in asymmetric synthesis are currently underway.

Experimental Section[9]

General Procedure for 1,3-Dioxolan-4-one Preparation. A solution of the carbonyl compound, acetal or ketal (1 equiv), in anhydrous dichloromethane (3 M) was added in a dropwise fashion to a solution of Me_3SiOTf or Me_3SiI (5%) and **2** (1.2–1.3 equiv) in dichloromethane at −78 °C (ca. 1 M final concentration). In some cases, di-*tert*-butylpyridine (2%) was also present. The solution was stirred at the temperature/time indicated in Table I. On occasion, additional Me_3SiOTf catalyst was necessary for complete reaction (TLC or GC analysis). Pyridine (1.3 equiv) was added, and the solution was poured into saturated aqueous sodium bicarbonate and extracted with ether. The organic phase was dried ($MgSO_4$), concentrated, and flash chromatographed[8] to provide the desired dioxolanone. Table I provides specific reaction scales and conditions.

Cyclohexanespiro-2′-(1′,3′-dioxolan-4′-one) (3):[3a] R_f 0.25 (SiO_2, 10% EtOAc/hexane); IR (film) 1807 (s), 1796 (s), 1674 (w), 1450 (w), 1300 (m), 1296 (m), 1222 (m), 1105 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.33 (2 H, s), 1.90–1.60 (8 H, m), 1.54–1.40 (2 H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.8, 112.7, 62.7, 34.8, 24.0, 22.6; MS (70 eV), *m/e* (relative intensity) 157 (3), 156 (M^+, 17), 113 (47), 98 (58), 70 (5), 69 (7), 56 (25), 55 (100), 54 (22), 43 (42).

(*R*)-3-Methylcyclohexanespiro-2′-(1′,3′-dioxolan-4′-one) (4A,B): R_f 0.24 (SiO_2, 10% EtOAc/hexane). Preparative HPLC or MPLC with 5% EtOAc/hexane provided **4A** and **4B** in a 1.1:1.0 ratio. The retention time of **4A** is longer than that of **4B**.

4A: $[\alpha]^{25}_D$ −18.86° (*c* 5.77, CH_2Cl_2); IR (film) 1804 (s), 1679 (m), 1457 (m), 1372 (m), 1228 (m), 1210 (m), 1165 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.35 (2 H, s), 1.96–1.90 (2 H, m), 1.88–1.70 (3 H, m), 1.70–1.54 (2 H, m), 1.30 (1 H, t, *J* = 12.6 Hz), 0.95 (3 H, d, *J* = 6.5 Hz), 0.92–0.85 (1 H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.0, 113.5, 63.0, 43.6, 35.0, 33.1, 29.8, 22.4, 21.7; MS (70 eV), *m/e* (relative intensity) 171 (3), 170 (M^+, 8), 127 (69), 113 (19), 94 (25), 69 (100), 56 (61), 55 (64), 43 (26), 42 (61). See **4B** for combustion analysis.

4B: $[\alpha]^{25}_D$ −12.39° (*c* 5.73, CH_2Cl_2); IR (film) 1808 (m), 1448 (m), 1358 (m), 1290 (s), 1238 (s), 1118 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.31 (2 H, s), 1.92–1.88 (2 H, m), 1.80–1.55 (5 H, m), 1.40 (1 H, t, *J* = 12.5 Hz), 0.96 (3 H, d, *J* = 6.5 Hz), 0.93–0.86 (1 H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.2, 113.4, 63.1, 43.0, 34.3, 33.0, 29.5, 22.1, 21.8; MS (70 eV), *m/e* (relative intensity) 171 (4), 170 (M^+, 8), 127 (70), 113 (19), 94 (25), 69 (100), 56 (62), 55 (64), 43 (26), 42 (63). Anal. Calcd for $C_9H_{14}O_3$: C, 63.51; H, 8.29. Found (for the mixture of isomers **4A** and **4B**): C, 63.42; H, 8.21.

(2*S*,5*R*)-2-(1-Methylethyl)-5-methylcyclohexanespiro-2′-(1′,3′-dioxolan-4′-one) (5A,B): R_f 0.18 (SiO_2, 5% EtOAc/hexane); bp 105–106 °C/9 mm Hg. Preparative HPLC or MPLC with 5% EtOAc/hexane provided **5A** and **5B** in a 1.1:1.0 ratio. The retention time of **5A** is longer than that of **5B**.

