A Novel Palladium Catalyzed Intramolecular Redox Reaction

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Supporting Information

General Experimental

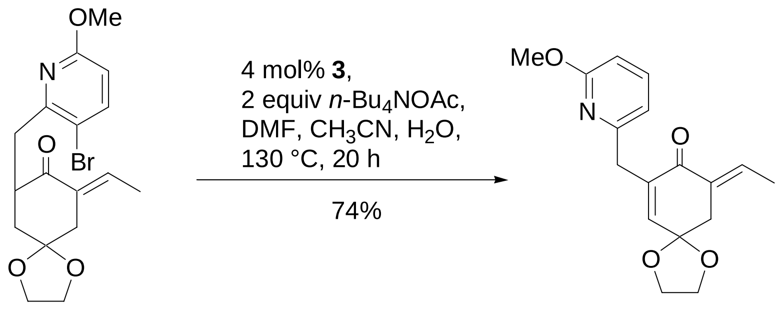
Unless otherwise stated, all commercially available compounds were used without further purification. Benzene was dried by refluxing over sodium metal and stored over 4 Å molecular sieves. THF was filtered over aluminium oxide, subsequently refluxed over potassium and used freshly distilled. Moisture sensitive reactions were carried out in flame dried glassware under an atmosphere of argon. Thin layer chromatography (TLC) was carried out on silica gel 60 plates with a 254 nm fluorescent indicator. Compounds on TLC were visualized by UV and ceric sulfate stain. Flash column chromatography was performed using silica gel 60 (230-400 mesh) and the solvent system indicated. ^{1}H- and ^{13}C NMR spectra were measured on a *Bruker* AMX 400 spectrometer. Chemical shifts are reported in ppm and coupling constants are quoted in hertz. Proton spectra are referenced to the residual $CHCl_3$ signal (7.26 ppm), carbon spectra are calibrated to the middle peak of $CDCl_3$ (77.0 ppm) and were recorded *J*-modulated. Spin multiplicity is quoted using the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets, dt = doublet of triplets, ddd = doublet of doublet of doublets, ddt = doublet of doublet of triplets, dq = doublet of quartets, tq = triplet of quartets. Broadening of peaks is indicated by the prefix br. Both low and high resolution mass spectra (LRMS and HRMS, resp.) were recorded under electron impact (EI) or field desorption (FD) using a *Finnigan* apparatus (MAT 8230, 900S). Infrared spectra (IR) were recorded on a *Perkin Elmer* machine (1600 FT) as liquid films on a silica plate. Elemental analyses (E.A.) were performed with a *Perkin Elmer* 240 instrument. Melting points were determined on a *Büchi* SMP 20 apparatus and are uncorrected.

General procedure for the alkylation of ketones *via* the pyrrolidine enamine (GP1)

Pyrrolidine (1.05 equiv) and a catalytic amount of *p*-TsOH were added to a solution of the ketone (1.0 equiv) in dry benzene (ca. 0.3 M). The resulting mixture was heated for 3 hours under reflux with a Dean-Stark trap. Then the bromide (1.05 equiv) was added and the reaction mixture was again heated for 16-24 h under reflux. After this time, the same volume of acetate buffer (NaOAc:HOAc:H_2O = 1:2:2) was added and the biphasic mixture was heated under reflux for 1 hour. The mixture was allowed to cool to rt and the aqueous layer was extracted with ether. The combined organic extracts were treated with water. Solid $NaHCO_3$ was added until the aqueous layer had a pH > 7. The aqueous layer was again extracted with ether. The combined organic extracts were dried with $MgSO_4$ and concentrated under reduced pressure. The product was purified by column chromatography.

General procedure for the palladium catalyzed redox reaction of bromoketones (GP2)

n-Bu$_4$NOAc (2 equiv) and palladacycle **3** (5 mol%) were added to a solution of bromoketone in DMF/CH$_3$CN/H$_2$O = 5/1/1 (ca. 0.1 M) and the resulting mixture was heated at 130 °C for the quoted time. After cooling to rt, the mixture was filtered through a short pad of celite, treated with water and the aqueous layer was extracted with ether. The combined organic extracts were dried with MgSO$_4$ and concentrated under reduced pressure. The product was purified by column chromatography.



1 **2**

9-Ethylidene-7-(6-methoxy-pyridine-2-ylmethyl)-1,4-dioxa-spiro[4.5]dec-6-ene-8-one (**2**)

n-Bu$_4$NOAc (316 mg, 1.05 mmol) and palladacycle **3** (19 mg, 4 mol%) were added to bromoketone **1** (200 mg, 0.52 mmol), dissolved in DMF (5 ml), acetonitrile (5 ml) and H$_2$O (1 ml). The resulting mixture was heated at 130 °C for 20 h. After cooling to rt, the solution was treated with water and the aqueous layer was extracted with ether. The combined organic extracts were dried with MgSO$_4$ and concentrated under reduced pressure. The crude product was purified by column chromatography, eluting with hexane/ethyl acetate (1/1), to yield dienone **2** (117 mg, 74%) as a clear, colourless oil.

