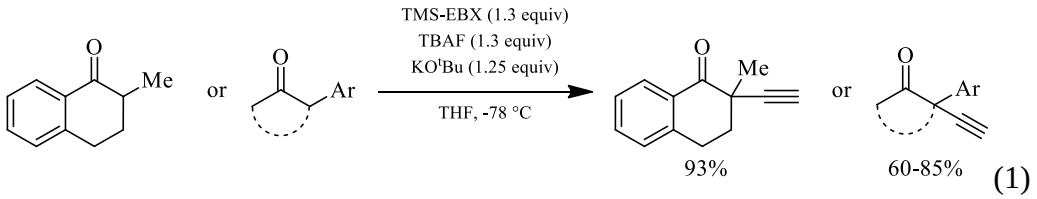
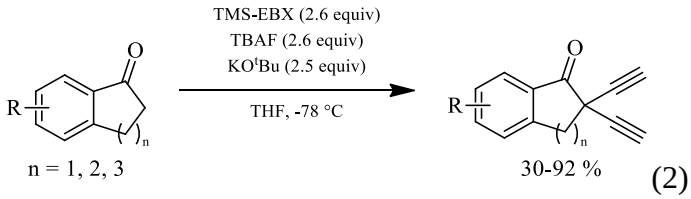
Alkynylation Reactions with TMS-EBX.

Alkynylations of C-Nucleophiles. After the alkynylation of β-ketoesters and other activated enolates with TMS-EBX was first reported in 2010,[7] it has been applied in the total synthesis of several complex natural products, including (−)-lingzhiol,[17] azadirachtin,[18] retigeranic acid,[19] perforanoid A,[20] and (+)-batzelladine B,[21] showing the robustness and versatility of this method. In addition, the scope of this transformation has been extended to other substrates than stabilized enolates, and enantioselective variants of the reaction have been studied.

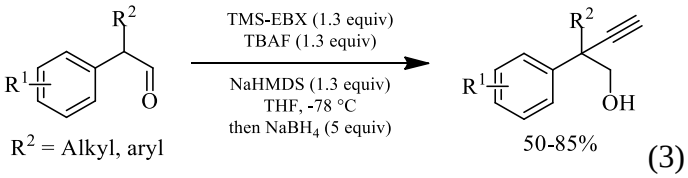
Alkynylation of Aromatic Ketones and Aldehydes. The α-ethynylation of ketones can be achieved with TMS-EBX in presence of KO^{t}Bu and TBAF as a source of fluoride, delivering directly the unprotected acetylene products.[22] Substrates bearing a substituent on the α-position are converted into mono-alkynylated derivatives in good to excellent yields (eq 1). Dialkynylation products are instead obtained starting from unsubstituted ketones (eq 2). In both cases, the transformation is limited to aryl or benzyl ketones. α-Arylaldehydes can be similarly alkynylated using TMS-EBX using NaHMDS as base.[23] In situ reduction using $NaBH_4$ provides propargyl alcohols in good to very good yields (eq 3).



(1)



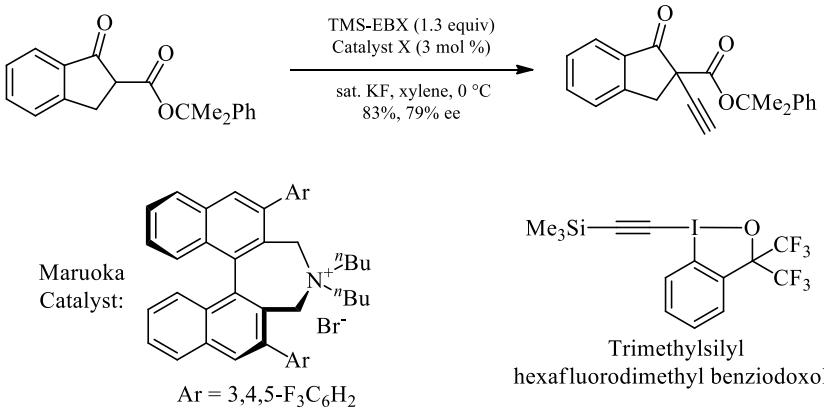
(2)



(3)

Alknylation of C-H Acidic Heterocycles TMS-EBX is utilized for the alkynylation of several C-H acidic nitrogen- or sulfur-containing heterocycles, including pyrazolones, rhodanine, azlactones, and oxindoles.[24,25,26] The reaction is performed in the presence of a tertiary amine[24,25] or TMG (tetramethyl guanidine)[26] as the base and occurs with concurrent desilylation of the alkyne in good to excellent yields. The alkynylated azlactones have been used for the synthesis of acetylene-containing C^{α}-tetrasubstituted α-amino acids derivatives.[25]

Enantioselective Alkynylation of Stabilized Enolates Asymmetric induction can be achieved in the ethynylation of β-ketoesters with TMS-EBX using Maruoka phase-transfer catalyst, in the presence of KF as a source of fluoride.[27] The highest enantiomeric excess is obtained with a bulky dimethylphenyl ester (eq 4). Higher enantioinduction (93% ee) has been achieved with the same catalyst but using trimethylsilyl hexafluorodimethyl benziodoxole instead of TMS-EBX.[28]

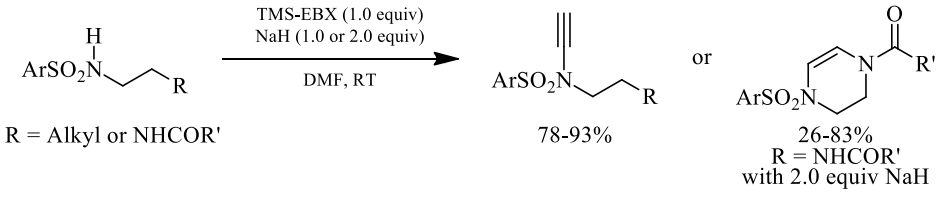


(4)

Moderate asymmetric induction is also observed in the alkynylation of nucleophilic fluorocarbons with TMS-EBX in the presence of a cinchona derived phase-transfer catalyst.[29]

Alkynylation of Heteroatoms.

The ethynylation of N-sulfonylamides is realized using TMS-EBX with stoichiometric NaH in very good to excellent yields.[30] Amides and carbamates are not alkynylated under these conditions, enabling the synthesis of tetrahydropyrazines when starting from orthogonally protected ethylene diamines (eq 5).



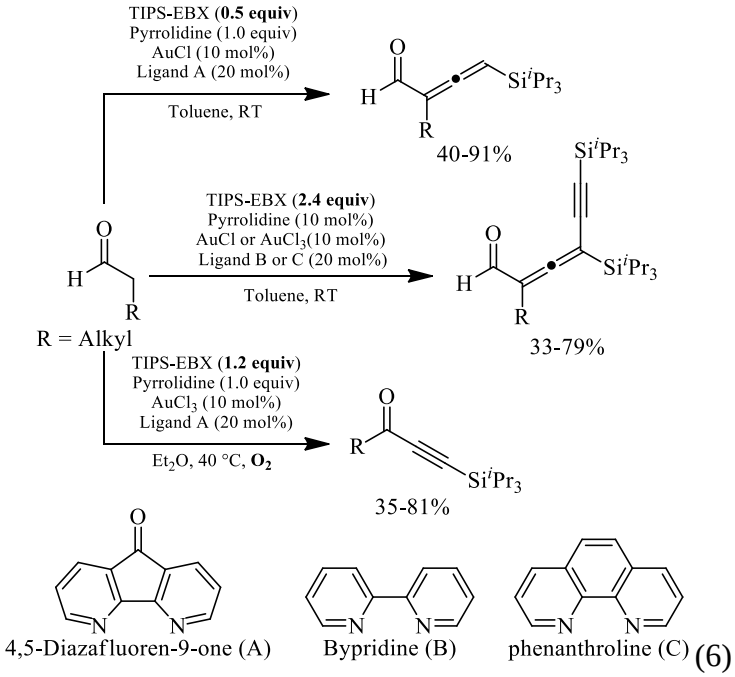
(5)

Alkynylation Reactions with TIPS-EBX

Transition Metal-Mediated Alkynylation of C-Nucleophiles. While the electrophilic α-alkynylation of carbonyl compounds has been accomplished with TMS-EBX under metal-free conditions, TIPS-EBX has been only rarely used.[23] One example is the base-mediated alkynylation of allyl β-ketoesters followed by a Pd-catalyzed asymmetric decarboxylation allylation to generate all-carbon quaternary stereocenters.[31] The synthetic potential of TIPS-EBX has been mostly exploited using transition metal catalysis. The scope of alkynylation using Au^{I} catalysts has been extended to enamines as well as a variety of electron-rich (hetero)arenes. Concurrently, many examples of alkynylation of aromatic and olefinic substrates have been reported relying on a directing-group approach.

