Supporting Information

Synthesis of Coumarins, 4-Hydroxycoumarins, and 4-Hydroxyquinolinones by Tellurium-Triggered Cyclizations

Donald C. Dittmer,* Qun Li, and Dimitry V. Avilov

Department of Chemistry, Room 1-014 CST, Syracuse University, Syracuse, NY 13244.

dcdittme@syr.edu

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General. NMR spectra were recorded on a 300 MHz instrument with tetramethylsilane as internal standard. Chemical shifts are reported in ppm downfield from tetramethylsilane. All reactions were conducted in the atmosphere of dry argon or nitrogen according to standard vacuum line techniques. Unless otherwise noted, all commercially available reagents were used as received without further purification. Tetrahydrofuran was distilled or vacuum-transferred from potassium benzophenone ketyl; ether from sodium benzophenone ketyl or lithium aluminum hydride; and dichloromethane from calcium hydride immediately before use. Pyridine and triethylamine were distilled from sodium hydroxide immediately before use. All other liquid reagents were distilled immediately before use. Thin layer chromatography was performed with the use of Silica Gel 60 plates impregnated with a fluorescent indicator (254 nm). Thin layer chromatography plates were visualized by exposure to ultraviolet light, iodine, anisaldehyde, and/or phosphomolybdic acid. Flash column chromatography was performed with the use of Premium Grade Silica Gel.

2-(Bromoacetoxy)benzaldehyde 2a.¹ Procedure B: Salicylaldehyde (2.6 g, 21 mmol) gave **2a**, colorless oil (4.5 g, 19 mmol, 90%). Compound **2a** decomposes slowly neat, in solution, or during chromatography, and may be contaminated with up to 4% of salicylaldehyde. This impurity did not interfere with the course of the telluride-triggered cyclization reactions. ¹H NMR (300 MHz, CDCl₃): δ 10.11 (s, 1 H), 7.88 (d, *J*=8.0 Hz, 1 H), 7.65 (m, 1 H), 7.44 (m, 1 H), 7.22 (d, *J*=8.0 Hz, 1 H), 4.17 (s, 2 H); ¹³C NMR (75 MHz, CDCl₃): δ 188.9, 165.5, 150.6, 135.4, 131.9, 127.6, 126.9, 122.9, 25.2; IR (CDCl₃): 1765 (s), 1702 (s), 1276 (m), 1254 (s), 1196 (s), 1118 (s) cm⁻¹.

Coumarin 3a.² Procedures D, E. See the main text.

2-(2-Bromopropionyloxy)benzaldehyde 2b. Procedure B: Salicylaldehyde (0.917 g, 7.51 mmol) gave **2b**, colorless oil (1.89 g, 7.36 mmol, 98.1%). ¹H NMR (300 MHz, CDCl₃): δ 10.15 (s, 1 H), 7.92-7.86 (dd, *J*=7.5, 1.5 Hz, 1 H), 7.68-7.59 (m, 1 H), 7.45-7.38 (m, 1 H), 7.24-7.18 (dd, *J*=7.8, 1.0 Hz, 1 H), 4.71-4.64 (q, *J*=6.9 Hz, 1 H), 1.99 (d, *J*=6.9 Hz, 3 H); ¹³C NMR (75 MHz, CDCl₃): δ 188.4, 168.4, 151.0, 135.4, 131.2, 128.0, 126.9, 122.9, 39.2, 21.3; IR (CH₂Cl₂): 2858 (w), 1768 (s), 1701 (s), 1666 (s), 1204 (m), 1130 (m) cm⁻¹. Anal. Calcd.: C, 46.70; H, 3.53. Found: C, 46.90; H, 3.40.

3-Methylcoumarin 3b.^{2c,3} Procedure D: 2-(2-Bromopropionyloxy)benzaldehyde **2b** (61 mg, 0.24 mmol) gave **3b** (24 mg, 0.15 mmol, 64%). The product was recrystallized from hexane/ether to give colorless needles: mp 88-90 °C (lit.^{3a} mp 90 °C); ¹H NMR (300 MHz, CDCl₃):

δ 7.55-7.36 (m, 3 H), 7.32-7.16 (m, 2 H), 2.21 (s, 3 H); ^{13}C NMR (75 MHz, CDCl_3): δ 162.7, 153.6, 139.6, 130.9, 127.4, 126.2, 124.7, 120.0, 116.9, 17.6.

