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Gold(III)-catalyzed direct nucleophilic substitution of propargylic alcohols

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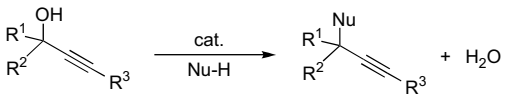
ABSTRACT

Gold-catalyzed nucleophilic substitution of propargylic alcohols with various nucleophiles (allylsilane, electron-rich aromatics, alcohols, thiols, hydrides, 1,3-dicarbonyl derivatives, sulfonamides) is described under very mild conditions (room temperature in dichloromethane). Preliminary mechanistic investigations suggest a mechanism through a carbocation intermediate. Nucleophilic substitutions on allylic and benzylic alcohols are also described.

1. Introduction

The direct (i.e., with non-pre-activated good leaving groups) substitution of propargylic alcohols (Scheme 1) has been for years a relatively unexplored reaction compared to reactions on allylic and benzylic substrates. These reactions are particularly interesting in the current context of the development of greener and atom-economic reactions because water is thus generated as the only by-product. These reactions have been traditionally carried under Nicholas conditions, using cobalt stabilized carbocations. However, the so-called Nicholas reaction requires a multi-step sequence and a stoichiometric amount of $[Co_2(CO)_8]$.[1] The development of greener catalytic reactions was thus highly desirable.



Scheme 1.

In 1994, Murahashi et al.[2] described, in a seminal paper, the propargylic substitution of monosubstituted (R^3=H) alkynes bearing a good leaving group on the propargylic alcohol moiety, where a mechanism through a copper–allenylidene intermediate was postulated.[3] Hidai et al. have there after developed a diruthenium complex catalyst for the direct substitution of 'true' (R^3=H) propargylic alcohols, in the presence of a large number of heteroatomic (alcohols, hydrides, amines, thiols, nitrogen, phosphorus,…) and carbon-centered nucleophiles.[4] Using enantiomerically pure catalysts, asymmetric propargylic substitutions were next developed using acetone, hydrides, and electron-rich aromatic nucleophiles.[5] The use of monoruthenium complexes was then described by Cadierno and Dixneuf.[6]

In 2003, oxo-rhenium catalysts have been described by Toste et al.[7–10] Substitution products are obtained in high yields with alcohols, allylsilanes, aromatics, and nitrogen nucleophiles. Interestingly, these reactions were not limited to 'true' propargylic alcohols. This methodology has been further used in a formal synthesis of podophyllotoxin.[10] The use of $[ReBr(CO)_3(THF)]_2$ was more recently described (in 2007) by Takai et al.[11]

In 2005, we described the direct Au(III)-catalyzed substitution of propargylic alcohols in the presence of various nucleophiles (allylsilanes, alcohols, thiols, electron-rich aromatics), and showed that gold probably acts as a Lewis acid to promote the formation of a stabilized propargylic carbocation intermediate.[12] A related reaction was subsequently reported by Dyker et al. in 2006, using azulene and 1,3-dimethoxybenzene in Friedel–Crafts type reactions with benzylic and propargylic alcohols.[13] Shortly after, Sanz and Zhan described that these reactions could also be carried out under Brønsted acid and $FeCl_3$ catalysis, respectively.[14–17] Later on, the use of copper, indium, bismuth, scandium, ytterbium, phosphomolybdic acid, and iodine catalysts has been reported by several groups.[18] These aspects have been recently reviewed by Kabalka et al.[19] A conceptually different approach, through the reaction of a propargylic alkoxide with allylsilane or organoboron dihalides, was also reported by Kabalka et al.[20] We would like to give herein a full account on our work related to gold(III)-catalyzed direct propargylic substitution.

2. Results

The initial starting point of this work is connected to early attempts to develop a strategy for the construction of the C13–C19 fragment of macrolactine **A**.[21] We initially planned to construct this fragment by applying an enantioselective alkynylation,[22] followed

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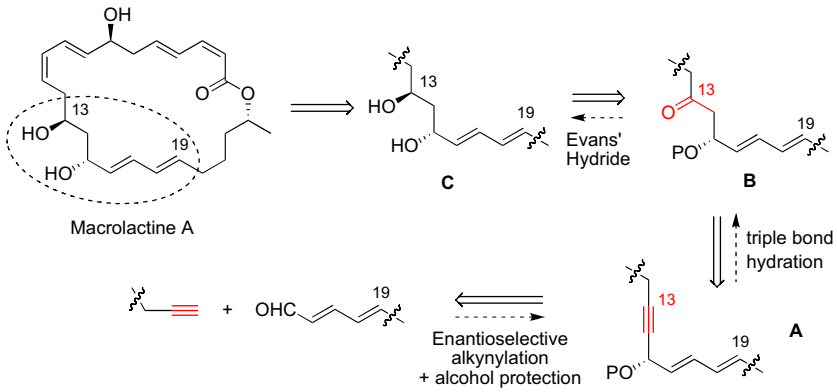
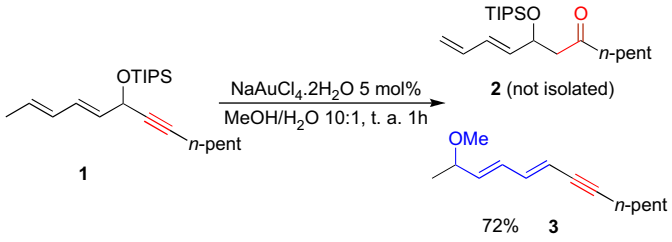


Scheme 2.

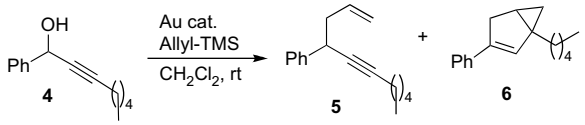
by a regioselective triple bond hydration to give the aldol surrogate **B**.[23] Finally, the β-keto alcohol could be reduced under Evans conditions[24] to give the C13–C15 1,3-*anti* diol **C** (Scheme 2).

We initially tested the triple bond hydration on model substrate **1**, obtained from the reaction between sorbaldehyde and heptyne, where the propargylic alcohol was further protected as a TIPS ether. When the hydration reaction was carried out in the presence of Au(III) catalyst, under Utimoto conditions,[23] the expected ketone **2** could not be isolated. The only, rather unexpected, isolated (in 72% yield) product was **3** resulting from the formal SN′ substitution of the OTIPS functional group by methanol (Scheme 3). We thus anticipated that gold(III) might be an interesting catalyst in the direct nucleophilic substitution of propargylic alcohols (Scheme 1).



Scheme 3.

The proof of concept was thus tested in the model reaction of **4** with allyltrimethylsilane in the presence of various gold(III) and gold(I) sources (Scheme 4, Table 1).



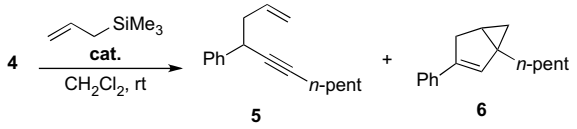
Scheme 4.

Gratifyingly, the expected product **5** could be isolated in good yields using various Au(III) catalysts (Table 1, entries 1–4), whereas more disappointing results have been obtained in the presence of Au(I) catalysts (Table 1, entries 5 and 6) and no reaction observed with $PtCl_2$ and $PdCl_2(PhCN)_2$ catalysts (Table 1, entries 7 and 8). After a short optimization, in the presence of $NaAuCl_4{\cdot}2H_2O$ (1 mol %) and after 2 h at room temperature, compound **5** was isolated in 71% yield (Table 1, entry 9). In the presence of $HAuCl_4{\cdot}3H_2O$ (Table 1, entry 4), the bicyclic compound **6**, probably resulting from the cycloisomerization of the 1,5-ene-yne **5**,[25,26] was also isolated as a minor product (11% yield). We thus next focused our efforts toward the development of reaction conditions able to

Table 1

Entry	Gold cat (%)	Time (H)	Isolated yield of **5** (%)
1	$NaAuCl_4{\cdot}2H_2O$ (**5**)	12	82
2	$AuBr_3$ (**5**)	12	68
3	$AuCl_3$ (**5**)	12	65
4	$HAuCl_4{\cdot}3H_2O$ (**5**)	12	60+**6** (11%)
5	AuCl	12	30
6	Ph_3PAuCl	12	NR
7	$PdCl_2(PhCN)_2$ (**5**)	12	NR
8	$PtCl_2$ (**5**)	12	NR
9	$NaAuCl_4{\cdot}2H_2O$ (**1**)	2	71