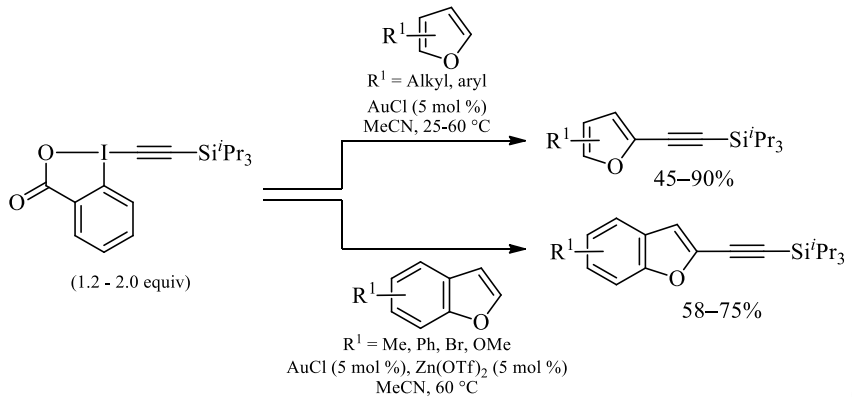
Reaction with Aldehydes under Gold/Enamine Dual Catalysis. The reaction of TIPS-EBX with non-aromatic aldehydes under enamine catalysis in the presence of a Au^{I} or Au^{III} co-catalyst results in α-vinylidenation in moderate to excellent yields (eq 6).[32] α-Alkynyl aldehydes are only generated as minor products. With an excess amount of TIPS-EBX, ethynylation of the allene occurs to deliver the corresponding enynes. By contrast, performing the transformation under an

O_2 atmosphere leads to the synthesis of ynones through the oxidative cleavage of the enamine intermediates.[33]

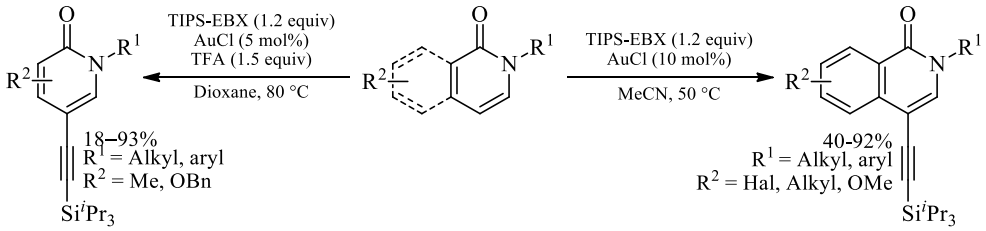


(6)

Au- and Pd-Catalyzed Alkynylation of Electron-Rich (Hetero)arenes and Alkynes. Furans undergo electrophilic alkynylation in good to excellent yield in the presence of catalytic AuCl at room temperature (eq 7).[34] Less reactive 2-aryl furans demand heating at 60 °C. The addition of a catalytic amount of $Zn(OTf)_2$ and a larger excess of TIPS-EBX are required to promote the alkynylation of benzofurans.[35] With both classes of substrates, the C-2 position is selectively functionalized; if the latter is substituted, the acetylene is transferred on the C-3 position. TIPS-EBX can be effectively used for the alkynylation of 2-pyridones[36] and isoquinolones at 50 to 80 °C (eq 8).[37] With less reactive 2-pyridones, the presence of an acidic additive (TFA) is necessary.

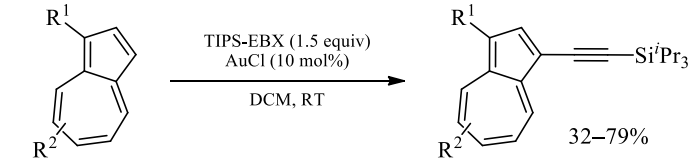


(7)



(8)

The Au^{I}-catalyzed alkynylation can be efficiently performed on azulenes at room temperature (eq 9).[38] The reaction exhibits high regio-selectivity for alkynylation of the five-membered ring.

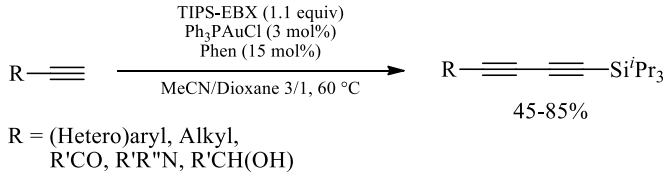


(9)

TIPS-EBX can also be used for the alkynylation of biologically relevant heterocycles. The indole ring of tryptophan is selectively ethynylated in the C-2 position using a Au^{I} catalyst in a 3/1 MeCN/water mixture as the solvent.[39,40] The alkynylation of protoporphyrin IX has also been accomplished with TIPS-EBX under Au^{I} catalysis in the presence of a Cu^{II} cocatalyst.[41] The introduced acetylene group can be exploited for biolabeling studies.

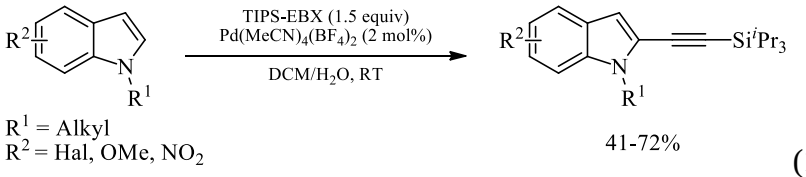
TIPS-EBX can also be employed for the alkynylation of terminal alkynes under Au^{I}-catalysis (eq 10).[42] Unsymmetrical diynes are obtained in up to excellent yields and both aryl and alkyl

substituted acetylenes can be engaged in the process. A similar reaction has also been reported still under Au^{I}-catalysis but using ethynyl hexafluorodimethyl benziodoxole reagents.[43]



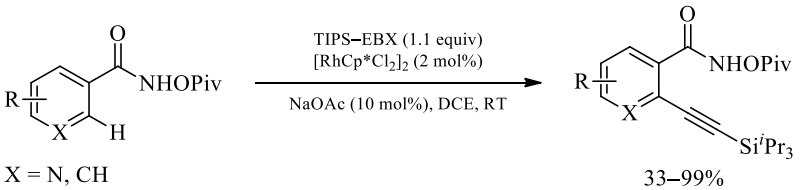
(10)

The selective C-3 alkynylation of indoles has been reported with TIPS-EBX under Au^{I}-catalysis.[9] Using instead a cationic Pd^{II} catalyst results in C-2 alkynylation (eq 11).[44] A broad range of substituents on both the benzene ring and the nitrogen atom are tolerated and the alkynylation products are generated in good yields under mild conditions (room temperature, water/DCM solvent, no additives).



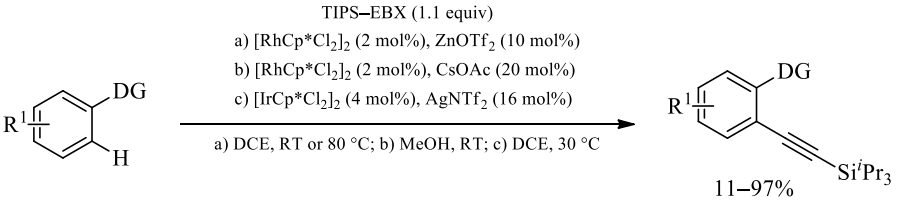
(11)

Rh- and Ir-Catalyzed Directed Alkynylation of (Hetero)arenes, Alkenes, and Aldehydes. Aromatic and heteroaromatic rings bearing a pivaloyl amide as a directing group are efficiently ethynylated at room temperature in the presence of a $Rh^{III}Cp^{*}$ catalyst (eq 12).[45,46] A large array of heterocyclic (pyridine, pyrimidine, pyrazole) and non-aromatic groups (oximes, nitrones, azomethine imines, amides) can also direct the reaction, although in these cases the activation of the rhodium catalyst with zinc triflate and higher temperatures are required (eq 13).[46] Under similar conditions, a cationic $Rh^{III}Cp^{*}$ complex enables the direct alkynylation of tertiary benzamides. An $Ir^{III}Cp^{*}$ complex also catalyzes effectively the alkynylation of N-methoxy benzamides and enamides (eq 13).[46]