2-Bromopropionate ester of 2-hydroxyacetophenone 2c. Procedure A: 2-Hydroxyacetophenone (1.0 g, 7.3 mmol) gave **2c**, colorless oil (1.8 g, 6.7 mmol, 92%); ^1H NMR (300 MHz, CDCl_3): δ 7.78 (dd, $J=7.8$, 1.7 Hz, 1 H), 7.55-7.45 (m, 1 H), 7.33-7.25 (m, 1 H), 7.13-7.09 (d, $J=1.2$ Hz, 1 H), 4.62 (q, $J=6.9$ Hz, 1 H), 2.50 (s, 3 H), 1.95 (d, $J=6.9$ Hz, 3 H); ^{13}C NMR (75 MHz, CDCl_3): δ 197.7, 169.1, 149.1, 134.1, 130.9, 130.6, 127.0, 123.8, 40.3, 29.7, 21.9; IR (CH_2Cl_2): 2954 (w), 1764 (s), 1726 (s), 1496 (m), 1201 (m), 1130 (s), 1084 (s) cm^{-1} . Anal. Calcd.: C, 48.71; H, 4.10. Found: C, 48.80; H, 4.10.

3,4-Dimethylcoumarin 3c.⁴ Procedure C: The 2-bromopropionate ester **2c** (0.54 g, 2.0 mmol) gave **3c**. The product was recrystallized from ether, yield 0.14 g (0.82 mmol, 41%); mp 113-115 $^\circ\text{C}$ (lit.⁴ mp 115 $^\circ\text{C}$); ^1H NMR (300 MHz, CDCl_3): δ 7.65-7.57 (m, 1 H), 7.51-7.42 (m, 1 H), 7.35-7.22 (m, 2 H), 2.41 (s, 3 H), 2.23 (s, 3 H); ^{13}C NMR (75 MHz, CDCl_3): δ 162.4, 152.3, 146.4, 130.8, 124.7, 124.5, 122.5, 120.9, 117.0, 15.4, 13.8.

2-Bromopropionate ester of methyl salicylate 4a. Procedure A: Methyl salicylate (1.5 g, 10 mmol) gave **4a**, colorless oil (2.2 g, 7.7 mmol, 77%); ^1H NMR (300 MHz, CDCl_3): δ 8.00 (m, 1 H), 7.58-7.51 (m, 1 H), 7.35-7.10 (m, 1 H), 7.13 (d, $J=8.1$ Hz, 1 H), 4.67 (q, $J=6.9$ Hz, 1 H), 3.83 (s, 3 H), 1.98 (d, $J=6.9$ Hz, 3 H); ^{13}C NMR (75 MHz, CDCl_3): δ 169.1, 165.1, 150.6, 134.4, 132.2, 126.9, 123.7, 123.4, 52.7, 40.2, 22.0; IR (CH_2Cl_2): 2954 (m), 1766 (s), 1730 (s), 1609 (m), 1125 (s), 1085 (s) cm^{-1} .

4-Hydroxy-3-methylcoumarin 5a.⁵ Procedure C: The 2-bromopropionate ester of methyl salicylate **4a** (1.4 g, 5.0 mmol) gave **5a** that was recrystallized from methanol, yield 0.48 g (2.7 mmol, 54%); mp 225-227 $^\circ\text{C}$ (lit.^{5a} mp 230 $^\circ\text{C}$ (methanol)); ^1H NMR (300 MHz, $\text{DMSO}-d_6$): δ 7.90-7.85 (m, 1 H), 7.59-7.51 (m, 1 H), 7.35-7.28 (m, 2 H), 1.97 (s, 3 H); ^{13}C NMR (75 MHz, $\text{DMSO}-d_6$): δ 164.0, 160.7, 152.5, 132.3, 124.7, 123.8, 117.2, 116.9, 101.1, 10.6. Anal. Calcd.: C, 68.17; H, 4.59. Found: C, 67.80; H, 4.60.