5A: $[\alpha]^{25}_D$ −36.26° (*c* 4.70, $CHCl_3$); IR (film) 1790 (s), 1445 (w), 1300 (m), 1275 (m), 1210 (m), 1105 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.32 (2 H, s), 2.00 (1 H, dt, *J* = 6.9, 2.2 Hz), 1.89 (1 H, ddd, *J* = 13.1, 3.5, 2.2 Hz), 1.80–1.60 (3 H, m), 1.58 (1 H, ddd, *J* = 12.9, 3.5, 2.3 Hz), 1.45 (1 H, dt, *J* = 12.9, 3.2 Hz), 1.34 (2 H, t, *J* = 12.8 Hz), 0.94 (3 H, d, *J* = 6.4 Hz), 0.93 (3 H, d, *J* = 7.0 Hz), 0.88 (3 H, d, *J* = 6.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.4, 115.8, 63.5, 48.8, 44.8, 34.0, 30.0, 24.8, 23.1, 22.8, 21.6, 18.5, MS (70 eV), *m/e* (relative intensity) 212 (M^+, 7), 197 (3), 153 (8), 136 (11), 127 (100), 112 (11), 99 (15), 69 (48), 55 (17), 41 (19). See **5B** for combustion analysis.

5B: $[\alpha]^{25}_D$ −0.77° (*c* 5.18, $CHCl_3$); IR (film) 1790 (s), 1450 (m), 1225 (s), 1155 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.37 (2 H, s), 2.09 (1 H, dt, *J* = 7.0, 1.5 Hz), 1.91 (1 H, ddd, *J* = 13.3, 3.5, 2.1 Hz), 1.86–1.60 (4 H, m), 1.50–1.40 (2 H, m), 1.27 (1 H, t, *J* = 12.6 Hz), 0.95 (3 H, d, *J* = 7.0 Hz), 0.92 (3 H, d, *J* = 6.5 Hz), 0.85 (3 H, d, *J* = 7.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.0, 115.6, 63.5, 49.4, 45.8, 34.1, 29.9, 24.8, 23.2 (2 C's), 21.6, 18.2; MS (70 eV), *m/e* (relative intensity) 212 (M^+, 6), 197 (3), 153 (8), 136 (11), 127 (100), 112 (11), 99 (16), 69 (55), 55 (20), 41 (22). Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.89; H, 9.50. Found (for the mixture of isomers **5A** and **5B**): C, 68.12; H, 9.44.

(2*S*,5*R*)-2-(1-Methyl-1-phenylethyl)-5-methylcyclohexanespiro-2′-(1′,3′-dioxolan-4′-one) (6A,B). 6A: R_f 0.25 (SiO_2, 5:15:80 MeCN/PhH/hexane); $[\alpha]^{25}_D$ −1.14° (*c* 3.95, $CHCl_3$); IR (film) 1807 (s), 1795 (s), 1455 (m), 1445 (m), 1318 (m), 1281 (s), 1217 (s), 1112 (s) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.35–7.14 (5 H, m), 4.01, 4.16 (2 H, AB, *J* = 15.4 Hz), 2.16–2.08 (1 H, m), 1.77–1.56 (5 H, m), 1.55–1.38 (1 H, m), 1.41 (3 H, s), 1.39 (3 H, s), 1.31 (1 H, t, *J* = 13.6 Hz), 0.88 (3 H, d, *J* = 6.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.4, 150.5, 127.9, 125.8, 125.5, 116.0, 62.5, 52.5, 46.1, 40.3, 34.4, 30.0, 29.1, 26.8, 25.1, 21.3; MS (70 eV), *m/e* (relative intensity) 288 (M^+, 2), 230 (0.2), 197 (0.4), 170 (12), 120 (10), 119 (100), 111 (5), 91 (20), 41 (12). Anal. Calcd for $C_{18}H_{24}O_3$: C, 74.97; H, 8.39. Found: C, 74.83; H, 8.64.