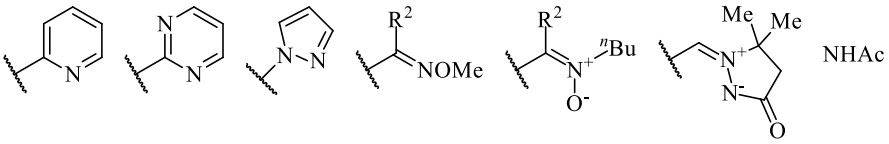


X = N, CH
R = Alkyl, aryl, OMe, Hal, CN, COR'

(12)



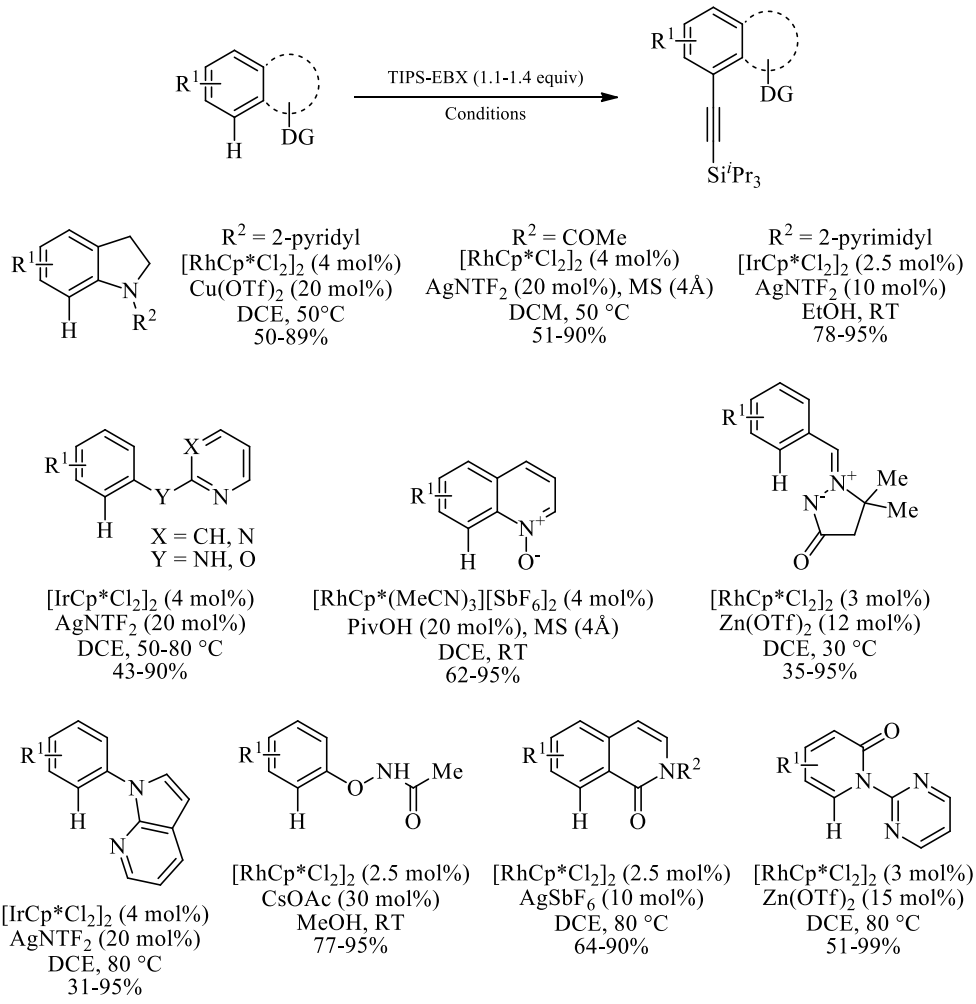
Conditions (a):

DG = 

Conditions (b): DG = NHOPiv
Conditions (c): DG = NHOMe

(13)

These seminal reports have been followed by a growing number of works describing the alkynylation of arenes and heteroarenes using a variety of directing groups, under $Rh^{III}Cp^*$ or $Ir^{III}Cp^*$ catalysis (eq 14). The alkynylation can be accomplished on N-functionalized indolines,[47,48,49] N-pyridyl and N-pyrimidyl anilines,[50] quinoline N-oxides,[51] aromatic hetero- and carbocycles bearing an azomethine ylide[52] or a 7-azaindole substituent,[53] N-phenoxyacetamides,[54] isoquinolones,[37] and N-pyrymidyl 2-quinolones.[36] The (di)alkynylation of ferrocenes can also be successfully performed using pyridine or quinoline as directing group.[55]

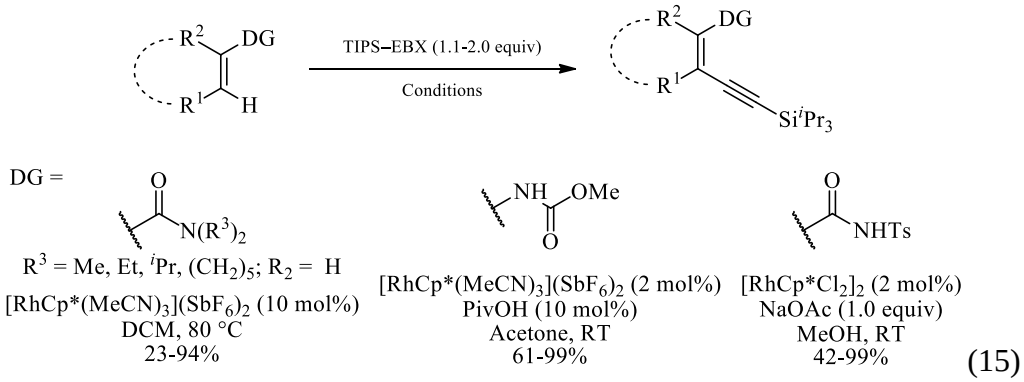


(14)

Similar procedures have also been developed relying on cheaper Ru^{II}-catalysis, in particular using activated [Ru(*p*-cymene)Cl_2]$_2$. Its use was first reported in the ethynylation of N-pyrimidyl isoquinolones,[56] and then extended to aromatic carbocycles and heterocycles with a N-methoxyamide,[57] or a pyridyl or pyrimidyl as directing group.[58] Finally, the alkynylation with TIPS-EBX using a Co^{III}Cp*-catalyst has been so far reported only with N-pyrimidyl indoles at 110 °C.[59]

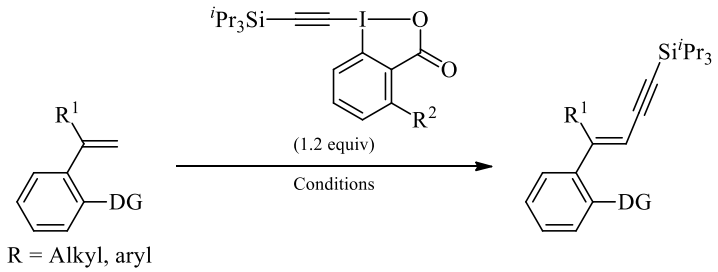
The C-H alkynylation of alkenes has also been described using rhodium or iridium catalysis with several directing groups (eq 15). Cationic Rh^{III}Cp* has been used for the selective β-alkynylation of α,β-unsaturated amides.[60] 1,3-Conjugated enynes are obtained in up to excellent yields starting

from acrylamides exhibiting a variety of aliphatic and aromatic substituents in the β-position, whereas the reaction does not work if the α-position is substituted. The same catalyst also allows the β-alkynylation of enamides using pivalic acid as an additive.[61] Both geminally and vicinally substituted alkenes are competent substrates for this transformation. Finally, α,β-unsaturated sulfonyl amides also undergo selective β-ethynylation at room temperature.[62] Best results are obtained with α-alkyl or aryl substituted N-tosyl acrylamides, whereas internal C=C double bonds are alkynylated in lower yields.



