Supporting Information

Palladium catalysed Sonogashira Reactions of 16-(Hydroxymethylidene)-3-methoxy-α-estrone

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General

For NMR spectra the substrates were dissolved in CDCl₃ and the spectra recorded on a Bruker AVANCE 300 III, 250 II or 500. The IR spectra were measured as ATR experiments with a Nicolet 6700 FT-IR spectrometer and a Nicolet 550 FT-IR spectrometer. MS and HRMS were measured by an Agilent 6890 N/5973 GC-MS and an Agilent 1200/6210 Time-of-Flight LC-MS. Melting points were determined by a Micro-Hot-Stage GalenTM III Cambridge Instruments.

Synthesis of (E)-16-(Trifluoromethanesulfonyloxymethylidene)-3-methoxy-α-estrone 2

16-(hydroxymethylidene)-3-methoxy-α-estrone 1 (1.8 mmol, 562 mg) and 2,6-Di-tert-butyl-4-methylpyridine (2.8 mmol, 575 mg) were dissolved in dichloromethane (10 mL) and cooled to 0 °C. Tf₂O (2.6 mmol, 734 mg) was added dropwise and the reaction was stirred for 1 h, while allowed to warm up to room temperature. Pentane (10 mL) was added and the precipitate was filtered. The filtrate was concentrated in vacuo and the crude product was purified by column chromatography (heptane/ethyl acetate 20:1) to yield 2 as white solid (605 mg, 76%). ¹H NMR (300 MHz, CDCl₃):
\[ \delta = 0.75–1.04 \text{ (m, 2H); } 1.10 \text{ (s, 3H, Me); } 1.40–1.56 \text{ (m, 3H); } 1.79–1.84 \text{ (m, 1H); } 2.03–2.09 \text{ (m, 1H); } 2.25–2.29 \text{ (m, 2H); } 2.37–2.43 \text{ (m, 1H); } 2.79–2.83 \text{ (m, 3H); } 3.76 \text{ (s, 3H, OMe); } 6.60 \text{ (d, } ^{3}J = 2.71 \text{ Hz, 1H); 6.71} \text{ (dd, } ^{3}J = 8.61 \text{ Hz, } ^{4}J = 2.77 \text{ Hz, 1H); 7.17} \text{ (d, } ^{3}J = 8.63 \text{ Hz, 1H); 7.56} \text{ (t, } ^{4}J = 2.45 \text{ Hz, 1H). } ^{13}\text{C NMR (75 MHz, CDCl}_3 \text{): } \delta = 25.1 \text{ (CH}_3 \text{), 26.2, 28.0, 28.1, 30.2, 31.7} \text{ (CH}_2 \text{); 41.2, 42.9, 46.5 \text{ (CH); } 51.6 \text{ (C); 55.2} \text{ (OCH}_3 \text{); 111.9, 113.5} \text{ (CH); 118.4 \text{ (q, } ^{3}J = 321.2 \text{ Hz, CF}_3); 125.8 \text{ (C); 126.9} \text{ (CH); 131.3, 137.8} \text{ (C); 141.9} \text{ (CH); 157.6} \text{ (C); 207.2} \text{ (C=O). } ^{19}\text{F NMR (282 MHz, CDCl}_3 \text{): } \delta = -73.62 \text{. IR (ATR, cm}^{-1} \text{): } \nu = 2918 \text{ (w), 1736} \text{ (m), 1658} \text{ (m), 1610} \text{ (w), 1500} \text{ (m), 1426} \text{ (s), 1206} \text{ (s), 1064} \text{ (s), 950} \text{ (s), 866} \text{ (m), 837} \text{ (s), 791} \text{ (m), 729} \text{ (m), 639} \text{ (m), 600} \text{ (s), 473} \text{ (m). MS (EI, 70 eV): } m/z \text{ (%) = 445 (22), 444 (M}^+ \text{, 85), 227} \text{ (10), 187} \text{ (12), 173} \text{ (25), 171} \text{ (17), 160} \text{ (12), 159} \text{ (15), 158} \text{ (12), 147} \text{ (23), 129} \text{ (11), 128} \text{ (13), 121} \text{ (11), 115} \text{ (23), 91} \text{ (18), 83} \text{ (23), 69} \text{ (100), 55} \text{ (18). HRMS (EI, 70 eV): Calculated for C}_{21}\text{H}_{23}\text{O}_{5}\text{F}_{3}\text{S} \text{ (M}^+ \text{), 444.12128; measured 444.12262.}

