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Ethynyl-cyclohexanol: an efficient acetylene surrogate in Sonogashira coupling

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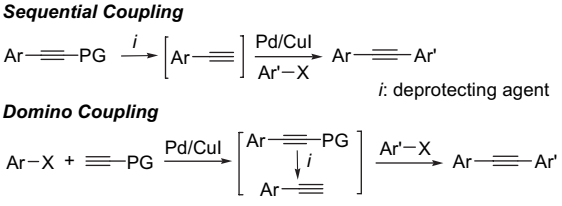
Dedicated to Professor Csaba Szántay on the occasion of his 80th birthday

Abstract—The Sonogashira coupling of aryl halides in the presence of 1-ethynyl-cyclohexanol as an acetylene source provides an efficient method for the synthesis of diarylacetylenes without the isolation of the appropriate arylacetylenes.

1. Introduction

The palladium-catalyzed coupling of terminal acetylenes with aryl and vinyl halides (Sonogashira reaction) is an important and widely used carbon–carbon bond forming reaction in organic synthesis,[1] enabling the efficient construction of triple bond containing synthetic intermediates,[2] condensed heterocycles,[3] and natural products.[3c,4] The Sonogashira coupling is also one of the most frequently used reactions for the preparation of conjugated oligomers and polymers[5] having interesting optical[2l,6] and electronic properties.[7]

The primary limitation in the preparation of diarylacetylenes is the availability of the appropriate monoarylacetylenes, which is greatly limited by their moderate stability. A convenient solution to this problem is offered by the sequential cross-coupling of masked arylacetylenes and aryl halides (Scheme 1),[8] where the release of the protecting group is combined with the Sonogashira coupling of an aryl halide giving the diarylacetylenes without the need to isolate the sensitive monoarylacetylene intermediate. The most frequently used masked acetylene moieties in lab-scale experiments are trimethylsilyl-acetylene[9] and 2-methyl-3-butyn-2-ol[10] derivatives. Since the masked arylacetylenes are usually also prepared in a Sonogashira coupling, it is possible to combine their formation with the sequential coupling. In the domino Sonogashira coupling both 2-methyl-3-butyn-2-ol and TMS-acetylene were applicable as acetylene surrogate and coupled with an aryl halide. Addition of the appropriate reagent—that initiated the release of the acetylene protecting group—followed by the second aryl halide led to the formation of the desired diarylacetylenes in a one-pot process. Extending the results of D'Auria[11] Brisbois and co-workers[12] described an efficient method for the preparation of diarylalkynes along the domino approach using trimethylsilyl-acetylene derivatives, while our research group followed a similar strategy using 2-methyl-3-butyn-2-ol as acetylene source.[13]



Scheme 1.

Although both TMS-acetylene and 2-methyl-3-butyn-2-ol usually work well, there is still a strong demand for the introduction of new protected acetylenes that would offer enhanced applicability. Utilizing the working principle of 2-methyl-3-butyn-2-ol, other ethynyl carbinols are expected to be useful as acetylene sources too. A plausible choice is 1-ethynyl-cyclohexanol, a commercially available chemical, whose price and 'mode of action' is very similar to 2-methyl-3-butyn-2-ol, with the only difference that it releases the chemically more inert cyclohexanone. The present paper reports the scope and limitations of the use of this protected acetylene in sequential and domino coupling reactions leading to diarylacetylenes.

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2. Results and discussion

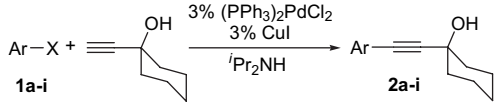
In order to obtain some model compounds for our studies first different aryl halides (**1a–i**) were coupled with 1-ethynyl-cyclohexanol in diisopropylamine (DIPA) to give the appropriate products (**2a–i**) in excellent yield (Table 1) on the multigram scale.

The first reaction we studied was the release of the protecting group (cyclohexanone) from the arylethynyl-cyclohexanols and the subsequent Sonogashira coupling with aryl halides. The optimal solvent–base combination was determined using **2a** and iodobenzene (**1a**) as test substrates (Table 2) and the reactions were monitored by GC–MS.

The use of KOH as base worked well to give full conversion and excellent selectivity in 60 min (entries 1 and 2). Cesium carbonate was less effective, while sodium hydride led to side reactions and the use of barium hydroxide resulted only in decomposition. Both DIPA and toluene work well as solvent, showing that the reaction is not too sensitive to the polarity of the media, although the use of DIPA was advantageous in certain cases. Since diisopropylamine acts not only as a solvent but also as a base in the Sonogashira coupling, for the further studies we chose the KOH–DIPA combination. It should also be noted that the biphasic conditions introduced by Rossi et al.[14] (entry 9) do also work well on this substrate. The reason for not pursuing this line further was our finding that under these conditions we also observed a considerable amount of decomposition with sensitive substrates (e.g., electron deficient heterocycles, halopurines).

Having established the optimal conditions for the sequential coupling we studied the reaction of arylethynyl-cyclohexanols (**2a–h**) and different aryl halides (**1a–j**). Since, several of these combinations are 'mirror images' of one another they also provided an opportunity to establish the influence of the coupling order on the yield of the process. The results summarized in Table 3 revealed the following trends. If one of the aryl groups is electron rich, such as 4-methoxyphenyl or 4-aminophenyl, then the order of the coupling has a significant effect on the yield. Coupling of the arylethynyl-cyclohexanol bearing the electron rich aromatic group with less electron rich aryl halides gave substantially higher yields than the other way around (cf. entries 5 and 6, 8 and 9, 10 and 11, 12 and 13, 16 and 17 or 31 and 32).

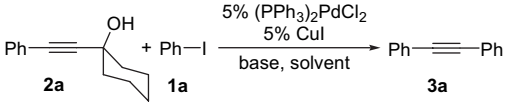
Table 1. The preparation of 1-arylethynyl-cyclohexanols



Entry	ArX	Product	Yield[a] (%)
1	Iodobenzene (**1a**)	**2a**	99
2	4-Iodoanisole (**1b**)	**2b**	91
3	2-Bromonaphtalene (**1c**)	**2c**	87
4	3-Bromopyridine (**1d**)	**2d**	75
5	2-Fluoroiodobenzene (**1e**)	**2e**	99
6	4-Iodoacetophenon (**1f**)	**2f**	98
7	4-Iodoaniline (**1g**)	**2g**	93
8	2-Bromothiophene (**1h**)	**2h**	85
9	2-Bromoiodobenzene (**1i**)	**2i**	97

[a] Isolated yields.

