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Available online 1 November 2007

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Keywords: Indole; Benzofuran; Aryl diynes; Cyclization

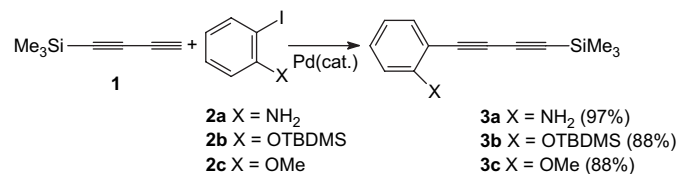
Substituted benzofurans and indoles form the core of numerous natural products and have considerable pharmacological potential.¹ Many synthetic methods for the construction of the indole ring have been reported.² Among these, palladium-catalyzed annulation of *o*-halo anilines and alkynes or of *o*-alkynyl anilines has been widely employed for the synthesis of indole derivatives, due to the versatile nature of this methodology and increased functional group tolerance.² Thus far, many kinds of reagents have been reported for indole synthesis from 2-ethynyl aniline derivatives.³ Moreover, there has been a growing interest in developing general and versatile methods for the synthesis of benzofuran derivatives, because of their activities as blood coagulation factor Xa inhibitors,⁴ as antagonists of angiotensin II receptors⁵ and potent calcium blockers.⁶ Various methods for the preparation of benzofurans are known⁷ but recent research has focused on the utilization of palladium-catalyzed coupling/cyclization reactions of alkynes with *o*-hydroxy aryl halides.^{7b,f,8}

In connection with our ongoing work^{9–13} in which we succeeded in synthesizing stereodefined conjugated polyunsaturated systems and a series of natural products^{10–13} using

unsaturated silylated compounds, and owing to the growing interest in the synthesis of the heterocyclic systems reported above, we decided to develop a procedure for the synthesis of unsaturated molecular frameworks linked to these heterocyclic systems. Thus, the wide application of the palladium-catalyzed coupling/cyclization reactions of alkynes with *ortho*-substituted aryl halides encouraged us to examine the possibility of preparing heterocyclic rings starting from *ortho*-substituted aryl diynes.

2. Results and discussion

As reported in [Scheme 1](#), starting from 1-trimethylsilyl-1,3-butadiyne **1**⁹ and 2-iodoaniline **2a**, protected 2-iodophenol **2b** and 2-iodoanisole **2c**, we have realized the synthesis of several *ortho*-substituted aryl diynes **3**, employing, with the appropriate modifications, as reported in [Section 3](#), the Sonogashira protocol.¹⁴



Scheme 1.

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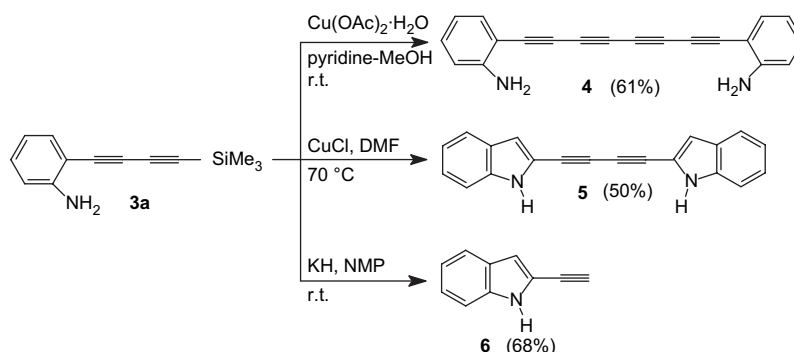
E-mail address: fianda@chimica.uniba.it (V. Fiandanese).

Compounds **3** have been synthesized in excellent yields (88–97%) and we started to investigate on their eventual conversion into heterocyclic systems. We have found (Scheme 2) that compound **3a**,¹⁵ when subjected to reaction with $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$ in pyridine/MeOH as solvent, at room temperature,^{3j} led easily to tetrayne **4**, derived from a dimerization of compound **3a**. However, by employing another copper salt, CuCl ¹⁶ in DMF as solvent at 70 °C, and performing the reaction in a capped flask, we obtained bis-(1*H*)-indole **5**, with the two indolyl moieties linked to the positions 2,2' by two triple bonds. (These results are in agreement with the literature data^{3j,16} because it is known that 2-ethynylanilines, without any substituent on the nitrogen atom, in the presence of copper acetate lead to the cyclized product in very low yield,^{3j} whereas the cyclization is favoured with copper chloride.)¹⁶ Finally, when we performed the reaction of compound **3a** with KH in *N*-methylpyrrolidone (NMP) as solvent,^{3m} this reaction led directly to the heterocyclic alkyne, 2-ethynylindole **6**.¹⁶ In an analogous manner, we have subjected also compounds **3b** and **3c**¹⁷ to similar reactions and for compound **3b** we have found a different selectivity towards the copper salts. In particular (Schemes 3 and 4), both compounds **3b** and **3c** have been easily dimerized leading to tetrayne derivative **7**

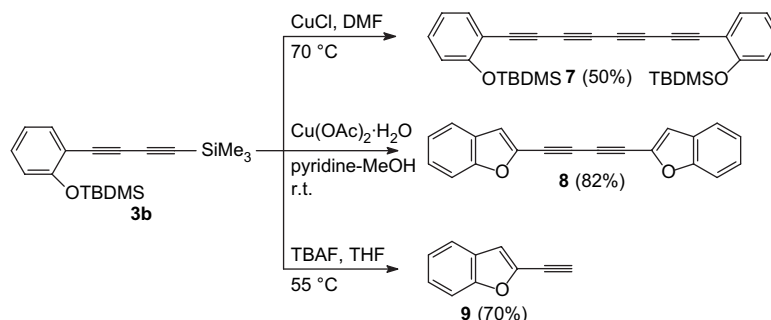
(Scheme 3) by treatment of compound **3b** with CuCl in DMF and to tetrayne derivative **10** (Scheme 4) by reaction of compound **3c** with $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$. However, when we performed the reaction of compound **3b** with $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$, we obtained directly the bis-benzofuran derivative **8** with the two rings linked to the positions 2,2' by two triple bonds. (The pyridine/MeOH system probably promotes the deprotection of the phenolic group and the cyclization reaction, whereas the dimerization reaction is promoted by the copper salt.)

