with a linear gradient of TEAB (0.05–0.8 M, total 1.2 L). Five-milliliter fractions were collected. Those fractions containing the main peak were collected, evaporated down to dryness, and coevaporated three times with water. The products were then lyophilized. The yields of the free oligoribonucleotides are as shown in Table III.

Enzyme Assay. Snake Venom Phosphodiesterase. An incubation solution of 1 M ammonium carbonate (230 μL) containing oligoribonucleotide (10 OD_{260}) and snake venom (20 mg/mL, 10 μL) was incubated at 37 °C for 12 h. The results of enzymatic hydrolysis are summarized in Table III.

New Synthesis and Some Selected Reactions of the Potential Ergot Alkaloid Precursor Indole-4-carboxaldehyde

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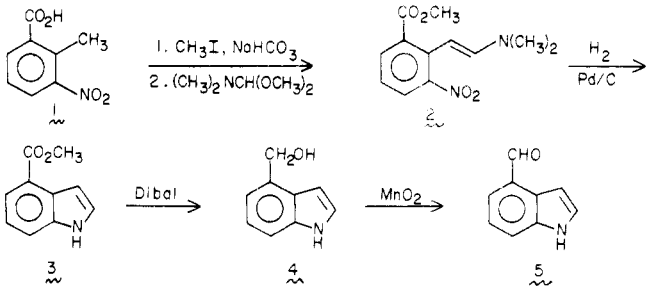
As a consequence of the potential use of the ergot alkaloids and their derivatives in the treatment of Parkinson's disease and for the inhibition of prolactin release, we have been greatly interested in designing new strategies for the preparation of these products.[2] Our retrosynthetic analysis of these compounds led us to consider routes based on the utilization of 4-C-substituted indoles as the key precursor molecules. Since no highly efficient procedures have been developed for the synthesis of such compounds, we initiated a study geared toward their production on a multigram scale.[3] We would now like to disclose an excellent method for producing methyl indole-4-carboxylate (**3**) from the commercially available 3-nitro-2-methylbenzoic acid as well as to describe some reactions of this compound.

Our synthesis of **3** is based on the straightforward extension of a general indole synthesis patented by Leimgruber and Batcho.[4] Thus, the benzoic acid **1** is esterified by reaction with iodomethane and potassium bicarbonate in DMF (Scheme I). This ester is heated with 3 equiv of *N,N*-dimethylformamide dimethyl acetal in dry DMF at 130 °C for 6 h. Removal of solvent and Kugelrohr distillation of the residue yields the enamine **2** in 80% yield. A solution of **2** in benzene is hydrogenated in a Parr shaker at 50 psi over 10% palladium on charcoal for 1.5 h. The reaction mixture is filtered, and the filtrate is washed with 5% HCl, dried ($MgSO_4$), and concentrated by rotary evaporation. The crude product is chromatographed on silica gel to afford **3** as a crystalline solid in 82% yield.

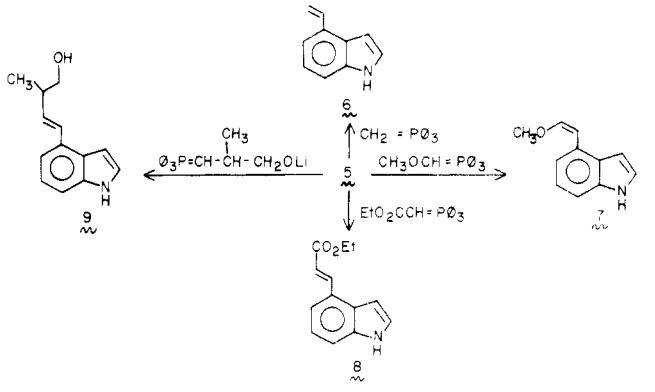
This entire sequence can be executed on a multigram scale in 2 days, thus making this the most efficient route presently designed for the preparation of **3**.