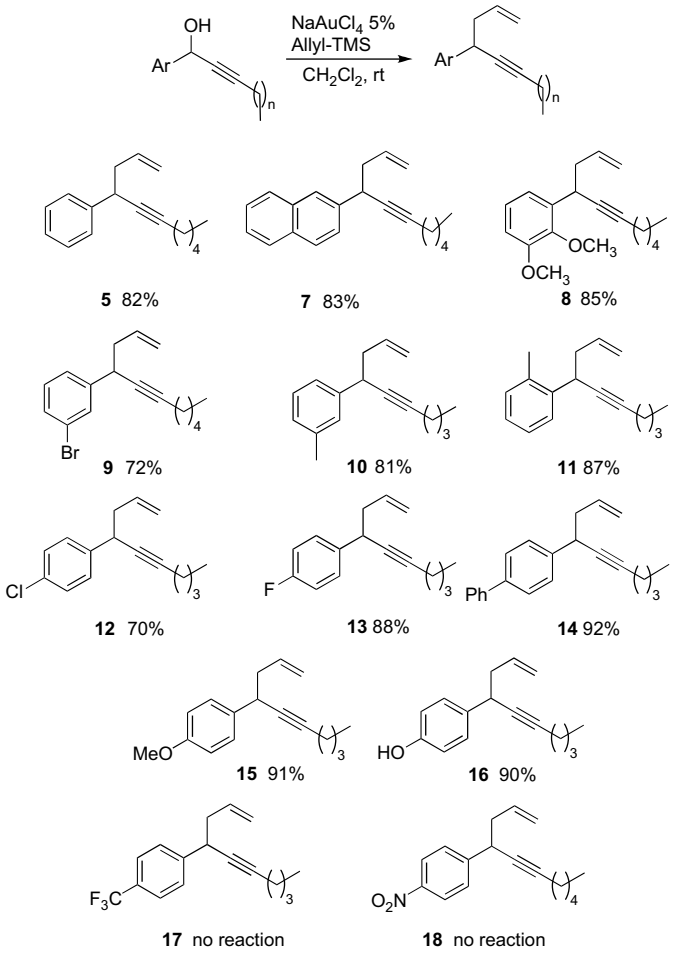
furnish **6** as the major product. After some experimentation, we ended up with two different sets of conditions: (i) in the presence of both $AuCl_3$ (5 mol %) and $Ph_3PAuSbF_6$ (5 mol %) catalysts, a 30:70 mixture of compounds **5** and **6** was obtained; (ii) a selective formation of **6**, isolated in 71% yield, was only achieved when the reaction mixture was first treated by $AuCl_3$ (5 mol %) to complete (TLC monitoring) the substitution reaction, and then by $Ph_3PAuSbF_6$ (5 mol %) to promote the cycloisomerization (Scheme 5). Similar experiments have been reported by Toste et al.[25] and more recently by Sanz et al.[16]



$AuCl_3$ 5% + $Ph_3PAuSbF_6$ 5%	30	70	64% (**5**+**6**)
$AuCl_3$ 5%, 5h then $Ph_3PAuOTf$ 5%	–	100	71%

Scheme 5.

Starting from the model reaction with **4** and allyltrimethylsilane, we set out to define the scope of the Au(III)-catalyzed propargylic substitutions. Variations on the aromatic group were first examined. Various substituents (naphthyl, OMe, Br, F, Cl, Me, Ph,…) are well tolerated (see compounds **5**–**16**) to the exception of the electron withdrawing nitro and CF_3 groups (compounds **17** and **18**) where no reaction could be observed (Scheme 6). These 1,5-ene-ynes have then been further transformed into cyclobutenes using an RCM reaction in the presence of the Grubbs–Hoveyda II catalyst.[27]



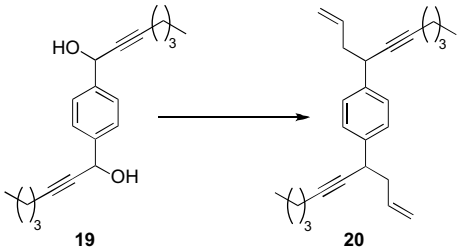
Scheme 6.

A double allylation reaction was also attempted on symmetrical bis-propargylic alcohol **19**, and the corresponding bis-allylated compound **20** was obtained in 69% yield (Scheme 7).

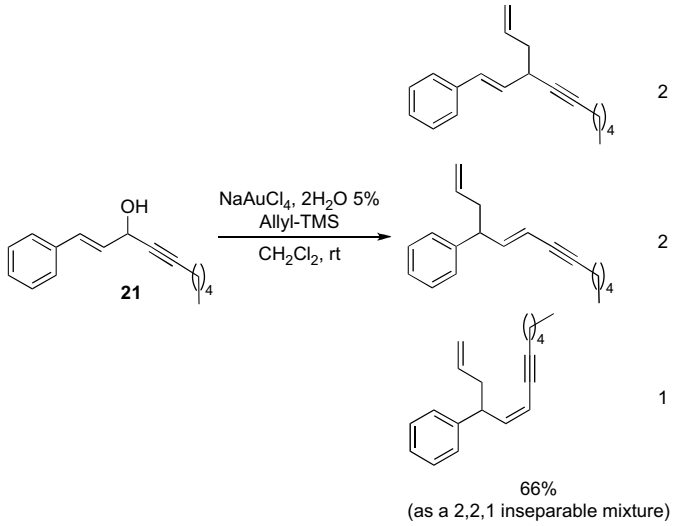
Starting from a cinnamyl derivative **21** (Scheme 8), an inseparable 2:2:1 mixture of α, γ(*E*), and γ(*Z*) isomers was obtained in 66% yield.

Substitutions at the alkyne position were next investigated. Starting from alkyl, aromatic, and silyl substituents on the alkyne position (R^3=alkyl, Ph, $SiMe_3$), the corresponding allylated compounds **4**, **22**–**24** were isolated in 71–97% yield. Limitations of this methodology were found with carboxylic esters substituents and 'true' alkynes where no reaction and a poor 9% yield were observed (compounds **25** and **26**) (Scheme 9).

Finally, tertiary benzylic and non-benzylic (in the propargylic position) substrates were investigated. Compounds **27** and **28** were

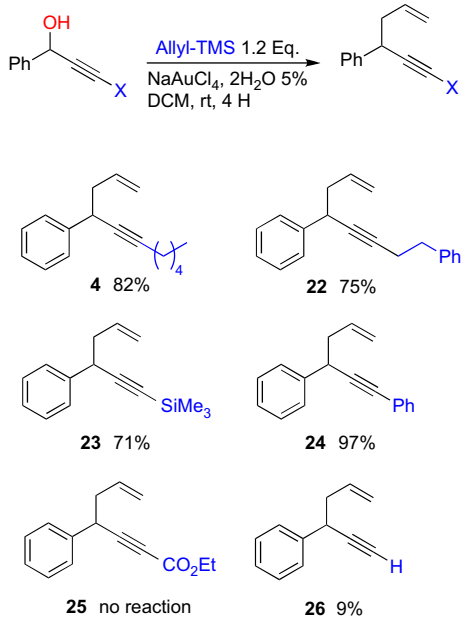


Scheme 7.

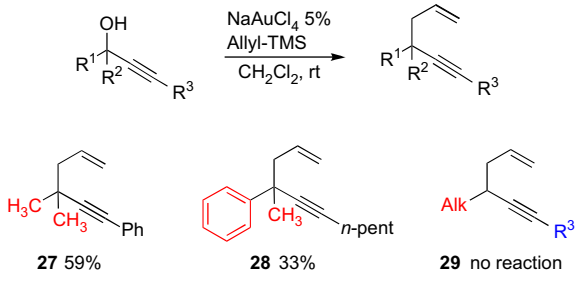


Scheme 8.