6B: R_f 0.29 (SiO_2, 5:15:80) MeCN/PhH/hexane); $[\alpha]^{25}_D$ + 38.68° (*c* 3.33, $CHCl_3$); IR (film) 1800 (s), 1455 (m), 1446 (m), 1314 (m), 1236 (s), 1225 (s), 1166 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.34–7.13 (5 H, m), 3.69, 4.07 (2 H, AB, *J* = 15.4 Hz), 2.07 (1 H, dd, *J* = 12.8, 3.6 Hz), 1.80–1.70 (4 H, m), 1.70–1.50 (2 H, m), 1.40 (3 H, s), 1.35 (3 H, s), 1.26 (1 H, t, *J* = 13.4 Hz), 0.87 (3 H, d, *J* = 6.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.9, 150.6, 127.8, 125.7, 125.4, 116.2, 62.4, 53.0, 47.5, 40.1, 34.6, 29.9, 28.6, 27.1, 25.9, 21.4; MS (70 eV), *m/e* (relative intensity) 288 (M^+, 2), 230 (0.2), 197 (0.4), 170 (12), 120 (10), 119 (100), 111 (5), 91 (21), 41 (12). Anal. Calcd for $C_{18}H_{24}O_3$: C, 74.97; H, 8.39. Found: C, 74.88; H, 8.25.

2-Cyclohexyl-1,3-dioxolan-4-one (7): R_f 0.29 (SiO_2, 10% EtOAc/hexane); IR (film) 1808 (s), 1451 (m), 1396 (w), 1351 (w), 1322 (m), 1218 (s), 1198 (s), 1080 (w) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.36 (1 H, d, *J* = 4.72 Hz), 4.21, 4.31 (2 H, AB, *J* = 15.1 Hz), 1.90–1.60 (6 H, m), 1.35–1.05 (5 H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.4, 109.2, 63.8, 41.7, 26.0, 25.9, 25.2; MS (70 eV) *m/e* (relative intensity) 171 (0.2), 170 (M^+, 0.2), 111 (55), 95 (11), 87 (92), 83 (87), 67 (30), 59 (61), 55 (100), 41 (82), 39 (47). Anal. Calcd for $C_9H_{14}O_3$: C, 63.51; H, 8.29. Found: C, 63.34; H, 8.31.

2-Phenyl-1,3-dioxolan-4-one (8):[4a] R_f 0.17 (SiO_2, 10% EtOAc/hexane); IR (film) 1811 (s), 1479 (m), 1395 (w), 1319 (w), 1225 (s), 1207 (m), 1188 (m), 1071 (w) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.55–7.25 (5 H, m), 6.45 (1 H, s), 4.34, 4.44 (2 H, AB, *J* = 15.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.0, 148.8, 130.4, 128.6, 126.3, 105.1, 64.0; MS (70 eV), *m/e* (relative intensity) 165 (5), 164 (M^+, 41), 163 (15), 119 (13), 106 (77), 105 (100), 90 (42), 78 (82), 77 (87), 63 (25), 51 (85), 39 (37). Anal. Calcd for $C_9H_8O_3$: C, 65.85; H, 4.91. Found: C, 65.76; H, 4.90.

Acknowledgment. We thank the Dreyfus Foundation and the National Institutes of Health for the support of this research.

A Convenient Synthesis of Cyclopenta[*cd*]pyrene[1]

Seshadri Veeraraghavan,* Scott Jostmeyer, J'né Myers, and James C. Wiley, Jr.

Chemsyn Science Laboratories, Eagle-Picher Industries, Inc., Lenexa, Kansas 66215-1297

