PMA–Silica Gel Catalyzed Propargylation of Aromatic Compounds with Arylpropargyl Alcohols under Solvent-Free Conditions[1]

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Abstract: PMA–silica gel has been utilized to catalyze efficiently the propargylation of aromatic compounds with arylpropargyl alcohols in the absence of solvent under environmentally benign conditions.

Key words: propargylation, nucleophilic substitution, Nicholas reaction, Friedel–Crafts alkylation

Electrophilic attack on an aromatic carbon is a useful method for the functionalization of aromatic compounds. Reactions such as the Friedel–Crafts alkylation or acylation and the Baylis–Hillman reaction, which provide functionalized aromatic compounds[2] with special properties, have been greatly studied as C–C bond forming reactions, however, very little attention has been focussed on the propargylation of aromatic compounds, which would afford scaffolds that are key intermediates for the synthesis of several natural products.[3a–g] Propargylation of aromatic compounds[3h,i] is achieved by the Nicholas reaction using a stoichiometric amount of octacarbonyldicobalt, and a few reports use Brønsted acids;[4] complexes involving metals such as rhenium,[5] ruthenium,[6] gold,[7,8] and bismuth[9] are also well precedented. Zhan et al. have recently achieved propargylation of aromatic compounds with propargyl acetates and nucleophilic substitution of propargylic alcohols employing iron(III) chloride as a catalyst.[10] The high cost of the reagents, multistep reactions, or harsh conditions limit many of these existing methodologies, thus an inexpensive reagent system, which could catalyze the reaction more efficiently, is always desirable.

Our efforts towards green chemistry[11] has led to the development of new synthetic methodologies. One of the key principles involved in green chemistry is to minimize stoichiometric amount of reagents to catalytic amounts and allow the process to run with high efficiency. Many heteropoly acids fall under this category as they exhibit high catalytic activity and good selectivity.[12] Recently, to this end, Montmorillonite K-10 was used as a mild acid[13] for the Nicholas reaction. We have shown that phosphomolybdic acid supported on silica gel (PMA–silica gel) works as an excellent solid reagent system that catalyzes acetal deprotection and Ferrier rearrangement reactions.[14]

In continuation of our investigations on PMA–silica gel as a solid reagent system, we disclose herein the propargylation of aromatic compounds with arylpropargyl alcohols **1** both in the presence and absence of solvent media (Scheme 1).

At the beginning of our study, phenol and PMA–silica gel were added to 1,3-diphenylprop-2-yn-1-ol (**1a**),[15] in acetonitrile and the reaction mixture was stirred until the starting material disappeared. The reaction mixture was filtered and the filtrate was concentrated to provide the crude product, which was further purified and characterized as the propargylated product, 4-(1,3-diphenylprop-2-ynyl)phenol (**2a**).

Encouraged by this result and to investigate further the efficiency of PMA–silica gel, phenol was propargylated with 1,3-diphenylprop-2-yn-1-ol (**1a**) using different concentrations of PMA, and the results show that as the concentration of PMA–silica gel increased from 0.025 mol% to 1 mol% the yield is enhanced and also the duration of the reaction is decreased (Table 1). Furthermore, to check the role of the catalyst, different acids such as 4-toluenesulfonic acid, phosphomolybdic acid, silica gel, silica gel supported sodium bisulfate, and silica gel supported perchloric acid, heterogeneous catalysts such as Amberlyst and Montmorillonite K-10 were also tested for propargylations. It was found that PMA–silica gel and perchloric acid were the best in terms of yields and reaction time, while others including phosphomolybdic acid without silica gel took longer for complete conversion (Table 2).

To study the role of the solvent, reactions were performed with 1,3-diphenylprop-2-yn-1-ol (**1a**) and cresol (Table 3) in different solvents such as nitromethane, dichloromethane, 1,2-dichloroethane, polyethylene glycol (PEG), and water and also under solvent-free conditions. We observed no solvent influence except that in PEG, where no reaction was observed, and in water where only 20% conversion was observed even after five hours at room temperature. Also, we found that the reaction proceeded much faster without the solvent (50% progress in absence of solvent against 10% in presence of solvent). However, the reaction went to completion in about the same time both in the presence and absence of solvent (Table 3). It is noteworthy to mention that, after completion of the reaction, the solid catalyst could be washed with diethyl ether and reused up to three times with small variations in yield.[16]

