7.55 (m, H_6 and $H_{6'}$), 2.91 (d of d, 2 H), 2.25 (t, 2 H), 2.16 (t, 2 H), 1.57 (quintet, 2 H); IR (KBr) 2940, 1565, 1500, 1455, 1330, 1220, 1140, 1090, 1050, 1020, 970, 940, 880, 840, 780, 750 cm^{-1}.

8,9,10,11,12,13,14,15-Octahydrocyclododeca[*b*]quinolin-6-(7*H*)-one (5). The same procedure described above for **2a** was followed, using 0.5 g (4.1 mmol) of 2-aminobenzaldehyde and 0.4 g (2.0 mmol) of 1,2-cyclododecanedione,[22] to give a crude product which was collected as an oil after chromatography. Kugelrohr distillation afforded 0.2 g (35%) of **5**: bp 210 °C (0.2 mm), mp 56-59 °C; ^1H NMR (80 MHz, $CDCl_3$) 7.7 (m, 5 H), 3.0 (m, 4 H), 1.7 (br m, 14 H); ^{13}C NMR (20 MHz, $CDCl_3$) 162.6, 146.5, 135.7, 128.5, 128.3, 126.7, 125.4, 32.7, 29.7, 28.4, 26.7, 26.4, 26.0, 25.4, 23.13, and 23.07 ppm; IR (KBr) 1670 cm^{-1}; 2,4-DNP mp 188 °C.

(22) Bauer, D. P.; Macomber, R. S. *J. Org. Chem.* **1975**, *40*, 1990.

Acknowledgment. Financial support from the Robert A. Welch Foundation and the donors of the Petroleum Research Fund, administered by the American Chemical Society, is gratefully acknowledged. We thank Helga Cohen for obtaining the 400-MHz NMR spectra at the South Carolina Magnetic Resonance Laboratory supported by NSF Grant CHE 82-07445 and Professor Tom Albright for enlightening comments on the singlet oxygen reaction.

Registry No. 1, 119-91-5; **2a**, 318-55-8; **2b**, 5967-35-1; **2c**, 94537-45-8; **2d**, 94537-46-9; **3**, 529-23-7; **4**, 23427-68-1; **5**, 94570-47-5; **7**, 94537-47-0; **8a**, 6907-48-8; **8b**, 94537-48-1; **8c**, 94537-49-2; **9a**, 6495-83-6; **9b**, 94537-50-5; **9c**, 94537-51-6; 1,2-cyclopentanedione, 3008-40-0; 1,2-cyclohexanedione, 765-87-7; 1,2-cycloheptanedione, 3008-39-7; 1,2-cyclooctanedione, 3008-37-5; 3,4-hexanedione, 4437-51-8.

Asymmetric Synthesis. 2.[1] Practical Method for the Asymmetric Synthesis of Indolizidine Alkaloids: Total Synthesis of (-)-Monomorine I

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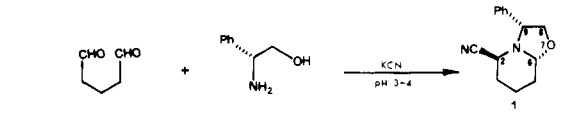
The alkylation of the chiral 2-cyano-6-oxazolopiperidine synthon (1) with the iodo ketal **2** gave, after selective cleavage of the cyano group, the oxazolopiperidine **4** having the 2*S* configuration. Compound **4** was alkylated with CH_3MgI, giving a 4:1 mixture of alcohols **6** and **7** in which the major product **6** possessed the desired 2,6-cis configuration. Treatment of **6** under acidic hydrogenation conditions (H_2, Pd/C, H^+) led to the desired (-)-monomorine I (**9**) having the 3*S*,5*R*,9*R* absolute configuration. This first asymmetric synthesis of (-)-monomorine I (**9**) establishes the absolute configuration of the natural (+)-monomorine I as 3*R*,5*S*,9*S*.

Since the isolation of monomorine I from *Monomorium pharaonis L.* by Ritter and co-workers[2] two total syntheses of the racemic form of this pharaoh ant trail pheromone[3] leading to the determination of its relative stereochemistry have been published.[4,5] More recently, a stereospecific synthesis of the racemic alkaloid **9** was reported.[6] However, no work concerning the asymmetric synthesis or the determination of the absolute configuration of monomorine I (**9**) and the related poison-dart frog gephyrotoxin 223 AB (**10b**) has appeared.[7]

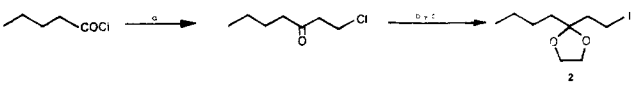
Herein we describe an enantiospecific total synthesis of (-)-monomorine I (**9**) which permitted us to assign the absolute configuration 3*R*,5*S*,9*S* to the natural (+) enantiomer.

