The Dianion Approach to Chiral Cyclopropene Carboxylic Acids

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Supporting Information

Experimental Procedures: 9 pages
Experimental Section

General Considerations: All reactions were carried out in glassware that was flame-dried under vacuum and cooled under nitrogen. THF was distilled under nitrogen from Na/benzophenone. Triethylamine was distilled under nitrogen from CaH₂. The methyllithium was made from methyl iodide and lithium metal following a literature procedure. Pd(PPh₃)₄ was purchased from Pressure Chemical Co. The other reagents were purchased from Aldrich and used without purification. Chromatography was performed on silica gel (ICN SiliTech 32-62D, 60Å). For ¹³C NMR, multiplicities were distinguished using an APT pulse sequence: typical methylene and quaternary carbons appear ‘up’ (u); methine and methyl carbons ‘down’ (dn). Exceptions are methine carbons of alkynes and cyclopropenes, which usually have the same phase as ‘normal’ methylenes and quaternary carbons. Yields in Tables refer to isolated yields (average of 2 runs) of compounds estimated to be >95% pure as determined by HPLC and ¹H NMR.

1-Phenyl-2-butyl-3-methylcycloprop-2-ene-1-carboxylic acid

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\text{1} \rightarrow \text{MeLi} \\
\text{2} \rightarrow \text{MeOTs or Mel}
\]

To a dried 100 mL round bottomed flask was added (+/–)-1-phenyl-2-butylcycloprop-2-ene-1-carboxylic acid (108 mg, 0.50 mmol). The flask was evacuated and then refilled with nitrogen. Freshly distilled ether (30 mL) was added via syringe, and the solution was cooled in a bath of dry ice/acetone. The solution was allowed to stir and MeLi (1.30 mL of a 0.85 M solution in Et₂O, 1.10 mmol) was added via syringe. After the mixture had stirred at −78°C for 5 min, the dry ice/acetone bath was removed and the reaction mixture gradually allowed to warm to rt. To the yellow solution was added methyl p-toluenesulfonate (186 mg, 1.00 mmol). After stirring at rt for 30 min, the reaction was quenched with saturated NaCl solution, and 5% aq HCl was added to render the solution acidic (pH ~ 1–2). The organic phase was separated, and the aqueous phase was extracted three times with CH₂Cl₂. The combined organics were dried (Na₂SO₄), filtered, and concentrated. The residue was chromatographed on silica gel (20% ethyl acetate in hexane) to provide 93 mg (81%) of the title compound as a colorless oil. An identical experiment using methyl iodide instead of methyl p-toluenesulfonyl gave 92 mg (80%) of the title compound. ¹H NMR (CDCl₃, 400MHz, δ): 7.25-7.31(m, 4H), 2.51(t, J= 7.0Hz, 2H), 2.18–2.14(m, 3H), 1.55-1.61(m, 2H), 1.34-1.40(m, 2H), 0.89(t, J= 7.3Hz, 3H); ¹³C NMR (CDCl₃, 90MHz, δ): 181.2, 141.7, 128.4, 128.0, 126.1, 110.5, 105.6, 34.5, 29.1, 23.9, 22.4, 13.7, 8.9; IR (neat, cm⁻¹): 3563, 2939, 1681, 1496, 1285,1095; HRMS-Cl(NH₃) m/z: [M+H], calcd for C₁₅H₁₉Ο₂, 231.1385; found, 231.1383.
1,2-Diphenyl-3-methylcycloprop-2-ene-1-carboxylic acid