^{1}H NMR (CDCl$_3$, 400 MHz): δ [ppm] 7.44 (1H, dd, *J* = 8.0, 7.5), 6.90 (1H, ddt, *J* = 14.2, 7.0, 1.6), 6.75 (1H, d, *J* = 7.5), 6.54 (1H, d, *J* = 8.0), 6.50 (1H, br s), 4.05-3.99 (4H, m), 3.87 (3H, s), 3.69 (2H, s), 2.90 (2H, s), 1.82 (3H, d, *J* = 7.0). **^{13}C NMR (CDCl$_3$, 100 MHz):** δ [ppm] 186.7, 163.6, 156.3, 142.3, 140.5, 138.8, 135.8, 131.3, 115.9, 107.9, 104.4, 65.0, 53.2, 37.5, 35.7, 13.8. **LRMS (EI, 70 eV, 70 °C):** *m/z* = 301 (M$^+$, 100%), 256 (30), 242 (43), 214 (50), 200 (35), 186 (46), 123 (41). **HRMS (EI, 70 eV, 70 °C):** calcd for C$_{17}$H$_{19}$NO$_4$: *m/z* = 301.1314 (M$^+$); found: *m/z* = 301.1308 ± 0.0015 (M$^+$). **IR (neat):** ν_{max} [cm^{-1}] = 2951, 1676, 1622, 1579, 1467, 1516, 1370, 1285, 1122.

2-(2-Bromobenzyl)-cyclopentanone (**4a**)

The title compound was prepared from cyclopentanone (0.67 ml, 7.57 mmol) and 2-bromobenzyl bromide using the general procedure (GP1). The crude product was purified by column chromatography, eluting with hexane/ethyl acetate (10/1→3/1), to yield bromoketone **4a** (1.39 g, 68%) as a clear, colourless oil.

^{1}H NMR ($CDCl_3$, 400 MHz): δ [ppm] 7.53 (1H, d, *J* = 8.1), 7.27-7.18 (2H, m), 7.10-7.03 (1H, m), 3.33 (1H, dd, *J* = 13.8, 4.4), 2.63 (1H, dd, *J* = 13.6, 9.6), 2.54-2.43 (1H, m), 2.34 (1H, dt, *J* = 8.3, 17.6), 2.16 (1H, dd, *J* = 19.0, 9.9), 2.10-1.93 (2H, m), 1.81-1.67 (1H, m), 1.64-1.52 (1H, m). **^{13}C NMR ($CDCl_3$, 100 MHz):** δ [ppm] 219.6, 139.5, 132.9, 131.0, 127.9, 127.4, 124.6, 49.6, 37.9, 35.6, 29.2, 20.5. **LRMS (EI, 70 eV, 40 °C):** *m/z* = 253 (M^+, 15%), 211 (15), 196 (30), 173 (86), 145 (90), 91 (78), 55 (100). **HRMS (EI, 70 eV, 40 °C):** calcd for $C_{12}H_{13}{}^{79}BrO$: *m/z* = 252.0150 (M^+); found: *m/z* = 252.0149 ± 0.0013 (M^+). **IR (neat):** ν_{max} [cm^{-1}] = 2961, 2870, 1739, 1472, 1439, 1153, 1025.

2-(2-Bromobenzyl)-cyclohexanone (**4b**)[1]

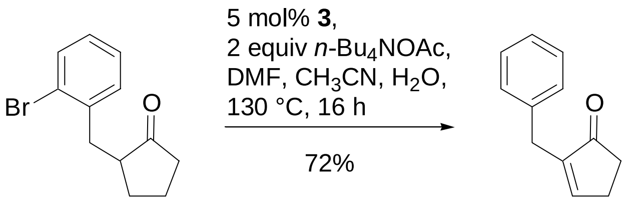
The title compound was prepared from cyclohexanone (1.50 g, 15.3 mmol) and 2-bromobenzyl bromide using the general procedure (GP1). The crude product was purified by column chromatography, eluting with hexane/ethyl acetate (20/1), to yield bromoketone **4b** (2.84 g, 70%) as a clear, colourless oil.

^{1}H NMR ($CDCl_3$, 400 MHz): δ [ppm] 7.51 (1H, dd, *J* = 7.9, 1.0), 7.25-7.16 (2H, m), 7.09-7.00 (1H, m), 3.35 (1H, dd, *J* = 13.5, 5.0), 2.77-2.63 (1H, m), 2.56 (1H, dd, *J* = 13.5, 8.0), 2.48-2.25 (2H, m), 2.14-1.97 (2H, m), 1.90-1.78 (1H, m), 1.72-1.33 (3H, m).

7-(2-Bromobenzyl)-1,4-dioxa-spiro[4.5]decan-8-one (**4c**)

The title compound was prepared from 1,4-cyclohexanedione monoethyleneacetal (1.30 g, 8.32 mmol) and 2-bromobenzyl bromide using the general procedure (GP1). The crude product was purified by column chromatography, eluting with hexane/ethyl acetate (3/1), to yield bromoketone **4c** (1.67 g, 62%) as a clear, colourless oil which solidified upon standing.

