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Synthesis of molecular chains: application of cross-coupling and bromo by iodo exchange reactions

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ABSTRACT

The synthesis of a series of molecular chains by use of C–S, C–N and *C*-Alkyne cross coupling, as well as bromo by iodo exchange reactions, has been reported. Two different types of chains R–C_6H_4–S–C_6H_4–C≡C–C_6H_4–NH–C_6H_4–Br, and R–C_6H_4–S–C_6H_4–NH–C_6H_4–C≡C–C_6H_4–Br (R=MeO, CN, NO_2) could be obtained starting from the same thioether but applying different reaction sequences. Compounds R–C_6H_4–C≡C–C_6H_4–S–C_6H_4–NH–C_6H_4–Br were prepared from diaryl acetylenes after two bromo by iodo replacements alternated with a C–S and a C–N cross coupling.

1. Introduction

In the last decades, the synthesis of molecular chains has attracted a growing interest as a consequence of its applications in a great variety of fields such as, pharmaceuticals,[1,2] sensors,[2,3] optoelectronic, non-linear optical and photonic devices,[4–6] catalysis,[7] etc.[8] One of the most common strategies to prepare this type of molecules involves the step-by-step repetition of coupling reactions.[9–11]

We have previously reported a stepwise synthesis of molecular chains.[10,11] Our approach involves the Pd-catalyzed C-X coupling between Ar–I and HXAr′Br (X=S, Ar=aryl, Ar′=phenylene) to give ArXAr′Br, taking advantage of the different reactivity of Br and I derivatives, followed by a Br by I replacement to give ArXAr′I. This unit could be reacted with HXAr′Br in the next growing step. In this way, we have proved that it is possible to prepare molecules of great interest such as phenylene thioethers of different sizes and ending groups. Thus, thioether oligomers R–C_6H_4–(S–C_6H_4)$_n$–Br, prepared by Pd-catalyzed C–S cross coupling, afforded molecules of the type R–C_6H_4–(S–C_6H_4)$_n$–I (Fig. 1) after the Cu-catalyzed replacement of bromo by iodo.[10] We also predicted the extension of this methodology to prepare chains such as Ar-(X–Ar′)$_n$-Br where X could be C≡C, NH, S or O. Indeed, introducing new functionalized groups would provide new interesting properties to the final chains. For example, ethynyl substituents are interesting because of their rigid structure and their π electrons, which could confer interesting photophysical properties that could lead to the possibility of using the final molecules in optoelectronic devices.[5,12,13] Additionally, amines are strong donor groups that have been included in oligomers with different applications.[4,12,14]

With the aim of extending the scope of this method, we present here the synthesis of six molecular chains of the type R–C_6H_4–X–C_6H_4–X′–C_6H_4–X″–C_6H_4–R′, R and R′ being either donor or acceptor groups such as NO_2, MeO, CN, Br or I and X, X′ and X″, S, NH or C≡C. The NH, and alkyne functions could be introduced into the chain by well-known C–N and *C*-alkyne cross coupling

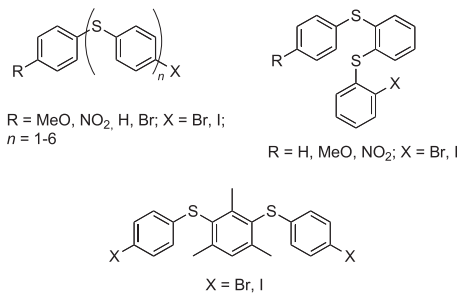

Fig. 1. Phenyl thioether described previously.

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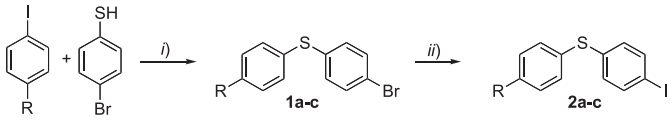
reactions of the appropriate Ar–I and HXAr′Br (X=N or alkyne) compounds. Thus, to illustrate the method, we have prepared chains with different sequential distribution of the functional groups by choosing the suitable starting material and reaction sequence.

2. Results and discussion

2.1. Synthesis of chains starting from a thioether

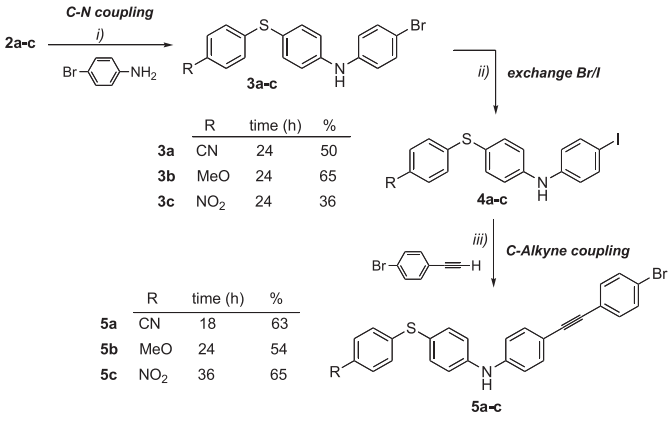
Compounds **2a**–**c** (Scheme 1) are the starting materials to synthesize several thioether chains containing the ethynyl phenylene amino unit. These compounds were prepared following the two steps procedure we have previously described:[10] *i*) the palladium-catalyzed C–S cross coupling reaction between iodoarenes and 4-bromobenzenethiol and *ii*) the copper-catalyzed replacement of bromo by iodo (Scheme 1). Interestingly, the C–S coupling reaction was significantly improved compared to what we previously described,[10] since the reaction time was reduced from 3 days to 2 h by increasing the temperature to 100 °C.



R = CN **a**
MeO **b**[a]
NO_2 **c**[a]

Scheme 1. Synthesis of iodo thioether compounds. *i*) NaO^{t}Bu (1 equiv), Pd(dba)$_2$ (5 mol %), dppf (5 mol %) 2 h at 100 °C; *ii*) CuI (7 mol %), dmcd (13 mol %), NaI (2 equiv); [a] Ref. 10.

Compounds **5a**–**c** (Scheme 2) or **7a**–**c** (Scheme 3) were prepared from the diaryl thiothers **2a**–**c**, but following different synthetic strategies.

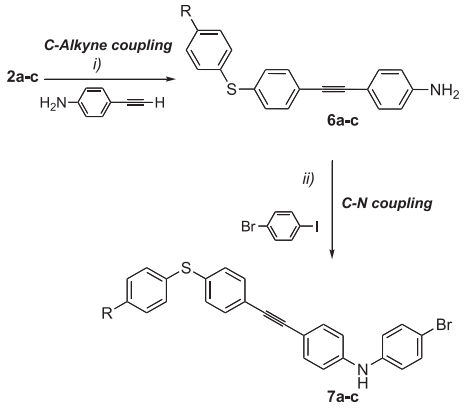


	R	time (h)	%
3a	CN	24	50
3b	MeO	24	65
3c	NO_2	24	36

	R	time (h)	%
5a	CN	18	63
5b	MeO	24	54
5c	NO_2	36	65

Scheme 2. Synthesis of the chains **5a**–**c**. *i*) Pd(dba)$_2$ (5 mol %), *rac*-Binap (5 mol %), NaO^{t}Bu (1.3 equiv), toluene at 100 °C; *ii*) CuI (7 mol %), NaI (2 equiv), dmcd (13%), dioxane, 48 h at 140 °C; *iii*) [PdCl$_2$(PPh$_3$)$_2$] (5 mol %), CuI (5 mol %), THF:^{i}Pr$_2$NH (50:1), rt.