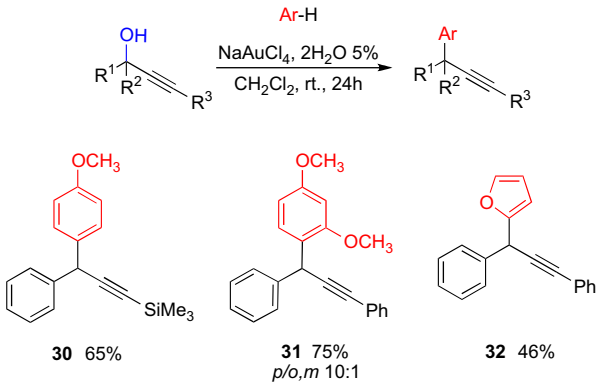
isolated in 59% and 33%, respectively.[28] However, using secondary propargyl alcohols bearing an alkyl group at the propargyl position (R^1=alkyl, R^2=H), no reaction is observed (see compound **29**) (Scheme 10).



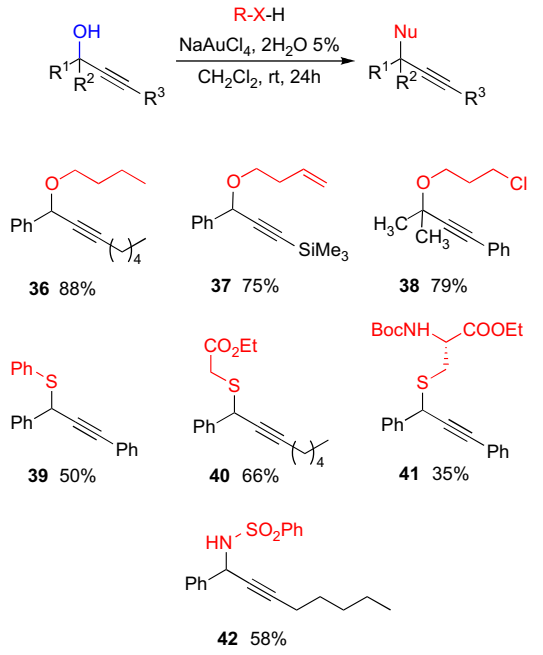
Scheme 9.



Scheme 10.



Scheme 11.



Scheme 13.

The Au(III)-catalyzed reaction was next tested for a diverse collection of nucleophiles. Carbon-centered nucleophiles were first examined: electron-rich aromatics, including the acid-sensitive furan, can be introduced in moderate to good yields and selectivities, at room temperature (Scheme 11).

The introduction of 1,3-dicarbonyl derivatives required harsher reaction conditions. Whereas no reaction occurs at room temperature, in refluxing dichloroethane, the expected product **33** could not be isolated and a mixture of the triple bond hydration product **34** and furan **35** were isolated in 69% and 26% yields, respectively. This result is in sharp contrast with results obtained by Sanz et al. using PTSA catalyst where substitution products, such as **33**, are obtained selectively (Scheme 12).[15]

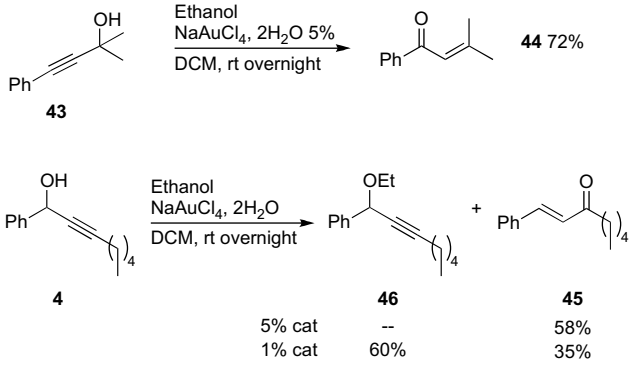
Moving to heteroatomic (O–, N–, and S–) nucleophiles, alcohols, thiols, and sulfonamides could be successfully introduced and compounds **36**–**42** were isolated in moderate to good yields. In the presence of Boc-Cys-OEt, a 1:1 inseparable mixture of the two possible diastereoisomers was obtained (Scheme 13).

Reactions with ethanol are more tricky, since unwanted Meyer–Schuster[29] rearranged by-products **44** and **45** are isolated as the sole isolated products from alcohols **43** and **4**, in 72% and 58%, respectively. However, by decreasing the catalyst amount to 1%, the expected ether **46** could be obtained in 60% yield, along with the Meyer–Schuster product (35% yield) (Scheme 14).

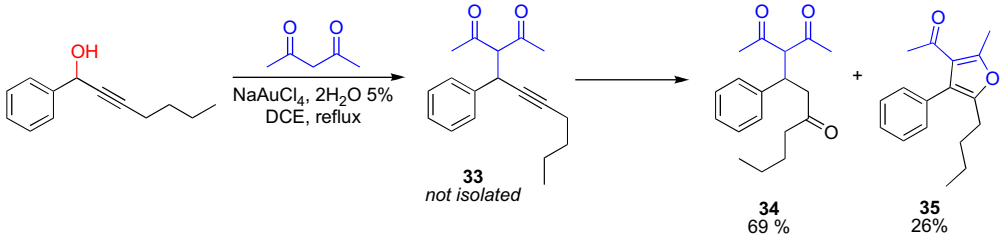
Finally, reduction of the propargylic alcohols in the presence of a hydride source was attempted. Indeed, in the presence of triethylsilane and $NaAuCl_4 \cdot 2H_2O$ 5 mol %, the corresponding reduction products were isolated in a 69–75% yield range (Scheme 15). Gratifyingly, polymethylhydrosiloxane (PMHS), a cheap and stable polymeric by-product of the silicone industry, could also be used in these reactions (Scheme 16).

The lack of reactivity in some examples prompts us to reconsider our initial mechanistic proposal. In our initial thoughts, we believed that gold may act, trough coordination to the π-bond, as a propargylic alcohol activating agent (Scheme 17, Eq. a). However, the lack of reactions in compounds **17**, **18**, **25**, and **29** suggested a mechanism through the formation of stabilized propargylic carbocation (Scheme 17, Eq. b).

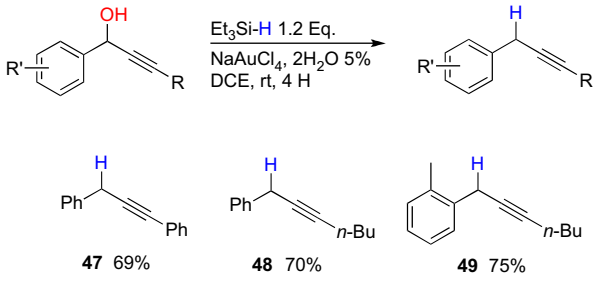
In order to test this hypothesis, the known[30] enantiomerically enriched (96% ee) propargylic alcohol (*R*)-**50** was engaged in a reaction in the presence of allyltrimethylsilane and Au(III) catalyst. The corresponding allylated product was obtained in a racemic form, thus suggesting a mechanism through the formation of a carbocation intermediate (Scheme 18).



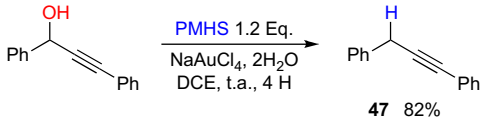
Scheme 14.



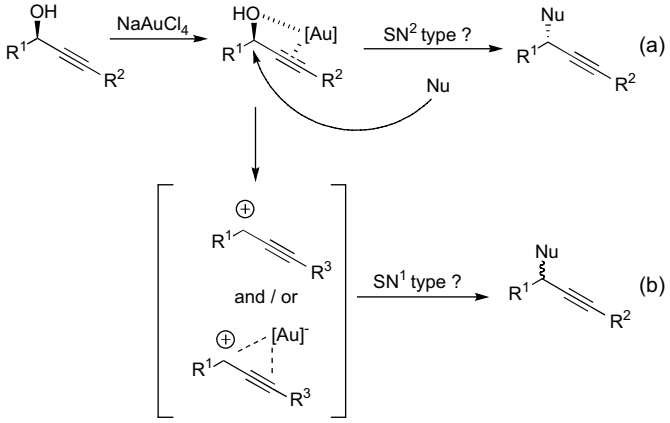
Scheme 12.



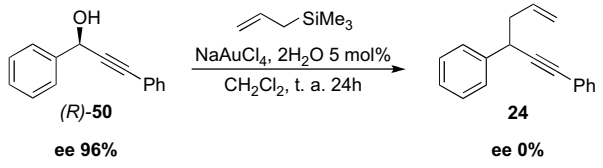
Scheme 15.



Scheme 16.