Moreover, the reaction of compound **3b** with a fluoride source, TBAF^{3o,8c} in THF at 55 °C, led to the heterocyclic product, 2-ethynylbenzofuran **9**¹⁸ in 70% yield. Thus, these results confirmed the full versatility of *ortho*-substituted aryl diynes **3a** and **3b** regarding their conversion into the heterocyclic compounds **5**, **6**, **8** and **9**.

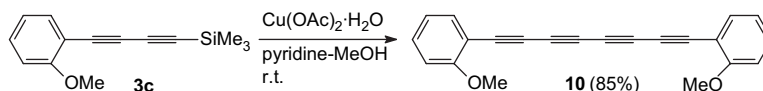
In order to evaluate the possibility of synthesizing other and more complex heterocyclic systems, we decided to employ compounds **6** and **9** as starting materials in a series of coupling reactions with different aryl or vinyl halides. Thus (Scheme 5), we found that when compound **6** was reacted with 2-iodophenol **11**, the reaction product **16** was easily cyclized with TBAF in THF, leading to the di-heterocyclic compound **21**,¹⁹ with the two rings (the indolyl and the benzofuran rings) linked



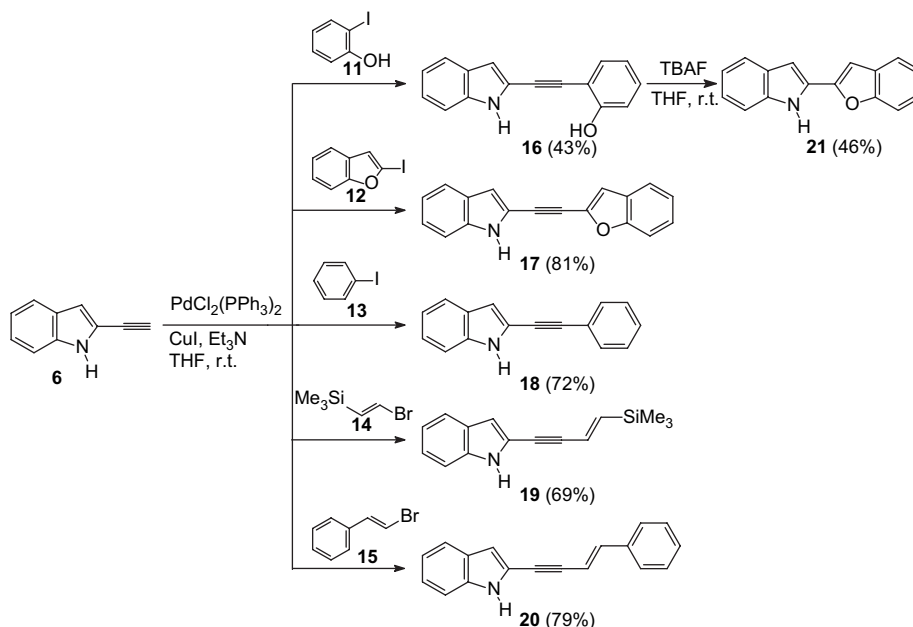
Scheme 2.



Scheme 3.



Scheme 4.



Scheme 5.

by a single bond. Moreover, the reaction of **6** with 2-iodobenzofuran **12**¹⁸ led to the di-heterocyclic compound **17** with the same two rings linked by a triple bond. Also the other reactions of compound **6** with the aryl and vinyl halides **13**–**15** proceeded very well, leading to the functionalized indole derivatives **18**–**20** in good yields.

In the case of compound **9**, we planned to realize a convenient procedure for the synthesis of benzofuran derivatives containing two benzofuran rings linked directly to the positions 2,2' by a single bond or by one triple bond and also by two triple bonds. Thus (Scheme 6), we reacted compound **9** with 2-iodophenol **11** and found that this reaction led directly to 2,2'-bi-benzofuran **22**,²⁰ by means of a tandem coupling/cyclization reaction. Moreover, to obtain compound **23**²¹ it was sufficient to perform the coupling reaction of **9** with 2-iodobenzofuran **12**. Finally, as reported in the scheme, the same dibenzofuran diyne **8** was easily obtained in an alternative

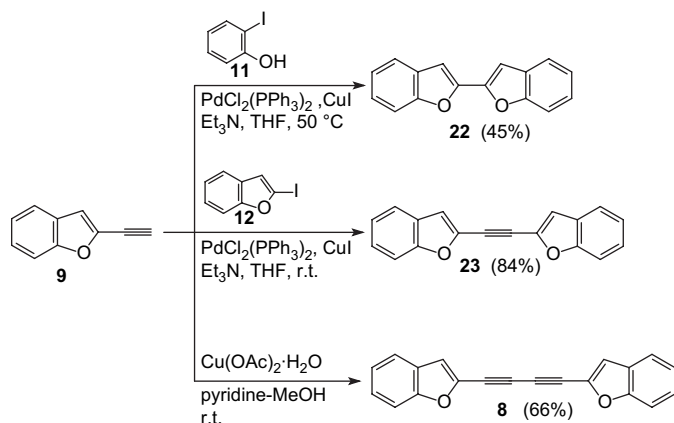
manner to the procedure reported in Scheme 3, by a dimerization reaction of compound **9**.

In summary, our synthetic approach to these heterocyclic systems compares favourably with other procedures. A special advantage of our strategy is represented by the possibility of synthesizing several heterocyclic compounds containing the benzofuran or the indole-benzofuran rings, starting from the same intermediates and employing simple coupling and dimerization reactions. Moreover, the simplicity of the operations involved, the mild reaction conditions and the ready availability of the silyl derivative employed are additional features making the procedure very promising.