A procedure for the preparation of methyl indole-4-carboxylate similar to our own has recently been published by Ponticello and Baldwin.[3] In contrast to our own results, these workers indicate that hydrogenation of **2** produces

Scheme I. Synthesis of Indole-4-carboxaldehyde



Scheme II



only trace amounts of **3**. Their scheme thus calls for a more tedious and lower yield Fe in AcOH–EtOH reduction to accomplish this conversion.

The indole ester **3** can be transformed readily into its corresponding aldehyde derivative. Accordingly, exposure of **3** to excess Dibal in ether at −70 °C for 2 h affords the hydroxymethyl derivative **4**. Oxidation of this alcohol with manganese dioxide in methylene chloride (40 h at room temperature) provides indole-4-carboxaldehyde in 84% yield after column chromatography. Attempts to reduce ester **3** directly to aldehyde **5** by use of controlled amounts of Dibal have not been successful.

A variety of reactions have been carried out with this indole aldehyde which serve to define some of the chemistry of this special heterocyclic system. Condensation of **5** with a number of phosphoranes provides, for example, ready access to a host of chain-elongated products of potential use for incorporation at various stages into an ergoline ring synthesis.[5] Methylenetriphenylphosphorane, (methoxymethylene)triphenylphosphorane, [(carboethoxy)methylene]triphenylphosphorane, and [3-(lithiooxy)-2-methylpropylidene]triphenylphosphorane[6] all give excellent yields of olefinic products **6**–**9** (Scheme II).

It is quite interesting to note here that this latter phosphorane, a γ-oxido ylide, leads to indole **9** which posseses a disubstituted olefin of *E* geometry as ascertained by ^1H NMR (J = 16 Hz). This ylide is thus capable of bringing about an internal Schlosser reaction in a manner such as noted previously by Berta, Salmond, and Havens in a single instance for a related γ-oxido ylide.[7] This result suggests that a certain amount of generality can be attached to a prediction that olefins of *E* geometry should arise

(1) Fellow of the Alfred P. Sloan Foundation, 1978–1980.

(2) (a) Kozikowski, A. P.; Kuniak, M. P. *J. Org. Chem.* **1978**, *43*, 2083. (b) Kozikowski, A. P.; Ishida, H. *Heterocycles* **1980**, *14*, 55. (c) Kozikowski, A. P.; Greco, M. *J. Am. Chem. Soc.* **1980**, *102*, 1165.

(3) Ponticello, G. S.; Baldwin, J. J. *J. Org. Chem.* **1979**, *44*, 4003. For other preparations of methyl indole-4-carboxylate, see: (a) Uhle, F. C. *J. Am. Chem. Soc.* **1949**, *71*, 761; (b) Watanabe, T.; Hamaguchi, F.; Ohki, S. *Chem. Pharm. Bull.* **1972**, *20*, 2123; (c) Plieninger, H. *Chem. Ber.* **1955**, *88*, 370; (d) Hardegger, E.; Corrodi, H. *Helv. Chim. Acta* **1954**, *37*, 1826.

(4) Leimgruber, W.; Batcho, A. D. Third International Congress of Heterocyclic Chemistry, Japan, Aug 23-27, 1971; U.S. Patent 3 976 639, 1976.

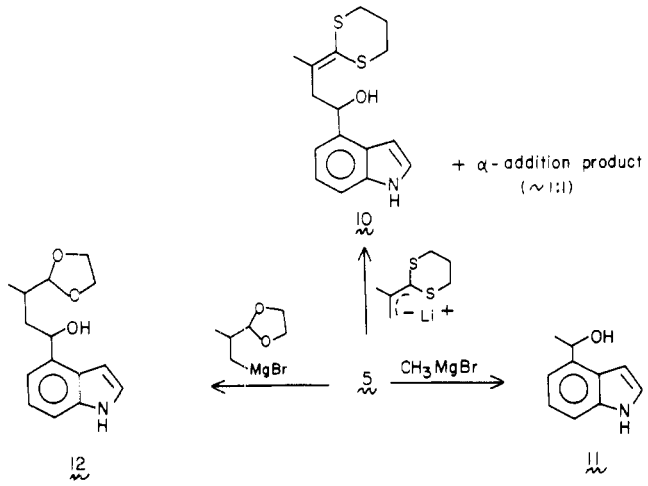
(5) For an earlier report on the reaction of indole-4-carboxaldehyde with an allylidenetriphenylphosphorane, see: Plieninger, H.; Höbel, M.; Liede, V. *Chem. Ber.* **1963**, *96*, 1618.