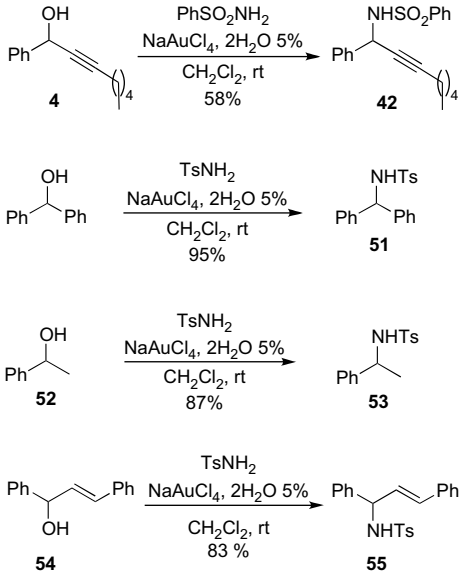


Scheme 17.



Scheme 18.

It thus appears that Au(III) catalyst may act as a Lewis Acid in these reactions. Consequently, the presence of a triple bond in the substrate is thus probably not necessary. Indeed, in collaboration with the group of Prim et al.,[31] the reactivity of benzylic alcohols was also investigated and various nitrogen nucleophiles could be introduced in these benzylic positions (Scheme 19).[32] The reaction of allylic alcohols was finally attempted. Starting from allylic alcohol **54** and tosylamide, the corresponding substitution product was isolated in 83% yield (Scheme 19).[33]



Scheme 19.

3. Conclusion

In conclusion, we developed efficient gold(III)-catalyzed substitutions on propargylic, benzylic, and allylic alcohols. Similar reactions have also been recently reported to be catalyzed by simpler, less expensive, catalysts such as $FeCl_3$ or PTSA.[14–16,34] Gold, however, allows reactions at room temperature and, due to the nature of the metal, different selectivities can be expected as illustrated, for example, by Dyker et al.[13] These aspects are currently under development in our laboratories. Another point of our current interest in these reactions is the development of direct propargylic substitutions, where the carbocation intermediate is not stabilized, with, for example, secondary propargyl alcohols bearing an alkyl group at the propargyl position (**29**). To the best of our knowledge, only one example of these reactions has been reported to date.[11]

4. Experimental

4.1. General information

Unless otherwise stated all commercial materials were used without further purification. Reactions were carried out in round bottom flasks equipped with a magnetic stirring bar and capped with a septum. Dichloromethane was distilled over CaH_2 and run over neutral alumina to remove any residual ethanol. TLC analysis of all reactions was performed on Merck silica gel 60 F_{254} TLC plates. Chromatography was carried out on Merck 60 silica gel (35–70 μm). FTIR spectra were recorded with a Perkin Elmer Spectrum BX spectrometer and Perkin Elmer Spectrum 1000. ^1H and ^{13}C NMR spectra were recorded with Bruker Avance-300, Avance-500 spectrometers and Bruker Ultra shield 400 plus and referenced to $CDCl_3$ unless otherwise noted. Mass spectra, elemental, and chiral HPLC analyses were obtained from the mass spectrometry, elemental analysis and HPLC facilities operated by the Institut de Chimie des Substances Naturelles and by the Centre Commun de Spectrométrie de Masse of University Claude Bernard Lyon 1.

4.2. General procedure for gold-catalyzed nucleophilic substitutions of propargylic alcohols

To a solution of propargylic alcohol (1 equiv) in dichloromethane or dichloroethane (0.2 M) was added the nucleophile

(1.5–5 equiv) followed by the catalyst (5 mol %). The reaction mixture was stirred at room temperature and monitored periodically by TLC. Upon completion, the mixture was concentrated in vacuo and loaded on to a silica gel column and chromatographed with an appropriate mixture of pentane and diethyl ether to give the substitution products described below.

4.2.1. Oct-1-en-5-yn-4-ylbenzene (**5**)[12]

Prepared with 1.5 equiv of allyltrimethylsilane and isolated as a clear oil.

^{1}H NMR ($CDCl_3$, 300 MHz) δ ppm 0.92 (t, J=7 Hz, 3H), 1.38 (m, 4H), 1.55 (m, 2H), 2.23 (td, J=2.2, 7 Hz, 2H), 2.47 (t, J=7 Hz, 2H), 3.68 (tt, J=2.2, 7 Hz, 1H), 5.04 (d, J=10.5 Hz, 1H), 5.05 (d, J=16.8 Hz, 1H), 5.87 (ddt, J=7, 10.4, 16.9 Hz, 1H), 7.20–7.39 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ ppm 14.2, 19.0, 22.4, 28.9, 31.2, 38.2, 43.2, 81.2, 84.0, 116.8, 126.7, 127.6, 128.5, 136.0, 142.3; MS (EI) m/z 185 (34), 91 (100), 77 (73), 41 (39). Anal. Calcd for $C_{17}H_{22}$: C, 90.20; H, 9.80. Found: C, 90.31; H, 10.15. IR (film) cm^{-1} 2955, 2929, 2357. Data are in accordance with previously reported results.[12]

4.2.2. 1-Pentyl-3-phenylbicyclo[3.1.0]hex-2-ene (**6**)[12]

Prepared with 1.5 equiv of allyltrimethylsilane, 0.05 equiv $HAuCl_4 \cdot 3H_2O$ and isolated as a colorless oil.

^{1}H NMR ($CDCl_3$, 300 MHz) δ ppm 0.26 (t, J=3.8 Hz, 1H), 0.8 (dd, J=3.7, 8 Hz, 1H), 0.91 (t, J=7 Hz, 3H), 1.32 (m, 4H), 1.46 (m, 3H), 1.67 (m, 1H), 2.70 (d, J=17 Hz, 1H), 3.05 (ddd, J=1.6, 7, 17 Hz, 1H), 6.32 (s, 1H), 7.26–7.39 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ ppm 14.1, 21.3, 22.7, 23.19, 28.2, 32.0, 33.4, 36.6, 36.9, 125.1, 126.6, 128.3, 132.3, 136.8, 138.6. The compound decomposes rapidly at room temperature.

4.2.3. 2-(Oct-1-en-5-yn-4-yl)naphthalene (**7**)[12]

Prepared with 1.5 equiv of allyltrimethylsilane and isolated as a clear oil.

^{1}H NMR ($CDCl_3$, 300 MHz) δ ppm 0.93 (t, J=7 Hz, 3H), 1.41 (m, 4H), 1.56 (m, 2H), 2.27 (td, J=2.2, 7 Hz, 2H), 2.60 (t, J=7 Hz, 2H), 3.85 (m, 1H), 5.05 (d, J=10 Hz, 1H), 5.06 (d, J=17 Hz, 1H), 5.90 (m, 1H), 7.47 (m, 3H), 7.8 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ ppm 14.0, 18.9, 22.2, 28.8, 31.1, 38.2, 42.9, 81.1, 84.1, 116.8, 125.5, 125.9, 126.0, 126.0, 127.6, 127.8, 128.0, 132.4, 133.5, 135.8, 139.6. Anal. Calcd for $C_{21}H_{24}$: C, 91.25; H, 8.75. Found: C, 91.17; H, 8.57. IR (film) cm^{-1} 3055, 2929. Data are in accordance with previously reported results.[12]

4.2.4. 1,2-Dimethoxy-3-(oct-1-en-5-yn-4-yl)benzene (**8**)[12]

Prepared with 1.5 equiv of allyltrimethylsilane and isolated as a clear oil.

^{1}H NMR ($CDCl_3$, 300 MHz) δ ppm 0.92 (t, J=7 Hz, 3H), 1.37 (m, 4H), 1.54 (m, 2H), 2.22 (td, J=2.2, 7 Hz, 2H), 2.45 (m, 2H), 3.86 (s, 3H), 3.87 (s, 3H), 4.10 (m, 1H), 5.04 (d, J=10 Hz, 1H), 5.05 (d, J=17 Hz, 1H), 5.90 (m, 1H), 6.80 (d, J=1.5, 8 Hz, 1H), 7.05 (t, J=8 Hz, 1H), 7.13 (dd, J=1.6, 7.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ ppm 14.0, 18.8, 22.2, 28.8, 31.1, 31.4, 41.8, 55.7, 60.8, 81.5, 82.8, 110.8, 116.4, 120.5, 123.8, 136.0, 136.2, 146.1, 152.5. Anal. Calcd for $C_{19}H_{26}O_2$: C, 79.68; H, 9.15. Found: C, 79.63; H, 9.28. IR (film) cm^{-1} 2929, 2359. Data are in accordance with previously reported results.[12]

4.2.5. 1-Bromo-3-(oct-1-en-5-yn-4-yl)benzene (**9**)[12]

Prepared with 1.5 equiv of allyltrimethylsilane and isolated as a colorless oil.