A dried 100 mL round bottomed flask was charged with (+/–)-1,2-diphenylcycloprop-2-ene-1-carboxylic acid $^{1,2}$ (118 mg, 0.50 mmol). The flask was evacuated and then refilled with nitrogen. Freshly distilled ether (30 mL) was added via syringe, and the solution was cooled in a bath of dry ice/acetone. The solution was allowed to stir and MeLi $^3$ (1.30 mL of a 0.85 M solution in Et$_2$O, 1.10 mmol) was added via syringe. After the mixture had stirred at –78°C for 5 min, the dry ice/acetone bath was removed and the reaction mixture gradually allowed to warm to rt. To the dark blue solution was added methyl p-toluenesulfonate (186 mg, 1.00 mmol). After stirring at rt for 30 min, the reaction was quenched with saturated NaCl solution, and 5% aq HCl was added to render the solution acidic (pH ~ 1–2). The organic phase was separated, and the aqueous phase was extracted three times with CH$_2$Cl$_2$. The combined organics were dried (Na$_2$SO$_4$), filtered, and concentrated. The residue was chromatographed on silica gel (25% ethyl acetate in hexane) to provide 106 mg (85%) of the title compound as a white semi-solid. An identical experiment using methyl iodide instead of methyl p-toluenesulfonate gave 104 mg (83%) of the title compound. $^1$H NMR (THF-d$_8$, 400MHz, δ): 7.56-7.52(m, 2H), 7.40-7.34(m, 4H), 7.29(app t, J=7.4Hz, 1H), 7.16(app t, J=8.0Hz, 2H), 7.05-7.09(m, 1H), 2.36(s, 3H); $^{13}$C NMR (THF-d$_8$, 90MHz, δ): 172.9(u), 140.4(u), 127.5(dn), 126.9(dn), 126.7(dn), 126.5(dn), 125.7(dn), 125.6(u), 123.7(dn), 110.0(u), 107.2(u), 33.1(u), 6.8(dn); IR(neat, cm$^{-1}$): 3520, 2936, 1687, 1500, 1275, 1091; HRMS-CI(NH$_3$) m/z: [M$^+$], calcd for C$_{17}$H$_{14}$O$_2$, 250.0993; found, 250.0987.

(R)-(–)-1,2-Diphenyl-3-methylcycloprop-2-ene-1-carboxylic acid

To a clean 100 mL round bottomed flask was added (4$R$)-3-[(1$R$)-1,2-diphenylcycloprop-2-en-1-oyl]-4-phenyloxazolidinone (160mg, 0.40mmol), THF (30mL) and water (10mL). The mixture was stirred and cooled by an ice bath (0–5°C). LiOH (45mg, 1.80mmol) and two drops of 35% hydrogen peroxide were added, and after the mixture had stirred at 0-5°C for 4 h, the reaction was quenched by aq NaHSO$_3$. The THF was removed under reduced pressure, and the mixture was extracted three times with CH$_2$Cl$_2$. The combined organics were dried (Na$_2$SO$_4$), filtered, and concentrated. The residue was chromatographed on silica gel (20% ethyl acetate in hexane) to provide 77 mg (82%) of
(R)-1,2-diphenylcycloprop-2-ene-1-carboxylic acid as a white semi-solid. $[\alpha]_D = −11.9^\circ$ (c 1.02 ethyl acetate). The enantioselectivity was measured to be 97% ee by HPLC using a CHIRALCEL AD column, eluting at 1 mL/min with 95.00/4.95/0.05 hexane/isopropanol/trifluoroacetic acid.

As described above for the analogous reaction of the racemate, a similar experiment that started with 60 mg of (R)-1,2-diphenylcycloprop-2-ene-1-carboxylic acid (97% ee)$^{2,3}$ gave 53 mg of (R)-1,2-diphenyl-3-methylcycloprop-2-ene-1-carboxylic acid, yield 85%. $[\alpha]_D = −5.8^\circ$ (c 0.98 ethyl acetate). The enantiomeric excess was measured to be 97% ee by chiral HPLC analysis (CHIRALCEL AD column, eluting at 1 mL/min with 95.00/4.95/0.05 hexane/isopropanol/trifluoroacetic acid.)

