Diastereoselective oxidative cross-coupling reactions of chiral alkylbenzenes with arenes and silyl nucleophiles

Supporting Information

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1. Synthetic Procedures and Analytical Data

General Methods:

All reactions, sensitive to air or moisture, were carried out in flame-dried glassware under positive pressure of argon using standard Schlenk techniques. Flash chromatography was performed on silica gel 60 (Merck, 230-400 mesh) with the eluent mixtures given for the corresponding procedures. Thin layer chromatography (TLC) was performed on silica coated glass plates (silica gel 60 F 254). Compounds were detected by UV (λ = 254 nm, 366 nm) and CAM (cerium ammonium molybdate solution). Technical solvents (n-pentane, ethyl acetate) employed for preparative column chromatography were purified by distillation prior to use. Chemical shifts are reported relative to the solvent (CHCl₃: δ (¹H) = 7.26 ppm, δ (¹³C) = 77.0 ppm) as reference. Anhydrous FeCl₂ was purchased from Sigma Aldrich and was stored in an argon-filled glove box. All other chemicals were used as received from commercial suppliers. The silyl nucleophiles were synthesized by following known procedures: [(3,3-dimethylbut-1-en-2-yl)oxy]trimethylsilane,¹ 4-[(trimethylsilyl)oxy]pent-3-en-2-one.² 2,3,3-trimethylbutanal was synthesized according to a previous used method.³

Initial Study towards the Oxidative Cross-Coupling Reaction of 3 to form 4a:

![Chemical structure of 3 and 4a]

<table>
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<th>Entryᵃ</th>
<th>Additive</th>
<th>DDQ</th>
<th>Solvent</th>
<th>T</th>
<th>Yield [%]</th>
<th>d.r.</th>
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<td>2.2 eq.</td>
<td>MeNO₂</td>
<td>r.t.</td>
<td>61</td>
<td>&gt;95:5</td>
</tr>
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<tr>
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<td>b</td>
<td>-</td>
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<td>5</td>
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<td>traces</td>
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<tr>
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<td>r.t.</td>
<td>55</td>
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</table>

ᵃAll reactions were carried out under anhydrous conditions within 60 min, 3 (200 μmol), Nu-TMS (800 μmol), Solvent (c = 200 mM).
ᵇOnly elimination takes place.
ᶜ3 (200 μmol), Nu-TMS (400 μmol), Solvent (c = 200 mM).
ᵈ3 (200 μmol), Nu-TMS (800 μmol), Solvent (c = 400 mM).
General Procedure 1 for the DDQ-mediated Oxidation of Benzylic C-H Bonds Catalyzed with FeCl₂

To a solution of the substrate 3 (200 μmol, 1.0 eq.), nucleophile (800 μmol, 4.0 eq.), FeCl₂ (40 μmol, 0.2 eq.) and nitromethane (c = 100 mM) in a flame-dried flask was added 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (260 μmol, 1.3 eq.) at room temperature. After one hour the solvent was removed under reduced pressure and the crude mixture was purified by flash column chromatography to afford the product.

General Procedure 2 for the DDQ-mediated Oxidation of Benzylic C-H Bonds

To a solution of the substrate 5 (200 μmol, 1.0 eq.), nucleophile (800 μmol, 4.0 eq.), and nitromethane (c = 100 mM) in a flame-dried flask was added 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (260 μmol, 1.3 eq.) at room temperature. After one hour the solvent was removed under reduced pressure and the crude mixture was purified by flash column chromatography to afford the product.

1-(2,4-Dimethoxyphenyl)-2,3,3-trimethylbutan-1-ol

A solution of 2.97 mL 1-bromo-2,4-dimethoxybenzene (4.48 g, 20.6 mmol, 1.2 eq.) in THF (34 mL) was cooled to –78 °C and within 15 minutes 7.57 mL n-BuLi (2.5 M in hexane, 18.9 mmol, 1.1 eq.) was added. After another 30 minutes at –78 °C, 1.96 g 2,3,3-trimethylbutanal (17.2 mmol, 1.0 eq.) in THF (6 mL) was added and the solution was stirred for 1 hour before it was allowed to warm to room temperature within 1 hour. After addition of NH₄Cl(aq) (40 mL), the layers were separated and the aqueous layer was extracted with diethylether (3×50 mL). The combined organic layers were washed with brine, dried over Na₂SO₄, filtered and the solvent was removed under reduced pressure. The residue was subjected to flash column chromatography (pentane : ethyl acetate = 20 : 1) to afford the alcohol as a yellow oil (1.86 g, 43%).

**TLC:** Rₕ = 0.51 (P:EtOAc 9:1 [UV/CAM]).

**IR** (ATR): \( \tilde{\nu} = 3545 \, (m, \, OH), \, 2942 \, (m, \, sp^3-CH), \, 1611 \, (m), \, 1585 \, (m), \, 1499 \, (m), \, 1463 \, (m), \, 1250 \, (s), \, 1206 \, (s), \, 1153 \, (s), \, 1125 \, (s), \, 1108 \, (s), \, 1038 \, (s), \, 835 \, (s) \, cm^{-1}. \)
$^1$H-NMR (360 MHz, CDCl$_3$, 300 K): $\delta$ [ppm] = 0.81 (d, $^3J = 7.2$ Hz, 3H, CHCH$_3$), 1.03 [s, 9H, C(CH$_3$)$_3$], 1.50 (qd, $^3J = 7.2$, 2.8 Hz, 1H, CHCH$_3$), 1.68 (d, $^3J = 4.8$ Hz, 1H, OH), 3.79 (s, 3H, OCH$_3$), 3.80 (s, 3H, OCH$_3$), 5.34 (d, $^3J = 2.8$ Hz, 1H, CHO), 6.43 (d, $^3J = 2.4$ Hz, 1H, CH$_{ar}$), 6.49 (dd, $^3J = 8.5$ Hz, $^4J = 2.4$ Hz, 1H, CH$_{ar}$), 7.30 (d, $^3J = 8.5$ Hz, 1H, CH$_{ar}$).

$^{13}$C-NMR (91 MHz, CDCl$_3$, 300 K): $\delta$ [ppm] = 7.0 (q, CHC$_3$), 28.4 [q, C(CH$_3$)$_3$], 33.5 [s, C(CH$_3$)$_3$], 47.2 (d, CHCH$_3$), 55.0 (q, OCH$_3$), 55.3 (q, OCH$_3$), 68.7 (d, CHO), 98.3 (d, C$_{ar}$), 103.5 (d, C$_{ar}$), 126.6 (s, C$_{ar}$), 127.1 (d, C$_{ar}$), 156.6 (s, C$_{ar}$), 159.5 (s, C$_{ar}$).

MS (EI, 70 eV): $m/z$ (%) = 252 (1) [C$_{15}$H$_{24}$O$_3$]$^+$, 234 (4) [C$_{15}$H$_{22}$O$_2$]$^+$, 167 (100) [C$_3$H$_{11}$O$_3$]$^+$.

CHN (C$_{15}$H$_{24}$O$_3$): calcd.: C: 71.39, H: 9.59; found: C: 71.40, H: 9.64.

2,4-Dimethoxy-1-(2,3,3-trimethylbutyl)benzene (3)

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\text{To a solution of 1.87 g 1-(2,4-dimethoxyphenyl)-2,3,3-trimethylbutan-1-ol (7.40 mmol, 1.0 eq.) in dichloromethane (20 mL) was added 2.36 mL Et$_3$SiH (1.72 g, 14.8 mmol, 2.0 eq.). The reaction was cooled to 0 °C and 1.83 mL BF$_3\cdot$Et$_2$O (2.10 g, 14.8 mmol, 2.0 eq.) was slowly added. After stirring for one hour at 0 °C the reaction was carefully quenched with saturated aqueous NaHCO$_3$ (10 mL). The organic layer was collected, washed with saturated aqueous NaCl (10 mL), dried over Na$_2$SO$_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (pentane) to give 3 (1.53 g, 88%) as a colorless oil.}

TLC: $R_f = 0.89$ (P:EtOAc 9:1 [UV/CAM]).

IR (ATR): $\tilde{\nu}$ = 2956 (m, sp$^3$-CH), 1611 (m), 1587 (m), 1505 (s), 1464 (m), 1285 (s), 1206 (s), 1154 (s), 1125 (s), 1132 (s), 1038 (s), 833 (m) cm$^{-1}$.

$^1$H-NMR (250 MHz, CDCl$_3$, 300 K): $\delta$ [ppm] = 0.70 (d, $^3J = 6.8$ Hz, 3H, CHCH$_3$), 0.95 [s, 9H, C(CH$_3$)$_3$], 1.45 (dqd, $^3J = 11.1$, 6.8, 2.6 Hz, 1H, CHCH$_3$), 2.00 (dd, $^3J = 13.0$ Hz, $^3J = 11.1$ Hz, 1H, CH$_2$), 2.87 (dd, $^3J = 13.0$ Hz, $^3J = 2.6$ Hz, 1H, C$_{ar}$), 3.78 (s, 3H, OCH$_3$), 3.80 (s, 3H, OCH$_3$), 6.38-6.45 (m, 2H, CH$_{ar}$), 6.98 (d, $^3J = 7.9$ Hz, 1H, C$_{ar}$).