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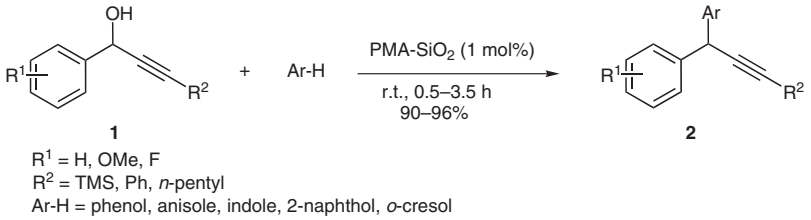


Scheme 1 Propargylation of aromatic compounds

Table 1 PMA–Silica Gel Catalyzed Propargylation of Phenol with 1,3-Diphenylprop-2-yn-1-ol (**1a**)[a]

Time	Conversion[b] (%) to **2a** with varying concentration of PMA–silica gel (mol%)									
	0.025 mol%	0.05 mol%	0.10 mol%	0.15 mol%	0.20 mol%	0.25 mol%	0.30 mol%	0.5 mol%	1.0 mol%	5.0 mol%
20 min	5	15	20	35	40	55	65	80	90	90
30 min	10	30	40	55	62	85	85	90	100	100
45 min	15	40	50	80	83	100	100	–	–	–
60 min	20	80	90	90	92	–	–	–	–	–
90 min	30	100	100	100	100	–	–	–	–	–

[a] 1,3-Diphenylprop-2-yn-1-ol (**1a**), PhOH, MeCN, r.t.
[b] Monitored and measured by TLC analysis.

Table 2 Acid-Catalyzed Propargylation of Phenol with 1-(4-Methoxyphenyl)-3-(trimethylsilyl)prop-2-yn-1-ol (**1b**)[a]

Acid[a]	Conversion[b] (%) to **2f** with varying time		
	45 min	2 h	3–5 h
silica gel	no reaction	no reaction	no reaction
PMA	65	70	85
PMA–silica gel	100	–	–
$HClO_4$	88	>90	–
PTSA	80	87	>90
$NaHSO_4$–silica gel	60	70	>90
$HClO_4$–silica gel	80	85	>90
Amberlyst	70	75	>90
Montmorillonite	72	75	>90

[a] 1-(4-Methoxyphenyl)-3-(trimethylsilyl)prop-2-yn-1-ol (**1b**) and PhOH were treated with 1 mol% of acid in MeCN, r.t.
[b] Monitored and measured by TLC analysis.

Table 3 PMA–Silica Gel Catalyzed Propargylation of Cresol with 1,3-Diphenylprop-2-yn-1-ol (**1a**) Using Various Solvents

Entry	Solvent	Catalyst	Time (h)	Conversion[b] (%) to **2c**
1	H_2O	PMA–silica gel (1 mol%)	1.0	>20
2	MeCN	PMA–silica gel (1 mol%)	1.0	>95
3	CH_2Cl_2	PMA–silica gel (1 mol%)	1.0	>95
4	DCE	PMA–silica gel (1 mol%)	1.0	>95
5	$MeNO_2$	PMA–silica gel (1 mol%)	1.0	>95
6	PEG 400	PMA–silica gel (1 mol%)	1.0	no reaction
7	no solvent	PMA–silica gel (1 mol%)	1.0	>95

[a] 1,3-Diphenylprop-2-yn-1-ol (**1a**) and cresol were treated with 1 mol% of PMA–silica gel at r.t.
[b] Monitored and measured by TLC analysis.

After standardizing the conditions, the generality of the reaction was studied further by examining the propargylation of various aromatic compounds with propargyl alcohols **1a–e** (Table 4).[17] Gratifyingly, phenols, anisole, and 2-naphthol responded well to these conditions and substitution was always present at the electron-rich position of the aromatic compounds (Table 4, entries 1–4, 6–8 10–12, 14–16).[18] Mechanistically,[19] we believe that a carbon nucleophile adds on to the propargylic cation. However, no attempts were made to study the exact mechanism. Simple benzene and toluene did not give the expected products whereas the heterocycle indole responded well under the present protocol (Table 4, entries 5, 9, 13). Even the arylpropargyl alcohol with a free terminal acetylene **1e** gave the corresponding product **2q** in good yield (Table 4, entry 17), A propargylic alcohol without the aryl group **1f** did not react under the present conditions (Table 4, entry 18). Attempts at the nucleophilic substitution reaction using heteroatom-centered nucleophiles (such as O-, S-, and N-centered nucleophiles) did not yield the required product under the present protocol. However, this could be achieved by heating the reaction mixture.[20]