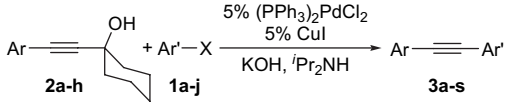
Table 2. The sequential deprotection and Sonogashira coupling of **2a** and iodobenzene (**1a**) under various conditions



Entry	Solvent	Base	Conversion[a] (%)	Time (h)
1	DIPA	KOH	100	1
2	Toluene	KOH	100	1
3	DIPA	NaH	100[b]	1
4	Toluene	NaH	100[c]	3.5
5	DIPA	Cs_2CO_3	100	3
6	Toluene	Cs_2CO_3	100	4.5
7	DIPA	$Ba(OH)_2$	35[d]	3
8	Toluene	$Ba(OH)_2$	100[d]	3
9	Toluene	aq NaOH[e]	100	1

[a] The reactions were run in a 80 °C oil bath. Conversions were determined by the GC–MS analysis of the reaction mixture.
[b] Containing 10% *Z*-stilbene as byproduct.
[c] Containing 25% *Z*-stilbene as byproduct.
[d] Decomposition.
[e] NaOH of 4 equiv in 2 M solution and 3 mol % TBAI.

Table 3. The sequential deprotection–Sonogashira coupling of arylethynyl-cyclohexanols (**2a–h**) with aryl halides (**1a–j**)



Entry	**2**	Ar′X	Product	Yield[a] (%)
1	**2a**	**1a**	**3a**	76
2	**2a**	**1j**[b]	**3a**	73
3	**2a**	**1d**	**3b**	73
4	**2d**	**1a**	**3b**	95
5	**2b**	**1a**	**3c**	70
6	**2b**	**1j**[b]	**3c**	54
7	**2b**	**1b**	**3d**	30
8	**2b**	**1c**	**3e**	87
9	**2c**	**1b**	**3e**	57
10	**2b**	**1d**	**3f**	82
11	**2d**	**1b**	**3f**	47
12	**2b**	**1e**	**3g**	84
13	**2e**	**1b**	**3g**	27
14	**2b**	**1g**	**3h**	31
15	**2g**	**1b**	**3h**	33
16	**2b**	**1h**	**3i**	67
17	**2h**	**1b**	**3i**	49
18	**2c**	**1a**	**3j**	70
19	**2c**	**1c**	**3k**	69
20	**2c**	**1d**	**3l**	61
21	**2d**	**1c**	**3l**	63
22	**2c**	**1e**	**3m**	83
23	**2e**	**1c**	**3m**	67
24	**2d**	**1d**	**3n**	72
25	**2e**	**1d**	**3o**	74
26	**2d**	**1e**	**3o**	66
27	**2e**	**1a**	**3p**	71
28	**2e**	**1j**[b]	**3p**	69
29	**2e**	**1e**	**3q**	82
30	**2f**	**1a**	**3r**	77
31	**2b**	**1f**	**3s**	78
32	**2f**	**1b**	**3s**	33

[a] Isolated yields.
[b] Compound **1j** stands for bromobenzene.

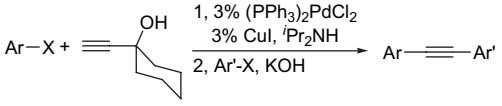
The only cases where the reaction performs poorly are couplings with two electron rich aryl groups (entries 7, 14 and 15). For most other reactions we observed good to excellent yields. The use of bromobenzene (**1j**) instead of iodobenzene gave usually comparable yields in longer reactions (cf. entries 1 and 2, 27 and 28) unless the other aryl group was electron rich (entries 5 and 6) where the decreased yield might be attributed to increased decomposition during the prolonged heating. Except for these limitations the sequential coupling performed reliably. Neutral and electron deficient aryl bromides and iodides gave comparable yields. Both five- and six-membered heterocycles can be included in the process and the presence of an *ortho*-substituent on the aryl halide had no significant influence on the efficiency of the coupling either.

Having established the scope and limitations of the sequential coupling of arylethynyl-cyclohexanols and aryl halides we also tested the possibility of carrying out this transformation as the domino coupling of two aryl halides and 1-ethynyl-cyclohexanol (Table 4). The test reactions were aimed at the weak points of the sequential approach, the synthesis of diarylacetylenes bearing two electron rich aromatic rings such as **3d** and **3h**.

Already in the first attempt, in the preparation of bis(*p*-anisyl)-acetylene (**3d**, entry 1) from 4-iodoanisole and 1-ethynyl-cyclohexanol we observed a substantial improvement of the yield to 76% from the 30% observed in the sequential coupling. The coupling of 4-iodoanisole (**1b**) and 4-iodoaniline (**1g**) was also more efficient in the domino fashion (entries 2 and 3), the yield increasing to 47% from 31%. When the electron rich 4-iodoanisole (**1b**) and the electron deficient 4-iodo-acetophenon (**1f**) were coupled with 1-ethynyl-cyclohexanol (entries 4 and 5) the yield depended largely on the coupling order.

Starting with the electron rich aryl halide in the domino coupling gave a yield that is comparable with the appropriate sequential coupling, while the reversal of the order led to diminished yields (alike in the analogous sequential coupling). It was also of interest to compare the efficiency of the present methodology with the analogous process utilizing 2-methyl-3-butyn-2-ol as acetylene surrogate. There are certain cases where the domino coupling of aryl halides with 2-methyl-3-butyn-2-ol gave only mediocre yields.[13] Some of these reactions were repeated using 1-ethynyl-cyclohexanol (Table 4, entries 6–9). The coupling of iodobenzene (**1a**) and 2-chloro-bromobenzene (**1k**) proceeded efficiently, irrespective of the order of the coupling. Coupling of the same bromobenzene derivative (**1k**) with 3-iodotoluene (**1l**) gave also improved yields. It is not only with bromoaromatics that the use of 1-ethynyl-cyclohexanol gives higher yields. The domino homocoupling of 4-iodoanisole (**1b**) was also more efficient with this acetylene surrogate (entry 1).