^{1}H NMR ($CDCl_3$, 300 MHz) δ ppm 0.92 (t, J=7 Hz, 3H), 1.37 (m, 4H), 1.50 (m, 2H), 2.23 (td, J=2.2, 7 Hz, 2H), 2.46 (t, J=7 Hz, 2H), 3.64 (td, J=2.1, 7 Hz, 2H), 5.04 (d, J=10 Hz, 1H), 5.05 (d, J=17 Hz, 1H), 5.84 (m, 1H), 7.23 (m, 1H), 7.37 (m, 2H), 7.52 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ ppm 14.1, 18.9, 22.3, 28.8, 31.2, 37.8, 43.0, 80.4, 84.6, 117.2, 122.5, 126.3, 129.8, 130.0, 130.8, 135.4, 144.6. Anal. Calcd for $C_{17}H_{21}Br$: C, 66.89; H, 6.93. Found: C, 66.68; H, 7.17. IR (film) cm^{-1} 2928, 670. Data are in accordance with previously reported results.[12]

4.2.6. 1-(Dec-1-en-5-yn-4-yl)-3-methylbenzene (**10**)

Prepared with 3 equiv of allyltrimethylsilane and isolated as a colorless oil.

^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 0.92 (t, J=7.2 Hz, 3H), 1.39–1.55 (m, 4H), 2.24 (dt, J=2.1, 6.9 Hz, 2H), 2.35 (s, 3H), 2.45 (t, J=7.2 Hz, 2H), 3.62 (tt, J=2.2, 7.3 Hz, 1H), 5.03 (d, J=9.9 Hz, 1H), 5.05 (d, J=17.0 Hz, 1H), 5.87 (tdd, J=7, 10.2, 17.1 Hz, 1H), 7.03 (d, J=7.1 Hz, 1H), 7.15 (t, J=7.1 Hz, 1H), 7.16 (s, 1H), 7.21 (d, J=7.3 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ ppm 13.6, 18.5, 21.4, 21.9, 31.1, 37.9, 43.0, 81.1, 83.6, 116.5, 124.4, 127.2, 128.1 (2C), 135.9, 137.8, 142.1; HREIMS m/z 226.1720, calcd for $C_{17}H_{22}$ 226.1722; IR (film) cm^{-1} 3077, 2952, 2228, 1689, 1642, 702.

4.2.7. 1-(Dec-1-en-5-yn-4-yl)-2-methylbenzene (**11**)

Prepared with 3 equiv of allyltrimethylsilane and isolated as a colorless oil.

^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 0.93 (t, J=7.2 Hz, 3H), 1.40–1.51 (m, 4H), 2.21 (dt, J=2.2, 6.9 Hz, 2H), 2.34 (s, 3H), 2.41 (t, J=7.1 Hz, 2H), 3.84 (tt, J=2.2, 7.3 Hz, 1H, H_7), 5.05 (d, J=10.1 Hz, 1H), 5.08 (d, J=16.8 Hz, 1H), 5.91 (tdd, J=7, 10.2, 17.1 Hz, 1H), 7.13 (m, 2H), 7.20 (m, 1H), 7.51 (d, J=7.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ ppm 13.6, 18.5, 19.2, 21.9, 31.1, 34.4, 41.5, 81.3, 82.9, 116.4, 126.1, 126.4, 127.4, 130.2, 134.7, 136.0, 140.3; HREIMS m/z 226.1720, calcd for $C_{17}H_{22}$ 226.1722; IR (film) cm^{-1} 3075, 2956, 1684, 1640, 1605, 754.

4.2.8. 1-Chloro-4-(dec-1-en-5-yn-4-yl)benzene (**12**)

Prepared with 3 equiv of allyltrimethylsilane and isolated as a colorless oil.

^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 0.92 (t, J=7.2 Hz, 3H), 1.37–1.54 (m, 4H), 2.23 (dt, J=2.2, 6.9 Hz, 2H), 2.45 (t, J=7.2 Hz, 2H), 3.64 (tt, J=2.2, 7.0 Hz, 1H), 5.02 (d, J=16.8 Hz, 1H), 5.03 (d, J=10.6 Hz, 1H), 5.81 (tdd, J=7, 10.3, 17.0 Hz, 1H), 7.27 (s, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ ppm 13.6, 18.4, 21.9, 31.0, 37.4, 42.9, 80.5, 84.1, 116.9, 128.3 (2C), 128.8 (2C), 132.2, 135.3, 140.6; HREIMS m/z 246.1176, calcd for $C_{16}H_{19}Cl$ 246.1175; IR (film) cm^{-1} 3078, 2961, 1686, 1641, 1609, 810.

4.2.9. 1-(Dec-1-en-5-yn-4-yl)-4-fluorobenzene (**13**)

Prepared with 3 equiv of allyltrimethylsilane and isolated as a colorless oil.

^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 0.92 (t, J=7.2 Hz, 3H), 1.38–1.55 (m, 4H), 2.23 (dt, J=2.2, 7.0 Hz, 2H), 2.44 (t, J=7.0 Hz, 2H), 3.65 (tt, J=2.1, 7.0 Hz, 1H), 5.03 (d, J=11.2 Hz, 1H), 5.02 (d, J=15.8 Hz, 1H), 5.89 (tdd, J=7, 10.4 Hz, J=16.6 Hz, 1H), 6.99 (m, 2H), 7.3 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ ppm 13.6, 18.4, 21.9, 31.1, 37.2, 43.1, 80.8, 83.9, 115.0 (d), 116.7, 128.9 (d), 135.4, 137.7, 160.3, 162.7; HREIMS m/z 230.1472, calcd for $C_{16}H_{19}F$ 230.1471; IR (film) cm^{-1} 3077, 2958, 1641, 1602, 834.

4.2.10. 1-(Biphenyl-4-yl)hept-2-yn-1-ol (**14**)

Prepared with 3 equiv of allyltrimethylsilane and isolated as a colorless oil.

^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 0.93 (t, J=7.2 Hz, 3H), 1.42–1.55 (m, 4H), 2.26 (dt, J=2.2, 7.0 Hz, 2H), 2.51 (t, J=7.2 Hz, 2H), 3.72 (tt, J=2.1, 7.1 Hz, 1H), 5.06 (d, J=10.2 Hz, 1H), 5.08 (d, J=17.1 Hz, 1H), 5.89 (tdd, J=7, 10.2, 17.2 Hz, 1H), 7.33 (m, 1H), 7.43 (m, 4H), 7.56 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ ppm 13.6, 18.5, 21.9, 31.1, 37.7, 43.0, 80.9, 83.8, 116.7, 127.0 (2C), 127.0 (3C), 127.8 (2C), 128.6 (2C), 135.7, 139.4, 140.9, 141.2; HREIMS m/z 288.1877, calcd for $C_{22}H_{24}$ 288.1878; IR (film) cm^{-1} 3062, 2932, 1683, 1635, 1601, 735.

4.2.11. 1-(Dec-1-en-5-yn-4-yl)-4-methoxybenzene (**15**)

Prepared with 3 equiv of allyltrimethylsilane and isolated as a colorless oil.

^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 0.92 (t, J=7.2 Hz, 3H), 1.40–1.56 (m, 4H), 2.23 (dt, J=2.2, 6.9 Hz, 2H), 2.44 (t, J=7.0 Hz, 2H), 3.62 (tt,

J=2.2, 7.0 Hz, 1H), 3.79 (s, 3H), 5.02 (d, *J*=10.2 Hz, 1H), 5.03 (d, *J*=17.1 Hz, 1H), 5.85 (tdd, *J*=7, 10.4, 17.3 Hz, 1H), 6.85 (m, 2H), 7.27 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ ppm 13.6, 18.5, 21.9, 31.1, 37.1, 43.1, 55.2, 81.3, 83.5, 113.0, 116.5, 128.3, 134.2, 135.9, 158.5; HREIMS *m*/*z* 242.1670, calcd for $C_{17}H_{22}O$ 242.1671; IR (film) cm^{-1} 3075, 2957, 1640, 1610, 828.

4.2.12. 4-(Dec-1-en-5-yn-4-yl)phenol (**16**)

Prepared with 3 equiv of allyltrimethylsilane and isolated as a colorless oil.

