Electrophilic Alkylations in Neutral Aqueous or Alcoholic Solutions**

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Analytical data:
NMR spectra were recorded on a Bruker ARX 300 (300 MHz) or Varian VXR 400 S (400 MHz). Chemical shifts are reported as $\delta$-values in ppm relative to tetramethylsilane ($\delta_H$: 0.00, $\delta_C$: 0.00) or relative to the deuterated solvent peak: CDCl$_3$ ($\delta_H$: 7.24, $\delta_C$: 77.0). Coupling constants are reported in Hz. For the characterization of the observed signal multiplicities the following abbreviations were applied: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), as well as br (broad).
GC-MS analysis were performed on an Agilent 5973 MSD: capillary column HP-5MS (Agilent Technologies; length 30 m; $\varnothing$ 0.25 mm); flow rate 1.0 mL/min; injector, split (23.9 mL/min), inlet heater 250 °C, carrier gas: He; temperature program: 70 °C (2 min) – 25 °C/min to 150 °C – 50 °C/min to 250 °C (12 min); quadrupole mass spectrometer.
Elemental analysis were carried out in the “Mikroanalytisches Laboratorium of the Department Chemie und Biochemie der LMU München”.
Melting points were determined on a Büchi B540 and are uncorrected.
1-(4-Methoxybenzyl)-2,4-dimethylbenzene (2a)

According to the typical reaction procedure, 4-methoxybenzyl chloride (517 mg, 3.33 mmol) was added to 10 mL of a solution of m-xylene (3.05 g, 10.0 mmol) in 2,2,2-trifluoroethanol (T) and ammonium hydrogencarbonate (395 mg, 5.00 mmol) and stirred for 1 h at ambient temperature. After the usual workup and purification by column chromatography on silica gel (pentane/ether : 7/1) 496 mg of 2a (2.19 mmol; 66%) was isolated as a colorless oil containing traces of the corresponding 1,2,3-substituted product.

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\begin{align*}
\text{H} \text{NMR (300 MHz, CDCl}_3\text{): } & \delta = 2.20, 2.29 (2 \text{ s}, 2 \times 3 \text{ H}, 2 \times \text{CH}_3), 3.76 (\text{s}, 3 \text{ H}, \text{OCH}_3), 3.87 (\text{s}, 2 \text{ H}, \text{CH}_2), 6.78 – 6.82 (\text{m}, 2 \text{ H}, \text{Ar-H}), 6.95 – 7.04 (\text{m}, 5 \text{ H}, \text{Ar-H}). \\
\text{C NMR (75.5 MHz, CDCl}_3\text{): } & \delta = 19.5, 20.9 (2 \text{ q}), 38.1 (\text{t}), 55.2 (\text{q, OCH}_3), 113.8 (\text{d}, 2 \times \text{C}_\text{ar}), 126.5, 129.7, 131.1 (3 \text{ d}, \text{C-3, C-5, C-6}), 129.6 (\text{d}, 2 \times \text{C}_\text{ar}), 132.7 (\text{s}, \text{C}_\text{ar}), 135.8, 136.2, 136.3 (3 \text{s}, \text{C-1, C-2, C-4}), 157.8 (\text{s}, \text{C}_\text{ar-OCH}_3). \text{ GC-MS: } t_R = 8.83 \text{ min; } m/z (\%) = 226 (92) [\text{M}^+] , 211 (100) [\text{M}^+ – \text{CH}_3], 195 (20) [\text{M}^+ – \text{OCH}_3], 165 (21) [\text{M}^+ – \text{OCH}_3 – 2 \text{CH}_3], 121 (19) [\text{H}_3\text{COC}_6\text{H}_4\text{CH}_2^+], 118 (62) [\text{M}^+ – \text{H}_3\text{COOC}_6\text{H}_5^+].
\end{align*}
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1-(4-Methoxybenzyl)-2,4,6-trimethylbenzene (2b)

According to the typical reaction procedure, 4-methoxybenzyl chloride (517 mg, 3.33 mmol) was added to 10 mL of a solution of mesitylene (1.20 g, 10.0 mmol) in 2,2,2-trifluoroethanol (T) and ammonium hydrogencarbonate (395 mg, 5.00 mmol) and stirred for 1 h at ambient temperature. After the usual workup and purification by column chromatography on silica gel (pentane/ether : 8/1) 702 mg of 2b (2.92 mmol; 88%) was isolated as a colorless oil.