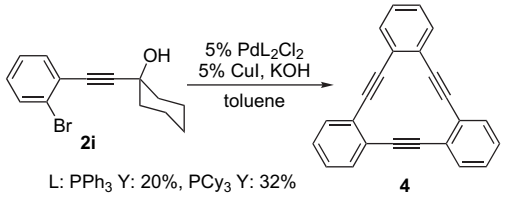
Table 4. The domino Sonogashira coupling of aryl halides using 1-ethynyl-cyclohexanol as acetylene surrogate



Entry	1	1′	Product	Yield[a] (%)
1	**1b**	**1b**	**3d**	76 (66)
2	**1b**	**1g**	**3h**	47
3	**1g**	**1b**	**3h**	40
4	**1b**	**1f**	**3s**	64
5	**1f**	**1b**	**3s**	24
6	**1a**	**1k**	**3t**	86 (47)
7	**1k**	**1a**	**3t**	83 (71)
8	**1k**	**1l**	**3u**	70 (59)
9	**1l**	**1k**	**3u**	43 (40)

[a] Isolated yields. Numbers in parentheses refer to the highest yield of the same product obtained by using 2-methyl-3-butyn-2-ol.

As a further test to the utility of 1-ethynyl-cyclohexanol as an acetylene surrogate we attempted to use it in the preparation of a [12]tribenzannulene derivative (Scheme 2). The sequential 'homocoupling' of (*o*-bromophenyl-ethynyl)-cyclohexanol (**2i**) in toluene gave the desired hexahydrotribenzo[12]annulene in 20% yield. Increasing the activity of the catalyst by using PCy_3 as ligand we obtained **4** in 32% yield, which is in line with the reported synthetic approaches utilizing 2-methyl-3-butyn-2-ol.[15]



Scheme 2. Synthesis of tribenzo[12]benzannulene.

In summary, an efficient method is reported for the use of 1-ethynyl-cyclohexanol as acetylene surrogate in Sonogashira couplings. It was demonstrated that using this reagent diarylacetylenes can be synthesized either in a sequential manner or in a one-pot domino Sonogashira coupling. In comparison with the use of the analogous 2-methyl-3-butyn-2-ol this method was found to work equally well or better on the substrates tested. It was also demonstrated that the order of the addition of the aryl halides might have a significant effect on the yield of the process. As a general rule the more electron rich aryl halides should be coupled first.

3. Experimental

3.1. General

Unless otherwise indicated, all starting materials were obtained from commercial suppliers (Aldrich, Fisher, Merck), and were used without further purification. All reactions were performed under an atmosphere of argon. Analytical thin-layer chromatography (TLC) was performed on Merck DC pre-coated TLC plates with 0.25 mm Kieselgel 60 F_{254}. Visualization was performed with a 254 nm UV lamp. Silica gel column chromatography was carried out with Flash silica gel (0.040–0.063 mm) from Merck. The ^1H and ^{13}C NMR spectra were recorded on a Brucker DRX-250 spectrometer in $CDCl_3$. Chemical shifts are expressed in parts per million (δ) using residual solvent protons as internal standards

(δ 7.26 for ^{1}H, δ 77.0 for ^{13}C). Coupling constants (J) are reported in hertz (Hz). Splitting patterns are designated as s (singlet), d (doublet), t (triplet), m (multiplet), dd (doublet of doublets), dt (doublet of triplets), td (triplet of doublets). Combination of gas chromatography and low resolution mass spectrometry was obtained on an Agilent 6890 N Gas Chromatograph (30 m×0.25 mm column with 0.25 μm HP-5MS coating, He carrier gas) and Agilent 5973 Mass Spectrometer (Ion source: EI$^+$, 70 eV, 230 °C; interface: 300 °C). All melting points were measured on Büchi 501 apparatus and are uncorrected.

3.2. General procedure for the synthesis of arylethynyl-cyclohexanols

Aryl halide (**1**) (10 mmol), 1.49 g of 1-ethynyl-cyclohexanol (12 mmol), 211 mg of $PdCl_2(PPh_3)_2$ (0.3 mmol, 3%), and 57 mg of CuI (0.3 mmol, 3%) were placed into a flame-dried Schlenk flask. Diisopropylamine of 20 mL was added, and the mixture was stirred under argon at 80 °C. The reaction was followed by TLC and GC–MS. When the coupling was complete (typically less than 30 min), the product (**2**) was separated by column chromatography, using hexane–ethylacetate eluent.

3.2.1. 1-Phenylethynyl-cyclohexanol (2a).[16] Pale yellow solid (1978 mg, 9.89 mmol, 99% yield). Mp: 57–59 °C. ^{1}H NMR ($CDCl_3$; 250 MHz): δ 7.44–7.39 (m, 2H), 7.31–7.25 (m, 3H), 2.28 (s, 1H), 2.03–1.94 (m, 2H), 1.79–1.55 (m, 7H), 1.33–1.25 (m, 1H); ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ 131.6, 128.2, 128.1, 122.9, 92.8, 84.3, 69.0, 40.0, 25.2, 23.4; MS (EI, 70 eV) *m/z* (% relative intensity, ion): 200 (20, [M$^+$]), 199 (43), 157 (100), 144 (30), 129 (70), 115 (61), 102 (64), 55 (48).

3.2.2. 1-(4′-Methoxyphenyl)ethynyl-cyclohexanol (2b).[16] Yellow solid (2095 mg, 9.10 mmol, 91% yield). Mp: 60–61 °C. ^{1}H NMR ($CDCl_3$; 250 MHz): δ 7.35 (d, 2H, J=8.7 Hz), 6.81 (d, 2H, J=8.7 Hz), 3.79 (s, 3H), 2.40 (s, 1H), 2.02–1.92 (m, 2H), 1.77–1.54 (m, 7H), 1.28–1.24 (m, 1H); ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ 159.4, 133.0, 115.0, 113.8, 91.4, 84.1, 69.0, 55.2, 40.0, 25.2, 23.4; MS (EI, 70 eV) *m/z* (% relative intensity, ion): 230 (46, [M$^+$]), 201 (33), 187 (100), 174 (33), 159 (39).

3.2.3. 1-(2′-Naphthyl)ethynyl-cyclohexanol (2c). White solid (2175 mg, 8.70 mmol, 87% yield). Mp: 120–121 °C. ^{1}H NMR ($CDCl_3$; 250 MHz): δ 7.97 (s, 1H), 7.82–7.74 (m, 3H), 7.51–7.46 (m, 3H), 2.62 (s, 1H), 2.12–2.08 (m, 2H), 1.80–1.59 (m, 7H), 1.33–1.30 (m, 1H); ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ 132.8, 132.6, 131.4, 128.4, 127.8, 127.6, 127.6, 126.5, 126.4, 120.1, 93.2, 84.6, 69.1, 40.0, 25.2, 23.4. IR (solid, cm^{-1}): 3240, 2931, 2854, 2158, 2033, 1604, 1568, 1507, 1446, 1412, 1342, 1302, 1285, 1244, 1182, 1170, 1157, 1134, 1105, 1067, 1038, 963, 828; MS (EI, 70 eV) *m/z* (% relative intensity, ion): 250 (61, [M$^+$]), 249 (50), 232 (19), 207 (100), 194 (23), 179 (64), 165 (63), 152 (80), 141 (20), 128 (17), 55 (83). Analysis calculated for $C_{18}H_{18}O$: C 86.36; H 7.25. Found: C 86.59; H 7.08.