^{1}H NMR ($CDCl_3$, 400 MHz): δ [ppm] 7.52 (1H, d, *J* = 7.8), 7.18-7.24 (2H, m), 7.06 (1H, ddd, *J* = 8.0, 6.0, 2.6), 3.90-4.01 (4H, m), 3.37 (1H, dd, *J* = 14.0, 5.4), 3.11-3.01 (1H, m), 2.69 (1H, dt, *J* = 6.5, 13.8), 2.57 (1H, dd, *J* = 13.9, 8.3), 2.41 (1H, ddd, *J* = 14.2, 4.9, 3.2), 2.10-1.92 (3H, m), 1.78 (1H, t, *J* = 13.3). **^{13}C NMR ($CDCl_3$, 100 MHz):** δ [ppm] 210.5, 139.2, 132.8, 131.6, 127.9, 127.3, 124.8, 107.3, 64.7, 46.4, 40.2, 38.2, 35.3, 34.7. **LRMS (EI, 70 eV, 50 °C):** *m/z* = 325 (M^+, 2%), 269 (64), 267 (61), 245 (90), 155 (88), 99 (100), 86 (80). **HRMS (EI, 70 eV, 50 °C):** calcd for $C_{15}H_{17}{}^{79}BrO_3$: *m/z* = 324.0361 (M^+); found: *m/z* = 324.0350 ± 0.0016 (M^+). **IR (neat):** ν_{max} [cm^{-1}] = 2957, 1712, 1472, 1438, 1306, 1117, 1041. **M.p.** 123-125 °C.



4a **6a**

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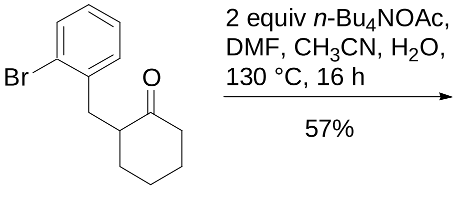
[1] Booth, S. E.; Jenkins, P. R.; Swain, C. J.; Sweeney, J. B. *J. Chem. Soc., Perkin Trans. 1* **1994**, 3499.

2-Benzylcyclopent-2-enone (**6a**)

The title compound was prepared from 2-(2-bromobenzyl)-cyclopentanone (**4a**) (100 mg, 0.40 mmol) using the general procedure (GP2, time = 16 hours). The crude product was purified by column chromatography, eluting with hexane/ethyl acetate (3/1), to yield enone **6a** (49 mg, 72%) as a clear, colourless oil.

^{1}H NMR ($CDCl_3$, 400 MHz): δ [ppm] 7.25-7.04 (6H, m), 3.46 (2H, d, *J* = 1.3), 2.49-2.43 (2H, m), 2.38-2.32 (2H, m). **^{13}C NMR ($CDCl_3$, 100 MHz):** δ [ppm] 209.1, 158.7, 146.0, 138.8, 128.9, 128.4, 126.2, 34.5, 31.3, 26.4. **LRMS (EI, 70 eV, 20 °C):** *m/z* = 172 (M^+, 100%), 129 (65), 115 (45), 91 (32), 84 (28). **HRMS (EI, 70 eV, 20 °C):** calcd for $C_{12}H_{12}O$: *m/z* = 172.0888 (M^+); found: *m/z* = 172.0891 ± 0.0009 (M^+). **IR (neat):** ν_{max} [cm^{-1}] = 3028, 2917, 1694, 1633, 1495, 1454, 1360, 1247, 1196, 1039, 1001.

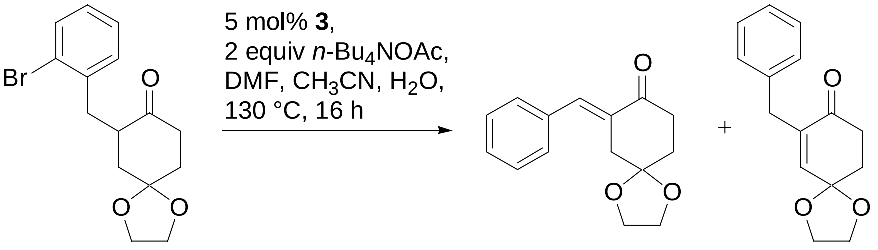


4b **6b**

2-Benzylcyclohex-2-enone (**6b**)

The title compound was prepared from 2-(2-bromobenzyl)-cyclohexanone (**4b**) (100 mg, 0.37 mmol) using the general procedure (GP2, time = 16 hours). The crude product was purified by column chromatography, eluting with toluene/ethyl acetate (10/1), to yield enone **6b** (40 mg, 57%) as a clear, colourless oil.

