One pot Sonogashira-coupling/Wittig olefination procedures

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Bromoarylcarbaldehydes, bromoheteroarylcarbaldehydes, and bromoalkenals can be subjected to a one pot Sonogashira coupling–Wittig olefination reaction to give easy access to molecules with extended pi-systems.

Keywords: sonogashira coupling, wittig olefination, diene-ynes

A larger number of conjugated phosphoranes are sufficiently stabilised not to be affected by oxygen or moisture, while still maintaining their reactivity towards carbaldehydes in form of Wittig olefination reactions.[1] Typical examples of such phosphoranes are **3a**–**3d**. This characteristic makes it possible to subject phosphoranes to reaction conditions used in metal catalysed C–C bond forming sequences, such as in Pd(0) catalysed Suzuki-[2] and Heck reactions and in Pd(0)/Cu(I) catalysed Sonogashira coupling without affecting the P=C moiety of the phosphoranes. In fact, it is possible to react haloaroylmethylidenetriphenylphosphoranes with arylboronic acids in a Suzuki type transformation[3] and with alkenes in a Heck reaction[4] in order to generate highly functionalised phosphoranes. The reaction of haloaroylmethylidenetriphenylphosphoranes in a Sonogashira type coupling reaction[3] leads to alkynyl-extended phosphoranes. In this paper, we show that Wittig olefination and Sonogashira coupling reactions can be carried out in a one pot procedure with haloarylcarbaldehydes and with haloalkenylcarbaldehydes. This can lead directly to diene-ynes in one step from readily available 3-bromoenaldehydes.

The Sonogashira coupling[5] is one of the standard C–C coupling reactions in the modern synthetic 'arsenal'. It has been used in one pot combinations previously in the preparation of polyenyne systems,[6] in tandem Sonogashira coupling reactions[7] and in Sonogashira coupling/intramolecular Diels–Alder reactions.[8] For the novel one pot combination Sonogashira coupling–Wittig olefination the authors used CuI/Pd$(PPh_3)_2Cl_2$ as the catalyst for the C–C coupling reaction, diisopropylamine as base and DME as solvent system. *p*-Bromobenzaldehyde (**1a**) and 5-bromothienyl-2-carbaldehyde (**1c**) gave good yields as substrates (see Scheme 1), where the reactions were complete after 15–24 h at 70 °C. Standard commercially available terminal acetylenes **2a**–**2c** were used in the transformations. 3-Bromo-ene-aldehydes, such as 4-bromo-3-formyl-1,2-dihydronaphthalene (**1b**), which is readily accessible via Arnold–Vilsmeier reaction[9-11] from α-tetralone were interesting substrates. The one pot sequence can also be employed with more complex starting materials, as with the steroidal derivative **5** (Scheme 2).[12]

The products, such as **4e** and **6a**, are potential starting materials for Pt- and Ru-catalysed diene-yne cyclisation reactions in the synthesis of areno-annelated compounds.[13,14]

Experimental

General: Melting points were measured on a Yanaco microscopic hot-stage and are uncorrected. IR spectra were measured with JASCO IR-700 and Nippon Denshi JIR-AQ2OM machines. ^1H and ^{13}C NMR spectra were recorded with a JEOL EX-270 spectrometer. The chemical shifts are relative to TMS (solvent $CDCl_3$, unless otherwise noted). Mass spectra were measured with a JMS-01-SG-2 spectrometer (EI, 70 eV). Column chromatography was carried out on Wakogel 300. Ethoxycarbonylmethylidenetriphenylphosphorane (**3a**),[15a] benzoylmethylidenetriphenylphosphorane (**3b**),[15b] acetylmethylidenetriphenylphosphorane (**3c**)[15b] and maleimidotriphenylphosphorane (**3d**)[15c] were prepared according to literature procedures.

1-Bromo-2-formyl-naphthalene (**1d**): A mixture of **1b** (1.0 g, 4.2 mmol), DDQ (1.04 g, 4.58 mmol) and benzoic acid (50 mg, 0.41 mmol) in toluene (5 ml) was kept at 65 °C for 14 h. The cooled solution was concentrated *in vacuo* and the residue was subjected to column chromatography on silica gel ($CHCl_3$/petrolether 60/70 4:1) to give **1d** (725 mg, 73%) as a colourless solid; ν_{max} (KBr)/cm^{-1} 3057, 2867, 1685, 1596, 1323, 1255, 1216, 811, 771, 752, 539 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 7.62 (2H, m), 7.73–7.87 (3H, m), 8.42 (1H, m), 10.60 (1H, s, CHO); δ_C (62.89 MHz, $CDCl_3$, DEPT) 123.88 (CH), 127.89 (CH), 128.05 (CH), 128.08 (CH), 128.30 (CH), 129.55 (CH), 130.97 (C_{quat}), 131.11 (C_{quat}), 131.86 (C_{quat}), 136.99 (C_{quat}), 192.53 (CHO); MS (70 eV) *m/z* (%): 236 (81) ([^{81}Br]M$^+$), 234 (60) ([^{79}Br]M$^+$), 207 (16), 205 (14), 128 (79), 126 (100). (Found: C, 56.20; H, 3.00; Br, 33.90. $C_{11}H_7BrO$ requires: C, 56.12; H, 3.19; Br, 33.86).