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\begin{align*}
\text{H} \text{NMR (300 MHz, CDCl}_3\text{): } & \delta = 2.20 (\text{s}, 6 \text{ H}, 2-\text{CH}_3, 6-\text{CH}_3), 2.28 (\text{s}, 3 \text{ H}, 4-\text{CH}_3), 3.75 (\text{s}, 3 \text{ H}, \text{OCH}_3), 3.94 (\text{s}, 2 \text{ H}, \text{CH}_2), 6.75 – 6.78 (\text{m}, 2 \text{ H}, \text{Ar-H}), 6.87 – 6.93 (\text{m}, 4 \text{ H}, \text{Ar-H}). \\
\text{C NMR (75.5 MHz, CDCl}_3\text{): } & \delta = 20.1 (\text{q}, 2 \times \text{CH}_3), 20.9 (\text{q}), 33.8 (\text{t}), 55.2 (\text{q, OCH}_3), 113.8 (\text{d}, \text{C}_\text{ar}), 128.7, 128.9 (2 \text{ d}, 4 \times \text{C}_\text{ar}), 132.1, 134.1, 135.5 (3 \text{s}, 3 \times \text{C}_\text{ar}), 136.9 (\text{s}, 2 \times \text{C}_\text{ar}) 157.7 (\text{s}, \text{C}_\text{ar-OCH}_3). \text{ GC-MS: } t_R = 9.15 \text{ min; } m/z (\%) = 240 (72) [\text{M}^+] , 225 (58) [\text{M}^+ – \text{CH}_3], 210 (10) [\text{M}^+ – 2 \text{CH}_3], 209 (8) [\text{M}^+ – \text{OCH}_3], 178 (11), 165 (13), 132 (100) [\text{M}^+ – \text{H}_3\text{COC}_6\text{H}_4\text{CH}_2^+], 121 (15) [\text{H}_3\text{COC}_6\text{H}_4\text{CH}_2^+].
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Bis(4-methoxyphenyl)methane (2c)

According to the typical reaction procedure, 4-methoxybenzyl chloride (517 mg, 3.33 mmol) was added to 10 mL of a solution of anisole (1.08 g, 10.0 mmol) in 2,2,2-trifluoroethanol (T) and ammonium hydrogencarbonate (395 mg, 5.00 mmol) and stirred for 30 min at ambient temperature. 

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\begin{align*}
\text{H} \text{NMR (300 MHz, CDCl}_3\text{): } & \delta = 2.20 (\text{s}, 6 \text{ H}, 2-\text{CH}_3, 6-\text{CH}_3), 2.28 (\text{s}, 3 \text{ H}, 4-\text{CH}_3), 3.75 (\text{s}, 3 \text{ H}, \text{OCH}_3), 3.94 (\text{s}, 2 \text{ H}, \text{CH}_2), 6.75 – 6.78 (\text{m}, 2 \text{ H}, \text{Ar-H}), 6.87 – 6.93 (\text{m}, 4 \text{ H}, \text{Ar-H}). \\
\text{C NMR (75.5 MHz, CDCl}_3\text{): } & \delta = 20.1 (\text{q}, 2 \times \text{CH}_3), 20.9 (\text{q}), 33.8 (\text{t}), 55.2 (\text{q, OCH}_3), 113.8 (\text{d}, \text{C}_\text{ar}), 128.7, 128.9 (2 \text{ d}, 4 \times \text{C}_\text{ar}), 132.1, 134.1, 135.5 (3 \text{s}, 3 \times \text{C}_\text{ar}), 136.9 (\text{s}, 2 \times \text{C}_\text{ar}) 157.7 (\text{s}, \text{C}_\text{ar-OCH}_3). \text{ GC-MS: } t_R = 9.15 \text{ min; } m/z (\%) = 240 (72) [\text{M}^+] , 225 (58) [\text{M}^+ – \text{CH}_3], 210 (10) [\text{M}^+ – 2 \text{CH}_3], 209 (8) [\text{M}^+ – \text{OCH}_3], 178 (11), 165 (13), 132 (100) [\text{M}^+ – \text{H}_3\text{COC}_6\text{H}_4\text{CH}_2^+], 121 (15) [\text{H}_3\text{COC}_6\text{H}_4\text{CH}_2^+].
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temperature. After the usual workup and purification by column chromatography on silica gel (pentane/ether : 7/1) 655 mg of 2c (2.87 mmol; 86%) was isolated as a white solid, m.p. 51 °C, containing traces of the corresponding 1,2-substituted product.

\[ ^{1}H \text{ NMR (300 MHz, CDCl}_3\text{): } \delta = 3.76 \text{ (s, 6 H, OCH}_3\text{)}, 3.86 \text{ (s, 2 H, CH}_2\text{)}, 6.80 - 6.83 \text{ (m, 4 H, Ar-H)}, 7.06 - 7.09 \text{ (m, 4 H, Ar-H)}. \]

\[ ^{13}C \text{ NMR (75.5 MHz, CDCl}_3\text{): } \delta = 40.1 \text{ (t, C-CH}_2\text{)}, 55.2 \text{ (s, 2 × OCH}_3\text{)}, 113.8 \text{ (d, 4 × C}_\text{ar}\text{)}, 129.7 \text{ (d, 4 × C}_\text{ar}\text{)}, 133.7 \text{ (s, 2 × C}_\text{ar}\text{)}, 157.9 \text{ (s, 2 × C}_\text{ar–OCH}_3\text{)}. \]

GC-MS: \( t_R = 9.11 \text{ min; } m/z \text{ (%) = 228 (100) [M}^+\text{], 213 (22) [M}^+\text{ – CH}_3\text{], 197 (57) [M}^+\text{ – OCH}_3\text{], 181 (13), 165 (12), 152 (16), 121 (32) [H}_3\text{COC}_6\text{H}_4\text{CH}_2^+\text{], 91 (22). } \]

NMR data for compound 2c are in accordance with the data previously published.[S1]

4-Methoxy-1-(4-methoxybenzyl)-2-methylbenzene (2d)