3. Experimental

3.1. General

Macherey–Nagel silica gel (60, particle size 0.040–0.063 mm) for column chromatography and Macherey–Nagel aluminum sheets with silica gel 60 F₂₅₄ for TLC were used. GC analysis was performed on a Varian 3900 gas chromatograph equipped with a J & W capillary column (DB-1301, 30 m×0.25 mm id). GC/mass-spectrometric analysis was performed on a Shimadzu GC–MS–QP5000 gas chromatograph-mass spectrometer equipped with a Zebron capillary column (methyl polysiloxane, 30 m×0.25 mm id). ¹H NMR spectra were recorded in deuteriochloroform or CD₃COCD₃ on a Bruker AM 500 spectrometer at 500 MHz or on a Varian Inova at 400 MHz. ¹³C NMR spectra were recorded in deuteriochloroform or CD₃COCD₃ on a Bruker AM 500 spectrometer at 125.7 MHz or on a Varian Inova at 100.6 MHz. IR spectra were recorded on a Perkin–Elmer FT-IR–Spectrum One and on a Shimadzu IR Prestige 21 spectrometers. Solvents



Scheme 6.

were dried before use as follows: tetrahydrofuran was distilled from sodium and *N,N*-dimethylformamide and acetonitrile were distilled over molecular sieves. Commercial NMP was used as supplied. Melting points (uncorrected) were determined on a Reichert Microscope. 2-Iodobenzofuran was prepared according to a literature procedure.¹⁸

3.2. Synthesis of 2-substituted aryl diynes **3**

3.2.1. 2-(4-Trimethylsilyl-1,3-butadiyn-1-yl)aniline (**3a**)¹⁵

A solution of 1-trimethylsilyl-1,3-butadiyne **1** (3.36 g, 27.54 mmol) in anhydrous CH₃CN (30 mL) was added at room temperature, under nitrogen, to a stirred mixture of 2-iodoaniline **2a** (3.02 g, 13.77 mmol), Pd(PPh₃)₄ (0.80 g, 0.69 mmol), CuI (0.26 g, 1.37 mmol) and Et₃N (1.393 g, 13.77 mmol) in CH₃CN (30 mL). After reaction completion (6 h), the mixture was quenched with a saturated aqueous solution of NH₄Cl (50 mL) and extracted with ethyl acetate (3×50 mL). The organic extracts were washed with H₂O (3×50 mL), dried over Na₂SO₄ and concentrated under vacuum. The residue was purified by column chromatography on silica gel (10% ethyl ether/petroleum ether) leading to 2.84 g of compound **3a** (97% yield) as a brown oil. $\nu_{\max}$ (neat) 3480, 3384, 2959, 2195, 2097, 1616, 1489, 1455, 1316, 1284, 1251, 849, 748, 705; δ_{H} (400 MHz, CDCl₃) 7.29 (dd, *J*=6.4, 1.2 Hz, 1H), 7.12 (ddd, *J*=6.4, 5.9, 1.2 Hz, 1H), 6.66–6.61 (m, 2H), 4.27 (br s, 2H), 0.23 (s, 9H); δ_{C} (100.6 MHz, CDCl₃) 149.8, 133.3, 130.7, 117.9, 114.3, 105.6, 91.7, 87.8, 79.3, 73.9, –0.4; MS *m/z* 213 (M⁺, 55), 199 (18), 198 (100), 182 (7), 170 (6), 168 (8), 158 (9), 144 (6), 141 (7), 130 (7), 117 (6), 99 (46), 85 (14), 77 (10), 72 (13), 53 (21), 44 (15), 43 (35%).

3.2.2. 2-(4-Trimethylsilyl-1,3-butadiyn-1-yl)-*tert*-butyldimethylsilylphenol (**3b**)

A solution of 2-(*tert*-butyldimethylsilyloxy)iodobenzene **2b** (3.83 g, 11.47 mmol), 1-trimethylsilyl-1,3-butadiyne **1** (2.80 g, 22.94 mmol), Pd(PPh₃)₄ (0.53 g, 0.46 mmol) and Et₃N (48.0 mL), under nitrogen, was stirred for 5 min at room temperature, then CuI (0.044 g, 0.23 mmol) was added and stirring was continued for another 2 min. The mixture was heated at 50 °C for 6 h, then was quenched with a saturated aqueous solution of NH₄Cl (50 mL) and extracted with ethyl acetate (3×50 mL). The organic extracts were washed with H₂O (3×50 mL), dried over Na₂SO₄ and concentrated under vacuum. The residue was purified by column chromatography on silica gel (petroleum ether) leading to 3.31 g of compound **3b** (88% yield) as a brown oil. [Found: C, 69.49; H, 8.60. C₁₉H₂₈OSi₂ requires: C, 69.45; H, 8.59%.] $\nu_{\max}$ (neat) 2958, 2930, 2858, 2205, 2102, 1593, 1485, 1448, 1288, 1252, 1019, 910, 843; δ_{H} (400 MHz, CDCl₃) 7.40 (dd, *J*=7.7, 1.7 Hz, 1H), 7.22 (td like, *J*=7.8, 1.7 Hz, 1H), 6.89 (td, *J*=7.7, 0.9 Hz, 1H), 6.82 (br d, *J*=8.2 Hz, 1H), 1.06 (s, 9H), 0.25 (s, 6H), 0.24 (s, 9H); δ_{C} (100.6 MHz, CDCl₃) 158.3, 134.1, 130.5, 121.2, 119.8, 114.1, 90.4, 88.2, 77.9, 74.4, 25.6, 18.2, –0.4, –4.4; MS *m/z* 328 (M⁺, 2), 273 (12), 272 (32), 271 (100), 255 (20), 243 (7), 232 (14), 231 (60), 128

(27), 98 (10), 97 (84), 83 (7), 73 (70), 69 (16), 59 (19), 57 (14), 45 (26), 43 (25), 41 (17%).