3.2.4. 1-(3′-Pyridyl)ethynyl-cyclohexanol (2d). White solid (1510 mg, 7.50 mmol, 75% yield). Mp: 75–76 °C. ^{1}H NMR ($CDCl_3$; 250 MHz): δ 8.72 (d, 1H, J=1.3 Hz), 8.47 (dd, 1H, J=4.9 Hz, J=1.5 Hz), 7.69 (dt, 1H, J=7.9 Hz, J=1.8 Hz), 7.22 (dd, 1H, J=7.9 Hz, J=4.9 Hz), 4.28 (m, 1H), 1.99–1.95 (m, 2H), 1.74–1.54 (m, 7H), 1.33–1.25 (m, 1H); ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ 151.9, 148.0, 138.8, 123.0, 120.4, 97.4, 80.4, 68.5, 39.8, 25.1, 23.2. IR (solid, cm^{-1}): 3223, 2948, 2934, 2854, 2159, 2030, 1977, 1626, 1596, 1498, 1447, 1353, 1343, 1293, 1266, 1186, 1155, 1070, 1033, 976, 858, 819, 747; MS (EI, 70 eV) *m/z* (% relative intensity, ion): 201 (8, [M$^+$]), 200 (23), 172 (16), 158 (100), 145 (36), 130 (57), 117 (13), 103 (14), 93 (16), 55 (33). Analysis calculated for $C_{13}H_{15}NO$: C 77.58; H 7.51; N 6.96. Found: C 77.21; H 7.50; N 6.63.

3.2.5. 1-(2′-Fluorophenyl)ethynyl-cyclohexanol (2e). Beige solid (2152 mg, 9.86 mmol, 99% yield). Mp: 60–61 °C. ^{1}H NMR ($CDCl_3$; 250 MHz): δ 7.40 (t, 1H, J=7.2 Hz), 7.30–7.22 (m, 1H), 7.08–7.00 (m, 2H), 2.64 (s, 1H), 2.06–1.97 (m, 2H), 1.75–1.55 (m, 7H), 1.31–1.24 (m, 1H); ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ 164.7, 160.7, 133.3, 133.3, 130.0, 129.7, 123.8, 123.7, 115.5, 115.1, 111.5, 111.3, 98.2, 98.1, 77.7, 77.7, 69.2, 39.9, 25.1, 23.3. IR (solid, cm^{-1}): 3343, 2926, 2855, 1572, 1488, 1443, 1391, 1340, 1297, 1263, 1241, 1208, 1187, 1100, 1063, 1029, 963, 903, 857, 845, 815, 754; MS (EI, 70 eV) *m/z* (% relative intensity, ion): 218 (13, [M$^+$]), 217 (15), 199 (7), 190 (8), 175 (100), 162 (37), 147 (74), 133 (56), 122 (24), 120 (24), 109 (15), 81 (31), 55 (43). Analysis calculated for $C_{14}H_{15}OF$: C 77.04; H 6.93. Found: C 76.83; H 7.14.

3.2.6. 1-(4′-Acetylphenyl)ethynyl-cyclohexanol (2f).[17] Pale brown solid (2380 mg, 9.83 mmol, 98% yield). Mp: 80–81 °C. ^{1}H NMR ($CDCl_3$; 250 MHz): δ 7.87 (d, 2H, J=8.5 Hz), 7.48 (d, 2H, J=8.5 Hz), 2.58 (s, 3H), 2.35 (s, 1H), 2.04–1.98 (m, 2H), 1.77–1.55 (m, 7H), 1.35–1.25 (m, 1H); ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ 197.4, 136.1, 131.7, 128.1, 127.8, 96.3, 83.5, 69.0, 39.8, 26.5, 25.1, 23.3; MS (EI, 70 eV) *m/z* (% relative intensity, ion): 242 (34, [M$^+$]), 199 (100), 171 (50), 143 (19), 129 (23), 115 (21), 55 (47).

3.2.7. 1-(4′-Aminophenyl)ethynyl-cyclohexanol (2g). Pale brown solid (2000 mg, 9.29 mmol, 93% yield). Mp: 117–118 °C. ^{1}H NMR ($CDCl_3$; 250 MHz): δ 7.22 (dt, 2H, J=8.6 Hz, J=2.2 Hz), 6.58 (dt, 2H, J=8.7 Hz, J=2.2 Hz), 3.79 (s, 2H), 2.27 (s, 1H), 2.0–1.91 (m, 2H), 1.73–1.51 (m, 7H), 1.28–1.24 (m, 1H); ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ 146.5, 132.9, 114.6, 112.2, 90.5, 84.8, 69.1, 40.1, 25.2, 23.4. IR (solid, cm^{-1}): 3374, 3237, 2929, 2853, 2213, 1605, 1509, 1446, 1337, 1269, 1179, 1156, 1134, 1058, 958, 901, 854, 834, 805; MS (EI, 70 eV) *m/z* (% relative intensity, ion): 215 (30, [M$^+$]), 197 (100), 186 (31), 172 (74), 169 (63), 159 (21), 144 (51), 130 (53), 117 (76), 106 (31), 55 (81). Analysis calculated for $C_{14}H_{17}NO$: C 78.10; H 7.96; N 6.51. Found: C 78.35; H 8.13; N 6.14.

3.2.8. 1-(2′-Thienyl)ethynyl-cyclohexanol (2h). Pale yellow solid (1750 mg, 8.49 mmol, 85% yield). Mp: 97–99 °C. ^{1}H NMR ($CDCl_3$; 250 MHz): δ 7.26–7.17 (m, 2H), 6.95 (dd, 1H, J=4.9 Hz, J=3.6 Hz), 2.36 (s, 1H), 2.02–1.97 (m, 2H), 1.75–1.55 (m, 7H), 1.31–1.25 (m, 1H); ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ 131.8, 126.9, 126.8, 122.8, 96.6, 77.5, 69.2, 39.8, 25.1, 23.2. IR (solid, cm^{-1}): 3213, 2931, 2853, 1515, 1446, 1423, 1344, 1285, 1256, 1229, 1183,

1069, 964, 938, 902, 851, 826, 731, 702, 694; MS (EI, 70 eV) *m/z* (% relative intensity, ion): 206 (26, [M$^+$]), 177 (17), 163 (100), 150 (37), 135 (63), 121 (23), 110 (27), 55 (40). Analysis calculated for $C_{12}H_{14}OS$: C 69.86; H 6.84. Found: C 69.54; H 7.04.