Table 4 PMA–Silica Gel Catalyzed Propargylation of Aromatic Compounds

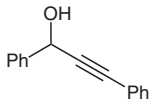
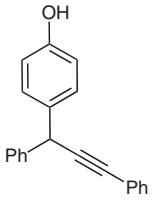
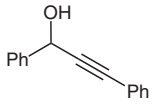
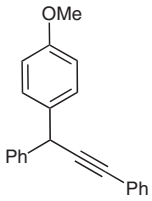
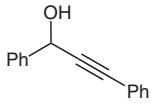
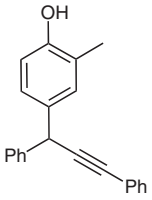
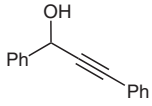
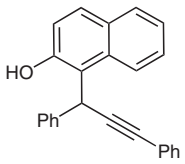
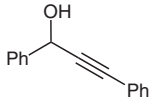
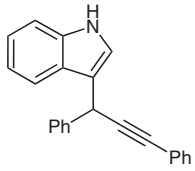
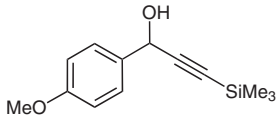
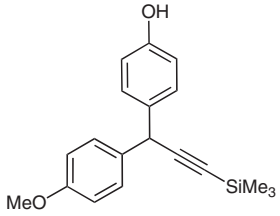
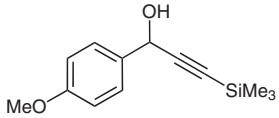
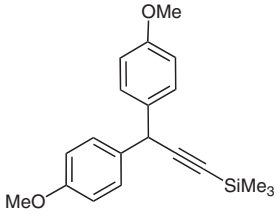
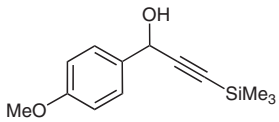
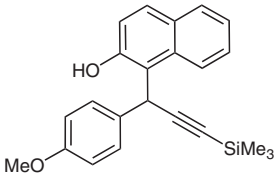
Entry	Propargyl alcohol		Aromatic compound	Product[a]		Time (h)	Yield[b] (%)
1		**1a**	phenol		**2a**	0.5 0.5	96 96[c]
2		**1a**	anisole		**2b**	2.0	92
3		**1a**	*o*-cresol		**2c**	1.0 1.0	96 96[c]
4		**1a**	2-naphthol		**2d**	2.0	95
5		**1a**	1*H*-indole		**2e**	3.5	92
6		**1b**	phenol		**2f**	0.45	96
7		**1b**	anisole		**2g**	2.0	91
8		**1b**	2-naphthol		**2h**	2.0 2.0	94 94[c]

Table 4 PMA–Silica Gel Catalyzed Propargylation of Aromatic Compounds (continued)

