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Synthesis of new 1-Vinyl and 1-Alkynyl Triazenes

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Abstract

The recent discovery of an N_2O-based synthesis of triazenes in our group has enabled the synthesis and investigation of 1-alkynyl triazenes. Early studies showed their potential for a functional group tolerant synthesis of 1-vinyl triazenes, which is further elaborated in this thesis. Furthermore, limitations in the synthesis of 1-alkynyl triazenes are addressed.

In the first part of the work, a Rh-catalyzed annulation reaction of 1-alkynyl triazenes with bifunctional boronic acids is presented. Indenyl triazenes were obtained and the acid-induced cleavage of the triazene group was studied.

Furthermore, cyclobutenyl triazenes were synthesized by Ficini-type cycloadditions of 1-alkynyl triazenes to electron deficient alkenes under Lewis-acid catalysis. Depending on the starting material, rearrangement of the addition products to bicyclooctenyl triazenes and subsequent derivatization was achieved.

New 1-alkynyl triazenes were synthesized among others γ-hydroxy substituted 1-alkynyl triazenes. The latter allow the synthesis of a terminal 1-alkynyl triazene, which can be derivatized to include a range of functional groups incompatible with the classical N_2O-based synthesis of 1-alkynyl triazenes.

Finally, the cytotoxicity of some of the newly synthesized 1-alkynyl and 1-vinyl triazenes was assessed.

Keywords: Triazenes, 1-Alkynyl triazenes, Annulation, Cycloaddition, Catalysis, 1-Vinyl triazenes, Terminal Alkyne, Indenes, Cyclobutenes, Triazenyl alkynes

Zusammenfassung

Die unlängst in unserer Gruppe entwickelte Synthese von Triazenen mit N_2O hat die Synthese und Erforschung von 1-Alkinyltriazenen ermöglicht. Erste Studien ergaben, dass sich 1-Alkinyltriazene für die Synthese von 1-Vinyltriazenen mit guter Toleranz funktioneller Gruppen eignen. Dieser Ansatz wird in der vorliegenden Arbeit fortgeführt. Ausserdem befasst sich die Arbeit mit den Grenzen der Synthese von 1-Alkinyltriazenen.

Im Ersten Teil der Arbeit wird eine Rh-katalysierte Annulierung von 1-Alkinyltriazenen mit bifunktionellen Phenylboronsäuren beschreiben. Indenyltriazene wurden erhalten und die Säure-induzierte Spaltung der Triazengruppe wurde untersucht.

Darüber hinaus wurden Cyclobutenyltriazene mittels Ficini-artiger, Lewis-Säure-katalysierter Cycloaddition von 1-Alkinyltriazenen an elektronenarme Alkene synthetisiert. Abhängig von dem jeweiligen Ausgangsmaterial eignen sich die Reaktionsprodukte zu Umlagerungen zu Bicyclooktenyltriazenen, welche wiederum derivatisiert werden können.

Neue 1-Alkinyltriazene wurden synthetisiert unter anderem γ-hydroxy-substituierte 1-Alkinyltriazene. Letzere erlauben die Synthese eines terminalen 1-Alkinyltriazens. Derivate dieses Produktes können verschiedene funktionelle Gruppen aufweisen, die mit der klassischen, N_2O-basierten Synthesemethode nicht kompatibel sind.

Schliesslich wurde die Cytotoxizität einiger neuer 1-Alkinyl- und 1-Vinyltriazenene untersucht.

Stichwörter: Triazene, 1-Alkinyltriazene, Annulierung, Cycloaddition, Katalyse, 1-Vinyltriazene, Terminales Alkin, Indene, Cyclobutene, Triazenylalkine

List of Abbreviations

[M]	Metal catalyzed
Ac	Acyl
Al	Aliphatic substituent
APCI	Atmospheric Pressure Chemical Ionization
APPI	Atmospheric Pressure Photoionization
Ar	Aryl
B(pin)	Boron Pinacolate
BCF	Tris(pentafluorophenyl)borane
Bn	Benzyl
Boc_2O	Di-*tert*-butyl dicarbonate
cat.	catalyzed
Cbz	Benzyloxy Carbamate
cod	1,5-Cyclooctadiene
Cp*	Pentamethylcyclopentadienyl
*c*Pent	Cyclopentyl
Cy	Cyclohexyl
CYP450	Cytochrome P450
DCE	1,2-Dichlorethan
DCM	Dichloromethane
DME	1,2-Dimethoxyethan
DMF	Dimethylformamide
DNA	Deoxyribonucleic acid
dppp	1,3-Bis(diphenylphosphino)propane
Et	Ethyl
esp	α,α,α′,α′-Tetramethyl-1,3-benzenedipropionate
EWG	Electron Withdrawing Group
ESI	Electrospray Ionization
FG	Functional Group
GC-MS	Gas chromatography-mass spectrometry
Hal	Halogen
HetAr	Heteroaryl
HMBC	Heteronuclear Multiple Bond Correlation
HRMS	High resolution mass spectrometry

*i*Pr	*iso*-Propyl
IR	Infrared
LiHMDS	Lithium bis(trimethylsilyl)amide
Me	Methyl
Mp	Melting Point
MTIC	5-(3-methyl-1-triazeno)imidazole-4-carboxamide
*n*Bu	*normal*-Butyl
NMR	Nuclear Magnetic Resonance
Nu	Nucleophile
Ph	Phenyl
Phe	Phenylalanine
ppm	parts per million
Pro	Proline
Py	Pyridine
QTOF	Quadrupole Time of Flight
ROMP	Ring Opening Metathesis Polymerization
RT	Room Temperature
rr	Ratio of Regioisomers
S_N	Nucleophilic Substitution
*t*Bu	*tert*-Butyl
TCNE	Tetracyanoethylene
Tf	Trifluoromethanesulfonyl
TFA	Trifluoroacetic acid
THF	Tetrahydrofuran
TM	Transition Metal
TMEDA	Tetramethylethylenediamine
TMS	Trimethylsilyl
Ts	*para*-Toluenesulfonyl
TS	Transition State

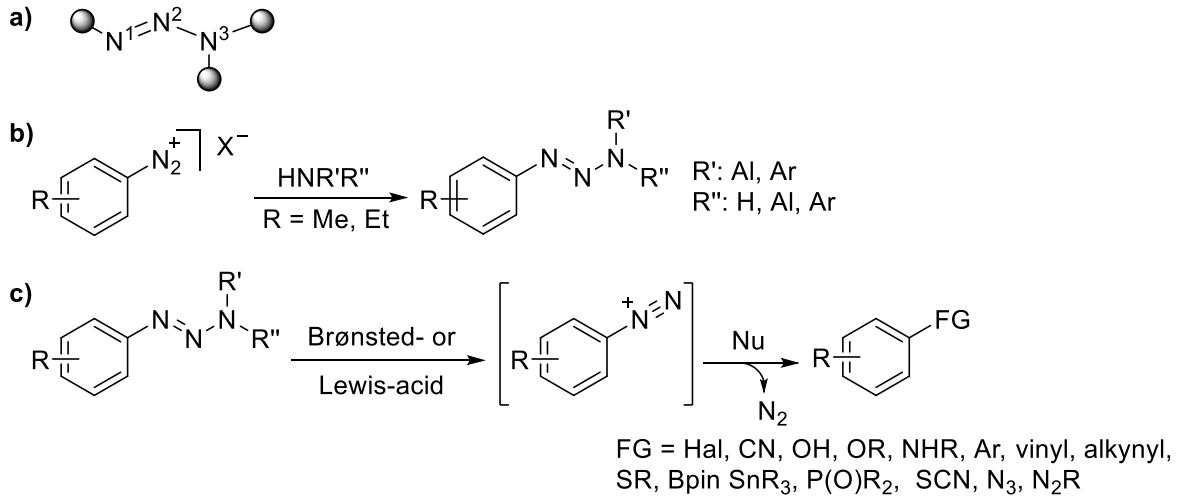
1. Introduction

1.1. Synthesis and Reactivity of Triazenes

1.1.1. 1-Ary Triazenes

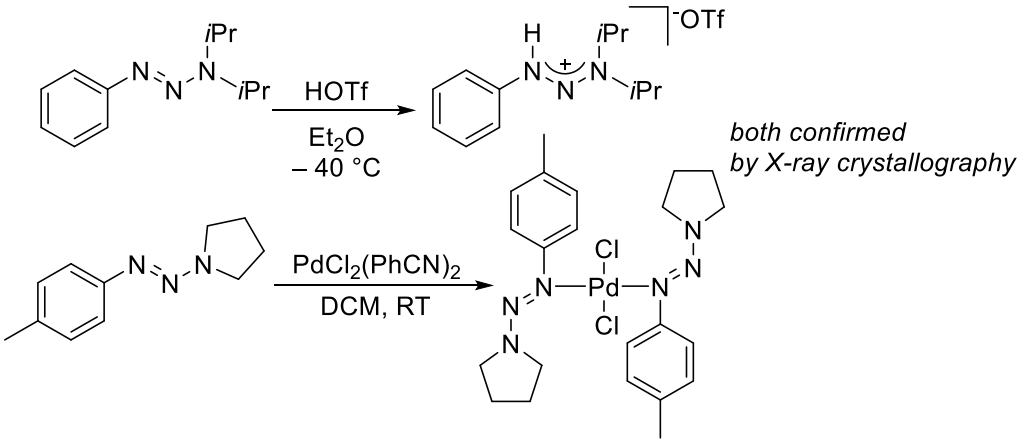
Triazenes contain a functional group made up of three, linearly arranged nitrogen, with a double bond between N1 and N2 (Scheme 1.1a).[1] Their utility in organic synthesis, material science and medicinal chemistry is documented in a range of reviews and monographs.[2–11]

The first triazene was synthesized by Griess in 1862,[12] but the structure was only elucidated later.[13,14] Soon after, Baeyer and Jäger's synthesis of 3,3-dimethyl- and 3,3-diethyl-1-phenyltriaz-1-ene by addition of dimethylamine or diethylamine to phenyldiazonium nitrate would establish the most popular method for the synthesis of 1-aryl triazenes. While other methods exist[7] diazotation of an aromatic amine and subsequent addition of amines is the "workhorse" of 1-aryl triazene synthesis. Primary or secondary, aromatic or aliphatic amines can be used (Scheme 1.1b).



Scheme 1.1. a) General structure of a triazene. b) Synthesis of a triazene by amine-diazonium coupling. c) Acid-induced cleavage reaction of a triazene

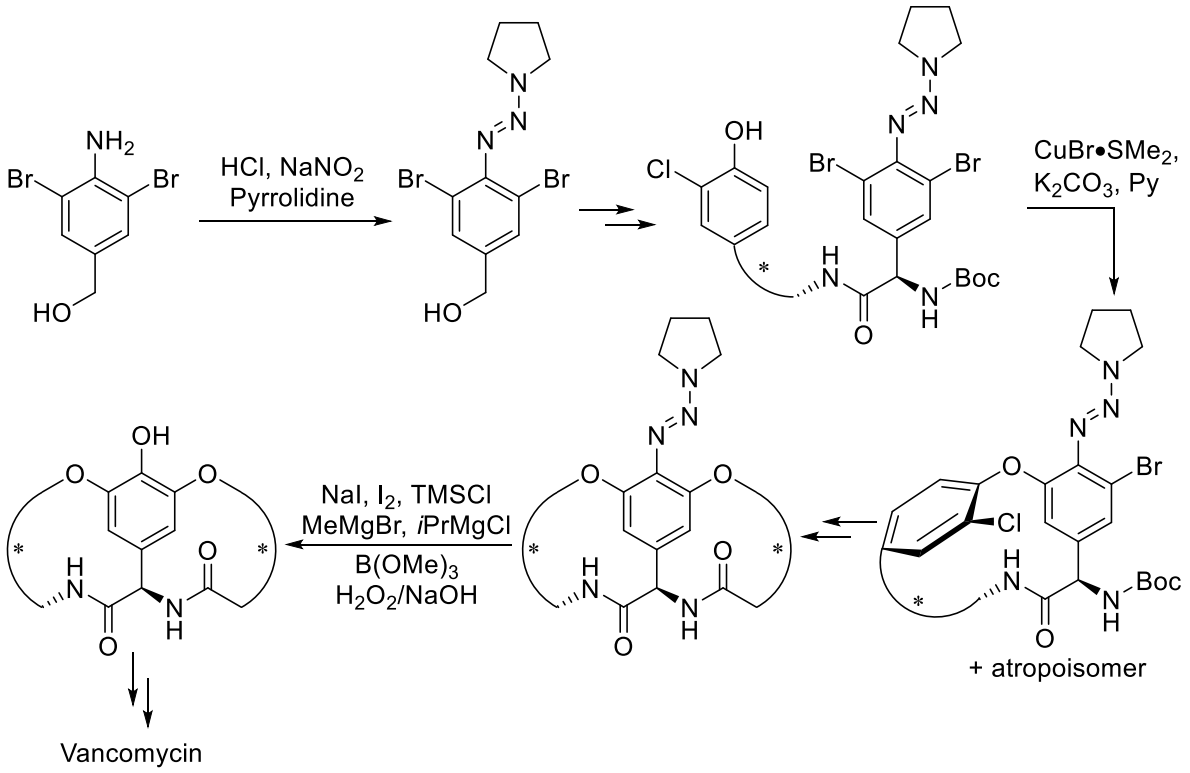
In stark contrast to their parent diazonium salts, triazenes are much more stable,[15] straightforwardly isolated, purified and handled, and can be stored under air for prolonged amounts of time. They are also resistant to bases, oxidants and most reducing agents.[16] However, under the influence of Brønsted- or Lewis-acids, the N2–N3 bond is ruptured to release the free amine and the corresponding diazonium salt (Scheme 1.1c), which can then undergo S_N-type reactions or engage in cross coupling reactions.[17] Accordingly, triazenes can be referred to as "masked diazonium salts"[8] and have been utilized to introduce halogens, C-,



Scheme 1.2. Brønsted (top) and Lewis (bottom) acid adducts of aryl triazenes.

O-, N-, S-, B-, or P-based nucleophiles as well as aryl-, vinyl- or alkynyl-groups or diazo functional groups. It is worth noting that N1 is the most Brønsted- and Lewis-basic nitrogen of the three (Scheme 1.2).[18] Both, a N1-protonated aryl triazene and a Pd complex with a N1-coordinated aryl triazene ligand have been synthesized and analyzed by X-ray crystallography.

N1-protonation is surprising to some extent, as liberation of the amine-end group and thus formation of the diazonium intermediate necessarily involves N3-protonation. N1-coordination



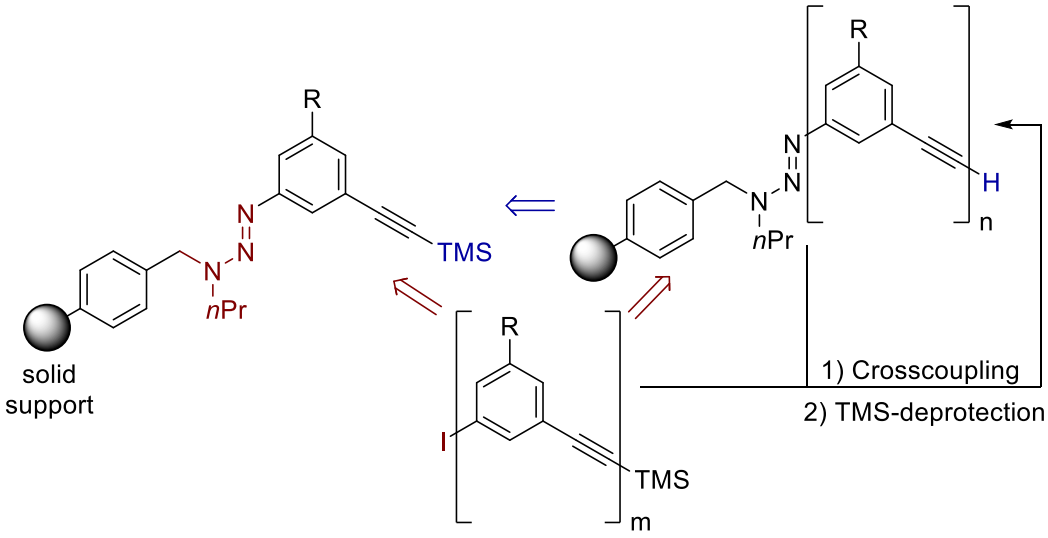
Scheme 1.3. Dual use of a triazene in the total synthesis of vancomycin; ortho-functionalization and functional group interconversion.

of metals had been described prior to the above discovery,[19,20] and it is known, that metal coordination to N1 can facilitate ortho functionalization of the respective aryl triazene.[6]

A combination of both ortho-functionalization and functional group interconversion was prominently featured in Nicolau's total synthesis of vancomycin. A triazene was introduced early on in the synthesis, with the goal to support a copper promoted ring closure to from ortho biarylethers.[21] Subsequently, the triazene functionality was replaced by a hydroxyl group (Scheme 1.3).[22,23] The persistence of the triazene throughout an extensive part of the synthesis is testimony to the stability of the triazene group to various reagents and conditions.

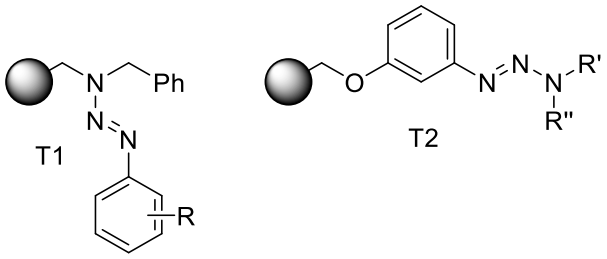
Aryl triazenes have also been used in a similar fashion in the synthesis of violaceic acid,[24] to first promote the formation of an aryl ether and then to be replaced by a phenol. Non-natural steroids have been synthesized from quinone diazides, which were obtained from para phenol triazenes.[25]

Phenylacetylene compounds have been synthesized for a range of applications, for example, in optical or electronic materials.[8] The group of Moore used a (2-alkynyl) phenyl triazene in the iterative synthesis of phenylacetylene oligomers. (Scheme 1.4).[26,27] Chain growth was achieved by Sonogashira reactions. As TMS-deprotection and synthesis of an aryl-iodide from the respective triazene are orthogonal, both the solid supported attachment point of the polymer chain (free alkyne) and the monomers (aryl iodide) could be obtained selectively from the same precursor. After each iteration, oligomers were released from the solid support as oligo(phenylacetylene) iodides and used in the growth of the chain, which multiplied the growth rate.



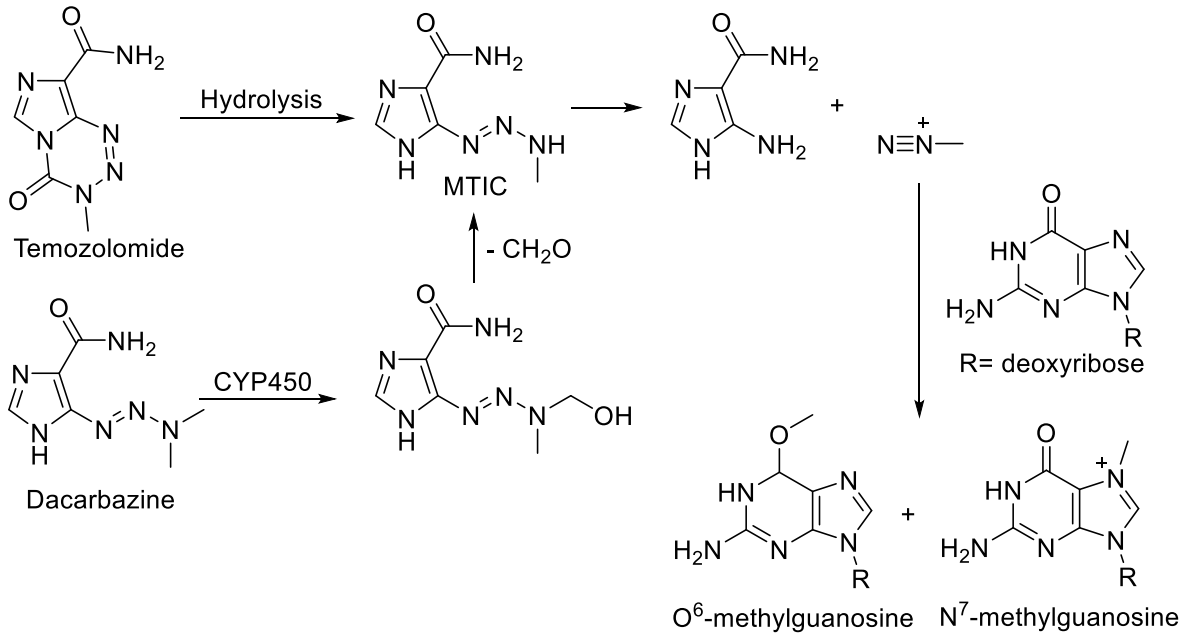
Scheme 1.4. Iterative synthesis of a phenylacetylene chain.

An alternative to the introduction of new functional groups via triazenes is the traceless removal of the group, which might be preferred in some cases, particularly in combinatorial chemistry, where traceless release from a polymer support is of interest. The group of Bräse developed several linkers to attach and tracelessly release arenes[28,29] or amines[30] to and from a solid support (Scheme 1.5). Notably, the so called T1 linker allows both traceless release with $SiHCl_3$ as well as the introduction of a variety of functional groups by methods known from aryl triazenes in solution.[31]



Scheme 1.5. Linkers used in solid phase synthesis to attach and tracelessly release arenes (T1) and amines (T2) to and from a polymer support.

The ability of triazenes to generate diazonium species has also been shown to be valuable in the context of medicinal chemistry. Dacarbazine and temozolomide are used against melanoma and Hodgkins lymphoma and brain cancer, respectively (Scheme 1.6).[3] The mechanism of action is similar for both compounds and involves the common intermediate 5-(3-methyl-1-triazeno)imidazole-4-carboxamide (MTIC), a 3-monomethyl triazene, which is generated by



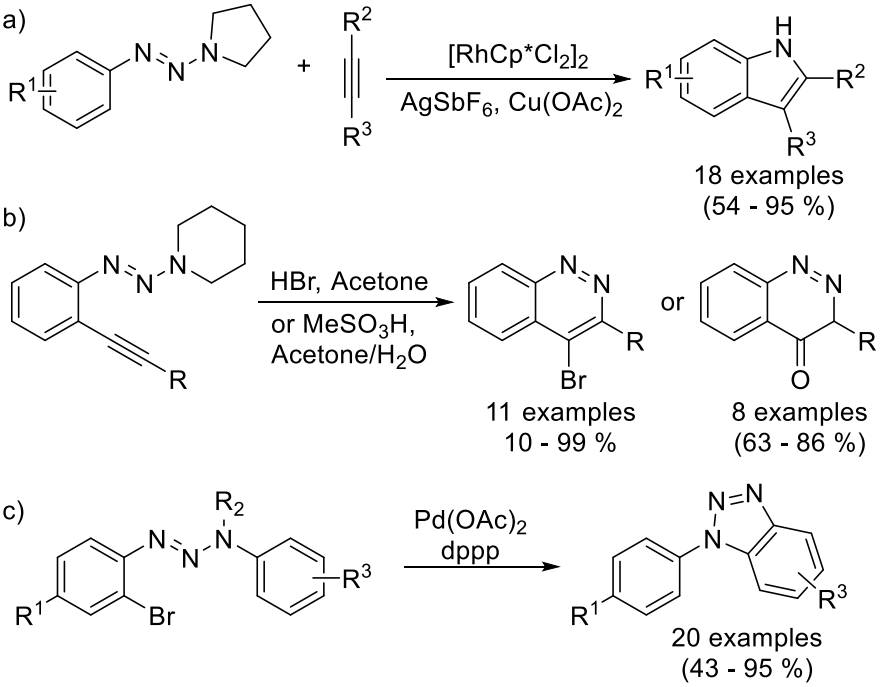
Scheme 1.6. Mechanism of action of temozolomide and dacarbazine (adapted from [3]).

hydrolysis of temozolomide or by liver metabolism of dacarbazine. MTIC spontaneously releases a methyldiazonium cation which then leads to N^7- or O^6-methylation of guanosine. The thusly methylated DNA is no longer functional, leading to cell death.

Apart from the acid-induced cleavage of the triazene group, it is also possible to incorporate one or several of the nitrogen atoms in the synthesis of aromatic heterocycles. Indoles were obtained by Rh^{III} catalyzed C-H activation of aryl triazenes (Scheme 1.7a).[32] Isotopic labelling studies proved that N1 of the starting triazene is incorporated in the product. The triazene group initially supports the C-H activation in ortho position via coordination to the catalyst. Exceptional rupture of the N1–N2 bond is proposed to proceed by solvolysis with methanol promoted by in situ formation of acetic acid.

A more conventional cleavage of the triazene group lead to the formation of cinnolines (Scheme 1.7b).[33] As a variation of the Richter reaction, where diazotation of a 2-alkynyl aniline leads to a diazonium salt, which then cyclizes intramolecularly to form the cinnoline,[34] Flynn and coworkers generated 2-alkynyl phenyldiazonium salts from a triazene under acidic conditions. Depending on the choice of acid, a benzylic vinyl bromide or ketone is obtained.

Synthesis of benzotriazoles from aryl triazenes has been achieved from 2-bromo aryl triazenes (Scheme 1.7c).[35] Notably, the procedure gives N1-substituted benzotriazoles selectively. After

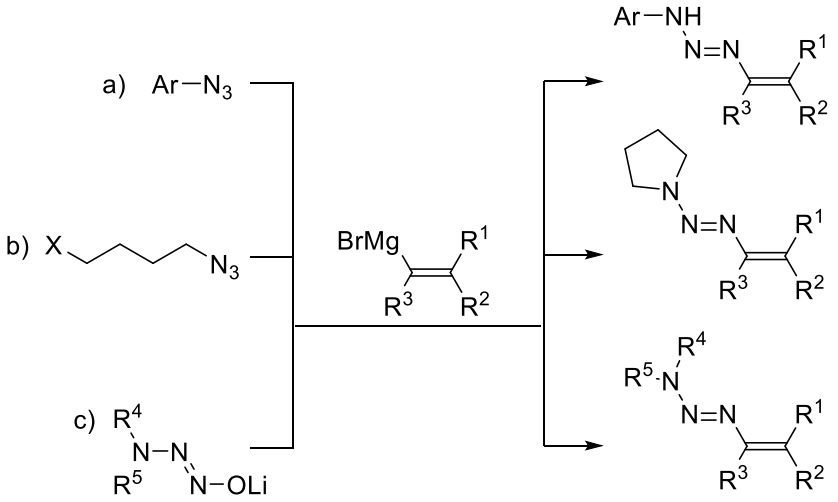


Scheme 1.7. Synthesis of aromatic N-heterocycles from aromatic triazenes. a) Indoles. b) Cinnolines. c) Benzotriazoles.

oxidative addition of aryl bromide to Pd, a 1,7-Pd migration/C-H activation is proposed. Attack of the N3-alkyl substituent of the triazene by base forms a six membered palladacylce, from which the product is formed through reductive elimination.

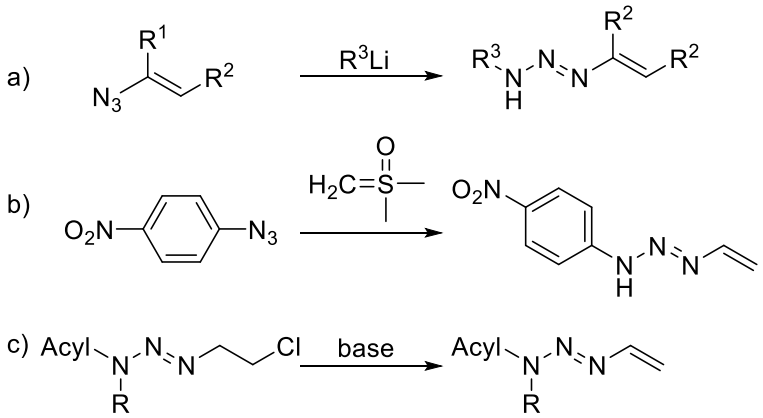
1.1.2. 1-Vinyl Triazenes

In contrast to 1-aryl triazenes, the chemistry of 1-vinyl triazenes is far less explored.[2] This might be due to the limited synthetic access. The pioneering work of the group of Jones in the late 1960's was enabled by the synthesis of vinyl triazenes from vinyl Grignard reagents and azides (Scheme 1.8a),[36–39] A modification of the vinyl Grignard/azide method recently published by our group involves a functionalized azide leading to an intramolecular alkylation step (Scheme 1.8b).[40] Lithium diazotates have been shown to undergo an analogous reaction, albeit with limited scope so far (Scheme 1.8c).[41] Common to all these methods is the limited functional group compatibility due to the use of Grignard reagents.



Scheme 1.8. Synthesis of 1-vinyl triazenes from vinyl Grignard reagents a) with aryl azides. b) with functionalized azides. c) with lithium diazotates.

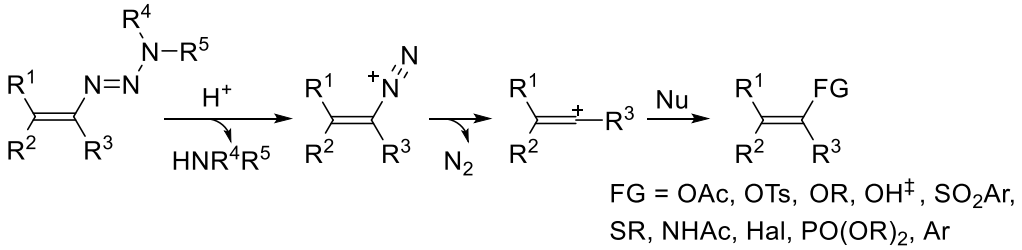
In a conceptually related fashion, vinyl azides can be combined with alkyllithium reagents to give vinyl triazenes (Scheme 1.9a).[42] Furthermore, reaction of para-nitro phenyl azide and sulfonium ylide gave a vinyl triazene (Scheme 1.8b)[43] and so did elimination of HCl from a chloroalkyl triazene (Scheme 1.9c).[44] All of these methods have limitations, namely restricted functional group tolerance and scope.



Scheme 1.9. Synthesis of 1-vinyl triazenes a) from vinyl azides and MeLi. b) from aryl azide and sulfonium ylide. d) from chloroalkyl triazene and base.

An alternative, potentially more functional group tolerant method for the synthesis of 1-vinyl triazenes are addition or annulation reactions to 1-alkynyl triazenes, the details of which are discussed in subchapter 1.1.3.

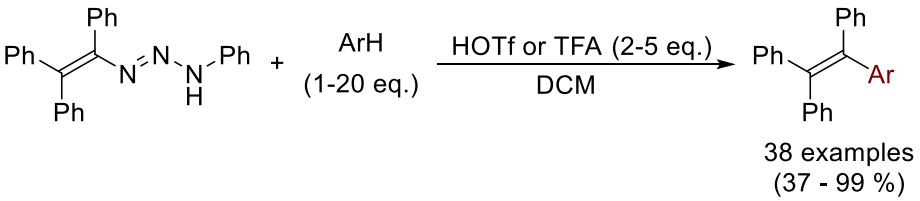
Despite the challenging synthesis of 1-vinyl triazenes, the reactivity of these compounds has been studied. Similarly to aryl triazenes, they undergo acid-induced cleavage of the triazene group, which leads to vinyl diazonium salts. Upon loss of dinitrogen, a vinyl cation is formed, which can undergo electrophilic vinylation (Scheme 1.10).[38,45]



Scheme 1.10. Reactivity of 1-vinyl triazenes (adapted from[2]). ‡Rearrangement to the respective ketone.

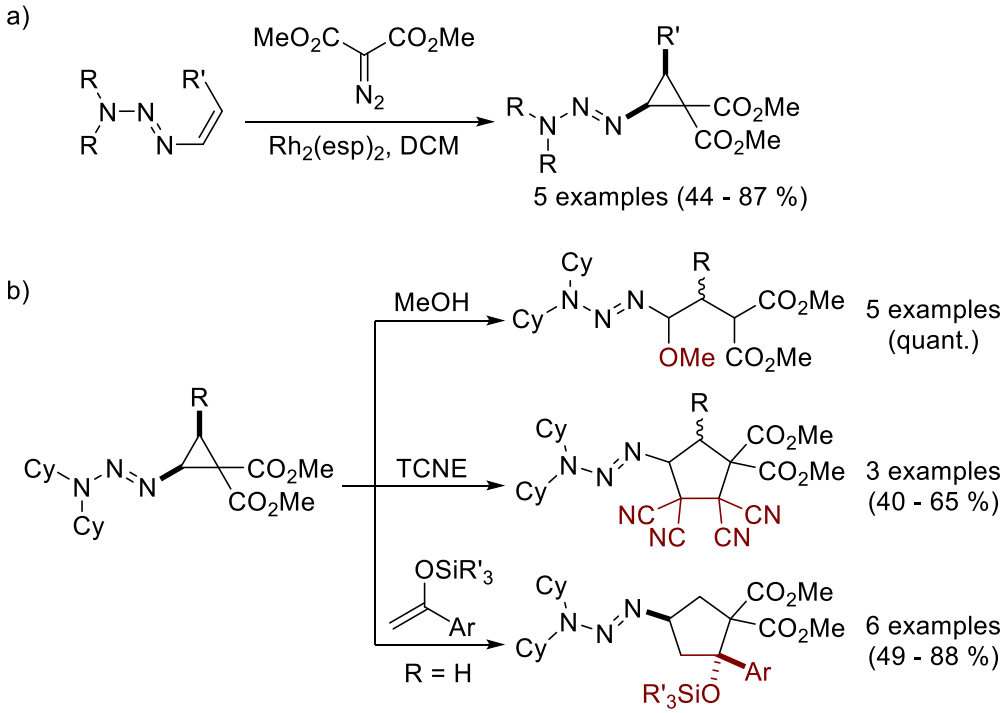
While the work of Jones et al. focused on the substitution with oxo-acids,[38,39] later reports revealed the possibility to introduce other functional groups, in particular synthetically valuable halogens.[46–48]

A notable example for the use of vinyl triazenes as vinylation reagents is the synthesis of tetraarylethenes by vinylation of arenes (Scheme 1.11).[49] A great variety of substituted (hetero)arenes as well as polycyclic aromatic hydrocarbons, supramolecular receptors, polymers or a β-estradiol derivative could be vinylated. The resulting compounds show aggregation induced emission (AIE), which is a property of interest for diverse applications.[50]



Scheme 1.11. Synthesis of tetraarylethenes by acid-induced cleavage of a 1-vinyl triazene (only one tautomer of the starting material is shown).

In comparison to the acid-induced cleavage of the triazene, reactions with the C–C double bond of vinyl triazenes have received far less attention. In collaboration with the group of Waser, our group recently published the synthesis of donor-acceptor cyclopropanes bearing a triazene as the donor group. Rh-catalyzed reaction of 1-vinyl triazenes with dimethyl diazomalonate lead to the desired cyclopropanes (Scheme 1.12a).[51] The triazene unit showed a strong electron donating effect, superior to other functional groups frequently used as donors in donor acceptor cyclopropanes. This high degree of activation was corroborated in reactivity studies with methanol, which lead to quantitative opening of the cyclopropane ring (Scheme 1.12b). Reaction with tetracyanoethylene (TCNE) lead to ring opening as well. Both reactions are not observed for donor-acceptor cyclopropanes activated with conventional donor groups. Silyl enol ethers were also suitable dipolarophiles (Scheme 1.12b). To the best of our knowledge,

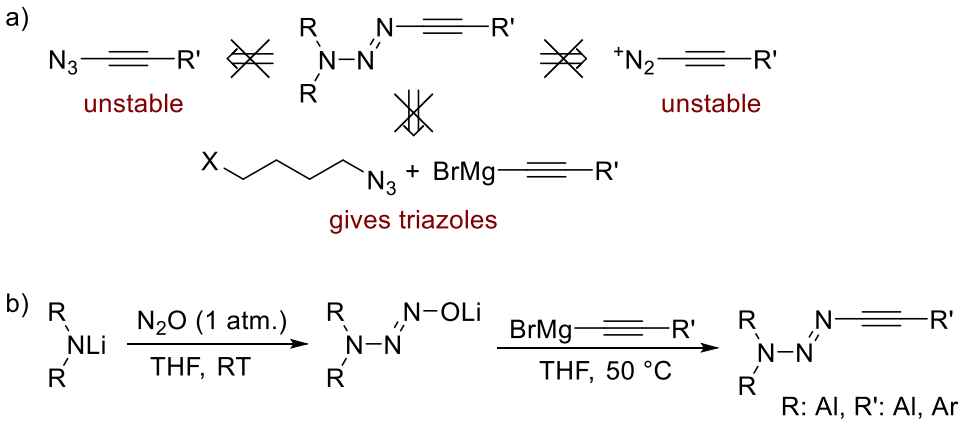


Scheme 1.12. a) Synthesis of donor-acceptor cyclopropanes from vinyl triazenes. b) Ring opening with methanol, tetracyanoethylene, and silyl enol ethers.

that work is the only example of a study on the reactivity of the C–C double bond of 1-vinyl triazenes.[52]

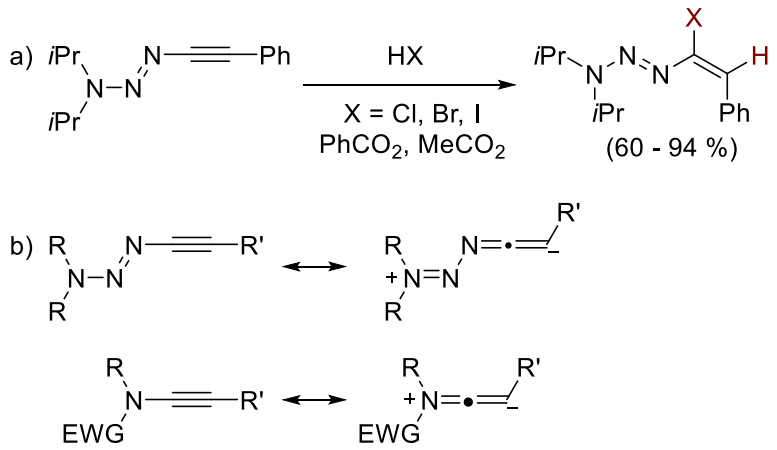
1.1.3. 1-Alkynyl Triazenes

The chemistry of 1-alkynyl triazenes has been completely uncharted territory until recently. Both 1-azidoalkynes[53] and alkynyl diazonium salts[54] are highly unstable and reactions of azides with metalated alkynes give triazoles.[40] Thus the classical methods for the synthesis of aryl and vinyl triazenes can not be applied (Scheme 1.13a). In 2015, our group discovered a synthesis of triazenes from nitrous oxide, lithium amides and Grignard reagents.[41,55] In a first step, lithium diazotate is formed by activation of N_2O with lithium amides. In the solid state, lithium diazotate is explosive, which is why it is directly consumed through reaction with a Grignard reagent. While aryl- and vinyl triazenes can be synthesized, this method is particularly useful for the synthesis of 1-alkynyl triazenes, as it represents the only available method to date (Scheme 1.13b). Alkynyl Grignard reagents bearing aromatic, heteroaromatic and aliphatic substituents have been used for the synthesis of 1-alkynyl triazenes by this method. The choice of functional groups has, however, been limited due to the necessity for alkynyl Grignard reagents.



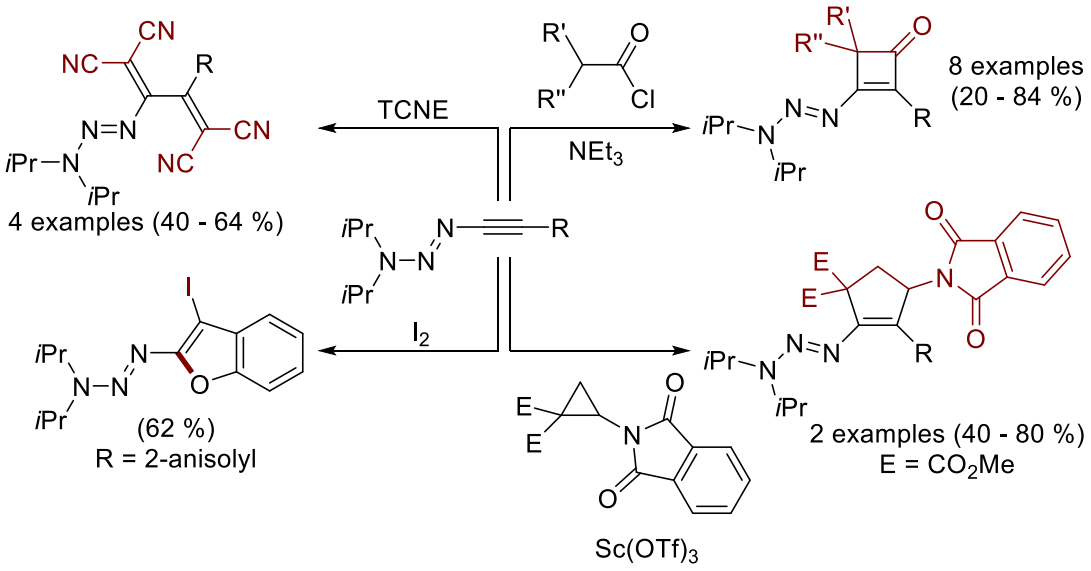
Scheme 1.13. a) Hypothetical substrates for the synthesis of 1-alkynyltriazenes by classical methods. b) Synthesis of 1-alkynyl triazenes from lithium amides, N_2O and alkynyl Grignard reagents.

In contrast to 1-aryl and 1-vinyl triazenes, 1-alkynyl triazenes do not undergo acid-induced cleavage. Instead, it was found, that acids add regioselectively across the triple bond to form a vinyl triazene (Scheme 1.14a).[56] This result indicates an electron-rich, polarized C–C triple bond. The regioselectivity of the addition can be rationalized with a charge-separated resonance structure, explaining the nucleophilicity of the β-carbon. The C–C triple bonds of ynamides, a versatile class of compounds in organic synthesis,[57] is similarly polarized, which lead to the



Scheme 1.14. a) Addition of Brønsted acids to 1-alkynyl triazenes. b) Analogy between charge-separated mesomeric structures of 1-alkynyl triazenes and ynamides.

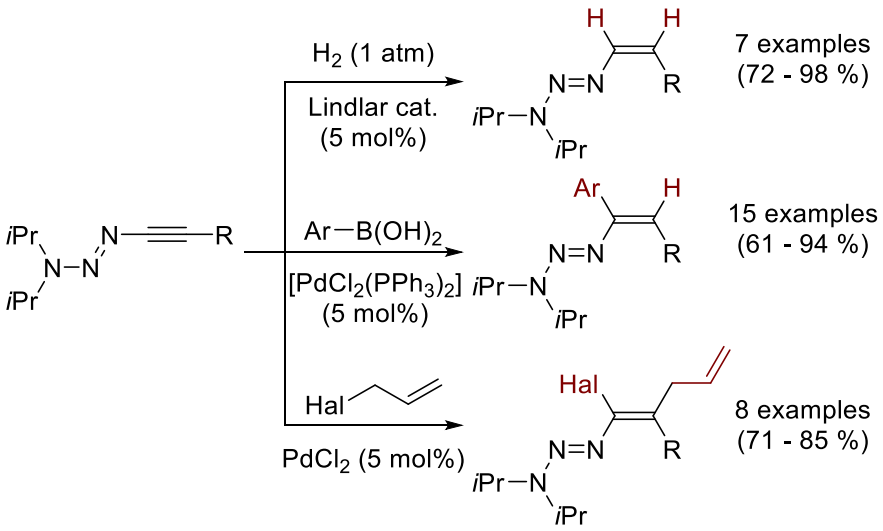
proposal of similarities in the reaction profile between the two compound classes (Scheme 1.14b). To put this proposition to the test, the reactivity of 1-alkynyl triazenes was further investigated (Scheme 1.15). Reactions with TCNE gave tetracyanobutadienes. Furthermore, cyclobutenones were obtained by addition of ketenes to 1-alkynyl triazenes. Under $Sc(OTf)_3$ catalysis, reactions with a donor-acceptor cyclopropane were achieved. In case of a 2-anisolyl substituent on the β-carbon, intramolecular cyclization upon ether cleavage with I_2 was achieved. All of those reactions proceeded with complete regioselectivity and analogously to the respective reactions of ynamides (Scheme 1.15).[56] The similarity in reactivity between 1-alkynyl triazenes and ynamides has also been corroborated in later studies.



Scheme 1.15. Examples for ynamide-like reactivity of 1-alkynyl triazenes.

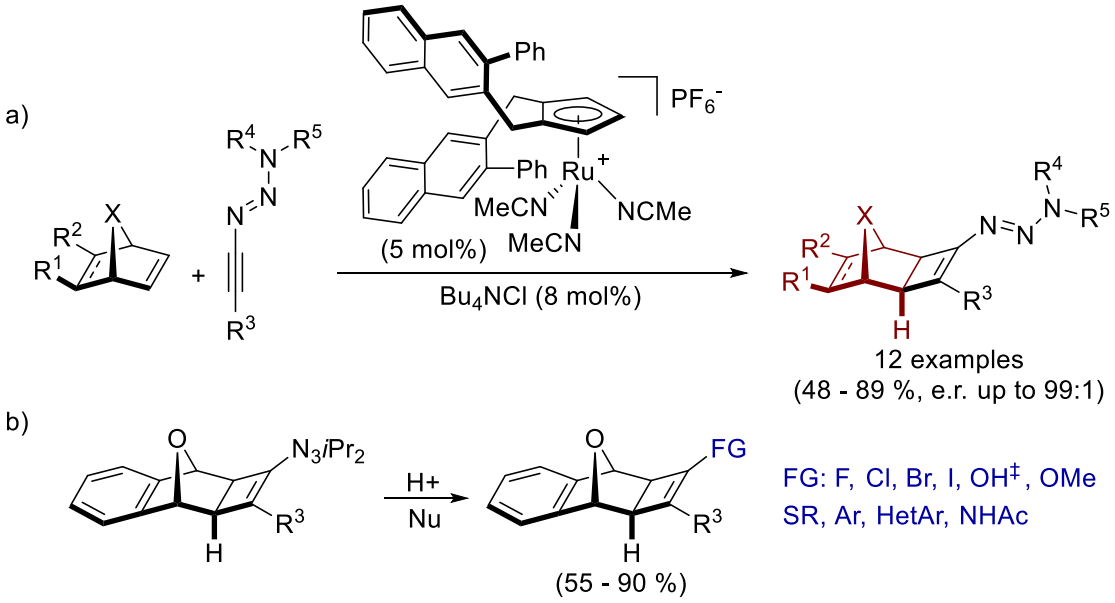
As the addition reactions described above gave sought after 1-vinyl triazenes (see chapter 1.1.2), further efforts were undertaken towards the synthesis of 1-vinyl triazenes from 1-alkynyl triazenes. In particular, addition reactions proceeding under mild conditions were of interest, to circumvent the limitations to functional group tolerance associated with the use of Grignard reagents in classical methods to synthesize 1-vinyl triazenes.

Indeed, an alternative path for the synthesis of 1-vinyl triazenes from 1-alkynyl triazenes was opened up by Pd catalysis (Scheme 1.16).[58] Hydrogenation using Lindlar catalyst gave disubstituted vinyl triazenes in good to excellent yields and full Z-selectivity. Disubstituted vinyl triazenes were obtained through Pd-catalyzed addition of arylboronic acids in moderate to excellent yields. Notably, the use of functionalized arylboronic acids allowed the introduction of several functional groups, which are incompatible with the organometallic approaches to 1-vinyl triazenes described above (CHO, NO_2, CN, NH_2, CO_2Et). Allyl halides could be added across the triple bond as well, leading to differentially trisubstituted vinyl triazenes with handles for further synthetic modifications. The latter two addition reactions proceeded with full regioselectivity, highlighting once again the polarized character of the C–C triple bond.



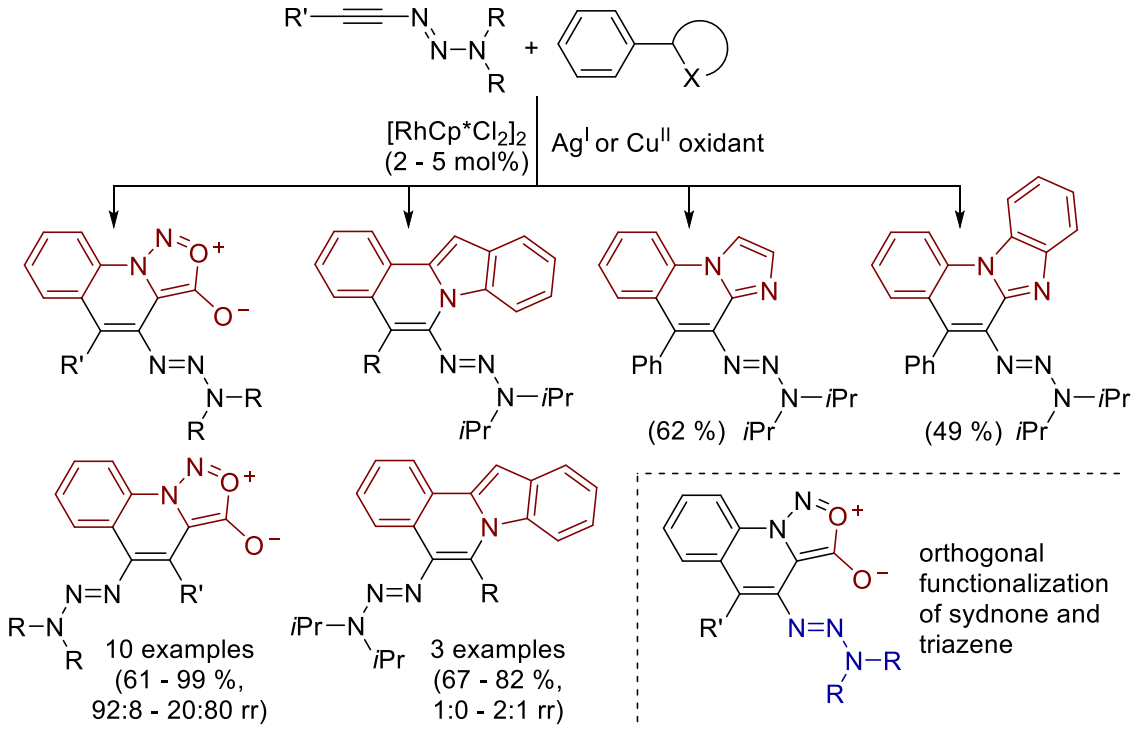
Scheme 1.16. Pd-catalyzed addition reactions of 1-alkynyl triazenes leading to 1-vinyl triazenes.

Furthermore, in collaboration with the group of Cramer, our group described an asymmetric, Ru-catalyzed [2+2] cycloaddition of 1-alkynyl triazenes to strained alkenes (Scheme 1.17a).[48] The desired products were obtained in good yields with high enantioselectivity. Gratifyingly, the resulting cyclobutenyl triazenes could be derivatized through acid-induced cleavage and a broad selection of functional groups could be introduced (Scheme 1.17b).



Scheme 1.17. a) Synthesis of asymmetric polycyclic vinyl triazenes from 1-alkynyl triazenes. b) Derivatization via acid-induced cleavage. ‡Rearrangement to the respective ketone.

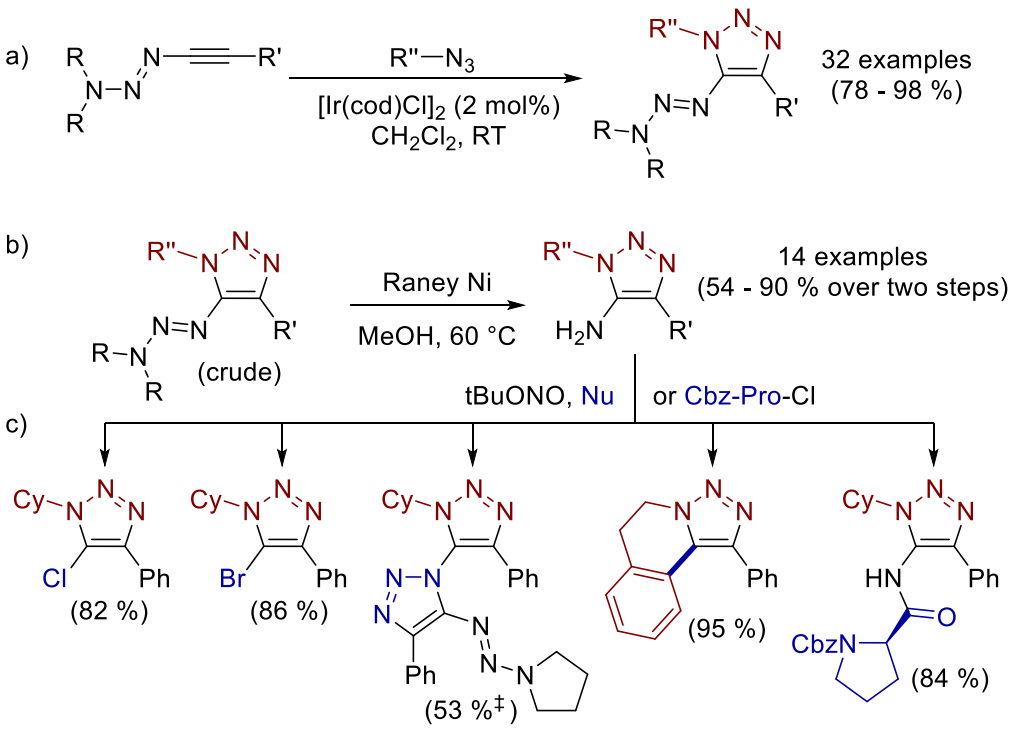
Apart from vinyl triazenes, the synthesis of aryl triazenes from 1-alkynyl triazenes has been investigated. While the products in question might be obtained through the methods described in chapter 1.1.1, the presented syntheses are still advantageous, as the functionalized starting materials, which would be needed for the respective reactions, are not straightforwardly available.



Scheme 1.18. Synthesis of heteroaromatic triazenes via C-H/N-H activation.

Heteroaryl triazenes were obtained by Rh^{III}-catalyzed double C-H and C-H/N-H activation of several biaryl precursors (Scheme 1.18).[59] Despite challenging side-product formation, suitable conditions were found for the reaction with phenylsydnone, 2-phenyl-1H-indole, 1-phenylimidazole and 1-phenylbenzimidazole, respectively. Phenylsydnone was a particularly valuable starting material, as reactions proceeded under mild conditions and the resulting products could be divergently functionalized both through cycloaddition reactions of the sydnone group and acid-induced cleavage of the triazene group. The respective functionalizations were found to be orthogonal to each other.

Triazolyl triazenes were synthesized by the group of Cui (Scheme 1.19a).[60] A broad range of azides and 1-alkynyl triazenes could be transformed by Ir-catalysis previously described for ynamides,[61] including azide derivatives of phenylalanine and glucose. 5-Amino triazoles, which represent a privileged scaffold in medicinal chemistry,[62] could be obtained by reduction with Raney-Ni from crude triazolyl triazene in generally good yields (Scheme 1.19b). Furthermore, diazotation of the amino group allowed the introduction of a chloride, bromide or azide, the latter of which could again undergo a cycloaddition with an alkynyl triazene. Intramolecular reaction of the diazonium salt or amidation of the amine were also reported (Scheme 1.19c).

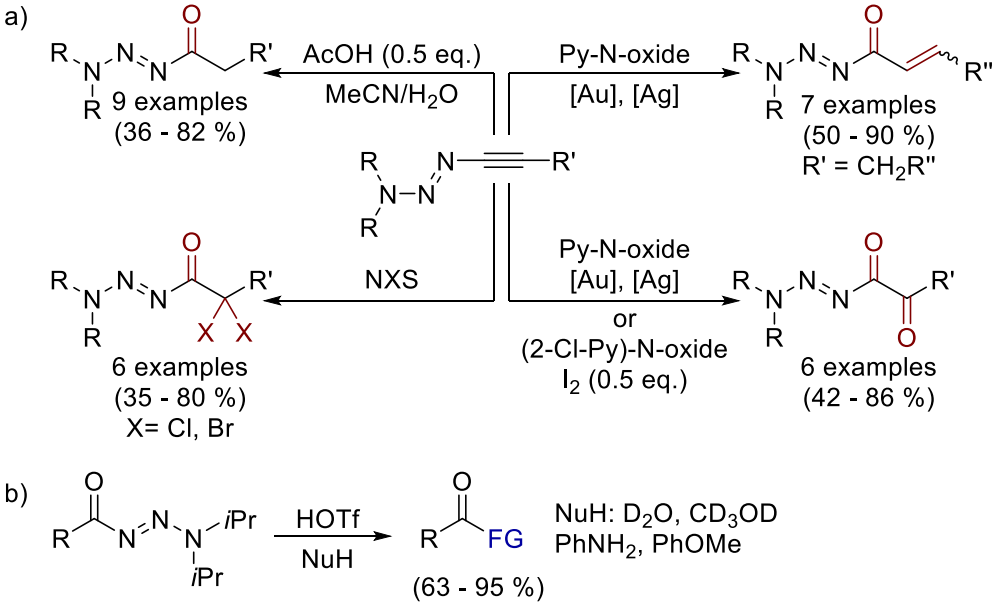


Scheme 1.19. a) Synthesis of 1-triazolyl alkynes from azides via Ir-catalyzed azide-alkyne cycloaddition. b) Synthesis of aminotriazoles as a two-step process. c) Derivatization of aminotriazoles. ‡Nu = $TMSN_3$, then cycloaddition to an alkynyl triazene according to a).

Apart from the synthesis of 1-vinyl and 1-aryl triazenes, 1-alkynyl triazenes allowed the exploration of entirely new compound classes.

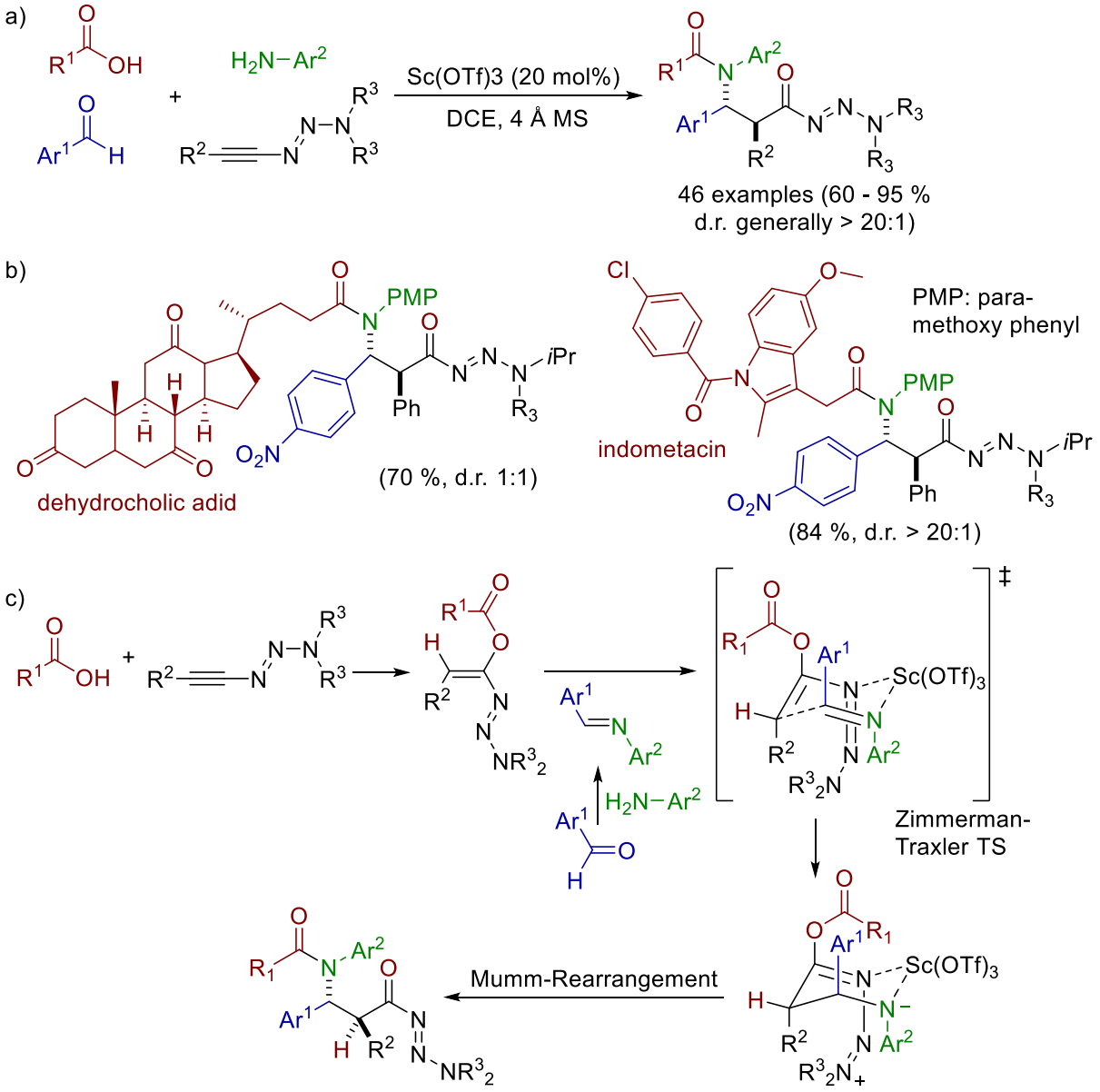
While 3-acyltriazenes have been rather well explored, in part due to their potential bioactivities,[7–9] 1-acyl triazenes were unknown until recently for lack of synthetic methods. However, 1-alkynyl triazenes could be transformed to 1-acyl triazenes trough hydration or oxidation (Scheme 1.20a).[63] Depending on the choice and quantity of the oxidation agent, α,β-unsaturated acyl triazenes, α-keto acyl triazenes or α-halogenated acyl triazenes were obtained. Exploration of the properties of 1-acyl triazenes revealed high thermal and hydrolytic stability and resistance to strong bases or oxidants. The electron withdrawing effect of the acyl group is assumed to contribute to the stability of 1-acyl triazenes. The electronic contribution of the acyl group is confirmed by comparatively short N2–N3 and long N1–N2 bonds.

Reactions of 1-acyl triazenes with acid proved to be dependent on temperature and solvent. N1-protonated 1-acyl triazenes could be synthesized and characterized upon treatment with triflic acid in Et_2O at RT.[18] The formation of stable acid-base adducts at RT is remarkable, given the usual acid sensitivity of triazenes and further highlights the stabilizing effect of the 1-acyl group on the triazene. When using nucleophilic solvents at RT or 70 °C instead, acylation of the solvent was observed. (Scheme 1.20b).



Scheme 1.20. a) Synthesis of 1-acyl triazenes through hydration and oxidation of 1-alkynyl triazenes. b) 1-Acyl triazenes as acylating agents.

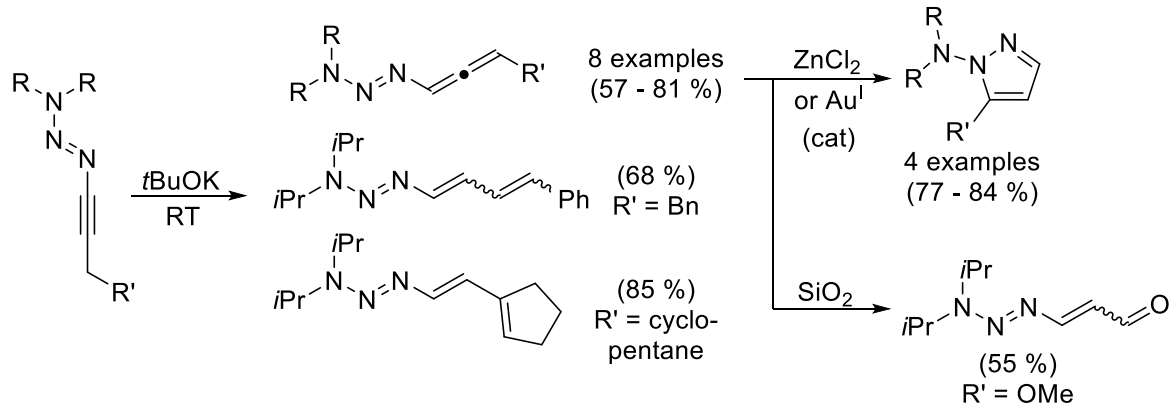
The synthesis of β-amido acyl triazenes by a Sc-catalyzed multicomponent reaction involving 1-alkynyl triazenes, carboxylic acids, anilines and aryl aldehydes was described by the group of Cui (Scheme 1.21a).[64] The reliability of the method was demonstrated by a thorough investigation of the scope. High diastereoselectivities and yields were usually obtained. Notable examples are the use of the synthetic steroid acid dehydrocholic acid and the anti-inflammatory drug indometacin as carboxylic acids (Scheme 1.21b). The proposed mechanism involves the initial addition of the carboxylic acid to the alkynyl triazene.[56] Subsequent reaction with an imine formed in situ through a Sc-stabilized Zimmerman-Traxler transition state then leads to



Scheme 1.21. a) Synthesis of β-amido 1-acyl triazenes in a multicomponent reaction from 1-alkynyl triazenes. b) Reaction products of dehydrocholic acid and indometacin. c) Proposed mechanism.

an intermediate imine, which undergoes a Mumm rearrangement to the final β-amido acyl triazene (Scheme 1.21c).

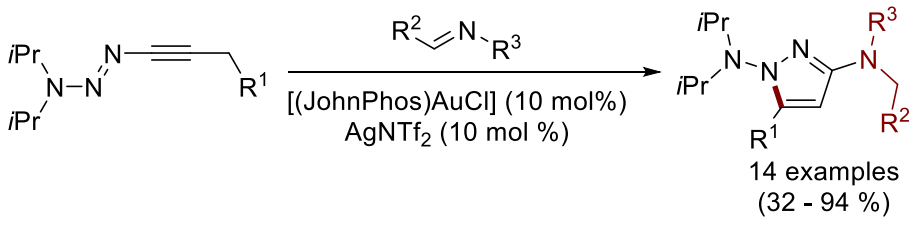
Another compound class so far exclusively accessible through 1-alkynyl triazenes are 1-allenyl triazenes. Base-induced isomerization of 1-alkynyl triazenes bearing an CH_2R-substituent in β-position lead to the aforementioned products in moderate to good yields (Scheme 1.22).[65] Depending on the β-substituent, dienyl triazenes could also be obtained. The 1-allenyl triazenes could be isomerized to amino-pyrazoles with stoichiometric amounts of $ZnCl_2$ or catalytic amounts of Au^I[66], while an OMe substituent on the allene lead to hydrolysis to the α,β-unsaturated aldehyde upon purification by column chromatography (Scheme 1.22).



Scheme 1.22. Base induced isomerization of 1-alkynyl triazenes to 1-allenyl triazenes and conjugated vinyl triazenes.

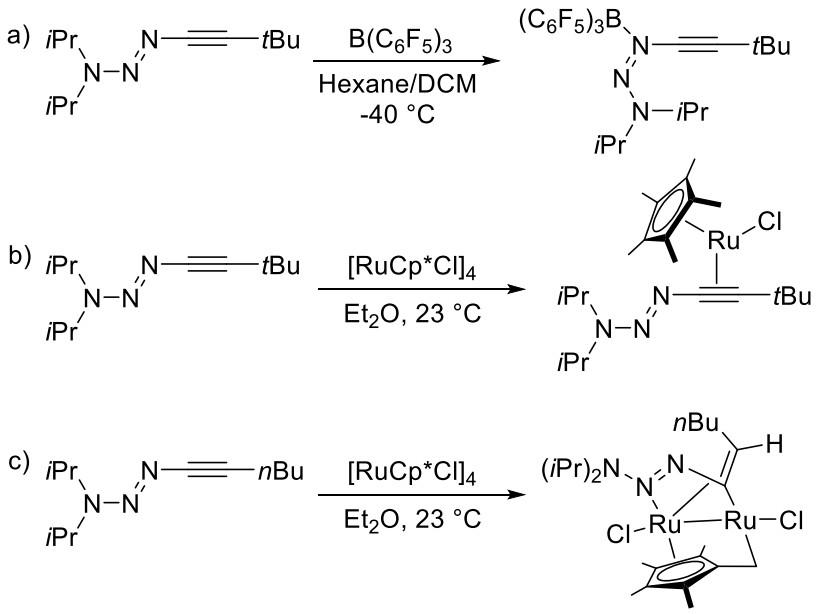
1,3-Diaminopyrazoles could also be obtained in one step from the same starting materials by Au^I-catalyzed reaction with imines (Scheme 1.23).[66] Even though 1-allenenyl triazenes can isomerize to aminopyrazoles (see above), they do not seem to be intermediates in the reaction. Instead, nucleophilic attack of the imine on the Au-activated alkyne followed by 1,5-H-shift and intramolecular attack of N2 is proposed as the mechanism.

The coordination chemistry of 1-alkynyl triazenes has only sparingly been explored. As for 1-aryl triazenes, the N1 atom of 1-alkynyl triazenes was found to be the most Lewis-basic



Scheme 1.23. Synthesis of 1,3-diaminopyrazoles from 1-alkynyl triazenes.

nitrogen of the three, as evidenced by a single crystal X-ray analysis of an adduct of a 1-alkynyl triazene with Tris(pentafluorophenyl)borane (BCF) (Scheme 1.24a).[18] An unusual isomerization of N1–N2 double bond was noted. The *Z*-geometry is assumed, presumably due to steric interactions between the diisopropylamine end-group and BCF. Reaction of the same 1-alkynyltriazene with $(Cp^*RuCl)_4$ gives a coordination complex with the C–C triple bond as a four electron donor ligand despite the steric bulk of the *t*Bu-group (Scheme 1.24b).[67] On the other hand, less bulky *n*Bu-substituted 1-alkynyl triazene gave a dinuclear vinyltriazene-Ru-complex in which both the C–C-double bond and N2 of the triazene are coordinated to Ru (Scheme 1.24c). The coordination chemistry of 1-alkynyl triazenes seems thus to be determined by a complex interplay of β-substituent and coordination partner.



Scheme 1.21. Coordination complexes of 1-alkynyl triazenes. All of the complexes were analyzed by X-ray crystallography.

1.2. Objectives of the Thesis

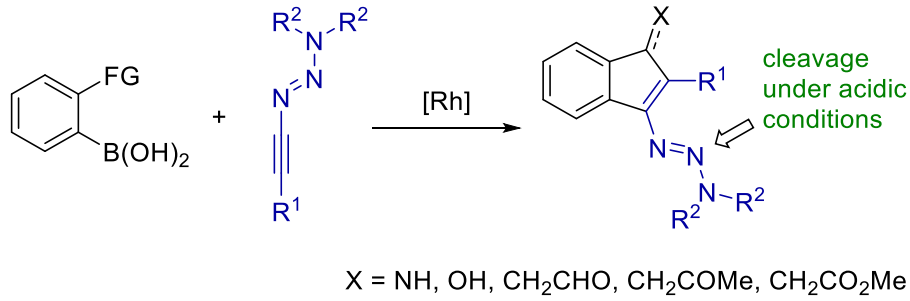
Despite the recent success in the synthesis of 1-vinyl and 1-alkynyl triazenes, their synthesis still suffers from severe drawbacks.

Organometallic reagents are common in the synthesis of vinyl triazenes. Addition reactions of 1-alkynyl triazenes have had some success and appear to be a promising approach to make the synthesis of vinyl triazenes more functional group tolerant. However, its potential is still underdeveloped.

Furthermore, the synthesis of the parent 1-alkynyl triazene requires alkynyl Grignard reagents, which severely limits the choice of substituents on the β-carbon and thus limits the versatility of structures attainable through aforementioned addition reactions.

The aim of the thesis is to push back those limitations to functional group tolerance in the synthesis of 1-vinyl and 1-alkynyl triazenes.

2. Synthesis of Indenyl Triazenes by Rhodium-Catalyzed Annulation Reactions



This chapter is based on a published article:

C. T. Bormann,‡ F. G. Abela,‡ R. Scopelliti, F. Fadaei-Tirani, K. Severin,* Synthesis of Indenyl Triazenes by Rhodium-Catalyzed Annulation Reactions. *Eur. J. Org. Chem.* **2020**, *2020*, 2130–2139.

‡These authors contributed equally.

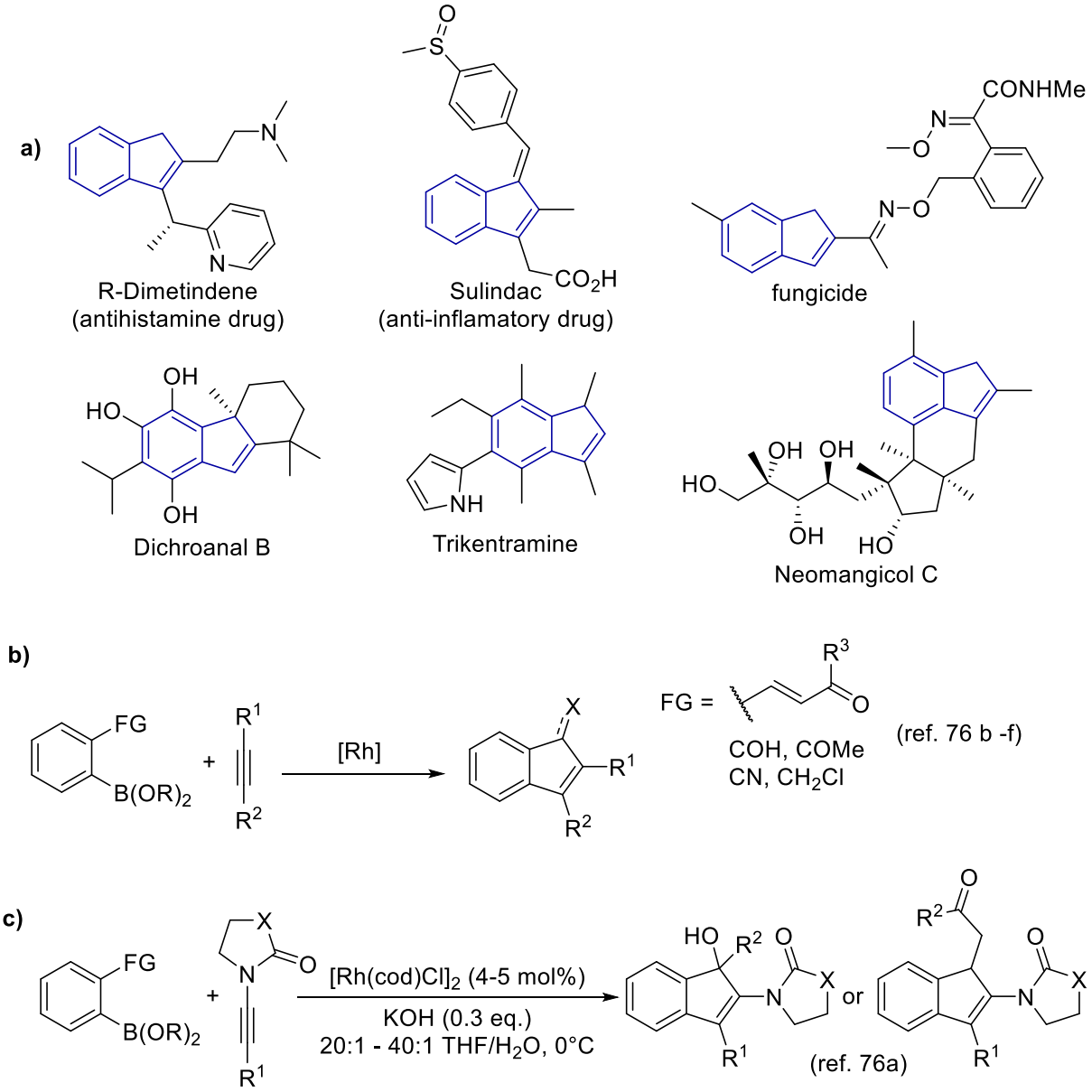
Some aspects of this work are also discussed in:

F. G. Perrin, Investigations of the Chemistry of 1-Alkynyltriazenes, PhD thesis No. 8667, École Polytechnique Fédérale de Lausanne, **2018**.

Author contributions: C.T.B. and F.G.A. performed the experiments. R.S. and F.F.T. performed X-ray structure analyses. K.S. supervised the project. K.S. and C.T.B. prepared the manuscript.

2.1. Introduction

The indene subunit can be found in many bioactive and natural compounds (Scheme 2.1a). Examples of reported bioactivities include histamine antagonism,[68] anti-inflammatory[69] and fungicidal activity.[70] Furthermore, several natural products containing the indene subunit have been isolated for example from plants (*Salvia dichroantha*, Dichroanal B)[71], sponges (*Trikentrion loeve*, Trikentramine)[72] and fungi (*Fusarium*, Neomangicol C).[73]



Scheme 2.1. a) Examples of indenes as bioactive compounds (top) or natural products (bottom). b) Synthesis of indenes from functionalized arylboronic acids and alkynes. b) Synthesis of indenyl amides from functionalized arylboronic acids and ynamides.

Numerous procedures for synthesizing substituted indenes have been reported in the literature.[74] For example, indenes can be synthesized by Rh-catalyzed [3+2] annulation

reactions of arylboronic acids bearing an electrophilic functional group in ortho position and alkynes (Scheme 2.1b).[75,76] Initial reports by Lautens et al.[76f] using α,β-unsaturated carbonyls as electrophiles were quickly followed up by Hayashi *et al.*,[76d] Murakami *et al.*[76c,76e] and Chatani *et al.*[76b] proving carbonyls, as well as the cyano group and benzylic chloride to be suited electrophiles. The reactions are typically performed with Rh^{I} complexes such as $[RhCl(cod)]_2$ as catalyst precursor under basic conditions.

Lam expanded explored the scope of alkyne substrates to ynamides (Scheme 2.1c). [76a] Since 1-alkynyl triazenes show a similar reactivity profile to ynamides,[56] we hypothesized that this particular methodology might be suited for the synthesis of indenyl triazenes. However, we also anticipated potential problems, such as insertion of the low-oxidation-state metal into the C–N bond of the triazene (as postulated for reactions of aryl triazenes with Pd complexes),[77,78] or attenuated catalytic activity due to the presence of a metal-binding triazene function.[79]

Indenyl triazenes appeared to be a worthwhile synthetic target because the triazene group itself can potentially trigger bioactivity (the bioactivity of a selection of triazenes is discussed in chapter 1.1 and chapter 5).[3,10,92] Furthermore, we anticipated that acid-induced cleavage reactions could allow further structural modifications of the indene scaffold.[81]

2.2. Scope of the Synthetic Method

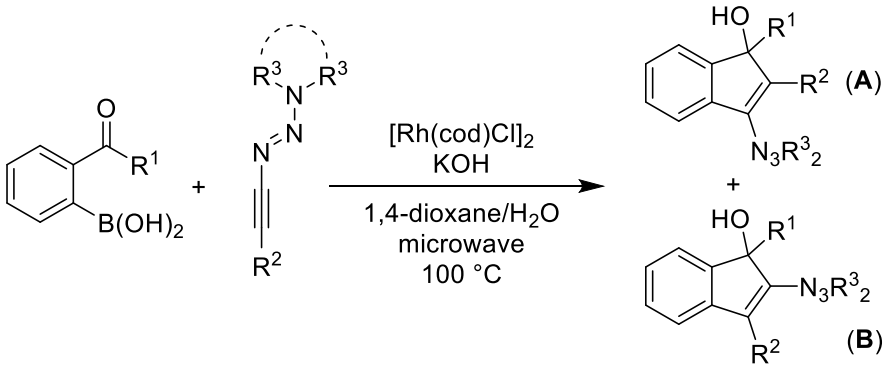
We started our investigations by performing reactions between 2-formylphenylboronic acid and 1-(3,3-dimethylbutynyl)-3,3-diisopropyl triazene in 1,4-dioxane/water (4:1). In analogy to published procedures,[76] we have used $[Rh(cod)Cl]_2$ as catalyst precursor (3 mol%) and KOH as base. A brief screening of reaction conditions revealed that a clean annulation reaction can be induced by microwave heating to 100 °C for 30 min. Indenol **2.1a** was isolated with good regioselectivity (8:1) in 90 % yield (Table 2.1, entry 1). Six other alkynyl triazenes were used as substrates for the coupling with 2-formylphenylboronic acid, providing the indenols **2.1b**–**g** in yields between 34 % and 72 %. Two regioisomers **A** and **B** are possible (Table 2.1), and an attribution was established by correlation NMR spectroscopy (HMBC). The results were corroborated by crystallographic analyses of the main isomers of **2.1a** and **2.1k**.[82]

The regioselectivity is strongly influenced by the substituents on the alkyne. Notably, a complete change in regioselectivity was observed when the substituent attached to the alkyne was changed from a *t*-butyl group to a methyl, *n*-butyl or cyclopentyl group (entry 1 vs. entry 5 – 7).