$^{13}$C-NMR (63 MHz, CDCl$_3$, 300 K): $\delta$ [ppm] = 13.7 (q, CHCH$_3$), 27.4 [q, C(CH$_3$)$_3$], 31.9 (t, CH$_2$), 33.2 [s, C(CH$_3$)$_3$], 43.5 (d, CHCH$_3$), 55.2 (q, OCH$_3$), 55.3 (q, OCH$_3$), 98.5 (d, C$_{ar}$), 103.6 (d, C$_{ar}$), 123.6 (s, C$_{ar}$), 130.9 (d, C$_{ar}$), 158.5 (s, C$_{ar}$), 158.9 (s, C$_{ar}$).

MS (EI, 70 eV): $m/z$ (%) = 236 (12) [C$_{15}$H$_{24}$O$_2$]$^+$, 151 (100) [C$_3$H$_{11}$O$_3$]$^+$.
2,3,3-Trimethyl-1-(2,4,6-trimethoxyphenyl)butan-1-ol

A solution of 2.98 g 1,3,5-trimethoxybenzene (17.7 mmol, 1.35 eq.) in THF (20 mL) was cooled to −40 °C and within 15 minutes 7.20 mL n-BuLi (2.5 M in hexane, 18.0 mmol, 1.37 eq.) was added. After another hour at −40 °C, 1.50 g 2,3,3-trimethylbutanal (13.1 mmol, 1.0 eq.) in THF (5 mL) was added and the solution was stirred for 1 hour before it was allowed to warm to room temperature within 1 hour. After addition of NH₄Cl(aq) (30 mL), the layers were separated and the aqueous layer was extracted with diethylether (3×30 mL). The combined organic layers were washed with brine, dried over Na₂SO₄, filtered and the solvent was removed under reduced pressure. The residue was subjected to flash column chromatography (pentane : ethyl acetate = 9 : 1) to afford the alcohol as a yellow oil (1.96 g, 46%).

**TLC:** Rᵋ = 0.26 (pentane : ethyl acetate = 9:1 [UV/CAM]).

**IR** (ATR): \( \tilde{\nu} = 3520 \text{ (w, OH)}, \ 2940 \text{ (m, sp}^3\text{-CH}), \ 1605 \text{ (s), 1592 (s), 1456 (m), 1416 (m), 1219 (s), 1203 (s), 1148 (s), 1121 (s), 813 \text{ cm}^{-1}. \)

**¹H-NMR** (250 MHz, CDCl₃, 300 K): δ [ppm] = 0.90 (d, \( ^3J = 7.2 \text{ Hz}, 3\text{H}, \text{CH}_3\)), 0.99 [s, 9H, C(CH₃)₃], 1.39 (qd, \( ^3J = 7.2, 2.3 \text{ Hz}, 1\text{H}, CHCH₃)), 3.80 (s, 3H, OCH₃), 3.81 (s, 6H, OCH₃), 4.15 (d, \( ^3J = 10.9 \text{ Hz}, 1\text{H}, OH\)), 5.40 (dd, \( ^3J = 10.9, 2.3 \text{ Hz}, 1\text{H}, CHOH\)), 6.13 (s, 2H, CH₉₆).

**¹³C-NMR** (91 MHz, CDCl₃, 300 K): δ [ppm] = 8.6 (q, CHCH₃), 28.4 [q, C(CH₃)₃], 33.6 [s, C(CH₃)₃], 48.8 (d, CHCH₃), 55.3 (q, OCH₃), 55.6 (q, OCH₃), 69.9 (d, CHOH), 91.2 (d, C₉₆), 113.6 (s, C₉₆), 158.2 (s, C₉₆), 159.7 (s, C₉₆).

**MS** (EI, 70 eV): \( m/z \) (%) = 264 (73) [C₁₆H₂₄O₃]⁺, 249 (100).

**CHN** (C₁₆H₂₆O₄): calcd.: C: 68.06, H: 9.28; found: C: 68.25, H: 9.33.

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1,3,5-Trimethoxy-2-(2,3,3-trimethylbutyl)benzene (5)

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**MS** (EI, 70 eV): \( m/z \) (%) = 264 (73) [C₁₆H₂₄O₃]⁺, 249 (100).

**CHN** (C₁₆H₂₆O₄): calcd.: C: 68.06, H: 9.28; found: C: 68.25, H: 9.33.
To a solution of 1.96 g 2,3,3-trimethyl-1-(2,4,6-trimethoxyphenyl)butan-1-ol (6.93 mmol, 1.0 eq.) in dichloromethane (20 mL) was added 2.22 mL Et₃SiH (1.62 g, 13.9 mmol, 2.0 eq.). The reaction was cooled to 0 °C and 1.97 mL BF₃·Et₂O (2.27 g, 13.9 mmol, 2.0 eq.) was slowly added. After stirring for one hour at 0 °C the reaction was carefully quenched with saturated aqueous NaHCO₃ (10 mL). The organic layer was collected, washed with saturated aqueous NaCl (10 mL), dried over Na₂SO₄, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (pentane : ethyl acetate = 50 : 1) to give 5 (1.79 g, 97%) as a colorless oil.

**TLC:** R<sub>f</sub> = 0.77 (P:EtOAc 9:1 [UV/CAM]).

**IR** (ATR): \( \tilde{\nu} = 2957 \text{ (m, sp}^3\text{-CH), 1594 (s), 1455 (m), 1217 (m), 1130 (s), 1062 (m), 951 (m), 809 (s) cm}^{-1}. \)

**1H-NMR** (250 MHz, CDCl₃, 300 K): \( \delta \text{ [ppm]} = 0.66 \text{ (d, } \frac{3}{2} J = 6.9 \text{ Hz, 3H, CHCH}_3), 0.94 \text{ [s, 9H, C(CH}_3)_3], 1.45 \text{ (dqd, } \frac{3}{2} J = 10.9, 6.9, 2.7 \text{ Hz, 1H, CHCH}_3), 2.3 \text{ (dd, } \frac{3}{2} J = 12.6 \text{ Hz, } \frac{3}{2} J = 10.9 \text{ Hz, 1H, CHH}), 2.63 \text{ (dd, } \frac{3}{2} J = 12.6 \text{ Hz, } \frac{3}{2} J = 2.7 \text{ Hz, 1H, CHH}), 3.78 \text{ (s, 6H, OCH}_3), 3.81 \text{ (s, 3H, OCH}_3), 6.13 \text{ (s, 2H, CH}_2). \)

**13C-NMR** (63 MHz, CDCl₃, 300 K): \( \delta \text{ [ppm]} = 13.7 \text{ (q, CHCH}_3), 24.6 \text{ (t, CH}_2), 27.4 \text{ [q, C(CH}_3)_3], 33.4 \text{ [s, C(CH}_3)_3], 43.1 \text{ (d, CHCH}_3), 55.3 \text{ (q, OCH}_3), 55.5 \text{ (q, OCH}_3), 90.5 \text{ (d, C}_ar), 112.0 \text{ (s, C}_ar), 158.9 \text{ (s, C}_ar), 159.1 \text{ (s, C}_ar). \)

**MS** (EI, 70 eV): \( m/z \% = 266 \text{ (10) [C}_{16}H_{26}O_3]^+, 181 \text{ (100) [C}_{16}H_{13}O_3]^+. \)

**CHN** (C₁₆H₂₆O₃): calcd.: C: 72.14, H: 9.84; found: C: 71.97, H: 9.90.

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5-(2,4-Dimethoxyphenyl)-2,2,6,7,7-pentamethyloctan-3-one (4a)

According to general procedure 1, 47.3 mg 2,4-dimethoxy-1-(2,3,3-trimethylbutyl) benzene (3) (200 μmol), 138 mg [(3,3-dimethylbut-1-en-2-yl)oxy]trimethylsilane (800 μmol), 5.1 mg FeCl₂ (40 μmol), 70.2 mg DDQ (260 μmol) and MeNO₂ (2 mL) yielded after one hour reaction time and flash column chromatography (pentane/ethyl acetate = 50 : 1) the product 4a as a colorless oil (43.5 mg, 65%). A single diastereoisomer (d.r. > 95/5) was obtained.

**TLC:** R<sub>f</sub> = 0.39 (P:EtOAc 20:1 [UV/CAM]).
IR (ATR): $\tilde{\nu} = 2956$ (m, sp$^3$-CH), 1704 (s, CO), 1610 (s), 1464 (s), 1291 (s), 1206 (s), 1156 (s), 1037 (s), 833 (m) cm$^{-1}$.

