Palladium(II)-Catalyzed Intramolecular 1,4-Oxyacyloxylation of Conjugated Dienes. A Stereocontrolled Route to Fused 6-Membered Lactones and Pyrans

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Supporting Information

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Experimental section

General Remarks. ^1H (400 or 300 MHz) and ^{13}C (100 or 75 MHz) NMR spectra were recorded on a Varian Mercury spectrometer. Chemical shifts (δ) are reported in ppm, using residual solvent proton resonance or tetramethylsilane as internal standard. Merck silica gel 60 (240-400 mesh) was used for flash chromatography and analytical thin-layer chromatography was performed on Merck precoated silica gel 60-F₂₅₄ plates. Unless otherwise noted, all materials were obtained from commercial suppliers and used without further purification. Tetrahydrofuran (THF) and diethyl ether (Et₂O) were freshly distilled from sodium benzophenone ketyl prior to use. Solvents for extraction and chromatography (pentane, ethyl acetate and diethyl ether) were technical grade and distilled. Elemental analysis was performed by Analytische Laboratorien, Lindlar, Germany. Mass spectra were recorded on a Finigan-MAT GCQ instrument. Triflates **1a-d** were prepared according to a literature procedure.¹³ 2-Cycloheptadien-1-one was prepared in 4 steps from cycloheptanol via acid-catalyzed elimination, palladium(II)-catalyzed allylic oxidation, hydrolysis and PDC oxidation, respectively.

5,5-Dimethylcyclohexa-1,3-dienyl-2-triflate (1c). Prepared from 4,4-dimethyl-2-cyclohexen-1-one following a literature procedure.¹³ ^1H NMR: δ 5.76-5.67 (m, 2H), 5.65-5.59 (m, 1H), 2.29 (d, J = 4.8 Hz, 2H), 1.07 (s, 6H). ^{13}C NMR: δ 142.7, 120.9, 118.4, 116.6, 114.0, 36.7, 31.4, 27.6.

(5R)-2-Methyl-5-(2-propenyl)cyclohexa-1,3-dienyl-3-triflate (1d). Prepared from *R*-(-)-carvone following a literature procedure.¹³ ^1H NMR: δ 5.70 (m, 1H), 5.65 (d, J = 4.3 Hz, 1H), 4.82 (m, 2H), 3.17 (ddd, J = 11.8, 9.2, 4.3 Hz, 1H), 2.40-2.20 (m, 2H), 1.82 (q, J = 1.9 Hz, 3H), 1.75 (br s, 3H). ^{13}C NMR: δ 147.8, 145.3, 127.2, 126.1, 118.5 (q, $J(^{13}\text{C}, ^{19}\text{F})$ = 320 Hz), 118.1, 111.8, 41.4, 27.6, 20.6, 16.6.

3-(2-Cycloheptadienyl)propanoic acid ethyl ester (2b). Reaction of diene triflate **1b** following the general procedure gave **2b** as a colorless oil in 86% yield. ^1H NMR: δ 5.85 (dt, J = 11.6, 5.2 Hz, 1H), 5.66 (m, 2H), 4.11 (q, J = 7.2 Hz, 2H), 2.42-2.30 (m, 4H), 2.27 (m, 2H), 2.20 (m, 2H), 1.82 (m, 2H), 1.24 (t, J = 7.2 Hz, 3H). ^{13}C NMR: δ 173.5, 135.4, 134.3, 129.6, 128.3, 60.4, 34.81, 34.76, 31.6, 30.0, 27.7, 14.4.

4-(2-Cyclohexadienyl)butanoic acid ethyl ester (2c). Reaction of diene triflate **1a** following the general procedure gave **2c** as a colorless oil in 86% yield. ^1H NMR: δ 5.86-5.78 (m, 2H), 5.50-5.45 (m, 1H), 4.15-4.08 (q, $J = 7.2$ Hz, 2H), 2.30-2.25 (t, $J = 7.6$ Hz, 2H), 2.12-2.07 (m, 4H), 2.07-2.01 (m, 2H), 1.77-1.69 (m, 2H), 1.27-1.22 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR: δ 173.8, 134.9, 127.1, 127.0, 121.1, 60.3, 34.9, 33.7, 23.7, 22.5, 22.5, 14.4.