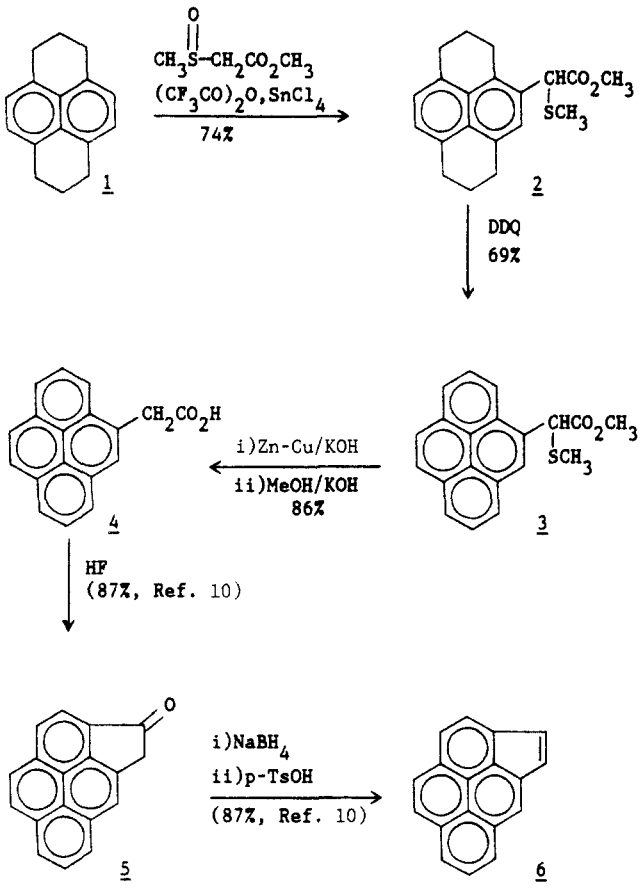
Received October 6, 1986

Cyclopenta[*cd*]pyrene (CPP, **6**), a non bay region polycyclic aromatic hydrocarbon of widespread environmental distribution,[2-4] has been shown to be carcinogenic to mice[5] and a very potent bacterial mutagen.[6] These findings have

(1) Work performed under a resource contract (NO1-CP-61037) with the National Cancer Institute.
(2) Gold, A. *Anal. Chem.* **1975**, *47*, 1469.
(3) Wallcave, L.; Nagel, D. L.; Smith, J. W.; Waniska, R. D. *Environ. Sci. Technol.* **1975**, *9*, 143.
(4) Grimmer, G.; Bohnke, H.; Glaser, A. *Zbl. Bakt. Hyg., I. Abt. Orig. B* **1977**, *164*, 218.
(5) Neal, J.; Trieff, N. M. *Health Lab Sci.* **1972**, *9*, 32.

0022-3263/87/1952-1355$01.50/0

Scheme I. Synthesis of Cyclopenta[*c d*]pyrene



aroused considerable interest in CPP, and a few syntheses of it have been reported to date.[7-13] None of the methods, however, are convenient. The route[7,9] using the Willgerodt reaction (or the Kindler modification thereof), for example, requires the use of sealed tubes and high temperatures while all our attempts to duplicate either the pyrene dianion approach[11] or the thallium trinitrate methodology[12] were unsuccessful.

In view of the importance of **6** and its potential metabolites in carcinogenesis research, a straightforward, high-yield synthesis of CPP was, therefore, required. We report herein a new synthesis of **6**. The strategy is patterned after a recent paper[14] on the application of the Pummerer rearrangement in organic synthesis.

Reaction of hexahydropyrene (**1**) with methyl (methylsulfinyl)acetate essentially as described[14] for other systems gave **2** in 74% yield (see Scheme I). Aromatization of **2** with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone afforded **3** in 69% yield. Although attempted desulfurization of **2** or **3** with Raney nickel (W-2 activity) or Zn–HOAc[15] failed, conversion of **3** into **4** via methyl pyren-4-ylacetate was conveniently accomplished by reaction with zinc–copper couple followed by alkaline hydrolysis.

The overall yield of pyren-4-ylacetic acid is 44%. Since pyren-4-ylacetic acid has previously[9,10] been converted into **6** in high overall yields, the method reported herein does indeed constitute a synthesis of **6**.

Experimental Section

General Procedures. Hexahydropyrene and methyl (methylsulfinyl)acetate were purchased from Aldrich Chemical Co. and were used as received. Infrared and ^{1}H NMR spectra were recorded on Beckman AccuLab-1 and Varian XL-300 spectrometers, respectively. Elemental analyses were performed by Galbraith Laboratories, Knoxville, TN. We thank Mike Stanga for the ^{1}H NMR spectra.