Ethyl 3-(tolan-4'-yl)acrylate (**4a**): general reaction procedure A: A mixture of *p*-bromobenzaldehyde (**1a**) (555 mg, 3.0 mmol), phenylacetylene (**2a**) (613 mg, 0.66 ml, 6.0 mmol), diisopropylamine (607 mg, 0.84 ml, 6.0 mmol), bis(triphenylphosphino)palladium (II) dichloride [$(PPh_3)_2PdCl_2$] (21.1 mg, 1 mol%), CuI (2.9 mg, 0.5 mol%), and ethoxycarbonylmethylidenetriphenylphosphorane (**3a**) (2.09 g, 6.0 mmol) in DME (15 ml) was kept at 70 °C for 12 h. Then, the mixture was poured into water (50 ml) and extracted with $CHCl_3$ (3×30 ml). The organic phase was dried over anhydrous $MgSO_4$ and evaporated *in vacuo*. Column chromatography of the residue on silica gel (hexane/ether 1:7) gave **4a** (450 mg, 1.6 mmol, 54%) as a colourless solid, m.p. 109 °C (ether/hexane 1:7); (Found: M$^+$, 276.1151. $C_{19}H_{16}O_2$ requires M$^+$, 276.11150). ν_{max} (KBr)/cm^{-1} 2988, 2206 (w), 1697, 1631, 1510, 1309, 1205, 1186, 1029, 991, 832, 759, 690, 517; δ_C (99.45 MHz, $CDCl_3$) 14.32, 60.58, 88.99, 91.52, 118.91, 122.92, 125.13, 127.95, 128.40, 128.56, 131.66, 132.01, 134.19, 143.65, 166.82; δ_H (270 MHz, $CDCl_3$) 1.34 (3H, t, ^3J=7.3 Hz), 4.27 (2H, q, ^3J=7.3 Hz), 6.44 (1H, d, ^3J=15.9 Hz), 7.29–7.56 (m, 9H), 7.66 (d, 1H, ^3J=15.9 Hz); MS (EI, 70 eV) *m/z* (%): 276 [M$^+$] (100), 231 (41), 202 (58). (Found: C, 82.81; H, 5.93. $C_{19}H_{16}O_2$ requires: C, 82.58; H, 5.84).

4-(Benzoylethenyl)-tolane (**4b**): A mixture of *p*-bromobenzaldehyde (**1a**) (555 mg, 3.0 mmol), phenylacetylene (**2a**) (613 mg, 0.66 ml, 6.0 mmol), diisopropylamine (607 mg, 0.84 ml, 6.0 mmol), bis(triphenylphosphino)palladium (II) dichloride (21.1 mg, 1 mol%), CuI (2.9 mg, 0.5 mol%), and benzoylmethylidenetriphenylphosphorane (**3b**) (2.28 g, 6.0 mmol) in DME (15 ml) was reacted for 12 h according to general reaction procedure A. Column chromatography on silica gel (hexane/ether 1:8) gave **4b** (570 mg, 1.6 mmol, 62%) as a colourless solid, m.p. 149 °C; (Found: M$^+$, 308.1198. $C_{23}H_{16}O$ requires: M$^+$, 308.1201); ν_{max} (KBr)/cm^{-1} 3046, 1658, 1606, 1335, 1220, 1034, 1018, 981, 833, 774, 751, 727, 690, 643, 526 cm^{-1}; δ_H (270 MHz, $CDCl_3$) 7.33–7.67 (m, 12H), 7.80 (d, 1H, ^3J=15.9 Hz), 8.04 (m, 3H); MS (70 eV) *m/z* (%): 308 (100) [M$^+$], 279 (8.7), 231 (11), 202 (36).