$^1$H-NMR (250 MHz, CDCl$_3$, 300 K): $\delta$ [ppm] = 0.84 [s, 9H, CHC(CH$_3$)$_3$], 0.84 (d, $^3J = 7.2$ Hz, 3H, CHCH$_3$), 1.03 [s, 9H, C(O)C(CH$_3$)$_3$], 1.46 (qd, $^3J = 7.2$, 3.7 Hz, 1H, CHCH$_3$), 2.78 (dd, $^2J = 17.4$ Hz, $^3J = 6.6$ Hz, 1H, C=H), 2.93 (dd, $^2J = 17.4$ Hz, $^3J = 7.6$ Hz, 1H, CHH), 3.73-3.76 (m, 1H, CH), 3.77 (s, 3H, OCH$_3$), 3.81 (s, 3H, OCH$_3$), 6.32-6.42 (m, 2H, CH$_{ar}$), 7.00-7.06 (m, 1H, CH$_{ar}$).

$^{13}$C-NMR (91 MHz, CDCl$_3$, 300 K): $\delta$ [ppm] = 11.7 (q, CHC(CH$_3$)$_3$), 26.2 [q, C(O)C(CH$_3$)$_3$], 26.8 (d, Ar-CH), 34.4 [s, CHC(CH$_3$)$_3$], 44.0 (t, CH$_2$), 44.0 [s, C(O)C(CH$_3$)$_3$], 46.9 (d, CHCH$_3$), 55.1 (q, OCH$_3$), 55.1 (q, OCH$_3$), 98.4 (d, C$_{ar}$), 103.5 (d, C$_{ar}$), 124.8 (s, C$_{ar}$), 130.4 (d, C$_{ar}$), 158.3 (s, C$_{ar}$), 158.7 (s, C$_{ar}$), 214.4 (s, C-3).

MS (EI, 70 eV): $m/z$ (%) = 334 (9) [C$_{21}$H$_{34}$O$_3$]$^+$, 249 (55) [C$_{15}$H$_{21}$O$_3$]$^+$, 57 (100) [C$_4$H$_9$]$^+$.

CHN (C$_{21}$H$_{34}$O$_3$): calcd.: C: 75.41, H: 10.25; found: C: 75.16, H: 10.30.

2,4-Dimethoxy-1-(5,6,6-trimethylhept-1-en-4-yl)benzene (4b)

![Structure of 2,4-Dimethoxy-1-(5,6,6-trimethylhept-1-en-4-yl)benzene (4b)](image)

d.r. 71:29

$\text{MW: 276.41}$

According to general procedure 1, 47.3 mg 2,4-dimethoxy-1-(2,3,3-trimethylbutyl) benzene (3) (200 $\mu$mol), 91.4 mg allyltrimethylsilane (800 $\mu$mol), 5.1 mg FeCl$_2$ (40 $\mu$mol), 70.2 mg DDQ (260 $\mu$mol) and MeNO$_2$ (2 mL) yielded after one hour reaction time and flash column chromatography (pentane : ethyl acetate = 50 : 1) the product 4b as a colorless oil (41.5 mg, 75%) with a syn/anti ratio of 71:29.

TLC: $R_f = 0.75$ (P:EtOAc 20:1 [UV/CAM]).

IR (ATR): $\tilde{\nu} = 2954$ (m, sp$^3$-CH), 1611 (m), 1585 (m), 1504 (s), 1464 (m), 1292 (m), 1207 (s), 1157 (s), 1134 (m), 1038 (s), 906 (m), 833 (m) cm$^{-1}$.

$^1$H-NMR (500 MHz, CDCl$_3$, 300 K): $\delta$ [ppm] = 0.85 (d, $^3J = 7.3$ Hz, 3H, CHCH$_3$), 0.97 [s, 9H, (CH$_3$)$_3$], 1.19 (qd, $^3J = 7.3$, 2.2 Hz, 1H, CHCH$_3$), 2.30-2.50 (m, 2H, CH$_2$), 3.43 (ddd, $^3J = 12.1$, 3.6, 2.2 Hz, 1H, ArCH), 3.79 (s, 3H, OCH$_3$), 3.79 (s, 3H, OCH$_3$), 4.81 (ddt, $^2J = 1.3$ Hz, $^3J = 10.2$ Hz, $^4J = 2.4$ Hz, 1H, C=CHH), 4.92 (ddt, $^2J = 1.3$ Hz, $^3J = 17.0$ Hz, $^4J = 1.6$ Hz, 1H, C=CHH), 5.59 (ddt, $^3J = 17.0$, 10.2, 6.6 Hz, 1H, $HC$=CHH), 6.40-6.46 (m, 2H, CH$_{ar}$), 7.07-7.11 (m, 1H, CH$_{ar}$).
\(^{13}\text{C NMR}\) (91 MHz, CDCl\(_3\), 300 K): \(\delta\) [ppm] = 9.81 (q, CHCH\(_3\)), 28.7 [q, (CH\(_3\))\(_3\)], 33.0 (t, CH\(_2\)), 34.4 [s, C(CH\(_3\))\(_3\)], 36.6 (d, ArCH), 47.3 (d, CHCH\(_3\)), 55.1 (q, OCH\(_3\)), 55.2 (q, OCH\(_3\)), 98.6 (d, C\(_{ar}\)), 103.4 (d, C\(_{ar}\)), 114.7 (t, HC=CH\(_2\)), 127.2 (s, C\(_{ar}\)), 128.1 (d, C\(_{ar}\)), 138.4 (d, HC=CH\(_2\)), 157.9 (s, C\(_{ar}\)), 158.6 (s, C\(_{ar}\)).

**anti-diastereomer**

\(^1\text{H-NMR}\) (500 MHz, CDCl\(_3\), 300 K): \(\delta\) [ppm] = 0.81 [s, 9H, (CH\(_3\))\(_3\)], 0.88 (d, \(3J = 7.2, 3H, CHCH_3\)), 1.55 (qd, \(3J = 7.2, 3.3 Hz, 1H, CHCH_3\)), 2.30-2.50 (m, 2H, CH\(_2\)), 3.49-3.58 (m, 1H, ArCH), 3.79 (s, 3H, OCH\(_3\)), 4.85 (ddt, \(2J = 1.5 Hz, 3J = 10.2 Hz, 4J = 2.3 Hz, 1H, C=CHH\)), 4.93 (ddt, \(2J = 1.5 Hz, 3J = 17.0 Hz, 4J = 1.9 Hz, 1H, C=CHH\)), 5.61-5.67 (m, 1H, HC=CH\(_2\)), 6.40-6.46 (m, 2H, CH\(_{ar}\)), 7.07-7.11 (m, 1H, CH\(_{ar}\)).

\(^{13}\text{C-NMR}\) (91 MHz, CDCl\(_3\), 300 K): \(\delta\) [ppm] = 9.81 (q, CHCH\(_3\)), 28.2 [q, C(CH\(_3\))\(_3\)], 33.0 (t, CH\(_2\)), 34.1 [s, C(CH\(_3\))\(_3\)], 36.6 (d, ArCH), 47.3 (d, CHCH\(_3\)), 55.1 (q, OCH\(_3\)), 55.1 (q, OCH\(_3\)), 98.2 (d, C\(_{ar}\)), 103.6 (d, C\(_{ar}\)), 114.9 (t, HC=CH\(_2\)), 125.0 (s, C\(_{ar}\)), 128.1 (d, C\(_{ar}\)), 138.4 (d, HC=CH\(_2\)), 157.9 (s, C\(_{ar}\)), 158.6 (s, C\(_{ar}\)).

**MS** (EI, 70 eV): \(m/z\) (%) = 276 (3) [C\(_{18}H_{28}O_2\]^+, 235 (29) [C\(_{12}H_{23}O_2\]^+, 191 (100) [C\(_{12}H_{15}O_2\]^+, 179 (52), 151 (82).

**CHN** (C\(_{18}H_{28}O_2\): calcd.: C: 78.21, H: 10.21; found: C: 77.71, H: 10.21.

\(2\)-[1-(2,4-Dimethoxyphenyl)-2,3,3-trimethylbutyl]-5-methylthiophene (4c)

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\begin{align*}
\text{C}_9\text{H}_{18}\text{O}_2\text{S} \\
\text{MW: 332.50}
\end{align*}
\]

According to general procedure 1, 47.3 mg 2,4-dimethoxy-1-(2,3,3-trimethylbutyl) benzene (3) (200 \(\mu\)mol), 78.5 mg 2-methylthiophene (800 \(\mu\)mol), 5.1 mg FeCl\(_2\) (40 \(\mu\)mol), 70.2 mg DDQ (260 \(\mu\)mol) and MeNO\(_2\) (2 mL) yielded after one hour reaction time and flash column chromatography (pentane : ethyl acetate = 40 : 1) the product 4c as a colorless oil (29.9 mg, 45%). A single diastereoisomer (d.r. > 95/5) was obtained.