^{1}H NMR ($CDCl_3$, 400 MHz): δ [ppm] 7.36-7.29 (2H, m), 7.27-7.19 (3H, m), 6.61 (1H, t, *J* = 4.2), 3.57 (2H, br d, *J* = 1.3), 2.53-2.47 (2H, m), 2.41-2.34 (2H, m), 2.03 (2H, qt, *J* = 6.3). **^{13}C NMR ($CDCl_3$, 100 MHz):** δ [ppm] 199.0, 146.4, 139.6, 139.5, 129.1, 128.3, 126.0, 38.5, 35.4, 26.1, 23.0. **LRMS (EI, 70 eV, 20 °C):** *m/z* = 186 (M^+, 100%), 158 (55), 129 (50), 115 (30), 91 (37). **HRMS (EI, 70 eV, 20 °C):** calcd for $C_{13}H_{14}O$: *m/z* = 186.1045 (M^+); found: *m/z* = 186.1047 ± 0.0009 (M^+). **IR (neat):** ν_{max} [cm^{-1}] = 2925, 1672, 1492, 1451, 1403, 1355, 1160, 1112.



4c **5c** (23%) **6c** (73%)

7*(E)*-Benzylidene-1,4-dioxa-spiro[4.5]decan-8-one (**5c**) and 7-benzyl-1,4-dioxa-spiro[4.5]dec-6-ene-8-one (**6c**)

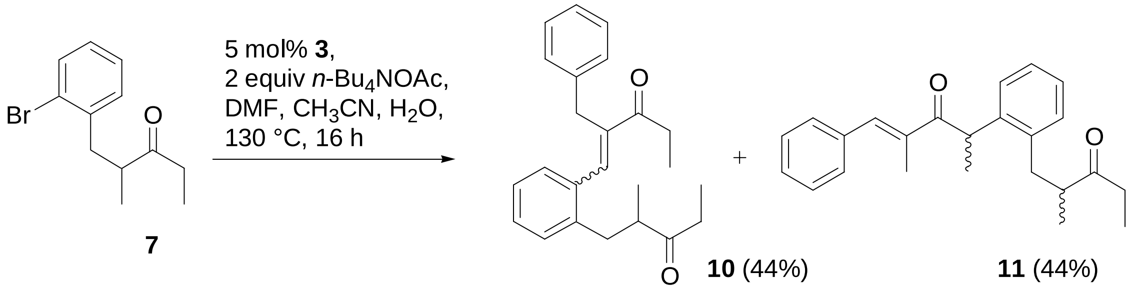
The title compounds were prepared from 7-(2-bromobenzyl)-1,4-dioxa-spiro[4.5]decan-8-one (**4c**) (100 mg, 0.31 mmol) using the general procedure (GP2, time = 16 hours). The crude product was purified by column chromatography, eluting with hexane/ethyl acetate (5/1), to yield enones **6c** (55 mg, 73%) and **5c** (17 mg, 23%) as clear, colourless oils.

data for **5c**: **^{1}H NMR ($CDCl_3$, 400 MHz):** δ [ppm] 7.58 (1H, t, *J* = 2.0), 7.42-7.30 (5H, m), 3.97 (4H, br d, *J* = 2.5), 3.06 (2H, br d, *J* = 1.0), 2.71 (2H, t, *J* = 7.1), 2.12 (2H, t, *J* = 7.0). **^{13}C NMR ($CDCl_3$, 100 MHz):** δ [ppm] 199.5, 137.9, 135.1, 132.6, 130.3, 128.8, 128.4, 107.3, 64.7, 38.3, 36.6, 31.5. **LRMS (EI, 70 eV, 50 °C):** *m/z* = 244 (M^+, 26%), 115 (35), 99 (100), 86 (31), 84 (47). **HRMS (EI, 70 eV, 50 °C):** calcd for $C_{15}H_{16}O_3$: *m/z* = 244.1099 (M^+); found: *m/z* = 244.1096 ± 0.0012 (M^+). **IR (neat):** ν_{max} [cm^{-1}] = 2957, 1685, 1596, 1446, 1273, 1177, 1114, 1056, 948.
data for **6c**: **^{1}H NMR ($CDCl_3$, 400 MHz):** δ [ppm] 7.31-7.11 (5H, m), 6.16 (1H, s), 3.97 (4H, s), 3.51 (2H, br s), 2.65 (2H, t, *J* = 6.6), 2.17 (2H, t, *J* = 6.4). **^{13}C NMR ($CDCl_3$, 100 MHz):** δ [ppm] 198.1, 142.3, 140.9, 138.2, 129.3, 128.5, 126.3, 104.8, 64.9, 35.6, 35.1, 33.1. **LRMS (EI, 70 eV, 30 °C):** *m/z* = 244 (M^+, 30%), 183 (61), 115 (44), 86, (64), 84 (100). **HRMS (EI, 70 eV, 30 °C):** calcd for $C_{15}H_{16}O_3$: *m/z* = 244.1099 (M^+); found: *m/z* = 244.1104 ± 0.0012 (M^+). **IR (neat):** ν_{max} [cm^{-1}] = 2958, 1681, 1494, 1453, 1368, 1276, 1122, 1066, 1044, 932.