3.2.3. 2-(4-Trimethylsilyl-1,3-butadiyn-1-yl)anisole (**3c**)¹⁷

To a stirred solution of 1-trimethylsilyl-1,3-butadiyne **1** (1.19 g, 9.74 mmol), 2-iodoanisole **2c** (1.14 g, 4.87 mmol), Pd(PPh₃)₂Cl₂ (0.14 g, 0.20 mmol) and Et₃N (9.5 mL), under nitrogen, at room temperature, after 5 min, CuI (0.019 g, 0.10 mmol) was added and stirring was continued at the same temperature for 12 h. Then, the mixture was quenched with a saturated aqueous solution of NH₄Cl (30 mL) and extracted with ethyl acetate (3×30 mL). The organic extracts were washed with H₂O (3×20 mL), dried over Na₂SO₄ and concentrated under vacuum. The residue was purified by percolation on Florisil column (10% ethyl acetate/petroleum ether) leading to 0.98 g of compound **3c** (88% yield) as a brown oil. $\nu_{\max}$ (neat) 2960, 2203, 2102, 1594, 1490, 1463, 1433, 1272, 1248, 1018, 847, 752; δ_{H} (400 MHz, CDCl₃) 7.44 (dd, *J*=7.4, 1.6 Hz, 1H), 7.36–7.29 (m, 1H), 6.92–6.85 (m, 2H), 3.89 (s, 3H), 0.23 (s, 9H); δ_{C} (100.6 MHz, CDCl₃) 161.7, 134.6, 130.8, 120.5, 110.6, 91.0, 88.0, 77.9, 73.3, 55.8, –0.4 (one coincident peak not observed); MS *m/z* 228 (M⁺, 37), 214 (21), 213 (100), 198 (7), 183 (21), 161 (8), 139 (8), 106 (21), 85 (11), 73 (9), 53 (10), 43 (19%).

3.3. Synthesis of compounds **4–6**

3.3.1. 2,2'-(Octa-1,3,5,7-tetrayne-1,8-diyl)dianiline (**4**)

To a solution of Cu(OAc)₂·H₂O (1.88 g, 9.40 mmol) in pyridine (18.5 mL) and methanol (18.5 mL) was added at room temperature, under nitrogen, 2-(4-trimethylsilyl-1,3-butadiyn-1-yl)aniline **3a** (1.00 g, 4.70 mmol). After reaction completion (12 h), the mixture was quenched with a saturated aqueous solution of NH₄Cl (50 mL) and extracted with ethyl acetate (3×50 mL). The organic extracts were washed with water (3×30 mL), dried over Na₂SO₄ and concentrated under vacuum. The residue was purified by column chromatography on silica gel (30% ethyl acetate/petroleum ether) leading to 0.40 g of compound **4** (61% yield) as a yellow solid (mp=130–132 °C). [Found: C, 85.74; H, 4.35; N, 9.93. C₂₀H₁₂N₂ requires: C, 85.69; H, 4.31; N, 9.99%.] $\nu_{\max}$ (KBr) 3307, 3191, 2186, 1609, 1564, 1485, 1449, 1245, 737; δ_{H} (500 MHz, CDCl₃) 7.32 (ddd, *J*=7.6, 1.5, 0.6 Hz, 2H), 7.16 (ddd, *J*=8.2, 7.3, 1.5 Hz, 2H), 6.67–6.63 (m, 4H), 4.34 (br s, 4H); δ_{C} (125.7 MHz, CDCl₃) 150.8, 133.7, 131.5, 118.0, 114.5, 104.4, 79.7, 75.5, 68.7, 64.4.

3.3.2. 2,2'-(Buta-1,3-diyne-1,4-diyl)bis(1*H*-indole) (**5**)

CuCl (0.19 g, 1.88 mmol) was added to a solution of **3a** (0.40 g, 1.88 mmol) in DMF (4 mL) and the mixture was warmed at 70 °C in a capped flask. After reaction completion (5 h), the mixture was quenched with a saturated aqueous solution of NH₄Cl (20 mL) and extracted with ethyl acetate (3×20 mL). The organic extracts were washed with a saturated solution of NaCl (3×20 mL), dried over Na₂SO₄ and concentrated under vacuum. The residue was purified by percolation

on silica gel (20% ethyl acetate/petroleum ether) leading to 0.13 g of compound **5** (50% yield) as a pale yellow solid (mp=218–220 °C). [Found: C, 85.60; H, 4.36; N, 9.95. C₂₀H₁₂N₂ requires: C, 85.69; H, 4.31; N, 9.99%.] $\nu_{\max}$ (KBr) 3370, 2147, 1606, 1441, 1391, 1342, 1259, 1092, 1019, 803, 748, 737, 652, 505; δ_{H} (500 MHz, acetone-*d*₆) 10.82 (br s, 2H), 7.59 (br d, *J*=7.9 Hz, 2H), 7.42 (dd, *J*=8.3, 0.7 Hz, 2H), 7.24 (ddd, *J*=8.3, 7.1, 1.0 Hz, 2H), 7.09 (ddd, *J*=7.9, 7.1, 0.7 Hz, 2H), 6.99 (br s, 2H); δ_{C} (125.7 MHz, acetone-*d*₆) 138.1, 128.3, 125.0, 121.7, 121.3, 117.8, 112.2, 112.2, 77.3, 76.9.