Methyl (1,2,3,6,7,8-Hexahydropyren-4-yl)(methylthio)acetate (2). To a well-stirred solution of hexahydropyrene (22.75 g, 0.109 mol) and methyl (methylsulfinyl)acetate (14.92 g, 0.110 mol) in dry methylene chloride (400 mL), maintained at 0 °C under an atmosphere of argon, was added trifluoroacetic anhydride (15.6 mL) over 15 min. After the contents were stirred for 5 min, stannic chloride (12.9 mL) was introduced dropwise over 10 min. The mixture was stirred at 0 °C for an additional 30 min, allowed to warm to ambient temperature, and then poured into 1 L of 1% aqueous sodium bicarbonate solution. Extraction with methylene chloride (3 × 100 mL) followed by the usual workup of the organic extract afforded 33.72 g (94%) of crude **2**, mp 105–111 °C. This was chromatographed on silica gel (E. Merck, 70–230 mesh) and eluted with benzene to obtain 26.69 g (74%) of pure **2**, mp 120–122 °C. A sample, mp 122–123 °C, for elemental analysis was prepared by recrystallization, with little loss, from ethanol. IR (Nujol): 1720, 1600 (w), 1305, 1210, 1165, 1020, 810 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.98–2.09 (4 H, m, aliphatic), 2.10 (3 H, s, SCH_3), 3.01–3.16 (8 H, m, aliphatic), 3.73 (3 H, s, CO_2CH_3), 5.03 (1 H, s, $CHCH_3$), 7.13–7.37 (3 H, m, aromatic). Anal. Calcd for $C_{20}H_{22}O_2S$: C, 73.60; H, 6.79; S, 9.82. Found: C, 73.76; H, 6.61; S, 10.05.

Methyl Pyren-4-yl(methylthio)acetate (3). A mixture of **2** (6.57 g, 20.5 mmol) and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (15 g, 66 mmol) in 650 mL of dry benzene was held at reflux for 2.5 h under an atmosphere of argon. The reaction mixture was then filtered hot through Celite and the filtrate chromatographed on alumina (Fisher A-540). Elution with benzene yielded 4.5 g (69%) of **3**, mp 108–111.5 °C. A sample, mp 114.5–116 °C, for elemental analysis was obtained by recrystallization, with little loss, from ethanol. IR (Nujol): 1730, 1600 (w), 1205, 1160, 1010, 880, 830, 720 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 2.22 (3 H, s, SCH_3), 3.77 (3 H, s, CO_2CH_3), 5.47 (1 H, s, $CHCH_3$), 7.25 (1 H, s, C_5-H aromatic), 8.02–8.46 (8 H, m, aromatic). Anal. Calcd for $C_{20}H_{16}O_2S$: C, 74.97; H, 5.03; O, 9.99; S, 10.01. Found: C, 74.81; H, 4.97; O, 9.79, S, 10.51.

Pyren-4-ylacetic Acid (4). A well-stirred mixture of **3** (6.99 g, 21.8 mmol), pyridine (70 mL), 20% aqueous KOH (70 mL), 50 mg of $CuSO_4 \cdot 5H_2O$, and activated zinc[16] was heated to 90 °C and held at that temperature for 4 h. The mixture was filtered hot through Celite, the filter cake was washed several times with benzene, and the washings and the filtrate were combined. Extraction with ether/benzene (1:1, v/v, 3 × 200 mL) followed by the usual workup afforded crude methyl pyren-4-ylacetate to which were added 45% aqueous KOH (25 mL) and methanol (150 mL). The mixture was held at reflux for 1.5 h, most of the methanol was distilled off under reduced pressure, and the contents were poured into a slurry of ice and concentrated HCl to obtain 4.86 g (86%) of pyren-4-ylacetic acid, mp 220–225 °C dec (lit.[10] mp 208–210 °C dec, 242–243 °C dec). Although a higher melting sample could be obtained by recrystallization from chlorobenzene, the product obtained above was of sufficient purity

(6) Eisenstadt, E.; Gold, A. *Proc. Natl. Acad. Sci. U.S.A.* **1978**, *75*, 1667.
(7) Gold, A.; Schultz, J.; Eisenstadt, E. *Tetrahedron Lett.* **1978**, 4491.
(8) Ittah, Y.; Jerina, D. M. *Tetrahedron Lett.* **1978**, 4495.
(9) Ruehle, P. H.; Fischer, D. L.; Wiley, J. C., Jr. *J. Chem. Soc., Chem. Commun.* **1979**, 302.
(10) Konieczny, M.; Harvey, R. G. *J. Org. Chem.* **1979**, *44*, 2158.
(11) Tintel, C.; Cornelisse, J.; Lugtenberg, J. *Recl.: J. R. Neth. Chem. Soc.* **1983**, *102*, 14.
(12) Sangaiah, R.; Gold, A. In *PAH-Mechanisms and Metabolism*, 8th International Symposium; Battelle: Columbus, OH, 1983; p 1147.
(13) Dr. Joseph E. Rice of the American Health Foundation has developed a new synthesis of pyren-4-ylacetic acid starting from pyrene and ethyl diazoacetate. The overall yields of **4** range from 20 to 25%. We thank Dr. Rice for sharing this information with us prior to publication.
(14) Stamos, I. K. *Tetrahedron Lett.* **1985**, *26*, 477.
(15) Tamura, Y.; Choi, H. D.; Shindo, H.; Ishibashi, H. *Chem. Pharm. Bull.* **1982**, *30*, 915.
(16) Commercial zinc (138 g) was activated by first stirring with 12% aqueous HCl (100 mL) for approximately 20 min. The acid was decanted off; the zinc was washed with about 100 mL of water and then treated with aqueous copper sulfate (25% w/v, 140 mL) solution. This suspension was used in the desulfurization reaction.