^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 0.91 (t, *J*=7.2 Hz, 3H), 1.37–1.54 (m, 4H), 2.22 (dt, *J*=2.2, 6.9 Hz, 2H), 2.42 (t, *J*=7.1 Hz, 2H), 3.60 (tt, *J*=2.2, 7.0 Hz, 1H), 4.66 (s, 3H), 5.01 (d, *J*=10.2 Hz, 1H), 5.02 (d, *J*=16.32 Hz, 1H), 5.83 (tdd, *J*=7, 10.4, 16.4 Hz, 1H), 6.77 (d, *J*=8.51 Hz, 2H), 7.24 (d, *J*=8.5 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ ppm 13.6, 18.4, 21.9, 31.1, 37.1, 43.1, 81.3, 83.5, 115.0, 116.6, 128.6, 134.4, 135.8, 154.0; HREIMS *m*/*z* 229.1591, calcd for $C_{16}H_{20}O$ 229.1592; IR (film) cm^{-1} 3321, 3055, 2929, 1638, 1613.

4.2.13. 1,4-Di(dec-1-en-5-yn-4-yl)benzene (**20**)

Prepared with 6 equiv of allyltrimethylsilane and isolated as a colorless oil.

^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 0.92 (t, *J*=7.2 Hz, 6H), 1.40–1.53 (m, 8H), 2.23 (dt, *J*=2.0, 6.9 Hz, 4H), 2.44 (t, *J*=6.9 Hz, 4H), 3.64 (tt, *J*=2.2, 7.1 Hz, 2H), 5.03 (d, *J*=9.9 Hz, 2H), 5.04 (d, *J*=18.5 Hz, 2H), 5.85 (tdd, *J*=7, 10.1, 17.3 Hz, 2H), 7.29 (s, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ ppm 13.6 (2C), 18.5 (2C), 21.9 (2C), 31.1 (2C), 37.6 (2C), 43.0 (2C), 81.1 (2C), 83.6 (2C), 116.5 (2C), 127.4 (4C), 135.8 (2C), 140.3 (2C); HREIMS *m*/*z* 346.2659, calcd for $C_{26}H_{34}$ 346.2661; IR (film) cm^{-1} 3076, 2930, 1640, 728.

4.2.14. Oct-7-en-3-yne-1,5-diyldibenzene (**22**)

Prepared with 6 equiv of allyltrimethylsilane and isolated as a colorless oil.

^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 2.44 (t, *J*=7.0 Hz, 2H), 2.54 (dt, *J*=2.2, 7.4 Hz, 2H), 2.85 (t, *J*=7.4 Hz, 2H), 3.64 (tt, *J*=2.2, 7.2 Hz, 1H), 5.01 (d, *J*=11.2 Hz, 1H), 5.02 (d, *J*=16 Hz, 1H), 5.86 (tdd, *J*=7, 11, 16.5 Hz, 1H), 7.20–7.31 (m, 10H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ ppm 21.0, 35.4, 37.9, 42.8, 81.9, 82.8, 116.6, 126.1, 126.5, 127.4 (3C), 128.2 (3C), 128.5 (2C), 135.7, 140.8, 141.8; HREIMS *m*/*z* 260.1561, calcd for $C_{20}H_{20}$ 260.1565; IR (film) cm^{-1} 3062, 2929, 1641, 1602, 739.

4.2.15. Trimethyl(3-phenylhex-5-en-1-ynyl)silane (**23**)[7]

Prepared with 1.5 equiv of allyltrimethylsilane and isolated as a clear oil.

^{1}H NMR ($CDCl_3$, 300 MHz) δ ppm 0.23 (s, 9H), 2.55 (t, *J*=7.1 Hz, 2H), 3.72 (t, *J*=7.1 Hz, 1H), 5.04 (d, *J*=11 Hz, 1H), 5.07 (d, *J*=15.5 Hz, 1H), 5.85 (m, 1H), 7.24 (m, 1H), 7.34 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ ppm 0.2, 38.8, 42.7, 87.7, 107.5, 116.8, 126.6, 127.4, 128.2, 135.1, 140.9. Data are in accordance with previously reported results.[7]

4.2.16. Hex-5-en-1-yne-1,3-diyldibenzene (**24**)[35]

Prepared with 1.5 equiv of allyltrimethylsilane and isolated as a clear oil.

^{1}H NMR ($CDCl_3$, 300 MHz) δ ppm 2.62 (t, *J*=7 Hz, 2H), 3.94 (t, *J*=7 Hz, 1H), 5.13 (m, 2H), 5.96 (ddt, *J*=7, 10.1, 17.1 Hz, 1H), 7.30–7.49 (m, 10H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ ppm 38.6, 42.8, 83.8, 90.9, 117.1, 123.7, 125.9, 126.3, 126.8, 127.3, 127.6, 127.8, 131.7, 131.9, 135.5, 141.4. Data are in accordance with previously reported results.[35]

4.2.17. Hex-5-en-1-yn-3-ylbenzene (**26**)[36]

Prepared with 1.5 equiv of allyltrimethylsilane and isolated as a clear oil.

^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 2.30 (s, 1H), 2.52 (t, *J*=7.1 Hz, 2H), 3.71 (t, *J*=7.0 Hz, 1H), 5.06 (d, *J*=10.4 Hz, 1H), 5.08 (d, *J*=15.8 Hz, 1H), 5.86 (m, 1H), 7.23–7.37 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ ppm 31.8, 38.7, 69.7, 85.5, 116.4, 125.9, 126.51 (2C), 128.42 (2C), 134.27, 140.02. Data are in accordance with previously reported results.[36]

4.2.18. (3,3-Dimethylhex-5-en-1-ynyl)benzene (**27**)[7]

Prepared with 1.5 equiv of allyltrimethylsilane and isolated as a clear oil.

^{1}H NMR ($CDCl_3$, 300 MHz) δ ppm 1.31 (s, 6H), 2.29 (d, *J*=7.2 Hz, 2H), 5.14 (d, *J*=8.8 Hz, 1H), 5.14 (d, *J*=16.8 Hz, 1H), 6.04 (m, 1H), 7.29 (m, 3H), 7.42 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ ppm 29.0, 31.5, 47.9, 80.7, 97.1, 117.5, 124.2, 127.5, 128.5, 131.8, 135.5. Data are in accordance with previously reported results.[7]

4.2.19. (4-Methyloct-1-en-5-yn-4-yl)benzene (**28**)[12]

Prepared with 1.5 equiv of allyltrimethylsilane and isolated as a clear oil.

^{1}H NMR ($CDCl_3$, 300 MHz) δ ppm 0.93 (t, *J*=7 Hz, 3H), 1.40 (m, 4H), 1.54 (s, 3H), 1.55 (m, 2H), 2.27 (t, *J*=6.9 Hz, 2H), 2.52 (m, 2H), 5.00 (d, *J*=15.5 Hz, 1H), 5.01 (d, *J*=12 Hz, 1H), 5.80 (m, 1H), 7.23 (m, 3H), 7.54 (d, *J*=7.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ ppm 14.0, 18.8, 22.2, 28.8, 29.5, 29.7, 31.1, 40.0, 48.9, 84.0, 84.9, 117.2, 126.2, 128.0, 135.2, 146.0. Data are in accordance with previously reported results.[12]

4.2.20. (3-(4-Methoxyphenyl)-3-phenylprop-1-ynyl)-trimethylsilane (**30**)[37]

Prepared with 1.1 equiv of anisole and isolated as a clear oil.

^{1}H NMR ($CDCl_3$, 300 MHz) δ ppm 0.27 (s, 9H), 2.96 (s, 3H), 5.00 (s, 1H), 6.86 (d, *J*=8.6 Hz, 2H), 7.20–7.33 (m, 5H), 7.38 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ ppm 0.1, 43.3, 55.3, 88.9, 107.1, 114.1, 126.7, 127.8, 128.5, 128.8, 133.8, 141.9, 158.5. Data are in accordance with previously reported results.[37]

4.2.21. (3-(2,4-Dimethoxyphenyl)prop-1-yne-1,3-diyl)-dibenzene (**31**)[10]

Prepared with 5 equiv of 1,3-dimethoxybenzene and isolated as a white solid.