1-(2-Bromophenyl)-2-methyl-pentan-3-one (**7**)

Under an argon atmosphere, *n*-BuLi (2.44 ml, 2.5 M in hexane, 6.09 mmol) was added dropwise to a solution of freshly distilled diisopropylamine (0.86 ml, 6.09 mmol) in dry THF (20 ml) at 0 °C. After stirring at 0 °C for 10 minutes, the solution was cooled to –78 °C. Diethylketone (500 mg, 5.80 mmol), dissolved in dry THF (5 ml), was added dropwise and the reaction mixture was stirred at –78 °C for 1 hour. After that time, a solution of 2-bromobenzyl bromide (1.52 g, 6.09 mmol) in dry THF (5 ml) was added dropwise and the reaction mixture was allowed to warm slowly to rt overnight (16 h). Ether (100 ml) and 1 M HCl (20 ml) were added and the aqueous layer was extracted with ether (3 × 50 ml). The combined organic extracts were washed with brine (20 ml), dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by column chromatography. The first column was eluted with hexane/ethyl acetate (30/1), the second column with toluene/ethyl acetate (100/1) to yield bromoketone **7** (962 mg, 65%) as a clear, colourless oil.

^{1}H NMR ($CDCl_3$, 400 MHz): δ [ppm] 7.53 (1H, dd, *J* = 8.0, 1.1), 7.23-7.12 (2H, m), 7.06 (1H, dt, *J* = 1.9, 7.6), 3.09 (1H, dd, *J* = 13.0, 7.0), 3.00 (1H, tq, *J* = 6.9, 6.9), 2.68 (1H, dd, *J* = 13.0, 7.2), 2.46 (1H, dq, *J* = 17.8, 7.2), 2.29 (1H, dq, *J* = 17.8, 7.3), 1.09 (3H, d, *J* = 6.8), 0.98 (3H, t, *J* = 7.3). **^{13}C NMR ($CDCl_3$, 100 MHz):** δ [ppm] 214.4, 139.1, 132.9, 131.6, 128.0, 127.3, 124.5, 45.4, 39.3, 35.2, 16.4, 7.6. **LRMS (EI, 70 eV, 20 °C):** *m/z* 256 (M^+, 1%), 254 (1), 227 (7), 225 (7), 199 (26), 197 (26), 175 (100), 115 (30), 57 (90). **HRMS (EI, 70 eV, 20 °C):** calcd for $C_{12}H_{15}{}^{79}BrO$: *m/z* = 254.0306 (M^+); found: *m/z* = 254.0312 ± 0.0013 (M^+). **IR (neat):** ν_{max} [cm^{-1}] = 2971, 1714, 1567, 1454, 1374, 1102, 1024.



2-Benzyl-1-[2-(2-methyl-3-oxopentyl)-phenyl]-pent-1-ene-3-one (**10**) and 2-methyl-4-[2-(2-methyl-3-oxo-pentyl)-phenyl]-1-phenyl-pent-1-ene-3-one (**11**)

The title compounds were prepared from 1-(2-bromophenyl)-2-methyl-pentan-3-one (**7**) (100 mg, 0.39 mmol) using the general procedure (GP2, time = 16 hours). The crude product was purified by column chromatography, eluting with hexane/ethyl acetate (30/1→10/1), to yield enones **11** (30 mg, 44%) and **10** (30 mg, 44%) as clear, colourless oils.