According to the typical reaction procedure, 4-methoxybenzyl bromide (750 mg, 3.73 mmol) was added to 25 mL of a solution of 3-methylanisole (3.05 g, 25.0 mmol) in 2,2,2-trifluoroethanol (T) and ammonium hydrogen carbonate (0.59 g, 7.46 mmol) and stirred for 1.5 h at ambient temperature. After the usual workup and purification by column chromatography on silica gel (pentane/ether : 7/1) 875 mg of 2d (3.61 mmol; 97%) was isolated in a mixture of regioisomers as a colorless oil. Fraction 1 of this separation was the pure isomer 2d which was identified spectroscopically.

\[ ^{1}H \text{ NMR (300 MHz, CDCl}_3\text{): } \delta = 2.20 \text{ (s, 3 H, CH}_3\text{), 3.76, 3.77 (2 s, 2 × 3 H, 2 × OCH}_3\text{), 3.85 (s, 2 H, CH}_2\text{), 6.66 – 6.72 (m, 2 H, Ar-H), 6.78 – 6.81 (m, 2 H, Ar-H), 6.98 – 7.03 (m, 3 H, Ar-H). } \]

\[ ^{13}C \text{ NMR (75.5 MHz, CDCl}_3\text{): } \delta = 19.9 \text{ (q, CH}_3\text{), 37.7 (t), 55.2 \text{ (q, 2 × OCH}_3\text{), 110.8 (d, C}_\text{ar}\text{), 113.8 (d, 2 × C}_\text{ar}\text{), 116.0 (d, C}_\text{ar}\text{), 129.5 (d, 2 × C}_\text{ar}\text{), 130.7 (d, C}_\text{ar}\text{), 131.6 (s, C}_\text{ar}\text{), 132.9 (s, C}_\text{ar}\text{), 137.8 (s, C-2), 157.8, 158.0 (2 s, 2 × C}_\text{ar–OCH}_3\text{). } \]

GC-MS: \( t_R = 9.56 \text{ min; } m/z \text{ (%) = 242 (100) [M}^+\text{], 227 (30) [M}^+\text{ – CH}_3\text{], 211 (22) [M}^+\text{ – OCH}_3\text{], 134 (55), 121 (56) [H}_3\text{COC}_6\text{H}_4\text{CH}_2^+\text{]. } \]


Fraction 2 was a 17:1 mixture of 2d and 2-methoxy-1-(4-methoxybenzyl)-4-methylbenzene, the latter of which was identified by its NMR spectra and GC-MS analysis.

NMR data for compound 2d were published previously.[S2]

2-(4-Methoxybenzyl)-5-methylthiophene (2e)

According to the typical reaction procedure, 4-methoxybenzyl bromide (783 mg, 5.00 mmol) was added to 25 mL of a solution of 2-methylthiophene (2.45 g, 25.0 mmol) and 2-
chloropyridine (625 mg, 5.50 mmol) in 2,2,2-trifluoroethanol (T) and stirred for 1 h at ambient temperature. After the usual workup and purification by column chromatography on silica gel (pentane/ether : 7/1) 920 mg of 2e (4.21 mmol; 84%) was isolated as a colorless oil. 

$^1$H NMR (300 MHz, CDCl$_3$): $\delta = 2.39$ (s, 3 H, 5-CH$_3$), 3.76 (s, 3 H, OCH$_3$), 3.99 (s, 2 H, CH$_2$), 6.52 – 6.55 (m, 2 H, 3-H, 4-H), 6.81 – 6.84 (m, 2 H, Ar-H), 7.13 – 7.16 (m, 2 H, Ar-H).

$^{13}$C NMR (75.5 MHz, CDCl$_3$): $\delta$ = 15.3 (q, 5-CH$_3$), 35.4 (t), 55.2 (q, OCH$_3$), 113.9 (d, 2 $\times$ C$_{ar}$), 124.5, 124.6 (2 d, C-3, C-4), 129.5 (d, 2 $\times$ C$_{ar}$), 132.7 (s, C$_{ar}$), 138.2, 142.4 (2 s, C-2, C-5), 158.2 (s, C$_{ar}$–OCH$_3$). GC-MS: $t_R = 8.45$ min; $m/z$ (%) = 218 (100) [M$^+$], 203 (95) [M$^+$ – CH$_3$], 187 (34) [M$^+$ – OCH$_3$], 121 (11) [H$_3$COC$_6$H$_4$CH$_2$]$^+$. $^1$H NMR and MS data for compound 2e were published previously.[S3]

2,4-Dimethoxy-1-(4-methoxybenzyl)benzene (2f)

According to the typical reaction procedure, 4-methoxybenzyl chloride (1.00 g, 6.39 mmol) was added to 25 mL of a solution of 1,3-dimethoxybenzene (3.45 g, 25.0 mmol) and 2,6-lutidine (1.03 g, 9.61 mmol) in 2,2,2-trifluoroethanol (T) and stirred for 30 min at ambient temperature. After the usual workup and purification by column chromatography on silica gel (pentane/ether : 8/1) 1.38 g of 2f (5.34 mmol; 84%) was isolated as a colorless oil containing 7% (GC-MS) of the corresponding 1,2,3-substituted product. The major fraction of this separation was the pure isomer 2d which was identified spectroscopically.