The C–N coupling of 4-bromoaniline with **2a**–**c** in the presence of a slight excess of NaO^{t}Bu, and 5 mol % of the catalytic mixture of Pd(dba)$_2$ and *rac*-Binap (toluene, 100 °C, 24 h) afforded compounds **3a**–**c** (Scheme 2). The Cu-catalyzed exchange reactions of bromo by iodo gave rise to iodo derivatives **4a**–**c**. The reaction is a slightly modified version of the Cu-catalyzed halogen exchange reaction reported by Buchwald,[15] using 7 mol % of CuI, 13 mol % of racemic *trans*-*N*,*N*′-dimethyl-1,2-cyclohexane diamine (dmcd), and 2 equiv of NaI (dioxane, 140 °C, 48 h). Compounds **5a**–**c** were prepared



	R	time (h)	%
6a	CN	16	70
6b	MeO	36	80
6c	NO_2	52	70

	R	time (h)	%
7a	CN	42	15
7b	MeO	16	80
7c	NO_2	24	35

Scheme 3. Synthesis of the chains **7a**–**c**. *i*) [PdCl$_2$(PPh$_3$)$_2$] (5 mol %), CuI (5 mol %), THF:^{i}Pr$_2$NH (50:1), rt; *ii*) Pd(dba)$_2$ (5 mol %), *rac*-Binap (5 mol %), NaO^{t}Bu (1.3 equiv), toluene at 80 °C.

following a modified Sonogashira *C*-alkyne coupling[16] of compounds **4a**–**c** with bromo-4-ethynylbenzene in the presence of 5 mol % of the catalytic mixture of PdCl$_2$(PPh$_3$)$_2$ and CuI in THF:^{i}Pr$_2$NH (50:1) at room temperature. Although the reaction time required to complete this last step increased from 18 h when R=CN (**5a**) to 36 h (R=NO_2, **5c**), the yields are very similar for the three prepared compounds. Thus, a priori, this process is independent of the mesomeric effect of the R substituent.

The isomers of type **7** were obtained inverting the coupling processes sequence (Scheme 3). In this case, we firstly carried out the *C*-alkyne coupling process, and then, the C–N coupling, without any Br by I exchange reaction between both steps (Scheme 3).

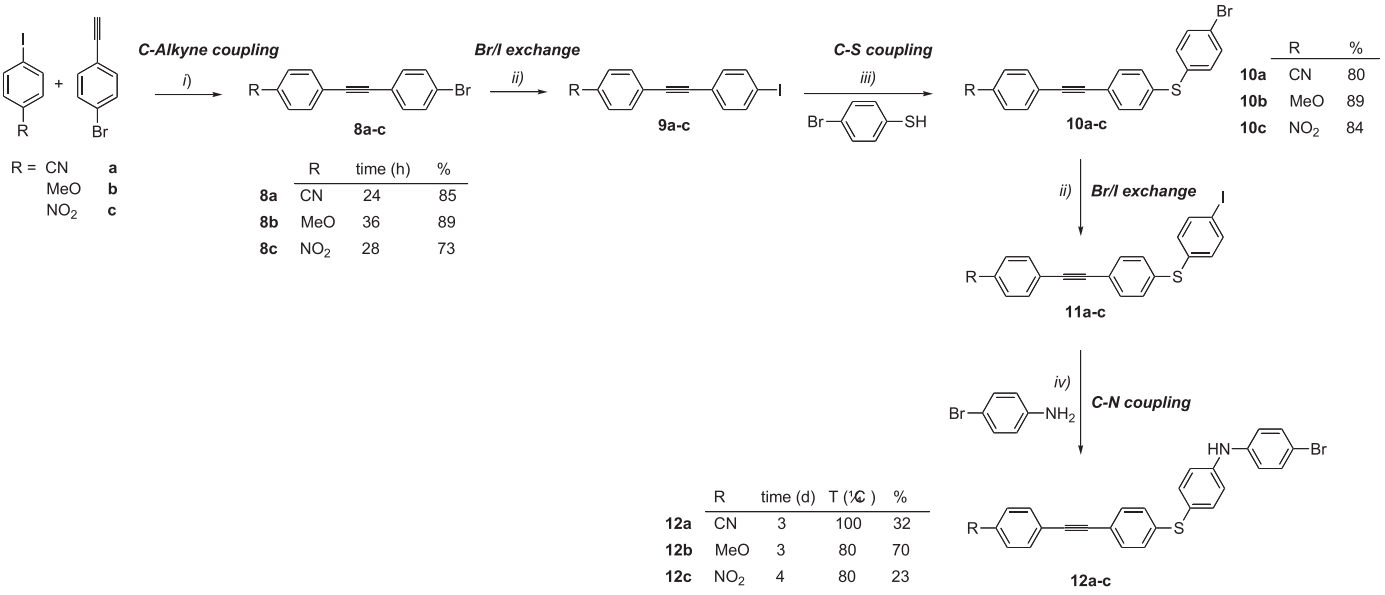
The reaction conditions of the *C*-alkyne and C–N cross couplings to afford compounds **6a**–**c** and **7a**–**c** were the same than those employed to obtain **5a**–**c** and **3a**–**c**, respectively, with the exception of the temperature, which ranges from 100 °C for **3a**–**c**, to 80 °C for **7a**–**c**. Observing the results in both cases, we could conclude that, the C–N cross coupling is more effective when 4-bromoaniline is used instead of 4-bromoiodobenzene. An exception to this is the reaction giving **7b** in which, despite of using a lower temperature than in the case of its analogous **3b**, both the reaction time and the yield are better.

Remarkably, when both coupling reactions required to obtain **7a**–**c** (Scheme 3) were performed via one-pot, the process stopped at the *C*-alkyne coupling to afford **6a**–**c**.

2.2. Synthesis of chains starting from alkynes

With the aim of introducing in the first step of the process the alkynyl unit, we have prepared compounds **8a**–**c** by a *C*-alkyne cross coupling reaction between the corresponding aryl iodide and bromo-4-ethynylbenzene (Scheme 4).[16] Subsequently, an exchange reaction of bromo by iodo was performed to give rise to **9a**–**c**. Just as we did for **7a**–**c**, we tried to obtain **9a**–**c** via one-pot reaction. However, when the *C*-alkyne coupling and the bromo by iodo exchange reactions were carried out in the same flask without isolating the bromo derivates, **8a**–**c** were obtained instead of **9a**–**c**. In this case, the reaction sequence also stopped at the *C*-alkyne coupling.

Compounds **10a**–**c** were obtained in good yields by a C–S cross coupling with 4-bromobenzenethiol, under the same reaction conditions as above. The arylamino group was introduced by an exchange of bromo by iodo to afford **11a**–**c**, followed by a C–N cross coupling with 4-bromoaniline to afford **12a**–**c** (Scheme 4). This last step of the process gave low yield for substrates containing electron withdrawing end groups (R=NO_2, CN).