3.3.3. 2-Ethynyl-1H-indole (**6**)¹⁶

KH (0.27 g, 6.77 mmol) was dissolved in NMP (5 mL) under nitrogen at room temperature, then a solution of **3a** (0.60 g, 2.82 mmol) in NMP (6 mL) was added dropwise and the mixture was stirred for 1 h at room temperature. The reaction was quenched with H₂O (20 mL) and extracted with ethyl acetate (3×20 mL), dried over Na₂SO₄ and concentrated under vacuum. The crude product was purified by column chromatography on silica gel (10% ethyl acetate/petroleum ether) affording 0.27 g of compound **6** (68% yield) as a yellow solid (mp=68–70 °C, lit.¹⁶ mp=68–69 °C). $\nu_{\max}$ (KBr) 3386, 3269, 2104, 1608, 1446, 1397, 1345, 1291, 1213, 1125, 1013, 800, 749, 680, 598, 499; δ_{H} (400 MHz, acetone-*d*₆) 10.61 (br s, 1H), 7.55 (br d, *J*=8.0 Hz, 1H), 7.38 (dd, *J*=8.2, 0.9 Hz, 1H), 7.18 (ddd, *J*=8.2, 7.1, 1.1 Hz, 1H), 7.05 (ddd, *J*=8.0, 7.1, 0.9 Hz, 1H), 6.78 (br s, 1H), 3.95 (s, 1H); δ_{C} (100.6 MHz, acetone-*d*₆) 137.3, 128.3, 124.0, 121.4, 120.9, 118.7, 112.0, 109.3, 82.1, 77.2; MS *m/z* 141 (M⁺, 100), 140 (26), 114 (23), 113 (13), 89 (11), 70 (20), 63 (19), 62 (10), 55 (7), 52 (7), 51 (7), 50 (7%).

3.4. Synthesis of compounds 7–10

3.4.1. 2,2'-(Octa-1,3,5,7-tetrayne-1,8-diyl)di-tert-butyltrimethylsilyldiphenol (**7**)

CuCl (0.15 g, 1.53 mmol) was added to a solution of **3b** (0.5 g, 1.53 mmol) in DMF (10 mL) and the mixture was warmed at 70 °C in a capped flask. After reaction completion (12 h), the mixture was quenched with a saturated aqueous solution of NH₄Cl (20 mL) and extracted with ethyl acetate (3×20 mL). The organic extracts were washed with a saturated solution of NaCl (3×20 mL), dried over Na₂SO₄ and concentrated under vacuum. The residue was purified by column chromatography on silica gel (petroleum ether) leading to 0.195 g of compound **7** (50% yield) as a yellow oil. [Found: C, 75.33; H, 7.38. C₃₂H₃₈O₂Si₂ requires: C, 75.24; H, 7.45%.] $\nu_{\max}$ (neat) 2954, 2930, 2857, 2197, 1593, 1563, 1484, 1448, 1289, 1256, 908, 838, 783, 755; δ_{H} (400 MHz, CDCl₃) 7.41 (dd, *J*=7.6, 1.8 Hz, 2H), 7.23 (ddd, *J*=8.3, 7.6, 1.8 Hz, 2H), 6.88 (td, *J*=7.6, 0.9 Hz, 2H), 6.80 (dd, *J*=8.3, 0.9 Hz, 2H), 1.02 (s, 18H), 0.22 (s, 12H); δ_{C} (100.6 MHz, CDCl₃) 159.1, 134.7, 131.2, 121.3, 119.9, 113.3, 77.9, 75.6, 67.5, 64.0, 25.6, 18.2, –4.3.

3.4.2. 2,2'-(Buta-1,3-diyne-1,4-diyl)bis(1-benzofuran) (**8**)

Compound **3b** (0.30 g, 0.92 mmol) was added, under nitrogen, to a solution of Cu(OAc)₂·H₂O (0.37 g, 1.84 mmol) in pyridine (4 mL) and methanol (4 mL), and the reaction was performed at room temperature. After reaction completion (12 h), the mixture was quenched with a saturated aqueous solution of NH₄Cl (20 mL) and extracted with ethyl acetate (3×20 mL). The organic extracts were washed with water (3×20 mL), dried over Na₂SO₄ and concentrated under vacuum. The residue was purified by column chromatography on silica gel (petroleum ether) leading to 0.106 g of compound **8** (82% yield) as a yellow solid (mp=165–168 °C). [Found: C, 85.03; H, 3.60. C₂₀H₁₀O₂ requires: C, 85.09; H, 3.57%.] $\nu_{\max}$ (KBr) 2141, 1439, 1342, 1245, 1176, 940, 883, 810, 733; δ_{H} (400 MHz, CDCl₃) 7.57 (ddd, *J*=7.8, 1.2, 0.7 Hz, 2H), 7.47 (dq like, *J*=8.3, 0.9 Hz, 2H), 7.38 (ddd, *J*=8.3, 7.2, 1.2 Hz, 2H), 7.26 (ddd, *J*=7.8, 7.2, 1 Hz, 2H), 7.15 (d, *J*=0.9 Hz, 2H); δ_{C} (100.6 MHz, CDCl₃) 155.3, 137.3, 127.1, 126.7, 123.7, 121.6, 115.4, 111.5, 79.4, 74.6.

3.4.3. 2-Ethynyl-1-benzofuran (**9**)¹⁸

TBAF (1 M in THF, 6.3 mL) was added at room temperature, under nitrogen, to a solution of **3b** (1.60 g, 4.88 mmol) in THF (27 mL) and the reaction mixture was stirred at 55 °C for 5 h. The mixture was quenched with a saturated aqueous solution of NH₄Cl (20 mL) and extracted with ethyl acetate (3×30 mL). The organic extracts were washed with H₂O (3×30 mL), dried over Na₂SO₄ and concentrated under vacuum. The residue was purified by column chromatography on silica gel (petroleum ether) leading to 0.485 g of compound **9** (70% yield) as a pale yellow oil. $\nu_{\max}$ (neat) 3290, 1555, 1447, 1260, 1245, 1183, 943, 813, 747, 684, 607; δ_{H} (400 MHz, CDCl₃) 7.57 (ddd, *J*=7.8, 1.3, 0.7 Hz, 1H), 7.46 (dq like, *J*=8.3, 0.9 Hz, 1H), 7.36 (ddd, *J*=8.3, 7.2, 1.3 Hz, 1H), 7.25 (ddd, *J*=7.8, 7.2, 1.0 Hz, 1H), 7.01 (dd, *J*=0.9, 0.4 Hz, 1H), 3.50 (d, *J*=0.4 Hz, 1H); δ_{C} (100.6 MHz, CDCl₃) 154.8, 137.7, 127.2, 126.0, 123.5, 121.4, 112.6, 111.4, 83.4, 74.1; MS *m/z* 142 (M⁺, 100), 114 (23), 113 (15), 88 (14), 63 (14), 62 (11%).