**General procedure A for the Sonogashira Reaction**

2 (0.225 mmol, 100 mg), copper iodide (0.006 mmol, 2.5 mol%, 1.1 mg), Pd(OAc)$_2$ (0.006 mmol, 2.5 mol%, 1.3 mg), XPhos (0.012 mmol, 5 mol%, 5.7 mg) and corresponding acetylene (0.338 mmol) were dissolved in THF (5 mL) and NEt$_3$ (1 mL). The reaction mixture was stirred at room temperature for 6 h. The solution was diluted with water and extracted with ethyl acetate (3x). The crude product 3 was purified by column chromatography.

(E)-16-(3-Phenylprop-2-ynylidene)-3-methoxy-α-estrone 3a

3a was synthesized according to general procedure A using phenylacetylene (0.338 mmol, 35 mg) and purified via column chromatography (heptane/ethyl acetate 20:1). Yield: 86 mg (97 %). mp. 54–55 °C. $^1$H NMR (250 MHz, CDCl$_3$): $\delta = 0.79–0.88$ (m, 3H); 1.10 (s, 3H, Me); 1.43–1.51 (m, 2H); 1.76–1.83 (m, 1H); 2.09–2.17 (m, 1H); 2.24–2.32 (m, 2H); 2.40–2.48 (m, 1H); 2.79–2.92 (m, 3H); 3.76 (s, 3H, OMe); 6.59 (d, $^3J = 2.71$ Hz, 1H); 6.67–6.72 (m, 2H); 7.18 (d, $^3J = 8.58$ Hz, 1H); 7.36–7.39 (m, 3H); 7.50–7.54 (m, 2H). $^{13}$C NMR (63 MHz, CDCl$_3$): $\delta = 25.5$ (CH$_3$), 28.1, 28.3, 29.9, 30.3, 32.2 (CH$_2$); 41.3, 43.0, 47.6 (CH), 50.8 (C), 55.2 (OCH$_3$); 87.2, 101.0 (C=C); 111.7, 113.5, 114.5 (CH); 122.7 (C); 126.9, 128.5, 129.2 (CH); 131.8 (C); 131.9 (CH); 138.0, 146.1, 157.5 (C); 207.4 (C=O). IR (ATR, cm$^{-1}$): $\nu = 2918$ (w), 2187 (w), 1711 (w), 1609 (w), 1498 (w), 1448 (w), 1257 (m), 1076 (m), 1016 (s), 870 (w), 793 (s), 755 (m), 688 (m), 531 (w). MS (EI, 70 eV): $m/z$ (%) = 397 (16), 396 (M$^+$, 78), 227 (15), 210 (14), 186
(E)-16-[3-(4-tert-Butylphenyl)-prop-2-ynylidene]-3-methoxy-α-estrone 3b