data for **10**: two isomers (ratio 3:2). **^{1}H NMR ($CDCl_3$, 400 MHz):** δ [ppm] 7.77 (0.6H, s), 7.75 (0.4H, s), 7.28-6.88 (9H, m), 3.82 (1.2H, dd, *J* = 16.8, 16.8), 3.75 (0.4H, d, *J* = 15.0), 3.70 (0.4H, d, *J* = 15.0), 3.00-2.02 (7H, m), 1.08 (1.8H, t, *J* = 7.2), 1.07 (1.2H, t, *J* = 7.3), 1.02 (1.8H, d, *J* = 6.6), 1.00 (1.2H, d, *J* = 6.8), 0.87 (1.8H, t, *J* = 7.2), 0.86 (1.2H, t, *J* = 7.2). **^{13}C NMR ($CDCl_3$, 100 MHz):** δ [ppm] 214.9, 214.3, 202.5, 202.3, 141.0, 140.4, 139.8, 139.2, 138.5 (2 signals), 137.9, 137.3, 135.3, 134.7, 130.3, 130.0, 129.1, 128.9, 128.7, 128.6 (2 signals), 128.4, 128.1, 126.9, 126.7, 126.4, 126.1, 125.9, 46.8, 45.9, 36.6, 36.3, 35.3, 35.1, 32.2, 31.5, 31.1, 29.7, 16.8 (2 signals), 8.7, 8.6, 7.6, 7.5. **LRMS (EI, 70 eV, 70 °C):** *m/z* = 348 (M^+,2%), 319 (1), 262 (13), 249 (8), 233 (6), 205 (9), 147 (100), 129 (29), 91 (34). **HRMS (EI, 70 eV, 70 °C):** calcd for $C_{24}H_{28}O_2$: *m/z* = 348.2089 (M^+); found: *m/z* = 348.2095 ± 0.0017 (M^+). **IR (neat):** ν_{max} [cm^{-1}] = 2975, 2937, 1713, 1673, 1376, 1212, 1170.
data for **11**: two isomers (ratio 3:1), NMR data given for the major isomer. **^{1}H NMR ($CDCl_3$, 400 MHz):** δ [ppm] 7.53 (1H, d, *J* = 1.3), 7.45-7.11 (9H, m), 3.51 (1H, q, *J* = 7.0), 3.08 (1H, dd, *J* = 15.2, 5.8), 2.84 (2H, q, *J* = 7.3), 2.90-2.80 (1H, m), 2.60-2.44 (1H, m), 2.07 (3H, d, *J* = 1.3), 1.51 (3H, d, *J* = 7.1), 1.24 (3H, d, *J* = 7.1), 1.18 (3H, t, *J* = 7.3). **^{13}C NMR ($CDCl_3$, 100 MHz):** δ [ppm] 214.3, 203.0, 138.1, 138.0, 137.2, 136.4, 136.0, 129.7, 128.4 (2 signals), 127.3, 126.9, 126.5, 125.8, 46.3, 40.7, 36.8, 30.8, 15.9, 14.5, 13.2, 8.8. **LRMS (EI, 70 eV, 20 °C):** *m/z* = 174 (M^+–$C_{12}H_{14}O$, 70%), 145 (55), 131 (80), 117 (92), 91 (100), 57 (36). **IR (neat):** ν_{max} [cm^{-1}] = 2975, 2937, 1713, 1673, 1376, 1212, 1170. **E.A.:** calcd for $C_{24}H_{28}O_2$: C, 82.72; H, 8.10; found: C, 82.89; H, 7.99.

7-(4-Bromobenzyl)-1,4-dioxa-spiro[4.5]decan-8-one (**12**)

The title compound was prepared from 1,4-cyclohexanedione monoethyleneacetal (1.30 g, 8.32 mmol) and 4-bromobenzyl bromide using the general procedure (GP1). The crude product was purified by column chromatography, eluting with hexane/ethyl acetate (3/1), to yield bromoketone **12** (2.10 g, 78%) as white crystals.

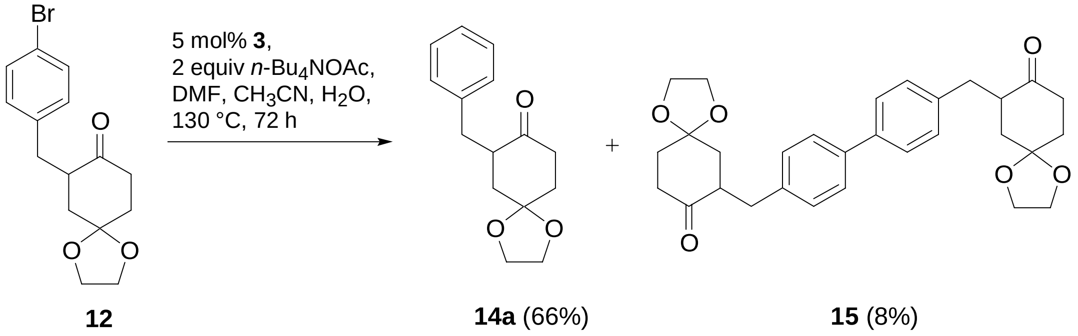
^{1}H NMR ($CDCl_3$, 400 MHz): δ [ppm] 7.38 (2H, ddd, *J* = 8.8, 2.2, 2.1), 7.02 (2H, ddd, *J* = 9.1, 1.6, 1.6), 4.00-3.90 (4H, m), 3.14 (1H, dd, *J* = 14.2, 5.3), 2.93-2.83 (1H, m), 2.66 (1H, ddt, *J* = 0.8, 6.7, 13.9), 2.45-2.36, (2H, m), 2.07-1.89 (3H, m), 1.67 (1H, t, *J* = 13.1).

^{13}C NMR (CDCl$_3$, 100 MHz): δ [ppm] 210.5, 138.6, 131.4, 130.9, 119.9, 107.2, 64.7, 64.5, 47.8, 40.0, 38.1, 34.6, 34.5. **LRMS (EI, 70 eV, 70 °C):** *m/z* = 326 (M$^+$, 20%), 324 (21), 269 (20), 267 (20), 155 (72), 99 (100), 84 (95). **HRMS (EI, 70 eV, 70 °C):** calcd for $C_{15}H_{17}{}^{79}BrO_3$: *m/z* = 324.0361 (M$^+$); found: *m/z* = 324.0356 ± 0.0016 (M$^+$). **IR (neat):** ν_{max} [cm^{-1}] 2969, 2931, 1710, 1566, 1470, 1376, 1022. **M.p.** 110-111 °C.