^{1}H NMR ($CDCl_3$, 300 MHz) δ ppm 3.82 (s, 3H), 3.83 (s, 3H), 5.63 (s, 1H), 6.48 (d, *J*=2.4 Hz, 1H), 6.53 (dd, *J*=2.4, 8.4 Hz, 1H), 7.22 (m, 1H), 7.31 (m, 5H), 7.49 (m, 4H), 7.52 (d, *J*=8.3 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ ppm 36.3, 55.6, 55.8, 83.6, 91.4, 98.8, 104.8, 123.1, 124.0, 126.6, 128.0, 128.4, 128.5, 129.7, 131.9, 142.3, 157.3, 160.1. Data are in accordance with previously reported results.[10]

4.2.22. 2-(1,3-Diphenylprop-2-ynyl)furan (**32**)[10]

Prepared with 1.5 equiv of furan and isolated as a yellow oil.

^{1}H NMR ($CDCl_3$, 300 MHz) δ ppm 5.29 (s, 1H), 6.30 (d, *J*=3.2 Hz, 1H), 6.34 (dd, *J*=1.9, 3.2 Hz, 1H), 7.32 (m, 7H), 7.50 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ ppm 38.0, 84.1, 87.6, 106.8, 110.5, 123.3, 127.5, 128.0, 128.4, 128.8, 131.9, 139.0, 142.4, 153.9. Data are in accordance with previously reported results.[10]

4.2.23. 3-Acetyl-4-phenyldecane-2,6-dione (**34**)

Prepared with 5 equiv of acetylacetone and isolated as a clear oil.

^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 0.79 (t, *J*=7.3 Hz, 3H), 1.08–1.18 (m, 2H), 1.32–1.40 (m, 2H), 1.86 (s, 3H), 2.06–2.25 (m, 2H), 2.24 (s, 3H), 2.59 (dd, *J*=4.3, 16.1 Hz, 1H), 2.74 (dd, *J*=9.0, 16.1 Hz, 1H), 4.02 (ddd, *J*=4.3, 9.0, 11.1 Hz, 1H), 4.21 (d, *J*=11.1 Hz, 1H), 7.17–7.28 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ ppm 13.7, 22.0, 25.4, 29.7, 29.9, 40.8, 43.2, 46.7, 74.7, 127.2, 128.0 (2C), 128.8 (2C), 140.3, 203.3, 203.3, 208.7; HREIMS *m*/*z* 2889.1793, calcd for $C_{18}H_{24}O_3$ 289.1804; IR (film) cm^{-1} 2957, 1704, 1682, 701.

*4.2.24. 1-(2-Methyl-5-pentyl-4-phenylfuran-3-yl)ethanone (**35**)*

Prepared with 5 equiv of acetylacetone and isolated as a clear oil.

^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 0.82 (t, J=7.1 Hz, 3H), 1.19–1.25 (m, 4H), 1.56 (m, 2H), 1.90 (s, 3H), 2.44 (t, J=7.7 Hz, 2H), 2.54 (s, 3H), 7.22–7.39 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ ppm 13.9, 14.3, 25.7, 28.1, 30.7, 30.7, 31.1, 120.5, 122.9, 127.3, 128.3 (2C), 129.9 (2C), 138.8, 151.1, 156.2, 196.2; HREIMS m/z 271.1698, calcd for $C_{18}H_{22}O_2$ 271.1699; IR (film) cm^{-1} 2955, 1670, 1612, 1557.

*4.2.25. (1-Butoxypent-2-ynyl)benzene (**36**)*[12]

Prepared with 1.5 equiv of 1-butanol and isolated as a clear oil.

^{1}H NMR ($CDCl_3$, 300 MHz) δ ppm 0.91 (t, J=7 Hz, 3H), 0.92 (t, J=7.3 Hz, 3H), 1.37 (m, 6H), 1.59 (m, 4H), 2.28 (td, J=2.2, 7 Hz, 2H), 3.48 (dt, J=6.7, 9 Hz, 1H), 3.64 (dt, J=6.7, 8.9 Hz, 1H), 5.15 (s, 1H), 7.34 (m, 3H), 7.52 (d, J=7.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ ppm 14.0, 14.1, 19.0, 19.5, 22.3, 28.5, 31.2, 31.9, 68.0, 71.8, 78.3, 88.3, 127.5, 128.2, 128.5, 139.8. Data are in accordance with previously reported results.[12]

*4.2.26. (3-(But-3-enyloxy)-3-phenylprop-1-ynyl)trimethylsilane (**37**)*[9]

Prepared with 1.5 equiv of 3-buten-1-ol and isolated as a clear oil.

^{1}H NMR ($CDCl_3$, 300 MHz) δ ppm 0.22 (s, 9H), 2.40 (q, J=6.8 Hz, 2H), 3.57 (dt, J=7.1, 8.5 Hz, 1H), 3.71 (dt, J=6.9, 8.8 Hz, 1H), 5.05 (d, J=10.2 Hz, 1H), 5.12 (d, J=17.3 Hz, 1H), 5.21 (s, 1H), 5.85 (ddt, J=6.7, 10.3, 17 Hz, 1H), 7.36 (m, 3H), 7.52 (d, J=7.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ ppm 0.06, 34.2, 67.6, 72.0, 92.7, 103.3, 116.5, 127.6, 128.4, 128.5, 135.4, 138.6. Data are in accordance with previously reported results.[9]

*4.2.27. (3-(3-Chloropropoxy)-3-methylbut-1-ynyl)benzene (**38**)*[9]

Prepared with 1.5 equiv of 3-chloropropan-1-ol and isolated as a clear oil.

^{1}H NMR ($CDCl_3$, 300 MHz) δ ppm 1.56 (s, 6H), 2.07 (m, 2H), 3.70 (t, J=6.4 Hz, 2H), 3.78 (t, J=5.8 Hz, 2H), 7.32 (m, 3H), 7.44 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ ppm 28.6, 33.3, 42.2, 60.6, 70.5, 84.0, 91.6, 122.9, 128.2, 128.3, 131.7. Data are in accordance with previously reported results.[9]

*4.2.28. (1,3-Diphenylprop-2-ynyl)(phenyl)sulfane (**39**)*[38]

Prepared with 1.5 equiv of thiophenol and isolated as a clear oil.

^{1}H NMR ($CDCl_3$, 300 MHz) δ ppm 5.24 (s, 1H), 7.32 (m, 9H), 7.40 (m, 2H), 7.48 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ ppm 44.4, 87.0, 87.5, 123.1, 128.0, 128.2, 128.4, 128.4, 128.6, 128.6, 128.8, 131.8, 133.5, 134.6, 138.2. Data are in accordance with previously reported results.[38]

*4.2.29. Ethyl 2-(1-phenylpent-2-ynylthio)acetate (**40**)*[12]

Prepared with 1.5 equiv of ethylmercaptoacetate and isolated as a clear oil.

^{1}H NMR ($CDCl_3$, 300 MHz) δ ppm 0.92 (t, J=7 Hz, 3H), 1.24–1.44 (m, 4H), 1.30 (t, J=7 Hz, 3H), 1.60 (m, 2H), 2.30 (td, J=2.2, 7 Hz, 2H), 3.23 (d, J=15 Hz, 1H), 3.50 (d, J=15 Hz, 1H), 4.19 (q, J=7 Hz, 2H), 5.01 (s, 1H), 7.30 (d, J=7.3 Hz, 1H), 7.52 (t, J=7.3 Hz, 2H), 7.53 (d, J=7.3 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ ppm 14.1, 14.3, 19.0, 22.3, 28.6, 31.2, 33.8, 39.7, 61.5, 77.0, 87.6, 127.5, 128.2, 128.7, 138.2, 170.4. Data are in accordance with previously reported results.[12]

*4.2.30. (2R)-Ethyl 2-(tert-butoxycarbonylamino)-3-(1,3-diphenylprop-2-ynylthio)propanoate (**41**)*[12]

Prepared with 1.5 equiv of Boc(L)-Cys-OEt and isolated as a 1:1 mixture of two diastereoisomers (clear oil).