$^1$H NMR (300 MHz, CDCl$_3$): $\delta = 3.75$, 3.76, 3.77 (3 s, 3 $\times$ 3 H, 3 $\times$ OCH$_3$), 3.83 (s, 2 H, CH$_2$), 6.37 – 6.45 (m, 2 H, Ar-H), 6.75 – 6.78 (m, 2 H, Ar-H), 6.80 – 6.82 (m, 1 H, Ar-H), 6.92 – 6.95 (m, 2 H, Ar-H). $^{13}$C NMR (75.5 MHz, CDCl$_3$): $\delta$ = 34.3 (t), 55.2 (q, 3 $\times$ OCH$_3$), 98.5, 103.9 (2 d, 2 $\times$ C$_{ar}$), 113.6 (d, 2 $\times$ C$_{ar}$), 122.5 (s, C$_{ar}$), 129.7 (d, 2 $\times$ C$_{ar}$), 130.3 (d, C$_{ar}$), 133.5 (s, C$_{ar}$), 157.7, 158.1, 159.0 (3 s, 3 $\times$ C$_{ar}$–OCH$_3$). GC-MS: $t_R = 10.13$ min; $m/z$ (%) = 258 (100) [M$^+$], 243 (18) [M$^+$ – CH$_3$], 227 (62) [M$^+$ – OCH$_3$], 151 (15) [M$^+$ – H$_3$COOC$_6$H$_5$], 121 (33) [H$_3$COC$_6$H$_5$]$^+$. Anal. Calcd. for C$_{16}$H$_{18}$O$_3$ (258.32): C, 74.40; H, 7.02. Found: C, 74.73; H, 7.03.

2,4,6-Trimethoxy-1-(4-methoxybenzyl)benzene (2g)

According to the typical reaction procedure, 4-methoxybenzyl chloride (1.00 g, 6.39 mmol) was added to 25 mL of a solution of 1,3,5-trimethoxybenzene (4.20 g, 25.0 mmol) and 2,6-lutidine (752 mg, 7.02 mmol) in 2,2,2-trifluoroethanol (T) and stirred for 2 h at ambient temperature. After the usual workup and purification by column chromatography on silica gel
(pentane/ether : 2/1) 1.62 g of 2g (5.62 mmol; 88%) was isolated as a white solid, m.p. 77 – 78 °C.

\(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta = 3.73\) (s, 3 H, OCH\(_3\)), 3.77 (s, 6 H, 2 \times OCH\(_3\)), 3.79 (s, 3 H, OCH\(_3\)), 3.86 (s, 2 H, CH\(_2\)), 6.14 (s, 2 H, Ar-H), 6.73 – 6.76 (m, 2 H, Ar-H), 7.13 – 7.16 (m, 2 H, Ar-H). \(^{13}\)C NMR (75.5 MHz, CDCl\(_3\)): \(\delta = 27.3\) (t), 55.1, 55.3 (2 q, 2 \times OCH\(_3\)), 55.7 (q, 2 \times OCH\(_3\)), 90.7 (d, 2 \times C\(_{ar}\)), 110.7 (s, C\(_{ar}\)), 113.4, 129.2 (2 d, 4 \times C\(_{ar}\)), 134.4 (s, C\(_{ar}\)), 157.3 (s, C\(_{ar-OCH3}\)), 158.7 (s, 2 \times C\(_{ar-OCH3}\)), 159.4 (s, C\(_{ar-OCH3}\)). GC-MS: \(t_R = 11.42\) min; \(m/z\) (%) = 288 (100) [M\(^+\)], 273 (8) [M\(^+\) – CH\(_3\)], 257 (37) [M\(^+\) – OCH\(_3\)], 181 (34) [M\(^+\) – H\(_3\)CO\(_6\)H\(_4\)], 121 (53) [H\(_3\)CO\(_6\)H\(_4^+\)], 91 (9). Anal. Calcd. for C\(_{17}\)H\(_{20}\)O\(_4\) (288.34): C, 70.81; H, 6.99. Found: C, 70.90; H, 7.05.

3-(4-Methoxybenzyl)-1H-indole (2h)

According to the typical reaction procedure, 4-methoxybenzyl bromide (1.01 g, 5.02 mmol) was added to 25 mL of a solution of indole (2.93 g, 25.0 mmol) in 80% aqueous acetone (v/v) (80A20W) and ammonium hydrogen carbonate (791 mg, 10.0 mmol) and stirred for 3 h at ambient temperature. After the usual workup and purification by column chromatography on silica gel (pentane/ether : 7/3) 890 mg of 2h (3.75 mmol; 75%) was isolated as a yellow solid, m.p. 77 – 78 °C, containing 17% of the corresponding 2-isomer. Fraction 1 of this separation was the pure isomer 2h which was identified spectroscopically.

3-Isomer: \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 3.76\) (s, 3 H, OCH\(_3\)), 4.04 (s, 2 H, CH\(_2\)), 6.80 – 7.51 (m, 9 H, Ar-H), 7.87 (br s, 1 H, NH). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 30.7\) (t), 55.2 (q, OCH\(_3\)), 102.4 (s, C-3), 111.0 (d, C-7), 113.8 (d, 2 \times C\(_{ar}\)), 119.2, 119.3, 120.4, 120.5 (4 d, C-2, C-4, C-5, C-6), 127.4 (s, C-3a), 129.7 (d, 2 \times C\(_{ar}\)), 133.3 (s, C\(_{ar}\)), 136.5 (s, C-7a), 157.8 (s, C\(_{ar-OCH3}\)). GC-MS: \(t_R = 12.13\) min; \(m/z\) (%) = 237 (100) [M\(^+\)], 236 (82) [M\(^+\) – H], 222 (10) [M\(^+\) – CH\(_3\)], 206 (17) [M\(^+\) – OCH\(_3\)], 192 (19), 130 (46) [M\(^+\) – H\(_3\)CO\(_6\)H\(_4\)]. Anal. Calcd. for C\(_{16}\)H\(_{15}\)NO (237.30): C, 80.98; H, 6.37; N, 5.90. Found: C, 80.91; H, 6.69; N, 5.80.