Methyl 2-[2-bromopropionyloxy]-5-methylbenzoate 4b. Procedure A: Methyl 2-hydroxy-5-methylbenzoate (0.96 g, 5.8 mmol) gave **4b**, colorless oil (1.7 g, 5.6 mmol, 97%); ^1H NMR (300 MHz, CDCl_3): δ 7.81 (m, 1 H), 7.34 (m, 1 H), 7.01 (d, $J=8.4$ Hz, 1 H), 4.66 (q, $J=6.9$ Hz, 1 H), 3.83 (s, 3 H), 2.36 (s, 3 H), 1.97 (d, $J=6.9$ Hz, 3 H); ^{13}C NMR (75 MHz, CDCl_3): δ 169.3, 165.2, 148.4,

136.7, 135.0, 132.5, 123.4, 122.9, 52.6, 40.3, 22.0, 21.2; IR (CH₂Cl₂): 2954 (w), 1764 (s), 1726 (s), 1496 (m), 1339 (m), 1201 (s), 1130 (s), 1084 (s) cm⁻¹.

4-Hydroxy-3,6-dimethylcoumarin 5b.⁶ Procedure C: Methyl 2-[2-bromopropionyloxy]-5-methylbenzoate **4b** (0.15 g, 0.50 mmol) gave **5b** (0.089 g, 0.47 mmol, 94%) (yield 74% after recrystallization from methanol); mp 262-263 °C (lit.⁶ mp 252-254 °C); ¹H NMR (300 MHz, DMSO-*d*₆): δ 7.65 (br s, 1 H), 7.37-7.32 (m, 1 H), 7.20 (d, *J*=8.4 Hz, 1 H), 2.34 (s, 3 H), 1.96 (s, 3 H); ¹³C NMR (75 MHz, DMSO-*d*₆): δ 164.1, 160.6, 150.7, 133.8, 133.0, 123.5, 116.8, 116.7, 101.0, 21.3, 10.6.

Methyl 2-[2-bromopropionyloxy]-5-methoxybenzoate 4c. Procedure A: Methyl 2-hydroxy-5-methoxybenzoate (1.9 g, 10 mmol) gave **4c**, colorless oil (3.0 g, 9.5 mmol, 93%); ¹H NMR (300 MHz, CDCl₃): δ 7.51 (d, *J*=3 Hz, 1 H), 7.10-7.02 (m, 2 H), 4.65 (q, *J*=6.9 Hz, 1 H), 3.87 (s, 3 H), 3.84 (s, 3 H), 1.99 (d, *J*=6.9 Hz, 3 H); ¹³C NMR (75 MHz, CDCl₃): δ 169.1, 164.6, 157.4, 143.6, 124.1, 123.5, 119.9, 115.8, 55.8, 52.33, 39.8, 21.6; IR (CH₂Cl₂): 2954 (w), 2841 (w), 1763 (s), 1725 (s), 1496 (m), 1196 (m), 1131 (m), 1076 (m), 1040 (m) cm⁻¹. Anal. Calcd.: C, 45.43; H, 4.14. Found: C, 45.47; H, 4.27.

4-Hydroxy-6-methoxy-3-methylcoumarin 5c.⁷ Procedure C: Methyl 2-[2-bromopropionyloxy]-5-methoxybenzoate **4c** (1.6 g, 5.0 mmol) gave **5c** (0.69 g, 3.4 mmol, 67%) which was recrystallized from methanol/DMSO; mp 225-226 °C (lit.⁷ mp 222 °C (methanol/water)); ¹H NMR (300 MHz, DMSO-*d*₆): δ 7.38 (d, *J*=3 Hz, 1 H), 7.24 (d, *J*=9 Hz, 1 H), 7.11 (dd, *J*=9, 3 Hz, 1 H), 3.77 (s, 3 H), 1.96 (s, 3 H); ¹³C NMR (75 MHz, DMSO-*d*₆): δ 164.2, 160.5, 156.1, 146.8, 119.7, 118.1, 117.5, 106.2, 101.4, 56.5, 10.7.