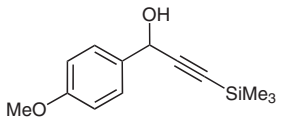
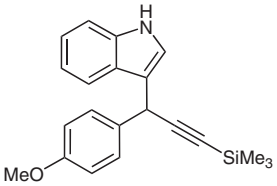
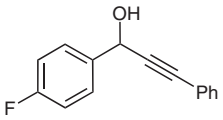
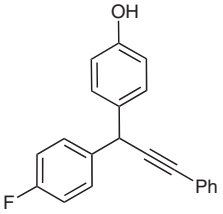
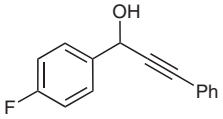
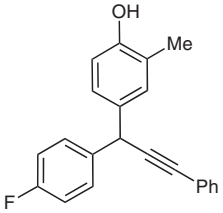
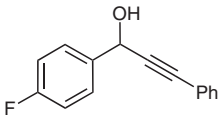
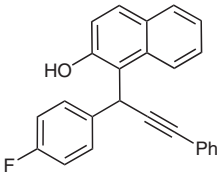
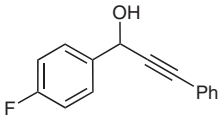
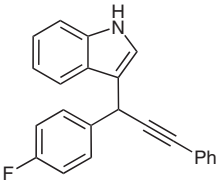
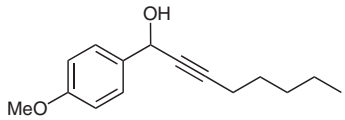
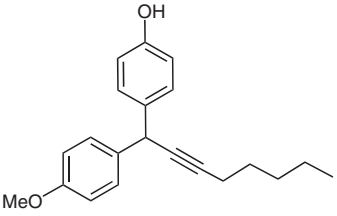
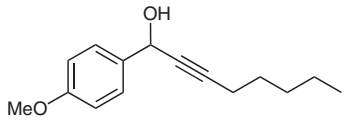
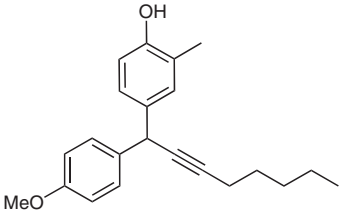
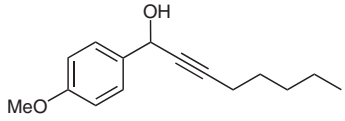
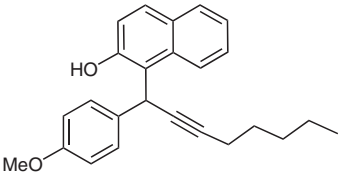
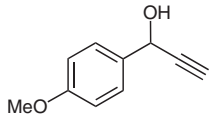
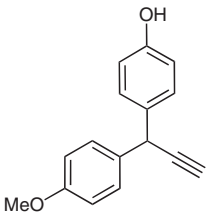
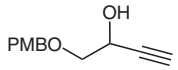
Entry	Propargyl alcohol		Aromatic compound	Product[a]		Time (h)	Yield[b] (%)
9		**1b**	1*H*-indole		**2i**	3.5	90
10		**1c**	phenol		**2j**	3.0 3.0	96 96[c]
11		**1c**	*o*-cresol		**2k**	1.5 1.5	95 95[c]
12		**1c**	2-naphthol		**2l**	2.0	94
13		**1c**	1*H*-indole		**2m**	3.5 3.5	91 91[c]
14		**1d**	phenol		**2n**	0.45 0.45	95 95[c]
15		**1d**	*o*-cresol		**2o**	1.0	94
16		**1d**	2-naphthol		**2p**	2.0 2.0	93 93[c]

Table 4 PMA–Silica Gel Catalyzed Propargylation of Aromatic Compounds (continued)

Entry	Propargyl alcohol		Aromatic compound	Product[a]		Time (h)	Yield[b] (%)
17		**1e**	phenol		**2q**	0.45	93
18		**1f**	phenol	no reaction			

[a] Products characterized by ^{1}H NMR and ^{13}C NMR spectroscopy and mass spectrometry.
[b] Isolated and optimized yields.
[c] Reactions were run under solvent-free conditions.

In conclusion, the PMA–silica gel reagent system works as a green catalyst for the propargylation of aromatic compounds with arylpropargyl alcohols. The simple reaction conditions involve an inexpensive catalyst and, also, the reusability of the catalyst system makes this an useful and attractive protocol over existing procedures. Further work on the exploration of PMA–silica gel for substitution reactions with tertiary propargylic alcohols/acetates is currently underway and the results will be published in due course.

Column chromatography was performed using silica gel (60–120 mesh). All solvents (MeCN, CH_2Cl_2, DCE, $MeNO_2$, and PEG 400) were of AR grade and commercially available and used without further drying. IR spectra were recorded on a Perkin-Elmer Infrared spectrophotometer as KBr wafers, neat, or a thin film ($CHCl_3$). ^{1}H NMR and ^{13}C NMR data were recorded on a Varian Gemini 200 or Bruker Avance 300 instrument using TMS as an internal standard. Mass spectra were recorded on a Micromass Quatro LC triple quadrupole mass spectrometer for ESI analysis. HRMS data were obtained through use of ESI-QTOF high-resolution techniques on an AB Systems QSTAR plus mass spectrometer.

Preparation of the PMA–Silica Gel Reagent

$H_3PMo_{12}O_{40}\cdot 2\,H_2O$ (1.0 g, 1 equiv by wt) was dissolved in MeOH (5 mL) and to this was added slowly silica gel (9 g, 9 equiv by wt, 60–120 mesh). The mixture was stirred at r.t. for 30 min and then the solvent was removed under vacuo to afford a dry yellowish green powder that contained 10% w/w of PMA.

3,3-Diarylpropy-1-ynols 2; General Procedure Using a Solvent

To a soln of arylpropargyl alcohol **1** (1 mmol) and nucleophile (1 mmol) in MeCN (5 mL) was added PMA–silica gel (1 mol%). The mixture was stirred at r.t. for the appropriate time. When the reaction was complete (TLC), the mixture was filtered and washed with CH_2Cl_2. The combined organic filtrates were evaporated to dryness in vacuo. The crude product was purified by column chromatography (EtOAc–hexane).

3,3-Diarylpropy-1-ynols 2; General Procedure under Solvent-Free Conditions

To a mixture of arylpropargyl alcohol **1** (1 mmol) and nucleophile (1 mmol) was added PMA–silica gel (1 mol%). The mixture was stirred at r.t. for the appropriate time. When the reaction was complete (TLC), the mixture was diluted with Et_2O and filtered. The combined organic filtrates were evaporated to dryness in vacuo to yield the crude product, which was purified by column chromatography (EtOAc–hexane). The silica gel supported PMA was separated and resubjected to this protocol with the same propargyl alcohol for propargylation to produce the products with consistent yields.

4-(1,3-Diphenylprop-2-ynyl)phenol (2a)

Brownish yellow sticky liquid. Data are in accordance with the literature.[5,9a]

^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.98 (br s, 1 H, OH), 5.09 (s, 1 H), 6.71 (d, *J* = 8.3 Hz, 2 H), 7.15–7.32 (m, 9 H), 7.36 (d, *J* = 7.5 Hz, 2 H), 7.41–7.47 (m, 1 H).

1-(1,3-Diphenylprop-2-ynyl)-4-methoxybenzene (2b)

Yellow sticky liquid.

IR (KBr): 3447, 3058, 3028, 2927, 2852, 2381, 2186, 1600, 1508, 1448, 1252, 1175, 1031, 756, 695 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.69 (s, 3 H), 5.04 (s, 1 H), 6.73 (d, *J* = 9.0 Hz, 2 H), 7.17–7.25 (m, 8 H), 7.27–7.32 (m, 2 H), 7.35–7.41 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 43.0, 55.3, 84.9, 90.7, 114.1, 123.7, 127.6, 127.9, 128.0, 128.3, 128.7, 129.0, 131.9, 134.0, 142.2, 158.7.

MS (ESI): *m*/*z* = 299 [M + H]$^+$.

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{19}O$: 299.1436; found: 299.1432.

4-(1,3-Diphenylprop-2-ynyl)-2-methylphenol (2c)

Brownish yellow sticky liquid.

IR (KBr): 3422, 3026, 2923, 2856, 2396, 2210, 1951, 1879, 1705, 1599, 1490, 1448, 1263, 1112, 756, 694 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.20 (s, 3 H), 4.53 (br s, 1 H, OH), 5.06 (s, 1 H), 6.63 (d, *J* = 7.5 Hz, 1 H), 7.03–7.11 (m, 2 H), 7.15–7.30 (m, 6 H), 7.35–7.39 (m, 2 H), 7.42–7.45 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.8, 42.8, 84.6, 90.6, 114.9, 123.5, 124.0, 126.3, 126.7, 127.7, 127.8, 128.1, 128.5, 130.4, 131.6, 133.8, 142.1, 152.6.

MS (ESI): *m*/*z* = 299 [M$^+$ + H].

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{19}O$: 299.1436; found: 299.1435.

1-(1,3-Diphenylprop-2-ynyl)naphthalen-2-ol (2d)
Brownish yellow sticky liquid. Data are in accordance with the literature.[5,9a]

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.21 (s, 1 H), 6.35 (br s, 1 H, OH), 7.10 (d, *J* = 9.0 Hz, 1 H), 7.15–7.35 (m, 7 H), 7.38–7.51 (m, 5 H), 7.68–7.79 (m, 2 H), 7.96 (d, *J* = 8.3 Hz, 1 H).

3-(1,3-Diphenylprop-2-ynyl)-1*H*-indole (2e)
Pale yellow sticky liquid.

IR (KBr): 3745, 3417, 3055, 2923, 2853, 2392, 2210, 1596, 1488, 1451, 1416, 1339, 1216, 1091, 1024, 749, 692 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 5.34 (s, 1 H), 6.90–7.13 (m, 3 H), 7.10–7.26 (m, 7 H), 7.33–7.50 (m, 5 H), 7.86 (br s, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 35.5, 83.3, 90.5, 111.2, 117.0, 119.6, 122.2, 122.5, 123.7, 126.1, 126.8, 127.8, 127.9, 128.1, 128.3, 128.4, 131.7, 136.7, 141.3.

MS (ESI): *m*/*z* = 308 [M^+ + H].