2-Isomer: GC-MS: \(t_R = 12.39\) min; \(m/z\) (%) = 237 (100) [M\(^+\)], 236 (39) [M\(^+\) – H], 222 (10) [M\(^+\) – CH\(_3\)], 206 (25) [M\(^+\) – OCH\(_3\)], 192 (17), 130 (22) [M\(^+\) – H\(_3\)CO\(_6\)H\(_4\)].

2-(4-Methoxybenzyl)-1-methyl-1H-pyrrole (2i)

According to the typical reaction procedure, 4-methoxybenzyl bromide (1.00 g, 4.97 mmol) was added to 25 mL of a solution of 1-methylpyrrole (2.03 g, 25.0 mmol) in 80% aqueous acetonitrile (v/v) (80A20W) and ammonium hydrogen carbonate (790 mg, 9.99 mmol) and
stirred for 30 min at ambient temperature. After the usual workup and purification by column chromatography on silica gel (pentane/ether : 7/1) 700 mg of 2i (3.48 mmol; 70%) was isolated as an orange oil containing 21% of the corresponding 3-substituted product. The major fraction 1 of this separation was the pure isomer 2i which was identified spectroscopically.

2-Isomer: $^1$H NMR (300 MHz, CDCl$_3$): $\delta = 3.42$ (s, 3 H, NCH$_3$), 3.78 (s, 3 H, OCH$_3$), 3.87 (s, 2 H, CH$_2$), 5.87 (m, 1 H, 3-H), 6.05 (m, 1 H, 4-H), 6.56 (m, 1 H, 5-H), 6.80 – 6.83 (m, 2 H, Ar-H), 7.05 – 7.08 (m, 2 H, Ar-H). $^{13}$C NMR (75.5 MHz, CDCl$_3$): $\delta = 32.0$ (t), 33.7 (q, NCH$_3$), 55.2 (q, OCH$_3$), 106.5, 107.7 (2 d, C-3, C-4), 113.8 (d, 2 × C$_{ar}$), 121.7 (d, C-5), 129.4 (d, 2 × C$_{ar}$), 131.5, 131.9 (2 s, C-2, C$_{ar}$), 158.0 (s, C$_{ar}$–OCH$_3$). GC-MS: $t_R = 8.20$ min; $m/z$ (%) = 201 (100) [M$^+$], 200 (54), 186 (11) [M$^+$ – CH$_3$], 170 (20) [M$^+$ – OCH$_3$], 94 (85) [M$^+$ – H$_3$COC$_6$H$_4$]. Anal. Calcd. for C$_{13}$H$_{15}$NO (201.27): C, 77.58; H, 7.51; N, 6.56. Found: C, 77.07; H, 7.65; N, 6.87.

Fraction 2 was a 2.3:1 mixture (NMR) of 2i and of 3-(4-methoxybenzyl)-1-methyl-1H-pyrrole, the latter of which was identified by the NMR spectra of the product mixture and GC-MS analysis.

3-Isomer: GC-MS: $t_R = 8.30$ min; shows the same fragmentation pattern as the 2-isomer.

3-(4-Methoxyphenyl)-2-methylpropanaldehyde (3a)

According to the typical reaction procedure, 4-methoxybenzyl bromide (500 mg, 2.49 mmol) was added to 25 mL of a solution of ethyl prop-1-enyl ether (2.15 g, 25.0 mmol) (mixture of cis/trans-isomers) in 90% aqueous acetonitrile (v/v) (90AN10W) and ammonium hydrogen carbonate (295 mg, 3.73 mmol) and stirred for 3 h at ambient temperature. After the usual workup and purification by column chromatography on silica gel (pentane/ether : 7/1) 266 mg of 3a (1.49 mmol; 60%) was isolated as a colorless liquid.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 1.07$ (d, $J = 6.7$ Hz, 3 H, CH$_3$), 2.53 – 2.64 (m, 2 H, CH$_2$), 2.98 – 3.03 (m, 1 H, CHCH$_3$), 3.77 (s, 3 H, OCH$_3$), 6.82 – 6.84 (m, 2 H, Ar-H), 7.06 – 7.08 (m, 2 H, Ar-H), 9.69 (s, 1 H, CHO). $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 13.1$ (q), 35.7 (t), 48.1 (d, CHCH$_3$), 55.1 (q, OCH$_3$), 113.9 (d, 2 × C$_{ar}$), 129.9 (d, 2 × C$_{ar}$), 130.7 (s, C$_{ar}$), 158.2 (s, C$_{ar}$–OCH$_3$), 204.4 (d, CHO). GC-MS: $t_R = 7.29$ min; $m/z$ (%) = 178 (18) [M$^+$], 163 (1) [M$^+$ – CH$_3$], 122 (12), 121 (100) [H$_3$COC$_6$H$_4$CH$_2$]^+, 108 (10), 91 (9), 77 (10).
4-(4-Methoxyphenyl)butan-2-one (3b)

According to the typical reaction procedure, 4-methoxybenzyl bromide (1.00 g, 4.97 mmol) was added to 25 mL of a solution of 2-methoxypropene (1.80 g, 25.0 mmol) and 2,6-lutidine (799 mg, 7.46 mmol) in 90% aqueous acetonitrile (v/v) (90AN10W) and stirred for 3 h at ambient temperature. After the usual workup and purification by column chromatography on silica gel (pentane/ether : 7/1) 594 mg of 3b (3.33 mmol; 67%) was isolated as a colorless liquid.