**1,2-Diphenyl-3-ethylcycloprop-2-ene-1-carboxylic acid**

![Reaction Scheme](Image)

A dried 100 mL round bottomed flask was charged with (+/–)-1,2-diphenylcycloprop-2-ene-1-carboxylic acid (118 mg, 0.50 mmol). The flask was evacuated and then refilled with nitrogen. Freshly distilled ether (30 mL) was added via syringe, and the solution was cooled in a bath of dry ice/acetone. The solution was allowed to stir and MeLi$^1$ (1.30 mL of a 0.85 M solution in Et$_2$O, 1.10 mmol) was added via syringe. After the mixture had stirred at $−78^\circ$C for 5 min, the dry ice/acetone bath was removed and the reaction mixture gradually allowed to warm to rt. To the dark blue solution was added ethyl iodide (156 mg, 1.0 mmol) and 12-crown-4 (5 mg, 0.03 mmol). After stirring at rt for 30 min, the reaction was quenched with saturated NaCl solution, and 5% aq HCl was added to render the solution acidic (pH ~1-2). The organic phase was separated, and the aqueous phase was extracted three times with dichloromethane. The combined organics were dried (Na$_2$SO$_4$), filtered, and concentrated. The residue was chromatographed on silica gel (25% Ethyl acetate in hexane) to provide 107 mg (81%) of the title compound as a white semi-solid. An identical experiment gave 110 mg (83%) of the title compound.$^1$H NMR (CDCl$_3$, 400MHz, $\delta$): 7.56-7.58(m, 2H), 7.38-7.41(m, 4H), 7.32-7.34(m, 1H), 7.23-7.27(m, 2H), 7.16-7.18(m, 1H), 2.77(dq, J=1.2 and 7.5Hz, 2H), 1.36(app t, J=7.5Hz, 3H); $^{13}$C NMR(CDCl$_3$, 90MHz, $\delta$): 179.8(u), 140.5(u), 129.3(dn), 128.9(dn), 128.9(dn), 128.3(dn), 128.0(dn), 126.3(dn), 126.1(u), 116.1(u), 107.5(u), 35.0(u), 18.5(u), 12.1(dn); IR(neat, cm$^{-1}$): 3456, 2928, 1780, 1763, 1595, 1190; HRMS-CI(NH$_3$) m/z: [M$^+$], calcd for C$_{18}$H$_{16}$O$_2$, 264.1150; found, 264.1140.
**1-Phenyl-2-butyl-3-methoxyethoxymethylcycloprop-2-ene-1-carboxylic acid**

To a dried 100 mL round bottomed flask was added (+/−)-1-phenyl-2-butylcycloprop-2-ene-1-carboxylic acid\(^2\) (216 mg, 1.0 mmol). The flask was evacuated and then refilled with nitrogen. Freshly distilled THF (30 mL) was added via syringe, and the solution was cooled in a bath of dry ice/acetone. The solution was allowed to stir and MeLi\(^1\) (1.40 mL of a 1.60 M solution in Et\(_2\)O, 2.20 mmol) was added via syringe. After the mixture had stirred at −78 °C for 5 min, the dry ice/acetone bath was replaced by an ice-water bath and gradually allowed to warm to 0–5 °C. To the dark blue solution was added MEMCl (150 mg, 1.20 mmol). After stirring at 0-5°C for 30 min, the reaction was quenched with saturated NaCl solution, and 5% aq HCl was added to render the solution acidic (pH ~ 1–2). The organic phase was separated, and the aqueous phase was extracted three times with CH\(_2\)Cl\(_2\). The combined organics were dried (Na\(_2\)SO\(_4\)), filtered, and concentrated. The residue was chromatographed on silica gel (35% ethyl acetate in hexane) to provide 231 mg (76%) of the title compound as a colorless oil. An identical experiment gave 237 mg (78%) of the title compound. \(^1\)H NMR (CDCl\(_3\), 400MHz, \(\delta\)): 7.26-7.33(m, 4H), 7.18-7.22(m, 1H), 4.60(t, J=1.5Hz, 2H), 3.62-3.65(m, 2H), 3.53(m, 2H), 3.38(s, 3H), 2.55-2.60(m, 2H), 1.57-1.64(m, 2H), 1.34-1.42(m, 2H), 0.89(t, J= 7.3Hz, 3H); \(^{13}\)C NMR (CDCl\(_3\), 100MHz, \(\delta\)): 181.2(u), 140.7(u), 128.6(dn), 128.0(dn), 126.4(dn), 114.6(u), 106.3(u), 71.7(u), 69.8(u), 63.9(u), 59.0(dn), 35.6(u), 28.9(u), 24.0(u), 22.4(u), 13.7(dn); IR (neat, cm\(^{-1}\)): 3556, 2931, 1713, 1681, 1495, 1243,1092; HRMS-Cl(NH\(_3\)) m/z: [M+Na], calcd for C\(_{18}\)H\(_{24}\)O\(_4\)Na, 327.1572; found, 327.1584.