**TLC**: \(R_f = 0.70\) (P:EtOAc 20:1 [UV/CAM]).

**IR** (ATR): \(\tilde{\nu} = 2954\) (m, sp\(^3\)-CH), 1609 (m), 1585 (m), 1503 (s), 1463 (m), 1291 (s), 1206 (s), 1155 (s), 1117 (m), 1037 (s), 925 (m), 795 (m) cm\(^{-1}\).

\(^1\text{H-NMR}\) (360 MHz, CDCl\(_3\), 300 K): \(\delta\) [ppm] = 0.84 [s, 9H, (CH\(_3\))\(_3\)], 0.93 (d, \(3J = 7.2 Hz, 3H, CHCH_3\)), 1.96 (qd, \(3J = 7.2, 5.3 Hz, 1H, CHCH_3\)), 2.40 (s, 3H, thiophene-CH\(_3\)), 3.77 (s, 3H,
OCH₃), 3.82 (s, 6H, OCH₃), 4.83 (d, ³J = 5.3 Hz, 1H, Ar-CH), 6.40-6.45 (m, 2H, CH_ar), 6.50-6.55 (m, 1H, thiophene-H), 7.27-7.31 (m, 1H, thiophene-H).

**1³C-NMR** (91 MHz, CDCl₃, 300 K): δ [ppm] = 12.8 (q, CH₃C), 15.2 (q, thiophene-CH₃), 28.4 [q, CHC(CH₃)₃], 34.6 [s, CHC(CH₃)₃], 40.2 (d, Ar-CH), 47.1 (d, CHCH₃), 55.3 (q, OCH₃), 55.4 (q, OCH₃), 98.7 (d, C_ar), 103.8 (d, C_ar), 124.2 (d, thiophene-C), 125.5 (d, thiophene-C), 127.4 (s, C_ar), 129.4 (d, C_ar), 137.3 (s, thiophene-C), 145.3 (s, thiophene-C), 156.8 (s, C_ar), 158.9 (s, C_ar).

**MS** (EI, 70 eV): m/z (%) = 332 (1) [C₂₀H₂₈O₂S]^+, 247 (100) [C₁₄H₁₅O₂S]^+, 111 (20).

**CHN** (C₂₀H₂₈O₂S): calcd.: C: 72.24, H: 8.49, S: 9.64; found: C: 72.34, H: 8.73, S: 9.14.

### 2-[1-(2,4-Dimethoxyphenyl)-2,3,3-trimethylbutyl]-1,3,5-trimethoxybenzene (4d)

According to general procedure 1, 47.3 mg 2,4-dimethoxy-1-(2,3,3-trimethylbutyl) benzene (3) (200 μmol), 134.6 mg 1,3,5-trimethoxybenzene (800 μmol), 5.1 mg FeCl₂ (40 μmol), 70.2 mg DDQ (260 μmol) and MeNO₂ (2 mL) yielded after one hour reaction time and flash column chromatography (pentane : ethyl acetate = 40 : 1) the product 4d as a colorless oil (70.0 mg, 87%) with a syn/anti ratio of 81:19.

**TLC:** R₉ = 0.49 (P:EtOAc 9:1 [UV/CAM]).

**IR** (ATR): v~ = 2955 (m, sp³-CH), 1722 (s, CO), 1610 (s), 1585 (m), 1504 (s), 1464 (m), 1293 (m), 1207 (s), 1157 (s), 1133 (m), 1035 (s), 922 (w), 834 (m) cm⁻¹.

**syn-diastereomer**

**¹H-NMR** (250 MHz, CDCl₃, 300 K): δ [ppm] = 0.62 (d, ³J = 7.0 Hz, 3H, CHCH₃), 0.78 [s, 9H, CHC(CH₃)₃], 2.53 (qd, ³J = 9.4, 7.0 Hz, 1H, CHCH₃), 3.60 (s, 3H, OCH₃), 3.67 (s, 3H, OCH₃), 3.74 (s, 3H, OCH₃), 3.75 (s, 6H, OCH₃), 3.88 (s, 6H, OCH₃), 4.98 (d, ³J = 9.4 Hz, 1H, Ar-CH), 5.96 (d, J = 2.4 Hz, 1H, CH_ar), 6.11 (d, J = 2.3 Hz, 1H, CH_ar), 6.29 (d, J = 2.6 Hz, 1H, CH_ar), 6.41 (dd, J = 8.7, 2.6 Hz, 1H, CH_ar), 7.63 (d, J = 8.6 Hz, 1H, CH_ar).

**¹³C-NMR** (91 MHz, CDCl₃, 300 K): δ [ppm] = 14.8 (q, CHCH₃), 26.6 [q, CHC(CH₃)₃], 32.9 [s, CHC(CH₃)₃], 35.0 (d, Ar-CH), 41.3 (d, CHCH₃), 55.0 (q, OCH₃), 55.1 (q, OCH₃), 55.1 (q,
OCH₃), 56.3 (q, OCH₃), 91.3 (d, Cₛ), 98.2 (d, Cₛ), 103.0 (s, Cₛ), 115.6 (d, Cₛ), 127.9 (s, Cₛ), 130.6 (d, Cₛ), 157.9 (s, Cₛ), 158.8 (s, Cₛ), 158.9 (s, Cₛ), 158.9 (s, Cₛ).

anti-diastereomer

¹H-NMR (250 MHz, CDCl₃, 300 K): δ [ppm] = 0.65 (d, 3J = 7.0 Hz, 3H, CHC₃H₃), 0.81 [s, 9H, CHC(CH₃)₃], 2.65 (qd, 3J = 9.1, 7.0 Hz, 1H, CHCH₃), 3.75 (s, 3H, OCH₃), 3.76 (s, 3H, OCH₃), 3.77 (s, 3H, OCH₃), 3.79 (s, 6H, OCH₃), 4.93 (d, 3J = 9.1 Hz, 1H, Ar-CH), 6.08 (s, 2H, CHar), 6.35-6.43 (m, 2H, CHar), 7.43-7.48 (m, 1H, CHar).

¹³C-NMR (91 MHz, CDCl₃, 300 K): δ [ppm] = 14.8 (q, CHC₃), 28.4 [q, CHC(CH₃)₃], 34.2 [s, CHC(CH₃)₃], 34.7 (d, Ar-CH), 42.8 (d, CHCH₃), 55.1 (q, OCH₃), 55.5 (q, OCH₃), 91.4 (d, Cₛ), 98.1 (d, Cₛ), 104.0 (s, Cₛ), 117.5 (d, Cₛ), 127.2 (s, Cₛ), 130.6 (d, Cₛ), 158.0 (s, Cₛ), 158.3 (s, Cₛ), 158.9 (s, Cₛ), 158.9 (s, Cₛ).

MS (EI, 70 eV): m/z (%) = 402 (1) [C₂₄H₃₄O₅]⁺, 317 (100) [C₁₈H₂₁O₃]⁺.

CHN (C₂₄H₃₄O₅): calcd.: C: 71.61, H: 8.51; found: C: 71.23, H: 8.61.

2-[1-(2,4-Dimethoxyphenyl)-2,3,3-trimethylbutyl]furan (4e)

According to general procedure 1, 47.3 mg 2,4-dimethoxy-1-(2,3,3-trimethylbutyl) benzene (3) (200 μmol), 112 mg 2-trimethylsilyl-furan (800 μmol), 5.1 mg FeCl₂ (40 μmol), 70.2 mg DDQ (260 μmol) and MeNO₂ (2 mL) yielded after one hour reaction time a mixture of product and TMS-substituted product. Removal of the solvent, addition of THF (5 mL) and TBAF (2 eq.), stirring the mixture over night and flash column chromatography (pentane : ethyl acetate = 40 : 1) yielded the product 4e as a colorless oil (40.5 mg, 67%) with a syn/anti ratio of 73:28.

TLC: Rf = 0.70 (P:EtOAc 10:1 [UV/CAM]).

IR (ATR): ν = 2954 (m, sp³-CH), 1610 (m), 1585 (m), 1504 (s), 1463 (m), 1292 (s), 1259 (s), 1207 (s), 1157 (s), 1117 (m), 1037 (s), 925 (m), 830 (m), 725 (m) cm⁻¹.

syn-diastereomer

¹H-NMR (360 MHz, CDCl₃, 300 K): δ [ppm] = 0.87 [s, 9H, (CH₃)₃], 0.99 (d, 3J = 7.2 Hz, 3H, CHCH₃), 1.89 (qd, 3J = 7.3, 4.1 Hz, 1H, CHCH₃), 3.81 (s, 3H, OCH₃), 3.86 (s, 3H, OCH₃), 4.86 (d, 3J = 4.1 Hz, 1H, Ar-CH), 6.10 (dd, J = 3.2, 0.9 Hz, 1H, furan-H3), 6.32 (dd, J = 3.2,
1.9 Hz, 1H, furan-H4), 6.43-6.49 (m, 2H, CH$_{ar}$), 7.24-7.28 (m, 1H, CH$_{ar}$), 7.38 (dd, $J = 1.9$, 0.9 Hz, 1H, furan-H5).