3.4.4. 2,2'-(Octa-1,3,5,7-tetrayne-1,8-diyl)dianisole (**10**)

Compound **3c** (0.30 g, 1.32 mmol) was added at room temperature, under nitrogen, to a solution of Cu(OAc)₂·H₂O (0.54 g, 2.72 mmol) in pyridine (6 mL) and methanol (6 mL). After reaction completion (12 h), the mixture was quenched with a saturated aqueous solution of NH₄Cl (20 mL) and extracted with ethyl acetate (3×30 mL). The organic extracts were washed with water (3×20 mL), dried over Na₂SO₄ and concentrated under vacuum. The residue was purified by percolation on a Florisil column (30% ethyl acetate/petroleum ether) leading to 0.179 g of compound **10** (85% yield) as a pale brown solid (mp=142–145 °C). [Found: C, 85.19; H, 4.50. C₂₂H₁₄O₂ requires: C, 85.14; H, 4.55%.] $\nu_{\max}$ (KBr) 2190, 1569, 1482, 1458, 1429, 1268, 1240, 1018, 733; δ_{H} (500 MHz, CDCl₃) 7.46 (dd, *J*=7.6, 1.5 Hz, 2H), 7.34 (ddd, *J*=8.4, 7.6, 1.5 Hz, 2H), 6.89 (td, *J*=7.6, 0.8 Hz, 2H), 6.86 (br d, *J*=8.4 Hz, 2H), 3.87 (s, 6H); δ_{C}

(125.7 MHz, CDCl₃) 162.4, 135.1, 131.5, 120.6, 110.7, 109.8, 78.2, 74.5, 68.0, 64.1, 55.8.

3.5. General procedure for the synthesis of compounds 16–20 and preparation of compound 21

A THF solution (0.60 M) of 2-ethynyl-1H-indole **6** (1.5 equiv) was added at room temperature, under nitrogen, to a stirred mixture of the halo derivatives **11–15** (1–1.5 equiv), PdCl₂(PPh₃)₂ (2 mol %), CuI (4 mol %) and Et₃N (1.5 equiv) in THF (0.60 M). After reaction completion (1–3 h), the mixture was quenched with a saturated aqueous solution of NH₄Cl (20 mL) and extracted with ethyl acetate (3×20 mL). The organic extracts were washed with H₂O (3×20 mL), dried over Na₂SO₄ and concentrated under vacuum. The residue was purified by column chromatography leading to compounds **16–20**.

3.5.1. 2-(1H-Indol-2-ylethynyl)phenol (**16**)

Product **16** was prepared from **6** (0.22 g, 1.56 mmol) and 2-iodophenol **11** (0.34 g, 1.56 mmol) in accordance with the general procedure. Purification by column chromatography (silica gel, 20% ethyl acetate/petroleum ether) afforded 0.156 g of product **16** (43% yield) as a brown solid (mp=104–107 °C). [Found: C, 82.33; H, 4.80; N, 5.95. C₁₆H₁₁NO requires: C, 82.38; H, 4.75; N, 6.00%.] $\nu_{\max}$ (KBr) 3396, 1443, 1406, 1260, 1092, 1020, 798; δ_{H} (400 MHz, CDCl₃) 8.38 (br s, 1H), 7.60 (d, $J=7.6$ Hz, 1H), 7.41 (dd, $J=7.7$, 1.5 Hz, 1H), 7.34–7.19 (m, 3H), 7.12 (t like, $J=7.3$ Hz, 1H), 6.97 (d, $J=8.4$ Hz, 1H), 6.91 (t like, $J=7.5$ Hz, 1H), 6.85 (br s, 1H); δ_{C} (100.6 MHz, CDCl₃) 156.6, 136.2, 131.8, 130.8, 127.6, 123.8, 121.0, 120.6, 120.6, 117.8, 115.0, 110.9, 109.4, 109.1, 88.4, 86.5; MS m/z 233 (M⁺, 100), 204 (30), 117 (42), 102 (33), 89 (19), 88 (14), 76 (11), 63 (10%).

3.5.2. 2-(1-Benzofuran-2-ylethynyl)-1H-indole (**17**)

Product **17** (0.20 g, 81% yield) was obtained from **6** (0.20 g, 1.43 mmol) and 2-iodobenzofuran **12** (0.23 g, 0.95 mmol), in accordance with the general procedure, after column chromatography (silica gel 10% ethyl acetate/petroleum ether) (yellow solid, mp=182–184 °C). [Found: C, 84.09; H, 4.30; N, 5.48. C₁₈H₁₁NO requires: C, 84.03; H, 4.31; N, 5.44%.] $\nu_{\max}$ (KBr) 3374, 2205, 1610, 1582, 1442, 1346, 1301, 1252, 1139, 1093, 932, 797, 738, 648, 499; δ_{H} (500 MHz, CDCl₃) 8.27 (br s, 1H), 7.62 (d, $J=7.9$ Hz, 1H), 7.58 (d, $J=7.6$ Hz, 1H), 7.49 (d, $J=8.1$ Hz, 1H), 7.39–7.32 (m, 2H), 7.30–7.23 (m, 2H), 7.15 (t like, $J=7.4$ Hz, 1H), 7.04 (s, 1H), 6.94 (br d, $J=1.0$ Hz, 1H); δ_{C} (125.7 MHz, CDCl₃) 155.0, 138.2, 136.4, 127.6, 127.5, 125.9, 124.2, 123.4, 121.3, 121.1, 120.8, 117.3, 112.1, 111.3, 110.9, 110.4, 87.6, 82.9; MS m/z 257 (M⁺, 100), 256 (14), 228 (13), 227 (10), 201 (6), 200 (6), 129 (37), 114 (27), 101 (16), 100 (10), 88 (11), 75 (5), 63 (6%).