Methyl 2-(2-chloro-2-phenylacetoxyl)benzoate 4d. Procedure A: Methyl 2-hydroxybenzoate (1.5 g, 10 mmol) gave **4d** (2.9 g, 9.4 mmol, 94%) which was recrystallized from ether/hexanes to give pale yellow crystals; mp 41-42 °C; ¹H NMR (300 MHz, CDCl₃): δ 8.07-8.01 (m, 1 H), 7.67-7.62 (m, 2 H), 7.58-7.52 (m, 1 H), 7.48-7.42 (m, 3 H), 7.37 (m, 1 H), 7.03 (m, 1 H), 5.70 (s, 1 H), 3.72 (s, 3 H); ¹³C NMR (75 MHz, CDCl₃): δ 167.4, 165.2, 150.3, 135.8, 134.3, 132.4, 129.9, 129.4, 128.8, 127.0, 123.6, 59.4, 52.6; IR (CH₂Cl₂): 2954 (w), 1777 (s), 1723 (s), 1304(m), 1202 (m), 1137 (s), 1085 (s) cm⁻¹.

4-Hydroxy-3-phenylcoumarin 5d.^{6b,8} Procedure C: Methyl 2-(2-chloro-2-phenylacetoxyl)benzoate **4d** (1.2 g, 3.9 mmol) gave **5d** which was isolated by flash chromatography and recrystallized from methanol (0.12 mg, 0.40 mmol, 10%); methyl 2-hydroxybenzoate was

obtained as a by product (0.3 g, 2.0 mmol, 50%). **5d**: mp 232-235 °C (lit.^{8a} mp 236 °C; ¹H NMR (300 MHz, DMSO-*d*₆ + CD₃OD): δ 8.01-7.93 (m, 1 H), 7.68-7.55 (m, 1 H), 7.45-7.27 (m, 7 H); ¹³C NMR (75 MHz, DMSO-*d*₆ + CD₃OD): δ 162.8, 160.9, 153.2, 133.10, 132.8, 131.8, 128.8, 128.3, 124.8, 124.5, 117.1, 117.0, 107.0.

Methyl 2-(N-bromoacetyl-N-methylamino)benzoate 12a.⁹ Procedure A: Methyl N-methylantranilate (1.7 g, 10 mmol) gave **12a** (2.3 g, 8.1 mmol, 81%) which was recrystallized from CH₂Cl₂/EtOAc; mp 82-84 °C (lit.⁹ mp 80-82 °C); ¹H NMR (300 MHz, CDCl₃): δ 8.06-8.00 (m, 1 H), 7.63 (m, 1 H), 7.51 (m, 1 H), 7.39 (m, 1 H), 3.87 (s, 3 H), 3.60, 3.54 (AB, *J*=11.1 Hz, 2 H), 3.21 (s, 3 H); ¹³C NMR (75 MHz, CDCl₃): δ 166.7, 166.0, 142.8, 134.4, 132.5, 130.3, 129.5, 128.7, 53.2, 38.2, 27.4; IR (CH₂Cl₂): 2954 (w), 1726 (s), 1668 (s), 1492 (m), 1125 (m), 1082 (s) cm⁻¹.

4-Hydroxy-1-methyl-1H-quinolin-2-one 13a.¹⁰ Procedure C: Methyl 2-(N-bromoacetyl-N-methylamino)benzoate **12a** (0.14 g, 0.50 mmol) gave **13a** (71 mg, 0.41 mmol, 81%); mp 269-270 °C (lit.^{10a} mp 259-260 °C, lit.^{10b} mp 271 °C); ¹H NMR (300 MHz, DMSO-*d*₆): δ 11.28 (s, 1 H), 7.89-7.83 (m, 1 H), 7.63-7.55 (m, 1 H), 7.46-7.41 (m, 1 H), 7.25-7.17 (m, 1 H), 5.84 (s, 1 H), 3.50 (s, 3 H); ¹³C NMR (75 MHz, DMSO-*d*₆) δ 163.4, 161.9, 140.8, 132.1, 123.9, 122.0, 116.9, 115.4, 98.8, 29.3.