$^{13}$C-NMR (91 MHz, CDCl$_3$, 300 K): $\delta$ [ppm] = 11.6 (q, CHCH$_3$), 27.9 [q, CHC(CH$_3$)$_3$], 34.1 [s, CHC(CH$_3$)$_3$], 37.6 (d, Ar-CH), 47.0 (d, CHCH$_3$), 55.2 (q, OCH$_3$), 55.3 (q, OCH$_3$), 98.5 (d, C$_{ar}$), 103.7 (d, C$_{ar}$), 107.3 (d, furan-C), 110.1 (d, furan-C), 125.2 (s, C$_{ar}$), 129.8 (d, C$_{ar}$), 140.4 (d, furan-C), 156.8 (s, furan-C), 157.3 (s, C$_{ar}$), 159.0 (s, C$_{ar}$).

anti-diastereomer

$^1$H-NMR (360 MHz, CDCl$_3$, 300 K): $\delta$ [ppm] = 0.78 (d, $^3J = 7.1$ Hz, 3H, CH$_2$CH$_3$), 0.87 [s, 9H, (CH$_3$)$_3$], 2.16-2.28 (m, 1H, CH$_2$CH$_3$), 3.81 (s, 3H, OCH$_3$), 3.84 (s, 3H, OCH$_3$), 4.66 (d, $^3J = 7.9$ Hz, 1H, Ar-CH), 6.04 (d, $J = 3.2$ Hz, 1H, furan-H3), 6.27 (dd, $J = 3.2$, 1.9 Hz, 1H, furan-H4), 6.43-6.49 (m, 2H, CH$_{ar}$), 7.24-7.28 (m, 1H, CH$_{ar}$), 7.30 (dd, $J = 1.8$, 0.9 Hz, 1H, furan-H5).

$^{13}$C-NMR (91 MHz, CDCl$_3$, 300 K): $\delta$ [ppm] = 13.4 (q, CHCH$_3$), 28.0 [q, CHC(CH$_3$)$_3$], 34.0 [s, CHC(CH$_3$)$_3$], 37.6 (d, Ar-CH), 45.8 (d, CHCH$_3$), 55.2 (q, OCH$_3$), 55.4 (q, OCH$_3$), 98.4 (d, C$_{ar}$), 104.3 (d, C$_{ar}$), 105.4 (d, furan-C), 110.1 (d, furan-C), 123.8 (s, C$_{ar}$), 130.1 (d, C$_{ar}$), 140.1 (d, furan-C), 157.6 (s, furan-C), 158.9 (s, C$_{ar}$), 159.6 (s, C$_{ar}$).

MS (EI, 70 eV): $m/z$ (%) = 302 (1) [C$_{19}$H$_{26}$O$_3$]$^+$, 217 (100) [C$_{13}$H$_{13}$O$_3$]$^+$.

CHN (C$_{19}$H$_{26}$O$_3$): calcd.: C: 75.46, H: 8.67; found: C: 75.38, H: 8.87.

2,2,6,7,7-Pentamethyl-5-(2,4,6-trimethoxyphenyl)octan-3-one (6a)

According to general procedure 2, 53.3 mg 1,3,5-trimethoxy-2-(2,3,3-trimethylbutyl)benzene (5) (200 $\mu$mol), 138 mg [(3,3-dimethylbut-1-en-2-yl)oxy]trimethylsilane (800 $\mu$mol), 70.2 mg DDQ (260 $\mu$mol) and MeNO$_2$ (2 mL) yielded after one hour reaction time and flash column chromatography (pentane : ethyl acetate = 40 : 1) the product 6a as a colorless oil (59.8 mg, 45%). A single diastereoisomer (d.r. > 95/5) was obtained.

TLC: $R_f = 0.49$ (P:EtOAc 9:1 [UV/CAM]).

IR (ATR): $\tilde{\nu} = 2954$ (m, sp$^3$-CH), 1703 (s, CO), 1604 (m), 1589 (m), 1456 (s), 1203 (s), 1148 (s), 1118 (s), 1063 (s), 955 (m), 812 (m) cm$^{-1}$. 
1H-NMR (250 MHz, CDCl₃, 300 K): δ [ppm] = 0.86 [s, 9H, CHC(CH₃)₃], 0.98 [s, 9H, C(O)C(CH₃)₃], 1.61 (qd, 3J = 7.2, 4.5 Hz, 1H, CHCH₃), 2.54 (dd, 2J = 16.9 Hz, 3J = 4.5 Hz, 1H, CHH), 3.28 (dd, 2J = 16.9 Hz, 3J = 9.8 Hz, 1H, CHH), 3.77 (s, 3H, OCH₃), 3.79 (s, 3H, OCH₃), 3.96 (dt, 3J = 9.8, 4.5 Hz, 1H, Ar-CH), 6.07 (s, 2H, CHar).

13C-NMR (91 MHz, CDCl₃, 300 K): δ [ppm] = 12.5 (q, CHC(CH₃)₃), 26.4 [q, C(O)C(CH₃)₃], 30.6 (d, Ar-CH), 34.8 [s, CHC(CH₃)₃], 44.1 [s, C(O)C(CH₃)₃], 46.8 (d, CHCH₃), 55.1 (q, OCH₃), 90.9 (d, C_ar), 117.1 (s, C_ar), 158.9 (s, C_ar), 215.6 (s, C-3).

MS (EI, 70 eV): m/z (%) = 364 (9) [C₂₂H₃₆O₄]+, 279 (100) [C₁₆H₂₃O₄]+, 57 (67) [C₄H₉]+.


1,3,5-Trimethoxy-2-(5,6,6-trimethylhept-1-en-4-yl)benzene (6b)

According to general procedure 2, 53.3 mg 1,3,5-trimethoxy-2-(2,3,3-trimethylbutyl)benzene (5) (200 μmol), 91.4 mg allyltrimethylsilane (800 μmol), 70.2 mg DDQ (260 μmol) and MeNO₂ (2 mL) yielded after one hour reaction time and flash column chromatography (pentane : ethyl acetate = 40 : 1) the product 6b as a colorless oil (60.7 mg, 99%). A single diastereoisomer (d.r. > 95/5) was obtained.

TLC: Rᵣ = 0.55 (P:EtOAc 20:1 [UV/CAM]).

IR (ATR): ν = 2953 (m, sp³-CH), 1604 (s), 1589 (s), 1455 (s), 1202 (s), 1149 (s), 1114 (s), 1062 (m), 1042 (m), 955 (m), 903 (m), 811 (s) cm⁻¹.

1H-NMR (360 MHz, CDCl₃, 300 K): δ [ppm] = 0.86 [s, 9H, (CH₃)₃], 1.02 (d, 3J = 7.2 Hz, 3H, CHCH₃), 1.67 (qd, 3J = 7.2, 4.4 Hz, 1H, CHCH₃), 2.18-2.29 (m, 1H, CHH), 2.58 (ddd, 2J = 13.9 Hz, 3J = 12.0, 7.2 Hz, 1H, CHH), 3.39 (dt, 3J = 12.0, 4.4 Hz, 1H, Ar-CH), 3.78 (s, 6H, OCH₃), 4.68-4.74 (m, 1H, C=CH₂), 4.77-4.85 (m, 1H, C=CH₂), 5.56 (ddt, 3J = 17.1, 10.3, 7.2 Hz, 1H, H=CHH), 6.08-6.13 (m, 2H, CHar).

13C-NMR (91 MHz, CDCl₃, 300 K): δ [ppm] = 12.2 (q, CHCH₃), 27.8 [q, C(CH₃)₃], 34.8 (t, CH₂), 34.8 (d, Ar-CH), 35.0 [s, C(CH₃)₃], 46.8 (d, CHCH₃), 55.0 (q, OCH₃), 55.1 (q, OCH₃), 55.7 (q, OCH₃), 90.5 (d, C_ar), 112.1 (d, C_ar), 113.6 (t, H=CH₂), 117.0 (s, C_ar), 139.6 (d, H=CH₂), 158.0 (s, C_ar), 158.8 (s, C_ar), 159.9 (s, C_ar).
MS (EI, 70 eV): \( m/z \) (%) = 306 (2) \([\text{C}_{19}\text{H}_{30}\text{O}_3]^+\), 265 (31) \([\text{C}_{16}\text{H}_{25}\text{O}_3]^+\), 221 (89) \([\text{C}_{13}\text{H}_{17}\text{O}_3]^+\), 181 (100).

CHN (\text{C}_{10}\text{H}_{30}\text{O}_3): \text{calcd.}: \text{C}: 74.47, \text{H}: 9.87; \text{found}: \text{C}: 74.04, \text{H}: 9.90.