7-(3-Bromobenzyl)-1,4-dioxa-spiro[4.5]decan-8-one (**13**)

The title compound was prepared from 1,4-cyclohexanedione monoethyleneacetal (1.30 g, 8.32 mmol) and 3-bromobenzyl bromide using the general procedure (GP1). The crude product was purified by column chromatography, eluting with hexane/ethyl acetate (5/1), to yield bromoketone **13** (1.39 g, 51%) as white crystals.

^{1}H NMR (CDCl$_3$, 400 MHz): δ [ppm] 7.34-7.28 (2H, m), 7.16-7.05 (2H, m). 4.01-3.90 (4H, m), 3.18 (1H, dd, *J* = 14.0, 5.2), 2.96-2.85 (1H, m), 2.67 (1H, dt, *J* = 6.4, 13.8), 2.47-2.37 (2H, m), 2.08-1.90 (3H, m), 1.69 (1H, t, *J* = 13.1). **^{13}C NMR (CDCl$_3$, 100 MHz):** δ [ppm] 210.3, 142.1, 132.1, 129.9, 129.2, 127.8, 122.4, 107.2, 64.7, 64.5, 47.8, 40.1, 38.1, 34.7, 34.6. **LRMS (EI, 70 eV, 70 °C):** *m/z* = 326 (M$^+$, 7%), 324 (7), 269 (16), 267 (16), 155 (57), 99 (100), 86 (45). **HRMS (EI, 70 eV, 70 °C):** calcd for $C_{15}H_{17}{}^{79}BrO_3$: *m/z* = 324.0361 (M$^+$); found: *m/z* = 324.0356 ± 0.0016 (M$^+$). **IR (neat):** ν_{max} [cm^{-1}] 2953, 1714, 1567, 1474, 1306, 1120, 1042, 997. **M.p.** 102-103 °C.



7-Benzyl-1,4-dioxa-spiro[4.5]decan-8-one (**14a**) and 7-({4'-[(8-oxo-1,4-dioxaspiro[4.5]dec-7-yl)methyl][1,1'-biphenyl]-4-yl}methyl)-1,4-dioxaspiro[4.5]decan-8-one (**15**)

The title compounds were prepared from 7-(4-bromobenzyl)-1,4-dioxa-spiro[4.5]decan-8-one (**12**) (200 mg, 0.62 mmol) using the general procedure (GP2, time = 72 hours). The crude product was purified by column chromatography, eluting with hexane/ethyl acetate (3/1→1/1), to yield aryl ketone **14a** (100 mg, 66%) and dimer **15** (12 mg, 8%) as clear, colourless oils.

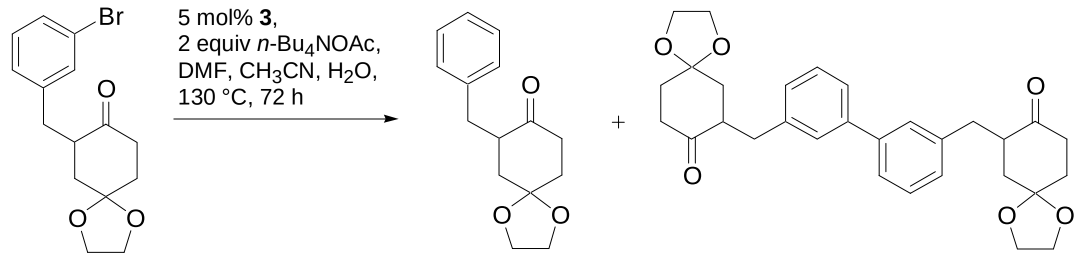
data for **14a**: **^{1}H NMR (CDCl$_3$, 400 MHz):** δ [ppm] 7.35-7.15 (5H, m), 3.92-4.05 (4H, m), 3.27 (1H, dd, *J* = 14.1, 5.1), 3.01-2.91 (1H, m), 2.76-2.65 (1H, m), 2.53-2.41 (2H, m), 2.12-1.97 (3H, m), 1.73 (1H, t, *J* = 13.0). **^{13}C NMR (CDCl$_3$, 100 MHz):** δ [ppm] 210.8, 139.6, 129.1, 128.3, 126.0, 107.3, 64.6, 64.5, 48.0, 39.9, 38.1, 35.0, 34.6. **LRMS (EI, 70 eV, 70 °C):** *m/z* = 246 (M$^+$, 30%), 189 (33), 155 (56), 99(100). **HRMS (EI, 70 eV, 70 °C):** calcd for