^{1}H NMR ($CDCl_3$, 300 MHz) δ ppm first diastereoisomer 1.25 (t, J=7.3 Hz, 3H), 1.46 (s, 9H), 2.93 (dd, J=7, 13.9 Hz, 1H), 3.43 (dd, J=3.9, 13.9 Hz, 1H), 4.23 (q, J=7.1 Hz, 2H), 4.65 (br s, 1H), 5.21 (s, 1H), 5.35 (t, J=7.7 Hz, 1H), 7.31–7.40 (m, 6H), 7.50–7.60 (m, 4H); second diastereoisomer 1.27 (t, J=7.3 Hz, 3H), 1.45 (s, 9H), 3.07 (dd, J=7, 13.9 Hz, 1H), 3.31 (dd, J=5.1, 14 Hz, 1H), 4.20 (q, J=7.1 Hz, 2H), 4.60 (br s, 1H), 5.21 (s, 1H), 5.35 (t, J=7.7 Hz, 1H), 7.31–7.40 (m, 6H), 7.50–7.60 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ ppm first diastereoisomer 14.3, 28.5, 34.8, 39.6, 53.1, 61.9, 80.2, 86.7, 86.9, 122.7, 128.1, 128.1, 128.4, 128.5, 128.8, 131.9, 137.8, 155.3, 171.1; second diastereoisomer 14.3, 28.5, 34.5, 39.9, 53.2, 61.9, 80.2, 86.5, 86.6, 122.8, 128.1, 128.2, 128.4, 128.6, 128.8, 131.9, 137.9, 155.4, 171.2.

*4.2.31. (1-Phenyloct-2-ynyl)benzenesulfonamide (**42**)*[40]

Prepared with 1.2 equiv of benzenesulfonamide and isolated as a clear oil.

^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 0.88 (t, J=7.3 Hz, 3H), 1.19–1.34 (m, 6H), 1.94–1.98 (m, 2H), 4.78 (d, J=8.8 Hz, 1H), 5.30 (d, J=8.8 Hz, 1H), 7.27–7.33 (m, 5H), 7.46–7.48 (m, 3H), 7.77 (d, J=8.3 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ ppm 13.9, 18.5, 22.1, 27.9, 31.0, 49.4, 76.6, 87.5, 127.2, 127.5, 128.1, 128.5, 129.3, 137.6, 138.2, 143.2. Data are in accordance with previously reported results.[40]

*4.2.32. 3-Methyl-1-phenylbut-2-en-1-one (**44**)*[39]

Prepared with 1.5 equiv of ethanol and isolated as a clear oil.

^{1}H NMR ($CDCl_3$, 300 MHz) δ ppm 2.03 (s, 3H), 2.22 (s, 3H), 6.75 (s, 1H), 7.43 (t, J=7.2 Hz, 2H), 7.52 (t, J=7.2 Hz, 1H), 7.93 (d, J=7.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ ppm 20.8, 27.6, 120.7, 127.7, 128.0, 131.8, 138.8, 156.4, 190.7. Data are in accordance with previously reported results.[39]

*4.2.33. (E)-1-Phenyloct-1-en-3-one (**45**)*[41]

Prepared with 1.5 equiv of ethanol and isolated as a clear oil.

^{1}H NMR ($CDCl_3$, 300 MHz) δ ppm 0.93 (t, J=7 Hz, 3H), 1.37 (m, 4H), 1.70 (m, 2H), 2.67 (t, J=7 Hz, 2H), 6.70 (d, J=16 Hz, 1H), 7.30–7.40 (m, 3H), 7.53 (m, 2H), 7.56 (d, J=16 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ ppm 13.9, 22.5, 24.1, 29.7, 40.9, 126.7, 128.2 (2C), 128.9 (2C), 130.4, 134.6, 142.3, 200.7. Data are in accordance with previously reported results.[41]

*4.2.34. (1-Ethoxyoct-2-ynyl)benzene (**46**)*[12]

Prepared with 1.5 equiv of ethanol and isolated as a clear oil.

^{1}H NMR ($CDCl_3$, 300 MHz) δ ppm 0.91 (t, J=7 Hz, 3H), 1.2 (t, J=7 Hz, 3H), 1.37 (m, 4H), 1.57 (m, 2H), 2.29 (dt, J=1.9, 7 Hz, 2H), 3.5 (m, 1H), 3.70 (m, 1H), 5.1 (s, 1H), 7.30–7.40 (m, 3H), 7.53 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ ppm 14.1, 15.2, 18.8, 22.2, 28.3, 31.1, 63.5, 71.6, 78.2, 88.2, 127.4 (2C), 128.1, 128.4 (2C), 139.6. Data are in accordance with previously reported results.[12]

*4.2.35. 1,3-Diphenylpropyne (**47**)*[42]

Prepared with 1.2 equiv of triethylsilane and isolated as a clear oil.

^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 3.83 (s, 2H), 7.23–7.46 (m, 10H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ ppm 25.7, 82.6, 84.5, 123.6, 126.6, 127.8 (2C), 127.9 (2C), 128.2, 128.5 (2C), 131.6 (2C), 136.7. Data are in accordance with previously reported results.[42]

*4.2.36. Hept-2-ynylbenzene (**48**)*

Prepared with 1.2 equiv of triethylsilane and isolated as a clear oil.

^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 0.84 (t, J=7.2 Hz, 3H), 1.30–1.47 (m, 4H), 2.12–2.16 (m, 2H), 3.49 (m, 2H), 7.11–7.27 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ ppm 13.6, 18.5, 22.0, 25.1, 31.1, 77.4, 82.6, 126.3, 127.8 (2C), 128.4 (2C), 137.6; HREIMS m/z 172.1253, calcd for $C_{13}H_{16}$ 172.1252; IR (film) cm^{-1} 3086, 3064, 3029, 2931, 2872, 2204, 1707, 1605.

*4.2.37. 1-(Hept-2-ynyl)-2-methylbenzene (**49**)*

Prepared with 1.2 equiv of triethylsilane and isolated as a clear oil.

^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 0.92 (t, 3H, J=7.2 Hz), 1.38–1.55 (m, 4H), 2.22 (tt, J=2.0, 7.1 Hz, 2H), 2.31 (s, 3H), 3.50 (t, J=2.3 Hz, 2H), 7.15–7.21 (m, 3H), 7.45 (d, J=6.9 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ ppm 13.6, 18.5, 19.2, 22.0, 23.3, 31.1, 77.0, 82.8, 126.0, 126.6, 128.1, 130.0, 135.8, 135.9; HREIMS m/z 186.1404, calcd for $C_{14}H_{18}$ 186.1409; IR (film) cm^{-1} 2960, 2931, 2873, 2199, 1707, 1602.

*4.2.38. N-Tosyl-1,1′-diphenylmethylamine (**51**)*[31]

Prepared with 3 equiv of tosylamine and isolated as a white solid.

^{1}H NMR ($CDCl_3$, 300 MHz) δ ppm 2.38 (s, 3H), 5.24 (d, J=7.1 Hz, 1H), 5.58 (d, J=7.1 Hz, 1H), 7.09–7.23 (m, 12H), 7.57 (d, J=8.3 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ ppm 21.4, 61.3, 127.2 (2C), 127.3 (4C), 127.5 (2C), 128.5 (4C), 129.3 (2C), 137.3, 140.5 (2C), 143.2. Data are in accordance with previously reported results.[31]

*4.2.39. N-Tosyl-1-phenylethylamine (**53**)*[31]

Prepared with 3 equiv of tosylamine and isolated as a white solid.

^{1}H NMR ($CDCl_3$, 300 MHz) δ ppm 1.42 (d, J=6.9 Hz, 3H), 2.39 (s, 3H), 4.47 (quint, J=6.9 Hz, 1H), 5.23 (d, J=7.1 Hz, 1H), 7.10–7.13 (m, 2H), 7.16–7.19 (m, 5H), 7.63 (d, J=8.1 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ ppm 21.4, 23.5, 53.6, 126.1 (2C), 127.0 (2C), 127.3, 128.4 (2C), 129.4 (2C), 137.6, 142.0, 143.0. Data are in accordance with previously reported results.[31]

*4.2.40. N-(1,3-Diphenyl-2(E)-propenyl)-4-methylbenzenesulfonamide (**55**)*[43]

Prepared with 1.1 equiv of tosylamine and isolated as a white solid.

^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 2.16 (s, 3H), 4.97 (dd, J=6.7, 6.9 Hz, 1H), 5.38 (d, J=7.5 Hz, 1H), 5.93 (dd, J=6.8, 15.8 Hz, 1H), 6.19 (d, J=15.7 Hz, 1H), 6.96–7.13 (m, 12H), 7.52 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ ppm 21.3, 59.7, 126.5 (2C), 127.0 (2C), 127.2 (2C), 127.7, 127.8, 128.1, 128.4 (2C), 128.6 (2C), 129.4 (2C), 131.9, 136.0, 137.6, 139.6, 143.2. Data are in accordance with previously reported results.[43]

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