**2-Hexyl-3-methylcycloprop-2-ene-1-carboxylic acid**

To a dried 100 mL round bottomed flask was added (+/−)-2-hexylcycloprop-2-ene-1-carboxylic acid\(^3\) (101 mg,0.60 mmol). The flask was evacuated and then refilled with nitrogen. Freshly distilled ether (30 mL) was added via syringe, and the solution was cooled in a bath of dry ice/acetone. The solution was allowed to stir and MeLi\(^1\) (1.60 mL of a 0.85 M solution in Et\(_2\)O, 1.32 mmol) was added via syringe. After the mixture had stirred at −78°C for 5 min, the dry ice/acetone bath was removed and the reaction mixture gradually allowed to warm to rt. To the yellow solution was added methyl p-toluenesulfonate (270 mg, 1.20 mmol). After stirring at rt for 30 min, the reaction was quenched with saturated NaCl solution, and 5% aq HCl was added to render the solution acidic (pH ~ 1–2). The organic phase was separated, and the aqueous phase was extracted three times with CH\(_2\)Cl\(_2\). The combined organics were dried (Na\(_2\)SO\(_4\)), filtered,
and concentrated. The residue was chromatographed on silica gel (25% ethyl acetate in hexane) to provide 73 mg (67%) of the title compound as a white colorless oil. An identical experiment gave 71 mg (65%) of the title compound.

$^1$H NMR (CDCl$_3$, 400MHz, δ): 2.43-2.38(m, 2H), 2.07(app t, J= 1.4Hz, 3H), 2.03(s, 1H), 1.55-1.59(m, 2H), 1.26-1.37(m, 6H), 0.89(t, J= 6.9Hz, 3H); $^{13}$C NMR (CDCl$_3$, 90MHz, δ): 182.2 (u), 106.0 (u), 101.3 (u), 31.4 (u), 28.8 (u), 26.7 (u), 24.4 (u), 22.5 (u), 22.2 (d), 13.9(d), 9.7(d); IR (neat, cm$^{-1}$): 3560, 2959, 1681, 1495, 1285, 1098; HRMS-CI(NH$_3$) m/z: [M+H], calcd for C$_{11}$H$_{19}$O$_2$, 183.1385; found, 183.1384.