(6) The precursor phosphonium salt was prepared from the bromide generated by hydroboration of methallyl alcohol followed by halogenolysis (Br_2, NaOMe) of the resulting trialkylborane: Brown, H. C.; Lane, C. F. *J. Am. Chem. Soc.* **1970**, *92*, 6660.

(7) Salmond, W. G.; Berta, M. A.; Havens, J. L. *J. Org. Chem.* **1978**, *43*, 790.

0022-3263/80/1945-3350$01.00/0

Scheme III



from the reaction of γ-oxido or perhaps other oxido ylides with aldehyde substrates.[8]

The reaction of **5** with an excess of strongly nucleophilic organometallic reagents also proceeds readily to give high yields of addition products. The new indoles **10–12** (Scheme III) are thus obtained on exposure of **5** to the lithio anion of 2-isopropylidene-1,3-dithiane,[9] methylmagnesium bromide, and [2-(1,3-dioxolan-2-yl)propyl]magnesium bromide, respectively. The latter organomagnesium reagent is easily prepared from the corresponding bromide generated on passing hydrogen bromide through a solution of methacrolein and ethylene glycol.

Although the aldehyde carbonyl group must experience strong resonance deactivation by the indolic nitrogen anion in these reactions, this feature precludes addition only in the case of the more weakly nucleophilic vinylmagnesium bromide. Prior protection of the indole nitrogen by acetylation is required to achieve a good yield of the carbinol in this case.

In summary, the *N,N*-dimethylformamide dimethyl acetal chemistry serves as a convenient link between 2-methyl-3-nitrobenzoic acid and a diverse number of 4-substituted indoles. The use of these products in the total synthesis of the ergot alkaloids will be reported in separate accounts.[10]

Experimental Section

Proton magnetic resonance spectra were obtained with a Varian Associates T-60A spectrometer and are calibrated in parts per million (δ) downfield from tetramethylsilane as an internal standard. Infrared spectra were recorded on a Perkin-Elmer 247 grating spectrophotometer. Low-resolution mass spectra were recorded on an LKB 9000 gas chromatograph/mass spectrometer and high-resolution mass spectra on a Varian MAT CH-5 double-focusing instrument.

The ether and tetrahydrofuran used in these experiments were dried by distillation from sodium benzophenone ketyl.

Methyl 2-Methyl-3-nitrobenzoate. A solution of 2-methyl-3-nitrobenzoic acid (54 g, 0.3 mol), methyl iodide (75 mL, 1.2 mol), and sodium bicarbonate (100 g, 1.2 mol) in 800 mL of freshly distilled *N,N*-dimethylformamide was heated at 60 °C under an argon atmosphere for 24 h with stirring. The reaction mixture was cooled and filtered and the filtrate concentrated. The residue was taken up in 300 mL of ethyl acetate, and the solution was washed sequentially with 100 mL of 5% sodium bicarbonate, 5% HCl, and saturated sodium chloride. After the solution was dried ($MgSO_4$) and concentrated, the crude product was recrystallized from ethanol to afford 50 g (86%) of the methyl ester: mp 66 °C; IR ($CHCl_3$) 3050, 3000, 1720, 1530, 1440 cm^{-1}; NMR ($CDCl_3$) δ 7.83–8.03 (m, 2 H), 7.33 (t, 1 H, J = 8 Hz), 3.93 (s, 3 H), 2.60 (s, 3 H); mass spectrum (15 eV), m/e 195 (M^+), 178, 164, 140, 129, 91.