3.5.3. 2-(Phenylethynyl)-1H-indole (**18**)²²

Product **18** was prepared from **6** (0.22 g, 1.56 mmol) and iodobenzene **13** (0.27 g, 1.3 mmol) in accordance with the general procedure. The residue was purified by column chromatography on silica gel (10% ethyl acetate/petroleum ether) leading to 0.20 g (72% yield) of compound **18** as a pale orange solid (mp=168–170 °C, lit.²² 161–162 °C). [Found: C, 88.38; H, 5.05; N, 6.49. C₁₆H₁₁N requires: C, 88.45; H, 5.10; N, 6.45%.] $\nu_{\max}$ (KBr) 3374, 1592, 1530, 1480, 1440, 1394, 1347, 1303, 1104, 1024, 794, 747, 687, 653, 507; δ_{H} (400 MHz, acetone-*d*₆) 10.69 (br s, 1H), 7.62–7.49 (m, 3H), 7.46–7.35 (m, 4H), 7.21 (t like, $J=7.6$ Hz, 1H), 7.08 (t like, $J=7.3$ Hz, 1H), 6.84 (br s, 1H); δ_{C} (100.6 MHz, acetone-*d*₆) 137.1, 131.4, 128.9, 128.1, 123.4, 122.9, 120.7, 120.3, 118.9, 111.4, 108.3, 91.9, 82.5 (one coincident peak not observed); MS m/z 217 (M⁺, 100), 216 (33), 189 (14), 109 (26), 94 (18), 83 (6), 81 (7), 63 (7), 51 (6%).

3.5.4. 2-[(3E)-4-Trimethylsilyl-3-buten-1-yn-1-yl]-1H-indole (**19**)

Compound **19** (0.20 g, 69% yield, pale brown oil) was obtained from **6** (0.21 g, 1.46 mmol) and (*E*)-2-bromovinylsilane **14** (0.22 g, 1.22 mmol) after purification by column chromatography (10% ethyl acetate/petroleum ether). [Found: C, 75.30; H, 7.20; N, 5.89. C₁₅H₁₇NSi requires: C, 75.26; H, 7.16; N, 5.85%.] $\nu_{\max}$ (neat) 3408, 3058, 2954, 2191, 1582, 1569, 1346, 1302, 1248, 972, 863, 840, 792, 748, 736; δ_{H} (400 MHz, CDCl₃) 8.12 (br s, 1H), 7.59 (d, $J=7.6$ Hz, 1H), 7.29 (d, $J=8.4$ Hz, 1H), 7.23 (t like, $J=7.4$ Hz, 1H), 7.12 (t like, $J=7.4$ Hz, 1H), 6.78 (br s, 1H), 6.59 (d, $J=19.6$ Hz, 1H), 6.20 (d, $J=19.6$ Hz, 1H), 0.15 (s, 9H); δ_{C} (100.6 MHz, CDCl₃) 146.6, 136.4, 128.0, 123.8, 122.8, 121.1, 120.7, 119.0, 111.0, 109.2, 93.2, 82.4, –1.4; MS m/z 239 (M⁺, 64), 238 (12), 224 (48), 199 (18), 198 (100), 180 (10), 174 (12), 154 (7), 146 (6), 141 (5), 130 (5), 112 (7), 105 (7), 99 (38), 85 (12), 73 (11), 59 (22), 53 (10), 45 (25), 43 (26%).

3.5.5. 2-[(3E)-4-Phenyl-3-buten-1-yn-1-yl]-1H-indole (**20**)

Product **20** was prepared from **6** (0.25 g, 1.78 mmol) and (*E*)-2-bromostyrene **15** (0.27 g, 1.48 mmol). The residue was purified by column chromatography (silica gel, 10% ethyl acetate/petroleum ether) leading to 0.28 g (79% yield) of **20** as a pale yellow solid (mp=174–177 °C). [Found: C, 88.90; H, 5.43; N, 5.80. C₁₈H₁₃N requires: C, 88.86; H, 5.39; N, 5.76%.] $\nu_{\max}$ (KBr) 3374, 2189, 1591, 1348, 1300, 1229, 1145, 1043, 1023, 951, 797, 745, 740, 689, 653, 509, 469; δ_{H} (400 MHz, CDCl₃) 8.14 (br s, 1H), 7.59 (br d, $J=6.8$ Hz, 1H), 7.44–7.40 (m, 2H), 7.38–7.26 (m, 4H), 7.25–7.20 (m, 1H), 7.16–7.10 (m, 1H), 7.06 (d, $J=16.2$ Hz, 1H), 6.81–6.78 (m, 1H), 6.39 (d, $J=16.2$ Hz, 1H); δ_{C} (100.6 MHz, CDCl₃) 141.8, 136.4, 136.3, 129.1, 129.0, 128.1, 126.6, 123.8, 121.1, 120.8, 119.2, 111.0, 109.1, 107.6, 92.6, 84.3; MS m/z 243 (M⁺, 100), 242 (63), 241 (56), 240 (15), 215 (16), 122 (38), 121 (46), 109 (11), 108 (14), 107 (16), 94 (19), 90 (10), 89 (18), 63 (11), 51 (11%).