Ethyl 3-(4'-[trimethylsilylethynyl]phenyl)acrylate (**4c**): A mixture of *p*-bromobenzaldehyde (**1a**) (555 mg, 3.0 mmol), trimethylsilylacetylene (**2b**) (884 mg, 0.66 ml, 6.0 mmol), diisopropylamine (607 mg, 0.84 ml, 6.0 mmol), bis(triphenylphosphino)palladium (II) dichloride (21.1 mg, 1 mol%), CuI (14.3 mg, 2.5 mol%), and ethoxycarbonylmethylidenetriphenylphosphorane (**3a**) (2.04 g, 6.0 mmol) in DME (15 ml) was kept for 15 h according to general reaction procedure A. Column chromatography on silica gel (hexane/ether 1:8) gave **4c** (716 mg, 88%) as an oil; (Found: M$^+$, 272.1234. $C_{16}H_{20}O_2Si$ requires: M$^+$, 272.1233); ν_{max} (neat)/cm^{-1} 3030, 2960, 2898, 2154, 1714, 1637, 1505, 1367, 1310, 1250, 1204, 1175, 860, 760, 637;

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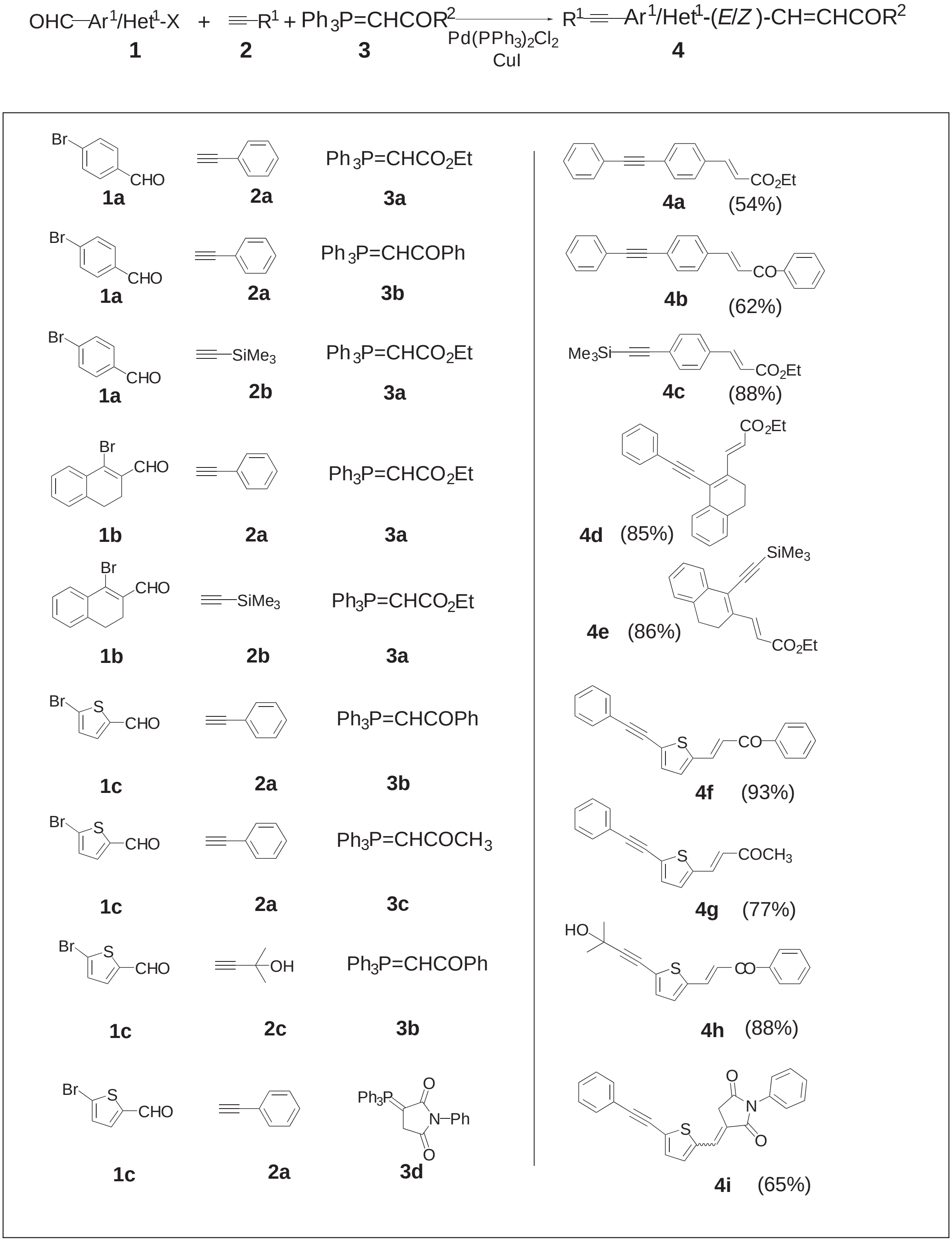
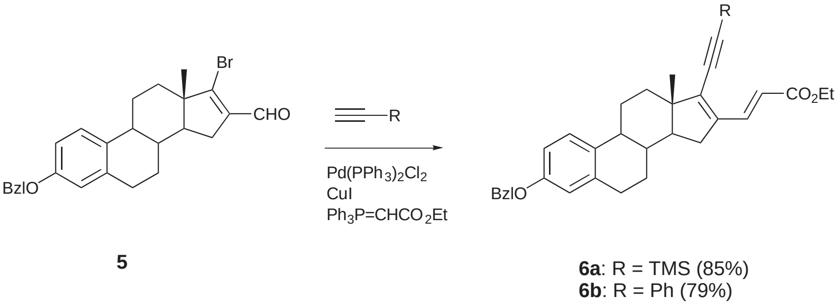


