Supporting Information for Palladium-Catalyzed Conjugate Reduction of Enones into α,β-Dideuterioketones with Hexamethyldisilane and Deuterium Oxide

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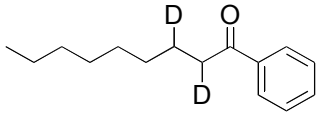
General Remarks. All manipulations of oxygen- and moisture-sensitive materials were conducted with a standard Schlenk technique under a nitrogen atmosphere. Nuclear magnetic resonance spectra were taken on a JEOL JNM LA-500 (^{1}H, 500 MHz; ^{13}C, 125 MHz; ^{31}P, 202 Hz) spectrometer using tetramethylsilane (^{1}H and ^{13}C) as an internal standard and 85% phosphoric acid (^{31}P) as an external standard. Elemental analyses were performed at the Microanalytical Center, Kyoto University. Unless otherwise noted, reagents are commercially available and were used without further purification. Anhydrous DMA was purchased from Aldrich Chemical Co. and was dried further with molecular sieves 3Å, which was evacuated at 260 °C for 12 h prior to use. Deuterium oxide (99.96%-*d*) was purchased from Cambridge Isotope Laboratories, Inc. Hexamethyldisilane (**2**) was purchased from Shin-Etsu Chemical Co. and was fractionally distilled. $[PdCl(\eta^3\text{-}C_3H_5)]_2$ (**3**),[1] $PdH(Cl)(PPh_3)_2$ (**5**),[2] chloro(benzoylmethyl)bis(triphenylphosphine)palladium (**7'**),[3] deuterio(dimethyl)phenylsilane (**6b-*d***),[4] 1-phenylnon-2-en-1-one (**1a**),[5] 4-methyl-1-phenylpent-2-en-1-one (**1b**),[6] 6-chloro-1-phenylhex-2-en-1-one (**1c**),[7] (*E*)-3-(4-methoxyphenyl)-1-phenylprop-2-en-1-one (**1e**),[8] (*E*)-1-phenyl-3-[4-(trifluoromethyl)phenyl]prop-2-en-1-one (**1f**),[9] (*E*)-1-(4-methoxyphenyl)-3-phenylprop-2-en-1-one (**1g**),[8] (*E*)-1-[4-(dimethylamino)phenyl]-3-phenylprop-2-en-1-one (**1h**),[10] and (*E*)-3-phenyl-1-[4-(trifluoromethyl)phenyl]prop-2-en-1-one (**1i**)[9] were prepared according to the literature methods.

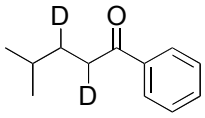
Palladium-Catalyzed Conjugate Reduction of Enones with Hexamethyldisilane and Deuterium Oxide. A General Procedure. To a solution of $[PdCl(\eta^3\text{-}C_3H_5)]_2$ (**3**: 3.7 mg, 0.010 mmol) and PPh_3 (10.5 mg, 0.0400 mmol) in DMA (0.50 mL) were added successively an enone (**1**: 0.40 mmol), hexamethyldisilane (**2**: 87.9 mg, 0.600 mmol) and D_2O (72 μL, 4.0 mmol). After stirring at 60 °C for 24 h, the resulting mixture was diluted with diethyl ether (20 mL), washed with water (10 mL x 5) and brine (10 mL), and dried over anhydrous magnesium sulfate. Filtration and evaporation of the solvent followed by PTLC on SiO_2 (hexane–ethyl acetate), column chromatography on SiO_2 (hexane–ethyl acetate) or bulb-to-bulb distillation gave the corresponding α,β-dideuterioketone (**4**). Deuterium ratios were determined by ^{1}H NMR. The results are summarized in Table 1.

The spectral data of all the α,β-dideuterioketones obtained here are in excellent agreement with the reported data of the corresponding ketones.



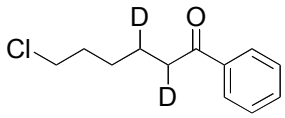
entry 1 of Table 1

2,3-Dideuterio-1-phenyl-1-nonanone (4a).[11] A colorless oil. Isolated by PTLC on SiO_2 (hexane:ethyl acetate = 15:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.88 (t, *J* = 7.0 Hz, 3 H), 1.18–1.42 (m, 10 H), 1.67–1.77 (m, 0.80 H, β), 2.89–2.98 (m, 0.75 H, α), 7.46 (t, *J* = 7.8 Hz, 2 H), 7.55 (t, *J* = 7.5 Hz, 1 H), 7.96 (d, *J* = 7.1 Hz, 2 H). Anal. Calcd for $C_{15}H_{19.55}D_{2.45}O$: C, 81.60; H, 11.16. Found: C, 81.76; H, 10.94.