3.2.9. 1-(2′-Bromophenyl)ethynyl-cyclohexanol (2i).[18] Pale yellow solid (2720 mg, 9.74 mmol, 97% yield). Mp: 67–68 °C. ^{1}H NMR ($CDCl_3$; 250 MHz): δ 7.48 (dd, 1H, J=8.0 Hz, J=0.9 Hz), 7.37 (dd, 1H, J=7.7 Hz, J=1.6 Hz), 7.18–7.03 (m, 2H), 2.35 (s, 1H), 1.99–1.95 (m, 2H), 1.75–1.48 (m, 7H), 1.22–1.12 (m, 1H); ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ 133.2, 132.3, 129.3, 126.9, 125.6, 125.0, 97.5, 83.0, 69.3, 39.9, 25.2, 23.3; MS (EI, 70 eV) *m/z* (% relative intensity, ion): 280 (3, [M$^+$]), 278 (3, [M$^+$]), 237 (17), 235 (17), 222 (4), 220 (4), 209 (7), 207 (7), 200 (13), 199 (100), 182 (7), 180 (6), 143 (7), 128 (19), 115 (23), 101 (9), 55 (43).

3.3. General procedure for the synthesis of diaryl-acetylenes

Sequential coupling: arylethynyl-cyclohexanol (**2**) (1 mmol), aryl halide (**1**) (1 mmol), 35 mg of $PdCl_2(PPh_3)_2$ (0.05 mmol, 5%), 9.5 mg of CuI (0.05 mmol, 5%), and 224 mg of KOH (4 mmol) were placed into a flame-dried Schlenk flask. Diisopropylamine of 7 mL was added, and the mixture was stirred under argon at 80 °C. The reaction was followed by TLC and GC–MS. When the coupling was complete the product (**3**) was separated by column chromatography using hexane–ethylacetate mixtures (100:0–80:20) as eluent.

Domino coupling: aryl halide (**1**) (1 mmol), 149 mg of 1-ethynyl-cyclohexanol (1.2 mmol), 21 mg of $PdCl_2(PPh_3)_2$ (0.03 mmol, 3%), and 5.7 mg of CuI (0.03 mmol, 3%) were placed into a flame-dried Schlenk flask. Diisopropylamine of 7 mL was added, and the mixture was stirred under argon at 80 °C. The reaction was followed by TLC and GC–MS. When the first coupling was complete (typically less than 30 min), the appropriate aryl halide (**1′**) (1 mmol), 21 mg of $PdCl_2(PPh_3)_2$ (0.03 mmol, 3%), 5.7 mg of CuI (0.03 mmol, 3%) and 224 mg of KOH (4 mmol) were added. The mixture was stirred under argon at 80 °C, until the reaction was complete. The product (**3**) was separated by column chromatography, using hexane–ethylacetate mixtures (100:0–80:20) as eluent.

3.3.1. Diphenylacetylene (3a).[12] White solid. Compounds **2a** and **1a** yielded 136 mg (0.76 mmol, 76% yield), while **2a** and **1j** gave 130 mg (0.73 mmol, 73% yield). Mp: 54–55 °C. ^{1}H NMR ($CDCl_3$; 250 MHz): δ 7.55–7.51 (m, 4H), 7.37–7.30 (m, 6H); ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ 131.1, 127.8, 127.7, 122.7, 88.9; MS (EI, 70 eV) *m/z* (% relative intensity, ion): 178 (100, [M$^+$]), 176 (21), 152 (17), 126 (8).

3.3.2. 3-Phenylethynyl-pyridine (3b).[19] Pale brown solid. Compounds **2a** and **1d** yielded 130 mg (0.73 mmol, 73% yield), while **2d** and **1a** gave 170 mg (0.95 mmol, 95% yield). Mp: 48–49 °C. ^{1}H NMR ($CDCl_3$; 250 MHz): δ 8.69 (d, 1H, J=1.3 Hz), 8.47 (dd, 1H, J=4.9 Hz, J=1.7 Hz), 7.73 (dt, 1H, J=7.9 Hz, J=2.0 Hz), 7.49–7.45 (m, 2H), 7.31–7.28 (m, 3H), 7.23–7.17 (m, 1H); ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ 152.2, 148.5, 138.4, 131.6, 128.8, 128.4, 123.0, 122.5, 120.4, 92.6, 85.9; MS (EI, 70 eV) *m/z* (% relative intensity, ion): 179 (100, [M$^+$]), 178 (22), 151 (14), 126 (21).

3.3.3. 4-Phenylethynyl-anisole (3c).[20] White solid. Compounds **2b** and **1a** yielded 145 mg (0.70 mmol, 70% yield), while **2b** and **1j** gave 112 mg (0.54 mmol, 54% yield). Mp: 59–60 °C. ^{1}H NMR ($CDCl_3$; 250 MHz): δ 7.42–7.34 (m, 4H), 7.23–7.18 (m, 3H), 6.74 (d, 2H, J=8.9 Hz), 3.65 (s, 3H); ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ 159.5, 133.0, 131.4, 128.2, 127.8, 123.5, 115.3, 113.9, 89.4, 88.0, 55.1; MS (EI, 70 eV) *m/z* (% relative intensity, ion): 209 (44), 208 (100, [M$^+$]), 193 (100), 165 (82), 139 (11).

3.3.4. Di-(4-methoxyphenyl)-acetylene (3d).[13] Pale yellow solid. Compounds **2b** and **1b** gave 71 mg (0.30 mmol, 30% yield). The domino coupling yielded 180 mg (0.76 mmol, 76% yield). Mp: 139–140 °C. ^{1}H NMR ($CDCl_3$; 250 MHz): δ 7.46 (dt, 4H, J=8.8 Hz, J=2.5 Hz), 6.87 (dt, 4H, J=9.1 Hz, J=2.4 Hz), 3.82 (s, 6H); ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ 159.4, 132.8, 115.7, 113.9, 87.9, 55.3; MS (EI, 70 eV) *m/z* (% relative intensity, ion): 238 (100, [M$^+$]), 223 (86), 195 (28), 180 (17), 152 (38).