3b was synthesized according to general procedure A using 4-tert-butylphenylacetylene (0.338 mmol, 54 mg) and purified via column chromatography (heptane/ethyl acetate 20:1). Yield: 47 mg (46 %). mp. 79–80 °C. 1H NMR (500 MHz, CDCl3): δ = 0.81–0.89 (m, 3H); 1.10 (s, 3H, Me); 1.33 (s, 9H, tBu); 1.43–1.57 (m, 3H); 1.77–1.80 (m, 1H); 2.09–2.13 (m, 1H); 2.26–2.30 (m, 2H); 2.42–2.46 (m, 1H); 2.80–2.92 (m, 2H); 3.76 (s, 3H, OMe); 6.59 (d, J = 2.67 Hz, 1H); 6.68–6.71 (m, 2H); 7.18 (d, J = 8.64 Hz, 1H); 7.38–7.40 (m, 2H), 7.45–7.46 (m, 2H). 13C NMR (125 MHz, CDCl3): δ = 25.6 (CH₃), 28.2, 28.3, 29.9, 30.3 (CH₂), 31.1 (tBu), 32.2 (CH₂), 34.9 (C), 41.4, 43.0, 46.6 (CH), 50.8 (C), 55.2 (OCH₃); 86.8, 101.5 (C≡C); 111.7, 113.5, 114.8 (CH); 119.7 (C); 125.5, 126.9, 131.7 (CH); 131.9, 138.0, 145.8, 152.7, 157.5 (C); 207.4 (C=O). IR (ATR, cm⁻¹): v = 3407 (w), 2924 (m), 2187 (m), 1712 (m), 1610 (m), 1499 (m), 1362 (w), 1237 (m), 1145 (m), 953 (m), 833 (s), 733 (m), 561 (s). MS (El, 70 eV): m/z (%) = 454 (20), 453 (77), 452 (M⁺, 100), 437 (26), 266 (35), 265 (94), 250 (16), 235 (12), 228 (12), 227 (32), 226 (25), 225 (16), 219 (20), 218 (58), 211 (10), 204 (13), 197 (22), 196 (75), 193 (11), 186 (14), 182 (13), 181 (74), 174 (17), 173 (18), 171 (13), 165 (15), 161 (16), 159 (12), 153 (10), 147 (21), 115 (14), 91 (18), 84 (40), 69 (15), 66 (41), 57 (19), 44 (11), 41 (12). HRMS (ESI): Calculated for C₉₃H₉₅O₂ (M+H⁺), 453.27881; measured 453.27886.

(E)-16-[3-(4-Trifluoromethylphenyl)-prop-2-ynylidene]-3-methoxy-α-estrone 3c
3c was synthesized according to general procedure A using 4-trifluoromethylphenylacetylene (0.338 mmol, 58 mg) and purified via column chromatography (heptane/ethyl acetate 5:1). Yield: 67 mg (64 %). mp. 169–170 °C. 1H NMR (300 MHz, CDCl₃): δ = 0.78–1.05 (m, 2H); 1.11 (s, 3H, Me); 1.44–1.57 (m, 3H); 1.78–1.84 (m, 1H); 2.09–2.14 (m, 1H); 2.25–2.32 (m, 2H); 2.41–2.48 (m, 1H); 2.80–2.94 (m, 3H); 3.76 (s, 3H, OMe); 6.59 (d, J = 2.73 Hz, 1H); 6.68–6.72 (m, 2H); 7.18 (d, J = 8.64 Hz, 1H); 7.62 (s, 4H). 13C NMR (125 MHz, CDCl₃): δ = 25.5 (CH₃), 28.1, 28.3, 30.0, 30.3, 32.2 (CH₂); 41.3, 43.1, 46.6 (CH), 50.8 (C), 55.2 (OCH₃); 89.1, 98.6 (C≡C); 111.7, 113.5, 113.6 (CH); 123.8 (q, J = 272.3 Hz, CF₃); 125.4 (q, J = 3.9 Hz, CH); 126.4 (q, J = 1.3 Hz, C); 126.9 (CH); 130.7 (q, J = 32.7 Hz, C-CF₃); 131.8 (C); 132.1 (CH); 137.9, 147.4, 157.6 (C); 207.2 (C=O). 19F NMR (282 MHz, CDCl₃): δ = -62.84. IR (ATR, cm⁻¹): ν = 3018 (w), 2926 (m), 2855 (m), 1710 (m), 1614 (s), 1575 (w), 1499 (m), 1401 (w), 1317 (s), 1256 (s), 1201 (m), 1146 (m), 1102 (s), 1066 (s), 1013 (m), 877 (m), 837 (s), 782 (m), 733 (m), 594 (m). MS (EI, 70 eV): m/z (%) = 466 (10), 465 (25), 464 (M⁺, 100), 227 (29), 209 (22), 208 (73), 207 (24), 197 (10), 188 (18), 186 (16), 185 (11), 183 (15), 182 (14), 175 (11), 174 (26), 173 (20), 172 (11), 171 (19), 165 (11), 160 (25), 159 (29), 158 (17), 147 (14), 145 (13), 144 (17), 141 (13), 139 (61), 129 (16), 128 (17), 115 (29), 91 (17). HRMS (ESI): Calculated for C₂₉H₂₈F₃O₂ (M+H⁺), 465.20359; measured 465.20373.

(E)-16-[3-(4-Fluorophenyl)-prop-2-ynylidene]-3-methoxy-α-estrone 3d

![Chemical Structure](image)

3d was synthesized according to general procedure A using 4-fluorophenylacetylene (0.338 mmol, 41 mg) and purified via column chromatography (heptane/ethyl acetate 10:1). Yield: 42 mg (45 %). mp. 139–140 °C. 1H NMR (500 MHz, CDCl₃): δ = 0.78–1.04 (m, 2H); 1.10 (s, 3H, Me); 1.41–1.54 (m, 2H); 1.78–1.81 (m, 1H); 2.10–2.13 (m, 1H); 2.26–2.30 (m, 2H); 2.42–2.46 (m, 1H); 2.80–2.96 (m, 4H); 3.76 (s, 3H, OMe); 6.59 (d, J = 2.64 Hz, 1H); 6.67–6.71 (m, 2H); 7.05–7.08 (m, 2H); 7.18 (d, J = 8.65 Hz, 1H); 7.49–7.52 (m, 2H). 13C NMR (125 MHz, CDCl₃): δ = 25.5 (CH₃), 28.1, 28.3, 29.9, 30.3, 32.2 (CH₂); 41.3, 43.1, 46.6 (CH), 50.8 (C), 55.2 (OCH₃); 87.0, 99.9 (C≡C); 111.7, 113.5, 114.3 (CH); 115.9 (d, J = 22.2 Hz, CH); 118.8 (d, J = 3.5 Hz, C); 126.9 (CH), 131.8 (C); 133.9 (d, J = 8.5 Hz, CH); 138.0, 146.2, 157.5 (C); 163.0 (d, J = 251.3 Hz, C); 207.3 (C=O). 19F NMR (282 MHz, CDCl₃): δ = -109.20. IR (ATR, cm⁻¹): ν = 2940 (m), 2840 (w), 1708 (m), 1611 (m), 1593 (m), 1503 (m), 1451 (w), 1427 (w), 1371 (w), 1253 (m), 1222 (m), 1146 (m), 1088 (w), 1032 (m), 940 (w), 875 (m), 782 (m), 733 (m), 594 (m). MS (EI, 70 eV): m/z (%) = 466 (10), 465 (25), 464 (M⁺, 100), 227 (29), 209 (22), 208 (73), 207 (24), 197 (10), 188 (18), 186 (16), 185 (11), 183 (15), 182 (14), 175 (11), 174 (26), 173 (20), 172 (11), 171 (19), 165 (11), 160 (25), 159 (29), 158 (17), 147 (14), 145 (13), 144 (17), 141 (13), 139 (61), 129 (16), 128 (17), 115 (29), 91 (17). HRMS (ESI): Calculated for C₂₉H₂₈F₂O₂ (M+H⁺), 465.20359; measured 465.20373.
830 (s), 790 (m), 754 (w), 526 (s). MS (El, 70 eV): m/z (%) = 415 (26), 414 (M+, 56), 227 (25), 213 (10), 174 (19), 173 (13), 171 (14), 160 (12), 159 (28), 158 (100), 157 (62), 147 (14), 145 (17), 144 (13), 133 (18), 129 (13), 128 (16), 115 (19), 91 (20). HRMS (ESI): Calculated for C_{28}H_{28}FO_{2} (M+H⁺), 415.20678; measured 415.20705.

(E)-16-[3-(4-Methoxyphenyl)-prop-2-ynylidene]-3-methoxy-α-estrone 3e

3e was synthesized according to general procedure A using 4-methoxyphenylacetylene (0.338 mmol, 45 mg) and purified via column chromatography (heptane/ethyl acetate 10:1). Yield: 55 mg (58 %). mp. 113–114 °C. ¹H NMR (300 MHz, CDCl₃): δ = 0.80–1.05 (m, 2H); 1.09 (s, 3H, Me); 1.43–1.50 (m, 3H); 1.75–1.81 (m, 1H); 2.08–2.14 (m, 1H); 2.24–2.31 (m, 2H); 2.40–2.47 (m, 1H); 2.80–2.92 (m, 3H); 3.75 (s, 3H, OMe); 3.84 (s, 3H, OMe); 6.58 (d, ³J = 2.72 Hz, 1H); 6.68–6.71 (m, 2H); 6.89 (d, ³J = 8.93 Hz, 2H); 7.18 (d, ³J = 8.61 Hz, 1H); 7.46 (d, ³J = 8.92 Hz, 2H). ¹³C NMR (75 MHz, CDCl₃): δ = 25.6 (CH₃), 28.2, 28.3, 29.8, 30.3, 32.2 (CH₂); 41.4, 43.0, 46.6 (CH), 50.8 (C), 55.2, 55.4 (OCH₃); 86.4, 101.7 (C≡C); 111.7, 113.5, 114.2 (CH); 114.7 (C); 114.9, 126.9 (CH); 131.9 (C); 133.6 (CH); 138.0, 145.1, 157.5, 160.4 (C); 207.4 (C=O). IR (ATR, cm⁻¹): v = 3015 (w), 2910 (m), 2542 (w), 2187 (m), 1707 (m), 1596 (s), 1500 (s), 1454 (m), 1375 (w), 1293 (m), 1246 (s), 1145 (m), 1088 (m), 1027 (s), 951 (m), 856 (m), 835 (s), 790 (m), 755 (m), 734 (m). MS (El, 70 eV): m/z (%) = 427 (27), 426 (M⁺, 70), 239 (27), 227 (15), 225 (11), 213 (13), 209 (11), 178 (10), 173 (11), 171 (40), 170 (100), 165 (27), 160 (13), 159 (18), 156 (11), 155 (26), 152 (12), 147 (15), 145 (22), 144 (16), 141 (11), 139 (11), 131 (13), 129 (11), 128 (23), 127 (40), 121 (12), 115 (25), 91 (25). HRMS (ESI): Calculated for C_{29}H_{31}O_{3} (M+H⁺), 427.22677; measured 427.22697.

(E)-16-[3-(4-Ethynylphenyl)-prop-2-ynylidene]-3-methoxy-α-estrone 3f
**3f** was synthesized according to general procedure A using 4-ethynylphenylacetylene (0.338 mmol, 43 mg) and purified via column chromatography (heptane/ethyl acetate 15:1). Yield: 70 mg (74 %).

mp. 123–124 °C. 1H NMR (250 MHz, CDCl3): \( \delta = 0.78–1.06 \) (m, 2H); 1.10 (s, 3H, Me); 1.43–1.51 (m, 3H); 1.76–1.83 (m, 1H); 2.08–2.14 (m, 1H); 2.24–2.28 (m, 2H); 2.41–2.46 (m, 1H); 2.79–2.87 (m, 3H); 3.21 (s, 1H, C≡CH); 3.75 (s, 3H, OMe); 6.58 (d, \( ^3J = 2.51 \) Hz, 1H); 6.69–6.71 (m, 2H); 7.18 (d, \( ^3J = 8.65 \) Hz, 1H); 7.47 (s, 4H). 13C NMR (63 MHz, CDCl3): \( \delta = 25.5 \) (CH3), 28.1, 28.3, 29.9, 30.3 (CH2); 30.9 (C≡CH); 41.3, 43.1, 46.7 (CH), 50.8 (C), 55.2 (OCH3); 79.5, 83.1, 89.0, 100.2 (3x C≡C + 1x C); 111.7, 113.5, 114.1 (CH); 122.8, 123.0 (C); 126.9, 131.8, 132.1 (CH); 138.0, 146.6, 157.5 (C); 207.3 (C=O). IR (ATR, cm\(^{-1}\)): \( \nu = 3282 \) (w), 2933 (m), 2193 (w), 1711 (m), 1612 (s), 1573 (m), 1497 (s), 1427 (m), 1280 (w), 1251 (s), 1199 (m), 1144 (m), 1077 (m), 1041 (m), 953 (m), 881 (m), 833 (s), 781 (m), 734 (w), 627 (m), 546 (s). MS (EI, 70 eV): m/z (%) = 421 (22), 420 (M+, 100), 355 (11), 346 (13), 342 (11), 325 (12), 315 (10), 311 (11), 281 (16), 255 (10), 254 (12), 233 (27), 227 (38), 210 (11), 209 (18), 207 (38), 203 (12), 202 (13), 197 (26), 194 (12), 193 (20), 191 (15), 189 (29), 186 (12), 179 (12), 178 (15), 174 (23), 173 (27), 172 (10), 171 (45), 170 (10), 169 (15), 166 (15), 165 (34), 164 (88), 163 (83), 160 (18), 158 (17), 155 (19), 150 (21), 147 (27), 145 (17), 139 (46), 138 (15), 135 (22), 131 (15), 129 (20), 128 (26), 115 (28), 91 (38), 77 (44), 73 (21). HRMS (ESI): Calculated for C\(_{30}\)H\(_{28}\)NaO\(_2\) (M+Na\(^+\)), 443.19815; measured 443.19818.

(E)-16-[3-(3-Aminophenyl)-prop-2-ynylidene]-3-methoxy-\( \alpha \)-estrone 3g

\[
\begin{align*}
\text{MeO} & \quad \text{MeO} \\
\text{H} & \quad \text{H} \\
\text{NH}_2 & \quad \text{H} \\
\end{align*}
\]

3g was synthesized according to general procedure A using 3-aminophenylacetylene (0.338 mmol, 40 mg) and purified via column chromatography (heptane/ethyl acetate 5:1). Yield: 64 mg (69 %).

mp. 68–69 °C. 1H NMR (500 MHz, CDCl3): \( \delta = 0.80–0.90 \) (m, 3H); 1.09 (s, 3H, Me); 1.40–1.52 (m, 2H); 1.77–1.80 (m, 1H); 2.10–2.13 (m, 1H); 2.25–2.29 (m, 2H); 2.41–2.45 (m, 1H); 2.80–2.91 (m, 3H); 3.75 (s, 3H, OMe); 6.59 (d, \( ^3J = 2.63 \) Hz, 1H); 6.67–6.70 (m, 2H); 6.74 (dd, \( ^3J = 8.05 \) Hz, \( ^4J = 1.65 \) Hz, 1H); 6.86–6.87 (m, 1H) 6.95 (d, \( ^3J = 7.61 \) Hz, 1H); 7.14–7.18 (m, 2H). 13C NMR (125 MHz, CDCl3): \( \delta = 25.5 \) (CH3), 28.1, 28.3, 29.9, 30.3, 32.2 (CH2); 41.3, 43.0, 46.6 (CH), 50.8 (C), 55.2 (OCH3); 86.7, 101.3 (C≡C); 111.7, 113.5, 114.6, 116.5, 118.3, 122.8 (CH); 123.4 (C); 126.9, 129.4 (CH); 131.8, 138.0, 145.7, 146.0, 157.5 (C); 207.4 (C=O). IR (ATR, cm\(^{-1}\)): \( \nu = 3457 \) (w), 3365 (w), 2919 (s), 2850 (m), 2185 (m), 1705 (m), 1607 (s), 1498 (m), 1447 (m), 1237 (m), 1145 (m), 1039 (m), 963 (m), 857 (m), 779 (s), 684 (m). MS (EI, 70 eV): m/z (%) = 412 (32), 411 (M+, 85), 227 (12), 224 (14), 173 (17), 171 (11), 165 (10), 160 (13),...
159 (20), 158 (10), 156 (30), 155 (100), 154 (40), 153 (10), 147 (12), 141 (22), 131 (14), 130 (17), 129 (19), 128 (39), 127 (23), 117 (15), 115 (21), 91 (21), 77 (13). HRMS (ESI): Calculated for C\textsubscript{28}H\textsubscript{30}NO\textsubscript{2} (M+H\textsuperscript{+}), 412.22711; measured 412.22746.

**\((E)-16-\{(3\text{-Thienyl})\text{-prop-2-ynylidene}\}-3\text{-methoxy-}\alpha\text{-estrone 3h}**

![Chemical Structure of 3h](image)

3h was synthesized according to general procedure A using 3-ethynylthiophene (0.338 mmol, 37 mg) and purified via column chromatography (heptane/ethyl acetate 10:1). Yield: 63 mg (70 %). mp. 53–54 °C. $^1$H NMR (500 MHz, CDCl\textsubscript{3}): $\delta = 0.80–1.04$ (m, 3H); 1.09 (s, 3H, Me); 1.43–1.52 (m, 2H); 1.77–1.80 (m, 1H); 2.09–2.14 (m, 1H); 2.25–2.30 (m, 2H); 2.42–2.46 (m, 1H); 2.80–2.91 (m, 3H); 3.76 (s, 3H, OMe); 6.59 (d, $^3J = 2.72$ Hz, 1H); 6.67–6.71 (m, 2H); 7.17–7.19 (m, 2H); 7.32 (dd, $^3J = 4.99$ Hz, $^3J = 2.99$ Hz, 1H); 7.57 (dd, $^3J = 2.97$ Hz, $^3J = 1.12$ Hz, 1H). $^{13}$C NMR (125 MHz, CDCl\textsubscript{3}): $\delta = 25.5$ (CH\textsubscript{3}), 28.1, 28.3, 29.9, 30.3, 32.2 (CH\textsubscript{2}); 41.3, 43.0, 46.6 (CH), 50.8 (C), 55.2 (OCH\textsubscript{3}); 87.0, 96.1 (C≡C); 111.7, 113.5, 114.4 (CH); 121.8 (C); 125.7, 126.9, 129.9, 130.1 (CH); 131.8, 138.0, 145.8, 157.5 (C); 207.3 (C=O). IR (ATR, cm\textsuperscript{-1}): $\nu = 3103$ (w), 2917 (m), 2187 (m), 1707 (s), 1607 (s), 1515 (s), 1498 (s), 1449 (m), 1281 (m), 1237 (m), 1145 (m), 1040 (m), 961 (s), 869 (m), 779 (s), 623 (s). MS (EI, 70 eV): $m/z$ (%) = 403 (20), 402 (M\textsuperscript{+}, 69), 227 (17), 215 (11), 186 (13), 185 (17), 174 (19), 151 (15), 160 (17), 159 (18), 158 (13), 147 (38), 146 (100), 145 (41), 141 (12), 132 (12), 129 (13), 128 (22), 127 (13), 121 (16), 120 (13), 115 (27), 102 (19), 91 (17). HRMS (ESI): Calculated for C\textsubscript{26}H\textsubscript{27}O\textsubscript{2}S (M+H\textsuperscript{+}), 403.17263; measured 403.17267.

**\((E)-16-\{(3\text{-Trimethylsilyl}\text{-prop-2-ynylidene}\}-3\text{-methoxy-}\alpha\text{-estrone 3i}**

![Chemical Structure of 3i](image)

3i was synthesized according to general procedure A using trimethylsilylacetylene (0.338 mmol, 33 mg) and purified via column chromatography (heptane/ethyl acetate 20:1). Yield: 40 mg (45 %). $^1$H NMR (250 MHz, CDCl\textsubscript{3}): $\delta = 0.25$ (s, 9H, TMS); 0.85–0.93 (m, 2H); 1.07 (s, 3H, Me); 1.33–1.49 (m, 3H); 1.73–1.79 (m, 1H); 2.06–2.11 (m, 1H); 2.22–2.30 (m, 2H); 2.39–2.44 (m, 1H); 2.79–2.85 (m, 3H); 3.76
(s, 3H, OMe); 6.46 (t, $^3J = 2.42$ Hz, 1H); 6.59 (d, $^4J = 2.63$ Hz, 1H); 6.69 (dd, $^3J = 8.59$ Hz, $^4J = 2.74$ Hz, 1H); 7.17 (d, $^3J = 8.61$ Hz, 1H). $^{13}$C NMR (63 MHz, CDCl$_3$): $\delta$ = -0.2 (TMS); 25.4 (Me), 28.1, 28.2, 29.8, 30.2, 32.1 (CH$_3$); 41.2, 43.0, 46.5 (CH), 50.7 (C), 55.2 (OMe); 88.3, 102.2 (C≡C); 111.7, 113.5, 114.2, 126.8 (CH); 131.8, 138.0, 147.3, 157.5 (C); 207.3 (C=O). IR (ATR, cm$^{-1}$): $\tilde{\nu}$ = 3392 (w), 2918 (w), 1693 (w), 1607 (m), 1499 (m), 1224 (s), 1171 (s), 1024 (s), 789 (m), 635 (s).

(E)-16-(Oct-2-ynylidene)-3-methoxy-α-estrone 3j

3j was synthesized according to general procedure A using 1-septyne (0.338 mmol, 33 mg) and purified via column chromatography (heptane/ethyl acetate 20:1). Yield: 52 mg (61%). $^1$H NMR (250 MHz, CDCl$_3$): $\delta$ = 0.76–0.85 (m, 2H); 0.93 (t, $^3J = 7.03$ Hz, 3H, Me); 1.06 (s, 3H, Me); 1.33–1.62 (m, 9H); 1.73–1.78 (m, 1H); 2.05–2.12 (m, 1H); 2.21–2.29 (m, 2H); 2.37–2.47 (m, 3H); 2.76–2.84 (m, 3H); 3.76 (s, 3H, OMe); 6.48 (t, $^4J = 2.35$ Hz, 1H); 6.59 (d, $^4J = 2.65$ Hz, 1H); 6.69 (dd, $^3J = 8.59$ Hz, $^4J = 2.71$ Hz, 1H); 7.17 (d, $^3J = 8.64$ Hz, 1H). $^{13}$C NMR (63 MHz, CDCl$_3$): $\delta$ = 14.0 (CH$_3$); 20.0, 22.2 (CH$_2$); 25.5 (CH$_3$); 28.1, 28.2, 28.3, 29.7, 30.3, 31.1, 32.2 (CH$_3$); 41.3, 42.9, 46.5 (CH), 50.7 (C), 55.2 (OCH$_3$); 78.6, 103.7 (C≡C); 111.6, 113.5, 115.6, 126.8 (CH); 131.9, 138.0, 145.1, 157.5 (C); 207.5 (C=O). IR (ATR, cm$^{-1}$): $\tilde{\nu}$ = 2925 (m), 2207 (w), 1713 (m), 1613 (m), 1499 (m), 1452 (m), 1376 (w), 1253 (w), 1144 (m), 1074 (m), 1041 (s), 964 (s), 872 (s), 792 (s), 628 (w), 594 (w). MS (EI, 70 eV): $m/z$ (%) = 391 (41), 390 (M$^+$, 100), 327 (14), 281 (11), 227 (11), 225 (19), 213 (10), 203 (23), 188 (11), 187 (15), 186 (20), 185 (10), 174 (24), 173 (17), 171 (13), 160 (21), 159 (31), 158 (18), 147 (42), 146 (12), 145 (21), 144 (15), 128 (34), 127 (16), 121 (19), 119 (21), 117 (33), 116 (14), 115 (16), 106 (11), 105 (36), 103 (11), 95 (13), 91 (60), 79 (18), 78 (37), 77 (40), 73 (14), 55 (13), 53 (11), 51 (20), 41 (18), 39 (11). HRMS (ESI): Calculated for C$_{27}$H$_{35}$O$_2$ (M+H$^+$), 391.25924; measured 391.26500.
(E)-16-(Trifluoromethanesulfonyloxymethylidene)-3-methoxy-α-estrone 2
(E)-16-(3-Phenylprop-2-ynylidene)-3-methoxy-α-estrone 3a
(E)-16-[3-(4-tert-Butylphenyl)-prop-2-ynylidene]-3-methoxy-α-estrone 3b
(E)-16-[3-(4-Trifluoromethylphenyl)-prop-2-ynylidene]-3-methoxy-α-estrone 3c
$^{(E)}$-16-[3-(4-Fluorophenyl)-prop-2-ynyldiene]-3-methoxy-α-estrone 3d
(E)-16-[3-(4-Methoxyphenyl)-prop-2-ynylidene]-3-methoxy-α-estrone 3e
(E)-16-[3-(4-Ethynylphenyl)-prop-2-ynylidene]-3-methoxy-α-estrone 3f
(E)-16-[3-(3-Aminophenyl)-prop-2-ynylidene]-3-methoxy-α-estrone 3g
(E)-16-[3-(3-Thienyl)-prop-2-ynyldene]-3-methoxy-α-estrone 3h
\[(E)-16-(3\text{-}\text{Trimethylsilylprop}-2\text{-}\text{ynylidene})\text{-}3\text{-}\text{methoxy}\text{-}\alpha\text{-}\text{estrone} \ 3i\]
(E)-16-(Oct-2-ynylidene)-3-methoxy-α-estrone 3j
References

1. EI and ESI were unable to find the product-mass, most likely due to instability of the TMS-group under MS-conditions.