In a recent paper[1] we reported a "one-pot" procedure for the preparation of the chiral 2-cyano-6-oxazolopiperidine synthon (**1**) from (-)-phenylglycinol, glutaraldehyde, and KCN (Scheme I). As chemo- and stereoselective reaction can be achieved at either the C-2 (α-amino nitrile) or C-6 (α-amino ether) centers of this molecule, and as hydrogenolysis produces a secondary nitrogen center capable of undergoing an intramolecular ring closure, the synthon **1** represents an ideal starting material for the chiral synthesis of the indolizidine system of **9**.

Scheme I



Scheme II



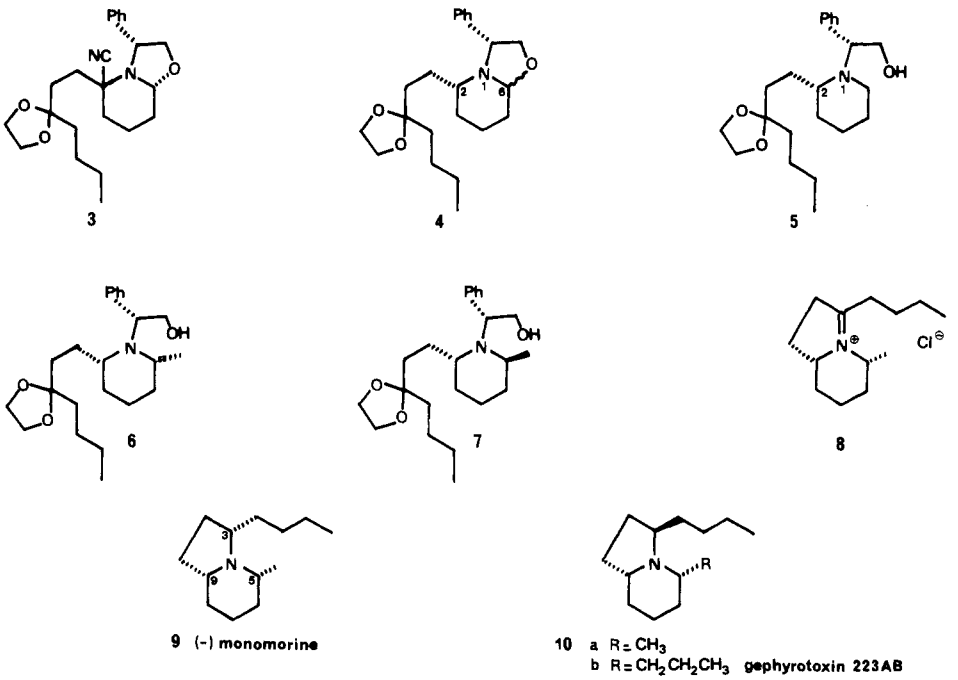
[a] Reagents: (a) $CH_2{=}CH_2$, $AlCl_3$, $CHCl_3$, 0 °C, 2 h (88% yield); (b) CH_2OHCH_2OH, PPTS, benzene, reflux, 1 h (83% yield); (c) KI, 18-crown-6, toluene, reflux, 15 h (74% yield).

Alkylation of the anion of **1** (LDA, THF, -78 °C) with iodo ketal **2** (prepared as outlined in Scheme II) led to the formation of a single product **3** isolated in 65% yield after flash chromatography on silica gel (Chart I). The amino nitrile moiety of **3** was then selectively reduced by prior complexation of the cyano group with silver ion ($AgBF_4$, THF, room temperature, 5 min) followed by reaction with $Zn(BH_4)_2$ at -50 °C (1 h). Compound **4** was obtained in 84% yield as a 3:2 mixture of C-6 epimeric oxazolidines having the 2*S* configuration.[1] A likely reversible opening of the oxazolidine ring during both the reaction workup