3.3.5. 2-(4′-Methoxyphenyl)ethynyl-naphthalene (3e). Yellow solid. Compounds **2b** and **1c** yielded 224 mg (0.87 mmol, 87% yield), while **2c** and **1b** gave 147 mg (0.57 mmol, 57% yield). Mp: 122–124 °C. ^{1}H NMR ($CDCl_3$; 250 MHz): δ 8.07 (s, 1H), 7.86–7.81 (m, 3H), 7.63–7.49 (m, 5H), 6.93 (d, 2H, J=8.9 Hz), 3.84 (s, 3H); ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ 159.6, 133.1, 133.0, 132.6, 131.6, 131.1, 128.4, 127.9, 127.7, 127.7, 126.4, 120.9, 115.3, 114.0, 89.8, 88.5, 55.2. IR (solid, cm^{-1}): 3054, 2996, 2836, 2213, 1592, 1566, 1508, 1464, 1436, 1303, 1283, 1269, 1243, 1172, 1137, 1106, 1030, 946, 899, 862, 829, 819, 741; MS (EI, 70 eV) *m/z* (% relative intensity, ion): 258 (100, [M$^+$]), 243 (51), 215 (45), 213 (34), 189 (11). Analysis calculated for $C_{19}H_{14}O$: C 88.34; H 5.46. Found: C 88.78; H 5.03.

3.3.6. 3-(4′-Methoxyphenyl)ethynyl-pyridine (3f).[13] Pale yellow solid. Compounds **2b** and **1d** gave 172 mg (0.82 mmol, 82% yield), while **2d** and **1b** yielded 98 mg (0.47 mmol, 47% yield). Mp: 46–48 °C. ^{1}H NMR ($CDCl_3$; 250 MHz): δ 8.75 (d, 1H, J=1.9 Hz), 8.51 (dd, 1H, J=4.9 Hz, J=1.6 Hz), 7.77 (dt, 1H, J=7.9 Hz, J=1.9 Hz), 7.48 (d, 2H, J=8.8 Hz), 7.25 (dd, 1H, J=8.0 Hz, J=5.0 Hz), 6.88 (d, 2H, J=8.8 Hz), 3.82 (s, 3H); ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ 159.9, 152.0, 148.1, 138.1, 133.1, 122.9, 120.7, 114.5, 114.0, 92.7, 84.7, 55.2; MS (EI, 70 eV) *m/z* (% relative intensity, ion): 209 (100, [M$^+$]), 194 (42), 166 (28), 139 (28), 113 (14).

3.3.7. (4′-Methoxyphenyl)ethynyl-fluorobenzene (3g). White solid. Compounds **2b** and **1e** yielded 190 mg (0.84 mol, 84% yield), while using **2e** and **1b** gave 61 mg (0.27 mmol, 27% yield). Mp: 56–57 °C. ^{1}H NMR ($CDCl_3$; 250 MHz): δ 7.37–7.32 (m, 3H), 7.16–7.07 (m, 1H), 6.97–6.90 (m, 2H), 6.72 (d, 2H, J=8.8 Hz); ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ 164.4, 160.4, 159.8, 133.2, 133.2, 133.1, 129.6, 129.5, 123.9, 123.8, 115.5, 115.2, 114.8, 113.9, 112.2, 112.0, 94.5, 94.5, 81.3, 81.3, 55.1. IR (solid, cm^{-1}):

1598, 1566, 1508, 1488, 1448, 1286, 1265, 1244, 1220, 1195, 1172, 1097, 1024, 940, 864, 835, 819, 751; MS (EI, 70 eV) *m/z* (% relative intensity, ion): 226 (100, [M$^+$]), 211 (52), 183 (72), 157 (18). Analysis calculated for $C_{15}H_{11}OF$: C 79.63; H 4.90. Found: C 79.85; H 4.91.

3.3.8. 4-(4′-Methoxyphenyl)ethynyl-aniline (3h).[21] Pale yellow solid. Compounds **2b** and **1g** yielded 70 mg (0.31 mmol, 31% yield), while using **2g** and **1b** gave 74 mg (0.33 mmol, 33% yield). The domino coupling according to Method B gave 105 mg product (0.47 mmol, 47% yield) when **1b** reacted first; 90 mg (0.40 mmol, 40% yield) product was obtained when **1g** reacted first. Mp: 138–139 °C. ^{1}H NMR ($CDCl_3$; 250 MHz): δ 7.35 (d, 2H, J=8.4 Hz), 7.24 (d, 2H, J=8.1 Hz), 6.77 (d, 2H, J=8.3 Hz), 6.54 (d, 2H, J=8.2 Hz), 3.73 (s, 5H); ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ 159.1, 146.3, 132.7, 116.0, 114.7, 113.9, 112.9, 88.6, 87.1, 55.2; MS (EI, 70 eV) *m/z* (% relative intensity, ion): 223 (100, [M$^+$]), 208 (92), 180 (35), 152 (32).

3.3.9. 2-(4′-Methoxyphenyl)ethynyl-thiophene (3i).[22] White solid. Compounds **2b** and **1h** yielded 144 mg (0.67 mmol, 67% yield), while using **2h** and **1b** gave 105 mg (0.49 mmol, 49% yield). Mp: 53–54 °C. ^{1}H NMR ($CDCl_3$; 250 MHz): δ 7.44 (dt, 2H, J=9.0 Hz, J=2.4 Hz), 7.26–7.23 (m, 2H), 6.98 (dd, 1H, J=4.9 Hz, J=3.9 Hz), 6.86 (dd, 2H, J=8.8 Hz, J=2.4 Hz), 3.80 (s, 3H); ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ 159.7, 132.9, 131.4, 127.0, 126.8, 123.7, 114.9, 114.0, 93.0, 81.2, 55.2; MS (EI, 70 eV) *m/z* (% relative intensity, ion): 214 (100, [M$^+$]), 199 (85), 171 (37), 127 (20).

3.3.10. 2-Phenylethynyl-naphthalene (3j).[23] White solid. Compounds **2c** and **1a** yielded 160 mg (0.70 mmol, 70% yield). Mp: 113–114 °C. ^{1}H NMR ($CDCl_3$; 250 MHz): δ 8.09 (s, 1H), 7.86–7.82 (m, 3H), 7.63–7.60 (m, 3H), 7.54–7.50 (m, 2H), 7.44–7.37 (m, 3H); ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ 133.0, 132.8, 131.6, 131.4, 128.4, 128.4, 128.3, 128.0, 127.8, 127.8, 126.6, 126.5, 123.3, 120.5, 89.8, 89.7; MS (EI, 70 eV) *m/z* (% relative intensity, ion): 228 (100, [M$^+$]), 226 (32), 207 (8), 114 (11).