Subsequently, we have investigated reactions with 2-acetylphenylboronic acid. Using similar conditions as described before, we were able to prepare indenols **2.1h**–**k** in yields between 46 % and 60 % (Table 2.1). The regioselectivity was again strongly influenced by the substituents on the triazene (entry 9 vs. entry 10).

Next, we examined reactions with arylboronate esters featuring α,β-unsaturated carbonyl substituents.[76a,f] THF/water (20:1) was found to be a suitable solvent system for these reactions. As catalyst precursor, we have used once more $[Rh(cod)Cl]_2$. Annulation reactions

Table 2.1. Rh-catalyzed reaction of 2-formyl- and 2-acetylphenylboronic acids with alkynyl triazenes.[a]



2.1

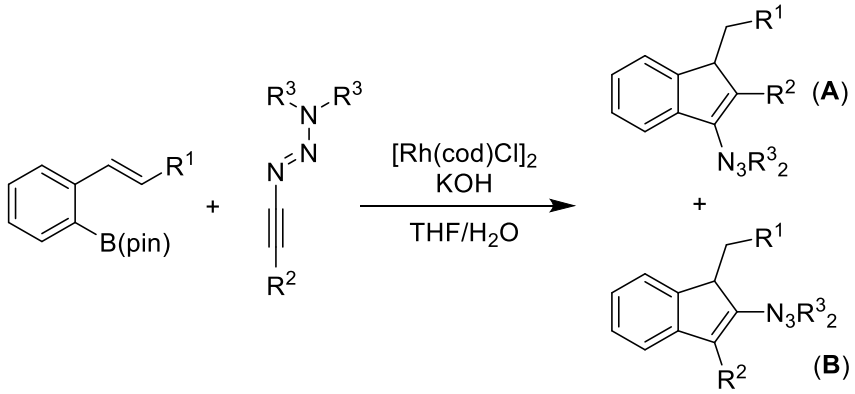
	Product	R^1	R^2	R^3	**A**:**B**[b]	Yield [%][c]
1	**2.1a**	H	*t*Bu	*i*Pr	8:1	90
2	**2.1b**	H	*t*Bu	$(CH_2)_4$	4:1	34
3	**2.1c**	H	*t*Bu	$(CH_2)_5$	> 20:1[d]	67
4	**2.1d**	H	Ph	*i*Pr	> 20:1[d]	48
5	**2.1e**	H	Me	Cy	< 1:20[d]	64
6	**2.1f**	H	*n*Bu	*i*Pr	< 1:20[d]	44
7	**2.1g**	H	*c*Pent	*i*Pr	< 1:20[d]	61
8	**2.1h**	Me	Ph	*i*Pr	6:1	60
9	**2.1i**	Me	*t*Bu	*i*Pr	> 20:1[d]	60
10	**2.1j**	Me	Me	*i*Pr	< 1:20[d]	46
11	**2.1k**	Me	Me	Cy	< 1:20[d]	54

a) Reaction conditions: boronic acid (1.2 equiv.), alkynyl triazene (1 equiv.), $[Rh(cod)Cl]_2$ (3–4 mol%), KOH (0.3–0.5 equiv.), 1,4-dioxane/H_2O (4:1), microwave, 100 °C, 15–45 min. b) Isomer ratio of the product as determined by ^1H NMR. c) Isolated yield. d) Ratio of the separated isomers.

with alkynyl triazenes gave the desired indene derivatives in moderate to good yields (Table 2.2). The reaction is compatible with boronate esters having aldehyde (entries 1 – 3), ketone (entries 4 – 6), and ester groups (entries 7 and 8).

The regioselectivity of the reaction was again strongly influenced by the substituents on the triazene. Alkynes with *t*-butyl or mesityl groups were found to favor isomer **A** with the triazene group in 3-position, as evidenced for instance by the single-crystal X-ray analysis of derivative **2.7** of **2.2g** (see Scheme 2.3).[82] A reversed selectivity was observed for alkynes with methyl substituents. For **2.2b,** the preferential formation of isomer **B** was confirmed by a single-crystal X-ray analysis.[82]

Table 2.2. Rh-catalyzed reaction of functionalized boronate esters with alkynyl triazenes.[a]



2.2

Entry	Product	R^1	R^2	R^3	**A**:**B**[b]	Yield [%][c]
1	**2.2a**	COH	*t*Bu	*i*Pr	9:1[d]	67
2	**2.2b**	COH	Me	Cy	< 1:20	69
3	**2.2c**	COH	Mes	*i*Pr	6:1	59[e]
4	**2.2d**	COMe	Ph	*i*Pr	1:1	80
5	**2.2e**	COMe	*t*Bu	*i*Pr	2:1	81
6	**2.2f**	COMe	Me	Cy	< 1:20[d]	66
7	**2.2g**	CO_2Me	*t*Bu	*i*Pr	6:1	68
8	**2.2h**	CO_2Me	Me	Cy	< 1:20	55[f]

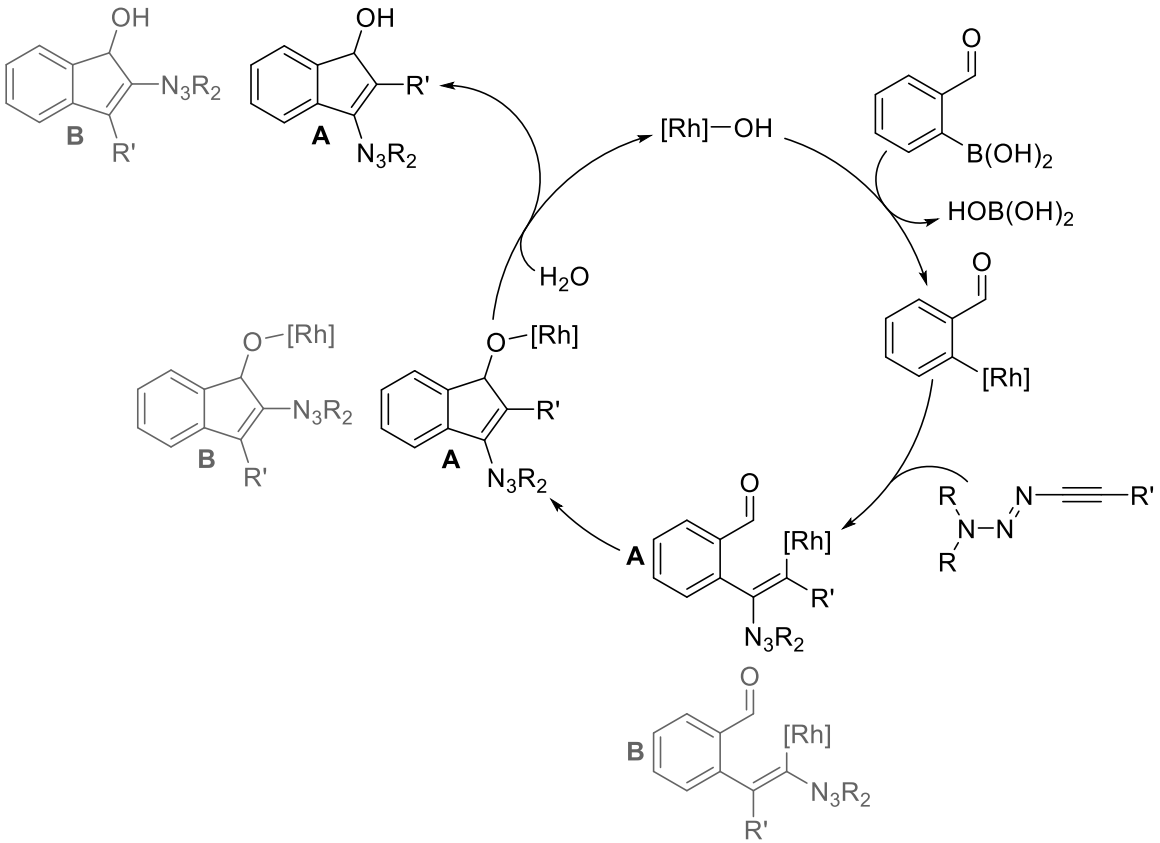
a) Reaction conditions: boronate ester (1.2 equiv.), alkynyl triazene (1 equiv.), $[RhCl(cod)]_2$ (3–5 mol%), KOH (0.3 equiv.), THF/H_2O (2.5–5 vol.-% H_2O), 0 °C (0–7 h) then RT (0–6.5 h). b) Isomer ratio of the product as determined by ^{1}H NMR. c) Isolated yield. d) Ratio of the separated isomers. e) 80 °C (15 min). f) 0 °C, then r.t. (overnight), then 50 °C (6 h).

2.3. Considerations on Mechanism and Regioselectivity

A plausible mechanism[75] for these reactions involves the formation of an aryl rhodium complex from the arylboronic acid, followed by insertion of the alkyne into the carbon–rhodium bond. The resulting styryl rhodium complex adds to the electrophilic substituent to give an alkoxy rhodium complex. The products are then formed by protonolysis (Scheme 2.2).

With regard to regioselectivity, one should note that alkynyl triazenes show a very polarized triple bond.[56] From an electronic point of view, the carborhodation step is expected to favor isomer **A**. In fact, this kind of selectivity was observed exclusively for reactions involving a carbopalladation step.[58] For reactions with alkynes having a methyl, *n*-butyl or cyclopentyl group next to the triple bond, electronic effects are apparently overruled. Aside from steric considerations, it is possible that mechanistic differences are at play. All 1-alkynyl triazenes leading to isomer **B** bear a proton next to the triple bond, which could allow for a different mechanistic pathway favoring isomer **B**.

The formation of indenes from ynamides[76a] is assumed to proceed through a similar mechanism, however the analogue of isomer **B** is favored, irrespective of the substituent. While



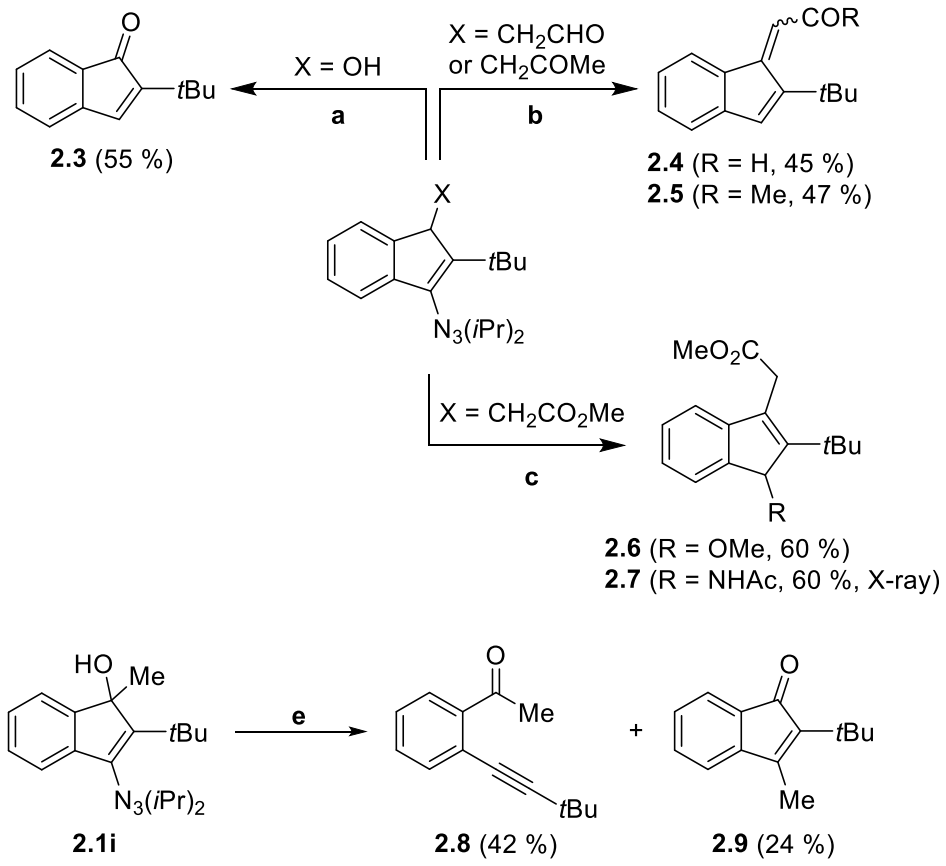
Scheme 2.2: Proposed mechanism for the formation of products **2.1a-g**. The formation of other indenyl triazenes **2.1h-k** and **2.2a-h** is assumed to proceed analogously.

electronic similarities between ynamides and 1-alkynyl triazenes would suggest a similar regioselectivity, it is assumed that chelation of the amide to the Rh-catalyst after the insertion step is responsible for the observed selectivity.[76a]

2.4. Acid-Induced Derivatization of Indenyl Triazenes

As discussed in chapter 1, triazenes can be cleaved under acidic conditions. In the case of 1-aryl triazenes, the addition of acid leads to formation of aryldiazonium compounds, which can be used for subsequent synthetic transformations.[4–8] In the case of 1-vinyl triazenes, the corresponding vinyl diazonium compounds are more reactive and prone to loose dinitrogen.[83]

For indenyl triazenes, nitrogen loss would result in the formation of high-energy cyclic vinyl cations,[84] and alternative decomposition pathways might be favored. Indeed, when indenyl

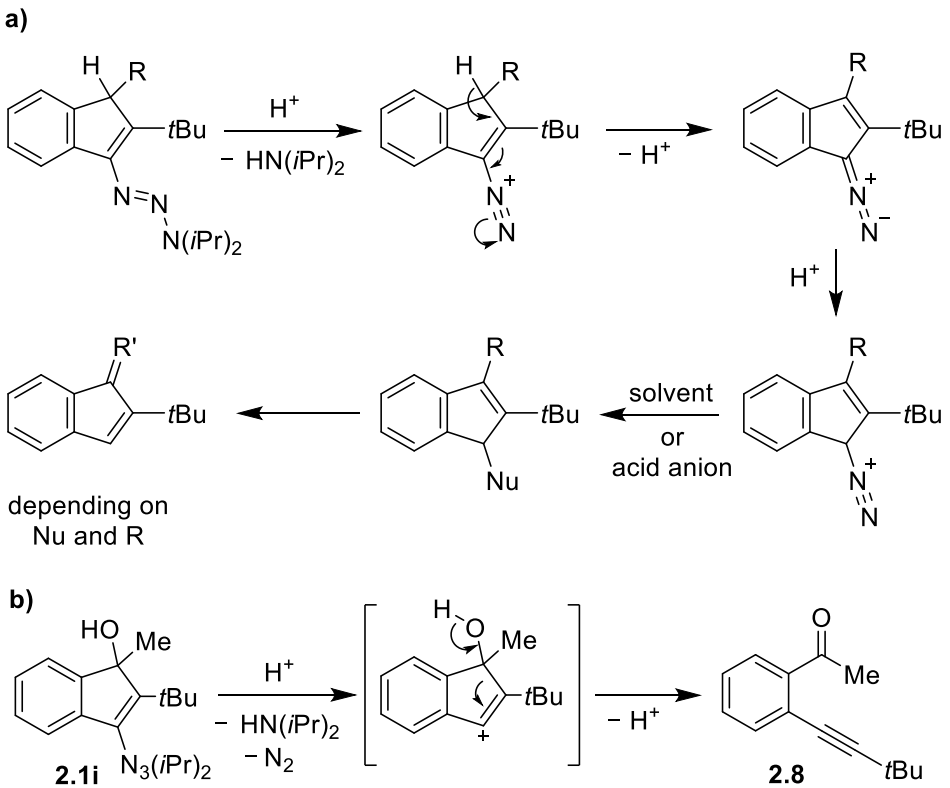


Scheme 2.3. Reactions of indenyl triazenes with acids. Conditions: a) TFA (3 equiv.), Et_2O, r.t., 4 h. b) TFA (2.5 equiv.), MeCN, 60 °C, 1 d (X = CH_2CHO) or 2 d (X = CH_2COMe). c) $HBF_4 \cdot Et_2O$ (3 equiv.), MeOH or MeCN, 40 °C, 2 d. d) HCl (6 equiv.), THF/H_2O (5:1), 60 °C 16 h. e) HF·Py (25 equiv.), 10 % THF in pentane, 30 °C, 1 h.

triazenes were subjected to strong acids, rearranged products were formed as opposed to addition products to hypothetical vinyl cations (Scheme 2.3). The addition of trifluoroacetic acid (TFA) to a solution of triazene **2.1a** in diethyl ether resulted in the formation of indenone **2.3**, which could be isolated in 55 % yield. A similar reactivity (triazene cleavage followed by deprotonation) was observed for reactions of **2.2a** and **2.2e** with TFA, which gave the 1-methylene-1*H*-indene derivatives **2.4** and **2.5.** An exchange of the triazene function against a methoxy or an acetamide group (via a Ritter-type reaction) was found for mixtures of **2.2g** and HBF_4 in methanol or acetonitrile (**2.6** and **2.7**). However, the substitution went along with a rearrangement of the double bond, as evidenced by NMR spectroscopy and by a crystallographic analysis of **2.7**.[82]

The reactions leading to **2.3** – **2.4** show that substitution of the triazene group by nucleophiles is disfavored in the presence of acidic protons. Compound **2.1i** does not feature acidic protons, and we thus attempted a displacement of the triazene by fluoride using HF·pyridine.[48,67] However, as main products of the reaction, we observed alkyne **2.8** along with minor amounts of indenone **2.9** (Scheme 2.3).

For cleavage reactions with triazenes having a hydrogen atom in 1-position, we propose the



Scheme 2.4. Proposed mechanism for the formation of cleavage products **2.3**–**2.7** (a). Proposed mechanism for the formation of cleavage product **2.10** (b).

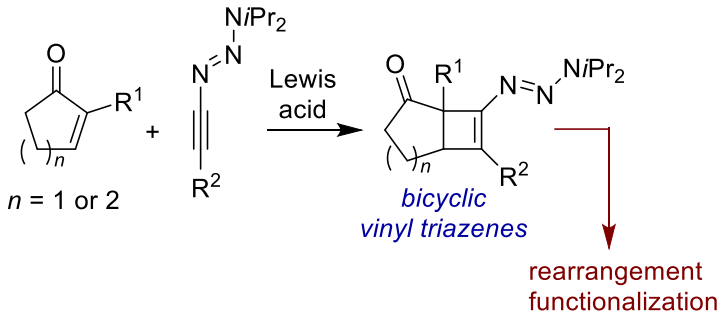
following tentative mechanism: The addition of a strong acid results in rupture of the N1–N2 bond of the triazene group and formation of a vinyl diazonium compound (Scheme 2.4a). Instead of N_2, a proton is lost to give a diazo compound. It is worth noting that there is literature precedence for the formation of diazo compounds from triazenes.[85] Acid-induced substitution of the diazo group by HNu then gives indenes with a rearranged double bond (e.g. **2.6** or **2.7**), or elimination products (e.g. **2.3** – **2.5**). The latter likely form via a TFA adduct (Nu = CF_3CO_2). In fact, for reactions leading to **2.4**, we have been able to characterize the intermediate TFA adduct by NMR spectroscopy (see chapter 7.2.5).

For reactions with **2.1i**, the formation of a diazo compound is not possible (no H atom in position 1). In this case, the reaction might proceed via a short-lived vinyl cation, which undergoes a ring-opening reaction to give alkyne **2.9** (Scheme 2.4b).

2.5. Conclusion

Vinyl triazenes are commonly prepared from vinyl Grignard reagents.[36–41,45] We have recently introduced a complementary approach, namely metal-catalyzed addition reactions to alkynyl triazenes. In continuation of studies about Ru- and Pd-catalyzed reactions,[48,58] we have now shown that substituted indenyl triazenes are accessible by Rh-catalyzed [3+2] annulation reactions. As substrates, we have employed arylboronic acid derivatives with aldehyde, ketone or ester groups. The regioselectivity of the reaction was mostly high, and strongly dependent on the substituent at the alkyne. The addition of acids allows cleavage of the triazene group in the products. This cleavage does not result in direct substitution of the triazene by nucleophiles, as observed for other vinyl triazenes. Instead, we observed substrate-specific rearrangements. Nevertheless, it is possible to use these cleavage reactions to prepare structurally complex indenes, as exemplified by the synthesis of compounds **2.5** – **2.8**.

3. Synthesis of Bicyclic Vinyl Triazenes by Ficini-Type Reactions



This chapter is based on a published article:

C. T. Bormann, F. Fadaei-Tirani, R. Scopelliti, K. Severin,* Synthesis of bicyclic vinyl triazenes by Ficini-type reactions. *Org. Biomol. Chem.* **2021**, *19*, 8113–8117.

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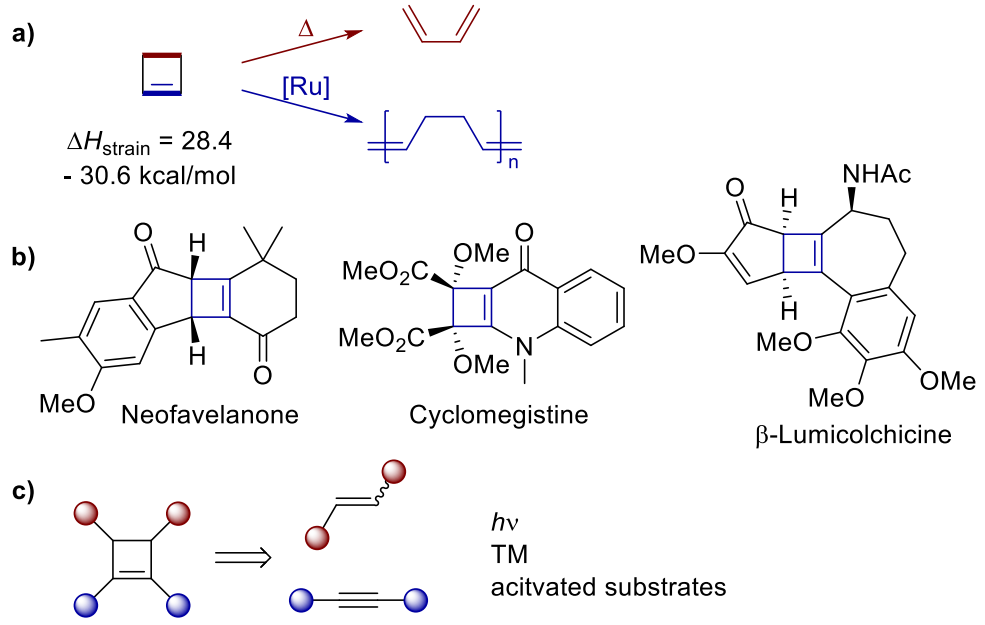
Author contributions: C.T.B. performed the experiments. F.F.T. and R.S. performed X-ray structure analyses. K.S. supervised the project. K.S. and C.T.B. prepared the manuscript

3.1. Introduction

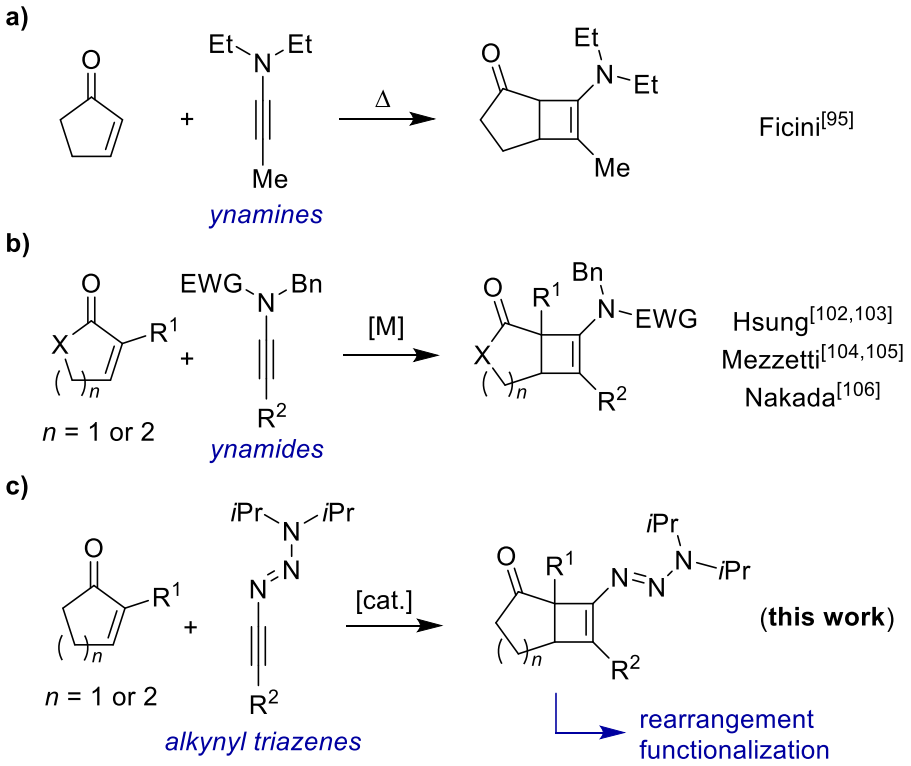
The ring strain of cyclobutenes is estimated to range from 28.4 – 30.6 kcal/mol, which is lower than cylcopropenes and slightly higher than cyclopropanes.[86] The intrinsic reactivity of cyclobutenes makes them valuable intermediates in organic synthesis and polymer chemistry. Two of the most widely encountered reactions to release the ring strain of cyclobutenes are the thermal ring opening leading to 1,3-dienes,[87] and ring opening metathesis polymerization (ROMP) results in polyenes (Scheme 3.1a).[88] While less common than cyclopropanes or cyclobutenes,[89] several natural products containing cyclobutene ring systems have been isolated (Scheme 3.1b).[90–92]



Scheme 3.1. a) Estimated ring strain of cyclobutenes and examples for ring opening reactions. b) Examples of natural products containing cyclobutenes. c) Alkyne-alkene [2+2]-cycloaddition as a retrosynthetic approach to cyclobutenes.

The [2+2] cycloaddition of alkenes and alkynes is the most popular approach for the synthesis cyclobutenes (Scheme 3.1c). To overcome or circumvent the energy barrier for the symmetry forbidden reaction, transition metal catalysis, light irradiation or specially activated substrates are used.[86,89,93,94] An example for the latter is the [2+2] cycloaddition between highly nucleophilic ynamines and enones. The coupling of cyclopentenone and N,N-diethylamino-1-propyne was first reported by Ficini and Krief in 1969 (Scheme 3.1a).[95] In subsequent studies, it was shown that other enones (e.g. cyclohexenones) are suited substrates as well.[96–101]

Due to the presence of an electron-withdrawing group on the nitrogen, ynamides are less reactive than ynamines. The tamed reactivity facilitates synthesis, handling, and storage, and thus ynamides have become popular reagents in synthetic chemistry.[57] Ficini-type reactions with ynamides were first reported by Hsung and co-workers (Scheme 3.2b).[102] Thermally induced cycloadditions were not successful, but the reactions proceeded in the presence of catalytic $CuCl_2$ and $AgSbF_6$. When $AgNTf_2$ was used instead of $AgSbF_6$, the reaction could also be performed without $CuCl_2$.[103] The asymmetric synthesis of cyclobutenyl amides starting from α-unsaturated β-ketoesters was reported by the groups of Mezzetti[104,105] and Nakada (Scheme 3.2b).[106] As catalysts, chiral Ru^{II} or Cu^{II} complexes were employed. A catalyst-free cycloaddition of ynamides with highly activated enones (cyclic isoimidium salts) has also been described.[107]

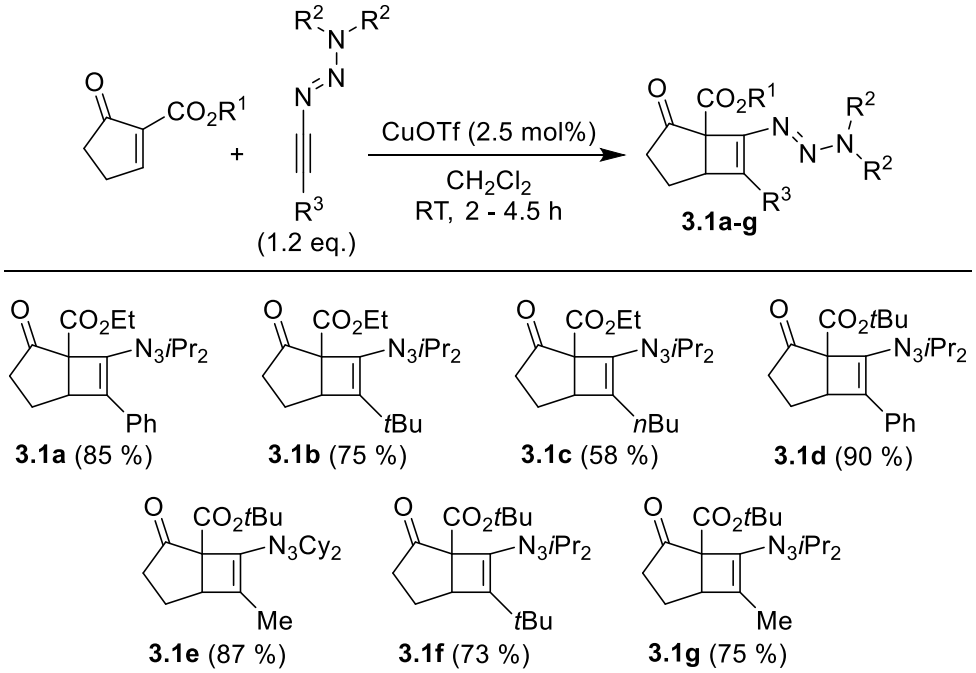


Scheme 3.2. [2+2] Cycloaddition reactions between enones and ynamines (**a**), ynamides (**b**), or 1-alkynyl triazenes (**c**).

Below, we show that Ficini-type reactions are possible with 1-alkynyl triazenes if appropriate Lewis acids are used as catalysts (Scheme 3.2c). The resulting cyclobutenyl triazenes can be rearranged under mild conditions into [3.2.1] bicyclooctenones, and the triazene group can be used for further functionalizations.

3.2. Synthesis from Unsaturated β-Ketoesters

First, we investigated the reaction of ester-substituted cyclopentenones with 1-alkynyl triazenes. Using CuOTf as Lewis-acidic catalyst (2.5 mol%) and dichloromethane as solvent, the desired cyclobutenyl triazenes were obtained in good yields (Scheme 3.3). Aliphatic and aromatic substituents on the alkyne were well tolerated. Changing from an ethyl to a more bulky *tert*-butyl ester did not adversely affect the yield.



Scheme 3.3. Synthesis of cyclobutenyl triazenes from ester-substituted cyclopentenones.

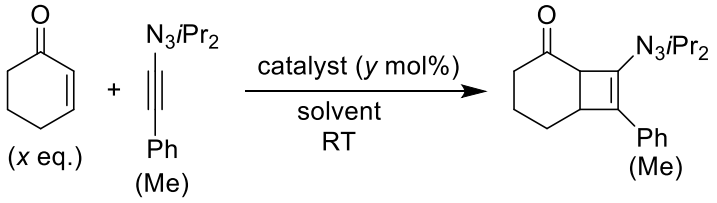
3.3. Synthesis from Enones

3.3.1. Optimization

Proceeding to less activated, hence more challenging substrates, we turned to α,β-unsaturated ketones. Silver and copper salts, which are suitable catalysts for the analogous reaction with ynamides,[102,103] were ineffective (Table 3.1, entries 1 and 2). Traces of product were observed with $AgBF_4$ and a methyl-substituted triazene. However, synthetically useful amounts were not obtained. Instead, tris(penta-fluorophenyl)borane (BCF) was found to be an effective catalyst (entry 3). A brief solvent screen revealed toluene as the most suitable solvent (entries 3 – 6). Lowering the catalyst concentration to from 5 to 2.5 mol% did benefit the yield (entry 7), but further reduction of the BCF concentration to 1 mol% led to a pronounced drop in yield

(entry 8). Finally, a longer reaction time of 24 h slightly improved the yield (entry 9). Reducing the excess of cyclohexenone from 2.5 to 1.2 equivalents was possible, but the catalyst loading had to be increased to achieve an acceptable yield (entry 10).

Table 3.1. Optimization of the reaction between cyclohexenone and 1-alkynyl triazenes.



Entry	*x*	Catalyst	*y*	Solvent[a]	Time [h]	Yield [%][b]
1	1.2	CuOTf	4.5	DCM	3.5	n.d.[c]
2	1.2	$AgBF_4$	10	DCM	28	12[d]
3	2.5	BCF	5	DCM	16	65
4	2.5	BCF	5	Ph-Cl	16	72
5	2.5	BCF	5	DCE	16	71
6	2.5	BCF	5	Toluene	16	80
7	2.5	BCF	2.5	Toluene	16	90[e]
8	2.5	BCF	1	Toluene	16	16[e]
9	**2.5**	**BCF**	**2.5**	**Toluene**	**24**	**98[d,e]**
10	1.2	BCF	5	Toluene	24	88[e]

a) Concentration: 0.2 M. b) Determined by NMR spectroscopy using $MeNO_2$ as internal standard after filtration over silica and removal of volatiles under vacuum. c) Me instead of Ph substituent. d) Isolated yield. e) Filtered over alumina

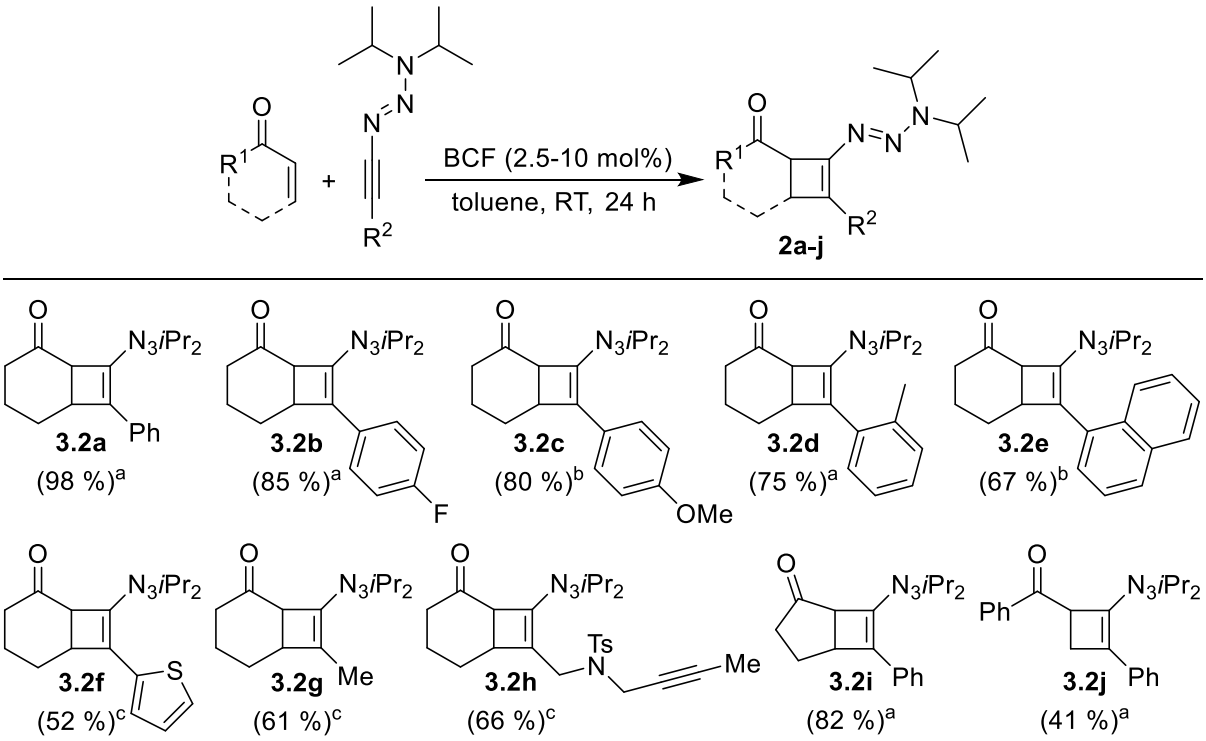
3.3.2. Scope

With the optimized conditions at hand, we started to investigate the scope of the reaction (Scheme 3.4). Triazenes with aromatic, heteroaromatic, and alkyl substituents at the triple bond could be used as substrates for the reaction, providing cyclobutenyl triazenes in yields between 52 % and 98 % (**3.2a**–**3.2g**).

The importance of the triazene function as an activating group was evidenced by a reaction with a substrate featuring two alkyne groups, one with a methyl substituent and one with an N_3iPr_2 substituent. Only the triazene-activated alkyne was found to react with cyclohexanone, giving **3.2h** in 66 % yield.

Using cyclopentenone instead of cyclohexanone gave the addition product **3.2i** in 82 % yield. For cycloheptenone, on the other hand, no conversion was observed. In terms of acyclic enones, we were able to convert phenyl vinyl ketone into a cyclobutenyl triazene,

albeit with low yield (41 %). No coupling reaction was observed for acrylate esters. It is worth noting that the BFC concentrations had to be adapted to the specific substrate.



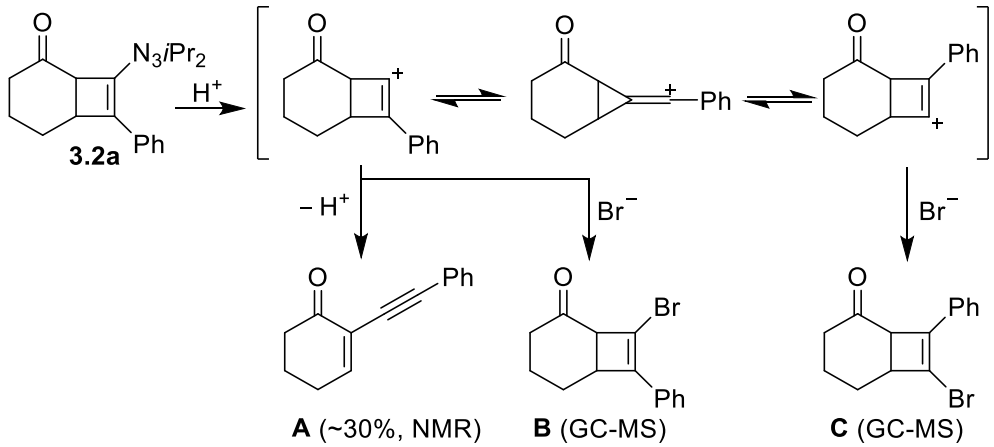
Scheme 3.4. Synthesis of cyclobutenyl triazenes from α,β-unsaturated ketones. a) 2.5 mol% BCF, b) 5 mol% BCF, c) 10 mol% BCF.

3.4. Derivatization

3.4.1. Acid-Induced Cleavage of the Triazene Group

Previously, we had reported Ru-catalyzed [2+2] cycloaddition reactions of 1-alkynyl triazenes and strained alkenes (e.g. 1,4-dihydro-1,4-epoxynaphthalene).[48] Under acidic conditions, the triazene group in the resulting products could be replaced by a variety of different nucleophiles. Attempts to perform similar substitution reactions with the cyclobutenyl triazenes described herein were largely unsuccessful. The addition of acids to the triazenes resulted in a conversion, but a complex mixture of products was observed in all cases. Potential problems are acid-promoted ring-opening reactions of the cyclobutene ring.[95–99] For example, we have examined the reaction of **2a** with HBr (Scheme 3.5). GC-MS and ^{1}H-NMR analysis of the crude reaction mixture revealed a complex mixture of products, including alkyne **A**, originating from ring-opening of the cyclobutene. The formation of **A** is facilitated by the inherent strain of the cyclobutenyl

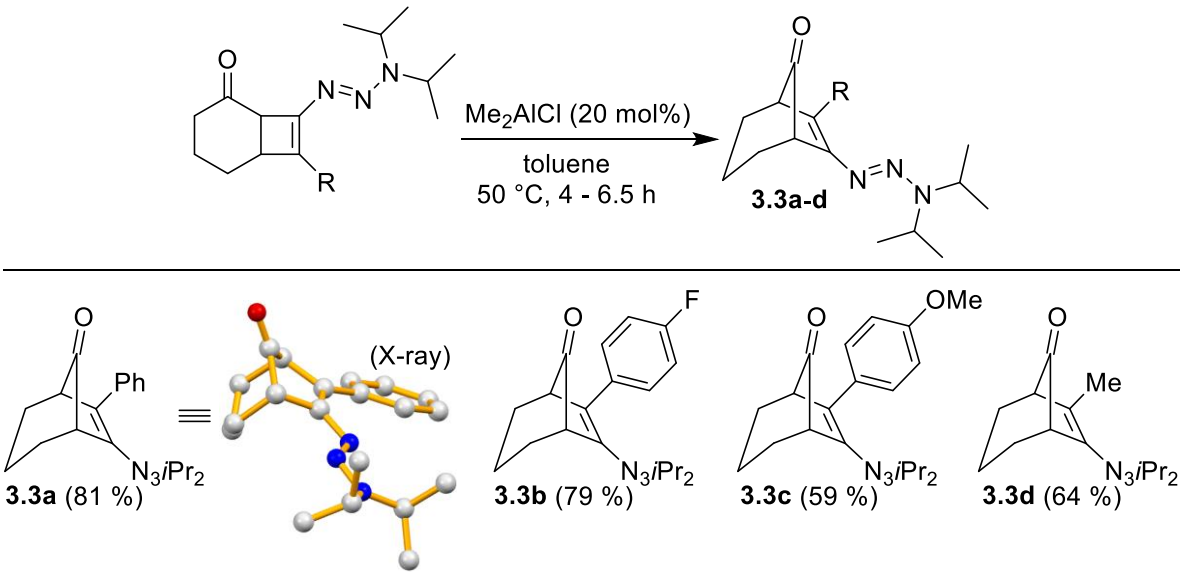
ring[108] and by the acidity of the proton α to the carbonyl group. Furthermore, several species with the expected mass and isotope pattern of the desired brominated product were detected via GC-MS (two potential products, **B** and **C**, are shown in Scheme 3.5). This result suggests that the putative vinyl cation,[109] which is generated upon acidic cleavage of the triazene group, undergoes various rearrangements before being trapped by bromide.



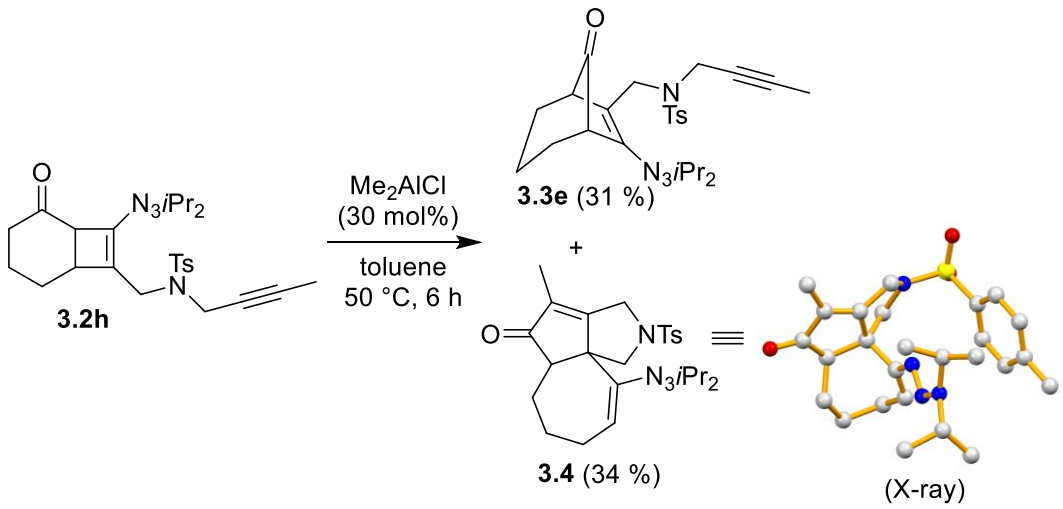
Scheme 3.5. Reaction of **3.2a** with HBr; Conditions: **3.2a** (1 eq.), HBr (6 eq.), Et_2O, 0 °C to RT, 3 h.

3.4.2. Lewis Acid-Catalyzed Rearrangements and Derivatization of the Products

The results prompted us to explore if we could perform targeted rearrangements of cyclobutenyl triazenes. Hsung and co-workers have reported the $AlCl_3$-catalyzed conversion of fused cyclobutenyl amides into [3.2.1]-bicyclic ketones.[110] An analogous

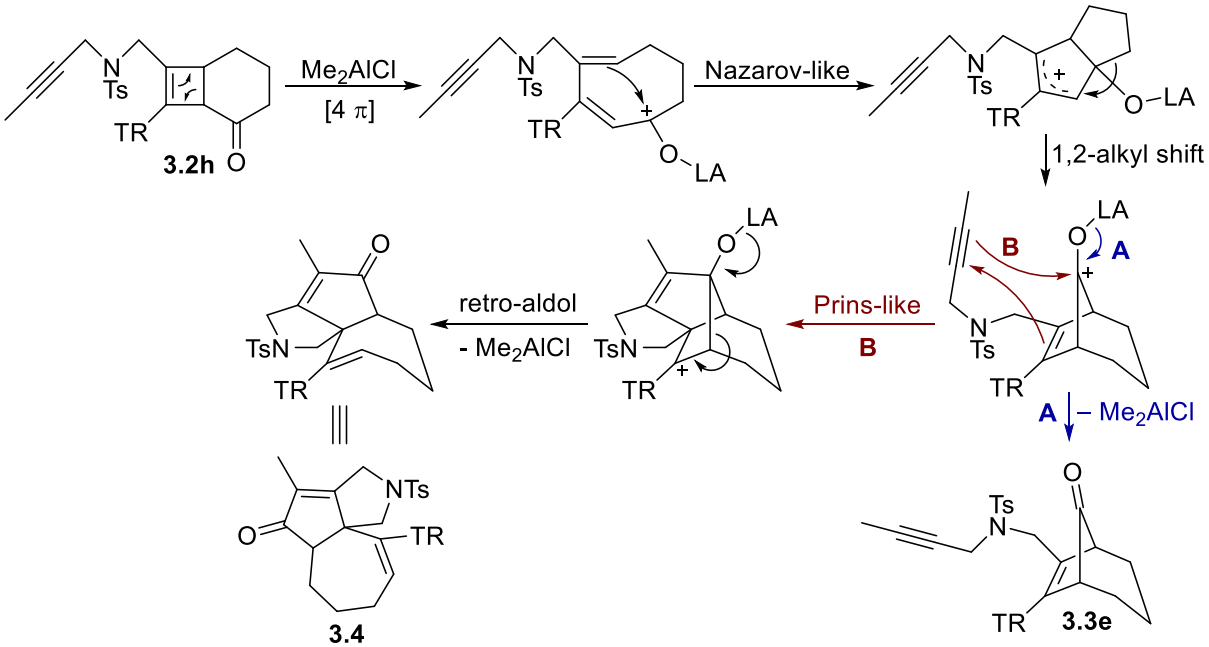


Scheme 3.6. Me_2AlCl-catalyzed rearrangement of cyclobutenyl triazenes.



Scheme 3.7. Me_2AlCl-catalyzed rearrangement of **3.2h** gives a mixture of **3.3e** and **3.4**.

reaction could be realized with cyclobutenyl triazenes **3.2**. In the presence of catalytic amounts of Me_2AlCl (20 mol%), bicyclooctenonyl triazenes (**3.3a**–**d**) were obtained in yields between 59 and 81% (Scheme 3.6). The structure of **3.3a** was confirmed by single-crystal X-ray analysis. It is worth noting that the rearrangements occurred under mild conditions when compared to what was reported by Hsung et al. (20 mol% Me_2AlCl vs. 40 mol% $AlCl_3$; 50 °C vs 105 °C).[110]

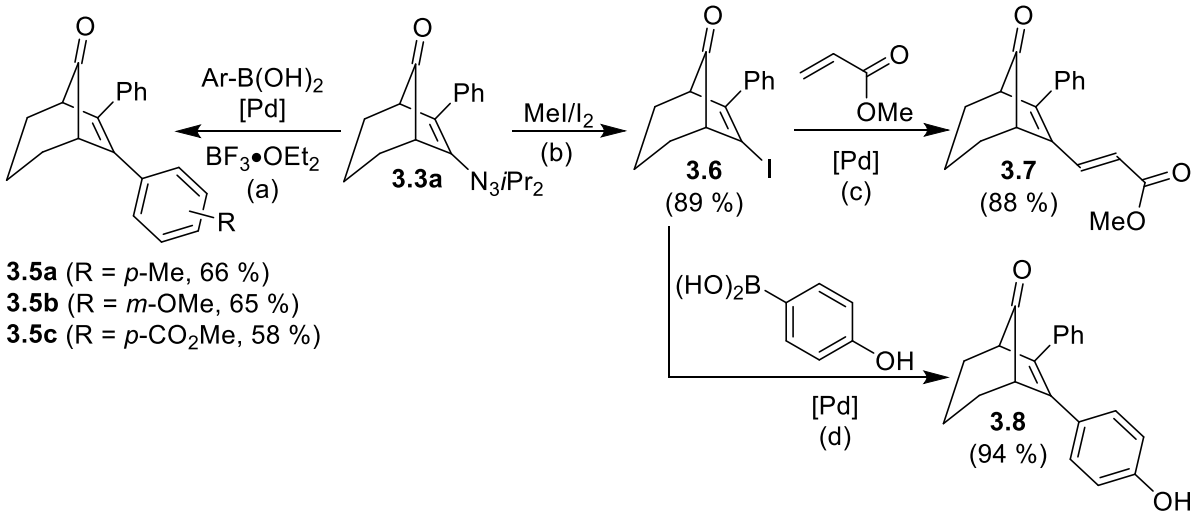


Scheme 3.8. Proposed mechanism for the formation of **3.3e** (pathway A) and **3.4** (pathway B) from **3.2h**. LA = Me_2AlCl, TR = 3,3-diisopropyltriaz-1-en-1-yl. The mechanism for the formation of **3.3e** and **3.3a** – **d** is assumed to be analogous.

In the case of **3.2h**, the tricyclic vinyl triazene **3.4** was obtained along with the expected [3.2.1]-bicyclic ketone **3.3e** in a 1.1:1 ratio (Scheme 3.7). The structure of **3.4** was confirmed by single-crystal X-ray analysis.

As suggested earlier,[110] the mechanism of the formation of rearrangement products **3a-e** and **4** likely involves a common intermediate originating from the initial formation of a strained *cis,trans*-cyclooctadienone, subsequent Nazarov-like ring closure and a 1,2-alkyl shift. Dissociation of the Lewis acid leads to rearrangement products **3.3a-e** (Scheme 3.8, A). On the other hand, **3.4** is likely formed by a Prins-like intramolecular reaction of the alkyne and retro-aldol addition (Scheme 3.8, B).

Subsequently, we have examined the possibility of using the triazene function for further derivatization of the bicyclooctene. The reactions were performed with the bicyclic ketone **3.3a** as a representative example. Brønsted-acid induced cleavages were not successful, possibly because of the high ring strain of the putative cyclopentenyl cation intermediate.[84]



Scheme 3.9. Derivatization of **3.3a;** a) Ar-B(OH)$_2$ (2 eq.), Pd(PPh$_3$)$_4$ (0.1 eq.), BF$_3$·OEt$_2$ (2 eq.), DME, 4 h, RT. b) I$_2$ (0.2 eq.), MeI, 130 °C, 4 h. c) methyl acrylate (1.5 eq.), Pd(OAc)$_2$ (0.1 eq.), NEt$_3$ (1.5 eq.), DMF, 50 °C, 14 h. d) Ar-B(OH)$_2$ (2 eq.), Pd(OAc)$_2$ (0.1 eq.), K$_2$CO$_3$ (2 eq.), DMF/H$_2$O 4:1, 85 °C, 6 h.

However, a BF$_3$·OEt$_2$-induced Suzuki-type reaction with arylboronic acids, as previously reported for aryl triazenes,[111] was successfully implemented to obtain substituted *Z*-stilbenes (Scheme 3.9a). By using a cross-coupling strategy, it is possible to obtain products with complete regioselectivity (**3.5a**), to override the inherent

regioselectivity for electrophilic substitutions (**3.5b**), or to introduce arenes, which display low reactivity in cationic vinylations (**3.5c**).

Conversion of the vinyl triazene **3.3a** to a vinyl iodide, **3.6**, was achieved in MeI in the presence of I_2 at elevated temperatures (Scheme 3.9b). This transformation could proceed via a radical pathway, as discussed for the iodination of aryl triazenes.[112,113] Vinyl iodide **3.6** was then used for Pd-catalyzed Heck- and Suzuki-reactions to give the coupling products **3.7** and **3.8** in high yields (Scheme 3.8c and 3.8d).

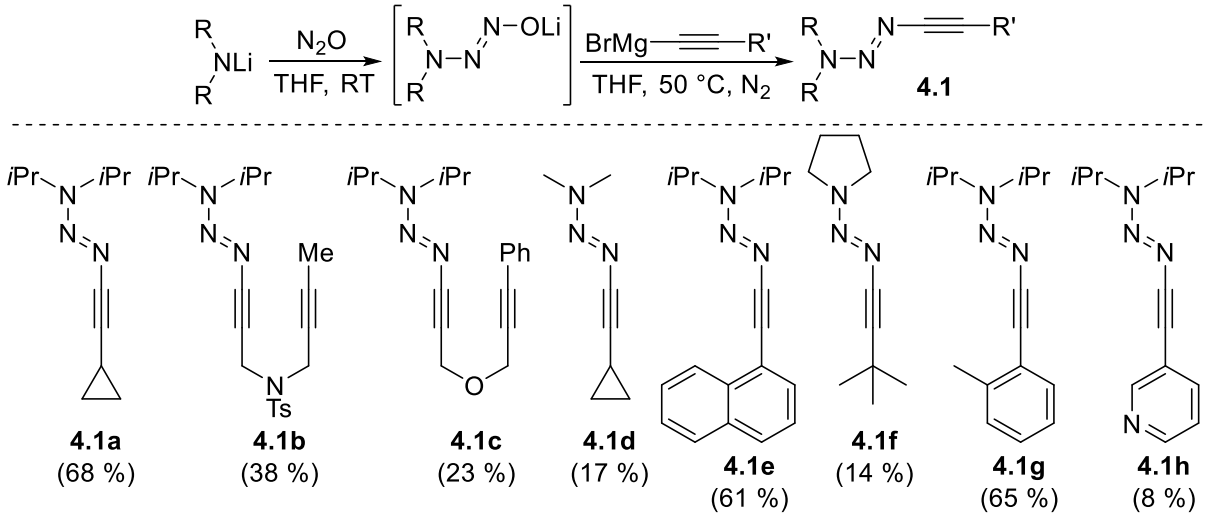
3.5. Conclusion

Cyclobutenyl triazenes fused to cyclopentanone or cyclohexanone rings were obtained by [2+2] cycloaddition reactions of 1-alkynyl triazenes and enones. Reactions with ester-substituted cyclopentenones are efficiently catalyzed by CuOTf, whereas cycloadditions with cyclohexenone are catalyzed by BCF. The bicyclic [4.2.0] triazenes derived from cyclohexenone can be rearranged into [3.2.1] ring systems. The triazene function in the latter enables further derivatizations. Notably, we demonstrate that vinyl triazenes can serve as substrates for Pd-catalyzed cross-coupling reactions with arylboronic acids.

4. Synthesis of New 1-Alkynyl Triazenes

4.1. Synthesis via the N_2O-Method

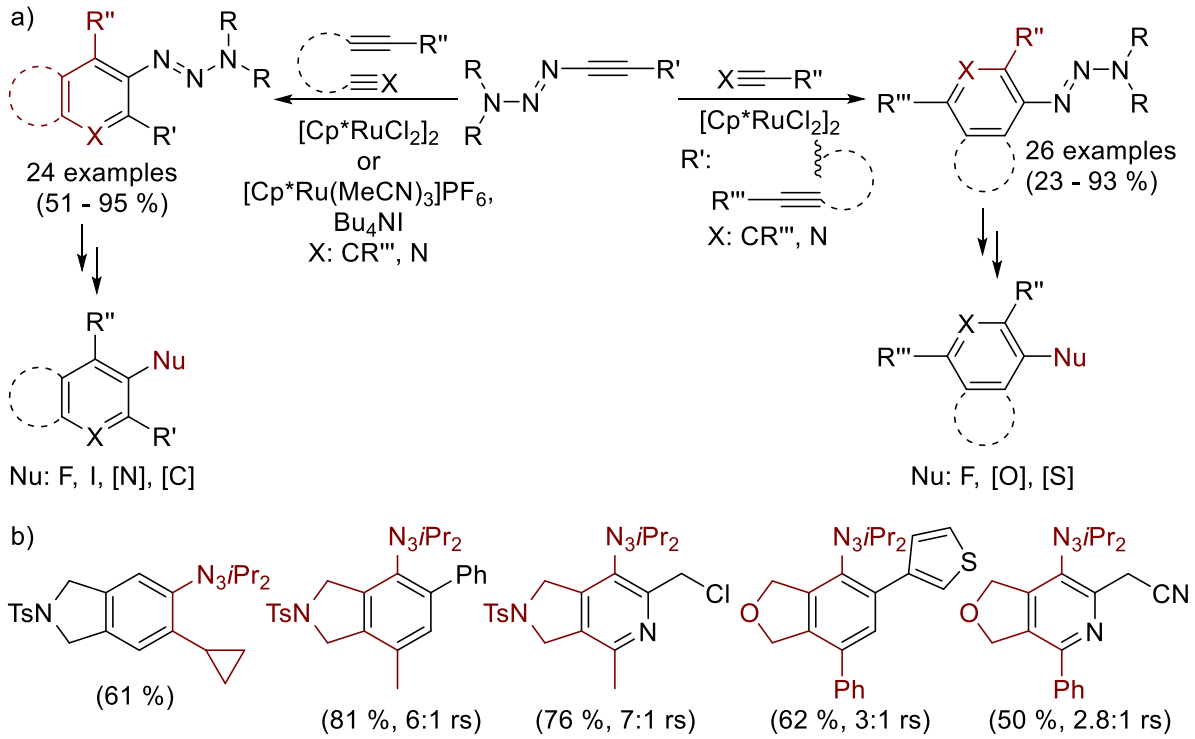
As discussed in chapter 1.1.3, the synthesis of 1-alkynyl triazenes from lithium amides, N_2O and alkynylmagnesium bromides has been established in 2015.[41] A range of new 1-alkynyl triazenes was synthesized during the completion of this thesis (Scheme 7.1). Starting alkynes for **4.1a** and **4.1d** – **4.1h** are commercially available, for **4.1b** and **4.1c**, the starting alkynes were provided by Jin Fay Tan, as part of a collaboration with the group of Nicolai Cramer (see below) and prepared according to literature procedures.[140,141] In all cases, the corresponding alkynyl Grignard reagent was freshly prepared by addition of ethylmagnesium bromide to the alkyne (see chapter 7.4.1 for details).



Scheme 4.1. Synthesis of novel 1-alkynyltriazenes via the N_2O-method.

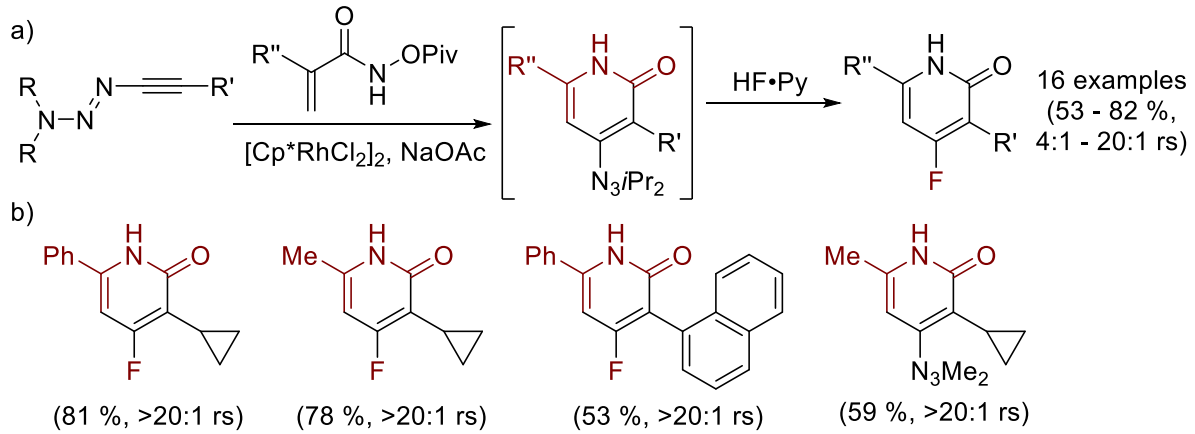
Compounds **4.1a – c** were initially provided to the group of Cramer for their investigations on Ru-catalyzed cyclotrimerization reactions involving 1-alkynyl triazenes. Densely substituted arenes and pyridines were obtained in generally good yields (Scheme 4.2a).[67] 1-Alkynyl triazenes were suited substrates with both an alkyl and aryl substituent as for **4.1a** as well as tethered to a second alkyne group as for **4.1b**, **c** (Scheme 4.2b). Upon acid-induced cleavage of the triazene group, a range of nucleophiles could be introduced. Notably, it was possible to introduce fluorine, which is relevant for biologically active compounds.

The concept of using 1-alkynyltriazenes as synthetic equivalents of generally unstable alkynyl fluorides[116,117] was expanded on by the group of Cramer by Rh^{III}-catalyzed synthesis of 4-fluoro-2-pyridones in a two-step reaction (Scheme 4.4).[47] Initial



Scheme 4.2. a) Synthesis and divergent functionalization of 1-aryl and 1-pyridyl triazenes from 1-alkynyl triazenes. b) Examples for products incorporating **4.1a** – **c**.

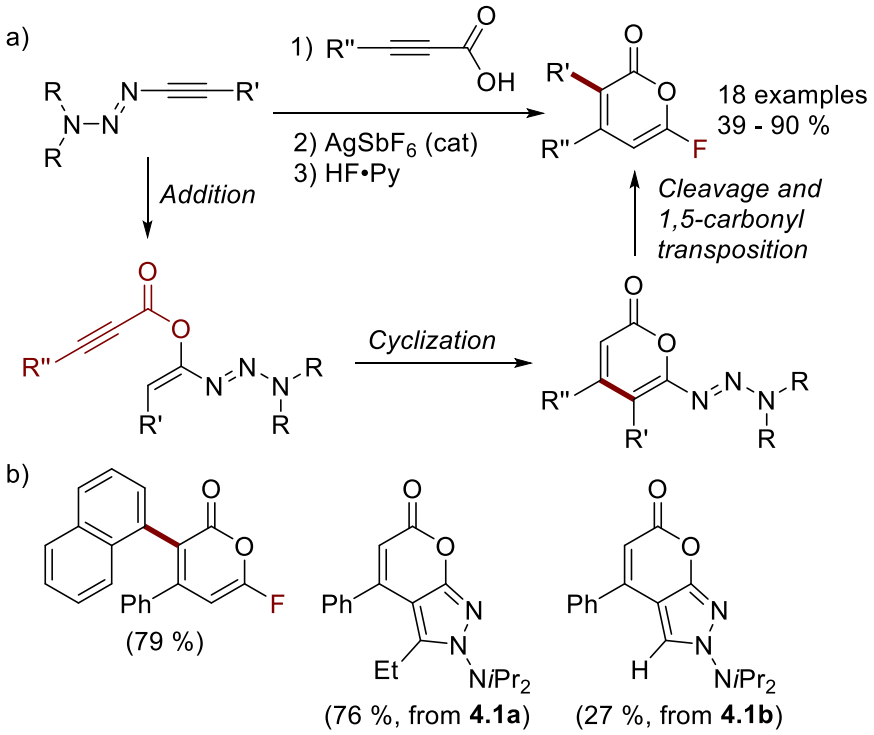
alkenyl C-H annulation of an N-(pivaloyloxy)acrylamide and subsequent Lossen-rearrangement is followed by treatment of the crude product with HF•Py to induce cleavage of the triazene group and installation of the fluorine (Scheme 4.3a). Alternative cleavages leading to fluorinated ethers or iodine were also demonstrated. Aromatic and aliphatic substituents were tolerated on both the N-(pivaloyloxy)acrylamide and triazene (e.g. **4.1a**,**e**). Dimethylamine-capped **4.1d** was also subjected to the annulation reaction, but cleavage of the triazene was not



Scheme 4.3. a) Synthesis of 4-fluoro-2-pyridones by Rh catalyzed alkenyl C-H annulation and subsequent treatment with HF•Py. b) Examples of products incorporating **4.1a**, **d**-**e**.

carried out, as the dimethylamine capped triazenes are potentially bioactive (see dacarbazine, chapter 1.1.1).

Furthermore, 1-alkynyl triazenes were provided to the group of Cramer as starting materials in their divergent synthesis of 2-fluoro pyrones, which had been unknown in the prior literature (Scheme 4.4a).[46] Initial addition of a propiolic acid across the C-C triple bond of the 1-alkynyl triazene (see as well chapter 1.3) is followed by Ag-catalyzed cyclization to give the triazenyl pyrone. Upon cleavage of the triazene group with HF•Py, a 1,5-carbonyl transposition is observed, along with introduction of a fluoride. An analogous transposition is also observed with cleavages induced by other acids. While **4.1e** underwent the reaction smoothly, **4.1a** and **b** gave N-amino pyrazoles, upon addition of acid to the triazenyl pyrone through intramolecular reactions (Scheme 4.4b).



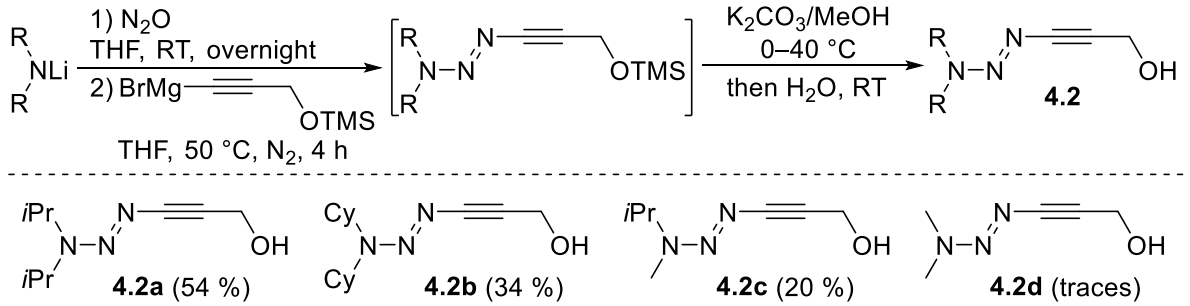
Scheme 4.4. a) Synthesis of 2-fluoro pyrones by addition of a propiolic acid to a 1-alkynyl triazene, Ag catalyzed cyclization and HF•Py-induced cleavage of the triazene and 1,5-carbonyl transposition. b) Products of the reaction with **4.1e**, **a** and **b** as starting materials.

Compounds **4.1f** and **4.1g** were synthesized for the work described in chapters 2 and 3 respectively. In the latter, **4.1b** was also used.

During the preparation of the alkynyl-Grignard reagent for the synthesis of **4.1h**, an unusual, grey precipitate was observed, which is believed to be caused by coordination of the pyridine

to magnesium[118] and likely interfered with the subsequent reaction with the lithium diazotate causing the low yield.

In extension of the N_2O-method, it was found that TMS-protected propargylic alcohols are suited substrates for the synthesis of 1-alkynyl triazenes (Scheme 4.3). While purification of the OTMS bearing 1-alkynyltriazene was not successful, removal of the protecting group from the crude product with K_2CO_3/MeOH yielded the free alcohol.



Scheme 4.3. Synthesis of 1-alkynyl triazenes bearing propargylic alcohols.

1-Alkynyl triazenes with diisopropylamine (**4.2a**), dicyclohexylamine (**4.2b**) and methyl(isopropyl)amine (**4.2c**) end-groups were synthesized from protected propargylic alcohol. Synthesis of dimethylamine capped 1-(propargylalcohol) triazene **4.2d** was not achieved. While traces of the desired product were detected, purification was not successful.

1-Alkynyl triazenes bearing propargylic alcohols are of potential interest in their own right.[119] However, we focused on the application of this discovery in the synthesis of functionalized 1-alkynyl triazenes, which is discussed in the subchapter below.

4.2. Synthesis and Reactivity of a Terminal 1-Alkynyl Triazene

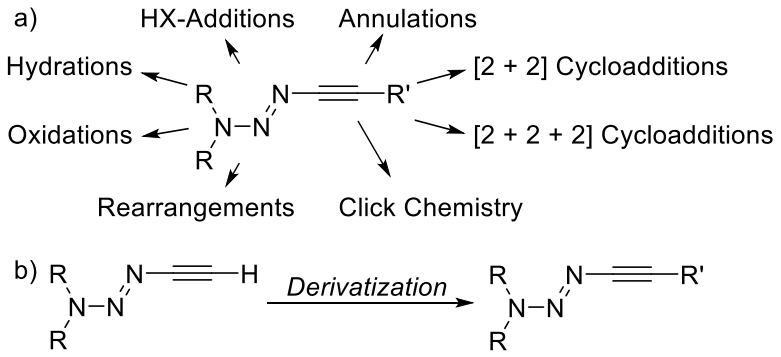
The work presented in this subchapter was supported by apprentices Aude Trotti and Margarida Mayimona Antonio.

4.2.1. Introduction

As demonstrated throughout this thesis, 1-alkynyl triazenes are versatile precursors to vinyl- and aryl triazenes, which can be obtained by an ever-growing variety of addition and annulation reactions of 1-alkynyl triazenes (Scheme 4.4a). Classically, alkynyl Grignard reagents are essential for the synthesis of 1-alkynyl triazenes (see above).[41] As a result, 1-alkynyl triazenes are limited with respect to the presence of substituents bearing functional groups on the

β-carbon. In particular, protic or nucleophilic substituents are not tolerated. This severely limits the use of 1-alkynyltriazenes in the synthesis of complex structures. As one of the key features of 1-alkynyl triazenes is the versatility of the triple bond in the synthesis of aryl and vinyl triazenes and the possibility for divergent functionalization of those products by acid induced cleavage of the triazene group, being limited at the β-carbon to almost exclusively hydrocarbon substituents is particularly striking.

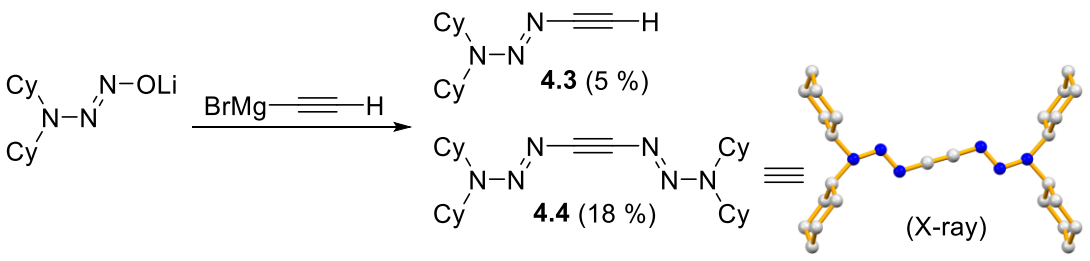
To overcome this limitation, we envisioned the synthesis of a terminal 1-alkynyl triazene, which can later be functionalized with a variety of substituents (Scheme 4.4b).



Scheme 4.4. a) 1-Alkynyl triazenes as versatile precursor to aryl and vinyl triazenes. b) Derivatization of a terminal 1-alkynyl triazene would allow for greater functional group tolerance.

4.2.2. Synthesis of the Terminal 1-Alkynyl Triazene

Initial attempts at synthesizing terminal 1-alkynyl triazene **4.3** from ethynylmagnesium bromide gave the desired product, however only in poor yield and purity (Scheme 4.5). Instead, 1,2-bis triazenyl ethyne **4.4** was obtained as the major product, albeit still in low yield. Presumably, **4.3** is deprotonated by excess ethynylmagnesium bromide and undergoes a second reaction with lithium diazotate to give **4.4**.

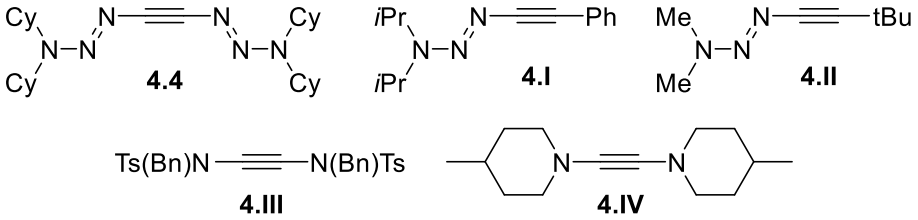


Scheme 4.5. Synthesis of terminal 1-alkynyl triazene **4.3** and 1,2-bis triazenyl ethyne **4.4.**

The structure of **4.4** was confirmed by single crystal X-ray crystallography.[120] Selected bond lengths are shown in Table 4.1. Compared to 1-alkynyl triazenes **4.I** and **II**,[41,120] the lengths

of the N3-N2 and the N2-N1 bonds don't differ relevantly. However, the N1-Cα bond is shortened and the Cα-Cβ triple bond is elongated in comparison to **4.I** and **4.II**. This comparison holds true also with respect to yndiamide **4.III**[120,121] and yndiamine **4.IV**.[120,122] Presumably, the presence of the two conjugated, strong electron donors,[123] leads to a decreased difference between N3-N2 and N1-Cα within the triazene group and to a weakening of the Cα-Cβ triple bond.

Table 4.1: Comparison of bond lengths for N-substituted alkynes.

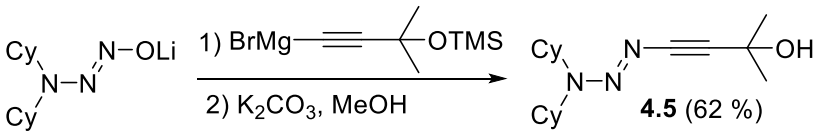


Compound	N3-N2 (Å)	N2-N1 (Å)	N1-Cα (Å)	Cα-Cβ (Å)
4.4	1.319(3)	1.297(3)	1.329(6)	1.228(10)
4.I	1.308(1)	1.294(1)	1.359(1)	1.202(1)
4.II	1.308(1)	1.289(1)	1.364(1)	1.203(1)
4.III	-	-	1.3483(9)	1.205(1)
4.IV	-	-	1.357(2)	1.206(2)

While not the primary objective of the study, **4.4** might be a promising compound for the introduction of a 1,2-bis triazenyl motif.[124] This motif is, to the best of our knowledge, so far undescribed in the literature. The acid induced cleavage of the 1,2-bis triazene could subsequently enable divergent 1,2-difunctionalization.

Given the limited success of the synthesis of **4.3** with the classical N_2O-method, we decided to follow a protecting group approach. In a first step, a protected terminal 1-alkynyl triazene would be synthesized and a second step would liberate the terminal alkyne.

Building on the discovery described in chapter 4.1, that 1-alkynyl triazenes bearing propargylic alcohols could be synthesized from the respective TMS-ethers, we chose the 2-hydroxy-prop-2-yl group to protect the acetylenic proton.



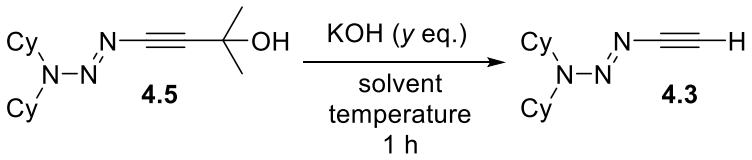
Scheme 4.6. Synthesis of protected terminal 1-alkynyl triazene **4.5**.

Apart from the similarity to successfully synthesized compounds, further desirable aspects were the removal of the protecting group with base, which is expected to be compatible with the triazene group and the commercial availability of the parent TMS-protected propargylic alcohol.

Protected terminal 1-alkynyl triazene **4.5** was straightforwardly synthesized analogously to compounds **4.2a** – **c** (Scheme 4.6). Only minor modifications were made to streamline the process and facilitate purification (see chapter 7.4.3 for details).

For the removal of the 2-hydroxy-prop-2-yl group, several literature methods were tested unsuccessfully.[125–128] Low conversion or complex mixtures of products were obtained. First successful results were achieved with KOH in DMSO at 100 °C. However, results were poorly reproducible, presumably due to inhomogeneity of the reaction mixture. Switching to higher alcohols, gave generally good yields (Table 4.2, entries 1 – 4). Despite initially not the best performing solvent at 75 % yield, optimization was continued with *t*BuOH. Lowering the temperature to 90 °C increased the yield to 80 % (entry 5). Using KO*t*Bu instead of KOH (entry 6) did not improve the reaction outcome, however lowering the temperature further to 80 °C gave a yield of 88 % (entry 7). Scale-up necessitated the increase of the amount of KOH to 1.5 eq., giving **4.3** in excellent yield on a 1.5 g scale (entry 8).

Table 4.2. Optimization of the deprotection of **4.5**.

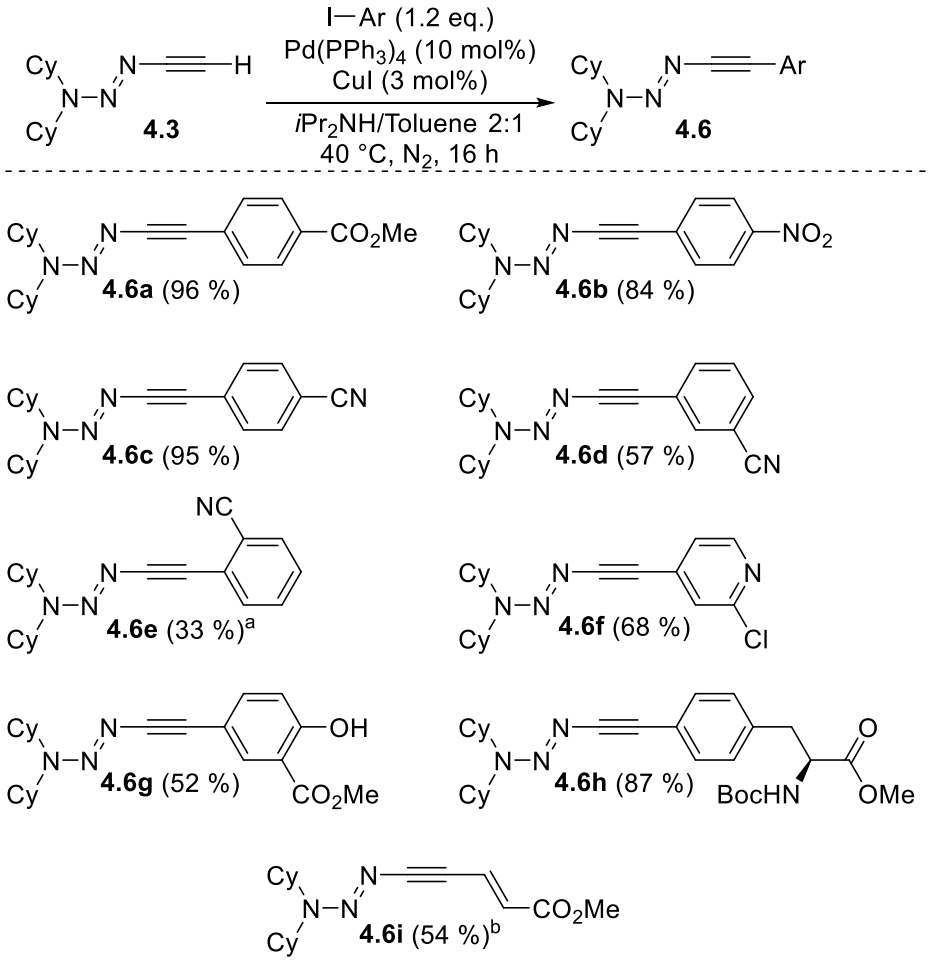


Entry	*y*	Solvent	Temperature [°C]	Yield [%][a]
1	1.1	*s*BuOH	100	77
2	1.1	*t*AmOH	100[b]	80
3	1.1	*t*BuOH	100[b]	75
4	1	*i*PrOH	90[b]	65
5	1.1	*t*BuOH	90[b]	80
6	1[c]	*t*BuOH	90[b]	70
7	1	*t*BuOH	80	88
8	1.5	*t*BuOH	80	93[d]

Conditions: **4.5** (5 – 21 mg, 17 – 71 µmol), KOH (y eq.) in the indicated solvent (0.07 – 0.1 M), at the indicated temperature for 1 h. a) NMR-yield with $MeNO_2$ as internal standard. b) in sealed vial. c) KO*t*Bu instead of KOH. d) **4.5** (2.0 g, 6.7 mmol), isolated yield, 1.5 g of **4.3**

Conveniently, purification of **4.3** can be achieved by a simple filtration over deactivated silica. The two-step synthesis can even be carried out without purifying the intermediate product **4.5**, albeit less efficiently (44 % vs 58 % overall yield).

While triazenes are generally more stable than diazonium salts,[15] we were initially cautious about the stability of **4.3**. Indeed, when trying to obtain the compound analogous to **4.3** with a diisopropylamine instead of dicyclohexylamine end-group, only traces of the desired product were obtained, presumably due to decomposition during the deprotection step. We also noticed, that prolonged storage of **4.3** in the condensed phase at ambient temperatures or at – 20 °C lead to decomposition to a dark solid, indicating polymerization. However, at – 40 °C, or dissolved in cyclohexane, samples of **4.3** were stable for several weeks without signs of decomposition. As a matter of precaution, **4.3** was stored as a 1 M solution in cyclohexane at – 20 °C.

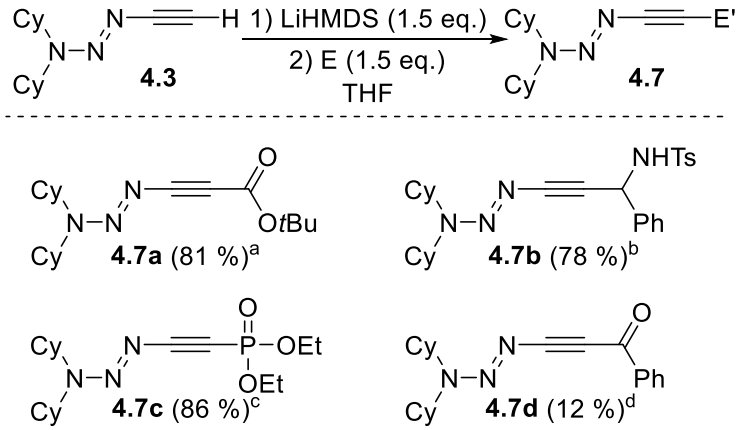


Scheme 4.7. Synthesis of 1-alkynyl triazenes via Sonogashira reaction. a) 31h, b) 1.5 eq. I-R, 10 mol% Cu, solvent: NEt_3.

4.2.1. Derivatization

To highlight the utility of **4.3** for the synthesis of new, functionalized 1-alkynyl triazenes, we explored its suitability for Sonogashira reactions (Scheme 4.7).

Another way to introduce new substituents to **4.3** is lithiation and subsequent reaction with an electrophile (Scheme 4.8). After lithiation with LiHMDS, addition of Boc_2O gave the respective alkynylated ester **4.7a** in very good yield. The strong polarization of the triple bond by the electron donating triazene group is further enhanced by the carbonyl, which should make **4.7a** an interesting reagent. N-Tosylbenzaldimine was also successfully used as electrophile and yielded propargylamine **4.7b**. Finally, alkynylphosphonate **4.7c** was analogously obtained. Alkynylphosphonates are important reagents, for example in the synthesis of bioactive substances.[129]



Scheme 4.8. Synthesis of 1-alkynyl triazenes via lithiation. a) – 78 °C to RT, b) – 40 °C, c) -78 °C to 0 °C, d) – 40 to 0 °C.

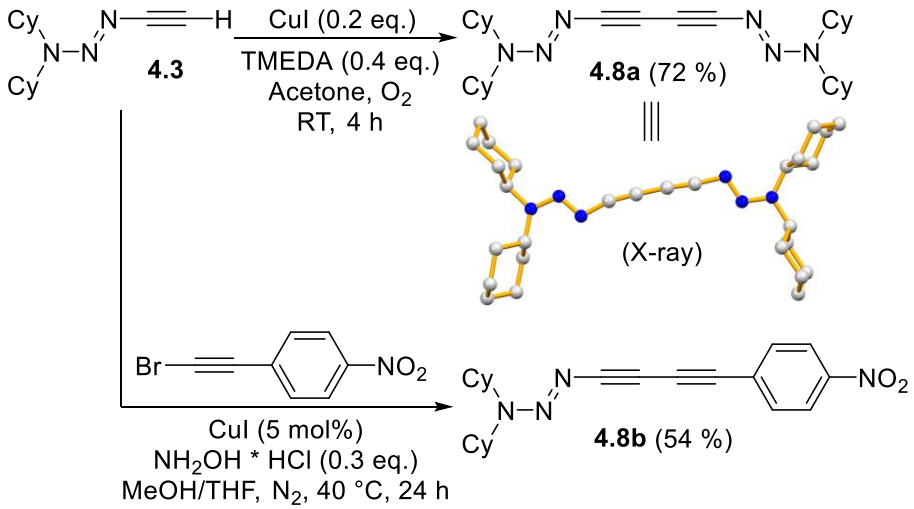
Remarkably, while **4.7a** could be synthesized straightforwardly, attempts to obtain the analogous product with a ketone instead of an ester functionality were met with very limited success. While benzoic acid chloride could be converted in low yield (**4.7d**), analogous attempts with pivalic acid chloride gave even lower yields and inseparable side products. Using a Cu-catalyzed method[130] was unsuccessful for either substrate. In comparison to **4.7a**, the C-C triple bond of **4.7d** and its *t*Bu analogue are even more polarized. The low yields and/or difficult purification could originate from side reactions occurring at this highly activated alkyne functionality.

1,3-Diynes are relevant building blocks in for example material science[131] and the synthesis of natural products.[132]. Based on a modified Hay reaction published by Saà et al. for terminal

ynamides,[133] we were able to carry out the homocoupling of **4.3** to obtain diynyl bistriazene **4.8a** (Scheme 4.9a).

The structure of **4.8** was confirmed by single crystal X-ray crystallography.[120] As with **4.4**, both N3–N2 and N2–N1 bond lengths (1.315(2) Å and 1.298(2) respectively) show no significant difference to previously synthesized 1-alkynyl triazenes. However, N1–Cα (1.347(2) Å) is slightly shorter and Cα–Cβ (1.209(2) Å) is slightly longer than in **4.I** and **4.II**, however the change of bond lengths is less pronounced than in **4.4**.

To obtain an unsymmetrical diyne, brominated 4-nitro ethynylbenzene was reacted under modified Cadiot-Chodkiewicz conditions published by Nemkovic et al. for ynamides,[134] to give diyne **4.8b** (Scheme 4.9).



Scheme 4.9. Synthesis of 1-diynyl triazenes.

Despite the successful synthesis of the derivatives of **4.3** described above, the introduction of several other functionalities was attempted without success (Scheme 4.10).

Attempts to introduce synthetically valuable halogens (**4.9a**, **b**) via lithiation and reaction with NBS[135] or I_2[136] or via Ag-catalyzed reaction with NBS[137] gave complex mixtures of products, the respective desired product was not detected.

Introduction of a trifluoromethyl substituent would be interesting given the importance of CF_3-groups in biologically active compounds and to increase the polarization of the C–C triple bond of the 1-alkynly triazene.[138] Synthesis of **4.9c** was attempted by several methods involving stoichiometric or catalytic "$CuCF_3$"-type reagents, none of which were successful. Reaction products were found to contain exclusively **4.3**[139] or a complex mixture of products with potential traces of **4.9c**, at best.[140,141] A method involving stoichiometric use of a

(phen)Cu(CF_3)$_3$ reagent gave encouraging results on a small scale, however, these results could not be reproduced on a synthetically useful scale.[141] Possibly, **4.8a** was formed as a side product in many of those reactions. Alternatively, lithiation of **4.3** and reaction with Umemoto's Reagent did also not lead to detection of the desired product.[143,144]

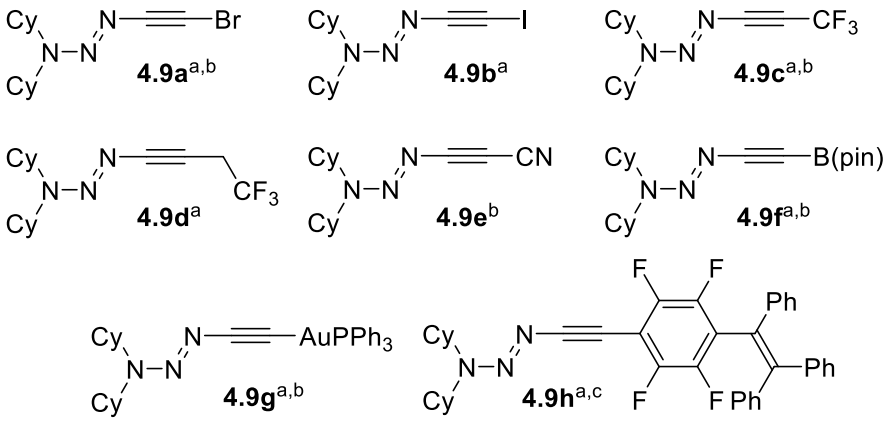
Substitution with CH_2CF_3 was also not successful by the lithiation and reaction with 2-iodo-1,1,1-trifluoroethane.[145] The presence of a β-CH_2-group might have led to the formation of a 1-allenyl triazene from the desired product **4.9d** in the presence of *n*BuLi (cf. chapter 1.1.3).

Attempted synthesis of nitrile substituted 1-alkynyl triazene **4.9e** lead to inseparable mixtures of products[146] or the desired product was not detected at all.[147]

Alkynyl boranes are of immense interest in organic chemistry due to the rich potential for further derivatization.[148] Neither lithiation of **4.3** and reaction with *i*PrOB(pin)[149] nor Ir-catalyzed dehydrogenative coupling with HB(pin)[150] gave **4.9f**.

Formation of alkynyl-Au^I-complex **4.9g** was attempted by reaction of lithiated **4.3** with $ClAuPPh_3$,[151] however the desired product was not detected.

Pentafluorophenyl triphenylethene was used in our group for the synthesis of tetraphenylethene-based AIE-luminogens[50] by SN-type reactions.[152] Neither lithiated **4.3** nor use of an in-situ generated amide-base[153] lead to **4.9h**, in both cases, **4.3** was recovered.



Scheme 4.10. Compounds, whose synthesis was unsuccessfully attempted. a) Lithiation + electrophile, b) Dehydr(ogen)ative coupling via metal catalysis, c) Catalytic amide base + electrophile.

4.3. Conclusion

New 1-alkynyl triazenes were synthesized by the classical N_2O-method, however this method lacks functional group tolerance. Based on the discovery that trimethylsilyl ethers are

compatible with the method, we were able to synthesize terminal 1-alkynyl triazene **4.3** via a protecting group strategy. **4.3** can be used to synthesize 1-alkynyl triazenes inaccessible by the classical method by Sonogashira reactions, lithiation and reaction with an electrophile or Cu-catalyzed alkyne-alkyne coupling. However, some limitations were encountered during the functionalization of **4.3**. The newly synthesized 1-alkynyl triazenes greatly expand the synthetic value of the compound class. The use of **4.3** as well as of the new, functionalized 1-alkynyl triazenes in the synthesis of new 1-aryl and 1-vinyl triazenes is currently under investigation.

5. Biological Activity of some 1-Vinyl and 1-Alkynyl Triazenes

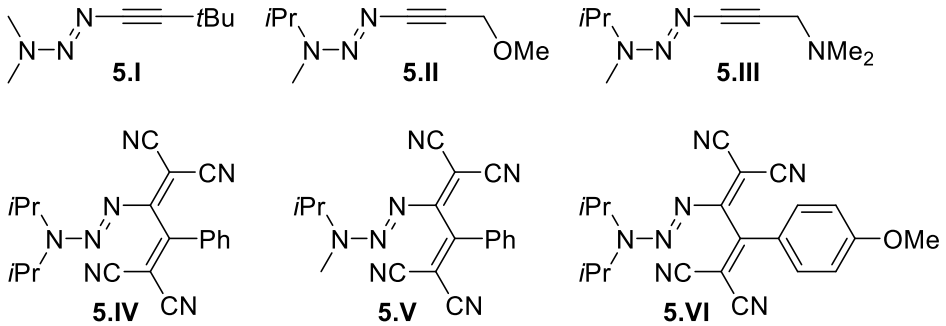
The work presented in this chapter was carried out in collaboration with Antoine Gibelin and Dr. Marc Chambon (Biomolecular Screening Core Facility, EPFL).

5.1. Introduction

1-Aryl triazenes have thoroughly been investigated for their biological activity. Apart from cancer medication dacarbazine and temozolomide (see chapter 1.1.1), several other 1-aryl triazenes continue to be topics of interest in medicinal chemistry.[3]

In contrast, the bioactivity of 1-vinyl and 1-alkynyl triazenes has hardly been explored. Following the discovery of the synthesis of triazenes via the N_2O-method, some newly synthesized 1-alkynyl and 1-vinyl triazenes were subjected to in vitro cytotoxicity tests with several human cancer (breast adenocarcinoma, MDA-MB-231; human ovarian carcinoma (A2780) and non-cancer (human embryonic kidney, HEK293; human mammary epithelium, MCF-10A) cell lines in a MTT assay.[41]

Furthermore the cytotoxicity of several tetracyanobutadienyl triazenes (cf. scheme 1.15 in chapter 1.1.1) was analyzed with the same cell lines as above and additionally human cervix adenocarcinoma (Hela) and human breast adenocarcinoma ((metastases from pleural effusion) MCF7) in a PrestoBlue assay.[154] The most active compounds of both assays are shown in Scheme 5.1.



Scheme 5.1. 1-Alkynyl and 1-vinyl triazenes subjected to cytotoxicity assays.

The activities (IC_{50}, concentration at which 50 % of the cells are killed) of the most active compounds are shown in Table 5.1. Since the assays were carried out with different techniques, the results are not directly comparable. Qualitatively, all tested compounds were found to be cytotoxic for A2780, MDA-MB-231 and HEK(T) cells. Overall the presence of at least one methyl substituent on N3 was found to be beneficial, but neither strictly necessary nor sufficient

for cytotoxicity. Furthermore, compounds lacking polar functional groups were found to be less likely to be cytotoxic, possibly due to solubility issues.

Table 5.1. IC_{50} (µM) of a selection of 1-alkynyl and 1-vinyl triazenes against several cell lines.

Compound	A2780	MDA-MB-231	Hela	MCF7	HEK293/ HEK293T	MCF-10A
5.I[a]	22	38	-	-	19	52
5.II[a]	20	32	-	-	14	208
5.III[a]	34	14	-	-	21	86
5.IV[b]	5.2	10.3	7.7	-[c]	7.3	-[c]
5.V[b]	2.6	11.7	9.6	-[c]	3.9	-[c]
5.VI[b]	9.3	9.7	11.6	-[c]	12.9	-[c]

a) MTT-assay, HEK293-cells. b) PrestoBlue assay, HEK293T-cells. c) Not determined due to inactivity in initial screening.

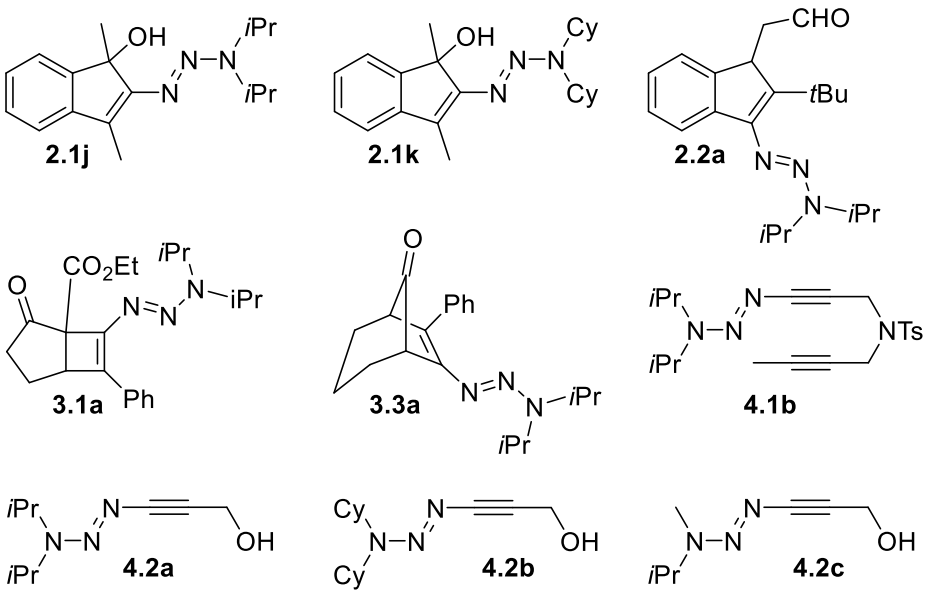
5.2. Results of Bioactivity Screening

To extend the study of cytotoxicity, several 1-alkynyl and 1-vinyl triazenes described in this thesis were submitted to an in vitro assay. A focus was put on the presence of (polar) functional groups in the submitted compounds.

Cell lines and assay method were chosen to match those used for compounds **5.IV** – **VI**. A PrestoBlue assay was carried out with four cancer (A2780, MDA-MB-231, MCF7, Hela) and two non-cancer (HEK293T, MCF-10A) cell lines. The cytotoxicity was assessed by measuring the fluorescence of resorufin, which is generated from resazurin (PrestoBlue) by living cells. Thus, the fluorescence measured is directly proportional to the number of living/surviving cells (see chapter 7.5 for experimental details).

The compounds submitted to the assay are shown in Scheme 5.2.

In a first phase, cells were exposed to a 10 µM solution of the compounds. Only **2.1j** and **4.2a** showed a measurable cytotoxicity for at least one of the cell lines, albeit both on a low level. Notably, replacing the OMe-group of **5.II** with an OH in **4.2c** lead to a complete loss in activity. Subsequently, dose response curves were recorded for **2.1j** and **4.2a** against all six cell lines.



Scheme 5.2. Structures submitted to in vitro assay of cytotoxicity against human cancer and non-cancer cell lines.

Compound **2.1j** showed an IC_{50} of 43 µM against non-cancer mammary epithelial cells (MCF-10A), while the corresponding IC_{50} against mammary cancer cells (MDA-MB-231) was beyond the limit of detection of the experiment (> 100 µM). This unwanted selectivity is in contrast to previously tested 1-alkynyl or 1-vinyl triazenes (see above), which were more active towards the cancer cell line in comparison to the non-cancer cell line. Against ovarian carcinoma cells (A2780), an IC_{50} > 100 µM was measured, despite this being the cell line, for which a low cytotoxicity was recorded in the first screening phase.

For compound **4.2a**, the IC_{50} against all cell lines was beyond the limits of detection of the experiment.

Table 5.2. IC_{50} (µM) of **2.1j** and **4.2a** against several cell lines.

	A2780	MDA-MB-231	MCF7	Hela	HEK	MCF-10A
2.1j	> 100	> 100	> 100	> 100	> 100	43
4.2a	> 100	> 100	> 100	> 100	> 100	> 100

Overall, none of the compounds subjected to the cytotoxicity screening showed activities, which are encouraging further investigation. Potentially, **2.1j** might be investigated for its toxicity, however as triazenes are generally prodrugs and require metabolism or hydrolysis to be converted into the active form, the result of the above in-vitro tests may not be representative of the behavior of the molecule in an organism. It is also possible, that the observed activity is governed by factors other than the reactivity of the triazene group.

5.3. Conclusion

The cytotoxicity of some new, functional group bearing 1-alkynyl and 1-vinyl triazenes was investigated. None of the compounds were cytotoxic against cancerous cell lines, however **2.1j** showed some cytotoxicity against one of the non-cancer cell lines.

6. Summary and Outlook

The synthesis and reactivity of 1-aryl triazenes is well established. The chemistry of 1-vinyl triazenes, and even more so 1-alkynyl triazenes, is still in need for investigation. This is partially due to the need for organometallic reagents in their synthesis, limiting the versatility. In this thesis, we present new methods for the synthesis of 1-vinyl and 1-alkynly triazenes.

In chapter 2, we describe a Rh-catalyzed annulation reaction between 1-alkynyl triazenes and ortho-functionalized phenylboronic acids giving 1-indenyl triazenes in generally good yields. Carbonyls and Michael-acceptors were suited substituents in the 2-position of the phenylboronic acid, leading to vinyl triazenes bearing alcohol, aldehyde, ketone or ester functionalities. Regioselectivity of the reaction was primarily determined by the β-substituent on the 1-alkynyl triazene. Under acidic conditions, cleavage of the triazene group was observed. The resulting vinyl cations underwent rearrangement reactions, before being trapped by a nucleophile or undergoing intramolecular elimination reactions.

In chapter 3, Ficini-type 2+2 cycloadditions between electron poor alkenes and 1-alkynyl triazenes are described. Cyclobutenyl triazenes are formed regioselectively from α-unsaturated β-ketoesters and enones in good yields. Brønsted acid-induced cleavage of these 1-vinyl triazenes did not give the nucleophilic substitution reactions observed for other cyclobutenyl triazenes. Rearrangements and intramolecular reactions were observed instead. Under Lewis acid catalysis however, rearrangement to bicyclooctenyl triazenes was observed, which could be transformed to the corresponding vinyl iodides. Furthermore, these new 1-vinyl triazenes were used as substrate in the BF_3-induced Suzuki-type cross coupling with phenylboronic acids, a reaction so far only described for 1-alkynyl triazenes.

In chapter 4, we describe several newly synthesized 1-alkynyl triazenes. Notably, it was found, that γ-hydroxy 1-alkynl triazenes could be synthesized from TMS-protected propargylic alcohols. This discovery lead to the development of a two-step reaction sequence to synthesize a terminal 1-alkynyl triazene, which is not accessible in useful yields via the classical N_2O-method. This new, promising compound was used in the synthesis of several 1-alkynyl triazenes bearing β-substituents, which are incompatible with the need for Grignard reagents in the classical N_2O-method, by Sonogashira reaction, lithiation and reaction with an electrophile and alkyne-alkyne coupling, greatly expanding the synthetic versatility of the compound class.

In chapter 5, we briefly report on the results of an in vitro cytotoxicity screening of several 1-alkynyl and 1-vinyl triazenes. One of the compounds showed low activity against healthy mammarian epithelial cells, all other experiments gave an activity below the limits of detection of the experiment.

For future research, the results presented in chapter 4 appear to be the most enticing.

Propargylic alcohols are a versatile compound class and have been used as carbocation or allene precursors as well as for addition reactions to the triple bond or as nucleophilic OH-reagents. It is worth investigating, whether γ-hydroxy 1-alkynl triazenes are suited substrates for those reactions. Several new methods to synthesize new 1-aryl or 1-vinyl triazenes can be envisioned.

Analogous considerations hold true for the terminal 1-alkynyl triazene and its derivatives. On the one hand, those newly synthesized 1-alkynyl triazenes could show interesting reaction properties depending on the substituents, in particular acceptor substituted 1-alkynyl triazenes or diynyl triazenes. On the other hand, synthesis of unnatural amino acids from the phenylalanine derived 1-alkynyl triazene could be of interest in chemical biology or medicinal chemistry. Finally, using the terminal 1-alkynyl triazene itself in (cyclo)addition or annulation reactions is worth exploring, both in reactions, which are known to work for internal 1-alkynyl triazenes, as well for new reactions, which are specific to terminal alkynes.

Furthermore, the synthesis of the serendipitously obtained 1,2-bis triazenyl ethyne could be optimized. The synthesis of 1,2-bis triazenyl compounds, which are undescribed to date, and their subsequent derivatization might lead to new 1,2-difunctionalization methods.

As a second priority, the issues encountered with rearrangements and intramolecular reactions of vinyl cations during acid induced cleavage of 1-vinyl triazenes could be worth addressing. A possible mitigation could be the elaboration of cleavages involving vinyl radicals as intermediates instead of cations.

7. Experimental

7.1. General Remarks

Copies of NMR spectra and X-ray data with CCDC numbers of published compounds can be found in Supporting Information files on web pages of the corresponding publications.

1-Alkynyltriazenes[41] were synthesized as described in the literature (see 7.4.4 for Details).

Air sensitive reactions were carried out under an atmosphere of dry nitrogen using standard Schlenk and glovebox techniques in oven-dried glassware. For the synthesis of 1-alkynyl triazenes, nitrous oxide (purity: 99.999 %, Messer Schweiz AG) was used. Other reactions were carried out under ambient atmosphere unless indicated otherwise. Reagents and solvents were purchased commercial suppliers and were used as obtained except where noted otherwise.

Dry solvents were obtained using a solvent purification system with an aluminum oxide column (Innovative Technologies).

Microwave assisted synthesis was carried out in a Biotage Initiator+.

Flash column chromatography was performed with Silicycle silica gel 60 (0.040–0.063 μm grade). For the purification of acid-sensitive compounds, silica gel 230– 400 mesh particle size (100 g) was deactivated prior to use by adding DCM containing 5 – 10 vol% triethylamine (300 mL), removal of the solvent under reduced pressure, and drying of the silica at RT under oil pump vacuum for at least 16 h. Residual NEt_3 in chromatography fractions was removed either by repeated co-evaporation with pentane or by addition of pentane and freeze-drying.

For vinyl triazenes and non-acid sensitive compounds, analytical thin-layer chromatography was performed with commercial aluminium plates coated with 0.25 mm silica gel (E. Merck, Kieselgel 60 F254). Compounds were either visualized under UV-light at 254 nm or by dipping the plates in an aqueous potassium permanganate solution followed by heating. For 1-alkynyl triazenes, the plates were deactivated by developing in 10 % NEt_3 in DCM and subsequent drying under air. Compounds were visualized under UV-light at 254 nm.

^{1}H-NMR spectra were recorded on a Bruker Avance 400 spectrometer with a BBFOz ATMA probe, Bruker DRX600 (600 MHz) and Bruker AvanceII (800 MHz) spectrometer. Chemical shifts (δ) are reported in parts per million (ppm) relative to residual chloroform (s, 7.26 ppm), and acetonitrile (quint, 1.94 ppm). Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; sept, septet; m, multiplet, br, broad or combinations of those. Proton decoupled Carbon-13 nuclear magnetic resonance (^{13}C NMR) data were acquired at 100 MHz

on a Bruker AV400 spectrometer. Chemical shifts are reported in ppm relative to $CDCl_3$ (77.16 ppm), and CD_3CN (1.32 ppm). Fluorine-19 nuclear magnetic resonance (^{19}F NMR) data were acquired at 376 MHz on a Bruker AV400 spectrometer and were not referenced. Phosphorous-31 nuclear magnetic resonance (^{31}P NMR) data were acquired at 162 MHz on a Bruker AV400 spectrometer and were not referenced.

High resolution mass are given in *m*/*z*. Electrospray-ionization (ESI) HRMS data were acquired on a Xevo G2-S QTOF (Waters) or an Agilent LC-MS TOF operated in the positive ionization mode. Data from the Lock-Spray were used to calculate a correction factor for the mass scale and provide accurate mass information of the analyte. Data were processed using the MassLynx 4.1 software. Atmospheric pressure photo-ionization (APPI) HRMS measurements were done on a LTQ– Orbitrap Elite instrument (Thermofisher) operated in the positive ionization mode. Data were processed using the XCalibur v2.2 software. Atmospheric-pressure chemical ionization (APCI) HRMS data were acquired on a Xevo G2-S QTOF (Waters) operated in the positive ionization mode. Data were processed using MassLynx 4.1 software.

IR spectra were recorded on a Perkin-Elmer FT-IR spectrometer. Absorbance frequencies are reported in reciprocal centimeters (cm^{-1}).

The X-ray analyses were performed by Dr. R. Scopelliti and Dr. F. Fadaei-Tirani at the EPF Lausanne.

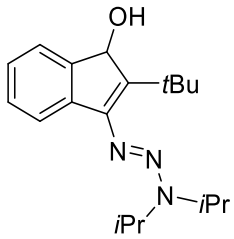
7.2. Experimental Details for Chapter 2

7.2.1. Synthesis of Starting Materials

Non-commercial boronic esters were synthesized according to literature procedures by Mancuso and Lautens.[155] All spectra were in good agreement with the reported data. The synthesis of 1-((3,3-dimethylbut-1-yn-1-yl)diazenyl)pyrrolidine is described in subchapter 7.4.1.

7.2.2. Synthesis of Indenyl Triazenes 2.1a–k

3-(*tert*-Butyl)-2-(3,3-diisopropyltriaz-1-en-1-yl)-1*H*-inden-1-ol (**2.1a**)



$[Rh(cod)Cl]_2$ (6 mg, 12 µmol, 0.03 eq., 6 mol% [Rh]), KOH (12 mg, 0.21 mmol, 0.55 eq.) and 1-(3,3-dimethylbut-1-yn-1-yl)-3,3-diisopropyltriaz-1-ene (80 mg, 0.38 mmol, 1.0 eq.) were dissolved in 1,4-dioxane/water (4:1, 4 mL) and stirred for 5 min at RT. 2-Formylphenylboronic acid (72 mg, 0.48 mmol, 1.2 eq.) was added and a slight color change could immediately be observed. The reaction flask was sealed and heated at 100 °C in the microwave for 30 min. The reaction mixture was diluted with water (4 mL) and the product was extracted with EtOAc (3 x 5 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under vacuum. Purification by flash column chromatography on deactivated silica (NEt_3) with a gradient of Et_2O in pentane (0 – 100 %) gave the product as a mixture of isomers in the form of a dark-red oil (107 mg, 0.34 mmol, 90 %, 8:1 rr).

^{1}H NMR (400 MHz, $CDCl_3$, 275 K) δ 8.03 – 7.85 (m, 1H, $C_{Ar}H$), 7.55 – 7.40 (m, 1H, $C_{Ar}H$), 7.32 – 7.13 (m, 2H, $C_{Ar}H$), 5.39 – 5.24 (m, 1H, $C_{i\mathrm{Pr}}H$), 5.23–5.13 (m, 1H, C*H*OH), 4.15 – 3.94 (m, 1H, $C_{i\mathrm{Pr}}H$), 1.74–1.62 (m, 1H, CHO*H*),[1] 1.52 – 1.47 (m, 9H, $C_{t\mathrm{Bu}}H_3$), 1.46 – 1.20 (m, 12H, $C_{i\mathrm{Pr}}H_3$).

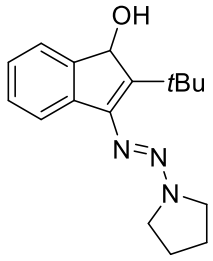
^{13}C NMR (101 MHz, $CDCl_3$) δ 145.0 (br, $C_{Ar,q}$ + C_{sp2}-N_3*i*Pr_2), 143.8 (C_{sp2}-*t*Bu), 140.0 ($C_{Ar,q}$), 128.0 ($C_{Ar}H$), 125.6 ($C_{Ar}H$), 123.4 ($C_{Ar}H$), 123.0 ($C_{Ar}H$), 76.4 (COH), 48.1 ($C_{i\mathrm{Pr}}H$), 45.3 ($C_{i\mathrm{Pr}}H$), 33.9 ($C_{t\mathrm{Bu,q}}$), 30.8 ($C_{t\mathrm{Bu}}H_3$), 24.2 ($C_{i\mathrm{Pr}}H_3$), 24.0 ($C_{i\mathrm{Pr}}H_3$), 19.6 ($C_{i\mathrm{Pr}}H_3$), 19.5 ($C_{i\mathrm{Pr}}H_3$).

IR (ν_{max}, cm^{-1}) 3284 (w), 2976 (w), 2914 (w), 2858 (w), 1699 (w), 1604 (w), 1464 (m), 1408 (m), 1402 (s), 1346 (m), 1313 (m), 1234 (s), 1206 (m), 1150 (s), 1094 (m), 999 (m), 926 (w), 893 (m), 770 (w), 742 (s).

[1] The shift of the OH-proton at 1.68 ppm is consistent with literature reports for indenols.[155]

HRMS (ESI–TOF): Calculated (MH+) 316.2389; Found 316.2390.

2-(*tert*-Butyl)-3-(pyrrolidin-1-yldiazenyl)-1*H*-inden-1-ol (**2.1b**)



$[Rh(cod)Cl]_2$ (6 mg, 12 μmol, 0.03 eq.), KOH (12 mg, 0.21 mmol, 0.5 eq.) and 1-((3,3-dimethylbut-1-yn-1-yl)diazenyl)pyrrolidine (74 mg, 0.41 mmol, 1 eq.) were dissolved in 1,4-dioxane/water (4:1, 3.75 mL) and stirred for 5 min at RT. 2-Formylphenylboronic acid (74 mg, 0.50 mmol, 1.2 eq.) was added, the reaction vessel was sealed and heated at 100 °C in the microwave for 30 min. The reaction mixture was diluted with H_2O (4 mL) and extracted with EtOAc (3 x 5 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under vacuum. Purification by flash column chromatography on deactivated silica (NEt_3) with a gradient of 5 – 20 % Et_2O in pentane gave the product in the form of a red solid (39 mg, 0.14 mmol, 34 %).

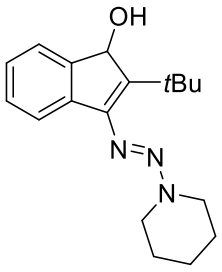
^{1}H NMR (400 MHz, $CDCl_3$, 298 K) δ 7.85 (dd, *J* = 7.1, 1.2 Hz, 1H, $C_{Ar}H$), 7.46 – 7.43 (m, 1H, $C_{Ar}H$), 7.21 (td, *J* = 7.5, 1.4 Hz, 1H, $C_{Ar}H$), 7.16 (td, *J* = 7.3, 1.3 Hz, 1H, $C_{Ar}H$), 5.19 (d, *J* = 10.1 Hz, 1H, C*H*OH), 3.81 (br, 4 H, NCH_2), 2.05 (td, *J* = 7.0, 5.6, 3.4 Hz, 4H, $(CH_2)_2$), 1.47 (s, 9H, $C_{tBu}H_3$), 1.37 (d, *J* = 10.2 Hz, 1H, CHO*H*).

^{13}C NMR (101 MHz, $CDCl_3$, 298 K) δ 144.95 (C_q), 144.80 (C_q), 144.63 (C_q), 140.01 (C_q), 127.95 ($C_{Ar}H$), 125.62 ($C_{Ar}H$), 123.22 ($C_{Ar}H$), 122.80 ($C_{Ar}H$), 76.48 (CHOH), 33.95 ($C_{tBu,q}$), 30.53 ($C_{tBu}H_3$).

IR (ν_{max}, cm^{-1}) 3385 (w), 2951 (m), 2871 (m), 1679 (w), 1604 (w), 1457 (w), 1411 (s), 1308 (s), 1126 (m), 1026 (w), 912 (w), 744 (m), 731 (m).

HRMS (ESI/QTOF): Calculated (MH+) 286.1914; Found 286.1911.

2-(*tert*-Butyl)-3-(piperidin-1-yldiazenyl)-1*H*-inden-1-ol (**2.1c**)



$[Rh(cod)Cl]_2$ (6 mg, 12 μmol, 0.03 eq.), KOH (11 mg, 0.2 mmol, 0.5 eq.) and 1-((3,3-dimethylbut-1-yn-1-yl)diazenyl)piperidine (77 mg, 0.40 mmol, 1 eq.) were dissolved in 1,4-dioxane/water (4:1, 3.75 mL) and stirred for 5 min at RT. 2-Formylphenylboronic acid (73 mg, 0.49 mmol, 1.2 eq.) was added, the reaction vessel was sealed and heated at 100 °C in the microwave for 15 min. The reaction mixture was diluted with H_2O (4 mL) and the product was extracted with EtOAc (3 x 5 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under vacuum. Purification by flash column chromatography on deactivated silica (NEt_3) with a gradient of 5 – 15 % Et_2O in pentane gave the product in the form of a yellow-orange solid (80 mg, 0.27 mmol, 67 %).

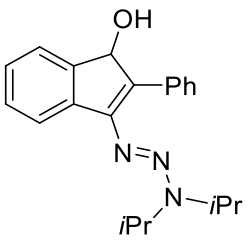
^{1}H NMR (400 MHz, $CDCl_3$, 298 K) δ 7.91 – 7.77 (m, 1H, $C_{Ar}H$), 7.49 – 7.40 (m, 1H, $C_{Ar}H$), 7.21 (td, *J* = 7.5, 1.6 Hz, 1H, $C_{Ar}H$), 7.17 (td, *J* = 7.3, 1.5 Hz, 1H, $C_{Ar}H$), 5.20 (d, *J* = 9.5 Hz, 1H, C*H*OH), 3.78 (m, 4H, NCH_2), 1.80 – 1.64 (m, 6H, $(CH_2)_3$), 1.46 (s, 9H, $C_{t\text{Bu}}H_3$), 1.39 (d, *J* = 10.2 Hz, 1H, CHO*H*).

^{13}C NMR (101 MHz, $CDCl_3$, 298 K) δ 145.98 (C_{sp2}-N), 144.99 (C_{sp2}-*t*Bu), 144.45 ($C_{Ar,q}$), 139.99 ($C_{Ar,q}$), 128.12 ($C_{Ar}H$), 125.87 ($C_{Ar}H$), 123.34 ($C_{Ar}H$), 123.02 ($C_{Ar}H$), 76.61 (CHOH), 34.17 ($C_{t\text{Bu,q}}$), 30.95 ($C_{t\text{Bu}}H_3$), 25.45 (CH_2), 24.59 (CH_2).

IR (ν_{max}, cm^{-1}) 3368 (w), 2941 (s), 2857 (m), 1428 (s), 1353 (s), 1320 (m), 1182 (s), 1105 (s), 1013 (m), 906 (m), 742 (s).

HRMS (ESI/QTOF): Calculated (MH+) 300.2070; Found 300.2065.

2-(3,3-Diisopropyltriaz-1-en-1-yl)-3-phenyl-1*H*-inden-1-ol (**2.1d**)



[Rh(cod)Cl]$_2$ (6 mg, 12 µmol, 0.03 eq., 6 mol% [Rh]), KOH (12 mg, 0.21 mmol, 0.5 eq.) and 3,3-diisopropyl-1-(phenylethynyl)triaz-1-ene (99 mg, 0.44 mmol, 1.0 eq.) were dissolved in 1,4-dioxane/water (4:1, 4 mL) and stirred for 5 min at RT. 2-Formylphenylboronic acid (78 mg, 0.52 mmol, 1.2 eq.) was added and a slight color change could immediately be observed. The reaction flask was sealed and heated at 100 °C in the microwave for 15 min. The reaction mixture was diluted with water (3 mL) and extracted with EtOAc (3 x 6 mL). The combined organic phases were dried over $MgSO_4$ and the solvent was removed under vacuum. Purification by column chromatography on deactivated silica (NEt_3) with 20 % Et_2O in pentane gave the product in the form of a dark-red solid (61 mg, 0.18 mmol, 48 %).

Alternative procedure:

[Rh(cod)Cl]$_2$ (6 mg, 12 µmol, 0.03 eq., 6 mol% [Rh]), Na_2CO_3 (50 mg, 0.47 mmol, 0.55 eq.) and 3,3-diisopropyl-1-(phenylethynyl)triaz-1-ene (100 mg, 0.43 mmol, 1.0 eq.) were dissolved in 1,4-dioxane/water (0.44 mL, 4:1) and stirred for 5 min at RT. 2-Formylphenylboronic acid (72 mg, 0.48 mmol, 1.2 eq.) was added and a slight color change could immediately be observed. The reaction flask was sealed and heated at 50 °C for 2 days. The reaction mixture was diluted with water (4 mL) and extracted with EtOAc (3 x 5 mL). The combined organic phases were dried over $MgSO_4$ and the solvent was removed under vacuum. Purification by column chromatography on deactivated silica (NEt_3) with a gradient of 10 – 50 % DCM in pentane gave the product in the form of a dark-red solid (83 mg, 0.34 mmol, 58 %).

^{1}H NMR (400 MHz, $CDCl_3$, 275 K) δ 8.10–7.93 (m, 3H, $C_{Ar}H$), 7.57 (d, *J* = 6.9 Hz, 1H, $C_{Ar}H$), 7.36 (d, *J* = 6.9 Hz, 2H, $C_{Ar}H$), 7.32–7.06 (m, 3H, $C_{Ar}H$), 5.62 (d, *J* = 9.0 Hz, 1H, C*H*OH),

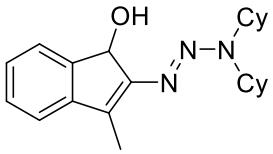
5.44–5.20 (m, 1H, C$_{i\text{Pr}}$H),)4.13–3.95 (m, 1H, C$_{i\text{Pr}}$H), 1.68 (d, *J* = 9.0 Hz, 1H, CHO*H*), 1.46–1.35 (m, 6H, C$_{i\text{Pr}}$H$_3$), 1.36–1.17 (m, 6H, C$_{i\text{Pr}}$H$_3$).

^{13}C NMR (101 MHz, $CDCl_3$, 298 K) δ 146.4 (C_{sp2}), 145.1 (C_{ar}), 139.5 (C_{ar}), 135.1 (C_{ar}), 129.6 (C_{ar}), 128.4 (C_{sp2}), 128.2 (C_{ar}), 126.6 (C_{ar}), 126.5 (C_{ar}), 124.2 (C_{ar}), 123.6 (C_{ar}), 75.1 (CHOH), 49.1 (C$_{i\text{Pr}}$H), 46.2 (C$_{i\text{Pr}}$H), 24.2 (C$_{i\text{Pr}}$H$_3$), 23.9 (C$_{i\text{Pr}}$H$_3$), 19.6 (C$_{i\text{Pr}}$H$_3$), 19.4 (C$_{i\text{Pr}}$H$_3$).

IR (ν_{max}, cm^{-1}) 3050 (w), 2975 (m), 2931 (w), 2875 (w), 1719 (m), 1600 (m), 1463 (m), 1396 (s), 1381 (s), 1341 (m), 1255 (s), 1148 (m), 1098 (m), 1068 (m), 1006 (m), 856 (w), 754 (m).

HRMS (ESI–TOF): Calculated (MH+) 336.2073; Found 336.2076.

2-(3,3-Dicyclohexyltriaz-1-en-1-yl)-3-methyl-1*H*-inden-1-ol (**2.1e**)



[Rh(cod)Cl]$_2$ (3.4 mg, 8.1 µmol, 0.04 eq., 8 mol% [Rh]), KOH (3.4 mg, 60 µmol, 0.3 eq.) and 3,3-dicyclohexyl-1-(prop-1-yn-1-yl)triaz-1-ene (49.8 mg, 201 µmol, 1 eq.) were dissolved in 1,4-dioxane/water (4:1, 2 mL) and stirred for 5 min at RT. 2-Formylphenylboronic acid (36.3 mg, 242 µmol, 1.2 eq.) was added, the reaction vessel was sealed and heated at 100 °C in the microwave for 15 min. The reaction mixture was extracted with DCM (3 x 5 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under vacuum. Purification by flash chromatography on deactivated silica (NEt_3) with a gradient of 4 – 8 % DCM in pentane gave the product in the form of a yellow solid (45.8 mg, 0.130 mmol, 64 %).

^{1}H NMR (400 MHz, $CDCl_3$, 298 K) δ 7.44 (d, *J* = 7.2 Hz, 1H, C$_{Ar}$H), 7.31–7.25 (m, 1H, C$_{Ar}$H), 7.17 (d, *J* = 7.4 Hz, 1H, C$_{Ar}$H), 7.16 (td, *J* = 7.3, 1.1 Hz, 1H, C$_{Ar}$H), 5.46 (s, 1H, C*H*OH), 4.96 (s, 1H, CH$_{Cy}$), 3.49 (s, 1H, CH$_{Cy}$), 3.33 (d, *J* = 1.9 Hz, 1H, OH), 2.19 (d, *J* = 1.4 Hz, 3H, CH_3), 1.95–1.12 (m, 20H, C$_{Cy}$H$_2$).

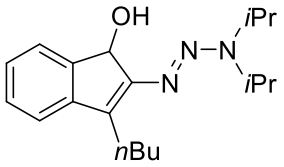
^{13}C NMR (101 MHz, $CDCl_3$, 298 K) δ 152.2 (C_{sp2}-N_3Cy_2), 145.1 ($C_{Ar,q}$), 141.5 ($C_{Ar,q}$), 128.5 (C$_{Ar}$H), 127.5 (C_{sp2}-Me), 125.5 (C$_{Ar}$H), 123.2 (C$_{Ar}$H), 118.6 (C$_{Ar}$H), 73.8 (CHOH), 34.8 (br, CH$_{2\ Cy}$), 30.0 (br, C$_{Cy}$H$_2$), 26.1 (br, C$_{Cy}$H$_2$), 9.4 (CH_3).[2]

IR (ν_{max}, cm^{-1}) 3357 (w), 2928 (m), 2850 (m), 2850 (m), 1602 (w), 1454 (w), 1394 (s), 1334 (m), 1320 (m), 1255 (s), 1213 (m), 1180 (m), 1142 (m), 1090 (m), 1012 (s), 798 (m), 758 (s), 728 (s).

HRMS (ESI/QTOF): Calculated (MH+) 354.2540; Found 354.2540.

[2] The NCH signals were not detected due to broadening. Based on HSQC spectroscopy, they are estimated to appear at ca 54 and 58 ppm, respectively.

2-Butyl-3-(3,3-diisopropyltriaz-1-en-1-yl)-1*H*-inden-1-ol (**2.1f**)



[Rh(cod)Cl]$_2$ (6 mg, 12 µmol, 0.03 eq., 6 mol% [Rh]), KOH (12 mg, 0.21 mmol, 0.5 eq.) and 1-(hex-1-yn-1-yl)-3,3-diisopropyltriaz-1-ene (85 mg, 0.41 mmol, 1 eq.) were dissolved in 1,4-dioxane/water (4:1, 4 mL) and stirred for 5 min at RT. 2-Formylphenylboronic acid (73 mg, 0.49 mmol, 1.2 eq.) was added, the reaction vessel was sealed and heated at 100 °C in the microwave for 15 min. The reaction mixture was diluted with water (4 mL) and extracted with EtOAc (3 x 5 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under vacuum. Purification by flash chromatography on deactivated silica (NEt_3) with 10 % Et_2O in pentane gave the product in the form of a red oil (56 mg, 0.18 mmol, 44 %).

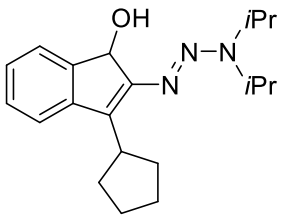
^{1}H NMR (400 MHz, $CDCl_3$, 298 K) δ 7.45 (d, *J* = 7.2 Hz, 1H, $C_{Ar}H$), 7.29 – 7.23 (m, 1H, $C_{Ar}H$), 7.21 (d, J = 7.3 Hz, 1H, $C_{Ar}H$), 7.15 (td, J = 7.3, 1.3 Hz, 1H, $C_{Ar}H$), 5.46 (d, J = 1.9 Hz, 1H, C*H*OH), 5.15 (s, 1H, $C_{i\text{Pr}}H$), 4.01 (s, 1H, $C_{i\text{Pr}}H$), 3.30 (d, J = 2.0 Hz, 1H, CHO*H*), 2.79 – 2.61 (m, 2H, $C_{n\text{Bu}}H_2$), 1.73 – 1.56 (m, 2H, $C_{n\text{Bu}}H_2$), 1.45 – 1.21 (m, 14H, $C_{n\text{Bu}}H_2$+ $C_{i\text{Pr}}H_3$), 0.93 (t, J = 7.3 Hz, 3H, $C_{n\text{Bu}}H_3$).

^{13}C NMR (101 MHz, $CDCl_3$, 298 K) δ 152.2 (C_{sp2}-N_3*i*Pr_2), 144.4 ($C_{Ar,q}$), 141.8 ($C_{Ar,q}$), 132.2 (C_{sp2}-*n*Bu), 128.4 ($C_{Ar}H$), 125.3 ($C_{Ar}H$), 123.4 ($C_{Ar}H$), 119.0 ($C_{Ar}H$), 73.7 (CHOH), 30.7 ($C_{n\text{Bu}}H_2$), 24.0 ($C_{n\text{Bu}}H_2$), 22.8 ($C_{n\text{Bu}}H_2$), 14.1 ($C_{n\text{Bu}}H_3$).[3]

IR (ν_{max}, cm^{-1}) 3544 (w), 2971 (m), 2958 (m), 2930 (m), 2871 (w), 2859 (w), 1606 (w), 1461 (m), 1401 (s), 1245 (s), 1205 (m), 1149 (s), 1032 (m), 731 (m).

HRMS (ESI/QTOF): Calculated (MH+) 316.2383; Found 316.2388.

3-Cyclopentyl-2-(3,3-diisopropyltriaz-1-en-1-yl)-1*H*-inden-1-ol (**2.1g**)



[Rh(cod)Cl]$_2$ (6 mg, 12 µmol, 0.03 eq., 6 mol% [Rh]), KOH (11 mg, 0.20 mmol, 0.5 eq.) and 1-(cyclopentylethynyl)-3,3-diisopropyltriaz-1-ene (90 mg, 406 µmol, 1 eq.) were dissolved in 1,4-dioxane/water (4:1, 3.75 mL) and stirred for 5 min at RT. 2-Formylphenylboronic acid (73 mg, 0.49 µmol, 1.2 eq.) was added, the reaction vessel was sealed and heated at 100 °C in the microwave for 15 min. The reaction mixture was diluted with H_2O (4 mL) and extracted with EtOAc (3 x 5 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under vacuum. Purification by flash column chromatography on deactivated silica (NEt_3) with a gradient of

[3] The NCH and the $C_{i\text{Pr}}H_3$ signals were not detected due to broadening. Based on HSQC spectroscopy, the $C_{i\text{Pr}}H_3$ signals are estimated to appear at 19 and 24 ppm respectively.

5 – 15 % Et_2O in pentane gave the product in the form of a red highly viscous oil (81 mg, 0.25 mmol, 61 %).

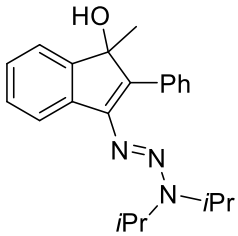
^{1}H NMR (400 MHz, $CDCl_3$, 298 K) δ 7.46 (d, *J* = 7.2 Hz, 1H, $C_{Ar}H$), 7.31 – 7.22 (m, 2H, $C_{Ar}H$), 7.15 (td, *J* = 6.9, 2.1 Hz, 1H, $C_{Ar}H$), 5.46 (d, *J* = 1.9 Hz, 1H, C*H*OH), 5.15 (s, 1H, $C_{i\text{Pr}}H$), 4.01 (s, 1H, $C_{i\text{Pr}}H$), 3.46 (p, *J* = 9.0 Hz, 1H, $C_{c\text{Pent}}H$), 3.35 (d, *J* = 2.0 Hz, 1H CHO*H*), 2.12 – 1.99 (m, 2H, $C_{c\text{Pent}}H_2$), 1.98 – 1.81 (m, 4H, $C_{c\text{Pent}}H_2$), 1.78 – 1.64 (m, 2H, $C_{c\text{Pent}}H_2$), 1.49 – 1.16 (m, 12H, $C_{i\text{Pr}}H_3$).

^{13}C NMR (101 MHz, $CDCl_3$, 298 K) δ 151.7 (C_{sp2}-N_3*i*Pr_2), 143.9 ($C_{Ar,q}$), 142.2 ($C_{Ar,q}$), 135.1 (C_{sp2}-*c*Pent), 128.4 ($C_{Ar}H$), 125.4 ($C_{Ar}H$), 123.7 ($C_{Ar}H$), 120.2 ($C_{Ar}H$), 73.9 (CHOH), 49.0 ($C_{i\text{Pr}}H$), 46.6 ($C_{i\text{Pr}}H$), 36.9 ($C_{c\text{Pent}}H$), 31.6 ($C_{c\text{Pent}}H_2$), 31.5 ($C_{c\text{Pent}}H_2$), 27.0 ($C_{c\text{Pent}}H_2$), 26.9 ($C_{c\text{Pent}}H_2$), 24.1 ($C_{i\text{Pr}}H_3$), 19.7 ($C_{i\text{Pr}}H_3$).

IR (ν_{max}, cm^{-1}) 2956 (m), 2868 (w), 2076 (w), 1601 (w), 1461 (m), 1400 (s), 1380 (s), 1365 (m), 1332 (m), 1244 (s), 1206 (m), 1149 (s), 1031 (m), 767 (m), 732 (s).

HRMS (ESI/QTOF): Calculated (MH+) 328.2383; Found 328.2387.

3-(3,3-Diisopropyltriaz-1-en-1-yl)-1-methyl-2-phenyl-1*H*-inden-1-ol (**2.1h**)



[Rh(cod)Cl]$_2$ (6 mg, 12 µmol, 0.03 eq., 6 mol% [Rh]), KOH (12 mg, 0.21 mmol, 0.5 eq.) and 3,3-diisopropyl-1-(phenylethynyl)triaz-1-ene (100 mg, 0.44 mmol, 1.0 eq.) were dissolved in 1,4-dioxane/water (4:1, 4 mL) and stirred for 5 min at RT. 2-Acetylphenylboronic acid (92.7 mg, 0.565 mmol, 1.3 eq.) was added, the reaction vessel was sealed and heated at 100 °C in the microwave for 45 min. The reaction mixture was diluted with $NaHCO_3$ (sat. aq., 4 mL) and extracted with EtOAc (3 x 5 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under vacuum. Purification by flash column chromatography on deactivated silica (NEt_3) with a gradient of 0 – 10 % Et_2O in pentane gave the product as a yellow solid (60 mg, 0.174 mmol, 40 %, major isomer) and as an oil (30 mg, 0.086 mmol, 20 %, 1.4:1 rr).

The data for the major isomer are reported.

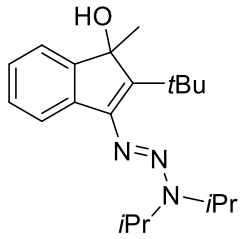
^{1}H NMR (400 MHz, $CDCl_3$ 298 K) δ 8.22–8.09 (m, 2H, $C_{Ar}H$), 8.08–7.98 (m, 1H, $C_{Ar}H$), 7.62–7.43 (m, 1H, $C_{Ar}H$), 7.43–7.33 (m, 2H, $C_{Ar}H$), 7.32–7.19 (m, 3H, $C_{Ar}H$), 5.39–5.14 (m, 1H, $C_{i\text{Pr}}H$), 4.20–3.97 (m, 1H, $C_{i\text{Pr}}H$), 1.99 (s, 1H, OH), 1.67 (s, 3H, $C_{t\text{Bu}}H_3$), 1.53–1.37 (m, 6H, $C_{i\text{Pr}}H_3$), 1.36–1.19 (m, 6H, $C_{i\text{Pr}}H_3$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 150.5 (C_{sp2}), 145.2 (C_{ar}), 138.1 (C_{ar}), 135.6 (C_{ar}), 135.2 (C_{ar}), 129.9 (C_{sp2}), 128.2 (C_{ar}), 127.6 (C_{ArH}),126.8 (C_{ArH}), 126.6 (C_{ArH}), 124.1 (C_{ArH}),121.5 (C_{ArH}), 81.6 (CHOH), 49.0 ($C_{i\mathrm{Pr}}$H), 45.9 ($C_{i\mathrm{Pr}}$H), 24.6 (CH_3), 19.7 ($C_{i\mathrm{Pr}}H_3$), 19.5 (br, $C_{i\mathrm{Pr}}H_3$).[4]

IR (ν_{max}, cm^{-1}) 3362 (w), 2976 (m), 2937 (w), 2864 (w), 1598 (w), 1453 (w), 1402 (s), 1380 (m), 1358 (m), 1279 (w), 1234 (s), 1156 (s), 1094 (s), 1022 (m), 910 (w), 842 (m), 753 (s), 691 (s).

HRMS (ESI–TOF): Calculated (MH+) 350.2227; Found 350.2231.

2-(*tert*-Butyl)-3-(3,3-diisopropyltriaz-1-en-1-yl)-1-methyl-1*H*-inden-1-ol **(2.1i)**



$[Rh(cod)Cl]_2$ (11 mg, 21 µmol, 0.04 eq., 8 mol% [Rh]), KOH (9 mg, 160 µmol, 0.3 eq.) and 1-(3,3-dimethylbut-1-yn-1-yl)-3,3-diisopropyltriaz-1-ene (112 mg, 0.535 mmol, 1 eq.) were dissolved in 1,4-dioxane/water (4:1, 4 mL). 2-Acetylphenylboronic acid (105 mg, 642 µmol, 1.2 eq.) was added, the reaction vessel was sealed and heated at 100 °C in the microwave for 15 min. The reaction mixture was extracted with DCM (3 x 10 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under vacuum. Purification by flash column chromatography on deactivated silica (NEt_3) with a gradient of 0 – 40 % DCM in pentane gave the product as separated isomers in the form of yellow solids (major: 102 mg, 0.311 mmol, 58 %, minor: 3.5 mg, 11 µmol, 2 %,).

^{1}H NMR (400 MHz, $CDCl_3$, 298 K) δ 7.90–7.78 (m, 1H, C_{ArH}), 7.42–7.33 (m, 1H, C_{ArH}), 7.24–7.13 (m, 2H, C_{ArH}), 5.49–5.07 (m, 1H, $C_{i\mathrm{Pr}}$H), 4.24–3.78 (m, 1H, $C_{i\mathrm{Pr}}$H), 1.77 (s, 3H, CH_3), 1.63 (s, 1H, OH), 1.51 (s, 9H, $C_{t\mathrm{Bu}}H_3$), 1.46–1.24 (m, 12H, $C_{i\mathrm{Pr}}H_3$).

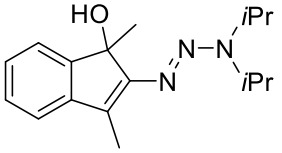
^{13}C NMR (101 MHz, $CDCl_3$, 298 K) δ 151.1 ($C_{Ar,q}$), 146.5 (C_{sp2}-*t*Bu), 144.2 (C_{sp2}-N_3*i*Pr_2), 138.3 ($C_{Ar,q}$), 127.7 (C_{ArH}), 125.9 (C_{ArH}), 123.4 (C_{ArH}), 120.7 (C_{ArH}), 82.8 (*C*(CH_3)OH), 34.9 ($C_{t\mathrm{Bu,q}}$), 31.4 ($C_{t\mathrm{Bu}}H_3$), 25.9 (CH_3).

IR (ν_{max}, cm^{-1}) 3317 (w), 2973 (m), 2948 (w), 2870 (w), 1601 (w), 1455 (w), 1415 (s), 1396 (m), 1363 (m), 1345 (m), 1307 (m), 1238 (s), 1224 (s), 1151 (s), 1120 (m), 1078 (s), 1040 (s), 1023 (s), 927 (m), 874 (m), 802 (m), 760 (s), 711 (s).

HRMS (ESI/QTOF): Calculated (MH+) 330.2540; Found 330.2540.

[4] An unknown impurity appears at 8.2 ppm only on the ^{13}C NMR spectrum. All other peaks match the obtained product.

2-(3,3-Diisopropyltriaz-1-en-1-yl)-1,3-dimethyl-1*H*-inden-1-ol (**2.1j**)



[Rh(cod)Cl]$_2$ (5.0 mg, 10.1 µmol, 0.04 eq., 8 mol% [Rh]), (4.2 mg, 75 µmol, 0.3 eq.) and 3-(3-isopropyl-3-methyltriaz-1-en-1-yl)prop-2-yn-1-ol (39 mg, 250 µmol, 1 eq.) were dissolved in 1,4-dioxane/water (4:1, 2.5 mL). 2-Acetylphenylboronic acid (49.5 mg, 302 µmol, 1.2 eq.) was added, the reaction vessel was sealed and heated at 100 °C in the microwave for 15 min. The reaction mixture was extracted with DCM (3 x 10 mL). The combined organic phases were dried over $MgSO_4$, filtered over a plug of deactivated Silica (NEt_3, eluent: EtOAc) and the solvent was removed under vacuum. Purification by flash chromatography on deactivated silica (NEt_3) with 10 % DCM in pentane gave the product in the form of a yellow, highly viscous oil that crystalizes upon storage at – 20 °C (33.1 mg, 0.115 mmol, 46 %).

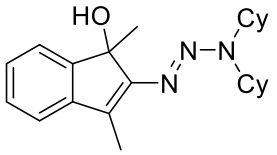
^{1}H NMR (400 MHz, $CDCl_3$, 298 K) δ 7.42–7.37 (m, 1H, $C_{Ar}H$), 7.32–7.25 (m, 1H, $C_{Ar}H$), 7.23–7.15 (m, 2H, $C_{Ar}H$), 5.30 (s, 1H, $C_{i\mathrm{Pr}}H$), 4.02 (s, 1H, $C_{i\mathrm{Pr}}H$), 3.60 (s, 1H, OH), 2.19 (s, 3H, C_{sp2}-CH_3), 1.66 (s, 3H, C(OH)CH_3), 1.51–1.16 (m, 12H, $C_{i\mathrm{Pr}}H_3$).

^{13}C NMR (101 MHz, $CDCl_3$, 298 K) δ 153.3 (C_{sp2}-N_3*i*Pr_2), 147.1 ($C_{Ar,q}$), 143.5 ($C_{Ar,q}$ or C_{sp2}-Me), 128.3 ($C_{Ar}H$), 126.6 ($C_{Ar,q}$ or C_{sp2}-Me), 125.8 ($C_{Ar}H$), 121.2 ($C_{Ar}H$), 118.9 ($C_{Ar}H$), 80.3 (C(OH)Me), 48.6 (br, $C_{i\mathrm{Pr}}H$), 45.7 (br, $C_{i\mathrm{Pr}}H$), 26.9 (C(OH)CH_3), 23.8 ($C_{i\mathrm{Pr}}H_3$), 19.5 ($C_{i\mathrm{Pr}}H_3$), 9.4 (C_{sp2}-CH_3).

IR (ν_{max}, cm^{-1}) 3542 (w), 3529 (w), 3055 (w), 2970 (w), 2927 (w), 2866 (w), 1605 (w), 1462 (w), 1397 (s), 1375 (m), 1316 (m), 1251 (s), 1209 (m), 1152 (s), 1089 (s), 1025 (s), 1014 (s), 933 (m), 748 (s).

HRMS (ESI/QTOF): Calculated (MH+) 288.2070; Found 288.2070.

2-(3,3-Dicyclohexyltriaz-1-en-1-yl)-1,3-dimethyl-1*H*-inden-1-ol (**2.1k**)



[Rh(cod)Cl]$_2$ (4.1 mg, 8.3 µmol, 0.04 eq., 8 mol% [Rh]), KOH (3.4 mg, 61 µmol, 0.3 eq.) and 3,3-dicyclohexyl-1-(prop-1-yn-1-yl)triaz-1-ene (50.8 mg, 0.206 mmol, 1.0 eq.) were dissolved in 1,4-dioxane/water (4:1, 2 mL). 2-Acetylphenylboronic acid (40.5 mg, 0.247 mmol, 1.2 eq.) was added, the reaction vessel was sealed and heated at 100 °C in the microwave for 15 min. The reaction mixture was extracted with DCM (3 x 5 mL). The combined organic phases were dried over $MgSO_4$, filtered over a plug of deactivated silica (NEt_3) and the solvent was removed under vacuum. Purification by flash column chromatography on deactivated silica (NEt_3) with a gradient of 4 – 15 % DCM in pentane gave the product in the form of a yellow solid (41.0 mg, 0.112 mmol 54 %).

Crystals suitable for X-ray diffraction analysis were obtained by slow evaporation from pentane.

^{1}H NMR (400 MHz, $CDCl_3$, 298 K) δ 7.42–7.08 (m, 4H, $C_{Ar}H$), 4.98 (s, 1H, $C_{Cy}H$), 3.64 (s, 1H, OH), 3.48 (s, 1H, $C_{Cy}H$), 2.15 (s, 3H, C_{sp2}-CH_3), 1.63 (s, 3H, C(OH)CH_3), 2.01–0.76 (m, 20H, $C_{Cy}H_2$).

^{13}C NMR (101 MHz, $CDCl_3$, 298 K) δ 153.3 (C_{sp2}-N_3Cy_2), 147.1 ($C_{Ar,q}$), 143.6 ($C_{Ar,q}$), 128.3 ($C_{Ar}H$), 126.3 (C_{sp2}-Me), 125.7 ($C_{Ar}H$), 121.10 ($C_{Ar}H$), 118.8 ($C_{Ar}H$), 80.3 (*C*(OH)CH_3), 57.6 ($C_{Cy}H$), 54.0 ($C_{Cy}H$), 34.8 (br, $C_{Cy}H_2$), 30.0 (br, $C_{Cy}H_2$), 26.9 (br, $C_{Cy}H_2$), 26.1 (C(OH)*C*H_3), 9.4 (C_{sp2}-*C*H_3).

IR (ν_{max}, cm^{-1}) 3503 (w), 2973 (w), 2924 (m), 2851 (m), 1608 (w), 1444 (m), 1398 (s), 1398 (s), 1379 (s), 1336 (m), 1313 (s), 1253 (m), 1209 (s), 1194 (s), 1086 (m), 1030 (s), 760 (s), 1140 (m), 1014 (m), 1274 (m), 1070 (m), 988 (m), 917 (m), 892 (m).

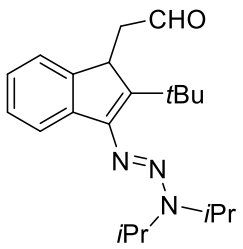
HRMS (nanochip-ESI/LTQ-Orbitrap): Calculated (MH+) 368.2696; Found 368.2696.

7.2.3. Synthesis of Indenyl Triazenes **2.2a – h**

2-(2-(*tert*-Butyl)-3-(3,3-diisopropyltriaz-1-en-1-yl)-1*H*-inden-1-yl)acetaldehyde (**2.2a**) and 2-(3-(*tert*-butyl)-2-(3,3-diisopropyltriaz-1-en-1-yl)-1*H*-inden-1-yl)acetaldehyde (**2.2a'**)

$[Rh(cod)Cl]_2$ (10.7 mg, 21.6 µmol, 0.05 eq., 10 mol% [Rh]), KOH (7.3 mg, 0.13 mmol, 0.3 eq.) and 1-(3,3-dimethylbut-1-yn-1-yl)-3,3-diisopropyltriaz-1-ene (90.5 mg, 0.432 mmol, 1 eq.) were dissolved in THF/water (20:1, 4.2 mL) at 0 °C. (*E*)-3-(2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-acryl-aldehyde (133.8 mg, 0.519 mmol, 1.2 eq.) was added and the reaction mixture was stirred at 0 °C for 1 h. The reaction mixture was allowed to warm to RT and stirring was continued for 6 h. The reaction mixture was filtered over a plug of deactivated silica (NEt_3, eluent: DCM), dried over $MgSO_4$ and the solvent was removed under vacuum. Purification by flash column chromatography on deactivated silica (NEt_3) with a gradient of 0 – 10 % DCM in pentane gave the product as separated isomers in the form of yellow solids (**2a**: 88.2 mg, 0.258 mmol, 60 %; **2a'**: 9.9 mg, 0.029 mmol, 7 %).

2.2a:



^{1}H NMR (400 MHz, $CDCl_3$, 298 K) δ 9.38 (dd, *J* = 2.8, 1.4 Hz, 1H, CHO), 7.97 (d, *J* = 7.7 Hz, 1H, $C_{Ar}H$), 7.32 (d, *J* = 7.4 Hz, 1H, $C_{Ar}H$), 7.23 (dd, *J* = 7.7, 1.3 Hz, 1H, td expected, partially covered by solvent signal, $C_{Ar}H$), 7.15 (td, *J* = 7.4, 1.2 Hz, 1H, $C_{Ar}H$), 5.22 (br, 1H, $C_{i\text{Pr}}H$), 4.09 (dd, *J* = 7.1, 3.2 Hz, 1H, C*H*CH_2COH), 4.03 (br, 1H, $C_{i\text{Pr}}H$), 3.17 (ddd, *J* = 17.4, 3.2,

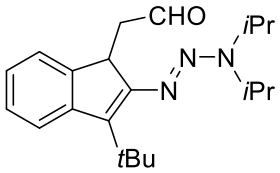
1.4 Hz, 1H, CH_2COH), 2.78 (ddd, J = 17.5, 7.1, 2.8 Hz, 1H, CH_2COH), 1.43 (s, 9H, $C_{t\mathrm{Bu}}H_3$), 1.34 (br, 12H, $C_{i\mathrm{Pr}}H_3$).

^{13}C NMR (101 MHz, $CDCl_3$, 298 K) δ 202.8 (CHO), 146.0 ($C_{\mathrm{Ar,q}}$ or C_{sp2}-$N_3i\mathrm{Pr}_2$), 145.8 ($C_{\mathrm{Ar,q}}$ or C_{sp2}-$N_3i\mathrm{Pr}_2$), 144.7 (C_{sp2}-tBu), 140.9 ($C_{\mathrm{Ar,q}}$), 126.8 (C_{Ar}H), 125.0 (C_{Ar}H), 123.4 (C_{Ar}H), 122.6 (C_{Ar}H), 46.2 (CH$_2$COH), 43.8 (CHCH$_2$COH), 34.4 ($C_{t\mathrm{Bu,q}}$), 31.2 ($C_{t\mathrm{Bu}}H_3$).

IR (ν_{max}, cm^{-1}) 2973 (m), 2823 (w), 2722 (w), 1718 (s), 1458 (m), 1399 (s), 1344 (m), 1241 (s), 1153 (s), 1127 (m), 1096 (m), 1023 (m), 938 (m), 757 (m), 744 (m).

HRMS (nanochip-ESI/LTQ-Orbitrap): Calculated (MNa+) 364.2359; Found 364.2358.

2.2a':



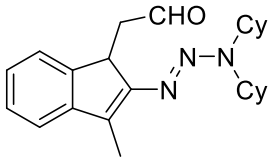
^{1}H NMR (400 MHz, $CDCl_3$, 298 K) δ 9.44 (s, 1H, CHO), 7.64 (d, J = 7.8 Hz, 1H, C_{Ar}H), 7.29 (d, J = 7.3 Hz, 1H, C_{Ar}H), 7.22 (td, J = 7.6, 1.3 Hz, 1H, C_{Ar}H), 7.09 (td, J = 7.4, 1.1 Hz, 1H, C_{Ar}H), 5.12 (s, 1H, $C_{i\mathrm{Pr}}$H), 4.23 (dd, J = 7.4, 3.5 Hz, 1H, CHCH$_2$COH), 3.97 (s, 1H, $C_{i\mathrm{Pr}}$H), 2.96 (ddd, J = 17.3, 3.5, 1.9 Hz, 1H, CH_2COH), 2.65 (ddd, J = 17.3, 7.4, 2.2 Hz, 1H, CH_2COH), 1.56 (s, 9H, $C_{t\mathrm{Bu}}H_3$), 1.39 – 1.11 (m, 12H, $C_{i\mathrm{Pr}}H_3$).

^{13}C NMR (101 MHz, $CDCl_3$, 298 K) δ 202.92 (CHO), 152.67 (C_{sp2}-$N_3i\mathrm{Pr}_2$), 144.97 ($C_{\mathrm{Ar,q}}$), 144.82 ($C_{\mathrm{Ar,q}}$), 137.69 (C_{sp2}-tBu), 126.52 (C_{Ar}H), 124.11 (C_{Ar}H), 123.29 (C_{Ar}H), 122.88 (C_{Ar}H), 45.84 (CH$_2$COH), 40.66 (CHCH$_2$COH), 35.26 ($C_{t\mathrm{Bu,q}}$), 31.40 ($C_{t\mathrm{Bu}}H_3$).

IR (ν_{max}, cm^{-1}) 2972 (m), 2953 (w), 2930 (w), 2906 (w), 2870 (w), 2191 (w), 1719 (s), 1457 (m), 1397 (s), 1379 (s), 1359 (s), 1243 (s), 1204 (m), 1158 (s), 1143 (s), 1098 (s), 1004 (m), 753 (s).

HRMS (ESI/QTOF): Calculated (MH+) 342.2540; Found 342.2536.

2-(2-(3,3-Dicyclohexyltriaz-1-en-1-yl)-3-methyl-1*H*-inden-1-yl)acetaldehyde (**2.2b**)



[Rh(cod)Cl]$_2$ (16.4 mg, 33.2 μmol, 0.05 eq., 10 mol% [Rh]), KOH (10.7 mg, 0.191 mmol, 0.3 eq.) and 3,3-dicyclohexyl-1-(prop-1-yn-1-yl)triaz-1-ene (159.7 mg, 0.646 mmol, 1.0 eq.) were dissolved in THF/water (33:1, 6.2 mL) at 0 °C. (*E*)-3-(2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)acrylaldehyde (200.0 mg, 0.775 mmol, 1.2 eq.) was added and the mixture was stirred at 0 °C for 2 h. The reaction mixture was filtered over a plug of deactivated silica (NEt_3, eluent: DCM) and the solvent was removed under vacuum. Purification by flash column chromatography on deactivated silica (NEt_3) with a gradient of 5 – 17 % DCM in pentane gave the product as a mixture of isomers in the form of a brown-orange solid (167.9 mg, 0.445 mmol, 69 %, > 20:1 rr).

Crystals suitable for X-ray diffraction analysis were obtained by slow evaporation from pentane.

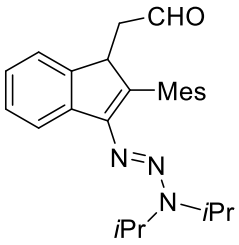
^{1}H NMR (400 MHz, $CDCl_3$, 298 K) δ 9.52 (s, 1H, CHO), 7.33–7.26 (m, 2H, $C_{Ar}H$), 7.33–7.23 (m, 3H, $C_{Ar}H$), 5.06–4.82 (m, 1H, CH_{Cy}), 4.25–4.14 (m, 1H, C*H*CH_2CHO), 3.80–3.37 (m, 1H, CH_{Cy}), 3.06 (ddd, *J* = 17.3, 3.6, 1.9 Hz, 1H, C*H*$_2$CHO), 2.70 (ddd, *J* = 17.3, 7.7, 2.2 Hz, 1H, C*H*$_2$CHO), 2.25 (s, 3H, CH_3), 1.93–1.10 (m, 20H, $CH_{2\ Cy}$).

^{13}C NMR (101 MHz, $CDCl_3$, 298 K) δ 202.7 (CHO), 153.1 (C_{sp2}-N_3Cy_2), 145.9 ($C_{Ar,q}$), 143.9 ($C_{Ar,q}$), 127.4 (C_{sp2}-Me), 127.0 ($C_{Ar}H$), 124.5 ($C_{Ar}H$), 123.0 ($C_{Ar}H$), 118.4 ($C_{Ar}H$), 57.7 (br, CH_{Cy}), 54.4 (br, CH_{Cy}), 45.1 (*C*H_2CHO), 40.4 (*C*HCH$_2$CHO), 34.5 (br, $CH_{2\ Cy}$), 34.3 (br, $CH_{2\ Cy}$), 30.0 (br, $CH_{2\ Cy}$), 29.8 (br, $CH_{2\ Cy}$), 26.1 (br, $CH_{2\ Cy}$), 9.56 (CH_3).

IR (ν_{max}, cm^{-1}) 3065 (w), 3041 (w), 3019 (w), 2930 (s), 2853 (m), 2718 (w), 1723 (s), 1604 (w), 1452 (m), 1399 (s), 1334 (m), 1276 (m), 1255 (m), 1206 (s), 1183 (m), 1140 (m), 1062 (w), 1015 (w), 990 (w), 893 (w), 758 (m).

HRMS (nanochip-ESI/LTQ-Orbitrap): Calculated (MNa+) 402.2516; Found 402.2520.

2-(3-(3,3-Diisopropyltriaz-1-en-1-yl)-2-mesityl-1*H*-inden-1-yl)acetaldehyde (**2.2c**)



[Rh(cod)Cl]$_2$ (4.3 mg, 8.7 μmol, 0.05 eq., 10 mol% [Rh]), KOH (3.3 mg, 0.59 mmol, 0.3 eq.) and 3,3-diisopropyl-1-(mesitylethynyl)triaz-1-ene (51.1 mg, 0.188 mmol, 1 eq.) were dissolved in 1,4-dioxane/water (20:1, 2.1 mL) at 0 °C. (*E*)-3-(2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl) phenyl) acryl-aldehyde (58.5 mg, 0.227 mmol, 1.2 eq.) was added and the reaction mixture was heated at 80 °C in the microwave for 15 min. The reaction mixture was filtered over plug of deactivated silica (NEt_3, eluent: DCM) and the solvent was removed under vacuum. Purification by flash column chromatography on deactivated silica (NEt_3) with a gradient of 0 – 33 % DCM in pentane gave the product as mixture of isomers in the form of an orange oil (45.2 mg, 0.112 mmol, 59 %, 6:1 rr).

^{1}H NMR (400 MHz, $CDCl_3$, 298 K) δ 9.68 (t, *J* = 1.6 Hz, 1H, CHO), 7.92 (d, *J* = 7.4 Hz, 1H, $C_{Indenyl}H$), 7.39 (d, *J* = 7.4 Hz, 1H, $C_{Indenyl}H$), 7.34 (td, *J* = 7.5, 1.2 Hz, 1H, $C_{Indenyl}H$), 7.22 (td, *J* = 7.5, 1.2 Hz, 1H, $C_{Indenyl}H$), 6.87 (s, 1H, $C_{Mes}H$), 6.86 (s, 1H, $C_{Mes}H$), 4.99 (s, 1H, $C_{i Pr}H$), 4.36 (dd, *J* = 8.4, 5.3 Hz, 1H, C*H*CH_2CHO), 3.89 (s, 1H, $C_{i Pr}H$), 2.68 (ddd, *J* = 17.5, 5.3, 1.5 Hz, 1H, C*H*$_2$CHO), 2.56 (ddd, *J* = 17.5, 8.4, 1.8 Hz, 1H, C*H*$_2$CHO), 2.28 (s, 3H, *p*-$CH_{3\ Mes}$), 2.19 (s, 3H *o*-$C_{Mes}H_3$), 2.07 (s, 4H *o*-$C_{Mes}H_3$), 1.34–0.95 (m, 12H, $C_{i Pr}H_3$).

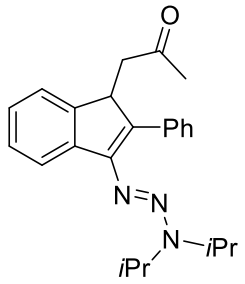
^{13}C NMR (101 MHz, $CDCl_3$, 298 K) δ 202.0 (CHO), 146.6 (C_{sp2}), 146.5 (C_{sp2}), 141.5 (C_{sp2}), 137.2 (*o*-$C_{q\ Mes}$), 137.1 (*o*-$C_{q\ Mes}$), 136.3 (*p*-$C_{q\ Mes}$), 132.9 (C_{sp2}), 132.8 (C_{sp2}), 128.3 ($C_{Mes}H$),

128.0 ($C_{Mes}H$), 127.0 ($C_{Indenyl}H$), 125.2 ($C_{Indenyl}H$), 123.4 ($C_{Indenyl}H$), 122.1 ($C_{Indenyl}H$), 45.2 (CH_2CHO), 44.5 ($CHCH_2CHO$), 21.2 (*p*-$C_{Mes}H_3$), 21.0 (*o*-$C_{Mes}H_3$), 20.9 (*o*-$C_{Mes}H_3$).

IR (ν_{max}, cm^{-1}) 2971 (m), 2924 (w), 2871 (w), 2821 (w), 2724 (w), 2065 (w), 1721 (s), 1610 (w), 1459 (m), 1400 (s), 1365 (m), 1347 (m), 1240 (s), 1219 (s), 1153 (s), 1125 (m), 1022 (m), 850 (m), 744 (m).

HRMS (ESI/QTOF): Calculated (MH+) 404.2696; Found 404.2689.

1-(3-(3,3-Diisopropyltriaz-1-en-1-yl)-2-phenyl-1*H*-inden-1-yl)propan-2-one (**2.2d**)



$[Rh(cod)Cl]_2$ (4.8 mg, 9.7 µmol, 0.04 eq. 8 mol% [Rh]), KOH (4.1 mg, 73 µmol, 0.3 eq.) and 3,3-diisopropyl-1-(phenylethynyl)triaz-1-ene (55.9 mg, 244 µmol, 1.0 eq.) were dissolved in THF/water (20:1, 2.1 mL) at 0 °C. (*E*)-4-(2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)but-3-en-2-one (79.6 mg, 292 µmol, 1.2 eq.) was added and the reaction mixture was stirred at 0 °C for 7 h. The reaction mixture was filtered over a plug of deactivated silica (NEt_3, eluent: DCM) and the solvent was removed under vacuum. Purification by flash column chromatography on deactivated silica (NEt_3) with a gradient of 0 – 33 % DCM in pentane gave the product as mixture of isomers in the form of an orange solid (74.0 mg, 0.197 mmol, 81 %, 1:1 rr[5]).

^{1}H NMR (400 MHz, $CDCl_3$, 298 K) δ 7.70 (dd, *J* = 8.3, 1.3 Hz, 2H, *o*-$C_{Ph}H$), 7.47 (d, *J* = 7.6 Hz, 1H, $C_{Indenyl}H$), 7.46–7.40 (m, 2H, *m*- $C_{Ph}H$), 7.35 (dd, *J* = 7.3, 1.1 Hz, 1H, $C_{Indenyl}H$), 7.31 (tt, *J* = 7.5, 1.2 Hz, 1H, *p*- $C_{Ph}H$), 7.28–7.19 (m, 1H, $C_{Indenyl}H$), 7.12 (td, *J* = 7.4, 1.2 Hz, 1H, $C_{Indenyl}H$), 5.22–5.01 (m, 1H, $C_{iPr}H$), 4.50 (dd, *J* = 9.8, 2.6 Hz, 1H, $CHCH_2COCH_3$), 4.08 – 3.89 (m, 1H, $C_{iPr}H$), 3.23 (dd, *J* = 17.5, 2.6 Hz, 1H, CH_2COCH_3), 2.52 (dd, *J* = 17.4, 9.8 Hz, 1H, CH_2COCH_3), 2.15 (s, 3H, CH_2COCH_3), 1.25 (dd, *J* = 54.3, 7.2 Hz, 12H, $C_{iPr}H_3$).

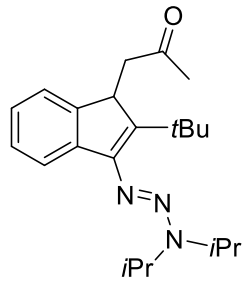
^{13}C NMR (101 MHz, $CDCl_3$, 298 K) δ 207.9 ($COCH_3$), 154.9 (C_{sp2}-Ph, 145.3 ($C_{q\ Indenyl}$), 144.1 ($C_{q\ Indenyl}$), 134.8 ($C_{q\ Ph}$), 130.0 (*o*- $C_{Ph}H$), 129.9 (C_{sp2}-N_3iPr_2), 127.9 (*m*- $C_{Ph}H$), 126.9 (*p*- $C_{Ph}H$ or $C_{Indenyl}H$), 126.8 (*p*- $C_{Ph}H$ or $C_{Indenyl}H$), 124.8 ($C_{Indenyl}H$), 123.7 ($C_{Indenyl}H$), 119.9 ($C_{Indenyl}H$), 49.1 (br, $C_{iPr}H$), 46.8 (CH_2COCH_3), 46.5 (br, $C_{iPr}H$), 41.3 ($CHCH_2COCH_3$), 30.5 ($COCH_3$), 24.0 (br, $C_{iPr}H_3$), 23.6 (br, $C_{iPr}H_3$), 19.7 (br, $C_{iPr}H_3$), 19.6 (br, $C_{iPr}H_3$).

IR (ν_{max}, cm^{-1}) 3061 (w), 3025 (w), 2972 (w), 2931 (w), 2870 (w), 2064 (w), 1714 (m), 1597 (w), 1493 (w), 1456 (m), 1398 (s), 1351 (s), 1242 (s), 1152 (s), 1024 (m), 761 (m), 745 (s).

[5] The ratio of regioisomers was determined from the NMR spectrum of the crude product before purification. A small amount of pure **2.2d** could be separated from the mixture of isomers, allowing a simplified characterization. Afterwards, due to the low amount, this sample was combined with the remaining mixture of regioisomers

HRMS (ESI/QTOF): Calculated (MH+) 376.2383; Found 376.2381.

1-(2-(*tert*-Butyl)-3-(3,3-diisopropyltriaz-1-en-1-yl)-1*H*-inden-1-yl)propan-2-one (**2.2e**)



$[Rh(cod)Cl]_2$ (6.4 mg, 13 µmol, 0.04 eq. 8 mol% [Rh]), KOH (5.1 mg, 91 µmol, 0.3 eq.) and 1-(3,3-dimethylbut-1-yn-1-yl)-3,3-diisopropyltriaz-1-ene (64.6 mg, 0.308 mmol, 1 eq.) in THF/water (24:1, 4.75 mL) at 0 °C. (*E*)-4-(2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)but-3-en-2-one (101 mg, 0.370 mmol, 1.2 eq.) was added and the mixture was stirred at 0 °C for 1 h. The reaction mixture was allowed to warm to RT and stirring was continued for 6.5 h. The reaction mixture was filtered over a plug of deactivated silica (NEt_3, eluent: DCM) and the solvent was removed under vacuum. Purification by flash column chromatography on deactivated silica (NEt_3) with a gradient of 0 – 20 % DCM in pentane gave the product as mixture of isomers in the form of a yellow solid (88.5 mg, 0.249 mmol, 81 %, 2:1 rr).

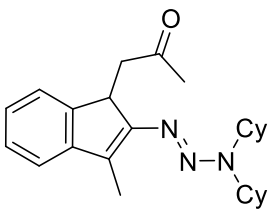
^{1}H NMR (400 MHz, $CDCl_3$, 298 K) δ 7.96 (d, *J* = 7.6 Hz, 1H, $C_{Ar}H$), 7.27–7.16* (m, 3H, $C_{Ar}H$), 7.08 (td, *J* = 7.5, 1.3 Hz, 1H, $C_{Ar}H$), 5.13 (s, 1H, $C_{i\mathrm{Pr}}H$), 4.23 (dd, *J* = 9.6, 2.3 Hz, 1H, C*H*CH_2CMeO), 3.95 (s, 1H, $C_{i\mathrm{Pr}}H$), 3.26 (dd, *J* = 17.7, 2.4 Hz, 1H, C*H*$_2$$COCH_3$), 2.41 (dd, *J* = 17.6, 9.6 Hz, 1H, C*H*$_2$$COCH_3$), 2.12 (s, 3H, COC*H*$_3$), 1.42 (s, 9H, $C_{t\mathrm{Bu}}H_3$), 1.46–1.15* (br s, 27H, $C_{i\mathrm{Pr}}H_3$). [6]

^{13}C NMR (101 MHz, $CDCl_3$, 298 K) δ 208.0 (*C*OCH_3), 147.5 ($C_{Ar,q}$), 145.9 (C_{sp2}-*t*Bu), 145.0 (C_{sp2}-N_3*i*Pr_2 or $C_{Ar,q}$), 140.5 (C_{sp2}-N_3*i*Pr_2 or $C_{Ar,q}$), 126.5 ($C_{Ar}H$), 124.7 ($C_{Ar}H$), 123.1 ($C_{Ar}H$), 122.5 ($C_{Ar}H$), 47.6 (*C*$H_2$$COCH_3$), 44.2 (*C*H$CH_2$$COCH_3$), 34.3 ($C_{t\mathrm{Bu},q}$), 31.1 ($C_{t\mathrm{Bu}}H_3$), 31.0 (CO*C*$H_3$), 24.2 (br, $C_{i\mathrm{Pr}}H_3$), 19.7 (br, $C_{i\mathrm{Pr}}H_3$).

IR (ν_{max}, cm^{-1}) 2972 (m), 2870 (w), 1717 (m), 1599 (w), 1459 (m), 1418 (m), 1397 (s), 1363 (m), 1316 (m), 1297 (w), 1237 (s), 1223 (s), 1150 (s), 1124 (m), 1097 (m), 1024 (m), 962 (w), 930 (w), 896 (w), 873 (w), 811 (w), 771 (m), 745 (s).

HRMS (APPI/LTQ-Orbitrap) Calculated (MH+) 356.2696; Found 356.2705.

1-(2-(3,3-Dicyclohexyltriaz-1-en-1-yl)-3-methyl-1*H*-inden-1-yl)propan-2-one (**2.2f**)



$[Rh(cod)Cl]_2$ (4.1 mg, 8.3 µmol, 0.04 eq., 8 mol% [Rh]), KOH (3.5 mg, 62 µmol, 0.3 eq.) and 3,3-dicyclohexyl-1-(prop-1-yn-1-yl)triaz-1-ene (50.9 mg, 0.206 mmol, 1 eq.) were dissolved in THF/water (50:1, 4.1 mL) and cooled to 0 °C. 4-(2-(4,4,5,5-Tetramethyl-1,3,2-

[6] Signals marked with an * correspond to overlapping signals from atoms of both isomers.

dioxaborolan-2-yl)phenyl)but-3-en-2-one (67.6 mg, 0.248 mmol, 1.2 eq.) was added and the reaction mixture was stirred at 0 °C for 1 h. The reaction mixture was allowed to warm to RT and stirring was continued for 3.5 h. The reaction mixture was filtered over a plug of deactivated silica (NEt_3) using DCM as eluent and the solvent was removed under vacuum. Purification by flash column chromatography on deactivated silica (NEt_3) using a gradient of 5 – 10 % DCM in pentane as eluent gave the product in the form of a yellow solid (53.9 mg, 0.137 mmol, 66 %).

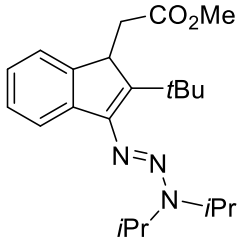
^{1}H NMR (400 MHz, $CDCl_3$, 298 K) δ 7.25 (m, *J* = 12.2, 6.0 Hz, 3H, $C_{Ar}H$), 7.07 (dq, *J* = 8.3, 4.1 Hz, 1H, $C_{Ar}H$), 5.35–4.68 (m, 1H, CH_{Cy}), 4.27 (d, *J* = 9.8 Hz, 1H, C*H*CH_2COCH_3), 3.71–3.31 (m, 1H, CH_{Cy}), 3.20 (dd, *J* = 17.3, 2.7 Hz, 1H, C*H*$_2$C(CH3)O), 2.36 (dd, *J* = 17.3, 9.9 Hz, 1H, C*H*$_2$C(CH3)O), 2.23 (s, 3H, C_{sp2}-CH_3), 2.12 (s, 3H, C(CH_3)O), 2.01–0.98 (m, 20H, $CH_{2\ Cy}$).

^{13}C NMR (101 MHz, $CDCl_3$, 298 K) δ 208.1 (*C*OCH_3), 153.9 (C_{sp2}-N_3Cy_2), 145.8 ($C_{Ar,q}$), 145.2 ($C_{Ar,q}$), 127.0 (C_{sp2}-Me), 126.8 ($C_{Ar}H$), 124.4 ($C_{Ar}H$), 123.2 ($C_{Ar}H$), 118.4 ($C_{Ar}H$), 57.6 (CH_{Cy}), 54.3 (CH_{Cy}), 46.3 (*C*H_2COCH_3), 41.2 (*C*HCH_2COCH_3), 34.7 (br, $CH_{2\ Cy}$), 34.4 (br, $CH_{2\ Cy}$), 30.4 (CO*C*H_3), 30.1 (br, $CH_{2\ Cy}$), 26.2 (br, $CH_{2\ Cy}$), 9.6 (C_{sp2}-*C*H_3).

IR (ν_{max}, cm^{-1}) 2928 (m), 2852 (m), 1718 (m), 1601 (w), 1446 (w), 1398 (s), 1332 (s), 1257 (m), 1202 (s), 1183 (s), 1138 (s), 1100 (m), 1059 (m), 1015 (m), 988 (m), 892 (m), 761 (s), 742 (m), 723 (w).

HRMS (APPI/LTQ-Orbitrap) Calculated (MH+) 394.2853; Found 394.2865.

Methyl 2-(3-(*tert*-butyl)-2-(3,3-diisopropyltriaz-1-en-1-yl)-1*H*-inden-1-yl)acetate (**2.2g**)



$[Rh(cod)Cl]_2$ (3 mg, 12 µmol, 0.03 eq., 6 mol% [Rh]), KOH (4 mg, 0.06 mmol, 0.3 eq.) and 1-(3,3-dimethylbut-1-yn-1-yl)-3,3-diisopropyltriaz-1-ene (42 mg, 0.2 mmol, 1.0 eq.) were dissolved in THF/water (40:1, 1 mL) and stirred for 5 min at 0 °C. Methyl (*E*)-3-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-acrylate (69 mg, 0.33 mmol, 1.2 eq.) was added and a color change could immediately be observed. The reaction flask was sealed and allowed to warm to RT and stirring was continued for 3 h. The reaction mixture was filtered over a plug of deactivated silica (NEt_3, eluent: DCM) and the solvent was removed under vacuum. Purification by flash column chromatography on deactivated silica (NEt_3) with 30 % DCM in pentane gave the product as mixture of isomers in the form of an orange oil (47 mg, 0.13 mmol, 68 %, 6:1 rr).[7]

[7] At RT, the $C_{iPr}H$-signals are broadened in both ^{1}H and ^{13}C-NMR.

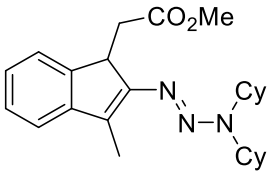
^{1}H NMR (400 MHz, $CDCl_3$, 298 K) δ 7.89 (d, *J*=7.7 Hz, 1H, $C_{Ar}H$), 7.20 (d, *J* = 7.2 Hz, 1H, $C_{Ar}H$), 7.14 (t, *J* = 7.5 Hz, 1H, $C_{Ar}H$), 7.08–6.98 (m, 1H, $C_{Ar}H$), 5.36–4.86 (m, 1H, $C_{i\text{Pr}}H$), 4.11–3.79 (m, 2H, $C_{i\text{Pr}}H$ +CH_2CO_2Me), 3.67 (s, 3H, CO_2Me), 3.17 (d, *J*=16.1 Hz, 1H, CH_2CO_2Me), 2.07 (dd, *J*=16.1, 10.2 Hz, 1H, CH), 1.37 (s, 9H, $C_{t\text{Bu}}H_3$), 1.32–1.18 (m, 12H, $C_{i\text{Pr}}H_3$).

^{13}C NMR (101 MHz, $CDCl_3$, 265K) δ 172.2 (CO_2Me), 145.6 (C_q), 144.1 (C_q), 143.9 (C_q), 139.4 (C_q), 125.5 ($C_{Ar}H$), 123.5 ($C_{Ar}H$), 122.0 ($C_{Ar}H$), 121.1 ($C_{Ar}H$), 50.6 (OCH_3), 46.6 (br, $C_{i\text{Pr}}H$), 44.5 (br, $C_{i\text{Pr}}H$), 44.3 (CH_2C=O), 37.3 ($C_{t\text{Bu,q}}$), 33.1 ($CHCH_2C$=O), 29.9 (CH_3), 22.5 (br, CH_3), 18.5 (br, CH_3).

IR (ν_{max}, cm^{-1}) 2976 (m), 2914 (m), 1744 (m), 1632 (w), 1464 (m), 1419 (m), 1397 (m), 1363 (m), 1346 (m), 1234 (s), 1156 (s), 1022 (m), 926 (w), 887 (w), 770 (m), 747 (m).

HRMS (ESI–TOF): Calculated (MH+) 371.2654; Found 371.2651.

Methyl 2-(3-(3,3-dicyclohexyltriaz-1-en-1-yl)-2-methyl-1*H*-inden-1-yl)acetate (**2.2h**)



[Rh(cod)Cl]$_2$ (6 mg, 12 µmol, 0.03 eq., 6 mol% [Rh]), KOH (4 mg, 0.06 mmol, 0.3 eq.) and 3,3-dicyclohexyl-1-(prop-1-yn-1-yl)triaz-1-ene (97 mg, 39 mmol, 1.0 eq.) were dissolved in THF/water (40:1, 1 mL) and stirred for 5 min at 0 °C. Methyl (*E*)-3-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)acrylate (130 mg, 0.45 mmol, 1.2 eq.) was added and a color change could immediately be observed. The reaction flask was sealed and allowed to warm to RT and stirring was continued overnight. The reaction was heated at 50 °C for 6 h. The reaction mixture was filtered over a plug of deactivated silica (NEt_3, eluent: DCM) and the solvent was removed under vacuum. Purification by flash column chromatography with a gradient of 0 – 100 % Et_2O in pentane gave the product as a mixture of isomers in the form of an orange oil (88 mg, 0.22 mmol, 55 %, >20:1).[8]

^{1}H NMR (400 MHz, $CDCl_3$, 298 K) δ 7.34–7.28 (m, 1H, $C_{Ar}H$), 7.26–7.23 (m, 2H, $C_{Ar}H$), 7.16–6.96 (m, 2H, $C_{Ar}H$), 5.09–4.85 (m, 1H, CH_{Cy}), 4.17 (d, *J* = 10.2 Hz, 1H,), 3.74 (s, 3H, CO_2Me), 3.54–3.38 (m, 1H, CH_{Cy}), 3.19 (dd, *J* = 15.9, 2.9 Hz, 1H, $CHCH_2$COOMe), 2.23 (s, 3H, CH_3), 2.10 (dd, *J* = 15.9, 10.6 Hz, 1H, $CHCH_2CO_2Me$), 1.87–1.66 (m, 13H, $CH_{2\ Cy}$), 1.46 – 1.29 (m, 7H, $CH_{2\ Cy}$).

[8] An impurity, which could not be separated, possibly the minor isomer is detected in the ^{1}H NMR spectrum. At RT, the $C_{Cy}H$-signals are broadened in both ^{1}H and ^{13}C-NMR.

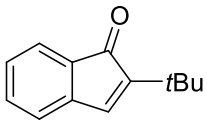
^{13}C NMR (101 MHz, $CDCl_3$, 265K) δ 173.9 (CO_2Me), 153.6 (C_q), 145.9 (C_q), 144.7 (C_q), 127.0 ($C_{Ar}H$), 126.9 (C_q), 124.5 ($C_{Ar}H$), 123.0 ($C_{Ar}H$), 118.5 ($C_{Ar}H$), 51.7 (OCH_3), 42.2 (CH_2CO_2Me), 36.8 ($CHCH_2CO_2Me$), 34.3 (br, CH_{Cy}), 30.2 (br, CH_{Cy}), 26.3 (br, $CH_{2\ Cy}$), 9.6 (CH_3).

IR (ν_{max}, cm^{-1}) 2926 (s), 2853 (m), 1734 (m), 1399 (s), 1334 (s), 1254 (s), 1202 (s), 1137 (s), 989 (s), 759 (s).

HRMS (ESI–TOF): Calculated (MH+) 410.2808; Found 410.2806.

7.2.4. Products of Acid Induced Cleavage

2-(*tert*-Butyl)-1*H*-inden-1-one (**2.3**)



Compound **2.1a** (31mg, 0.1 mmol, 1.0 eq., mixture of isomers as indicated above) was dissolved in Et_2O (0.5 mL). Trifluoroacetic acid (22.6 µL, 34.2 mg, 0.3mmol, 3.0 eq.) was added and the mixture was stirred at RT for 4 h. The reaction mixture was quenched by $NaHCO_3$ (sat. aq., 1 mL) and extracted with EtOAc (3 x 1 mL). The combined organic phases were dried over $MgSO_4$ and the solvent was removed under vacuum. Purification by flash column chromatography on silica with a gradient of 0 – 100 % Et_2O in pentane gave the product in the form of a yellow oil (10 mg, 0.054 mmol, 54 %). The spectroscopic data are in good agreement with literature reports.[157]

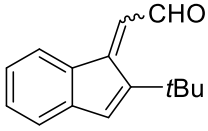
^{1}H NMR (400 MHz, $CDCl_3$, 298 K) δ 7.57 – 7.42 (m, 3H, $C_{Ar}H$), 7.30 (t, J = 7.4 Hz, 1H, $C_{Ar}H$), 7.13 (d, J = 7.1 Hz, 1H, $C_{Ar}H$), 1.44 (s, 9H, $C_{t\text{Bu}}H_3$).

^{13}C NMR (101 MHz, $CDCl_3$, 298 K) δ 198.1 (C=O) 148.9 (C_q), 144.0 (C_q), 140.9 (CH), 133.8 (CH), 131.6 (C_q), 128.1 (CH), 122.5 (CH), 121.3 (CH), 32.2 ($C_{t\text{Bu,q}}$), 29.14 ($C_{t\text{Bu}}H_3$).

IR (ν_{max}, cm^{-1}) 2987 (w), 2897 (w), 1705 (w), 1604 (w), 1397 (w), 1296 (w), 1240 (w), 1050 (w), 910 (s), 719 (s).

HRMS (APCI): Calculated (MH+) 187.1117; Found 187.1116.

2-(2-(*tert*-Butyl)-1*H*-inden-1-ylidene)acetaldehyde (**2.4**)



Compound **2.2a** (50.2 mg, 0.147 mmol, 1 eq.) was dissolved in acetonitrile (2 mL). Trifluoroacetic acid (27.3 µL, 368 µmol, 2.5 eq.) was added and the mixture was stirred at 60 °C for 18.5 h. The mixture was diluted with EtOAc (30 mL), washed with H_2O (2 x 10 mL), $NaHCO_3$ (sat. aq., 1 x 10 mL) and NaCl (sat. aq. 1 x 10 mL), dried over $MgSO_4$ and the solvent was removed under vacuum. Purification by flash column chromatography on silica with a gradient of 17 – 50 % DCM in pentane gave the product in the form of an orange solid (14.0 mg, 66.1µmol, 45 %).

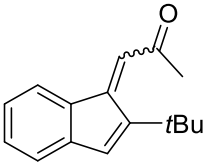
^{1}H NMR (400 MHz, $CDCl_3$, 298 K) δ 10.79 (d, *J* = 7.9 Hz, 1H, CHO), 7.68 (d, *J* = 7.5 Hz, 1H, C*H*-CHO), 7.25 (td, *J* = 7.5, 1.0 Hz, 1H, $C_{Ar}H$), 7.14–7.06 (m, 2H, $C_{Ar}H$), 6.74 (d, *J* = 7.8 Hz, 1H, $C_{Ar}H$), 6.67 (s, 1H, HC=C-*t*Bu), 1.35 (s, 9H, $C_{tBu}H_3$).

^{13}C NMR (101 MHz, $CDCl_3$, 298 K) δ 191.2 (C=O), 154.3 ($C_{Ar,q}$), 152.4 (C_{sp2}-*t*Bu), 143.2 ($C_{Ar,q}$), 135.2 (*C*=CH-CHO), 133.8 (H*C*=C-tBu), 130.6 ($C_{Ar}H$), 128.9 (*C*H-CHO), 126.4 ($C_{Ar}H$), 126.0 ($C_{Ar}H$), 121.4 ($C_{Ar}H$), 33.1 ($C_{tBu,q}$), 31.3 ($C_{tBu}H_3$).

IR (ν_{max}, cm^{-1}) 3060 (w), 2967 (w), 2957 (w), 2910 (w), 2871 (w), 1712 (w), 1657 (s), 1597 (w), 1479 (w), 1464 (w), 1397 (w), 1368 (w), 1324 (w), 1242 (w), 1170 (w), 1152 (m), 1120 (s), 1083 (m), 1024 (w), 939 (w), 890 (w), 865 (m), 773 (m), 747 (s).

HRMS (APPI/LTQ-Orbitrap): Calculated (M+) 212.1196; Found 212.1205.

1-(2-(*tert*-Butyl)-1*H*-inden-1-ylidene)propan-2-one (**2.5**)



Compound **2.2e** (49.5 mg, 0.139 mmol, 1 eq., mixture of isomers as indicated above) was dissolved in acetonitrile (2.4 mL). Trifluoroacetic acid (25.9 µL, 349 µmol, 2.5 eq.) was added and the mixture was heated at 60 °C for 48 h. The reaction was quenched with $NaHCO_3$ (sat. aq., 5 mL) and extracted with EtOAc (3 x 15 mL). The combined organic phases were dried over $MgSO_4$ and the solvent was removed under vacuum. Purification by flash column chromatography on silica with a gradient of 17–33 % DCM in pentane gave the product as an orange oil (14.9 mg, 0.0657 mmol, 47 %).

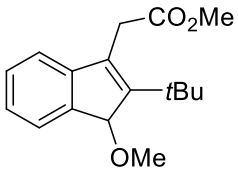
^{1}H NMR (400 MHz, CDCl3, 298 K) δ 8.07 – 7.97 (m, 1H, $C_{Ar}H$), 7.18 (td, *J* = 7.6, 7.2, 1.0 Hz, 1H, $C_{Ar}H$), 7.10–7.02 (m, 2H, $C_{Ar}H$), 6.91 (s, 1H, C*H*(CH_3)O), 6.63 (s, 1H, HC=C-*t*Bu), 2.47 (s, 3H, CH_3), 1.37 (s, 9H, $C_{tBu}H_3$).

^{13}C NMR (101 MHz, $CDCl_3$, 298 K) δ 200.8 (C=O), 151.5 (C_{sp2}-*t*Bu), 146.0 (*C*=CH-$COCH_3$), 143.0 ($C_{Ar,q}$), 134.6 ($C_{Ar,q}$), 132.2 (H*C*=C-*t*Bu), 130.0 ($C_{Ar}H$), 128.0 (*C*H-$COCH_3$), 126.3 ($C_{Ar}H$), 125.5 ($C_{Ar}H$), 120.5 ($C_{Ar}H$), 33.1 ($C_{tBu,q}$), 32.2 (CO*C*H_3), 31.7 ($C_{tBu}H_3$).

IR (ν_{max}, cm^{-1}) 3068 (w), 2965 (m), 2936 (w), 2909 (w), 2869 (w), 1689 (s), 1610 (m), 1595 (m), 1583 (m), 1457 (s), 1366 (s), 1354 (s), 1289 (w), 1289 (w), 1241 (w), 1195 (s), 1178 (s), 975 (m), 859 (m), 774 (m), 749 (s).

HRMS (APPI/LTQ-Orbitrap): Calculated (MH+) 171.0804; Found 171.0806.

Methyl 2-(2-(*tert*-butyl)-1-methoxy-1*H*-inden-3-yl)acetate (**2.6**)



Compound **2.2g** (37 mg, 0.1 mmol, 1.0 eq., mixture of isomers as indicated above) was dissolved in methanol (2 mL). HBF_4 in Et_2O (40 µL, 7.5 M, 0.3 mmol, 3.0 eq.) was added and the reaction mixture was stirred at 40 °C for 2 days. The reaction mixture was quenched with K_2CO_3 (69 mg, 0.5 mmol, 5.0 eq.), filtered and the solvent was removed under vacuum. Purification by flash column chromatography on silica with 50 % Et_2O in pentane gave the product in the form of a yellow oil (23 mg, 7.8 mmol, 60 %).

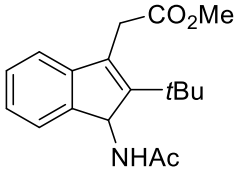
^{1}H NMR (400 MHz, $CDCl_3$, 298 K) δ 7.33 (d, *J* = 7.2 Hz, 1H, $C_{Ar}H$), 7.24–7.15 (m, 1H, $C_{Ar}H$), 7.12–6.99 (m, 2H, $C_{Ar}H$), 5.16–5.01 (m, 1H, CH), 3.68 – 3.64 (m, 2H, CH_2), 3.61 (s, 3H, COOMe), 2.97 (s, 3H, OMe), 1.30 (s, 9H, CH_3).

^{13}C NMR (101 MHz, $CDCl_3$, 298 K) δ 171.3 (CO_2Me), 151.6 (C_q), 145.2 (C_q), 140.8 (C_q), 132.0 (C_q), 128.5 ($C_{Ar}H$), 125.5 ($C_{Ar}H$), 123.4 ($C_{Ar}H$), 118.5 ($C_{Ar}H$), 84.1 (CHOMe), 52.3 (OCH_3), 51.2 (OCH_3), 34.0 (CH_2), 32.9 ($C_{tBu,q}$), 30.8 ($C_{tBu}H_3$).

IR (ν_{max}, cm^{-1}) 2970 (m), 2903 (w), 1727 (w), 1470 (w), 1391 (w), 1369 (w), 1246 (w), 1195 (m), 1167 (m), 1066 (m), 910 (s), 725 (s).

HRMS (ESI–TOF): Calculated (MNa+) 298.1468; Found 298.1467.

Methyl 2-(1-acetamido-2-(*tert*-butyl)-1*H*-inden-3-yl)acetate (**2.7**)



Compound **2.2g** (48 mg, 0.13 mmol, 1.0 eq., mixture of isomers as indicated above) was dissolved in wet acetonitrile (2 mL). HBF_4 in Et_2O (40 µL, 7.5 M, 0.3 mmol, 3.0 eq.) was added and the reaction mixture was stirred at 40 °C for 2 days. The reaction mixture was quenched with K_2CO_3 (69 mg, 0.5 mmol, 3.8 eq.), filtered and the solvent was removed under vacuum. Purification by flash column chromatography on silica with a gradient of 60–100 % EtOAc in pentane gave the product in the form of a white solid (23 mg, 7.8 mmol, 60 %). Crystals suitable for X-ray diffraction were grown by layering a saturated solution of **8** in CH_2Cl_2 with pentane.

^{1}H NMR (400 MHz, $CDCl_3$, 298 K) δ 7.30–7.25 (m, 1H, $C_{Ar}H$), 7.22–7.15 (m, 1H, $C_{Ar}H$), 7.10–7.04 (m, 2H, $C_{Ar}H$), 5.89 (d, *J* = 9.9 Hz, 1H, C*H*NH), 5.43 (d, *J* = 9.6 Hz, 1H, CHN*H*), 3.83–3.66 (m, 5H, CH_2+CO_2CH_3), 2.04 (s, 3H, CH_3C=O), 1.33 (s, 9H, CH_3).

^{13}C NMR (101 MHz, $CDCl_3$, 298 K) δ 170.2 (CO_2Me), 168.8 (NHC=O), 150.8 (C_q), 143.4 (C_q), 142.6 (C_q), 130.8 (C_q), 127.0 ($C_{Ar}H$), 124.8 ($C_{Ar}H$), 121.8 ($C_{Ar}H$), 117.4 ($C_{Ar}H$), 56.8 (CHNH), 51.1 (CH_2), 33.0 (CHNH), 31.7 ($C_{tBu,q}$), 30.0 ($C_{tBu}H_3$), 22.6 (OCH_3).

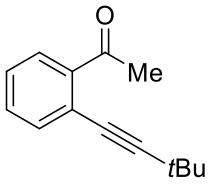
IR (ν_{max}, cm^{-1}) 3239 (w), 3049 (w), 2959 (m), 2914 (w), 1733 (s), 1643 (s), 1542 (s), 1470 (m), 1430 (s), 1369 (s), 1318 (m), 1302 (m), 1268 (m), 1212 (m), 1201 (s), 1162 (s), 999 (m), 971 (m), 792 (w), 758 (s).

HRMS (ESI–TOF): Calculated (MNa+) 324.1586; Found 324.1576.

1-(2-(3,3-Dimethylbut-1-yn-1-yl)phenyl)ethan-1-one (**2.8**) and 2-(tert-Butyl)-3-methyl-1*H*-inden-1-one (**2.9**)

A Falcon tube was charged with compound **2.1f** (30.9 mg, 93.8 µmol, 1 eq.). A mixture of *n*-pentane (1.8 mL) and tetrahydrofuran (0.2 mL) was added and the mixture was homogenized by sonication. Hydrogen fluoride pyridine (70 % HF, 60.9 µL, 2.34 mmol, 25 eq.) was added and the mixture was heated to 30 °C for 1 h. The reaction was quenched with calcium gluconate (1.01 g, 2.34 mmol, 25 eq.). The resulting slurry was filtered and rinsed with EtOAc (40 mL). The solvent was removed under vacuum. Purification by flash column chromatography on silica with a gradient of 3–4 % Et_2O in pentane gave **2.8** (7.9 mg, 0.039 mmol, 42 %) in the form of a faint purple liquid and **2.9 (**4.6 mg, 0.023 mmol, 24 %) in the form of a yellow solid. The spectroscopic data are in good agreement with literature reports.[158]

2.8:



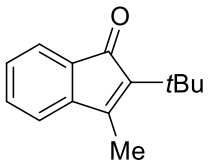
^{1}H NMR (400 MHz, CDCl3, 298 K) δ 7.66 (dd, *J* = 7.8, 1.5 Hz, 1H, $C_{Ar}H$), 7.47 (dd, *J* = 7.7, 1.4 Hz, 1H, $C_{Ar}H$), 7.39 (td, *J* = 7.5, 1.5 Hz, 1H, $C_{Ar}H$), 7.32 (td, *J* = 7.6, 1.4 Hz, 1H, $C_{Ar}H$), 2.74 (s, 3H, CH_3), 1.33 (s, 9H, $C_{tBu}H_3$).

^{13}C NMR (101 MHz, $CDCl_3$, 298 K) δ 201.5 (C=O), 141.2 ($C_{Ar,q}$-C_{sp}), 134.0 ($C_{Ar}H$), 131.2 ($C_{Ar}H$), 128.4 ($C_{Ar}H$), 127.7 ($C_{Ar}H$), 122.6 ($C_{Ar,q}$-C=O), 104.8 (C_{sp}-$C_{Ar,q}$), 78.6 (C_{sp}-*t*Bu), 30.8 ($C_{tBu}H_3$), 30.4 (CH_3), 28.4 ($C_{tBu,q}$).

IR (ν_{max}, cm^{-1}) 2968 (m), 2927 (w), 2869 (w), 2235 (w), 1684 (s), 1594 (w), 1473 (m), 1441 (w), 1357 (m), 1278 (m), 1234 (m), 1201 (w), 1010 (w), 963 (m), 801 (m), 760 (s).

HRMS (ESI/QTOF): Calculated (MH+) 201.1274; Found 201.1276.

2.9:



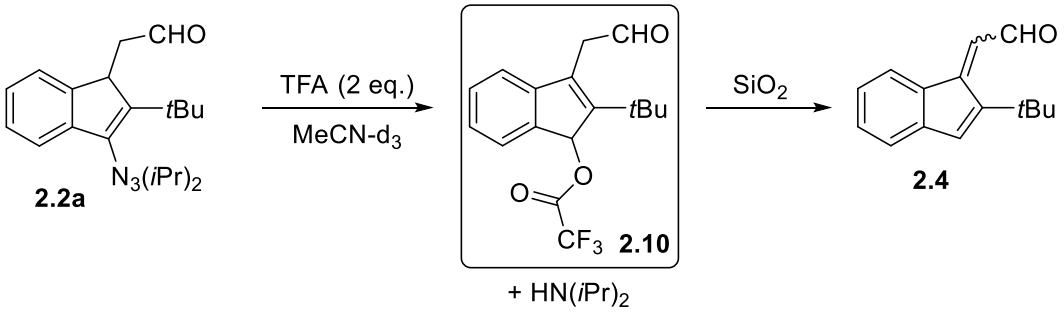
^{1}H NMR (400 MHz, CDCl3, 298 K) δ 7.36 – 7.29 (m, 2H, $C_{Ar}H$), 7.16 (td, *J* = 7.2, 0.9 Hz, 1H, $C_{Ar}H$), 7.05 (d, *J* = 7.5 Hz, 1H, $C_{Ar}H$), 2.29 (s, 3H, CH_3) 1.36 (s, 9H, $C_{tBu}H_3$).

^{13}C NMR (101 MHz, $CDCl_3$, 298 K) δ 198.7 (C=O), 151.2 (C_{sp2}-Me), 147.0 ($C_{Ar,q}$), 140.3 (C_{sp2}-*t*Bu), 133.3 ($C_{Ar}H$), 130.7 ($C_{Ar,q}$), 128.2 ($C_{Ar}H$), 121.3 ($C_{Ar}H$), 118.5 ($C_{Ar}H$), 34.0 ($C_{tBu,q}$), 30.6 ($C_{tBu}H_3$), 13.3 (CH_3).

IR (ν_{max}, cm^{-1}) 2955 (m), 2918 (w), 2868 (w), 1701 (s), 1605 (m), 1457 (m), 1312 (m), 1184 (w), 1126 (w), 1083 (w), 997 (w), 881 (w), 755 (s), 718 (m).

HRMS (ESI/QTOF): Calculated (MH+) 201.1274; Found 201.1276.

7.2.5. Characterization of Intermediate **2.10**



In an NMR-tube, **2.2a** (10.2 mg, 30.0 µmol, 1 eq.) was dissolved in CD_3CN (0.5 mL). Addition of trifluoroacetic acid (2.22 µL, 29.9 µmol, 1 eq.) led to an incomplete reaction with starting material and intermediate **2.10** being observed by ^1H NMR and ^{13}C NMR. Further addition of trifluoroacetic acid (2.22 µL, 29.9 µmol, 1.0 eq.) resulted in complete conversion to **2.10**, which was characterized in situ by NMR spectroscopy. The mixture was subsequently diluted with EtOAc (20 mL), washed with H_2O (3 x 10 mL), dried over $MgSO_4$ and freeze dried to give an orange-brown solid, which was stored at – 20 °C. Attempted purification by flash column chromatography on silica with a gradient of 0 – 50 % DCM in pentane resulted in a roughly 1:1 mixture of **10** and **2.4** according to ^1H-NMR, suggesting transformation of **2.10** to **2.4** on the column.

In situ:

^{1}H NMR (400 MHz, CD_3CN) δ 9.75 (t, *J* = 1.2 Hz, 1H, C*H*O), 7.39–7.32 (m, 2H, $C_{Ar}H$), 7.20 (td, *J* = 7.5, 1.0 Hz, 1H, $C_{Ar}H$), 7.14 (d, *J* = 7.6 Hz, 1H, $C_{Ar}H$), 6.58 (s, 1H, C*H*OCOCF$_3$), 3.98 (d, *J* = 18.0 Hz, 1H, C*H*$_2$CHO), 3.89 (d, *J* = 18.0 Hz, 1H, C*H*$_2$CHO), 3.42 (hept, *J* = 6.4 Hz, 3H, NCH), 1.29 -128 (m, 26 H, $C_{tBu}H_3$ (9H)+ $C_{iPr}H_3$ (17 H),overlapping).[9]

^{13}C NMR (101 MHz, CD_3CN) δ 199.4 (CHO), 150.0 (C_{sp2}-*t*Bu), 146.0 (CAr,q), 139.5 (CAr,q), 135.6 (*C*$_{sp2}$-CH$_2$CHO), 130.9 ($C_{Ar}H$), 127.5 ($C_{Ar}H$), 124.8 ($C_{Ar}H$), 120.3 ($C_{Ar}H$), 82.9 (*C*HOCOCF$_3$), 48.3 ($C_{iPrNH2}H$), 43.0 (*C*H$_2$CHO), 34.2 *C*$_{tBu,q}$), 30.8 (*C*$_{tBu}$*H*$_3$), 19.2 ($C_{iPrNH2}H_3$).

After column chromatography:

^{19}F NMR (376 MHz, CDCl3) *δ* (ppm) – 74.95.

HRMS (APCI): Calculated (M+) 326.1124; Found 326.1132.

[9] The 1:1.4 ratio of **12** to *i*Pr$_2$NH suggests the formation of side products.

7.3. Experimental Details for Chapter 3

7.3.1. General Information

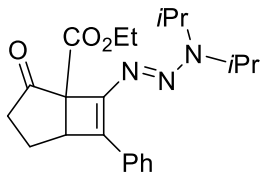
Cyclopentenone and cyclohexenone were dried over molecular sieves prior to use. Iodomethane was degassed using standard freeze-pump-thaw technique.

α-Unsaturated β-ketoesters,[159] and phenyl vinyl ketone[160] were synthesized as described in the literature.

Melting points were acquired using a Edmund Bueler SP6 apparatus and are uncorrected.

7.3.2. Synthesis of 1-Vinyl Triazenes 3.1a–g

Ethyl 7-(3,3-diisopropyltriaz-1-en-1-yl)-2-oxo-6-phenylbicyclo[3.2.0]hept-6-ene-1-carboxylate (**3.1a**)



$CuOTf{\cdot}C_6H_6$ (13.0 mg, 25.8 μmol, 2.5 mol%), ethyl 5-oxocyclopent-1-ene-1-carboxylate (156 mg, 1.01 mmol, 1 eq.), and 3,3-diisopropyl-1-(phenylethynyl)triaz-1-ene (280 mg, 1.21 mmol, 1.2 eq.) were dissolved in dichloromethane (10 mL). The mixture was stirred at RT under exclusion of light. The reaction was determined complete by TLC after 2 h 15 min. The mixture was filtered over cotton and the solvent was removed under vacuum. Purification by flash chromatography with a gradient of 5 – 10 % EtOAc in pentane gave the product as a yellow solid. (327 mg, 853 μmol, 85 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (dd, *J* = 8.1, 1.5 Hz, 2H, $C_{Ph}H$), 7.37 (t, *J* = 7.7 Hz, 2H, $C_{Ph}H$), 7.25 – 7.19 (m, 1H, $C_{Ph}H$), 5.27 (br s, 1H, $C_{iPr}H$), 4.33 – 4.08 (m, 2H, $C_{Et}H_2$), 3.95 (s, 1H, $C_{iPr}H$), 3.83 – 3.72 (m, 1H, $C_{sp3}H$), 2.89 (ddd, *J* = 18.0, 12.0, 9.4 Hz, 1H, $C_{sp3}HH$), 2.42 – 2.09 (m, 3H, $C_{sp3}H_2$), 1.39 – 1.25 (m, 12H, $C_{iPr}H_3$), 1.22 (t, *J* = 7.1 Hz, 4H, $C_{Et}H_3$).

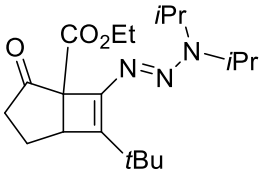
^{13}C NMR (101 MHz, $CDCl_3$) δ 208.4 (CO), 169.4 (COOEt), 142.0 (C_{sp2}-N_3*i*Pr_2), 133.9 (C_{sp2}-Ph), 128.6 ($C_{Ph}H$), 127.2 ($C_{Ph}H$), 127.0 ($C_{Ph,q}$), 63.1 ($C_{sp3,q}$), 60.8 ($C_{Et}H_2$), 49.8 ($C_{iPr}H$), 46.9 ($C_{iPr}H$), 45.8 ($C_{sp3}H$), 36.1 ($C_{sp3}H_2$), 23.5 ($C_{iPr}H_3$), 23.4 ($C_{iPr}H_3$), 21.6 ($C_{sp3}H_2$), 19.4 ($C_{iPr}H_3$), 19.3 ($C_{iPr}H_3$), 14.4 ($C_{Et}H_3$).

IR (ν_{max}, cm^{-1}) 2974 (s), 2934 (s), 2873 (s), 1744 (s), 1732 (s), 1636 (s), 1407 (s), 1377 (s), 1338 (s), 1292 (s), 1249 (s), 1156 (s), 1023 (s), 913 (s), 753 (s), 729 (s).

Mp: 107 °C.

HRMS (ESI/QTOF) *m/z*: $[M + Na]^+$ Calcd for $C_{22}H_{29}N_3NaO_3^+$ 406.2101; Found 406.2103.

Ethyl 6-(tert-butyl)-7-(3,3-diisopropyltriaz-1-en-1-yl)-2-oxobicyclo[3.2.0]hept-6-ene-1-carboxylate (**3.1b**)



3.1b was synthesized analogously to **3.1a** from ethyl 5-oxocyclopent-1-ene-1-carboxylate (15.4 mg, 100 µmol, 1 eq.) and 1-(3,3-dimethylbut-1-yn-1-yl)-3,3-diisopropyltriaz-1-ene (26mg, 124 µmol, 1.2 eq.) within 4 h 30 min. The product was obtained as a yellow solid (27.2 mg, 74.8 µmol, 75 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.96 (hept, *J* = 6.9 Hz, 1H, $C_{i\mathrm{Pr}}H$), 4.25 – 4.03 (m, 2H, $C_{\mathrm{Et}}H_2$), 3.85 (hept, *J* = 6.7 Hz, 1H, $C_{i\mathrm{Pr}}H$), 3.43 – 3.34 (m, 1H, $C_{sp3}H$), 2.92 (ddd, *J* = 17.6, 12.2, 9.3 Hz, 1H, C_{sp3}*H*H), 2.29 – 2.15 (m, 1H, C_{sp3}*H*H), 2.12 – 2.01 (m, 2H, $C_{sp3}H$), 1.27 (dd, *J* = 22.4, 6.3 Hz, 5H), 1.26 (s, 9H, $C_{t\mathrm{Bu}}H_3$), 1.21 (t, *J* = 7.1 Hz, 3H $C_{\mathrm{Et}}H_3$)., 1.15 (dd, *J* = 6.8, 3.9 Hz, 6H), 1.30 (d, *J* = 6.6 Hz, 3H, $C_{i\mathrm{Pr}}H_3$), 1.26 (s, 9H, $C_{t\mathrm{Bu}}H_3$), 1.24 (d, *J* = 6.0 Hz, 3H, $C_{i\mathrm{Pr}}H_3$), 1.21 (t, *J* = 7.1 Hz, 3H, $C_{\mathrm{Et}}H_3$), 1.15 (d, *J* = 6.7 Hz, 3H, $C_{i\mathrm{Pr}}H_3$), 1.14 (d, J = 6.3 Hz, 3H, $C_{i\mathrm{Pr}}H_3$).

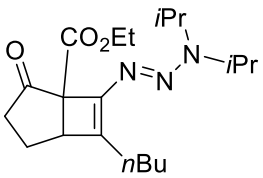
^{13}C NMR (101 MHz, $CDCl_3$) δ 209.1 (CO), 169.7 (CO_2Et), 140.9 (C_{sp2}-N_3*i*Pr_2), 139.1 (C_{sp2}-*t*Bu), 62.1 ($C_{sp3,q}$), 60.5 ($C_{\mathrm{Et}}H_2$), 49.4 ($C_{i\mathrm{Pr}}H$), 46.6 ($C_{sp3}H$), 46.4 ($C_{i\mathrm{Pr}}H$), 35.8 ($C_{sp3}H_2$), 34.1 ($C_{t\mathrm{Bu,q}}$), 29.2 ($C_{t\mathrm{Bu}}H_3$), 23.4 ($C_{i\mathrm{Pr}}H_3$), 22.8 ($C_{sp3}H_2$), 19.3 ($C_{i\mathrm{Pr}}H_3$), 19.2 ($C_{i\mathrm{Pr}}H_3$), 14.4 ($C_{\mathrm{Et}}H_3$).

IR (ν_{max}, cm^{-1}) 2968 (s), 2933 (s), 2870 (s), 1735 (s), 1463 (s), 1408 (s), 1365 (s), 1312 (s), 1290 (s), 1244 (s), 1197 (s), 1158 (s), 1111 (s), 1072 (s), 1029 (s), 961 (s).

Mp: 35 °C.

HRMS (ESI/QTOF) *m*/*z*: $[M + Na]^+$ Calcd for $C_{20}H_{33}N_3NaO_3^+$ 386.2414; Found 386.2409.

Ethyl 6-butyl-7-(3,3-diisopropyltriaz-1-en-1-yl)-2-oxobicyclo[3.2.0]hept-6-ene-1-carboxylate (**3.1c**)



3.1c was synthesized analogously to **3.1a** from ethyl 5-oxocyclopent-1-ene-1-carboxylate (14.9 mg, 96.8 µmol, 1 eq.) and 1-(3,3-dimethylbut-1-yn-1-yl)-3,3-diisopropyltriaz-1-ene (25.2 mg, 120 µmol, 1.2 eq.) within 2 h 30 min. The product was obtained as a yellow solid (20.5 mg, 56.4 µmol, 58 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.08 (br s, 1H, $C_{i\mathrm{Pr}}H$), 4.25 – 4.02 (m, 2H, $C_{\mathrm{Et}}H_2$), 3.84 (br s, 1H, $C_{i\mathrm{Pr}}H$), 3.33 (d, *J* = 6.7 Hz, 1H, $C_{sp3}H$), 2.87 (ddd, *J* = 17.8, 11.9, 9.4 Hz, 1H, C_{sp3}*H*H), 2.39 (dt, *J* = 15.5, 7.7 Hz, 1H, C_{sp3}-C*H*H), 2.33 – 2.19 (m, 2H, C_{sp3}*H*H + C_{sp2}-C*H*H), 2.12 – 1.91 (m, 2H, $C_{sp3}CH_2$), 1.62 (p, *J* = 7.4 Hz, 2H, C_{sp2}-CH_2-CH_2), 1.41 (hd, *J* = 7.3, 2.1 Hz, 2H, C_{sp2}-CH_2-CH_2-CH_2), 1.34 – 1.04 (m, 12H, $C_{i\mathrm{Pr}}H_3$), 1.22 (t, *J* = 7.1 Hz, 3H, $C_{\mathrm{Et}}H_3$), 0.93 (t, *J* = 7.3 Hz, 3H, $C_{n\mathrm{Bu}}H_3$).

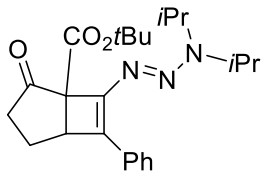
^{13}C NMR (101 MHz, CDCl3) δ 209.1 (CO), 169.6 (COOEt), 142.7 (C_{sp2}-N_3*i*Pr_2), 132.5 (C_{sp2}-*n*Bu), 63.0 ($C_{sp3,q}$), 60.6 ($C_{Et}H_2$), 49.1 ($C_{i Pr}H$), 47.5 ($C_{sp3}H$), 45.9 ($C_{i Pr}H$), 36.0 ($C_{sp3}H_2$), 29.4 (C_{sp2}-CH_2-*C*H_2), 26.8 (C_{sp2}-*C*H_2-CH_2), 23.4 ($C_{i Pr}H_3$), 22.9 (C_{sp2}-CH_2-CH_2-C*H*$_2$), 21.2 ($C_{sp3}H_2$), 19.4 ($C_{i Pr}H_3$), 14.4 ($C_{Et}H_3$), 14.0 ($C_{n Bu}H_3$).

IR (ν_{max}, cm^{-1}) 2969 (s), 2933 (s), 2873 (s), 1735 (s), 1467 (s), 1408 (s), 1366 (s), 1246 (s), 1157 (s), 1118 (s), 1032 (s).

Mp: 47 °C.

HRMS (ESI/QTOF) *m*/*z*: $[M + Na]^+$ Calcd for $C_{20}H_{33}N_3NaO_3^+$ 386.2414; Found 386.2432.

tert-Butyl 7-(3,3-diisopropyltriaz-1-en-1-yl)-2-oxo-6-phenylbicyclo[3.2.0]hept-6-ene-1-carboxylate (**3.1d**)



3.1d was synthesized analogously to **3.1a** from tert-butyl 5-oxocyclopent-1-ene-1-carboxylate (18.4 mg, 101 µmol, 1 eq.) and 3,3-diisopropyl-1-(phenylethynyl)triaz-1-ene (26.7 mg, 116 µmol, 1.2 eq.) within 2 h 10 min. The product was obtained as a yellow solid (37.4 mg, 90.9 µmol, 90 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 – 7.65 (m, 2H, $C_{Ph}H$), 7.36 (dd, *J* = 7.7 Hz, 2H, $C_{Ph}H$), 7.25 – 7.19 (m, 1H, $C_{Ph}H$), 5.31 – 5.15 (br m, 1H, $C_{i Pr}H$), 3.95 (br s, 1Hz, $C_{i Pr}H$), 3.72 (dd, *J* = 6.2, 1.5 Hz, 1H, $C_{sp3}H$), 2.85 (ddd, *J* = 17.4, 11.6, 9.3 Hz, 1H, C_{sp3}*H*H), 2.33 – 2.12 (m, 3H, C_{sp3}*H*H + $C_{sp3}H_2$), 1.44 (s, 9H, $C_{t Bu}H_3$), 1.36 (d, *J* = 6.3 Hz, 6H, $C_{i Pr}H_3$), 1.25 (d, *J* = 6.8 Hz, 6H, $C_{i Pr}H_3$).

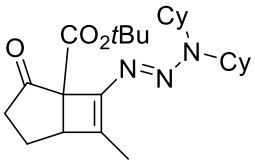
^{13}C NMR (101 MHz, $CDCl_3$) δ 208.7 (CO), 168.6 (CO_2*t*Bu), 142.3 (C_{sp2}-N_3*i*Pr_2), 134.1 (C_{sp2}-Ph), 128.5 ($C_{Ph}H$), 127.0 ($C_{Ph}H$), 126.9 ($C_{Ph}H$), 126.9 ($C_{Ph,q}$), 80.8 ($C_{tBu,q}$), 64.3 ($C_{sp3,q}$), 49.9 ($C_{i Pr}H$), 46.8 ($C_{i Pr}H$), 45.9 ($C_{sp3}H$), 36.2 ($C_{sp3}H_2$), 28.2 ($C_{t Bu}H_3$), 23.6 ($C_{i Pr}H_3$), 23.4 ($C_{i Pr}H_3$), 21.6 ($C_{sp3}H_2$), 19.4 ($C_{i Pr}H_3$), 19.2 ($C_{i Pr}H_3$).

IR (ν_{max}, cm^{-1}) 2974 (w), 2934 (w), 2872 (w), 1730 (m), 1368 (s), 1340 (m), 1300 (m), 1250 (s), 1148 (s), 1082 (m), 1024 (m), 910 (m), 730 (s).

Mp: 116 – 119 °C.

HRMS (ESI/QTOF) *m*/*z*: $[M + Na]^+$ Calcd for $C_{24}H_{33}N_3NaO_3^+$ 434.2414; Found 434.2424.

tert-Butyl 7-(3,3-dicyclohexyltriaz-1-en-1-yl)-6-methyl-2-oxobicyclo[3.2.0]hept-6-ene-1-carboxylate (**3.1e**)



3.1e was synthesized analogously to **3.1a** from *tert*-butyl 5-oxocyclopent-1-ene-1-carboxylate (17.8 mg, 97.7 µmol, 1 eq.) and 3,3-dicyclohexyl-1-(prop-1-yn-1-yl)triaz-1-ene (29.3 mg, 118 µmol, 1.2 eq.) within 2 h 10 min. The product was obtained as a yellow solid (36.7 mg, 85.4 µmol, 87 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.84 (br s, 1H, $C_{Cy}H$), 3.33 (m, 1H, $C_{Cy}H$), 3.23 (d, *J* = 6.8 Hz, 1H, $C_{sp3}H$), 2.82 (ddd, *J* = 17.8, 11.7, 9.4 Hz, 1H, $C_{sp3}HH$), 2.21 (ddd, *J* = 17.7, 8.4, 1.7 Hz, 1H, $C_{sp3}HH$), 2.07 – 1.93 (m, 2H, $C_{sp3}H_2$), 1.91 (d, *J* = 1.3 Hz, 3H, CH_3), 1.87 – 1.57 (m, 12H, $C_{Cy}H_2$), 1.42 (s, 9H, $C_{tBu}H_3$), 1.41 – 1.07 (m, 8H, $C_{Cy}H_2$).

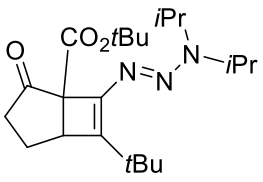
^{13}C NMR (101 MHz, $CDCl_3$) δ 209.4 (CO), 168.9 (CO_2tBu), 143.3 (C_{sp2}-N_3Cy_2), 127.8 (C_{sp2}-Me), 80.5 ($C_{tBu,q}$), 64.8 ($C_{sp3,q}$), 57.8 ($C_{Cy}H$), 53.6 ($C_{Cy}H$), 48.7 ($C_{sp3}H$), 36.0 ($C_{sp3}H_2$), 34.0 ($C_{Cy}H_2$), 33.69 ($C_{Cy}H_2$), 30.0 ($C_{Cy}H_2$), 29.9 ($C_{Cy}H_2$), 28.2 ($C_{tBu}H_3$), 26.3 ($C_{Cy}H_2$), 25.9 ($C_{Cy}H_2$), 25.5 ($C_{Cy}H_2$), 20.6 ($C_{sp3}H_2$), 11.7 ($C_{Me}H_3$).

IR (ν_{max}, cm^{-1}) 2930 (m), 2854 (w), 1732 (m), 1452 (m), 1408 (s), 1368 (m), 1338 (m), 1302 (m), 1254 (s), 1210 (m), 1146 (s), 910 (m), 798 (m), 730 (s).

Mp: 74 °C.

HRMS (ESI/QTOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{25}H_{40}N_3O_3^+$ 430.3064; Found 430.3064.

tert-Butyl 6-(tert-butyl)-7-(3,3-diisopropyltriaz-1-en-1-yl)-2-oxobicyclo[3.2.0]hept-6-ene-1-carboxy-late (**3.1f**)



3.1f was synthesized analogously to **3.1a** from *tert*-butyl 5-oxocyclopent-1-ene-1-carboxylate (17.9 mg, 98.2 µmol, 1 eq.) and 1-(3,3-dimethylbut-1-yn-1-yl)-3,3-diisopropyltriaz-1-ene (24.7 mg, 118 µmol, 1.2 eq.) within 2 h 15 min. The product was obtained as a yellow solid (28.0 mg, 71.5 µmol, 73 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.97 – 4.84 (m, 1H, $C_{iPr}H$), 3.90 – 3.78 (m, 1H, $C_{iPr}H$), 3.32 (dd, *J* = 5.3, 2.1 Hz, 1H, $C_{sp3}H$), 2.89 (ddd, *J* = 17.4, 11.9, 9.5 Hz, 1H, $C_{sp3}HH$), 2.27 – 2.14 (m, 1H, $C_{sp3}HH$), 2.11 – 1.97 (m, 2H, $C_{sp3}H_2$), 1.41 (s, 9H, $C_{O\text{-}tBu}H_3$), 1.30 (d, *J* = 5.9 Hz, 6H, $C_{iPr}H_3$), 1.25 (s, 9H, $C_{tBu}H_3$), 1.15 (d, *J* = 6.9 Hz, 6H, $C_{iPr}H_3$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 209.3 (CO), 168.9 (CO_2tBu), 141.1 (C_{sp2}-N_3iPr_2), 139.1 (C_{sp2}-*t*Bu), 80.3 ($C_{O\text{-}tBu,q}$), 63.0 ($C_{sp3,q}$), 49.6 ($C_{iPr}H$), 46.7 ($C_{sp3}H$), 46.5 ($C_{iPr}H$), 36.0 ($C_{sp3}H_2$), 34.0

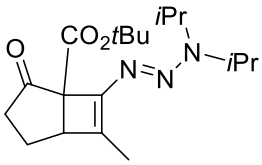
($C_{tBu,q}$), 29.2 ($C_{tBu}H_3$), 28.2 ($C_{O\text{-}tBu}H_3$), 23.5 ($C_{iPr}H_3$), 23.4 ($C_{iPr}H_3$), 22.8 ($C_{sp3}H_2$), 19.3 ($C_{iPr}H_3$), 19.2 ($C_{iPr}H_3$).

IR (ν_{max}, cm^{-1}) 2968 (m), 2932 (w), 2870 (w), 1732 (s), 1460 (w), 1406 (s), 1366 (m), 1296 (m), 1244 (s), 1152 (s), 1110 (s), 1074 (m), 1028 (m), 998 (m), 964 (w), 920 (w), 874 (w), 844 (w), 818 (w), 732 (w).

Mp: 44 °C.

HRMS (ESI/QTOF) *m*/*z*: $[M + Na]^+$ Calcd for $C_{22}H_{37}N_3NaO_3^+$ 414.2727; Found 414.2721.

tert-Butyl 7-(3,3-diisopropyltriaz-1-en-1-yl)-6-methyl-2-oxobicyclo[3.2.0]hept-6-ene-1-carboxylate (**3.1g**)



3.1g was synthesized analogously to **3.1a** from *tert*-butyl 5-oxocyclopent-1-ene-1-carboxylate (18.1 mg, 99.3 µmol, 1 eq.) and 3,3-diisopropyl-1-(prop-1-yn-1-yl)triaz-1-ene (20.2 mg, 121 µmol, 1.22 eq.) within 2 h 10 min. The product was obtained as a yellow oil (28.0 mg, 71.5 µmol, 75 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.14 (br s, 1H, $C_{iPr}H$), 3.84 (br s, 1H, $C_{iPr}H$), 3.24 (d, *J* = 6.8 Hz, 1H, $C_{sp3}H$), 2.82 (ddd, *J* = 17.8, 11.8, 9.4 Hz, 1H, $C_{sp3}HH$), 2.21 (ddd, *J* = 17.9, 8.3, 1.7 Hz, 1H, $C_{sp3}HH$), 2.07 – 1.92 (m, 2H), 1.90 (d, *J* = 1.4 Hz, 3H, $C_{Me}H_3$), 1.42 (s, 9H, $C_{tBu}H_3$), 1.28 (d, *J* = 6.4 Hz, 6H, $C_{iPr}H_3$), 1.14 (d, *J* = 6.7 Hz, 6H, $C_{iPr}H_3$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 209.3 (CO), 168.8 (CO_2tBu), 143.3 (C_{sp2}-N_3iPr_2), 128.1 (C_{sp2}-Me), 80.5 ($C_{tBu,q}$), 64.7 ($C_{sp3,q}$), 48.9 ($C_{iPr}H$), 48.7 ($C_{sp3}H$), 45.4 ($C_{iPr}H$), 36.0 ($C_{sp3}H_2$), 28.2 ($C_{tBu}H_3$), 23.6 ($C_{iPr}H_3$), 23.4 ($C_{iPr}H_3$), 20.5 ($C_{sp3}H_2$), 19.5 ($C_{iPr}H_3$), 19.6 ($C_{iPr}H_3$), 11.6 ($C_{Me}H_3$).

IR (ν_{max}, cm^{-1}) 2973 (w), 2933 (w), 2874 (w), 1731 (s), 1408 (s), 1366 (m), 1303 (m), 1248 (s), 1146 (s), 1116 (s), 1092 (m), 1028 (m), 1002 (m), 967 (m), 917 (w), 842 (w), 803 (w), 773 (w), 731 (m).

HRMS (ESI/QTOF) *m*/*z*: $[M + Na]^+$ Calcd for $C_{19}H_{31}N_3NaO_3^+$ 372.2258; Found 372.2269.

7.3.3. Determination of Regioisomer for 1-Vinyl Triazenes 3.1a–g

The structure of products **3.1a** – **g** was corroborated by ^{1}H-^{13}C-HSQC spectroscopy. In **3.1b**, for example, the protons from both the CH_2-group adjacent to the bridgehead (2.12 – 2.01 ppm (m, 2H)) and the *t*Bu-group (1.26 ppm (s, 9H)) couple to the same vinylic carbon (139.1 ppm) (Figure 7.1). Such a coupling pattern requires the reported isomer **A**. In case of isomer **B**, the respective protons would each couple to different vinylic protons (139.1 ppm and 140.9 ppm), which is not observed.

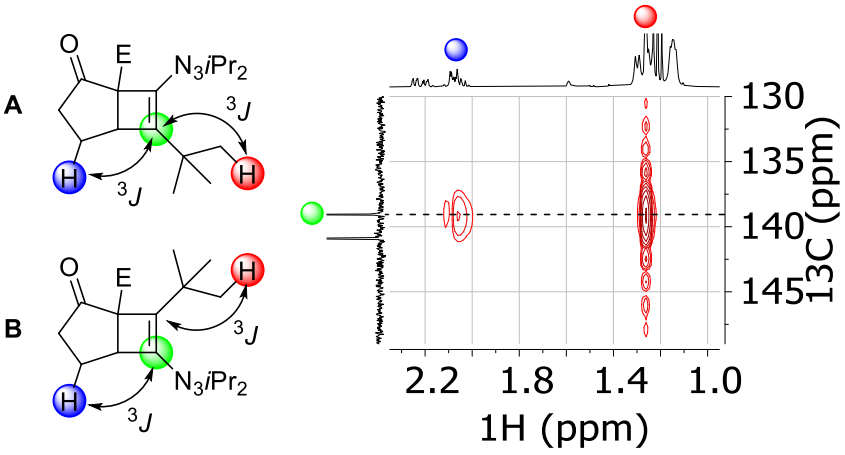
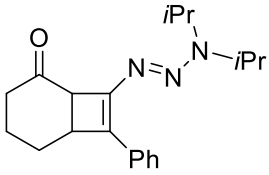


Figure 7.1. Left: Possible regioisomers and coupling partners of the vinylic carbons of **3.1b**. E = CO_2Et Right: Section of the ^{1}H-^{13}C-HSQC spectrum showing the actual coupling pattern.

7.3.4. Synthesis of 1-Vinyl Triazenes 3.2a–j

8-(3,3-Diisopropyltriaz-1-en-1-yl)-7-phenylbicyclo[4.2.0]oct-7-en-2-one (**3.2a**)



Tris(pentafluorophenyl)borane (5.6 mg, 11 µmol, 2.5 mol%.), 3,3-diisopropyl-1-(phenylethynyl)triaz-1-ene (100 mg, 437 µmol, 1 eq.) and 2-cyclohexen-1-one (106 µL, 1.09 mmoles, 2.5 eq.) were dissolved in toluene (2 mL). The mixture was stirred at RT for 24 h. K_2CO_3 (sat. aq., 5.4 µL) was added and the mixture was stirred vigorously for 20 min. The mixture was then filtered over a plug of $MgSO_4$ and basic alumina and eluted with Et_2O. The solvent was removed under vacuum. Purification by flash chromatography with a gradient of 0 – 15 % Et_2O in pentane gave the product in the form of a yellow solid (139 mg, 428 µmol, 98 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 – 7.64 (m, 2H, $C_{Ph}H$), 7.35 (t, *J* = 7.7 Hz, 2H, $C_{Ph}H$), 7.25 – 7.15 (m, 1H, $C_{Ph}H$), 5.23 (hept, *J* = 6.8 Hz, 1H, $C_{iPr}H$), 3.92 (hept, *J* = 6.6 Hz, 1H, $C_{iPr}H$), 3.76 (dd, *J* = 4.8, 1.8 Hz, 1H, $C_{CO\text{-}sp3}H$), 3.58 (td, *J* = 4.8, 2.0 Hz, 1H, $C_{sp3}H$), 2.55 – 2.44 (m, 1H, $C_{sp3}HH$), 2.28 – 2.17 (m, 2H, 2 x $C_{sp3}HH$), 2.16 – 2.00 (m, 1H, $C_{sp3}HH$), 1.77 – 1.61 (m, 2H, $C_{sp3}H_2$), 1.33 (d, *J* = 6.6 Hz, 3H, $C_{iPr}H_3$), 1.29 – 1.20 (m, 9H, $C_{iPr}H_3$).

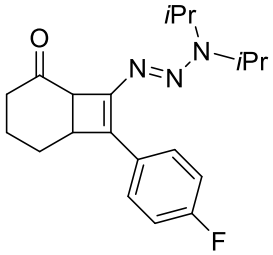
^{13}C NMR (101 MHz, $CDCl_3$) δ 212.8 (CO), 142.6 (C_{sp2}-N_3iPr_2), 134.6 ($C_{Ph,q}$), 128.5 ($C_{Ph}H$), 127.2 (C_{sp2}-Ph), 126.9 ($C_{Ph}H$), 126.6 ($C_{Ph}H$), 53.8 ($C_{CO\text{-}sp3}H$), 49.6 ($C_{iPr}H$), 46.7 ($C_{iPr}H$), 38.9 ($C_{sp3}H_2$), 38.2 ($C_{sp3}H$), 25.2 ($C_{sp3}H_2$), 23.5 ($C_{iPr}H_3$), 23.3 ($C_{iPr}H_3$), 19.3 ($C_{iPr}H_3$), 18.3 ($C_{sp3}H_2$).

IR (ν_{max}, cm^{-1}) 2973 (w), 2933 (w), 2905 (w), 2876 (w), 2852 (w), 1699 (s), 1633 (w), 1492 (w), 1448 (m), 1379 (s), 1338 (m), 1249 (s), 1155 (s), 1114 (m), 1095 (m), 1031 (m), 977 (m), 758 (s).

Mp: 97 °C.

HRMS (ESI/QTOF) *m*/*z*: [M + H]+ Calcd for C20H28N3O+ 326.2227; Found 326.2229.

8-(3,3-Diisopropyltriaz-1-en-1-yl)-7-(4-fluorophenyl)bicyclo[4.2.0]oct-7-en-2-one (**3.2b**)



3.2b was synthesized analogously to **3.2a** from 1-((4-fluorophenyl)ethynyl)-3,3-diisopropyltriaz-1-ene (59.5 mg, 241 µmol, 1 eq.) and 2-cyclohexen-1-one (58 µL, 599 µmol, 2.5 eq.). The product was obtained as a highly viscous yellow liquid (70.0 mg, 203 µmol, 85 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 – 7.58 (m, 2H, $C_{Ph}H$), 7.11 – 6.97 (m, 2H, $C_{Ph}H$), 5.21 (hept, *J* = 6.8 Hz, 1H, $C_{iPr}H$), 3.92 (hept, *J* = 6.6 Hz, 1H, $C_{iPr}H$), 3.75 (dd, *J* = 4.8, 1.7 Hz, 1H, $C_{CO\text{-}sp3}H$), 3.54 (td, *J* = 4.6, 4.2, 1.8 Hz, 1H, $C_{sp3}H$), 2.54 – 2.42 (m, 1H, $C_{sp3}HH$), 2.29 – 2.14 (m, 2H2 x $C_{sp3}HH$), 2.14 – 1.97 (m, 1H, $C_{sp3}HH$), 1.78 – 1.60 (m, 2H, $C_{sp3}H_2$), 1.32 (d, *J* = 6.6 Hz, 3H, $C_{iPr}H_3$), 1.28 – 1.18 (m, 9H, $C_{iPr}H_3$).

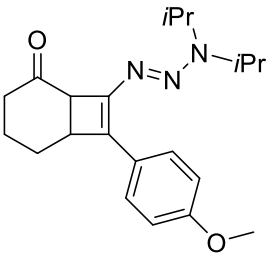
^{13}C NMR (101 MHz, $CDCl_3$) δ 212.5 (CO), 161.7 (d, *J* = 246.7 Hz, $C_{Ph}F$), 142.0 (d, *J* = 2.8 Hz, C_{sp2}-N_3iPr_2), 131.0 (d, *J* = 3.4 Hz, $C_{Ph,q}$), 128.5 (d, *J* = 7.7 Hz, $C_{Ph}H$), 126.1 (d, *J* = 1.4 Hz, C_{sp2}-Ph), 115.5 (d, *J* = 21.5 Hz, $C_{Ph}H$), 53.7 ($C_{CO\text{-}sp3}H$), 49.6 ($C_{iPr}H$), 46.6 ($C_{iPr}H$), 38.9 ($C_{sp3}H_2$), 38.2 ($C_{sp3}H$), 25.1 ($C_{sp3}H_2$), 23.5 ($C_{iPr}H_3$), 23.3 ($C_{iPr}H_3$), 19.3 ($C_{iPr}H_3$), 18.3 ($C_{sp3}H_2$).

^{19}F NMR (377 MHz, $CDCl_3$) δ – 114.6.

IR (ν_{max}, cm^{-1}) 2974 (w), 2935 (w), 2907 (w), 2878 (w), 1700 (m), 1636 (w), 1506 (s), 1380 (s), 1331 (s), 1251 (s), 1232 (s), 1154 (s), 1113 (m), 1095 (m), 979 (m), 839 (s), 731 (m).

HRMS (ESI/QTOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{20}H_{27}FN_3O^+$ 344.2133; Found 344.2125.

8-(3,3-Diisopropyltriaz-1-en-1-yl)-7-(4-methoxyphenyl)bicyclo[4.2.0]oct-7-en-2-one (**3.2c**)



3.2c was synthesized analogously to **3.2a** from 3,3-diisopropyl-1-((4-methoxyphenyl)ethynyl)triaz-1-ene (62.3 mg, 240 µmol, 1 eq.) and cyclohexen-1-one (58 µL, 599 µmol, 2.5 eq.) using tris(penta-fluorophenyl)-borane (6.1 mg, 12 µmol, 5 mol%). The product was obtained as a yellow solid (68.1 mg, 192 µmol, 80 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 – 7.58 (m, 2H, $C_{Ph}H$), 6.95 – 6.87 (m, 2H, $C_{Ph}H$), 5.21 (hept, *J* = 6.8 Hz, 1H, $C_{iPr}H$), 3.91 (hept, *J* = 6.6 Hz, 1H, $C_{iPr}H$), 3.83 (s, 3H, O-$C_{Me}H_3$), 3.74 (dd, *J* = 4.8, 1.7 Hz, 1H, $C_{CO\text{-}sp3}H$), 3.53 (m, 1H, $C_{sp3}H$), 2.48 (dd, *J* = 18.4, 7.6 Hz, 1H, $C_{sp3}HH$), 2.21 (m, 2H 2 x $C_{sp3}HH$), 2.08 (dddd, *J* = 18.1, 16.7, 9.4, 4.0 Hz, 1H, $C_{sp3}HH$), 1.72 (dt, *J* = 13.5, 3.9 Hz, 1H, $C_{sp3}HH$), 1.68 – 1.58 (m, 1H, $C_{sp3}HH$), 1.32 (d, *J* = 6.5 Hz, 3H, $C_{iPr}H_3$), 1.24 (m, 9H, $C_{iPr}H_3$).

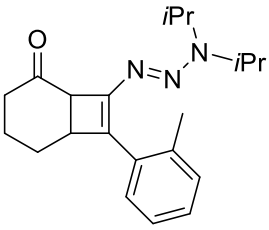
^{13}C NMR (101 MHz, $CDCl_3$) δ 213.0 (CO), 158.5 (C_{Ph}-OMe), 140.5 (C_{sp2}-N_3*i*Pr_2), 128.3 ($C_{Ph}H$), 127.7 ($C_{Ph,q}$), 127.1 (C_{sp2}-Ph), 114.1 ($C_{Ph}H$), 55.4 (O-$C_{Me}H_3$), 53.8 ($C_{CO\text{-}sp3}H$), 49.4 ($C_{i\text{Pr}}H$), 46.4 ($C_{i\text{Pr}}H$), 38.9 ($C_{sp3}H_2$), 38.2 ($C_{sp3}H$), 25.2 ($C_{sp3}H_2$), 23.5 ($C_{i\text{Pr}}H_3$), 23.3 ($C_{i\text{Pr}}H_3$), 19.4 ($C_{i\text{Pr}}H_3$), 18.3 ($C_{sp3}H_2$).

IR (ν_{max}, cm^{-1}) 2972 (w), 2933 (w), 2837 (w), 1700 (m), 1605 (w), 1508 (m), 1392 (m), 1333 (m), 1243 (s), 1157 (m), 1034 (m), 979 (m), 836 (m).

Mp: 91 °C.

HRMS (ESI/QTOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{21}H_{30}N_3O_2^+$ 356.2333; Found 356.2346.

8-(3,3-Diisopropyltriaz-1-en-1-yl)-7-(o-tolyl)bicyclo[4.2.0]oct-7-en-2-one (**3.2d**)



3.2d was synthesized analogously to **3.2a** from 3,3-diisopropyl-1-(o-tolylethynyl)triaz-1-ene (58.3 mg, 240 µmol, 1 eq.) and 2-cyclohexen-1-one (58 µL, 599 µmol, 2.5 eq.). The product was obtained as a yellow, highly viscous resin (60.8 mg 179 µmol, 75 %).

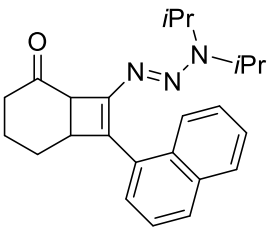
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 – 7.52 (m, 1H, $C_{Ph}H$), 7.24 – 7.10 (m, 3H, $C_{Ph}H$), 5.13 (hept, *J* = 6.9 Hz, 1H, $C_{i\text{Pr}}H$), 3.90 (hept, *J* = 6.5 Hz, 1H, $C_{i\text{Pr}}H$), 3.78 (dd, *J* = 4.8, 1.8 Hz, 1H, $C_{CO\text{-}sp3}H$), 3.70 (td, *J* = 3.8, 3.2, 1.4 Hz, 1H, $C_{sp3}H$), 2.54 (s, 3H, $C_{Ph\text{-}Me}H_3$), 2.57 – 2.46 (m, 1H, C_{sp3}*H*H), 2.22 (dddd, *J* = 18.5, 10.3, 8.5, 1.9 Hz, 1H, C_{sp3}*H*H), 2.15 – 1.91 (m, 2H, $C_{sp3}H_2$), 1.72 – 1.58 (m, 2H, $C_{sp3}H_2$), 1.32 (d, *J* = 6.6 Hz, 3H, $C_{i\text{Pr}}H_3$), 1.26 (d, *J* = 6.6 Hz, 3H, $C_{i\text{Pr}}H_3$), 1.20 (d, *J* = 6.8 Hz, 3H, $C_{i\text{Pr}}H_3$), 1.16 (d, *J* = 6.8 Hz, 3H, $C_{i\text{Pr}}H_3$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 212.9 (CO), 142.4 (C_{sp2}-N_3*i*Pr_2), 136.4 ($C_{Ph,q}$), 133.7 (C_{Ph}-Me), 130.9 ($C_{Ph}H$), 129.1 ($C_{Ph}H$), 128.4 (C_{sp2}-Ph), 127.1 ($C_{Ph}H$), 125.6 ($C_{Ph}H$), 53.4 ($C_{CO\text{-}sp3}H$), 49.4 ($C_{i\text{Pr}}H$), 46.6 ($C_{i\text{Pr}}H$), 40.2 ($C_{sp3}H$), 38.9 ($C_{sp3}H_2$), 25.2 ($C_{sp3}H_2$), 23.5 ($C_{i\text{Pr}}H_3$), 23.4 ($C_{i\text{Pr}}H_3$), 21.6 ($C_{Ph\text{-}Me}H_3$), 19.4 ($C_{i\text{Pr}}H_3$), 19.2 ($C_{i\text{Pr}}H_3$), 18.5 ($C_{sp3}H_2$).

IR (ν_{max}, cm^{-1}) 2972 (w), 2933 (w), 2874 (w), 2852 (w), 1696 (m), 1392 (s), 1380 (s), 1316 (m), 1249 (s), 1156 (s), 1103 (m), 1034 (m), 977 (m), 908 (m), 753 (s), 731 (s).

HRMS (ESI/QTOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{21}H_{30}N_3O^+$ 340.2383; Found 340.2374.

8-(3,3-Diisopropyltriaz-1-en-1-yl)-7-(naphthalen-1-yl)bicyclo[4.2.0]oct-7-en-2-one (**3.2e**)



3.2e was synthesized analogously to **3.2a** from 3,3-diisopropyl-1-(naphthalen-1-ylethynyl)triaz-1-ene (150 mg, 538 µmol, 1 eq.) and cyclohexen-1-one (130 µL, 1.34 mmol, 2.5 eq.) using tris(pentafluorophenyl)-borane (13.8 mg, 27.0 µmol, 5 mol%) within 16 h. The product was obtained as a yellow solid (135 mg, 359 µmol, 67 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.21 – 8.63 (m, 1H, $C_{Naph}H$), 7.87 – 7.83 (m, 1H $C_{Naph}H$), 7.78 – 7.73 (m, 1H $C_{Naph}H$), 7.63 (dd, *J* = 7.3, 1.2 Hz, 1H $C_{Naph}H$), 7.48 (m, 3H $C_{Naph}H$), 5.14 (hept, *J* = 6.8 Hz, 1H, $C_{iPr}H$), 3.96 (hept, *J* = 6.6 Hz, 1H, overlapping with following m), 3.91 – 3.86 (m, 2H, $C_{CO\text{-}sp3}H$, $C_{sp3}H$), 2.65 – 2.52 (m, 1H, $C_{sp3}HH$), 2.26 (dddd, *J* = 18.3, 10.1, 8.5, 1.7 Hz, 1H, $C_{sp3}HH$), 2.17 – 2.01 (m, 2H, 2 x $C_{sp3}HH$), 1.71 (tt, *J* = 13.6, 3.5 Hz, 1H, $C_{sp3}HH$), 1.66 – 1.59 (m, 1H, $C_{sp3}HH$), 1.35 (d, *J* = 6.5 Hz, 3H, $C_{iPr}H_3$), 1.30 (d, *J* = 6.6 Hz, 3H, $C_{iPr}H_3$), 1.28 (d, *J* = 6.8 Hz, 3H, $C_{iPr}H_3$), 1.18 (d, *J* = 6.8 Hz, 3H, $C_{iPr}H_3$).

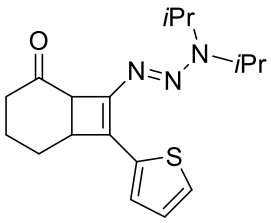
^{13}C NMR (101 MHz, $CDCl_3$) δ 212.8 (CO), 142.6 (C_{sp2}-N_3iPr_2), 134.2 ($C_{Naph,q}$), 132.1 ($C_{Naph,q}$), 131.2 ($C_{Naph,q}$), 128.4 ($C_{Naph}H$), 127.9 ($C_{Naph}H$), 127.5 ($C_{Naph}H$), 127.1 (C_{sp2}-Naph), 126.3 ($C_{Naph}H$), 125.9 ($C_{Naph}H$), 125.8 ($C_{Naph}H$), 125.6 ($C_{Naph}H$), 53.2 ($C_{CO\text{-}sp3}H$), 49.8 ($C_{iPr}H$), 47.1 ($C_{iPr}H$), 39.8 ($C_{sp3}H$), 39.0 ($C_{sp3}H_2$), 24.9 ($C_{sp3}H_2$), 23.5 ($C_{iPr}H_3$), 23.4 ($C_{iPr}H_3$), 19.4 ($C_{iPr}H_3$), 19.2 ($C_{iPr}H_3$), 18.6 ($C_{sp3}H_2$).