Methyl 2-(N-(2-bromopropionyl)-N-methylamino)benzoate 12b. Procedure A: Methyl N-methylantranilate (1.7 g, 10 mmol) gave **12b** (3.0 g, 9.9 mmol, 99%) which was recrystallized from CH₂Cl₂/EtOAc; mp 70-71 °C; ¹H NMR (300 MHz, CDCl₃)(mixture of amide rotamers in solution): δ 8.08-8.04 (m, 0.2 H), 7.96-7.92 (m, 0.8 H), 7.65-7.42 (m, 2.8 H), 7.20-7.15 (m, 0.2 H), 4.08-3.96 (m, 1 H), 3.86 (s, 0.6 H), 3.82 (s, 2.4 H), 3.23 (s, 0.6 H), 3.14 (s, 2.4 H), 1.70-1.63 (m, 3 H); ¹³C NMR (75 MHz, CDCl₃): δ 170.1, 169.1, 166.2, 165.8, 142.7, 142.6, 134.3, 134.3, 133.1, 132.1, 130.5, 130.0, 129.5, 129.3, 129.2, 128.7, 53.12, 53.10, 40.1, 39.7, 38.5, 38.0, 22.6, 21.8; IR (CH₂Cl₂): 2954 (w), 1725 (s), 1668 (s), 1492 (m), 1389 (w), 1128 (m), 1079 (m) cm⁻¹. Anal. Calcd.: C, 48.00; H, 4.71; N, 4.67. Found: C, 47.79; H, 4.44; N, 4.60.

4-Hydroxy-1,3-dimethyl-1H-quinolin-2-one 13b.¹¹ Procedure C: Methyl 2-(N-(2-bromopropionyl)-N-methylamino)benzoate **12b** (1.5 g, 5.0 mmol) gave **13b** which was recrystallized from methanol/CH₂Cl₂, (0.52 g, 2.8 mmol, 55%); mp 216-218 °C (lit.¹¹ mp 220-221 °C); ¹H NMR (300 MHz, DMSO-*d*₆): δ 7.97-7.92 (m, 1 H), 7.58-7.51 (m, 1 H), 7.46-7.41 (m, 1 H), 7.25-7.18 (m, 1 H), 3.56 (s, 3 H), 2.02 (s, 3 H); ¹³C NMR (75 MHz, DMSO-*d*₆): δ 163.9, 156.8, 138.9, 130.9, 123.7, 122.0, 117.1, 115.0, 107.3, 30.0, 11.1.

Methyl 2-(N-(2-chloro-2-phenylacetyl)-N-methylamino)benzoate 12c. Procedure A: Methyl N-methylanthranilate (1.7 g, 10 mmol) gave **12c** (2.8 g, 8.9 mmol, 89%) which was recrystallized from CH₂Cl₂/ether to afford pale yellow crystals: mp 77-79 °C; ¹H NMR (300 MHz, CDCl₃)(mixture of amide rotamers in solution): δ 8.09-7.59 (m, 1 H), 7.73-7.64 (m, 0.5 H), 7.57-7.15 (m, 7 H), 6.81-6.76 (m, 0.5 H), 5.14 (s, 0.5 H), 5.07 (s, 0.5 H), 3.95 (s, 1.5 H), 3.41 (s, 1.5 H), 3.23 (s, 3 H), 3.21 (s, 3 H); ¹³C NMR (75 MHz, CDCl₃): δ 167.6, 167.4, 166.1, 165.2, 142.6, 142.3, 136.9, 136.3, 134.7, 133.9, 132.8, 132.7, 131.0, 130.5, 129.7, 129.5, 129.4, 129.2, 129.13, 129.07, 129.05, 128.9, 128.8, 128.6, 58.5, 57.1, 53.4, 52.7, 38.53, 38.47; IR (CH₂Cl₂): 2953 (w), 1727 (s), 1680 (s), 1492 (m), 1380 (m), 1128 (m), 1083 (m) cm⁻¹.

4-Hydroxy-1-methyl-3-phenyl-1H-quinolin-2-one 13c.¹² Procedure C: Methyl 2-(N-(2-chloro-2-phenylacetyl)-N-methylamino)benzoate **12c** (0.15 mg, 0.50 mmol) gave **13c** (0.11 g, 0.38 mmol, 77%) which was recrystallized from methanol; mp 222-224 °C (lit.¹² mp 221-223 °C); ¹H NMR (300 MHz, DMSO-*d*₆): δ 8.05-8.00 (m, 1 H), 7.66-7.59 (m, 1 H), 7.53-7.47 (m, 1 H), 7.42-7.22 (m, 6 H), 3.59 (s, 3 H); ¹³C NMR (75 MHz, DMSO-*d*₆): δ 162.8, 157.0, 139.8, 134.6, 132.0, 131.9, 128.6, 127.8, 124.4, 122.2, 117.2, 115.3, 113.2, 30.1.