and could be used as such in the next step. ^{1}H NMR (Me_2SO-d_6): δ 4.29 (2 H, s, benzylic), 7.95-8.35 (9 H, m, aromatic), 12.49 (1 H, br s, CO_2H).

When the above reaction was performed on a 1-g scale, isolation of the methyl ester was not required and the acid was obtained in quantitative yield.

Acid-Catalyzed Decomposition of 4(5)-Nitroso-5(4)-phenylimidazole in Methanol and Water

Shelley M. Brothers and Robert A. McClelland*

Department of Chemistry, University of Toronto, Toronto, Ontario, Canada M5S 1A1

Received September 16, 1986

Metronidazole [1-(2-hydroxyethyl)-2-methyl-5-nitroimidazole] and other 5-nitroimidazoles are used extensively for the treatment of infections with protozoa and anaerobic bacteria.[1,2] Although exact details are unknown, these drugs are believed to be activated by reduction of the nitro group,[3-5] with an implication that one (or more) of the reduction products is the cause of biological activity. The amine derivative from metronidazole[6,7] is observed in biological systems, but it lacks antimicrobial activity.[7] This focuses attention on the nitroso and hydroxylamine derivatives, but little is known of their chemistry. Various reductions of metronidazole give ring-fragmented products,[8-10] some of which have also been observed as metabolites in biological systems.[8,11,12] The fragmentation indicates that a product (or products) of intermediate oxidation states is not stable. An examination of the literature reveals no examples of simple 5-hydroxylamino or 5-nitrosoimidazoles. There is one 4-hydroxylamine[13] and two reports of 4(5)-nitroso-5(4)-phenylimidazoles.[14,15] Frustrated in our attempts to prepare derivatives of metronidazole, we have reexamined the latter system. We find that the nitroso compound can be prepared, but it is unstable in aqueous solution, undergoing ring opening via a nucleophilic addition reaction that may model some of the fragmentations associated with metronidazole reduction.

Table I. NMR Spectral Characteristics

	nitroso[a] compd	methanol[b] adduct	intermed[c] in water	major product[a] in water
H_2'	8.53	8.28	8.43	8.26
H_3'	7.85-7.90	7.49	7.85	7.73
H_4'		7.58	7.75	7.90
H_2	8.22	6.39	6.67	9.62
		(CH_3) 3.38[f]		
C_1'	132.1	132.03		134.8
C_2'[d]	131.1	131.2		130.3
C_3'[d]	130.9	130.1		129.0
C_4'	132.3	133.7		135.0
C_2	140.3	103.7		168.0
C_4[e]	147.3	154.3		164.3
C_5[e]	159.6	167.6		192.9
		(CH_3) 51.0[f]		

[a] ^{1}H NMR, 1:1 Me_2SO-d_6/D_2O; ^{13}C NMR, Me_2SO-d_6. [b] CD_3OD. [c] 1:1 Me_2SO-d_6/D_2O. [d] C_2', C_3' cannot be distinguished. [e] C_4, C_5 cannot be distinguished. [f] Signal does not correspond to CH_3OH.

Results and Discussion

The literature route[14] to 4(5)-nitroso-5(4)-phenylimidazole involves the reaction of 4(5)-phenylimidazole with isoamyl nitrite in ethanol containing sodium ethoxide, followed by acidification. With this procedure we obtained the green solid previously reported in good yield, although there was substantial loss of material on recrystallization. Our experiments with 4(5)-methylimidazole and with 2-phenylimidazole failed to give characterizable products. The procedure however did work with 2,4(2,5)-diphenylimidazole.[14] The indication therefore is that a 4(5)-phenyl is required.