3.3.11. Di-(naphth-2′-yl)acetylene (3k).[24] White solid. Compounds **2c** and **1c** yielded 192 mg (0.69 mmol, 69% yield). Mp: 215–216 °C. ^{1}H NMR ($CDCl_3$; 250 MHz): δ 8.11 (s, 2H), 7.86–7.83 (m, 6H), 7.40 (dd, 2H, J=8.3 Hz, J=1.3 Hz), 7.53–7.49 (m, 4H); ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ 133.1, 132.9, 131.5, 128.4, 128.0, 127.8, 127.8, 126.7, 126.6, 120.6, 90.2; MS (EI, 70 eV) *m/z* (% relative intensity, ion): 278 (100, [M$^+$]), 276 (30), 139 (26), 138 (26), 125 (9).

3.3.12. 3-(Naphth-2′-yl)ethynyl-pyridine (3l). White solid. Compounds **2c** and **1d** yielded 140 mg (0.61 mmol, 61% yield), while using **2d** and **1c** gave 144 mg (0.63 mmol, 63% yield). Mp: 70–72 °C. ^{1}H NMR ($CDCl_3$; 250 MHz): δ 8.71 (d, 1H, J=1.4 Hz), 8.42 (dd, 1H, J=4.8 Hz, J=1.4 Hz), 7.94 (s, 1H), 7.70–7.66 (m, 4H), 7.45 (dd, 1H, J=8.6 Hz, J=1.5 Hz), 7.39–7.33 (m, 2H), 7.12 (dd, 1H, J=7.8 Hz, J=4.9 Hz); ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ 152.1, 148.4, 138.3, 132.9, 132.8, 131.7, 128.0, 128.0, 127.7, 127.7, 126.8, 126.6, 122.9, 120.4, 119.6, 93.0, 86.2. IR (solid, cm^{-1}): 3054, 2215, 1594, 1557, 1498, 1477, 1402, 1270, 1242, 1183, 1107, 1019, 951, 902, 865, 830, 803, 741, 701; MS (EI, 70 eV) *m/z* (% relative intensity, ion): 229 (100, [M$^+$]), 200 (13), 176 (13), 88 (21). Analysis calculated for $C_{17}H_{11}N$: C 89.06; H 4.84; N 6.11. Found: C 88.55; H 4.73; N 5.83.

3.3.13. 2-(Naphth-2-yl)ethynyl-fluorobenzene (3m). White solid. Compounds **2c** and **1e** yielded 204 mg (0.83 mmol, 83% yield), while using **2d** and **1c** gave 165 mg (0.67 mmol, 67% yield). Mp: 90–91 °C. ^{1}H NMR ($CDCl_3$; 250 MHz): δ 8.12 (s, 1H), 7.87–7.83 (m, 3H), 7.66–7.51 (m, 4H), 7.39–7.30 (m, 1H), 7.19–7.12 (m, 2H); ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ 164.7, 160.7, 133.5, 133.4, 132.9, 131.7, 130.0, 129.9, 128.3, 128.0, 127.8, 127.8, 126.8, 126.6, 124.0, 123.9, 120.2, 120.2, 115.7, 115.4, 112.0, 111.8, 94.9, 94.8, 83.0, 83.0. IR (solid, cm^{-1}): 3051, 2159, 1592, 1573, 1492, 1466, 1444, 1345, 1309, 1264, 1238, 1219, 1139, 1116, 1093, 1028, 951, 940, 906, 867, 822, 753, 744; MS (EI, 70 eV) *m/z* (% relative intensity, ion): 247 (18), 246 (100, [M$^+$]), 244 (28), 123 (11). Analysis calculated for $C_{18}H_{11}F$: C 87.78; H 4.50. Found: C 87.77; H 4.14.

3.3.14. Di-(3-pyridyl)-acetylene (3n).[25] White solid. Compounds **2d** and **1d** yielded 130 mg (0.72 mmol, 72% yield). Mp: 59–60 °C. ^{1}H NMR ($CDCl_3$; 250 MHz): δ 8.72 (s, 2H), 8.51 (d, 2H, J=2.7 Hz), 7.75 (dt, 2H, J=7.9 Hz, J=1.7 Hz), 7.24 (dd, 2H, J=7.6 Hz, J=4.7 Hz); ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ 152.2, 149.0, 138.4, 123.0, 119.7, 89.1; MS (EI, 70 eV) *m/z* (% relative intensity, ion): 180 (100, [M$^+$]), 179 (27), 152 (11), 127 (17), 100 (10), 74 (18).

3.3.15. 3-(2′-Fluorophenyl)ethynyl-pyridine (3o). Colorless liquid. Compounds **2d** and **1e** yielded 130 mg (0.66 mmol, 66% yield), while using **2e** and **1d** gave 145 mg (0.74 mmol, 74% yield). ^{1}H NMR ($CDCl_3$; 250 MHz): δ 8.79 (d, 1H, J=1.3 Hz), 8.55 (dd, 1H, J=4.9 Hz, J=1.4 Hz), 7.80 (dt, 1H, J=7.9 Hz, J=1.9 Hz), 7.52 (td, 1H, J=7.3 Hz, J=1.7 Hz), 7.37–7.23 (m, 2H), 7.15–7.06 (m, 2H); ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ 164.4, 160.4, 152.0, 148.6, 138.3, 133.2, 133.2, 130.4, 130.3, 123.9, 123.8, 122.8, 119.8, 115.6, 115.2, 111.1, 110.8, 90.7, 90.7, 85.8, 85.8. IR (oil, cm^{-1}): 3031, 2224, 1560, 1492, 1472, 1450, 1406, 1263, 1221, 1186, 1145, 1120, 1098, 1022, 942, 864, 801, 753, 700; MS (EI, 70 eV) *m/z* (% relative intensity, ion): 197 (100, [M$^+$]), 170 (13), 144 (30). Analysis calculated for $C_{13}H_8FN$: C 79.18; H 4.09; N 7.10. Found: C 79.30; H 4.11; N 7.17.