3.5.6. 2-(1-Benzofuran-2-yl)-1H-indole (**21**)¹⁹

TBAF (1 M in THF, 1.39 mmol) was added to a solution of 2-(1H-indol-2-ylethynyl)phenol **16** (0.25 g, 1.07 mmol) in THF (5 mL). The mixture was stirred at room temperature for 2 h. The mixture was quenched with a saturated aqueous solution of NH₄Cl (20 mL) and extracted with ethyl acetate (3×20 mL). The organic extracts were washed with H₂O (3×20 mL), dried over Na₂SO₄ and concentrated under vacuum. The residue was purified by column chromatography (10% ethyl acetate/petroleum ether) leading to 0.115 g of compound **21** (46% yield) as a pale yellow solid (mp=220–222 °C, lit.¹⁹ mp=213–214 °C). $\nu_{\max}$ (KBr) 3422, 1601, 1414, 1261, 1102, 1054, 1021, 979, 749, 731; δ_{H} (400 MHz, CDCl₃) 8.65 (br s, 1H), 7.66 (dd, $J=7.9$, 0.8 Hz, 1H), 7.61–7.58 (m, 1H), 7.53 (br d, $J=8.1$ Hz, 1H), 7.43 (dd, $J=8.1$, 0.8 Hz, 1H), 7.34–7.22 (m, 3H), 7.16 (ddd, $J=8.0$, 7.1, 1.0 Hz, 1H), 7.00–6.97 (m, 2H); δ_{C} (100.6 MHz, CDCl₃) 154.4, 149.3, 136.4, 129.0, 128.7, 128.5, 124.4, 123.3, 123.1, 121.0, 120.9, 120.6, 111.1, 111.0, 101.4, 101.2; MS m/z 233 (M⁺, 100), 232 (19), 204 (31), 117 (34), 102 (34), 89 (17), 88 (14), 76 (9), 63 (8), 51 (5%).

3.6. Synthesis of dibenzofuran derivatives **22**, **23** and **8**

3.6.1. 2,2'-Bi-1-benzofuran (**22**)²⁰

A solution of 2-ethynyl-1-benzofuran **9** (0.30 g, 2.11 mmol) in THF (2.5 mL) was added at room temperature, under nitrogen, to a stirred mixture of 2-iodophenol **11** (0.23 g, 1.06 mmol), PdCl₂(PPh₃)₂ (0.037 g, 0.053 mmol), CuI (0.020 g, 0.106 mmol) and Et₃N (9 mL) in THF (2.5 mL) and then the reaction mixture was warmed at 50 °C. After reaction completion (6 h), the mixture was quenched with a saturated aqueous solution of NH₄Cl (20 mL) and extracted with ethyl acetate (3×20 mL). The organic extracts were washed with H₂O (3×20 mL), dried over Na₂SO₄ and concentrated under vacuum. The residue was purified by column chromatography on silica gel (petroleum ether) leading to 0.11 g of compound **22** (45% yield) as a white solid (mp=176–178 °C, lit.²⁰ mp=176 °C). $\nu_{\max}$ (KBr) 1439, 1255, 1171, 1049, 874, 804, 748, 732; δ_{H} (400 MHz, CDCl₃) 7.61 (dd, $J=7.7$, 0.6 Hz, 2H), 7.53 (br d, $J=8.1$ Hz, 2H), 7.39–7.20 (m, 4H), 7.14 (br s, 2H); δ_{C} (100.6 MHz, CDCl₃) 155.1, 147.7, 128.5, 125.1, 123.3, 121.4, 111.3, 103.7; MS m/z 234 (M⁺, 100), 205 (21), 176 (11), 117 (30), 89 (11), 88 (14), 76 (30), 63 (11%).

3.6.2. 2,2'-Ethyne-1,2-diylbis(1-benzofuran) (**23**)²¹

A solution of 2-ethynyl-1-benzofuran **9** (0.30 g, 2.11 mmol) in THF (3.5 mL) was added at room temperature, under nitrogen, to a stirred mixture of 2-iodobenzofuran **12** (0.43 g, 1.76 mmol), PdCl₂(PPh₃)₂ (0.025 g, 0.035 mmol), CuI (0.013 g, 0.070 mmol) and Et₃N (0.37 mL) in THF (3.5 mL). After reaction completion (3 h), the mixture was quenched with a saturated aqueous solution of NH₄Cl (20 mL) and extracted with ethyl acetate (3×20 mL). The organic extracts were washed with H₂O (3×20 mL), dried over Na₂SO₄ and concentrated under vacuum. The crude product was purified

by column chromatography on silica gel (petroleum ether) leading to 0.38 g of compound **23** (84% yield) as a pale yellow solid (mp=143–145 °C). $\nu_{\max}$ (KBr) 1449, 1349, 1295, 1253, 1142, 960, 799, 747, 730; δ_{H} (400 MHz, CDCl₃) 7.60 (ddd, $J=7.8$, 1.3, 0.7 Hz, 2H), 7.50 (br dd, $J=8.3$, 0.9 Hz, 2H), 7.37 (ddd, $J=8.3$, 7.3, 1.3 Hz, 2H), 7.27 (ddd, $J=7.8$, 7.3, 1.0 Hz, 2H), 7.12 (d, $J=0.9$ Hz, 2H); δ_{C} (100.6 MHz, CDCl₃) 155.2, 137.6, 127.4, 126.2, 123.5, 121.4, 113.2, 111.4, 85.2; MS m/z 258 (M⁺, 100), 229 (7), 202 (10), 201 (10), 200 (13), 129 (27), 101 (14), 100 (9), 88 (21), 75 (7), 63 (6%).

3.6.3. 2,2'-(Buta-1,3-diyne-1,4-diyl)bis(1-benzofuran) (**8**)

2-Ethynyl-1-benzofuran **9** (0.20 g, 1.41 mmol) was added at room temperature, under nitrogen, to a solution of Cu(OAc)₂·H₂O (0.56 g, 2.82 mmol) in pyridine (5.6 mL) and methanol (5.6 mL). After reaction completion (12 h), the mixture was quenched with a saturated aqueous solution of NH₄Cl (20 mL) and extracted with ethyl acetate (3×20 mL). The organic extracts were washed with water (3×20 mL), dried over Na₂SO₄ and concentrated under vacuum. The residue was purified by column chromatography on silica gel (petroleum ether) leading to 0.13 g of compound **8** (66% yield) as a yellow solid (mp=165–168 °C).

Acknowledgements

This work was financially supported by the Ministero dell'Università e della Ricerca (M.U.R.), Rome, and the University of Bari (National Project 'Stereoselezione in Sintesi Organica. Metodologie ed Applicazioni').

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