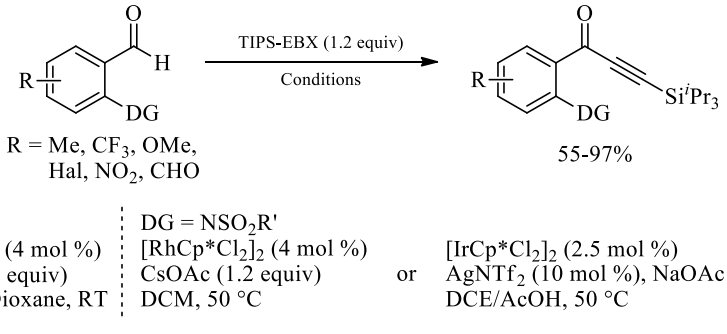
(15)

Free OH and NH_2 directing groups can be used in the alkynylation of olefins in vinyl phenols[63] and vinyl anilines to give Z-enyne products with high selectivity (eq. 16).[64] With vinyl phenols as the substrates, best results are obtained under $Rh^{III}Cp^*$ catalysis. The *ortho*-methyl substituent in this reagent is likely to prevent the counterproductive insertion of $Rh^{III}Cp^*$ into 2-iodobenzoic acid, the by-product when using simple TIPS-EBX. When the reaction is run with N-unprotected vinyl anilines, $Ir^{III}Cp^*$ catalysis gives better results. In this case, TIPS-EBX can be effectively used as $Ir^{III}Cp^*$ does not easily undergo insertion into 2-iodobenzoic acid.



(16)

ortho-Hydroxy benzaldehydes bearing a diversity of substituents can be converted into the corresponding aryl ethynyl ketones under Ir^{III}-Cp*-catalysis (eq 17).[65] The same transformation has been also reported with benzaldehydes bearing an *ortho*-sulfonamide substituent using either a rhodium[65] or an iridium catalyst.[66] Quinoline also serves as a competent directing group in the Rh^{III}Cp*-catalyzed alkynylation of aldehydes.[66]



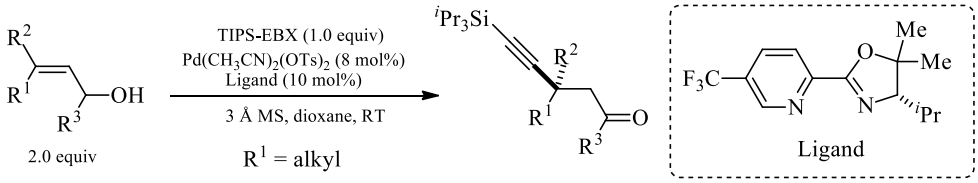
(17)

Metal-Catalyzed Alkynylations in Multiple Bond-Forming Processes. Domino reactions are of high interest because several bond-forming events are happening in a single process, thus improving the overall efficiency of a transformation. TIPS-EBX has been particularly successful in metal-catalyzed domino processes involving alkenes, alkynes and diazo compounds.

Alkenes substrates. The previously reported aminoalkynylation tandem reactions of homoallylic carbamates[16] has been successfully applied in the total synthesis of (-)-Chanoclavine.[67] An extension of aminoalkynylation tandem reactions has been achieved based on a copper catalyst to

functionalize terminal and internal alkenes.[68] A single example using TIPS-EBX is shown, in which the cyclic alkynylated Weinreb amide product is obtained in 36% yield using 1 mol% of $Cu(CH_3CN)_4BF_4$ at 60 °C.

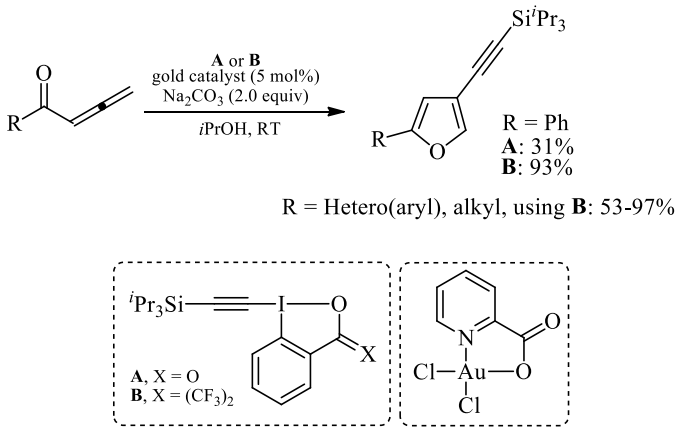
A palladium-catalyzed enantioselective redox relay Heck alkynylation for the synthesis of chiral β-alkynyl carbonyl compounds has been reported (eq 18).[69] This transformation affords high enantioselectivity for aldehydes (>94:6 er) and tolerates the formation of methylketone, albeit in low yield (30%, 94:6 er). Formation of propargylic quaternary stereocenters in low yield is possible.



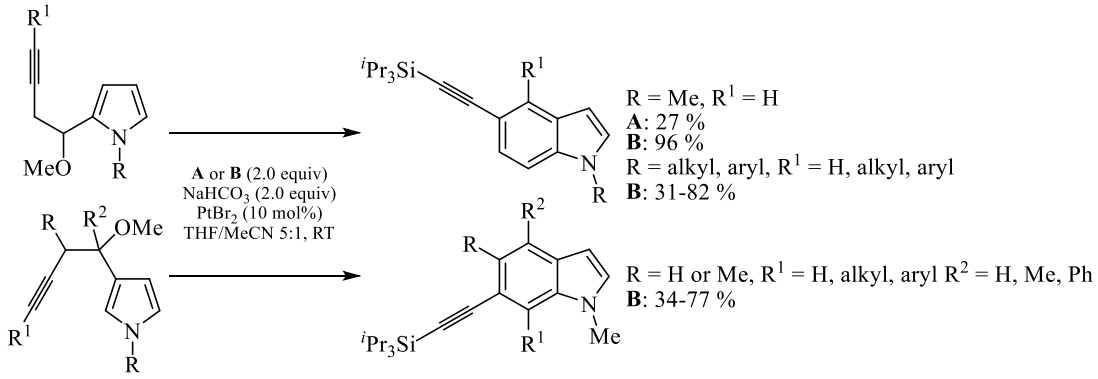
$R^2 = R^3 = H$, 46-68%, 88-93 %ee
$R^2 = Me$, $R^3 = H$, 25-36%, 88-90 %ee

(18)

Alkynes substrates. The synthesis of C-3 ethynylated furans can be realized by a gold promoted cascade starting from allenic ketones in presence of a preformed gold catalyst (eq 19).[34] TIPS-EBX gives low yield in this transformation, however the use of the corresponding bis(trifluoromethyl) reagent greatly increases the efficiency of the domino reaction. The superiority of this reagent has also been shown in the platinum mediated synthesis of C-5 and C-6 ethynylated indoles (eq 20),[70] as well as in the synthesis of C-3 ethynylated benzofurans and benzothiophenes via gold and platinum catalyzed cascades respectively.[71]

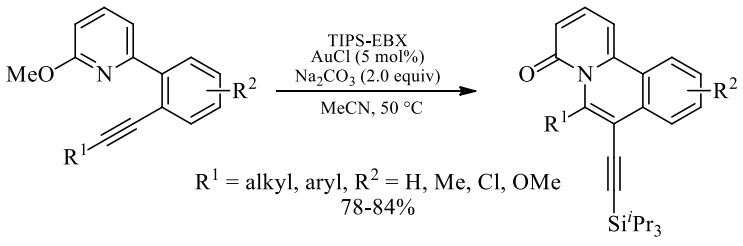


(19)



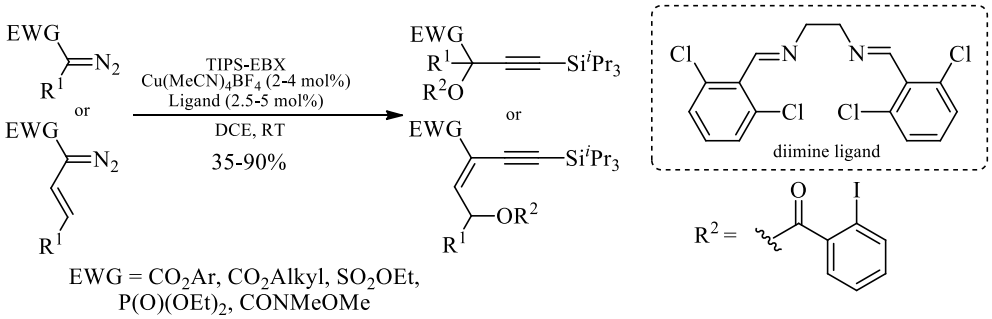
(20)

A Au^I catalyzed aminoalkynylation of alkynes has been developed to access alkynylated quinalizinones (eq 21).[72] Best results are obtained with simple Au^I chloride.