3-(2-(5,5-Dimethylcycloheptadienyl))propanoic acid ethyl ester (2d). Reaction of diene triflate **1c** following the general procedure gave **2d** as a colorless oil in 74% yield. ^1H NMR: δ 5.69-5.65 (dd, $J = 10.0, 1.6$ Hz, 1H), 5.56-5.52 (dd, $J = 9.6, 0.8$ Hz, 1H), 5.43-5.39 (m, 1H), 4.15-4.09 (q, $J = 7.2$ Hz, 2H), 2.43-2.37 (m, 2H), 2.37-2.31 (m, 2H), 2.07-2.04 (dt, $J = 4.4, 1.6$ Hz, 2H), 1.27-1.22 (t, $J = 7.2$ Hz, 3H), 0.96 (s, 6H). ^{13}C NMR: δ 173.4, 138.8, 133.0, 124.2, 120.1, 60.4, 38.0, 33.7, 31.0, 30.6, 27.9, 14.4.

2-(2-Cycloheptadienyl)benzoic acid methyl ester (2f). Reaction of the organozinc reagent **5** (1.33 g, 6.2 mmol) with diene triflate **1b** (1.0 g, 4.1 mmol) following the same procedure as for **2e** gave 321 mg (34%) of the title compound as a colorless oil. ^1H NMR: δ 7.72-7.69 (ddd, $J = 7.6, 1.6, 0.8$ Hz, 1H), 7.44-7.39 (dt, $J = 7.6, 1.6$ Hz, 1H), 7.31-7.28 (dt, $J = 7.6, 1.6$ Hz, 1H), 7.28-7.24 (ddd, $J = 7.6, 1.6, 0.8$ Hz, 1H), 5.95-5.84 (m, 2H), 5.81-5.76 (m, 1H), 3.80 (s, 3H), 2.43-2.38 (m, 4H), 2.03-1.95 (m, 2H). ^{13}C NMR: δ 169.4, 145.5, 139.1, 133.6, 132.2, 131.4, 130.5, 129.9, 129.6, 128.8, 126.7, 52.0, 31.6, 30.4, 28.1.

(5R)-3-[3-(2-Methyl-5-(2-propenyl)cyclohexa-1,3-dienyl)]propanoic acid ethyl ester (2g). Reaction of diene triflate **1d** following the general procedure gave **2g** as a colorless oil in 75% yield. ^1H NMR (300 MHz): δ 5.57 (br s, 1H), 5.41 (d, $J = 3.5$ Hz, 1H), 4.73 (d, $J = 1$ Hz, 2H), 4.13 (q, $J = 7.1$ Hz, 2H), 2.83 (m, 1H), 2.43 (m, 4H), 2.09 (m, 2H), 1.79 (d, $J = 2$ Hz, 3H), 1.72 (d, $J = 1$ Hz, 3H), 1.25 (t, $J = 7.1$ Hz, 3H). ^{13}C NMR (300 MHz): δ 173.2, 147.9, 136.3, 132.2, 124.9, 122.5, 110.1, 60.3, 41.7, 33.7, 28.1, 27.8, 20.8, 19.1, 14.2. MS m/z 234 (M^+ , 24), 188 (13), 160 (62), 131 (100), 105 (60), 91 (24), 77 (9). IR (neat) 2936, 1737, 1646, 1436, 1373, 1158, 891 cm^{-1} .

3-(2-Cycloheptadienyl)propanoic acid (3b). Hydrolysis of diene **2b** following the general procedure gave **3b** as a colorless oil in 98% yield. ^1H NMR: δ 5.87 (dt, $J = 11.6, 5.2$ Hz, 1H),

5.67 (m, 2H), 2.50-2.42 (m, 2H), 2.39-2.32 (m, 2H), 2.32-2.17 (m, 4H), 1.87-1.78 (m, 2H). ^{13}C NMR: δ 179.5, 135.1, 134.6, 129.8, 128.1, 34.42, 34.40, 31.7, 30.0, 27.6. MS m/z 166 (M^+ , 27), 106 (32), 91 (100), 77 (22). IR (neat) 2927, 1708, 1425, 1300, 1213, 934 cm^{-1} .

4-(2-Cyclohexadienyl)butanoic acid (3c). Hydrolysis of diene **2c** following the general procedure gave **3c** as a colorless oil in 98% yield. ^1H NMR: δ 5.87-5.77 (m, 2H), 5.51-5.46 (m, 1H), 2.36-2.32 (m, 2H), 2.12-2.04 (m, 6H), 1.79-1.70 (m, 2H). ^{13}C NMR: δ 180.6, 134.7, 127.2, 126.9, 121.3, 34.8, 33.4, 23.3, 22.5, 22.4.