	R	time (h)	%
8a	CN	24	85
8b	MeO	36	89
8c	NO_2	28	73

	R	%
10a	CN	80
10b	MeO	89
10c	NO_2	84

	R	time (d)	T (°C)	%
12a	CN	3	100	32
12b	MeO	3	80	70
12c	NO_2	4	80	23

Scheme 4. Synthesis of chains derived from bromo-4-ethynylbenzene. *i*) $[PdCl_2(PPh_3)_2]$ (5 mol %), CuI (5 mol %), THF:$^iPr_2NH$ (50:1), rt; *ii*) CuI (7 mol %), NaI (2 equiv), dcm (13%), dioxane, 48 h at 140 °C; *iii*) $Pd(dba)_2$ (5 mol %), dppf (5 mol %), NaO^{t}Bu (1 equiv), toluene, 2 h at 100 °C; *iv*) $Pd(dba)_2$ (5 mol %), *rac*-Binap (5 mol %), NaO^{t}Bu (2 equiv), toluene.

3. Conclusions

We have prepared a series of molecular chains containing an alkynyl, a thio and an amino group. Their syntheses are based on the application of a step-by-step sequential method consisting of C–N, C–S, or *C*-Alkyne cross coupling reaction including a bromo by iodo exchange reaction. Thus, starting from the same thioether compound, two types of chains could be prepared depending on the next step being a C–N or a *C*-alkyne coupling. Isomeric chains have also been prepared, but using a different starting material and reactions sequence. In conclusion, the application of several cross coupling and exchange reactions allows the formation of isomeric chains R–C_6H_4–X–C_6H_4–X′–C_6H_4–X″–C_6H_4–R′, where R, R′, could be either donor or acceptor groups, NO_2, MeO, CN, Br or I, while X, X′ and X″ could be S, NH or C≡C. The presence of a C–Br end group allows the easy additional growing of the chains.

4. Experimental section

4.1. General

4-Bromobenzenethiol, 4-iodonitrobenzene, 4-iodoanisole, 4-bromobenzonitrile, 4-bromoiodobenzene, KO^{t}Bu, NaO^{t}Bu, dppf (1,1′-Bis(diphenylphosphino)ferrocene), *rac*-Binap (*rac*-1,1′-binaphthalene-2,2′-diyl)bis(diphenylphosphine)), dmcd (*trans*-*N*,*N*′-Dimethylcyclohexane-1,2-diamine), and dba (dibenziylideneacetone) were obtained from commercial sources. 4-Ethynylaniline,[17] bromo-4-ethynylbenzene, $Pd(dba)_2$[18] and $PdCl_2(PPh_3)_2$ were prepared according to previously reported methods. Compounds **1b**, **1c**, **2b** and **2c** were prepared following a slightly modified version of a procedure previously reported by our group.[10,11] The reactions were carried out under an inert atmosphere. CH_2Cl_2, Et_2O and Toluene were degassed and dried using a Pure Solv MD-5 solvent purification system while 1,4-dioxane was obtained from commercial sources and deoxygenated by bubbling N_2. *n*-Hexane and *n*-pentane were used as received. Elemental analyses were carried out with Carlo Erba 1106 and LECO CHNS-932 microanalyzers. NMR spectra were recorded on Bruker Avance 200, 300, and 400 instruments. ^{1}H chemical shifts were referenced to TMS, and $^{13}C\{^1H\}$ NMR spectra were referenced to $CDCl_3$ (77.0 ppm). The temperature values in NMR experiments were not corrected. Abbreviations used: br (broad), s (singlet), d (doublet), m (multiplet), v (virtual). Chromatographic separations were carried out on silica gel either by preparative TLC using a fluorescent indicator or by column chromatography. High-resolution ESI mass spectra were recorded on an Agilent 6220 Accurate-Mass TOF LC/MS spectrometer.

4.2. General method for the bromo by iodo exchange

The exchange of bromo by iodo was carried out as previously described.[11] A Carius tube was charged successively with the bromo derivate, CuI (7 mol %), NaI (2 equiv), dmcd (13 mol %) and 1,4-dioxane. The reaction mixture was stirred at 140 °C for 2 days. After cooling down to room temperature, the solvent was removed under vacuum, and the residue extracted with Et_2O (30 mL) and filtered. The filtrate was concentrated to dryness, and the residue was purified by washing with cold *n*-hexane (**Method A**) or by chromatography in CH_2Cl_2/*n*-hexane (1:1) (**Method B**).

*4.2.1. 4-((4-Iodophenyl)thio)benzonitrile (**2a**). Method A.* Colourless solid. Yield: 88%. ^{1}H NMR (300.1 MHz, $CDCl_3$): δ 7.74 (vd, 2H, *J*=8.0 Hz), 7.50 (vd, 2H, *J*=8.0 Hz), 7.22–7.18 (m, 4H). $^{13}C\{^1H\}$ NMR (75.45 MHz, $CDCl_3$): δ 144.4 (CN), 138.9 (CH), 135.6 (CH), 132.4 (CH), 131.2 (C), 127.8 (CH), 118.5 (C), 109.2 (C), 95.3 (C). Elemental analyses (%) calcd for $C_{13}H_8INS$: C, 46.31; H, 2.39; N, 4.15; S, 9.51; found: C, 46.48; H, 2.45; N, 4.50; S, 9.49. MS (EI) *m*/*z* (%): 337 (95), 338 (30), 339 (11).

*4.2.2. 4-((4-((4-Iodophenyl)amino)phenyl)thio)benzonitrile (**4a**). Method A.* Colourless solid. Yield: 95%. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 7.62–7.58 (m, 2H), 7.47–7.44 (m, 2H), 7.43–7.39 (m, 2H), 7.12–7.10 (m, 2H), 7.09–7.05 (m, 2H), 6.94–6.91 (m, 2H), 5.88 (br s, 1H, NH). $^{13}C\{^1H\}$ NMR (100.8 MHz, $CDCl_3$): δ 147.4 (C), 144.4 (C), 141.3 (C), 138.3 (CH), 136.9 (CH), 132.2 (CH), 126.1 (CH), 121.1 (CH), 119.9 (C), 118.9 (C), 117.7 (CH), 108.0 (C), 84.4 (C). Elemental analyses (%) calcd for $C_{19}H_{13}IN_2S$: C, 53.28; H, 3.06; N, 6.54; S, 7.49; found: C, 53.40; H, 3.08; N, 6.55; S, 7.61. MS (EI) *m*/*z* (%): 428.1 (100), 429.1 (20), 430 (6).

*4.2.3. 4-Iodo-N-(4-((4-methoxyphenyl)thio)phenyl)aniline (**4b**). Method B.* Colourless solid. Yield: 70%. ^{1}H NMR (400.9 MHz,

$CDCl_3$): δ 7.50 (vd, 2H, *J*=16.0 Hz), 7.32 (vd, 2H, *J*=8.8 Hz), 7.20 (vd, 2H, *J*=8.4 Hz), 6.94 (vd, 2H, *J*=8.4 Hz), 6.85 (vd, 2H, *J*=8.8 Hz), 6.79 (vd, 2H, *J*=8.4 Hz), 5.73 (br s, 1H, NH), 3.79 (s, 3H, Me). $^{13}C\{^1H\}$ NMR (100.8 MHz, $CDCl_3$): δ 159.1 (C), 142.6 (C), 141.3 (C), 138.1 (CH), 133.3 (CH), 131.9 (CH), 128.7 (C), 126.7 (C), 119.6 (CH), 118.8 (CH), 114.8 (CH), 82.6 (C), 55.3 (MeO). Elemental analyses (%) calcd for $C_{19}H_{16}INOS$: C, 52.67; H, 3.72; N, 3.23; S, 7.40; found: C, 52.61; H, 3.72; N, 3.20; S, 7.46. HRMS (ESI+) *m*/*z* calcd for $[M+H]^+$: 434.0076; found: 434.0075. Δ=0.23 ppm.