Methyl *trans*-2-[β-(Dimethylamino)vinyl]-3-nitrobenzoate (2). A solution of methyl 2-methyl-3-nitrobenzoate (9.75 g, 0.05 mol) and *N,N*-dimethylformamide dimethyl acetal (17.85 g, 0.15 mol) in 50 mL of dry *N,N*-dimethylformamide was heated at 130 °C for 6 h. The *N,N*-dimethylformamide was removed under reduced pressure, and the residue was bulb-to-bulb distilled (120–130 °C, 0.2 mm) to yield 10.7 g (86%) of **2**: IR ($CHCl_3$) 1720, 1600, 1530, 1260 cm^{-1}; NMR (CCl_4) δ 7.60 (m, 2 H), 7.02 (t, 1 H, J = 8 Hz), 6.28 (d, 1 H, J = 14 Hz), 5.58 (d, 1 H, J = 14 Hz), 3.80 (s, 3 H), 2.80 (s, 6 H); mass spectrum (70 eV), m/e 250 (M^+), 219, 186, 117.

Methyl Indole-4-carboxylate (3). A mixture of 7.0 g (28 mmol) of methyl *trans*-2-[β-(dimethylamino)vinyl]-3-nitrobenzoate in 140 mL of dry benzene containing 1.4 g of 10% palladium on carbon was shaken in a Parr apparatus under a hydrogen atmosphere of 50 psi for 1.5 h. The catalyst was removed by filtration, and the benzene solution was washed with 30 mL of 5% HCl and saturated sodium chloride, dried over magnesium sulfate, and concentrated by rotary evaporation. Chromatography of the residue on silica gel with 25% ethyl acetate–hexane afforded 6.9 g (82%) of **3**: mp 63 °C (lit.[3b] mp 64–65 °C); IR ($CHCl_3$) 3500, 3400, 3050, 3000, 1710, 1440, 1330, 1290, 1200, 1150, 920 cm^{-1}; NMR ($CDCl_3$) δ 8.80 (br s, 1 H), 7.97 (dd, 1 H, J = 1,7 Hz), 7.20–7.70 (m, 4 H) 3.97 (s, 3 H); mass spectrum (15 eV), m/e 175 (M^+), 144, 116.

Indole-4-methanol (4). To a stirred solution of 16.5 g (93 mmol) of methyl indole-4-carboxylate in 300 mL of dry ether cooled to −70 °C was added dropwise 250 mL of a 1 M solution of diisobutylaluminum hydride in toluene. After 4 h, 20 mL of water was added, and the reaction mixture was slowly warmed to room temperature. Saturated sodium chloride (100 mL) was added, and the resulting mixture was extracted with ethyl acetate (4 × 100 mL). The combined organic portions were washed with saturated sodium chloride, dried ($MgSO_4$), and concentrated by rotary evaporation. The crude product was purified by silica gel chromatography with 25% ethyl acetate–hexane as eluent to yield 13.34 g (97%) of **4**: mp 54 °C (lit.[3d] mp 56–57 °C); IR ($CHCl_3$) 3600, 3450 cm^{-1}; NMR ($CDCl_3$) δ 8.40 (br s, 1 H), 7.00–7.40 (m, 4 H), 6.63 (m, 1 H), 4.93 (br s, 2 H), 1.93 (br s, 1 H), mass spectrum (15 eV), m/e 147 (M^+), 129, 117, 91.

Indole-4-carboxaldehyde (5). A mixture of 13.34 g of indole-4-methanol (91 mmol) and 50 g of active manganese dioxide in 500 mL of methylene chloride was stirred at room temperature for 2 days. The reaction mixture was then filtered, the filter cake was washed with chloroform, and the filtrate was concentrated by rotary evaporation to yield 11.90 g (90.4%) of **5**: mp 138 °C (lit.[5] mp 142–144 °C); IR ($CHCl_3$) 3500, 3350, 2750, 1680 cm^{-1}; NMR ($CDCl_3$) δ 10.60 (s, 1 H), 8.80 (br s, 1 H), 7.58–7.76 (m, 2 H), 7.43–7.53 (m, 3 H); mass spectrum (15 eV) m/e 145 (M^+), 116, 89.

4-Vinylindole (6). To a suspension of methyltriphenylphosphonium bromide (5.7 g, 16 mmol) in 60 mL of dry tetrahydrofuran was added 10 mL of a 1.6 M solution of *n*-BuLi in hexane. After 30 min at room temperature, a solution of indole-4-carboxaldehyde (1.16 g, 8 mmol) in 10 mL of tetrahydrofuran was added dropwise at a rate such that the reaction temperature remained below 30 °C. After 1 h, 40 mL of water was added, and the reaction mixture was extracted with ethyl acetate (3 × 50 mL). The ethyl acetate extracts were dried ($MgSO_4$) and concentrated to give a brown liquid. The crude product was chromatographed on neutral silica gel with 25% ethyl acetate–hexane as eluent to give 1.078 g (94%) of **6**: IR ($CHCl_3$) 3500, 3050, 1710, 1605, 1520, 1400, 1350, 1200, 1060, 1000, 940, 920, 800 cm^{-1}; NMR ($CDCl_3$) δ 8.00 (br s, 1 H), 7.06–7.30 (m, 4 H), 7.10 (dd, 1 H, J = 11, 18 Hz), 6.73 (m, 1 H), 5.68 (dd, 1 H, J = 2, 18 Hz), 5.37 (dd, 1 H, J = 2, 11 Hz); mass spectrum, m/e calcd 143.0735, obsd 143.0739.

(8) We have observed this phenomenon in one additional case in which benzaldehyde was reacted with the phosphorane prepared from (3-hydroxy-2-methylbutyl)triphenylphosphonium iodide (*E/Z* ratio of 85:15): Kozikowski, A. P.; Schmiesing, R. M., unpublished results.

(9) The site selectivity which the anions of ketene thioacetals display in their reactions with carbonyl compounds has been the subject of a thorough study: Kozikowski, A. P.; Chen, Y. Y. *J. Org. Chem.*, **1980**, *45*, 2236.

(10) Kozikowski, A. P.; Ishida, H. *J. Am. Chem. Soc.* **1980**, *102*, 4265.

(Z)-4-(2-Methoxyvinyl)indole (7). To a stirred suspension of (methoxymethyl)triphenylphosphonium chloride (1.38 g, 4 mmol) in 5 mL of dry tetrahydrofuran was added 2.5 mL of a 1.6 M solution of *n*-BuLi in hexane. After 30 min at room temperature, a solution of indole-4-carboxaldehyde (0.29 mg, 2 mmol) in 4 mL of dry tetrahydrofuran was added dropwise at a rate such that the reaction temperature remained below 30 °C. After 1 h, 10 mL of water was added, and the reaction mixture was extracted with ether (4 × 10 mL). The ether extracts were dried ($MgSO_4$) and concentrated to afford a brown liquid. The crude product was chromatographed on neutral alumina with methylene chloride as eluent to yield 235 mg (73%) of **7**: mp 90–93 °C; IR ($CHCl_3$) 3500, 3025, 2950, 2900, 1640, 1410, 1350, 1275, 1200, 1160, 1100, 1080, 940 cm^{-1}; NMR ($CDCl_3$) δ 7.80–8.20 (br s, 1 H), 7.67 (t, 1 H, J = 4 Hz), 7.00–7.17 (m, 3 H), 6.43–6.70 (m, 1 H), 6.23 (d, 1 H, J = 7 Hz), 5.60 (d, 1 H, J = 7 Hz), 3.70 (s, 3 H); mass spectrum, m/e calcd 173.0841, obsd 173.0838.

Ethyl (E)-3-(4-Indolyl)propenoate (8). A solution of indole-4-carboxaldehyde (37 mg, 0.25 mmol) and [(carboethoxy)-methylene]triphenylphosphorane (175 mg, 0.50 mmol) in 2.5 mL of dry tetrahydrofuran was stirred at 50 °C for 24 h. The reaction mixture was concentrated, and the crude product was chromatographed on silica gel with 20% ethyl acetate–hexane as eluent to give 48 mg (89%) of **8**: mp 72–73.5 °C; IR ($CHCl_3$) 3450, 3000, 1690, 1625, 1280, 1230, 1195, 1182 cm^{-1}; NMR ($CDCl_3$) δ 8.02–8.34 (br s, 1 H), 7.94 (d, 1 H, J = 16 Hz), 6.98–7.34 (m, 4 H), 6.58–6.70 (m, 1 H), 6.46 (d, 1 H, J = 16 Hz), 4.18 (q, 2 H, J = 7 Hz), 1.32 (t, 3 H, J = 7 Hz); mass spectrum, m/e calcd 215.0946, obsd 215.0946.

(E)-4-(4-Hydroxy-3-methyl-1-butenyl)indole (9). To a suspension of (2-methyl-3-hydroxypropyl)triphenylphosphonium bromide (9 g, 20 mmol) in 100 mL of dry tetrahydrofuran cooled to −78 °C was added dropwise 26 mL of a 1.6 M solution of *n*-BuLi in hexane. The reaction mixture was brought to room temperature, and after 2 h, a solution of indole-4-carboxaldehyde (2.18 g, 15 mmol) in 15 mL of tetrahydrofuran was added to the red homogeneous solution of the phosphorane. After 20 h, the reaction mixture was poured into 100 mL of ethyl acetate and the mixture washed once with 200 mL of a saturated ammonium chloride solution and twice with 200 mL of a saturated sodium chloride solution. The organic layer was dried over sodium sulfate, filtered, and concentrated by rotary evaporation. The isolated crude product was chromatographed on silica gel with 25% ethyl acetate–hexane to yield 1.78 g (59%) of Wittig product **9**: IR ($CHCl_3$) 3550, 3450, 3000, 2975, 2900, 1710, 1405, 1350, 1210, 1050, 990 cm^{-1}; NMR ($CDCl_3$) δ 8.30 (br s, 1 H), 6.50–7.40 (m, 6 H), 6.17 (dd, 1 H, J = 16, 7 Hz), 3.57 (d, 2 H, J = 6 Hz), 2.60 (m, 1 H), 1.73 (br s, 1 H), 1.15 (d, 3 H, J = 6 Hz); mass spectrum, m/e calcd 201.1154, obsd 201.1154.

4-[1-Hydroxy-3-(1,3-dioxolan-2-yl)butyl]indole (12). To a flask containing 0.53 g (21.8 mmol) of magnesium foil (freshly washed with absolute ether and oven dried) covered with 15 mL of dry tetrahydrofuran was added 2.13 g (10.9 mmol) of 2-(2-bromo-1-methylethyl)-1,3-dioxolane. After being stirred 2 h at room temperature, the reaction mixture was cooled in an ice bath, and a solution of indole-4-carboxaldehyde (0.264 g, 1.82 mmol) in 2 mL of dry tetrahydrofuran was added by syringe. After 30 min, 20 mL of ether and 20 mL of saturated ammonium chloride were added. The organic layer was separated, dried ($MgSO_4$), filtered, and concentrated by rotary evaporation. The residue was chromatographed on silica gel with 40% ethyl acetate–hexane to yield 0.475 g (100%) of **12**: IR ($CHCl_3$) 3600, 3475, 2990, 2975, 2880, 1405, 1340, 1155, 1100, 1070, 940 cm^{-1}; NMR ($CDCl_3$) δ 8.56 (br s, 1 H), 7.18 (m, 4 H), 6.66 (m, 1 H), 5.30 (m, 1 H), 4.78 (d, 1 H, J = 5 Hz), 3.93 (m, 4 H), 1.00 (d, 3 H, J = 7 Hz); mass spectrum, m/e calcd 261.1365, obsd 261.1367.

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Registry No. 1, 1975-50-4; 2, 73816-11-2; 3, 39830-66-5; 4, 1074-85-7; 5, 1074-86-8; 6, 68900-05-0; 7, 73805-09-1; 8, 73805-10-4; 9, 73805-11-5; 10, 73805-12-6; 11, 73805-13-7; 12, 73805-14-8; methyl 2-methyl-3-nitrobenzoate, 59382-59-1; *N,N*-dimethylformamide dimethyl acetal, 4637-24-5; methyltriphenylphosphonium bromide, 1779-49-3; (methoxymethyl)triphenylphosphonium chloride, 4009-98-7; [(carboethoxy)methylene]triphenylphosphorane, 1099-45-2; (2-methyl-3-hydroxypropyl)triphenylphosphonium bromide, 73805-15-9; 2-(2-bromo-1-methylethyl)-1,3-dioxolane, 33498-32-7; CH_3Br, 74-83-9; 2-isopropylidene-1,3-dithiane, 36998-38-6.

Product Stereospecificity in the Microbial Reduction of α-Haloaryl Ketones

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The importance of arene oxides as intermediates in the metabolism of aromatic compounds stimulated several studies on the absolute configurations of these compounds and of products from their enzymatic hydration.[1] The procedure used for determining the absolute stereochemistry of the diols formed on enzymatic hydration of the corresponding arene oxides of di- and tricyclic aromatic compound involved reducing the oxirane or diol to a hydroaromatic alcohol.[1b] The latter was then synthesized, resolved, and oxidized (after protecting the hydroxyl group) to a derivative hydroxy dicarboxylic acid of known configuration. In those instances, however, where the hydroaromatic alcohol is achiral, e.g., 2-indanol obtained from hydrogenolysis of *cis*- and *trans*-1,2-indandiol (metabolites of indene and 2-indanone), an alternative method of ascertaining the configuration is required. In the cases of *cis*- and *trans*-1,2-indandiol, microbial reduction of 2-bromoindan-1-one (**1a**) produced optically active *trans*-2-bromoindan-1-ol (**2a**) which was then stereospecifically converted to the two diols and indene oxide.[2] In addition to establishing the configurations of these metabolites, the presence of an α-bromo atom significantly increased the scope and potential value of microbially mediated ketone reductions. In continuing our studies of these carbonyl reductions, we have therefore examined the effect of an α-chloro atom as well as some stereochemical questions raised in the earlier study.[2,3] The compounds employed as substrates and the results are summarized in Table I.

These findings demonstrate that microbial reduction of α-haloaryl ketones generally yield halohydrins with enantiomeric excesses of 80% or more in good yield which serve as convenient intermediates for the preparation of optically active oxiranes. In addition, the intermediate halohydrin is frequently more useful than the oxirane in establishing the absolute stereochemistry at the benzylic carbon (see Figure 1). The presence of a heteroatom in the aromatic system does not appear to influence the

(1) (a) Donald M. Jerina and John W. Daly, *Science (Washington, DC)*, **185**, 573 (1974); (b) Masato Koreeda, M. Naseem Akhtar, Derek R. Boyd, John D. Neill, David T. Gibson, and Donald M. Jerina, *J. Org. Chem.*, **43**, 1023 (1978); (c) Haruhiko Yagi, H. Akagi, Dhiren R. Thakker, H. D. Mah, Masato Koreeda, and Donald M. Jerina, *J. Am. Chem. Soc.*, **99**, 2358 (1977); (d) Koji Nakanishi, H. Kasai, H. Cho, R. G. Harvey, A. M. Jeffrey, K. W. Jannette, and I. B. Weinstein, *ibid.*, **99**, 258 (1977).

(2) Mitsuru Imuta and Herman Ziffer, *J. Org. Chem.*, **43**, 4540 (1978).

(3) Ridley et al. have described the microbial reduction of some α-chloro ketones: Robyn L. Crumbie, Damon D. Ridley, and Gregory W. Simpson, *J. Chem. Soc., Chem. Commun.*, 315 (1977).