$$\underset{\mathbf{1}}{\text{OHC—Ar}^1/\text{Het}^1\text{-X}} + \underset{\mathbf{2}}{\equiv\!\text{—R}^1} + \underset{\mathbf{3}}{\text{Ph}_3\text{P=CHCOR}^2} \xrightarrow[\text{CuI}]{\text{Pd(PPh}_3)_2\text{Cl}_2} \underset{\mathbf{4}}{\text{R}^1\!\equiv\!\text{—Ar}^1/\text{Het}^1\text{-}(E/Z)\text{-CH=CHCOR}^2}$$

Scheme 1



5

6a: R = TMS (85%)
6b: R = Ph (79%)

Scheme 2

δ_H (270 MHz, $CDCl_3$) 0.25 (9H, s, $SiMe_3$), 1.36 (3H, t, ^3J=7.0 Hz), 4.27 (2H, q, ^3J=7.0 Hz), 6.41 (1H, d, ^3J=15.9 Hz), 7.44 (4H, s), 7.63 (1H, d, ^3J=15.9 Hz); MS (EI, 70 eV) *m/z* (%): 272 (43) [M^+], 257 (100).

Ethyl 3'-(4-phenylethynyl-1,2-dihydronapthalen-3-yl)acrylate (**4d**): A mixture of 4-bromo-3-formyl-1,2-dihydronaphthalene (**1b**) (474 mg, 2.0 mmol), phenylacetylene (**2a**) (409 mg, 0.44 ml, 4.0 mmol), diisopropylamine (607 mg, 0.84 ml, 6.0 mmol), bis(triphenylphosphino)palladium (II) dichloride (70.2 mg, 5 mol%), CuI (9.5 mg, 2.5 mol%), and ethoxycarbonylmethylidenetriphenylphosphorane (**3a**) (1.39 g, 4.0 mmol) in DME (10 ml) was reacted for 18h according to general procedure A. Column chromatography on silica gel (hexane/ether 1:8) gave **4d** (559 mg, 1.7 mmol, 85%) as a pale yellow solid, m.p. 125 °C; (Found: M^+, 328.1467, $C_{23}H_{20}O_2$ requires: M^+, 328.1463); ν_{max} (neat)/cm^{-1} 3062, 3022, 2954, 2198, 1710, 1611, 1489, 1443, 1366, 1303, 1263, 1173, 1042, 981, 756; δ_H (270 MHz, $CDCl_3$) 1.35 (3H, t, ^3J=7.0 Hz), 2.61 (2H, t, ^3J=8.4 Hz), 2.90 (2H, t, ^3J=8.4 Hz), 4.27 (2H, t, ^3J=7.0 Hz), 6.14 (1H, d, ^3J=15.7 Hz), 7.61–7.65 (2H, m), 7.16–7.41 (6H, m), 7.81–7.84 (1H, m), 8.36 (1H, d, ^3J=15.7 Hz); δ_C (67.8 MHz, $CDCl_3$) 14.8, 24.0, 27.6, 60.9, 85.6, 100.5, 119.5, 123.4, 126.6, 127.3, 127.4, 127.8, 128.9, 129.1, 129.4, 132.1, 133.4, 136.4, 139.5, 143.9, 144.1, 167.8; MS (EI, 70eV) *m/z* (%): 328 (47) [M^+], 301 (24), 300 (100).

Ethyl 3'-(4-trimethylsilylethynyl-1,2-dihydronapthalen-3-yl)acrylate (**4e**): A mixture of 4-bromo-3-formyl-1,2-dihydronaphthalene (**1b**) (1.18 g, 5.0 mmol), trimethylsilylacetylene (**2b**) (1.47 g, 2.12 ml, 15.0 mmol), diisopropylamine (1.01 g, 1.40 ml, 10.0 mmol), bis(triphenylphosphino)palladium (II) dichloride (175.5 mg, 5 mol%), CuI (23.8 mg, 2.5 mol%), and ethoxycarbonylmethylidenetriphenylphosphorane (**3a**) (3.48 g, 10.0 mmol) in DME (25 ml) was reacted at 70 °C for 14 h according to reaction procedure A. Column chromatography on silica gel (hexane/ether 1:8) gave **4e** (1.40 g, 4.3 mmol, 86%) as a pale yellow oil, (Found: M^+, 324.1549. $C_{20}H_{24}O_2Si$ requires: M^+, 324.1546); ν_{max} (neat)/cm^{-1} 3068, 2958, 2892, 2136, 1708, 1613, 1302, 1169, 1042, 984; δ_H (270 MHz, $CDCl_3$) 0.31 (9H, s, $SiMe_3$), 1.37 (3H, q, ^3J=7.3 Hz), 2.55 (2H, t, ^3J=8.4 Hz), 2.85 (2H, t, ^3J=8.4 Hz), 4.26 (2H, q, ^3J=7.3 Hz), 6.11 (1H, d, ^3J=15.9 Hz), 7.13–7.31 (3H, m), 7.73 (1H, m), 8.26 (1H, d, ^3J=15.9 Hz); δ_C (99.45 MHz, $CDCl_3$) –0.06, 14.31, 23.39, 26.99, 60.43, 100.23, 105.82, 119.38, 125.90, 126.80, 126.88, 127.19, 128.76, 132.68, 135.78, 140.07, 143.29, 167.19; MS (EI,. 70 eV) *m/z* (%): 324 (100) [M^+], 309 (21), 295 (28), 279 (28), 251 (32), 235 (35), 221 (35), 205 (59), 178 (52). (Found: C, 74.09; H, 7.46. $C_{20}H_{24}O_2Si$ requires: C, 74.03; H, 7.45).

2-Phenylethynyl-5-benzoylethenylthiophene (**4f**): A mixture of **1c** (573 mg, 3.0 mmol), phenylacetylene (**2a**) (613 mg, 0.66 ml, 6.0 mmol), diisopropylamine (0.84 ml, 9.0 mmol), **3b** (2.28 g, 4.0 mmol), $Pd(PPh_3)_2Cl_2$ (105 mg, 5 mol%), and CuI (14.3 mg, 2.5 mol%) in DME (15 ml) was reacted for 16 h according to general procedure A. Column chromatography on silica gel (hexane/ether/$CHCl_3$ 6:1:1) gave **4f** (876 mg, 93%) as a yellow solid, m.p. 127 °C; (Found: 314.0766. $C_{21}H_{14}OS$ requires: M^+, 314.0765); ν_{max} (KBr)/cm^{-1} 1651, 1587, 1573, 1336, 1221, 1013, 973, 815, 755, 702, 690; δ_H (270 MHz, $CDCl_3$) 7.22–7.62 (11H, m), 7.95 (1H, d, ^3J=16.2 Hz), 8.02 (2H, m); δ_C (99.45 MHz, $CDCl_3$) 82.51, 96.05, 121.25, 122.38, 126.43, 128.36, 128.48, 128.53, 128.69, 131.53, 132.84, 136.45, 138.02, 141.44, 189.61; MS (70 eV) *m/z* (%): 314 (100) [M^+], 285 (14), 237 (20), 208 (20), 184 (18), 149 (27). (Found: C, 80.35; H, 4.49. $C_{21}H_{14}OS$ requires: C, 80.22; H, 4.49).

5-Acetylethenyl-2-phenylethynylthiophene (**4g**): **1c** (573 mg, 3.0 mmol), phenylacetylene (**2a**) (613 mg, 6.0 mmol), diisopropylamine (0.84 ml, 6.0 mmol), $(PPh_3)_2PdCl_2$ (105 mg, 5 mol%), CuI (14.3 mg, 2.5 mol%), **3c** (1.91 g, 6.0 mmol) in DME (15 ml) were reacted for 12 h according to general procedure A. Column chromatography on silica gel (hexane/ether 4:1) gave **4g** (582 mg, 77%) as a yellow solid, m.p. 79 °C; (Found: M^+, 252.0607. $C_{16}H_{12}OS$ requires: M^+, 252.0609); IR (KBr) ν 3074, 2924, 2354 (w), 1666, 1612, 1253, 962, 794, 756, 689 cm^{-1}; δ_H (270 MHz, $CDCl_3$) 2.35 (3H, s, CH_3), 6.51 (1H, d, ^3J=15.9 Hz), 7.17 (1H, d, ^3J=4.6 Hz), 7.21 (1H, d, ^3J=4.6 Hz), 7.37 (3H, m), 7.52 (2H, m), 7.56 (1H, d, ^3J=15.9 Hz); δ_C (99.45 MHz, $CDCl_3$) 27.79, 82.39, 96.00, 122.33, 126.13, 126.55, 128.42, 128.53, 128.87, 131.52, 134.93, 135.01, 140.76, 197.45; MS (EI, 70 eV) *m/z* (%) 252 (M^+, 97), 237 (100), 208 (30). (Found: C, 76.30; H, 4.85. $C_{16}H_{12}OS$ requires C, 76.16; H, 4.79).