$^1$H NMR (300 MHz, CDCl$_3$): $\delta = 2.12$ (s, 3 H, CH$_3$), 2.69 – 2.74 (m, 2 H, COCH$_2$), 2.81 – 2.86 (m, 2 H, ArCH$_2$), 3.77 (s, 3 H, OCH$_3$), 6.79 – 6.84 (m, 2 H, Ar-H), 7.07 – 7.12 (m, 2 H, Ar-H). $^{13}$C NMR (75.5 MHz, CDCl$_3$): $\delta = 28.8$ (t, COCH$_2$C), 30.0 (q, COCH$_3$), 45.4 (t, COCH$_2$), 55.2 (q, OCH$_3$), 113.8, 129.1 (2 d, 4 × C$_{ar}$), 133.0 (s, C$_{ar}$), 157.9 (s, C$_{ar}$–OCH$_3$), 208.0 (s, CO). GC-MS: $t_R = 7.41$ min; $m/z$ (%) = 178 (35) [M$^+$], 163 (5) [M$^+$ – CH$_3$], 135 (8) [M$^+$ – COCH$_3$], 121 (100) [H$_3$COCH$_2$H$_2$C$_{6}$H$_5$], 108 (10), 91 (9), 77 (8).

NMR and MS data for compound 3b were published previously.$^{[S4]}$

3-(4-Methoxyphenyl)-1-phenylpropan-1-one (3c)

According to the typical reaction procedure, 4-methoxybenzyl bromide (250 mg, 1.24 mmol) was added to 10 mL of a solution of 1-phenyl-1-(trimethylsiloxy)ethene (1.92 g, 10.0 mmol) in 90% aqueous acetonitrile (v/v) (90AN10W) and ammonium hydrogen carbonate (147 mg, 1.86 mmol) and stirred for 4.5 h at ambient temperature. After the usual workup the resulting acetophenone was removed in vacuo. Purification by column chromatography on silica gel (pentane/ether : 7/1) and recrystallization yielded 98.3 mg of 3c (409 µmol; 33%) as a white solid, m.p. 66 °C.

$^1$H NMR (300 MHz, CDCl$_3$): $\delta = 2.98 – 3.03$ (m, 2 H, ArCH$_2$), 3.24 – 3.29 (m, 2 H, COCH$_2$), 3.78 (s, 3 H, OCH$_3$), 6.82 – 6.85 (m, 2 H, Ar-H), 7.15 – 7.18 (m, 2 H, Ar-H), 7.42 – 7.57 (m, 3 H, C$_6$H$_3$), 7.94 – 7.96 (m, 2 H, C$_6$H$_3$). $^{13}$C NMR (75.5 MHz, CDCl$_3$): $\delta = 29.3$ (t, ArCH$_2$), 40.7 (t, COCH$_2$), 55.3 (q, OCH$_3$), 113.9 (d, 2 × C$_{ar}$), 128.0 (d, 2 × C$_{ar}$), 128.6 (d, 2 × C$_{ar}$), 129.3 (d, 2 × C$_{ar}$), 133.0 (d, C$_{ar}$), 133.2, 136.9 (2 s, 2 × C$_{ar}$), 158.0 (s, C$_{ar}$–OCH$_3$), 199.3 (s, CO). GC-MS: $t_R = 9.92$ min; $m/z$ (%) = 220 (25) [M$^+$], 205 (100) [M$^+$ – CH$_3$], 189 (4) [M$^+$ – OCH$_3$], 177 (8), 145 (10).

NMR and MS data for compound 3c were published previously.$^{[S5]}$
2-[Bis(4-methoxyphenyl)methyl]-5-methylfuran (4a)

According to the typical reaction procedure, chlorobis(4-methoxyphenyl)-methane (1.00 g, 3.81 mmol) (dissolved in 3.00 mL acetonitrile) was added to 20 mL of a solution of 2-methylfuran (1.64 g, 20.0 mmol) and 2-chloropyridine (433 mg, 3.81 mmol) in 2,2,2-trifluoroethanol (T) and stirred for 1 min at ambient temperature. After the usual workup and purification by column chromatography on silica gel (pentane/ether : 7/1) 895 mg of 4a (3.24 mmol; 85%) was isolated as a colorless oil.

$^1$H NMR (300 MHz, CDCl$_3$): $\delta = 2.24$ (s, 3 H, 5-CH$_3$), 3.77 (s, 6 H, 2 × OCH$_3$), 5.29 (s, 1 H, 2-CH), 5.71, 5.86 (2 m, 2 H, 3-H, 4-H), 6.80 – 6.85 (m, 4 H, Ar-H), 7.02 – 7.06 (m, 4 H, Ar-H). $^{13}$C NMR (75.5 MHz, CDCl$_3$): $\delta = 13.6$ (q, 5-CH$_3$), 49.3 (d, 2-CH), 55.2 (q, 2 × OCH$_3$), 105.8, 108.7 (2 d, C-3, C-4), 113.7 (d, 4 × C$_{ar}$), 134.6 (s, 2 × C$_{ar}$), 151.3, 155.5 (2 s, C-2, C-5), 158.2 (s, 2 × C$_{ar}$-OCH$_3$). GC-MS: $t_R = 12.36$ min; $m/z$ (%) = 308 (100) [M$^+$], 293 (9) [M$^+$ – CH$_3$], 277 (27) [M$^+$ – OCH$_3$], 265 (93), 250 (29), 234 (8), 218 (6), 201 (71), 185 (18), 115 (12).