3-[2,3,3-Trimethyl-1-(2,4,6-trimethoxyphenyl)butyl]pentan-2,4-dione (6c)

According to general procedure 2, 53.3 mg 1,3,5-trimethoxy-2-(2,3,3-trimethylbutyl)benzene (5) (200 \( \mu \text{mol} \)), 138 mg 4-[(trimethylsilyl)oxy]pent-3-en-2-one (800 \( \mu \text{mol} \)), 70.2 mg DDQ (260 \( \mu \text{mol} \)) and MeNO\(_2\) (2 mL) yielded after one hour reaction time and flash column chromatography (pentane : ethyl acetate = 10 : 1) the product 6c as a colorless oil (62.7 mg, 86%). A single diastereoisomer (d.r. > 95/5) was obtained.

TLC: \( R_f = 0.16 \) (P:EtOAc 10:1 [UV/CAM]).

IR (ATR): \( \tilde{\nu} = 2924 \text{ (m, } \text{sp}^3\text{-CH}), 1693 \text{ (s, CO), 1605 (m), 1589 (m), 1459 (m), 1204 (s), 1148 (s), 1117 (s), 1063 (s), 951 (m), 810 (m) } \text{cm}^{-1}. \)

\(^1\text{H-NMR}\) (500 MHz, CDCl\(_3\), 300 K): \( \delta \ [\text{ppm}] = 0.78 \text{ [s, } 9\text{H, } \text{(CH}_3)_3\text{], 0.78 } \text{[d, } ^3\text{J} = 7.3 \text{ Hz, 3H, CHCH}_3\text{], 1.70 } \text{[s, } 3\text{H, C(O)CH}_3\text{], 1.84 } \text{[quint., } ^3\text{J} = 7.3 \text{ Hz, 1H, CHCH}_3\text{], 2.19 } \text{[s, } 3\text{H, C(O)CH}_3\text{], 3.75 } \text{[s, } 3\text{H, OCH}_3\text{], 3.79 } \text{[s, } 3\text{H, OCH}_3\text{], 3.82 } \text{[s, } 3\text{H, OCH}_3\text{], 4.28 } \text{[dd, } ^3\text{J} = 10.9, 7.3 \text{ Hz, 1H, ArCH], 4.65 } \text{[d, } ^3\text{J} = 10.9 \text{ Hz, 1H, H}_3\text{C(O)CCHC(O)CH}_3\text{], 5.99-6.01 } \text{[m, } 1\text{H, CH}_{ar}\text{], 6.04-6.06 } \text{[m, 1H, CH}_{ar}\text{].}

\(^{13}\text{C-NMR}\) (91 MHz, CDCl\(_3\), 300 K): \( \delta \ [\text{ppm}] = 13.9 \text{ [q, CHCH}_3\text{], 26.7 } \text{[q, C(O)CH}_3\text{], 28.0 } \text{[q, CHC(CH}_3\text{)]}, 30.3 \text{ [q, C(O)CH}_3\text{], 34.3 } \text{[d, Ar-CH],34.5 } \text{[s, CHC(CH}_3\text{)]}, 47.7 \text{ (d, CHCH}_3\text{), 55.1 } \text{[q, OCH}_3\text{], 55.3 } \text{[q, OCH}_3\text{], 55.4 } \text{[q, OCH}_3\text{], 73.5 } \text{[d, H}_3\text{C(O)CCHC(O)CH}_3\text{], 90.5 } \text{[d, C}_{ar}\text{], 91.2 } \text{[d, C}_{ar}\text{], 114.0 } \text{[s, C}_{ar}\text{], 157.0 } \text{[s, C}_{ar}\text{], 159.8 } \text{[s, C}_{ar}\text{], 159.9 } \text{[s, C}_{ar}\text{], 204.3 } \text{[s, H}_3\text{C(O)CCHC(O)CH}_3\text{], 204.7 } \text{[s, H}_3\text{C(O)CCHC(O)CH}_3\text{].}

MS (EI, 70 eV): \( m/z \) (%) = 364 (5) \([\text{C}_{21}\text{H}_{32}\text{O}_5]^+\), 279 (15) \([\text{C}_{12}\text{H}_{19}\text{O}_5]^+\), 237 (100).

CHN (\text{C}_{21}\text{H}_{32}\text{O}_5): \text{calcd.}: \text{C}: 69.20, \text{H}: 8.85; \text{found}: \text{C}: 69.53, \text{H}: 9.16.

4,5,5-Trimethyl-3-(2,4,6-trimethoxyphenyl)hexanal (6d)
According to general procedure 2, 53.3 mg 1,3,5-trimethoxy-2-(2,3,3-trimethylbutyl)benzene (5) (200 μmol), 93.0 mg trimethyl(vinylhexyloxy)silane (800 μmol), 70.2 mg DDQ (260 μmol) and MeNO₂ (2 mL) yielded after one hour reaction time and flash column chromatography (pentane : ethyl acetate = 20 : 1) the product 6d as a colorless oil (25.3 mg, 86%). A single diastereoisomer (d.r. > 95/5) was obtained.

**TLC:** R₆ = 0.30 (P:EtOAc 20:1 [UV/CAM]).

**IR (ATR):** υ = 2944 (m, sp³-CH), 1719 (s, CO), 1605 (s), 1588 (s), 1455 (m), 1202 (s), 1149 (s), 1119 (s), 1060 (s), 813 (s) cm⁻¹.

**¹H-NMR (360 MHz, CDCl₃, 300 K):** δ [ppm] = 0.85 [s, 9H, (CH₃)₃], 0.96 (d, ³J = 7.2 Hz, 3H, CHCH₃), 1.74 (qd, ³J = 7.2, 4.9 Hz, 1H, CHCH₃), 2.46 (ddd, ²J = 15.4 Hz, ³J = 4.9, 2.0 Hz, 1H, CHH), 2.86 (ddd, ²J = 15.4 Hz, ³J = 11.7, 3.7 Hz, 1H, CHH), 3.78 (s, 9H, OCH₃), 3.88 (dt, ²J = 11.7, 4.9 Hz, 1H, Ar-CH), 6.09 (s, 2H, CHar), 9.46 (dd, ³J = 3.7, 2.0 Hz, 1H, CHO).

**¹³C-NMR (91 MHz, CDCl₃, 300 K):** δ [ppm] = 12.6 (q, CHCH₃), 27.8 [q, C(CH₃)₃], 30.1 (d, ArCH), 34.7 [s, C(CH₃)₃], 45.3 (t, CH₂), 46.3 (d, CHCH₃), 55.2 (q, OCH₃), 55.3 (q, OCH₃), 90.9 (d, C_ar), 115.0 (s, C_ar), 159.6 (s, C_ar), 159.6 (s, C_ar), 205.1 (d, CHO).

**MS (EI, 70 eV):** m/z (%) = 308 (8) [C₁₈H₂₈O₄]+, 223 (100) [C₁₂H₁₅O₄]+, 195 (65).

**CHN (C₁₈H₂₈O₄):** calcd.: C: 70.10, H: 9.15; found: C: 69.38, H: 9.22.

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2-Methyl-5-[2,3,3-trimethyl-1-(2,4,6-trimethoxyphenyl)butyl]thiophene (6e)

According to general procedure 2, 53.3 mg 1,3,5-trimethoxy-2-(2,3,3-trimethylbutyl)benzene (5) (200 μmol), 78.5 mg 2-methylthiophene (800 μmol), 70.2 mg DDQ (260 μmol) and MeNO₂ (2 mL) yielded after one hour reaction time and flash column chromatography (pentane : ethyl acetate = 40 : 1) the product 6e as a colorless oil (55.1 mg, 76%). A single diastereoisomer (d.r. > 95/5) was obtained.
TLC: R_f = 0.59 (P:EtOAc 20:1 [UV/CAM]).

IR (ATR): \( \tilde{\nu} = 2954 \) (m, sp\(^3\)-CH), 1604 (s), 1589 (s), 1454 (s), 1224 (m), 1203 (s), 1150 (s), 1119 (s), 1060 (m), 1040 (m), 952 (m), 810 (m), 792 (m) cm\(^{-1}\).

\(^1\)H-NMR (500 MHz, CDCl\(_3\), 300 K): \( \delta \) [ppm] = 0.81 [s, 9H, (CH\(_3\))\(_3\)], 0.81 (d, \(^3\)J = 7.0 Hz, 3H, CHCH\(_3\)), 2.36 (d, \(^3\)J = 1.1 Hz, 3H, thiophene-CH\(_3\)), 2.40 (m, 1H, CHCH\(_3\)), 3.77 (s, 3H, OCH\(_3\)), 3.83 (s, 6H, OCH\(_3\)), 4.69 (d, \(^3\)J = 8.0 Hz, 1H, Ar-CH), 6.09 (s, 2H, CH\(_{ar}\)), 6.42 (m, 1H, thiophene-H), 6.58 (d, \(^3\)J = 3.4 Hz, 1H, thiophene-H).

