between ethyl acetate (30 mL) and water (25 mL). The organic layer was washed with water (2 × 25 mL) and brine (1 × 25 mL). This solution was dried and then spin evaporated in vacuo to give a greenish-yellow oil. The oil was triturated with pentane (25 ml) to give a yellow, amorphous solid that was recrystallized from hexane–EtOAc to give crystalline **2a**: yield 0.171 g (34%); mp 117–120 °C; TLC (EtOAc/cyclohexane (1:2)); NMR (Me_2SO-d_6) δ 7.38 (br s, 1 H, NH), 7.20 (s, 4 H, Ar H), 5.10 (d, J = 1.3 Hz, 2 H, NCH_2N), 4.54 (s, 2 H, CH_2Ar), 2.30 (s, 3 H, CH_3); UV (pH 7) λ_{max} 310 nm; mass spectrum, m/e 328 (M^+), 223 ($M^+ - C_8H_9$). Anal. Calcd for $C_{14}H_{12}ClF_3N_4$: C, 51.15; H, 3.68; N, 17.04. Found: C, 51.54; H, 3.51; N, 17.27.

7,8-Dihydro-9-(4-methylbenzyl)-2-(trifluoromethyl)purine (2b). Compound **2b** was isolated from a remake of **2a** in the following manner. A solution of 2.81 g (8.60 mmol) of **1a**, 0.651 g (17.2 mmol) of sodium borohydride, and 60 mL of dry tetrahydrofuran was refluxed with stirring for 1 h. The solvent was spin evaporated in vacuo, and the residue was partitioned between ethyl acetate (75 mL) and water (50 mL). The organic layer was washed with water (1 × 50 mL) and brine (1 × 50 mL). The solution was dried over anhydrous sodium sulfate and then spin evaporated in vacuo. The crude residue was dissolved in dichloromethane and added to 25 g of silica gel. This mixture was spin evaporated in vacuo, and the solids were introduced onto a column of silica gel 60. The column was eluted with ethyl acetate/hexane (1:2) by the flash chromatography technique.[11] The major product **2a** was eluted first and collected in 15 50-mL fractions. The yield of **2a** was 2.40 g (85%). The column was then eluted with ethyl acetate/hexane (3:2). The appropriate fractions were combined and spin evaporated in vacuo to give a white solid. Recrystallization from hexane–ethyl acetate gave analytically pure **2b**: yield 0.078 g (3.1%); mp 123–125 °C; TLC (EtOAc/cyclohexane (1:1)); NMR (Me_2SO-d_6) δ 7.18 (s, 4 H, Ar H), 7.13 (s, 1 H, C-6), 6.83 (br s, 1 H, NH), 5.02 (s, 2 H, NCH_2N), 4.51 (s, 2 H, CH_2Ar), 2.28 (s, 3 H, CH_3); UV (pH 7) λ_{max} 310 nm; mass spectrum, m/e 294 (M^+), 292 ($M^+ - 2$ H). Anal. Calcd for $C_{14}H_{13}F_3N_4$: C, 57.14; H, 4.45; N, 19.04. Found: C, 57.17; H, 4.46; N, 19.04.

9-(4-Methylbenzyl)-2-(trifluoromethyl)purine (3). Base-Mediated Dehydrochlorination. To a stirred solution of 0.200 g (0.608 mmol) of **2a** in 3.3 mL of tetrahydrofuran was added 0.61 mL (0.61 mmol) of 1 N NaOH. The orange solution was stirred for 18 h and then spin evaporated in vacuo to a volume of 1 mL. The solution was acidified with 1 N HCl and then extracted with ethyl acetate (1 × 20 mL). The extract was washed with water (1 × 15 mL) and brine (1 × 15 mL), dried (Na_2SO_4), and spin evaporated in vacuo. The crude oil was dissolved in dichloromethane and added to 1 g of silica gel. The volatiles were evaporated and the residue was introduced onto a column (2 cm × 9 cm) of silica gel 60. The column was eluted with ethyl acetate/hexane (1:1) by the flash chromatography technique.[11] The appropriate fractions were combined and spin evaporated in vacuo to give a solid residue. Recrystallization from hexane gave **3**: yield 0.051 g (29%); mp 107.5–108.5 °C; TLC (ethyl acetate/cyclohexane (1:1)); NMR (Me_2SO-d_6) δ 9.37 (s, 1 H, C-6), 8.96 (s, 1 H, C-8), 7.21 (AB q, 4 H, Ar H), 5.52 (s, 2 H, CH_2), 2.25 (s, 3 H, CH_3); UV (pH 7) λ_{max} 263 nm; mass spectrum, m/e 292 (M^+). Anal. Calcd for $C_{14}H_{11}F_3N_4$: C, 57.54; H, 3.79; N, 19.17. Found: C, 57.41; H, 3.67; N, 19.08.