NMR data for compound 4a are in accordance with the previously published data.\[S6\]

2-[1-(4-Methoxyphenyl)ethyl]-5-methylfuran (4b)

According to the typical reaction procedure, 1-(1-chloroethyl)-4-methoxybenzene (1.00 g, 5.86 mmol) was added to 25 mL of a solution of 2-methylfuran (2.05 g, 25.0 mmol) and 2,6-lutidine (691 mg, 6.45 mmol) in 2,2,2-trifluoroethanol (T) and stirred for 30 min at ambient temperature. After the usual workup and purification by column chromatography on silica gel (pentane/ether : 7/1) 887 mg of 4b (4.10 mmol; 70%) was isolated as a colorless oil.

$^1$H NMR (300 MHz, CDCl$_3$): $\delta = 1.53$ (d, $J = 7.2$ Hz, 3 H, CH$_3$), 2.22 (s, 3 H, 5-CH$_3$), 3.77 (s, 3 H, OCH$_3$), 4.01 (q, $J = 7.2$ Hz, 1 H, 2-CH), 5.83 – 5.87 (m, 2 H, 3-H, 4-H), 6.81 – 6.83 (m, 2 H, Ar-H), 7.12 – 7.15 (m, 2 H, Ar-H). $^{13}$C NMR (75.5 MHz, CDCl$_3$): $\delta = 13.5$ (q, 5-CH$_3$), 20.8 (q), 38.4 (d, 2-CH), 55.2 (q, OCH$_3$), 105.3, 105.7 (2 d, C-3, C-4), 113.8 (d, 2 × C$_{ar}$), 128.2 (d, 2 × C$_{ar}$), 136.6 (s, C$_{ar}$), 150.7 (s, C-2), 157.5, 158.1 (2 s, C-5, C$_{ar}$-OCH$_3$). GC-MS: $t_R = 7.85$ min; $m/z$ (%) = 216 (25) [M$^+$], 201 (100) [M$^+$ – CH$_3$], 186 (9), 158 (10). Anal. Calcd. for C$_{14}$H$_{16}$O$_2$ (216.28): C, 77.75; H, 7.46. Found: C, 77.47; H, 7.32.

2-Methyl-5-(1-thiophen-2-ylethyl)furan (4c)

According to the typical reaction procedure, 2-chloro-2-thiencylethane (1.56 g, 10.6 mmol) was added to 50 mL of a solution of 2-methylfuran (4.11 g, 50.0 mmol) in 90% aqueous
acetonitrile (v/v) (90AN10W) and ammonium hydrogen carbonate (1.68 g, 21.2 mmol) and stirred for 24 h at ambient temperature. After the usual workup, purification by column chromatography on silica gel (CH₂Cl₂) and distillation, 980 mg of 4c (5.10 mmol; 48%) was isolated as a colorless oil, b.p. 115 – 117 °C/3.0 mbar.

1H NMR (400 MHz, CDCl₃): δ = 1.65 (d, J = 7.2 Hz, 3 H, CH₂CH₃), 2.25 (s, 3 H, 2-CH₃), 4.35 (q, J = 7.2 Hz, 1 H, CHCH₃), 5.87, 5.93 (2 m, 2 × 1 H, 3-H, 4-H), 6.85, 6.92, 7.14 (3 m, 3 × 1 H, C₆H₅S). 13C NMR (100 MHz, CDCl₃): δ = 13.5 (q, 2-CH₃), 21.5 (q), 34.6 (d, CHCH₃), 105.4, 105.8 (2 d, C-3, C-4), 123.4, 123.7, 126.5 (3 d), 148.1, 150.9, 156.4 (3 s). GC-MS: t_R = 7.01 min; m/z (%) = 192 (33) [M⁺], 177 (100) [M⁺ – CH₃], 149 (7), 134 (9), 115 (8).

2-Benzhydryl-5-methylfuran (4d)

According to the typical reaction procedure, benzhydryl chloride (1.01 g, 5.00 mmol) was added to 25 mL of a solution of 2-methylfuran (2.05 g, 25.0 mmol) in 2,2,2-trifluoroethanol (T) and ammonium hydrogen carbonate (589 mg, 5.50 mmol) and stirred for 2 h at ambient temperature. After the usual workup and purification by column chromatography on silica gel (pentane/ether : 7/1) 1.08 g of 4d (4.35 mmol; 87%) was isolated as a yellow oil.