2-(2-Cycloheptadienyl)benzoic acid (3e). Hydrolysis of diene **2f**, following the same procedure as for **3d**, gave **3e** as a colorless oil in 96% yield. ^1H NMR: δ 7.91-7.87 (dd, J = 7.5, 1.2 Hz, 1H), 7.51-7.45 (dt, J = 7.5, 1.5 Hz, 1H), 7.36-7.30 (dt, J = 7.5, 1.5 Hz, 1H), 7.30-7.26 (dd, J = 7.5, 1.5 Hz, 1H), 5.96-5.80 (m, 3H), 2.44-2.36 (m, 4H), 2.05-1.96 (m, 2H). ^{13}C NMR: δ 174.0, 146.6, 139.0, 133.8, 132.3, 132.2, 130.4, 130.3, 129.1, 128.7, 126.8, 31.6, 30.5, 27.9.

(5R)-3-[3-(2-Methyl-5-(2-propenyl)cyclohexa-1,3-dienyl)]propanoic acid (3f). Hydrolysis of diene **2g** following the general procedure gave **3f** as a colorless oil in 97% yield. ^1H NMR: δ 5.59 (m, 1H), 5.44 (d, J = 3.5 Hz, 1H), 4.74 (m, 2H), 2.85 (m, 1H), 2.47 (m, 4H), 2.19-2.01 (m, 2H), 1.79 (app. q, J = 1.9 Hz, 3H), 1.72 (br s, 3H). ^{13}C NMR: δ 179.5, 147.9, 136.0, 125.2, 122.8, 110.2, 41.8, 33.5, 28.2, 27.6, 20.8, 19.1. MS m/z 206 (M^+ , 45), 191 (13), 145 (27), 131 (74), 105 (100), 91 (42). IR (neat) 2938, 1713, 1440, 1376, 1286, 1026, 892, 823 cm^{-1} .

3-(2-cycloheptadienyl)propanol (4b). Reduction of ethyl ester **2b** with LiAlH_4 gave **4b** as a colorless oil in 98% yield. ^1H NMR: δ 5.89-5.80 (m, 1H), 5.71-5.63 (m, 2H), 3.66-3.60 (t, J = 6.6 Hz, 2H), 2.32-2.17 (m, 4H), 2.14-2.07 (m, 2H), 1.87-1.78 (m, 2H), 1.72-1.62 (m, 2H), 1.51 (s, 1H). ^{13}C NMR: δ 136.4, 134.0, 129.2, 128.6, 62.6, 35.8, 32.3, 31.7, 30.0, 27.7.

3-(2-(5,5-Dimethylcyclohexadienyl))propanol (4c). Reduction of ethyl ester **2d** with LiAlH_4 gave **4d** as a colorless oil in 94% yield. ^1H NMR: δ 5.72-5.67 (dd, J = 9.6, 1.5 Hz, 1H), 5.56-5.51 (dd, J = 9.6, 0.9 Hz, 1H), 5.44-5.38 (m, 1H), 3.67-3.61 (t, J = 6.6 Hz, 2H), 2.15-2.05 (m,

4H), 1.73-1.63 (m, 2H), 1.37 (br s, 1H), 0.97 (s, 6H). ^{13}C NMR: δ 138.6, 133.9, 124.4, 119.8, 62.6, 38.1, 31.5, 31.4, 31.0, 28.0.

Compound 9c. Using the same procedure and amounts as for **9a**, but without added LiCl and LiOAc $\cdot$ 2H $_2$ O, lactone **9c** was isolated in 53% yield as a white solid. Mp. 63-65°C. ^1H -NMR, δ : 5.66 (br s, 1H), 5.32 (m, 1H), 4.83 (m, 1H), 2.71-2.42 (m, 4H), 2.26 (ddt, J = 13.1, 5.7, 3.0 Hz, 1H), 2.16 (m, 1H), 2.01 (s, 3H), 1.77 (ddt, J = 13.1, 8.9, 3.0 Hz, 1H), 1.56 (ddt, J = 12.9, 8.6, 2.7 Hz, 1H). ^{13}C NMR: δ 171.7, 170.4, 135.5, 125.0, 74.9, 68.7, 29.6, 27.2, 26.0, 25.2, 21.0. MS m/z 210 (M^+ , 0.9), 168 (100), 150 (52), 122 (43), 108 (28), 95 (51), 79 (33). IR (neat) 2938, 1734, 1438, 1366, 1244, 1185, 1154, 1023 cm^{-1} .

Compound 10a. Following the general procedure, **3b** was allowed to react in the presence of 1 equiv. LiAOc $\cdot$ 2H $_2$ O but without added LiCl. The substrate was added at once and the reaction was stirred at 40 °C for 36 h. Chromatography (pentane/Et $_2$ O 1:3) gave an inseparable mixture of two isomers **10a** and **10b** (91:9) in 98% yield. A pure sample of **10a** was obtained by recrystallization from pentane/Et $_2$ O. ^1H NMR: δ 5.56 (br s, 1H), 5.33-5.24 (br d, J = 10.9 Hz, 1H), 4.99-4.93 (br d, J = 10.9 Hz, 1H), 2.60-2.45 (m, 4H), 2.14-2.00 (m, 2H), 2.06 (s, 3H), 1.88-1.73 (m, 2H), 1.72-1.50 (m, 2H). ^{13}C NMR: δ 172.0, 170.3, 135.8, 127.7, 80.9, 73.0, 33.7, 31.9, 30.5, 28.7, 23.7, 21.3. MS m/z 182 (86), 164 (42), 136 (100), 109 (43), 79 (39). Anal. Calc. for C $_{12}$ H $_{16}$ O $_4$: C, 64.27; H, 7.19; Found: C, 64.39; H, 7.16.

Compound 10b. ^1H NMR (Distinguishable peaks in mixture of isomers): δ 6.08-5.99 (dt, J = 11.7, 6.3 Hz, 1H), 5.59 (d, J = 11.7 Hz, 1H), 5.04-4.99 (dd, J = 8.4, 3.3 Hz, 1H), 2.08 (s, 3H).

Compound 11a. Following the general procedure, **3d** was allowed to react in the presence of 2 equiv. LiAOc $\cdot$ 2H $_2$ O and 0.5 equiv. LiCl, using 2 equiv. of *p*-benzoquinone as the oxidant. Chromatography (pentane/Et $_2$ O 1:3) gave **11a** and **11b** in a 55:45 ratio in 50% combined yield.

White solid. Mp. 89-91°C. ^1H NMR: δ 8.14 (dd, J = 7.9, 1.3 Hz, 1H), 7.64-7.54 (m, 2H), 7.48 (m, 1H), 6.48 (ddd, J = 4.7, 2, 1 Hz, 1H), 5.41 (m, 1H), 5.06 (m, 1H), 2.30-2.20 (m, 2H), 2.08 (s, 3H), 2.10-2.02 (m, 1H), 1.90 (m, 1H). ^{13}C NMR: δ 170.6, 164.2, 136.2, 134.1, 130.4, 129.5, 124.1, 123.8, 123.3, 74.7, 66.5, 25.4, 24.5, 21.1. IR (KBr) 2938, 1719, 1654, 1601, 1368, 1265, 1234, 1116, 1041, 775.

Compound 11b. White solid. Mp. 146-148°C. ^1H NMR: δ 8.16 (dd, $J = 7.8, 1.4$ Hz, 1H), 7.64-7.46 (m, 3H), 6.49 (ddd, $J = 5.0, 2, 1$ Hz, 1H), 5.12 (ddd, $J = 9.9, 5.9, 1.8$ Hz, 1H), 4.84 (m, 1H), 2.49-2.38 (m, 1H), 2.35-2.24 (m, 2H), 2.21-2.10 (m, 1H). ^{13}C NMR: δ 164.1, 135.8, 134.1, 132.1, 130.5, 129.7, 126.0, 123.9, 123.2, 74.7, 53.9, 29.3, 24.0.

Compound 11c. Following the general procedure, **3d** was allowed to react in the absence of $\text{LiOAc}\cdot 2\text{H}_2\text{O}$ and LiCl , using 2 equiv. of *p*-benzoquinone as the oxidant. Chromatography (pentane/ Et_2O 1:3) gave **11c** as a single isomer in 47% yield. White solid. Mp. 101-102°C. ^1H NMR: δ 8.13 (dd, $J = 7.9, 1$ Hz, 1H), 7.63-7.54 (m, 2H), 7.47 (m, 1H), 6.34 (m, 1H), 5.58 (m, 1H), 5.14 (m, 1H), 2.45 (m, 1H), 2.32 (m, 1H), 2.12 (s, 3H), 2.03 (ddt, $J = 13.6, 9.4, 2.9$ Hz, 1H), 1.69 (ddt, $J = 13.3, 9.4, 2.9$ Hz, 1H). ^{13}C NMR: δ 170.6, 164.5, 136.1, 134.2, 132.6, 130.5, 129.5, 126.6, 123.8, 123.4, 74.7, 69.0, 27.5, 26.5, 21.3. IR (KBr) 2944, 1732, 1600, 1463, 1365, 1234, 1123, 1027, 972, 918, 769.

Compound 12. Following the general procedure, **3e** was allowed to react in the presence of 2M $\text{LiOAc}\cdot 2\text{H}_2\text{O}$ but without added LiCl . The substrate was added at once and the reaction was stirred at 40 °C for 36 h. Chromatography (pentane/ Et_2O 1:2) gave **12** as a single isomer in 63% yield as a white solid. ^1H NMR: δ 8.14-8.10 (ddd, $J = 7.8, 1.5, 0.6$ Hz, 1H), 7.63-7.59 (dd, $J = 8.1, 1.8$ Hz, 1H), 7.59-7.53 (dt, $J = 7.5, 1.5$ Hz, 1H), 7.44-7.37 (ddd, $J = 8.1, 6.6, 1.5$ Hz, 1H), 6.44 (dd, $J = 4.5, 1.8$ Hz, 1H), 5.66-5.58 (dddd, $J = 11.1, 4.8, 3.3, 1.5$, 1H), 5.38-5.32 (m, 1H), 2.26-2.15 (m, 1H), 2.11 (s, 3H), 2.09-1.86 (m, 4H), 1.79-1.66 (m, 1H). ^{13}C NMR: δ 170.3, 163.7, 135.6, 134.1, 131.1, 130.4, 129.9, 128.9, 122.8, 122.3, 79.9, 72.3, 32.3, 31.4, 21.8, 21.3. Anal. Calc. For $\text{C}_{16}\text{H}_{16}\text{O}_4$: C, 70.57; H, 5.92; Found: C, 70.42; H, 5.94.

Compound 14. Following the general procedure, **3f** was allowed to react in the presence of 2 equiv. $\text{LiOAc}\cdot 2\text{H}_2\text{O}$ and 0.5 equiv. LiCl , using 2 equiv. of *p*-benzoquinone as the oxidant. Chromatography (pentane/ Et_2O 1:3) gave **7** in 23% yield. ^1H NMR: δ 5.22 (br s, 1H), 4.92 (br s, 1H), 4.88 (s, 1H), 4.69 (d, $J = 9.7$ Hz, 1H), 2.71-2.48 (m, 5H), 2.09 (s, 3H), 1.89 (ddd, $J = 14.6, 3.3, 2.2$ Hz, 1H), 1.79 (m, 1H), 1.77 (s, 3H), 1.66 (s, 3H). ^{13}C NMR: δ 172.5, 170.8, 144.1, 130.5, 129.0, 113.0, 78.4, 70.1, 41.7, 32.1, 29.1, 23.6, 21.2, 20.6, 16.3. IR (neat) 2977, 1713, 1648, 1509, 1442, 1372, 1231, 1014, 897, 829.

Compound 18a. Following the general procedure, **4d** was allowed to react in the presence of 2.5M LiOAc·2H₂O and 0.3 equiv. LiCl. After 8 h additional stirring and workup, chromatography (pentane/Et₂O 2:1) gave an inseparable mixture of **18a** and **18b** in a 88:12 ratio in 90% yield. ¹H NMR: δ 7.66-7.62 (m, 1H), 7.25-7.21 (m, 2H), 7.04-7.00 (m, 1H), 6.40-6.37 (dt, *J* = 4.8, 1.6 Hz, 1H), 5.41-5.37 (m, 1H), 4.90-4.86 (d, *J* = 14.8 Hz, 1H), 4.84-4.80 (d *J* = 14.8 Hz, 1H), 4.18-4.12 (m, 1H), 2.14-2.07 (m, 1H), 2.06 (s, 3H), 2.05-1.97 (m, 1H), 1.95-1.80 (m, 2H). ¹³C NMR: δ 171.0, 137.6, 135.0, 130.0, 128.4, 127.1, 124.8, 123.5, 116.8, 73.8, 68.3, 67.4, 26.2, 25.0, 21.5.

Compound 18b. Following the general procedure, **4d** was allowed to react in the absence of LiCl and LiOAc·2H₂O. After 8 h additional stirring and workup, chromatography (pentane/Et₂O 2:1) gave a mixture of **18a** and **18b** in a 20:80 ratio in 80% yield. A pure sample of **18b** was obtained by recrystallization from pentane/Et₂O as white crystals. ¹H NMR: δ 7.65-7.58 (m, 1H), 7.27-7.19 (m, 2H), 7.05-6.98 (m, 1H), 6.21 (m, 1H), 5.63-5.54 (m, 1H), 4.93-4.87 (d, *J* = 15.0 Hz, 1H), 4.84-4.78 (d, *J* = 15.0 Hz, 1H), 4.27-4.20 (m, 1H), 2.34-2.23 (m, 2H), 2.11 (s, 3H), 1.80-1.54 (m, 2H). ¹³C NMR: δ 170.9, 135.9, 134.7, 130.1, 128.2, 127.1, 124.7, 123.5, 119.6, 73.4, 70.5, 68.4, 28.2, 26.8, 21.5. Anal. Calc. for C₁₅H₁₆O₃: C, 73.75; H, 6.60; Found: C, 73.94; H, 6.72.

***N*-tosyl-3-(2-cycloheptadienyl)propylamide (19).** Diene alcohol **4b** (400 mg, 2.63 mmol) was dissolved in 4 mL CH₂Cl₂, and Et₃N (552 μL, 3.95 mmol) was added. The solution was cooled to 0 °C and methanesulfonyl chloride (254 μL, 3.29 mmol) was added dropwise. Stirring was continued for 1.5 h at rt. After evaporation of the solvent, the product was dissolved in Et₂O, the organic phase was washed with water and brine, dried (MgSO₄) and evaporated.

The mesylated diene alcohol was dissolved in 7 mL DMF and sodium *p*-toluenesulfonamide (605 mg, 3.13 mmol) was added. The solution was stirred for 12h at rt. The solvent was evaporated and Et₂O was added. The organic phase was washed with water and brine, dried (MgSO₄) and evaporated. Column chromatography (pentane/EtOAc 2:1) gave 431 mg (54%) of **19** as a colorless oil. ¹H NMR: δ 7.76-7.72 (m, 2H), 7.32-7.28 (m, 2H), 5.84-5.77 (m, 1H), 5.58-5.50 (m, 2H), 4.58 (br s, 1H), 2.96-2.88 (m, 2H), 2.42 (s, 3H), 2.27-2.21 (m, 2H), 2.19-2.12 (m, 2H), 2.01-1.96 (m, 2H), 1.81-1.74 (m, 2H), 1.59-1.51 (m, 2H). ¹³C NMR: δ 143.4, 137.1, 135.5, 134.3, 129.8 (2C), 128.2, 127.3, 42.7, 36.4, 31.7, 30.0, 28.9, 27.6, 21.6.

Benzyl carbamic acid (20). Diene alcohol **4b** (595 mg, 3.91 mmol) was dissolved in 6 mL CH₂Cl₂, and Et₃N (820 μ L, 5.87 mmol) was added. The solution was cooled to 0 °C and methanesulfonyl chloride (379 μ L, 4.89 mmol) was added dropwise. Stirring was continued for 1.5 h at rt. After evaporation of the solvent, the product was dissolved in Et₂O, the organic phase was washed with water and brine, dried (MgSO₄) and evaporated.

Potassium phthalimide (797 mg, 4.30 mmol) and KI (80 mg, 0.03 mmol) were suspended in DMF (12 mL). The mesylated alcohol, dissolved in 3 mL DMF, was added and the reaction was stirred overnight at r.t. The solvent was evaporated and the product was dissolved in ether. The organic phase was washed with water and brine, dried (MgSO₄) and evaporated. Column chromatography (pentane/Et₂O 1:1) gave 857 mg (78 %) of the phthalimide as a colorless oil. ¹H NMR: δ 7.83-7.78 (dd, *J* = 3.2, 5.6 Hz, 2H), 7.73-7.65 (dd, *J* = 3.2, 5.6 Hz, 2H), 5.88-5.78 (m, 1H), 5.69-5.61 (m, 2H), 3.70-3.61 (t, *J* = 6.6 Hz, 2H), 2.28-2.11, (m, 4H), 2.11-2.03, (m, 2H), 1.84-1.72 (m, 4H). ¹³C NMR: δ 168.5, 135.7, 134.0, 133.9, 132.3, 129.4, 128.5, 123.2, 37.9, 36.8, 31.6, 30.0, 28.1, 27.8.

The phthalimide (625 mg, 2.22 mmol) was dissolved in 95% EtOH (50 mL) and hydrazine monohydrate (162 μ L, 3.34 mmol) was added. The solution was stirred at r.t. for 1 h followed by 40 °C overnight. EtOH was evaporated *in vacuo* and the material was dissolved in 2M NaOH and stirred at rt for 1h. The solution was acidified to neutral pH and the product was extracted with EtOAc, after which the organic phase was dried (Na₂SO₄) and evaporated. Column chromatography (pentane/Et₂O 1:1) gave 240 mg (71 %) of the amine as a colorless oil.

The amine (240 mg, 1.59 mmol) was dissolved in THF (2 mL) and H₂O (1 mL) under argon and NaOH (70 mg, 1.75 mmol) was added. The solution was cooled to 0 °C and benzyl chloroformate (250 μ L, 1.75 mmol) was added dropwise. The solution was stirred at that temperature for 2 h and then at r.t for 12 h. Ethyl acetate was added and the organic phase was washed with brine (x 2), dried (Na₂SO₄) and evaporated. Column chromatography (pentane/Et₂O 1:1) gave 205 mg (45%) of **20** as a colorless oil. ¹H NMR: δ 7.37-7.29 (m, 5H), 5.88-5.81 (m, 1H), 5.68-5.61 (m, 2H), 5.09 (s, 2H), 4.76 (br s, 1H), 3.22-3.15 (m, 2H), 2.31-2.25 (m, 2H), 2.24-2.18 (m, 2H), 2.09-2.03 (m, 2H), 1.86-1.78 (m, 2H), 1.66-1.57 (m, 2H). ¹³C NMR: δ 156.5, 136.8, 135.9, 134.2, 129.5, 128.6, 128.4, 128.2 (2C), 66.7, 40.7, 36.8, 31.7, 30.0, 29.5, 27.7.

Compound 26. Following the same procedures for hydrolysis and esterification as for compound **25**, acetate ester **18b** was transformed into formate ester **26** in 75% (2 steps). ^1H NMR: δ 8.14 (d, $J = 0.9$ Hz, 1H), 7.63-7.58 (m, 1H), 7.27-7.21 (m, 2H), 7.06-6.99 (m, 1H), 6.21 (m, 1H), 5.77-5.68 (m, 1H), 4.94-4.87 (d, $J = 15.0$ Hz, 1H), 4.85-4.78 (d, $J = 15.0$ Hz, 1H), 4.29-4.22 (m, 1H), 2.38-2.27 (m, 2H), 1.83-1.60 (m, 2H). ^{13}C NMR: δ 160.9, 136.5, 134.7, 129.9, 128.3, 127.1, 124.8, 123.5, 118.8, 73.2, 70.3, 68.4, 28.1, 26.8. Anal. Calc. for $\text{C}_{14}\text{H}_{14}\text{O}_3$: C, 73.03; H, 6.13; Found: C, 72.86; H, 6.11.

Compound 28b. Following the general procedure, **18b** was allowed to react with the cuprate to give compound **28b** in 89% as a colorless oil. ^1H NMR: δ 7.38-7.32 (m, 1H), 7.23-7.13 (m, 2H), 7.02-6.98 (m, 1H), 6.29-6.23 (dt, $J = 9.9, 2.1$ Hz, 1H), 5.71-5.64 (dt, $J = 9.9, 3.6$ Hz, 1H), 5.06-4.99 (d, $J = 15.3$ Hz, 1H), 4.99-4.93 (d, $J = 15.3$ Hz, 1H), 3.77-3.71 (dd, $J = 12.0, 4.2$ Hz, 1H), 2.32-2.16 (m, 2H), 2.08-1.84 (m, 2H), 1.78-1.56 (m, 2H), 1.30-1.10 (m, 4H), 0.83-0.78 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR: δ 141.2, 134.3, 130.7, 126.7, 125.9, 125.6, 125.5, 124.8, 78.5, 68.8, 40.8, 38.6, 26.4, 25.2, 23.8, 23.7, 14.2.

1c-1H

Pulse Sequence: s2pul

1c-13C

Pulse Sequence: s2pul

13C OBSERVE

Solvent: CDCl₃
 Temp: 25.0 C / 298.1 K
 UNITY-400 "uppkems2"
 User andersp
 Date Apr 6 98
 Pulse sequence
 1st pulse arrayed
 2nd pulse arrayed
 Acq. time 1.49 sec
 Width 25000.0 Hz
 Observed resolution
 OBSERVE C13: 100.5671759 MHz
 DECOUPLE H1: 398.9510961 MHz
 Power 46 dB
 Continuously on
 Water gated
 DATA PROCESSING
 Line broadening 1.0 Hz
 FT size 65536
 Total time 9 minutes

2a-1H

Pulse Sequence: s2pul

2a

2a-13C

Pulse Sequence: s2pul

2b-1H

Pulse Sequence: s2pul

2b-13C

Pulse Sequence: s2pul

2c-1H

Pulse Sequence: s2pul

2c

2c-13C

Pulse Sequence: s2pul

2d-1H

Pulse Sequence: s2pul

2d-13C

Pulse Sequence: s2pul

2e**¹³C OBSERVE**

Solvent: CDCl₃
 Temp: 25.0 C / 288.1 K
 UNITY-400 "uppkemw62"
 User andersp
 Date May 28 98
 Pulse SEQUENCE arrayed
 1st pulse arrayed
 2nd pulse arrayed
 Acq. time 1.199 sec
 Width 25000.0 Hz
 Offset 100.625000 MHz
 OBSERVE C13 100.5671788 MHz
 DECOUPLE H1 399.9510961 MHz
 Power 46 dB
 Continuously on
 Water gated
 DATA PROCESSING
 Line broadening 1.0 Hz
 FT size 65536
 Total time 4 minutes

2f-1H

Pulse Sequence: s2pul

2f

2f-13C

Pulse Sequence: zgpg30

2f

STANDARD 1H OBSERVE

Solvent: cdc13
 Temp: 25.0 C / 298.1 K
 UNITY-400 "uppkemw2"
 User andersp
 Date Apr 28 98
 PREPARED BY
 Date SEQUOIE
 Relax delay arrayed
 1st pulse arrayed
 2nd pulse arrayed
 Acq. time 3.744 sec
 Width 5000.0 Hz
 Freq 500.136 MHz
 Acquired 16384000
 OBSERVE H1 399.5486782 MHz
 DATA PROCESSING
 Line broadening 0.2 Hz
 F1 size 85536
 Total time 1 minute

3a-1H

Pulse Sequence: zgpg30

3b-1H

Pulse Sequence: s2pul

3b

3b-13C

Pulse Sequence: zgpg30

3c-1H

Pulse Sequence: s2pul

3c

3c-13C

Pulse Sequence: zgpg30

3c

3d

3e-1H

Pulse Sequence: s2pul

3e

Solvent: cdd-13
 Temp: 288.1 K
 UNITY-400 "supkmems2"
 User andersp
 Date 11/11/2010
 PULSE SEQUENCE
 Relax, delay arrayed
 1st pulse arrayed
 2nd pulse 31.6 degrees
 Acq. time 3.744 sec
 Width 5000.0 Hz
 F2 399.5466782 MHz
 OBSERVE H 399.5466782 MHz
 DATA PROCESSING
 Line broadening 0.2 Hz
 FT size 65536
 Total time 1 minute

4b-1H

Pulse Sequence: s2pul

4b

4b-13C

Pulse Sequence: s2pul

4b

4c-1H

Pulse Sequence: zgpg30

4c-13C

Pulse Sequence: s2pul

STANDARD 1H OBSERVE

Solvent: cdc13
 Temp: 25.0 C / 298.1 K
 UNITY-400 "uppkemws2"
 User andersp
 Date Apr 9 98
 Pulse sequence
 Relax delay arrayed
 1st pulse arrayed
 2nd pulse arrayed
 Acq. time 3.744 sec
 Relax delay arrayed
 Arrayed 300.000 Hz
 Arrayed 300.000 Hz
 OBSERVE H1 385.3486782 MHz
 DATA PROCESSING
 Line broadening 0.2 Hz
 F1 size 65536
 Total time 1 minute

STANDARD 1H OBSERVE

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Solvent: cdcl3
Temp: 25.0 C / 298.1 K
UNIT1-400 13C NMR
=====
User      descsp
Date      Dec 14 1998
PULSE SEQUENCE: s2pu1
Pulse 28.6 degrees
Acq. time 3.744 sec
Width 6000.6 Hz
Single scan
=====
OBSERVE H1,
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 1 minute
=====

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11c-1H

Pulse Sequence: s2pul

11c

11c-13C
Pulse Sequence: zgpg30

13C-1H

Pulse Sequence: s2pul

13c-13C

Pulse Sequence: s2pul

STANDARD 1H OBSERVE

Solvent: cdc13
 Temp: 25.0 C / 298.1 K
 UNITY-400 "uppkems2"
 User andersp
 Date Jun 2 98
 Pulse sequence
 Relax delay arrayed
 1st pulse arrayed
 2nd pulse 31.6 degrees
 Acq. time 3.744 sec
 Relax delay arrayed
 Arrayed repetitions
 OBSERVE H1 399.9486782 MHz
 DATA PROCESSING
 Line broadening 0.2 Hz
 F1 size 65536
 Total time 1 minute

14

16a-1H

Pulse Sequence: s2pul

16a

16a-13C

Pulse Sequence: s2pul

16a

16b-1H

Pulse Sequence: s2pul

16b

16b-13C

Pulse Sequence: s2pul

17-1H

Pulse sequence: s2pul

17

17-13C

Pulse Sequence: zgpg30

17

18a-1H

Pulse Sequence: s2pul

18a

18a-13C

Pulse Sequence: zgpg30

18a

19-13C

Pulse sequence: s2pul

25-1H

Pulse Sequence: s2pul

25

25-13C

Pulse Sequence: s2pul

25

28a-1H

Pulse sequence: zgpg30

28a

28a-13C

Pulse Sequence: s2pul

28a

28b-1H

Pulse Sequence: s2pul

28b

28b-13C

Pulse Sequence: zgpg30

28b