Catalytic Hydrogenolysis. A mixture of 0.500 g (1.53 mmol) of **1a**, 0.208 g (1.53 mmol) of sodium acetate trihydrate, 0.250 g of 5% palladium on carbon, and 25 mL of methanol was shaken at 2–3 atm of hydrogen for 1.5 h. The reaction was filtered and spin evaporated in vacuo. The residue was partitioned between ethyl acetate (25 mL) and water (25 mL). The ethyl acetate layer was washed with brine (15 mL), dried (Na_2SO_4), and spin evaporated in vacuo to give an oil. The oil was crystallized from pentane–hexane to give crystalline **3**: yield 0.226 g (50%); mp 106.5–108 °C identical with that prepared from **2a**.

5-Formamido-6-[(4-methylbenzyl)amino]-2-(trifluoromethyl)pyrimidine (4). A stirred solution of 0.500 g (1.52 mmol) of **2a**, 3.0 mL (3.0 mmol) of 1 N NaOH, and 8.2 mL of ethanol was stirred at ambient temperature for 18 h. The solvent was spin evaporated in vacuo, and the residue was dissolved in 40 mL of ethyl acetate. This solution was washed with water (1 × 25 mL) and brine (1 × 25 mL). The combined aqueous phases were back-washed with 50 mL of EtOAc. The combined extracts and wash were extracted with brine (1 × 50 mL), dried (Na_2SO_4), and spin evaporated in vacuo to give an orange oil. The crude oil was preadsorbed onto 3 g of silica gel and purified by flash column (3.5 cm × 17 cm) chromatography[11] on silica gel 60 using EtOAc/hexane (3:2) as eluant. The appropriate fractions were combined and spin evaporated in vacuo to give a light yellow solid. Recrystallization from EtOAc–hexane gave **4**: yield 0.091 g (19%); mp 191.5–192 °C; TLC (EtOAc/cyclohexane (1:1)); NMR (Me_2SO-d_6) δ 9.72 (br t, 1 H, N*H*CHO), 8.53 (s, 1 H, C-4), 8.37 (s over d, J = 11 Hz, 1 H, CHO, collapsed to s with D_2O exchange), 7.92 (br t, 1 H, N*H*CH_2), 7.20 (q, 4 H, Ar H), 4.57 (d, J = 5 Hz, 2H, CH_2), 2.27 (s, 3 H, CH_3); UV (pH 7) λ_{max} 253 nm; mass spectrum, m/e 310 (M^+), 295 ($M^+ - CH_3$), 281 ($M^+ - CHO$). Anal. Calcd for $C_{14}H_{13}F_3N_4O$: C, 54.19; H, 4.22; N, 18.06. Found: C, 54.22; H, 4.27; N, 18.01.

Acknowledgment. We thank D. A. Brent and R. L. Johnson for the mass spectra, B. S. Hurlbert, R. C. Crouch, A. Ragouzeos, and J. L. Miller for the nuclear magnetic resonance measurements, and Dr. R. W. Morrison for helpful comments during the preparation of this manuscript.

Registry No. **1a**, 105183-02-6; **1b**, 105183-07-1; **2a**, 105183-03-7; **2b**, 105183-04-8; **3**, 105183-05-9; **4**, 105183-06-0; 6-chloro-2-(trifluoromethyl)purine, 1998-63-6; 4-methylbenzyl bromide, 104-81-4.

Benzylic Hydroperoxide Rearrangement: Observations on a Viable and Convenient Alternative to the Baeyer–Villiger Rearrangement

Dale L. Boger*[1a] and Robert S. Coleman[1b]

Department of Chemistry, Purdue University, West Lafayette, Indiana 47906

Received August 7, 1986

In three recent and independent studies requiring the preparation of phenol substrates we have encountered difficulties implementing successful Baeyer–Villiger oxidations of highly substituted, electron-rich acetophenones possessing one or two substituents ortho to the aryl acetyl group.[2] The combination of steric and electronic features of the acetophenone substrates, which slow or preclude the formation of the initial tetrahedral peracyl hemiketal, could not be addressed effectively by the use of recent variants[3-6] of the peracid Baeyer–Villiger reaction. Furthermore, under vigorous reaction conditions, substrates bearing sensitive functionality or groups susceptible to oxidation (e.g., indolines and electron-rich aromatic systems) underwent secondary reactions and oxidation processes involving the reaction of substrate or solvent with the peracid, at the expense of the desired Baeyer–Villiger reaction.

(1) (a) National Institutes of Health Research Career Development Award recipient, 1983–1988 (No. CA 00898/01134). Searle Scholar recipient, 1981–1985. Alfred P. Sloan Research Fellow, 1985–1989. (b) National Institutes of Health Predoctoral fellow, 1984–1985 (No. GM 07775). David Ross fellow of Purdue University, 1986–1987.