5-Benzoylethenyl-2-(3'-hydroxy-3'-methylbutynyl)thiophene (**4h**): A mixture of **1c** (573 mg, 3.0 mmol), 3-hydroxy-methylbutynol (505 mg, 0.66 ml, 6.0 mmol), diisopropylamine (0.84 ml, 9.0 mmol), **3b** (2.28 g, 4.0 mmol), $Pd(PPh_3)_2Cl_2$ (105 mg, 5 mol%), and CuI (14.3 mg, 2.5 mol%) in DME (15 ml) was reacted for 18 h according to general reaction procedure A. Column chromatography of the residue on silica gel (hexane/ether 1:1) gave **4h** (876 mg, 88%) as a slowly crystallising yellow oil, m.p. 89 °C; (Found: 297.0950. Calcd. for $C_{18}H_{17}O_2S$: 297.0949); ν (neat)/cm^{-1} 3418 (bs, OH), 3062, 2980, 1654, 1589, 1518, 1446, 1355, 1310, 1285, 1207, 1178, 1014, 962, 773, 694, 616; δ_H (270 MHz, $CDCl_3$) 1.63 (6H, s, 2 CH_3), 2.24 (1H, bs, OH), 7.11 (1H, d, ^3J=3.8 Hz), 7.19 (1H, d, ^3J=3.8 Hz), 7.27 (1H, d, ^3J=15.4 Hz), 7.47–7.62 (3H, m), 7.83 (1H, d, ^3J=15.4 Hz), 8.00 (2H, m); δ_C (99.45 MHz, $CDCl_3$) 31.19 (2 CH_3), 65.75, 75.32, 100.34, 121.25, 125.74, 128.38, 128.64, 132.87, 133.03, 136.42, 137.92, 189.61; MS (FAB, 3-nitrobenzyl alcohol) *m/z* (%) 297 (100) [MH^+], 279 (29) [MH^+–H_2O].

*2'-(Phenylethynyl)thien-5'-yl-N-phenyl-H-methylidenemaleimide (E/Z-***4i**): A mixture of **1c** (191 mg, 1.0 mmol), phenylacetylene (**2a**) (204 mg, 0.22 ml, 2.0 mmol), diisopropylamine (202 mg, 0.28 ml, 2.0 mmol), **3d** (653 mg, 1.5 mmol), $(PPh_3)_2PdCl_2$ (35.1 mg, 5 mol%) and CuI (4.8 mg, 2.5 mol%) was reacted according to general procedure A. Column chromatography on silica gel (hexane/ether/$CHCl_3$ 2:1:1) gave **4i** (240 mg, 65%) as a yellow solid, m.p. 210 °C (dec.); (Found: 370.0904. Calcd. for $C_{23}H_{16}O_2NS$: 370.0902); (KBr)/cm^{-1} ν_{max} 1766, 1704, 1641, 1499, 1390, 1194, 1171, 897, 754, 690; δ_H (270 MHz, $CDCl_3$) 3.68 (A/B, 2H, d, ^4J=2.2 Hz), 7.18–7.64 (A/B, 12H, m), 7.87 (B, 1H, t, ^4J=2.2 Hz), 7.94 (A, 1H, t, ^4J=2.2 Hz); MS (FAB, 3-nitrobenzyl alcohol) *m/z* (%) 370 (‘5.5) [MH^+].

Ethyl 3'-(4-ethynyl-1,2-dihydronapthalen-3-yl)acrylate (**4j**): A solution of **4e** (700 mg, 2.16 mmol) and tetrabutylammonium fluoride (TBAF) in THF (20 ml) was stirred at rt for 8 h. Then the reaction mixture is poured into water and extracted with $CHCl_3$ (3 × 50 ml). The organic phase was dried over anhydrous $MgSO_4$ and concentrated *in vacuo* to give **4j** as a pale yellow solid (370 mg, 68%), m.p. 74 °C; (Found: M^+, 252.1153. $C_{17}H_{16}O_2$ requires: M^+, 252.1150); ν_{max} (neat)/cm^{-1} 3280, 2934, 1708, 1612, 1303, 1173, 1037; δ_H (270 MHz, $CDCl_3$) 1.31 (3H, t, ^3J=7.3 Hz), 2.57 (2H, t ^3J=8.4 Hz), 2.87 (2H, t, ^3J=8.4 Hz), 3.66 (1H, s), 4.26 (2H, q, ^3J=7.3 Hz), 6.14 (1H, d, ^3J=15.8 Hz), 7.73 (1H, m), 7.14–727 (3H, m), 8.21 (1H, d ^3J=15.8 Hz); δ_C (67.8 MHz, $CDCl_3$) 14.31, 23.48, 26.95, 60.51, 78.96, 87.64, 119.79, 124.97, 126.04, 126.78, 127.23, 128.86, 132.67, 135.71, 140.57, 142.96, 167.19; MS (70 eV) *m/z* (%): 252 (37) [M^+], 223 (13), 207 (18), 195 (13), 179 (100), 178 (88), 152 (29).