The 4(5)-nitroso-5(4)-phenylimidazole had ^{1}H and ^{13}C NMR spectra (Table I), mass spectrum, and analysis consistent with this structure. The absorption spectrum in water had a strong band at 365 nm with a weak band at 725 nm. It is well established that a *C*-nitroso compound can exist as the simple monomer or as an azodioxy dimer.[16] A weak visible band near 700 nm is characteristic of the monomer, the dimer usually not absorbing above 400 nm.[16] Thus, the presence of the 725-nm band indicates that 4(5)-nitroso-5(4)-phenylimidazole is monomeric. Moreover, in methanol, the visible absorbance followed Beer's law in solutions as concentrated as 20 mM, implying that this compound remains monomeric at least up to this point. The brilliant green indicates that the solid form is also monomeric.

By following the change in absorbance at 365 nm, a pK_a of 7.1 was obtained for deprotonation. Thus, the nitrosoimidazole is relatively acidic, probably more acidic than the corresponding nitroimidazole. This acidity constant, for 4(5)-nitro-5(4)-phenylnitroimidazole, is not known. However, 4(5)-nitroimidazole has a pK_a of 9.3,[17] and the additional phenyl is unlikely to have a large effect.

Under acid conditions, the nitrosoimidazole is not stable. In the absorption spectrum, the 365-nm band and the visible band were observed to disappear, with a new band eventually (see later text) appearing at 260 nm. The absorbance decreases obeyed excellent first-order kinetics at constant pH, with the first-order rate constants k_{obsd} being proportional to H^+ concentration over the range of pH studied (pH 1-6). A second-order rate constant at 25 °C was obtained by plotting k_{obsd} vs. H^+ concentration; the value is 1.3×10^2 M^{-1} s^{-1}. The half-life at pH 6 is 1.5 h; in 0.1 M HCl it is only 50 ms.

(1) Grunberg, E.; Titsworth, E. H. *Ann. Rev. Microbiol.* **1973**, *27*, 317-347.
(2) Goldman, P. *Johns Hopkins Med. J.* **1980**, *147*, 1-9.
(3) Lindmark, D. G.; Muller, M. *Antimicrob. Agents Chemother.* **1976**, *10*, 476-482.
(4) Muller, M. *Scand. J. Infect. Dis., Suppl.* **1981**, *No. 26*, 31-41.
(5) Rauth, A. M. *Int. J. Radiat. Oncology Biol. Phys.* **1984**, *10*, 1293-1300.
(6) Sullivan, C. E.; Tally, F. P.; Goldin, B. R.; Vouros, P. *Biochem. Pharm.* **1982**, *31*, 2689-2691.
(7) Elhardt, W. J.; Beaulieu, B. B.; Goldman, P. *Biochem. Pharmacol.*, in press.
(8) Zinc/ammonium chloride: Koch, R. L.; Goldman, P. *J. Pharm. Exp. Theor.* **1979**, *206*, 406-410.
(9) Enzymic (xanthine oxidase): Chrystal, E. J. T.; Koch, R. L.; Goldman, P. *Mol. Pharmacol.* **1980**, *18*, 105-111.
(10) Electrochemical: Knox, R. J.; Knight, R. C.; Edwards, D. I. *Biochem. Pharmacol.* **1983**, *32*, 2149-2156.
(11) Koch, R. L.; Chrystal, E. J. T.; Beaulieu, B. B.; Goldman, P. *Biochem. Pharmacol.* **1979**, *28*, 3611-3615.
(12) Beaulieu, B. B.; McLafferty, M. A.; Koch, R. L.; Goldman, P. *Antimicrob. Agents Chemother.* **1981**, *20*, 410-414.
(13) 5-Cyano-4-(hydroxyamino)-1-methylimidazole: Taylor, E. C.; Loeffler, P. K. *J. Org. Chem.* **1959**, *24*, 2035-2036.
(14) Cusmano, S.; Didonna, G. *Gazz. Chim. Ital.* **1955**, *85*, 208-216.
(15) Ruccia, M.; Werber, G. *Atti Acad. Sci., Lett. Arti Palermo, Parte 1* **1961/62**, *22*, 95.
(16) Rao, C. N. R.; Bhaskar, K. R. In *Chemistry of the Nitro and Nitroso Group, Part 1*; Interscience: New York, 1969; pp 137-163.
(17) Barlin, G. B. *J. Chem. Soc. B* **1967**, 641-647.

0022-3263/87/1952-1357$01.50/0