(2) (a) Boger, D. L.; Coleman, R. S. *J. Org. Chem.* **1986**, *51*, 3250. (b) Boger, D. L.; Mullican, M. D. *Tetrahdron Lett.* **1983**, *24*, 4939; *J. Org. Chem.* **1984**, *49*, 4033. (c) Boger, D. L; Yohannes, D., unpublished observations.

(3) Emmons, W. D.; Lucas, G. B. *J. Am. Chem. Soc.* **1955**, *77*, 2287. Wetter, H. *Helv. Chim. Acta* **1981**, *64*, 761.

(4) Rastetter, W. H.; Richard, T. J.; Lewis, M. D. *J. Org. Chem.* **1978**, *43*, 3163.

(5) Ogata, Y.; Tomizawa, K.; Ikeda, T. *J. Org. Chem.* **1978**, *43*, 2417.

(6) Tsunokawa, Y.; Iwasaki, S.; Okuda, S. *Tetrahedron Lett.* **1982**, *23*, 2113; *Chem. Pharm. Bull.* **1983**, *31*, 4578.

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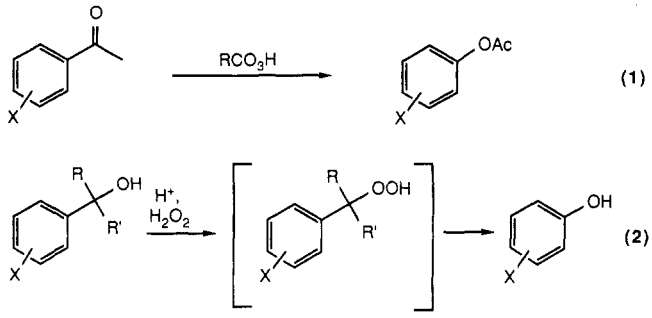
In the search for alternatives to the Baeyer–Villiger oxidation for the conversion of a substituted acetophenone to the corresponding phenol (eq 1), we have investigated



the scope and preparative synthetic utility of the benzylic hydroperoxide rearrangement[7] (eq 2). Unexpectantly mild conditions that permit the use of either secondary or tertiary benzylic alcohols derived from the corresponding acetophenone or benzoate esters are detailed in Table I. Comparative yields for Baeyer–Villiger oxidation of the parent acetophenones are given in Table II.

Examination of a series of acid catalysts for promoting the formation of benzylic hydroperoxides and their subsequent rearrangement to phenols led to the observation that *p*-toluenesulfonic acid (*p*-TsOH) was a suitable acid catalyst for providing reasonable rates for these two reaction processes. Secondary and tertiary alcohols derived from methoxyacetophenones, methoxybenzaldehydes, or methyl methoxybenzoates (Table I, entries 4–9) required mildly acidic conditions for hydroperoxide formation/rearrangement (10–15 mol % *p*-TsOH in Et_2O or THF, excess 30–90% H_2O_2, room temperature) and provided excellent yields of the resulting methoxyphenols. These results contrast the moderate yields generally obtained in the Baeyer–Villiger oxidations of the corresponding *o*-alkoxyacetophenones (Table II, entries 2, 3, and 5).

The presence of basic functionality in the substrate, e.g. an indoline nitrogen (Table I, entries 1 and 2), necessarily required the use of more than 1 mol equiv of *p*-TsOH, and under these conditions substrate nitrogen protonation slowed the rate of the desired benzylic hydroperoxide formation/rearrangement sufficiently to allow secondary processes to effectively compete. Use of 55% aqueous sulfuric acid[7g] provided a satisfactory rate of hydroperoxide formation/rearrangement, but again secondary processes were observed and the desired phenol **4** was isolated in an optimized yield of 44% after acetylation. Boron trifluoride etherate (BF_3·Et_2O)[8] proved to be an ideal catalyst for the hydroperoxide rearrangement of the tertiary alcohol **3** derived from 7-acetylindoline (**1**; entry 2), providing **4** in 57% yield after acetylation. Thus, basic functionality may survive the hydroperoxide formation/rearrangement processes as a consequence of either protic acid protonation or Lewis acid coordination during the reaction. Protection of the indoline nitrogen as the acetate prior to hydroperoxide rearrangement was unsuccessful in providing the corresponding phenol. Oxidation of the indoline to the indole prior to rearrangement (Table I, entry 3) did not lead to improved yields of phenol **7**, and again secondary oxidation processes appeared to predominate.

In contrast to the hydroperoxide rearrangement of the *secondary* and *tertiary* alcohols derived from **1**, Baeyer–Villiger oxidation (CF_3CO_3H, Na_2HPO_4, CH_2Cl_2)[3] of *N*-acetyl-7-acetylindoline (**17**) was only modestly successful (Table II, entry 1), providing 20–25% of *N,O*-diacetyl-7-hydroxyindoline (**4**) and 20–25% recovered starting material under optimal conditions. Additional peracids (*m*-chloroperbenzoic acid,[9] 3,5-dinitroperbenzoic acid,[4] permonophosphoric acid[5], or *O*-alkoxypercarbonic acids[6]) and other methods for effecting Baeyer–Villiger oxidations (acidic H_2O_2[10]) were unsuccessful in providing significant yields of **4** from **17**.

Benzylic secondary and tertiary alcohol substrates derived from hindered, electron-rich acetophenones as well as those possessing an oxidizable amino group, which consequently fail to effectively participate in the conventional Baeyer–Villiger rearrangement, appear to be ideally suited for use in the benzylic hydroperoxide rearrangement. Although both secondary and tertiary alcohols participated in hydroperoxide formation/rearrangement (e.g., compare entries 4 and 5, Table I), in those instances where secondary oxidation processes effectively competed with the desired rearrangement, the tertiary alcohol substrate provided consistently higher yields of product phenol (e.g., compare entries 1 and 2, Table I). Thus, the benzylic hydroperoxide rearrangement provides an effective complement to the Baeyer–Villiger rearrangement of acetophenones especially suited for use on occasions in which peracid treatment would prove to be expectantly poor.

Experimental Section[12]

7-Acetylindoline (1). A solution of indoline[13] (1 g, 8.39 mmol) in 17 mL of dry benzene was carefully added to a cooled (0 °C) solution of BCl_3 in CH_2Cl_2 (9.25 mL of 1 M solution), and the resulting solution was warmed to reflux (80 °C bath) under N_2 for 1 h. The reaction mixture was cooled to room temperature,

(7) (a) Anderson, G. H.; Smith, J. G. *Can. J. Chem.* **1968**, *46*, 1553, 1561. Kharasch, M. S.; Fono, A.; Nudenberg, W.; Poshkus, A. C. *J. Org. Chem.* **1950**, *15*, 775. (c) Deno, N. C.; Billups, W. E.; Kramer, K. E.; Lastomirsky, R. R. *J. Org. Chem.* **1970**, *35*, 3080. (d) Hawkins, E. G. E. *Organic Peroxides*; Van Nostrand: New York, 1961. (e) Davies, A. G. *Organic Peroxides*; Butterworths: London, 1961. (f) Lee, J. B.; Uff, B. C. *Q. Rev. Chem. Soc.* **1967**, *21*, 449. (g) For application of a hydroperoxide rearrangement in the total synthesis of triumferol see: Kusumi, T.; Chang, C. C.; Wheeler, M.; Kubo, I.; Nakanishi, K.; Naoki, H. *Tetrahedron Lett.* **1981**, *22*, 3451. (h) For application of a hydroperoxide rearrangement in the synthesis of 4-hydroxypyrazoles see: Albrand, M.; Gelin, S. *Synthesis* **1983**, 1030.

(8) McClure, J. D.; Williams, P. H. *J. Org. Chem.* **1962**, *27*, 24.

(9) Godfrey, I. M.; Sargent, M. V.; Elix, J. A. *J. Chem. Soc., Perkin Trans. 1* **1974**, 1353.

(10) Matsumoto, M.; Kobayashi, H.; Hotta, Y. *J. Org. Chem.* **1984**, *49*, 4740.

(11) Smissman, E. E.; Li, J. P.; Israili, Z. H. *J. Org. Chem.* **1968**, *33*, 4231.

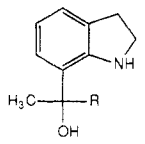
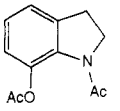
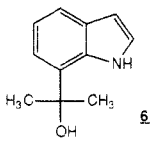
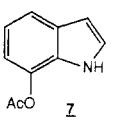
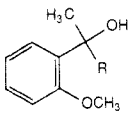
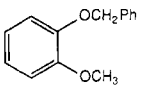
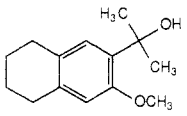
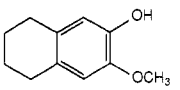
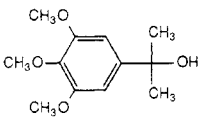
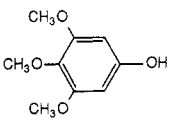
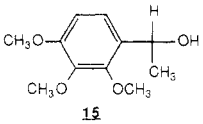
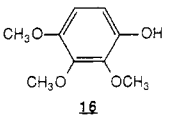
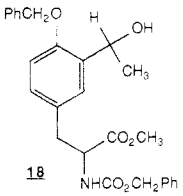
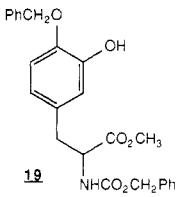
(12) Proton nuclear magnetic resonance spectra (^1H NMR) were recorded on a Varian FT-80, Varian XL-200, Nicolet NT-200, or Nicolet NT-470 spectrometer. Infrared spectra (IR) were recorded on a Perkin-Elmer 1710 Fourier transform spectrophotometer. Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Electron-impact mass spectra (EIMS) and chemical ionization mass spectra (CIMS) were recorded on a Finnigan 4000 spectrometer. High-resolution mass spectra (HRMS) were recorded on a Kratos MS-50 spectrometer. Medium-pressure liquid chromatography (MPLC)[14a] and flash chromatography[14b] were performed on silica gel 60 (240–400 mesh). Preparative centrifugal thin-layer chromatography (PCTLC)[14c] was performed on a Harrison Model 7924 chromatotron (Harrison Research, Palo Alto, CA) using Merck silica gel 60 PF_{254} containing $CaSO_4$·$^1/_2H_2O$ binder. Diethyl ether (Et_2O) and tetrahydrofuran (THF) were distilled from sodium benzophenone ketyl, methylene chloride (CH_2Cl_2) was distilled from P_2O_5, benzene was distilled from CaH_2, and ethanol (EtOH) was distilled from MgOEt prior to use. All extraction and chromatographic solvents (CH_2Cl_2, Et_2O, EtOAc, hexane) were distilled before use. 90% hydrogen peroxide (H_2O_2) was obtained from the FMC Corp. All other reagents were used as received from commercial sources.

(13) For use of this procedure in the ortho acylation of anilines see: Sugasawa, T.; Toyoda, T.; Adachi, M. Sasakura, K. *J. Am. Chem. Soc.* **1978**, *100*, 4842.

(14) (a) Meyers, A. I.; Slade, J.; Smith, R. K.; Mihelich, E. D.; Hershenson, F. M.; Liang, C. D. *J. Org. Chem.* **1979**, *44*, 2247. (b) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923. (c) Stahl, E.; Müller, J. *Chromatographia* **1982**, *15*, 493.

(15) (a) Bretschneider, H.; Hohenlohe-Oehringen, K.; Kaiser, A.; Wölcke, U. *Helv. Chim. Acta* **1973**, 2857. (b) Konda, M.; Shioiri, T.; Yamada, S.-I. *Chem. Pharm. Bull.* **1975**, *23*, 1063.

Table I. Benzylic Hydroperoxide Rearrangements

entry	substrate	conditions	product	yield, %
		(a) 5 equiv of H_2O_2, 10 equiv BF_3·Et_2O, CH_2Cl_2, 22 °C, 18–22 h (b) Ac_2O, K_2CO_3, 100 °C, 6–12 h	 **4**	
1	R=H **2**			19
2	R=CH_3 **3**			57
3	 **6**	(a) 10 mol % *p*-TsOH, 3 equiv of H_2O_2, THF, 23 °C, 24 h (b) Ac_2O, K_2CO_3, 100 °C, 6 h	 **7**	37
		(a) 9–12 mol % *p*-TsOH, 20 equiv of H_2O_2, Et_2O, 22 °C, 5 h (R = CH_3) 24 h (R = H) (b) $PhCH_2Br$, acetone, K_2CO_3, catalyst *n*-Bu_4NI, reflux, 14 h	 **10**	
4	R=H **8**			86
5	R=CH_3 **9**			89
6	 **11**	10 mol % *p*-TsOH, 10 equiv of H_2O_2, THF, 22 °C, 6 h	 **12**	85
7	 **13**	11 mol % *p*-TsOH, 20 equiv of H_2O_2, THF, 22 °C, 4 h	 **14**	73
8	 **15**	10 mol % *p*-TsOH, 10 equiv of H_2O_2, THF, 24 °C, 21 h	 **16**	95
9	 **18**	40 mol % *p*-TsOH, 10 equiv of H_2O_2, 22 °C, 6 days	 **19**	50

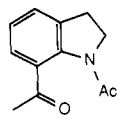
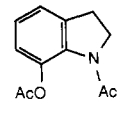
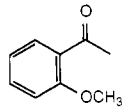
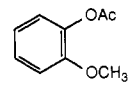
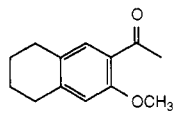
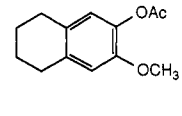
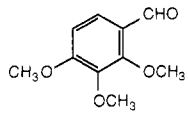
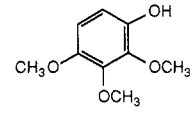
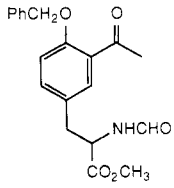
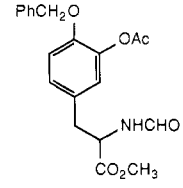
and CH_3CN (2.2 mL, 42 mmol, 5 equiv) was added followed by $AlCl_3$ (1.5 g, ca. 10 mmol). The mixture was warmed to reflux (80 °C bath) for an additional 15 h and was cooled to room temperature. 10% HCl (10 mL) was added, and the reaction mixture was warmed at 80 °C for 0.5 h. The reaction mixture was cooled, diluted with 100 mL of water, and made basic with solid K_2CO_3. The mixture was extracted with CH_2Cl_2 (4 × 100 mL), the combined extracts were dried ($MgSO_4$), and the solvent removed in vacuo. Chromatography (MPLC, 1.5 × 100 cm SiO_2, 10–30% Et_2O in hexane gradient) afforded 948 mg of **1** [1.35 g theor., (70%)] as a yellow crystalline solid: mp 85–86 °C (Et_2O–hexane); ^1H NMR ($CDCl_3$, 80 MHz, ppm) 7.41 (dd, 1 H, J = 1, 8 Hz, C6-H), 7.14 (dd, 1 H, J = 1, 7 Hz, C4-H), 6.51 (dd, 1 H, J = 7, 8 Hz, C5-H), 3.73 (t, 2 H, J = 8.5 Hz, NCH_2CH_2), 3.02 (t, 2 H, J = 8.5 Hz, NCH_2CH_2), 2.49 (s, 3 H, $ArCOCH_3$); IR (KBr) ν_{max} 3403, 3062, 2993, 2904, 2846, 1642, 1580, 1504, 1479, 1391, 1307, 1290, 1264, 1226, 1193, 1118, 1058, 1037, 981, 741, 625 cm^{-1}; EIMS, m/e (relative intensity) 161 (M^+, base), 146 (69), 118 (56), 91 (29); CIMS (isobutane), m/e 162 (M^+ + H, base).

Anal. Calcd for $C_{10}H_{11}NO$: C, 74.51; H, 6.88; N, 8.69. Found: C, 74.37; H, 7.06; N, 8.77.

***N,O*-Diacetyl-7-hydroxyindoline (4).** A solution of **3** (56 mg, 0.316 mmol) in 1.2 mL of CH_2Cl_2 was cooled to 0 °C and was treated with a 2:1 (mol/mol) mixture of BF_3·Et_2O–90% H_2O_2[8] (0.43 mL, ca. 1.5 mmol of H_2O_2, ca. 5 equiv). The reaction mixture was allowed to warm to 22 °C and was stirred 22 h. The reaction mixture was diluted with water and was poured onto 5 mL of cold (0 °C) saturated Na_2SO_3. After 5 min solid Na_2CO_3 was carefully added until the mixture was basic. Extraction with EtOAc (8 × 4 mL), drying the combined extracts ($NaSO_4$), and removal of the solvent in vacuo afforded crude 7-hydroxyindoline as a brown solid. This solid was dissolved in 2 mL of Ac_2O and treated with excess K_2CO_3 and catalytic (*N,N*-dimethylamino)pyridine, and the resulting mixture was warmed at 100 °C for 6 h. The volatiles were removed in vacuo and the residue partitioned between 10 mL of water and 10 mL of CH_2Cl_2. The aqueous phase was extracted with CH_2Cl_2 (2 × 10 mL), the combined organic extracts were dried ($MgSO_4$), and the solvent was removed in vacuo to afford crude **4** as a brown oil. Chromatography (PCTLC, 1 mm SiO_2, EtOAc) afforded 39.6 mg of **4** [69.3 mg theor., (57%)] as a white, crystalline solid: mp 125–126 °C (CH_2Cl_2–hexane); ^1H NMR ($CDCl_3$, 80 MHz, ppm) 6.8–7.1 (m, 3 H, ArH), 4.10 (t, 2 H, J = 8 Hz, NCH_2CH_2), 3.09 (t, 2 H, J = 8Hz, NCH_2CH_2), 2.28 (s, 3 H, acetyl), 2.21 (s, 3 H, acetyl); IR (KBr) ν_{max} 2931, 2879, 1765, 1676, 1608, 1477, 1460, 1395, 1366, 1355, 1341, 1324, 1248, 1222, 1187, 1019, 879, 851, 781, 740 cm^{-1}; EIMS, m/e (relative intensity) 219 (M^+, 11), 177 (25), 135 (base), 116 (6), 104 (3); CIMS (isobutane), m/e 220 (M^+ + H, base), 178 (38).

Anal. Calcd for $C_{12}H_{13}NO_3$: C, 65.74; H, 5.98; N, 6.39. Found: C, 65.62; H, 5.96; N, 6.61.

Table II. Comparative Baeyer–Villiger Reactions

entry	substrate	conditions	product	yield, %
1		CF_3CO_3H, Na_2HPO_4, CH_2Cl_2[a]		20–25
2[b]		CF_3CO_3H, $CHCl_3$, reflux, 5 h		60
3[c]		*m*-CPBA, CH_2Cl_2, 25 °C, 22 h		60
4[d]		*m*-CPBA, CH_2Cl_2, reflux; KOH, MeOH, room temp		83
5[e]		*m*-CPBA, $CHCl_3$, reflux, 48 h		33

[a] For preparation and use of this reagent system see ref 3. [b] See ref 11. [c] See ref 2b. [d] See ref 9. [e] See ref 15b.

7-Acetoxyindole (7): ^1H NMR ($CDCl_3$, 80 MHz, ppm) 8.5 (br s, 1 H, NH), 6.4–7.5 (m, 5 H, ArH), 2.37 (s, 3 H, $OCOCH_3$); IR (neat) ν_{max} 3368, 3110, 3079, 2933, 1735, 1636, 1580, 1495, 1443, 1369, 1342, 1287, 1228, 1204, 1109, 1036, 907, 892, 846, 791, 722 cm^{-1}; EIMS, *m/e* (relative intensity) 175 (M^+, 38), 133 (base), 105 (25), 104 (29); CIMS (isobutane), *m/e* 176 ($M^+ + H$, base), 134 (8); HRMS, *m/e* 175.0635 ($C_{10}H_9NO_2$ requires 175.0633).

***O*-Benzyl-*O*-methylcatechol (10).** A solution of 90% H_2O_2 in Et_2O (14.4 mmol in 2.0 mL) was added to **9** (108.7 mg, 0.654 mmol) followed by *p*-TsOH·H_2O (11 mg, 0.06 mmol, 9 mol %). The resulting solution was stirred 5 h at 22 °C. The reaction mixture was poured onto 10 mL of 10% Na_2CO_3, and the mixture was extracted with CH_2Cl_2 (5 × 10 mL). The combined organic extracts were dried ($MgSO_4$), and the solvent was removed in vacuo (bath temperature <25 °C) to afford crude 2-methoxyphenol as a light yellow oil. This crude oil dissolved in 1.5 mL of dry acetone was treated with K_2CO_3 (0.46 g, 3.3 mmol, 5 equiv), benzyl bromide (0.25 mL, 2.1 mmol, 3.2 equiv), and *n*-Bu_4NI (catalyst). The reaction mixture was warmed to 55 °C under N_2 for 14 h, cooled to room temperature, and partitioned between 50 mL of Et_2O and 15 mL of water. The Et_2O layer was washed with 20 mL of brine and was dried over $MgSO_4$. Removal of the solvent in vacuo followed by chromatography (PCTLC, 2 mm SiO_2, hexane and then 50% Et_2O–hexane) afforded 124 mg of **10** [140 mg theor., (89%)] as a colorless oil: ^1H NMR ($CDCl_3$, 80 MHz, ppm) 7.2–7.4 (m, 5 H, $PhCH_2$), 6.89 (br s, 4 H, ArH), 5.14 (s, 2 H, $PhCH_2$), 3.88 (s, 3 H, OCH_3); IR (neat) ν_{max} 3034, 2951, 2935, 2919, 2838, 1591, 1508, 1456, 1290, 1258, 1220, 1185, 1125, 1022, 1010, 741, 699 cm^{-1}; EIMS, *m/e* (relative intensity) 214 (M^+, 4), 91 (base); CIMS (isobutane), *m/e* 215 ($M^+ + H$, base), 147 (6), 137 (14), 91 (12); HRMS, *m/e* 214.0999 ($C_{14}H_{14}O_2$ requires 214.0994).

A solution of 30% H_2O_2 (0.8 mL, 7.8 mmol, 10.0 equiv) was added to a solution of **9** (129 mg, 0.78 mmol) in 0.8 mL of THF. *p*-TsOH·H_2O (15 mg, 0.08 mmol, 10 mol %) was added and the reaction mixture was stirred 24 h at 22 °C. Workup, benzylation, and purification as described above afforded 132 mg of **10** [166 mg theor., (80%)].

3-Methoxy-5,6,7,8-tetrahydro-2-naphthalenol (12): mp 80–81 °C (hexane); ^1H NMR ($CDCl_3$, 470 MHz, ppm) 6.62 (s, 1 H, C1-H), 6.54 (s, 1 H, C4-H), 5.40 (s, 1 H, OH), 3.84 (s, 3 H, OCH_3), 2.67 (m, 4 H, C5-H and C8-H), 1.74 (m, 4 H, C6-H and C7-H); IR (KBr) ν_{max} 3413, 2927, 2837, 1518, 1450, 1433, 1373, 1322, 1291, 1266, 1249, 1209, 1109, 1020, 865, 846, 808 cm^{-1}; EIMS, *m/e* (relative intensity) 178 (M^+, base), 163 (15), 150 (36), 135 (31), 117 (12), 107 (24), 91 (18); CIMS (isobutane), *m/e* 179 ($M^+ + H$, base), 177 (6); HRMS, *m/e* 178.0993 ($C_{11}H_{14}O_2$ requires 178.0994).

***N*-(Carbobenzyloxy)-4-*O*-benzyl-3-hydroxy-L-tyrosine methyl ester (19)**: ^1H NMR ($CDCl_3$, 200 MHz, ppm) 7.39 (br s, 5 H, $PhCH_2O$), 7.34 (br s, 5 H, $PhCH_2O$), 6.81 (d, 1 H, J = 8.2 Hz, C5-H), 6.69 (d, 1 H, J = 2.0 Hz, C2-H), 6.54 (dd, 1 H, J = 8, 2 Hz, C6-H), 5.64 (s, 1 H, OH), 5.22 (d, 1 H, J = 7.7 Hz, NH), 5.10 (s, 2 H, $PhCH_2O$), 5.06 (s, 2 H, $PhCH_2O$), 4.60 (m, 1 H, $NHCHCH_2$), 3.72 (s, 3 H, OCH_3), 3.01 (d, 2 H, J = 5.6 Hz, $CHCH_2$); IR (neat) ν_{max} 3518, 3364, 3064, 3033, 2952, 1718, 1592, 1510, 1455, 1438, 1382, 1343, 1275, 1215, 1129, 1061, 1025, 738, 698 cm^{-1}; EIMS, *m/e* (relative intensity) 435 (M^+, 1), 392, 374, 332, 303, 284, 268, 241, 224, 213, 211, 204, 195, 181, 91 (base); CIMS (isobutane), *m/e* 436 ($M^+ + H$, 14), 392 (base).

Acknowledgment. We gratefully acknowledge the financial support of the National Institutes of Health (Grant CA 42056, 41986), the Searle Scholars Foundation, and the Alfred P. Sloan Foundation. We thank Purdue University for providing financial support in the form of a David Ross Fellowship to R.S.C.

Registry No. **1**, 104019-19-4; **2**, 105205-61-6; **3**, 105205-62-7; **4**, 105205-63-8; **5**, 104019-20-7; **6**, 105205-64-9; **7**, 5526-13-6; **7** (alcohol), 4770-38-1; **8**, 13513-82-1; **9**, 21022-73-1; **10**, 835-79-0; **11**, 105205-65-0; **12**, 3579-88-2; **13**, 105205-66-1; **14**, 642-71-7; **15**, 41038-42-0; **16**, 19676-64-3; **17**, 105205-67-2; **18**, 105205-68-3; **18** (3-acetyl), 105205-69-4; **19**, 105229-41-2; *p*-TsOH, 104-15-4; $PhCH_2Br$, 100-39-0; *o*-$MeOC_6H_4OH$, 90-05-1; *o*-$MeOC_6H_4COMe$, 579-74-8; indoline, 496-15-1; methyl 2-methoxy-5,6,7,8-tetrahydronaphthalene-3-carboxylate, 78112-34-2; methyl 3,4,5-trimethoxybenzoate, 1916-07-0; 2,3,4-trimethoxybenzaldehyde, 2103-57-3.

Supplementary Material Available: Preparative information and full spectral and physical characterization of substrates **2**, **3**, **5**, **6**, **8**, **9**, **11**, **13**, **15**, **17**, and **18** (5 pages). Ordering information is given on any current masthead page.

Use of Chiral Lanthanide Shift Reagents in the Determination of Enantiomer Composition and Absolute Configuration of Epoxides and Arene Oxides

Herman J. C. Yeh,[†] Suresh K. Balani,[†] Haruhiko Yagi,[†] Ruth M. E. Greene,[‡] Narain D. Sharma,[‡] Derek R. Boyd,[‡] and Donald M. Jerina*[†]

Laboratories of Bioorganic Chemistry and Analytical Chemistry, NIDDK, The National Institutes of Health, Bethesda, Maryland 20892, and Department of Chemistry, Queen's University of Belfast, Belfast BT95AG, Northern Ireland

Received July 30, 1986

The metabolism of olefins and arenes in plants, animals, and fungi often proceeds via epoxide and arene oxide intermediates[1,2] which are frequently formed in high optical yields. Earlier studies from these laboratories have been concerned with the synthesis and determination of optical purity and absolute configuration of epoxides[3-5] and arene oxides[2] using a wide range of methods. Chiral shift reagents have been used previously to estimate the optical purity of acyclic epoxides[6-13] including keto epoxides[13] but have not been used in the determination of absolute con-

[†] The National Institutes of Health.
[‡] Queen's University of Belfast.