Ethyl 3'-(1-ethynylnapthalen-2-yl)acrylate (**4k**): Procedure A: A solution of **4j** (350 mg, 1.39 mmol) and DDQ (567 mg, 2.5 mmol) in benzene (20 ml) was heated at 80 °C for 90 min. Thereafter, the mixture was concentrated *in vacuo*. The residue was subjected to column chromatography on silica soild (hexane/ether 6:1) to give **4k** (225 mg, 65%) as a colourless soild, m.p. 108 °C; (Found: 250.0989. $C_{17}H_{14}O_2$ requires: M^+, 250.0994); ν_{max} (KBr)/cm^{-1} 3240, 2980, 1700, 1631, 1306, 1257, 1181, 1034, 989, 816, 755; δ_H (270 MHz, $CDCl_3$) 1.36 (3H, t, ^3J=7.0 Hz), 3.88 (1H, s), 4.30 (2H, q, ^3J=70 Hz), 6.59 (1H, d, ^3J=15.9 Hz), 7.52–7.83 (5H, m), 8.42 (1H, d, ^3J=8.4 Hz), 8.47 (1H, d, ^3J=15.9 Hz); δ_C (6.78 MHz, $CDCl_3$), 14.35, 60.64, 78.99, 89.22, 120.56, 121.28, 122.30, 127.05, 127.59, 127.65, 128.15, 129.22, 133.50, 133.76, 135.14, 142.52, 166.88; MS (70 eV) *m/z* (%): 250 (9.9) [M^+], 176 (16), 58 (100). Found: C, 81.75; H, 5.70. Calcd. for $C_{17}H_{14}O$: C, 81.58; H, 5.64).

Procedure B: A solution of **4m** (447 mg, 1.39 mmol) and TBAF (2.0 mmol) in THF (7 ml) was stirred for 2 h at r.t. Thereafter, water (30 ml) was added and the mixture was extracted with chloroform (3 × 15 ml). The combined organic phase was dried over anhydrous $MgSO_4$, concentrated *in vacuo*, and the residue was subjected to column chromatogrphy on silica gel (hexane/ether 5:1) to give **4k** (236 mg, 68%).

Trimethylsilylethynyl-2-ethoxycarbonylethenylnaphthalene (**4m**): A mixture of **4e** (973 mg, 3.0 mmol) and DDQ (1.36 g, 6.0 mmol) in toluene (30 ml) was held at reflux for 36 h. Thereafter, the cooled solution was concentrated *in vacuo* and the residue was subjected to column chromatography on silica gel (hexane/ether 10:1) to give **4m** (830 mg, 85%) as an oil; (Found: MH^+, 323.1468. $C_{20}H_{23}O_2Si$ requires: MH^+, 323.1467); ν_{max} (neat)/cm^{-1} 3058, 2150, 1713, 1632, 1294, 1260, 1175, 1041, 846 cm^{-1}; δ_H (270 MHz, $CDCl_3$) 0.40 (9H, s, $SiMe_3$), 1.39 (3H, t, ^3J=7.3 Hz), 4.32 (2H, q, ^3J=7.3 Hz), 6.61 (1H, d, ^3J=16.2 Hz), 7.55–7.84 (3H, m), 8.40 (1H, m), 8.50 (1H, d, ^3J=16.2 Hz); δ_C (67.8 MHz, $CDCl_3$) 0.00, 14.34, 60.53, 100.27, 107.66, 120.20, 122.30, 122.36, 127.23, 127.48, (2C), 127.50, 128.08, 128.83, 133.50, 134.74, 142.76, 166.88; MS (FAB, 3-nitrobenzyl alcohol) *m/z* (%): 323 (100) [MH^+], 277 (32), 205(29).