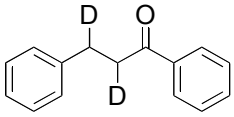
entry 2 of Table 1

2,3-Dideuterio-4-methyl-1-phenyl-1-pentanone (4b).[12] A colorless oil. Isolated by column chromatography on SiO_2 (hexane:ethyl acetate = 25:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.95 (d, *J* = 6.6 Hz, 6 H), 1.54–1.70 (m, β + γ), 2.88–3.00 (m, α), 7.46 (t, *J* = 7.7 Hz, 2 H), 7.55 (t, *J* = 7.4 Hz, 1 H), 7.96 (d, *J* = 7.2 Hz, 2 H); (500 MHz, DMSO) δ 0.90 (d, *J* = 7.1 Hz, 6 H), 1.44–1.53 (m, 0.87 H, β), 1.59 (octet, *J* = 6.7 Hz, 0.78 H, γ), 2.94–3.03 (m, 0.56 H, α), 7.52 (t, *J* = 7.8 Hz, 2 H), 7.63 (t, *J* = 7.5 Hz, 1 H), 7.97 (d, *J* = 7.6 Hz, 2 H). The deuterium ratio was determined by ^{1}H NMR using DMSO-*d* as a solvent, as the peak of the β protons overlap with that of water in $CDCl_3$ as a solvent. Anal. Calcd for $C_{12}H_{13.40}D_{2.60}O$: C, 80.58; H, 10.48. Found: C, 80.35; H, 10.22.



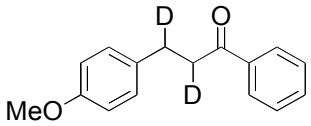
entry 3 of Table 1

6-Chloro-2,3-dideuterio-1-phenyl-1-hexanone (4c).[13] A colorless oil. Isolated by PTLC on SiO_2 (hexane:ethyl acetate = 10:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.53 (q, *J* = 7.5 Hz, 2 H), 1.69–1.79 (m, 0.83 H, β), 1.83 (quint, *J* = 7.2 Hz, 2 H), 2.93–3.01 (m, 0.44 H, α), 3.55 (t, *J* = 6.7 Hz, 2 H), 7.46 (t, *J* = 7.7 Hz, 2 H), 7.56 (t, *J* = 7.4 Hz, 1 H), 7.96 (d, *J* = 7.0 Hz, 2 H). Anal. Calcd for $C_{12}H_{12.27}D_{2.73}ClO$: C, 67.53; H, 8.37. Found: C, 67.68; H, 8.30.



entry 4 of Table 1

2,3-Dideuterio-1,3-diphenyl-1-propanone (4d).[11] A white solid. Isolated by PTLC on SiO_2 (hexane:ethyl acetate = 5:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.01–3.10 (m, 0.98 H, β), 3.23–3.33 (m, 0.79 H, α), 7.21 (t, *J* = 7.3 Hz, 1 H), 7.26 (d, *J* = 7.3 Hz, 2 H), 7.30 (t, *J* = 7.5 Hz, 2 H), 7.45 (t, *J* = 7.5 Hz, 2 H), 7.56 (t, *J* = 7.5 Hz, 1 H), 7.96 (d, *J* = 8.2 Hz, 2 H). Anal. Calcd for $C_{15}H_{11.77}D_{2.23}O$: C, 84.78; H, 7.70. Found: C, 84.94; H, 7.59.



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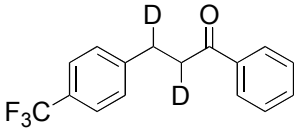
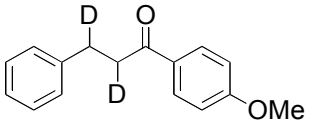
2,3-Dideuterio-3-(4-methoxyphenyl)-1-phenyl-1-propanone (4e). [14] A white solid. Isolated by PTLC on SiO_2 (hexane:ethyl acetate = 5:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.96–3.03 (m, 0.91 H, β), 3.20–3.28 (m, 0.69 H, α), 3.79 (s, 3 H), 6.84 (d, *J* = 8.8 Hz, 2 H), 7.17 (d, *J* = 8.8 Hz, 2 H), 7.45 (t, *J* = 7.4 Hz, 2 H), 7.55 (t, *J* = 7.4 Hz, 1 H), 7.95 (d, *J* = 7.4 Hz, 2 H). Anal. Calcd for $C_{16}H_{13.60}D_{2.40}O_2$: C, 79.18; H, 7.64. Found: C, 79.09; H, 7.64.