*4.2.4. 4-Iodo-N-(4-((4-nitrophenyl)thio)phenyl)aniline (**4c**). Method B*. Orange solid. Yield: 70%. ^1H NMR (400.9 MHz, $CDCl_3$): δ 8.07–8.03 (m, 2H), 7.62–7.58 (m, 2H), 7.44–7.40 (m, 2H), 7.14–7.11 (m, 2H), 7.10–7.06 (m, 2H), 6.95–6.92 (m, 2H), 5.96 (br s, 1H, NH). $^{13}C\{^1H\}$ NMR (100.8 MHz, $CDCl_3$): δ 150.2 (C), 144.9 (C), 144.6 (C), 141.2 (C), 138.3 (CH), 137.0 (CH), 132.4 (C), 125.6 (C), 123.9 (CH), 121.2 (CH), 119.5 (C), 117.7 (CH), 84.6 (C). Elemental analyses (%) calcd for $C_{18}H_{13}IN_2O_2S$: C, 48.23; H, 2.92; N, 6.25; S, 7.15; found: C, 48.13; H, 3.01; N, 6.04; S, 7.17. HRMS (ESI+) *m*/*z* calcd for $[M+H]^+$: 448.9815; found: 448.9827. Δ=2.67 ppm.

*4.2.5. 4-((4-Iodophenyl)ethynyl)benzonitrile (**9a**). Method B*. Colourless solid. Yield 83%. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.74–7.71 (m, 2H), 7.66–7.59 (m, 4H), 7.27–7.25 (m, 2H). $^{13}C\{^1H\}$ NMR (100.8 MHz, $CDCl_3$): δ 137.2 (CH), 132.6 (C), 131.6 (CH), 131.5 (CH), 127.3 (C), 121.2 (C), 117.9 (C), 111.2 (C), 94.8 (C), 92.2 (C), 88.5 (C). Elemental analyses (%) calcd for $C_{15}H_8IN$: C, 54.74, H, 2.45; N, 4.26; found: C, 54.81; H, 2.41; N, 4.21. HRMS (ESI+) *m*/*z* calcd for $[M+Na]^+$: 351.9594; found: 351.9588. Δ=1.70 ppm.

*4.2.6. 1-Iodo-4-((4-methoxyphenyl)ethynyl)benzene (**9b**). Method A*. Colourless solid. Yield: 90%. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.69–7.65 (m, 2H), 7.48–7.43 (m, 2H), 7.26–7.21 (m, 2H), 6.90–6.85 (m, 2H), 3.83 (s, 3H, MeO). $^{13}C\{^1H\}$ NMR (100.8 MHz, $CDCl_3$): δ 159.8 (C), 137.5 (CH), 133.1 (C), 132.9 (CH), 123.2 (C), 115.0 (C), 114.1 (C), 93.6 (C), 90.9 (C), 87.2 (C), 55.3 (MeO). Elemental analyses (%) calcd for $C_{15}H_{11}IO$: C, 53.92; H, 3.32; found: C, 53.62; H, 3.45. MS (EI) *m*/*z* (%): 334 (100), 335 (24).

*4.2.7. 1-Iodo-4-((4-nitrophenyl)ethynyl)benzene (**9c**). Method B*. Pale yellow solid. Yield: 84%. ^1H NMR (200.1 MHz, $CDCl_3$): δ 8.23 (vd, 2H, *J*=16.0 Hz), 7.74–7.64 (m, 4H), 7.30–7.26 (m, 2H). $^{13}C\{^1H\}$ NMR (50.3 MHz, $CDCl_3$): δ 147.1 (C), 137–7 (CH), 133.1 (CH), 132.2 (CH), 129.8 (C), 123.6 (CH), 121.6 (C), 95.4 (C), 93.6 (C), 88.8 (C). Elemental analyses (%) calcd for $C_{14}H_8INO_2$: C, 48.16; H, 2.31; N, 4.01 found: C, 48.54; H, 2.38; N, 3.95. Owing to the poor ionization of the compound, we were not able to obtain a useful mass spectrum.

*4.2.8. 4-((4-((4-Iodophenyl)thio)phenyl)ethynyl)benzonitrile (**11a**). Method B*. Colourless solid. Yield: 90%. ^1H (300.8 MHz, $CDCl_3$): δ 7.68–7.57 (m, 6H), 7.46–7.43 (m, 2H), 7.27–7.24 (m, 2H), 7.14–7.11 (m, 2H). $^{13}C\{^1H\}$ (75.45 MHz, $CDCl_3$): δ 138.5 (CH), 137.6 (C), 134.2 (C), 133.6 (CH), 132.4 (CH), 132.0 (CH), 129.0 (CH), 127.9 (C), 120.7 (C), 118.5 (C), 111.6 (C), 93.3 (C), 93.1 (C), 88.6 (C). Elemental analyses (%) calcd for $C_{21}H_{12}INS$: C, 57.68; H, 2.77; N, 3.20; S, 7.33; found: C, 57.85; H, 2.79; N, 3.14; S, 7.72. HRMS (ESI+) *m*/*z* calcd for MNa^+ 459.9627; found: 459.9620. Δ=1.52 ppm.

*4.2.9. (4-Iodophenyl)(4-((4-methoxyphenyl)ethynyl)phenyl)thioether (**11b**). Method B*. Pale yellow solid. Yield: 76%. ^1H NMR (300.8 MHz, $CDCl_3$): δ 7.62 (vd, 2H, *J*=12.0 Hz), 7.47–7.42 (m, 4H), 7.29–7.24 (m, 2H), 7.07 (vd, 2H, *J*=12.0 Hz), 6.87 (vd, 2H, *J*=12.0 Hz), 3.83 (MeO). $^{13}C\{^1H\}$ NMR (75.45 MHz, $CDCl_3$): δ 159.7 (C), 138.3 (CH), 135.5 (C), 135.1 (C), 133.1 (CH), 132.8 (CH), 132.2 (CH), 130.7 (CH), 122.7 (C), 115.1 (C), 114.0 (CH), 92.6 (C), 90.6 (C), 87.4 (C), 55.3 (MeO). Elemental analyses (%) calcd for $C_{21}H_{15}IOS$: C, 57.02; H, 3.42; S, 7.25 found: C, 57.07; H, 3.62; S, 7.22. HRMS (ESI+) *m*/*z* calcd for MH^+: 442.9967; found: 442.9965. Δ=0.45 ppm.

*4.2.10. (4-Iodophenyl)(4-((4-nitrophenyl)ethynyl)phenyl)thioether (**11c**). Method B*. Pale yellow solid. Yield: 84%. ^1H NMR (400.9 MHz, $CDCl_3$): δ 8.24–8.20 (m, 2H, Ar), 7.68–7.64 (m, 4H, Ar), 7.47–7.45 (m, 2H, Ar), 7.27–7.25 (m, 2H, Ar), 7.15–7.12 (m, 2H, Ar). $^{13}C\{^1H\}$ NMR (100.8 MHz, $CDCl_3$): δ 146 (C), 138.4 (CH), 137.8 (C), 134.1 (C), 133.7 (CH), 132.4 (CH), 132.2 (CH), 129.9 (C), 129.7 (CH), 123.7 (CH), 120.4 (C), 94.1 (C), 93.5 (C), 88.4 (C). Elemental analyses (%) calcd for $C_{20}H_{12}INO_2S$: C, 52.53; H, 2.65; N, 3.06; S, 7.01; found: C, 52.42; 2.98; 3.06; S, 6.84. MS (EI) *m*/*z* (%): 457 (100), 458 (27), 459 (8).