3-Benzyloxy-16-(2'-carbethoxy)ethenyl-17-(trimethylsilylethynyl-estra-1,3,5(10),16-tetraene (**6a**): Trimethylsilylacetylene (0.42 ml, 3.0 mmol) was added to a solution of **5** (450 mg, 1.0 mmol), dichlorobis(triphenylphosphine)palladium (7.0 mg, 10 µmol), CuI (1.0 mg, 5 μmol), ethoxycarbonylmethylidenetriphenylphosphorane (697 mg, 2 mmol) and diisopropylamine (0.28 ml, 2 mmol) in DME (5 ml). The solution was stirred for 24 h at 70 °C under an argon atmosphere. The reaction mixture was concentrated *in vacuo*, and the residue was subjected to column chromatography on silica gel (hexane: ether 8/1) to give **6a** (457 mg, 85%) as a colourless solid, m.p. 162 °C; (Found: MH^+, 539.2980. $C_{35}H_{43}O_3Si$ requires: MH^+, 539.2981); ν_{max} (KBr)/cm^{-1} 3032, 2971, 2929, 2855, 2128, 1713, 1620, 1577, 1499, 1452, 1366, 1337, 1306, 1277, 1253, 1208, 1161, 1119, 1096, 1039, 983, 944, 928, 856, 785, 760, 735, 695, 631; δ_H (270 MHz, $CDCl_3$) 0.24 (9H, s, $(CH_3)_3Si$), 0.91 (3H, s, CH_3, C-18), 1.31 (3H, t, ^3J=7.1 Hz), 1.43–1.69 (3H, m), 1.93–2.01 (2H, m), 2.12–2.53 (6H, m), 2.87–2.93 (2H, m), 4.23 (2H, q, ^3J=7.1Hz), 5.04 (s, 2H, OCH_2Ph), 5.88 (1H, d, ^3J=15.7 Hz), 6.73 (1H, d, ^4J=2.7 Hz, C-4), 6.79 (1H, dd, ^3J=8.5, ^4J=2.7 Hz, C-2), 7.19 (1H, d, ^3J=8.6Hz, C-1), 7.26–7.45 (5H, m), 7.74 (1H, d, ^3J=15.7Hz); δ_C (100 MHz, $CDCl_3$) 0.0, 14.2, 16.3, 26.3, 27.7, 29.6, 31.0, 34.3, 37.4, 44.2, 49.8, 54.2, 60.3, 70.0, 112.3, 114.9, 119.4, 126.0, 127.4, 127.8, 128.5, 132.8, 137.3, 137.8, 139.1, 144.6, 167.2; MS (FAB, 3-nitrobenzyl alcohol) *m/z* (%): 539 (21) [MH^+].

3-Benzyloxy-16-(2'-carbethoxy)ethenyl-17-phenylethynyl-estra-1,3,5(10),16-tetraene (**6b**): Phenylacetylene (0.32 ml, 3 mmol) was added to **5** (675 mg, 1.5 mmol), dichlorobis(triphenylphosphine)palladium (10.5 mg, 15 μmol), CuI (1.4 mg, 7.5 μmol), diisopropylamine (0.42 ml, 3 mmol) and ethoxycarbonylmethylidenetriphenylphosphorane (1.05 g, 3.0 mmol) in DME (8 ml). The solution was stirred for 24 h at 70 °C under an argon atmosphere. The reaction mixture was concentrated *in vacuo*, and was subjected to column chromatography on silica gel (hexane: ether 8/1 to 2/1) to give **6b** (1.04 g, 79%) as a colourless solid. M.p. 103 °C; (Found: MH^+, 543.2903. $C_{38}H_{39}O_3$ requires: MH^+, 543.2899); ν_{max} (KBr)/cm^{-1} 2928, 1710, 1613, 1574, 1497, 1451, 1366, 1304, 1258, 1165, 1039, 976, 860, 786, 755, 732, 689, 565, 526, 464; δ_H (270 MHz, $CDCl_3$) 0.97 (3H, s, CH_3, C-18), 1.32 (3H, t, ^3J=7.1 Hz), 1.43–1.76 (5H, m), 1.96–2.59 (6H, m), 2.89–2.95 (2H, m), 4.24 (2H, q, ^3J=7.1 Hz), 5.04 (2H, s, OCH_2Ph), 5.91 (1H, d, ^3J=15.7 Hz), 6.74 (1H, d, ^4J=2.6 Hz, C-4), 6.79 (1H, dd, ^3J=8.5 Hz, ^4J=2.6 Hz, C-2), 7.20 (1H, d, ^3J=8.5 Hz, C-1), 7.31–7.54 (10H, m), 7.84 (1H, d, ^3J=15.7 Hz); δ_C (100 MHz, $CDCl_3$) 14.3, 16.5, 26.4, 27.7, 29.7, 31.1, 34.5, 37.5, 44.3, 50.0, 54.2, 60.4, 70.0, 83.6, 101.4, 112.2, 114.8, 115.0, 123.1, 126.0, 127.4, 127.8, 128.0, 128.4, 128.6, 131.8, 132.8, 137.3, 137.8, 139.2, 142.8, 143.7, 156.8, 167.3; MS (FAB, 3-nitrobenzyl alcohol) *m/z* (%): 543 (14) [MH^+].

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