1-(2-Thienyl)-2,3-diphenylcycloprop-2-ene-1-carboxylic acid

To a dried 100 mL round bottomed flask was added (+/–)-1-(2-thienyl)-2-phenylcycloprop-2-ene-1-carboxylic acid$^{12}$ (121 mg,0.50 mmol). The flask was evacuated and then refilled with nitrogen. Freshly distilled THF (30 mL) was added via syringe, and the solution was cooled in a bath of dry ice/acetone. The solution was allowed to stir and MeLi$^1$ (1.30 mL of a 0.85 M solution in Et$_2$O, 1.10 mmol) was added via syringe. After the mixture had stirred at –78°C for 5 min, the dry ice/acetone bath was removed and the reaction mixture gradually allowed to warm to rt. The mixture was again cooled in the dry ice/acetone bath, and to the brown solution was added ZnCl$_2$ (0.5 mL of a 1.0 M solution in ether, 0.50 mmol), tetrakis(triphenylphosphine) palladium(0) (29 mg, 0.025 mmol) and iodobenzene (306 mg, 1.50 mmol). The cold bath was removed, and the reaction was stirred for 2 h as it warmed to rt. The reaction was quenched with saturated NaCl solution, and 5% aq HCl was added to render the solution acidic (pH ~ 1–2). The organic phase was separated, and the aqueous phase was extracted three times with dichloromethane. The combined organics were dried (Na$_2$SO$_4$), filtered, and concentrated. The residue was chromatographed on silica gel (25% Ethyl acetate in hexane) to provide 103 mg (65%) of the title compound as a light yellow semisolid. An identical experiment gave 105 mg (66%) of the title compound. $^1$H NMR (CDCl$_3$, 400MHz, δ): 7.75-7.72(m, 4H), 7.51-7.45(m, 4H), 7.44-7.39(m, 2H), 7.13(dd, J=1.2, 5.1 Hz, 1H), 7.02(dd, J=1.2, 3.6 Hz, 1H), 6.86(dd, J=3.6, 5.1 Hz, 1H); $^{13}$C NMR (CDCl$_3$, 90MHz, δ): 174.1(u), 144.2(u), 129.9(dn), 129.8(dn), 126.4(dn), 125.2(u), 124.8(dn), 124.4(dn), 110.2(u), 30.5(u); IR (neat, cm$^{-1}$): 3553, 2959, 1687, 1495, 1285,1075; HRMS-CI(NH$_3$) m/z: [M$^+$], calcd for C$_{20}$H$_{14}$O$_2$S, 318.0714; found, 318.0723.
1-Phenyl-2-(4-methylphenyl)-3-(p-methylphenyl-1-hexyl-6-yl)cycloprop-2-ene-1-carboxylic acid (10)

To a dried 100 mL round bottomed flask was added (+/-)-1-phenyl-2-(1-hexyn-6-yl)cycloprop-2-ene-1-carboxylic acid \(^3\) (120 mg, 0.50 mmol). The flask was evacuated and then refilled with nitrogen. Freshly distilled THF (30 mL) was added via syringe, and the solution was cooled in a bath of dry ice/acetone. The solution was allowed to stir and MeLi \(^1\) (2.0 mL of a 0.85 M solution in Et\(_2\)O, 1.65 mmol) was added via syringe. After the mixture had stirred at –78°C for 5 min, the dry ice/acetone bath was removed and the reaction mixture gradually allowed to warm to rt. The mixture was again cooled in the dry ice/acetone bath, and to the yellow solution was added ZnCl\(_2\) (0.5 mL of a 1.0 M solution in ether, 0.50 mmol), tetrakis(triphenylphosphine) palladium(0) (29 mg, 0.025 mmol) and 4-iodotoluene (550 mg, 2.50 mmol). The cold bath was removed, and the reaction was stirred for 2 h as it warmed to rt. The reaction was quenched with saturated NaCl solution, and 5% aq HCl was added to render the solution acidic (pH ~ 1–2). The organic phase was separated, and the aqueous phase was extracted three times with dichloromethane. The combined organics were dried (Na\(_2\)SO\(_4\)), filtered, and concentrated. The residue was chromatographed on silica gel (30% Ethyl acetate in hexane) to provide 143 mg (65%) of the title compound as a white semi-solid. An identical experiment gave 146 mg (69%) of the title compound.