Methyl 2-(N-(2-bromopropionyl)-N-phenylamino)benzoate 12d was prepared according to a modified literature procedure.¹³ To a solution of methyl N-phenylanthranilate (98 mg, 0.43 mmol) in CH₂Cl₂ (0.3 mL) was added a solution of 2-bromopropionyl bromide (132 mg, 0.61 mmol) in CH₂Cl₂ (0.2 mL) at 0 °C. The mixture was warmed to rt, stirred overnight, quenched with 1 mL of aqueous KOH (1 M), and extracted with chloroform (4 x 2 mL). The organic phase was dried (MgSO₄), and the crude mixture was purified by flash chromatography (hexanes/EtOAc 3:1) to afford the recovered methyl N-phenylanthranilate (9 mg, 9%) and **12d** (128 mg, 0.35 mmol, 82%). ¹H NMR (300 MHz, CDCl₃)(mixture of amide rotamers in solution): δ 8.01-7.86 (m, 2 H), 7.65-7.10 (m, 16 H), 4.49 (m, 1 H), 4.29 (m, 1 H), 3.90 (s, 3 H), 3.89 (s, 3 H), 1.82 (m, 6 H); ¹³C NMR (75 MHz, CDCl₃): δ 170.3, 170.1, 166.9, 166.6, 142.4, 142.3, 141.7, 141.4, 134.1, 133.1, 132.0, 131.9, 131.0, 130.3, 130.0, 129.31, 129.25, 129.01, 129.00, 128.7, 127.5, 126.7, 126.3, 53.2, 52.9, 41.8, 40.1, 22.1, 21.5; IR (CH₂Cl₂): 2954 (w), 2871 (w), 1725 (s), 1680 (s), 1492 (m), 1373 (m), 1090 (m) cm⁻¹. For compounds **12a-d** two sets of amide rotamer signals are present in solution at room temperature. At higher temperature, the rotamer signals coalesce to give one set of signals, as demonstrated for compound **12d** (coalescence temperature ~55 °C). This behavior is characteristic for amides.¹⁴ See pages S 52 - S 54 of this Supporting Information.

4-Hydroxy-1-phenyl-3-methyl-1H-quinolin-2-one 13d.¹⁵ Procedure C: Methyl 2-(N-(2-bromopropionyl)-N-phenyl)benzoate **12d** (0.18 g, 0.50 mmol) gave **13d** (0.11 g, 0.44 mmol, 88%) which was recrystallized from methanol; mp 275-277 °C (lit.^{15a} mp >250 °C (EtOH), lit.^{15b} mp 275-277 °C (EtOH)); ¹H NMR (300 MHz, DMSO-*d*₆): δ 8.0-7.94 (m, 1 H), 7.60-7.45 (m, 3 H), 7.37-7.29 (m, 1 H), 7.28-7.15 (m, 3 H), 6.47-6.40 (d, *J*=8.1 Hz, 1 H), 2.04 (s, 3 H); ¹³C NMR (75 MHz, DMSO-*d*₆) δ 163.9, 157.5, 139.9, 139.2, 130.7, 130.6, 130.2, 129.2, 123.7, 122.3, 116.9, 115.8, 107.4, 10.8.

Benzyl phenylacetamide 11.¹⁶ See the main text. ¹H NMR (300 MHz, CDCl₃): δ 7.39-7.14 (m, 10 H), 5.69 (br s, 1 H), 4.41 (d, *J*=5.7 Hz, 2 H), 3.63 (s, 2H); ¹³C NMR (75 MHz, CDCl₃): δ 170.9, 138.1, 134.7, 129.5, 129.1, 128.7, 127.5, 127.4, 43.8, 43.6.

DA220-6

DA247-8

DA247-8

DA275-5

DA275-6

13b

DA279-2

DA279-2

in toluene- d_8 at various temperatures; signals of ester methyl group shown.

13d

References.