3.3.16. 2-Phenylethynyl-fluorobenzene (3p).[26] White solid. Compounds **2e** and **1a** yielded 140 mg (0.71 mmol, 71% yield), while using **2e** and **1j** gave 135 mg (0.69 mmol, 69% yield). Mp: 45–46 °C. ^{1}H NMR ($CDCl_3$; 250 MHz): δ 7.60–7.51 (m, 3H), 7.40–7.28 (m, 4H), 7.17–7.08 (m, 2H); ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ 164.6, 160.6, 133.4, 133.4, 131.7, 130.0, 129.9, 128.6, 128.3, 124.0, 123.9, 122.9, 115.7, 115.3, 112.0, 111.8, 94.4, 94.4, 82.7, 82.6; MS (EI, 70 eV) *m/z* (% relative intensity, ion): 197 (17), 196 (100, [M$^+$]), 194 (13), 170 (11), 98 (11).

3.3.17. Di-(2-fluorophenyl)-acetylene (3q).[12] White solid. Compounds **2e** and **1e** yielded 175 mg (0.82 mmol, 82%

yield). Mp: 50–52 °C. ^{1}H NMR ($CDCl_3$; 250 MHz): δ 7.59–7.52 (m, 2H), 7.39–7.30 (m, 2H), 7.18–7.08 (m, 4H); ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ 164.6, 160.6, 133.5, 133.5, 130.4, 130.3, 124.0, 123.9, 115.7, 115.4, 111.7, 111.4, 87.7, 87.6; MS (EI, 70 eV) *m/z* (% relative intensity, ion): 214 (100, [M$^+$]), 193 (10), 144 (6), 107 (13), 94 (8).

3.3.18. 4-Phenylethynyl-acetophenone (3r).[27] Pale yellow solid. Compounds **2f** and **1a** yielded 170 mg (0.77 mmol, 77% yield). Mp: 95–96 °C. ^{1}H NMR ($CDCl_3$; 250 MHz): δ 7.83 (d, 2H, J=8.7 Hz), 7.52–7.44 (m, 4H), 7.28–7.25 (m, 3H), 2.50 (s, 3H); ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ 197.2, 136.1, 131.7, 131.6, 128.7, 128.4, 128.2, 128.1, 122.5, 92.6, 88.6, 26.5; MS (EI, 70 eV) *m/z* (% relative intensity, ion): 220 (55, [M$^+$]), 205 (100), 176 (61), 151 (25), 102 (11), 88 (20).

3.3.19. 4-(4′-Methoxyphenyl)ethynyl-acetophenone (3s).[28] Pale yellow solid. Compounds **2b** and **1f** yielded 195 mg (0.78 mmol, 78% yield), while using **2f** and **1b** gave 83 mg (0.33 mmol, 33% yield). The domino coupling according to Method B obtained 160 mg (0.64 mmol, 64% yield) product when **1b** reacted first, and 60 mg (0.24 mmol, 24% yield) product when **1f** reacted first. Mp: 123–124 °C. ^{1}H NMR ($CDCl_3$; 250 MHz): δ 7.91 (d, 2H, J=8.4 Hz), 7.57 (d, 2H, J=8.2 Hz), 7.48 (d, 2H, J=8.7 Hz), 6.88 (d, 2H, J=8.7 Hz), 3.82 (s, 3H), 2.59 (s, 3H); ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ 197.2, 160.0, 135.8, 133.2, 131.4, 128.5, 128.2, 114.6, 114.0, 92.9, 87.5, 55.2, 26.5; MS (EI, 70 eV) *m/z* (% relative intensity, ion): 250 (94, [M$^+$]), 235 (100), 207 (20), 192 (17), 176 (14), 164 (50), 163 (58), 117 (18).

3.3.20. (2′-Chlorophenylethynyl)-benzene (3t).[13] Pale yellow liquid. The domino coupling according to Method B yielded 183 mg (0.86 mmol, 86%), when **1a** reacted first, and 83% (177 mg, 0.83 mmol) when **1k** reacted first. ^{1}H NMR ($CDCl_3$; 250 MHz): δ 7.58–7.51 (m, 3H), 7.41–7.37 (m, 1H), 7.35–7.30 (m, 3H), 7.23–7.15 (m, 2H); ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ 135.8, 133.1, 131.7, 129.2, 129.2, 128.6, 128.3, 126.4, 123.1, 122.8, 94.5, 86.1; MS (EI, 70 eV) *m/z* (% relative intensity, ion): 212 (100, [M$^+$]), 176 (50), 151 (21), 88 (19).

3.3.21. 3-(2′-Chlorophenylethynyl)-toluene (3u).[13] Yellow solid. Domino coupling yielded 70% (160 mg, 0.70 mmol) when **1k** reacted first, and 97 mg (0.43 mmol, 43%), when **1l** reacted first. Mp: 39–41 °C. ^{1}H NMR ($CDCl_3$; 250 MHz): δ 7.54–7.49 (m, 1H), 7.40–7.31 (m, 3H), 7.24–7.10 (m, 4H), 2.31 (s, 3H); ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ 137.9, 135.8, 133.1, 132.2, 129.5, 129.2, 129.1, 128.7, 128.2, 126.4, 123.2, 122.6, 94.7, 85.8, 21.1; MS (EI, 70 eV) *m/z* (% relative intensity, ion): 226 (100, [M$^+$]), 189 (65), 165 (17), 94 (23).

3.3.22. Hexadehydrotribenzo[12]annulene (4).[29] 1-(2′-Bromophenylethynyl)-1-cyclohexanol (**2i**) (279 mg, 1 mmol), 5% of $PdCl_2L_2$ (0.05 mmol), 9.5 mg of CuI (0.05 mmol, 5%), and 224 mg of KOH (4 mmol) were placed into a flame-dried Schlenk flask. Absolute toluene of 7 mL was added, and the mixture was stirred under argon at 80 °C. The reaction was followed by TLC and GC–MS. When the sequential coupling was complete, the product (**4**) was separated by column chromatography, using hexane as eluent. Yellow solid, using 35 mg of $Pd(PPh_3)_2Cl_2$ yielded 20 mg product (0.066 mmol, 20% yield), while using 37 mg $Pd(PCy_3)_2Cl_2$ gave 32 mg product (0.107 mmol, 32% yield). Mp: 202–204 °C (decomp.). ^{1}H NMR ($CDCl_3$; 250 MHz): δ 7.31–7.23 (m, 6H), 7.14–7.07 (m, 6H); ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ 132.0, 128.5, 126.6, 92.8; MS (EI, 70 eV) *m/z* (% relative intensity, ion): 301 (25), 300 (100, [M$^+$]), 298 (36), 150 (26), 149 (33), 136 (13).

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