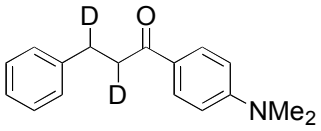
entry 6 of Table 1

2,3-Dideuterio-1-phenyl-3-[4-(trifluoromethyl)phenyl]-1-propanone (4f). [15] A white solid. Isolated by column chromatography on SiO_2 (hexane:ethyl acetate = 15:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.08–3.16 (m, 1.03 H, β), 3.27–3.35 (m, 0.65 H, α), 7.37 (d, *J* = 7.8 Hz, 2 H), 7.46 (t, *J* = 7.8 Hz, 2 H), 7.55 (d, *J* = 7.9 Hz, 2 H), 7.57 (t, *J* = 7.8 Hz, 1 H), 7.95 (d, *J* = 7.9 Hz, 2 H). Anal. Calcd for $C_{16}H_{10.68}D_{2.32}F_3O$: C, 68.49; H, 5.50. Found: C, 68.53; H, 5.72.



entry 7 of Table 1

2,3-Dideuterio-1-(4-methoxyphenyl)-3-phenyl-1-propanone (4g). [16] A white solid. Isolated by column chromatography on SiO_2 (hexane:ethyl acetate = 10:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.00–3.08 (m, 0.95 H, β), 3.19–3.26 (m, 0.55 H, α), 3.87 (s, 3 H), 6.93 (d, *J* = 8.9 Hz, 2 H), 7.21 (t, *J* = 7.2 Hz, 1 H), 7.25 (d, *J* = 7.2 Hz, 2 H), 7.30 (t, *J* = 7.2 Hz, 2 H), 7.94 (d, *J* = 8.9 Hz, 2 H). Anal. Calcd for $C_{16}H_{13.50}D_{2.50}O_2$: C, 79.14; H, 7.68. Found: C, 79.06; H, 7.58.



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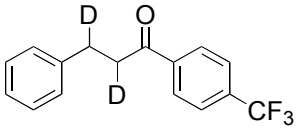
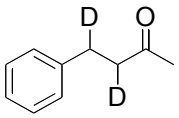
2,3-Dideuterio-1-[4-(dimethylamino)phenyl]-3-phenyl-1-propanone (4h). [17] A white solid. Isolated by PTLC on SiO_2 (hexane:ethyl acetate = 5:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.00–3.08 (m, β), 3.06 (s, 6 H, $N(CH_3)_2$), 3.13–3.22 (m, α), 6.66 (d, *J* = 9.1 Hz, 2 H), 7.20 (t, *J* = 7.0 Hz, 1 H), 7.23–7.28 (m, 2 H), 7.29 (t, *J* = 7.7 Hz, 2 H), 7.88 (d, *J* = 9.1 Hz, 2 H); (500 MHz, DMSO) δ 2.83–2.91 (m, 1.04 H, β), 2.99 (s, 6 H), 3.12–3.19 (m, 0.42 H, α), 6.69 (d, *J* = 9.2 Hz, 2 H), 7.12–7.18 (m, 1 H), 7.20–7.29 (m, 4 H), 7.81 (d, *J* = 9.2 Hz, 2 H). The deuterium ratio was determined by ^{1}H NMR using DMSO-*d* as a solvent, as the peak of the β

protons overlap with that of the dimethylamino group in $CDCl_3$ as a solvent. Anal. Calcd for $C_{17}H_{16.46}D_{2.54}ON$: C, 79.79; H, 8.48. Found: C, 79.55; H, 8.21.



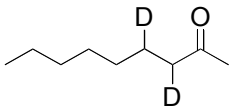
entry 9 of Table 1

2,3-Dideuterio-3-phenyl-1-[4-(trifluoromethyl)phenyl]-1-propanone (4i). [18] A white solid. Isolated by PTLC on SiO_2 (hexane:ethyl acetate = 8:1). ^1H NMR (500 MHz, $CDCl_3$) δ 3.01–3.11 (m, 0.95 H, β), 3.24–3.35 (m, 0.69 H, α), 7.18–7.27 (m, 3 H), 7.31 (t, J = 7.4 Hz, 2 H), 7.72 (d, J = 8.1 Hz, 2 H), 8.05 (d, J = 8.1 Hz, 2 H). Anal. Calcd for $C_{16}H_{10.64}D_{2.36}OF_3$: C, 68.48; H, 5.51. Found: C, 68.48; H, 5.77.