1. Fuson, R. C.; Thomas, N. *J. Org. Chem.* **1953**, *18*, 1762.
2. (a) Zwenger, C.; Dronke, F. *Justus Liebigs Ann. Chem.* **1862**, *123*, 145-157. (b) Meyer, H.; Beer, R.; Lasch, G. *Monatsh. Chem.* **1913**, *34*, 1665-1672. (c) Rowbotham, J. B.; Schaefer, T. *Can. J. Chem.* **1973**, *51*, 953-960.
3. (a) Perkin, W. H. *J. Chem. Soc.* **1875**, 10-15. (b) Ernst, L. *J. Magn. Reson.* **1976**, *21*, 241-246.
4. Peters, F.; Simonis, H. *Ber. Dtsch. Chem. Ges.* **1908**, *41*, 830-837.
5. (a) Heilbron, I. M.; Hill, D. W. *J. Chem. Soc.* **1927**, 1705-1708. (b) Rabaron, A.; Didry, J.-R.; Kirkiacharian, B. S.; Plat, M. M. *Org. Magn. Reson.* **1979**, *12*, 284-288. (c) Mizuno, T.; Nishiguchi, I.; Hirashima, T.; Ogawa, A.; Kambe, N.; Sonoda, N. *Synthesis* **1988**, 257-259.
6. (a) Walker, T. K.; Suthers, A. J.; Roe, L. L.; Shaw, H. *J. Chem. Soc.* **1931**, 514-520. (b) da Re, P.; Sandri, E. *Chem. Ber.* **1960**, *93*, 1085-1088.
7. Garden, J. F.; Hayes, N. F.; Thomson, R. H. *J. Chem. Soc.* **1956**, 3315-3318.
8. (a) Pauley, H.; Lockemann, K. *Ber. Dtsch. Chem. Ges.* **1915**, *48*, 28-32. (b) Neelakantan, S.; Raman, P. V.; Tinabaye, A. *Indian J. Chem.* **1982**, *21B*, 256-257.
9. (a) Uskokovic, M.; Wenner, W. U.S. Patent 3244698, 1966; *Chem. Abstr.* **1966**, *64*, 104316. (b) Showell, G. A.; Bourrain, S.; Neduvelil, J. G.; Fletcher, S. R.; Baker, R.; Watt, A. P.; Fletcher, A. E.; Freedman, S. B.; Kemp, J. A.; Marshall, G. R.; Patel, S.; Smith, A. J.; Matassa, V. G. *J. Med. Chem.* **1994**, *37*, 719-721.
10. (a) Friedländer, P.; Müller, F. *Ber. Dtsch. Chem. Ges.* **1887**, *20*, 2009-2017. (b) Meyer, A.; Heimann, P. *C. R. Hebd. Seances Acad. Sci.* **1936**, *203*, 335-337. (c) Tomita, K. *Yakugaku Zasshi* **1951**, *71*, 1100-1112; *Chem. Abstr.* **1952**, *46*, 5044.
11. Ohta, T.; Mori, Y. *Tokyo Yakka Daigaku Kenkyu Nenpo* **1958**, *8*, 34-36; *Chem. Abstr.* **1960**, *54*, 4588.
12. (a) Baumgarten, P.; Kärger, W. *Ber. Dtsch. Chem. Ges.* **1927**, *60*, 832-842. (b) Coppola, G. M. *Synth. Commun.* **1985**, *15*, 135-139.
13. Gogerty, J. H.; Griot, R. G.; Habeck, D.; Iorio, L. C.; Houlihan, W. J. *J. Med. Chem.* **1977**, *20*, 952-956.
14. Pople, J. A.; Schneider, W. G.; Bernstein, H. J. *High Resolution Nuclear Magnetic Resonance*; McGraw-Hill: New York, 1959; Chapter 13, pp. 366-371.
15. (a) Pfister, R.; Haeffliger, F. U. S. Patent 3,025,299, 1962; *Chem. Abstr.* **1962**, *57*, 12444. (b)

Kafka, S.; Klásek, A.; Kosmrlj, J. *J. Org. Chem.* **2001**, 66, 6394-6399.

16. (a) Olah, G. A.; Narang, S. C.; Garcia-Luna, A. *Synthesis* **1980**, 8, 661-662. (b) Perreux, L.; Loupy, A.; Volatron, F. *Tetrahedron* **2002**, 58, 2155-2162.