(1) For Part 1 see: Guerrier, L.; Royer, J.; Grierson, D. S.; Husson, H.-P. *J. Am. Chem. Soc.* **1983**, *105*, 7754.
(2) Ritter, F. J.; Rotgans, I. E. M.; Talman, E.; Verwiel, P. E. J.; Stein, F. *Experientia* **1973**, *29*, 530.
(3) Monomorine I exhibits trail pheromone activity but is not the only active compound, see: Ritter, F. J.; Bruggemann-Rotgans, I. E. M.; Verweil, P. E. J.; Persoons, C. J.; Talman, E. *Tetrahedron Lett.* **1977**, 2617.
(4) (a) Oliver, J. E.; Sonnet, P. E. *J. Org. Chem.* **1974**, *39*, 2662. (b) Sonnet, P. E.; Oliver, J. E. *J. Heterocycl. Chem.* **1975**, *12*, 289. (c) Sonnet, P. E.; Netzel, D. A.; Mendoza, R. *Ibid.* **1979**, *16*, 1041.
(5) Macdonald, T. L. *J. Org. Chem.* **1980**, *45*, 193.
(6) Stevens, R. V.; Lee, A. W. M. *J. Chem. Soc., Chem. Commun.* **1982**, 102.
(7) For recent stereoselective synthesis of (±)-gephyrotoxin 223AB, see: Stevens, R. V.; Lee, A. W. M. *J. Chem. Soc. Chem. Commun.* **1982**, 103. Hart, D. J.; Tsai, Y.-M. *J. Org. Chem.* **1982**, *47*, 4403.

0022-3263/85/1950-0670$01.50/0

Chart I



and subsequent chromatographic purification accounts for the observed epimerization at C-6.

A single alcohol **5** was obtained on further reduction of **4**, demonstrating that the above reaction at C-2 was stereospecific. This stereospecificity was interpreted in terms of an elimination–addition mechanism wherein hydride ion approaches a preferred iminium conformer[1] under complete stereoelectronic control[8] from the axial direction. The reaction of **4** with CH_3MgI (−70 °C, ether, 3 h) afforded a 4:1 mixture of the desired cis alcohol **6** and its trans isomer **7**. An analogous mechanism involving a C-2 pseudoaxial substituted iminium ion was invoked to rationalize the stereoselectivity of this reaction.[9] After separation of the two isomers by column chromatography (SiO_2; CH_2Cl_2:MeOH, 96:4) alcohol **6** (55% from **4**) was treated under catalytic hydrogenation conditions (H_2, 10% Pd/C, MeOH containing 1% 1 M HCl, 1 atm). Under these conditions the hydrogenolysis of the chiral auxiliary and liberation of the ketone function were followed by formation of the iminium intermediate **8** which was slowly reduced to the desired indolizidine system. (−)-Monomorine I (**9**) $[\alpha]^{20}_D$ −35.8° (*n*-hexane, *c* 1.35),[10] having the expected "all-cis" stereochemistry was obtained pure in 70% yield after separation from the isomeric product **10a** [10% yield, **10a·HCl** $[\alpha]^{20}_D$ −69.2° (MeOH, *c* 0.55)] by column chromatography on alumina.

Synthetic (−)-monomorine I (**9**) exhibited spectral data (^1H and ^{13}C NMR and mass spectra) identical with the published data for the racemic material[4c] and was indistinguishable with an authentic sample by GLC analysis. As the absolute configuration at the C-5 and C-9 centers of **9** were known on the basis of previous results,[1] we concluded that the absolute configuration of (−)-monomorine I (**9**) is 3*S*,5*R*,9*R*. The natural monomorine I being dextrorotatory therefore has the 3*R*,5*S*,9*S* absolute configuration.

In a further experiment the iminium ion **8** was isolated and reduced with $NaBH_3CN$ (MeOH, pH 6) to a 3:2 mixture of indolizidines **9** and **10a**. The latter product **10a** possesses the same relative configuration as the structurally related alkaloid gephyrotoxin 223AB (**10b**). These latter results illustrate the potential flexibility of our approach to the syntheses of the indolizidine alkaloids from the common chiral synthon **1**.