\(^13\)C-NMR (91 MHz, CDCl\(_3\), 300 K): \( \delta \) [ppm] = 15.3 (q, CHCH\(_3\)), 15.3 (q, Thiophen-CH\(_3\)), 28.0 [q, CHC(CH\(_3\))\(_3\)], 34.6 [s, CHC(CH\(_3\))\(_3\)], 38.7 (d, Ar-CH), 44.9 (d, CHCH\(_3\)), 55.2 (q, OCH\(_3\)), 91.1 (d, C\(_{ar}\)), 100.0 (s, C\(_{ar}\)), 123.3 (d, thiophene-C), 125.0 (d, thiophene-C), 136.9 (s, thiophene-C), 147.2 (s, thiophene-C), 159.3 (s, C\(_{ar}\)), 159.3 (s, C\(_{ar}\)).

MS (EI, 70 eV): \( m/z \) (%) = 362 (1) \([\text{C}_{21}\text{H}_{30}\text{O}_{3}\text{S}]^+\), 277 (100) \([\text{C}_{13}\text{H}_{17}\text{O}_{5}\text{S}]^+\).

CHN (C\(_{21}\)H\(_{30}\)O\(_3\)S): calcd.: C: 69.57, H: 8.34, S: 8.84; found: C: 69.95, H: 8.59, S: 8.59.

2-[1-(2,4-Dimethoxyphenyl)-2,3,3-trimethylbutyl]-1,3,5-trimethoxybenzene (6f)

According to general procedure 2, 53.3 mg 1,3,5-trimethoxy-2-(2,3,3-trimethylbutyl)benzene (5) (200 \( \mu \)mol), 111 mg 1,3-dimethoxybenzene (800 \( \mu \)mol), 70.2 mg DDQ (260 \( \mu \)mol) and MeNO\(_2\) (2 mL) yielded after one hour reaction time and flash column chromatography (pentane : ethyl acetate = 40 : 1) the product 6f as a colorless solid (38.6 mg, 48%) with a syn/anti ratio of 77:23.

TLC: R_f = 0.49 (P:EtOAc 9:1 [UV/CAM]).

IR (ATR): \( \tilde{\nu} = 2955 \) (m, sp\(^3\)-CH), 1722 (s, CO), 1610 (s), 1585 (m), 1504 (s), 1464 (m), 1293 (m), 1207 (s), 1157 (s), 1133 (m), 1035 (s), 922 (w), 834 (m) cm\(^{-1}\).

\(^1\)H-NMR (250 MHz, CDCl\(_3\), 300 K): \( \delta \) [ppm] = 0.65 (d, \(^3\)J = 7.0 Hz, 3H, CHCH\(_3\)), 0.81 [s, 9H, CHC(CH\(_3\))\(_3\)], 2.65 (qd, \(^3\)J = 9.1, 7.0 Hz, 1H, CHCH\(_3\)), 3.75 (s, 3H, OCH\(_3\)), 3.76 (s, 3H, OCH\(_3\)).
OCH₃), 3.77 (s, 3H, OCH₃), 3.79 (s, 6H, OCH₃), 4.93 (d, J = 9.1 Hz, 1H, Ar-CH), 6.08 (s, 2H, CH₃), 6.35-6.43 (m, 2H, CH₃), 7.43-7.48 (m, 1H, CH₃).

13C-NMR (91 MHz, CDCl₃, 300 K): δ [ppm] = 14.8 (q, CH₃C(H)₃), 28.4 [q, CHC(CH₃)₃], 34.2 [s, CHC(CH₃)₃], 34.7 (d, Ar-CH), 42.8 (d, CHCH₃), 55.1 (q, OCH₃), 55.5 (q, OCH₃), 91.4 (d, C₉H), 98.1 (d, C₉H), 104.0 (s, C₉H), 117.5 (d, C₉H), 127.2 (s, C₉H), 130.6 (d, C₉H), 158.0 (s, C₉H), 158.3 (s, C₉H), 158.9 (s, C₉H), 158.9 (s, C₉H).

anti-diastereomer

1H-NMR (250 MHz, CDCl₃, 300 K): δ [ppm] = 0.62 (d, J = 7.0 Hz, 3H, CH₂C(CH₃)₃), 0.78 [s, 9H, CH(CH₃)₃], 2.53 (qd, J = 9.4, 7.0 Hz, 1H, CHCH₃), 3.60 (s, 3H, OCH₃), 3.67 (s, 3H, OCH₃), 3.74 (s, 3H, OCH₃), 3.75 (s, 6H, OCH₃), 3.88 (s, 6H, OCH₃), 4.98 (d, J = 9.4 Hz, 1H, Ar-CH), 5.96 (d, J = 2.4 Hz, 1H, CH₃), 6.11 (d, J = 2.3 Hz, 1H, CH₃), 6.29 (d, J = 2.6 Hz, 1H, CH₃), 6.41 (dd, J = 8.7, 2.6 Hz, 1H, CH₃), 7.63 (d, J = 8.6 Hz, 1H, CH₃).

13C-NMR (91 MHz, CDCl₃, 300 K): δ [ppm] = 14.8 (q, CH₃C(H)₃), 26.6 [q, CHC(CH₃)₃], 32.9 [s, CHC(CH₃)₃], 35.0 (d, Ar-CH), 41.3 (d, CHCH₃), 55.0 (q, OCH₃), 55.1 (q, OCH₃), 55.1 (q, OCH₃), 56.3 (q, OCH₃), 91.3 (d, C₉H), 98.2 (d, C₉H), 103.0 (s, C₉H), 115.6 (d, C₉H), 127.9 (s, C₉H), 130.6 (d, C₉H), 157.9 (s, C₉H), 158.8 (s, C₉H), 158.9 (s, C₉H), 158.9 (s, C₉H).

MS (EI, 70 eV): m/z (%) = 402 (1) [C₂₄H₃₄O₅]+, 317 (100) [C₁₈H₂₁O₃]⁺.

CHN (C₂₄H₃₄O₅): calcd.: C: 71.61, H: 8.51; found: C: 71.23, H: 8.61.

2-[2,3,3-Trimethyl-1-(2,4,6-trimethoxyphenyl)butyl]furan (6g)

According to general procedure 2, 53.3 mg 1,3,5-trimethoxy-2-(2,3,3-trimethylbutyl)benzene (5) (200 µmol), 112 mg 2-trimethylsilyl-furan (800 µmol), 70.2 mg DDQ (260 µmol) and MeNO₂ (2 mL) yielded after one hour reaction time and flash column chromatography (pentane : ethyl acetate = 40 : 1) the product 6g as a colorless oil (28.6 mg, 43%). A single diastereoisomer (d.r. > 95/5) was obtained.

TLC: Rf = 0.65 (P:EtOAc 10:1 [UV/CAM]).

IR (ATR): ν = 2939 (m, sp³-CH), 1604 (s), 1588 (s), 1456 (s), 1203 (s), 1150 (s), 1114 (s), 1061 (m), 1042 (m), 1010 (m), 952 (m), 812 (s), 723 (s) cm⁻¹.

1H-NMR (360 MHz, CDCl₃, 300 K): δ [ppm] = 0.74 (d, J = 7.1 Hz, 3H, CHCH₃), 0.81 [s, 9H, (CH₃)₃], 2.12 (qd, J = 7.1, 5.8 Hz, 1H, CHCH₃), 3.74 (s, 3H, OCH₃), 3.75 (s, 6H, OCH₃),
4.60 (d, $^3J = 5.8$ Hz, 1H, Ar-CH), 5.84-5.85 (m, 1H, furan-H3), 6.08 (s, 2H, CH$_{ar}$), 6.14 (dd, $^3J = 3.2$, 1.8 Hz, 1H, furan-H4), 7.17 (dd, $^3J = 1.8$, 0.9 Hz, 1H, furan-H5).

$^{13}$C-NMR (91 MHz, CDCl$_3$, 300 K): δ [ppm] = 13.7 (q, CHCH$_3$), 27.7 [q, CHC(CH$_3$)$_3$], 34.6 [s, CHC(CH$_3$)$_3$], 35.7 (d, Ar-CH), 46.8 (d, CHCH$_3$), 55.2 (q, OCH$_3$), 55.6 (q, OCH$_3$), 91.3 (d, C$_{ar}$), 114.9 (s, C$_{ar}$), 105.8 (d, furan-C), 109.9 (d, furan-C), 139.4 (d, furan-C), 158.6 (s, furan-C), 159.2 (s, C$_{ar}$), 159.4 (s, C$_{ar}$).

MS (EI, 70 eV): $m/z$ (%) = 332 (1) [C$_{20}$H$_{28}$O$_4$]$^+$, 247 (100) [C$_{14}$H$_{15}$O$_4$]$^+$.