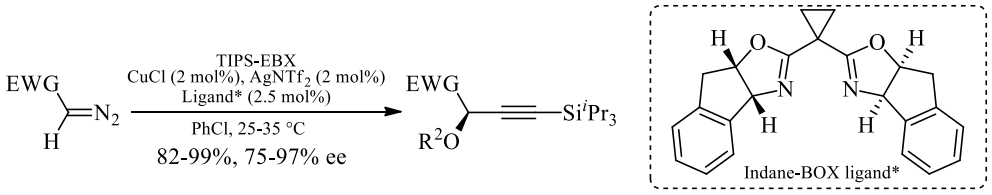


(eq 21)

Diazo Compounds. An atom economical oxyalkynylation of diazo compounds via a copper-catalyzed domino process has recently been developed (eq 22).[73] A diimine ligand is important for achieving good yields. The vinylogous reaction with vinyldiazo compounds is also successful. An enantioselective variant using copper chloride, silver triflimide as cocatalyst and an indane-BOX ligand has been also reported (eq 23).[74]



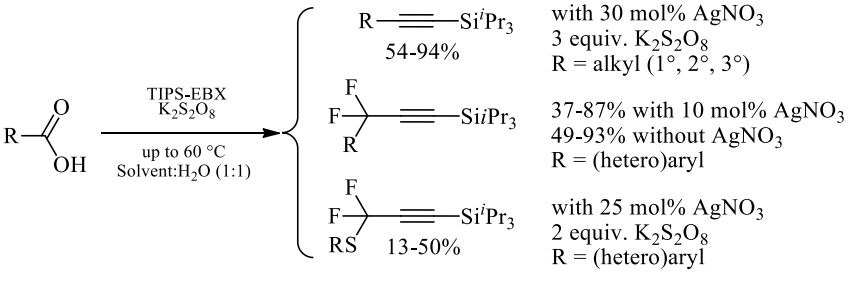
(22)



(23)

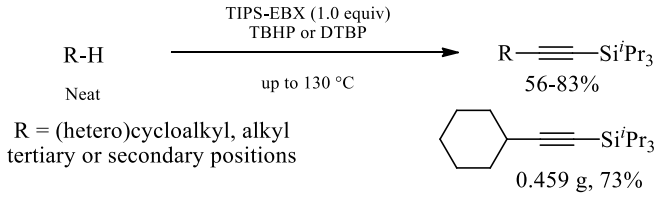
Alkynylations of radicals. The alkynylation of radicals with EBX reagents has recently emerged as a powerful alternative to two-electron chemistry. Nowadays, a broad range of strategies are available using either peroxides, silver catalysis or photoredox catalysis for the generation of either C(sp^3)-centered radicals, acyl radicals, O-centered radicals and iminyl radicals. The latter two are usually used in subsequent radical cascades.

Alkynylation of C(sp^3)-centered radicals. The alkynylation of C-centered radical has first been described in 2012 (eq 24).[75] In this seminal work, a silver nitrate mediated decarboxylation generates an alkyl radical, which is trapped by TIPS-EBX to deliver the alkynylated product in good to excellent yields. Stoichiometric amounts of potassium persulfate are necessary to regenerate the silver catalyst. This general mode of activation has been further extended to α,α-difluoroarylacetic acids.[76] A metal free procedure has been developed, highlighting that silver catalyst is not necessary to achieve high yields.[77] More recently, the alkynylation α,α-difluorothio(hetero)arylacetic acids has been described. [78,79]



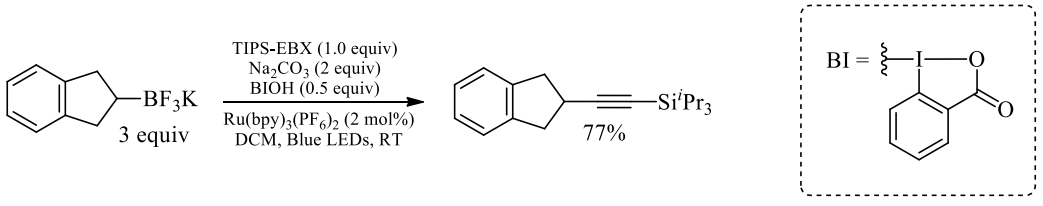
(24)

Concerning the direct alkynylation of C-H bonds using TIPS-EBX, several examples have been first reported in modest yields using *tert*-butylperoxide (TBHP) as hydrogen atom transfer (HAT) reagent at 100 °C using the neat ether starting material (eq 25).[80] The reaction scope has been extended to non-activated C-H bonds, using di-*tert*-butylperoxide (DTBP), and could be scaled to gram quantities.[81]



(25)

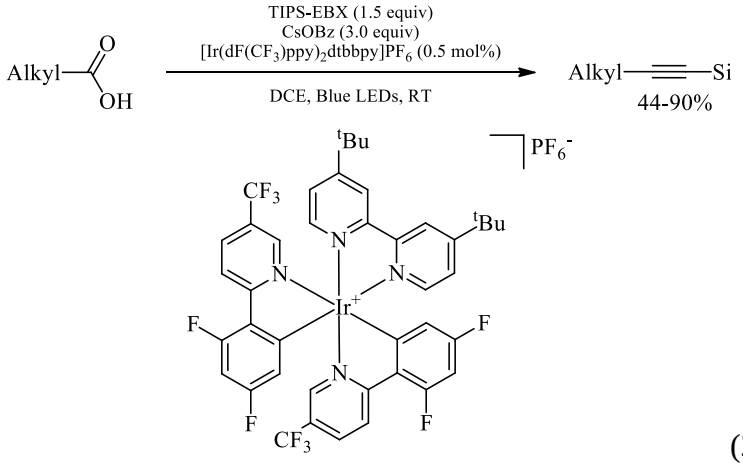
Avoiding the use of external oxidants in overstoichiometric amounts and elevated temperature, a photoredox-catalyzed deboronative alkynylation with TIPS-EBX has been reported using $Ru(bpy)_3^{2+}(PF_6^-)_2$ as photocatalyst and 3 equivalents of potassium alkyl trifluoroborate salts (eq 26).[82]



(26)

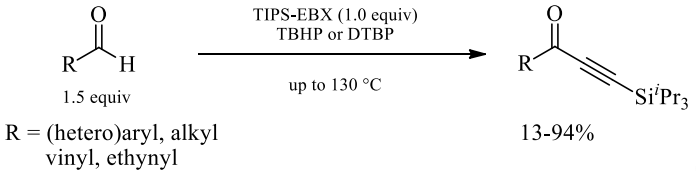
A decarboxylative alkynylation has been developed by using $[Ir(dF(CF_3)ppy)_2dtbbpy]PF_6$ as photocatalyst and cesium benzoate as a mild base (eq 26).[83,84] Blue LEDs or sunlight can be used with similar efficiency. Mechanistic investigations support the radical mechanism.[85,86] In 2016, the

decarboxylative alkynylation of Cbz-protected proline have been reported using the organic dye 9,10-DiCyanoAnthracene (DCA) as a cheap replacement of iridium photocatalyst (eq 27).[87]



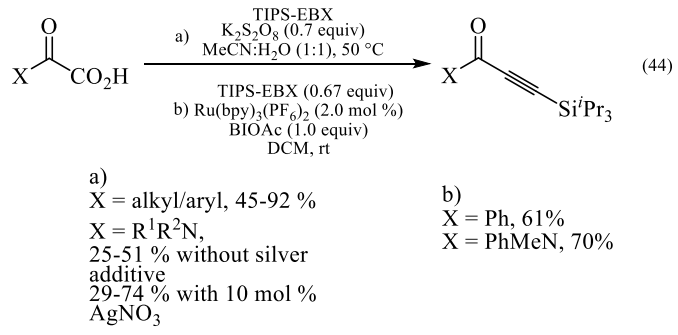
(27)

Alkynylation of acyl radicals. The alkynylation of acyl radicals has been extensively studied in 2015 by several groups. The efficient radical alkynylation of a broad range of aldehydes (including (hetero)aryl-, vinyl-, ethynyl-, and alkylaldehydes) using DTBP at 130 °C has been first described (eq 28).[88] The same reaction using TBHP at 100-120 °C has then been developed with (hetero)arylaldehydes[89,90] and alkylaldehydes.[90]



(28)

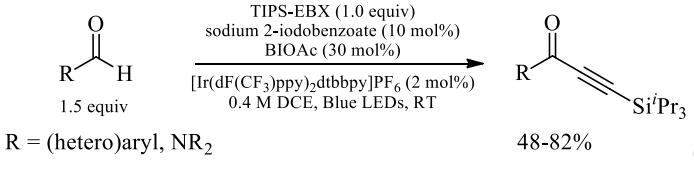
The metal free decarboxylative alkynylation of ketoacids and oxamic acids in aqueous media can be accomplished using potassium persulfate as oxidant (eq 29).[91,92] The addition of 10 mol% of silver nitrate results in higher yields for oxamic acids substrates. The decarboxylative alkynylation can be also performed using dual photoredox and cyclic hypervalent iodine reagent catalysis for the *in-situ* activation of ketoacids and oxamic acids.[93]



(eq 29)

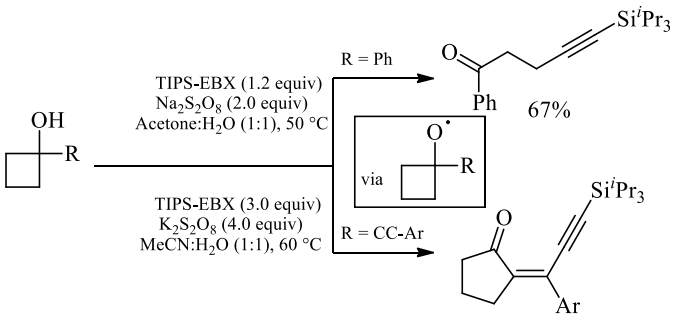
In addition, a single example of a decarboxylative carbonylative alkynylation using TIPS-EBX has been reported in 2015 under an atmospheric pressure of CO.[84]

The efficient photoredox catalyzed alkynylation of aldehydes and formamides via a HAT process has been described. It has been successfully applied to the alkynylation of complex molecules such as cholestoreol and pharmaceuticals derivatives (eq 30).[94]



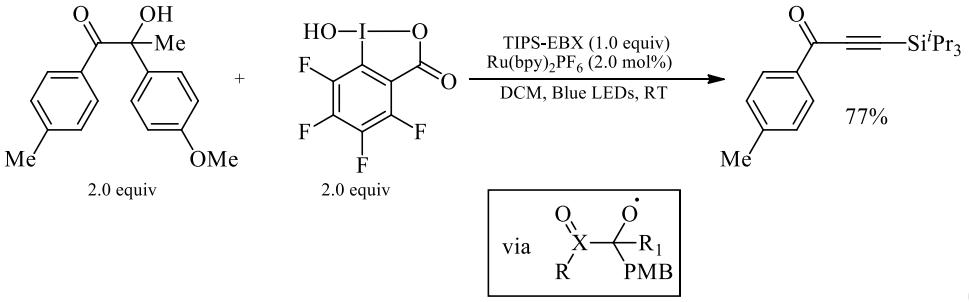
(eq 30)

Hydroxy radicals mediated fragmentation alkynylation cascade. The remote alkynylation of ketones alkyl radicals can be achieved by the ring opening of tertiary cyclopropanols and cyclobutanols (and cyclopentanols with catalytic amount of silver nitrate) via oxidative C-C bond cleavage in presence of sodium persulfate (eq 31).[95] Only a single example has been reported with TIPS-EBX as radical trap: most of the scope has been explored with the similar TBS-EBX. The scope has been extended to tertiary alkynylcyclobutanols affording enyne products in good yields with low to good E/Zselectivity.[96]

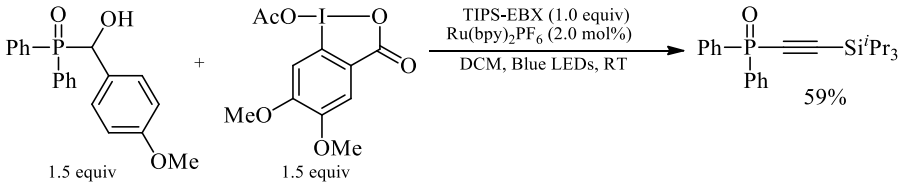


(31)

Oxygen-centered radicals have also been generated to cleave the C-C or C-P bond in α-position of non-strained alcohols. This strategy, involving dual photoredox and hypervalent iodine catalysis, was successfully applied for the synthesis of an alkynylarylketone (eq 32),[97] and a TIPS-protected phosphonoalkyne (eq 33).[98]

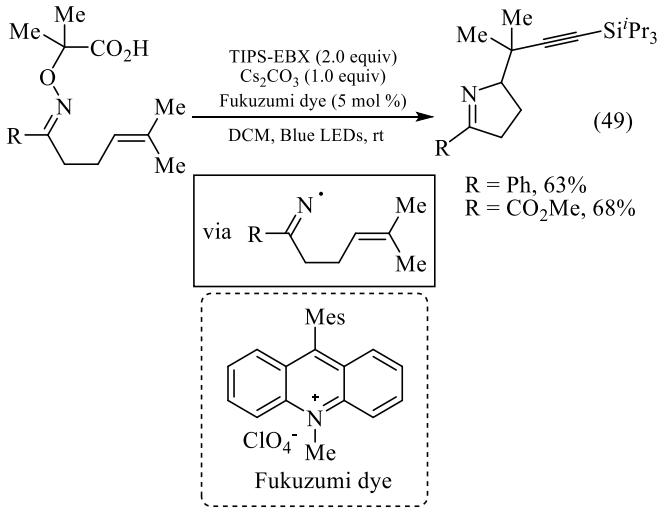


(32)



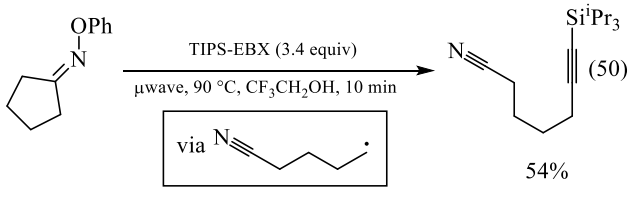
(33)

Iminyl radicals mediated fragmentation alkynylation cascade. A photoredox driven decarboxylation – acetone extrusion – iminyl radical cyclization – alkynylation cascade to give pyrroline products has been developed under metal-free conditions, using Fukuzumi dye as a catalyst (eq 34).[99]

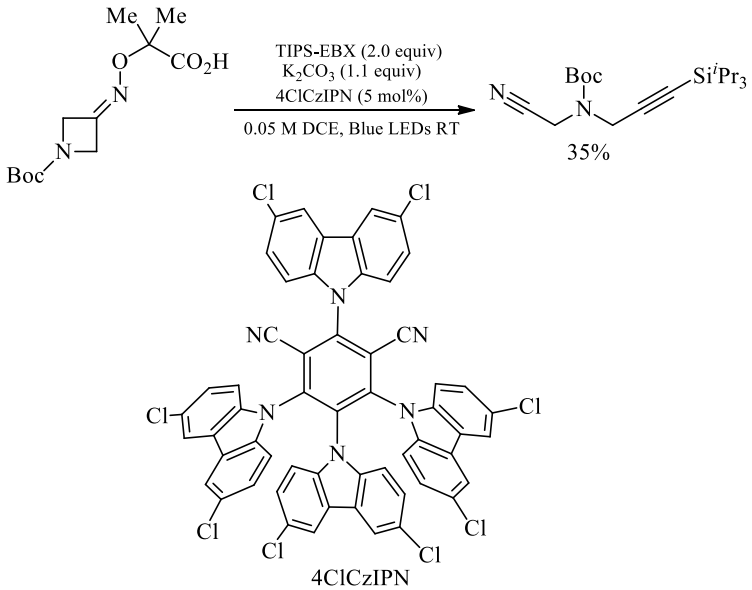


(34)

More recently, one example of a microwave assisted (90 °C) ring opening – alkynylation cascade of cyclobutyloxime ethers via iminyl radical promoted C-C bond fragmentation has been described (eq 35).[100] This transformation can be performed at room temperature under photoredox catalysis using the organic dye 4ClCzIPN and commercially available blue LEDs (eq 36).[101]

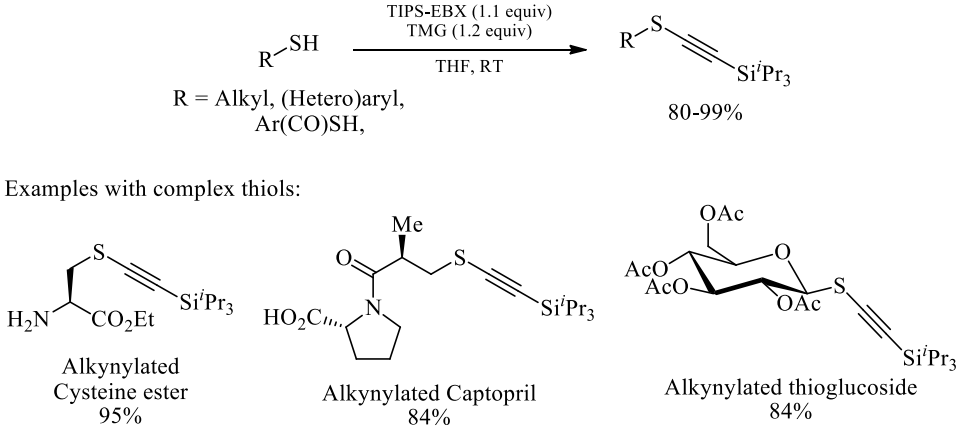


(35)



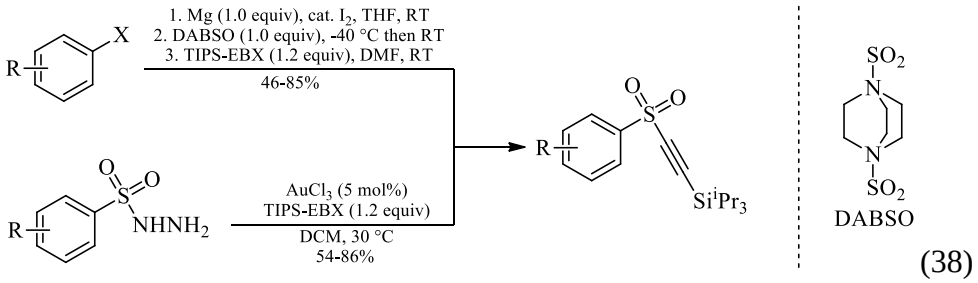
(36)

Alkynylations of Heteroatoms. The alkynylation of thiols can be efficiently accomplished using TIPS-EBX (eq 37).[102] In the presence of TMG as a base, both aromatic and aliphatic substrates are converted into the corresponding ethynyl sulfides in few minutes. The reaction works under very mild condition (room temperature, open flask) and the products are obtained in almost quantitative yields with broad functional group tolerance. N-unprotected cysteine can be alkynylated with TIPS-EBX as well as cysteine-containing peptides, thiogylcosides and proteins.[103,104] The scope of the reaction also encompasses thiobenzoic acids and sulfide salts. Not only TIPS-EBX but also other silyl EBX as well as alkyl and aryl EBX reagents perform excellently in the alkynylation of thiols. The resulting silylethynyl sulfides have found several applications. For instance, they undergo [3+2] cycloadditions with Donor-Acceptor cyclopropanes under Lewis Acid catalysis.[105] In another work, the products obtained through the reaction of arene thiols with TMS-EBX can be utilized to generate useful α,α-difluoroethyl thioethers following treatment with HF·Py.[106]



(37)

Sulfinate anions generated in situ through the reaction of (hetero)aryl and allyl Grignard reagents with the SO_2-source DABSO (1,4-diazobicyclo[2.2.2]octane-bis(sulfur dioxide)) can be trapped with TIPS-EBX to generate alkynyl sulfones in up to very good yields (eq 38).[107] In an alternative approach, the synthesis of alkynyl sulfones is achieved through the Au^{III}-catalyzed dehydrazinative coupling of arylsulfonyl hydrazides and TIPS-EBX.[108]



(38)

Phosphites, phosphinates, and secondary phosphinoxides are ethynylated with TIPS-EBX as well. The reaction, which occurs in the presence of DBU as a base, delivers alkynyl phosphorus compounds in good to excellent yields under mild conditions.[109]

17. Long, R.; Huang, J.; Shao, W.; Liu, S.; Lan, Y.; Gong, J.; Yang, Z. *Nat. Commun.* **2014**, *5*, 5707.

18. Shi, H.; Tan, C.; Zhang, W.; Zhang, Z.; Long, R.; Luo, T.; Yang, Z. *Org. Lett.* **2015**, *17*, 2342.

19. Zhang, J.; Wang, X.; Li, S.; Li, D.; Liu, S.; Lan, Y.; Gong, J.; Yang, Z. *Chem. Eur. J.* **2015**, *21*, 12596.

20. Lv, C.; Yan, X.; Tu, Q.; Di, Y.; Yuan, C.; Fang, X.; Ben-David, Y.; Xia, L.; Gong, J.; Shen, Y.; et al. *Angew. Chem. Int. Ed.* **2016**, *55*, 7539.

21. Parr, B. T.; Economou, C.; Herzon, S. B. *Nature* **2015**, *525*, 507.

22. Utaka, A.; Cavalcanti, L. N.; Silva, L. F. *Chem. Commun.* **2014**, *50*, 3810.

23. Teodoro, B. V. M.; Silva, L. F. *J. Org. Chem.* **2017**, *82*, 11787.

24. Kamlar, M.; Cisarova, I.; Vesely, J. *Org. Biomol. Chem.* **2015**, *13*, 2884.

25. Finkbeiner, P.; Weckenmann, N. M.; Nachtsheim, B. J. *Org. Lett.* **2014**, *16*, 1326.

26. Roy, A.; Das, M. K.; Chaudhuri, S.; Bisai, A. *J. Org. Chem.* **2018**, *83*, 403.

27. Fernández González, D.; Brand, J. P.; Mondière, R.; Waser, J. *Adv. Synth. Catal.* **2013**, *355*, 1631.

28. Wu, X.; Shirakawa, S.; Maruoka, K. *Org. Biomol. Chem.* **2014**, *12*, 5388.

29. Kamlar, M.; Putaj, P.; Veselý, J. *Tetrahedron Lett.* **2013**, *54*, 2097.

30. Aubineau, T.; Cossy, J. *Chem. Commun.* **2013**, *49*, 3303.

31. Vita, M. V.; Mieville, P.; Waser, J. *Org. Lett.* **2014**, *16*, 5768.

32. Wang, Z.; Li, X.; Huang, Y. *Angew. Chem. Int. Ed.* **2013**, *52*, 14219.

33. Wang, Z.; Li, L.; Huang, Y. *J. Am. Chem. Soc.* **2014**, *136*, 12233.

34. Li, Y.; Brand, J. P.; Waser, J. *Angew. Chem. Int. Ed.* **2013**, *52*, 6743.

35. Li, Y.; Waser, J. *Beilstein J. Org. Chem.* **2013**, *9*, 1763.

36. Li, Y.; Xie, F.; Li, X. *J. Org. Chem.* **2016**, *81*, 715.

37. Shaikh, A. C.; Shinde, D. R.; Patil, N. T. *Org. Lett.* **2016**, *18*, 1056.

38. Székely, A.; Péter, Á.; Aradi, K.; Tolnai, G. L.; Novák, Z. *Org. Lett.* **2017**, *19*, 954.

39. Tolnai, G. L.; Brand, J. P.; Waser, J. *Beilstein J. Org. Chem.* **2016**, *12*, 745.

40. Hansen, M. B.; Hubálek, F.; Skrydstrup, T.; Hoeg-Jensen, T. *Chem. Eur. J.* **2016**, *22*, 1572.

41. Nierth, A.; Marletta, M. A. *Angew. Chem. Int. Ed.* **2014**, *53*, 2611.

42. Banerjee, S.; Patil, N. T. *Chem. Commun.* **2017**, *53*, 7937.

43. Li, X., Xie. X., Sun, N. Liu, Y. *Angew. Chem. Int. Ed.* **2017**, *56*, 6994.

44. Tolnai, G. L.; Ganss, S.; Brand, J. P.; Waser, J. *Org. Lett.* **2013**, *15*, 112.

45. Feng, C.; Loh, T.-P. *Angew. Chem. Int. Ed.* **2014**, *53*, 2722.

46. Xie, F.; Qi, Z.; Yu, S.; Li, X. *J. Am. Chem. Soc.* **2014**, *136*, 4780.

47. Yang, X.-F.; Hu, X.-H.; Feng, C.; Loh, T.-P. *Chem. Commun.* **2015**, *51*, 2532.

48. Jin, N.; Pan, C.; Zhang, H.; Xu, P.; Cheng, Y.; Zhu, C. *Adv. Synth. Catal.* **2015**, *357*, 1149.

49. Wu, Y.; Yang, Y.; Zhou, B.; Li, Y. *J. Org. Chem.* **2015**, *80*, 1946.

50. Tang, G.-D.; Pan, C.-L.; Xie, F. *Org. Biomol. Chem.* **2016**, *14*, 2898.

51. Jeong, J.; Patel, P.; Hwang, H.; Chang, S. *Org. Lett.* **2014**, *16*, 4598.

52. Zhang, X.; Qi, Z.; Gao, J.; Li, X. *Org. Biomol. Chem.* **2014**, *12*, 9329.

53. Liu, B.; Wang, X.; Ge, Z.; Li, R. *Org. Biomol. Chem.* **2016**, *14*, 2944.

54. Hu, S.; Lu, L.; Zhu, T.; Wu, Q.; Chen, Y.; Li, J. J.; Zhao, J. *Org. Biomol. Chem.* **2018**, *16*, 43.

55. Wang, S.-B.; Gu, Q.; You, S.-L. *J. Org. Chem.* **2017**, *82*, 11829.

56. Kang, D.; Hong, S. *Org. Lett.* **2015**, *17*, 1938.

57. Boobalan, R.; Gandeepan, P.; Cheng, C.-H. *Org. Lett.* **2016**, *18*, 3314.

58. Liu, Y.; Chang, F.; Jiang, Q.; Ma, Z.; Liu, C. *Synlett* **2018**, *14*, 658.

59. Zhang, Z.-Z.; Liu, B.; Wang, C.-Y.; Shi, B.-F. *Org. Lett.* **2015**, *17*, 4094.

60. Collins, K. D.; Lied, F.; Glorius, F. *Chem. Commun.* **2014**, *50*, 4459.

61. Feng, C.; Feng, D.; Loh, T.-P. *Chem. Commun.* **2014**, *50*, 9865.

62. Feng, C.; Feng, D.; Luo, Y.; Loh, T.-P. *Org. Lett.* **2014**, *16*, 5956.

63. Finkbeiner, P.; Kloeckner, U.; Nachtsheim, B. J. *Angew. Chem. Int. Ed.* **2015**, *54*, 4949.

64. Caspers, L. D.; Finkbeiner, P.; Nachtsheim, B. J. *Chem. Eur. J.* **2017**, *23*, 2748.

65. Wang, H.; Xie, F.; Qi, Z.; Li, X. *Org. Lett.* **2015**, *17*, 920.

66. Ai, W.; Wu, Y.; Tang, H.; Yang, X.; Yang, Y.; Li, Y.; Zhou, B. *Chem. Commun.* **2015**, *51*, 7871.

67. Lu, J.-T.; Shi, Z.-F.; Cao, X.-P. *J. Org. Chem.* **2017**, *82*, 7774.

68. Shen, K.; Wang, Q. *Chem. Sci.* **2017**, *8*, 8265.

69. Chen, Z.-M.; Nervig, C. S.; DeLuca, R. J.; Sigman, M. S. *Angew. Chem. Int. Ed.* **2017**, *56*, 6651.

70. Li, Y.; Waser, J. *Angew. Chem. Int. Ed.* **2015**, *54*, 5438.

71. Li, Y.; Gryn'ova, G.; Saenz, F.; Jeanbourquin, X.; Sivula, K.; Corminboeuf, C.; Waser, J. *Chem. Eur. J.* **2017**, *23*, 8058.

72. Shinde, P. S.; Shaikhab, A. C.; Patil, N. T. *Chem. Commun.*, **2016**, *52*, 8152.

73. Hari, D. P.; Waser, J. *J. Am. Chem. Soc.* **2016**, *138*, 2190.

74 Hari, D. P.; Waser, J. *J. Am. Chem. Soc.* **2017**, *139*, 8420.

75. Liu, X.; Wang, Z.; Cheng, X.; Li, C. *J. Am. Chem. Soc.* **2012**, *134*, 14330.

76. Chen, F.; Hashmi, A. S. K. *Org. Lett.* **2016**, *18*, 2880.

77. Li, X.; Li, S.; Sun, S.; Yang, F.; Zhu, W.; Zhu, Y.; Wu, Y.; Wu, Y. *Adv. Synth. Catal.* **2016**, *358*, 1699.

78. Shen, F.; Zhang, P.; Lu, L.; Shen, Q. *Org. Lett.* **2017**, *19*, 1032.

79. Ismalaj, E.; Glenadel, Q.; Billard, T. *Eur. J. Org. Chem.* **2017**, *14*, 1911.

80. Zhang, R.-Y.; Xi, L.-Y.; Zhang, L.; Liang, S.; Chen, S.-Y.; Yu, X.-Q. *RSC Adv.* **2014**, *4*, 54349.

81. Cheng, Z.-F.; Feng, Y.-S.; Rong, C.; Xu, T.; Wang, P.-F.; Xu, J.; Daia, J.-J.; Xu, H.-J. *Green Chem.* **2016**, *18*, 4185.

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

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

84. Zhou, Q.-Q.; Guo, W.; Ding, W.; Wu, X.; Chen, X.; Lu, L.-Q.; Xiao, W.-J. *Angew. Chem. Int. Ed.* **2015**, *54*, 11196.

85. Le Vaillant, F.; Wodrich, M. D.; Waser, J. *Chem. Sci.* **2017**, *8*, 1790.

86. Le Vaillant, F.; Waser, J. *Chimia* **2017**, *71*, 226.

87. Yang, C.; Yang, J.-D.; Li, Y.-H.; Li, X.; Cheng, J.-P. *J. Org. Chem.* **2016**, *81*, 12357.

88. Liu, X.; Yu, L.; Luo, M.; Zhu, J.; Wei, W. *Chem. Eur. J.* **2015**, *21*, 8745.

89. Zhang, R.-Y.; Xi, L.-Y.; Zhang, L.; Chen, S.-Y.; Yu, X.-Q. *Tetrahedron*, **2015**, *71*, 6176.

90. Ouyang, X.-H.; Song, R.-J.; Wang, C.-Y.; Yanga, Y.; Li, J.-H. *Chem. Commun.* **2015**, *51*, 14497.

91. Wang, H.; Guo, L.-N.; Wang, S.; Duan, X.-H. *Org. Lett.* **2015**, *17*, 3054.

92. Wang, P.-F.; Feng, Y.-S.; Cheng, Z.-F.; Wu, Q.-M.; Wang, G.-Y.; Liu, L.-L.; Dai, J.-J.; Xu, J.; Xu, H.-J. *J. Org. Chem.* **2015**, *80*, 9314.

93 Huang, H.; Zhang, G.; Chen, Y. *Angew. Chem. Int. Ed.* **2015**, *54*, 7872.

94. Mukherjee, S.; Garza-Sanchez, R. A.; Tlahuext-Aca, A.; Glorius, F. *Angew. Chem. Int. Ed.* **2017**, *56*, 14723.

95. Wang, S.; Guo, L.-N.; Wang, H.; Duan, X.-H. *Org. Lett.* **2015**, *17*, 4798.

96. Zhang, R.-Y.; Xi, L.-Y.; Shi, L.; Zhang, X.-Z.; Chen, S.-Y.; Yu, X.-Q. *Org. Lett.* **2016**, *18*, 4024.

97. Jia, K.; Pan, Y.; Chen, Y. *Angew. Chem. Int. Ed.* **2017**, *56*, 2478.

98. Jia, K.; Li, J.; Chen, Y. *Chem. Eur. J.* **2018**, *24*, 3174.

99. Davies, J.; Sheikh, N. S.; Leonori, D. *Angew. Chem. Int. Ed.* **2017**, *56*, 13361.

100. Jackman, M. M.; Im, S.; Bohman, S. R.; Lo, C. C. L.; Garrity, A. L.; Castle, L. S. *Chem. Eur. J.* **2018**, *24*, 594.

101. Le Vaillant, F.; Garreau, M.; Nicolai, S.; Gryn'ova, G.; Corminboeuf, C.; Waser, J. *Chem. Sci.* **2018**, accepted for publication, DOI: 10.1039/C8SC01818A.

102. Frei, R.; Waser, J. *J. Am. Chem. Soc.* **2013**, *135*, 9620.

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

104. Abegg, D.; Frei, R.; Cerato, L.; Hari, D. P.; Wang, C.; Waser, J.;Adibekian, A. *Angew. Chem. Int. Ed.* **2015**, *54*, 10852

105. Racine, S.; Hegedus, B.; Scopelliti, R.; Waser, J. *Chem. Eur. J.* **2016**, *22*, 11997.

106. Tomita, R.; Al-Maharik, N.; Rodil, A.; Buhl, M.; O'Hagan, D. *Org. Biomol. Chem.* **2018**, *16*, 1113.

107. Chen, C. C.; Waser, J. *Org. Lett.* **2015**, *17*, 736.

108. Shinde, P. S., S.; Patil, N. T.. *Eur. J. Org. Chem.* **2017**, 3512.

109. Chen, C. C.; Waser, J. *Chem. Commun.* **2014**, *50*, 12923.