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{23}H_{18}N$: 308.1470; found: 308.1458.

4-[1-(4-Methoxyphenyl)-3-(trimethylsilyl)prop-2-ynyl]phenol (2f)
Pale yellow sticky liquid.

IR (neat): 3415, 2957, 2927, 2855, 2376, 2169, 1608, 1508, 1459, 1248, 1174, 1034, 842, 761, 573 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.12 (s, 9 H), 3.69 (s, 3 H), 4.66 (br s, 1 H, OH), 4.77 (s, 1 H), 6.62 (d, *J* = 8.3 Hz, 2 H), 6.71 (d, *J* = 9.0 Hz, 2 H), 7.07 (d, *J* = 8.3 Hz, 2 H),7.12 (d, *J* = 8.3 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 1.0, 42.4, 55.2, 88.6, 107.2, 113.9, 115.3, 128.7, 128.9, 134.0, 134.2, 154.3, 158.4.

MS (ESI): *m*/*z* = 311 [M^+ + H].

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{23}O_2Si$: 311.1475; found: 311.1467.

[3,3-Bis(4-methoxyphenyl)prop-1-ynyl]trimethylsilane (2g)
Pale yellow sticky liquid.

IR (KBr): 3444, 2959, 2382, 2171, 1614, 1511, 1460, 1249, 1173, 1030, 845, 761 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.18 (s, 9 H), 3.75 (s, 6 H), 4.85 (s, 1 H), 6.77 (d, *J* = 8.9 Hz, 4 H), 7.19 (d, *J* = 7.5 Hz, 4 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.1, 37.6, 55.1, 92.42, 104.0, 113.1, 113.6, 128.8, 129.3, 131.2, 134.2, 159.1, 159.7.

MS (ESI): *m*/*z* = 325 [M^+ + H].

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{24}NaO_2Si$: 347.1443; found: 347.1441.

1-[1-(4-Methoxyphenyl)-3-(trimethylsilyl)prop-2-ynyl]naphthalen-2-ol (2h)
Yellow sticky liquid.

IR (neat): 3414, 2958, 2835, 2381, 2166, 1625, 1508, 1250, 1176, 1027, 843, 751 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.15 (s, 9 H), 3.63 (s, 3 H), 5.79 (s, 1 H), 6.66 (d, *J* = 9.5 Hz, 2 H), 6.79 (s, 1 H), 7.01–7.34 (m, 5 H), 7.55–7.67 (m, 2 H), 7.75 (d, *J* = 8.1 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.07, 33.6, 55.2, 90.8, 106.0, 114.3, 117.5, 119.4, 123.1, 123.5, 126.4, 128.3, 128.8, 129.4, 129.7, 131.1, 132.3, 152.6, 158.5.

MS (ESI): *m*/*z* = 359 [M – H]$^+$.

HRMS: *m*/*z* [M – H]$^+$ calcd for $C_{23}H_{23}O_2Si$: 359.1480; found: 359.1467.

3-[1-(4-Methoxyphenyl)-3-(trimethylsilyl)prop-2-ynyl]-1*H*-indole (2i)
Yellow sticky liquid.

IR (KBr): 3415, 3056, 2958, 2836, 2369, 2169, 1610, 1508, 1458, 1250, 1176, 1031, 844, 744 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.11 (s, 9 H), 3.68 (s, 3 H), 5.07 (s, 1 H), 6.71 (d, *J* = 8.3 Hz, 2 H), 6.90–6.94 (m, 2 H), 7.03 (t, *J* = 8.3 Hz, 1 H), 7.15–7.24 (m, 3 H), 7.37 (d, *J* = 7.5 Hz, 1 H), 7.77 (br s, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.08, 35.0, 55.1, 87.0, 107.4, 111.1, 113.7, 116.6, 119.2, 119.5, 121.9, 122.4, 125.8, 128.7, 133.2, 136.6, 158.2.

MS (ESI): *m*/*z* = 333 [M^+].

HRMS: *m*/*z* [M – H]$^+$ calcd for $C_{21}H_{22}NOSi$: 332.1476; found: 332.1470.

4-[1-(4-Fluorophenyl)-3-phenylprop-2-ynyl]phenol (2j)
Yellow sticky liquid.

IR (KBr): 3379, 2924, 2386, 2169, 1600, 1506, 1443, 1226, 1156, 832, 757, 691 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.82 (br s, 1 H, OH), 5.08 (s, 1 H), 6.73 (d, *J* = 9.0 Hz, 2 H), 6.96 (t, *J* = 9.0 Hz, 2 H), 7.20–7.26 (m, 5 H), 7.31–7.35 (m, 2 H), 7.40–7.44 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 42.1, 84.9, 90.2, 115.2, 115.5, 123.3, 128.1, 128.3, 129.1, 129.3, 129.4, 131.6, 133.9, 137.3, 137.7, 138.1, 154.5, 163.5, 167.2.

MS (ESI): *m*/*z* = 301 [M – H]$^+$.

HRMS: *m*/*z* [M – H]$^+$ calcd for $C_{21}H_{14}FO$: 301.1032; found: 301.1028.

4-[1-(4-Fluorophenyl)-3-phenylprop-2-ynyl]-2-methylphenol (2k)
Light brownish yellow sticky liquid.

IR (KBr): 3418, 2924, 2391, 2016, 1599, 1505, 1265, 1224, 1113, 1017, 840, 756, 690 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.14 (s, 3 H), 4.80 (br s, 1 H, OH), 4.97 (s, 1 H), 6.59 (d, *J* = 7.5 Hz, 1 H), 6.87–7.00 (m, 4 H), 7.17–7.22 (m, 3 H), 7.25–7.30 (m, 2 H), 7.34–7.38 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 16.0, 42.4, 64.6, 85.0, 90.5, 115.2, 115.3, 115.6, 123.6, 124.2, 126.6, 128.2, 128.4, 129.4, 129.5, 130.6, 131.8, 133.9, 138.1, 153.0, 160.3, 163.5.

MS (ESI): *m*/*z* = 317 [M + H]$^+$.

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{18}FO$: 317.1342; found: 317.1338.

1-[1-(4-Fluorophenyl)-3-phenylprop-2-ynyl]naphthalen-2-ol (2l)
Brownish yellow sticky liquid.

IR (KBr): 3422, 3059, 2924, 2853, 2163, 1870, 1626, 1439, 1224, 1157, 814, 751 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.18 (s, 1 H), 6.33 (br s, 1 H, OH), 6.94 (t, *J* = 8.6 Hz, 2 H), 7.12 (d, *J* = 8.8 Hz, 1 H), 7.23–7.32 (m, 4 H), 7.36–7.47 (m, 5 H), 7.70–7.78 (m, 2 H), 7.93 (d, *J* = 8.4 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 33.2, 86.2, 88.5, 115.5, 115.7, 117.7, 119.2, 122.6, 123.2, 123.6, 127.0, 128.5, 128.7, 128.9, 129.0, 129.5, 129.9, 131.1, 131.9, 132.4, 135.5, 135.6, 152.3, 160.4, 163.6.

MS (ESI): m/z = 353 $[M + H]^+$.

HRMS: m/z $[M + H]^+$ calcd for $C_{25}H_{18}OF$: 353.1341; found: 353.1334.

3-[1-(4-Fluorophenyl)-3-phenylprop-2-ynyl]-1*H*-indole (2m)
Pale yellow sticky liquid.

IR (KBr): 3751, 3416, 3057, 2962, 2379, 2176, 1890, 1601, 1505, 1453, 1341, 1261, 1222, 1094, 1018, 801, 748, 691 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 5.33 (s, 1 H), 6.88–7.00 (m, 2 H), 7.04–7.11 (m, 2 H), 7.17–7.26 (m, 5 H), 7.34–7.44 (m, 5 H), 7.88 (br s, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 34.9, 83.7, 90.4, 111.5, 115.3, 115.6, 116.8, 119.7, 119.8, 122.5, 122.8, 123.7, 126.1, 128.1, 128.4, 129.5, 129.6, 131.8, 136.9, 137.1, 137.2, 160.3, 163.5.

MS (ESI): m/z = 326 $[M + H]^+$.

HRMS: m/z $[M + H]^+$ calcd for $C_{23}H_{17}FN$: 326.1345; found: 326.1342.

4-[1-(4-Methoxyphenyl)oct-2-ynyl]phenol (2n)
Brownish yellow sticky liquid.

IR (KBr): 3750, 3447, 2928, 2857, 2382, 2192, 1612, 1510, 1252, 1028, 761 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.85 (t, J = 6.8 Hz, 3 H), 1.25–1.35 (m, 4 H), 1.44–1.51 (m, 2 H), 2.19 (t, J = 6.8 Hz, 2 H), 3.73 (s, 3 H), 5.27 (s, 1 H), 6.73–6.80 (m, 4 H), 7.13–7.19 (m, 2 H), 7.35 (d, J = 8.3 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0, 18.8, 22.6, 28.7, 31.1, 41.6, 55.3, 81.2, 84.8, 113.8, 115.3, 128.7, 128.9, 134.8, 135.2, 154.4, 158.1.

MS (ESI): m/z = 307 $[M – H]^+$.

HRMS: m/z $[M – H]^+$ calcd for $C_{21}H_{23}O_2$: 307.1699; found: 307.1698.

4-[1-(4-Methoxyphenyl)oct-2-ynyl]-2-methylphenol (2o)
Yellow sticky liquid.

IR (KBr): 3422, 2957, 2929, 2859, 2393, 2056, 1882, 1607, 1507, 1460, 1252, 1176, 1110, 1033, 811, 610 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 0.84 (t, J = 6.2 Hz, 3 H), 1.18–1.52 (m, 6 H), 2.09–2.22 (m, 5 H), 3.69 (s, 3 H), 4.50 (br s, 1 H, OH), 4.69 (s, 1 H), 6.53 (d, J = 7.8 Hz, 1 H), 6.69 (d, J = 8.6 Hz, 2 H), 6.91 (d, J = 11.7 Hz, 2 H), 7.12 (d, J = 8.6 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.2, 16.0, 19.1, 22.4, 28.9, 31.3, 41.8, 55.4, 81.4, 84.9, 114.0, 115.0, 123.9, 126.4, 128.8, 130.5, 135.2, 135.3, 152.7, 158.4.

MS (ESI): m/z = 323 $[M + H]^+$.

HRMS: m/z $[M + Na]^+$ calcd for $C_{22}H_{26}NaO_2$: 345.1824; found: 345.1830.

1–[1-(4-Methoxyphenyl)oct-2-ynyl]naphthalen-2-ol (2p)
Brownish yellow sticky liquid.

IR (KBr): 3403, 3057, 2929, 2858, 2383, 2067, 1626, 1508, 1462, 1248, 1214, 1174, 1031, 961, 810, 748 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.81 (t, J = 6.9 Hz, 3 H), 1.17–1.45 (m, 4 H), 1.44–1.58 (m, 2 H), 2.21 (t, J = 7.2 Hz, 2 H), 3.62 (s, 3 H), 5.77 (s, 1 H), 6.66 (d, J = 8.3 Hz, 2 H), 6.81 (br s, 1 H, OH), 6.93 (d, J = 7.0 Hz, 1 H), 7.04 (d, J = 8.7 Hz, 1 H), 7.12–7.21 (m, 2 H), 7.25–7.33 (m, 1 H), 7.55–7.66 (m, 2 H), 7.78 (d, J = 8.5 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.6, 17.7, 21.0, 27.3, 30.0, 31.6, 54.0, 78.3, 86.0, 108.4, 112.9, 116.8, 118.3, 122.0, 122.3, 125.3, 125.6, 126.6, 127.1, 127.6, 128.4, 131.2, 151.5, 157.3.

MS (ESI): m/z = 381 $[M + Na]^+$.

HRMS: m/z $[M + Na]^+$ calcd for $C_{25}H_{26}NaO_2$: 381.1843; found: 381.1830.

4-[1-(4-Methoxyphenyl)prop-2-ynyl]phenol (2q)
Light yellow liquid.

^1H NMR (200 MHz, $CDCl_3$): δ = 2.46 (d, J = 2.7 Hz, 1 H), 3.77 (s, 3 H), 4.77 (d, J = 2.4 Hz, 1 H), 5.41 (br s, 1 H, OH), 6.75 (d, J = 8.7 Hz, 2 H), 6.83 (d, J = 8.7 Hz, 2 H), 7.21 (d, J = 9.0 Hz, 2 H), 7.25 (d, J = 9.0 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 41.4, 55.5, 72.7, 85.4, 114.2, 115.6, 128.9, 129.1, 133.8, 154.7, 158.7.

MS (ESI): m/z = 239 $[M + H]^+$.

HRMS: m/z $[M + K]^+$ calcd for $C_{16}H_{14}KO_2$: 277.0630; found: 277.0628.

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(17) All the reactions were run with 1 mol% PMA–silica gel at r.t. in MeCN unless specified.

(18) Substitution was present at the *para* position (least hindered site with high electron density) and was confirmed by ^{1}H NMR spectroscopy. No other products were formed in this reaction.

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