4.3. General method for the C–S coupling reactions

The C–S coupling was carried out by a modification of a procedure described recently by our group.[10] The reaction time was reduced from 3 days to 2 h by increasing the temperature to 100 °C. Thus, a Carius tube was charged with the corresponding thiol (1 equiv), aryl iodide (1.05 equiv), $Pd(dba)_2$ (5 mol %), dppf (5 mol %), NaOtBu (1 equiv), and toluene. The resulting mixture was heated at 100 °C for 2 h. After removing the solvent under vacuum, the residue was extracted with CH_2Cl_2 (30 mL) and filtered. The organic filtrate was concentrated and purified by chromatography using CH_2Cl_2/*n*-hexane (1:1) as eluent.

*4.3.1. 4-((4-Bromophenyl)thio)benzonitrile (**1a**).* Colourless solid. Yield: 80%. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.57–7.53 (m, 2H), 7.52–7.48 (m, 2H), 7.37–7.35 (m, 2H), 7.20–7.17 (m, 2H). $^{13}C\{^1H\}$ NMR (100.8 MHz, $CDCl_3$): δ 144.6 (CN), 135.6 (CH), 133.1 (CH), 132.5 (CH), 130.3 (C), 127.7 (CH), 123.8 (C), 118.6 (C), 109.3 (C). Elemental analyses (%) calcd for $C_{13}H_8BrNS$: C, 53.81; H, 2.78; N, 4.83; S, 11.05; found: C, 53.88; H, 2.69; N, 5.19; S, 10.82. MS (EI) *m*/*z* (%): 289 (90), 290 (16), 291 (87), 292 (15).

*4.3.2. 4-((4-((4-Bromophenyl)thio)phenyl)ethynyl)benzonitrile (**10a**).* Colourless solid. Yield: 80%. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.65–7.58 (m, 4H), 7.49–7.43 (m, 4H), 7.29–7.23 (m, 4H). $^{13}C\{^1H\}$ NMR (100.8 MHz, $CDCl_3$): δ 137.8 (C), 133.7 (CH), 133.2 (C), 132.6 (CH), 132.4 (CH), 132.0 (CH), 132.0 (CH), 129.5 (CH), 128.0 (C), 122.1 (C), 120.5 (C), 118.4 (C), 111.5 (C), 93.1(C), 88.5 (C). Elemental analyses (%) calcd for $C_{21}H_{12}BrNS$: C, 64.62; H, 3.10; N, 3.59; S, 8.22; found: C, 64.55; H, 3.12; N, 3.71; S, 8.02. HRMS (ESI+) *m*/*z* calcd for MNa^+: 411.9746; found: 411.9744. Δ=4.85 ppm.

*4.3.3. (4-Bromophenyl)(4-((4-methoxyphenyl)ethynyl)phenyl)thioether (**10b**).* Colourless solid. Yield: 80%. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.45 (m, 6H), 7.26–7.21 (m, 4H), 6.89–6.87 (m, 2H), 3.83 (s, 3H, MeO). $^{13}C\{^1H\}$ NMR (100.8 MHz, $CDCl_3$): δ 159.7 (C), 135.4 (C), 134.4 (C), 133.1 (CH), 132.8 (CH), 132.4 (CH), 132.2 (CH), 130.5 (CH), 122.5 (C), 121.5 (C), 115.1 (C), 114.0 (C), 90.5 (C), 87.4 (C). Elemental analyses (%) calcd for $C_{21}H_{15}BrOS$: C, 63.80; H, 3.82; S, 8.11; found: C, 63.74; H, 3.92; S, 8.20. HRMS (ESI+) *m*/*z* calcd for MH^+: 395.0105; found: 395.0107. Δ=0.51 ppm.

*4.3.4. (4-Bromophenyl)(4-((4-nitrophenyl)ethynyl)phenyl)thioether (**10c**).* Pale yellow solid. Eluent CH_2Cl_2/*n*-hexane (1:3), R_f=0.33. Yield: 65%. ^1H NMR (400.9 MHz, $CDCl_3$): δ 8.24–8.21 (m, 2H), 7.67–7.64 (m, 2H), 7.50–7.44 (m, 4H), 7.30–7.27 (m, 2H), 7.26–7.23 (m, 2H). $^{13}C\{^1H\}$ NMR (100.8 MHz, $CDCl_3$): δ 147.0 (C), 138.2 (C), 133.9 (CH), 133.1 (C), 132.6 (CH), 132.5 (CH), 132.2 (CH), 130.0 (C), 129.5 (CH), 123.7 (CH), 122.3 (C), 120.4 (C), 94.0 (C), 88.3 (C). Elemental analyses (%) calcd for $C_{20}H_{12}BrNO_2S$: C, 58.55; H, 2.95; N,

3.41; S, 7.82 found: C, 58.28; H, 2.77; N, 3.35; S, 8.04. HRMS (ESI+) m/z calcd for MH^+: 409.9850; found: 409.9863. Δ=3.17 ppm.

4.4. General method for the *C*-alkyne coupling reactions

A Schlenk tube under a nitrogen atmosphere was charged with the iododerivate, 4-ethynylaniline (1.1 equiv) or bromo-4-ethynylbenzene (1.1 equiv), CuI (5 mol %), and $[PdCl_2(PPh_3)_2]$ (5 mol %). Sequentially, THF (5 mL) and $^iPr_2NH$ (0.1 mL) were added. The reaction mixture was stirred for X h at room temperature, and extracted with CH_2Cl_2 (30 mL) and water (2×10 mL). The organic phase was dried over $MgSO_4$, and the resulting solution was concentrated to about 1 mL. Addition of cold Et_2O (**Method A**) or column chromatography (**Method B**) gave the desired compound.

*4.4.1. 4-((4-((4-Bromophenyl)ethynyl)phenyl)amino)phenyl) thio)benzonitrile (**5a**). Method B.* X=18. Eluent EtOAc/*n*-hexane (1:4), R_f=0.5. Pale yellow solid. Yield 63%. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 7.49–7.42 (m, 8H), 7.39–7.36 (m, 2H), 7.16–7.09 (m, 6H), 6.03 (br s, 1H, NH). $^{13}C\{^1H\}$ NMR (100.8 MHz, $CDCl_3$): δ 147.3 (C), 143.9 (C), 141.9 (C), 136.9 (CH), 133.0 (CH), 132.8 (CH), 132.3 (CH), 131.6 (CH), 126.2 (CH), 122.4 (C), 122.2 (C), 120.5 (C), 118.9 (C), 118.3 (CH), 118.0 (CH), 116.0 (C), 108.1 (C), 90.5 (C), 87.6 (C). Elemental analyses (%) calcd for $C_{27}H_{17}BrN_2S$: C, 67.3; H, 3.56; N, 5.82; S, 6.66; found: C, 67.46; H, 3.42; N, 6.03; S, 6.85. HRMS (ESI+) m/z calcd for MNa^+: 503.0188; found: 503.0190. Δ=0.40 ppm.

*4.4.2. 4-((4-Bromophenyl)ethynyl)-N-(4-((4-methoxyphenyl)thio) phenyl)aniline (**5b**). Method B.* X=24. Eluent EtOAc/*n*-hexane (1:4), R_f=0.34. Pale yellow solid. Yield 54%. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 7.46 (vd, 2H, J=8.0 Hz), 7.41–7.33 (m, 6H), 7.22 (vd, 2H, J=8.0 Hz), 7.03–6.96 (m, 4H), 6.87 (vd, 2H, J=8.0 Hz), 5.83 (br s, 1H, NH), 3.80 (s, 3H, MeO). $^{13}C\{^1H\}$ NMR (100.8.8 MHz, $CDCl_3$): δ 159.2 (C), 143.3 (C), 140.7 (C), 133.5 (CH), 132.9 (CH), 132.8 (CH), 131.7 (CH), 131.5 (CH), 129.5 (C), 126.5 (C), 122.6 (C), 121.9 (C), 119.4 (C), 116.5 (CH), 115.8 (CH), 114.5 (C), 90.9 (C), 87.2 (C), 55.3 (MeO). Elemental analyses (%) calcd for $C_{27}H_{20}BrNOS$: C, 66.67; H, 4.14; N, 2.88; S, 6.59; found: C, 66.54; H, 4.42; N, 3.10; S, 6.59. MS (EI) m/z (%): 485 (100), 486 (43), 487 (91), 488 (41), 489 (13).

*4.4.3. 4-((4-Bromophenyl)ethynyl)-N-(4-((4-nitrophenyl)thio)phenyl)aniline (**5c**). Method B.* X=36. Eluent EtOAc/*n*-hexane (1:4), R_f=0.21. Reddish Solid. Yield: 65%. ^{1}H NMR (300.1 MHz, $CDCl_3$): δ 8.09–8.04 (m, 2H), 7.49–7.44 (m, 6H), 7.40–7.35 (m, 2H), 7.18–7.10 (m, 6H), 6.04 (br s, 1H, NH). $^{13}C\{^1H\}$ NMR (75.45 MHz, $CDCl_3$): δ 150.0 (C) 145.0 (C), 144.1 (C), 141.8 (C), 137.0 (CH), 133.0 (CH), 132.9 (CH), 131.6 (CH), 125.7 (CH), 124.0 (CH), 122.4 (C), 122.2 (C), 120.1 (C), 118.3 (CH), 118.2 (C), 116.1 (C), 90.5 (C), 87.7 (C). Elemental analyses (%) calcd for $C_{26}H_{17}BrN_2O_2S$: C, 62.28; H, 3.42; N, 5.59; S, 6.40; found: C, 61.88; H, 3.39; N, 5.56; S, 6.42. MS (ESI) m/z (%): $[M+H]^+$ calcd 501.0272; found: 501.0279. Δ=1.39 ppm.

*4.4.4. 4-((4-((4-Aminophenyl)ethynyl)phenyl)thio)bezonitrile (**6a**). Method A.* X=16. Colourless solid. Yield: 70%. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 7.53–7.48 (m, 4H), 7.45–7.43 (m, 2H), 7.36–7.33 (m, 2H), 7.22–7.19 (m, 2H), 6.66–6.63 (m, 2H), 3.90 (br s, 2H, NH_2).). $^{13}C\{^1H\}$ NMR (100.8 MHz, $CDCl_3$): δ 147.0 (C), 145.1 (C), 133.9 (CH), 133.0 (CH), 132.5 (CH), 132.4 (CH), 130.3 (C), 127.7 (CH), 125.1 (C), 118.0 (C), 114.7 (CH), 111.9 (C), 109.0 (C), 92.4 (C≡), 86.4 (C≡). Elemental analyses (%) calcd for $C_{21}H_{14}N_2S$: C, 77.27; H, 4.32; N, 8.58; S, 9.82; found: C, 76.98; H, 4.52; N, 8.55; S, 9.93. MS (EI) m/z (%): 326 (100), 327 (52), 328 (25), 329 (5).

*4.4.5. 4-((4-((4-Methoxyphenyl)thio)phenyl)ethynyl)aniline (**6b**). Method A.* X=36. Pale yellow solid, unstable in silica gel. Yield: 70%. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 7.44–7.40 (m, 2H), 7.35–7.28 (m, 4H), 7.08–7.05 (m, 2H), 6.93–7.89 (m, 2H), 6.93–7.89 (m, 2H), 6.61–6.59 (m, 2H), 3.82 (s, 3H, MeO), 3.80 (s, 2H, NH_2). $^{13}C\{^1H\}$ NMR (100.8 MHz, $CDCl_3$): δ 160.0 (C), 146.6 (C), 138.7 (C), 135.7 (CH), 132.9 (CH), 131.7 (CH), 127.4 (CH), 123.4 (C), 121.0 (C), 115.1 (CH), 114.7 (CH), 112.5 (C), 90.4 (C≡), 87.0 (C≡), 55.3 (MeO). Elemental analyses (%) calcd for $C_{21}H_{17}NOS$: C, 76.10; H, 5.17; N, 4.23; S, 9.68; found: C, 75.96; H, 5.31; N, 4.35; S, 9.89. HRMS (ESI+) m/z calcd for MH^+: 332.1104; found: 332.1095. Δ=2.71 ppm.

*4.4.6. 4-((4-((4-Nitrophenyl)thio)phenyl)ethynyl)aniline (**6c**). Method A.* X=52. Pale orange crystals. Further compound could be obtained from the mother liquor. Yield: 70%. ^{1}H NMR (300.8 MHz, $CDCl_3$): δ 8.08 (vd, 2H, J=9.0 Hz), 7.56–7.46 (m, 4H), 7.3 (vd, 2H, J=9.0 Hz), 7.21 (vd, 2H, J=9.0 Hz), 6.65 (vd, 2H, J=9.0 Hz), 3.86 (br s, 2H, NH_2). $^{13}C\{^1H\}$ NMR (100.8 MHz, $CDCl_3$): δ 147.9, 147.0, 145.5, 134.2 (CH), 133.0 (CH), 132.6 (CH), 129.8, 127.0 (CH), 125.4, 124.1 (CH), 114.7 (CH), 111.8, 92.6 (C≡), 86.3 (C≡). Elemental analyses (%) calcd for $C_{20}H_{14}IN_2O_2S$: C, 69.35; H, 4.07; N, 8.09; S, 9.26; found: C, 69.14; H, 3.97; N, 8.28; S, 9.20. MS (EI) m/z (%): 346 (100), 347 (35), 348 (11).

*4.4.7. 4-((4-Bromophenyl)ethynyl)benzonitrile (**8a**). Method B.* X=24. Eluent CH_2Cl_2/*n*-hexane (1:5), R_f=0.43. Colourless solid. Yield: 85%. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 7.66–7.59 (m, 8H), 7.54–7.50 (m, 2H), 7.42–7.39 (m, 2H). $^{13}C\{^1H\}$ NMR (100.8 MHz, $CDCl_3$): δ 133.2 (CH), 132.1 (CH), 131.8 (CH), 127.8 (C), 123.5 (C), 121.1 (C), 118.4 (CN), 111.7 (C), 92.6 (C≡), 88.7 (C≡). Elemental analyses (%) calcd for $C_{15}H_8BrN$: C, 63.86; H, 2.86; N, 4.96; found: C, 63.73; H, 2.63; N, 4.98. MS (EI) m/z (%): 281 (100), 282 (36), 283 (99), 284 (33).

*4.4.8. 1-Bromo-4-((4-methoxyphenyl)ethynyl)benzene (**8b**). Method B.* X=24. Eluent CH_2Cl_2/*n*-hexane (1:5), R_f=0.43. Colourless solid. Yield: 89%. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 7.48–7.44 (m, 4H), 7.38–7.35 (m, 2H), 6. 90–6.86 (m, 2H), 3.83 (s, 3H, MeO). $^{13}C\{^1H\}$ NMR (75.45 MHz, $CDCl_3$): δ 159.7 (C), 133.0 (CH), 132.8 (CH), 131.5 (CH), 122.5 (C), 122.0 (C), 114.9 (C), 114.0 (CH), 90.5 (C≡), 87.0 (C≡), 55.3 (MeO). Elemental analyses (%) calcd for $C_{15}H_{11}BrO$: C, 62.74; H, 3.86; found: C, 62.69; H, 3.83. MS (EI) m/z (%): 286 (100), 287 (25), 288 (99), 289 (25).

*4.4.9. 1-Bromo-4-((4-nitrophenyl)ethynyl)benzene (**8c**). Method B.* X=28. Eluent CH_2Cl_2/*n*-hexane (1:3), R_f=0.45. Pale yellow solid. Yield: 73%. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 8.25–8.21 (m, 2H), 7.68–7.65 (m, 2H), 7.55–7.52 (m, 2H), 7.44–7.41 (m, 2H). $^{13}C\{^1H\}$ NMR (100.8 MHz, $CDCl_3$): δ 147.1 (C), 133.1 (CH), 132.2 (CH), 131.8 (CH), 129.8 (C), 123.6 (CH), 121.0 (C), 93.4 (C), 88.5 (C). One C signal was not detected. Elemental analyses (%) calcd for $C_{14}H_8BrNO_2$: C, 55.66; H, 2.67; N, 4.64; found: C, 55.31; H, 2.69; N, 4.94. MS (EI) m/z calcd for M^+: 300.9738; found: 300.9697.

4.5. General method for the C–N coupling reactions

A Schlenk tube under a nitrogen atmosphere was charged with the corresponding iododerivate (1 equiv), 4-bromoaniline (1.1 equiv) or 1-bromo-4-iodobenzene (1 equiv), $Pd(dba)_2$ (5 mol %), *rac*-Binap (5 mol %), Na^tOBu (1.3–2 equiv). Subsequently, toluene (10 mL) was added and the reaction mixture was stirred for X h at Y °C. The resulting mixture was extracted with CH_2Cl_2 (30 mL) and water (2×10 mL). The organic phase was dried over $MgSO_4$. The solution was concentrated to about 1 mL and purified by column chromatography.

*4.5.1. 4-((4-((4-Bromophenyl)amino)phenyl)thio)benzonitrile (**3a**).* X=24, Y=100. Eluent EtOAc/*n*-hexane (1:5), R_f=0.34. Colourless solid. Yield: 50%. ^{1}H NMR (200.1 MHz, $CDCl_3$): δ 7.49–7.40

(m, 6H), 7.14–7.02 (m, 6H), 5.88 (br s, 1H, NH). $^{13}C\{^1H\}$ NMR (50.30 MHz, $CDCl_3$): δ 147.4 (C), 144.7 (C), 140.5 (C), 136.9 (CH), 132.4 (CH), 132.2 (CH), 126.1 (CH), 121.0 (CH), 119.7(C), 119.0 (C), 117.5 (CH), 114.6 (C), 107.9 (C). Elemental analyses (%) calcd for $C_{19}H_{13}BrN_2S$: C, 59.85; H, 3.44; N, 7.35; S, 8.41; found: C, 59.30; H, 3.70; N, 7.08; S, 8.25. MS (EI) *m*/*z* (%): 380 (82, M^+), 381 (26), 382 (73), 383 (23), 384 (6).

*4.5.2. 4-Bromo-N-(4-((4-methoxyphenyl)thio)phenyl)aniline (**3b**).* *X*=24, *Y*=100. Eluent CH_2Cl_2/*n*-hexane (1:2), R_f=0.33. Colourless solid. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.34–7.31 (m, 4H), 7.23–7.20 (m, 2H), 6.92–6.88 (m, 6H), 5.70 (br s, 1H, NH), 3.80 (s, 3H, MeO). $^{13}C\{^1H\}$ NMR (100.8 MHz, $CDCl_3$): δ 159.1 (C), 141.8 (C), 141.5 (C), 133.2 (CH), 132.2 (CH), 132.1 (CH), 128.5, 126.8 (C), 119.4 (CH), 118.5(CH), 114.8 (CH), 113.1 (C), 55.3 (MeO). Elemental analyses (%) calcd for $C_{19}H_{16}BrNOS$: C, 59.07; H, 4.17; N, 3.63; S, 8.30; found: C, 59.11; H, 4.22; N, 3.48; S, 8.53. MS (EI) *m*/*z* (%): 385 (100, M^+), 387 (49), 388 (25), 389 (10).

*4.5.3. 4-Bromo-N-(4-((4-nitrophenyl)thio)phenyl)aniline (**3c**).* *X*=24, *Y*=100. Eluent CH_2Cl_2/*n*-hexane (1:1), R_f=0.47. Colourless solid. ^1H NMR (400.9 MHz, $CDCl_3$): δ 8.07–8.03 (m, 2H), 7.44–7.42 (m, 4H), 7.08–7.04 (m, 6H), 5.91 (br s, 1H, NH). $^{13}C\{^1H\}$ NMR (100.8 MHz, $CDCl_3$): δ 150.2 (C), 145.0 (C), 144.9 (C), 140.4 (C), 137.0 (CH), 132.5 (CH), 125.6 (CH), 124.0 (CH), 121.1 (CH), 119.4 (C), 117.5 (CH), 114.8 (C). Elemental analyses (%) calcd for $C_{18}H_{13}BrN_2O_2S$: C, 53.88; H, 3.27; N, 6.98; S, 7.99; found: C, 53.69; H, 3.34; N, 7.29; S, 8.12. HRMS (ESI+) *m*/*z* (%): $[M+H]^+$ calcd 400.9959; found: 400.9951. Δ=2.00 ppm.

*4.5.4. 4-((4-((4-((4-Bromophenyl)amino)phenyl)ethynyl)phenyl)thio)benzonitrile (**7a**).* *X*=42, *Y*=80. Eluent CH_2Cl_2/*n*-hexane (1:1), R_f=0.36. Orange solid. Yield: 15%. ^1H NMR (300.1 MHz, $CDCl_3$): δ 7.55–7.38 (m, 10H), 7.22–7.19 (m, 2H), 7.01–6.97 (m, 4H), 5.83 (s, 1H, NH). $^{13}C\{^1H\}$ NMR (75.45 MHz, $CDCl_3$): δ 145.0 (C), 143.3 (C), 140.9 (C), 133.9 (CH), 133.1 (CH), 132.6 (CH), 132.5 (CH), 132.4 (CH), 130.8 (C), 127.8 (CH), 124.8 (C), 120.5 (CH), 118.7 (C), 116.5 (CH), 114.5(C), 114.2 (C), 109.1 (C), 91.9 (C), 87.3 (C). Elemental analyses (%) calcd for $C_{27}H_{17}BrN_2S$: C, 67.36; H, 3.56; N, 5.82; S, 6.66; found: C, 67.76; H, 3.37; N, 5,44; S, 6.65. MS (EI) *m*/*z* (%): 480 (100), 481 (30), 482 (100), 483 (30), 484 (9).