\(^{1}\)H NMR (CDCl\(_3\), 400MHz, \(\delta\)): 7.46(d, \(J=8.0\)Hz, 2H), 7.37-7.39(m, 2H), 7.16-7.29(m, 7H), 7.07(d, \(J= 7.9\)Hz, 2H), 2.78(t, \(J=7.2\)Hz, 2H), 2.41(t, \(J=6.9\)Hz, 2H), 2.36(s, 3H), 2.33(s, 3H), 1.92-1.97(m, 2H), 1.66-1.71(m, 2H); \(^{13}\)C NMR (CDCl\(_3\), 90MHz, \(\delta\)): 179.7(u), 140.5(u), 139.2(u), 137.5(u), 131.4(dn), 129.6(dn), 129.3(dn), 128.9(dn), 128.3(dn), 128.0(dn), 126.3(dn), 123.2(u), 120.7(u), 113.6(u), 107.4(u), 88.8(u), 81.1(u), 29.7(u), 28.2(u), 26.7(u), 24.5(u), 21.5(dn), 21.4(dn), 19.1(u); IR (neat, cm\(^{-1}\)): 3568, 2935, 1680, 1505, 1275, 1096; HRMS-Cl(NH\(_3\)) m/z: [M+Na], calcd for C\(_{30}\)H\(_{28}\)O\(_2\), 443.1987; found, 443.1966.

1-Phenylcycloprop-2-ene-1-carboxylic acid

To a clean 100 mL round bottomed flask was added methyl 1-phenyl-2-trimethylsilylcycloprop-2-ene-1-carboxylic acid ester \(^4\) (850 mg, 3.46 mmol) and methanol (20 mL). The mixture was cooled in an ice bath and allowed to stir. A solution of 1.5 M aq KOH (30mL) was added. The ice bath was removed. After the mixture had stirred overnight rt, the methanol was removed under reduced pressure. HCl (conc. aq) was added to render the solution acidic (pH ~ 1–2), and the mixture was extracted three times with CH\(_2\)Cl\(_2\). The combined organics were dried (Na\(_2\)SO\(_4\)), filtered, and concentrated. The
residue was chromatographed on silica gel (25% ethyl acetate in hexane) to provide 483 mg (87%) of the title compound as a white solid. An identical experiment using 8.70 g of starting material gave 4.97 g (88%) of the title compound. mp = 78-80°C. ¹H NMR (DMSO-d₆, 400 MHz, δ): 7.73 (d, J=0.5 Hz, 2H), 7.21-7.28 (m, 4H), 7.14-7.18 (m, 1H); ¹³C NMR (DMSO-d₆, 100 MHz, δ): 176.5 (u), 142.8 (u), 128.4 (dn), 127.9 (dn), 126.0 (dn), 107.7 (u), 29.2 (u); IR (neat, cm⁻¹): 3523, 2931, 1694, 1650, 1228, 1096; HRMS-CI (NH₃) m/z: [M⁺], calcd for C₁₀H₈O₂, 160.0524; found, 160.0521.

1-Phenyl-2-(α-hydroxybenzyl)cycloprop-2-ene-1-carboxylic acid (13)

To a dried 100 mL round bottomed flask was added 1-phenylcycloprop-2-ene-1-carboxylic acid (160 mg, 1.00 mmol). The flask was evacuated and then refilled with nitrogen. Freshly distilled THF (30 mL) was added via syringe, and the solution was cooled in a bath of dry ice/acetone. The solution was allowed to stir and MeLi (2.60 mL of a 0.85 M solution in Et₂O, 2.20 mmol) was added via syringe. After the mixture had stirred at −78°C for 5 min, the dry ice/acetone bath was removed and the reaction mixture gradually allowed to warm to 0-5°C. To the yellow solution was added benzaldehyde (0.5 mL, 0.48 g, 4.5 mmol). After stirring at rt for 10 min, the reaction was quenched with saturated NaCl solution, and 5% aq HCl was added to render the solution acidic (pH ~ 1–2). The organic phase was separated, and the aqueous phase was extracted three times with CH₂Cl₂. The combined organics were dried (Na₂SO₄), filtered, and concentrated. The residue was chromatographed on silica gel (35% ethyl acetate in hexane) to provide 241 mg (91%) of a colorless oil that was a 1:1 mixture of diastereomers. An identical experiment gave 236 mg (89%) of the diastereomers.