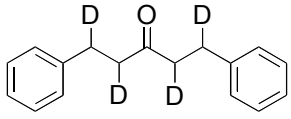
entry 10 of Table 1

3,4-Dideuterio-3-phenyl-2-butanone (4j).[19] A colorless oil. Isolated by PTLC on SiO_2 (hexane:ethyl acetate = 8:1). ^1H NMR (500 MHz, $CDCl_3$) δ 2.08–2.16 [m, 1.57 H, C(=O)C$\underline{H}_3$], 2.70–2.78 (m, 0.44 H, α), 2.84–2.91 (m, 1.02 H, β), 7.16–7.22 (m, 3 H), 7.28 (t, J = 7.5 Hz, 2 H). Anal. Calcd for $C_{10}H_{8.03}D_{3.97}O$: C, 78.92; H, 10.57. Found: C, 78.88; H, 10.34.



entry 11 of Table 1

3,4-Dideuterio-2-nonanone (4k).[20] A colorless oil. Isolated by column chromatography on SiO_2 (hexane:ethyl acetate = 10:1) followed by bulb-to-bulb distillation (110 °C/12 mmHg). ^1H NMR (500 MHz, $CDCl_3$) δ 0.87 (t, J = 6.9 Hz, 3 H), 1.20–1.35 (m, 8 H), 1.50–1.60 (m, β), 2.08–2.14 [m, C(=O)C$\underline{H}_3$], 2.34–2.43 (m, α); (500 MHz, DMSO) δ 0.90 (t, J = 7.0 Hz, 3 H), 1.17–1.37 (m, 8 H), 1.40–1.51 (m, 0.94 H, β), 2.05–2.12 [m, 2.80 H, C(=O)C$\underline{H}_3$], 2.37–2.45 (m, 0.95 H, α). The deuterium ratio was determined by ^1H NMR using DMSO-*d* as a solvent, as the peak of the β protons overlap with that of water in $CDCl_3$ as a solvent. Anal. Calcd for $C_9H_{15.68}D_{2.32}O$: C, 74.77; H, 14.16. Found: C, 74.98; H, 14.04.



entry 12 of Table 1

1,2,4,5-Tetradeuterio-1,5-diphenyl-3-pentanone (4l).[21] A white solid. Isolated by PTLC on SiO_2 (hexane:ethyl acetate = 5:1). ^1H NMR (500 MHz, $CDCl_3$) δ 2.62–2.72 (m, 0.78 H, α), 2.82–2.90 (m, 2.0 H, β), 7.15 (d, J = 7.4 Hz, 4 H), 7.18 (tt, J = 7.6, 1.9 Hz, 2 H), 7.27 (t, J = 7.5 Hz, 4 H). Anal. Calcd for $C_{17}H_{12.78}D_{5.22}O$: C, 83.83; H, 9.60. Found: C, 84.02; H, 9.33.

The Assignment of the Peaks of α- and β-Methylenes in ^{1}H NMR.

4d-*h*, **4e-*h***, **4f-*h***, **4g-*h***, **4h-*h*** and **4i-*h***: On treatment of 1,3-diphenyl-1-propane (**4d-*h***: 20.3 mg, 0.965 mmol) with NaH (11.1 mg, 56% in oil, 0.259 mmol) and D_2O (1.0 mL) in THF (0.50 mL) at room temperature for 18 h, the triplet at 3.31 ppm (J = 7.7 Hz) had disappeared, whereas the triplet at 3.07 ppm (J = 7.7 Hz) had changed to a broad singlet. Consequently, the triplets at 3.31 ppm and 3.07 ppm were assigned to the α- and β-methylenes, respectively. The chemical shifts of the α- and β-methylenes of the other chalcon derivatives (**4e-*h***, **4f-*h***, **4g-*h***, **4h-*h*** and **4i-*h***) were assigned based on those of **4d-*h***.

4a-*h*, **4b-*h***, **4c-*h***, **4j-*h***, **4k-*h*** and **4l-*h***: The chemical shifts of the α- and β-methylenes of **4j-*h*** [22] and **4k-*h*** [4] were assigned according to the literature. Those of **4a-*h***, **4b-*h*** and **4c-*h*** were assigned based on those of **4k-*h***, whereas the assignment was done for **4l-*h*** based on **4j-*h***.

The Reaction of a α-Palladioacetophenone with Deuterio(dimethyl)phenylsilane. A solution of chloro(benzoylmethyl)bis(triphenylphosphine)palladium (**7'**: 7.9 mg, 0.010 mmol), 1,8-bis(dimethylamino)naphthalene (**10**: 6.5 mg, 0.030 mmol) and *p*-dimethoxybenzene as an internal standard (2.6 mg) in DMF-d_7 (0.60 mL) was stirred at room temperature. To the resulting mixture were added a solution of deuterio(dimethyl)phenylsilane (**6b-*d***: 2.1 mg, 15 mmol) in DMF-d_7 (20 μL). After the mixture was stirred at room temperature for 1 h, 1-(dimethylphenylsiloxy)-1-phenylethene **9a**, α-deuterioacetophenone (**11**) and acetophenone (**12**) were determined by ^{1}H NMR.

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