*4.5.5. 4-Bromo-N-(4-((4-((4-methoxyphenyl)thio)phenyl)ethynyl)phenyl)aniline (**7b**).* *X*=16, *Y*=80. Eluent CH_2Cl_2/*n*-hexane (1:1), R_f=0.53. Pale orange solid. Yield: 80%. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.45–7.34 (m, 8H), 7.09–7.06 (vd, 2H, *J*=8.0), 6.99–6.91 (m, 6H), 5.79 (br s, 1H, NH), 3.84 (s, 3H, MeO). $^{13}C\{^1H\}$ NMR (100.8 MHz, $CDCl_3$): δ 160.1 (C), 142.8 (C), 141.1 (C), 139.2 (C), 135.8 (CH), 132.9 (CH), 132.3 (CH), 131.8 (CH), 127.3 (CH), 123.3 (C), 120.7 (C), 120.2 (CH), 116.7 (CH), 115.3 (C), 115.1 (CH), 113.8 (C), 89.9 (C≡), 88.0 (C≡), 55.4 (MeO). Elemental analyses (%) calcd for $C_{27}H_{20}BrNOS$: C, 66.67; H, 4.14; N, 2.88; S, 6.59; found: C, 66.86; H, 4.14; N, 3.15; S, 6.73. MS (EI) *m*/*z* (%): 485 (98), 486 (28), 487 (100), 488 (29), 489 (9).

*4.5.6. 4-Bromo-N-(4-((4-((4-nitrophenyl)thio)phenyl)ethynyl)phenyl)aniline (**7c**).* *X*=24, *Y*=80. Eluent CH_2Cl_2/*n*-hexane (1:1), R_f=0.2. Orange solid. Yield: 35%. ^1H NMR (400.9 MHz, $CDCl_3$): δ 8.09–8.07 (m, 2H), 7.56 (vd, 2H, *J*=8.0 Hz), 7.48 (vd, 2H, *J*=8.0 Hz), 7.44–7.38 (m, 4H), 7.24–7.20 (m, 2H), 7.01–6.98 (m, 4H), 5.85 (br s, 1H, NH). $^{13}C\{^1H\}$ NMR (100.8 MHz, $CDCl_3$): δ 147.8 (C), 145.5 (C), 143.3 (C), 140.8 (C), 134.2 (CH), 133.1 (CH), 132.7 (CH), 132.4 (CH),130.3 (C), 127.2 (CH), 125.1 (C), 124.1 (CH), 120.6 (CH), 116.5 (CH), 114.5 (C), 114.2 (C), 92.1 (C≡), 87.3 (C≡). Elemental analyses (%) calcd for $C_{26}H_{17}BrN_2O_2S$: C, 62.28; H, 3.42; N, 5.59; S, 6.40; found: C, 62.14; H, 3.60; N, 5.60; S, 6.39. MS (EI) *m*/*z* (%): 500 (100), 501 (30), 502 (98), 503 (27), 504 (8).

*4.5.7. 4-((4-((4-((4-Bromophenyl)amino)phenyl)thio)phenyl)ethynyl)benzonitrile (**12a**).* *X*=72, *Y*=100. Eluent EtOAc/*n*-hexane (1:4), R_f=0.37. Yellowish solid. Yield: 32%. ^1H NMR (300.1 MHz, $CDCl_3$): δ 7.63–7.55 (m, 4H), 7.42–7.37 (m, 6H), 7.15–7.10 (m, 2H), 7.06–6.98 (m, 4H), 5.82 (br s, NH). $^{13}C\{^1H\}$ NMR (75.45 MHz, $CDCl_3$): δ 143.8 (C), 141.3 (C), 140.9 (C), 136.0 (CH), 132.4 (CH), 132.1 (CH), 132.0 (CH), 132.0 (CH), 127.0 (C), 122.3 (C), 120.5 (CH), 119.0 (C), 118.5 (C), 117.7 (CH), 114.2 (C), 111.3 (C), 93.7 (C), 88.0 (C). Elemental analyses (%) calcd for $C_{27}H_{17}BrN_2S$: C, 67.36; H, 3.56; N, 5.82; S, 6.66; found: C, 66.84; H, 3.67; N, 5.66; S, 6.92. HRMS (ESI+) *m*/*z* (%): $[M+H]^+$ calcd 481.0369; found: 481.0377. Δ=1.66 ppm.

*4.5.8. 4-Bromo-N-(4-((4-((4-methoxyphenyl)ethynyl)phenyl)thio)phenyl)aniline (**12b**).* *X*=72, *Y*=80. Eluent CH_2Cl_2/*n*-hexane (1:1), R_f=0.4. Yellowish solid. Yield. 70%. ^1H NMR (300.1 MHz, $CDCl_3$): δ 7.46–7.43 (m, 2H), 7.41–7.35 (m, 6H), 7.14–7.11 (m, 2H), 7.03–6.98 (m, 4H), 6.88–6.85 (m, 2H), 5.80 (br s, 1H, NH), 3.82 (s, 1H, MeO). $^{13}C\{^1H\}$ NMR (75.45 MHz, $CDCl_3$): δ 159.6 (C), 143.3 (C), 141.1 (C), 139.0 (C), 135.5 (CH), 133.0 (CH), 132.3 (CH), 131.8 (CH), 127.6 (CH), 123.4 (C), 120.8 (C), 120.3 (CH), 117.8 (CH), 115.3(C), 114.0 (CH), 113.9 (C), 89.7 (C), 87.8 (C), 55.3 (MeO). Elemental analyses (%) calcd for $C_{27}H_{20}BrNOS$: C, 66.67; H, 4.14; N, 2.88; S, 6.59; found: C, 66.20; H, 4.93; N, 3.01; S, 6.10. MS (EI) *m*/*z* (%): 485 (100), 486 (37), 487 (90), 488 (32), 489 (10).

*4.5.9. 4-Bromo-N-(4-((4-((4-nitrophenyl)ethynyl)phenyl)thio)phenyl)aniline (**12c**).* *X*=96, *Y*=80. Eluent CH_2Cl_2/*n*-hexane (1:1), R_f=0.70. Yellow solid. Yield: 23%. ^1H NMR (300.1 MHz, $CDCl_3$): δ 8.21 (m, 2H), 7.63 (m, 2H), 7.42–7.39 (m, 6H), 7.12 (m, 2H), 7.03 (m, 4H), 5.85 (br s, 1H, NH). $^{13}C\{^1H\}$ NMR (75.45 MHz, $CDCl_3$): δ 146.9 (C), 143.8 (C), 141.6 (C), 140.9 (C), 138.5 (CH), 136.1 (CH), 132.4 (CH), 132.18 (CH), 132.15 (CH), 130.3 (C), 126.9 (CH), 123.6 (CH), 122.2 (C), 120.6 (CH), 118.8 (C), 117.7 (CH), 114.3 (C), 94.6 (C), 87.8 (C). Elemental analyses (%) calcd for $C_{26}H_{17}BrN_2O_2S$: C, 62.28; H, 3.42; N, 5.59; S, 6.40; found: C, 62.28; H, 3.42; N, 5.39; S, 6.28. MS (EI) *m*/*z* (%): 501 (94), 502 (28), 503 (100), 504 (29), 505 (9).

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Supplementary data

Supplementary data (^1H and ^{13}C NMR spectra of the new compounds) related to this article can be found at http://dx.doi.org/10.1016/j.tet.2015.06.072.

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