Spectral data is reported for both diastereomers—a total of ¹H NMR (CDCl₃, 400 MHz, δ): 7.30-7.37 (m, 2H), 7.33-7.36 (m, 6H), 7.28-7.30 (m, 10H), 7.21-7.23 (m, 2H), 7.19-7.21 (m, 2H), 6.97 (d, J=1.2 Hz, 1H), 6.92 (d, J=1.6 Hz, 1H), 5.86 (d, J=0.8 Hz, 1H), 5.65 (d, J=1.6 Hz, 1H), 2.09 (s, 2H); ¹³C NMR (CDCl₃, 90 MHz, δ): 181.2 (u), 180.8 (u), 139.8 (u), 139.6 (u), 139.4 (u), 138.9 (u), 128.7 (dn), 128.5 (dn), 2x128.4 (dn), 2x128.3 (dn), 2x128.1 (dn), 126.8 (dn), 126.7 (dn), 126.6 (dn), 126.4 (dn), 122.2 (u), 121.3 (u), 107.1 (u), 100.5 (u), 69.0 (dn), 68.9 (dn), 35.1 (u), 34.8 (u); IR (neat, cm⁻¹): 3563, 2931, 1694, 1650, 1228, 1096; HRMS-CI (NH₃) m/z: [M⁺], calcd for C₁₇H₁₄O₃, 266.0969; found, 266.0935.

1-Phenyl-2-(4-n-butylphenyl)cycloprop-2-ene-1-carboxylic acid (14)

S-8
To a dried 100 mL round bottomed flask was added 1-phenylcycloprop-2-ene-1-carboxylic acid (160 mg, 1.0 mmol). The flask was evacuated and then refilled with nitrogen. Freshly distilled THF (30 mL) was added via syringe, and the solution was cooled in a bath of dry ice/acetone. The solution was allowed to stir and MeLi\(^1\) (1.30 mL of a 0.85 M solution in Et\(_2\)O, 1.10 mmol) was added via syringe. After the mixture had stirred at \(-78^\circ\text{C}\) for 5 min, the dry ice/acetone bath was removed and the reaction mixture gradually allowed to warm to rt. The mixture was again cooled in the dry ice/acetone bath, and to the yellow solution was added ZnCl\(_2\) (0.5 mL of a 1.0 M solution in ether, 0.50 mmol), tetrakis(triphenylphosphine) palladium(0) (29 mg, 0.025 mmol) and 1-iodo-4-n-butylbenzene (390 mg, 1.50 mmol). The cold bath was removed, and the reaction was stirred for 2 h as it warmed to rt. The reaction was quenched with saturated NaCl solution, and 5% aq HCl was added to render the solution acidic (pH ~ 1–2). The organic phase was separated, and the aqueous phase was extracted three times with dichloromethane. The combined organics were dried (Na\(_2\)SO\(_4\)), filtered, and concentrated. The residue was chromatographed on silica gel (25% ethyl acetate in hexane) to provide 184 mg (63%) of the title compound as a white semi-solid. An identical experiment gave 190 mg (65%) of the title compound. \(^1\)H NMR (CDCl\(_3\), 400MHz, \(\delta\)): 7.54-7.56(m, 2H), 7.41-7.43(m, 2H), 7.19-7.30(m, 5H), 7.13(s, 1H), 2.64(t, J=5.8Hz, 2H), 1.56-1.64(m, 2H), 1.33-1.39(m, 2H), 0.93(t, J=7.3Hz, 3H); \(^{13}\)C NMR (CDCl\(_3\), 90MHz, \(\delta\)): 181.4(u), 146.0(u), 140.6(u), 130.4(dn), 129.5(dn), 128.9(dn), 128.5(dn), 127.0(dn), 122.8(u), 117.1(u), 98.9(u), 36.1(u), 33.9(u), 33.5(u), 22.7(u), 14.4(dn); IR (neat, cm\(^{-1}\)): 3530, 2929, 1685, 1498, 1282, 1045; HRMS-CI(NH\(_3\)) m/z: [M\(^+\)], calcd for C\(_{20}\)H\(_{20}\)O\(_2\), 292.1463; found, 292.1467.

References