1H NMR (300 MHz, CDCl₃): δ = 2.24 (s, 3 H, 5-CH₃), 5.39 (s, 1 H, 2-CH), 5.74 – 5.75, 5.86 – 5.87 (2 m, 2 H, 3-H, 4-H), 7.16 – 7.31 (m, 10 H, Ar-H). 13C NMR (75.5 MHz, CDCl₃): δ = 13.6 (q, 5-CH₃), 51.0 (d, 2-CH), 105.9, 109.1, (2 d, C-3, C-4), 126.6 (d, 2 × C₆H₅), 128.3, 128.8 (2 d, 8 × C₆H₅), 142.1 (s, 2 × C₆H₅), 151.5, 154.8 (2 s, C-2, C-5). GC-MS: t_R = 8.80 min; m/z (%) = 248 (95) [M⁺], 233 (14) [M⁺ – CH₃], 205 (87), 171 (100) [M⁺ – C₆H₅], 167 (19) [Ph₂CH⁺], 128 (18).

2-(4-Methoxybenzyl)-5-methylfuran (4e)

According to the typical reaction procedure, 4-methoxybenzyl bromide (1.00 g, 4.97 mmol) was added to 25 mL of a solution of 2-methylfuran (2.05 g, 25.0 mmol) in 90% aqueous acetonitrile (v/v) (90AN10W) and ammonium hydrogen carbonate (786 mg, 9.94 mmol) and stirred for 2 h at ambient temperature. After the usual workup and purification by column chromatography on silica gel (pentane/ether : 7/1) 737 mg of 4e (3.64 mmol; 73%) was isolated as a colorless liquid.

1H NMR (300 MHz, CDCl₃): δ = 2.30 (s, 3 H, CH₃), 3.77 (s, 3 H, OCH₃), 3.84 (s, 2 H, CH₂), 5.81 – 5.84 (m, 2 H, 3-H, 4-H), 6.81 – 6.84 (m, 2 H, Ar-H), 7.13 – 7.16 (m, 2 H, Ar-H). 13C
NMR (75.5 MHz, CDCl3): δ = 13.5 (q, 5-CH₃), 33.7 (t), 55.2 (q, OCH₃), 105.9, 106.6 (2 d, C-3, C-4), 113.8, 129.6 (2 d, 4 × C_ar), 130.5 (s, C_ar), 150.8, 153.2 (2 s, C-2, C-5), 158.2 (s, C_ar–OCH₃). GC-MS: t_R = 7.76 min; m/z (%) = 202 (100) [M⁺], 187 (41) [M⁺ – CH₃], 171 (39) [M⁺ – OCH₃], 159 (35), 144 (35), 115 (16), 95 (12). Anal. Calcd. for C₁₃H₁₄O (202.25): C, 77.20; H, 6.98. Found: C, 76.90; H, 6.53.

1H NMR and MS data for compound 4e were published previously.[⁸³]

2-Methyl-5-(3-phenylallyl)furan (4f)

According to the typical reaction procedure, cinnamyl bromide (985 mg, 5.00 mmol) was added to 25 mL of a solution of 2-methylfuran (2.05 g, 25.0 mmol) in 90% aqueous acetonitrile (v/v) (90AN10W) and ammonium hydrogen carbonate (791 mg, 10.0 mmol) and stirred for 1 d at ambient temperature. After the usual workup and purification by column chromatography on silica gel (PE/EA : 10/1) 605 mg (3.05 mmol; 61%) of a mixture (5.2:1; NMR) of 4f and the allylic isomer 2-Methyl-5-(1-phenylallyl)furan were isolated as an orange oil. The following NMR data were derived from the mixture of isomers.

2-Methyl-5-(3-phenylallyl)furan: 1H NMR (300 MHz, CDCl₃): δ = 2.26 (s, 3 H, 2-CH₃), 3.49 (d, J = 6.8 Hz, 2 H, 5-CH₂), 5.87 – 5.92 (m, 2 × 1 H, 3-H, 4-H), 6.24 – 6.32 (m, 1 H, 2-CH₂C=CH), 6.46 – 6.51 (m, 1 H, 2-CH₂CH=CH₂), 7.22 – 7.37 (m, 5 H, Ar-H). 13C NMR (75.5 MHz, CDCl₃): δ = 13.5 (q, 2-CH₃), 31.8 (t), 106.0, 106.2 (2 d, C-3, C-4), 125.9 (d, C_ar), 126.2 (d, 2 × C_ar), 127.2 (d, CH₂CH=CH₂), 128.5 (d, 2 × C_ar), 131.7 (d, CH₂CH=CH₂), 137.3 (s, C_ar), 150.8, 152.1 (2 s, C-2, C-5). GC-MS: t_R = 7.85 min; m/z (%) = 198 (100) [M⁺], 183 (20) [M⁺ – CH₃], 155 (99), 141 (22), 128 (24), 115 (35), 95 (32), 77 (26) [Ph⁺].

2-Methyl-5-(1-phenylallyl)furan: 1H NMR (300 MHz, CDCl₃): δ = 2.24 (s, 3 H, 2-CH₃), 4.67 (d, J = 6.0 Hz, 1 H, 5-CH), 5.01 – 5.07, 5.16 – 5.19 (2 m, 2 H, C=CH₂), 5.37 – 5.92 (m, 3-H, 4-H), 6.13 – 6.22 (m, 1 H, CH=CH₂), 7.22 – 7.37 (m, 5 H, Ar-H). GC-MS: t_R = 7.23 min; m/z (%) = 198 (95) [M⁺], 183 (32) [M⁺ – CH₃], 171 (60) [M⁺ – CH₂CH₂], 155 (100), 128 (25), 115 (35), 91 (19), 77 (33) [Ph⁺].

1H NMR and MS data for compounds 4f and its allylic isomer were published previously.[⁸⁷]
References:


