Copper-Catalyzed Oxy-Alkynylation of Diazo Compounds with Hypervalent Iodine Reagents

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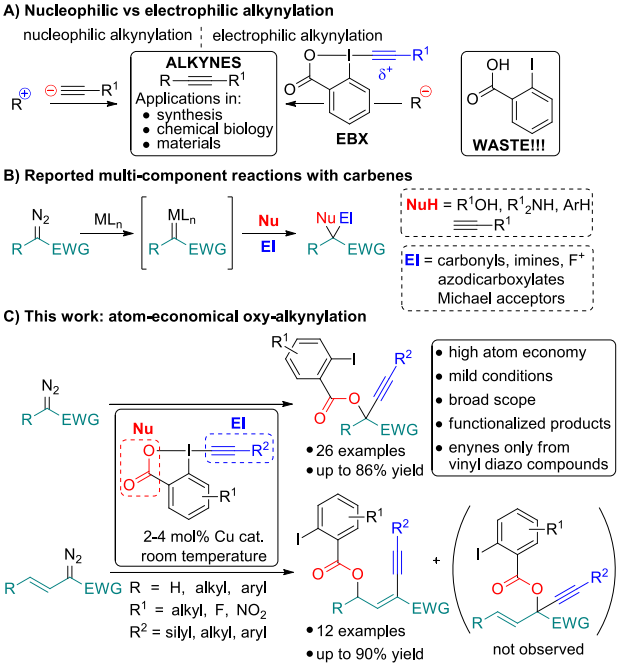
Supporting Information Placeholder

ABSTRACT: Alkynes have found widespread applications in synthetic chemistry, biology and materials sciences. In recent years, methods based on electrophilic alkynylation with hypervalent iodine reagents have made acetylene synthesis more flexible and efficient, but they lead to the formation of one equivalent of an iodoarene as side-product. Herein, a more efficient strategy involving a copper-catalyzed oxy-alkynylation of diazo compounds with ethynylbenziodoxol(on)e (EBX) reagents is described, which proceeds with generation of nitrogen gas as the only waste. This reaction is remarkable for its broad scope in both EBX reagents and diazo compounds. In addition, vinyl diazo compounds gave enynes selectively as single geometric isomers. The functional groups introduced during the transformation served as easy handles to access useful building blocks for synthetic and medicinal chemistry.

The carbon-carbon triple bond is among the most valuable functional groups in organic chemistry because of its versatile reactivity.[1] Alkynes are broadly applied as chemical building blocks for the synthesis of fine chemicals.[2] In past years, they have also gained a lot of interest for applications in biochemistry or material sciences.[1,3] As a result of this growing importance of alkynes, developing more efficient and versatile methods for their synthesis is of fundamental importance. Alkynes are often accessed by the addition of acetylides on electrophilic positions of molecules.[4] However, introducing triple bonds only to electrophilic positions strongly limits the flexibility and efficiency of alkyne synthesis. Major efforts have therefore been made to develop electrophilic alkynylation methods, relying on the umpolung of the innate reactivity of acetylenes (Scheme 1A).[5]

Hypervalent iodine reagents such as alkynyliodonium salts have been particularly successful for the electrophilic alkynylation of nucleophiles.[6] However, the use of alkynyliodonium salts is limited due to their low stability. Recently, EthynylBenziodoX-ol(on)es (EBX)[7a,b] have been introduced as excellent electrophilic reagents for the alkynylation of ketoesters,[7c] thiols,[7d] and aromatic C-H bonds using transition metal catalysis,[7e-g] among many other successful transformations.[7h] Nevertheless, the developed methods are often restricted to the transfer of one type of acetylenes (either silyl-, aryl- or alkyl- substituted). Furthermore, 2-iodobenzoic acid is usually obtained as a stoichiometric byproduct after alkynylation, resulting in low atom economy.[8] Recently, Greaney and co-workers[9a] and Dauban and co-workers[9b] reported more atom economical transformations based on the use of the formed aryl iodides in cross-coupling reactions with aryliodonium salts and $PhI(OPiv)_2$, respectively. With EBX reagents, progress in this area has been limited to a report of Yoshikai and co-workers on the palladium-catalyzed reaction of imines with alkynylbenziodoxolones to give furan derivatives.[10]

Scheme 1. Alkynylation strategies and multi-component reactions using diazo compounds



To develop more efficient transformations with EBX reagents, we intended to make use of the nucleophilic properties of the formed iodobenzoate side products. In this context, metal carbene species are interesting reactive intermediates, as they display both nucleophilic and electrophilic reactivity on a single carbon atom and can be easily generated from α-diazo carbonyl compounds.[11] They have been used in a broad range of transformations such as X–H bond insertions, cyclopropanation, ylide formation and 1,2- migration reactions and have been successfully applied in total synthesis.[12] Recently, research in the area has focused on the development of multi-component reactions to afford products with high structural diversity, complexity, and atom economy (Scheme 1B).[13] The only approach for the synthesis of alkynes from diazo compounds has been reported by Wang and co-workers for a reaction involving metal carbene migratory insertion with nucleophilic

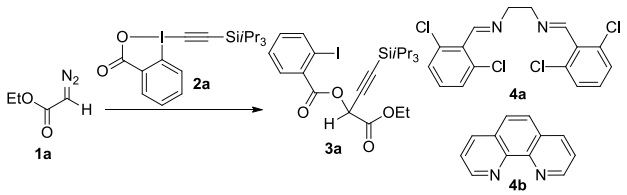
alkynes.[14] We envisioned a different strategy making use of the carboxylate of the EBX reagent as a nucleophile, and the alkyne as an electrophile.

Herein, we report the successful implementation of this strategy, resulting in a highly efficient and atom economical oxy-alkynylation of diazo compounds under mild conditions using a non-expensive copper catalyst (Scheme 1C). The reaction exhibits a broad scope towards both diazo compounds and EBX-reagents, and tolerates many functional groups. It provides access to both secondary and tertiary propargylic alcohol derivatives and can be used for the synthesis of silyl-, aryl- and alkyl- substituted acetylenes. The iodine atom, the ester and the triple bond of the product can serve as versatile handles for further transformations. Interestingly, when vinyl diazo compounds were used as starting materials, only 1,4-addition to give enynes was observed.

We first attempted the oxy-alkynylation of ethyl diazoacetate (**1a**) with 1-[(tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (TIPS-EBX, **2a**) using 5 mol% of $Rh_2(OAc)_4$ in DCM at 40 °C, but did not obtain the desired product **3a** (Table 1, entry 1). Replacing $Rh_2(OAc)_4$ with $Cu(OTf)_2$ gave the desired product **3a** in 19% yield after 20 h at 40 °C (Table 1, entry 2). Product **3a** was obtained in 24% yield when $Cu(CH_3CN)_4BF_4$ was used (Table 1, entry 3), whereas the use of other metal catalysts such as CuCl, $Cu(OAc)_2$, $PdCl_2(PPh_3)_2$, and $AuBr_3$ did not lead to the formation of the desired product **3a** (Table 1, entries 4-7). Use of DCE as a solvent at 65 °C gave **3a** in 30% yield (Table 1, entry 8). With two equivalents of **1a**, the yield could be raised to 46% (Table 1, entry 9). Decreasing the catalyst loading to 2 mol% gave **3a** in 54% yield (Table 1, entry 10). Alkyne **3a** was then obtained in 60% yield when the concentration of the reaction was decreased to 0.05 M (Table 1, entry 11). Finally, a major improvement was obtained when using 2.5 mol% of 1,2 diimine **4a** as ligand:[15] the yield increased to 86% and the reaction could be performed at room temperature (Table 1, entry 12). In contrast, the reaction did not take place when using 1,10-phenanthroline (**4b**) as ligand (Table 1, entry 13). In the absence of $Cu(CH_3CN)_4BF_4$, no product was obtained, demonstrating that the copper catalyst is necessary for the reaction (Table 1, entry 14).

The scope of the reaction was first examined using TIPS-EBX (**2a**) and a variety of *α*-diazo compounds (Figure 1A). *Tert*-butyl and benzyl diazoacetates provided the oxy-alkynylation products **3b** and **3c** in high yields. The transformation was also successful for disubstituted diazo compounds, leading to products **3d-f** with tertiary propargylic centers. Noteworthy, a cyclic diazo compound also afforded the desired product **3g** in 80% yield. Derivatives of *α*-hydroxy-alkynyl lactones are present in pharmaceutical molecules,[16] but have never been synthesized directly from lactones to the best of our knowledge. In addition to *α*-diazo esters, several other diazo compounds including 2-diazo-*N,N*-diethylacetamide, ethyl diazomethanesulfonate, and diethyl (diazomethyl)phosphonate underwent the desired transformation in good to high yields (products **3h-j**). We then turned our attention to the scope of R-EBX reagents (Figure 1B). Electron-donating and –withdrawing groups were well tolerated on the aryl ring of TIPS-EBX (**2a**) (products **3k-m**). EBX reagents bearing aryl substituents on the alkyne worked efficiently in this transformation, giving products **3n-p** in 80–84% yield. Bromide-substituted product **3p**, which is useful for further chemical transformations, could be isolated in 83% yield. Several aliphatic EBX reagents bearing functional groups such as a chloro, an azido, and an ether also gave the desired products in moderate to high yields (products **3q-3t**). A cyclopropyl derived EBX reagent can also be used in this reaction (product **3u**). A TMS-alkyne substituted EBX reagent gave product **3v** in 75% yield. In addition, ethyl 2-diazopropanoate can also be oxy-alkynylated successfully with aryl-substituted EBX reagents to furnish products **3w** and **3x** with tertiary propargylic centers in 78% and 72% yield, respectively.

Table 1. Optimization of the reaction conditions.[a]



Entry	Catalyst (x mol %)	Solvent (conc.)	Time/T (°C)	Yield
1	$Rh_2(OAc)_4$ (5.0)	DCM (0.1 M)	20 h/40	<5%
2	$Cu(OTf)_2$ (5.0)	DCM (0.1 M)	20 h/40	19%
3	$Cu(CH_3CN)_4BF_4$ (5.0)	DCM (0.1 M)	20 h/40	24%
4	CuCl (5.0)	DCM (0.1 M)	20 h/40	<5%
5	$Cu(OAc)_2$ (5.0)	DCM (0.1 M)	20 h/40	<5%
6	$PdCl_2(PPh_3)_2$ (5.0)	DCM (0.1 M)	2 h/40	<5%
7	$AuBr_3$ (5.0)	DCM (0.1 M)	18 h/40	<5%
8	$Cu(CH_3CN)_4BF_4$ (5.0)	DCE (0.1 M)	2 h/65	30%
9[b]	$Cu(CH_3CN)_4BF_4$ (5.0)	DCE (0.1 M)	1 h/65	46%
10[b]	$Cu(CH_3CN)_4BF_4$ (2.0)	DCE (0.1 M)	1.5 h/65	54%
11[b]	$Cu(CH_3CN)_4BF_4$ (2.0)	DCE (0.05 M)	2.5 h/65	60%
12[b,c]	$Cu(CH_3CN)_4BF_4$ (2.0)	DCE (0.05 M)	1 h/RT	86%
13[b,d]	$Cu(CH_3CN)_4BF_4$ (2.0)	DCE (0.05 M)	20 h/RT	<5%
14[b]	No catalyst	DCE (0.05 M)	20 h/65	<5%

[a]Reaction conditions: 0.30 mmol ethyldiazoacetate (**1a**), 0.25 mmol TIPS-EBX (**2a**). The reaction was run for 20 h or until full conversion of the EBX reagent. Yield after purification by column chromatography. [b]With 0.50 mmol **1a**. [c]With 2.5 mol % of **4a**. [d]With 2.5 mol % of **4b**.

Next, the developed method was applied to the oxy-alkynylation of vinyl diazo compounds (Figure 1C). Controlling the selectivity in the reaction of nucleophiles with vinyl diazo compounds is challenging, as they display electrophilic reactivity at both the carbenoid and the vinylogous center.[17] Gratifyingly, only vinylogous product **6a** was obtained as a single geometric isomer when using (*E*)-methyl 2-diazopent-3-enoate (**5a**) with TIPS-EBX (**2a**). We were pleased to see that (*E*)-methyl 2-diazohex-3-enoate (**5b**) and cyclic diazo compounds **5c** and **5d** could be used to give the desired vinylogous products **6b**, **6c** and **6d** in good to high yields.[18] Various R-EBX reagents were then examined. TIPS-EBX reagents having substituents on the aromatic ring led to the desired products **6e** and **6f** in high yields. The reaction was also successful with aryl-substituted EBX reagents, and products **6g** and **6h** were obtained in 82% and 75% yield, respectively. Substituents containing a long alkyl chain, a chloro, and a cyclopropyl functional group were well tolerated in this reaction (products **6i-6k**). A TMS-alkyne substituted EBX reagent gave the vinylogous product **6l** in 72% yield.

Modification of steroidal drugs provides an efficient route for the fine-tuning of their biological activity. Therefore, our method was applied to the late-stage oxy-alkynylation of diazo derivatives **7** and **8** of steroids,[19] which could be smoothly converted to the desired products **9** and **10** in 82% and 75% yield, respectively (Scheme 2A). This transformation highlights the chemoselectivity of the method in the presence of carbon-hydrogen bonds, olefins and carbonyls, which can react with carbene intermediates.[20]

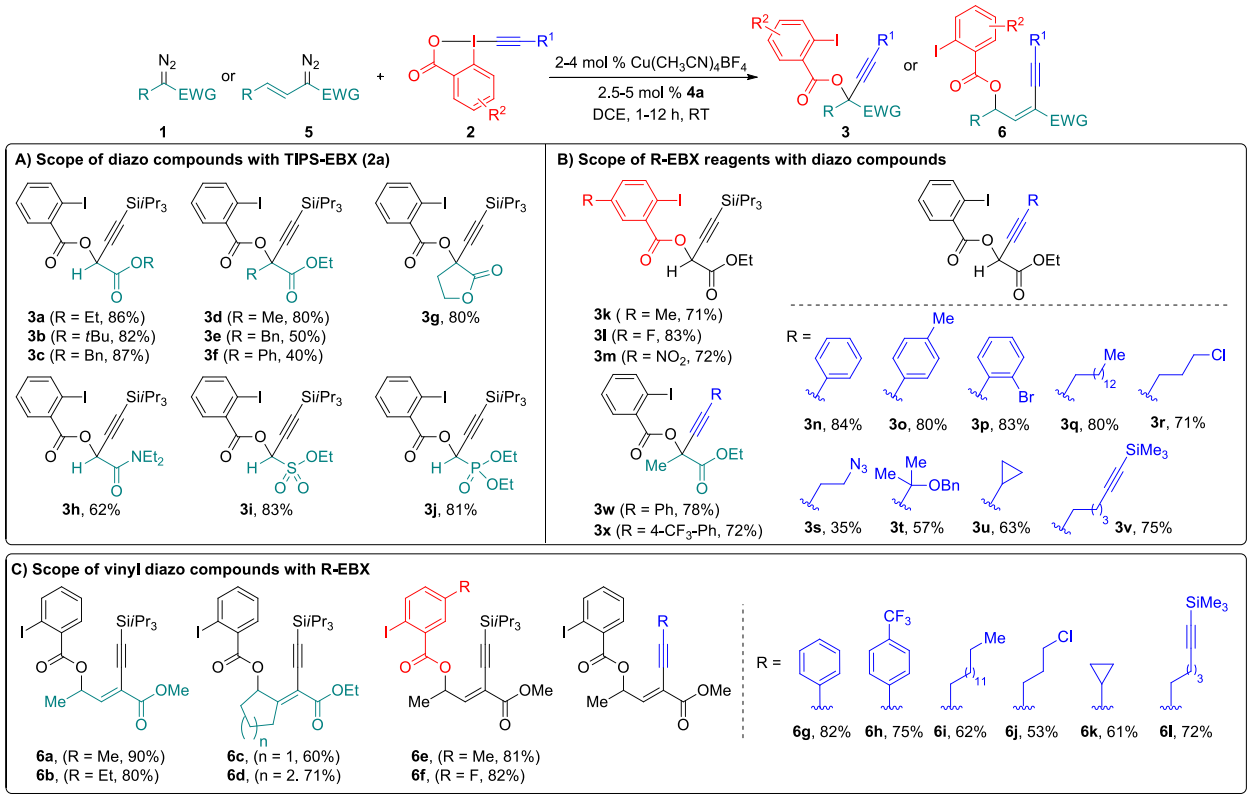
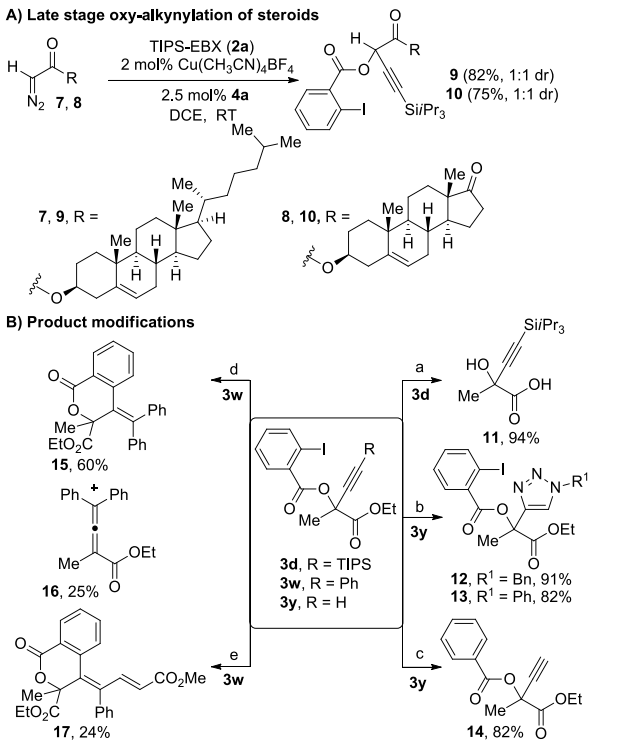


Figure 1. Scope of the copper-catalyzed oxy-alkynylation of diazo compounds with EBX reagents.

The obtained products contain three valuable functional groups: an alkyne, an iodide, and an ester. Oxy-alkynylated products **3a**, **3d**, and **3w** were synthesized on gram scale in 91%, 84%, and 79% yield, respectively. Ester **3d** could be readily hydrolyzed, affording the alkyne substituted α-hydroxy acid **11** in 94% yield (Scheme 2B). Copper-catalyzed cycloaddition of terminal alkyne **3y**, obtained by desilylation of **3d**, with benzyl and phenyl azides gave triazoles **12** and **13** in high yields. Deiodination of **3y** was achieved using visible light photoredox catalysis to give product **14** in 82% yield.[21] Isocoumarins derivative **15** could be synthesized using a domino carbopalladation/Suzuki cascade reaction[22] in 60% yield from **3w**. Tetra-substituted allene **16** was also obtained as a side product in the coupling reaction. Finally, a domino carbopalladation/Heck cascade reaction was also possible to furnish product **17** in 24% yield from **3w**.

Based on literature reports[5,13,17] and our own results, we propose a tentative mechanism for the reaction (Scheme 3A). The Cu(I) catalyst **I** first reacts with diazo compound **1** to form copper-carbene intermediate **II**. Then the carboxylate group of EBX reagent **2** adds to carbene intermediate **II** to form organocopper species **III**. Finally, intramolecular alkyne transfer gives product **3**. For vinyl diazo compounds **5**, conjugate addition on the formed carbene intermediate would give organocopper species **IV**, which affords to enyne product **6** as a single geometric isomer after alkyne transfer. For the alkyne transfer step, several mechanisms could be envisaged (Scheme 3B): nucleophilic attack on either the α or β position of the alkynyliodonium salt (pathways **a** and **b**), or oxidative alkyne transfer to copper (pathway **c**). In case of α-addition, β-elimination of the iodine would led directly to the product from the formed intermediate **V**. Alternatively, a concerted reaction could also be envisaged.[7d] On the other hand, β-addition would furnish first to a vinylidene intermediate via α-elimination on addition product **VI**. A fast 1,2-silicon shift would then lead to product **3**.

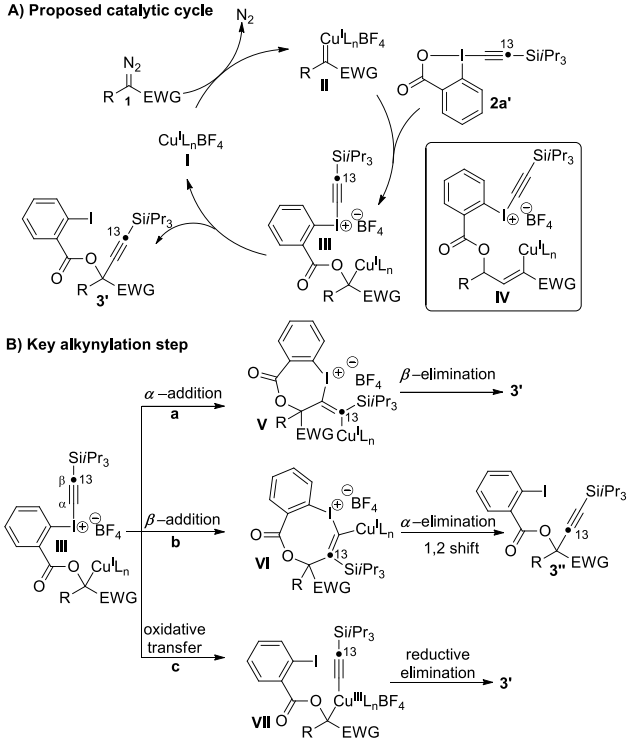
Scheme 2. Late stage Reaction and Product Modifications.



Reaction conditions: a) K_2CO_3, EtOH. b) R^1N_3, 20 mol % $CuSO_4$•$5H_2O$, sodium ascorbate, triazole ligand, tBuOH/H_2O. c) 2.5 mol % *fac*-Ir(ppy)$_3$, NBu_3, HCO_2H, blue LED, MeCN. d) 5 mol % $Pd(PPh_3)_4$, K_2CO_3, $PhB(OH)_2$, DMF. e) Ethyl acrylate, 5 mol % $Pd(PPh_3)_4$, NEt_3, DMF.

When ^{13}C labeled TIPS-EBX reagent **2a'** was used in the reaction, product **3'** without 1,2 shift of the silyl group was obtained exclusively, which indicated that addition on the β position is less probable. On the other hand, oxidative alkyne transfer to give copper(III) intermediate **VII**, followed by reductive elimination (pathway **c**) would also lead to the observed product **3'**. Consequently, further investigations will be needed to elucidate the mechanism of the alkyne-transfer step.

Scheme 3. Proposed mechanism for oxy-alkynylation.



In conclusion, we have developed an atom economical oxy-alkynylation of diazo compounds using EBX reagents. The reaction protocol is highly practical and characterized by mild reaction conditions, high yields, and the use of an inexpensive copper catalyst. A remarkably broad range of R-EBX reagents and diazo compounds were well tolerated in this transformation. In the case of vinyl diazo compounds, we obtained enyne products as single olefin isomers in high yields. The obtained products were efficiently transformed into useful building blocks such as α-hydroxy acids, triazoles, and isocoumarins. Further investigation using other hypervalent iodine reagents, studies to confirm the proposed mechanism of the reaction, and the development of an asymmetric version of the transformation are currently ongoing in our laboratories.

ASSOCIATED CONTENT

Supporting Information

Experimental procedures and analytical data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interests.

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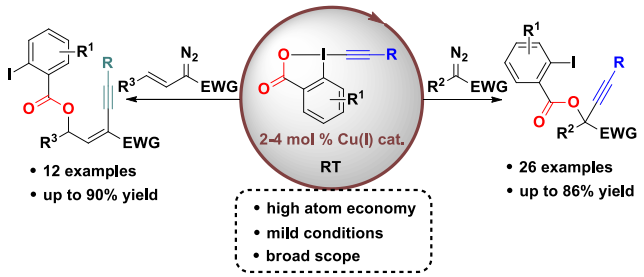
• 12 examples
• up to 90% yield
2-4 mol % Cu(I) cat.
RT
• high atom economy
• mild conditions
• broad scope
• 26 examples
• up to 86% yield

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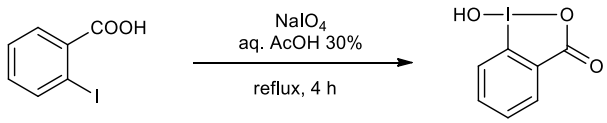
1. General Methods

All reactions were carried out in oven dried glassware under an atmosphere of nitrogen, unless stated otherwise. For quantitative flash chromatography technical grade solvents were used. For flash chromatography for analysis, HPLC grade solvents from Sigma-Aldrich were used. THF, Et_2O, CH_3CN, toluene, hexane and CH_2Cl_2 were dried by passage over activated alumina under nitrogen atmosphere (H_2O content < 10 ppm, *Karl-Fischer* titration). The solvents were degassed by Freeze-Pump-Thaw method when mentioned. All chemicals were purchased from Acros, Aldrich, Fluka, VWR, Aplichem or Merck and used as such unless stated otherwise. Chromatographic purification was performed as flash chromatography using Macherey-Nagel silica 40-63, 60 Å, using the solvents indicated as eluent with 0.1-0.5 bar pressure. TLC was performed on Merck silica gel 60 F_{254} TLC glass plates or aluminium plates and visualized with UV light, permanganate stain, CAN stain or Anisaldehyde stain. Melting points were measured on a Büchi B-540 melting point apparatus using open glass capillaries, the data is uncorrected. ^{1}H-NMR spectra were recorded on a Brucker DPX-400 400 MHz spectrometer in chloroform-d, DMSO-d_6 or CD_3OD, all signals are reported in ppm with the internal chloroform signal at 7.26 ppm, the internal DMSO signal at 2.50 ppm or the internal methanol signal at 3.30 ppm as standard. The data is being reported as (s = singlet, d = doublet, t = triplet, q = quadruplet, qi = quintet, m = multiplet or unresolved, br = broad signal, app = apparent, coupling constant(s) in Hz, integration, interpretation).^{13}C-NMR spectra were recorded with ^{1}H-decoupling on a Brucker DPX-400 100 MHz spectrometer in chloroform-d, DMSO-d_6 or CD_3OD, all signals are reported in ppm with the internal chloroform signal at 77.0 ppm, the internal DMSO signal at 39.5 ppm or the internal methanol signal at 49.0 ppm as standard. Infrared spectra were recorded on a JASCO FT-IR B4100 spectrophotometer with an ATR PRO410-S and a ZnSe prisma and are reported as cm^{-1} (w = weak, m = medium, s = strong, br = broad). High resolution mass spectrometric measurements were performed by the mass spectrometry service of ISIC at the EPFL on a MICROMASS (ESI) Q-TOF Ultima API.

2. Preparation of EBX reagents

The synthesis of R-EBX reagents **2a-2l** had been already described before. The procedures are taken here from the indicated publications to facilitate reproduction of the results by having all the data in the same file.

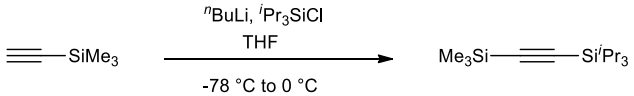
1-Hydroxy-1,2-benziodoxol-3-(1H)-one (19)



18 **19**

Following a reported procedure,[1] $NaIO_4$ (7.24 g, 33.8 mmol, 1.05 equiv) and 2-iodobenzoic acid (**18**) (8.00 g, 32.2 mmol, 1.00 equiv) were suspended in 30% (v/v) aq. AcOH (48 mL). The mixture was vigorously stirred and refluxed for 4 h. The reaction mixture was then diluted with cold water (180 mL) and allowed to cool to room temperature, protecting it from light. After 1 h, the crude product was collected by filtration, washed on the filter with ice water (3 x 20 mL) and acetone (3 x 20 mL), and air-dried in the dark to give the pure product **19** (8.3 g, 31 mmol, 98%) as a white solid. ^{1}H NMR (400 MHz, $(CD_3)_2SO$): δ 8.02 (dd, *J* = 7.7, 1.4 Hz, 1H, Ar*H*), 7.97 (m, 1H, Ar*H*), 7.85 (dd, *J* = 8.2, 0.7 Hz, 1H, Ar*H*), 7.71 (td, *J* = 7.6, 1.2 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $(CD_3)_2SO$): δ 167.7, 134.5, 131.5, 131.1, 130.4, 126.3, 120.4; IR ν 3083 (w), 3060 (w), 2867 (w), 2402 (w), 1601 (m), 1585 (m), 1564 (m), 1440 (m), 1338 (s), 1302 (m), 1148 (m), 1018 (w), 834 (m), 798 (w), 740 (s), 694 (s), 674 (m), 649 (m). The values of the NMR spectra are in accordance with reported literature data.[1]

Tri*iso*propylsilyl trimethylsilylacetylene (21)



20 **21**

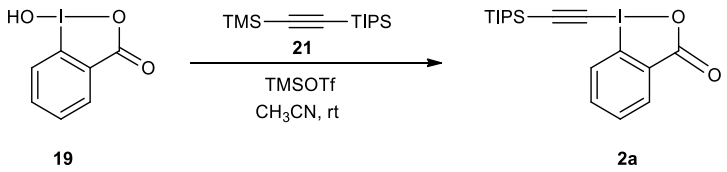
Following a reported procedure,[2] ^{n}BuLi (2.5 M in hexanes, 12.0 mL, 29.9 mmol, 0.98 equiv) was added dropwise to a stirred solution of ethynyltrimethylsilane (**20**) (3.0 g, 30 mmol, 1.0 equiv) in THF (48 mL) at -78 °C. The mixture was then warmed to 0 °C and stirred for 5 min. The mixture

[1] Kraszkiewicz, L.; Skulski, L. *Arkivoc* **2003**, *6*, 120.

[2] Helal, C. J.; Magriotis, P. A.; Corey, E. J. *J. Am. Chem. Soc.* **1996**, *118*, 10938.

was then cooled back to -78 °C and chlorotri*iso*propylsilane (6.4 mL, 30 mmol, 1.0 equiv) was added dropwise. The mixture was then allowed to warm to room temperature and stirred overnight. A saturated solution of ammonium chloride (40 mL) was added, and the reaction mixture was extracted with diethyl ether (2 x 60 mL). The organic layer was washed with water and brine, then dried over $MgSO_4$, filtered and concentrated under reduced pressure to obtain a colorless liquid which was further purified by Kugelrohr distillation (56-57 °C/0.25 mm of Hg) to yield **21** (7.16 g, 28.0 mmol, 92% yield) as a colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.08 (m, 21H, TIPS), 0.18 (s, 9H, TMS); IR ν 2959 (m), 2944 (m), 2896 (w), 2867 (m), 1464 (w), 1385 (w), 1250 (m), 996 (w), 842 (s), 764 (s), 675 (m), 660 (m). The values of the NMR spectra are in accordance with reported literature data.[2]

1-[(Tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (2a)

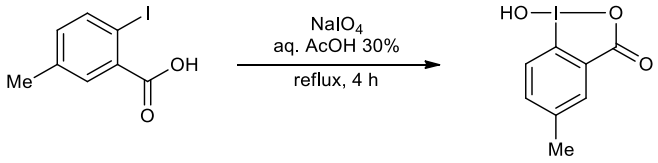


Following a reported procedure,[3] 2-iodosylbenzoic acid (**19**) (21.7 g, 82.0 mmol, 1.00 equiv) was charged in oven-dried three-neck 1L flask equipped with a magnetic stirrer. After 3 vacuum/nitrogen cycles, anhydrous acetonitrile (500 mL) was added *via* canula and cooled to 0 °C. Trimethylsilyltriflate (16.4 mL, 90.0 mmol, 1.10 equiv) was added dropwise *via* a dropping funnel over 30 min (no temperature increase was observed). After 15 min, (trimethylsilyl)(tri*iso*propylsilyl)acetylene (**21**) (23.0 g, 90.0 mmol, 1.10 equiv) was added *via* canula over 15 min (no temperature increase was observed). After 30 min, the suspension became an orange solution. After 10 min, pyridine (7.0 mL, 90 mmol, 1.1 equiv) was added *via* syringe. After 15 min, the reaction mixture was transferred in a one-neck 1L flask and reduced under vacuum until a solid was obtained. The solid was dissolved in CH_2Cl_2 (200 mL) and transferred in a 1L separatory funnel. The organic layer was added and washed with 1 M HCl (200 mL) and the aqueous layer was extracted with CH_2Cl_2 (200 mL). The organic layers were combined, washed with a saturated solution of $NaHCO_3$ (2 x 200 mL), dried over $MgSO_4$, filtered and the solvent was evaporated under reduced pressure. Recrystallization from acetonitrile (*ca* 120 mL)

[3] Brand, J. P.; Waser, J. *Angew. Chem., Int. Ed.* **2010**, *49*, 7304.

afforded **2a** (30.1 g, 70.2 mmol, 86%) as colorless crystals. Mp (Dec.): 170-176 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.44 (m, 1H, Ar*H*), 8.29 (m, 1H, Ar*H*), 7.77 (m, 2H, Ar*H*), 1.16 (m, 21H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.4, 134.6, 132.3, 131.4, 131.4, 126.1, 115.6, 114.1, 64.6, 18.4, 11.1; IR ν 2943 (m), 2865 (m), 1716 (m), 1618 (m), 1604 (s), 1584 (m), 1557 (m), 1465 (m), 1439 (w), 1349 (m), 1291 (m), 1270 (w), 1244 (m), 1140 (m), 1016 (m), 999 (m), 883 (m), 833 (m), 742 (m), 702 (s), 636 (m). The values of the NMR spectra are in accordance with reported literature data.[3]

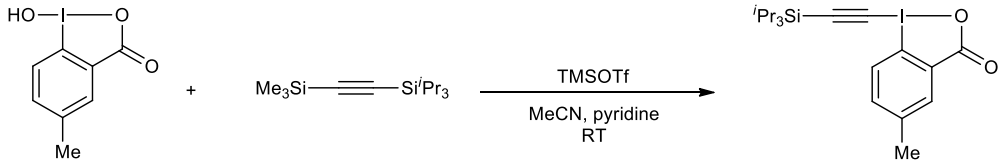
5-Methyl-2-iodosylbenzoic acid (23)



22 **23**

Following a reported procedure,[4] $NaIO_4$ (1.25 g, 5.84 mmol, 1.05 equiv) and 2-iodo-5-methylbenzoic acid (**22**) (1.46 g, 5.56 mmol, 1.00 equiv) were suspended in 30% (v/v) aq. AcOH (15 mL). The mixture was vigorously stirred and refluxed for 4 h. The reaction mixture was then diluted with cold water (40 mL) and allowed to cool to room temperature, protecting it from light. The crude product was collected by filtration, washed on the filter with ice water (3 x 4 mL) and acetone (3 x 4 mL), and air-dried in the dark to give the pure product **23** (1.39 g, 5.00 mmol, 90%) as a colorless solid. ^{1}H NMR (400 MHz, $(CD_3)_2SO$): δ 7.84 (s, 1H, Ar*H*), 7.78 (m, 1H, Ar*H*), 7.69 (m, 1H, Ar*H*), 2.47 (s, 3H, C*H*$_3$).

5-Methyl-1-[(tri*iso*propylsilyl)ethynyl]-1,2-benziodoxol-3(1*H*)-one (2b)



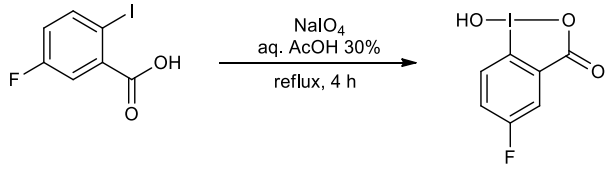
23 **21** **2b**

Following a reported procedure,[4] trimethylsilyltriflate (400 μL, 2.20 mmol, 1.10 equiv) was added dropwise to a stirred solution of **23** (556 mg, 2.00 mmol, 1.00 equiv) in acetonitrile (10 mL). After 20 min, (trimethylsilyl)(tri*iso*-propylsilyl)acetylene (**21**) (560 mg, 2.20 mmol, 1.10

[4] Brand, J. P.; Chevalley, C.; Scopelliti, R.; Waser, J. *Chem. - Eur. J.* **2012**, *18*, 5655.

equiv) was then added dropwise, followed, after 20 min, by the addition of pyridine (180 µL, 2.20 mmol, 1.10 equiv). The mixture was stirred for 20 min. The solvent was then removed under reduced pressure and the yellow crude oil was dissolved in CH_2Cl_2 (20 mL). The organic layer was washed with 1 M HCl (20 mL) and the aqueous layer was extracted with CH_2Cl_2 (20 mL). The organic layers were combined, washed with a saturated solution of $NaHCO_3$ (40 mL), dried over $MgSO_4$, filtered and the solvent was evaporated under reduced pressure. Recrystallization from acetonitrile (*ca* 25 mL) and wash with hexanes afforded **2b** (559 mg, 1.26 mmol, 63%) as colorless crystals. Mp (Dec.): 192-197 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.23 (d, *J* = 1.5 Hz, 1H, Ar*H*), 8.12 (d, *J* = 8.5 Hz, 1H, Ar*H*), 7.57 (dd, *J* = 8.5, 1.8 Hz, 1H, Ar*H*), 2.51 (s, 3H, ArC*H*$_3$), 1.16 (m, 21H, TIPS); ^{13}C NMR (101 MHz, $CDCl_3$): δ 166.6, 142.5, 135.6, 133.0, 131.2, 125.8, 113.8, 111.8, 64.6, 20.7, 18.5, 11.2. The characterization data corresponded to the reported values.[4]

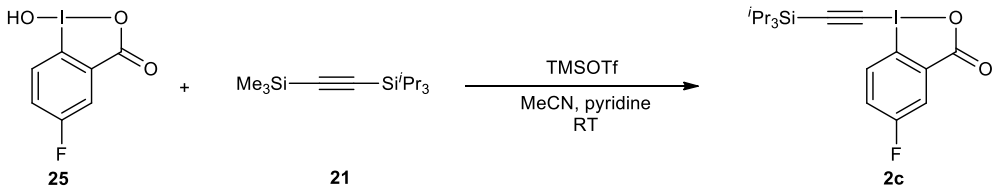
5-Fluoro-2-iodosylbenzoic acid (25)



24 **25**

Following a reported procedure,[4] $NaIO_4$ (656 mg, 3.07 mmol, 1.05 equiv) and 2-iodo-4-fluorobenzoic acid (**24**) (778 mg, 2.92 mmol, 1.00 equiv) were suspended in 30% (v/v) aq. AcOH (7 mL). The mixture was vigorously stirred and refluxed for 4 h. The reaction mixture was then diluted with cold water (20 mL) and allowed to cool to room temperature, protecting it from light. The crude product was collected by filtration, washed on the filter with ice water (3 x 4 mL) and acetone (3 x 4 mL), and air-dried in the dark to give the pure product **25** (738 mg, 2.62 mmol, 90%) as a white solid. ^{1}H NMR (400 MHz, $(CD_3)_2SO$): δ 7.88-7.79 (m, 3H, Ar*H* and O*H*), 7.75 (m, 1H, Ar*H*).

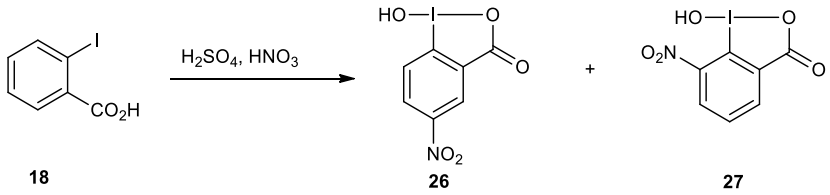
5-Fluoro-1-[(tri*iso*propylsilyl)ethynyl]-1,2-benziodoxol-3(1*H*)-one (2c)



25 **21** **2c**

Following a reported procedure,[4] trimethylsilyltriflate (247 µL, 1.36 mmol, 1.10 equiv, freshly distilled) was added dropwise to a stirred solution of **25** (350 mg, 1.24 mmol, 1.00 equiv) in acetonitrile (5 mL). (Trimethylsilyl)(tri*iso*-propylsilyl)acetylene (**21**) (349 mg, 1.36 mmol, 1.10 equiv) was then added dropwise, followed, after 15 min, by the addition of pyridine (110 µL, 1.36 mmol, 1.10 equiv). The mixture was stirred for 10 min. The solvent was then removed under reduced pressure and the yellow crude oil was dissolved in CH_2Cl_2 (50 mL). The organic layer was washed with 1 M HCl (50 mL) and the aqueous layer was extracted with CH_2Cl_2 (50 mL). The organic layers were combined, washed with a saturated solution of $NaHCO_3$ (2 x 50 mL), dried over $MgSO_4$, filtered and the solvent was evaporated under reduced pressure. Recrystallization from acetonitrile (*ca* 5 mL) afforded **2c** (381 mg, 0.854 mmol, 69%) as a white solid. Mp (Dec.); 185-189 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.22 (dd, *J* = 9.0, 4.2 Hz, 1H, Ar*H*), 8.10 (dd, *J* = 7.9, 2.9 Hz, 1H, Ar*H*), 7.48 (m, 1H, Ar*H*), 1.16 (m, 21H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.6 (d, *J* = 254 Hz), 165.2 (d, *J* = 7 Hz), 134.2 (d, *J* = 7 Hz), 127.8 (d, *J* = 8 Hz), 122.2 (d, *J* = 24 Hz), 119.4 (d, *J* = 24 Hz), 115.0, 108.0 (d, *J* = 1 Hz), 64.0, 18.5, 11.2. The characterization data corresponded to the reported values.[4]

2-Iodosyl-5-nitrobenzoic acid (26) and 2-iodosyl-3-nitrobenzoic acid (27)

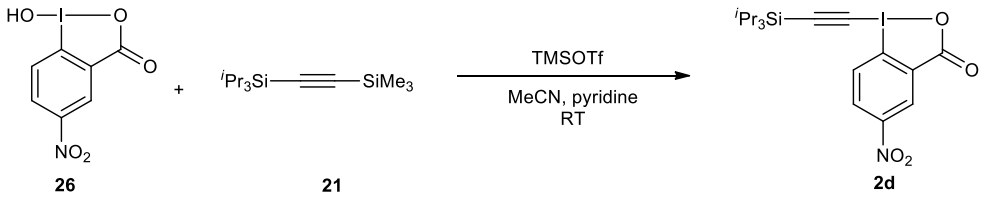


18 26 27

Following a reported procedure,[4] fuming nitric acid (3.3 mL) was added to 2-iodobenzoic acid (**18**) (5.0 g, 20 mmol, 1.0 equiv) in concentrated H_2SO_4 (6.7 mL). The reaction was equipped with a cooler and a nitrous vapor trap and was heated at 100 °C for 1 h. The reaction mixture was then poured in ice-water and filtered. The resulting solid was refluxed in water (50 mL) and filtered. A second crop of precipitate was filtered from the mother liquors. Both solids were combined, washed with acetone (10 mL) and dried under vacuum to afford **26** (2.19 g, 7.10 mmol, 36 %). The mother liquors were reduced to one third and then kept at 4 °C, the resulting precipitate was filtered, washed with acetone (10 mL) and dried under vacuum to afford **27** (630 mg, 2.04 mmol, 10 %). **26**: ^{1}H NMR (400 MHz, $(CD_3)_2SO$): δ 8.73 (dd, *J* = 8.8, 2.6 Hz, 1H, Ar*H*), 8.58 (d, *J* = 2.4

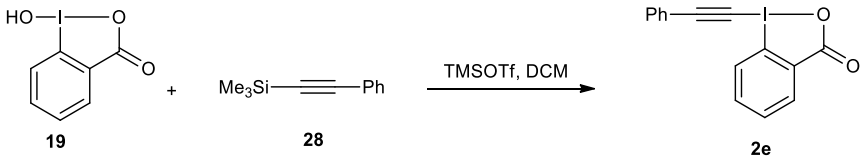
Hz, 1H, Ar*H*), 8.54 (br s, 1H, O*H*), 8.11 (d, *J* = 8.8 Hz, 1H, Ar*H*). **27**: ^{1}H NMR (400 MHz, $(CD_3)_2SO$): δ 7.92 (dd, *J* = 7.9, 1.5 Hz, 1H, Ar*H*), 7.79 (m, 1H, Ar*H*), 7.67 (m, 1H, Ar*H*).

5-Nitro-1-[(tri*iso*propylsilyl)ethynyl]-1,2-benziodoxol-3(1*H*)-one (2d)



Following a reported procedure,[4] trimethylsilyltriflate (646 µL, 3.56 mmol, 1.10 equiv, freshly distilled over CaH_2) was added dropwise to a stirred solution of 2-iodosylbenzoic acid **26** (1.00 g, 3.23 mmol, 1.00 equiv) in acetonitrile (15 mL) at 0 °C. After 15 min at room temperature, (trimethylsilyl)(tri*iso*-propylsilyl)acetylene (**21**) (906 mg, 3.56 mmol, 1.10 equiv) was then added dropwise, followed, after 30 min, by the addition of pyridine (290 µL, 3.56 mmol, 1.10 equiv). The mixture was stirred for 20 min. The solvent was then removed under reduced pressure and the yellow crude oil was dissolved in CH_2Cl_2 (25 mL). The organic layer was washed with 1 M HCl (25 mL) and the aqueous layer was extracted with CH_2Cl_2 (25 mL). The organic layers were combined, washed with a saturated solution of $NaHCO_3$ (20 mL), dried over $MgSO_4$, filtered and the solvent was evaporated under reduced pressure. Recrystallization from acetonitrile (*ca* 20 mL) afforded **2d** (960 mg, 2.02 mmol, 63%) as a white solid. Mp (Dec.); 198-206 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.20 (d, *J* = 2.6 Hz, 1H, Ar*H*), 8.60 (ddd, *J* = 9.0, 2.5, 0.4 Hz, 1H, Ar*H*), 8.53 (d, *J* = 8.9 Hz, 1H, Ar*H*), 1.30-1.14 (m, 21H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.4, 150.7, 134.4, 129.0, 128.2, 126.5, 122.7, 115.2, 63.1, 18.5, 11.3. The characterization data corresponded to the reported values.[4]

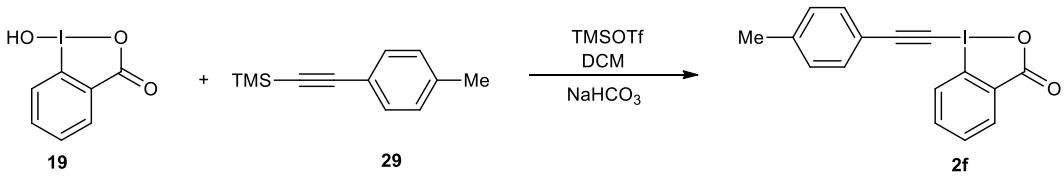
1-[Phenylethynyl]-1,2-benziodoxol-3(1*H*)-one (2e)



Following a reported procedure,[4] trimethylsilyl triflate (7.50 mL, 41.5 mmol, 1.10 equiv) was added to a suspension of 2-iodosylbenzoic acid (**19**) (10.0 g, 37.7 mmol, 1.00 equiv) in CH_2Cl_2 (100 mL) at room temperature. The resulting yellow mixture was stirred for 1 h, followed by the

dropwise addition of trimethyl(phenylethynyl)silane (**28**) (8.10 mL, 41.5 mmol, 1.10 equiv) (slightly exothermic). The resulting suspension was stirred for 6 h at room temperature, during this time a white solid was formed. A saturated solution of $NaHCO_3$ (100 mL) was then added and the mixture was stirred vigorously. The resulting suspension was filtered on a glass filter of porosity 4. The two layers of the mother liquors were separated and the organic layer was washed with saturated solution of $NaHCO_3$ (100 mL), dried over $MgSO_4$, filtered and evaporated under reduced pressure. The resulting mixture was combined with the solid obtained by filtration and boiled in CH_3CN (*ca* 300 mL). The mixture was cooled down, filtered and dried under high vacuum to afford **2e** (6.08 g, 17.4 mmol, 46 %) as a white solid. Mp (Dec.); 155–160 °C (lit 153-155°C); ^{1}H NMR (400 MHz, $CDCl_3$); δ 8.46 (m, 1H, Ar*H*), 8.28 (m, 1H, Ar*H*), 7.80 (m, 2H, Ar*H*), 7.63 (m, 2H, Ar*H*), 7.48 (m, 3H, Ar*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.9, 134.9, 132.9, 132.5, 131.6, 131.3. 130.8, 128.8, 126.2, 120.5, 116.2, 106.6, 50.2. The characterization data corresponded to the reported values.[4]

1-(*p*-Tolylethynyl)-1,2-benziodoxol-3(1H)-one (2f)

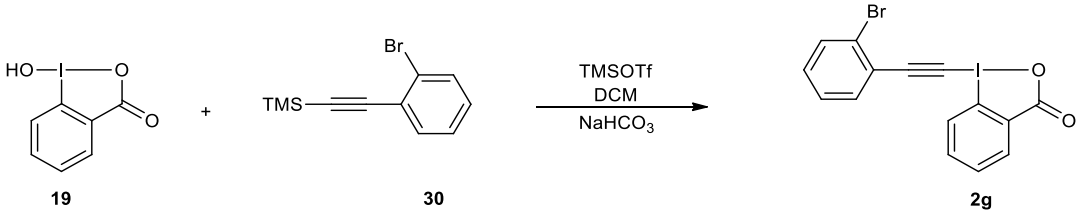


Following a reported procedure,[5]trimethylsilyl triflate (1.0 mL, 5.5 mmol, 1.1 equiv) was added to a suspension of 2-iodosylbenzoic acid (**19**) (1.32 g, 5.00 mmol, 1.00 equiv) in CH_2Cl_2 (15 mL) at room temperature. The resulting suspension was stirred for 3 h, followed by the drop wise addition of trimethyl(*p*-tolylethynyl)silane (**29**) (1.04 g, 5.50 mmol, 1.10 equiv). The resulting suspension was stirred for 6 h at room temperature. A saturated solution of $NaHCO_3$ (20 mL) was then added and the mixture was stirred vigorously for 30 minutes, the two layers were separated and the organic layer was washed with saturated solution of $NaHCO_3$ (20 mL), dried over $MgSO_4$, filtered and evaporated under reduced pressure. The resulting solid was boiled in CH_3CN (*ca* 20 mL). The mixture was cooled down, filtered and dried under high vacuum to afford **2f** (0.540 g, 1.49 mmol, 30%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.43 (dd, *J* = 6.1, 2.9

[5] Huang, H.; Zhang, G.; Gong, L.; Zhang, S.; Chen, Y. *J. Am. Chem. Soc.* **2014**, *136*, 2280.

Hz, 1H, Ar*H*), 8.30– 8.14 (m, 1H, Ar*H*), 7.77 (dd, *J* = 6.9, 3.1 Hz, 2H, Ar*H*), 7.50 (d, *J* = 7.8 Hz, 2H, Ar*H*), 7.25 (d, *J* = 7.6 Hz, 2H, Ar*H*), 2.43 (s, 3H, ArC*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.6, 141.5, 134.9, 132.8, 132.5, 131.6, 131.3, 129.5, 126.2, 117.4, 116.2, 107.25, 49.1, 21.7. The characterization data corresponded to the reported values.[5]

1-[2-Bromophenylethynyl]-1,2-benziodoxol-3(1H)-one (2g)

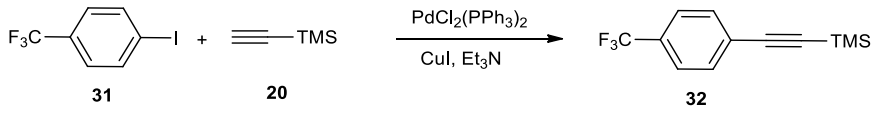


19 **30** **2g**

Following a reported procedure,[6] trimethylsilyl triflate (1.0 mL, 5.5 mmol, 1.1 equiv) was added to a suspension of 2-iodosylbenzoic acid (**19**) (1.32 g, 5.00 mmol, 1.00 equiv) in CH_2Cl_2 (15 mL) at room temperature. The resulting suspension was stirred for 3 h, followed by the drop wise addition of ((2-bromophenyl)ethynyl)trimethylsilane (**30**) (1.17 g, 5.50 mmol, 1.10 equiv). The resulting suspension was stirred for 6 h at room temperature. A saturated solution of $NaHCO_3$ (20 mL) was then added and the mixture was stirred vigorously for 30 minutes, the two layers were separated and the organic layer was washed with saturated solution of $NaHCO_3$ (20 mL), dried over $MgSO_4$, filtered and evaporated under reduced pressure. The resulting solid was boiled in CH_3CN (*ca* 20 mL). The mixture was cooled down, filtered and dried under high vacuum to afford **2g** (1.50 g, 3.51 mmol, 70%) as a white solid. Mp (Dec.): 174-177 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.44 (td, *J* = 7.3, 2.1 Hz, 2H, Ar*H*), 7.84–7.74 (m, 2H, Ar*H*), 7.68 (d, *J* = 1.1 Hz, 1H, Ar*H*), 7.61 (dd, *J* = 7.6, 1.7 Hz, 1H, Ar*H*), 7.36 (dtd, *J* = 22.4, 7.5, 1.5 Hz, 2H, Ar*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.6, 135.2, 134.7, 133.0, 132.7 , 131.8, 131.3, 127.6, 126.8, 126.4, 123.2, 116.5, 104.3, 55.4; IR ν 2358 (w), 2155 (w), 1638 (s), 1616 (m), 1585 (w), 1466 (w), 1316 (m), 1147 (w). The characterization data corresponded to the reported values.[6]

Trimethyl((4-(trifluoromethyl)phenyl)ethynyl)silane (32)

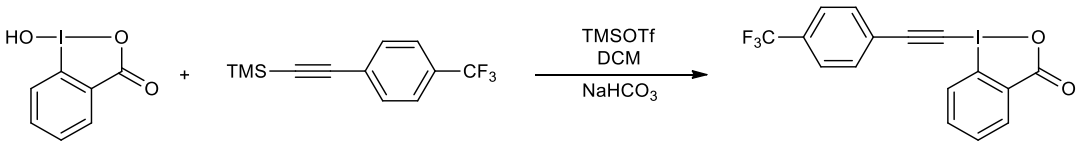
[6] Le Vaillant, F.; Courant, T.; Waser, J. *Angew. Chem., Int. Ed.* **2015**, *54*, 11200.



31 20 32

Following a reported procedure,[5] a solution of trimethylsilyl acetylene (**20**) (2.13 mL, 15.0 mmol, 1.50 equiv) was added drop wise to a mixture of 1-iodo-4-(trifluoromethyl) benzene (**31**) (2.72 g, 10.0 mmol, 1.00 equiv), $Pd(PPh_3)_2C1_2$ (70 mg, 0.10 mmol, 0.010 equiv), and copper (I) iodide (38 mg, 0.20 mmol, 0.020 equiv) in triethylamine (30 mL). The reaction mixture was stirred at room temperature for 3 h, concentrated and purified by column chromatography (pure pentane) to afford the corresponding product **32** (1.60 g, 6.60 mmol, 66%) as a colorless oil. TLC (pentane): R_f = 0.8, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 (s, 4H, Ar*H*), 0.27 (s, 9H, TMS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 132.2, 130.1 (q, *J* = 32.7 Hz), 126.9 (q, *J* = 3.9 Hz), 125.2 (q, *J* = 3.8 Hz), 123.9 (q, *J* = 272.1 Hz), 103.6, 97.2, -0.2.

1-[4-Trifluoromethylphenylethynyl]-1,2-benziodoxol-3(1H)-one (2h)

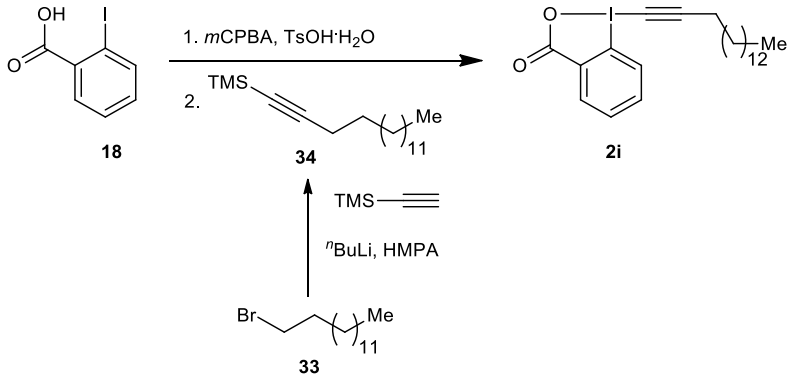


19 32 2h

Following a reported procedure,[5] trimethylsilyl triflate (0.80 mL, 4.4 mmol, 1.1 equiv) was added to a suspension of 2-iodosylbenzoic acid (**19**) (1.06 g, 4.00 mmol, 1.00 equiv) in CH_2Cl_2 (15 mL) at room temperature. The resulting yellow mixture was stirred for 1 h, followed by the dropwise addition of trimethyl((4-(trifluoromethyl)phenyl)ethynyl)silane (**32**) (1.07 g, 4.40 mmol, 1.10 equiv). The resulting suspension was stirred for 6 h at room temperature. A saturated solution of $NaHCO_3$ (20 mL) was then added and the mixture was stirred vigorously for 30 minutes, the two layers were separated and the organic layer was washed with a saturated solution of $NaHCO_3$ (20 mL), dried over $MgSO_4$, filtered and evaporated under reduced pressure. The resulting solid was recrystallized in CH_3CN (*ca* 20 mL) to afford **2h** (850 mg, 2.04 mmol, 51%) as a pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.46–8.38 (m, 1H, Ar*H*), 8.28–8.19 (m, 1H, Ar*H*), 7.84–7.74 (m, 2H, Ar*H*), 7.74–7.65 (m, 4H, Ar*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.8, 135.2, 133.3 (two signals overlapped), 132.7, 132.2, 130.1 (q, $J_{C\text{-}F}$ = 32.0 Hz), 126.5, 125.8 (q, $J_{C\text{-}F}$ = 3.6 Hz),

124.9, 123.4 (q, $J_{C\text{-}F}$ = 270.0 Hz), 116.3, 104.3, 53.9. The characterization data corresponded to the reported values.[5]

Hexadecynyl-1,2-benziodoxol-3(1*H*)-one (2i)

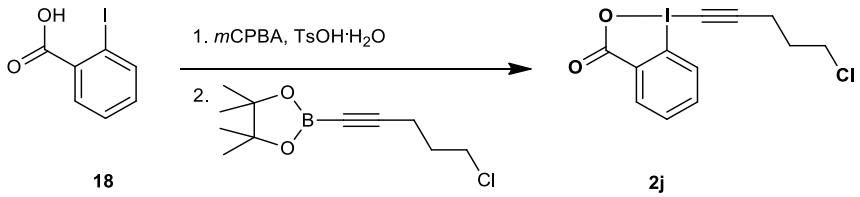


Following a reported procedure,[7] to a mixture of trimethylsilylacetylene (8.33 g, 85.0 mmol, 1.20 equiv) and dry THF (46 mL) was added at -78 °C under nitrogen 2.5 M ^{n}BuLi in hexanes (33.9 mL, 85.0 mmol, 1.20 equiv) over a 10 minute time period. The resulting light yellow solution was stirred at -78 °C for 1 h, after which a mixture consisting of 1-bromotetradecane (**33**) (19.6 g, 70.7 mmol, 1.00 equiv), hexamethylphosphoramide (HMPA, 14.2 mL, 78.0 mmol, 1.10 equiv) and dry THF (23 mL) was slowly added *via* cannula over a 20 minutes time period. The reaction mixture was stirred for 1 h at -78 °C, followed by 24 h of stirring at room temperature. The reaction was quenched at 0 °C with saturated aq. NH_4Cl (50 mL) and diluted with water (10 mL) and EtOAc (50 mL). The two layers were separated and the aq. layer was extracted with additional portions of EtOAc (3 x 50 mL). The combined organic layers were washed with water (2 x 100 mL), brine (100 mL), dried over $MgSO_4$, filtered and concentrated in vacuo. The light brown crude liquid was finally pushed through a small plug of silica gel with pentane as eluent to afford pure hexadec-1-yn-1-yltrimethylsilane (**34**) (19.3 g, 65.5 mmol, 92.7% yield) as a colorless liquid. TLC (pentane): R_f = 0.78, $KMnO_4$; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.19 (t, J = 7.1 Hz, 2H, CCC*H*$_2$), 1.54-1.44 (m, 2H, C*H*$_2$), 1.42-1.18 (m, 22H, C*H*$_2$), 0.87 (t, J = 6.7 Hz, 3H, CH_2CH_3), 0.13 (s, 9H, TMS); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 107.7, 84.3, 32.2, 29.9, 29.8, 29.7, 29.6, 29.3, 29.0, 28.9, 22.9, 20.0, 14.3, 0.3; IR ν 2924 (m), 2854 (m), 2175 (w), 1461 (w), 1249 (w), 910 (w), 841 (s), 761 (w), 736 (m). The characterization data corresponded to the reported values.[7]

[7] Frei, R.; Wodrich, M. D.; Hari, D. P.; Borin, P.-A.; Chauvier, C.; Waser, J. *J. Am. Chem. Soc.* **2014**, *136*, 16563.

Following a reported procedure,[7] 2-iodobenzoic acid (**18**) (8.00 g, 32.2 mmol, 1.00 equiv), *para*-toluenesulfonic acid monohydrate ($TsOH.H_2O$, 6.13 g, 32.2 mmol, 1.00 equiv) and *meta*-chloroperoxybenzoic acid (mCPBA-70%, 8.74 g, 35.5 mmol, 1.10 equiv) were dissolved in CH_2Cl_2 (60 mL) and 2,2,2-trifluoroethanol (60 mL). The mixture was stirred at room temperature under nitrogen for 1 h, after which hexadec-1-yn-1-yltrimethylsilane (**34**) (13.3 g, 45.1 mmol, 1.40 equiv) was added in one portion. The reaction mixture was stirred for 14 h at room temperature, filtered and concentrated in vacuo. The resulting oil was dissolved in CH_2Cl_2 (400 mL) and under vigorous stirring, saturated solution of $NaHCO_3$ (400 mL) was added. The mixture was stirred for 1 h, the two layers were separated and the aqueous layer was extracted with additional portions of CH_2Cl_2 (3 x 100 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated in vacuo. The crude product was purified by flash column chromatography using EtOAc to afford **2i** (6.02 g, 12.9 mmol, 40%) as a white solid. TLC (EtOAc): R_f = 0.36, $KMnO_4$; Mp: 102.6-105.3 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.44-8.37 (m, 1H, Ar*H*), 8.21-8.14 (m, 1H, Ar*H*), 7.80-7.70 (m, 2H, Ar*H*), 2.59 (t, *J* = 7.1 Hz, 2H, CCC*H*$_2$), 1.65 (p, *J* = 7.1 Hz, 2H, CCCH$_2$C*H*$_2$), 1.52-1.40 (m, 2H), 1.39-1.19 (m, 20H, C*H*$_2$), 0.86 (t, *J* = 6.7 Hz, 3H, CH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 166.6, 134.7, 132.5, 131.7, 131.6, 126.2, 115.7, 109.9, 39.5, 32.1, 29.8, 29.7, 29.6, 29.5, 29.2, 29.1, 28.3, 22.8, 20.6, 14.3; IR ν 2924 (s), 2853 (m), 2166 (w), 1649 (m), 1623 (m), 1439 (w), 908 (m), 736 (s). The characterization data corresponded to the reported values.[7]

(5-Chloropent-1-ynyl)-1,2-benziodoxol-3(1H)-one (2j)

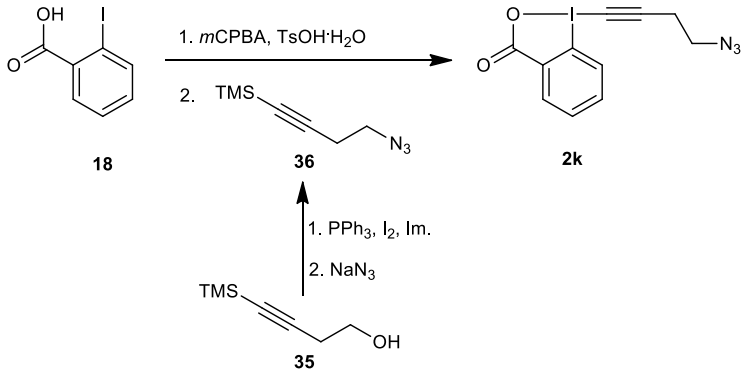


Following a reported procedure,[7, 8] 2-iodobenzoic acid (**18**) (3.76 g, 15.2 mmol, 1.00 equiv), *para*-toluenesulfonic acid monohydrate ($TsOH.H_2O$, 2.88 g, 15.2 mmol, 1.00 equiv) and *meta*-chloroperoxybenzoic acid (mCPBA-70%, 4.11 g, 16.7 mmol, 1.10 equiv) were dissolved in CH_2Cl_2 (30 mL) and 2,2,2-trifluoroethanol (30 mL). The mixture was stirred at room temperature under nitrogen for 1 h, after which 5-chloro-1-pentynyl-1-boronic acid pinacol ester (4.85 g, 21.2 mmol, 1.40 equiv) was added in one portion. The reaction mixture was stirred for 90 minutes at

[8] Bouma, M. J.; Olofsson, B. *Chem. - Eur. J.* **2012**, *18*, 14242.

room temperature, filtered and concentrated in vacuo. The resulting oil was dissolved in CH_2Cl_2 (15 mL) and under vigorous stirring, saturated solution of $NaHCO_3$ (15 mL) was added. The mixture was stirred for 10 minutes, the two layers were separated and the aqueous layer was extracted with additional portions of CH_2Cl_2 (3 x 15 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated in vacuo. The crude product was purified by flash column chromatography using ethyl acetate to afford **2j** (3.76 g, 10.8 mmol, 71%) as a white solid. TLC (EtOAc): R_f = 0.15, $KMnO_4$; Mp: 138.5-141.7 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.41-8.34 (m, 1H, Ar*H*), 8.22-8.13 (m, 1H, Ar*H*), 7.82-7.68 (m, 2H, Ar*H*), 3.71 (t, *J* = 6.1 Hz, 2H, ClC*H*$_2$CH$_2$), 2.82 (t, *J* = 6.9 Hz, 2H, CCC*H*$_2$CH$_2$), 2.18-2.05 (m, 2H, ClCH$_2$C*H*$_2$); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 166.8, 134.9, 132.5, 131.6, 131.6, 126.4, 115.8, 107.1, 43.4, 41.2, 30.7, 18.0; IR ν 2942 (w), 2866 (w), 2171 (w), 2091 (w), 1727 (w), 1617 (s), 1556 (w), 1441 (w), 1339 (m), 1213 (w), 1023 (w), 846 (w), 742 (s). The characterization data corresponded to the reported values.[7]

(4-Azidobut-1-ynyl)-1,2-benziodoxol-3(1H)-one (2k)



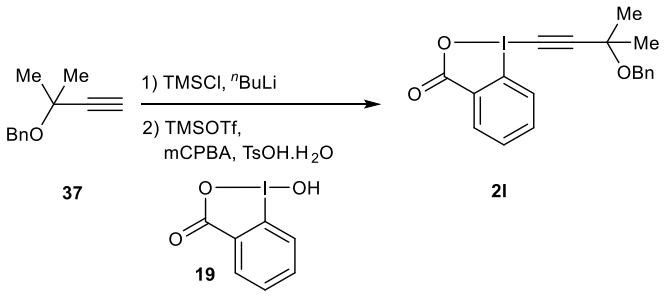
Following a reported procedure,[7] triphenylphosphine (27.7 g, 105 mmol, 1.00 equiv) was added at 0 °C to a colorless solution of 4-(trimethylsilyl)but-3-yn-1-ol (**35**) (15.0 g, 105 mmol, 1.00 equiv) in THF (400 mL). After dissolution, imidazole (7.18 g, 105 mmol, 1.00 equiv) and iodine (26.8 g, 105 mmol, 1.00 equiv) were added to the mixture. The cooling bath was removed after 5 minutes and the reaction mixture was stirred at room temperature for 2 h. Next, the mixture was diluted with diethyl ether (300 mL) and washed with 10% aq. $Na_2S_2O_3$ (300 mL). The aq. layer was washed with additional portions of diethyl ether (2 x 100 mL) and the combined organic layers were washed with brine (300 mL), dried over $MgSO_4$, filtered and concentrated in vacuo. The resulting white suspension was filtered and the filtrate was purified by Kugelrohr distillation (95 °C at 0.5 mbar) to furnish pure (4-iodobut-1-yn-1-yl)trimethylsilane (25.3 g, 100 mmol, 95%

yield) as a colorless liquid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.19 (t, *J* = 7.5 Hz, 2H, CH_2CH_2I), 2.76 (t, *J* = 7.5 Hz, 2H, CH_2CH_2I), 0.13 (s, 9H, TMS); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 105.1, 86.8, 25.2, 1.1, 0.1. The characterization data corresponded to the reported values.[7]

0.5 M sodium azide in DMSO (220 ml, 110 mmol, 1.10 equiv) was added to (4-iodobut-1-yn-1-yl)trimethylsilane (25.2 g, 99.9 mmol, 1.00 equiv) and the reaction mixture was stirred for 24 h at room temperature. The mixture was next slowly added to ice water (500 mL) and extracted with diethyl ether (3 x 200 mL). The combined organic layers were washed with water (2 x 100 mL), brine (100 mL), dried over $MgSO_4$, filtered and concentrated in vacuo. The light yellow crude liquid was finally pushed through a small plug of silica gel with pentane as eluent to afford pure (4-azidobut-1-yn-1-yl)trimethylsilane (**36**) (15.8 g, 94.5 mmol, 95% yield) as a colorless liquid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.36 (t, *J* = 6.8 Hz, 2H, $CH_2CH_2N_3$), 2.50 (t, *J* = 6.9 Hz, 2H, $CH_2CH_2N_3$), 0.14 (s, 9H, TMS); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 102.7, 87.3, 49.8, 21.1, -0.1. The characterization data corresponded to the reported values.[7]

Following a reported procedure,[7] 2-iodobenzoic acid (**18**) (15.9 g, 64.0 mmol, 1.00 equiv), *para*-toluenesulfonic acid monohydrate ($TsOH.H_2O$, 12.2 g, 64.0 mmol, 1.00 equiv) and *meta*-chloroperoxybenzoic acid (mCPBA-70%, 17.4 g, 70.5 mmol, 1.10 equiv) were dissolved in CH_2Cl_2 (120 mL) and 2,2,2-trifluoroethanol (120 mL). The mixture was stirred at room temperature under nitrogen for 1 h, after which (4-azidobut-1-yn-1-yl)trimethylsilane (**36**) (15.0 g, 90.0 mmol, 1.40 equiv) was added in one portion. The reaction mixture was stirred for 14 h at room temperature, filtered and concentrated in vacuo. The resulting oil was dissolved in CH_2Cl_2 (750 mL) and under vigorous stirring, saturated solution of $NaHCO_3$ (750 mL) was added. The mixture was stirred for 1 h, the two layers were separated and the aqueous layer was extracted with additional portions of CH_2Cl_2 (3 x 250 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated in vacuo. The crude product was purified by flash column chromatography using ethyl acetate to afford **2k** (9.20 g, 27.0 mmol, 42%) as a light beige solid. TLC (EtOAc:MeOH, 9:1 v/v): R_f = 0.47, $KMnO_4$; Mp (explosive decomposition): 114-125 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.32 (dd, *J* = 7.0, 2.1 Hz, 1H, Ar*H*), 8.21 (d, *J* = 7.9 Hz, 1H, Ar*H*), 7.79-7.63 (m, 2H, Ar*H*), 3.54 (t, *J* = 6.5 Hz, 2H, $CH_2CH_2N_3$), 2.85 (t, *J* = 6.5 Hz, 2H, $CH_2CH_2N_3$); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.2, 134.9, 132.3, 131.5, 131.4, 126.8, 115.8, 104.5, 49.4, 42.7, 21.5; IR ν 3452 (w), 2170 (w), 2112 (s), 1647 (s), 1624 (s), 1439 (w), 1331 (m), 1297 (m), 835 (w), 749 (m). The characterization data corresponded to the reported values.[7]

3-(Benzyloxy)-3-methyl-but-1-yn-1-yl)-1,2-benziodoxol-3(1H)-one (2l)

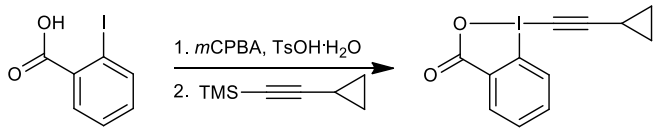


Following a reported procedure,[7] **37** (850 mg, 4.90 mmol, 1.00 equiv) was dissolved in dry THF (10 mL). Next, ^{n}BuLi (2.5 M in hexane, 5.1 mL, 13 mmol, 2.6 equiv) was added through syringe dropwise over 10 minutes and the reaction mixture was stirred for another 10 minutes to get a brownish-red solution. Next, TMSCl (0.70 mL, 5.5 mmol, 1.1 equiv) was added dropwise to get a clear solution and the reaction mixture was stirred for 1.5 h at 0 °C. The resulting reaction mixture was continuously stirred at room temperature for 2.5 h until a white solid precipitated. It was then diluted with hexane (30 mL), washed with water (3 x 20 mL), brine (20 mL), dried over $MgSO_4$, filtered and concentrated in vacuo. The crude product was purified by flash chromatography using EtOAc:Pentane 1:20 as mobile phase to afford (3-(benzyloxy)-3-methylbut-1-yn-1-yl)trimethylsilane (362 mg, 1.47 mmol, 33%), which was used directly in the next step.

Trimethylsilyltriflate (1.60 mL, 8.56 mmol, 1.10 equiv) was added dropwise to a stirred solution of 2-iodosylbenzoic acid (**19**) (2.12 g, 7.99 mmol, 1.00 equiv) in acetonitrile (40 mL) at 0 °C. After 15 minutes, (3-(benzyloxy)-3-methylbut-1-yn-1-yl)trimethylsilane (2.07 g, 8.89 mmol, 1.05 equiv) was added dropwise, followed, after 30 min, by the addition of pyridine (6 mL). The mixture was stirred for 20 minutes. The solvent was then removed under reduced pressure and the crude oil was dissolved in CH_2Cl_2 (100 mL). The organic layer was washed with 0.5 M HCl (100 mL) and the aqueous layer was extracted with CH_2Cl_2 (100 mL). The organic layers were combined, washed with a saturated solution of $NaHCO_3$ (2 x 100 mL), brine (100 mL), dried over $MgSO_4$, filtered and the solvent was evaporated under reduced pressure. Recrystallization from hot EtOAc afforded **2l** (770 mg, 0.183 mmol, 23%) as a light yellow solid. Mp: 146.6-148.0 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.39 (dd, *J* = 7.3, 1.8 Hz, 1H, Ar*H*), 8.11 (dd, *J* = 8.2, 1.1 Hz, 1H, Ar*H*), 7.78-7.62 (m, 2H, Ar*H*), 7.39-7.31 (m, 4H, Ar*H*), 7.31-7.27 (m, 1H, Ar*H*), 4.70 (s, 2H,

ArC*H*$_2$), 1.69 (s, 6H, 2 x C*H*$_3$); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 166.6, 138.3, 135.0, 132.6, 131.7, 131.4, 128.6, 127.9, 127.6, 126.1, 115.8, 110.0, 71.9, 67.2, 45.5, 28.8; IR ν 2986 (w), 2868 (w), 2159 (w), 1618 (s), 1561 (m), 1446 (w), 1330 (m), 1299 (m), 1224 (m), 1159 (m), 1054 (m), 888 (w), 834 (m), 742 (s). The characterization data corresponded to the reported values.[7]

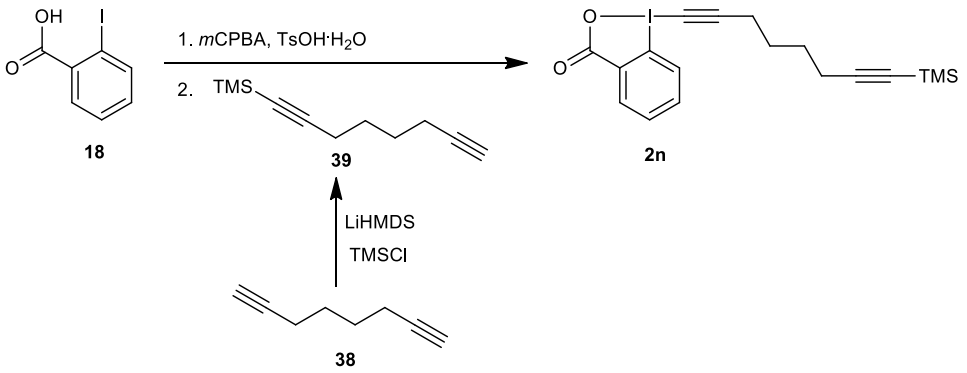
2-Cyclopropylethynyl-1,2-benziodoxol-3(1*H*)-one (2m)



18 **2m**

Following a slightly modified procedure,[8] 2-iodobenzoic acid (**18**) (6.41 g, 25.8 mmol, 1.00 equiv), *para*-toluenesulfonic acid monohydrate ($TsOH{\cdot}H_2O$, 4.91 g, 25.8 mmol, 1.00 equiv) and *meta*-chloroperoxybenzoic acid (*m*CPBA-70%, 7.00 g, 28.4 mmol, 1.10 equiv) were dissolved in dichloromethane (48 mL) and 2,2,2-trifluoroethanol (48 mL). The mixture was stirred at room temperature under nitrogen for 1 h, after which (cyclopropylethynyl)trimethylsilane (5.00 g, 36.2 mmol, 1.40 equiv) was added in one portion. The reaction mixture was stirred for 12 h at room temperature, filtered and concentrated in vacuo. The resulting oil was dissolved in CH_2Cl_2 (400 mL) and under vigorous stirring, a saturated solution of $NaHCO_3$ (400 mL) was added. The mixture was stirred for 1 h, the two layers were separated and the aqueous layer was extracted with additional portions of CH_2Cl_2 (3 x 100 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated in vacuo. The crude product was purified by flash column chromatography using ethyl acetate to afford **2m** (2.11 g, 6.76 mmol, 26 %) as a white solid. Mp (Dec.): 174.2–177.6 °C; TLC (EtOAc:MeOH, 9:1 v/v): R_f = 0.46, $KMnO_4$; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.34 (dd, *J* = 7.0, 2.1 Hz, 1H, Ar*H*), 8.18-8.09 (m, 1H, Ar*H*), 7.81-7.63 (m, 2H, Ar*H*), 1.59 (tt, *J* = 8.2, 5.0 Hz, 1H, C*H*), 1.07-0.85 (m, 4H, C*H*$_2$C*H*$_2$); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 166.7, 134.7, 132.3, 131.7, 131.4, 126.2, 115.9, 113.3, 35.0, 9.8, 1.1; IR ν 3464 (w), 3077 (w), 3012 (w), 2238 (w), 2159 (m), 1607 (s), 1559 (m), 1438 (m), 1338 (m), 1298 (m), 833 (m), 744 (s), 691 (m). HRMS (ESI) calcd. for $C_{12}H_{10}IO_2^+$ $[M+H]^+$ 312.9720; found 312.9719.

8-(Trimethylsilyl)octa-1,7-diyn-1-yl-1,2-benziodoxol-3(1*H*)-one (2n)



Following a slightly modified procedure,[9] to a solution of 1,7-octadiyne **38** (10.6 g, 100 mmol, 1.00 equiv) in dry THF (150 mL) was added at -78 °C under nitrogen 1 M lithium bis(trimethylsilyl)amide in THF (LiHMDS, 100 mL, 100 mmol, 1.00 equiv). The solution was stirred at -78 °C for 30 minutes, after which trimethylsilyl chloride (TMSCl, 13.0 mL, 100 mmol, 1.00 equiv) was added dropwise. The reaction was warmed to room temperature and stirred for 2 h. The reaction was cooled to 0 °C and quenched by adding water (10 mL). The mixture was diluted with 1 M HCl (200 mL) and extracted with diethyl ether (100 mL and 2 x 75 mL). The combined organic layers were washed with brine (200 mL), dried over $MgSO_4$, filtered and concentrated in vacuo. The crude product was purified by vacuum distillation using a 20 cm Vigreux column (oil bath set to 98 °C at 0.3 mbar) furnishing pure trimethyl(octa-1,7-diyn-1-yl)silane (**39**) (8.37 g, 46.9 mmol, 47%) as a colorless liquid. TLC (pentane): R_f = 0.2, $KMnO_4$; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.28-2.17 (m, 4H), 1.93 (t, *J* = 2.7 Hz, 1H, CC*H*), 1.68-1.57 (m, 4H), 0.13 (s, 9H, TMS); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 107.0, 84.9, 84.2, 68.6, 27.7, 27.6, 19.5, 18.1, 0.3; IR ν 3309 (w), 2951 (w), 2175 (w), 1250 (m), 912 (w), 841 (s), 761 (m), 734 (m).). The characterization data corresponded to the reported values.[9]

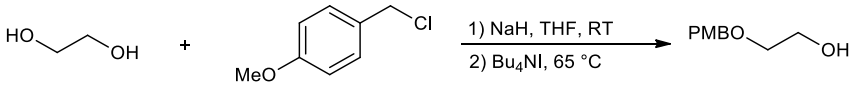
Following a slightly modified procedure,[8] 2-iodobenzoic acid (**18**) (8.43 g, 33.3 mmol, 1.00 equiv), *para*-toluenesulfonic acid monohydrate ($TsOH.H_2O$, 6.40 g, 33.3 mmol, 1.00 equiv) and *meta*-chloroperoxybenzoic acid (mCPBA-70%, 9.04 g, 36.7 mmol, 1.10 equiv) were dissolved in CH_2Cl_2 (60 mL) and 2,2,2-trifluoroethanol (60 mL). The mixture was stirred at room temperature under nitrogen for 1 h, after which trimethyl(octa-1,7-diyn-1-yl)silane (**39**) (8.32 g, 46.7 mmol, 1.40 equiv) was added. The reaction mixture was stirred for 15 h at room temperature and then filtered and concentrated in vacuo. The resulting light being solid was dissolved in CH_2Cl_2 (500

[9] Trost, B. M.; Rudd, M. T. *Org. Lett.* **2003**, *5*, 4599.

mL) and under vigorous stirring, saturated solution of $NaHCO_3$ (500 mL) was added. The mixture was stirred for 1 h, the two layers were separated and the aqueous layer was extracted with additional portions of CH_2Cl_2 (3 x 150 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated in vacuo. The crude product was purified by flash column chromatography using ethyl acetate to afford **2n** (4.2 g, 9.9 mmol, 30%) as a white solid. Mp: 152.3–155.6 °C; TLC (EtOAc:MeOH, 9:1 v/v): R_f = 0.59, $KMnO_4$; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.37 (dd, *J* = 6.7, 2.3 Hz, 1H, Ar*H*), 8.17 (dd, *J* = 7.8, 1.5 Hz, 1H, Ar*H*), 7.82-7.66 (m, 2H, Ar*H*), 2.63 (t, *J* = 6.8 Hz, 2H,), 2.29 (t, *J* = 6.7 Hz, 2H), 1.83-1.62 (m, 4H), 0.13 (s, 9H, TMS); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 166.7, 134.8, 132.4, 131.7, 131.5, 126.3, 115.7, 109.1, 106.4, 85.4, 40.0, 27.7, 27.3, 20.2, 19.4, 0.3; IR ν 2955 (w), 2170 (w), 1647 (m), 1621 (s), 1439 (w), 1329 (m), 1296 (w), 1249 (m), 840 (s), 746 (s). HRMS (ESI) calcd. for $C_{18}H_{22}IO_2Si^+$ $[M+H]^+$ 425.0428; found 425.0433.

Preparation of ^{13}C-labeled reagent 2a'

2-(4-Methoxybenzyloxy)ethanol (42)



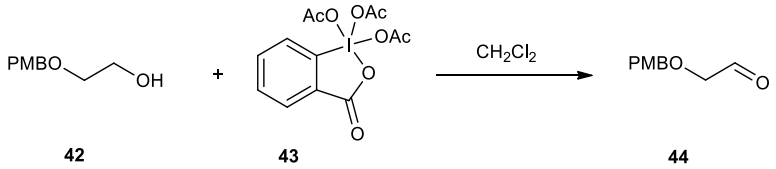
40 **41** **42**

Following a reported procedure,[10] NaH (60% in mineral oil, 0.70 g, 17 mmol, 1.0 equiv) was added to a solution of ethylene glycol (**40**) (freshly distilled from drierite (p = 0.3 mbar, T = 46 °C), 2.8 mL, 50 mmol, 3.0 equiv) in THF (30 mL). After stirring 30 min at room temperature, 4-methoxybenzyl chloride (**41**) (2.60 g, 16.6 mmol, 1.00 equiv) and Bu_4NI (0.61 g, 1.7 mmol, 0.10 equiv) were added, and the reaction mixture was heated to reflux. After 4.5 h, the reaction mixture was cooled to room temperature, the reaction was quenched with saturated solution of NH_4Cl (30 mL) and extracted with Et_2O (3 x 30 mL). The combined organic layers were washed with brine (30 mL), dried over $MgSO_4$ and the solvent was removed under reduced pressure. The crude product was purified by flash column chromatography (PET/AcOEt, 5/1-1/1) to yield protected alcohol **42** (2.54 g, 13.9 mmol, 84%) as a yellow oil. TLC (EtOAc:pentane, 1:1 v/v): R_f = 0.25, $KMnO_4$; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.27 (dm, *J* = 8.2 Hz, 2H, Ar*H*), 6.89 (dm, *J* = 8.6 Hz, 2H, Ar*H*), 4.49 (s, 2H, ArC*H*$_2$), 3.81 (s, 3H, OC*H*$_3$), 3.74 (t, *J* = 4.3 Hz, 2H, C*H*$_2$OPMB),

[10] Brand, J. P.; Charpentier, J.; Waser, J. *Angew. Chem., Int. Ed.* **2009**, *48*, 9346.

3.57 (m, 2H, C*H*$_2$OH), 2.08 (br s, 1H, O*H*). The characterization data corresponded to the reported values.[10]

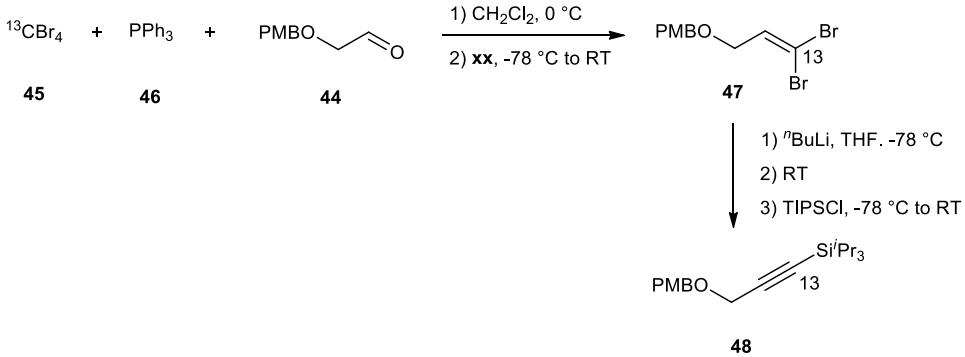
2-(4-Methoxybenzyloxy)acetaldehyde (44)



42 **43** **44**

Following a reported procedure,[10] Dess-Martin Periodinane (**43**) (0.53 g, 1.3 mmol, 1.1 equiv) was added to a solution of alcohol **42** (0.21 g, 1.2 mmol, 1.0 equiv) in wet CH_2Cl_2 (9 mL). After stirring 2.5 h at room temperature, the reaction was quenched with saturated solution of $NaHCO_3$ (10 mL) and saturated sodium thiosulfate solution (10 mL) and the mixture was stirred vigorously for 10 min until two clear layers were obtained. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure to give aldehyde **44** (0.21 g, 1.2 mmol, quant.) as a yellow oil, which was used immediately in the next step without further purification. TLC (EtOAc:pentane, 1:1 v/v): R_f = 0.35, $KMnO_4$; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.71 (t, *J* = 0.9 Hz, C*H*O), 7.29 (dm, *J* = 8.8 Hz, 2H, ArH), 6.90 (dm, *J* = 8.8 Hz, 2H, ArH), 4.57 (s, 2H, ArC*H*$_2$), 4.07 (d, *J* = 0.9 Hz, 2H, C*H*$_2$CHO), 3.81 (s, 3H, OC*H*$_3$). The characterization data corresponded to the reported values.[10]

Labeled 1-((3,3-dibromoallyloxy)methyl)-4-methoxybenzene (47) and tri*iso*propyl(3-(4-methoxybenzyloxy)prop-1-ynyl)silane (48)



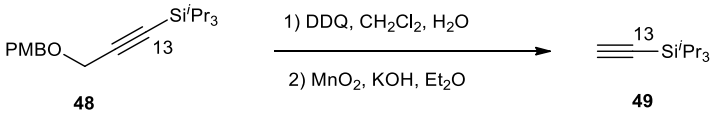
45 **46** **44** **47** **48**

Following a reported procedure,[10] a solution of PPh_3 (**46**) (1.6 g, 6.0 mmol, 2.0 equiv) in CH_2Cl_2 (9 mL) was added to a solution of CBr_4 (**45**) (1.0 g, 3.0 mmol, 1.0 equiv, 20% ^{13}C, prepared from 0.80 g natural CBr_4 and 0.20 g 99% ^{13}C-enriched CBr_4) in CH_2Cl_2 (12 mL) at 0 °C over 15 min.

After stirring for 15 min at 0 °C, the yellow-orange solution was cooled to -78 °C and a solution of aldehyde **44** (freshly synthesized, 0.66 g, 3.6 mmol, 1.2 equiv) in CH_2Cl_2 (9 mL) was added over 10 min, whereas the reaction mixture turned dark red-brown. The reaction mixture was left to warm to room temperature over 17 h, quenched with saturated solution of $NaHCO_3$ (30 mL) and extracted with CH_2Cl_2 (3 x 30 mL). The combined organic layers were washed with brine (30 mL), dried over $MgSO_4$ and the solvent was removed under reduced pressure. The crude product was purified by flash column chromatography (PET/CH_2Cl_2, 3/1-1.5/1) to yield dibromide **47** (501 mg, 1.55 mmol, 52%) as a slightly yellow oil, which was used directly in the next step. TLC (PET: CH_2Cl_2, 2:1 v/v): R_f = 0.30, $KMnO_4$; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.28 (dm, *J* =8 .6 Hz, 2H, Ar*H*), 6.90 (dm, *J* = 8.6 Hz, 2H, Ar*H*), 6.64 (tm, *J* = 6.1 Hz, 1H, alkene *H*), 4.46 (s, 2H, ArCH_2), 4.04 (m, 2H, alkene CH_2), 3.81 (s, 3H, OCH_3); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 159.3, 135.6, 129.5, 129.4, 113.8, 91.3 (labeled 20 X more intensive), 72.2, 69.4, 55.2. The characterization data corresponded to the reported values.[10]

Following a literature procedure,[10] ^{n}BuLi (2.5 M in hexane, 1.4 mL, 3.4 mmol, 2.2 equiv) was added dropwise to a solution of dibromide **47** (0.50 g, 1.5 mmol, 1.0 equiv) in THF (9 mL) at -78 °C. The yellow solution was stirred 1 h at -78 °C and 1 h at room temperature. After cooling to -78 °C, TIPSCl (0.43 mL, 2.0 mmol, 1.3 equiv) was added and the reaction was left to warm to room temperature over 12 h. The reaction was quenched with saturated solution of $NaHCO_3$ (10 mL) and extracted with Et_2O (3 x 20 mL). The combined organic layers were washed with brine (10 mL), dried over $MgSO_4$ and the solvent was removed under reduced pressure. The crude product was purified by flash column chromatography (PET/CH_2Cl_2, 4/1-2/1) to yield alkyne **48** (372 mg, 1.12 mmol, 72%) as a colorless oil. Comparison of the ^{13}C NMR with an unlabeled sample (synthesized following the same procedure) showed 20% ^{13}C incorporation at the indicated position only. TLC (PET: CH_2Cl_2, 2:1 v/v): R_f = 0.35, $KMnO_4$; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.30 (dm, *J* = 8.4 Hz, 2H, Ar*H*), 6.89 (dm, *J* = 8.6 Hz, 2H, Ar*H*), 4.59 (s, 2H, ArCH_2), 4.19 (s, 2H, alkyne CH_2), 3.81 (s, 3H, OCH_3), 1.12 (m, 21H, TIPS); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 159.3, 129.8, 129.5, 113.8, 103.4, 87.7 (labeled 20 X more intensive), 70.6, 57.4, 55.2, 18.6, 11.1; IR 2961 (w), 2944 (w), 2931 (w), 2866 (w), 2171 (w), 1663 (w), 1614 (w), 1515 (w), 1463 (w), 1444 (w), 1378 (w), 1250 (w), 1078 (m), 1036 (w), 907 (s), 730 (s), 651 (m). The characterization data corresponded to the reported values.[10]

Labeled tri*iso*propyl acetylene (49)

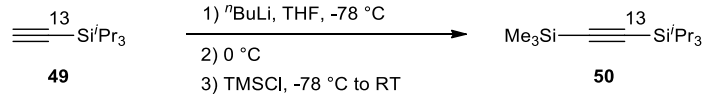


48 **49**

Following a reported procedure,[10] DDQ (0.38 g, 1.7 mmol, 1.5 equiv) was added to a solution of protected alcohol **48** (372 mg, 1.12 mmol, 1.00 equiv) in CH_2Cl_2 (11 mL) and water (1.1 mL) at 0 °C. The reaction mixture was stirred for 15 min at 0 °C and 3 h at room temperature. The resulting dark red thick suspension was quenched with saturated solution of $NaHCO_3$ (20 mL) and extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were washed with saturated solution of $NaHCO_3$ (20 mL) and brine (20 mL), dried over $MgSO_4$ and the solvent was removed under reduced pressure. TLC (PET/EtOAc, 6:1 v/v): R_f = 0.5, $KMnO_4$. This mixture was directly used as such in the next step.

Following a reported procedure,[10] the obtained mixture was diluted with Et_2O (14 mL) and MnO_2 (Aldrich activated, 1.2 g, 13 mmol, 12 equiv) and KOH (freshly grounded, 0.38 g, 6.8 mmol, 6.0 equiv) were added in 4 portions every hour. After stirring for further 3 h, TLC (PET/EtOAc, 6:1 v/v, $KMnO_4$) showed complete conversion and the reaction mixture was filtered over SiO_2 and the filter cake was washed with Et_2O (50 mL). The solvent was removed under reduced pressure and the crude mixture was purified by flash column chromatography using PET to yield alkyne **49** (167 mg, 0.915 mmol, 82%) as a colorless oil. Comparison of the ^{13}C NMR with an unlabeled sample (synthesized following the same procedure) showed 20% ^{13}C incorporation at the indicated position only. TLC (PET): R_f = 0.8, $KMnO_4$; ^1H NMR (CD_2Cl_2, 400 MHz): δ 2.38 (s, 1H, CC*H*), 1.07 (m, 21H, TIPS); ^{13}C NMR (CD_2Cl_2, 100 MHz): δ 94.9, 86.2 (labeled 20 X more intensive), 18.3, 11.1. The characterization data corresponded to the reported values.[10]

Labeled tri*iso*propyl((trimethylsilyl)ethynyl)silane (50)

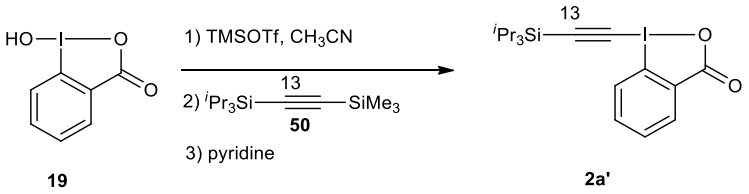


49 **50**

^{n}BuLi (2.5 M in hexane, 0.44 mL, 1.1 mmol, 1.2 equiv) was added to a solution of acetylene **49** (167 mg, 0.915 mmol, 1.00 equiv) in THF (2 mL) at -78 °C. The reaction mixture was stirred 15 min at 0 °C and the yellow solution was cooled back to -78 °C. TMSCl (freshly distilled, 0.15 mL, 1.2 mmol, 1.3 equiv) was added and the colorless solution was left to warm to room

temperature over 6 h. The reaction was quenched with saturated solution of NH_4Cl (3 mL) and extracted with Et_2O (3 x 10 mL). The combined organic layers were washed with brine (5 mL), dried over $MgSO_4$ and the solvent was removed under reduced pressure. The crude mixture was purified by flash column chromatography using PET to yield protected alkyne **50** (184 mg, 0.722 mmol, 79%) as a colorless oil. Comparison of the ^{13}C NMR with an unlabeled sample showed 20% ^{13}C incorporation at the indicated position only. TLC (PET): R_f = 0.8, $KMnO_4$; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.07 (m, 21H, TIPS), 0.17 (s, 9H, TMS); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 116.2, 110.1 (labeled 20 X more intensive), 18.6, 11.1, 0.0; IR 2959 (m), 2944 (m), 2896 (w), 2867 (m), 1464 (w), 1385 (w), 1250 (m), 996 (w), 842 (s), 764 (s), 675 (m), 660 (m). The characterization data corresponded to the reported values.[10]

Labeled 1-[(tri*iso*propyllsilyl)ethynyl]-1,2-benziodoxol-3(1*H*)-one (2a')

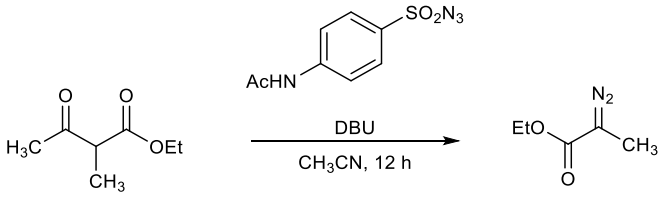


Following a reported procedure,[10] TMSOTf (freshly distilled, 0.15 mL, 0.82 mmol, 1.1 equiv) was added to a suspension of 2-iodosylbenzoic acid (**19**) (freshly synthesized, 0.19 g, 0.72 mmol, 1.0 equiv) in CH_3CN (6.5 mL). After 10 min, a solution of acetylene **50** (0.18 g, 0.72 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL) was added to the slightly yellow solution. After stirring 15 min at room temperature, pyridine (70 µL, 0.87 mmol, 1.2 equiv) was added and the solvent was removed under reduced pressure below 30 °C. The reaction mixture was diluted with CH_2Cl_2 (15 mL) and washed with 1 M HCl (5 mL). The water layer was extracted with CH_2Cl_2 (2 x 5 mL) and the combined organic layers were washed with saturated solution of Na_2CO_3 (2 x 10 mL). The combined basic aqueous layers were extracted with CH_2Cl_2 (10 mL) and the combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure to give labeled reagent **2a'** (>95% pure by ^1H NMR, containing traces of acetylene **50**, 259 mg, 0.604 mmol, 84%) as a slightly yellow solid. Comparison of the ^{13}C NMR with an unlabeled sample showed 20% ^{13}C incorporation at the indicated position only. ^1H NMR ($CDCl_3$, 400 MHz): δ 8.40 (m, 1H, Ar*H*), 8.28 (m, 1H, Ar*H*), 7.74 (m, 2H, Ar*H*), 1.13 (m, 21H, TIPS); ^{13}C

NMR ($CDCl_3$, 100 MHz): δ 166.3, 134.6, 132.4, 131.5, 131.4, 126.0, 115.6, 114.1 (labeled 20 X more intensive), 64.7, 18.4, 11.1. The characterization data corresponded to the reported values.[10]

3. Preparation of diazo compounds

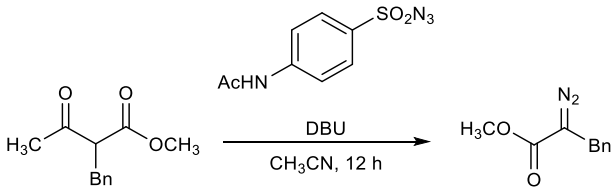
Ethyl 2-diazopropanoate (1b)



51 **1b**

Following a modified reported procedure,[11] DBU (2.2 mL, 15 mmol, 3.0 equiv) was added slowly to a stirred solution of ethyl 2-methyl-3-oxobutanoate (**51)** (0.72 g, 5.0 mmol, 1.0 equiv) and *p*-acetamidobenzenesulfonyl azide (*p*-ABSA) (1.92 g, 7.50 mmol, 1.50 equiv) in MeCN (10 mL) at 0 °C. The reaction mixture was then allowed to warm to room temperature. After stirring for 12 h, the reaction mixture was quenched with 1 M HCl (10 mL), and extracted with hexane (3 x 50 mL). The organic layers were combined and washed with saturated solution of $NaHCO_3$ (50 mL), brine (50 mL), and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and purified by flash column chromatography using 1:50 Et_2O:pentane as mobile phase affording the corresponding ethyl 2-diazopropanoate (**1b)** as a yellow oil (500 mg, 3.90 mmol, 78%). TLC (Et_2O:pentane, 1:50 v/v): R_f = 0.4, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.20 (q, *J* = 7.1 Hz, 2H, C*H*$_2$CH$_3$), 1.94 (s, 3H, N_2CC*H*$_3$), 1.25 (t, *J* = 7.1 Hz, 3H, CH_2C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.9, 60.7, 14.5, 8.4. The values of the NMR spectra are in accordance with reported literature data.[12] One carbon was not resolved at 100 MHz.

Methyl 2-diazo-3-phenylpropanoate (1c)



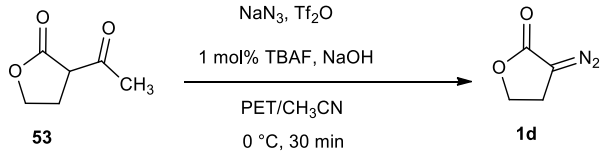
52 **1c**

[11] Hashimoto, T.; Naganawa, Y.; Maruoka, K. *J. Am. Chem. Soc.* **2011**, *133*, 8834.

[12] Huang, L.; Wulff, W. D. *J. Am. Chem. Soc.* **2011**, *133*, 8892.

Following a reported procedure,[11] to a stirred solution of methyl 2-benzyl-3-oxobutanoate (**52**) (1.03 g, 5.00 mmol, 1.00 equiv) and *p*-acetamidobenzenesulfonyl azide (1.82 g, 7.50 mmol, 1.50 equiv) in dry CH_3CN (10 mL) was added DBU (2.3 mL, 15 mmol, 3.0 equiv) at 0 °C. The reaction mixture was then allowed to warm to room temperature. After stirring for 12 h, the resulting mixture was quenched with 10 mL of 1 M HCl, and extracted with hexane (3 x 50 mL). The combined organic layers were washed with saturated solution of $NaHCO_3$ (50 mL), brine (50 mL), and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and purified by flash column chromatography using 1:20 EtOAc:pentane as mobile phase affording the corresponding methyl 2-diazo-3-phenylpropanoate (**1c**) as a yellow oil (0.790 g, 4.15 mmol, 81%). TLC (EtOAc:pentane, 1:20 v/v): R_f = 0.4, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36–7.22 (m, 5H, Ar*H*), 3.79 (s, 3H, OC*H*$_3$), 3.64 (s, 2H, ArC*H*$_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.5, 137.1, 128.8, 128.3, 127.1, 52.0, 29.3.The values of the NMR spectra are in accordance with reported literature data.[11] Diazo signal was not resolved.

3-Diazodihydrofuran-2(3H)-one (1d)

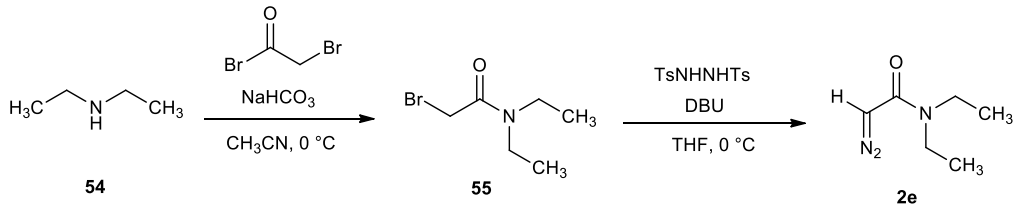


Following a reported procedure,[13] sodium azide (4.83 g, 74.3 mmol, 4.00 equiv), sodium hydroxide (155 mL of 2 M in water), tetrabutylammonium bromide (60 mg, 0.19 mmol, 0.010 equiv), and petroleum ether (80 mL) were mixed in a 500 mL round-bottom flask with magnetic stir bar open to the air and allowed to cool to 0 °C. With vigorous stirring, Tf_2O (6.2 mL, 37 mmol, 2.0 equiv) was added dropwise. After 10 min, a solution of 2-acetyl-butyrolactone (**53**) (2.00 mL, 18.6 mmol, 1.00 equiv) in CH_3CN (70 mL) was poured into the round-bottom flask through a funnel, followed by an additional CH_3CN (10 mL) to complete the transfer. The initially colorless reaction mixture immediately turned yellow. After allowing to stir for 30 min at 0 °C, the mixture was diluted with ice water (50 mL) and chilled EtOAc (50 mL) and transferred to a separatory funnel. After phase separation and removal of the organic layer, the aqueous layer was washed with cold EtOAc (2 x 100 mL). The combined organic layers were dried over

[13] Sattely, E. S.; Meek, S. J.; Malcolmson, S. J.; Schrock, R. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2009**, *131*, 943.

$MgSO_4$, filtered, and concentrated under reduced pressure. The resulting orange-brown oily residue was purified by column chromatography using 1:1 EtOAc:pentane as mobile phase affording the corresponding 3-diazodihydrofuran-2(3H)-one (**1d)** as a bright yellow crystalline solid (1.25 g, 11.6 mmol, 60%). TLC (EtOAc:pentane, 1:1 v/v): R_f = 0.39, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.38 (t, *J* = 8.0 Hz, 2H, C*H*$_2$), 3.36 (t, *J* = 8.0 Hz, 2H, C*H*$_2$); ^{13}C NMR (100 MHz, $CDCl_3$): 170.6, 65.3, 49.4, 23.1. The values of the NMR spectra are in accordance with reported literature data.[13]

2-Diazo-N,N-diethylacetamide (1e)

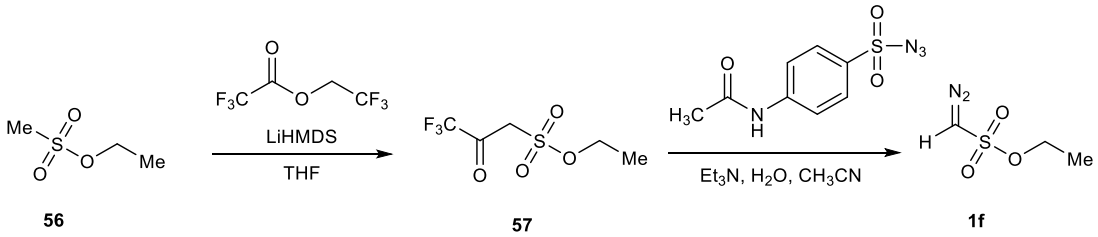


Following a reported procedure,[14] diethyl amine (**54**) (0.73 g, 10 mmol, 1.0 equiv) and $NaHCO_3$ (2.52 g, 30.0 mmol, 3.00 equiv) were dissolved in dry CH_2Cl_2 (20 mL) and bromoacetyl bromide (1.75 mL, 20.0 mmol, 2.00 equiv) was added slowly at 0 °C and stirred for 6 h at room temperature, the reaction was quenched with 100 mL of H_2O and the solution was extracted with CH_2Cl_2 (3 x 50 mL). The combined organic layers were washed with water (100 mL) and dried over $MgSO_4$, the solvent was evaporated and the residue was used in the next step without purification. The resulting bromoacetamide **55** and *N,N′*-ditosylhydrazine (2.10 g, 6.08 mmol, 0.60 equiv) were dissolved in dry THF (20 mL) and cooled down to 0 ˚C, then DBU (2.30 mL, 15.2 mmol, 1.52 equiv) was added dropwise and stirred at room temperature for 1 h and then quenched with saturated solution of $NaHCO_3$ (50 mL) and extracted with diethyl ether (3 x 50 mL). The combined organic layers were dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and purified by flash column chromatography using 1:2 EtOAc:pentane as mobile phase affording the corresponding 2-diazo- *N,N′*-diethylacetamide (**1e)** as a yellow oil (0.725 g, 5.14 mmol, 52%). TLC (EtOAc:pentane, 1:2 v/v): R_f = 0.2, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.92 (s, 1H, C*H*N_2), 3.26 (br s, 4H, 2 X C*H*$_2$$CH_3$), 1.14 (t, *J* = 7.2 Hz, 6H, 2 X

[14] Chanthamath, S.; Thongjareun, S.; Shibatomi, K.; Iwasa, S. *Tetrahedron Lett.* **2012**, *53*, 4862.

CH_2CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): 165.8, 46.4, 41.4, 13.9. The values of the NMR spectra are in accordance with reported literature data.[15]

Ethyl diazomethanesulfonate (1f)



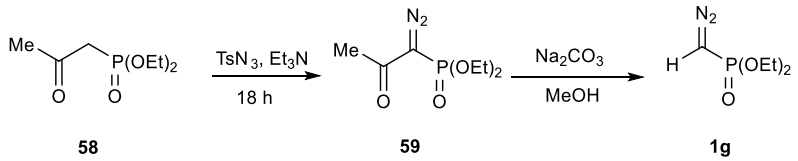
56 57 1f

Following a reported procedure,[16] to a solution of ethyl methanesulfonate (**56)** (1.86 g, 15.0 mmol, 1.00 equiv) in dry THF (50 mL) was added a 1 M LiHMDS solution in hexane (18 mL, 18 mmol, 1.2 equiv) at -78 °C. After stirring the reaction mixture for 30 min at this temperature, 2,2,2-trifluoroethyl trifluoroacetate (2.4 mL, 18 mmol, 1.2 equiv) was added rapidly in one portion *via* syringe. After 10 min, the reaction mixture was poured into a solution of diethyl ether (20 mL) and 5% HCl (50 mL). The mixture was extracted with diethyl ether (3 x 50 mL), washed with brine (50 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure to give a yellow oil **57**. This yellow oil was immediately dissolved in dry CH_3CN (30 mL). To this solution was added *p*-acetamidobenzenesulfonyl azide (4.32 g, 18.0 mmol, 1.20 equiv), Et_3N (2.5 mL, 18 mmol, 1.2 equiv), and water (0.27 mL, 15 mmol, 1.0 equiv). After stirring the reaction mixture overnight at room temperature, the solvent was removed under reduced pressure and the residue was filtered on short silica gel and washed with a mixture of ethyl acetate (100 mL) and hexane (100 mL). The filtrate was concentrated under vacuum and the residue was purified by flash column chromatography using 1:10 EtOAc:pentane as mobile phase affording the corresponding ethyl diazomethanesulfonate (**1f)** as a yellow oil (0.9 g, 6 mmol, 40%). TLC (EtOAc:pentane, 1:10 v/v): R_f = 0.25, $KMnO_4$; ^1H NMR (400 MHz, $CDCl_3$): δ 5.25 (s, 1H, C*H*N_2), 4.26 (q, *J* = 7.1 Hz, 2H, CH_2CH_3), 1.41 (t, *J* = 7.1 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 67.4, 52.4, 14.6.The values of the NMR spectra are in accordance with reported literature data.[16]

Diethyl (diazomethyl)phosphonate (1g)

[15] Gauthier, D.; Dodd, R. H.; Dauban, P. *Tetrahedron* **2009**, *65*, 8542.

[16] Ye, T.; Zhou, C. *New J. Chem.* **2005**, *29*, 1159.



58 **59** **1g**

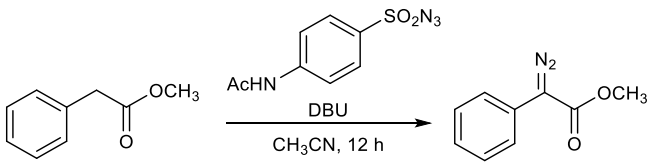
Following a reported procedure,[17] a mixture of diethyl (2-oxopropyl)phosphonate (**58**) (1.15 mL, 6.00 mmol, 1.00 equiv), tosyl azide (1.3 g, 6.6 mmol, 1.1 equiv) and triethylamine (6 mL) was stirred at room temperature for 18 h. After evaporation of triethylamine under reduced pressure, the residue was dissolved in diethyl ether (50 mL). The precipitate was filtered off, the filtrate was evaporated and the residue was purified by column chromatography using 1:1 EtOAc:pentane as mobile phase affording the corresponding diethyl (1-diazo-2-oxopropyl)phosphonate (**59**) as a yellow oil (0.810 g, 3.68 mmol, 61%). TLC (EtOAc:pentane, 1:4 v/v): R_f = 0.49, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.04– 4.19 (m, 4H, 2 X C*H*$_2$CH$_3$) 2.19 (s, 3H, C*H*$_3$), 1.30 (t, *J* = 7.0 Hz, 6H, 2 X CH$_2$C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): 190.1 (d, *J* = 13.2 Hz), 63.4 (d, *J* = 5.6 Hz), 27.1, 16.0 (d, *J* = 6.8 Hz). The values of the NMR spectra are in accordance with reported literature data.[18]

To a solution of diethyl (1-diazo-2-oxopropyl)phosphonate (**59**) (694 mg, 3.15 mmol, 1.00 equiv) in MeOH (9 mL) was added Na_2CO_3 (401 mg, 3.78 mmol, 1.20 equiv). The mixture was stirred at room temperature for 15 min. The precipitate was filtered off, the filtrate was evaporated and the residue was purified by column chromatography using 1:1 EtOAc:pentane as mobile phase affording the corresponding diethyl (diazomethyl)phosphonate (**1g)** as a yellow oil (533 mg, 2.99 mmol, 95%). TLC (EtOAc:pentane, 1:4 v/v): R_f = 0.41, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.17–4.08 (m, 4H, 2 X C*H*$_2$CH$_3$), 3.75 (d, *J* = 11.1 Hz, 1H, C*H*N$_2$), 1.34 (td, *J* = 7.1, 0.7 Hz, 6H, 2 X CH$_2$C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 62.6 (d, *J* = 5.3 Hz), 16.1 (d, *J* = 6.9 Hz). The values of the NMR spectra are in accordance with reported literature data.[18] One carbon was not resolved at 100 MHz.

Methyl 2-diazo-2-phenylacetate (1h)

[17] Chanthamath, S.; Ozaki, S.; Shibatomi, K.; Iwasa, S. *Org. Lett.* **2014**, *16*, 3012.

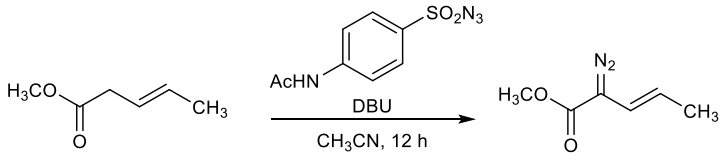
[18] Müller, S.; Sasse, F.; Maier, M. E. *Eur. J. Org. Chem.* **2014**, 1025.



60 **1h**

Following a modified reported procedure,[19] DBU (4.2 mL, 28 mmol, 1.4 equiv) was added slowly to a stirred solution of methyl 2-phenylacetate (**60**) (3.0 g, 20 mmol, 1.0 equiv) and *p*-acetamidobenzenesulfonyl azide (5.77 g, 24.0 mmol, 1.20 equiv) in dry CH_3CN (60 mL) at 0 °C. The reaction mixture was then allowed to warm to room temperature. After stirring for 14 h, the reaction mixture was quenched with water (15 mL), and extracted with diethyl ether (3 x 20 mL). The organic layers were combined and washed with 10% NH_4Cl (3 x 20 mL), brine (50 mL), and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and purified by flash column chromatography using 1:20 Et_2O:pentane as mobile phase affording the corresponding methyl 2-diazo-2-phenylacetate (**1h**) as a red oil (2.50 g, 14.2 mmol, 71%). TLC (Et_2O:pentane, 1:20 v/v): R_f = 0.36, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52–7.45 (m, 2H, Ar*H*), 7.42–7.34 (m, 2H, Ar*H*), 7.19 (td, *J* = 7.3, 1.2 Hz, 1H, Ar*H*), 3.87 (s, 3H, OC*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.6, 128.9, 125.8, 125.4, 124.0, 52.0. The values of the NMR spectra are in accordance with reported literature data.[19] One carbon was not resolved at 100 MHz.

(*E*)-methyl 2-diazopent-3-enoate (5a)



61 **5a**

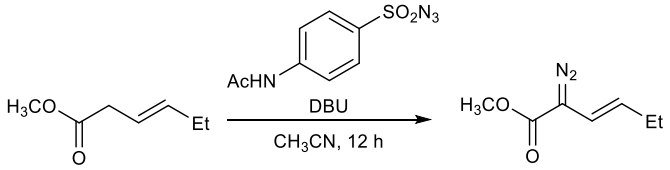
Following a slightly modified reported procedure,[20] to a stirred solution of methyl trans-pent-3-enoate (**61)** (500 mg, 4.40 mmol, 1.00 equiv) and *p*-acetamidobenzenesulfonyl azide (1.58 g, 6.57 mmol, 1.50 equiv) in dry CH_3CN (10 mL) at 0 °C, was added DBU (1.30 mL, 8.76 mmol, 2.00 equiv) slowly in 5 min. The reaction mixture was stirred at 0 °C for 1 h and then 12 h at room

[19] Muthusamy, S.; Sivaguru, M. *Org. Lett.* **2014**, *16*, 4248.

[20] Davies, H. M. L.; Walji, A. M. *Angew. Chem., Int. Ed.* **2005**, *44*, 1733.

temperature. The reaction mixture was quenched with saturated solution of NH_4Cl (10 mL). The aqueous layer was extracted with diethyl ether (3 X 20 mL) and the combined organic layers were washed with brine (20 mL) and dried over $MgSO_4$, filtered and concentrated in vacuo. The resulting crude product was purified by flash chromatography using pentane affording **5a** (400 mg, 2.85 mmol, 65%) as an orange oil. TLC (pentane): R_f = 0.2, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.73 (dd, *J* = 15.8, 1.7 Hz, 1H, CH_3CHCH), 5.38–5.29 (m, 1H, CH_3CHCH), 3.79 (s, 3H, OCH_3), 1.84 (dd, *J* = 6.7, 1.7 Hz, 3H, CH_3CHCH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.1, 120.4, 112.6, 52.0, 18.2. The values of the NMR spectra are in accordance with reported literature data.[20] One carbon was not resolved at 100 MHz.

(*E*)-methyl 2-diazohex-3-enoate (5b)

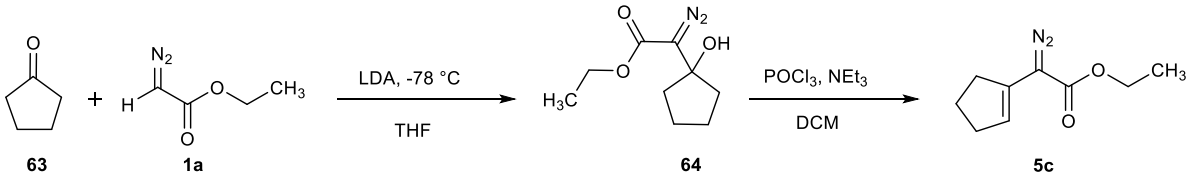


62 **5b**

Following a slightly modified reported procedure,[20] to a stirred solution of (*E*)-methyl hex-3-enoate (**62**) (1.0 g, 7.8 mmol, 1.0 equiv) and *p*-acetamidobenzenesulfonyl azide (2.81 g, 11.7 mmol, 1.50 equiv) in dry CH_3CN (15 mL) at 0 °C, was added DBU (2.35 mL, 15.6 mmol, 2.00 equiv) slowly in 5 min. The reaction mixture was stirred at 0 °C for 1 h and then 12 h at room temperature. The reaction mixture was quenched with saturated solution of NH_4Cl (15 mL). The aqueous layer was extracted with diethyl ether (3 X 30 mL) and the combined organic layers were washed with brine (30 mL) and dried over $MgSO_4$, filtered and concentrated in vacuo. The resulting crude product was purified by flash chromatography using Et_2O:pentane 1:50 as mobile phase affording (*E*)-methyl 2-diazohex-3-enoate (**5b**) (574 mg, 3.72 mmol, 48%) as an orange oil. TLC (Et_2O:pentane, 1:50 v/v): R_f = 0.25, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.71 (dt, *J* = 15.8, 1.6 Hz, 1H, CH_3CHCH), 5.36 (dt, *J* = 15.9, 6.6 Hz, 1H, CH_3CHCH), 3.79 (s, 3H, OCH_3), 2.25–2.12 (m, 2H, $CHCH_2CH_3$), 1.03 (t, *J* = 7.4 Hz, 3H, CH_3CH_2CH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.1, 127.2, 110.8, 52.0, 25.8, 13.8; IR ν 2965 (m), 2081 (m), 1713 (s), 1437 (m),

1311 (m), 1218 (s), 1142 (m), 1050 (m), 956 (w), 828 (w). One carbon was not resolved at 100 MHz.[21]

Ethyl 2-(cyclopent-1-en-1-yl)-2-diazoacetate (5c)



63 1a 64 5c

Following a reported procedure,[22] to a solution of ethyl diazoacetate (**1a**) (1.2 mL, 10 mmol, 1.0 equiv) and cyclopentanone (**63**) (0.89 mL, 10 mmol, 1.0 equiv) in dry THF (10 mL) at -78 °C, was added LDA (6.0 mL, 12 mmol, 2 M in THF, 1.2 equiv) over 15 minutes. The resulting solution was stirred at -78 °C for 1 h and quenched with 30% aqueous NH_4Cl (20 mL). The reaction mixture was extracted with diethyl ether (2 x 30 mL), dried over $MgSO_4$, filtered and concentrated in vacuo. The resulting crude product was purified by flash chromatography using EtOAc:pentane 1:10 as mobile phase affording **64** (1.75 g, 8.83 mmol, 88%) as a yellow oil. TLC (EtOAc:pentane, 1:10 v/v): R_f = 0.29, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.24 (q, *J* = 7.1 Hz, 2H, C*H*$_2$CH$_3$), 3.26 (s, 1H, O*H*), 2.10–1.99 (m, 2H, cy-C*H*$_2$), 1.97–1.63 (m, 6H, cy-C*H*$_2$), 1.28 (t, *J* = 7.1 Hz, 3H, CH$_2$C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.2, 78.6, 60.8, 39.3, 22.9, 14.4. The values of the NMR spectra are in accordance with reported literature data.[23] One carbon was not resolved at 100 MHz.

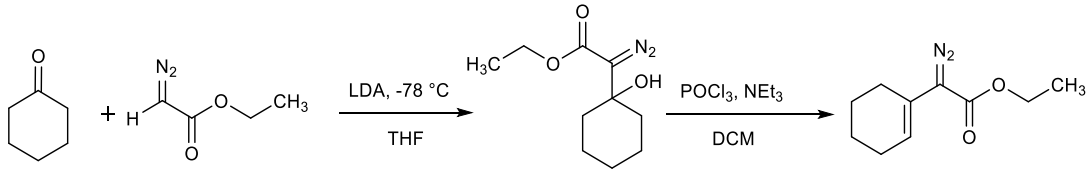
To a solution of ethyl 2-diazo-2-(1-hydroxycyclopentyl)acetate (**64**) (793 mg, 4.00 mmol, 1.00 equiv), NEt_3 (2.24 mL, 16.0 mmol, 4.00 equiv) in dry CH_2Cl_2 (20 mL) at 0 °C, was slowly added a solution of $POCl_3$ (0.56 mL, 6.0 mmol, 1.5 equiv) in dry CH_2Cl_2 (4 mL) over 30 minutes using syringe pump. The resulting solution was warmed to room temperature and further stirred for 12 h. The solution was washed with water (2 x 20 mL) and dried over $MgSO_4$, filtered and concentrated in vacuo. The resulting crude product was purified by flash chromatography using Et_2O:pentane 1:50 as mobile phase affording **5c** (610 mg, 3.39 mmol, 85%) as an orange oil. TLC (Et_2O:pentane, 1:50 v/v): R_f = 0.32, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.06–5.84 (m,

[21] Due to the low stability of compound **5b**, HRMS data could not be obtained.
[22] Doyle, M. P.; Yan, M.; Hu, W.; Gronenberg, L. S. *J. Am. Chem. Soc.* **2003**, *125*, 4692.

[23] Pellicciari, R.; Natalini, B.; Sadeghpour, B. M.; Marinozzi, M.; Snyder, J. P.; Williamson, B. L.; Kuethe, J. T.; Padwa, A. *J. Am. Chem. Soc.* **1996**, *118*, 1.

1H, olefinic *H*), 4.26 (q, *J* = 7.1 Hz, 2H, C*H*$_2$CH$_3$), 2.55–2.39 (m, 4H, Cy-C*H*$_2$), 2.04–1.81 (m, 2H, Cy-C*H*$_2$), 1.29 (t, *J* = 7.1 Hz, 3H, CH$_2$C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.8, 124.4, 124.2, 60.8, 33.9, 33.7, 22.6, 14.4; IR ν 2979 (w), 2849 (w), 2362 (w), 2084 (s), 1709 (s), 1375 (m), 1287 (m), 1235 (s), 1143 (m), 1045 (w), 862 (w). One carbon was not resolved at 100 MHz.[24]

Ethyl 2-(cyclohex-1-en-1-yl)-2-diazoacetate (5d)



65 1a 66 5d

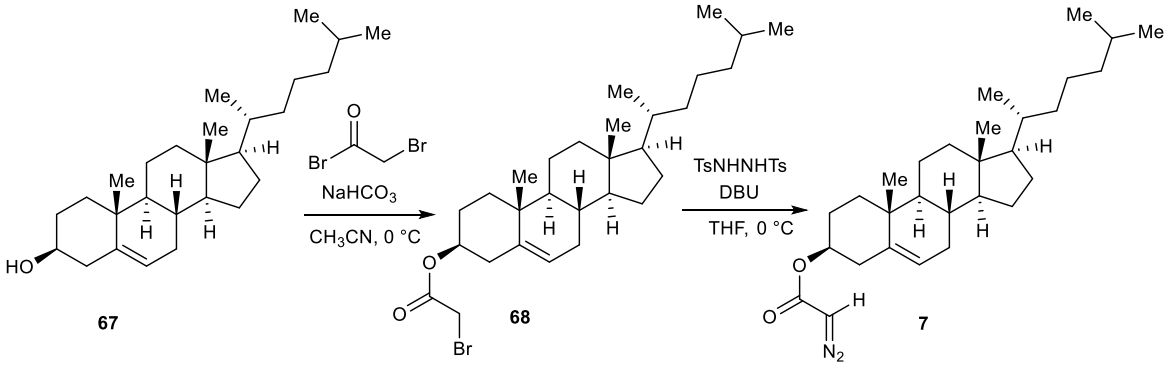
Following a reported procedure,[22] to a solution of ethyl diazoacetate (**1a**) (1.2 mL, 10 mmol, 1.0 equiv) and cyclohexanone (**65**) (1.04 mL, 10.0 mmol, 1.00 equiv) in dry THF (10 mL) at -78 °C, was added LDA (6.0 mL, 12 mmol, 2 M in THF, 1.2 equiv) over 15 minutes. The resulting solution was stirred at -78 °C for 1 h and quenched with 30% aqueous NH_4Cl (20 mL). The reaction mixture was extracted with diethyl ether (2 x 30 mL), dried over $MgSO_4$, filtered and concentrated in vacuo. The resulting crude product was purified by flash chromatography using EtOAc:pentane 1:15 as mobile phase affording **66** (1.7 g, 8.0 mmol, 80%) as a yellow oil. TLC (EtOAc:pentane, 1:15 v/v): R_f = 0.25, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.23 (q, *J* = 7.1 Hz, 2H, C*H*$_2$CH$_3$), 3.47 (s, 1H, O*H*), 1.94–1.31 (m, 10H, (C*H*$_2$)$_5$), 1.28 (t, *J* = 7.1 Hz, 3H, CH$_2$C*H*$_3$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.2, 70.2, 60.7, 36.4, 25.2, 22.0, 14.4. The values of the NMR spectra are in accordance with reported literature data.[22] One carbon was not resolved at 100 MHz.

To a solution of ethyl 2-(1-hydroxyl-1- cyclohexyl)-2-diazoacetate (**66**) (849 mg, 4.00 mmol, 1.00 equiv) and NEt_3 (2.24 mL, 16.0 mmol, 4.00 equiv) in dry CH_2Cl_2 (20 mL) at 0 °C, was slowly added a solution of $POCl_3$ (0.56 mL, 6.0 mmol, 1.5 equiv) in dry CH_2Cl_2 (4 mL) over 30 minutes using syringe pump. The resulting solution was warmed to room temperature and further stirred for 12 h. The solution was washed with water (2 x 20 mL) and dried over $MgSO_4$, filtered and concentrated in vacuo. The resulting crude product was purified by flash chromatography

[24] Due to the low stability of compound **5c**, HRMS data could not be obtained.

using Et_2O:pentane 1:50 as mobile phase affording **5d** (420 mg, 2.15 mmol, 54%) as an orange oil. TLC (Et_2O:pentane, 1:50 v/v): R_f = 0.22, $KMnO_4$; ^1H NMR (400 MHz, $CDCl_3$): δ 6.07 (tt, *J* = 4.1, 1.6 Hz, 1H, olefinic *H*), 4.23 (q, *J* = 7.1 Hz, 2H, C*H*$_2$CH$_3$), 2.20–2.12 (m, 2H, cy-C*H*$_2$), 2.10–2.06 (m, 2H, cy-C*H*$_2$), 1.75–1.67 (m, 2H, cy-C*H*$_2$), 1.62–1.56 (m, 2H, cy-C*H*$_2$), 1.27 (t, *J* = 7.1 Hz, 3H, CH$_2$C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.0, 123.6, 119.9, 60.5, 26.2, 25.7, 22.6, 21.8, 14.4. The values of the NMR spectra are in accordance with reported literature data.[22] One carbon was not resolved at 100 MHz.

3S,8S,9S,10R,13R,14S,17R)-10,13-Dimethyl-17-((R)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl 2-diazoacetate (7)

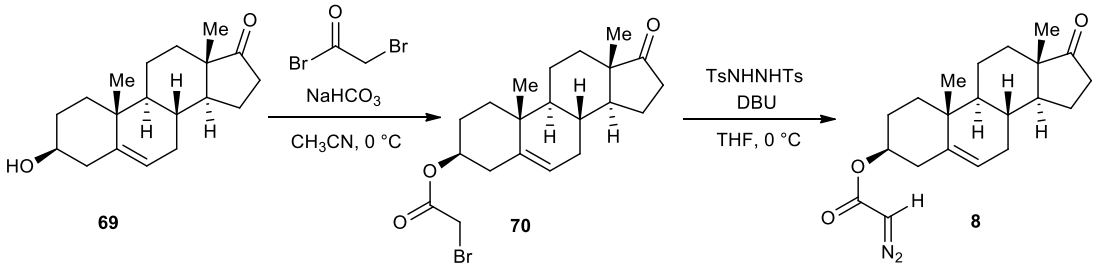


Following a slightly modified reported procedure,[25] cholesterol **67** (773 mg, 2.00 mmol, 1.00 equiv) and $NaHCO_3$ (840 mg, 10.0 mmol, 5.00 equiv) were dissolved in dry CH_2Cl_2 (10 mL) and bromoacetyl bromide (0.53 mL, 6.0 mmol, 3.0 equiv) was added slowly at 0 °C and stirred for 6 h at room temperature, the reaction was quenched with H_2O (25 mL) and the solution was extracted with CH_2Cl_2 (3 x 50 mL). After washing with water (50 mL) and drying over $MgSO_4$, the solvent was evaporated and the residue was used in the next step without further purification. The resulting crude bromoacetamide **68** and *N,N′*-ditosylhydrazine (1.36 g, 4.00 mmol, 2.00 equiv) were dissolved in dry THF (10 mL) and cooled down to 0 ˚C, then DBU (1.5 mL, 10 mmol, 5.0 equiv) was added dropwise and stirred at room temperature for 1 h. After quenching with saturated solution of $NaHCO_3$ (20 mL) and extracting with diethyl ether (3 x 50 mL), the organic layer was dried over $MgSO_4$, filtered and concentrated in vacuo. The resulting crude

[25] (a) Chanthamath, S.; Thongjareun, S.; Shibatomi, K.; Iwasa, S. *Tetrahedron Lett.* **2012**, *53*, 4862. (b) Toma, T.; Shimokawa, J.; Fukuyama, T. *Org. Lett.* **2007**, *9*, 3195.

product was purified by flash chromatography using Et_2O:pentane 1:20 as mobile phase affording **7** (750 mg, 1.65 mmol, 82%) as a pale yellow solid. TLC (Et_2O:pentane, 1:20 v/v): R_f = 0.4, $KMnO_4$; ^1H NMR (400 MHz, $CDCl_3$): δ 5.38 (d, *J* = 5.1 Hz, 1H, olefinic *H*), 4.75–4.65 (m, 2H, N_2C*H* and OC*H*), 2.45–2.23 (m, 2H), 2.08–1.76 (m, 5H), 1.64–0.80 (m, 33H), 0.68 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.3, 139.5, 122.8, 74.6, 56.7, 56.1, 50.0, 46.3, 42.3, 39.7, 39.5, 38.3, 36.9, 36.5, 36.2, 35.8, 31.9, 31.8, 28.2, 28.0, 28.0, 24.3, 23.8, 22.8, 22.5, 21.0, 19.3, 18.7, 11.8. The values of the NMR spectra are in accordance with reported literature data.[23b]

(3S,8R,9S,10R,13S,14S)-10,13-Dimethyl-17-oxo-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl 2-diazoacetate (8)



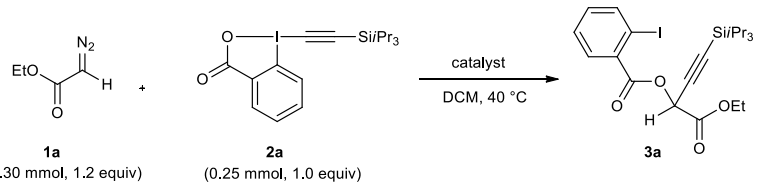
Following a slightly modified reported procedure,[25] dehydroepiandrosterone **69** (1.16 g, 4.00 mmol. 1.00 equiv) and $NaHCO_3$ (1.6 g, 20 mmol, 5.0 equiv) were dissolved in dry CH_2Cl_2 (20 mL) and bromoacetyl bromide (0.7 mL, 8 mmol, 2.0 equiv) was added slowly at 0 °C and the reaction mixture was stirred for 6 h at room temperature. The reaction was then quenched with water (50 mL) and the solution was extracted with CH_2Cl_2 (3 x 100 mL). After washing with water (100 mL) and drying over $MgSO_4$, the solvent was evaporated and the residue was used in the next step without further purification. The resulting crude bromoacetamide **70** and *N,N′*-ditosylhydrazine (2.72 g, 8.00 mmol, 2.00 equiv) were dissolved in dry THF (20 mL) and cooled down to 0 ˚C, then DBU (3.0 mL, 20 mmol, 5.0 equiv) was added dropwise and stirred at room temperature for 1 h. After quenching with saturated solution of $NaHCO_3$ (40 mL) and extracting with diethyl ether (3 X 100 mL), the organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting crude product was purified by flash chromatography using EtOAc:pentane 1:5 as mobile phase affording **8** (1.1 g, 3.1 mmol, 77%) as a pale yellow solid. Mp (Dec.): 192.3–196.8 °C; TLC (EtOAc:pentane, 1:5 v/v): R_f = 0.42, $KMnO_4$; ^1H NMR (400 MHz, $CDCl_3$): δ 5.41 (d, *J* = 5.0 Hz, 1H, olefinic *H*), 4.84–4.54 (m, 2H, N_2C*H* and OC*H*), 2.56–2.24 (m, 3H), 2.17–2.02 (m, 2H), 2.00–1.78 (m, 4H), 1.74–1.41 (m, 6H), 1.34–1.22 (m, 2H), 1.16

(td, J = 13.9, 13.2, 4.2 Hz, 1H), 1.08–0.97 (m, 4H), 0.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 221.0, 166.3, 139.8, 122.0, 75.0, 51.6, 50.1, 47.5, 46.3, 38.2, 36.9, 36.7, 35.8, 31.4, 31.4, 30.7, 27.9, 21.8, 20.3, 19.3, 13.5; IR ν 3126 (w), 2946 (w), 2861 (w), 2111 (s), 1736 (m), 1686 (s), 1377 (m), 1336 (w), 1240 (m), 1193 (w), 1033 (m); HRMS (ESI) calcd. for $C_{21}H_{28}N_2NaO_3^+$ $[M+Na]^+$ 379.1992; found 379.1994.

4. General method for the optimization

a) Screening of catalysts

A flame dried 5 mL microwave vial was charged under nitrogen with catalyst (12.5 µmol, 0.05 equiv) and dry DCM (1 mL). To this solution was added a mixture of 1-[(tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2a**) (0.25 mmol, 1.0 equiv) and ethyl 2-diazoacetate (**1a**) (0.3 mmol, 1.2 equiv) in dry DCM (1.5 mL) in 2 min and the resulting reaction mixture was stirred at 40 °C. After the reaction was completed (monitored by TLC, EtOAc:pentane, 1:40 v/v), the solvent was evaporated under reduced pressure and the crude product was purified by column chromatography (EtOAc:pentane, 1:40 v/v) directly without any further work-up.



1a (0.30 mmol, 1.2 equiv) **2a** (0.25 mmol, 1.0 equiv) **3a**

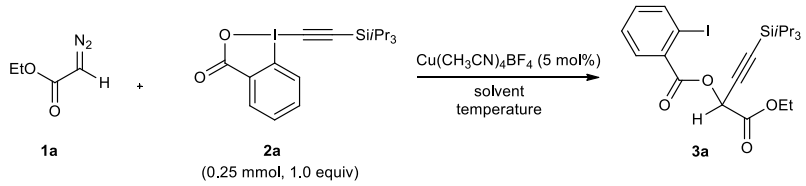
Entry	Catalyst (5 mol%)	Time	Yield (%)
1	$Rh_2(OAc)_4$	20 h	0
2	$Cu(OTf)_2$	20 h	19
3	CuOTf	20 h	19
4	$Cu(CH_3CN)_4BF_4$	20 h	24
5	CuCl	20 h	0
6	$Cu(OAc)_2$	20 h	0
7	CuBr	20 h	0
8	CuI	20 h	0
9*	$PdCl_2(PPh_3)_2$	2 h	0
10*	$PdCl_2$	2 h	0
11*	$Pd(OAc)_2$	2 h	0
12	$AuBr_3$	20 h	0
13	AuCl	20 h	0

14	$PtCl_2$		20 h	0

*Diazo compound was decomposed in 2 h.

b) Screening of equivalents of diazo compound

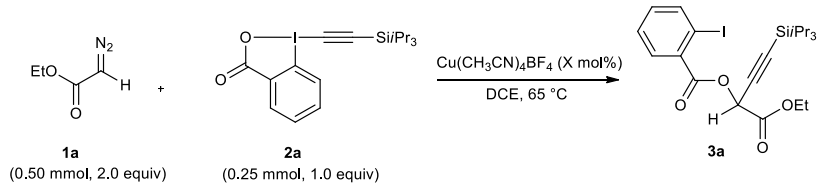
A flame dried 5 mL microwave vial was charged under nitrogen with $Cu(MeCN)_4BF_4$ (12.5 µmol, 0.05 equiv) and dry DCE (1 mL). To this solution was added a mixture of 1-[(tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2a**) (0.25 mmol, 1.0 equiv) and ethyl 2-diazoacetate (**1a**) in dry DCE (1.5 mL) in 2 min and the resulting reaction mixture was stirred at 65 °C. After the reaction was completed (monitored by TLC, EtOAc;pentane, 1:40 v/v), the solvent was evaporated under reduced pressure and the crude product was purified by column chromatography (EtOAc;pentane, 1:40 v/v) directly without any further work-up.



Entry	1a (equiv)	Time	T (°C)	Yield (%)
1	1.2	2 h	65	30
2	2	1 h	65	46
3	4	1 h	65	46

c) Screening of catalyst loading

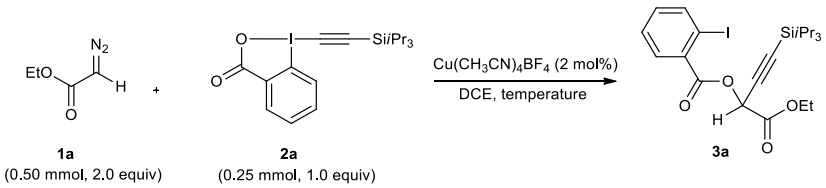
A flame dried 5 mL microwave vial was charged under nitrogen with $Cu(MeCN)_4BF_4$ and dry DCE (1 mL). To this solution was added a mixture of 1-[(tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2a**) (0.25 mmol, 1.0 equiv) and ethyl 2-diazoacetate (**1a**) (0.50 mmol, 2.0 equiv) in dry DCE (1.5 mL) in 2 min and the resulting reaction mixture was stirred at 65 °C. After the reaction was completed (monitored by TLC, EtOAc:pentane, 1:40 v/v), the solvent was evaporated under reduced pressure and the crude product was purified by column chromatography (EtOAc:pentane, 1:40 v/v) directly without any further work-up.



Entry	$Cu(CH_3CN)_4BF_4$	Time	T (°C)	Yield (%)
1	20 mol%	1 h	65	28
2	10 mol%	1 h	65	37
3	5 mol%	1 h	65	46
4	2 mol%	1 h	65	54
5	1 mol%	2 h	65	53

d) Screening of temperature

A flame dried 5 mL microwave vial was charged under nitrogen with $Cu(MeCN)_4BF_4$ (1.6 mg, 5.0 µmol, 0.02 equiv) and dry DCE (1 mL). To this solution was added a mixture of 1-[(tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2a**) (0.25 mmol, 1.0 equiv) and ethyl 2-diazoacetate (**1a**) (0.50 mmol, 2.0 equiv) in dry DCE (1.5 mL) in 2 min and the resulting reaction mixture was stirred until the reaction was completed (monitored by TLC, EtOAc;pentane, 1:40 v/v), the solvent was evaporated under reduced pressure and the crude product was purified by column chromatography (EtOAc;pentane, 1:40 v/v) directly without any further work-up.

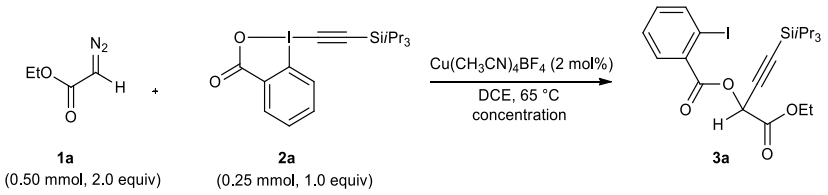


Entry	Time	T (°C)	Yield (%)
1	24 h	RT	0
2	20 h	40	20
3	20 h	50	47
4	1 h	65	54

5	1 h	70	51
6	1 h	90	51

e) Screening of concentration

A flame dried 5 mL microwave vial was charged under nitrogen with $Cu(MeCN)_4BF_4$ (1.6 mg, 5.0 µmol, 0.02 equiv) and dry DCE (1 mL). To this solution was added a mixture of 1-[(tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2a**) (0.25 mmol, 1.0 equiv) and ethyl 2-diazoacetate (**1a**) (0.50 mmol, 2.0 equiv) in dry DCE (1.5 mL) in 2 min and the resulting reaction mixture was stirred at 65 °C. After the reaction was completed (monitored by TLC, EtOAc:pentane, 1:40 v/v), the solvent was evaporated under reduced pressure and the crude product was purified by column chromatography (EtOAc:pentane, 1:40 v/v) directly without any further work-up.

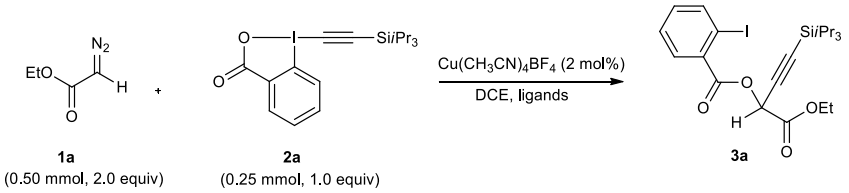


Entry	Time	Concentration	Yield
1	3 h	0.2 M	47
2	1 h	0.1 M	54
3	2.5 h	0.05 M	60
4	2.5 h	0.025 M	60

f) Screening of ligands

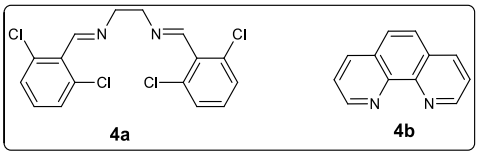
A flame dried 5 mL microwave vial was charged under nitrogen with $Cu(MeCN)_4BF_4$ (1.6 mg, 5.0 µmol, 0.02 equiv), ligand (6.25 µmol, 0.025 equiv) and dry DCE (2 mL). The resulting solution was stirred at room temperature for 30 minutes. To this solution was added a mixture of 1-[(tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2a**) (0.25 mmol, 1.0 equiv) and ethyl

2-diazoacetate (**1a**) (0.50 mmol, 2.0 equiv) in dry DCE (3 mL) in 2 min and the resulting reaction mixture was stirred until the reaction was completed (monitored by TLC, EtOAc:pentane, 1:40 v/v), the solvent was evaporated under reduced pressure and the crude product was purified by column chromatography (EtOAc:pentane, 1:40 v/v) directly without any further work-up.



1a (0.50 mmol, 2.0 equiv) **2a** (0.25 mmol, 1.0 equiv) **3a**

Entry	Ligands	T (°C)	Time	Yield (%)
1	no ligand	65	2.5 h	60
2	2.5 mol% **4a**	65	1 h	89
3	2.5 mol% **4b**	65	20 h	0
4	2.5 mol% **4a**	RT	1 h	90



4a **4b**

5. Oxy-alkynylation of diazo compounds

General procedure A: Oxy-alkynylation of diazo compounds:

A flame dried 5 mL microwave vial was charged under nitrogen with $Cu(MeCN)_4BF_4$ (1.6 mg, 5.0 µmol, 0.02 equiv), 1,2 diimine ligand **4a** (2.40 mg, 6.25 µmol, 0.025 equiv) and dry DCE (2 mL). The resulting solution was stirred at room temperature for 30 minutes. To this solution was added a mixture of R-EBX (0.25 mmol, 1.0 equiv) and diazo compound (0.50 mmol, 2.0 equiv) in dry DCE (3 mL) in 2 min and the resulting reaction mixture was stirred at room temperature. After the reaction was completed (monitored by TLC, EtOAc;pentane), the solvent was evaporated under reduced pressure and the crude product was purified by column chromatography (EtOAc:pentane) directly without any further work-up.

General procedure B: Oxy-alkynylation of diazo compounds:

A flame dried 5 mL microwave vial was charged under nitrogen with $Cu(MeCN)_4BF_4$ (1.6 mg, 5.0 µmol, 0.02 equiv), 1,2 diimine ligand **4a** (2.40 mg, 6.25 µmol, 0.025 equiv) and dry DCE (2 mL). The resulting solution was stirred at room temperature for 30 minutes and then added to a mixture of R-EBX (0.25 mmol, 1.0 equiv) and diazo compound (0.50 mmol, 2.0 equiv) in dry DCE (3 mL) in 2 min and the resulting reaction mixture was stirred at room temperature. After the reaction was completed (monitored by TLC, EtOAc:pentane), the solvent was evaporated under reduced pressure and the crude product was purified by column chromatography (EtOAc:pentane) directly without any further work-up.

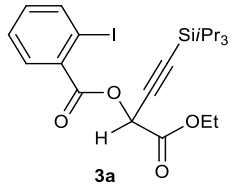
General procedure C: Oxy-alkynylation of vinyl diazo compounds:

A flame dried 5 mL microwave vial was charged under nitrogen with $Cu(MeCN)_4BF_4$ (3.2 mg, 10 µmol, 0.04 equiv), 1,2 diimine ligand **4a** (4.80 mg, 12.5 µmol, 0.05 equiv) and dry DCE (2 mL). The resulting solution was stirred at room temperature for 30 minutes. To this solution was added a mixture of R-EBX (0.25 mmol, 1.0 equiv) and diazo compound (0.50 mmol, 2.0 equiv) in dry DCE (3 mL) in 2 min and the resulting reaction mixture was stirred at room temperature. After the reaction was completed (monitored by TLC, EtOAc:pentane), the solvent was evaporated under reduced pressure and the crude product was purified by column chromatography (EtOAc:pentane) directly without any further work-up.

General procedure D: Oxy-alkynylation of vinyl diazo compounds:

A flame dried 5 mL microwave vial was charged under nitrogen with $Cu(MeCN)_4BF_4$ (3.2 mg, 10 µmol, 0.04 equiv), 1,2 diimine ligand **4a** (4.80 mg, 12.5 µmol, 0.05 equiv) and dry DCE (2 mL). The resulting solution was stirred at room temperature for 30 minutes and then added to a mixture of R-EBX (0.25 mmol, 1.0 equiv) and diazo compound (0.50 mmol, 2.0 equiv) in dry DCE (3 mL) in 2 min and the resulting reaction mixture was stirred at room temperature. After the reaction was completed (monitored by TLC, EtOAc:pentane), the solvent was evaporated under reduced pressure and the crude product was purified by column chromatography (EtOAc:pentane) directly without any further work-up.

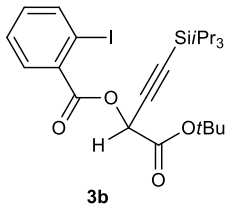
1-Ethoxy-1-oxo-4-(tri*iso*propylsilyl)but-3-yn-2-yl 2-iodobenzoate (3a)



3a

Following general procedure **A**, 1-[(tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2a**) (107 mg, 0.250 mmol, 1.00 equiv) and ethyl 2-diazoacetate (**1a**) (60 µL, 0.50 mmol, 13 wt. % dichloromethane, 2.0 equiv) were stirred for 1 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 1:40 as mobile phase affording **3a** (116 mg, 0.225 mmol, 86%) as a colorless oil. TLC (EtOAc:pentane, 1:40 v/v): R_f = 0.14, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02 (dd, *J* = 7.9, 1.2 Hz, 1H, Ar*H*), 7.99 (dd, *J* = 7.8, 1.7 Hz, 1H, Ar*H*), 7.44 (td, *J* = 7.6, 1.2 Hz, 1H, Ar*H*), 7.18 (td, *J* = 7.7, 1.7 Hz, 1H, Ar*H*), 5.98 (s, 1H, OC*H*CC), 4.44–4.17 (m, 2H, C*H*$_2$CH$_3$), 1.32 (t, *J* = 7.1 Hz, 3H, CH$_2$C*H*$_3$), 1.11–1.03 (m, 21H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.4, 164.9, 141.5, 133.3, 133.2, 131.8, 128.0, 97.6, 94.5, 90.6, 63.9, 62.6, 18.5, 14.0, 11.0; IR ν 2945 (m), 2866 (m), 2188 (w), 1745 (s), 1583 (w), 1464 (m), 1241 (s), 1203 (s), 1092 (s), 1020 (s), 883 (m); HRMS (ESI) calcd. for $C_{22}H_{32}IO_4Si^+$ $[M+H]^+$ 515.1109; found 515.1095.

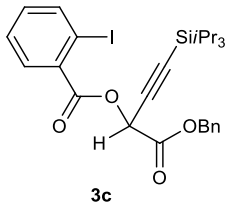
1-(*Tert*-butoxy)-1-oxo-4-(tri*iso*propylsilyl)but-3-yn-2-yl 2-iodobenzoate (3b)



3b

Following general procedure **A**, 1-[(tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2a**) (107 mg, 0.250 mmol, 1.00 equiv) and *tert*-butyl 2-diazoacetate (82 µL, 0.50 mmol, 15 wt. % dichloromethane, 2.0 equiv) were stirred for 2 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 1:60 as mobile phase affording **3b** (111 mg, 0.205 mmol, 82%) as a colorless oil. TLC (EtOAc:pentane, 1:40 v/v): R_f = 0.25, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04–7.97 (m, 2H, Ar*H*), 7.43 (td, *J* = 7.6, 1.2 Hz, 1H, Ar*H*), 7.18 (td, *J* = 7.7, 1.7 Hz, 1H, Ar*H*), 5.87 (s, 1H, OC*H*CC), 1.51 (s, 9H, C(C*H*$_3$)$_3$), 1.09 (s, 21H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.0, 164.2, 141.5, 133.6, 133.2, 131.9, 128.0, 98.2, 94.5, 89.8, 83.6, 64.4, 27.8, 18.5, 11.1; IR ν 2944 (m), 2867 (m), 2188 (w), 1744 (s), 1584 (w), 1465 (m), 1371 (m), 1245 (s), 1158 (s), 1097 (s), 1017 (m), 881 (w), 846 (w); HRMS (ESI) calcd. for $C_{24}H_{35}INaO_4Si^+$ $[M+Na]^+$ 565.1242; found 565.1245.

1-(Benzyloxy)-1-oxo-4-(tri*iso*propylsilyl)but-3-yn-2-yl 2-iodobenzoate (3c)

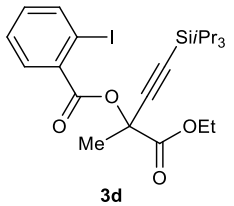


3c

Following general procedure **A**, 1-[(tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2a**) (107 mg, 0.250 mmol, 1.00 equiv) and benzyl 2-diazoacetate (0.985 mL, 0.500 mmol, 10% in toluene, 2.00 equiv) were stirred for 2 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 1:60 as mobile phase affording **3c** (125 mg, 0.217 mmol, 87%) as a colorless oil. TLC (EtOAc:pentane, 1:40 v/v): R_f = 0.29, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02 (dd, *J* = 7.9, 1.1 Hz, 1H, Ar*H*), 7.97 (dd, *J* = 7.8, 1.7 Hz, 1H, Ar*H*), 7.43 (td, *J* = 7.6, 1.2 Hz, 1H, Ar*H*), 7.39–7.32 (m, 5H, Ar*H*), 7.19 (td, *J* = 7.7, 1.7 Hz, 1H, Ar*H*), 6.05 (s, 1H, OC*H*CC), 5.35 (d, *J* = 12.2 Hz, 1H, ArC*H*$_2$), 5.20 (d, *J* = 12.2 Hz, 1H, ArC*H*$_2$), 1.07–1.00 (m, 21H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.3, 164.9, 141.5,

134.8, 133.3, 133.2, 131.9, 128.6, 128.5, 128.3, 128.0, 97.2, 94.6, 90.9, 68.0, 63.9, 18.5, 11.0; IR ν 2943 (m), 2865 (m), 2189 (w), 1763 (s), 1741 (s), 1584 (w), 1463 (m), 1381 (w), 1324 (m), 1242 (s), 1192 (s), 1094 (s), 1016 (s), 883 (m); HRMS (ESI) calcd. for $C_{27}H_{33}INaO_4Si^+$ $[M+Na]^+$ 599.1085; found 599.1092.

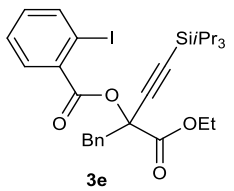
1-Ethoxy-2-methyl-1-oxo-4-(tri*iso*propylsilyl)but-3-yn-2-yl 2-iodobenzoate (3d)



3d

Following general procedure **A**, 1-[(tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2a**) (107 mg, 0.250 mmol, 1.00 equiv) and ethyl 2-diazopropanoate (**1b**) (64 mg, 0.50 mmol, 2.0 equiv) were stirred for 1 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 1:40 as mobile phase affording **3d** (106 mg, 0.201 mmol, 80%) as a colorless oil. TLC (EtOAc:pentane, 1:40 v/v): R_f = 0.15, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98 (dd, *J* = 7.9, 1.1 Hz, 1H, Ar*H*), 7.81 (dd, *J* = 7.8, 1.7 Hz, 1H, Ar*H*), 7.41 (td, *J* = 7.6, 1.2 Hz, 1H, Ar*H*), 7.16 (td, *J* = 7.7, 1.7 Hz, 1H, Ar*H*), 4.28 (qq, *J* = 10.7, 7.1 Hz, 2H, C*H*$_2$CH$_3$), 1.93 (s, 3H, OCOCC*H*$_3$), 1.32 (t, *J* = 7.1 Hz, 3H, CH$_2$C*H*$_3$), 1.08 (s, 21H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.3, 164.6, 141.2, 134.8, 132.7, 131.2, 127.8, 102.7, 93.8, 88.6, 73.7, 62.4, 26.1, 18.6, 14.0, 11.1; IR ν 2943 (m), 2866 (m), 2186 (w), 2120 (w), 1746 (s), 1579 (w), 1465 (m), 1372 (w), 1294 (s), 1250 (s), 1198 (m), 1133 (s), 1078 (s), 1017 (s), 884 (m); HRMS (ESI) calcd. for $C_{23}H_{33}INaO_4Si^+$ $[M+Na]^+$ 551.1085; found 551.1090.

2-Oxo-3-((tri*iso*propylsilyl)ethynyl)tetrahydrofuran-3-yl 2-iodobenzoate (3e)

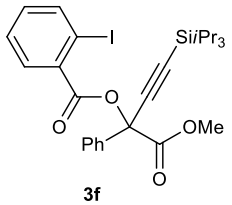


3e

Following general procedure **A**, 1-[(tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2a**) (107 mg, 0.250 mmol, 1.00 equiv) and methyl 2-diazo-3-phenylpropanoate (**1c**) (95 mg, 0.50 mmol, 2.0 equiv) were stirred for 2 h. The crude reaction mixture was concentrated in vacuo and

purified by flash chromatography using EtOAc:pentane 1:40 as mobile phase affording **3e** (74.0 mg, 0.125 mmol, 50%) as a colorless oil. TLC (EtOAc:pentane, 1:20 v/v): R_f = 0.3, $KMnO_4$; ^1H NMR (400 MHz, $CDCl_3$): δ 7.98 (dd, *J* = 7.9, 1.1 Hz, 1H, Ar*H*), 7.69 (dd, *J* = 7.8, 1.7 Hz, 1H, Ar*H*), 7.43– 7.32 (m, 3H, Ar*H*), 7.30–7.26 (m, 3H, Ar*H*), 7.16 (td, *J* = 7.7, 1.7 Hz, 1H, Ar*H*), 3.76 (s, 3H, OCH_3), 3.54 (d, *J* = 13.5 Hz, 1H, ArCH_2), 3.39 (d, *J* = 13.5 Hz, 1H, ArCH_2), 1.08–1.03 (m, 21H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.2, 164.4, 141.3, 134.5, 133.6, 132.8, 131.2, 130.8, 128.0, 127.8, 127.4, 101.0, 94.0, 91.1, 77.1, 53.1, 44.4, 18.5, 11.1; IR ν 2949 (m), 2866 (m), 2178 (w), 1749 (s), 1583 (w), 1463 (m), 1289 (s), 1245 (s), 1126 (m), 1091 (m), 1045 (m), 1017 (m), 885 (w), 826 (w); HRMS (ESI) calcd. for $C_{28}H_{35}INaO_4Si^+$ $[M+Na]^+$ 613.1242; found 613.1247.

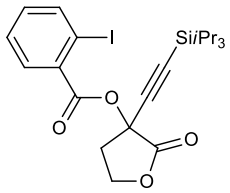
1-Methoxy-1-oxo-2-phenyl-4-(tri*iso*propylsilyl)but-3-yn-2-yl 2-iodobenzoate (3f)



3f

Following general procedure **A**, 1-[(tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2a**) (107 mg, 0.250 mmol, 1.00 equiv) and methyl 2-diazo-2-phenylacetate (**1h**) (88 mg, 0.50 mmol, 2.0 equiv) were stirred for 1.5 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 1:40 as mobile phase affording **3f** (58.0 mg, 0.101 mmol, 40%) as a colorless oil. TLC (EtOAc:pentane, 1:30 v/v): R_f = 0.3, $KMnO_4$; ^1H NMR (400 MHz, $CDCl_3$): δ 7.93 (dd, *J* = 7.9, 1.1 Hz, 1H, Ar*H*), 7.84–7.79 (m, 3H, Ar*H*), 7.39–7.31 (m, 4H, Ar*H*), 7.11 (td, *J* = 7.7, 1.7 Hz, 1H, Ar*H*), 3.71 (s, 3H, OCH_3), 1.07–1.01 (m, 21H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.6, 164.4, 141.3, 135.7, 134.7, 132.8, 131.2, 129.3, 128.5, 127.9, 126.7, 101.1, 93.9, 91.6, 77.7, 53.6, 18.6, 11.2; IR ν 2947 (m), 2865 (m), 2175 (w), 1749 (s), 1584 (w), 1461 (m), 1247 (s), 1123 (s), 1090 (s), 1018 (s), 883 (w); HRMS (ESI) calcd. for $C_{27}H_{33}INaO_4Si^+$ $[M+Na]^+$ 599.1085; found 599.1088.

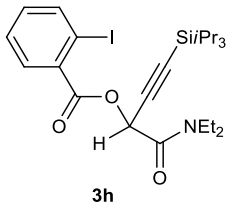
2-Oxo-3-((tri*iso*propylsilyl)ethynyl)tetrahydrofuran-3-yl 2-iodobenzoate (3g)



3g

Following general procedure **A**, 1-[(tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2a**) (107 mg, 0.250 mmol, 1.00 equiv) and 3-diazodihydrofuran-2(3H)-one (**1d**) (56 mg, 0.50 mmol, 2.0 equiv) were stirred for 3 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 1:10 as mobile phase affording **3g** (103 mg, 0.201 mmol, 80%) as a colorless oil. TLC (EtOAc:pentane, 1:9 v/v): R_f = 0.6, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.03 (dd, *J* = 7.9, 1.1 Hz, 1H, Ar*H*), 7.93 (dd, *J* = 7.8, 1.8 Hz, 1H, Ar*H*), 7.46 (td, *J* = 7.6, 1.2 Hz, 1H, Ar*H*), 7.21 (td, *J* = 7.7, 1.7 Hz, 1H, Ar*H*), 4.62 (td, *J* = 8.7, 2.4 Hz, 1H, CH_2^1), 4.49 (td, *J* = 9.5, 6.5 Hz, 1H, CH_2^2), 3.14–2.92 (m, 2H, CH_2), 1.14–1.08 (m, 21H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.1, 164.3, 141.5, 133.4, 133.3, 131.7, 128.0, 98.8, 94.3, 92.8, 73.3, 65.2, 36.8, 18.5, 11.0; IR ν 2945 (s), 2866 (m), 2177 (w), 1801 (s), 1742 (s), 1584 (w), 1465 (m), 1379 (w), 1289 (m), 1245 (s), 1178 (s), 1118 (s), 1021 (s), 883 (m); HRMS (ESI) calcd. for $C_{22}H_{29}INaO_4Si^+$ $[M+Na]^+$ 535.0772; found 535.0777.

1-(Diethylamino)-1-oxo-4-(tri*iso*propylsilyl)but-3-yn-2-yl 2-iodobenzoate (3h)

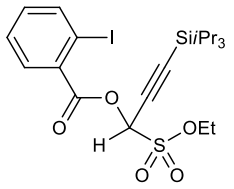


3h

Following general procedure **A**, 1-[(tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2a**) (107 mg, 0.250 mmol, 1.00 equiv) and 2-diazo-*N*,*N*-diethylacetamide (**1e**) (71 mg, 0.50 mmol, 2.0 equiv) were stirred for 5 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 1:10 as mobile phase affording **3h** (84.0 mg, 0.155 mmol, 62%) as a colorless oil. TLC (EtOAc:pentane, 1:10 v/v): R_f = 0.35, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.10 (dd, *J* = 7.8, 1.7 Hz, 1H, Ar*H*), 7.98 (dd, *J* = 8.0, 1.1 Hz, 1H, Ar*H*), 7.43 (td, *J* = 7.6, 1.1 Hz, 1H, Ar*H*), 7.16 (td, *J* = 7.7, 1.8 Hz, 1H, Ar*H*), 6.13 (s, 1H, OC*H*CC), 3.67 (tq, *J* = 14.1, 7.2 Hz, 2H, CH_2CH$_3$), 3.39 (dq, *J* = 14.5, 7.1 Hz, 1H, CH_2CH$_3$),

3.17 (dq, *J* = 14.1, 7.1 Hz, 1H, C*H*$_2$CH$_3$), 1.33 (t, *J* = 7.1 Hz, 3H, CH$_2$C*H*$_3$), 1.14 (t, *J* = 7.1 Hz, 3H, CH$_2$C*H*$_3$), 1.07–1.01 (m, 21H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.4, 163.5, 141.2, 133.8, 133.0, 132.2, 128.0, 98.4, 94.3, 91.0, 63.7, 41.5, 40.6, 18.5, 14.0, 12.5, 11.0; IR ν 2942 (m), 2865 (m), 2184 (w), 1738 (m), 1677 (s), 1463 (m), 1433 (m), 1288 (m), 1246 (s), 1130 (m), 1098 (s), 1069 (s), 1016 (s), 884 (m), 828 (w); HRMS (ESI) calcd. for $C_{24}H_{37}INO_3Si^+$ $[M+H]^+$ 542.1582; found 542.1597.

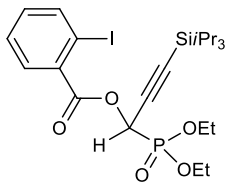
1-(Ethoxysulfonyl)-3-(tri*iso*propylsilyl)prop-2-yn-1-yl 2-iodobenzoate (3i)



3i

Following general procedure **A**, 1-[(tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2a**) (107 mg, 0.250 mmol, 1.00 equiv) and ethyl diazomethanesulfonate (**1f**) (75 mg, 0.50 mmol, 2.0 equiv) were stirred for 1 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 1:20 as mobile phase affording **3i** (114 mg, 0.207 mmol, 83%) as a colorless oil. TLC (EtOAc:pentane, 1:20 v/v): R_f = 0.3, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05 (dd, *J* = 7.9, 1.2 Hz, 1H, Ar*H*), 7.94 (dd, *J* = 7.8, 1.7 Hz, 1H, Ar*H*), 7.46 (td, *J* = 7.6, 1.2 Hz, 1H, Ar*H*), 7.23 (td, *J* = 7.7, 1.7 Hz, 1H, Ar*H*), 6.71 (s, 1H, OC*H*CC), 4.51 (q, *J* = 7.1 Hz, 2H, C*H*$_2$CH$_3$), 1.43 (t, *J* = 7.1 Hz, 3H, CH$_2$C*H*$_3$), 1.13–1.07 (m, 21H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.1, 141.8, 133.8, 132.2, 131.9, 128.2, 95.6, 94.9, 93.6, 73.9, 70.8, 18.5, 15.3, 11.0; IR ν 2947 (m), 2868 (m), 1755 (s), 1584 (w), 1466 (m), 1383 (s), 1238 (s), 1180 (m), 1078 (s), 1009 (m), 924 (s), 887 (w); HRMS (ESI) calcd. for $C_{21}H_{31}INaO_5SSi^+$ $[M+Na]^+$ 573.0598; found 573.0599.

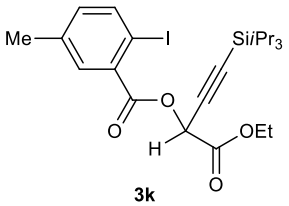
1-(Diethoxyphosphoryl)-3-(tri*iso*propylsilyl)prop-2-yn-1-yl 2-iodobenzoate (3j)



3j

Following general procedure **A**, 1-[(tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2a**) (107 mg, 0.250 mmol, 1.00 equiv) and diethyl (diazomethyl)phosphonate (**1g**) (89 mg, 0.50 mmol, 2.0 equiv) were stirred for 1 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 1:4 as mobile phase affording **3j** (117 mg, 0.202 mmol, 81%) as a colorless oil. TLC (EtOAc:pentane, 1:4 v/v): R_f = 0.35, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00 (dd, *J* = 8.0, 1.1 Hz, 1H, Ar*H*), 7.84 (dd, *J* = 7.9, 1.7 Hz, 1H, Ar*H*), 7.42 (td, *J* = 7.6, 1.1 Hz, 1H, Ar*H*), 7.18 (td, *J* = 7.7, 1.6 Hz, 1H, Ar*H*), 6.05 (d, *J* = 17.0 Hz, 1H, OC*H*P), 4.35–4.18 (m, 4H, 2 X C*H*$_2$CH$_3$), 1.35 (td, *J* = 7.1, 3.5 Hz, 6H, 2 X CH$_2$C*H*$_3$), 1.08 (s, 21H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.4 (d, *J* = 8.0 Hz), 141.4, 133.8, 133.1, 131.4, 127.9, 97.4 (d, *J* = 5.8 Hz), 94.4, 91.8 (d, *J* = 8.2 Hz), 64.1 (d, *J* = 6.9 Hz), 64.0 (d, *J* = 6.5 Hz), 60.2 (d, *J* = 174.4 Hz), 18.5, 16.4 (t, *J* = 5.4 Hz, 2 X C), 11.1; IR ν 2944 (w), 2866 (w), 2181 (w), 1744 (m), 1464 (w), 1270 (m), 1241 (m), 1020 (s), 977 (m), 884 (w); HRMS (ESI) calcd. for $C_{23}H_{37}IO_5PSi^+$ $[M+H]^+$ 579.1187; found 579.1195.

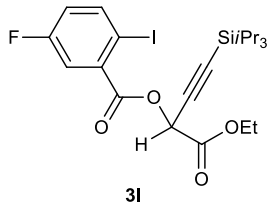
1-Ethoxy-1-oxo-4-(tri*iso*propylsilyl)but-3-yn-2-yl 2-iodo-5-methylbenzoate (3k)



3k

Following general procedure **A**, 5-methyl-1-[(tri*iso*propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2b**) (111 mg, 0.250 mmol, 1.00 equiv) and ethyl 2-diazoacetate (**1a**) (60 µL, 0.50 mmol, 13 wt. % dichloromethane, 2.0 equiv) were stirred for 0.5 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 1:60 as mobile phase affording **3k** (94.0 mg, 0.178 mmol, 71%) as a colorless oil. TLC (EtOAc:pentane, 1:40 v/v): R_f = 0.26, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 (d, *J* = 8.0 Hz, 1H, Ar*H*), 7.79 (d, *J* = 1.7 Hz, 1H, Ar*H*), 7.01 (ddd, *J* = 8.1, 2.3, 0.8 Hz, 1H, Ar*H*), 5.98 (s, 1H, OC*H*CC), 4.39–4.22 (m, 2H, C*H*$_2$CH$_3$), 2.35 (s, 3H, ArC*H*$_3$), 1.32 (t, *J* = 7.2 Hz, 3H, CH$_2$C*H*$_3$), 1.11–1.05 (m, 21H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.5, 165.0, 141.2, 138.2, 134.3, 133.1, 132.5, 97.7, 90.6, 90.4, 63.8, 62.5, 20.8, 18.5, 14.0, 11.0; IR ν 2945 (m), 2866 (m), 2190 (w), 1763 (s), 1743 (s), 1466 (m), 1248 (s), 1196 (s), 1098 (s), 1036 (m), 885 (w); HRMS (ESI) calcd. for $C_{23}H_{33}INaO_4Si^+$ $[M+Na]^+$ 551.1085; found 551.1095.

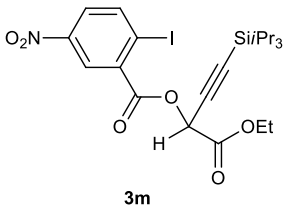
1-Ethoxy-1-oxo-4-(tri*iso*propylsilyl)but-3-yn-2-yl 5-fluoro-2-iodobenzoate (3l)



3l

Following general procedure **A**, 5-fluoro-1-[(tri*iso*propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2c**) (112 mg, 0.250 mmol, 1.00 equiv) and ethyl 2-diazoacetate (**1a**) (60 µL, 0.50 mmol, 13 wt. % dichloromethane, 2.0 equiv) were stirred for 0.5 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 1:60 as mobile phase affording **3l** (110 mg, 0.207 mmol, 83%) as a colorless oil. TLC (EtOAc:pentane, 1:40 v/v): R_f = 0.29, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96 (dd, *J* = 8.7, 5.3 Hz, 1H, Ar*H*), 7.72 (dd, *J* = 8.9, 3.0 Hz, 1H, Ar*H*), 6.97 (ddd, *J* = 8.7, 7.7, 3.1 Hz, 1H, Ar*H*), 5.97 (s, 1H, OC*H*CC), 4.44–4.16 (m, 2H, C*H*$_2$CH$_3$), 1.33 (t, *J* = 7.1 Hz, 3H, CH$_2$C*H*$_3$), 1.13–1.05 (m, 21H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.2, 163.8 (d, *J* = 2.2 Hz), 162.3 (d, *J* = 249.6 Hz), 142.9 (d, *J* = 7.2 Hz), 134.8 (d, *J* = 7.1 Hz), 120.9 (d, *J* = 21.5 Hz), 119.3 (d, *J* = 24.3 Hz), 97.2, 91.0, 87.6 (d, *J* = 3.5 Hz), 64.1, 62.7, 18.5, 14.0, 11.0; IR ν 2945 (m), 2867 (m), 2190 (w), 1749 (s), 1576 (w), 1466 (m), 1396 (w), 1324 (m), 1242 (s), 1192 (s), 1087 (s), 1024 (m), 886 (m), 823 (m); HRMS (ESI) calcd. for $C_{22}H_{30}FINaO_4Si^+$ $[M+Na]^+$ 555.0834; found 555.0840.

1-Ethoxy-1-oxo-4-(tri*iso*propylsilyl)but-3-yn-2-yl 2-iodo-5-nitrobenzoate (3m)

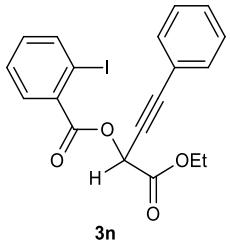


3m

Following general procedure **A**, 5-nitro-1-[(tri*iso*propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2d**) (118 mg, 0.250 mmol, 1.00 equiv) and ethyl 2-diazoacetate (**1a**) (60 µL, 0.50 mmol, 13 wt. % dichloromethane, 2.0 equiv) were stirred for 1 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 1:50 as mobile phase affording **3m** (100 mg, 0.179 mmol, 72%) as a pale yellow solid. Mp: 61.9–65.7 °C; TLC (EtOAc:pentane, 1:40 v/v): R_f = 0.2, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.76 (d, *J* = 2.7 Hz,

1H, Ar*H*), 8.24 (d, *J* = 8.7 Hz, 1H, Ar*H*), 8.01 (dd, *J* = 8.7, 2.7 Hz, 1H, Ar*H*), 6.00 (s, 1H, OC*H*CC), 4.44–4.21 (m, 2H, CH_2CH$_3$), 1.34 (t, *J* = 7.1 Hz, 3H, CH$_2$CH_3), 1.11–1.07 (m, 21H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.9, 163.2, 147.7, 142.9, 134.9, 126.9, 126.3, 102.9, 96.8, 91.6, 64.5, 62.8, 18.5, 14.0, 11.0; IR ν 3101 (w), 2944 (m), 2866 (m), 2189 (w), 1749 (s), 1604 (m), 1530 (s), 1463 (m), 1348 (s), 1237 (s), 1207 (s), 1123 (s), 1090 (s), 1021 (s), 919 (m), 882 (m), 838 (m); HRMS (ESI) calcd. for $C_{22}H_{31}INO_6Si^+$ $[M+H]^+$ 560.0960; found 560.0965.

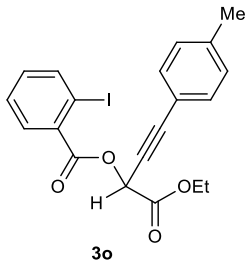
1-Ethoxy-1-oxo-4-phenylbut-3-yn-2-yl 2-iodobenzoate (3n)



3n

Following general procedure **B**, 1-[phenylethynyl]-1,2-benziodoxol-3(1H)-one (**2e**) (87 mg, 0.25 mmol, 1.0 equiv) and ethyl 2-diazoacetate (**1a**) (60 µL, 0.50 mmol, 13 wt. % dichloromethane, 2.0 equiv) were stirred for 1 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 1:30 as mobile phase affording **3n** (93.0 mg, 0.210 mmol, 84%) as a colorless oil. TLC (EtOAc:pentane, 1:20 v/v): R_f = 0.39, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.10–7.99 (m, 2H, Ar*H*), 7.53–7.48 (m, 2H, Ar*H*), 7.45 (td, *J* = 7.6, 1.2 Hz, 1H, Ar*H*), 7.40–7.29 (m, 3H, Ar*H*), 7.20 (td, *J* = 7.7, 1.7 Hz, 1H, Ar*H*), 6.19 (s, 1H, OC*H*CC), 4.35 (q, *J* = 7.1 Hz, 2H, CH_2CH$_3$), 1.36 (t, *J* = 7.1 Hz, 3H, CH$_2$CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.5, 164.9, 141.6, 133.3, 133.1, 132.1, 131.9, 129.3, 128.3, 128.0, 121.4, 94.6, 87.6, 80.2, 64.1, 62.8, 14.1; IR ν 2985 (w), 2239 (w), 1740 (s), 1582 (w), 1466 (w), 1242 (s), 1202 (s), 1127 (m), 1094 (s), 1041 (s), 1022 (s), 860 (w); HRMS (ESI) calcd. for $C_{19}H_{15}INaO_4^+$ $[M+Na]^+$ 456.9907; found 456.9910.

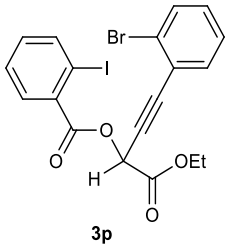
1-Ethoxy-1-oxo-4-(*p*-tolyl)but-3-yn-2-yl 2-iodobenzoate (3o)



3o

Following general procedure **B**, 1-(*p*-tolylethynyl)-1,2-benziodoxol-3(1H)-one (**2f**) (91 mg, 0.25 mmol, 1.0 equiv) and ethyl 2-diazoacetate (**1a**) (60 µL, 0.50 mmol, 13 wt. % dichloromethane, 2.0 equiv) were stirred for 1 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 1:30 as mobile phase affording **3o** (90.0 mg, 0.201 mmol, 80%) as a colorless oil. TLC (EtOAc:pentane, 1:20 v/v): R_f = 0.32, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06–8.01 (m, 2H, Ar*H*), 7.44 (td, *J* = 7.6, 1.2 Hz, 1H, Ar*H*), 7.39 (d, *J* = 8.1 Hz, 2H, Ar*H*), 7.19 (td, *J* = 7.7, 1.7 Hz, 1H, Ar*H*), 7.14 (d, *J* = 8.2 Hz, 2H, Ar*H*), 6.18 (s, 1H, OC*H*CC), 4.34 (q, *J* = 7.1 Hz, 2H, C*H*$_2$CH$_3$), 2.35 (s, 3H, ArC*H*$_3$), 1.35 (t, *J* = 7.1 Hz, 3H, CH$_2$C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.5, 164.9, 141.5, 139.5, 133.3, 133.1, 131.9, 131.8, 129.1, 128.0, 118.2, 94.6, 87.9, 79.5, 64.1, 62.7, 21.5, 14.0; IR ν 2984 (w), 2237 (w), 1741 (s), 1582 (w), 1511 (w), 1464 (w), 1242 (s), 1203 (s), 1094 (s), 1022 (s), 859 (w), 818 (m); HRMS (ESI) calcd. for $C_{20}H_{17}INaO_4^+$ $[M+Na]^+$ 471.0064; found 471.0067.

4-(2-Bromophenyl)-1-ethoxy-1-oxobut-3-yn-2-yl 2-iodobenzoate (3p)

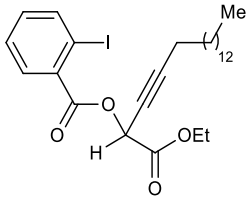


3p

Following general procedure **B**, 1-[2-bromophenylethynyl]-1,2-benziodoxol-3(1H)-one (**2g**) (107 mg, 0.250 mmol, 1.00 equiv) and ethyl 2-diazoacetate (**1a**) (60 µL, 0.50 mmol, 13 wt. % dichloromethane, 2.0 equiv) were stirred for 1 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 1:30 as mobile phase affording **3p** (106 mg, 0.207 mmol, 83%) as a pale yellow solid. Mp: 81.2–86.5 °C; TLC (EtOAc:pentane, 1:20 v/v): R_f = 0.26, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07–8.00 (m, 2H, Ar*H*), 7.59 (dd, *J* = 7.9, 1.3 Hz, 1H, Ar*H*), 7.52 (dd, *J* = 7.6, 1.8 Hz, 1H, Ar*H*), 7.45 (td, *J* = 7.6,

1.2 Hz, 1H, Ar*H*), 7.30–7.26 (m, 1H, Ar*H*), 7.21 (dtd, *J* = 7.9, 7.4, 1.8 Hz, 2H, Ar*H*), 6.23 (s, 1H, OC*H*CC), 4.36 (qd, *J* = 7.2, 4.6 Hz, 2H, CH_2CH$_3$), 1.37 (t, *J* = 7.1 Hz, 3H, CH$_2$CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.2, 164.8, 141.6, 133.8, 133.3, 133.1, 132.5, 131.9, 130.4, 128.0, 127.0, 125.9, 123.6, 94.7, 86.0, 84.6, 63.9, 62.8, 14.1; IR ν 3065 (w), 2983 (w), 2242 (w), 1739 (s), 1583 (w), 1468 (m), 1431 (m), 1241 (s), 1201 (s), 1092 (s), 1018 (s), 860 (w); HRMS (ESI) calcd for $C_{19}H_{14}BrINaO_4^+$ $[M+Na]^+$ 534.9012; found 534.9016.

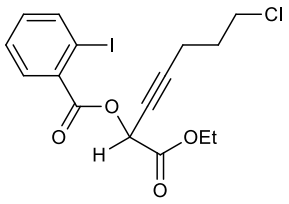
1-Ethoxy-1-oxooctadec-3-yn-2-yl 2-iodobenzoate (3q)



3q

Following general procedure **A**, hexadecynyl-1,2-benziodoxol-3(1H)-one (**2i**) (117 mg, 0.250 mmol, 1.00 equiv) and ethyl 2-diazoacetate (**1a**) (60 µL, 0.50 mmol, 13 wt. % dichloromethane, 2.0 equiv) were stirred for 12 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 1:40 as mobile phase affording **3q** (111 mg, 0.200 mmol, 80%) as a colorless oil. TLC (EtOAc:pentane, 1:20 v/v): R_f = 0.47, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00–7.85 (m, 2H, Ar*H*), 7.36 (t, *J* = 7.6 Hz, 1H, Ar*H*), 7.11 (td, *J* = 7.7, 1.6 Hz, 1H, Ar*H*), 5.97–5.68 (m, 1H, OC*H*CCCH$_2$), 4.24 (qd, *J* = 7.1, 1.4 Hz, 2H, CO$_2$CH_2CH$_3$), 2.19 (td, *J* = 7.1, 2.2 Hz, 2H, CCCH_2), 1.54–1.41 (m, 2H), 1.34–1.14 (m, 25H), 0.81 (t, *J* = 6.7 Hz, 3H, CH$_2$CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.9, 165.0, 141.5, 133.3, 133.2, 131.8, 127.9, 94.5, 89.5, 71.4, 64.0, 62.5, 31.9, 29.7, 29.7, 29.6, 29.5, 29.3, 29.1, 28.8, 28.1, 22.7, 18.8, 14.1, 14.0; IR ν 2925 (s), 2854 (m), 2245 (w), 1743 (s), 1583 (w), 1463 (m), 1326 (m), 1244 (s), 1203 (s), 1127 (m), 1096 (s), 1023 (s), 860 (w); HRMS (ESI) calcd. for $C_{27}H_{39}INaO_4^+$ $[M+Na]^+$ 577.1785; found 577.1792. Two carbons were not resolved at 100 MHz.

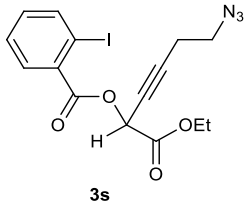
7-Chloro-1-ethoxy-1-oxohept-3-yn-2-yl 2-iodobenzoate (3r)



3r

Following general procedure **A**, (5-chloropent-1-ynyl)-1,2-benziodoxol-3(1H)-one (**2j**) (87 mg, 0.25 mmol, 1.0 equiv) and ethyl 2-diazoacetate (**1a**) (60 µL, 0.50 mmol, 13 wt. % dichloromethane, 2.0 equiv) were stirred for 1 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 1:20 as mobile phase affording **3r** (77.0 mg, 0.177 mmol, 71%) as a colorless oil. TLC (EtOAc:pentane, 1:15 v/v): R_f = 0.16, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02 (dd, *J* = 8.0, 1.2 Hz, 1H, Ar*H*), 7.98 (dd, *J* = 7.8, 1.7 Hz, 1H, Ar*H*), 7.44 (td, *J* = 7.6, 1.2 Hz, 1H, Ar*H*), 7.19 (ddd, *J* = 7.9, 7.4, 1.7 Hz, 1H, Ar*H*), 5.92 (t, *J* = 2.3 Hz, 1H, OC*H*CC), 4.31 (qd, *J* = 7.1, 1.4 Hz, 2H, $CO_2CH_2CH_3$), 3.65 (t, *J* = 6.3 Hz, 2H, CH_2CH_2Cl), 2.48 (td, *J* = 6.8, 2.3 Hz, 2H, CCCH_2), 2.06–1.94 (m, 2H, CH_2CH_2Cl), 1.34 (t, *J* = 7.1 Hz, 3H, $CO_2CH_2CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.7, 164.9, 141.5, 133.3, 131.7, 128.0, 94.5, 87.2, 72.7, 63.8, 62.6, 43.4, 30.8, 16.3, 14.0; IR ν 2961 (w), 2247 (w), 1738 (s), 1583 (w), 1465 (w), 1431 (w), 1370 (w), 1327 (m), 1244 (s), 1205 (s), 1130 (m), 1094 (s), 1017 (s), 858 (w); HRMS (ESI) calcd. for $C_{16}H_{16}ClINaO_4^+$ $[M+Na]^+$ 456.9674; found 456.9681. One carbon was not resolved at 100 MHz.

6-Azido-1-ethoxy-1-oxohex-3-yn-2-yl 2-iodobenzoate (3s)

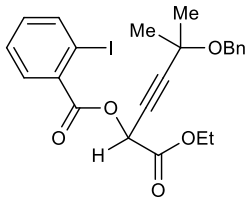


3s

Following general procedure **C**, (4-azidobut-1-ynyl)-1,2-benziodoxol-3(1H)-one (2i) (85 mg, 0.25 mmol, 1.0 equiv) (**2k**) and ethyl 2-diazoacetate (**1a**) (60 µL, 0.50 mmol, 13 wt. % dichloromethane, 2.0 equiv) were stirred for 6 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 1:9 as mobile phase affording **3s** (37.0 mg, 0.087 mmol, 35%) as a colorless oil. TLC (EtOAc:pentane, 1:9 v/v): R_f = 0.21, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04–7.98 (m, 2H, Ar*H*), 7.43 (td, *J* = 7.6, 1.2 Hz, 1H,

Ar*H*), 7.19 (td, *J* = 7.7, 1.7 Hz, 1H, Ar*H*), 5.94 (t, *J* = 2.2 Hz, 1H, OC*H*CC), 4.31 (q, *J* = 7.1 Hz, 2H, $CO_2CH_2CH_3$), 3.43 (t, *J* = 6.8 Hz, 2H, $CH_2CH_2N_3$), 2.58 (td, *J* = 6.9, 2.2 Hz, 2H, $CH_2CH_2N_3$), 1.33 (t, *J* = 7.2 Hz, 3H, $CO_2CH_2CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.4, 164.8, 141.5, 133.3, 133.1, 131.8, 128.0, 94.6, 84.9, 73.7, 63.6, 62.7, 49.3, 20.0, 14.0; IR ν 2982 (w), 2938 (w), 2250 (w), 2107 (m), 1739 (s), 1584 (w), 1465 (w), 1246 (s), 1208 (s), 1131 (m), 1096 (s), 1019 (m), 858 (w); HRMS (ESI) calcd. for $C_{15}H_{14}IN_3NaO_4^+$ $[M+Na]^+$ 449.9921; found 449.9925.

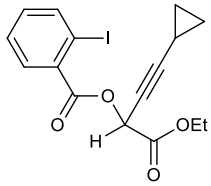
5-(Benzyloxy)-1-ethoxy-5-methyl-1-oxohex-3-yn-2-yl 2-iodobenzoate (3t)



3t

Following general procedure **A**, 3-(benzyloxy)-3-methyl-but-1-yn-1-yl)-1,2-benziodoxol-3(1H)-one (**2l**) (105 mg, 0.250 mmol, 1.00 equiv) and ethyl 2-diazoacetate (**1a**) (60 µL, 0.50 mmol, 13 wt. % dichloromethane, 2.0 equiv) were stirred for 1 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 1:50 as mobile phase affording **3t** (72.0 mg, 0.142 mmol, 57%) as a colorless oil. TLC (EtOAc:pentane, 1:40 v/v): R_f = 0.16, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02 (dd, *J* = 7.9, 1.1 Hz, 1H, Ar*H*), 7.99 (dd, *J* = 7.8, 1.7 Hz, 1H, Ar*H*), 7.43 (td, *J* = 7.6, 1.2 Hz, 1H, Ar*H*), 7.39–7.30 (m, 4H, Ar*H*), 7.29–7.23 (m, 1H, Ar*H*), 7.19 (td, *J* = 7.7, 1.7 Hz, 1H, Ar*H*), 6.02 (s, 1H, OC*H*CC), 4.64 (s, 2H, $ArCH_2$), 4.40–4.16 (m, 2H, CH_2CH_3), 1.57 (s, 6H, $C(CH_3)_2$), 1.31 (t, *J* = 7.1 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.4, 164.8, 141.5, 138.7, 133.3, 133.2, 131.8, 128.3, 128.0, 127.7, 127.4, 94.5, 90.3, 75.8, 70.6, 66.8, 63.5, 62.7, 28.5, 28.5, 14.0; IR ν 2987 (w), 2934 (w), 2867 (w), 2248 (w), 1741 (s), 1584 (w), 1463 (m), 1376 (w), 1240 (s), 1207 (s), 1162 (s), 1096 (s), 1025 (s), 934 (w), 858 (w); HRMS (ESI) calcd. for $C_{23}H_{23}INaO_5^+$ $[M+Na]^+$ 529.0482; found 529.0493.

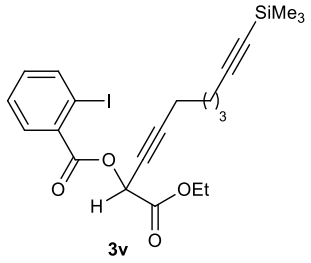
4-Cyclopropyl-1-ethoxy-1-oxobut-3-yn-2-yl 2-iodobenzoate (3u)



3u

Following general procedure **A**, 2-cyclopropylethynyl-1,2-benziodoxol-3(1H)-one (**2m**) (78 mg, 0.25 mmol, 1.0 equiv) and ethyl 2-diazoacetate (**1a**) (60 µL, 0.50 mmol, 13 wt. % dichloromethane, 2.0 equiv) were stirred for 4 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 1:30 as mobile phase affording **3u** (62.0 mg, 0.156 mmol, 63%) as a colorless oil. TLC (EtOAc:pentane, 1:20 v/v): R_f = 0.3, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02–7.97 (m, 2H, Ar*H*), 7.42 (td, *J* = 7.6, 1.2 Hz, 1H, Ar*H*), 7.18 (td, *J* = 7.7, 1.7 Hz, 1H, Ar*H*), 5.88 (d, *J* = 2.1 Hz, 1H, OC*H*CC), 4.29 (q, *J* = 7.1 Hz, 2H, C*H*$_2$CH$_3$), 1.35–1.27 (m, 4H, CH$_2$C*H*$_3$ and cy-C*H*), 0.85–0.72 (m, 4H, cy-C*H*$_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.8, 165.0, 141.5, 133.3, 133.2, 131.7, 127.9, 94.5, 92.3, 66.6, 64.0, 62.5, 14.0, 8.4, -0.5; IR ν 3017 (w), 2247 (w), 1737 (s), 1582 (w), 1465 (w), 1430 (w), 1368 (w), 1326 (m), 1244 (s), 1214 (s), 1129 (m), 1094 (s), 1019 (s), 925 (w), 856 (w), 815 (w); HRMS (ESI) calcd. for $C_{16}H_{16}IO_4^+$ $[M+H]^+$ 399.0088; found 399.0088.

1-Ethoxy-1-oxo-10-(trimethylsilyl)deca-3,9-diyn-2-yl 2-iodobenzoate (3v)

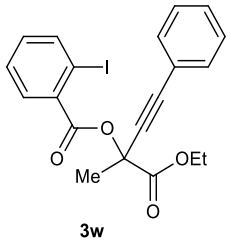


3v

Following general procedure **A**, 8-(trimethylsilyl)octa-1,7-diyn-1-yl-1,2-benziodoxol-3(1H)-one (**2n**) (106 mg, 0.250 mmol, 1.00 equiv) and ethyl 2-diazoacetate (**1a**) (60 µL, 0.50 mmol, 13 wt. % dichloromethane, 2.0 equiv) were stirred for 1 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 1:30 as mobile phase affording **3v** (95.0 mg, 0.186 mmol, 75%) as a colorless oil. TLC (EtOAc:pentane, 1:20 v/v): R_f = 0.29, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.03–7.97 (m, 2H, Ar*H*), 7.43 (td, *J* = 7.6, 1.2 Hz, 1H, Ar*H*), 7.18 (td, *J* = 7.7, 1.7 Hz, 1H, Ar*H*), 5.92 (t, *J* = 2.3 Hz, 1H, OC*H*CC), 4.30 (qd, *J*

= 7.2, 2.1 Hz, 2H, C*H*$_2$CH$_3$), 2.35–2.20 (m, 4H, 2 X C*H*$_2$), 1.69–1.61(m, 4H, 2 X C*H*$_2$), 1.33 (t, *J* = 7.1 Hz, 3H, CH$_2$C*H*$_3$), 0.14 (s, 9H, TMS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.9, 165.0, 141.5, 133.3, 133.2, 131.7, 128.0, 106.7, 94.5, 88.8, 84.8, 71.8, 63.9, 62.5, 27.5, 28.0, 19.3, 18.4, 14.0, 0.1; IR ν 2953 (w), 2246 (w), 2173 (w), 1739 (s), 1584 (w), 1464 (w), 1430 (w), 1247 (s), 1204 (m), 1131 (m), 1094 (s), 1018 (m), 842 (s); HRMS (ESI) calcd. for $C_{22}H_{27}INaO_4Si^+$ $[M+Na]^+$ 533.0616; found 533.0629.

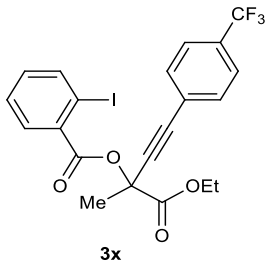
1-Ethoxy-2-methyl-1-oxo-4-phenylbut-3-yn-2-yl 2-iodobenzoate (3w)



3w

Following general procedure **B**, 1-[phenylethynyl]-1,2-benziodoxol-3(1H)-one (**2e**) (87 mg, 0.25 mmol, 1.0 equiv) and ethyl 2-diazopropanoate (**1b**) (64 mg, 0.50 mmol, 2.0 equiv) were stirred for 4 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 1:25 as mobile phase affording **3w** (87.0 mg, 0.194 mmol, 78%) as a colorless oil. TLC (EtOAc:pentane, 1:15 v/v): R_f = 0.21, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02–7.96 (m, 1H, Ar*H*), 7.88 (dd, *J* = 7.8, 1.6 Hz, 1H, Ar*H*), 7.50 (dd, *J* = 7.6, 1.9 Hz, 2H, Ar*H*), 7.42 (td, *J* = 8.5, 7.7, 1.0 Hz, 1H, Ar*H*), 7.37–7.27 (m, 3H, Ar*H*), 7.17 (td, *J* = 7.7, 1.7 Hz, 1H, Ar*H*), 4.34 (qq, *J* = 7.0, 3.6 Hz, 2H, C*H*$_2$CH$_3$), 2.03 (s, 3H, OCOCC*H*$_3$), 1.35 (t, *J* = 7.1 Hz, 3H, CH$_2$C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.4, 164.7, 141.3, 134.4, 132.9, 132.0, 131.3, 128.8, 128.2, 127.9, 121.9, 94.0, 86.5, 85.1, 74.2, 62.6, 25.9, 14.1; IR ν 2988 (w), 2938 (w), 2238 (w), 1743 (s), 1583 (w), 1491 (w), 1465 (w), 1373 (w), 1291 (m), 1252 (s), 1132 (s), 1095 (m), 1072 (m), 1018 (m), 863 (w); HRMS (ESI) calcd. for $C_{20}H_{17}INaO_4^+$ $[M+Na]^+$ 471.0064; found 471.0051.

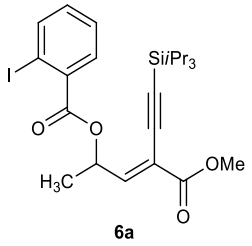
1-Ethoxy-2-methyl-1-oxo-4-(4-(trifluoromethyl)phenyl)but-3-yn-2-yl 2-iodobenzoate (3x)



3x

Following general procedure **B**, 1-[4-trifluoromethylphenylethynyl]-1,2-benziodoxol-3(1H)-one (**2h**) (104 mg, 0.250 mmol, 1.00 equiv) and ethyl 2-diazopropanoate (**1b**) (64 mg, 0.50 mmol, 2.0 equiv) were stirred for 4 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 1:25 as mobile phase affording **3x** (93 mg, 0.18 mmol, 72%) as a colorless oil. TLC (EtOAc:pentane, 1:10 v/v): R_f = 0.31, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01 (dd, *J* = 7.9, 0.9 Hz, 1H, Ar*H*), 7.88 (dd, *J* = 7.8, 1.6 Hz, 1H, Ar*H*), 7.64–7.54 (m, 4H, Ar*H*), 7.43 (td, *J* = 7.7, 1.0 Hz, 1H, Ar*H*), 7.18 (td, *J* = 7.7, 1.7 Hz, 1H, Ar*H*), 4.42–4.26 (m, 2H, C*H*$_2$CH$_3$), 2.03 (s, 3H, OCOCC*H*$_3$), 1.35 (t, *J* = 7.1 Hz, 3H, CH$_2$C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.2, 164.7, 141.4, 134.2, 133.0, 132.2, 131.3, 130.5 (q, *J* = 32.8 Hz), 127.9, 125.7, 125.1 (q, *J* = 3.7 Hz), 123.9 (d, *J* = 272.4 Hz), 94.1, 87.5, 85.0, 73.8, 62.8, 25.9, 14.0; IR ν 2988 (w), 1750 (s), 1618 (w), 1325 (s), 1253 (s), 1169 (m), 1131 (s), 1072 (m), 1019 (m), 848 (w); HRMS (ESI) calcd. for $C_{21}H_{16}F_3INaO_4^+$ $[M+Na]^+$ 538.9938; found 538.9935.

(*E*)-4-(Methoxycarbonyl)-6-(tri*iso*propylsilyl)hex-3-en-5-yn-2-yl 2-iodobenzoate (6a)

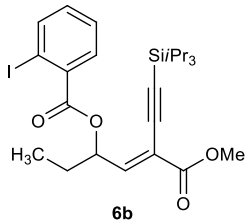


6a

Following general procedure **C**, 1-[(tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2a**) (107 mg, 0.250 mmol, 1.00 equiv) and (*E*)-methyl 2-diazopent-3-enoate (**5a**) (70 mg, 0.50 mmol, 2.0 equiv) were stirred for 1 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 1:60 as mobile phase affording **6a** (122 mg, 0.226 mmol, 90%) as a colorless oil. TLC (EtOAc:pentane, 1:60 v/v): R_f = 0.13, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92 (dd, *J* = 7.9, 1.2 Hz, 1H, Ar*H*), 7.73 (dd, *J* = 7.8, 1.7 Hz, 1H, Ar*H*), 7.33 (td, *J* = 7.6, 1.2 Hz, 1H, Ar*H*), 7.21 (d, *J* = 7.7 Hz, 1H, CH$_3$CHC*H*), 7.08 (td, *J* = 7.7,

1.7 Hz, 1H, Ar*H*), 5.98 (dq, *J* = 7.7, 6.6 Hz, 1H, CH_3CHCH), 3.73 (s, 3H, OCH_3), 1.51 (d, *J* = 6.6 Hz, 3H, CH_3CHCH), 1.12–0.93 (m, 21H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.5, 164.5, 150.6, 141.3, 135.0, 132.7, 131.0, 127.9, 117.6, 102.3, 98.4, 94.0, 71.2, 52.6, 18.9, 18.6, 11.2; IR ν 2945 (m), 2865 (m), 2153 (w), 1732 (s), 1585 (w), 1464 (m), 1436 (w), 1283 (m), 1249 (s), 1131 (m), 1101 (m), 1041 (m), 1017 (m), 884 (w), 851 (w); HRMS (ESI) calcd. for $C_{24}H_{33}INaO_4Si^+$ $[M+Na]^+$ 563.1085; found 563.1092.

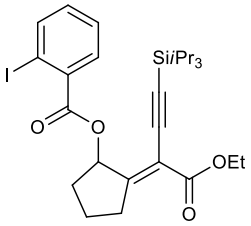
(*E*)-5-(Methoxycarbonyl)-7-(tri*iso*propylsilyl)hept-4-en-6-yn-3-yl 2-iodobenzoate (6b)



6b

Following general procedure **C**, 1-[(tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2a**) (107 mg, 0.250 mmol, 1.00 equiv) and (*E*)-methyl 2-diazohex-3-enoate (**5b**) (77 mg, 0.50 mmol, 2.0 equiv) were stirred for 1 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 1:60 as mobile phase affording **6b** (111 mg, 0.200 mmol, 80%) as a colorless oil. TLC (EtOAc:pentane, 1:40 v/v): R_f = 0.32, $KMnO_4$; ^1H NMR (400 MHz, $CDCl_3$): δ 7.99 (dd, *J* = 7.9, 1.2 Hz, 1H, Ar*H*), 7.81 (dd, *J* = 7.8, 1.7 Hz, 1H, Ar*H*), 7.40 (td, *J* = 7.6, 1.2 Hz, 1H, Ar*H*), 7.21 (d, *J* = 8.0 Hz, 1H, CH_2CHCH), 7.15 (td, *J* = 7.7, 1.7 Hz, 1H, Ar*H*), 5.97–5.88 (m, 1H, CH_2CHCH), 3.80 (s, 3H, OCH_3), 2.08–1.80 (m, 2H, CH_2CH_3) 1.17–1.01 (m, 24H, TIPS and CH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.6, 164.4, 149.6, 141.3, 135.1, 132.6, 131.0, 127.9, 118.3, 101.8, 98.7, 94.0, 75.6, 52.6, 26.7, 18.6, 11.2, 9.6; IR ν 2944 (m), 2865 (m), 2725 (w), 2153 (w), 1731 (s), 1584 (w), 1464 (m), 1435 (m), 1241 (s), 1096 (m), 1016 (m), 883 (m), 852 (w); HRMS (ESI) calcd. for $C_{25}H_{36}IO_4Si^+$ $[M+H]^+$ 555.1422; found 555.1441.

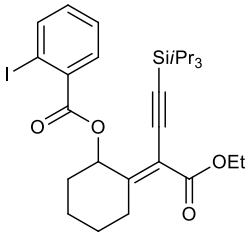
(*E*)-2-(1-Ethoxy-1-oxo-4-(tri*iso*propylsilyl)but-3-yn-2-ylidene)cyclopentyl 2-iodobenzoate (6c)



6c

Following general procedure **C**, 1-[(tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2a**) (107 mg, 0.250 mmol, 1.00 equiv) and ethyl 2-(cyclopent-1-en-1-yl)-2-diazoacetate (**5c**) (90 mg, 0.50 mmol, 2.0 equiv) were stirred for 1 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 1:60 as mobile phase affording **6c** (87 mg, 0.15 mmol, 60%) as a white solid. Mp: 95.4–99.2 °C; TLC (EtOAc:pentane, 1:60 v/v): R_f = 0.14, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99 (dd, *J* = 7.9, 1.2 Hz, 1H, Ar*H*), 7.90 (dd, *J* = 7.8, 1.8 Hz, 1H, Ar*H*), 7.35 (td, *J* = 7.6, 1.2 Hz, 1H, Ar*H*), 7.12 (td, *J* = 7.7, 1.8 Hz, 1H, Ar*H*), 6.10–6.04 (m, 1H, OC*H*CH_2), 4.23 (qd, *J* = 7.2, 2.4 Hz, 2H, C*H*$_2$$CH_3$), 3.20–3.04 (m, 1H, cy-*H*), 2.93–2.71 (m, 1H, cy-*H*), 2.18–1.76 (m, 4H, cy-*H*), 1.31 (t, *J* = 7.2 Hz, 3H, CH_2C*H*$_3$), 1.04–0.88 (m, 21H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.4, 164.9, 164.8, 141.5, 133.9, 132.7, 131.72, 127.7, 114.6, 101.0, 97.9, 94.5, 78.9, 61.1, 33.0, 32.9, 23.9, 18.5, 14.1, 11.2; IR ν (w), 3063 (w), 2943 (m), 2865 (m), 2722 (w), 2148 (w), 1721 (s), 1464 (m), 1274 (s), 1245 (s), 1205 (s), 1112 (s), 1017 (s), 885 (m); HRMS (ESI) calcd. for $C_{27}H_{38}IO_4Si^+$ $[M+H]^+$ 581.1579; found 581.1581.

(*E*)-2-(1-Ethoxy-1-oxo-4-(tri*iso*propylsilyl)but-3-yn-2-ylidene)cyclohexyl 2-iodobenzoate (6d)

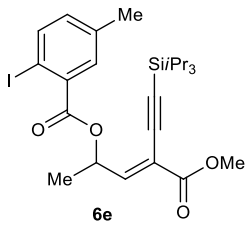


6d

Following general procedure **C**, 1-[(tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2a**) (107 mg, 0.250 mmol, 1.00 equiv) and ethyl 2-(cyclohex-1-en-1-yl)-2-diazoacetate (**5d**) (97 mg, 0.50 mmol, 2.0 equiv) were stirred for 3 h. The crude reaction mixture was concentrated in vacuo

and purified by flash chromatography using EtOAc:pentane 1:60 as mobile phase affording **6d** (105 mg, 0.177 mmol, 71%) as a colorless oil. TLC (EtOAc:pentane, 1:40 v/v): R_f = 0.22, $KMnO_4$; ^1H NMR (400 MHz, $CDCl_3$): δ 7.97 (d, *J* = 7.9 Hz, 1H, Ar*H*), 7.75 (dd, *J* = 7.9, 1.7 Hz, 1H, Ar*H*), 7.39 (t, *J* = 7.6 Hz, 1H, Ar*H*), 7.13 (t, *J* = 7.6 Hz, 1H, Ar*H*), 6.43 (s, 1H, OC*H*CH_2), 4.23 (q, *J* = 7.1 Hz, 2H, C*H*$_2$$CH_3$), 3.39 (d, *J* = 13.5 Hz, 1H, cy-*H*), 2.40 (td, *J* = 13.6, 4.8 Hz, 2H, cy-*H*), 2.06–1.78 (m, 2H, cy-*H*), 1.77–1.56 (m, 2H, cy-*H*), 1.48 (tt, *J* = 13.3, 3.7 Hz, 1H, cy-*H*), 1.31 (t, *J* = 7.1 Hz, 3H, CH_2C*H*$_3$), 1.11 (s, 21H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.2, 165.0, 157.7, 141.1, 135.8, 132.3, 130.8, 127.8, 113.7, 100.2, 98.6, 93.7, 73.9, 61.2, 31.9, 27.6, 27.5, 20.5, 18.7, 14.0, 11.3; IR ν 3429 (w), 2942 (m), 2864 (m), 2148 (w), 1724 (s), 1585 (w), 1464 (m), 1286 (m), 1243 (s), 1217 (s), 1110 (s), 1017 (m), 934 (m), 881 (m); HRMS (ESI) calcd. for $C_{28}H_{39}INaO_4Si^+$ $[M+Na]^+$ 617.1555; found 617.1566.

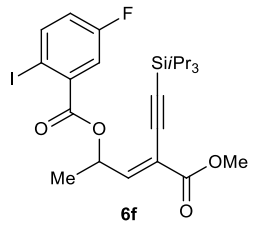
(*E*)-4-(Methoxycarbonyl)-6-(tri*iso*propylsilyl)hex-3-en-5-yn-2-yl 2-iodo-5-methylbenzoate (6e)



6e

Following general procedure **C**, 5-methyl-1-[(tri*iso*propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2b**) (111 mg, 0.250 mmol, 1.00 equiv) and (*E*)-methyl 2-diazopent-3-enoate (**5a**) (70 mg, 0.50 mmol, 2.0 equiv) were stirred for 3 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 1:60 as mobile phase affording **6e** (112 mg, 0.202 mmol, 81%) as a colorless oil. TLC (EtOAc:pentane, 1:40 v/v): R_f = 0.24, $KMnO_4$; ^1H NMR (400 MHz, $CDCl_3$): δ 7.83 (d, *J* = 8.1 Hz, 1H, Ar*H*), 7.60 (d, *J* = 1.8 Hz, 1H, Ar*H*), 7.28 (d, *J* = 7.6 Hz, 1H, CH_3CHC*H*), 7.05–6.89 (m, 1H, Ar*H*), 6.04 (dq, *J* = 7.7, 6.6 Hz, 1H, CH_3C*H*CH), 3.80 (s, 3H, OC*H*$_3$), 2.33 (s, 3H, ArC*H*$_3$), 1.58 (d, *J* = 6.6 Hz, 3H, C*H*$_3$CHCH), 1.16–1.07 (m, 21H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.6, 164.5, 150.7, 141.0, 138.1, 134.7, 133.7, 131.7, 117.6, 102.2, 98.4, 89.9, 71.1, 52.6, 20.8, 18.9, 18.6, 11.2; IR ν 2945 (m), 2865 (m), 2153 (w), 1731 (s), 1464 (m), 1288 (m), 1248 (s), 1200 (s), 1106 (m), 1040 (m), 1014 (m), 883 (m), 852 (w); HRMS (ESI) calcd. for $C_{25}H_{35}INaO_4Si^+$ $[M+Na]^+$ 577.1242; found 577.1242.

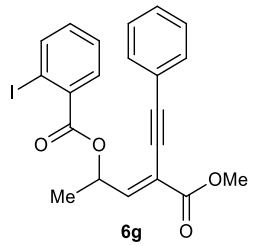
(E)-4-(Methoxycarbonyl)-6-(tri*iso*propylsilyl)hex-3-en-5-yn-2-yl 5-fluoro-2-iodobenzoate (6f)



6f

Following general procedure **C**, 5-fluoro-1-[(tri*iso*propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2c**) (112 mg, 0.250 mmol, 1.00 equiv) and (*E*)-methyl 2-diazopent-3-enoate (**5a**) (70 mg, 0.50 mmol, 2.0 equiv) were stirred for 3 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 1:60 as mobile phase affording **6f** (114 mg, 0.204 mmol, 82%) as a colorless oil. TLC (EtOAc:pentane, 1:40 v/v): R_f = 0.3, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 (dd, *J* = 8.7, 5.4 Hz, 1H, Ar*H*), 7.54 (dd, *J* = 9.0, 3.1 Hz, 1H, Ar*H*), 7.25 (d, *J* = 7.8 Hz, 1H, CH_3CHCH), 6.93 (ddd, *J* = 8.7, 7.7, 3.1 Hz, 1H, Ar*H*), 6.04 (dq, *J* = 7.7, 6.6 Hz, 1H, CH_3CHCH), 3.80 (s, 3H, OCH_3), 1.58 (d, *J* = 6.7 Hz, 3H, CH_3CHCH), 1.14–1.07 (m, 21H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.4, 164.3 (d, *J* = 2.2 Hz), 162.4 (d, *J* = 249.4 Hz), 150.0, 142.7 (d, *J* = 7.2 Hz), 136.4 (d, *J* = 6.9 Hz), 120.3 (d, *J* = 21.4 Hz), 118.5 (d, *J* = 24.2 Hz), 117.9, 102.4, 98.3, 87.1 (d, *J* = 3.5 Hz), 71.5, 52.7, 18.9, 18.6, 11.2; IR ν 2947 (m), 2866 (m), 2153 (w), 1733 (s), 1464 (m), 1291 (m), 1248 (s), 1196 (s), 1041 (w), 885 (w); HRMS (ESI) calcd. for $C_{24}H_{32}FINaO_4Si^+$ $[M+Na]^+$ 581.0991; found 581.0995.

(*E*)-4-(Methoxycarbonyl)-6-phenylhex-3-en-5-yn-2-yl 2-iodobenzoate (6g)

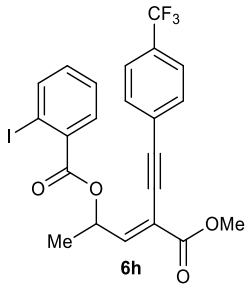


6g

Following general procedure **D**, 1-[phenylethynyl]-1,2-benziodoxol-3(1H)-one (**2e**) (87 mg, 0.25 mmol, 1.0 equiv) and (*E*)-methyl 2-diazopent-3-enoate (**5a**) (70 mg, 0.50 mmol, 2.0 equiv) were stirred for 4 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 1:25 as mobile phase affording **6g** (94.0 mg, 0.204 mmol,

82%) as a colorless oil. TLC (EtOAc:pentane, 1:10 v/v): R_f = 0.3, $KMnO_4$; ^1H NMR (400 MHz, $CDCl_3$): δ 7.99 (dd, *J* = 7.9, 1.1 Hz, 1H, Ar*H*), 7.82 (dd, *J* = 7.8, 1.7 Hz, 1H, Ar*H*), 7.57–7.49 (m, 2H, Ar*H*), 7.45–7.32 (m, 4H, Ar*H*), 7.30 (d, *J* = 7.7 Hz, 1H, CH_3CHCH), 7.15 (td, *J* = 7.7, 1.7 Hz, 1H, Ar*H*), 6.14 (dq, *J* = 7.7, 6.6 Hz, 1H, CH_3CHCH), 3.86 (s, 3H, OCH_3), 1.62 (d, *J* = 6.6 Hz, 3H, CH_3CHCH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.6, 164.5, 149.5, 141.3, 134.8, 132.7, 131.8, 131.1, 129.0, 128.3, 127.9, 122.3, 117.6, 98.8, 94.1, 81.5, 70.8, 52.8, 19.2; IR ν 2211 (w), 1729 (s), 1584 (w), 1492 (w), 1438 (w), 1252 (s), 1133 (m), 1105 (w), 1040 (m), 859 (w); HRMS (ESI) calcd. for $C_{21}H_{17}INaO_4^+$ $[M+Na]^+$ 483.0064; found 483.0069.

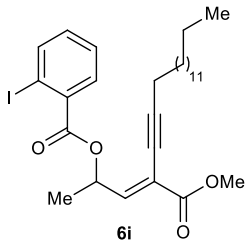
(*E*)-4-(Methoxycarbonyl)-6-(4-(trifluoromethyl)phenyl)hex-3-en-5-yn-2-yl 2-iodobenzoate (6h)



6h

Following general procedure **D**, 1-[4-trifluoromethylphenylethynyl]-1,2-benziodoxol-3(1H)-one (**2h**) (104 mg, 0.250 mmol, 1.00 equiv) and (*E*)-methyl 2-diazopent-3-enoate (**5a**) (70 mg, 0.50 mmol, 2.0 equiv) were stirred for 4 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 1:25 as mobile phase affording **6h** (99.0 mg, 0.187 mmol, 75%) as a colorless oil. TLC (EtOAc:pentane, 1:10 v/v): R_f = 0.33, $KMnO_4$; ^1H NMR (400 MHz, $CDCl_3$): δ 7.99 (dd, *J* = 8.0, 1.2 Hz, 1H, Ar*H*), 7.82 (dd, *J* = 7.8, 1.7 Hz, 1H, Ar*H*), 7.66–7.56 (m, 4H, Ar*H*), 7.39 (td, *J* = 7.6, 1.2 Hz, 1H, Ar*H*), 7.34 (d, *J* = 7.8 Hz, 1H, CH_3CHCH), 7.19–7.07 (m, 1H, Ar*H*), 6.13 (dq, *J* = 7.7, 6.6 Hz, 1H, CH_3CHCH), 3.86 (s, 3H, OCH_3), 1.62 (d, *J* = 6.7 Hz, 3H, CH_3CHCH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.5, 164.2, 150.5, 141.4, 134.6, 132.8, 132.0, 131.0, 130.61 (q, *J* = 32.7 Hz), 127.9, 126.0, 125.3 (q, *J* = 3.9 Hz), 123.8 (q, *J* = 272.4 Hz), 117.3, 97.0, 94.1, 83.7, 70.5, 52.9, 19.2; IR ν 2953 (w), 2214 (w), 1728 (s), 1618 (w), 1584 (w), 1436 (m), 1322 (s), 1247 (s), 1167 (s), 1126 (s), 1105 (s), 1063 (s), 1038 (s), 1016 (s), 976 (w), 844 (s); HRMS (ESI) calcd. for $C_{22}H_{16}F_3INaO_4^+$ $[M+Na]^+$ 550.9938; found 550.9941.

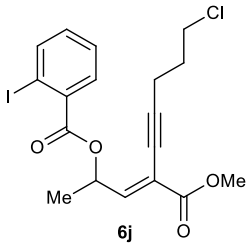
(*E*)-4-(Methoxycarbonyl)icos-3-en-5-yn-2-yl 2-iodobenzoate (6i)



6i

Following general procedure **C**, hexadecynyl-1,2-benziodoxol-3(1H)-one (**2i**) (117 mg, 0.250 mmol, 1.00 equiv) and (*E*)-methyl 2-diazopent-3-enoate (**5a**) (70 mg, 0.50 mmol, 2.0 equiv) were stirred for 2 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 1:60 as mobile phase affording **6i** (90.0 mg, 0.155 mmol, 62%) as a colorless oil. TLC (EtOAc:pentane, 1:40 v/v): R_f = 0.26, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99 (dd, *J* = 8.0, 1.1 Hz, 1H, Ar*H*), 7.81 (dd, *J* = 7.8, 1.7 Hz, 1H, Ar*H*), 7.40 (td, *J* = 7.6, 1.2 Hz, 1H, Ar*H*), 7.20–7.06 (m, 2H, Ar*H* and CH_3CHCH), 6.12–5.90 (m, 1H, CH_3CHCH), 3.80 (s, 3H, OCH_3), 2.42 (t, *J* = 7.1 Hz, 2H, $CCCH_2$), 1.63–1.56 (m, 2H, $CCCH_2CH_2$), 1.55 (d, *J* = 6.6 Hz, 3H, CH_3CHCH), 1.47–1.38 (m, 2H), 1.34–1.22 (m, 20H, 10 **X** CH_2), 0.87 (t, *J* = 6.8 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.5, 164.9, 148.4, 141.3, 134.9, 132.7, 131.0, 127.9, 117.9, 100.8, 94.1, 73.0, 70.9, 52.6, 31.9, 29.7, 29.6, 29.5, 29.3, 29.1, 28.9, 28.4, 22.7, 19.7, 19.1, 14.1; IR ν 2924 (m), 2854 (m), 2227 (w), 1729 (s), 1436 (w), 1281 (m), 1246 (s), 1132 (m), 1044 (m), 1017 (m); HRMS (ESI) calcd. for $C_{29}H_{41}INaO_4^+$ $[M+Na]^+$ 603.1942; found 603.1949. Some carbons were not resolved at 100 MHz.

(*E*)-9-Chloro-4-(methoxycarbonyl)non-3-en-5-yn-2-yl 2-iodobenzoate (6j)

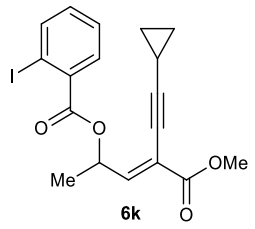


6j

Following general procedure **C**, (5-chloropent-1-ynyl)-1,2-benziodoxol-3(1H)-one (**2j**) (87 mg, 0.25 mmol, 1.0 equiv) and (*E*)-methyl 2-diazopent-3-enoate (**5a**) (70 mg, 0.50 mmol, 2.0 equiv) were stirred for 7 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 1:30 as mobile phase affording **6j** (61.0 mg, 0.132 mmol,

53%) as a colorless oil. TLC (EtOAc:pentane, 1:20 v/v): R_f = 0.24, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92 (dd, *J* = 7.9, 1.2 Hz, 1H, Ar*H*), 7.74 (dd, *J* = 7.8, 1.7 Hz, 1H, Ar*H*), 7.34 (td, *J* = 7.6, 1.2 Hz, 1H, Ar*H*), 7.15–7.01 (m, 2H, Ar*H* and CH_3CHCH), 5.94 (dq, *J* = 7.9, 6.6 Hz, 1H, CH_3CHCH), 3.74 (s, 3H, OCH_3), 3.65 (t, *J* = 6.3 Hz, 2H, $ClCH_2CH_2$), 2.57 (t, *J* = 6.8 Hz, 2H, $CCCH_2CH_2$), 1.99 (p, *J* = 6.7 Hz, 2H, $ClCH_2CH_2$), 1.48 (d, *J* = 6.7 Hz, 3H, CH_3CHCH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.5, 164.7, 148.8, 141.3, 134.8, 132.7, 131.0, 127.9, 117.7, 98.3, 94.1, 74.0, 70.7, 52.7, 43.6, 31.0, 19.1, 17.1; IR ν 2953 (w), 2850 (w), 2230 (w), 1725 (s), 1583 (w), 1435 (m), 1245 (s), 1133 (m), 1043 (m), 1016 (m), 912 (w), 854 (w); HRMS (ESI) calcd. for $C_{18}H_{18}ClINaO_4^+$ $[M+Na]^+$ 482.9831; found 482.9844.

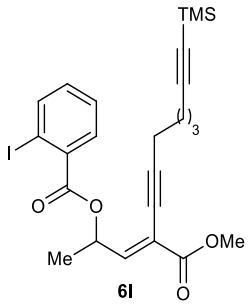
(*E*)-6-Cyclopropyl-4-(methoxycarbonyl)hex-3-en-5-yn-2-yl 2-iodobenzoate (6k)



6k

Following general procedure **C**, 2-cyclopropylethynyl-1,2-benziodoxol-3(1H)-one (**2m**) (78 mg, 0.25 mmol, 1.0 equiv) and (*E*)-methyl 2-diazopent-3-enoate (**5a**) (70 mg, 0.50 mmol, 2.0 equiv) were stirred for 7 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 1:25 as mobile phase affording **6k** (65.0 mg, 0.153 mmol, 61%) as a colorless oil. TLC (EtOAc:pentane, 1:20 v/v): R_f = 0.25, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): 7.99 (dd, *J* = 8.0, 1.2 Hz, 1H, Ar*H*), 7.80 (dd, *J* = 7.8, 1.7 Hz, 1H, Ar*H*), 7.40 (td, *J* = 7.6, 1.2 Hz, 1H, Ar*H*), 7.22–7.06 (m, 2H, Ar*H* and CH_3CHCH), 6.04–5.92 (m, 1H, CH_3CHCH), 3.79 (s, 3H, OCH_3), 1.53 (d, *J* = 6.6 Hz, 3H, CH_3CHCH), 1.46 (tt, *J* = 8.2, 5.1 Hz, 1H, cy-C*H*), 0.96–0.70 (m, 4H, 2 X cy-CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.5, 164.8, 148.4, 141.3, 134.8, 132.7, 131.0, 127.9, 117.9, 103.8, 94.1, 70.8, 68.1, 52.7, 19.1, 9.1, 9.0, 0.5; IR ν 2951 (w), 2221 (w), 1724 (s), 1583 (w), 1434 (w), 1283 (m), 1245 (s), 1165 (w), 1132 (m), 1100 (m), 1038 (m), 1016 (m), 996 (w), 917 (w), 844 (w); HRMS (ESI) calcd. for $C_{18}H_{17}INaO_4^+$ $[M+Na]^+$ 447.0064; found 447.0065.

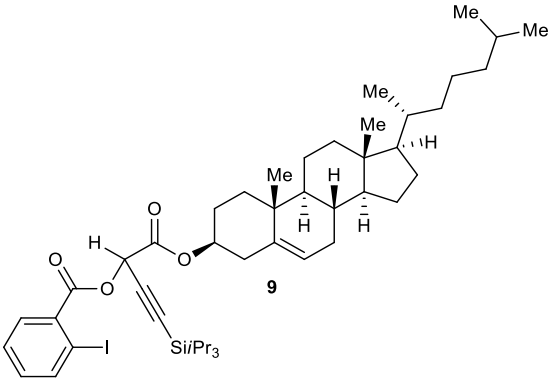
(*E*)-4-(Methoxycarbonyl)-12-(trimethylsilyl)dodeca-3-en-5,11-diyn-2-yl 2-iodobenzoate (6l)



6l

Following general procedure **C**, 8-(trimethylsilyl)octa-1,7-diyn-1-yl-1,2-benziodoxol-3(1H)-one (**2n**) (106 mg, 0.250 mmol, 1.00 equiv) and (*E*)-methyl 2-diazopent-3-enoate (**5a**) (70 mg, 0.50 mmol, 2.0 equiv) were stirred for 4 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 1:30 as mobile phase affording **6l** (96.0 mg, 0.179 mmol, 72%) as a colorless oil. TLC (EtOAc:pentane, 1:15 v/v): R_f = 0.31, $KMnO_4$; ^1H NMR (400 MHz, $CDCl_3$): δ 7.99 (dd, *J* = 7.9, 1.1 Hz, 1H, Ar*H*), 7.81 (dd, *J* = 7.8, 1.7 Hz, 1H, Ar*H*), 7.40 (td, *J* = 7.6, 1.2 Hz, 1H, Ar*H*), 7.23–7.04 (m, 2H, Ar*H* and CH_3CHCH), 6.02 (dq, *J* = 7.8, 6.6 Hz, 1H, CH_3CHCH), 3.80 (s, 3H, OCH_3), 2.54–2.37 (m, 2H, CH_2), 2.35–2.21 (m, 2H, CH_2), 1.77–1.59 (m, 4H, 2 X CH_2), 1.55 (d, *J* = 6.6 Hz, 3H, CH_3CHCH), 0.14 (s, 9H, TMS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.5, 164.8, 148.6, 141.3, 134.8, 132.7, 131.0, 127.9, 117.8, 106.9, 100.1, 94.1, 84.7, 73.4, 70.9, 52.7, 27.7, 27.4, 19.4, 19.2, 19.1, 0.1; IR ν 2953 (w), 2228 (w), 2173 (w), 1727 (s), 1435 (w), 1248 (s), 1132 (m), 1044 (m), 1021 (m), 845 (s); HRMS (ESI) calcd. for $C_{24}H_{29}INaO_4Si^+$ $[M+Na]^+$ 559.0772; found 559.0777.

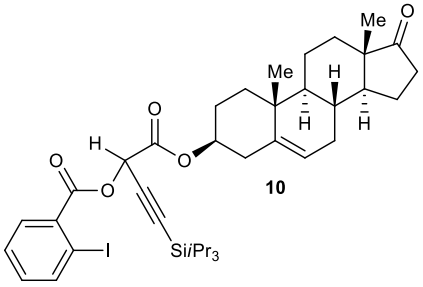
1-(((3S,8S,9S,10R,13R,14S,17R)-10,13-Dimethyl-17-((R)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl)oxy)-1-oxo-4-(tri*iso*propylsilyl)but-3-yn-2-yl 2-iodobenzoate (9)



9

Following general procedure **A**, 1-[(tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2a**) (107 mg, 0.250 mmol, 1.00 equiv) and 3S,8S,9S,10R,13R,14S,17R)-10,13-dimethyl-17-((R)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl 2-diazoacetate (**7**) (227 mg, 0.500 mmol, 2.00 equiv) were stirred for 1 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using Et_2O:pentane 1:60 as mobile phase affording **9** (175 mg, 0.205 mmol, 82%, 1:1 mixture of diastereoisomers as determined by ^{13}C NMR) as a thick colorless oil. TLC (Et_2O:pentane, 1:50 v/v): R_f = 0.2, $KMnO_4$; ^1H NMR (400 MHz, $CDCl_3$): δ 8.02–7.98 (m, 2H, Ar*H*), 7.44 (td, *J* = 7.6, 1.1 Hz, 1H, Ar*H*), 7.18 (td, *J* = 7.7, 1.7 Hz, 1H, Ar*H*), 5.96 (s, 1H, OC*H*CC), 5.42–5.31 (m, 1H, olefinic *H*), 4.74 (tt, *J* = 11.3, 4.4 Hz, 1H, OC*H*), 2.44–2.33 (m, 2H), 2.09–1.75 (m, 5H), 1.71–0.94 (m, 45H), 0.91 (d, *J* = 6.5 Hz, 3H), 0.86 (dd, *J* = 6.6, 1.8 Hz, 6H), 0.68 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.9, 164.8, 141.5, 139.2, 133.4, 133.2, 131.8, 128.0, 97.7, 94.5, 90.4, 64.0, 56.6, 56.1, 49.9, 42.3, 39.7, 39.5, 37.7, 37.6, 36.8, 36.5, 36.2, 35.8, 31.9, 31.8, 28.2, 28.0, 27.5, 27.3, 24.3, 23.8, 22.8, 22.5, 21.0, 19.2, 18.7, 18.5, 11.8, 11.0; IR ν 2943 (s), 2866 (s), 2189 (w), 1744 (s), 1584 (w), 1464 (m), 1377 (w), 1239 (s), 1205 (s), 1095 (s), 1016 (s), 884 (m); HRMS (ESI) calcd. for $C_{47}H_{71}INaO_4Si^+$ $[M+Na]^+$ 877.4059; found 877.4069.

1-(((3S,8R,9S,10R,13S,14S)-10,13-Dimethyl-17-oxo-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl)oxy)-1-oxo-4-(tri*iso*propylsilyl)but-3-yn-2-yl 2-iodobenzoate (10)



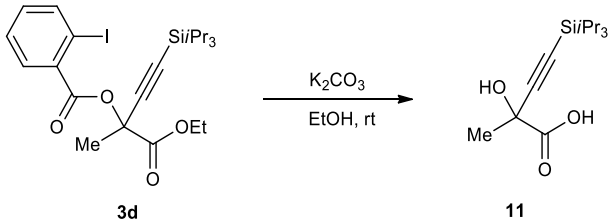
10

Following general procedure **A**, 1-[(tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2a**) (107 mg, 0.250 mmol, 1.00 equiv) and (3S,8R,9S,10R,13S,14S)-10,13-dimethyl-17-oxo-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl 2-diazoacetate (**8**) (178 mg, 0.500 mmol, 2.00 equiv) were stirred for 1 h. The crude reaction

mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 1:10 as mobile phase affording **10** (142 mg, 0.188 mmol, 75%, 1:1 mixture of diastereoisomers as determined by ^{13}C NMR) as a thick colorless oil. TLC (EtOAc:pentane, 1:10 v/v): R_f = 0.24, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02–7.98 (m, 2H, Ar*H*), 7.44 (t, *J* = 7.6 Hz, 1H, Ar*H*), 7.19 (t, *J* = 7.7 Hz, 1H, Ar*H*), 5.95 (s, 1H, OC*H*CC), 5.42 (t, *J* = 5.5 Hz, 1H, olefinic *H*), 4.78–4.70 (m, 1H, OC*H*), 2.54–2.30 (m, 3H), 2.16–2.04 (m, 2H), 2.01–1.78 (m, 4H), 1.76–1.58 (m, 4H), 1.58–1.40 (m, 2H), 1.32–1.25 (m, 2H), 1.19–0.97 (m, 26H), 0.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 221.0, 164.9, 164.8, 141.5, 139.4, 131.8, 128.0, 122.3, 97.7, 94.5, 90.5, 76.2, 64.0, 51.6, 50.0, 47.5, 37.7, 37.6, 36.8, 36.7, 35.8, 31.5, 31.4, 30.7, 27.4, 27.3, 21.9, 20.3, 19.3, 18.5, 13.5, 11.0; IR ν 3056 (w), 2948 (m), 2867 (m), 2190 (w), 1739 (s), 1464 (w), 1265 (s), 1212 (m), 1095 (m), 1018 (m), 885 (w); HRMS (ESI) calcd. for $C_{39}H_{53}INaO_5Si^+$ $[M+Na]^+$ 779.2599; found 779.2598. Other diastereomer, ^{13}C NMR (100 MHz, $CDCl_3$): 221.0, 164.9, 164.8, 139.4, 131.8, 97.7, 36.7. Some carbons are not resolved at 100 MHz.

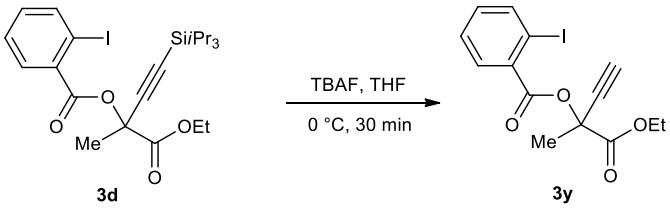
6. Product modifications

2-Hydroxy-2-methyl-4-(tri*iso*propylsilyl)but-3-ynoic acid (11)



Following a slightly modified procedure,[26] a flame dried 5 mL microwave vial with a rubber septum and magnetic stir bar was charged with compound **3d** (106 mg, 0.200 mmol, 1.00 equiv), K_2CO_3 (69 mg, 0.50 mmol, 2.5 equiv) and EtOH (2 mL). The mixture was stirred at room temperature for 36 h, then the solvent was evaporated and the crude product was purified by flash chromatography using CH_2Cl_2 to CH_2Cl_2:MeOH (7:1) as mobile phase affording **11** (51 mg, 0.19 mmol, 94%) as a white solid. Mp (Dec.): 156-160 °C; TLC (MeOH:CH_2Cl_2, 1:5 v/v): R_f = 0.29, $KMnO_4$; ^{1}H NMR (400 MHz, CD_3OD): δ 1.68 (s, 3H, OCOCC*H*$_3$), 1.15–1.01 (m, 21H, TIPS); ^{13}C NMR (100 MHz, CD_3OD): δ 177.7, 110.9, 84.2, 71.3, 29.3, 19.0, 12.5; IR ν 2943 (s), 2867 (s), 2176 (w), 1735 (m), 1663 (s), 1464 (s), 1381 (s), 1193 (s), 967 (m), 889 (s), 840 (m); HRMS (ESI) calcd. for $C_{14}H_{25}O_3Si$ $[M-H]^+$ 269.1573; found 269.1578.

1-Ethoxy-2-methyl-1-oxobut-3-yn-2-yl 2-iodobenzoate (3y)



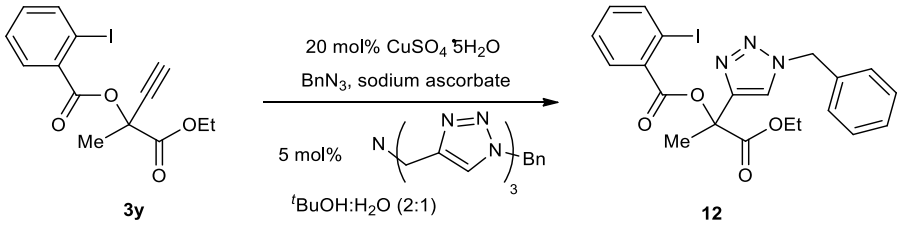
Following a reported procedure,[27] TIPS alkyne **3d** (1.05 g, 2.00 mmol, 1.00 equiv) was dissolved in dry THF (25 mL) in a flame dried flask and the solution was cooled to 0 °C. Then TBAF (2.4 mL, 2.4 mmol, 1.2 equiv, 1 M in hexanes) was added slowly and the reaction was left for 30 minutes at 0 °C and then quenched with saturated NH_4Cl solution (40 mL). The mixture was extracted with diethyl ether (3 x 20 mL) and the combined organic layers were dried over

[26] Janson, P. G.; Ghoneim, I.; Ilchenko, N. O.; Szabó, K. J. *Org. Lett.* **2012**, *14*, 2882–2885.

[27] Li, Y.; Waser, J. *Angew. Chem., Int. Ed.* **2015**, *54*, 5438–5442.

$MgSO_4$, filtered and concentrated in vacuo. The resulting crude product was purified by flash chromatography using EtOAc:pentane 1:15 as mobile phase affording **3y** (610 mg, 1.64 mmol, 82%) as a pale yellow oil. TLC (EtOAc:pentane, 1:15 v/v): R_f = 0.2, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00 (d, *J* = 7.9 Hz, 1H, Ar*H*), 7.86 (dd, *J* = 7.8, 1.5 Hz, 1H, Ar*H*), 7.42 (t, *J* = 7.6 Hz, 1H, Ar*H*), 7.17 (td, *J* = 7.7, 1.5 Hz, 1H, Ar*H*), 4.31 (qd, *J* = 7.1, 5.0 Hz, 2H, C*H*$_2$CH$_3$), 2.71 (s, 1H, CC*H*), 1.94 (s, 3H, OCOCC*H*$_3$), 1.33 (t, *J* = 7.1 Hz, 3H, CH$_2$C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.1, 164.5, 141.4, 133.9, 133.0, 131.4, 127.9, 94.1, 79.7, 75.1, 73.2, 62.7, 25.9, 14.0; IR ν 3283 (w), 2998 (w), 2122 (w), 1741 (s), 1583 (w), 1464 (w), 1373 (w), 1293 (s), 1252 (s), 1189 (m), 1130 (s), 1078 (s), 1013 (s), 860 (w); HRMS (ESI) calcd. for $C_{14}H_{13}INaO_4^+$ $[M+Na]^+$ 394.9751; found 394.9751.

2-(1-Benzyl-1H-1,2,3-triazol-4-yl)-1-ethoxy-1-oxopropan-2-yl 2-iodobenzoate (12)

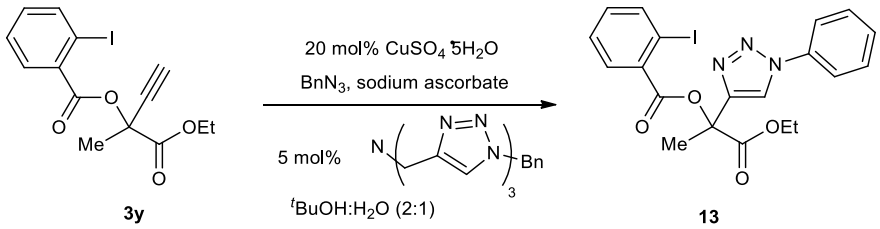


Following a reported procedure,[28] alkyne **3y** (50.0 mg, 0.134 mmol, 1.0 equiv), (azidomethyl)benzene (20 µL, 0.16 mmol, 1.2 equiv), sodium ascorbate (11 mg, 60 µmol, 0.40 equiv), $CuSO_4.5H_2O$ (5 mg, 0.03 mmol, 0.2 equiv) and tris((1-benzyl-1H-1,2,3-triazol-4-yl)methyl)amine (4.0 mg, 6.7 µmol, 0.05 equiv) were dissolved in 1.5 mL of ^{t}BuOH:H_2O (2:1) in an open flask and stirred for 2 h. The reaction mixture was diluted with water (20 mL) and extracted with CH_2Cl_2 (3×15 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated in vacuo. The resulting crude product was purified by flash chromatography using EtOAc:pentane 1:4 as mobile phase affording **12** (62.0 mg, 0.123 mmol, 91%) as a thick colorless oil. TLC (EtOAc:pentane, 1:4 v/v): R_f = 0.25, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 (dd, *J* = 7.9, 1.0 Hz, 1H, Ar*H*), 7.84 (s, 1H, C*H* triazole), 7.81 (dd, *J* = 7.8, 1.6 Hz, 1H, Ar*H*), 7.42–7.31 (m, 4H, Ar*H*), 7.30–7.25 (m, 2H, Ar*H*), 7.18–7.09 (m, 1H, Ar*H*), 5.52 (s, 2H. ArC*H*$_2$), 4.37–4.13 (m, 2H, C*H*$_2$CH$_3$), 2.17 (s, 3H, OCOCC*H*$_3$), 1.28 (t, *J* = 7.1 Hz, 3H, CH$_2$C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.1, 165.4, 145.8, 141.1, 134.5, 134.4, 132.8, 131.2,

[28] Deng, Q.-H.; Bleith, T.; Wadepohl, H.; Gade, L. H. *J. Am. Chem. Soc.* **2013**, *135*, 5356–5359.

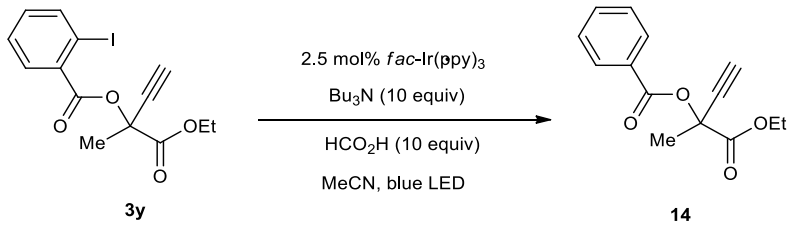
129.1, 128.7, 128.1, 127.9, 124.1, 93.8, 77.8, 62.1, 54.2, 23.7, 14.0; IR ν 2988 (w), 2939 (w), 1584 (w), 1462 (m), 1295 (s), 1256 (s), 1190 (m), 1134 (s), 1099 (s), 1048 (m), 1017 (m), 859 (w); HRMS (ESI) calcd. for $C_{21}H_{21}IN_3O_4^+$ $[M+H]^+$ 506.0571; found 506.0577.

1-Ethoxy-1-oxo-2-(1-phenyl-1H-1,2,3-triazol-4-yl)propan-2-yl 2-iodobenzoate (13)



Following a reported procedure,[28] alkyne **3y** (50.0 mg, 0.134 mmol, 1.00 equiv), azidobenzene (0.33 mL, 0.16 mmol, 1.2 equiv, 0.5 M in THF), sodium ascorbate (11 mg, 60 µmmol, 0.40 equiv), $CuSO_4.5H_2O$ (5 mg, 0.03 mmol, 0.2 equiv) and tris((1-benzyl-1H-1,2,3-triazol-4-yl)methyl)amine (4.0 mg, 6.7 µmol, 0.05 equiv) were dissolved in 1.5 mL of ^{t}BuOH:H_2O (2:1) in an open flask and stirred for 2 h. The reaction mixture was diluted with water (20 mL) and extracted with CH_2Cl_2 (3×15 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated in vacuo. The resulting crude product was purified by flash chromatography using EtOAc:pentane 1:5 as mobile phase affording **13** (54 mg, 0.11 mmol, 82%) as a thick colorless oil. TLC (EtOAc:pentane, 1:4 v/v): R_f = 0.29, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.37 (s, 1H, C*H* triazole), 7.97 (dd, *J* = 7.9, 1.1 Hz, 1H, Ar*H*), 7.88 (dd, *J* = 7.8, 1.8 Hz, 1H, Ar*H*), 7.78–7.73 (m, 2H, Ar*H*), 7.54–7.48 (m, 2H, Ar*H*), 7.46–7.37 (m, 2H, Ar*H*), 7.16 (td, *J* = 7.7, 1.7 Hz, 1H, Ar*H*), 4.34 (qt, *J* = 7.0, 3.6 Hz, 2H, C*H*$_2$CH$_3$), 2.24 (s, 3H, OCOCC*H*$_3$), 1.35 (t, *J* = 7.2 Hz, 3H, CH$_2$C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.2, 165.4, 146.1, 141.2, 136.9, 134.3, 133.0, 131.4, 129.7, 128.8, 128.0, 122.3, 120.6, 94.0, 77.7, 62.3, 23.9, 14.1; IR ν 3151 (w), 3066 (w), 2985 (w), 2934 (w), 2111 (w), 1735 (s), 1598 (w), 1504 (m), 1465 (m), 1295 (s), 1253 (s), 1115 (s), 1040 (s), 1017 (s), 911 (w), 859 (w); HRMS (ESI) calcd. for $C_{20}H_{19}IN_3O_4^+$ $[M+H]^+$ 492.0415; found 492.0415.

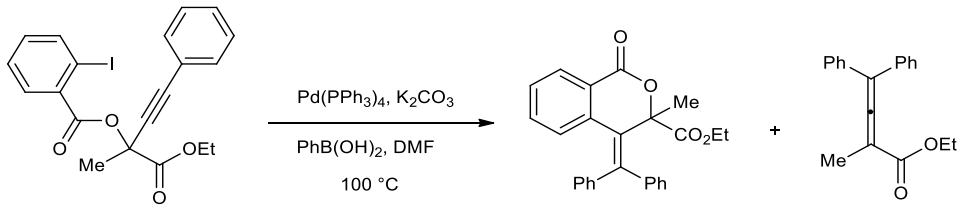
1-Ethoxy-2-methyl-1-oxobut-3-yn-2-yl benzoate (14)



Following a reported procedure,[29] A flame dried 2 mL microwave vial with a rubber septum and magnetic stirring bar was charged with aryl iodide **3y** (37.2 mg, 0.100 mmol, 1.00 equiv), MeCN (1.0 mL), tributylamine (180 mg, 1.00 mmol, 10.0 equiv), formic acid (46 mg, 1.0 mmol, 10 equiv) and *fac*-Ir(ppy)$_3$ (1.7 mg, 2.5 µmol, 0.025 equiv). The resulting reaction mixture was degassed by "pump-freeze-thaw" cycles (×2) *via* a syringe needle and placed in a 250 mL beaker with blue LEDs wrapped inside. The reaction mixture was stirred at 25−30 °C for 12 h. The solvent was removed from the crude mixture and was dissolved in EtOAc (10 mL), then transferred to a separatory funnel containing EtOAc (10 mL) and 2 M HCl (10 mL) solution. The layers were separated and the aqueous layer was extracted with EtOAc (2 × 10 mL). The combined organic layers were washed with saturated $NaHCO_3$ solution (10 mL), brine (10 mL), dried over $MgSO_4$, filtered and concentrated in vacuo. The resulting crude product was purified by flash chromatography using EtOAc:pentane 1:5 as mobile phase affording **14** (54 mg, 0.11 mmol, 82%) as a colorless oil. TLC (EtOAc:pentane, 1:4 v/v): R_f = 0.25, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.12–8.04 (m, 2H, Ar*H*), 7.62–7.55 (m, 1H, Ar*H*), 7.45 (t, *J* = 7.7 Hz, 2H, Ar*H*), 4.30 (qd, *J* = 7.1, 1.4 Hz, 2H, C*H*$_2$CH$_3$), 2.68 (s, 1H, CC*H*), 1.95 (s, 3H, OCOCC*H*$_3$), 1.30 (t, J = 7.1 Hz, 3H, CH$_2$C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.4, 164.8, 133.5, 129.9, 129.1, 128.4, 80.1, 74.7, 72.5, 62.6, 26.0, 13.9; IR ν 3275 (w), 2990 (w), 2122 (w), 1752 (s), 1731 (s), 1601 (w), 1451 (m), 1374 (w), 1282 (s), 1189 (m), 1131 (s), 1099 (s), 1022 (m), 860 (w); HRMS (ESI) calcd. for $C_{14}H_{14}NaO_4^+$ $[M+Na]^+$ 269.0784; found 269.0785.

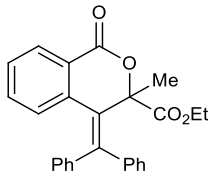
Ethyl 4-(diphenylmethylene)-3-methyl-1-oxo*iso*chroman-3-carboxylate (15) and ethyl 2-methyl-4,4-diphenylbuta-2,3-dienoate (16)

[29] Nguyen, J. D.; D'Amato, E. M.; Narayanam, J. M. R.; Stephenson, C. R. J. *Nat. Chem.* **2012**, *4*, 854–859.



3w **15** **16**

Following a reported procedure,[30] a mixture of 1-ethoxy-2-methyl-1-oxo-4-phenylbut-3-yn-2-yl 2-iodobenzoate (**3w**) (45 mg, 0.10 mmol, 1.0 equiv), $PhB(OH)_2$ (15 mg, 0.12 mmol, 1.2 equiv), K_2CO_3 (28 mg, 0.20 mmol, 2.0 equiv), $Pd(PPh_3)_4$ (6 mg, 5 µmol, 0.05 equiv) and DMF (1.0 mL) was placed in a 2 mL microwave vial under nitrogen. The resulting mixture was then heated under nitrogen at 100 °C. After 14 h, the reaction mixture was cooled to room temperature, quenched with saturated NH_4Cl solution (10 mL) and extracted with EtOAc (3 x 10 mL). The combined organic layers were washed with water (10 mL), brine (10 mL), dried over $MgSO_4$, filtered and concentrated under vacuo. The resulting crude product was purified by flash chromatography using EtOAc:pentane 1:10 as mobile phase affording **15** (24 mg, 60 µmol, 60%) as a pale yellow oil. In addition, the compound **16** was isolated as a pale yellow oil by flash chromatography using EtOAc:pentane 1:30 as mobile phase (7.0 mg, 25 µmol, 25%).

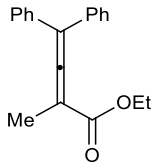


15

TLC (EtOAc:pentane, 1:10 v/v): R_f = 0.2, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99 (dd, *J* = 7.7, 1.4 Hz, 1H, Ar*H*), 7.71 (dt, *J* = 7.5, 1.6 Hz, 1H, Ar*H*), 7.42 (td, *J* = 7.4, 1.6 Hz, 1H, Ar*H*), 7.39–7.28 (m, 2H, Ar*H*), 7.27–7.22 (m, 1H, Ar*H*), 7.20–7.08 (m, 4H, Ar*H*), 7.05 (dt, *J* = 7.4, 1.7 Hz, 1H, Ar*H*), 6.98 (dd, *J* = 8.0, 1.6 Hz, 2H, Ar*H*), 6.82 (dd, *J* = 8.0, 1.1 Hz, 1H, Ar*H*), 3.97 (qd, *J* = 7.1, 1.2 Hz, 2H, C*H*$_2$CH$_3$), 1.38 (s, 3H, OCOCC*H*$_3$), 1.00 (t, *J* = 7.1 Hz, 3H, CH$_2$C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.1, 164.7, 146.3, 142.8, 141.9, 138.8, 132.3, 131.0, 131.0, 130.2, 130.0, 128.9, 128.7, 128.5, 128.3, 128.2, 128.2, 127.9, 127.7, 125.9, 86.6, 62.1, 24.9, 13.7; IR ν 3060 (w), 2985 (w), 2255 (w), 1733 (s), 1599 (w), 1451 (m), 1293 (m), 1254 (s), 1123 (m), 1075

[30] Guo, L.-N.; Duan, X.-H.; Hu, J.; Bi, H.-P.; Liu, X.-Y.; Liang, Y.-M. *Eur. J. Org. Chem.* **2008**, 1418–1425.

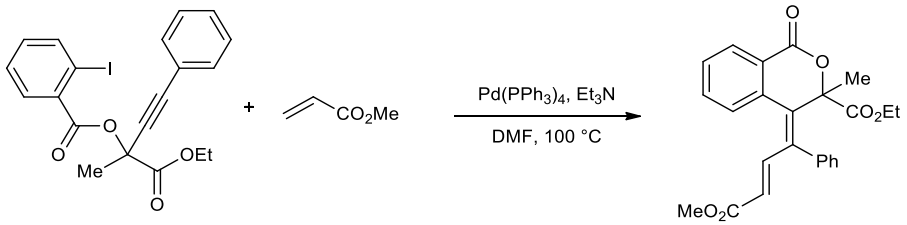
(s), 954 (w), 914 (w), 858 (w); HRMS (ESI) calcd. for $C_{26}H_{22}NaO_4^+$ $[M+Na]^+$ 421.1410; found 421.1417. Two carbons are not resolved at 100 MHz.



16

TLC (EtOAc:pentane, 1:20 v/v): R_f = 0.5, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40–7.30 (m, 10H, Ar*H*), 4.22 (q, *J* = 7.1 Hz, 2H, C*H*$_2$CH$_3$), 2.05 (s, 3H, OCOCC*H*$_3$), 1.29 (t, *J* = 7.1 Hz, 3H, CH$_2$C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 212.4, 167.3, 135.5, 128.7, 128.5, 127.9, 112.4, 98.2, 61.1, 15.2, 14.3; IR ν 3060 (w), 2983 (w), 1772 (w), 1714 (s), 1599 (w), 1491 (w), 1451 (w), 1371 (w), 1267 (s), 1120 (m), 1030 (w), 973 (w), 910 (w); HRMS (ESI) calcd. for $C_{19}H_{18}NaO_2^+$ $[M+Na]^+$ 301.1199; found 301.1205.

(Z)-Ethyl 4-((E)-4-methoxy-4-oxo-1-phenylbut-2-en-1-ylidene)-3-methyl-1-oxoisochroman-3-carboxylate (17)

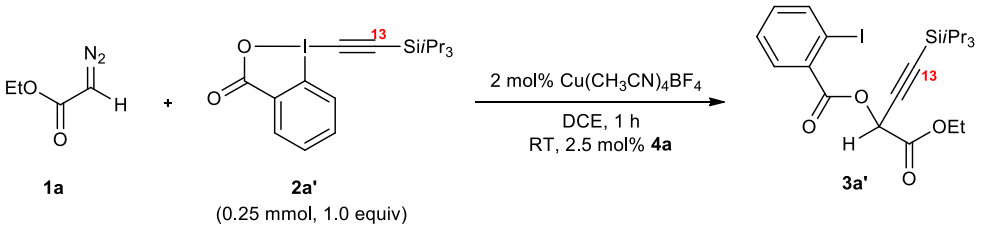


3w **17**

Following a reported procedure,[30] a mixture of 1-ethoxy-2-methyl-1-oxo-4-phenylbut-3-yn-2-yl 2-iodobenzoate (**3w**) (36 mg, 0.080 mmol, 1.0 equiv), methyl acrylate (8.3 mg, 0.096 mmol, 1.2 equiv), Et_3N (16.3 mg, 0.161 mmol, 2.00 equiv), $Pd(PPh_3)_4$ (4.6 mg, 4.0 µmol, 0.05 equiv) and DMF (1.0 mL) was placed in a 2 mL microwave vial under nitrogen. The resulting mixture was then heated under nitrogen at 100 °C. After 14 h, the reaction mixture was cooled to room temperature, quenched with saturated NH_4Cl (10 mL) solution and extracted with EtOAc (3 x 10 mL). The combined organic layers were washed with water (10 mL), brine (10 mL), dried over $MgSO_4$, filtered and concentrated under vacuo. The resulting crude product was purified by flash chromatography using EtOAc:pentane 1:4 as mobile phase affording **17** (7.5 mg, 19 µmol, 24%) as a thick colorless oil. TLC (EtOAc:pentane, 1:4 v/v): R_f = 0.25, $KMnO_4$; ^{1}H NMR (400 MHz,

$CDCl_3$): δ 8.12 (dd, *J* = 7.6, 1.4 Hz, 1H, Ar*H*), 7.83 (d, *J* = 15.5 Hz, 1H, C*H*CHCO$_2$Me), 7.65 (td, *J* = 7.6, 1.5 Hz, 1H, Ar*H*), 7.56 (td, *J* = 7.6, 1.2 Hz, 1H, Ar*H*), 7.47–7.38 (m, 5H, Ar*H*), 7.21–7.24 (m, 1H, Ar*H*), 5.50 (d, *J* = 15.5 Hz, 1H, CHC*H*CO$_2$Me), 3.95 (qd, *J* = 7.1, 1.1 Hz, 2H, C*H*$_2$CH$_3$), 3.69 (s, 3H, COOC*H*$_3$), 1.22 (s, 3H, C*H*$_3$CCO$_2$Et), 0.92 (t, *J* = 7.1 Hz, 3H, CH$_2$C*H*$_3$). ^{13}C NMR (100 MHz, $CDCl_3$): 170.7, 167.0, 163.8, 146.1, 140.0, 137.6, 136.3, 136.2, 133.2, 131.1, 130.5, 130.3, 130.2, 129.6, 128.8, 128.5, 128.2, 126.1, 125.9, 86.0, 62.2, 51.8, 24.3, 13.7. IR ν 2931 (w), 2858 (w), 1746 (s), 1610 (w), 1454 (w), 1294 (s), 1261 (m), 1176 (m), 1080 (w), 1024 (w), 868 (w); HRMS (ESI) calcd. for $C_{24}H_{22}NaO_6^+$ $[M+Na]^+$ 429.1309; found 429.1312.

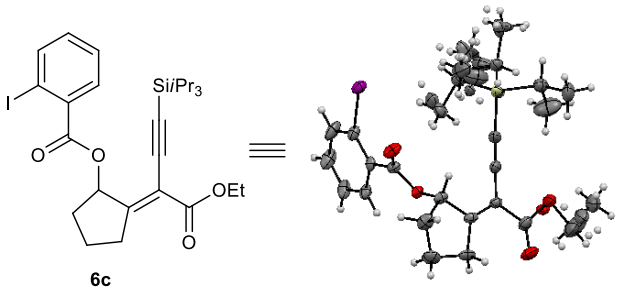
7. Reaction with ^{13}C labeled TIPS-EBX (2a') reagent



A flame dried 2 mL microwave vial under nitrogen was charged with $Cu(MeCN)_4BF_4$ (0.2 mg, 0.5 µmol, 0.02 equiv), 1,2 diimine ligand **4a** (0.30 mg, 0.63 µmol, 0.025 equiv) and dry DCE (0.5 mL). The resulting solution was stirred at room temperature for 30 min. To this solution was added a mixture of **2a'** (11.0 mg, 0.025 mmol, 1.00 equiv) and ethyl diazoacetate (**1a**) (6 µmol, 0.05 mmol, 2 equiv) in dry DCE (0.5 mL) in 2 min and the resulting reaction mixture was stirred at room temperature for 1 h. The solvent was evaporated under reduced pressure and the crude product was purified by column chromatography using EtOAc:pentane 1:40 as mobile phase affording **3a'** (11.0 mg, 0.021 mmol, 86%) as a colorless oil. TLC (EtOAc:pentane, 1:40 v/v): R_f = 0.15, $KMnO_4$; ^1H NMR (400 MHz, $CDCl_3$): δ 8.02 (dd, *J* = 7.9, 1.2 Hz, 1H, Ar*H*), 7.99 (dd, *J* = 7.8, 1.7 Hz, 1H, Ar*H*), 7.44 (td, *J* = 7.6, 1.2 Hz, 1H, Ar*H*), 7.19 (td, *J* = 7.7, 1.7 Hz, 1H, Ar*H*), 5.98 (s, 1H, OC*H*CC), 4.43–4.16 (m, 2H, C*H*$_2$CH$_3$), 1.32 (t, J = 7.1 Hz, 3H, CH$_2$C*H*$_3$), 1.11–1.06 (m, 21H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.4, 164.9, 141.5, 133.3, 133.2, 131.8, 128.0, 97.6, 94.6 , 90.6 (labeled 20 X more intense), 63.9, 62.6, 18.5, 14.0, 11.0; Comparison of the ^{13}C NMR with an unlabeled sample showed 20% ^{13}C incorporation at the indicated position only.

8. X-ray diffraction parameters and data for 6c

CCDC 1444412



Empirical formula	$C_{27}H_{37}IO_4Si$	
Formula weight	580.56	
Temperature	120(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1/n$	
Unit cell dimensions	a = 15.4542(13) Å	α= 90°.
	b = 11.4011(11) Å	β= 100.951(6)°.
	c = 16.3020(14) Å	γ = 90°.
Volume	2820.0(4) Å^3	
Z	4	
Density (calculated)	1.367 Mg/m^3	
Absorption coefficient	1.206 mm^{-1}	
F(000)	1192	
Crystal size	0.43 x 0.32 x 0.24 mm^3	
Theta range for data collection	2.68 to 30.00°.	
Index ranges	$-21 \le h \le 18$, $-16 \le k \le 15$, $-22 \le l \le 22$	
Reflections collected	38860	
Independent reflections	8180 [R(int) = 0.0348]	
Completeness to theta = 30.00°	99.7 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7460 and 0.6682	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	8180 / 0 / 402	
Goodness-of-fit on F^2	1.144	

Final R indices [I>2sigma(I)]	R1 = 0.0367, wR2 = 0.0616
R indices (all data)	R1 = 0.0655, wR2 = 0.0729
Largest diff. peak and hole	0.657 and -0.634 e.Å^{-3}