IR (ν_{max}, cm^{-1}) 3044 (w), 2973 (w), 2934 (w), 2874 (w), 2853 (w), 1700 (m), 1404 (s), 1391 (s), 1379 (s), 1366 (m), 1314 (m), 1253 (s), 1156 (m), 1129 (m), 1102 (m), 1033 (m), 803 (m), 779 (s).

Mp: 58 °C.

HRMS (ESI/QTOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{24}H_{30}N_3O^+$ 376.2383; Found 376.2385.

8-(3,3-Diisopropyltriaz-1-en-1-yl)-7-(thiophen-2-yl)bicyclo[4.2.0]oct-7-en-2-one (**3.2f**)



3.2f was synthesized analogously to **3.2a** from 3,3-diisopropyl-1-(thiophen-2-ylethynyl)triaz-1-ene (56.5 mg, 240 µmol, 1 eq.) and 2-cyclohexen-1-one (58 µL, 600 µmol, 2.5 eq.) using tris(pentafluorophenyl)borane (12.3 mg, 24.0 µmol, 10 mol%). The product was obtained as a yellow-brown oil (41.5 mg, 125 µmol, 52 %).

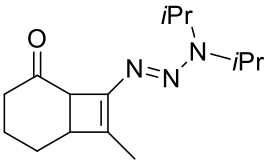
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.23 (m, 1H, $C_{Thioph}H$), 7.10 – 7.06 (m, 1H, $C_{Thioph}H$), 7.03 (dd, *J* = 5.1, 3.6 Hz, 1H, $C_{Thioph}H$), 5.18 (hept, *J* = 6.7 Hz, 1H, $C_{iPr}H$), 3.93 (hept, *J* = 6.6 Hz, 1H, $C_{iPr}H$), 3.78 (dd, *J* = 4.8, 1.7 Hz, 1H, $C_{CO\text{-}sp3}H$), 3.55 (dt, *J* = 6.5, 3.5 Hz, 1H, $C_{sp3}H$), 2.63 – 2.41 (m, 1H, $C_{sp3}HH$), 2.31 – 2.01 (m, 3H, 3 x $C_{sp3}HH$), 1.78 – 1.62 (m, 2H 2 x $C_{sp3}HH$), 1.32 (d, *J* = 6.6 Hz, 3H, $C_{iPr}H_3$), 1.29 – 1.21 (m, 9H, $C_{iPr}H_3$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 212.0 (CO), 139.3 (C_{sp2}-N_3iPr_2), 136.8 ($C_{Thioph,q}$), 127.3 ($C_{Thioph}H$), 125.7 ($C_{Thioph}H$), 123.8 ($C_{Thioph}H$), 122.1 (C_{sp2}-Thioph), 54.0 ($C_{CO\text{-}sp3}H$), 49.9 ($C_{iPr}H$), 47.0 ($C_{iPr}H$), 39.4 ($C_{sp3}H$), 39.0 ($C_{sp3}H_2$), 25.2 ($C_{sp3}H_2$), 23.5 ($C_{iPr}H_3$), 23.3 ($C_{iPr}H_3$), 19.3 ($C_{iPr}H_3$), 19.3 ($C_{iPr}H_3$), 18.2 ($C_{sp3}H_2$).

IR (ν_{max}, cm^{-1}) 3103 (w), 3070 (w), 2972 (w), 2933 (w), 2874 (w), 2852 (w), 1699 (s), 1637 (w), 1405 (s), 1391 (s), 1380 (s), 1314 (m), 1253 (s), 1157 (m), 1033 (m).

HRMS (ESI/QTOF) *m/z*: $[M + H]^+$ Calcd for $C_{18}H_{26}N_3OS^+$ 332.1791; Found 332.1797.

8-(3,3-Diisopropyltriaz-1-en-1-yl)-7-methylbicyclo[4.2.0]oct-7-en-2-one (**3.2g**)



3.2g was synthesized analogously to **3.2a** from 3,3-diisopropyl-1-(prop-1-yn-1-yl)triaz-1-ene (500 mg, 2.99 mmol, 1 eq.) and 2-cyclohexen-1-one (720 µL, 7.44 mmol, 2.5 eq.) using tris(pentafluorophenyl)borane (12.3 mg, 24.0 µmol, 10 mol%). The product was obtained as a yellow solid (477 mg, 1.81 mmol, 61 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.12 (br s, 1H, $C_{iPr}H$), 3.82 (br s, 1H, $C_{iPr}H$), 3.60 (dt, *J* = 4.2, 2.1 Hz, 1H, $C_{CO\text{-}sp3}H$), 3.04 (dtq, *J* = 4.2, 2.6, 1.3 Hz, 1H, $C_{sp3}H$), 2.50 – 2.37 (m, 1H, $C_{sp3}HH$), 2.15 (dddd, *J* = 18.0, 10.0, 8.2, 1.8 Hz, 1H, $C_{sp3}HH$), 2.09 – 1.95 (m, 1H, $C_{sp3}HH$), 1.96 – 1.86 (m, 1H, $C_{sp3}HH$), 1.85 (t, *J* = 1.8 Hz, 3H $C_{Me}H_3$), 1.73 – 1.50 (m, 2H, 2 x $C_{sp3}HH$), 1.35 – 1.06 (m, 12H, $C_{iPr}H_3$).

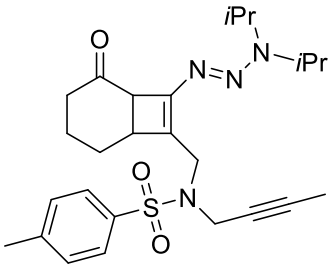
^{13}C NMR (101 MHz, $CDCl_3$) δ 213.3 (CO), 142.7 (C_{sp2}-N_3iPr_2), 128.3 (C_{sp2}-Me), 54.2 ($C_{CO\text{-}sp3}H$), 48.7 ($C_{iPr}H$), 45.3 ($C_{iPr}H$), 40.4 ($C_{sp3}H$), 38.6 ($C_{sp3}H_2$), 24.4 ($C_{sp3}H_2$), 23.4 ($C_{iPr}H_3$), 19.5 ($C_{iPr}H_3$), 18.2 ($C_{sp3}H_2$), 11.3 ($C_{Me}H_3$).

IR (ν_{max}, cm^{-1}) 2971 (w), 2932 (m), 2905 (w), 2849 (w), 1700 (s), 1407 (s), 1366 (m), 1294 (m), 1235 (s), 1159 (m), 1128 (m), 1105 (s), 1028 (s).

Mp: 48 – 52 °C.

HRMS (ESI/QTOF) *m/z*: $[M + H]^+$ Calcd for $C_{15}H_{26}N_3O^+$ 264.2070; Found 264.2069.

N-(But-2-yn-1-yl)-N-((8-(3,3-diisopropyltriaz-1-en-1-yl)-2-oxobicyclo[4.2.0]oct-7-en-7-yl)methyl)-4-methylbenzenesulfonamide (**3.2h**)



3.2h was synthesized analogously to **3.2a** from N-(but-2-yn-1-yl)-N-(3-(3,3-diisopropyltriaz-1-en-1-yl) prop-2-yn-1-yl)-4-methyl-benzenesulfon-amide[10] (50 mg, 129 µmol, 1 eq.) and 2-cyclohexen-1-one (31.2 µL, 322 µmol, 2.5 eq.) using tris(penta-fluorophenyl)borane (6.6 mg, 12.9 µmol, 10 mol%). The product was obtained as an off-white solid (41.0 mg, 84.6 µmol, 66 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 – 7.73 (d, *J* = 8.3 Hz, 2H, $C_{Ph}H$), 7.28 (d, *J* = 8.1 Hz, 2H, $C_{Ph}H$), 5.00 (hept, *J* = 7.0 Hz, 1H, $C_{iPr}H$), 4.22 (dq, *J* = 18.0, 2.4 Hz, 1H, NC*H*H), 4.11 – 3.95 (m, 3H, NC*H*H + NCH_2), 3.86 (hept, *J* = 7.6, 6.9 Hz, 1H, $C_{iPr}H$), 3.60 – 3.55 (m, 1H, $C_{CO\text{-}sp3}H$), 3.16 – 3.09 (m, 1H, $C_{sp3}H$), 2.42 (s, 3H, $C_{Ph\text{-}Me}H_3$), 2.47 – 2.35 (m, 1H, $C_{sp3}HH$), 2.16 (dddd, *J* = 18.3, 10.1, 8.2, 1.7 Hz, 1H, $C_{sp3}HH$), 2.09 – 1.93 (m, 2H, 2 x $C_{sp3}HH$), 1.75 – 1.66 (m, 1H,

[10] The synthesis of this alkynyl triazene is described in 7.5.2.

C_{sp3}*H*H), 1.65 – 1.55 (m, 1H, C_{sp3}*H*H), 1.56 – 1.52 (m, 3H, $C_{C\equiv CMe}H_3$), 1.28 (d, *J* = 6.6 Hz, 3H, $C_{i\mathrm{Pr}}H_3$), 1.20 (d, *J* = 6.6 Hz, 3H, $C_{i\mathrm{Pr}}H_3$), 1.18 – 1.10 (m, 6H, $C_{i\mathrm{Pr}}H_3$).

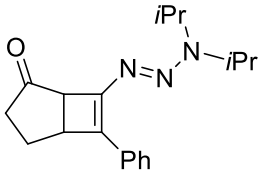
^{13}C NMR (101 MHz, $CDCl_3$) δ 212.0 (CO), 146.5 (C_{sp2}-N_3*i*Pr_2), 143.2 (C_{Ph}-Me), 136.6 ($C_{Ph,q}$), 129.3 (C_{Ph}H), 128.0 (C_{Ph}H), 123.6 (*C*$_{sp2}$-CH_2), 81.4 (C≡C), 72.3 (C≡C), 53.9 ($C_{CO\text{-}sp3}$H), 49.5 ($C_{i\mathrm{Pr}}$H), 46.4 ($C_{i\mathrm{Pr}}$H), 41.8 (C_{sp2}-*C*H_2), 39.1 (C_{sp3}H), 39.0 ($C_{sp3}H_2$), 37.5 (NCH_2), 24.6 ($C_{sp3}H_2$), 23.5 ($C_{i\mathrm{Pr}}H_3$), 23.2 ($C_{i\mathrm{Pr}}H_3$), 21.7 ($C_{Ph\text{-}Me}H_3$), 19.3 ($C_{i\mathrm{Pr}}H_3$), 18.4 ($C_{sp3}H_2$), 3.4 ($C_{C\equiv CMe}H_3$).

IR (ν_{max}, cm^{-1}) 2972 (w), 2934 (w), 2876 (w), 2854 (w), 1700 (m), 1406 (m), 1346 (m), 1304 (m), 1248 (m), 1160 (s), 1094 (m), 994 (w), 902 (w), 740 (w).

Mp: 110 °C.

HRMS (ESI/QTOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{26}H_{37}N_4O_3S^+$ 485.2581; Found 485.2584.

7-(3,3-Diisopropyltriaz-1-en-1-yl)-6-phenylbicyclo[3.2.0]hept-6-en-2-one (**3.2i**)



3.2i was synthesized analogously to **3.2a** from 3,3-diisopropyl-1-(phenylethynyl)triaz-1-ene (54.9 mg, 239 µmol, 1 eq.) and 2-cyclopentenone (50.2 µL, 599 µmol, 2.5 eq.). The product was obtained as a yellow solid (60.8 mg, 195 µmol, 82 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 – 7.65 (m, 2H, C_{Ph}H), 7.36 (t, *J* = 7.6 Hz, 2H, C_{Ph}H), 7.20 (t, *J* = 7.4 Hz, 1H, C_{Ph}H), 5.21 (hept, *J* = 6.8 Hz, 1H, $C_{i\mathrm{Pr}}$H), 3.97 (hept, *J* = 6.6 Hz, 1H, $C_{i\mathrm{Pr}}$H), 3.67 – 3.52 (m, 2H, $C_{CO\text{-}sp3}$H + C_{sp3}H), 2.86 (ddd, *J* = 15.3, 11.2, 8.8 Hz, 1H, C_{sp3}*H*H), 2.26 (dd, *J* = 12.3, 9.0 Hz, 1H, C_{sp3}*H*H), 2.15 – 1.99 (m, 2H, $C_{sp3}H_2$), 1.37 (dd, *J* = 6.6, 1.9 Hz, 6H, $C_{i\mathrm{Pr}}H_3$), 1.25 (dd, *J* = 6.9, 3.9 Hz, 6H, $C_{i\mathrm{Pr}}H_3$).

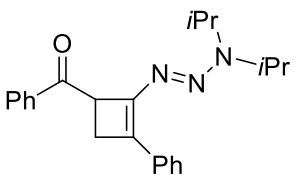
^{13}C NMR (101 MHz, $CDCl_3$) δ 215.1 (CO), 143.8 (C_{sp2}-N_3*i*Pr_2), 134.6 ($C_{Ph,q}$), 128.6 (C_{Ph}H), 127.5 (C_{sp2}-Ph), 126.8 (C_{Ph}H), 126.6 (C_{Ph}H), 52.4 ($C_{CO\text{-}sp3}$H), 49.8 ($C_{i\mathrm{Pr}}$H), 46.8 ($C_{i\mathrm{Pr}}$H), 37.7 (C_{sp3}H), 35.0 ($C_{sp3}H_2$), 23.6 ($C_{i\mathrm{Pr}}H_3$), 23.4 ($C_{i\mathrm{Pr}}H_3$), 22.4 ($C_{sp3}H_2$), 19.4 ($C_{i\mathrm{Pr}}H_3$), 19.3 ($C_{i\mathrm{Pr}}H_3$).

IR (ν_{max}, cm^{-1}) 2973 (w), 2933 (w), 2871 (w), 1733 (s), 1628 (w), 1407 (m), 1390 (s), 1379 (s), 1341 (m), 1251 (s), 1154 (s), 975 (m), 752 (m).

Mp: 81 °C.

HRMS (ESI/QTOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{19}H_{26}N_3O^+$ 312.2070; Found 312.2061.

(2-(3,3-Diisopropyltriaz-1-en-1-yl)-3-phenylcyclobut-2-en-1-yl)(phenyl)methanone (**3.2j**)



3.2j was synthesized analogously to **3.2a** from 3,3-diisopropyl-1-(phenylethynyl)triaz-1-ene (55.0 mg, 240 µmol, 1 eq.) and phenyl vinyl ketone (79.5 mg, 602 µmol, 2.5 eq.). The product was obtained as a yellow solid (35.5 mg, 98.2 µmol, 41 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 – 8.04 (m, 2H, $C_{Ph\text{-}CO}H$), 7.70 – 7.62 (m, 2H, $C_{Ph}H$), 7.57 – 7.51 (m, 1H, $C_{Ph\text{-}CO}H$), 7.50 – 7.41 (m, 2H, $C_{Ph\text{-}CO}H$), 7.38 – 7.30 (m, 2H, $C_{Ph}H$), 7.22 – 7.16 (m, 1H, $C_{Ph}H$), 5.23 (hept, *J* = 6.8, 6.3 Hz, 1H, $C_{i\text{Pr}}H$), 4.89 (dd, *J* = 5.3, 2.3 Hz, 1H, $C_{CO\text{-}sp3}H$), 3.76 (hept, *J* = 6.6 Hz, 1H, $C_{i\text{Pr}}H$), 2.93 (dd, *J* = 12.0, 5.3 Hz, 1H, $C_{sp3}H\mathit{H}$), 2.80 (dd, *J* = 12.0, 2.3 Hz, 1H, $C_{sp3}H\mathit{H}$), 1.25 – 1.17 (m, 6H, $C_{i\text{Pr}}H_3$), 1.07 (d, *J* = 6.6 Hz, 3H, $C_{i\text{Pr}}H_3$), 0.83 (d, *J* = 6.6 Hz, 3H, $C_{i\text{Pr}}H_3$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 199.8 (CO), 145.0 (C_{sp2}-$N_3i\text{Pr}_2$), 137.8 ($C_{Ph\text{-}CO,q}$), 135.2 ($C_{Ph,q}$), 132.7 ($C_{Ph\text{-}CO}H$), 128.6 ($C_{Ph\text{-}CO}H$), 128.5 ($C_{Ph\text{-}CO}H$), 128.3 ($C_{Ph}H$), 126.9 ($C_{Ph}H$), 126.5 ($C_{Ph}H$), 125.7 (C_{sp2}-Ph), 49.0 ($C_{i\text{Pr}}H$), 46.8 ($C_{i\text{Pr}}H$), 45.3 ($C_{CO\text{-}sp3}H$), 29.1 ($C_{sp3}H_2$), 23.3 ($C_{i\text{Pr}}H_3$), 22.9 ($C_{i\text{Pr}}H_3$), 19.3 ($C_{i\text{Pr}}H_3$), 19.3 ($C_{i\text{Pr}}H_3$).

IR (ν_{max}, cm^{-1}) 3058 (w), 3024 (w), 2974 (w), 2930 (w), 2912 (w), 2870 (w), 1252 (s), 1674 (m), 1344 (s), 1214 (s), 1154 (m), 1022 (m), 760 (m), 1378 (s), 1390 (m), 1406 (m), 1448 (m), 1596 (w).

Mp: 137 °C.

HRMS (ESI/QTOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{23}H_{28}N_3O^+$ 362.2227; Found 362.2226.

7.3.5. Determination of Regioisomer for 1-Vinyl Triazenes 3.2a–3.2j

The structure of products **3.2a** – **3.1j** was corroborated by ^{1}H-^{13}C-HSQC spectroscopy. In **3.2b**, for example, one of protons from both the CH_2-group adjacent to the bridgehead (part of the multiplet 1.78 – 1.60 ppm (m, 2H)) and two of the protons from the Ph-group (7.69 – 7.58 ppm (m, 2H)) couple to the same vinylic carbon (126.1 ppm (d, *J* = 1.4 Hz)) (Figure 7.2). Such a coupling pattern requires the reported isomer **A**. In case of isomer **B**, the respective protons would each couple to different vinylic protons (126.1 ppm (d, *J* = 1.4 Hz) and 142.0 ppm (d, *J* = 2.8 Hz)), which is not observed.

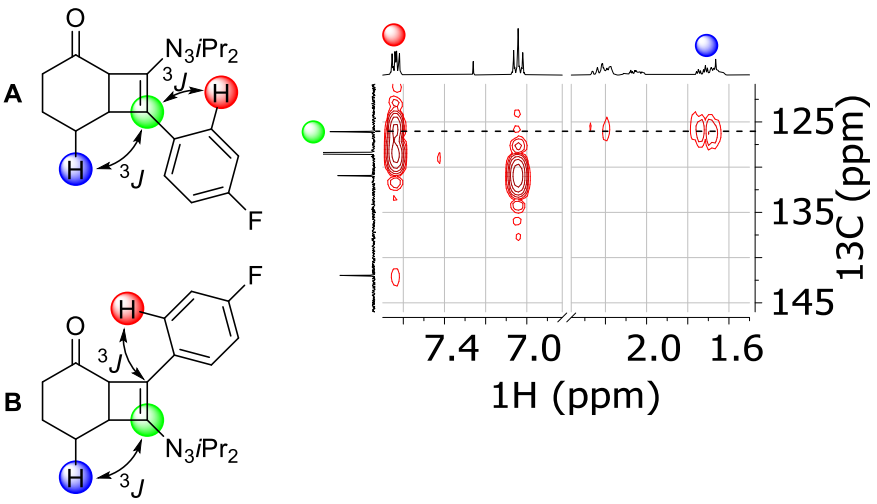
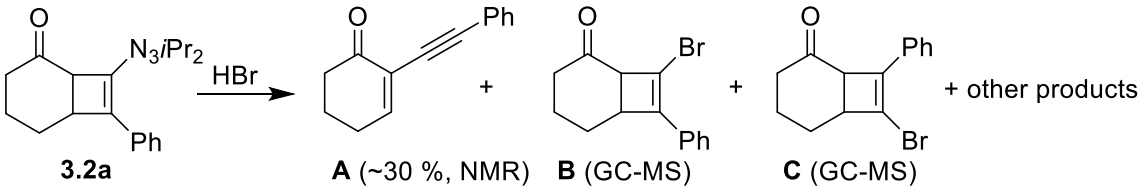


Figure 7.2. Left: Possible regioisomers and coupling partners of the vinylic carbons of **3.2b**. Right: Section of the ^{1}H-^{13}C-HSQC spectrum showing the actual coupling pattern.

7.3.6. Reaction of **3.2a** with HBr

A solution of **3.2a** (15.0 mg, 46.1 µmol, 1 eq.) in Et_2O (0.46 mL) was cooled to 0 °C. HBr (47 % aq., 32.0 µL, 275 µmol, 6 eq.) was added and the mixture was stirred at 0 °C for 1 h. The ice bath was removed and stirring was continued for additional 2 h. The reaction mixture was quenched with K_2CO_3 (38.5 mg, 279 µmol, 6 eq.) and stirred vigorously for 15 min. The mixture was filtered over a plug of silica (rinsed with Et_2O), and the solvent was removed under vacuum. The residue was dissolved in $CDCl_3$ (ca. 0.5 mL) and the solution was transferred into an NMR tube. After addition of nitromethane (1.5 µL, 27.5 µmol, 0.597 eq.) as internal standard, ^{1}H and ^{13}C NMR spectra were recorded.



Scheme 7.1. Reaction of **3.2a** with HBr.

The presence of alkyne **A** was evidenced by ^{13}C NMR signals at 92.2 and 83.9 ppm,[161] and the yield of **A** was estimated by integration of the ^{1}H NMR signal at 7.52 – 7.47 (m).

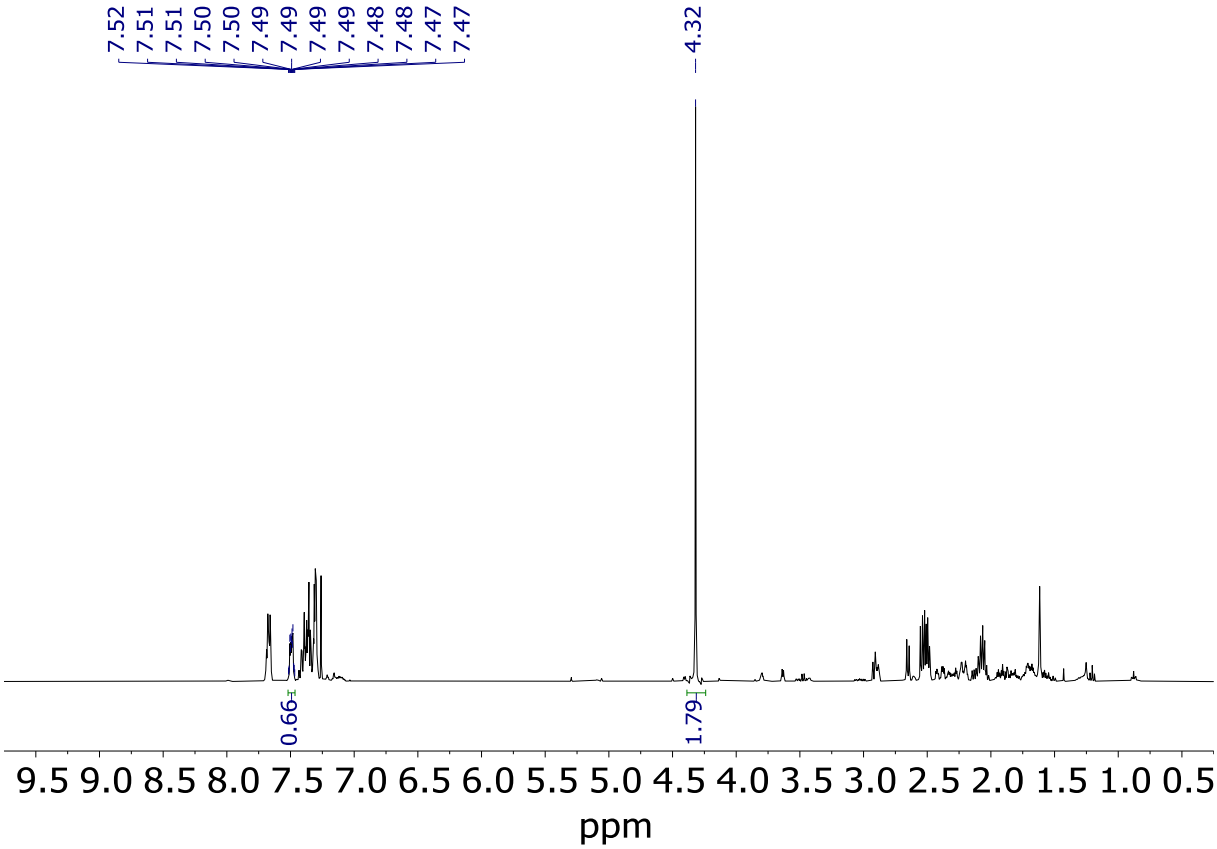
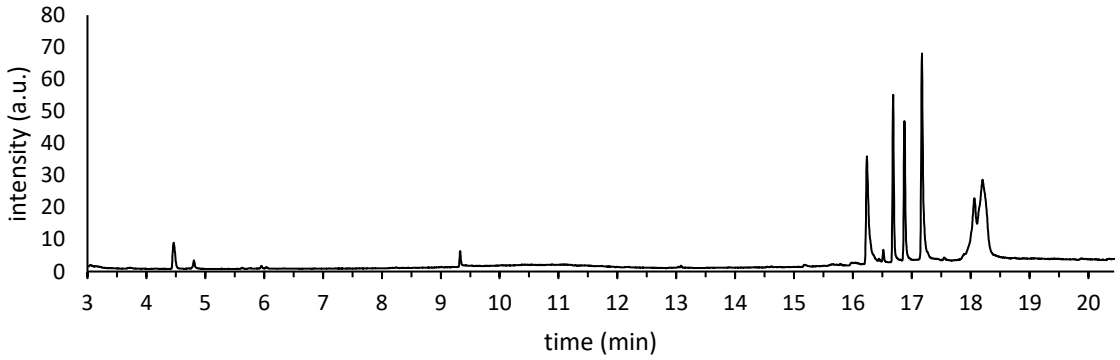


Figure 7.3. ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of crude product with $MeNO_2$ as internal standard

The crude product was also analyzed by GC-MS, and the results are summarized below.



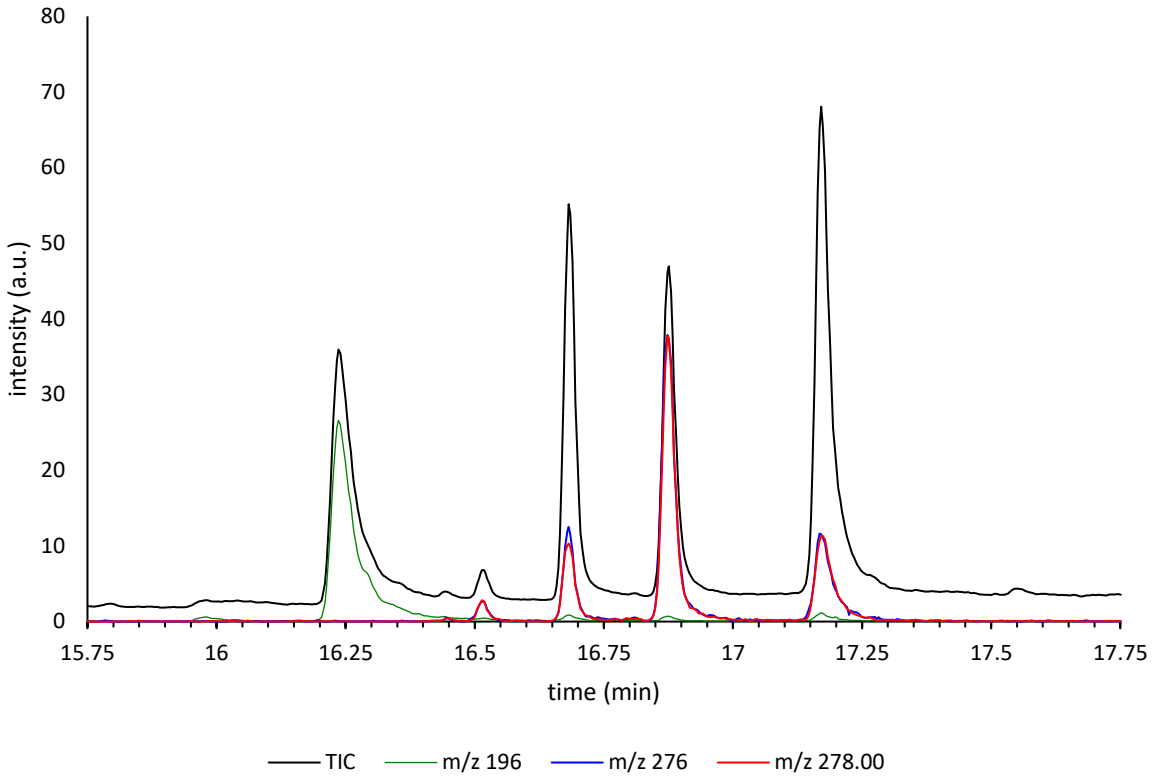
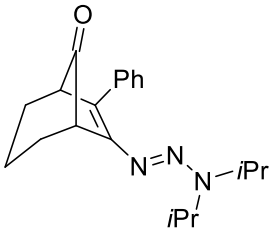


Figure 7.4. Full GC-MS chromatogram of the product mixture (top) and enlarged view on signals with *m*/*z* = 196 (green trace, mass of alkyne **A**) or *m*/*z* = 276, 278 (blue and red trace, mass of brominated products such as **B** and **C**). The compounds responsible for the signals at 18 – 18.5 min could not be identified.

7.3.7. Synthesis 1-Vinyl Triazenes 3.3a–e and 3.4

6-(3,3-Diisopropyltriaz-1-en-1-yl)-7-phenylbicyclo[3.2.1]oct-6-en-8-one (**3.3a**)



A solution of **3.2a** (200 mg, 615 µmol, 1 eq.) in toluene (1 mL) was dried over molecular sieves (10 – 20 vol %) overnight. The solution was diluted with more toluene (8 mL), dimethylaluminium chloride (0.9 M in hexanes, 140 µL, 126 µmol, 0.2 eq.) was added, and the mixture was heated to 50 °C under exclusion of light for 4 h. The mixture was allowed to cool to RT and filtered over a plug of deactivated silica (eluent: Et_2O). The solvent was removed under vacuum. Purification by flash column chromatography on deactivated silica (NEt_3) with 5 % Et_2O in pentane gave the product in the form of a yellow solid (161 mg, 495 µmol, 81 %).

Crystals suitable for X-ray diffraction analysis were obtained by slow evaporation from pentane.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 – 7.86 (m, 2H, $C_{Ph}H$), 7.35 (dd, *J* = 8.5, 7.1 Hz, 2H, $C_{Ph}H$), 7.23 – 7.17 (m, 1H, $C_{Ph}H$), 5.21 (hept, *J* = 6.8 Hz, 1H, $C_{i\text{Pr}}H$), 4.00 (hept, *J* = 6.6 Hz, 1H, $C_{i\text{Pr}}H$), 3.56 (dt, *J* = 4.2, 2.0 Hz, 1H, $C_{sp3}H$), 3.42 (dt, *J* = 4.0, 1.9 Hz, 1H, $C_{sp3}H$), 2.21 – 2.09 (m, 1H, $C_{sp3}HH$), 2.04 – 1.96 (m, 1H, $C_{sp3}HH$), 1.89 (dddd, *J* = 13.4, 11.9, 5.9, 2.1 Hz, 1H, $C_{sp3}HH$), 1.79 (tdd, *J* = 12.7, 5.9, 2.3 Hz, 1H, $C_{sp3}HH$), 1.72 – 1.51 (m, 2H, $C_{sp3}H_2$), 1.38 – 1.22 (m, 12H, $C_{i\text{Pr}}H_3$).

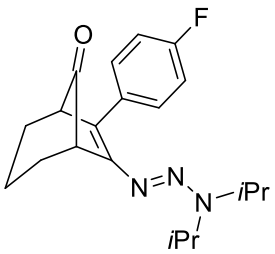
^{13}C NMR (101 MHz, $CDCl_3$) δ 215.9 (CO), 145.1 (C_{sp2}-$N_3i\text{Pr}_2$), 135.3 ($C_{Ph,q}$), 128.4 ($C_{Ph}H$), 128.3 ($C_{Ph}H$), 126.3 ($C_{Ph}H$), 121.1 (C_{sp2}-Ph), 53.4 ($C_{sp3}H$), 51.1 ($C_{sp3}H$), 49.2 ($C_{i\text{Pr}}H$), 47.1 ($C_{i\text{Pr}}H$), 30.2 ($C_{sp3}H_2$), 29.3 ($C_{sp3}H_2$), 23.9 ($C_{i\text{Pr}}H_3$), 23.7 ($C_{i\text{Pr}}H_3$), 19.4 ($C_{i\text{Pr}}H_3$), 18.4 ($C_{sp3}H_2$).

IR (ν_{max}, cm^{-1}) 2974 (m), 2939 (m), 2858 (w), 1760 (s), 1493 (w), 1446 (w), 1396 (m), 1354 (m), 1252 (s), 1155 (m), 1033 (w), 770 (w).

Mp: 86 °C.

HRMS (ESI/QTOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{20}H_{28}N_3O^+$ 326.2227; Found 326.2222.

6-(3,3-Diisopropyltriaz-1-en-1-yl)-7-(4-fluorophenyl)bicyclo[3.2.1]oct-6-en-8-one (**3.3b**)



3.3b was synthesized analogously to **3.3a** from a dried solution of **3.2b** (25.0 mg, 72.8 µmol, 1 eq.) in toluene (1.1 mL). The product was obtained as a yellow solid (19.7 mg, 57.4 µmol, 79 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (dd, *J* = 8.5, 5.6 Hz, 2H, $C_{Ph}H$), 7.04 (t, *J* = 8.6 Hz, 2H, $C_{Ph}H$), 5.18 (hept, *J* = 6.8 Hz, 1H, $C_{i\text{Pr}}H$), 4.00 (hept, *J* = 6.7 Hz, 1H, $C_{i\text{Pr}}H$), 3.55 (dd, *J* = 4.4, 2.1 Hz, 1H, $C_{sp3}H$), 3.37 (dd, *J* = 3.6, 1.7 Hz, 1H, $C_{sp3}H$), 2.12 (dt, *J* = 13.3, 3.9 Hz, 1H, $C_{sp3}HH$), 1.99 (dt, *J* = 12.9, 4.1 Hz, 1H, $C_{sp3}HH$), 1.88 (td, *J* = 12.2, 7.3 Hz, 1H, $C_{sp3}HH$), 1.79 (td, *J* = 12.0, 7.4 Hz, 1H, $C_{sp3}HH$), 1.66 – 1.53 (m, 2H, $C_{sp3}H_2$), 1.35 – 1.20 (m, 12H, $C_{i\text{Pr}}H_3$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 215.5 (CO), 161.4 (d, *J* = 247.0 Hz, $C_{Ph}F$), 144.6 (d, *J* = 2.2 Hz, C_{sp2}-$N_3i\text{Pr}_2$), 131.5 (d, *J* = 3.3 Hz, $C_{Ph,q}$), 129.9 (d, *J* = 7.4 Hz, $C_{Ph}H$), 120.1 (C_{sp2}-Ph), 115.2 (d, *J* = 21.2 Hz, $C_{Ph}H$), 53.4 ($C_{sp3}H$), 50.9 ($C_{sp3}H$), 49.2 ($C_{i\text{Pr}}H$), 47.1 ($C_{i\text{Pr}}H$), 30.1 ($C_{sp3}H_2$), 29.2 ($C_{sp3}H_2$), 23.9 ($C_{i\text{Pr}}H_3$), 23.7 ($C_{i\text{Pr}}H_3$), 19.3 ($C_{i\text{Pr}}H_3$), 19.3, 18.4 ($C_{sp3}H_2$).

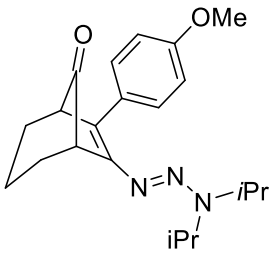
^{19}F NMR (376 MHz, $CDCl_3$) δ – 115.6.

IR (ν_{max}, cm^{-1}) 2974 (w), 2938 (m), 2860 (w), 1756 (s), 1506 (s), 1394 (s), 1382 (m), 1354 (s), 1248 (s), 1156 (s), 836 (m).

Mp: 113 °C.

HRMS (nanochip-ESI/LTQ-Orbitrap) *m*/*z*: $[M + Na]^+$ Calcd for $C_{20}H_{26}FN_3NaO^+$ 366.1952; Found 366.1961.

6-(3,3-Diisopropyltriaz-1-en-1-yl)-7-(4-methoxyphenyl)bicyclo[3.2.1]oct-6-en-8-one (**3.3c**)



3.3c was synthesized analogously to **3.3a** from a dried solution of **3.2c** (25.1 mg, 70.6 µmol, 1 eq.) in toluene (1 mL) within 6.5 h. The product was obtained as a yellow solid (14.8 mg, 41.6 µmol, 59 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.4 Hz, 2H, $C_{Ph}H$), 6.91 (d, *J* = 8.4 Hz, 2H, $C_{Ph}H$), 5.28 – 5.11 (m, 1H, $C_{iPr}H$), 4.05 – 3.91 (m, 1H, $C_{iPr}H$), 3.83 (s, 3H, $C_{OMe}H_3$), 3.57 – 3.50 (m, 1H, $C_{sp3}H$), 3.38 (s, 1H, $C_{sp3}H$), 2.17 – 2.06 (m, 1H, $C_{sp3}HH$), 2.00 (dd, *J* = 12.4, 5.9 Hz, 1H, $C_{sp3}HH$), 1.87 (td, *J* = 12.4, 5.6 Hz, 1H, $C_{sp3}HH$), 1.77 (td, *J* = 12.3, 5.7 Hz, 1H, $C_{sp3}HH$), 1.66 – 1.52 (m, 2H, $C_{sp3}H_2$), 1.38 – 1.19 (m, 12H, $C_{iPr}H_3$).

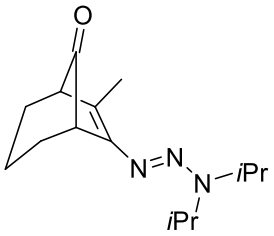
^{13}C NMR (101 MHz, $CDCl_3$) δ 215.9 (CO), 158.2(C_{Ph}-OMe), 143.2 (C_{sp2}-N_3iPr_2), 129.6 ($C_{Ph}H$), 128.1 ($C_{Ph,q}$), 121.0 (C_{sp2}-Ph), 113.9 ($C_{Ph}H$), 55.4 ($C_{OMe}H_3$), 53.4 ($C_{sp3}H$), 50.9 ($C_{sp3}H$), 49.0 ($C_{iPr}H$), 46.9 ($C_{iPr}H$), 30.1 ($C_{sp3}H_2$), 29.2 ($C_{sp3}H_2$), 24.0 ($C_{iPr}H_3$), 23.7 ($C_{iPr}H_3$), 19.4 ($C_{iPr}H_3$), 18.4 ($C_{sp3}H_2$).

IR (ν_{max}, cm^{-1}) 2972 (w), 2936 (w), 2856 (w), 2836 (w), 1756 (m), 1604 (w), 1508 (m), 1396 (m), 1354 (m), 1248 (s), 1180 (m), 1154 (m), 1032 (m), 832 (m).

Mp: 91 – 95 °C.

HRMS (ESI/QTOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{21}H_{30}N_3O_2^+$ 356.2333; Found 356.2333.

6-(3,3-Diisopropyltriaz-1-en-1-yl)-7-methylbicyclo[3.2.1]oct-6-en-8-one (**3.3d**)



3.3d was synthesized analogously to **3.3a** from a dried solution of **3.2g** (25.0 mg, 94.9 µmol, 1 eq.) in toluene (1.4 mL). The product was obtained as a yellow solid (16.1 mg, 61.1 µmol, 64 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.14 (br, 1H, $C_{iPr}H$), 3.91 (br, 1H, $C_{iPr}H$), 3.24 (t, *J* = 3.2 Hz, 1H, $C_{sp3}H$), 2.73 (dt, *J* = 3.8, 1.7 Hz, 1H, $C_{sp3}H$), 2.01 (s, 3H, $C_{Me}H_3$), 1.95 – 1.84 (m, 2H, $C_{sp3}H_2$), 1.76 – 1.60 (m, 2H, $C_{sp3}H_2$), 1.57 – 1.43 (m, 2H, $C_{sp3}H_2$), 1.27 – 1.18 (m, 12H, $C_{iPr}H_3$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 216.7 (CO), 143.6 (C_{sp2}-N_3iPr_2), 122.3 (C_{sp2}-Me), 55.3 ($C_{sp3}H$), 49.5 ($C_{sp3}H$), 28.8 ($C_{sp3}H_2$), 28.7 ($C_{sp3}H_2$), 18.3 ($C_{sp3}H_2$), 11.4 ($C_{Me}H_3$).[11]

IR (ν_{max}, cm^{-1}) 2974 (m), 2931 (m), 2858 (w), 1755 (s), 1409 (s), 1244 (s), 1214 (s), 1155 (m), 1103 (s), 1379 (m), 1367 (m), 1331 (m), 1140 (m), 1015 (m), 1034 (m), 1128 (m).

Mp: 61 – 64 °C.

[11] The signals of $C_{iPr}H$ and $C_{iPr}H_3$ are strongly broadened. They can tentatively be assigned to broad peaks at 48.4 ppm, 46.0 ppm and 23.6 ppm, 19.6 ppm respectively.

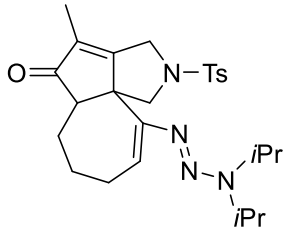
HRMS (ESI/QTOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{15}H_{26}N_3O^+$ 264.2070; Found 264.2073.

10-(3,3-Diisopropyltriaz-1-en-1-yl)-4-methyl-2-tosyl-2,3,5a,6,7,8-hexahydroazuleno[1,8a-c]pyrrol-5(1H)-one (**3.4**) and N-(But-2-yn-1-yl)-N-(((1S,5R)-7-(3,3-diisopropyltriaz-1-en-1-yl)-8-oxobicyclo[3.2.1]oct-6-en-6-yl)methyl)-4-methylbenzenesulfonamide (**3.3e**)

3.4 and **3.3e** were obtained as a separable mixture of isomers analogously to **3.3a** from a dried solution of **3.2h** (50 mg, 103 µmol, 1 eq.) in toluene (1.6 mL) and dimethylaluminium chloride (0.9 M in hexanes, 34.4 µL, 31.0 µmol, 0.3 eq.) within 6 h. The products were obtained as colorless solids (**3.4**: 17.0 mg, 35.1 mmol, 34 %, **3.3e**: 15.3 mg, 31.6 mmol, 31 %).

Crystals suitable for X-ray diffraction analysis were obtained by slow diffusion of pentane into a solution of **3.4** in toluene.

3.4:



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.3 Hz, 2H, $C_{Ph}H$), 7.25 (d, *J* = 8.3 Hz, 2H, $C_{Ph}H$), 5.30 (t, *J* = 7.9 Hz, 1H, $C_{sp2}H$), 4.34 (dd, *J* = 14.0, 1.6 Hz, 1H, NC*H*H), 4.22 (d, *J* = 8.7 Hz, 1H, NC*H*H), 3.99 (d, *J* = 14.0 Hz, 1H, NC*H*H), 2.96 (d, *J* = 8.8 Hz, 1H, NC*H*H), 2.39 (s, 3H, $C_{Ph\text{-}Me}H_3$), 2.19 (td, *J* = 8.6, 5.7 Hz, 2H, $C_{sp3}H_2$), 2.07 (m, 2H, C_{sp3}*H*H + C_{sp3}H), 1.64 (d, *J* = 1.3 Hz, 3H, $C_{Me}H_3$), 1.61 – 1.47 (m, 2H, $C_{sp3}H_2$), 1.44 – 1.31 (m, 1 H, C_{sp3}*H*H) 1.19 (br, 12H, $C_{i\text{Pr}}H_3$). [12]

^{13}C NMR (101 MHz, $CDCl_3$) δ 209.3 (CO), 173.0 (C_{sp2}), 152.6 (C_{sp2}-N_3*i*Pr_2), 143.5 (C_{Ph}-Me), 134.6 ($C_{Ph,q}$), 133.4 (C_{sp2}-Me), 129.7 ($C_{Ph}H$), 127.6 ($C_{Ph}H$), 106.1 ($C_{sp2}H$), 61.7 (NCH_2), 57.7 (C_{sp3}), 52.9 ($C_{sp3}H$), 48.6 (NCH_2), 24.4 ($C_{sp3}H_2$), 23.0 ($C_{sp3}H_2$), 21.7 ($C_{Ph\text{-}Me}H_3$), 20.9 ($C_{sp3}H_2$), 8.9 ($C_{Me}H_3$).[13]

IR (ν_{max}, cm^{-1}) 2972 (w), 2936 (w), 2864 (w), 1712 (m), 1680 (m), 1404 (m), 1346 (m), 1222 (m), 1156 (s), 1094 (m), 1036 (m), 732 (m), 814 (w), 914 (w).

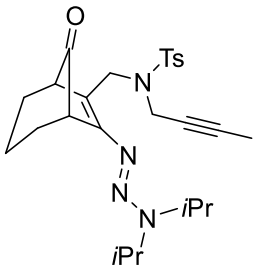
Mp: 130 °C (decomposition).

HRMS (ESI/QTOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{26}H_{37}N_4O_3S^+$ 485.2581; Found 485.2580.

[12] The signals of $C_{i\text{Pr}}H$ are strongly broadened. They can tentatively be assigned to broad peaks at 4.50 ppm and 3.85 ppm respectively.

[13] The signals of $C_{i\text{Pr}}H$ and $C_{i\text{Pr}}H_3$ are not detected, presumably due to broadening.

3.3e:



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 – 7.73 (m, 2H, $C_{Ph}H$), 7.29 (d, *J* = 8.1 Hz, 2H, $C_{Ph}H$), 5.11 (hept, *J* = 6.1 Hz, 1H, $C_{i\text{Pr}}H$), 4.28 (s, 2H, NCH_2), 4.02 (dq, *J* = 7.0, 2.4 Hz, 2H, NCH_2), 3.89 (hept, *J* = 7.5, 7.0 Hz, 1H, $C_{i\text{Pr}}H$), 3.29 (dt, *J* = 4.1, 1.9 Hz, 1H, $C_{sp3}H$), 2.98 (dt, *J* = 3.8, 1.8 Hz, 1H, $C_{sp3}H$), 2.42 (s, 3H, $C_{Ph\text{-}Me}H_3$), 2.06 – 1.96 (m, 1H, $C_{sp3}HH$), 1.94 – 1.85 (m, 1H, $C_{sp3}HH$), 1.79 – 1.65 (m, 2H, $C_{sp3}H_2$), 1.56 – 1.47 (m, 5H, $C_{sp3}H_2$ + $C_{C\equiv CMe}H_3$), 1.26 (d, *J* = 6.3 Hz, 6H, $C_{i\text{Pr}}H_3$), 1.17 (d, *J* = 6.8 Hz, 3H, $C_{i\text{Pr}}H_3$), 1.14 (d, *J* = 6.7 Hz, 3H, $C_{i\text{Pr}}H_3$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 215.9 (CO), 148.6 (C_{sp2}-N_3iPr_2), 143.2 (C_{Ph}-Me), 136.9 ($C_{Ph,q}$), 129.3 ($C_{Ph}H$), 128.0 ($C_{Ph}H$), 119.1 (C_{sp2}-CH_2), 80.8 (C≡C), 72.7 (C≡C), 52.4 ($C_{sp3}H$), 49.9 ($C_{sp3}H$), 49.1 ($C_{i\text{Pr}}H$), 46.3 ($C_{i\text{Pr}}H$), 42.0 (NCH_2), 37.1 (NCH_2), 29.6 ($C_{sp3}H_2$), 28.8 ($C_{sp3}H_2$), 23.8 ($C_{i\text{Pr}}H_3$), 23.6 ($C_{i\text{Pr}}H_3$), 21.7 ($C_{Ph\text{-}Me}H_3$), 19.4 ($C_{i\text{Pr}}H_3$), 18.5 ($C_{sp3}H_2$), 3.4 ($C_{C\equiv CMe}H_3$).

IR (ν_{max}, cm^{-1}) 2970 (w), 2926 (w), 2858 (w), 1756 (m), 1406 (m), 1346 (m), 1246 (m), 1158 (s), 1094 (m), 900 (m).

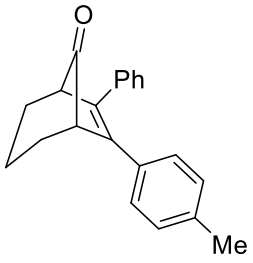
Mp: 140 °C.

HRMS (ESI/QTOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{26}H_{37}N_4O_3S^+$ 485.2581; Found 485.2592.

7.3.8. Pd-Catalyzed Cross-Coupling Reactions with 3.3a

The compounds **3.5a**–**c** were synthesized in analogy to a published procedure, in which aryl triazenes are used as substrates.[111]

6-Phenyl-7-(p-tolyl)bicyclo[3.2.1]oct-6-en-8-one (**3.5a**)



BF_3*OEt_2 (19.0 µL, 154 µmol, 2 eq.) was added to a solution of **3.3a** (25.0 mg, 76.8 µmol, 1 eq.), 4-tolylboronic acid (21.3 mg, 157 µmol, 2.04 eq.) and $Pd(PPh_3)_4$ (9.0 mg, 7.8 µmol, 0.1 eq.) in DME (0.77 mL), and the mixture was stirred at for 4 h. The reaction was quenched with NaOH (1 M, 0.5 mL), and the product was extracted with Et_2O (3 x 1.5 mL). The combined organic phases were dried over $MgSO_4$, filtered over celite, and the solvent was removed under vacuum. Purification by flash column chromatography on silica with a gradient of 0 – 5 % Et_2O in pentane gave the product in the form of a yellow solid (14.7 mg, 51.0 µmol, 66 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.20 (m, 5H, $C_{Ph}H$), 7.15 (d, *J* = 8.2 Hz, 2H, $C_{Tol}H$), 7.06 (d, *J* = 7.9 Hz, 2H, $C_{Tol}H$), 3.22 (s, 1H, $C_{sp3}H$), 3.21 (s, 1H, $C_{sp3}H$), 2.32 (s, 3H, $C_{Ph\text{-}Me}H_3$), 2.15

– 2.06 (m, 2H, $C_{sp3}H_2$), 1.97 – 1.85 (m, 3H, $C_{sp3}H_2$ + $C_{sp3}H$*H*), 1.67 (dtd, *J* = 7.9, 5.9, 5.4, 2.7 Hz, 1H, $C_{sp3}H$*H*).

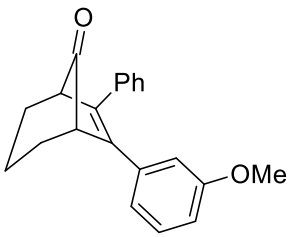
^{13}C NMR (101 MHz, $CDCl_3$) δ 216.1 (CO), 137.6 (C_{Ph}-Me), 136.2 ($C_{Ph,q}$), 134.9 (C_{sp2}-Tol), 134.2 (C_{sp2}-Ph), 132.8 ($C_{Tol,q}$), 129.3 ($C_{Tol}H$), 128.6 ($C_{Ph}H$), 128.1 ($C_{Ar}H$), 128.0 ($C_{Ar}H$), 127.6 ($C_{Ph}H$), 56.3 ($C_{sp3}H$), 56.2 ($C_{sp3}H$), 30.0 ($C_{Ph\text{-}Me}H_3$), 21.4 ($C_{sp3}H_2$)[14], 18.1 ($C_{sp3}H_2$).

IR (ν_{max}, cm^{-1}) 3078 (w), 3052 (w), 3026 (w), 2940 (w), 2858 (w), 1758 (s), 1512 (w), 1444 (w), 1268 (w), 1228 (w), 1076 (w), 828 (w), 818 (w), 768 (w).

Mp: 109 °C.

HRMS (ESI/QTOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{21}H_{21}O^+$ 289.1587; Found 289.1585.

6-(3-Methoxyphenyl)-7-phenylbicyclo[3.2.1]oct-6-en-8-one (**3.5b**)



3.5b was synthesized analogously to **3.5a** from **3.3a** (25.0 mg, 76.8 µmol, 1 eq.) and 3-methoxyphenylboronic acid (23.2 mg, 153 µmol, 2 eq.). The product was obtained as a light yellow solid (15.1 mg, 49.6 µmol, 65 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.20 (m, 5H, $C_{Ph}H$), 7.20 – 7.15 (m, 1H, $C_{PhOMe}H$), 6.83 (dt, *J* = 7.7, 1.3 Hz, 1H, $C_{PhOMe}H$), 6.78 (t, *J* = 2.9 Hz, $C_{PhOMe}H$), 6.77 (d, *J* = 1.6 Hz, $C_{PhOMe}H$), 3.64 (s, 3H, $C_{OMe}H_3$), 3.23 (s, 1H, $C_{sp3}H$), 3.22 (s, 1H, $C_{sp3}H$), 2.17 – 2.05 (m, 2H, $C_{sp3}H_2$), 1.98 – 1.85 (m, 3H, $C_{sp3}H_2$ + $C_{sp3}H$*H*), 1.69 (dd, *J* = 9.2, 5.3 Hz, 1H, $C_{sp3}H$*H*).

^{13}C NMR (101 MHz, $CDCl_3$) δ 215.9 (CO), 159.6 (C_{Ph}-OMe), 137.1 ($C_{PhOMe,q}$), 136.0 ($C_{Ph,q}$), 135.2 (C_{sp2}-Ph), 134.7 (C_{sp2}PhOMe), 129.7 ($C_{PhOMe}H$), 128.7 ($C_{Ph}H$), 128.1 ($C_{Ph}H$), 127.8 ($C_{Ph}H$), 120.5 ($C_{PhOMe}H$), 113.5 ($C_{PhOMe}H$), 113.5 ($C_{PhOMe}H$), 56.4 ($C_{sp3}H$), 56.2 ($C_{sp3}H$), 55.2 ($C_{OMe}H_3$), 30.0 ($C_{sp3}H_2$), 30.0 ($C_{sp3}H_2$), 18.1 ($C_{sp3}H_2$).

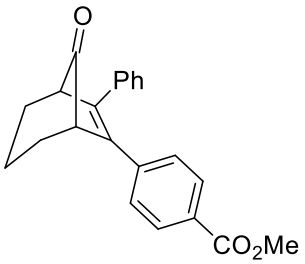
IR (ν_{max}, cm^{-1}) 3076 (w), 3054 (w), 3028 (w), 3000 (w), 2940 (w), 2858 (w), 2834 (w), 1762 (s), 1598 (w), 1576 (w), 1444 (w), 1288 (w), 1260 (w), 788 (w), 768 (w).

Mp: 87 – 90 °C.

HRMS (ESI/QTOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{21}H_{21}O_2^+$ 305.1536; Found 305.1530.

[14] The signals for the two $C_{sp3}H_2$ adjacent to the bridgehead are not resolved.

Methyl 4-(8-oxo-7-phenylbicyclo[3.2.1]oct-6-en-6-yl)benzoate (**3.5c**)



3.5c was synthesized analogously to **3.5a** from **3.3a** (25.0 mg, 76.8 µmol, 1 eq.) and 4-methoxycarbonylphenylboronic acid (27.6 mg, 153 µmol, 2 eq.). The product was obtained as a light yellow solid (14.7 mg, 44.2 µmol, 58 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.5 Hz, 2H, $C_{PhCO2Me}H$), 7.33 – 7.29 (m, 2H, $C_{PhCO2Me}H$), 7.29 – 7.20 (m, 5H, $C_{Ph}H$), 3.90 (s, 3H, $C_{OMe}H_3$), 3.26 (s, 1H, $C_{sp3}H$), 3.25 (s, 1H, $C_{sp3}H$), 2.15 – 2.07 (m, 2H, $C_{sp3}H_2$), 2.01 – 1.84 (m, 3H, $C_{sp3}H_2$ + $C_{sp3}H$*H*), 1.75 – 1.67 (m, 1H, $C_{sp3}H$*H*).

^{13}C NMR (101 MHz, $CDCl_3$) δ 215.3 (CO), 166.8 (CO_2Me), 140.6 (*C*$_{Ph}$-CO_2Me), 137.3 (C_{sp2}-Ph), 135.4 ($C_{Ar,q}$), 134.0 (*C*s_{p2}-PhCO2Me), 129.9 ($C_{PhCO2Me}H$), 129.1 ($C_{Ar,q}$), 128.8 ($C_{Ar}H$), 128.1 ($C_{Ph}H$), 128.1 ($C_{Ar}H$), 128.0 ($C_{Ar}H$), 56.5 ($C_{sp3}H$), 56.1 ($C_{sp3}H$), 30.1 ($C_{sp3}H_2$), 30.0 ($C_{sp3}H_2$), 18.1 ($C_{sp3}H_2$).

IR (ν_{max}, cm^{-1}) 3076 (w), 3054 (w), 3022 (w), 2996 (w), 2946 (w), 2860 (w), 1762 (s), 1720 (s), 1606 (m), 1436 (m), 1276 (s), 1182 (w), 1110 (m), 770 (m).

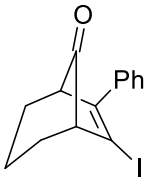
Mp: 104 – 107 °C.

HRMS (ESI/QTOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{22}H_{21}O_3^+$ 333.1485; Found 333.1480.

7.3.9. Synthesis of Iodo-Bicyclooctenone **3.6** and Derivatization

3.6 was synthesized in analogy to a published procedure.[162] The cross-coupling products **3.7** and **3.8** were synthesized according to modified literature procedures.[163,164]

6-Iodo-7-phenylbicyclo[3.2.1]oct-6-en-8-one (**3.6**)



In a microwave-vial, **3.3a** (50 mg, 154 µmol, 1 eq.) and iodine (7.8 mg, 30.7 µmol, 0.2 eq.) were dissolved in dry, degassed iodomethane (3 mL). The vial was sealed and heated in the microwave to 130 °C for 4 h. The mixture was allowed to cool to RT, diluted with Et_2O (15 mL), and washed with $Na_2S_2O_3$ (sat. aq., 5 mL) and NaCl (sat. aq., 5 mL). The organic phase was dried over $MgSO_4$, and the solvent was removed under vacuum. Purification by flash column chromatography on silica with a gradient of 4 – 6 % Et_2O in pentane gave the product in the form of a light yellow solid (44.3 mg, 137 µmol, 89 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 – 7.56 (m, 2H, $C_{Ph}H$), 7.47 – 7.31 (m, 3H, $C_{Ph}H$), 3.17 (dt, *J* = 4.5, 1.6 Hz, 1H, $C_{sp3}H$), 3.06 (m, 1H, $C_{sp3}H$), 2.14 – 2.00 (m, 2H, 2 x C_{sp3}*H*H), 1.85 – 1.60 (m, 4H, 2 x C_{sp3}*H*H + $C_{sp3}H_2$).

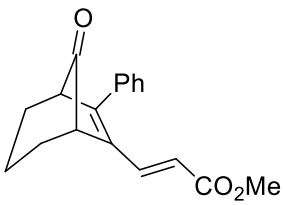
^{13}C NMR (101 MHz, $CDCl_3$) δ 213.8 (CO), 144.0 (C_{sp2}-Ph), 135.5 ($C_{Ph,q}$), 128.7 ($C_{Ph}H$), 128.6 ($C_{Ph}H$), 127.2 ($C_{Ph}H$), 87.2 (C_{sp2}-I), 62.6 ($C_{sp3}H$), 56.2 ($C_{sp3}H$), 29.9 ($C_{sp3}H_2$), 28.4 ($C_{sp3}H_2$), 17.5 ($C_{sp3}H_2$).

IR (ν_{max}, cm^{-1}) 2940 (w), 2857 (w), 1762 (s), 1491 (w), 1443 (w), 1279 (w), 1267 (w), 1073 (w), 764 (m), 694 (m).

Mp: 48 °C.

HRMS (APPI/LTQ-Orbitrap) *m*/*z*: $[M + H]^+$ Calcd for $C_{14}H_{14}IO^+$ 325.0084; Found 325.0096.

Methyl (*E*)-3-(8-oxo-7-phenylbicyclo[3.2.1]oct-6-en-6-yl)acrylate (**3.7**)



A solution of $Pd(OAc)_2$ (1.7 mg, 7.6 μmol, 0.1 eq.) in DMF (0.3 mL) was added to a solution containing **3.6** (25.0 mg, 77.1 μmol, 1 eq.), methyl acrylate (10.4 μL, 116 μmol, 1.5 eq.) and triethylamine (16.1 μL, 116 μmol, 1.5 eq.) in DMF (0.5 mL). The mixture was heated to 50 °C for 14 h. The mixture was allowed to cool to RT, diluted with Et_2O (15 mL), and washed with H_2O (3 x 5 mL). The combined aqueous phases were extracted with Et_2O (2 x 15 mL). The combined organic phases were washed with NaCl (sat. aq., 2 x 15 mL), dried over $MgSO_4$, and the solvent was removed under vacuum. Purification by flash column chromatography on silica with 20 % Et_2O in pentane gave the product in the form of a light yellow, highly viscous liquid, which solidified upon standing (19.1 mg, 67.7 μmol, 88 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 15.8 Hz, 1H, CO-C*H*=CH), 7.48 – 7.32 (m, 5H, C_{Ph}-H), 5.92 (d, *J* = 15.7 Hz, 1H, CO-CH=C*H*), 3.76 (s, 3H, CH_3), 3.29 (dd, *J* = 4.2, 2.0 Hz, 1H, $C_{sp3}H$), 3.23 (dd, *J* = 4.1, 2.0 Hz, 1H, $C_{sp3}H$), 2.11 – 2.00 (m, 2H, 2 x C_{sp3}*H*H), 1.98 – 1.81 (m, 2H, 2 x C_{sp3}*H*H), 1.70 – 1.53 (m, 2H, $C_{sp3}H_2$).

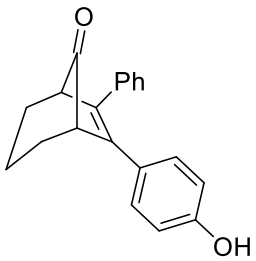
^{13}C NMR (101 MHz, $CDCl_3$) δ 214.8 (CO), 167.6 (CO_2Me), 145.4 (C_{sp2}-Ph), 136.9 (CO-*C*H=CH), 134.5 ($C_{Ph,q}$), 132.0 (*C*$_{sp2}$-CH=CH-CO), 129.0 (C_{Ph}-H), 129.0 (C_{Ph}-H), 128.5 (C_{Ph}-H), 120.4 (CO-CH=*C*H), 56.7 ($C_{sp3}H$), 51.9 (CH_3), 51.6 ($C_{sp3}H$), 30.1 ($C_{sp3}H_2$), 29.6 ($C_{sp3}H_2$), 17.8 ($C_{sp3}H_2$).

IR (ν_{max}, cm^{-1}) 2946 (w), 2860 (w), 1760 (s), 1710 (s), 1615 (m), 1444 (m), 1435 (m), 1324 (m), 1306 (m), 1272 (s), 1166 (s), 984 (m), 768 (m).

Mp: 95 °C.

HRMS (APCI/QTOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{18}H_{19}O_3^+$ 283.1329; Found 283.1325.

6-(4-Hydroxyphenyl)-7-phenylbicyclo[3.2.1]oct-6-en-8-one (**3.8**)



3.6 (25.0 mg, 77.1 µmol, 1 eq.), 4-hydroxyphenylboronic acid (21.3 mg, 154 µmol, 2 eq.), potassium carbonate (21.3 mg, 154 µmol, 2 eq.), and $Pd(OAc)_2$ (1.7 mg, 7.6 µmol, 0.1 eq.) were dissolved in DMF (1.2 mL) and water (0.3 mL) and purged with N_2 at RT for 30 min. The mixture was heated to 85 °C for 6 h. The mixture was allowed to cool to RT, diluted with Et_2O (15 mL), washed with LiCl (10 % aq., 2 x 5 mL) H_2O (1 x 5 mL) and NaCl (sat. aq., 2 x 4 mL), dried over $MgSO_4$, and the solvent was removed under vacuum. Purification by flash column chromatography on silica with 18 % EtOAc in pentane gave the product in the form of an off-white solid (21.1 mg, 72.7 µmol, 94 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 – 7.18 (m, 5H, C_{Ph}-H), 7.17 – 7.07 (m, 2H, $C_{Ph\text{-}OH}$-H), 6.84 – 6.66 (m, 2H, Ph_{OH}-H), 5.08 (s, 1H, OH), 3.26 – 3.16 (m, 2H, C_{sp3}H), 2.15 – 2.06 (m, 2H, 2 x C_{sp3}*H*H), 1.96 – 1.83 (m, 3H, 3 x C_{sp3}*H*H), 1.71 – 1.63 (m, 1H, C_{sp3}*H*H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 216.4 (CO), 155.2 (C_{Ph}-OH), 136.2 ($C_{Ph,q}$), 134.4 (C_{sp2}-Ph-OH), 133.5 (C_{sp2}-Ph), 129.6 ($C_{Ph\text{-}OH}$-H), 128.7 (C_{Ph}-H), 128.3 ($C_{Ph\text{-}OH,q}$), 128.1 (C_{Ph}-H), 127.6 (C_{Ph}-H), 115.6 ($C_{Ph\text{-}OH}$-H), 56.3 (C_{sp3}H), 56.1 (C_{sp3}H), 30.0 ($C_{sp3}H_2$), 30.0 ($C_{sp3}H_2$), 18.1 ($C_{sp3}H_2$).

IR (ν_{max}, cm^{-1}) 3346 (w), 2941 (m), 2858 (w), 1743 (s), 1609 (m), 1513 (s), 1443 (m), 1267 (m), 1217 (m), 1173 (m), 837 (m), 731 (m).

Mp: 149 °C (decomposition).

HRMS (ESI/QTOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{20}H_{19}O_2^+$ 291.1380; Found 291.1366.

7.4. Experimental Details for Chapter 4

7.4.1. General information

The synthesis of 1-alkynyl triazenes is based on a published procedure (see below).[41]

Dicyclohexylamine and 3-methyl-3-trimethylsilyloxy-1-butyne were dried over molecular sieves overnight prior to use.

Diisopropylamine used in the synthesis of **4.5a** – **i** was degassed (3 x freeze-pump-thaw) and dried over molecular sieves overnight prior to use.

N-(but-2-yn-1-yl)-4-methyl-N-(prop-2-yn-1-yl)benzenesulfonamide[114] and (3-(prop-2-yn-1-yloxy)prop-1-yn-1-yl)benzene[115] were provided by the group of Cramer and prepared according to a published procedure.

Methyl (S)-2-((tert-butoxycarbonyl)amino)-3-(4-iodophenyl)propanoate (Boc-(I-Phe)-OMe) was obtained in two steps from iodo-phenylalanine according to a literature procedure.[165]

Methyl 2-hydroxy-5-iodobenzoate was obtained from 2-hydroxy-5-iodobenzoic acid in one step according to a literature procedure.[166] 1-(Bromoethynyl)-4-nitrobenzene from 1-ethynyl-4-nitrobenzene according to a literature procedure.[168]

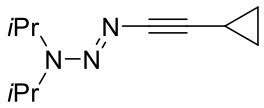
7.4.2. Synthesis of New 1-Alkynyl Triazenes via the N_2O-Method

General procedure for the synthesis of non-commercial alkynyl Grignard reagents: Ethylmagnesium bromide (1 M, 1.0 eq.) was added to a solution of the respective alkyne in dry THF (2 M) under an atmosphere of N_2. The mixture was stirred at RT for 1 h and subsequently heated to 50 °C for 1 h. The solution was allowed to cool to RT, and it was then used for the triazene syntheses described below.

General Procedure for the synthesis of alkynyl triazenes with nitrous oxide:

The corresponding lithium amide (2 mmol, 1.0 eq.) was dissolved in THF (4 mL), and the resulting solution was stirred vigorously under an atmosphere of N_2O for 3 h or overnight at RT. A white precipitate formed. The N_2O atmosphere was then replaced by an atmosphere of dry N_2 and the corresponding Grignard reagent (1.5 eq.) in THF was added, resulting in formation of a yellow solution. The solution was stirred for 3 h at 50 ˚C. The mixture was quenched with water (20 mL), the product was extracted with ethyl acetate (3 x 20 mL), and the combined organic phases were dried $MgSO_4$. After removal of the solvent under vacuum, the product was purified by column chromatography.

1-(Cyclopropylethynyl)-3,3-diisopropyltriaz-1-ene (**4.1a**)



4.1a was obtained according to the general procedure from lithium diisopropylamide (1.7 g, 16 mmol, 1.0 eq.), N_2O (overnight) and ethynylcyclopropane (2.1 mL, 25 mmol, 1.5 eq.). Purification by flash column chromatography on deactivated silica (NEt_3) with a gradient of 0 – 5 % Et_2O in pentane gave the product in the form of a yellow solid (2.1 g, 11 mmol, 68 %).

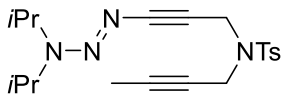
^{1}H NMR (400 MHz, $CDCl_3$) δ 5.09 – 4.88 (m, 1H, $C_{i\mathrm{Pr}}H$), 4.04 – 3.87 (m, 1H, $C_{i\mathrm{Pr}}H$), 1.50 (tt, *J* = 8.2, 5.0 Hz, 1H, $C_{sp3}H$), 1.31 (d, *J* = 6.7 Hz, 6H, $C_{i\mathrm{Pr}}H_3$), 1.18 (d, *J* = 6.9 Hz, 6H, $C_{i\mathrm{Pr}}H_3$), 0.81 (ddt, *J* = 8.1, 5.6, 3.0 Hz, 2H, $C_{sp3}H_2$), 0.74 (tt, *J* = 5.0, 2.8 Hz, 2H, $C_{sp3}H_2$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 83.7 (C_{sp}-C), 80.8 (C_{sp}-N), 50.0 ($C_{i\mathrm{Pr}}H$), 46.9 ($C_{i\mathrm{Pr}}H$), 23.5 ($C_{i\mathrm{Pr}}H_3$), 19.2 ($C_{i\mathrm{Pr}}H_3$), 8.8 ($C_{sp3}H_2$), 0.5 ($C_{sp3}H$).

IR (ν_{max}, cm^{-1}) 2975 (w), 2935 (w), 2873 (w), 2207 (w), 1394 (s), 1365 (s), 1351 (s), 1262 (m), 1236 (s), 1154 (m), 1021 (m), 916 (w), 867 (w), 808 (w).

HRMS (APCI/QTOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{11}H_{20}N_3^+$ 194.1652; Found 194.1649.

N-(but-2-yn-1-yl)-N-(3-(3,3-diisopropyltriaz-1-en-1-yl)prop-2-yn-1-yl)-4-methylbenzenesulfonamide (**4.1b**)



4.1b was obtained according to the general procedure from lithium diisopropylamide (0.19 g, 1.8 mmol, 1.0 eq.), N_2O (3 h) and N-(but-2-yn-1-yl)-4-methyl-N-(prop-2-yn-1-yl)benzenesulfonamide (0.69 g, 2.7 mmol, 1.5 eq.). Purification by flash column chromatography on deactivated silica (NEt_3) with a gradient of 10 – 20 % EtOAc in pentane gave the product in the form of a yellow solid (0.26 g, 0.66 mmol, 38 %).

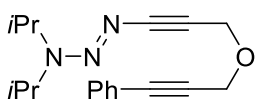
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 – 7.72 (m, 2H, $C_{Ph}H$), 7.26 (d, *J* = 8.1 Hz, 2H, $C_{Ph}H$), 4.96 (hept, *J* = 6.9 Hz, 1H, $C_{i\mathrm{Pr}}H$), 4.42 (s, 2H, $C_{sp3}H_2$), 4.13 (q, *J* = 2.4 Hz, 2H, $C_{sp3}H_2$), 3.99 (hept, *J* = 6.6 Hz, 1H, $C_{i\mathrm{Pr}}H$), 2.39 (s, 3H, $C_{Tol}H_3$), 1.63 (t, *J* = 2.4 Hz, 3H, $C_{Me}H_3$), 1.32 (d, *J* = 6.7 Hz, 6H, $C_{i\mathrm{Pr}}H_3$), 1.18 (d, *J* = 6.8 Hz, 6H, $C_{i\mathrm{Pr}}H_3$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 143.3 (C_{Ph}-Me), 136.0 (C_{Ph}-C_{sp}), 129.4 ($C_{Ph}H$), 128.2 ($C_{Ph}H$), 89.5 (C_{sp}-N), 81.7 (C_{sp}-$C_{sp3}H_2$), 72.1 (C_{sp}-Me), 71.5 (C_{sp}-$C_{sp3}H_2$), 50.4 ($C_{i\mathrm{Pr}}H$), 47.4 ($C_{i\mathrm{Pr}}H$), 37.7 ($C_{sp3}H_2$), 36.8 ($C_{sp3}H_2$), 23.5 ($C_{i\mathrm{Pr}}H_3$), 21.7 ($C_{Tol}H_3$), 19.1 ($C_{i\mathrm{Pr}}H_3$), 3.6 ($C_{Me}H_3$).

IR (ν_{max}, cm^{-1}) 2976 (w), 2935 (w), 2923 (w), 2875 (w), 2851 (w), 2209 (w), 1598 (w), 1412 (m), 1345 (s), 1270 (m), 1241 (m), 1159 (s), 1093 (m), 900 (m), 815 (w), 746 (m).

HRMS (ESI/QTOF) *m*/*z*: $[M + Na]^+$ Calcd for $C_{20}H_{28}N_4NaO_2S^+$ 411.1825; Found 411.1826.

3,3-Diisopropyl-1-(3-((3-phenylprop-2-yn-1-yl)oxy)prop-1-yn-1-yl)triaz-1-ene (**4.1c**)



4.1c was obtained according to the general procedure from lithium diisopropylamide (0.12 g, 1.1 mmol, 1.0 eq.), N_2O (overnight) and (3-(prop-2-yn-1-yloxy)prop-1-yn-1-yl)benzene (0.29 g, 1.7 mmol, 1.5 eq.). Purification by flash column chromatography on deactivated silica (NEt_3) with a gradient of 10 – 15 % DCM in pentane gave the product in the form of a yellow liquid (0.26 g, 0.66 mmol, 38 %).

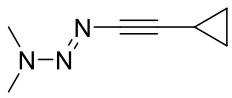
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 – 7.42 (m, 2H, $C_{Ph}H$), 7.34 – 7.28 (m, 3H, $C_{Ph}H$), 5.05 (hept, *J* = 6.8 Hz, 1H, $C_{iPr}H$), 4.63 (s, 2H, $C_{sp3}H_2$), 4.53 (s, 2H, $C_{sp3}H_2$), 4.02 (hept, *J* = 6.7 Hz, 1H, $C_{iPr}H$), 1.34 (d, *J* = 6.6 Hz, 6H, $C_{iPr}H_3$), 1.21 (d, *J* = 6.8 Hz, 6H, $C_{iPr}H_3$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 131.9 ($C_{Ph}H$), 128.5 ($C_{Ph}H$), 128.4 ($C_{Ph}H$), 122.9 (C_{Ph}-C_{sp}), 91.0 (C_{sp}-N), 86.5 (C_{sp}-Ph), 85.1 (C_{sp}-$C_{sp3}H_2$), 73.9 (C_{sp}-$C_{sp3}H_2$), 58.1 ($C_{sp3}H_2$), 57.1 ($C_{sp3}H_2$), 50.4 ($C_{iPr}H$), 47.5 ($C_{iPr}H$), 23.5 ($C_{iPr}H_3$), 19.1 ($C_{iPr}H_3$).

IR (ν_{max}, cm^{-1}) 2975 (s), 2934 (s), 2871 (s), 2850 (s), 2203 (s), 1490 (s), 1414 (s), 1343 (s), 1267 (s), 1240 (s), 1151 (s), 1067 (s), 1028 (s), 1028 (s), 921 (s), 891 (s), 757 (s).

HRMS (nanochip-ESI/LTQ-Orbitrap) *m*/*z*: $[M + H]^+$ Calcd for $C_{18}H_{24}N_3O^+$ 298.1914; Found 298.1909.

1-(Cyclopropylethynyl)-3,3-dimethyltriaz-1-ene (**4.1d**)



4.1d was obtained according to the general procedure from lithium dimethylamide (5 % in hexanes, 8.4 mL, 5.5 mmol, 1 eq.), N_2O (overnight) and ethynylcyclopropane (0.70 mL, 8.3 mmol, 1.5 eq.). Purification by flash column chromatography on deactivated silica (NEt_3) with a gradient of 5– 20 % Et_2O in pentane gave the product in the form of a yellow oil (0.13 g, 0.96 mmol, 17 %).

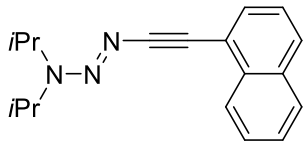
^{1}H NMR (400 MHz, $CDCl_3$) δ 3.45 (s, 3H, $C_{Me}H_3$), 3.08 (s, 3H, $C_{Me}H_3$), 1.47 (tt, *J* = 8.2, 5.0 Hz, 1H, $C_{sp3}H$), 0.85 – 0.79 (m, 2H, $C_{sp3}H_2$), 0.75 – 0.69 (m, 2H, $C_{sp3}H_2$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 84.0 (C_{sp}-C), 80.1 (C_{sp}-N), 43.5 ($C_{Me}H_3$), 36.3($C_{Me}H_3$), 8.8 ($C_{sp3}H_2$), 0.3 ($C_{sp3}H$).

IR (ν_{max}, cm^{-1}) 3092 (w), 3008 (w), 2911 (w), 2859 (w), 2206 (w), 1479 (m), 1403 (m), 1379 (m), 1349 (s), 1306 (s), 1091 (s), 1026 (m), 915 (m), 810 (m).

HRMS (APPI/LTQ-Orbitrap) *m*/*z*: $[M + H]^+$ Calcd for $C_7H_{12}N_3^+$ 138.1026; Found 138.1021.

3,3-Diisopropyl-1-(naphthalen-1-ylethynyl)triaz-1-ene (**4.1e**)



4.1e was obtained according to the general procedure from lithium diisopropylamide (0.53 g, 5.0 mmol, 1 eq.), N_2O (overnight) and 1-ethynylnaphthalene (1.1 mL, 7.7 mmol, 1.5 eq.). Purification by flash

column chromatography on deactivated silica (NEt_3) with a gradient of 0 – 10 % Et_2O in pentane gave the product in the form of a yellow solid (0.84 g, 3.0 mmol, 61 %).

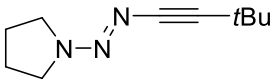
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (d, *J* = 8.3 Hz, 1H, $C_{Naph}H$), 7.83 (d, *J* = 8.0 Hz, 1H, $C_{Naph}H$), 7.75 (d, *J* = 8.3 Hz, 1H, $C_{Naph}H$), 7.67 (d, *J* = 7.2 Hz, 1H, $C_{Naph}H$), 7.55 (t, *J* = 7.4 Hz, 1H, $C_{Naph}H$), 7.49 (t, *J* = 7.4 Hz, 1H, $C_{Naph}H$), 7.42 (t, *J* = 7.7 Hz, 1H, $C_{Naph}H$), 5.21 (hept, *J* = 7.9, 7.3 Hz, 1H, $C_{i\text{Pr}}H$), 4.08 (hept, *J* = 6.7 Hz, 1H, $C_{i\text{Pr}}H$), 1.42 (d, *J* = 6.7 Hz, 6H, $C_{i\text{Pr}}H_3$), 1.29 (d, *J* = 6.8 Hz, 6H, $C_{i\text{Pr}}H_3$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 133.4 ($C_{Naph,q}$), 133.2 ($C_{Naph,q}$), 129.4 ($C_{Naph}H$), 128.2 ($C_{Naph}H$), 127.4 ($C_{Naph}H$), 126.9 ($C_{Naph}H$), 126.3 ($C_{Naph}H$), 126.2 ($C_{Naph}H$), 125.5 ($C_{Naph}H$), 122.8 (C_{Naph}-C_{sp}), 99.0 (C_{sp}-N), 78.0 (C_{sp}-C), 50.5 ($C_{i\text{Pr}}H$), 47.6 ($C_{i\text{Pr}}H$), 23.6 ($C_{i\text{Pr}}H_3$), 19.3 ($C_{i\text{Pr}}H_3$).

IR (ν_{max}, cm^{-1}) 3057 (w), 2975 (w), 2935 (w), 2872 (w), 2183 (m), 1411 (m), 1352 (s), 1258 (s), 1247 (s), 1216 (m), 1154 (m), 1094 (m), 799 (m), 774 (s).

HRMS (APPI/LTQ-Orbitrap) *m*/*z*: $[M + H]^+$ Calcd for $C_{18}H_{22}N_3^+$ 280.1808; Found 280.1807.

1-((3,3-Dimethylbut-1-yn-1-yl)diazenyl)pyrrolidine (**4.1f**)



4.1f was obtained according to the general procedure from lithium pyrrolidinide (1.6 g, 21 mmol, 1.0 eq.), N_2O (overnight) and 3,3-dimethyl-1-butyne (3.9 mL, 31 mmol, 1.5 eq.). Purification by flash column chromatography on deactivated silica (NEt_3) with a gradient of 0 – 15 % DCM in pentane gave the product in the form of a colorless solid (0.55g, 2.9 mmol, 14 %).

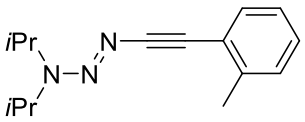
^{1}H NMR (400 MHz, $CDCl_3$, 298 K) δ 3.80 (t, *J* = 6.8 Hz, 2H, NCH_2), 3.45 (t, *J* = 6.9 Hz, 2H, NCH_2), 2.01 – 1.85 (m, 4H, $(CH_2)_2$), 1.22 (s, 9H, $C_{t\text{Bu}}H_3$).

^{13}C NMR (101 MHz, $CDCl_3$, 298 K) δ 88.27 (C_{sp}-*t*Bu), 84.03 (C_{sp}-N), 51.55 (NCH_2), 46.72 (NCH_2), 31.53 ($C_{t\text{Bu}}H_3$), 28.10 ($C_{t\text{Bu,q}}$), 23.98 (CH_2), 23.58 (CH_2).

IR (neat): *ν* = 2965 (m), 2926 (w), 2865 (w), 2212 (w), 2182 (w), 1400 (s), 1360 (s), 1309 (m), 1275 (m), 1248 (m), 1213 (m), 1204 (m), 1097 (m)

HRMS (ESI/QTOF): Calculated (MH+) 180.1495; Found 180.1497.

3,3-Diisopropyl-1-(o-tolylethynyl)triaz-1-ene (**4.1g**)



4.1g was obtained according to the general procedure from lithium diisopropylamide (0.54 g, 5.0 mmol, 1.0 eq.), N_2O (overnight) and 1-ethynyl-2-methylbenzene (0.94 mL, 7.5 mmol, 1.5 eq.). Purification by flash column chromatography on deactivated silica (NEt_3) with a gradient of 0 – 10 % Et_2O in pentane gave the product in the form of a yellow solid (0.79 g, 3.2 mmol, 65 %).

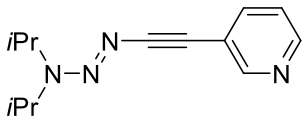
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (dd, *J* = 7.2, 2.0 Hz, 1H, $C_{Ph}H$), 7.19 (dd, *J* = 6.8, 2.2 Hz, 1H, $C_{Ph}H$), 7.17 – 7.09 (m, 2H, $C_{Ph}H$), 5.16 (hept, *J* = 6.8 Hz, 1H, $C_{iPr}H$), 4.04 (hept, *J* = 6.7 Hz, 1H, $C_{iPr}H$), 2.48 (s, 3H, $C_{Me}H_3$), 1.38 (d, *J* = 6.7 Hz, 6H, $C_{iPr}H_3$), 1.25 (d, *J* = 6.8 Hz, 6H, $C_{iPr}H_3$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 139.4 (C_{Ph}-Me), 131.6 ($C_{Ph}H$), 129.3 ($C_{Ph}H$), 127.1 ($C_{Phr}H$), 125.5 ($C_{Ph}H$), 124.7 (C_{Ph}-C_{sp}), 98.0 (C_{sp}-N), 78.8 (C_{sp}-C), 50.3 ($C_{iPr}H$), 47.3 ($C_{iPr}H$), 23.6 ($C_{iPr}H_3$)), 21.1 ($C_{Me}H_3$), 19.3 ($C_{iPr}H_3$)).

IR (ν_{max}, cm^{-1}) 2976 (w), 2936 (w), 2873 (w), 2188 (m), 1486 (w), 1466 (w), 1457 (w), 1411 (m), 1357 (s), 1251 (s), 1212 (m), 1157 (m), 1130 (w), 1096 (m), 756 (m).

HRMS (APCI/QTOF) *m/z*: $[M + H]^+$ Calcd for $C_{15}H_{22}N_3^+$ 244.1808; Found 244.1810.

3-((3,3-Diisopropyltriaz-1-en-1-yl)ethynyl)pyridine (**4.1h**)



4.1h was obtained according to the general procedure from lithium diisopropylamide (0.19 g, 1.8 mmol, 1.0 eq.), N_2O and 3-ethynylpyridine (0.28 g, 2.7 mmol, 1.5 eq.). Purification by flash column chromatography on deactivated silica (NEt_3) with a gradient of 10–50 % EtOAc in pentane gave the product in the form of a yellow oil (0.034 g, 0.15 mmol, 8 %).

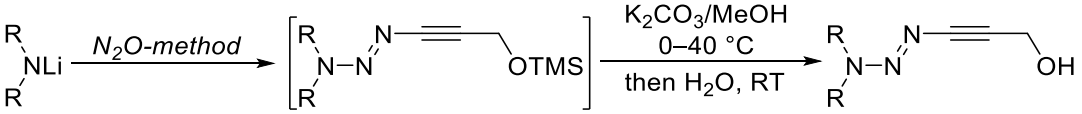
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 (dd, *J* = 2.2, 1.0 Hz, 1H, $C_{Py}H$), 8.43 (dd, *J* = 4.9, 1.7 Hz, 1H, $C_{Py}H$), 7.70 (dt, *J* = 7.9, 1.9 Hz, 1H, $C_{Py}H$), 7.20 (ddd, *J* = 7.9, 4.9, 0.9 Hz, 1H, $C_{Py}H$), 5.12 (hept, *J* = 6.8 Hz, 1H, $C_{iPr}H$), 4.07 (hept, *J* = 6.7 Hz, 1H, $C_{iPr}H$), 1.37 (d, *J* = 6.7 Hz, 6H, $C_{iPr}H_3$), 1.25 (d, *J* = 6.8 Hz, 6H, $C_{iPr}H_3$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 151.9 ($C_{Py}H$), 147.4 ($C_{Py}H$), 137.8 ($C_{Py}H$), 123.0 ($C_{Py}H$), 122.1 ($C_{Py,q}$), 96.9 (C_{sp}-N), 76.6 (C_{sp}-C), 50.8 ($C_{iPr}H$), 47.9 ($C_{iPr}H$), 23.5 ($C_{iPr}H_3$), 19.2 ($C_{iPr}H_3$).

IR (ν_{max}, cm^{-1}) 2976 (w), 2935 (w), 2874 (w), 2189 (m), 1413 (m), 1353 (s), 1256 (s), 1212 (m), 1157 (m), 1097 (m), 1002 (m), 803 (m), 706 (m).

HRMS (ESI/QTOF) *m/z*: $[M + H]^+$ Calcd for $C_{13}H_{19}N_4^+$ 231.1604; Found 231.1605.

7.4.3. Synthesis of 1-Alkynyl Triazenes from Protected Propargylic Alcohols

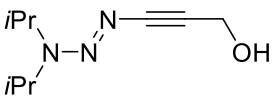


General method for the synthesis of γ-hydroxy 1-alkynyl triazenes:

3-(Trimethylsilyl)oxy)prop-1-yn-1-yl)triaz-1-enes were synthesized from lithium amides, N_2O and propargyloxytrimethylsilane according to the general procedure above.

The crude product was dissolved in MeOH (25 mL) and cooled to 0 °C. K_2CO_3 (1.4 g, 10 mmol, 1 eq.) was added and the mixture was stirred at 0 °C for 10 min. The solvent was evaporated under vacuum (rotavap, 40 °C) and H_2O (10 mL) was added. The suspension was stirred at RT for 5 min. The product was extracted with EtOAc (3 x 20 mL) and the combined organic phases were dried over $MgSO_4$. After removal of the solvent under vacuum, the product was purified by column chromatography.

3-(3,3-Diisopropyltriaz-1-en-1-yl)prop-2-yn-1-ol (**4.2a**)



4.2a was obtained according to the general procedure from lithium diisopropylamide (1.1 g, 10 mmol, 1 eq.), N_2O, propargyloxy-trimethylsilane (2.4 mL, 16 mmol, 1.6 eq.) and K_2CO_3 (1.4 g, 10 mmol, 1 eq.). Purification by flash column chromatography on deactivated silica (NEt_3) with a gradient of 20 – 30 % EtOAc in in pentane gave the product in the form of a dark red solid (0.98 g, 5.4 mmol, 54 %).

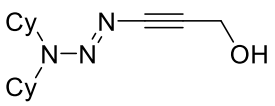
^{1}H NMR (400 MHz, $CDCl_3$) δ 5.02 (hept, J = 6.9 Hz, 1H, $C_{i\mathrm{Pr}}H$), 4.55 (s, 2H, $C_{sp3}H_2$), 4.01 (hept, J = 6.7 Hz, 1H, $C_{i\mathrm{Pr}}H$), 1.69 (s, 1H, OH), 1.33 (d, J = 6.6 Hz, 6H, $C_{i\mathrm{Pr}}H_3$), 1.20 (d, J = 6.8 Hz, 6H, $C_{i\mathrm{Pr}}H_3$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 90.0 (C_{sp}-N), 76.9 (C_{sp}-C), 52.1 ($C_{sp3}H_2$), 50.4 ($C_{i\mathrm{Pr}}H$), 47.5 ($C_{i\mathrm{Pr}}H$), 23.4 ($C_{i\mathrm{Pr}}H_3$), 19.1 ($C_{i\mathrm{Pr}}H_3$).

IR (ν_{max}, cm^{-1}) 3233 (w), 2974 (m), 2934 (w), 2871 (w), 2202 (w), 1466 (w), 1414 (s), 1354 (s), 1262 (s), 1239 (s), 1149 (s), 1149 (s), 1094 (s), 1004 (s), 797 (m).

HRMS (nanochip-ESI/LTQ-Orbitrap) m/z: $[M + H]^+$ Calcd for $C_9H_{18}N_3O^+$ 184.1444; Found 184.1447.

3-(3,3-Dicyclohexyltriaz-1-en-1-yl)prop-2-yn-1-ol (**4.2b**)



4.2b was obtained according to the general procedure from lithium dicyclohexylamide (1.9 g, 10 mmol, 1 eq.), N_2O, propargyloxy-trimethylsilane (2.3 mL, 15 mmol, 1.5 eq.) and K_2CO_3 (1.4 g, 10 mmol, 1 eq.). Purification by flash column chromatography on deactivated silica (NEt_3) with a gradient of 30 – 40 % EtOAc in pentane gave the product in the form of a dark red solid (0.89 g, 3.4 mmol, 34 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.80 (tt, J = 11.8, 3.5 Hz, 1H, $C_{Cy}H$), 4.55 (s, 2H, $C_{sp3}H_2$), 3.53 (tt, J = 11.2, 4.0 Hz, 1H, $C_{Cy}H$), 1.90 – 1.55 (m, 14H, $C_{Cy}H_2$), 1.55 – 1.08 (m, 10H, $C_{Cy}H_2$).[15]

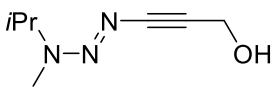
^{13}C NMR (101 MHz, $CDCl_3$) δ 90.2 (C_{sp}-N), 77.0 (C_{sp}-C), 58.9 ($C_{Cy}H$), 55.7 ($C_{Cy}H$), 52.2, 34.0 ($C_{sp3}H_2$), 29.6 ($C_{Cy}H_2$), 26.1 ($C_{Cy}H_2$), 25.7 ($C_{Cy}H_2$), 25.7 ($C_{Cy}H_2$), 25.3 ($C_{Cy}H_2$), 25.2 ($C_{Cy}H_2$).

[15] Excess protons in the aliphatic region are believed to originate from traces of unreacted dicyclohexylamine. The OH-signal is not detected due to broadening.

IR (ν_{max}, cm^{-1}) 3368 (w), 2928 (s), 2852 (m), 2201 (m), 1449 (m), 1411 (m), 1371 (s), 1340 (s), 1278 (m), 1254 (s), 1206 (s), 1154 (m), 1142 (m), 1008 (s), 987 (s), 893 (m), 831 (m), 831 (m), 779 (m).

HRMS (ESI/QTOF) *m*/*z*: $[M + Na]^+$ Calcd for $C_{15}H_{25}N_3NaO^+$ 286.1890; Found 286.1888.

3-(3-Isopropyl-3-methyltriaz-1-en-1-yl)prop-2-yn-1-ol (**4.2c**)



4.2c was obtained according to the general procedure from lithium isopropyl(methyl)amide (0.55 g, 6.9 mmol, 1 eq.), N_2O, propargyloxy-trimethylsilane (2.3 mL, 15 mmol, 1.5 eq.) and K_2CO_3 (1.4 g, 10 mmol, 1.4 eq.). Purification by flash column chromatography on deactivated silica (NEt_3) with a gradient of 10 – 25 % EtOAc in pentane gave the product in the form of a dark red liquid (0.21 g, 1.4 mmol, 20 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.53 (d, *J* = 4.2 Hz, 2H, $C_{sp3}H_2$), 4.20 (hept, *J* = 6.8 Hz, 1H, $C_{iPr}H$), 3.04 (s, 3H, $C_{Me}H_3$), 1.64 (s, 1H, OH), 1.31 (d, *J* = 6.8 Hz, 6H, $C_{iPr}H_3$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 89.7 (C_{sp}-N), 76.3 (C_{sp}-C), 57.8 ($C_{sp3}H_2$), 52.0 ($C_{iPr}H$), 31.9 ($C_{Me}H_3$), 20.8 ($C_{iPr}H_3$).

IR (ν_{max}, cm^{-1}) 3364 (w), 2978 (w), 2934 (w), 2868 (w), 2202 (m), 1470 (m), 1428 (m), 1340 (s), 1302 (m), 1264 (m), 1098 (s), 1002 (s).

HRMS (ESI/QTOF) *m*/*z*: $[M + Ag]^+$ Calcd for $C_7H_{13}AgN_3O^+$ 262.0104; Found 262.0101.

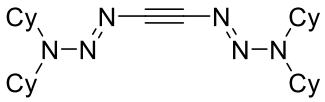
7.4.4. Synthesis of Terminal 1-Alkynyl Triazene **4.3** and its Derivatives

Synthesis of 3,3-dicyclohexyl-1-ethynyltriaz-1-ene (**4.3**) and 1,2-bis(3,3-dicyclohexyltriaz-1-en-1-yl)ethyne (**4.4**) from ethynylmagnesium bromide:

Under N_2-atmosphere, lithium dicyclohexylamide (2.51 mmol, 1 eq.) was dissolved in tetrahydrofuran (5.2 mL) The N_2-atmosphere was replaced by N_2O (3 vacuum/N_2O cycles) and the mixture was stirred under N_2O-atmosphere overnight to give a colorless to light red suspension. The N_2O-atmosphere was replaced by N_2 (3 vacuum/N_2 cycles). Ethynylmagnesium bromide (0.5 M in THF, 7.5 mL, 3.75 mmol, 1.5 eq.) was added and the mixture was stirred at 50 °C for 4 h. The heating was stopped and the reaction was quenched by addition of H_2O (15 mL) and allowed to cool to RT. The product was extracted with EtOAc (3 x 20 mL). The combined organic phases were washed with $CuSO_4$ (10 % aq., 3 x 20 mL), dried over $MgSO_4$ and the solvent was removed under vacuum. The resulting brown solid was suspended in MeOH (15 mL) and filtered.

The filtrate was concentrated under vacuum and purified by filtration over a plug of deactivated silica eluting with pentane to give **4.3** (31.8 mg, 0.136 mmol, 5 %, purity not determined). For the characterization of **4.3** see below.

The filter cake was purified flash column chromatography on deactivated silica (NEt_3) with a gradient of 0 – 100 % DCM in pentane to give **4.4** as a yellow solid (98.8 mg, 0.224 mmol, 18 %).



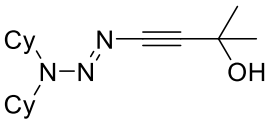
^{1}H NMR (400 MHz, $CDCl_3$) δ 4.83 (s, 2H, $C_{Cy}H$), 3.46 (s, 2H, $C_{Cy}H$), 1.87 – 1.59 (m, 24H, $C_{Cy}H_2$), 1.50 – 1.06 (m, 16H, $C_{Cy}H_2$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 88.1 (C_{sp}), 58.4 ($C_{Cy}H$), 55.0 ($C_{Cy}H$), 34.1 ($C_{Cy}H_2$), 29.8 ($C_{Cy}H_2$), 26.2 ($C_{Cy}H_2$), 25.8 ($C_{Cy}H_2$), 25.4 ($C_{Cy}H_2$).

IR (ν_{max}, cm^{-1}) 2925 (m), 2855 (m), 1450 (w), 1413 (w), 1387 (m), 1365 (s), 1335 (s), 1277 (m), 1255 (m), 1240 (m), 1200 (s), 1162 (w), 1141 (m), 1122 (w), 1030 (w), 1010 (w), 987 (w), 894 (w), 783 (w).

HRMS (ESI/QTOF) *m/z*: $[M + H]^+$ Calcd for $C_{26}H_{45}N_6^+$ 441.3700; Found 441.3693.

4-(3,3-Dicyclohexyltriaz-1-en-1-yl)-2-methylbut-3-yn-2-ol (**4.5**)



Under N_2-atmosphere, lithium dicyclohexylamide (2.55 g, 13.6 mmol, 1 eq.) was dissolved in THF (28 mL). The N_2-atmosphere was replaced by N_2O (3 vacuum/N_2O cycles) and the mixture was stirred under N_2O-atmosphere overnight to give a colorless to light red suspension. The N_2O-atmosphere was replaced by N_2 (3 vacuum/N_2 cycles).

Under N_2-atmopshere, ethylmagnesium bromide (0.9 M in THF, 23.0 mL, 20.7 mmol, 1.5 eq.) was added to a solution of 3-methyl-3-trimethylsilyloxy-1-butyne (4.00 mL, 20.7 mmol, 1.5 eq.) in tetrahydrofuran (10 mL) and the mixture was stirred at RT for 1 h and then at 50 °C for 1 h. The resulting solution was added to the lithium diazotate suspension and the mixture was stirred at 50 °C for 4 h. The mixture was allowed to cool to RT. Methanol (200 mL) and K_2CO_3 (8.43 g, 61.0 mmol, 4.5 eq.) were added and the mixture was heated to 40 °C for 30 min. Volatiles were removed under vacuum. Water (100 mL) was added and the mixture was stirred at 70 °C for 15 min. After cooling to RT, the product was extracted with EtOAc (3 x 200 mL). The combined organic phases were washed with $CuSO_4$ (10 % aq.)/NaCl (sat. aq.) (10:1, 3 x 110 mL), dried over $MgSO_4$ and the solvent was removed under vacuum. Purification by flash column chromatography on deactivated silica (NEt_3) with a gradient of 5 – 20 % EtOAc in pentane gave the product in the form of a yellow solid (2.43 g, 8.34 mmol, 62 %).

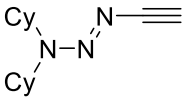
^{1}H NMR (400 MHz, $CDCl_3$) δ 4.80 (tt, *J* = 11.7, 3.5 Hz, 1H, $C_{Cy}H$), 3.50 (tt, *J* = 10.9, 4.4 Hz, 1H, $C_{Cy}H$), 2.02 (s, 1H, OH), 1.88 – 1.61 (m, 12H, $C_{Cy}H_2$), 1.59 (s, 6H, $C_{Me}H_3$), 1.50 – 1.08 (m, 8H $C_{Cy}H_2$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 87.0 (C_{sp}-N), 83.6 (C_{sp}-C), 66.1 ($C_{sp3,q}$), 58.8 ($C_{Cy}H$), 55.3 ($C_{Cy}H$), 34.0 ($C_{Cy}H_2$), 32.1 ($C_{Cy}H_2$) ($C_{Me}H_3$), 29.6 ($C_{Cy}H_2$), 26.1 ($C_{Cy}H_2$), 25.7 ($C_{Cy}H_2$), 25.3 ($C_{Cy}H_2$).

IR (ν_{max}, cm^{-1}) 3397 (w), 2930 (s), 2976 (w), 2855 (m), 2205 (w), 1376 (s), 1344 (s), 1196 (s), 1144 (s), 951 (m), 895 (m), 737 (m), 1452 (m), 1409 (m), 1092 (m), 1277 (m), 1243 (m), 989 (m).

HRMS (ESI/QTOF) *m*/z: $[M + H]^+$ Calcd for $C_{17}H_{30}N_3O^+$ 292.2383; Found 292.2385.

Synthesis of 3,3-dicyclohexyl-1-ethynyltriaz-1-ene (**4.3**) from **4.5**



A round bottom flask was charged with **4.4** (2.00 g, 6.86 mmol, 1 eq.), *t*-butanol (70 mL) and KOH (579 mg, 10.3 mmol, 1.5 eq.). The flask was equipped with a cooler and placed in a pre-heated oil bath and the mixture was stirred at 80 °C for 1 h. The mixture was allowed to cool to RT and the reaction was quenched with NH_4Cl (0.1 M, 103 mL) and NaCl (sat. aq., 20 mL). The product was extracted with cyclohexane (3 x 150 mL). The combined organic phases were dried over $MgSO_4$ and the solvent was removed under vacuum. Purification by filtration over a plug of deactivated silica eluting with pentane gave the product as a dark red liquid containing traces of pentane (1.50 g, 99 % purity, 6.37 mmol, 93 %). The red color of the product is likely caused by small amounts of an unknown side product.

The product was diluted with cyclohexane (4.2 mL) and dried over molecular sieves overnight. Three aliquots of 21.4 µL were taken, the solvent was evaporated under vacuum and the remaining liquid was analyzed by NMR with nitromethane (1 µL) as internal standard to determine the concentration of the stock solution to be 1.13 M.

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.82 (tt, *J* = 11.7, 3.5 Hz, 1H, $C_{Cy}H$), 3.56 (s, 1H, $C_{sp}H$), 3.52 (dq, *J* = 11.0, 4.1, 3.6 Hz, 1H, $C_{Cy}H$), 1.89 – 1.60 (m, 12H, $C_{Cy}H_2$), 1.52 – 1.07 (m, 8H, $C_{Cy}H_2$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 87.9 (C_{sp}-N), 66.1 ($C_{sp}H$), 58.9 ($C_{Cy}H$), 55.7 ($C_{Cy}H$), 34.0 ($C_{Cy}H_2$), 29.5 ($C_{Cy}H_2$), 26.1 ($C_{Cy}H_2$), 25.6 ($C_{Cy}H_2$), 25.2 ($C_{Cy}H_2$).

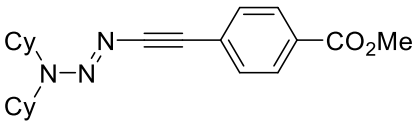
IR (ν_{max}, cm^{-1}) 3318 (w), 2929 (s), 2855 (m), 2076 (w), 1373 (s), 1411 (m), 1451 (m), 1344 (s), 1216 (m), 1254 (m), 894 (w).

HRMS (nanochip-ESI/LTQ-Orbitrap) *m*/z: $[M + H]^+$ Calcd for $C_{14}H_{24}N_3^+$ 234.1965; Found 234.1964.

Sonogashira Reactions

Sonogashira reaction products **4.6a** – **i** were obtained according to a modified published procedure.[168] In a Schlenck tube under N_2-atmosphere, the aryl iodide (1.2 eq.) and $Pd(PPh_3)_4$ (23.2 mg, 10 mol%) were dissolved in *i*Pr_2NH (3 mL) and toluene (1.5 mL) and **4.3** (0.2 mmol, 1 eq., stock solution in cyclohexane, ca. 1 M) was added and the mixture was stirred at RT for 10 min. CuI (1.2 mg, 3 mol%) was added and the headspace of the Schlenck tube was flushed with N_2 for 5 min. The mixture was stirred at 40 °C for 16 h. The reaction was quenched with H_2O (10 mL) and the product was extracted with EtOAc (3 x 10 mL). The combined organic phases were washed with NaCl (sat. aq., 2 x 10 mL), dried over $MgSO_4$ and the solvent was removed under vacuum.

Methyl 4-((3,3-dicyclohexyltriaz-1-en-1-yl)ethynyl)benzoate (**4.6a**)



4.6a was obtained from **4.3** and methyl 4-iodobenzoate according to the general procedure in 96 % yield. Purification by flash column chromatography on deactivated silica (NEt_3) with a gradient of 0 – 10 % Et_2O in pentane.

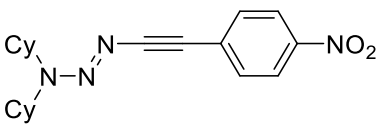
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 – 7.89 (m, 2H, $C_{Ph}H$), 7.53 – 7.43 (m, 2H, $C_{Ph}H$), 4.90 (tt, *J* = 11.7, 3.4 Hz, 1H, $C_{Cy}H$), 3.90 (s, 3H, $C_{Me}H_3$), 3.58 (tt, *J* = 11.0, 4.2 Hz, 1H, $C_{Cy}H$), 1.93 – 1.63 (m, 12H, $C_{Cy}H_2$), 1.57 – 1.10 (m, 8H, $C_{Cy}H_2$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.0 (CO), 131.0 ($C_{Ph}H$), 130.1 (C_{Ph}-CO), 129.5 ($C_{Ph}H$), 128.1 (C_{Ph}-C_{sp}), 97.3 (C_{sp}-N), 79.6 (C_{sp}-C), 59.2 ($C_{Cy}H$), 56.0 ($C_{Cy}H$), 52.2 ($C_{Me}H_3$), 34.0 ($C_{Cy}H_2$), 29.6 ($C_{Cy}H_2$), 26.1 ($C_{Cy}H_2$), 25.7 ($C_{Cy}H_2$), 25.6 ($C_{Cy}H_2$), 25.2 ($C_{Cy}H_2$).

IR (ν_{max}, cm^{-1}) 2931 (m), 2855 (w), 2185 (m), 1719 (s), 1602 (m), 1412 (m), 1366 (s), 1342 (s), 1272 (s), 1249 (s), 1214 (s), 1172 (m), 1107 (m), 769 (m).

HRMS (ESI/QTOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{22}H_{30}N_3O_2^+$ 368.2333; Found 368.2331.

3,3-dicyclohexyl-1-((4-nitrophenyl)ethynyl)triaz-1-ene (**4.6b**)



4.6b was obtained from **4.3** and 1-iodo-4-nitrobenzene according to the general procedure in 84 % yield. Purification by flash column chromatography on deactivated silica (NEt_3) with a gradient of 0 – 2 % Et_2O in pentane.

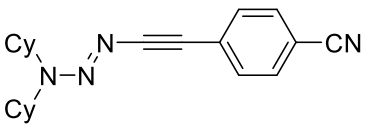
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 – 8.09 (m, 2H, $C_{Ph}H$), 7.59 – 7.48 (m, 2H, $C_{Ph}H$), 4.92 (tt, *J* = 11.9, 3.5 Hz, 1H, $C_{Cy}H$), 3.61 (tt, *J* = 11.4, 3.9 Hz, 1H, $C_{Cy}H$), 1.79 (m, 12H, $C_{Cy}H_2$), 1.55 – 1.07 (m, 6H, $C_{Cy}H_2$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 146.0 (C_{Ph}-NO_2), 132.6 (C_{Ph}-C_{sp}), 131.5 ($C_{Ph}H$), 123.7 ($C_{Ph}H$), 99.9 (C_{sp}-N), 78.9 (C_{sp}-C), 59.5 ($C_{Cy}H$), 56.4 ($C_{Cy}H$), 34.0 ($C_{Cy}H_2$), 29.6 ($C_{Cy}H_2$), 26.1 ($C_{Cy}H_2$), 25.6 ($C_{Cy}H_2$), 25.6 ($C_{Cy}H_2$), 25.2 ($C_{Cy}H_2$).

IR (ν_{max}, cm^{-1}) 2932 (m), 2856 (w), 2182 (m), 1591 (m), 1512 (m), 1451 (w), 1416 (w), 1367 (m), 1331 (s), 1300 (m), 1248 (m), 1216 (m), 854 (w).

HRMS (ESI/QTOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{20}H_{27}N_4O_2^+$ 355.2129; Found 355.2128.

4-((3,3-Dicyclohexyltriaz-1-en-1-yl)ethynyl)benzonitrile (**4.6c**)



4.6c was obtained from **4.3** and 4-iodobenzonitrile according to the general procedure in 95 % yield. Purification by flash column chromatography on deactivated silica (NEt_3) with a gradient of 0 – 2 % Et_2O in pentane.

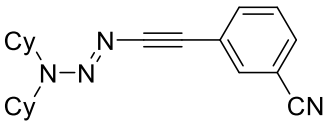
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 8.4 Hz, 2H, $C_{Ph}H$), 7.49 (d, *J* = 8.4 Hz, 2H, $C_{Ph}H$), 4.91 (tt, *J* = 11.8, 3.5 Hz, 1H, $C_{Cy}H$), 3.60 (tt, *J* = 11.2, 3.9 Hz, 1H, $C_{Cy}H$), 1.92 – 1.63 (m, 12H, $C_{Cy}H_2$), 1.55 – 1.11 (m, 8H, $C_{Cy}H_2$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 132.0 ($C_{Ph}H$), 131.5 ($C_{Ph}H$), 130.4 (C_{Ph}-C_{sp}), 119.2 (CN), 109.8 (C_{Ph}-CN), 98.7 (C_{sp}-N), 78.8 (C_{sp}-C), 59.4 ($C_{Cy}H$), 56.3 ($C_{Cy}H$), 34.0 ($C_{Cy}H_2$), 29.6 ($C_{Cy}H_2$), 26.1 ($C_{Cy}H_2$), 25.6 ($C_{Cy}H_2$), 25.6 ($C_{Cy}H_2$), 25.2 ($C_{Cy}H_2$).

IR (ν_{max}, cm^{-1}) 2931 (m), 2855 (m), 2225 (w), 2181 (s), 1601 (m), 1414 (m), 1364 (s), 1340 (s), 1300 (m), 1249 (s), 1215 (s), 1172 (m), 837 (m), 732 (m).

HRMS (ESI/QTOF) *m*/*z*: $[M + Na]^+$ Calcd for $C_{21}H_{26}N_4Na^+$ 357.2050; Found 357.2040.

3-((3,3-Dicyclohexyltriaz-1-en-1-yl)ethynyl)benzonitrile (**4.6d**)



4.6d was obtained from **4.3** and 3-iodobenzonitrile according to the general procedure in 57 % yield. Purification by flash column chromatography on deactivated silica (NEt_3) with a gradient of 0 – 10 % Et_2O in pentane.

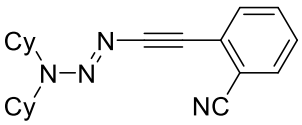
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (t, *J* = 1.4 Hz, 1H, $C_{Ph}H$), 7.63 (dt, *J* = 7.8, 1.5 Hz, 1H, $C_{Ph}H$), 7.47 (dt, *J* = 7.8, 1.5 Hz, 1H, $C_{Ph}H$), 7.37 (t, *J* = 7.8 Hz, 1H, $C_{Ph}H$), 4.89 (tt, *J* = 11.8, 3.4 Hz, 1H, $C_{Cy}H$), 3.59 (tt, *J* = 11.2, 4.0 Hz, 1H, $C_{Cy}H$), 1.91 – 1.63 (m, 12H, $C_{Cy}H_2$), 1.55 – 1.11 (m, 8H, $C_{Cy}H_2$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 135.2 ($C_{Ph}H$), 134.4 ($C_{Ph}H$), 130.0 ($C_{Ph}H$), 129.1 ($C_{Ph}H$), 126.8 (C_{Ph}-C_{sp}), 118.7 (CN), 112.7 (C_{Ph}-CN), 96.5 (C_{sp}-N), 77.7 (C_{sp}-C), 59.2 ($C_{Cy}H$), 56.1 ($C_{Cy}H$), 34.0 ($C_{Cy}H_2$), 29.6 ($C_{Cy}H_2$), 26.1 ($C_{Cy}H_2$), 25.6 ($C_{Cy}H_2$), 25.6 ($C_{Cy}H_2$), 25.2 ($C_{Cy}H_2$).

IR (ν_{max}, cm^{-1}) 2931 (m), 2855 (m), 2230 (w), 2186 (m), 1452 (w), 1413 (m), 1366 (s), 1342 (s), 1261 (w), 1216 (m), 1199 (m), 1145 (w), 894 (w), 795 (w).

HRMS (APCI/QTOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{21}H_{27}N_4^+$ 335.2230; Found 335.2224.

2-((3,3-Dicyclohexyltriaz-1-en-1-yl)ethynyl)benzonitrile (**4.6e**)



4.6e was obtained from **4.3** and 2-iodobenzonitrile according to the general procedure with a reaction time of 31 h in 33 % yield. Purification by flash column chromatography on deactivated silica (NEt_3) with a gradient of 10 – 15 % Et_2O in pentane.

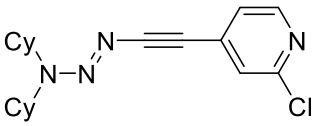
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (dd, *J* = 7.8, 1.2 Hz, 1H, $C_{Ph}H$), 7.52 (dd, *J* = 8.0, 1.5 Hz, 1H, $C_{Ph}H$), 7.47 (td, *J* = 7.6, 1.3 Hz, 1H, $C_{Ph}H$), 7.27 (td, *J* = 7.6, 1.5 Hz, 1H, $C_{Ph}H$), 4.94 (tt, *J* = 11.8, 3.5 Hz, 1H, $C_{Cy}H$), 3.59 (tt, *J* = 11.1, 4.1 Hz, 1H, $C_{Cy}H$), 1.92 – 1.62 (m, 12H, $C_{Cy}H_2$), 1.55 – 1.10 (m, 8H, $C_{Cy}H_2$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 132.7 ($C_{Ph}H$), 132.2 ($C_{Ph}H$), 131.9 ($C_{Ph}H$), 129.4 (C_{Ph}-C_{sp}), 126.7 ($C_{Ph}H$), 118.3 (CN), 114.2 (C_{Ph}-CN), 100.4 (C_{sp}-N), 76.4 (C_{sp}-C), 59.3 ($C_{Cy}H$), 56.2 ($C_{Cy}H$), 34.0 ($C_{Cy}H_2$), 29.6 ($C_{Cy}H_2$), 26.1 ($C_{Cy}H_2$), 25.6 ($C_{Cy}H_2$), 25.2 ($C_{Cy}H_2$).

IR (ν_{max}, cm^{-1}) 2932 (m), 2856 (w), 2226 (w), 2184 (s), 1451 (w), 1416 (m), 1365 (s), 1342 (s), 1280 (w), 1249 (m), 1216 (m), 761 (m).

HRMS (ESI/QTOF) *m*/*z*: $[M + Na]^+$ Calcd for $C_{21}H_{26}N_4Na^+$ 357.2050; Found 357.2056.

2-Chloro-4-((3,3-dicyclohexyltriaz-1-en-1-yl)ethynyl)pyridine (**4.6f**)



4.6f was obtained from **4.3** and 2-chloro-4-iodopyridine according to the general procedure in 68 % yield. Purification by flash column chromatography on deactivated silica (NEt_3) with a gradient of 5 – 10 % Et_2O in pentane.

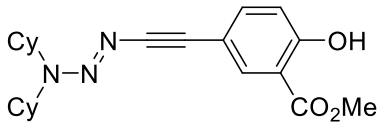
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (dd, *J* = 5.3, 0.8 Hz, 1H, $C_{Py}H$), 7.32 – 7.31 (m, 1H, $C_{Py}H$), 7.18 (dd, *J* = 5.2, 1.4 Hz, 1H, $C_{Py}H$), 4.91 (tt, *J* = 11.8, 3.4 Hz, 1H, $C_{Cy}H$), 3.62 (tt, *J* = 11.4, 3.9 Hz, 1H, $C_{Cy}H$), 1.92 – 1.63 (m, 12H, $C_{Cy}H_2$), 1.56 – 1.11 (m, 9H, $C_{Cy}H_2$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 151.5 (C_{Py}-Cl), 149.3 ($C_{Py}H$), 136.5 (C_{Py}-C), 125.4 ($C_{Py}H$), 123.9 ($C_{Py}H$), 100.3 (C_{sp}-N), 76.5 (C_{sp}-C), 59.6 ($C_{Cy}H$), 56.6 ($C_{Cy}H$), 34.0 ($C_{Cy}H_2$), 29.5 ($C_{Cy}H_2$), 26.0 ($C_{Cy}H_2$), 25.6 ($C_{Cy}H_2$), 25.6 ($C_{Cy}H_2$), 25.2 ($C_{Cy}H_2$).

IR (ν_{max}, cm^{-1}) 2932 (m), 2856 (w), 2188 (s), 1584 (s), 1452 (w), 1416 (m), 1364 (s), 1341 (s), 1309 (m), 1280 (w), 1249 (m), 1217 (m), 1082 (w), 828 (m).

HRMS (ESI/QTOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{19}H_{26}ClN_4^+$ 345.1841; Found 345.1839.

Methyl 5-((3,3-dicyclohexyltriaz-1-en-1-yl)ethynyl)-2-hydroxybenzoate (**4.6g**)



4.6g was obtained from **4.3** and methyl 2-hydroxy-5-iodobenzoate according to the general procedure in 52 % yield. Purification by flash column chromatography on deactivated silica (NEt_3) with 5 % Et_2O in pentane.

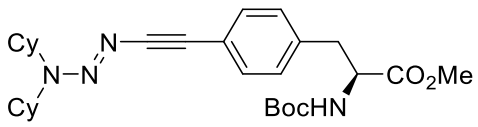
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.78 (s, 1H, OH), 7.96 (d, *J* = 2.2 Hz, 1H, $C_{Ph}H$), 7.53 (dd, *J* = 8.7, 2.2 Hz, 1H, $C_{Ph}H$), 6.91 (d, *J* = 8.7 Hz, 1H, $C_{Ph}H$), 4.87 (tt, *J* = 11.7, 3.4 Hz, 1H, $C_{Cy}H$), 3.94 (s, 3H, $C_{Me}H_3$), 3.55 (tt, *J* = 10.8, 4.4 Hz, 1H, $C_{Cy}H$), 1.91 – 1.62 (m, 12H, $C_{Cy}H_2$), 1.53 – 1.11 (m, 8H, $C_{Cy}H_2$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.4 (CO), 160.6 (C_{Ph}-OH), 138.4 ($C_{Ph}H$), 132.7 ($C_{Ph}H$), 117.8 ($C_{Ph}H$), 116.1 (C_{Ph}-CO), 112.5 (C_{Ph}-C_{sp}), 92.9 (C_{sp}-N), 79.0 (C_{sp}-C), 58.9 ($C_{Cy}H$), 55.6 ($C_{Cy}H$), 52.5 ($C_{Me}H_3$), 34.1 ($C_{Cy}H_2$), 29.6 ($C_{Cy}H_2$), 26.1 ($C_{Cy}H_2$), 25.7 ($C_{Cy}H_2$), 25.7 ($C_{Cy}H_2$), 25.3 ($C_{Cy}H_2$).

IR (ν_{max}, cm^{-1}) 3165 (w), 2931 (m), 2855 (w), 2193 (w), 1678 (m), 1490 (m), 1441 (m), 1370 (s), 1342 (s), 1288 (m), 1240 (m), 1207 (s), 1144 (m), 1091 (m).

HRMS (ESI/QTOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{22}H_{30}N_3O_3^+$ 384.2282; Found 384.2274.

Methyl (S)-2-((tert-butoxycarbonyl)amino)-3-(4-((3,3-dicyclohexyltriaz-1-en-1-yl)ethynyl)phenyl)-propanoate (**4.6h**)



4.6h was obtained from **4.3** and methyl (S)-2-((tert-butoxycarbonyl) amino) -3- (4-iodophenyl) propanoate (Boc-(I-Phe)-OMe) according to the general procedure in 87 % yield. Purification by flash column chromatography on deactivated silica (NEt_3) with a gradient of 10 – 15 % EtOAc in pentane.

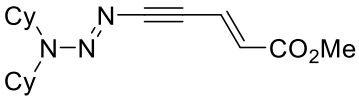
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.33 (m, 2H, $C_{Ph}H$), 7.04 (d, *J* = 7.9 Hz, 2H, $C_{Ph}H$), 4.99 – 4.83 (m, 2H, $C_{Cy}H$, NH), 4.57 (m, $C_{Cy}H$), 3.69 (s, 3H, $C_{OMe}H_3$), 3.55 (tt, *J* = 10.3, 4.6 Hz, 1H, $C_{Cy}H$), 3.07 (td, *J* = 12.1, 10.6, 6.1 Hz, 2H, CH_2), 1.94 – 1.63 (m, 12H, $C_{Cy}H_2$), 1.54 – 1.10 (m, 17H, $C_{Cy}H_2$, $C_{tBu}H_3$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 172.4 (C-*C*O), 155.2 (N-CO), 134.8 (C_{Ph}-CH_2), 131.3 ($C_{Ph}H$), 129.2 ($C_{Ph}H$), 123.7 (C_{Ph}-C_{sp}), 94.3 (C_{sp}-N), 80.1 $C_{tBu,q}$), 79.8 (C_{sp}-C), 58.9 ($C_{Cy}H$), 55.6 ($C_{Cy}H$), 54.5 (CH-NH), 52.3 ($C_{OMe}H_3$), 38.4 ($C_{Cy}H_2$), 34.0 ($C_{Cy}H_2$), 29.6 ($C_{Cy}H_2$), 28.4 ($C_{tBu}H_3$), 26.1 ($C_{Cy}H_2$), 25.7 ($C_{Cy}H_2$), 25.7 ($C_{Cy}H_2$), 25.3 ($C_{Cy}H_2$).

IR (ν_{max}, cm^{-1}) 3365 (w), 2932 (m), 2856 (m), 2189 (w), 1745 (m), 1715 (m), 1500 (m), 1451 (m), 1411 (m), 1368 (s), 1344 (s), 1250 (m), 1212 (s), 1167 (s), 732 (w).

HRMS (ESI/QTOF) *m*/*z*: $[M + Na]^+$ Calcd for $C_{29}H_{42}N_4NaO_4^+$ 533.3098; Found 533.3097.

Methyl (*E*)-5-(3,3-dicyclohexyltriaz-1-en-1-yl)pent-2-en-4-ynoate (**4.6h**)



A Schlenck-tube was charged with **4.3** (0.89 M in cyclohexane, 225 µL, 200 µmol, 1 eq.) and the solvent was removed under vacuum. $Pd(PPh_3)_4$ (23.1 mg, 20 µmol, 0.1 eq.), methyl (*E*)-3-iodoacrylate (63.6 mg, 300 µmol, 1.5 eq.) and triethylamine (dry, degassed, 4 mL) were added and the mixture was stirred at RT for 10 min. A solution of CuI (3.8 mg, 20 µmol, 0.1 eq.) in triethylamine (dry, degassed, 0.5 mL) was added and the mixture was stirred at 40 °C for 16 h. The reaction was quenched with H_2O (10 mL) and the product was extracted with EtOAc (3 x 10 mL). The combined organic phases were washed with brine (2 x 10 mL), dried over $MgSO_4$ and the solvent was removed under vacuum. Purification by flash column chromatography on deactivated silica (NEt_3) with 10 % Et_2O in pentane gave the product in the form of a brown, highly viscous resin (34.1 mg, 0.107 mmol, 54 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11 (d, *J* = 15.6 Hz, 1H, C_{sp2}-C_{sp}), 6.12 (d, *J* = 15.6 Hz, 1H, C_{sp2}-CO), 4.88 (tt, *J* = 11.7, 3.5 Hz, 1H, $C_{Cy}H$), 3.74 (s, 3H, CH_3), 3.59 (tt, *J* = 11.4, 3.9 Hz, 1H, $C_{Cy}H$), 1.90 – 1.62 (m, 12H, $C_{Cy}H_2$), 1.54 – 1.10 (m, 8H, $C_{Cy}H_2$).

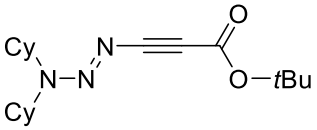
^{13}C NMR (101 MHz, $CDCl_3$) δ 167.3 (CO), 127.4 (C_{sp2}-C_{sp}), 125.7 (C_{sp2}-CO), 103.5 (C_{sp}-N), 78.0 (C_{sp}-C), 59.5 ($C_{Cy}H$), 56.5 ($C_{Cy}H$), 51.7 (CH_3), 34.0 ($C_{Cy}H_2$), 29.5 ($C_{Cy}H_2$), 26.0 ($C_{Cy}H_2$), 25.6 ($C_{Cy}H_2$), 25.6 ($C_{Cy}H_2$), 25.2 ($C_{Cy}H_2$).

IR (ν_{max}, cm^{-1}) 2931 (m), 2856 (m), 2168 (s), 1716 (s), 1608 (m), 1416 (m), 1361 (s), 1336 (s), 1264 (s), 1232 (s), 1213 (m), 1191 (m), 1157 (s), 1033 (w), 1014 (w), 956 (m).

HRMS (ESI/QTOF) *m*/*z*: $[M + Na]^+$ Calcd for $C_{18}H_{27}N_3NaO_2^+$ 340.1995; Found 340.1998.

*Synthesis of Products from Lithiated **4.3***

tert-Butyl 3-(3,3-dicyclohexyltriaz-1-en-1-yl)propiolate (**4.7a**)



Under N_2-atmosphere, a solution of **4.3** (1.13 M in cyclohexane, 177 µL, 0.200 mmol, 1 eq.) was diluted with THF (2 mL) and cooled to – 40 °C. LiHMDS (1 M in THF, 0.3 mL, 300 µmol, 1.5 eq.) was added dropwise and the mixture was stirred at – 40 °C for 1 h and was subsequently cooled to – 78 °C. Di-*tert*-butyl dicarbonate (64.2 µL, 300 µmol, 1.5 eq.) was dissolved in THF (2 mL) and the solution was added dropwise to the lithium acetylide solution. The mixture was stirred at – 78 °C for 1 h and then allowed to warm to RT over 6 h and was stirred at RT overnight. The reaction was quenched with NH_4Cl (sat. aq., 5 mL) and the product was extracted with Et_2O (3 x 10 mL). The combined organic phases were dried over $MgSO_4$ and the solvent was removed under vacuum. Purification by flash column chromatography on

deactivated silica (NEt_3) with 4 % Et_2O in pentane gave **4.7a** in the form of a yellow, highly viscous resin (53.8 mg, 161 µmol, 81 %).

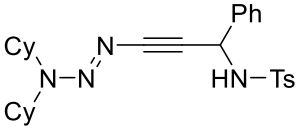
^{1}H NMR (400 MHz, $CDCl_3$) δ 4.82 (tt, *J* = 11.9, 3.5 Hz, 1H, $C_{Cy}H$), 3.60 (tt, *J* = 11.4, 3.8 Hz, 1H, $C_{Cy}H$), 1.89 – 1.60 (m, 12H, $C_{Cy}H_2$), 1.50 – 1.07 (m, 17H, $C_{Cy}H_2$ (8) + $C_{t\text{Bu}}H_3$ (9)).

^{13}C NMR (101 MHz, $CDCl_3$) δ 154.8 (CO), 88.9 (C_{sp}-N), 82.0 ($C_{t\text{Bu,q}}$), 73.4 (C_{sp}-C), 59.9 ($C_{Cy}H$), 57.1 ($C_{Cy}H$), 33.8 ($C_{Cy}H_2$), 29.3 ($C_{Cy}H_2$), 28.2 ($C_{t\text{Bu}}H_3$), 25.9 ($C_{Cy}H_2$), 25.5 ($C_{Cy}H_2$), 25.4 ($C_{Cy}H_2$), 25.1 ($C_{Cy}H_2$).

IR (ν_{max}, cm^{-1}) 2976 (w), 2932 (m), 2857 (w), 2178 (s), 1687 (s), 730 (s), 1092 (s), 1130 (s), 1155 (s), 1199 (m), 1244 (s), 1291 (s), 1365 (s), 1343 (m), 910 (m), 746 (m).

HRMS (ESI/QTOF) *m*/*z*: $[M + Ag]^+$ Calcd for $C_{19}H_{31}AgN_3O_2^+$ 440.1462; Found 440.1454.

N-(3-(3,3-Dicyclohexyltriaz-1-en-1-yl)-1-phenylprop-2-yn-1-yl)-4-methylbenzenesulfonamide (**4.7b**)



Under N_2-atmosphere, a solution of **4.3** (1.07 M in cyclohexanae, 200 µL, 0.214 mmol, 1 eq.) was diluted with THF (2.1 mL) and cooled to – 40 °C. LiHMDS (1 M in THF, 0.32 mL, 0.320 mmol, 1.5 eq.) was added dropwise and the mixture was stirred at – 40 °C for 1 h. A solution of N-tosylbenzaldimine (83.1 mg, 0.320 mmol, 1.5 eq.) in THF (2.1 mL) was added and the mixture was stirred at – 40 °C for 4 h. H_2O (10 mL) was added and the mixture was allowed to warm to RT and diluted with EtOAc (25 mL). The phases were separated and the product was extracted from the aqueous layer with EtOAc (2 x 25 mL). The combined organic phases were washed with NaCl (sat. aq., 1 x 25 mL), dried over $MgSO_4$ and the solvent was removed under vacuum. Purification by flash column chromatography on deactivated silica (NEt_3) with 20 % EtOAc in pentane gave **4.7b** in the form of a yellow-orange solid (81.9 mg, 0.166 mmol, 78 %).

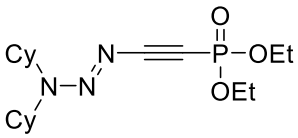
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.4 Hz, 2H, $C_{Ar}H$), 7.57 – 7.48 (m, 2H, $C_{Ar}H$), 7.35 – 7.20 (m, 5H, $C_{Ar}H$), 5.60 (d, *J* = 8.3 Hz, 1H, $C_{sp3}H$), 4.87 (d, *J* = 8.4 Hz, 1H, NH), 4.73 (tt, *J* = 11.7, 3.6 Hz, 1H, $C_{Cy}H$), 3.51 (tt, *J* = 11.5, 3.9 Hz, 1H, $C_{Cy}H$), 2.38 (s, 3H, $C_{Me}H_3$), 1.91 – 1.60 (m, 12H, $C_{Cy}H_2$), 1.49 – 1.06 (m, 8H, $C_{Cy}H_2$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 143.1 ($C_{Ts,q}$-Me), 139.0 ($C_{Ph,q}$), 137.7 ($C_{Ts,q}$-S), 129.5 ($C_{Ar}H$), 128.6 ($C_{Ar}H$), 128.1 ($C_{Ar}H$), 127.7 ($C_{Ar}H$), 127.5 ($C_{Ar}H$), 90.9 (C_{sp}-N), 75.5 (C_{sp}-C), 58.8 ($C_{Cy}H$), 55.6 ($C_{Cy}H$), 50.6 ($C_{sp3}H$), 34.0 ($C_{Cy}H_2$), 29.5 ($C_{Cy}H_2$), 26.1 ($C_{Cy}H_2$), 25.7 ($C_{Cy}H_2$), 25.6 ($C_{Cy}H_2$), 25.3 ($C_{Cy}H_2$), 21.7 ($C_{Me}H_3$).

IR (ν_{max}, cm^{-1}) 3270 (w), 2931 (m), 2855 (m), 2204 (m), 1451 (m), 1414 (m), 1371 (s), 1329 (s), 1253 (m), 1209 (m), 1156 (s), 1026 (m), 909 (m), 811 (m), 731 (s).

HRMS (ESI/QTOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{28}H_{37}N_4O_2S^+$ 493.2632; Found 493.2640.

Diethyl ((3,3-dicyclohexyltriaz-1-en-1-yl)ethynyl)phosphonate (**4.7c**)



Under N2-atmosphere, a solution of **4.3** (1.07 M in cyclohexane, 187 µL, 0.200 mmol, 1 eq.) (in CyH) in THF (2 mL) was cooled to – 40 °C. LiHMDS (1 M in THF, 300 µL, 0.300 mmol, 1.5 eq.) was added dropwise and the mixture was stirred at – 40 °C for 1 h. Diethyl chlorophosphate (43.5 µL, 0.300 µmol, 1.5 eq.) was dissolved in THF (2 mL) and cooled to – 78 °C. The solution of the lithium acetylide was added via slow cannula transfer to the chlorphosphate and the mixture was stirred at – 78 °C for 1 h, at – 40 °C for 2 h and at 0 °C for 2 h. The reaction was quenched with NH_4Cl (sat. aq., 6 mL) and allowed to warm to RT. The product was extracted with Et_2O (3 x 15 mL, Et2O). The combined organic phases were dried over $MgSO_4$ and the solvent was removed under vacuum. Purification by flash column chromatography on deactivated silica (NEt_3) with 40 % EtOAc in pentane gave **4.7c** in the form of a brown solid (63.7 mg, 172 µmol, 86 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.85 (tt, *J* = 12.0, 3.6 Hz, 1H, $C_{Cy}H$), 4.25 – 4.08 (m, 4H, $C_{Et}H_2$), 3.63 (tt, *J* = 11.5, 3.8 Hz, 1H, $C_{Cy}H$), 1.90 – 1.61 (m, 12H, $C_{Cy}H_2$),1.37 (t, *J* = 7.1 Hz, 6H). 1.54 – 1.09 (m, 14H, $C_{Et}H_3$ (6)[16] + $C_{Cy}H_2$ (8)).

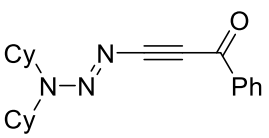
^{13}C NMR (101 MHz, $CDCl_3$) δ 102.6 (d, *J* = 61.2 Hz, C_{sp}-N), 66.3 (d, *J* = 322.3 Hz, C_{sp}-P), 62.7 (d, *J* = 5.5 Hz, $C_{Et}H_2$), 60.1 ($C_{Cy}H$), 57.3 ($C_{Cy}H$), 33.9 ($C_{Cy}H_2$), 29.3 ($C_{Cy}H_2$), 25.9 ($C_{Cy}H_2$), 25.5 ($C_{Cy}H_2$), 25.5 ($C_{Cy}H_2$), 25.2 ($C_{Cy}H_2$), 16.3 (d, *J* = 7.4 Hz, $C_{Et}H_3$).

^{31}P NMR (162 MHz, $CDCl_3$) δ – 1.8.

IR (ν_{max}, cm^{-1}) 2981 (w), 2932 (m), 2857 (w), 2139 (s), 1451 (w), 1425 (m), 1365 (s), 1339 (s), 1234 (m), 1051 (m), 1026 (s), 967 (m), 766 (m).

HRMS (ESI/QTOF) *m/z*: $[M + H]^+$ Calcd for $C_{18}H_{33}N_3O_3P^+$ 370.2254; Found 370.2255.

3-(3,3-Dicyclohexyltriaz-1-en-1-yl)-1-phenylprop-2-yn-1-one (**4.7c**)



Under N_2-atmosphere, a solution of **4.3** (1.07 M in cyclohexane, 187 µL, 200 µmol, 1 eq.) in THF (2 mL) was cooled to – 40 °C. LiHMDS (1 M in THF, 300 µL, 300 µmol, 1.5 eq.) was added and the mixture was stirred at – 40 °C for 1 h. benzoyl chloride (35 µL, 301 µmol, 1.5 eq.) was dissolved in THF (2 mL) and was cooled to – 78 °C. The solution of the lithium acetylide was added via slow cannula transfer to the electrophile and the mixture was stirred at – 78 °C for 1 h, at – 40 °C for 2 h and at 0 °C for 2 h. The reaction was quenched with $NaHCO_3$ (sat. aq., 6 mL) and allowed to warm to RT. The product was extracted with Et_2O (3 x 15 mL). The combined organic phases

[16] The signal has the shape of a triplet with *J* = 7.1 Hz.

were dried over $MgSO_4$ and the solvent was removed under vacuum. Purification by flash column chromatography on deactivated silica (NEt_3) with a gradient of 15 – 20 % Et_2O in pentane gave **4.7d** in the form of a red-brown solid (8.1 mg, 24 µmol, 12 %)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 – 8.06 (m, 2H, $C_{Ph}H$), 7.60 – 7.52 (m, 1H, $C_{Ph}H$), 7.47 (dd, *J* = 8.3, 6.8 Hz, 2H, $C_{Ph}H$), 4.99 (tt, *J* = 11.9, 3.4 Hz, 1H, $C_{Cy}H$), 3.68 (tt, *J* = 11.4, 3.9 Hz, 1H, $C_{Cy}H$), 1.93 – 1.61 (m, 12H, $C_{Cy}H_2$), 1.55 – 1.13 (m, 10H[17], $C_{Cy}H_2$).

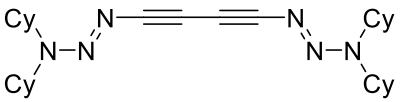
^{13}C NMR (101 MHz, $CDCl_3$) δ 178.8 (CO), 138.1 ($C_{Ph,q}$), 133.3 ($C_{Ph}H$), 129.6 ($C_{Ph}H$), 128.4 ($C_{Ph}H$), 99.4 (C_{sp}-N), 79.4 (C_{sp}-C), 60.3 ($C_{Cy}H$), 57.5 ($C_{Cy}H$), 33.9 ($C_{Cy}H_2$), 29.4 ($C_{Cy}H_2$), 26.0 ($C_{Cy}H_2$), 25.5 ($C_{Cy}H_2$), 25.5 ($C_{Cy}H_2$), 25.2 ($C_{Cy}H_2$).

IR (ν_{max}, cm^{-1}) 2932 (m), 2856 (w), 2157 (s), 1627 (m), 1422 (m), 1363 (m), 1341 (m), 1310 (m), 1244 (s), 1201 (s), 1170 (m), 951 (m).

HRMS (ESI/QTOF) *m*/*z*: $[M + Na]^+$ Calcd for $C_{21}H_{27}N_3NaO^+$ 360.2046; Found 360.2041.

Diynes

1,4-bis(3,3-dicyclohexyltriaz-1-en-1-yl)buta-1,3-diyne (**4.8a**)



According to a published procedure,[134] a Schlenck tube was charged with CuI (7.6 mg, 40 µmol, 0.2 eq.) and was placed under O_2-atmosphere by three vacuum/O_2-cycles. TMEDA (12 µL, 80 µmol, 0.4 eq.) and dry acetone (2 mL) were added and the mixture was stirred at RT for 15 min. A second Schlenck tube was filled with **4.3** (0.89 M in cyclohexane, 225 µL, 200 µmol, 1 eq.) and the solvent was removed under vacuum. The residue was dissolved in dry acetone (2 mL) and added to the CuI/TMEDA solution via cannula transfer. The mixture was stirred at RT for 4 h. The mixture was filtered over a plug of deactivated silica. The plug was rinsed with acetone until the filtrate no longer appeared orange-yellow. The solvent was removed under vacuum. The crude product was suspended in MeOH (5 x 1 mL) and filtered. The filter cake was washed off the filter with DCM and the solvent was removed under vacuum to give **4.8a** in the form of a yellow-brown solid (33.3 mg, 71.7 µmol, 72 %). Crystals suitable for X-ray crystallographic analysis were obtained by layering a solution of **4.8a** in DCM with MeCN.

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.83 (tt, *J* = 11.7, 3.5 Hz, 2H, $C_{Cy}H$), 3.53 (tt, *J* = 11.0, 4.3 Hz, 2H, $C_{Cy}H$), 1.90 – 1.59 (m, 24H, $C_{Cy}H_2$), 1.50 – 1.08 (m, 16H, $C_{Cy}H_2$).

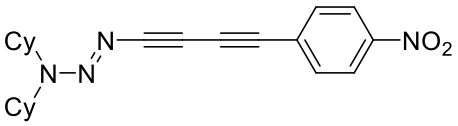
^{13}C NMR (101 MHz, $CDCl_3$) δ 88.2 (C_{sp}-N), 66.8 (C_{sp}-C), 58.9 ($C_{Cy}H$), 55.8 ($C_{Cy}H$), 33.9 ($C_{Cy}H_2$), 29.5 ($C_{Cy}H_2$), 26.0 ($C_{Cy}H_2$), 25.5 ($C_{Cy}H_2$), 25.2 ($C_{Cy}H_2$).

[17] The reason for the larger than expected integral (10 instead of 8) is unknown, all ^{1}H signals are correlated to ^{13}C-signals originating from CyH in ^{1}H-^{13}C-HSQC.

IR (ν_{max}, cm^{-1}) 2931 (m), 2855 (m), 2119 (w), 1411 (m), 1359 (s), 1330 (s), 1278 (m), 1253 (m), 1214 (m), 1200 (s), 1143 (m).

HRMS (ESI/QTOF) *m*/*z*: $[M + Na]^+$ Calcd for $C_{28}H_{44}N_6Na^+$ 487.3520; Found 487.3518.

3,3-Dicyclohexyl-1-((4-nitrophenyl)buta-1,3-diyn-1-yl)triaz-1-ene (**4.8b**)



According to a published procedure,[135] under N_2-atmosphere, CuI (1.9 mg, 9.98 µmol, 5 mol%) and hydroxylamine hydrochloride (4.2 mg, 60.4 µmol, 0.3 eq.) were added to a Schlenck tube and the N_2-atmosphere was reestablished (3 x vac/N_2). *n*-Butylamine (39.5 µL, 400 µmol, 2 eq.) and dry MeOH (0.7 mL) were added and the mixture was heated to 40 °C. A second Schlenck tube was filled with **4.3** (1.13 M in cyclohexane, 177 µL, 200 µmol, 1 eq.), the solvent was removed under vacuum. The residue was dissolved in dry MeOH (0.6 mL)/ dry THF (0.3 mL) and added to the mixture. A solution of 1-(bromoethynyl)-4-nitrobenzene (67.4 mg, 298 µmol, 1.5 eq.) in MeOH (0.7 mL) was added to the mixture in small portions over 20 min. The mixture was stirred at 40 °C for 24 h. The reaction was quenched with NaCl (sat. aq., 8 mL). The product was extracted with DCM (3 x 10 mL). The combined organic phases were washed with NaCl (sat. aq., 1 x 10 mL) dried over $MgSO_4$ and the solvent was removed under vacuum. Purification by flash column chromatography on deactivated silica (NEt_3) with 5 % Et_2O in pentane gave **4.8b** in the form of a yellow-orange solid (40.6 mg, 107 µmol, 54 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 – 7.92 (m, 2H, $C_{Ar}H$), 7.66 – 7.49 (m, 2H, $C_{Ar}H$), 4.86 (tt, *J* = 11.7, 3.5 Hz, 1H, $C_{Cy}H$), 3.62 (tt, *J* = 11.4, 3.8 Hz, 1H, $C_{Cy}H$), 1.91 – 1.63 (m, 12H, $C_{Cy}H_2$), 1.54 – 1.10 (m, 8H, $C_{Cy}H_2$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 146.9 (C_{Ph}-NO_2), 132.7 ($C_{Ar}H$), 130.7 (C_{Ph}-C_{sp}), 123.7 ($C_{Ar}H$), 87.8 (C_{sp}-N), 82.8 (C_{sp}-C_{Ph}), 80.9 (C_{sp}), 65.1 (C_{sp}), 59.8 ($C_{Cy}H$), 57.2 ($C_{Cy}H$), 34.0 ($C_{Cy}H_2$), 29.5 ($C_{Cy}H_2$), 26.0 ($C_{Cy}H_2$), 25.6 ($C_{Cy}H_2$), 25.5 ($C_{Cy}H_2$), 25.2 ($C_{Cy}H_2$).

IR (ν_{max}, cm^{-1}) 2932 (m), 2856 (w), 2185 (s), 2132 (w), 1590 (m), 1515 (m), 1420 (m), 1389 (w), 1365 (m), 1336 (s), 1316 (s), 1252 (m), 1220 (m), 1203 (m), 851 (m).

HRMS (APCI/QTOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{22}H_{27}N_4O_2^+$ 379.2129; Found 379.2119.

7.5. Experimental Details for Chapter 5

The cytotoxicity assay was carried out by Antoine Gibelin and Dr. Marc Chambon at the Biomolecular Screening Core Facility at EPFL.

Compounds were stored in the dark, at – 20 C under dry air, using an automated storage system and their chemical integrity was controlled regularly by RP-HPLC, coupled to ESI-MS and CAD detector.

A2780 human ovarian carcinoma cells (ECACC 93112519) and MDA-MB-231 human breast adenocarcinoma cells (ECACC 92020424) were obtained from the European Collection of Cell Cultures. Hela human cervix adenocarcinoma cells (ATCC CCL-2), MCF7 human breast adenocarcinoma (metastases from pleural effusion) cells (ATC HTB-22) and MCF-10A human epithelial breast cells (ATC CRL-10317) were obtained from ATCC. HEK293T human embryonic kidney cells were obtained from Prof. Aebisher.

All cell culture media, buffers and reagents were obtained from Gibco Life Technologies.

Cells were grown as adherent monolayer cultures in 75 cm^2 culture flasks (TPP) without antibiotics using the media listed in Table 7.1, supplemented with 10 % heatinactivated fetal bovine serum (FBS, Invitrogen 10101-145).

Medium for MCF-10A was supplemented with 10 μg/mL insulin, 20 μg/mL hydrocortisone, 20 ng/mL epidermal growth factor and 100 ng/mL cholera toxin. Cultures were maintained in an incubator at 37 °C in a humidified atmosphere containing 5 % CO_2 and 95 % air. Cells were subcultured 2 to 3 times per week. Briefly, the cells were harvested with trypsin 0.05 %-EDTA (Life Technologies 25300062) and diluted with growth medium. Cells used for the assays were harvested from culture when the level of confluence was between 60 % and 80 %, while cell viability was > 90 %.

Table 7.1. Cell lines and their respective media.

Cell line	Medium (Invitrogen)
A2780	RPMI1640 61870-010
Hela	DMEM 32430-027
MDA-MB-231	DMEM 61965-026
MCF7	DMEM 31966-021
MCF-10A	DMEMF12 31331-028
HEK293T	DMEM 32430-027

All compounds were dissolved in DMSO at a stock concentration of 10 mM.

For primary testing at a single concentration (10 µM - DMSO content of 0.1%), compounds were platted as 100 nl of stock solution using an Echo acoustic dispenser (Labcyte). Compound dilution series for dose-response curves were also generated using an Echo acoustic dispenser (Labcyte), with a final DMSO content normalized to 0.5 %. Compounds were tested at 8 concentrations, with 2 replicates per concentration.

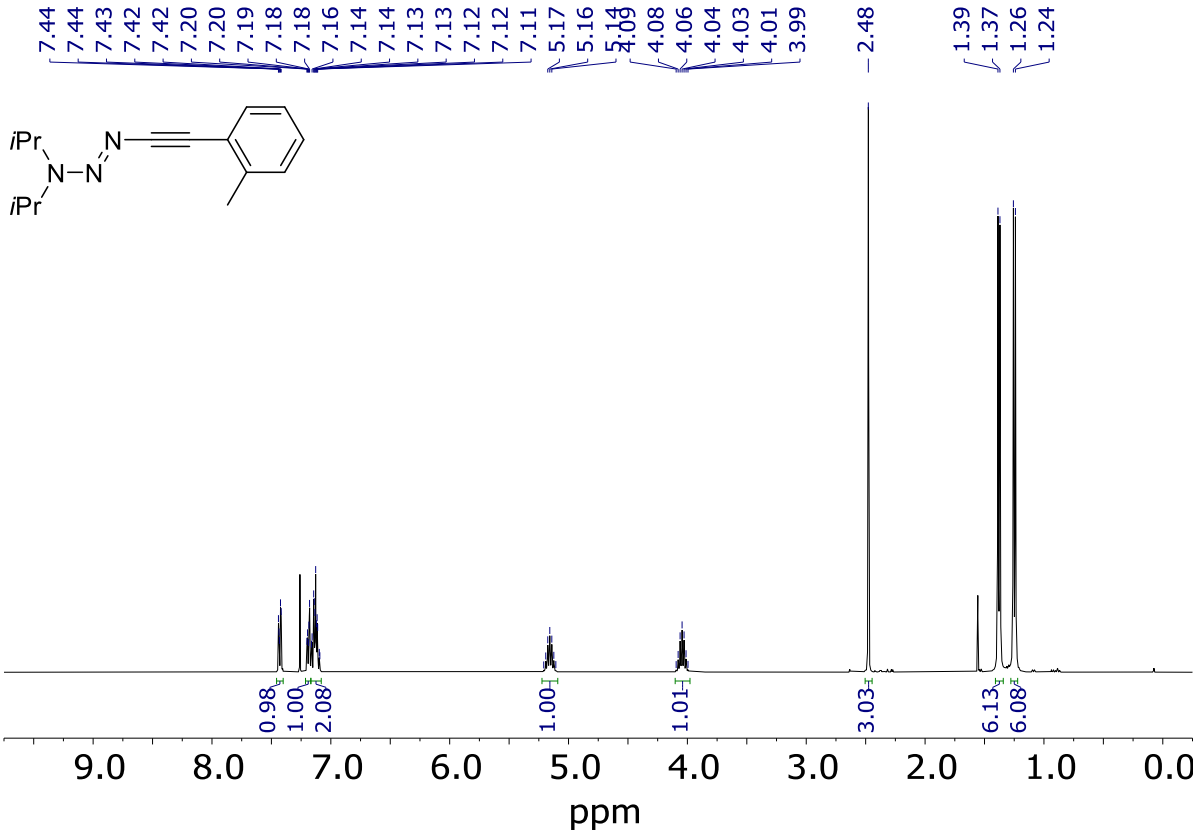
Cells were added at top of compounds in the assay plates in volumes of 100 µL/well (using a multi-drop dispenser, ThermoFisher) at seeding density of ca. 10 000 cells per well for A2780, Hela, HEK293T and MCF-10A and ca. 15000 cells per well for MCF7 and MDA-MB-231. Incubation time in cell incubator was set to 24 h. Subsequently, 10 µL of PrestoBlue was added to the cells and the plates were incubated for a further 1 h.

$CuSO_4$ (at 10 mM) was used as positive control and DMSO (0.1 % for primary screening, 0.5 % for dose-response curves) was used as negative control.

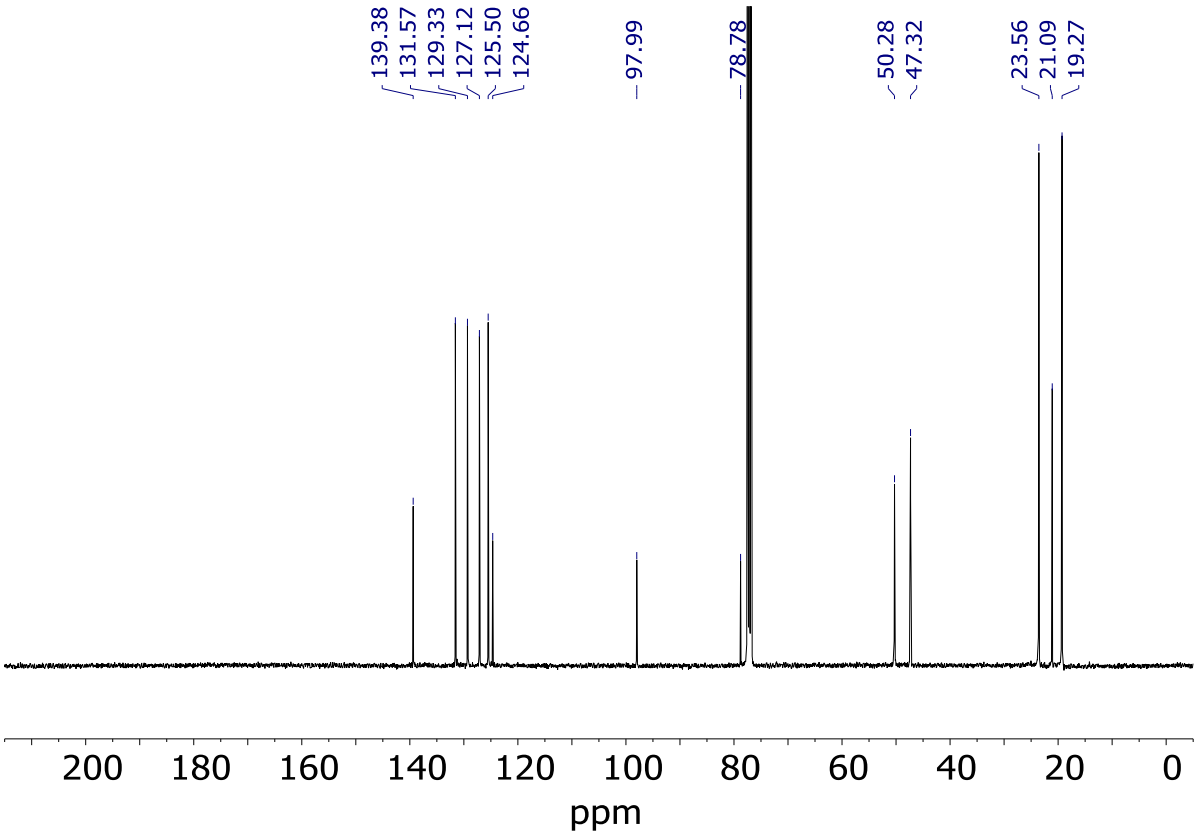
Cell viability was determined by the resazurin assay.[169] The fluorescence emission was read at 590 nm after excitation at 560 nm using an Infinite F500 microplate reader (Tecan).

Dose-response curves and IC_{50} determination were generated by using the in-house developed software within LIMS based on four-parameters nonlinear regression Hill model.

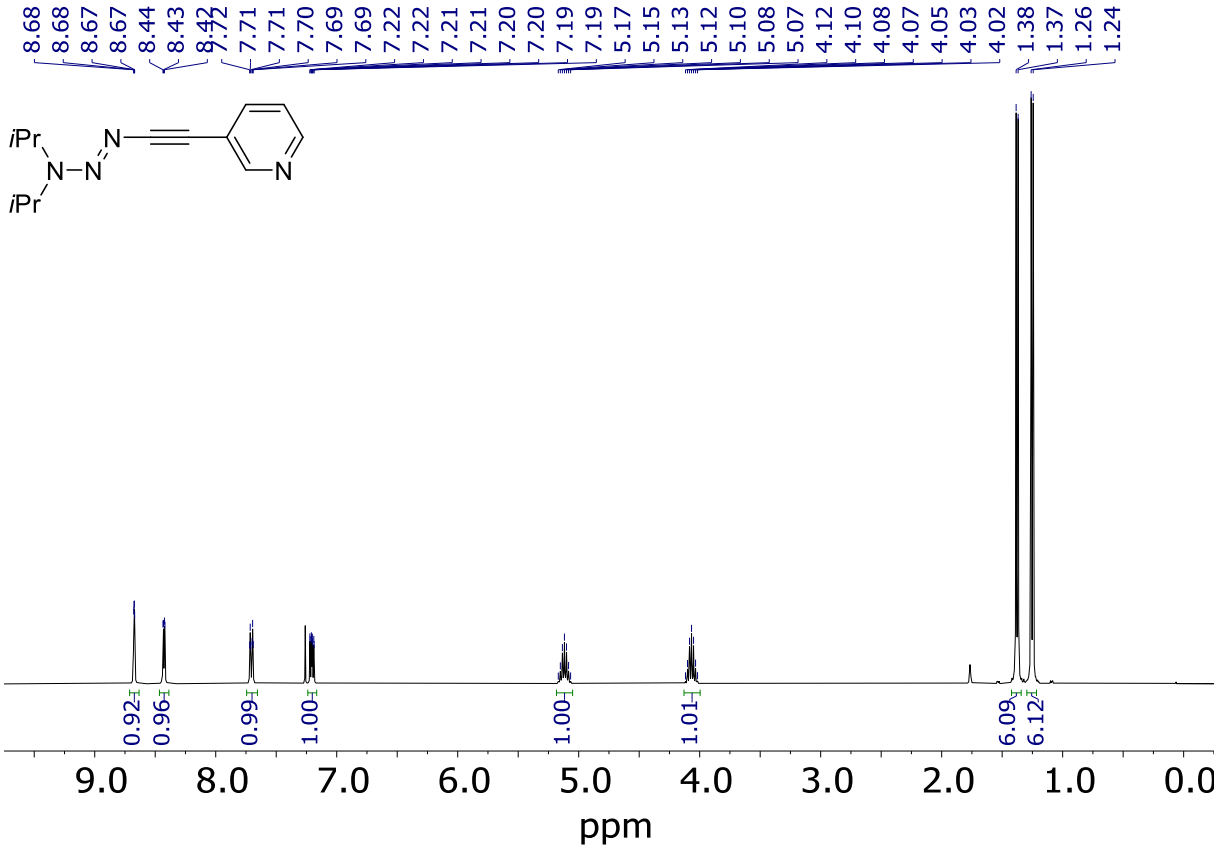
7.6. NMR-Spectra



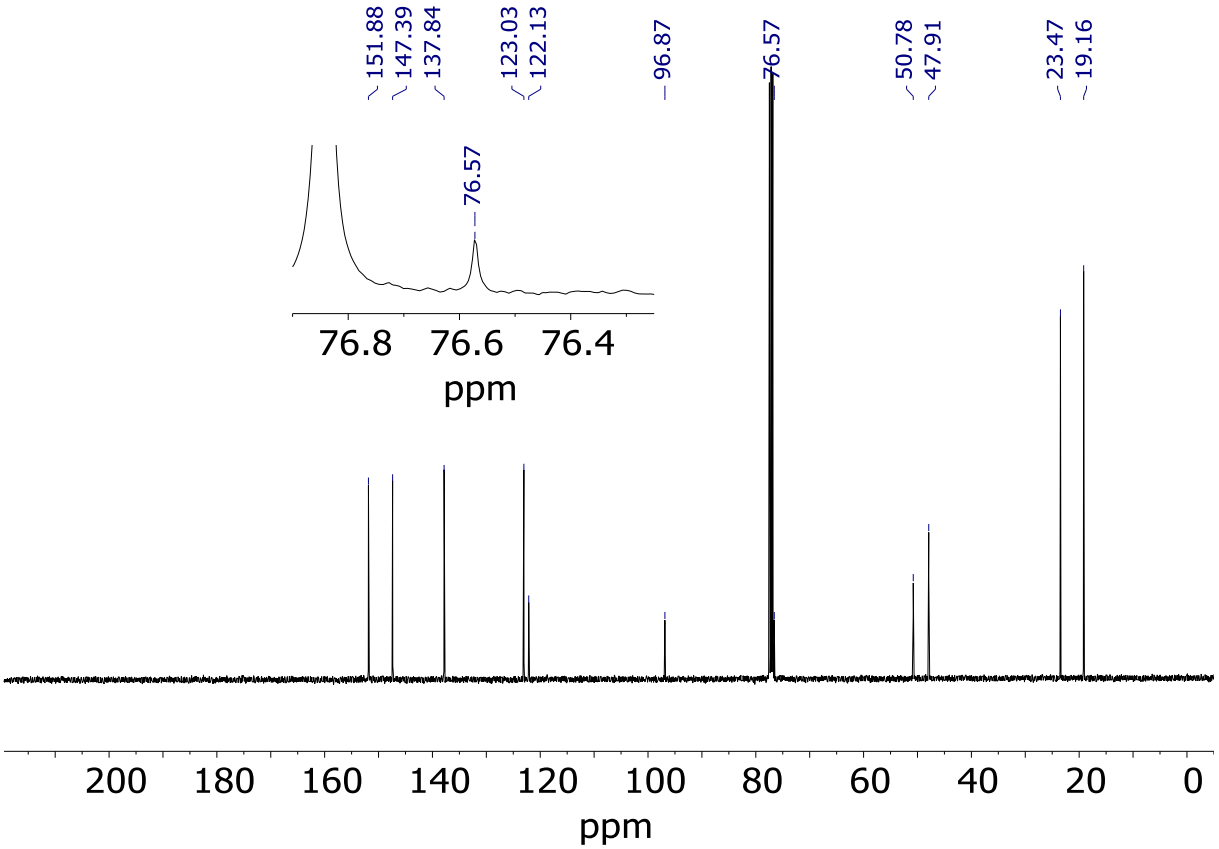
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **4.1g**.



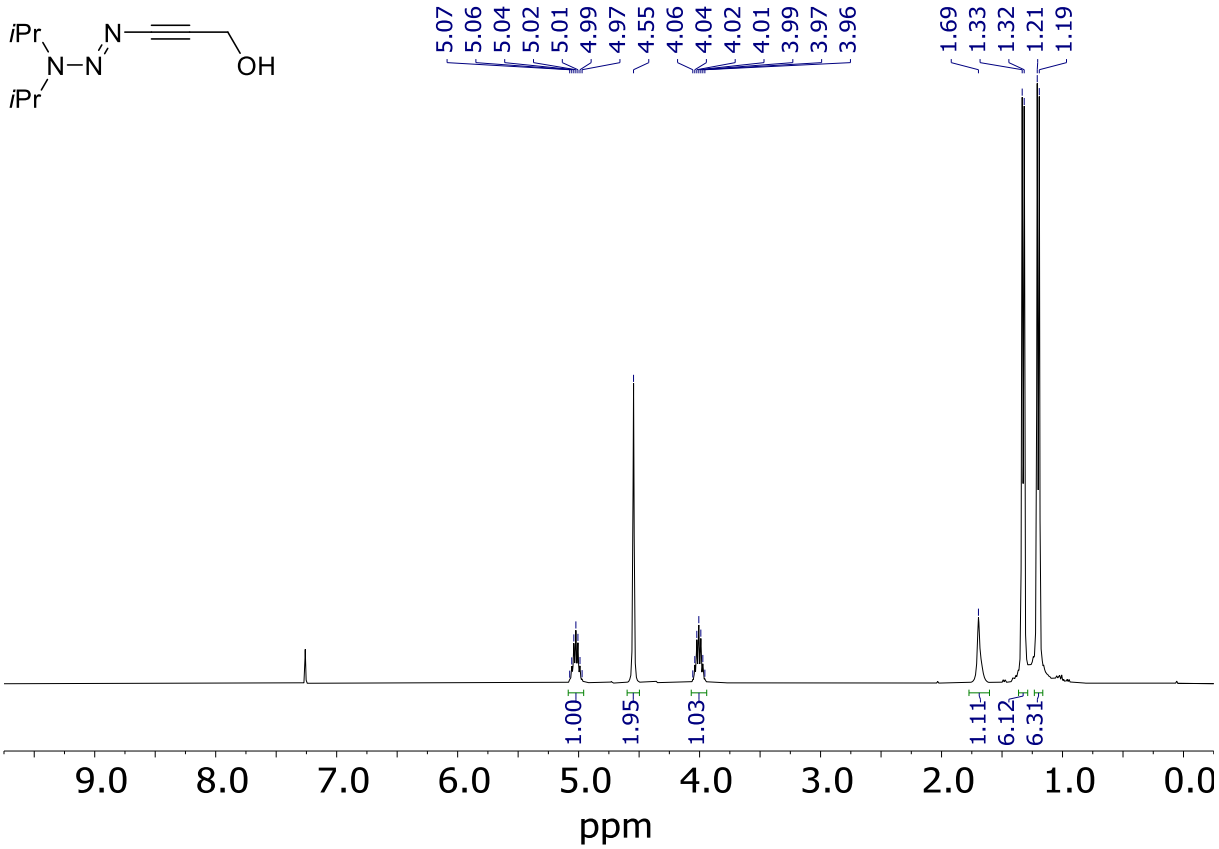
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of compound **4.1g**.



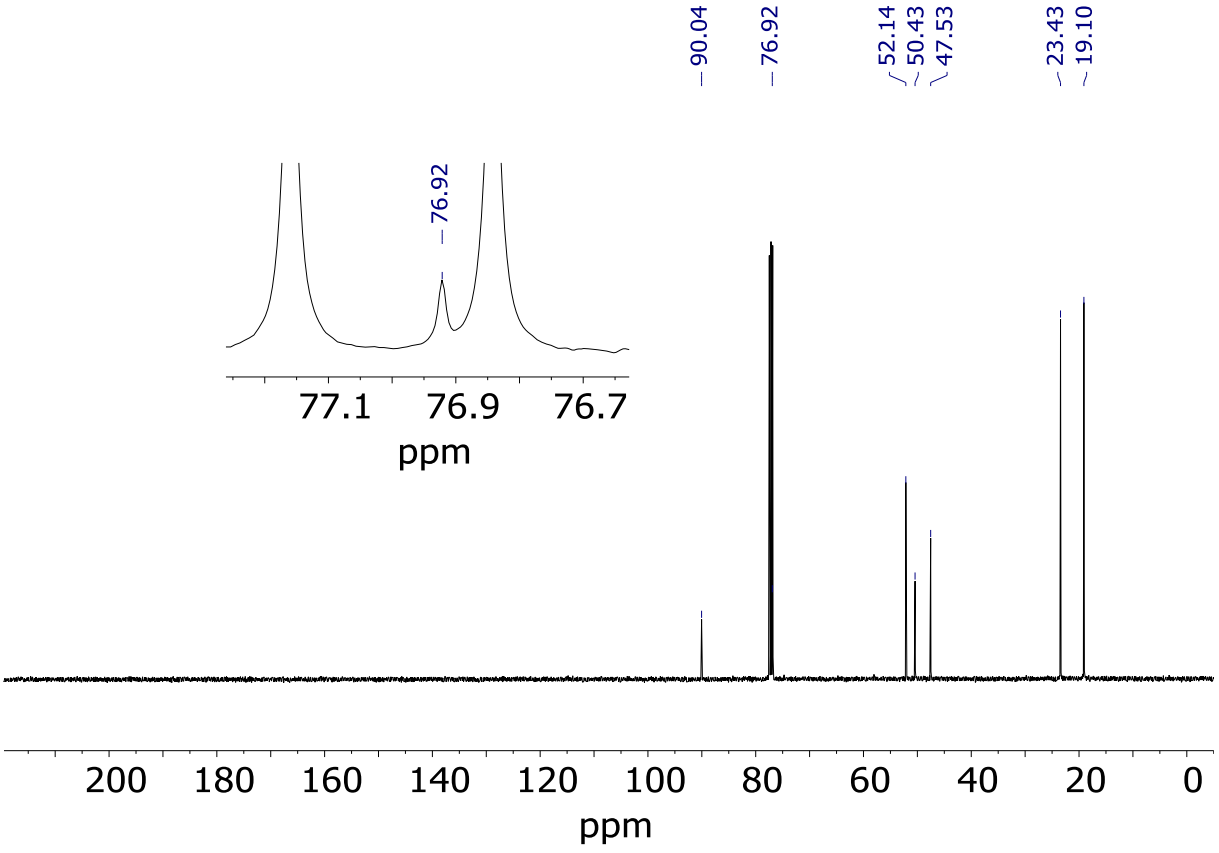
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **4.1h**.



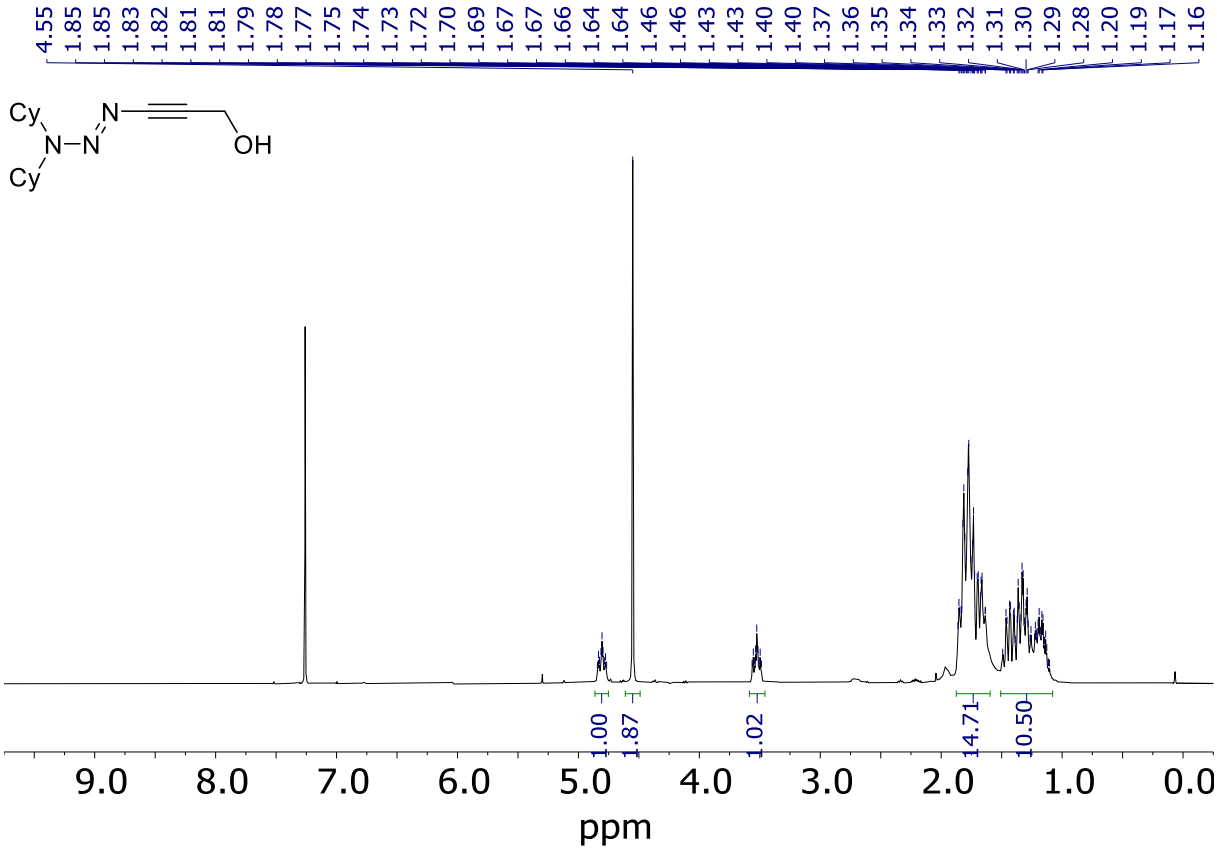
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of compound **4.1h**.



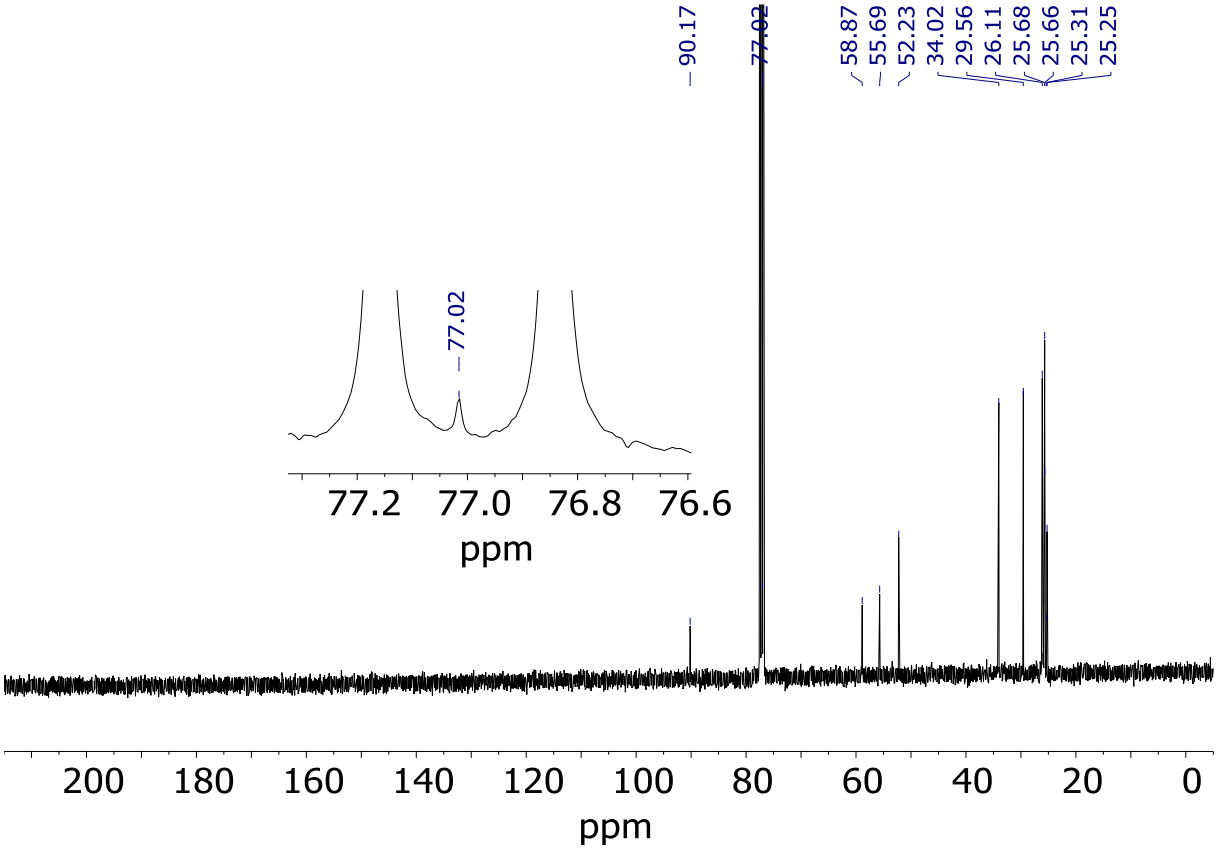
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **4.2a**.



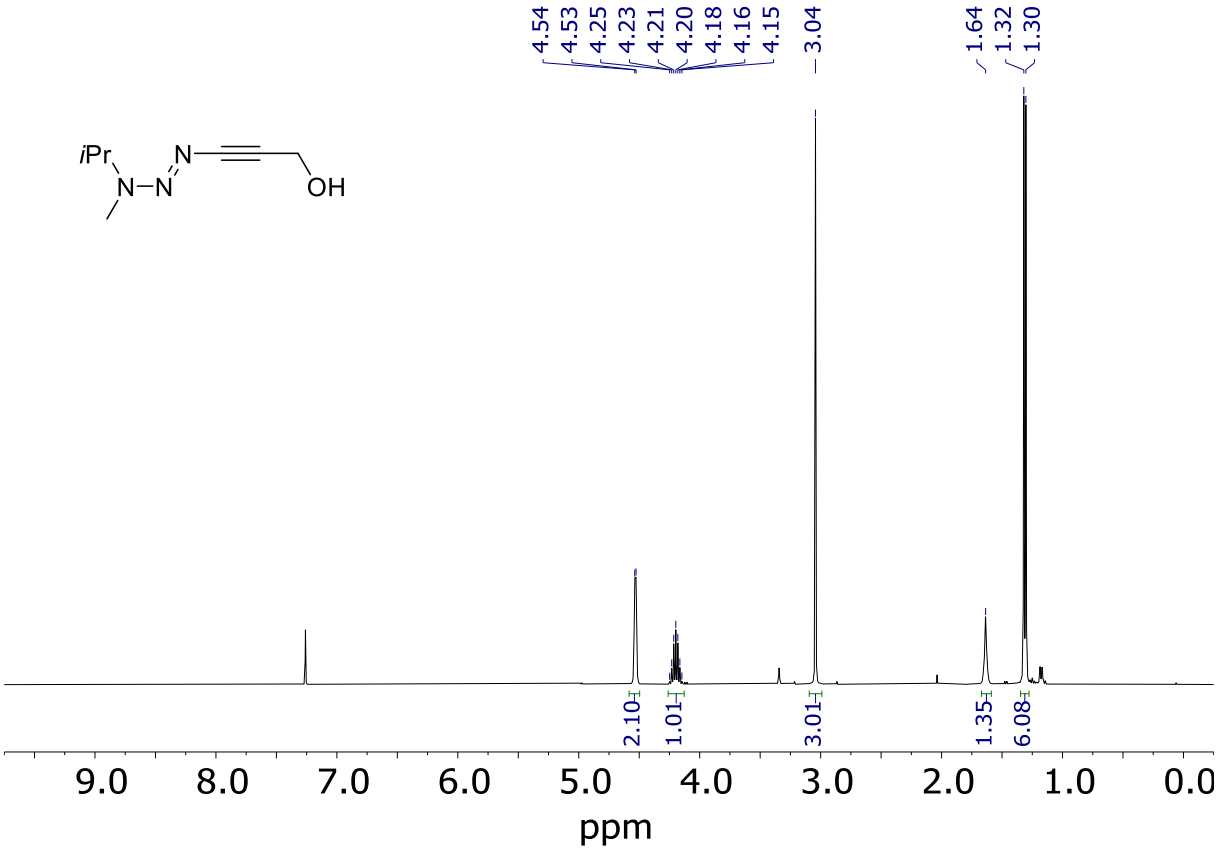
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of compound **4.2a**.



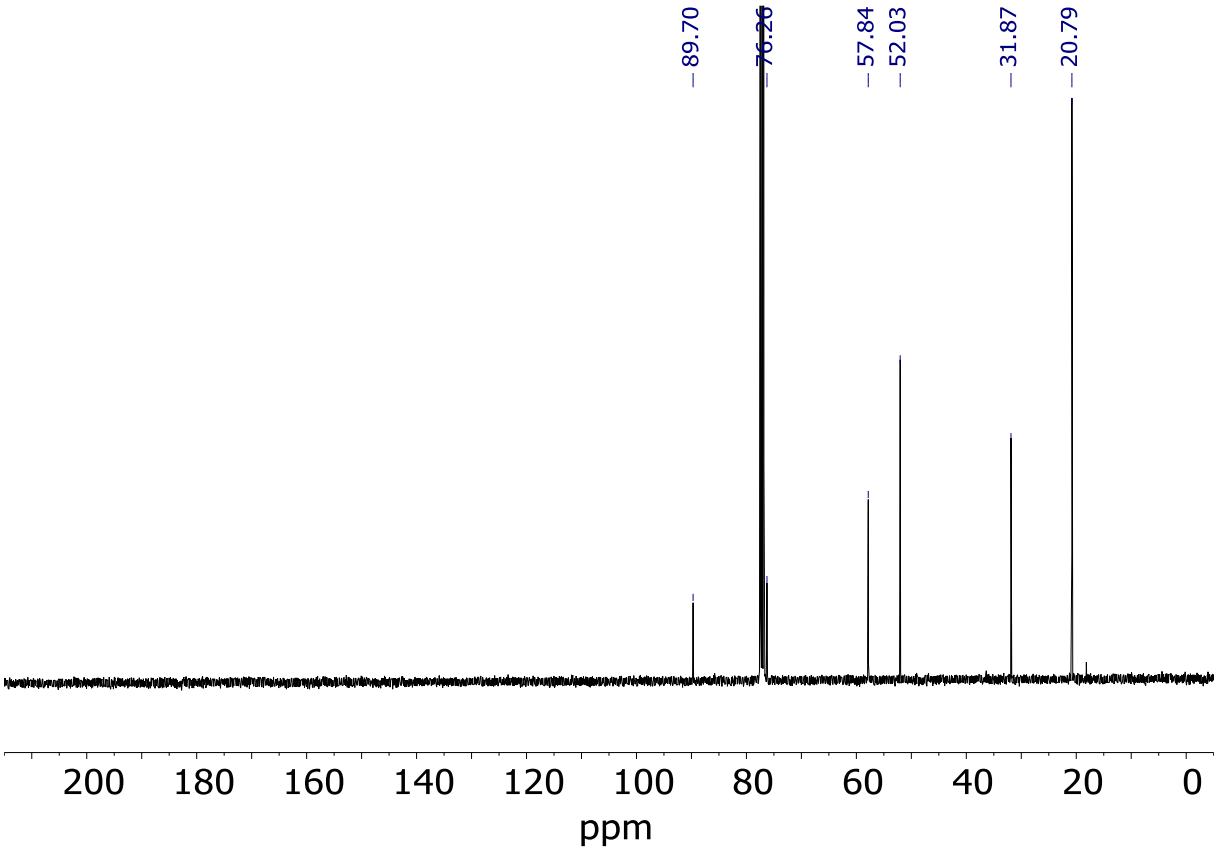
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **4.2b**.



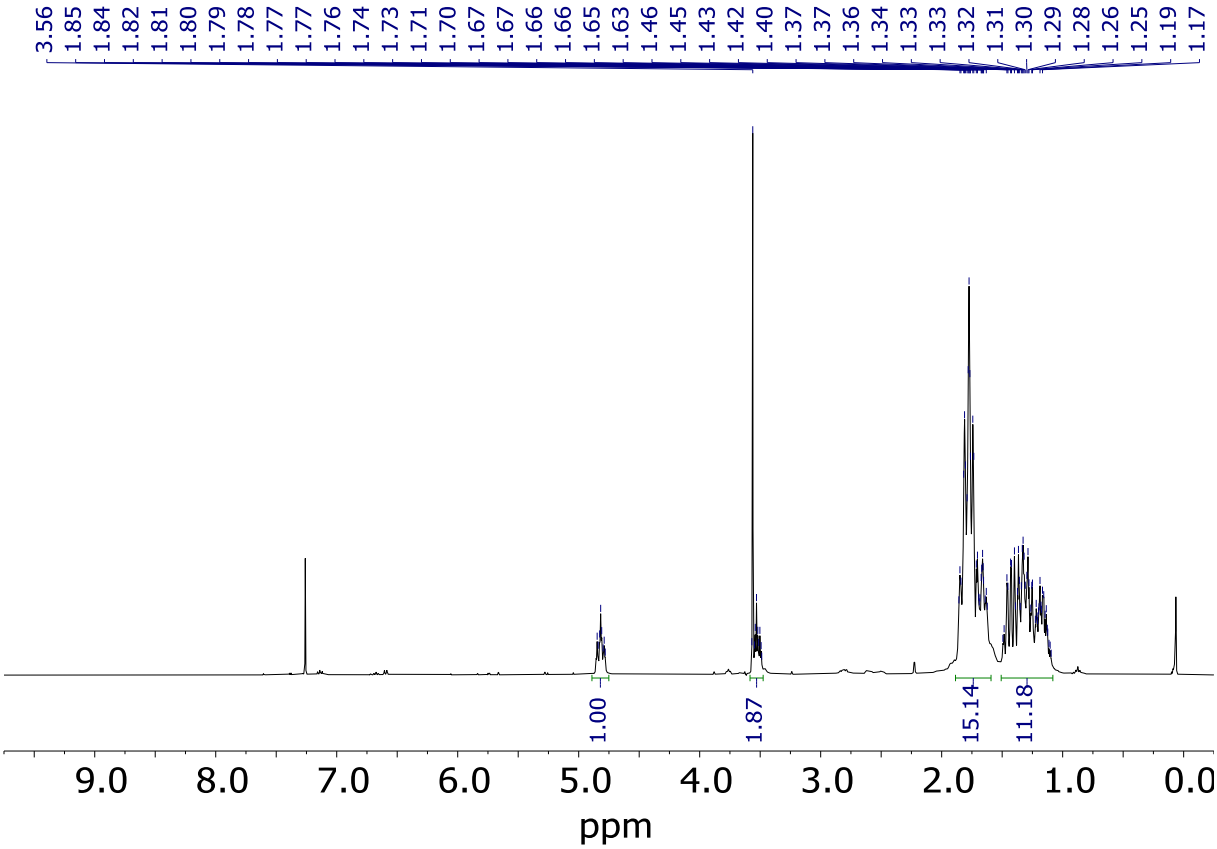
^{13}C-NMR (101 MHz, $CDCl_3$) of compound **4.2b**.



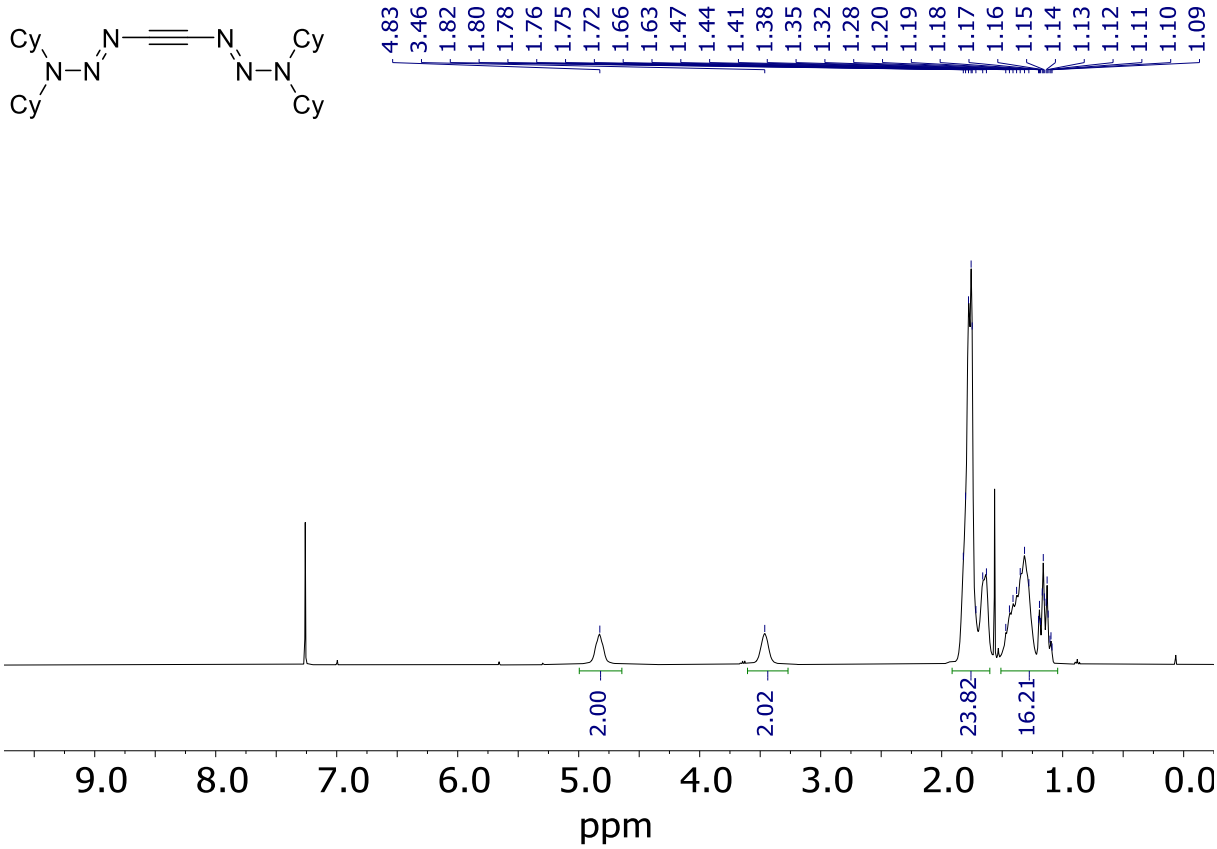
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **4.2c**.



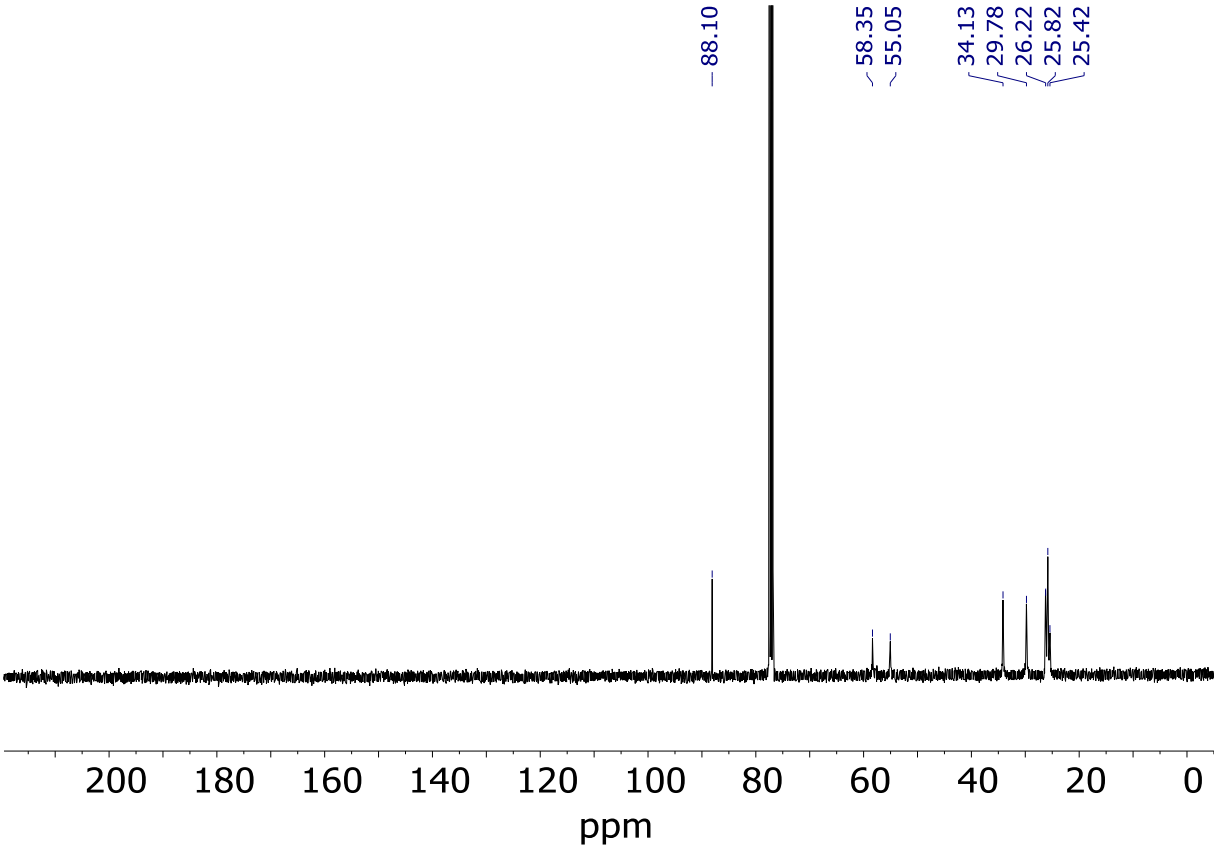
^{13}C-NMR (101 MHz, $CDCl_3$) of compound **4.2c**.



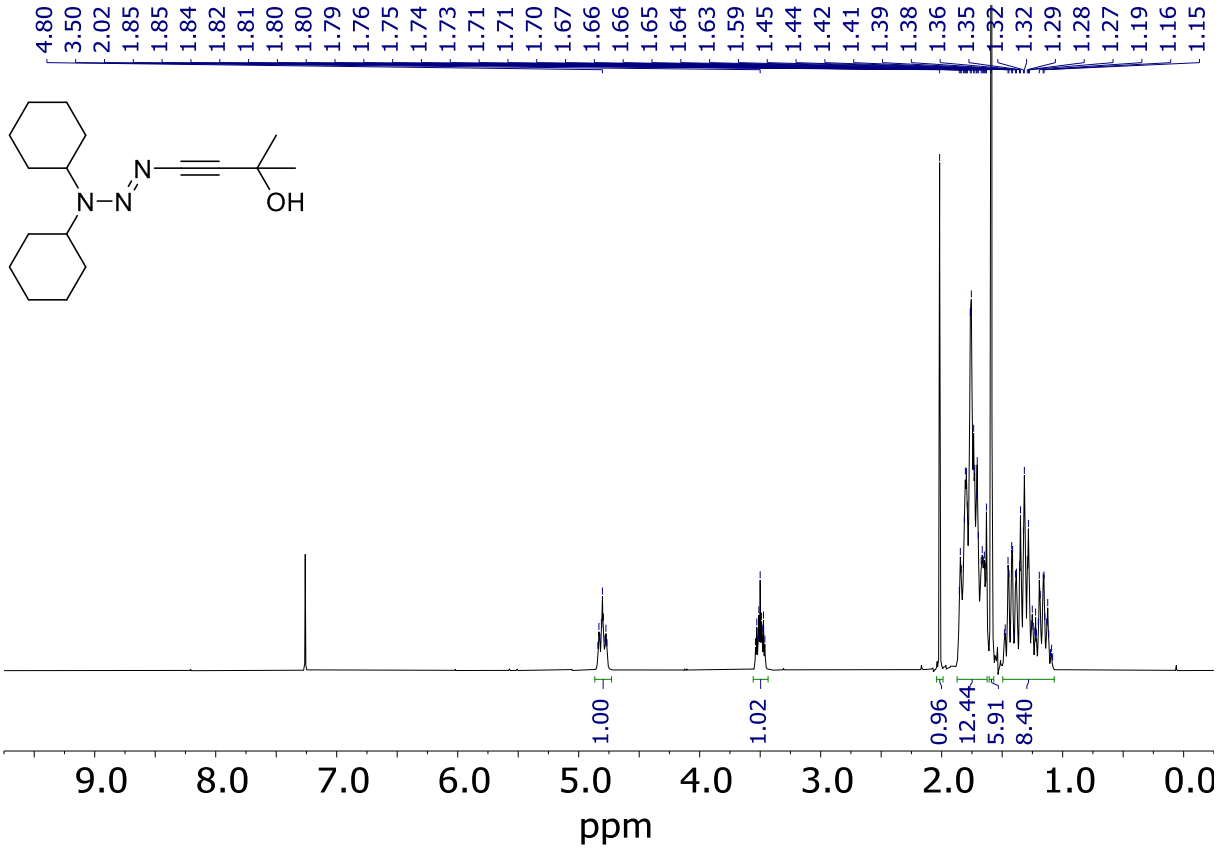
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **4.3** synthetized from Ethynylmagnesium bromide.



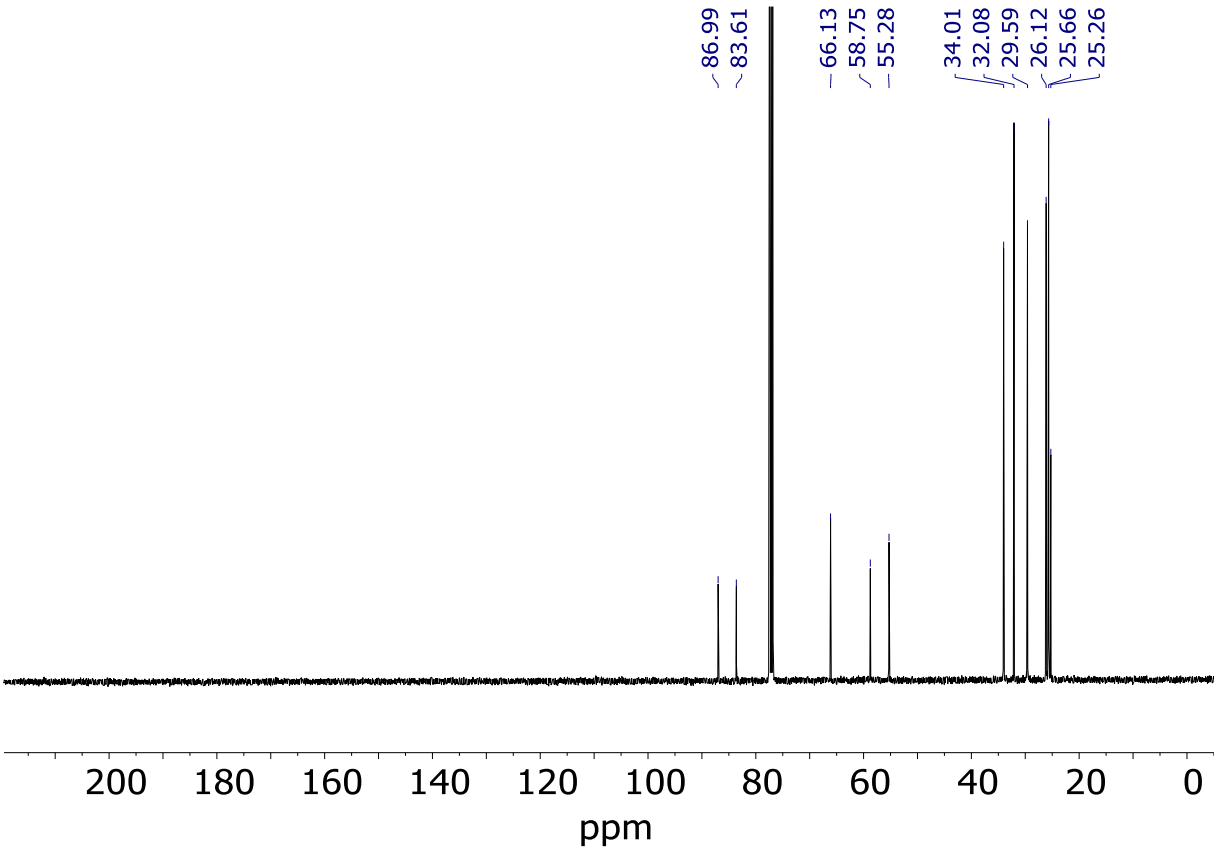
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **4.4**.



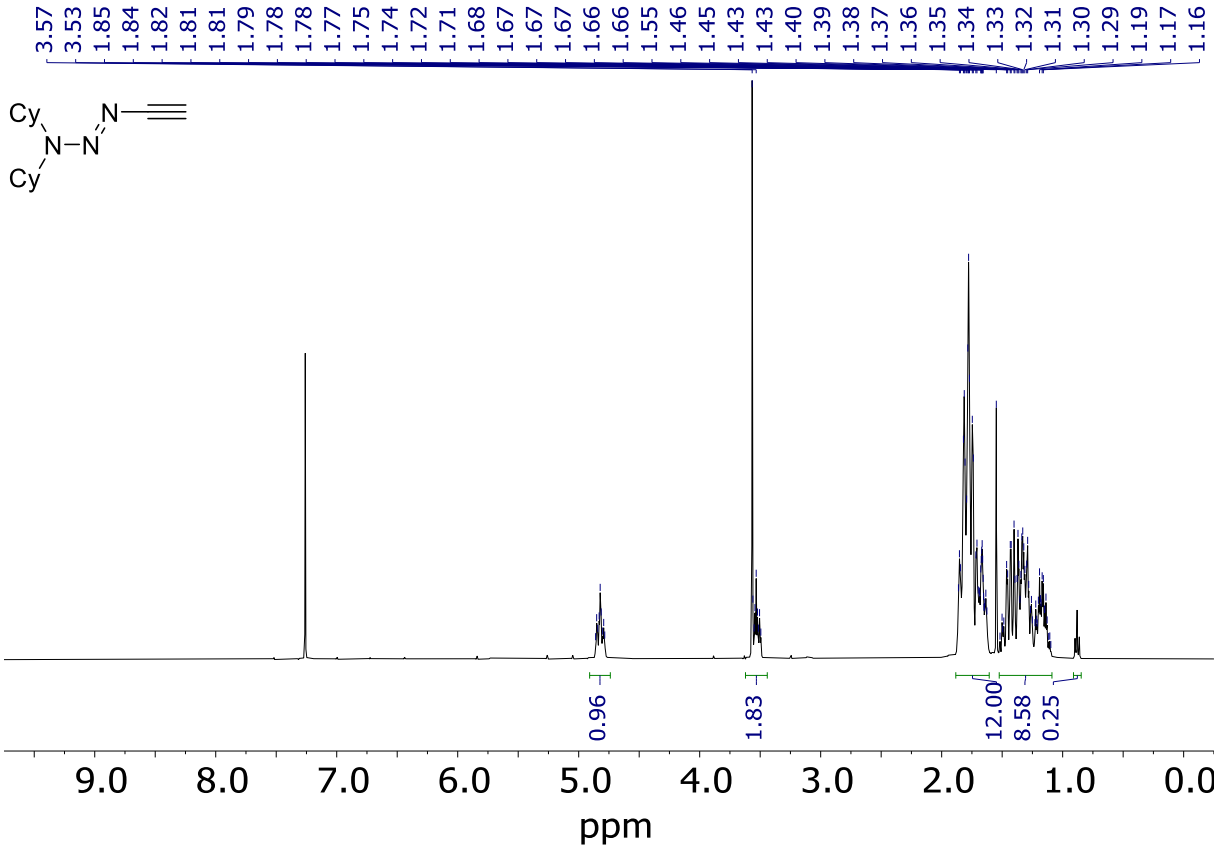
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of compound **4.4**.



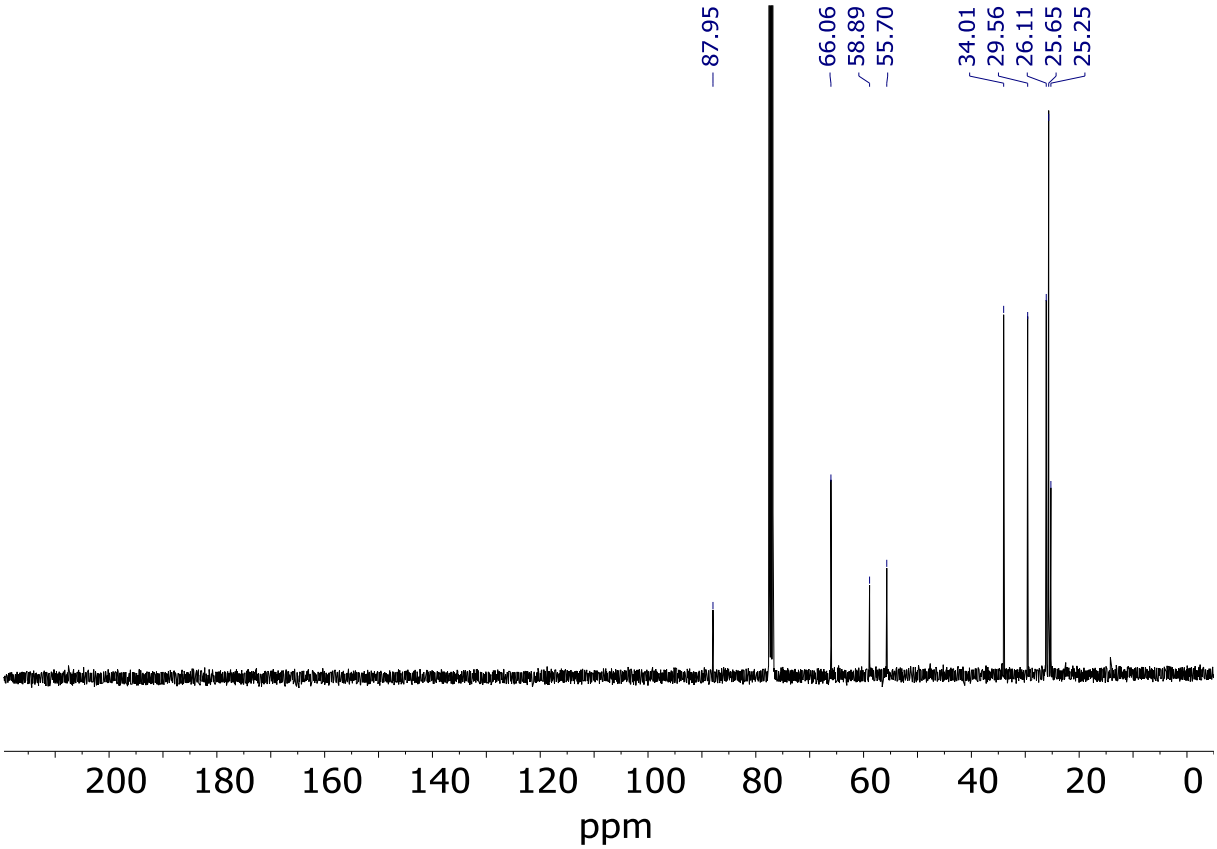
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **4.5**.



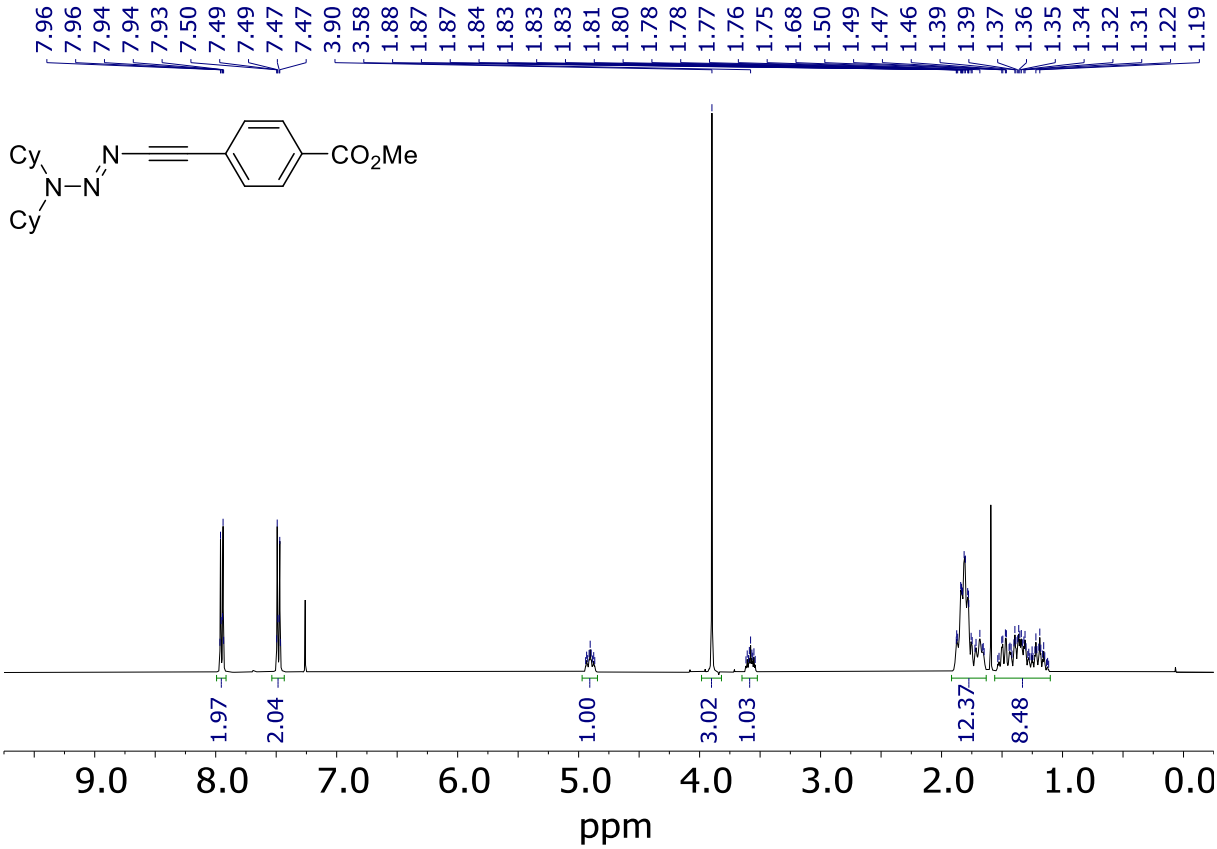
^{13}C-NMR (101 MHz, $CDCl_3$) of compound **4.5**.



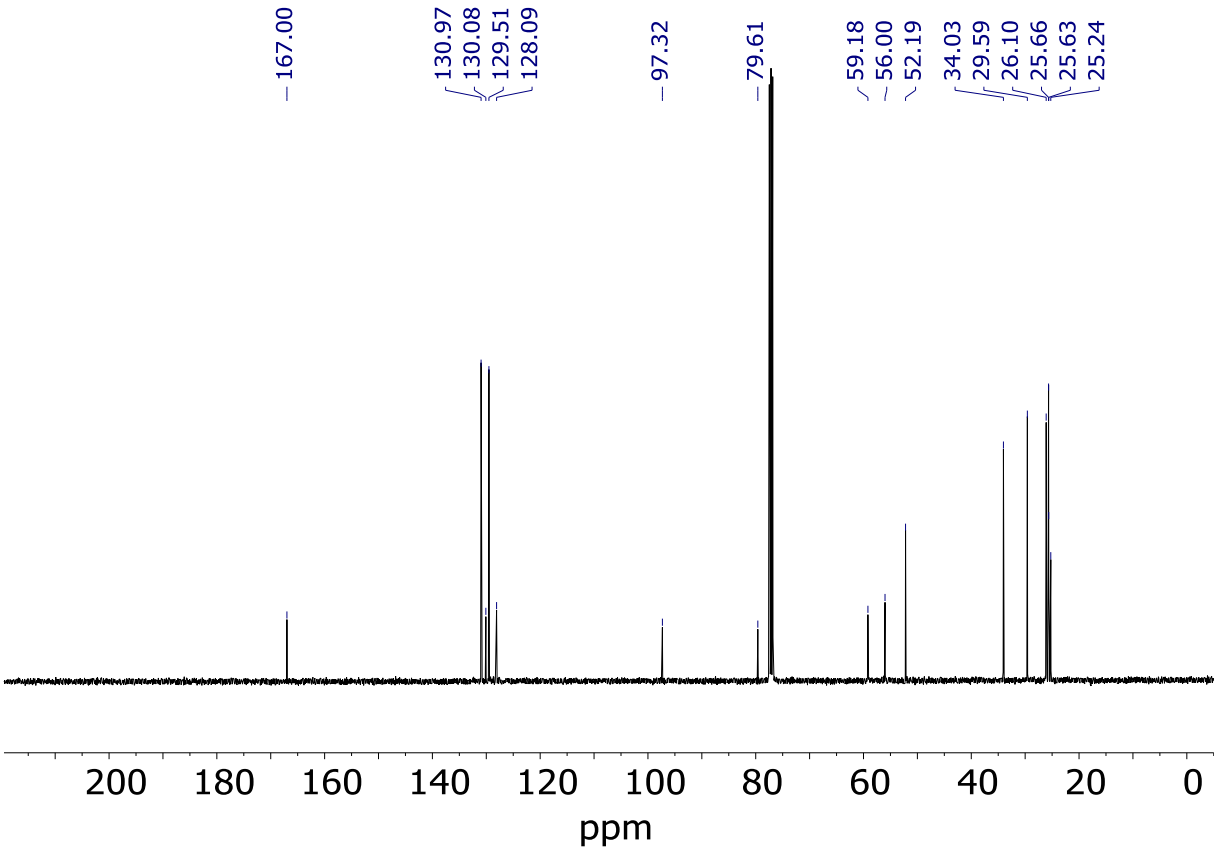
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **4.3** synthetized from **4.5**.



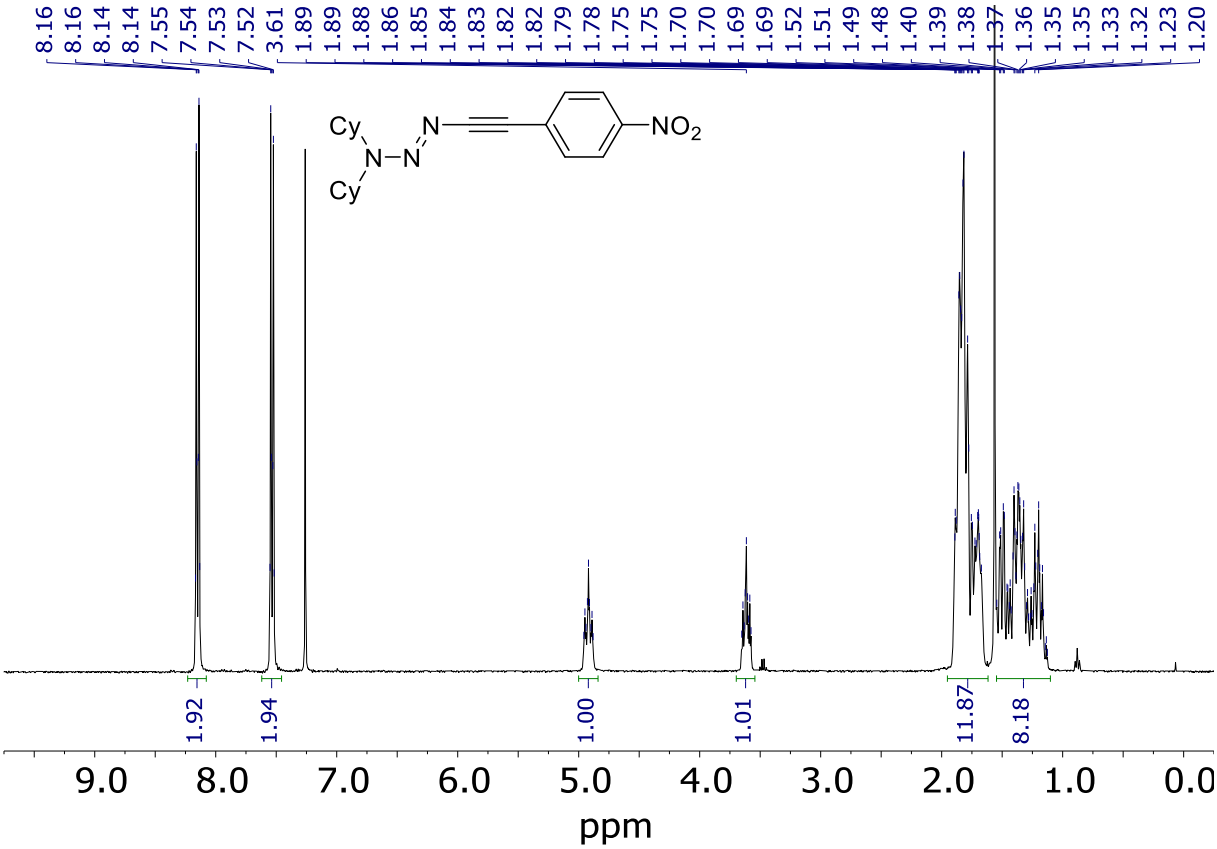
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of compound **4.3** synthetized from **4.5**.



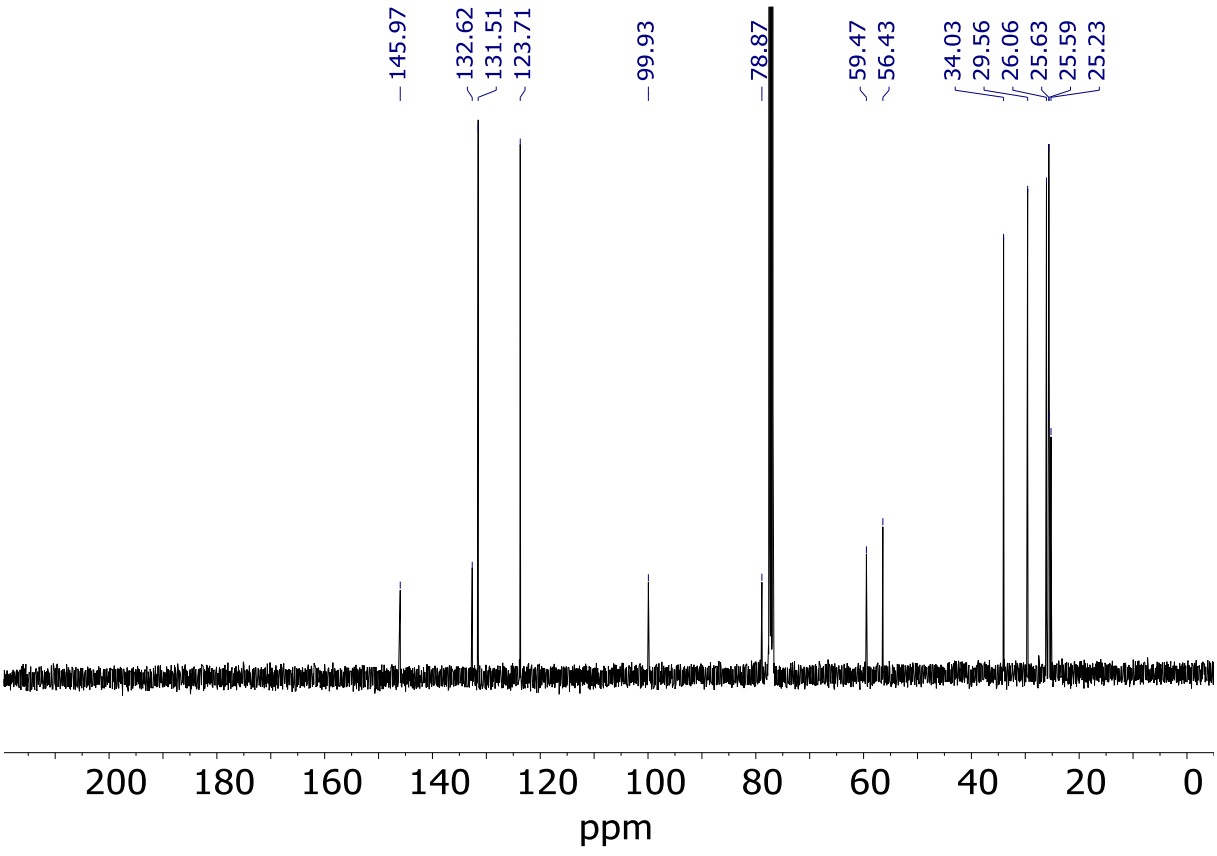
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **4.6a**



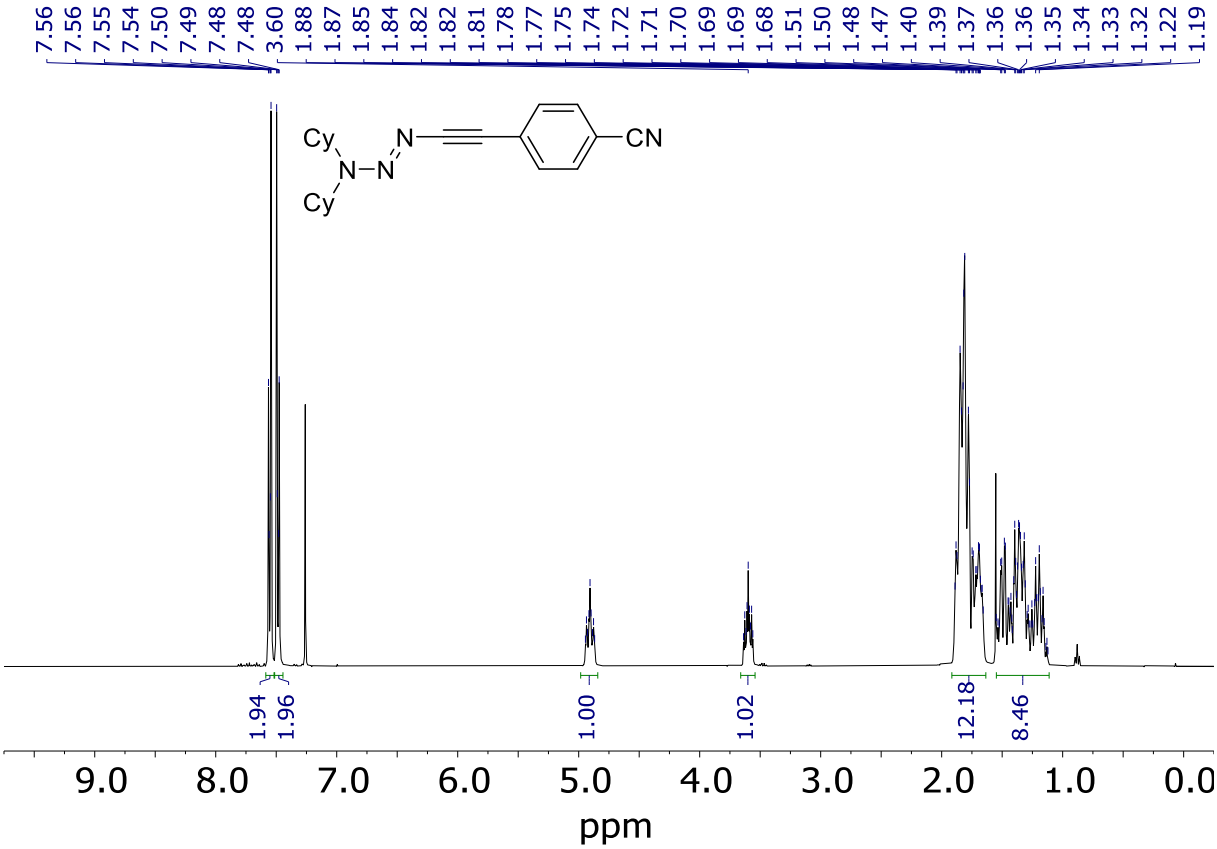
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of compound **4.6a**.



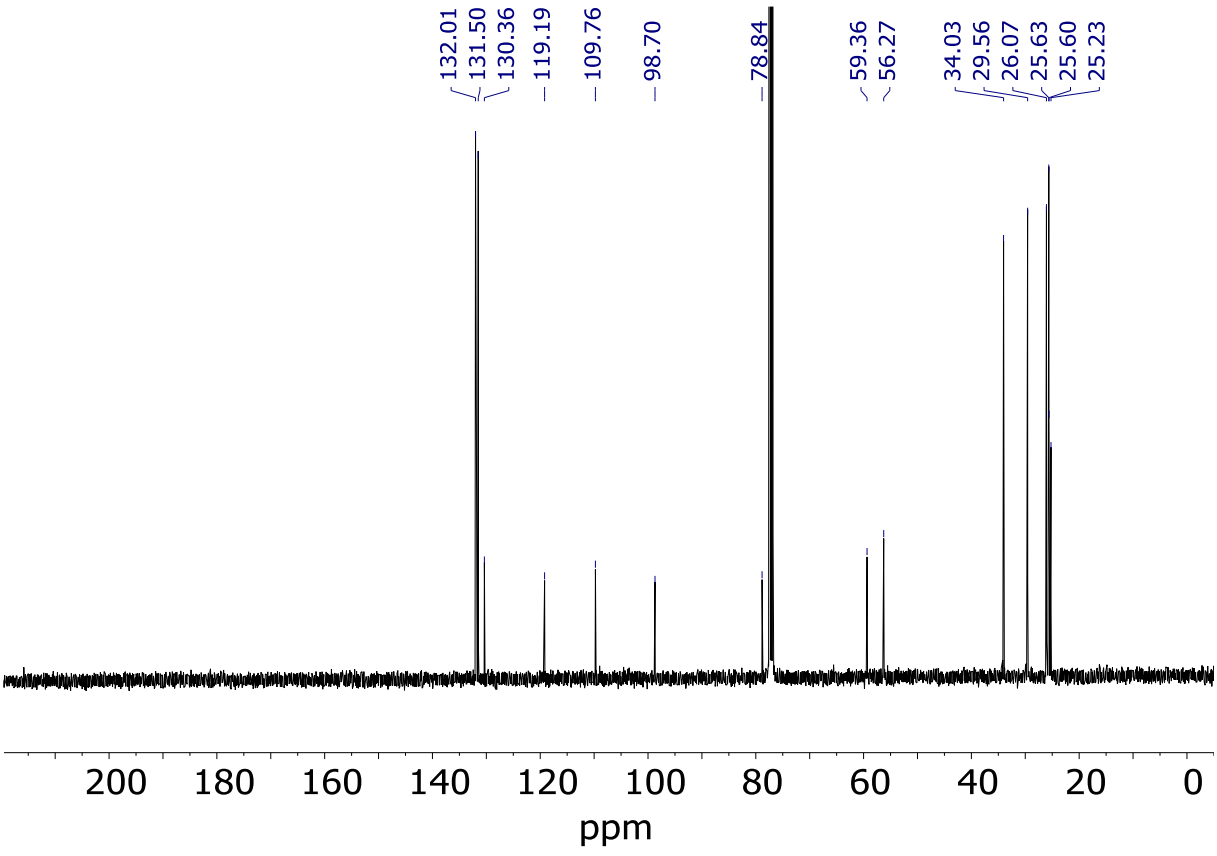
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **4.6b**.



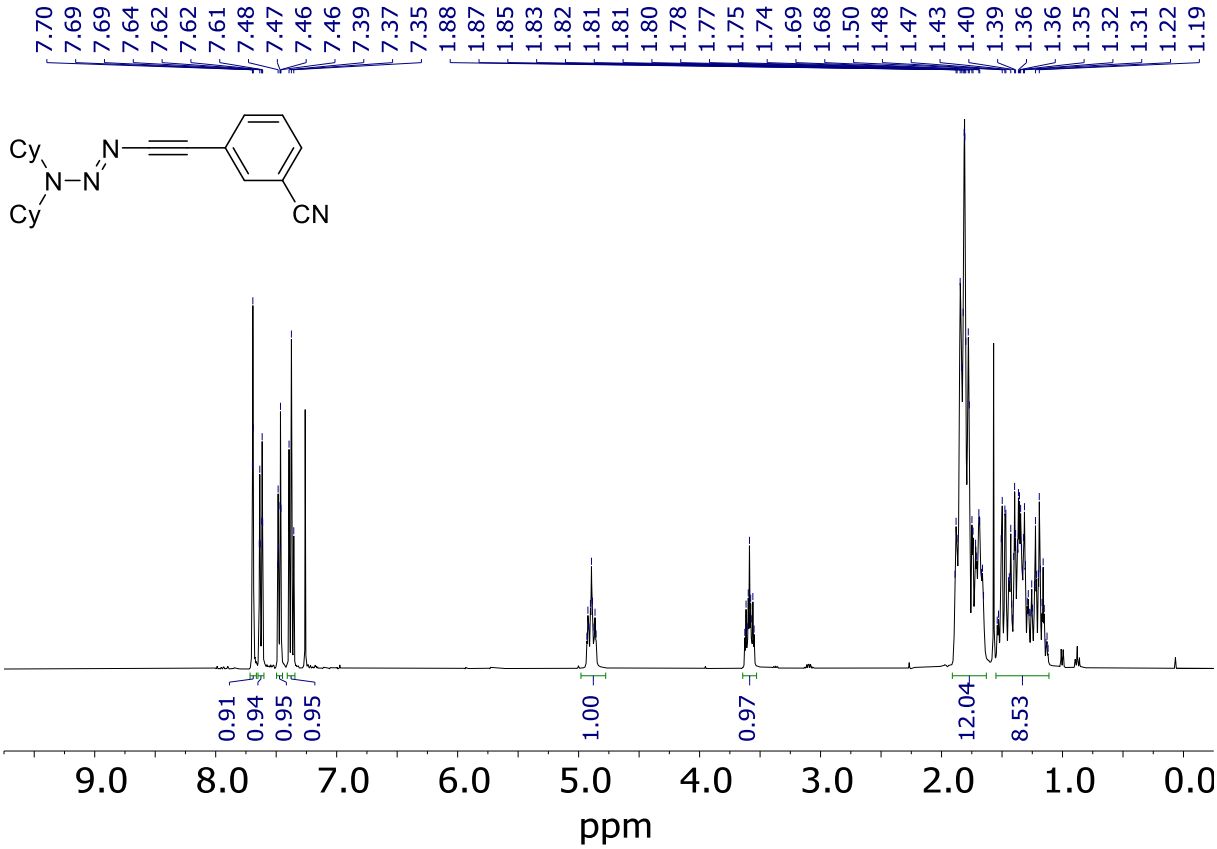
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of compound **4.6b**.



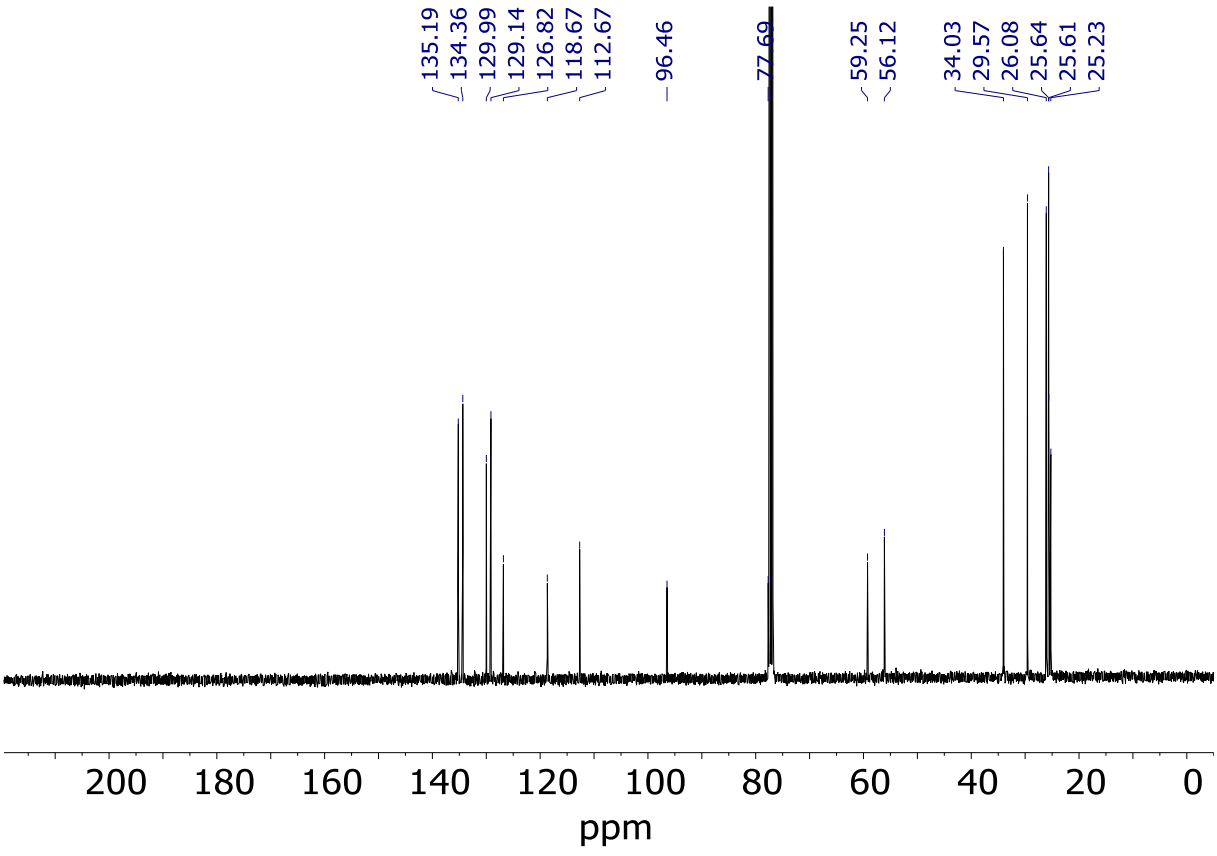
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **4.6c**.



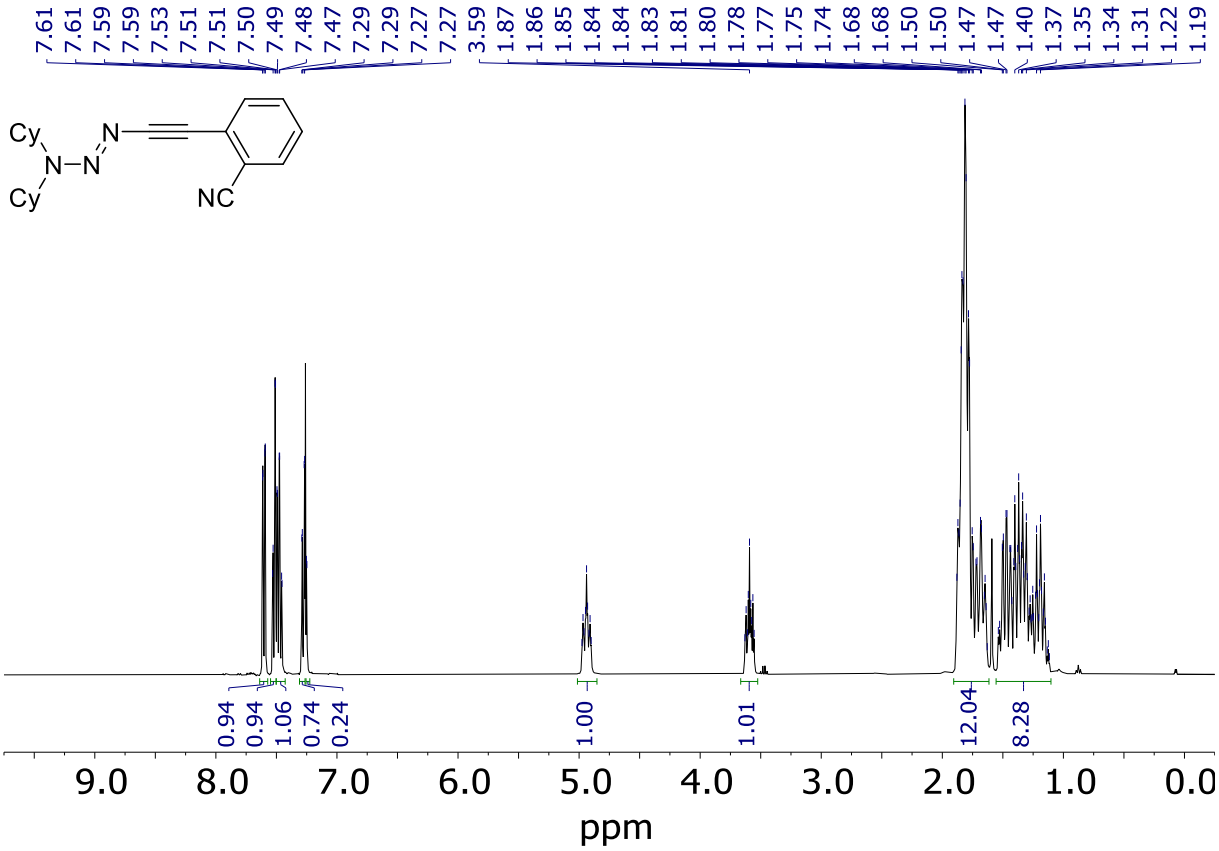
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of compound **4.6c**.



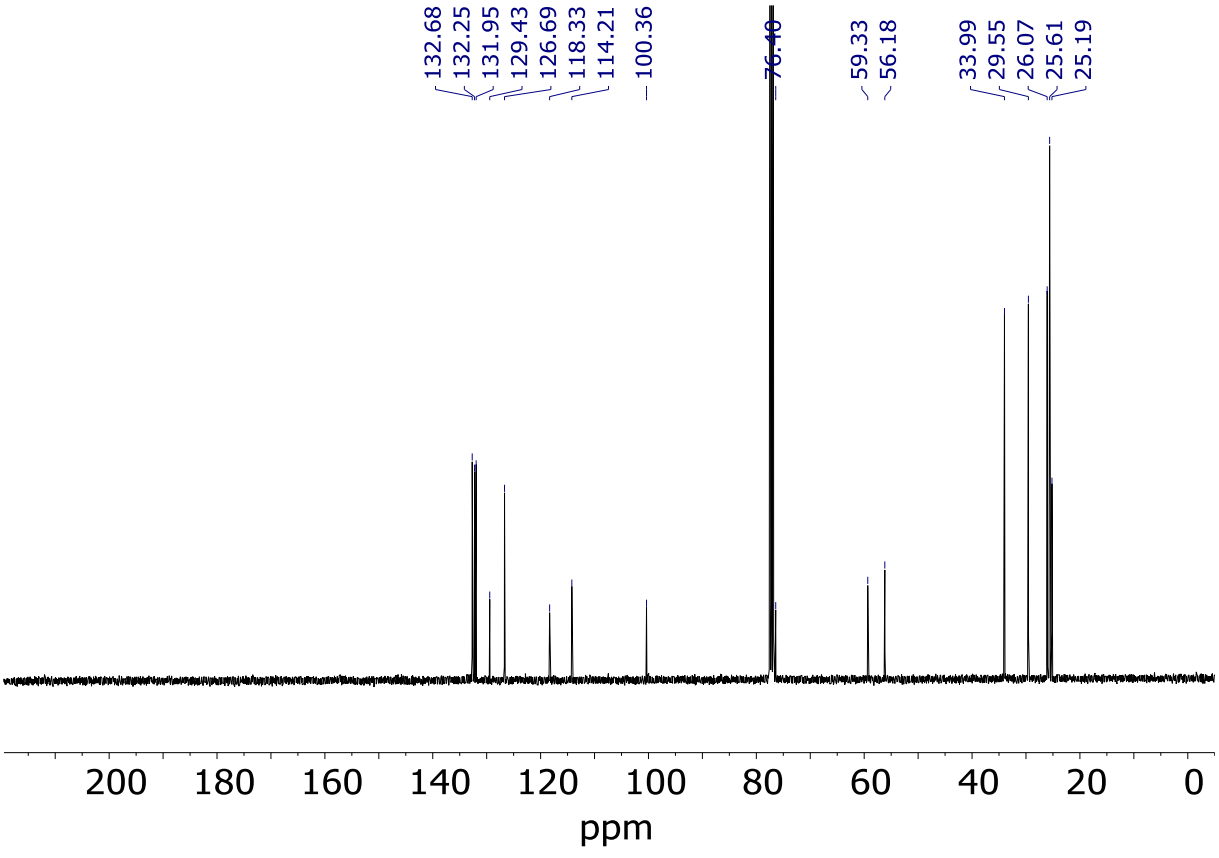
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **4.6d**.



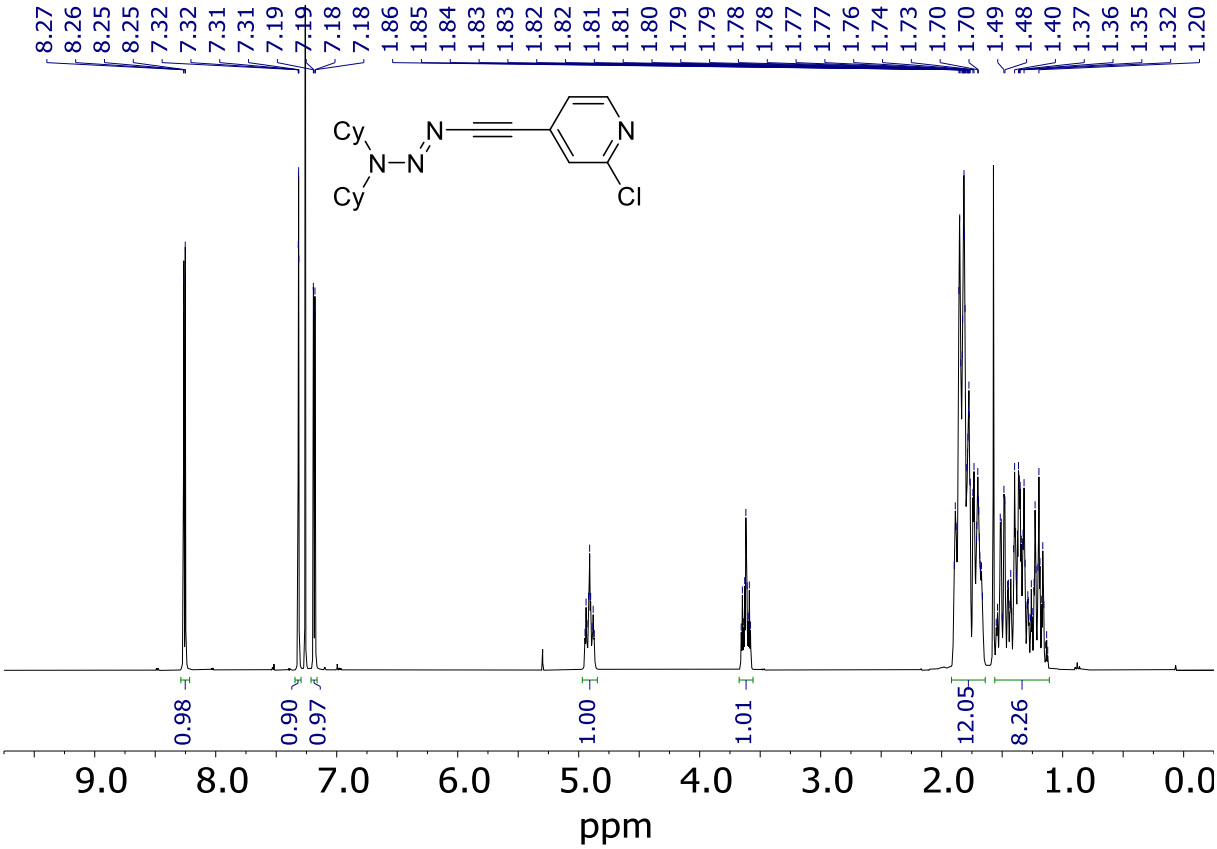
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of compound **4.6d**.



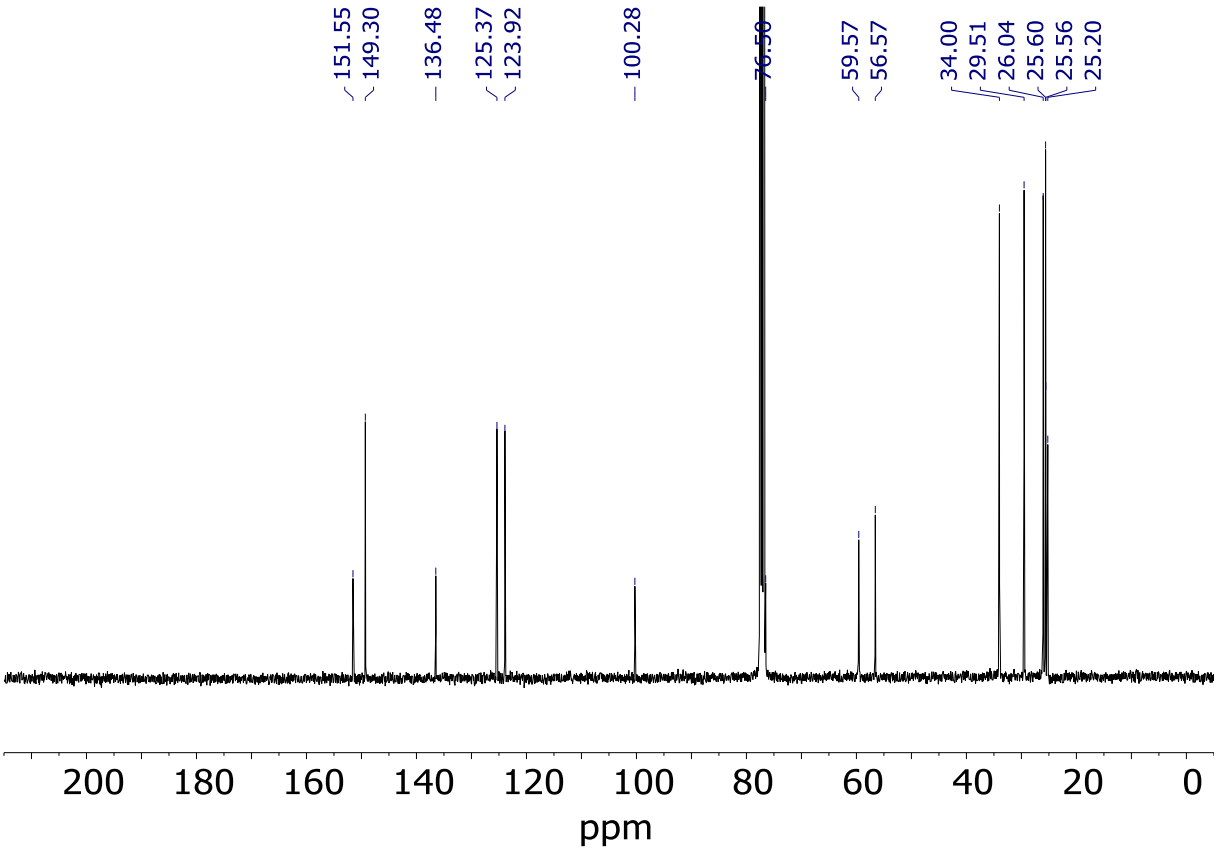
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **4.6e**.



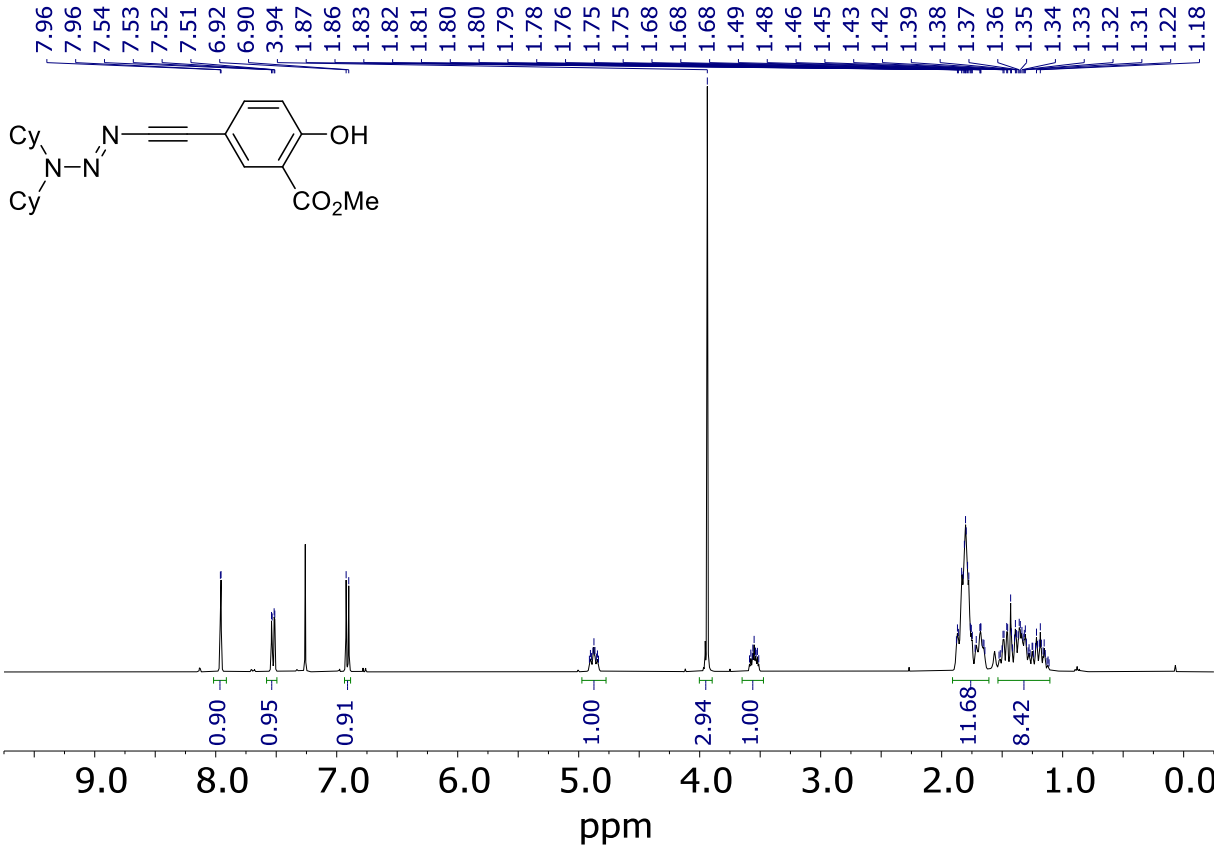
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of compound **4.6e**.



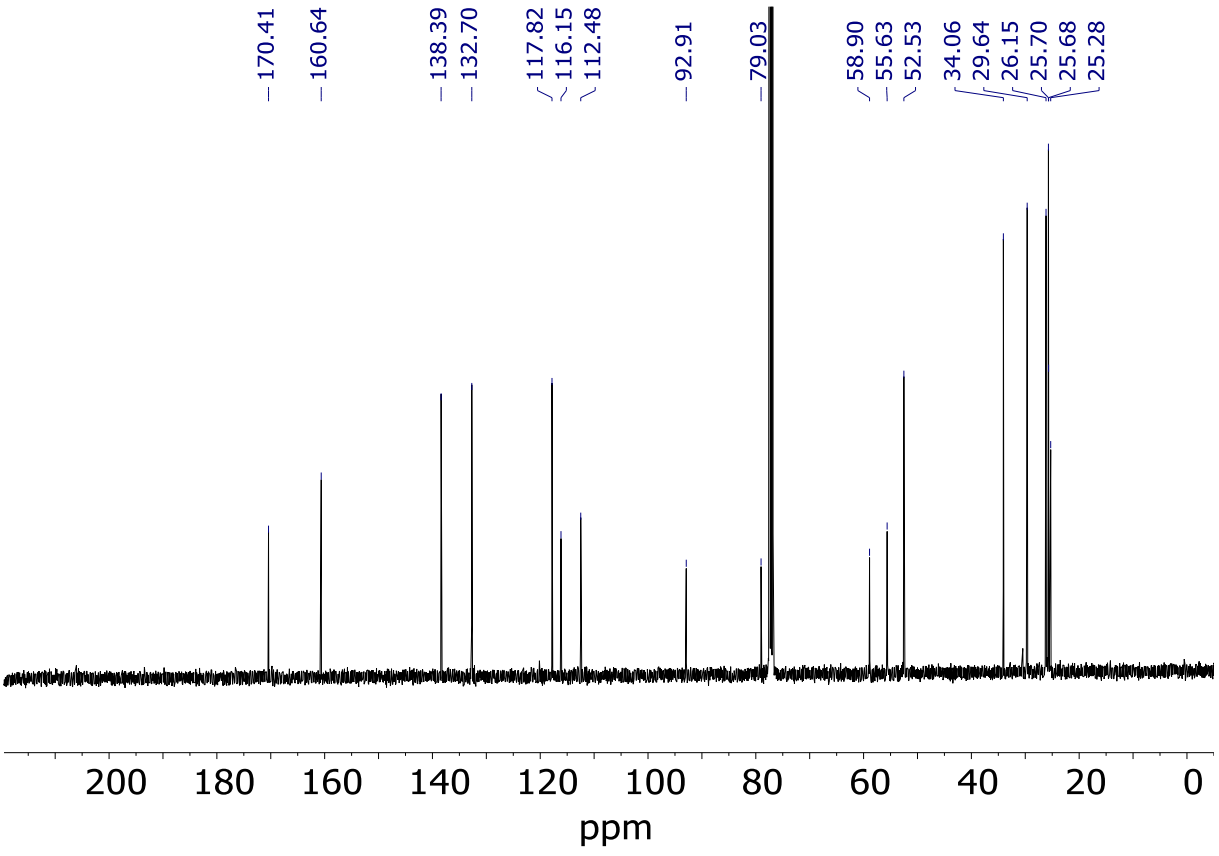
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **4.6f**.



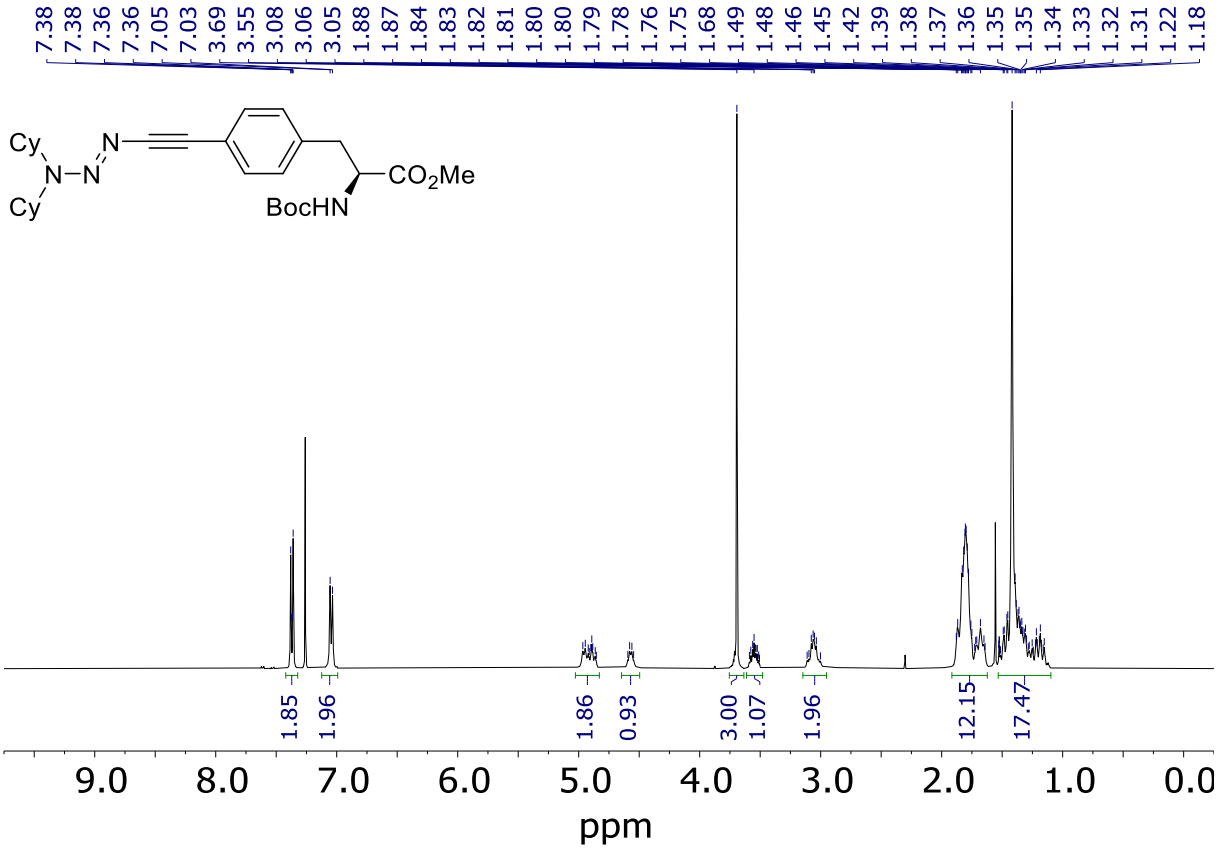
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of compound **4.6f**.



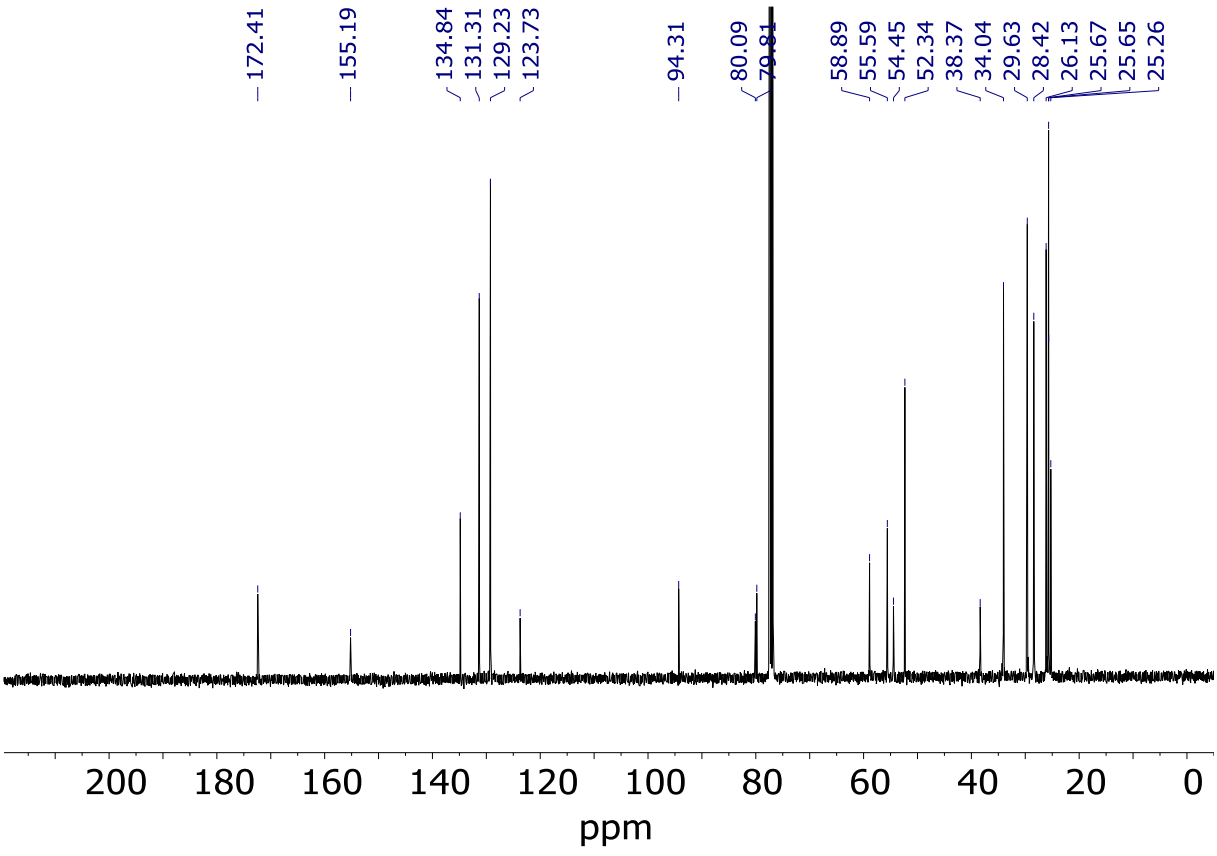
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **4.6g**.



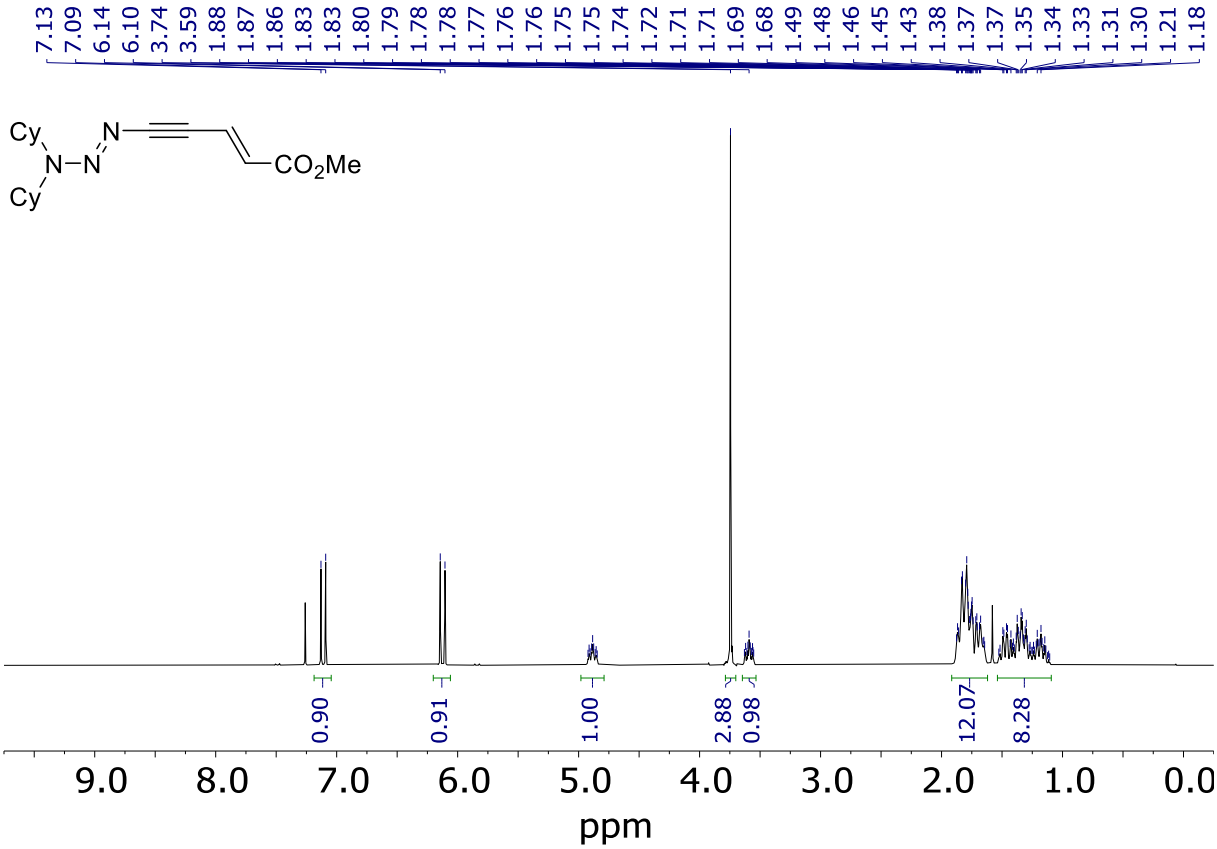
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of compound **4.6g**.



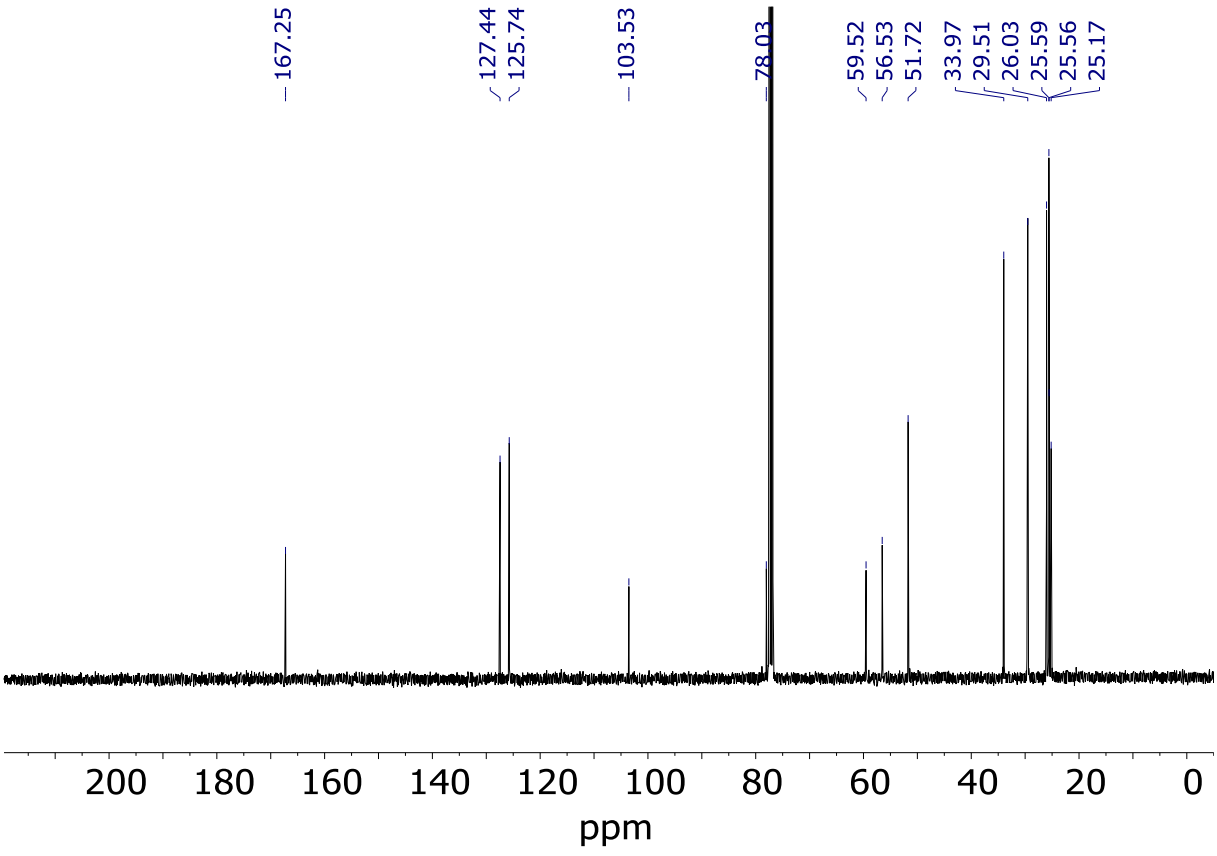
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **4.6h**.



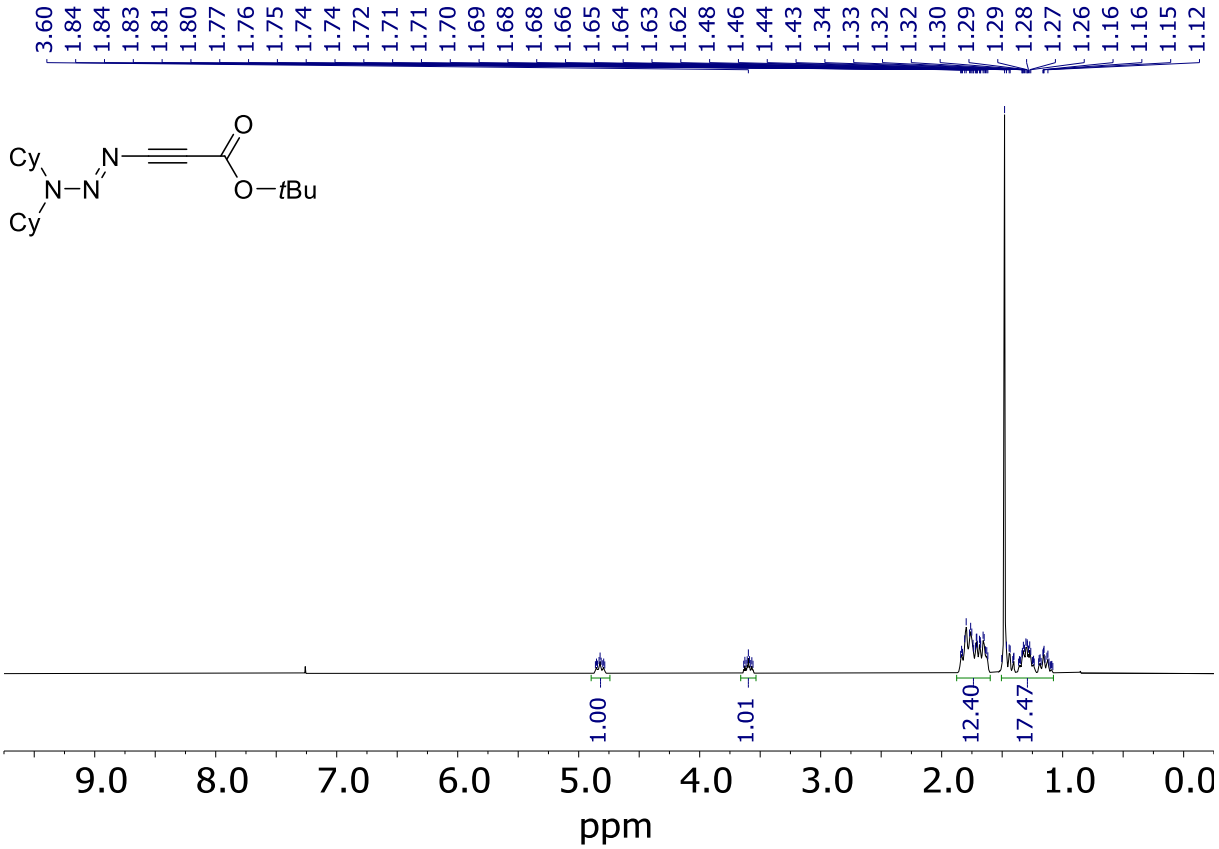
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of compound **4.6h**.



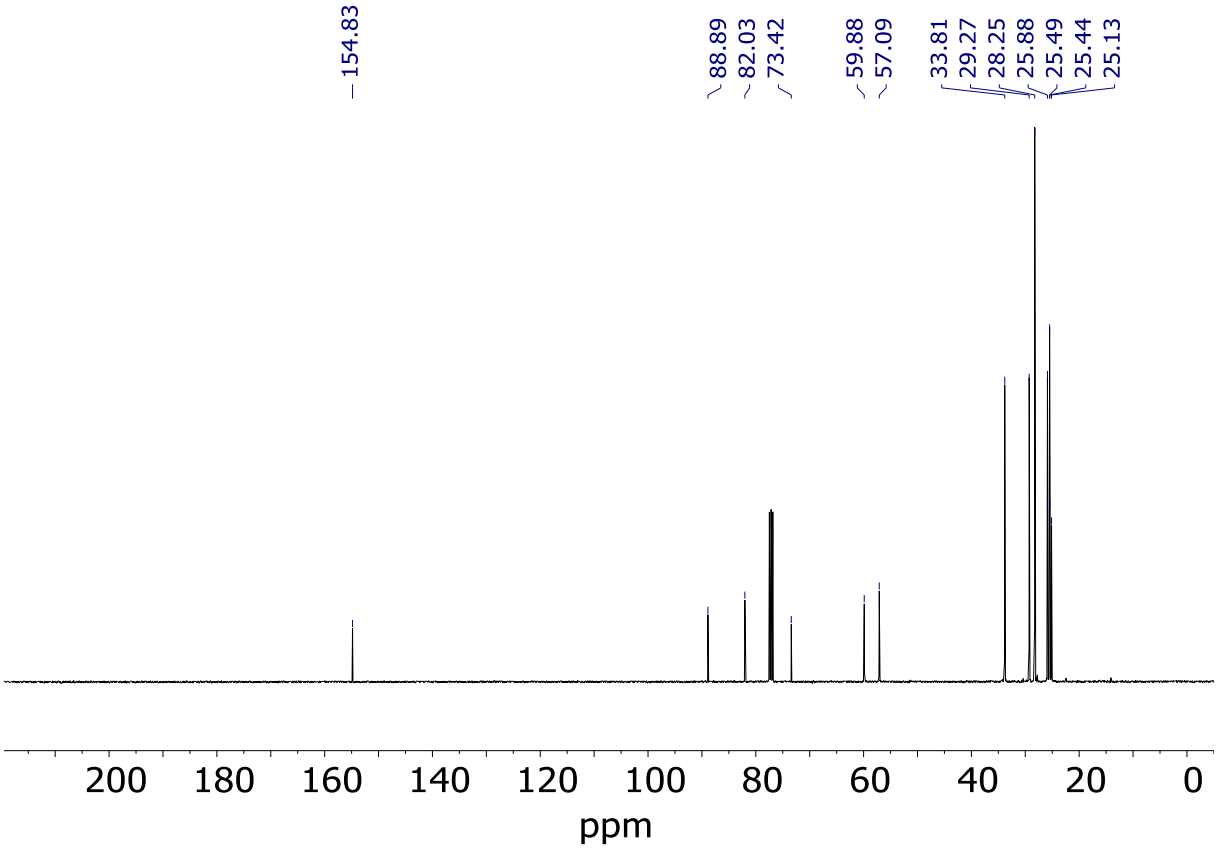
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **4.6i**.



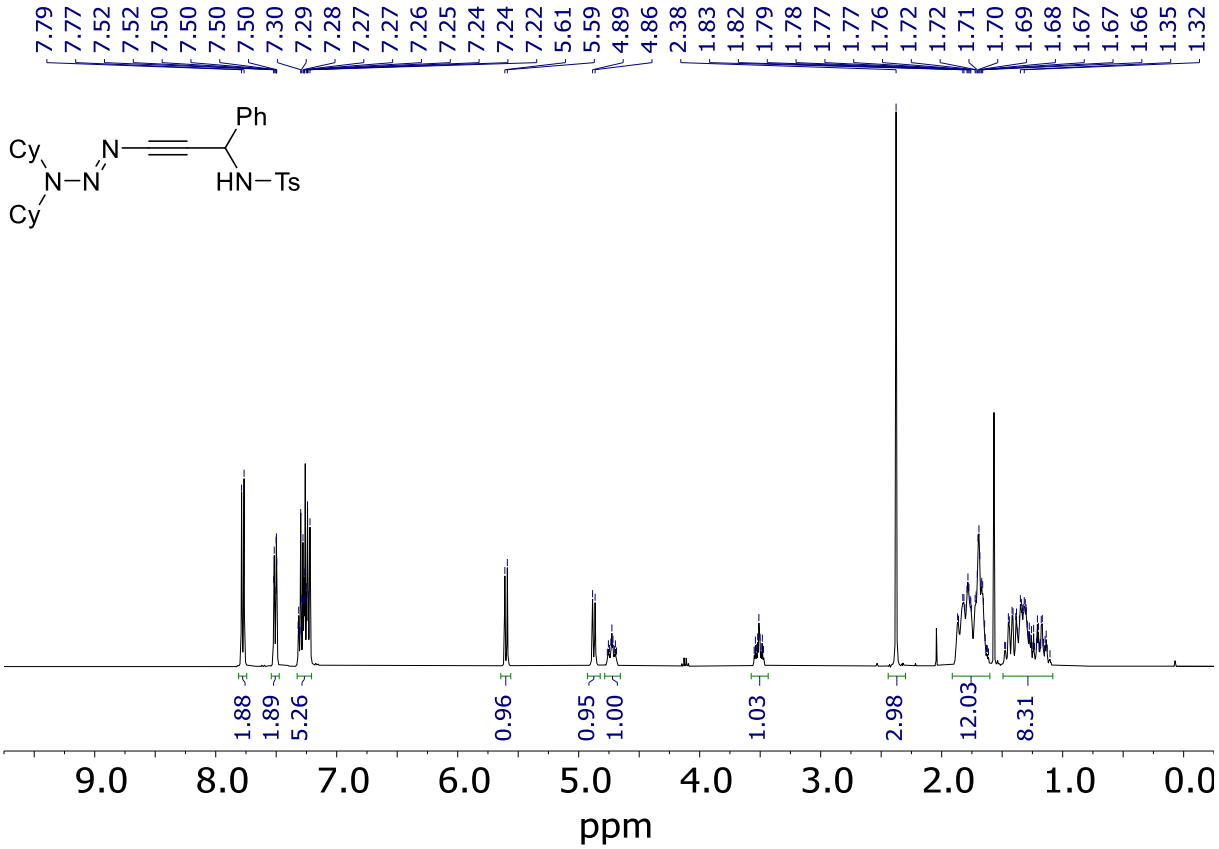
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of compound **4.6i**.



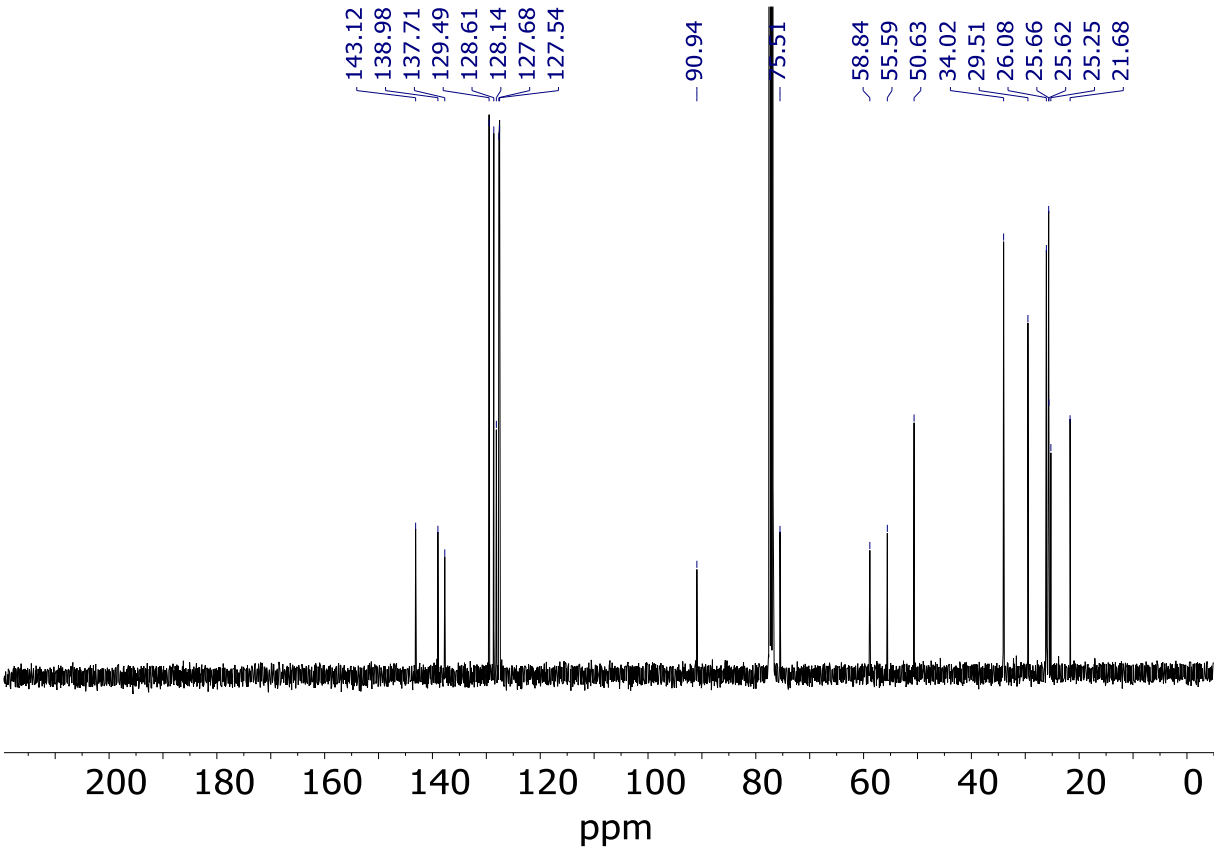
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **4.7a**.



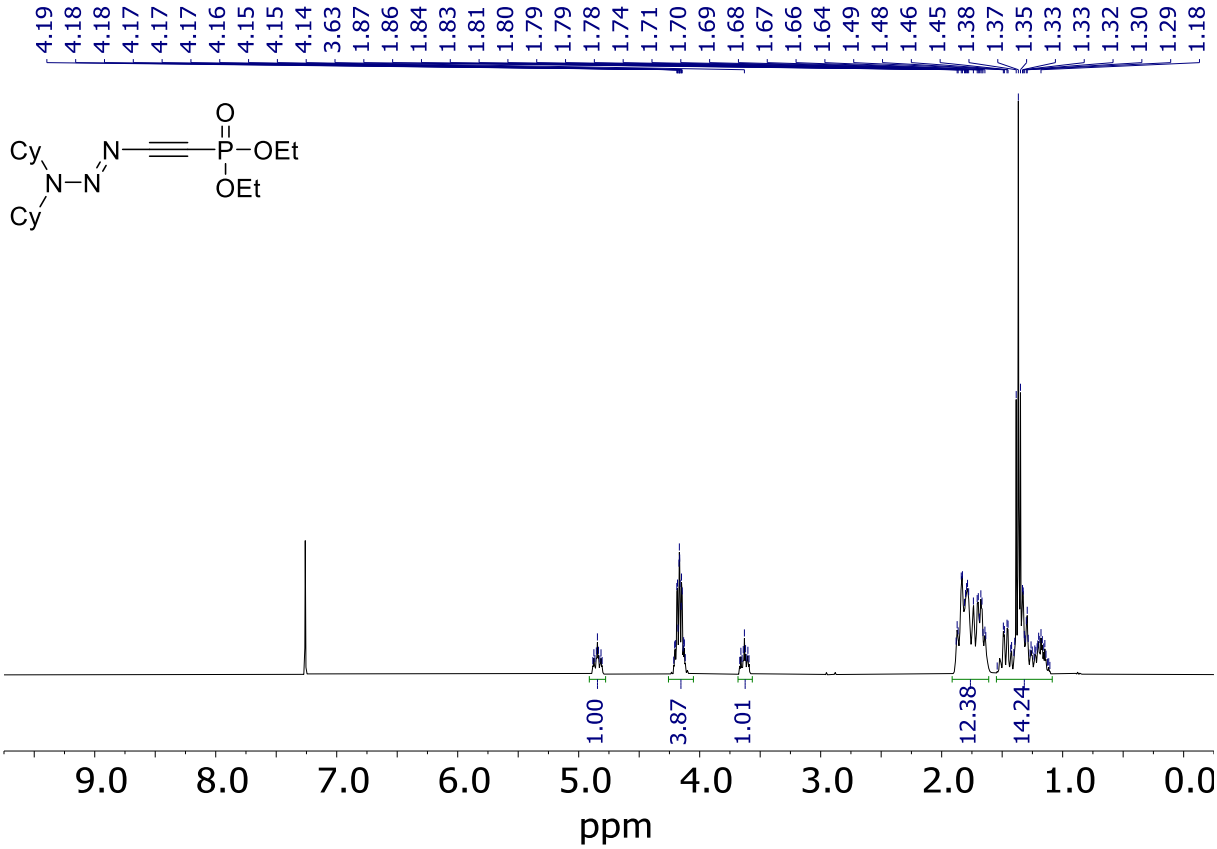
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of compound **4.7a**.



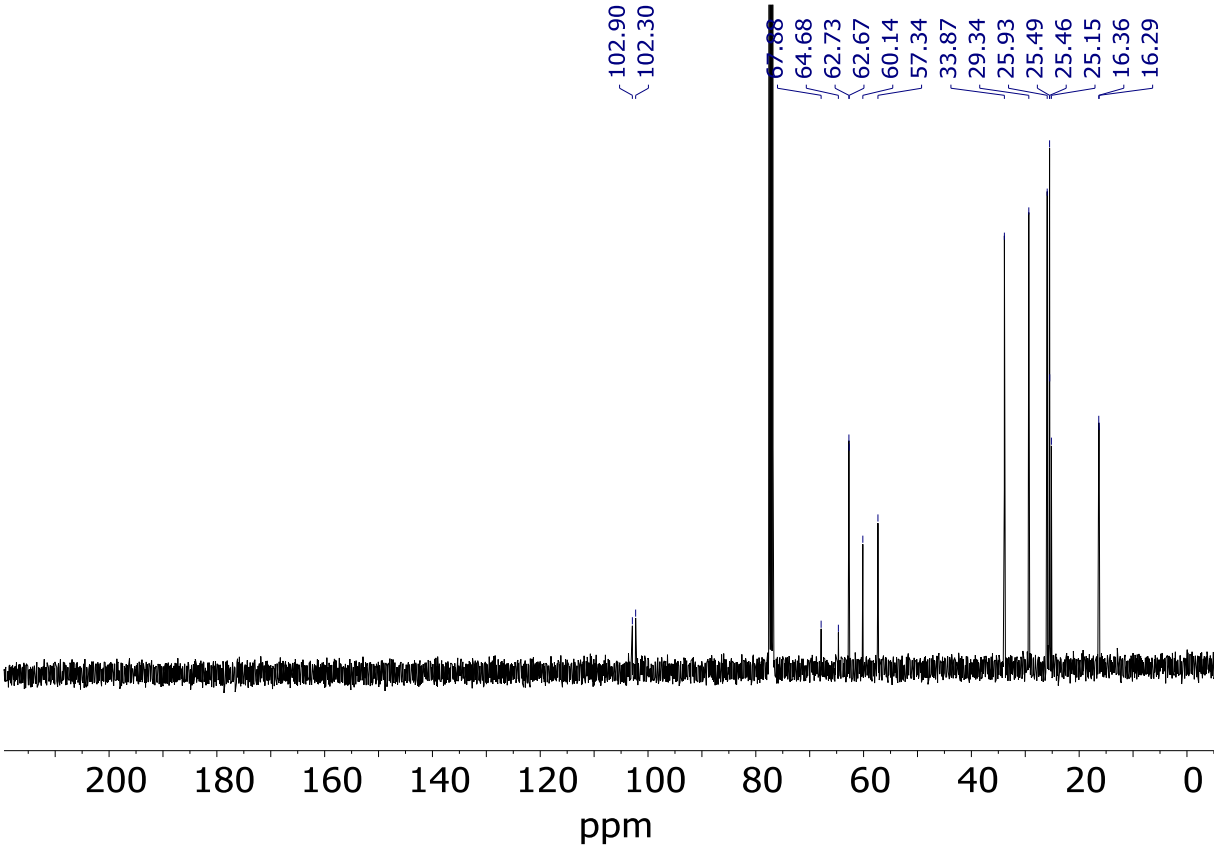
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **4.7b**.



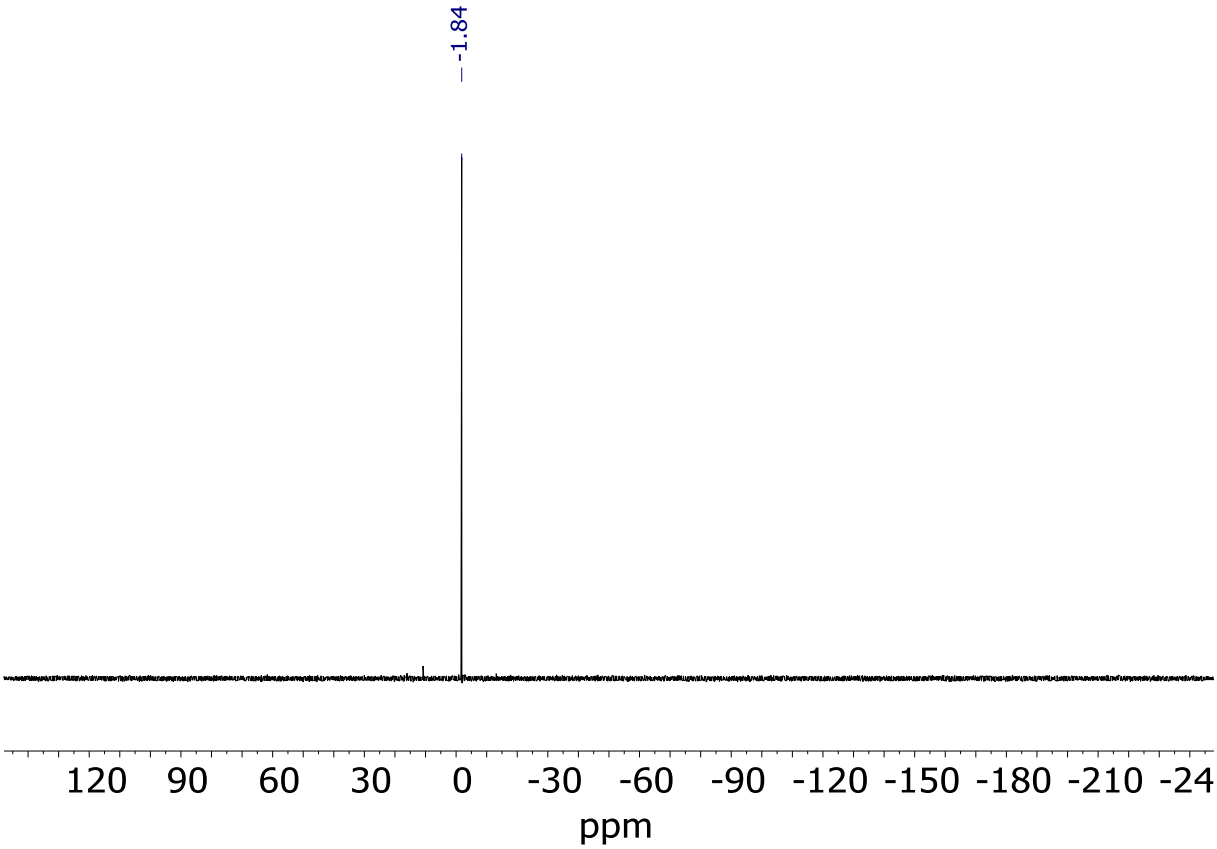
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of compound **4.7b**.



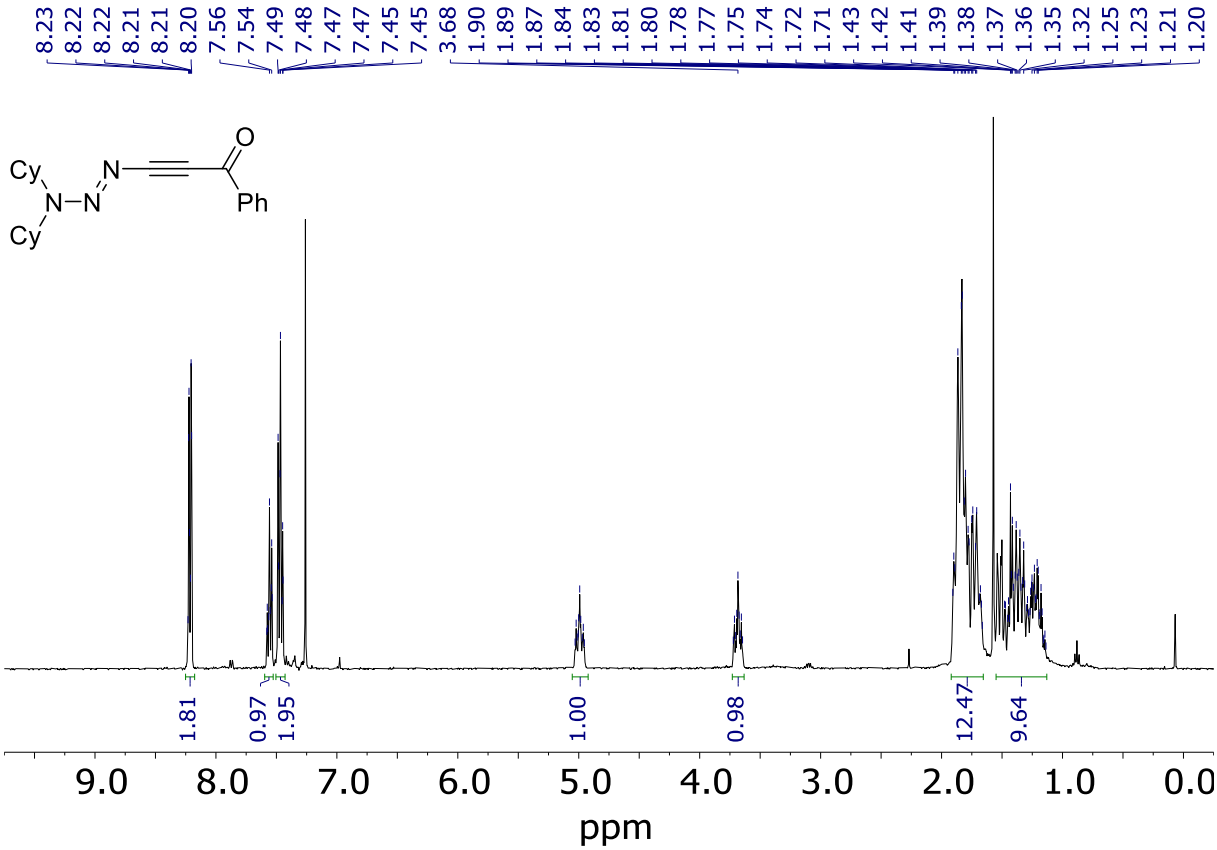
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **4.7c**.



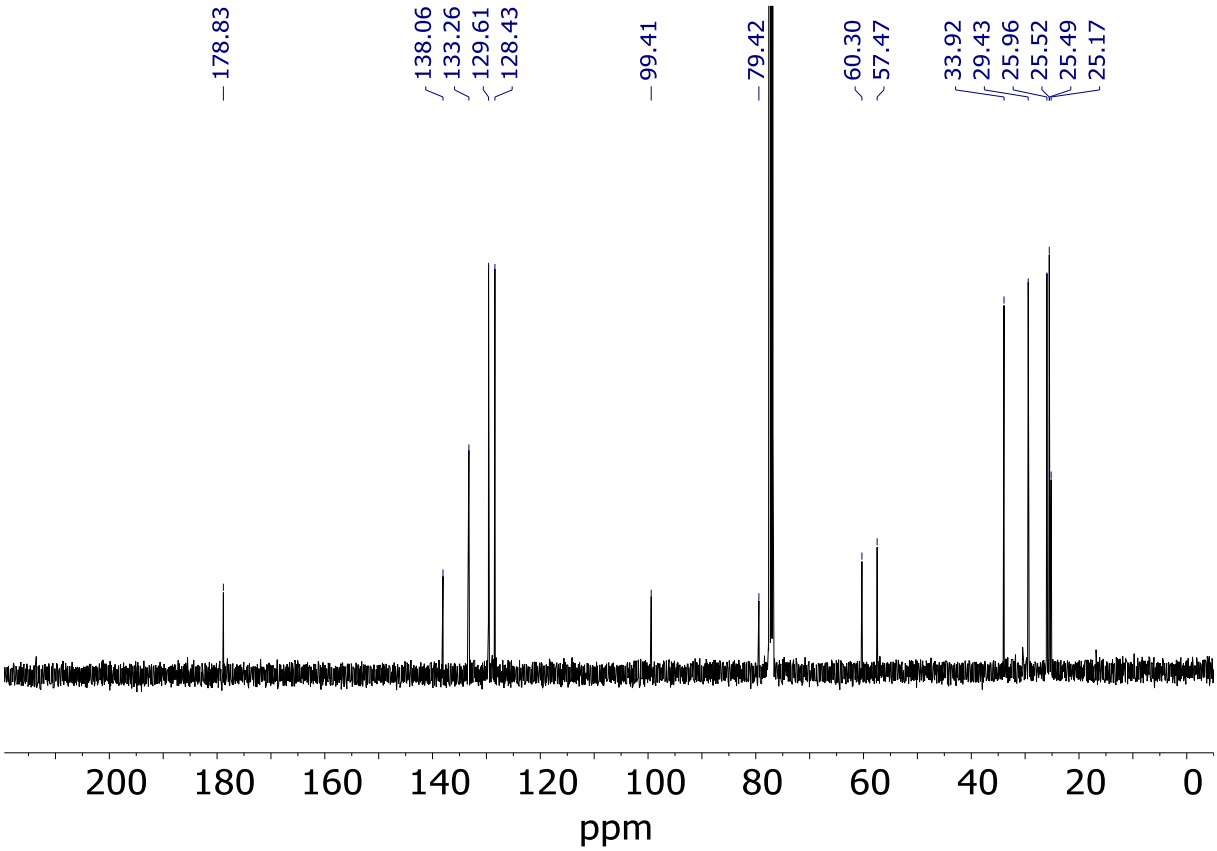
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of compound **4.7c**.



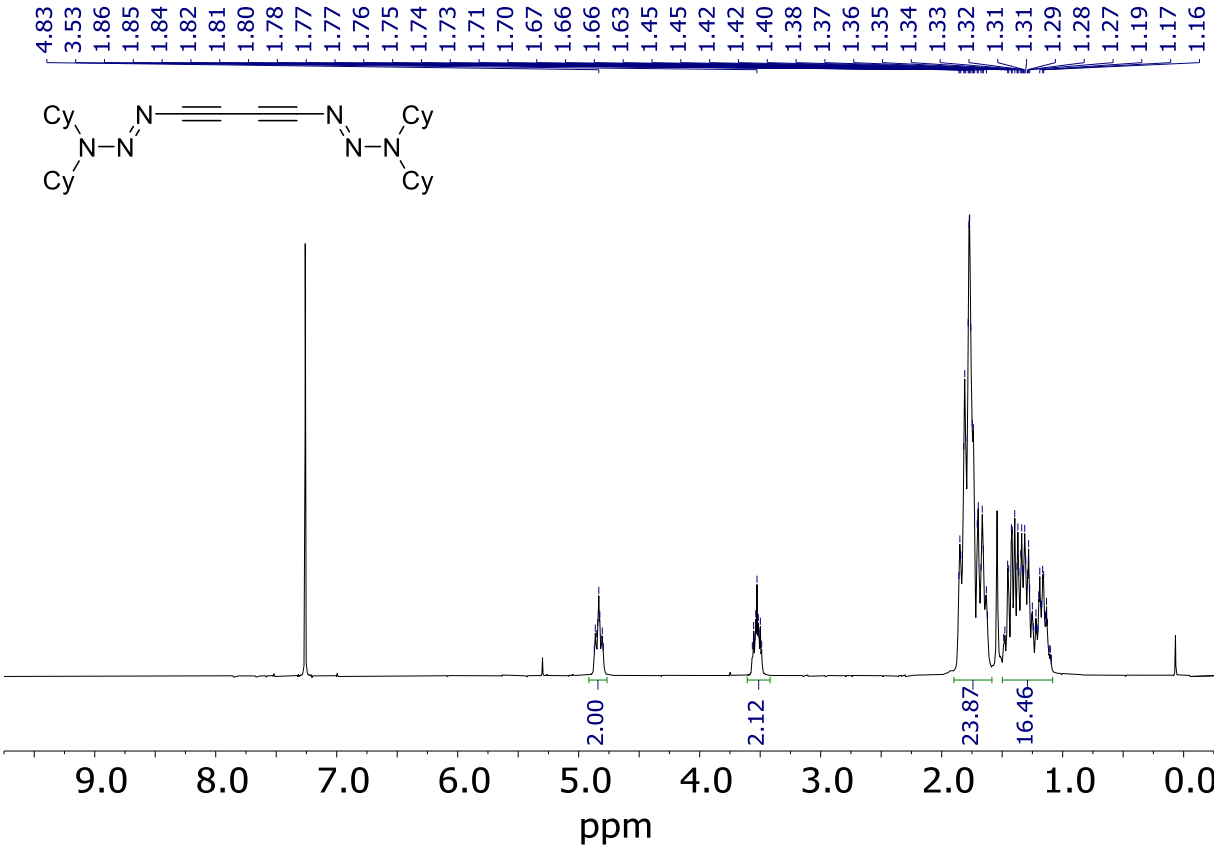
^{31}P NMR spectrum (162 MHz, $CDCl_3$) of compound **4.7c**.



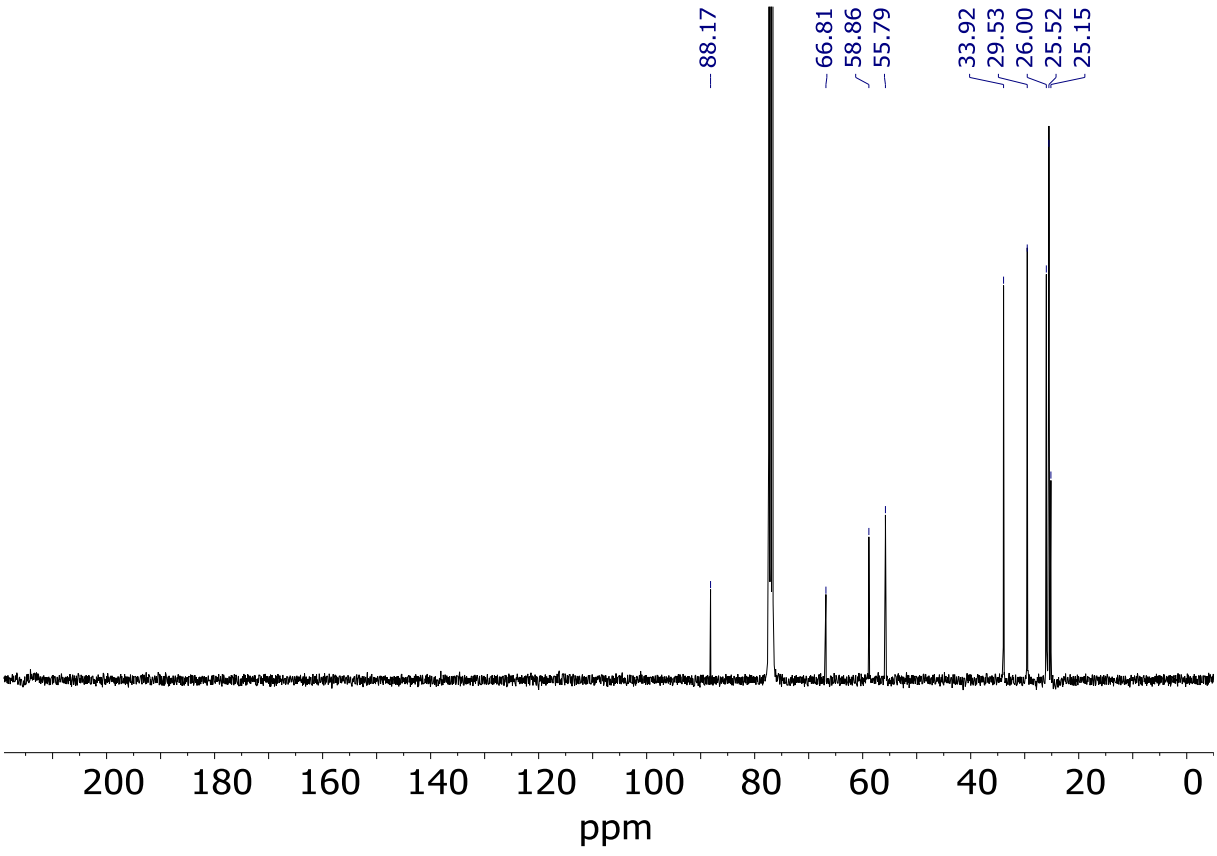
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **4.7d**.



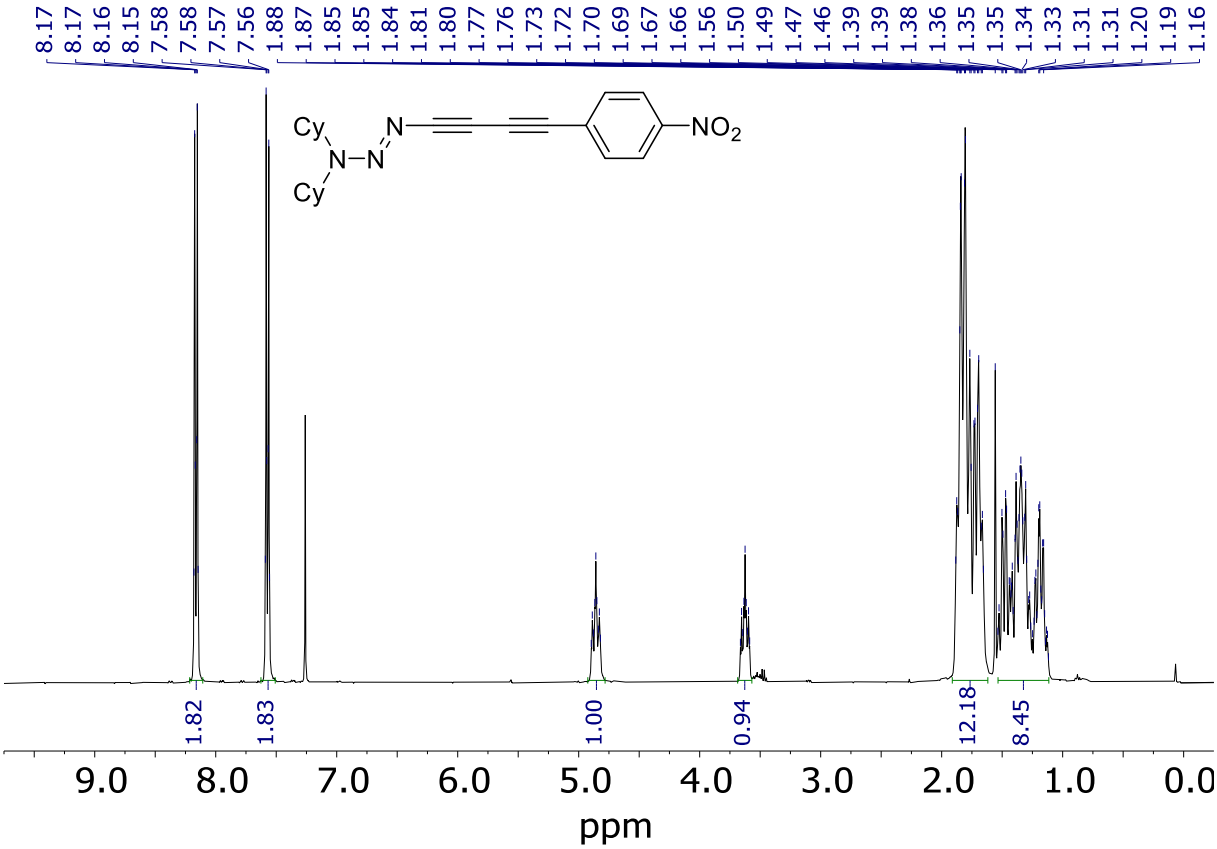
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of compound **4.7d**.



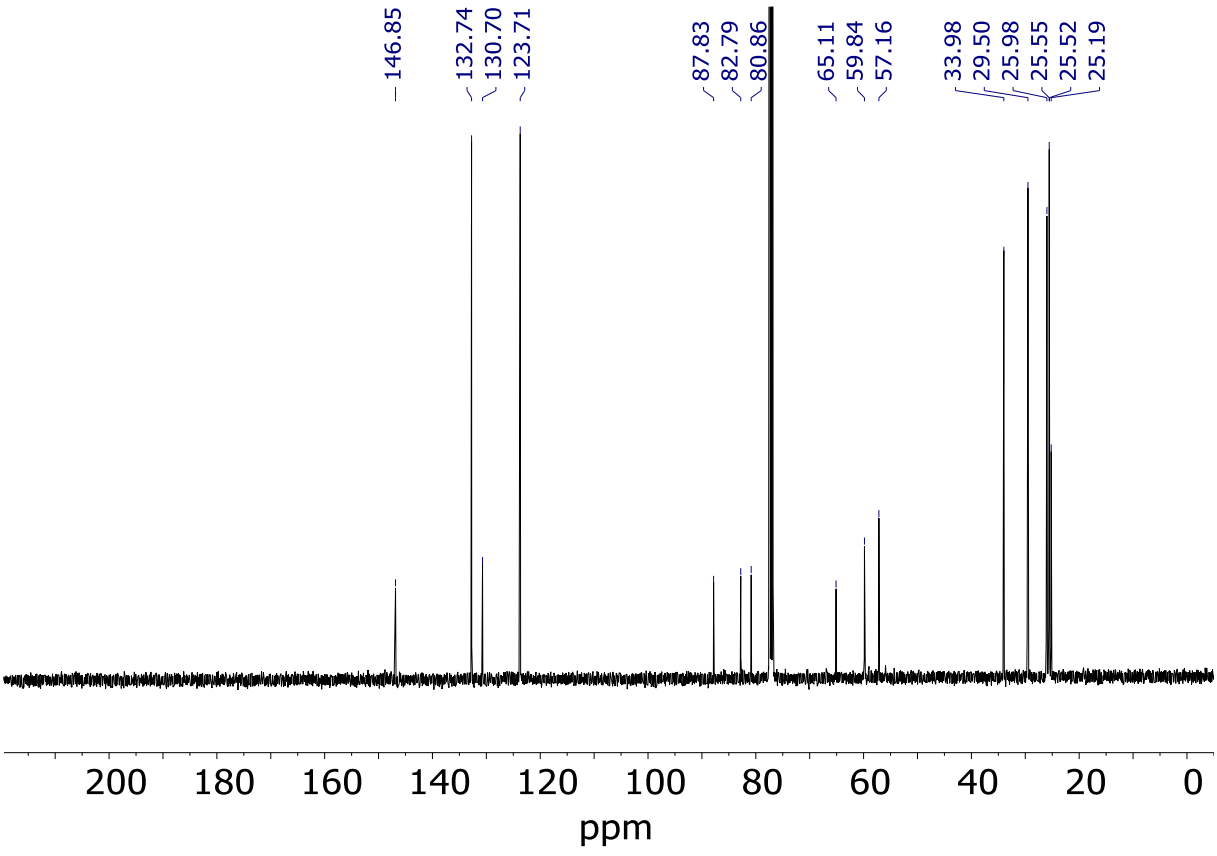
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **4.8a**.



^{13}C NMR spectrum (101 MHz, $CDCl_3$) of compound **4.8a**.



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **4.8b**.



^{13}C NMR spectrum (101 MHz, $CDCl_3$) of compound **4.8b**.

7.7. X-Ray Crystallography

A clear intense yellow plate-shaped crystal of **4.4** with dimensions of 0.69 × 0.35 × 0.08 mm^3 and a clear intense yellow prism-shaped crystal of **4.8a** with dimensions of 0.80 × 0.41 × 0.29 mm^3 were mounted. Data were collected using a SuperNova, Dual, Cu at home/near, Atlas diffractometer operating at T = 230.00(10) K for **4.4** and AtlasS2 diffractometer operating at T = 140.00(10) K for **4.8a**.

Data were measured using ω scans with Cu$K\alpha$ radiation. The diffraction pattern was indexed and the total number of runs and images was based on the strategy calculation from the program CrysAlis^{Pro}.[170] The maximum resolution achieved was Θ = 76.321° (0.79 Å) for **4.4** and Θ = 76.012° (0.79 Å) for **4.8a**.

The unit cells were refined using CrysAlis^{Pro}[170] on 7954 reflections, 54% of the observed reflections (**4.4**) and on 40431 reflections, 61% of the observed reflections (**4.8a**).

Data reduction, scaling and absorption corrections were performed using CrysAlis^{Pro}.[170] The final completeness is 100.00 % out to 76.321° (**4.4**)/ 76.012° (**4.8a**) in Θ. A Gaussian absorption correction was performed using CrysAlis^{Pro}.[170] Numerical absorption correction based on Gaussian integration over a multifaceted crystal model. Empirical absorption correction using spherical harmonics as implemented in SCALE3 ABSPACK scaling algorithm. The absorption coefficient μ of these materials are 0.491 mm^{-1} (**4.4**) and 0.528 mm^{-1} (**4.8a**) at this wavelength (λ = 1.54184Å) and the minimum and maximum transmissions are 0.283 and 1.000 (**4.4**) and 0.253 and 1.000 (**4.8a**).

The structures were solved in the space groups are $I4/mcm$ (# 140) for **4.4** and $P2_1/c$ (# 14) for **4.8a** by the ShelXT 2018/2 structure solution program[171] using dual methods and refined by full matrix least squares minimization on F^2 using ShelXL 2018/3.[172] All non-hydrogen atoms were refined anisotropically. Hydrogen atom positions were calculated geometrically and refined using the riding model.

In the structure **4.4**, the value of Z' is 0.125. This means that there are one-eighth independent molecules in the asymmetric unit.

In the structure **4.8a**, the value of Z' is 2. This means that there are two independent molecules in the asymmetric unit.

Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre and correspond to the codes 2127787 (**4.4**) and 2128261 (**4.8a**). These data can be obtained free of charge via www.ccdc.cam.ac.uk/structures/.

Table 7.2. X-Ray Crystallographic Data for compounds **4.4** and **4.8a**.

Compound	**4.4**	**4.8a**
Formula	$C_{26}H_{44}N_6$	$C_{28}H_{44}N_6$
$D_{calc.}$/ g cm^{-3}	1.055	1.136
μ/mm^{-1}	0.491	0.528
Formula Weight	440.67	464.69
Color	clear intense yellow	clear intense yellow
Shape	plate-shaped	prism-shaped
Size/mm^3	0.69×0.35×0.08	0.80×0.41×0.29
T/K	230.00(10)	140.00(10)
Crystal System	tetragonal	monoclinic
Space Group	*I*4/*mcm*	$P2_1/c$
a/Å	11.93083(17)	19.16181(12)
b/Å	11.93083(17)	13.48827(7)
c/Å	19.4982(5)	22.85254(14)
α/°	90	90
β/°	90	113.0659(7)
γ/°	90	90
V/Å^3	2775.47(11)	5434.26(6)
Z	4	8
Z'	0.125	2
Wavelength/Å	1.54184	1.54184
Radiation type	Cu$K\alpha$	Cu$K\alpha$
Θ_{min}/°	4.535	3.894
Θ_{max}/°	76.321	76.012
Measured Refl's.	14624	66214
Indep't Refl's	814	11298
Refl's I≥2σ(I)	735	10799
R_{int}	0.0226	0.0192
Parameters	76	745
Restraints	112	493
Largest Peak/e Å^{-3}	0.214	0.605
Deepest Hole/e Å^{-3}	-0.201	-0.249
GooF	1.153	1.040
wR_2 (all data)	0.1799	0.1528
wR_2	0.1745	0.1513
R_1 (all data)	0.0553	0.0585
R_1	0.0517	0.0569
CCDC number	2127787	2128261

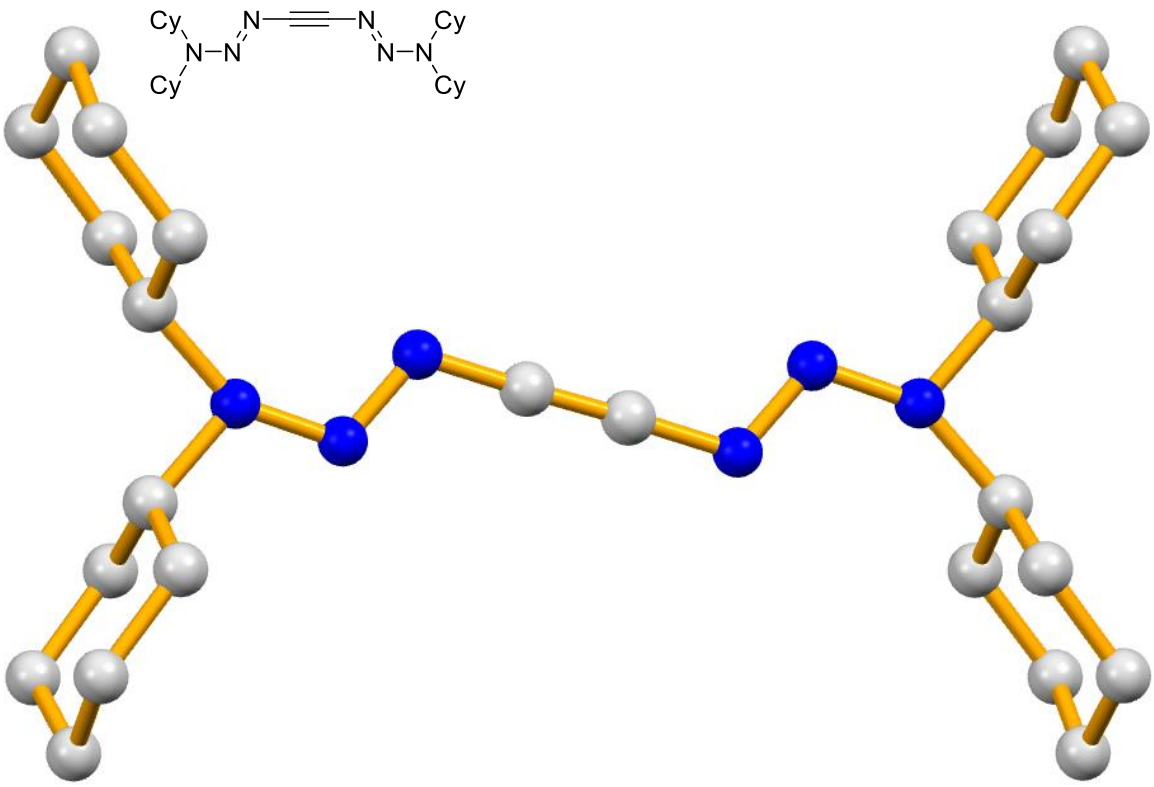


Figure 7.5. Molecular structure of compound **4.4** determined by X-ray diffraction. Ellipsoids are set at a 50% probability level. Color-coding: C: grey, N: blue. Hydrogen atoms and disorder are omitted for clarity.

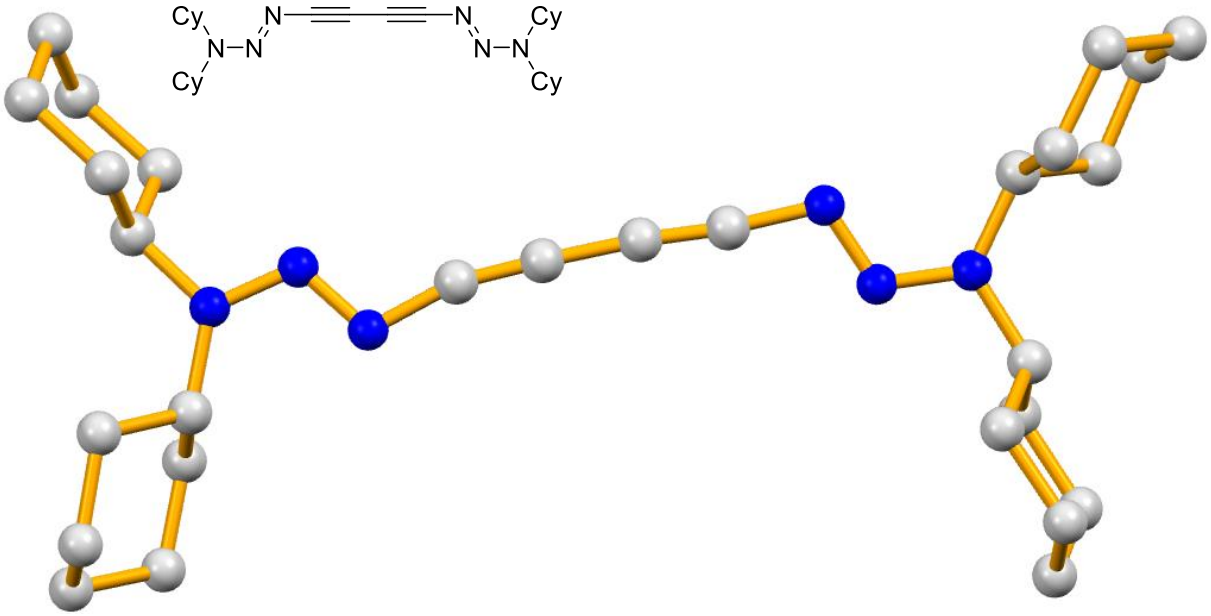


Figure 7.6. Molecular structure of compound **4.8a** determined by X-ray diffraction. Ellipsoids are set at a 50% probability level. Color-coding: C: grey, N: blue. Hydrogen atoms and second molecule in the unit cell are omitted for clarity.

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Bachelor and Master of Science ETH in Chemistry

Heimschule Lender, Sasbach (Germany) 05/2011
Abitur (secondary diploma); Chemistry Award of the Society of German Chemists (GDCh)

Experience

Institute of Chemistry and Chemical Engineering, Severin-Group, EPFL 11/2017 – 03/2022
"Synthesis of new 1-Vinyl and 1-Alkynyl Triazenes" (Doctoral Thesis)
Synthesis of 1-vinyl and 1-alkynyl triazenes with improved functional group tolerance. Development of three synthetic methods for previously inaccessible, new molecules with classically incompatible functional groups. Recipient of the "Teaching Excellence Award". Supervision of two apprentices (laboratory technicians) in the laboratory.

BASF Research Center, Basel 10/2016 – 09/2017
Internship
Development optical materials. Synthesis of organic mono- and polymers with a high refractive index. Collaboration with the Centre Suisse d'Electronique et de Microtechnique (CSEM) and the University of Applied Sciences and Arts Northwestern Switzerland (FHNW).

Laboratory of Inorganic Chemistry, Grützmacher-Group, ETHZ 01/2016 – 07/2016
"Click-able Bis(acyl)phosphane oxides for the Synthesis of Dendritic Photoinitiators" (Master Thesis)
Synthesis of branched photoinitators for polymerizations via click-chemistry. Characterization of hydrolytic stability and photoactivity via NMR.

Laboratory of Organic Chemistry, Carreira-Group, ETHZ 03/2015 – 07/2015
Research project
Synthesis of model compounds for NMR-based assignment of relative stereochemistry of polybrominated natural products.

Laboratory of Inorganic Chemistry, Togni-Group, ETHZ 09/2014 – 02/2015
Research project
Synthesis of trifluoromethylated NHC-Pd complexes and investigation of catalytic properties for hydrosilylation via NMR.

Publications

Alkynyl triazenes enable divergent syntheses of 2-pyrones
J.-F. Tan, C. T. Bormann, K. Severin, N. Cramer, *Chem. Sci.* **2021**, *12*, 9140–9145.

Synthesis of bicyclic vinyl triazenes by Ficini-type reactions
C. T. Bormann, F. Fadaei-Tirani, R. Scopelliti, K. Severin, *Org. Biomol. Chem.*, **2021**, ***19***, 8113-8117

Alkynyl Triazenes as Fluoroalkyne Surrogates: Regioselective Access to 4-Fluoro-2-pyridones by a Rh(III)-Catalyzed C–H Activation–Lossen Rearrangement–Wallach Reaction
J.-F. Tan, C. T. Bormann, K. Severin, N. Cramer, *ACS Catal.* **2020**, 3790–3796.

Synthesis of Indenyl Triazenes by Rhodium-Catalyzed Annulation Reactions
C. T. Bormann, F. G. Abela, R. Scopelliti, F. Fadaei-Tirani, K. Severin, *Eur. J. Org. Chem.* **2020**, *14*, 2130-2139.

Divergent Synthesis of Densely Substituted Arenes and Pyridines via Cyclotrimerization Reactions of Alkynyl Triazenes
J.-F. Tan, C. T. Bormann, F. G. Perrin, F. M. Chadwick, K. Severin, N. Cramer, *J. Am. Chem. Soc.* **2019**, *141*, 10372–10383.

Conferences and Summer Schools

Big Data and Machine Learning for Chemistry, Lausanne 06/2021
Attendance

Fall Meeting of the Swiss Chemical Society, Online 08/2020
Virtual Poster Presentation “Ficini-Type Reactions with 1-Alkynyl Triazenes”

Fall Meeting of the Swiss Chemical Society, Zürich 09/2019
Poster Presentation “Rh-Catalyzed Synthesis of Indenyl Triazenes”

Swiss Summer School: Trends in Organic Synthesis, Villars 08/2019
Oral Presentation “Rh-Catalyzed Synthesis of Indenyl Triazenes”

Languages

English: Fluent (C1)
German: Native Language (C2)
French: Good (B1)

Extracurricular Activities

Board of PolyDoc (PhD-student association of EPFL) 12/2019 – 12/2021
Coordination of PhD-student representatives (2019/20), management of the finances (2020/21).

Teaching Commission of the Section of Chemistry and Chem. Engineering 10/2019 – 12/2021
Exchange with professors and students on teaching related topics.

Faculty Council of the School of Basic Sciences 09/2018 – 08/2020
Participation in EPFL-consultations, election of institute and section directions.

IDEA-League Challenge Program 11/2015 – 04/2016
Four modules at TU Delft, RWTH Aachen, Chalmers Gothenburg and ETH Zürich; exploring issues at the intersection of technology and society.

Board of VSETH (official student association of ETH Zürich, half-time) 09/2013 – 09/2014
Representation of students towards ETHZ and others, participation in the national student association, organization of workshops and events within the association.

9. References

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