CHN (C$_{20}$H$_{28}$O$_4$): calcd.: C: 72.26, H: 8.49; found: C: 72.65, H: 8.79.
2. $^{1}$H- and $^{13}$C-NMR Spectra for New Compounds

1-(2,4-Dimethoxyphenyl)-2,3,3-trimethylbutan-1-ol

$^{1}$H-NMR (300 K, CDCl$_3$)

$^{13}$C-NMR (300 K, CDCl$_3$)
2,4-Dimethoxy-1-(2,3,3-trimethylbutyl)benzene (3)

$^1$H-NMR (300 K, CDCl$_3$)

$^{13}$C-NMR (300 K, CDCl$_3$)
2,3,3-Trimethyl-1-(2,4,6-trimethoxyphenyl)butan-1-ol

$^1$H-NMR (300 K, CDCl$_3$)

$^{13}$C-NMR (300 K, CDCl$_3$)
1,3,5-Trimethoxy-2-(2,3,3-trimethylbutyl)benzene (5)

$^1$H-NMR (300 K, CDCl$_3$)

$^{13}$C-NMR (300 K, CDCl$_3$)
5-(2,4-Dimethoxyphenyl)-2,2,6,7,7-pentamethyloctan-3-one (4a)

$^1$H-NMR (300 K, CDCl$_3$)

$^{13}$C-NMR (300 K, CDCl$_3$)
2,4-Dimethoxy-1-(5,6,6-trimethylhept-1-en-4-yl)benzene (4b)

$^1$H-NMR (300 K, CDCl$_3$)

$^{13}$C-NMR (300 K, CDCl$_3$)
2-[1-(2,4-Dimethoxyphenyl)-2,3,3-trimethylbutyl]-5-methylthiophene (4c)

$^1$H-NMR (300 K, CDCl$_3$)

$^{13}$C-NMR (300 K, CDCl$_3$)
2-[1-(2,4-Dimethoxyphenyl)-2,3,3-trimethylbutyl]-1,3,5-trimethoxybenzene (4d)

$^1$H-NMR (300 K, CDCl$_3$)

$^{13}$C-NMR (300 K, CDCl$_3$)
2-[1-(2,4-Dimethoxyphenyl)-2,3,3-trimethylbutyl]furan (4e)

$^1$H-NMR (300 K, CDCl$_3$)

$^{13}$C-NMR (300 K, CDCl$_3$)
2,2,6,7,7-Pentamethyl-5-(2,4,6-trimethoxyphenyl)octan-3-on (6a)

$^1$H-NMR (300 K, CDCl$_3$)

$^{13}$C-NMR (300 K, CDCl$_3$)
1,3,5-Trimethoxy-2-(5,6,6-trimethylhept-1-en-4-yl)benzene (6b)

$^1$H-NMR (300 K, CDCl$_3$)

$^{13}$C-NMR (300 K, CDCl$_3$)
3-[2,3,3-Trimethyl-1-(2,4,6-trimethoxyphenyl)butyl]pentan-2,4-dion (6c)

$^1$H-NMR (300 K, CDCl$_3$)

$^{13}$C-NMR (300 K, CDCl$_3$)
4,5,5-Trimethyl-3-(2,4,6-trimethoxyphenyl)hexanal (6d)

$^{1}H$-NMR (300 K, CDCl$_3$)

$^{13}C$-NMR (300 K, CDCl$_3$)
2-Methyl-5-[2,3,3-trimethyl-1-(2,4,6-trimethoxyphenyl)butyl]thiophene (6e)

$^1$H-NMR (300 K, CDCl$_3$)

$^{13}$C-NMR (300 K, CDCl$_3$)
2-[1-(2,4-Dimethoxyphenyl)-2,3,3-trimethylbutyl]-1,3,5-trimethoxybenzene (6f)

\[^1\text{H-NMR}\ (300 \text{ K, CDCl}_3)\]

\[^{13}\text{C-NMR}\ (300 \text{ K, CDCl}_3)\]
2-[2,3,3-Trimethyl-1-(2,4,6-trimethoxyphenyl)butyl]furan (6g)

$^1$H-NMR (300 K, CDCl$_3$)

$^{13}$C-NMR (300 K, CDCl$_3$)
3. Crystallographic Data

Experimental Part

CCDC 1016616 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Single Crystal X-Ray Determination (CCDC 1016616) of 6f.

Figure S1. ORTEP style representation of compound 6f. Ellipsoids are shown at the 30% probability level.

A clear colorless fragment-like specimen of C_{24}H_{34}O_{5}, approximate dimensions 0.121 mm x 0.126 mm x 0.132 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured on a Bruker Kappa APEX II CCD system equipped with a MONTEL mirror monochromator and a Mo FR591 rotating anode (λ = 0.71073 Å).

A total of 699 frames were collected. The total exposure time was 3.88 hours. The frames were integrated with the Bruker SAINT software package using a narrow-frame algorithm. The integration of the data using a monoclinic unit cell yielded a total of 16558 reflections to a maximum θ angle of 23.26° (0.90 Å resolution), of which 3089 were independent (average redundancy 5.360, completeness = 98.4%, R_{int} = 10.67%) and 1913 (61.93%) were greater than 4σ(F^2). The final cell constants of a = 13.558(3) Å, b = 11.365(2) Å, c = 15.410(3) Å, β = 112.740(6)°, volume = 2189.9(7) Å^3, are based upon the refinement of the XYZ-centroids of 5437 reflections above 20 σ(I) with 4.589° < 2θ < 50.75°. Data were corrected for absorption effects using the multi-scan method (SADABS). The ratio of minimum to maximum apparent
transmission was 0.557. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.9890 and 0.9900.

The final anisotropic full-matrix least-squares refinement on $F^2$ with 272 variables converged at $R1 = 8.16\%$, for the observed data and $wR2 = 20.73\%$ for all data. The goodness-of-fit was 1.049. The largest peak in the final difference electron density synthesis was 0.861 e/Å$^3$ and the largest hole was -0.271 e/Å$^3$ with an RMS deviation of 0.062 e/Å$^3$. On the basis of the final model, the calculated density was 1.221 g/cm$^3$ and $F(000)$, 872 e$^-$.  

Table S1. Sample and crystal data.

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<tr>
<th>Identification code</th>
<th>NitDo2 AP6174-123</th>
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<tr>
<td>Chemical formula</td>
<td>$C_{24}H_{34}O_5$</td>
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<tr>
<td>Formula weight</td>
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<tr>
<td>Temperature</td>
<td>123(2) K</td>
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<tr>
<td>Wavelength</td>
<td>0.71073 Å</td>
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<tr>
<td>Crystal size</td>
<td>0.121 x 0.126 x 0.132 mm</td>
</tr>
<tr>
<td>Crystal habit</td>
<td>clear colorless fragment</td>
</tr>
<tr>
<td>Crystal system</td>
<td>monoclinic</td>
</tr>
<tr>
<td>Space group</td>
<td>$P \overline{2}_1/n$</td>
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<tr>
<td>Unit cell dimensions</td>
<td>$a = 13.558(3)$ Å $\alpha = 90^\circ$</td>
</tr>
<tr>
<td></td>
<td>$b = 11.365(2)$ Å $\beta = 112.740(6)^\circ$</td>
</tr>
<tr>
<td></td>
<td>$c = 15.410(3)$ Å $\gamma = 90^\circ$</td>
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<tr>
<td>Volume</td>
<td>2189.9(7) Å$^3$</td>
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<tr>
<td>Z</td>
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<tr>
<td>Density (calculated)</td>
<td>1.221 g/cm$^3$</td>
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<tr>
<td>Absorption coefficient</td>
<td>0.084 mm$^{-1}$</td>
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<td>F(000)</td>
<td>872</td>
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Table 3. Data collection and structure refinement.

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<th>Diffractometer</th>
<th>Bruker Kappa APEX II CCD</th>
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<td>Radiation source</td>
<td>FR591 rotating anode, Mo</td>
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<td>Theta range for data collection</td>
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<td>Index ranges</td>
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<td>Reflections collected</td>
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<tr>
<td>Independent reflections</td>
<td>3089 [R(int) = 0.1067]</td>
</tr>
<tr>
<td>Coverage of independent</td>
<td>98.4%</td>
</tr>
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</table>
reflections
Absorption correction multi-scan
Max. and min. transmission 0.9900 and 0.9890
Refinement method Full-matrix least-squares on F²
Refinement program SHELXL-2014 (Sheldrick, 2014)
Function minimized Σ w(F_o² - F_c²)²
Data / restraints / parameters 3089 / 0 / 272
Goodness-of-fit on F² 1.049
Final R indices 1913 data; I>2σ(I) R1 = 0.0816, wR2 = 0.1855
all data R1 = 0.1330, wR2 = 0.2073
Weighting scheme w=1/[σ²(F_o²)+(0.0730P)²+3.6926P]
where P=(F_o²+2F_c²)/3
Extinction coefficient 0.0087(18)
Largest diff. peak and hole 0.861 and -0.271 eÅ⁻³
R.M.S. deviation from mean 0.062 eÅ⁻³