$C_{15}H_{18}O_3$: *m/z* = 246.1256 (M^+); found: *m/z* = 246.1262 ± 0.0012 (M^+). **IR (neat):** ν_{max} [cm^{-1}] = 2956, 1714, 1682, 1054, 933, 701.
<u>data for **15**:</u> **^{1}H NMR ($CDCl_3$, 400 MHz):** δ [ppm] 7.48 (4H, d, *J* = 8.3), 7.21 (4H, d, *J* = 8.3), 4.00-3.89 (8H, m), 3.25 (2H, dd, *J* = 14.2, 5.1), 3.00-2.90 (2H, m), 2.69 (2H, dt, *J* = 6.1, 13.8), 2.54-2.46 (2H, m), 2.43 (2H, ddd, *J* = 14.3, 5.0, 3.2), 2.09-1.92 (6H, m), 1.72 (2H, t, *J* = 13.0). **^{13}C NMR ($CDCl_3$, 100 MHz):** δ [ppm] 210.8, 138.7, 138.6, 129.5, 126.8, 107.4, 64.7, 64.5, 48.0, 40.0, 38.2, 34.7, 34.6. **LRMS (FD):** *m/z* 491 (M^+, 15%), 321 (100). **IR (neat):** ν_{max} [cm^{-1}] = 2955, 1714, 1498, 1436, 1366, 1306, 1120, 1043. **E.A.:** calcd for $C_{30}H_{34}O_6$: C, 73.45; H, 6.99; found: C, 73.66; H, 6.89.

7-Benzyl-1,4-dioxa-spiro[4.5]decan-8-one *d1* (**14b**)

The title compound was prepared from 7-(4-bromobenzyl)-1,4-dioxa-spiro[4.5]decan-8-one (**12**) (50 mg, 0.15 mmol) using the general procedure (GP2, d7-DMF instead of DMF, time = 72 hours). The crude product was purified by column chromatography, eluting with hexane/ethyl acetate (3/1), to yield the deuterated aryl ketone **14b** (23 mg, 60%) as a clear, colourless oil.

^{1}H NMR ($CDCl_3$, 400 MHz): δ [ppm] 7.26 (2H, d, *J* = 7.1), 7.14 (2H, d, *J* = 7.1), 3.99-3.88 (4H, m), 3.22 (1H, dd, *J* = 14.0, 4.9), 2.96-2.86 (1H, m), 2.66 (1H, dt, *J* = 6.6, 13.8), 2.44 (1H, dd, *J* = 14.4, 8.6), 2.45-2.37 (1H, m), 2.07.1.90 (3H, m), 1.68 (1H, t, *J* = 13.1). **^{13}C NMR ($CDCl_3$, 100 MHz):** δ [ppm] 210.8, 139.6, 129.1, 128.2, 125.8 (t, *J* = 24.5), 107.3, 64.6, 64.5, 48.0, 39.9, 38.2, 35.0, 34.6. **LRMS (EI, 70 eV, 40 °C):** *m/z* 247 (M^+, 12%), 190 (20), 155 (47), 142 (20), 99 (100), 86 (40). **HRMS (EI, 70 eV, 40 °C):** calcd for $C_{15}H_{17}DO_3$: *m/z* = 247.1318 (M^+); found: *m/z* = 247.1312 ± 0.0012 (M^+). **IR (neat):** ν_{max} [cm^{-1}] = 2954, 2887, 1714, 1492, 1438, 1365, 1307, 1141, 1120, 1042.



13 **14a** (55%) **16** (30%)

7-Benzyl-1,4-dioxa-spiro[4.5]decan-8-one (**14a**) and 7-({3'-[(8-oxo-1,4-dioxaspiro[4.5]dec-7-yl)methyl][1,1'-biphenyl]-3-yl}methyl)-1,4-dioxaspiro[4.5]decan-8-one (**16**)

The title compounds were prepared from 7-(3-bromobenzyl)-1,4-dioxa-spiro[4.5]decan-8-one (**13**) (100 mg, 0.31 mmol) using the general procedure (GP2, time = 72 hours). The crude product was purified by column chromatography, eluting with hexane/ethyl acetate (3/1→1/1), to yield aryl ketone **14a** (42 mg, 55%) and dimer **16** (23 mg, 30%) as clear, colourless oils.

data for **16**: **^{1}H NMR (CDCl$_3$, 400 MHz):** δ [ppm] 7.42-7.27 (6H, m), 7.12 (2H, d, *J* = 7.3), 3.97-3.88 (8H, m), 3.28 (2H, dd, *J* = 13.9, 5.1), 3.00-2.90 (2H, m), 2.67 (2H, dt, *J* = 6.7, 13.7), 2.49 (2H, dd, *J* = 14.0, 8.7), 2.41 (2H, ddd, *J* = 14.3, 5.0, 3.2), 2.07-1.90 (6H, m), 1.71 (2H, t, *J* = 13.0). **^{13}C NMR (CDCl$_3$, 100 MHz):** δ [ppm] 210.8, 141.2, 140.2, 128.7, 128.1, 127.9, 125.0, 107.3, 64.9, 64.5, 48.1, 40.1, 38.2, 35.2, 34.6. **LRMS (EI, 70 eV, 150 °C):** *m/z* = 491 (M^+, 5%), 305 (65), 286 (16), 91 (100). **HRMS (EI, 70 eV, 150 °C):** calcd for $C_{30}H_{34}O_6$: *m/z* = 490.2355 (M^+); found: *m/z* = 490.2339 ± 0.0025 (M^+). **IR (neat):** ν_{max} [cm^{-1}] = 2955, 1714, 1602, 1438, 1307, 1120, 1043.