Experimental Section

Infrared spectra (IR) were recorded neat or in chloroform solution on a Perkin-Elmer 297 spectrophotometer. Peaks yielding structural information are reported. ^1H NMR spectra were recorded in $CDCl_3$ (tetramethylsilane as an internal standard, δ = 0) on a Brucker WP 80 (80 MHz) and/or the I.E.F.[11] 400 MHz spectrometer. ^{13}C NMR spectra were recorded in $CDCl_3$ (Me_4Si, δ = 0) on a Brucker WP 200 (50 MHz) instrument. Mass spectrometry was performed on an AEI MS 50 spectrometer by the Mass Spectrometry Service of the ICSN at Gif. Flash chromatography refers to the medium pressure technique described by W. C. Still.[12]

Preparation of 2-Cyano-6-oxazolopiperidine (1). A solution of 25% aqueous glutaraldehyde (28 mL, 76 mmol) was added over a period of 20 min to a cooled (0 °C) solution of (−)-phenylglycinol (5.48 g, 40 mmol) and citric acid (20 g) in water (900 mL), and the resulting mixture was stirred for 1 h at 0 °C. An aqueous solution of potassium cyanide (3.64 g, 56 mmol, 40 mL) was then added and vigorous stirring was continued for 65 h at room temperature. During this reaction a viscous green oil was observed to precipitate from the medium. The reaction mixture was then neutralized with $NaHCO_3$ and extracted with CH_2Cl_2. The CH_2Cl_2 fractions were combined, dried over anhydrous sodium sulfate and concentrated in vacuo to give a green oil. The crude reaction product was separated by flash chromatography on silica (hexane–ether, 8:2). 2-Cyano-6-oxazolopiperidine (**1**) was obtained as white crystals (4.65 g, 51%): mp 81 °C (hexane); $[\alpha]^{20}_D$ −278° ($CHCl_3$, *c* 1); IR 2100 cm^{-1} (CN); ^1H NMR ($CDCl_3$, 400 MHz) δ 1.5–2.2 (m, 6 H, piperidine ring CH_2), 3.75 (t, J = 8 Hz, 1 H, H-8 or H-9), 3.87 (br d, J = 2.5 Hz, 1 H, H-2), 3.92 (t, J = 8 Hz, 1 H,

(8) Overman, L. E.; Freerks, R. L. *J. Org. Chem.* **1981**, *46*, 2833.
(9) Bonin, M.; Romero, J. R.; Grierson, D. S.; Husson, H.-P. *J. Org. Chem.* **1984**, *49*, 2392.
(10) $[\alpha]_D$ value was found opposite to that of natural product determined with a very low quantity of material and kindly communicated by Dr. Bruggeman as $[\alpha]^{23}_D$ 46.5° (*n*-hexane, *c* 0.032). Despite the slight difference of the absolute value we found an excellent correlation with the ORD curve. It must be noticed that the synthetic monomorine I salt (**9**, HCl) was found to be dextrorotatory $[\alpha]^{20}_D$ 32.0° (MeOH, *c* 0.5).
(11) Institut d'Électronique Fondamentale, Université Paris-Sud, 91405-Orsay, France. We thank Dr. S. K. Kan for the use of his 400-MHz ^1H NMR spectrophotometer.
(12) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

H-8 or H-9), 4.16 (dd, J = 9.5 Hz, J' = 2.5 Hz, 1 H, H-6), 4.28 (t, J = 8 Hz, 1 H, H-8 or H-9), 7.4 (m, 5 H, Ar); ^{13}C NMR ($CDCl_3$, 15 MHz) δ 19.3, 28.0, 30.0 (piperidine ring CH_2), 47.4 (C-2), 63.9 (C-9), 73.0 (C-8), 89.9 (C-6), 116 (CN), 128.2, 128.6, 129.0 (Ar); MS m/e (relative intensity) 228 (M^+, 10), 201 (10), 170 (15), 117 (8), 104 (100), 91 (15). Anal. Calcd for $C_{14}H_{16}N_2O$: C, 73.64; H, 7.07; N, 12.28. Found: C, 73.39; H, 7.20; N, 12.20.

1-Iodo-3,3-(ethylenedioxy)heptane (2). 1-Chloro-2-heptanone was prepared according to the procedure described by E. Brown.[13] Valeryl chloride (2.4 g, 20 mmol) was added slowly to a cooled (0 °C) suspension of aluminium chloride (3 g, 2.2 mmol) in methylene chloride (100 mL). Ethylene gas was bubbled through the resulting solution for 2 h. The reaction mixture was then poured into a vigorously stirred mixture of concentrated HCl (5 mL) in ice–water (25 mL). The aqueous layer was separated and extracted with CH_2Cl_2. The organic layer and CH_2Cl_2 extracts were washed with water and saturated $NaHCO_3$, then dried (Na_2SO_4), and concentrated in vacuo to yield 2.61 g (88%) of an essentially pure oil which was carried through directly to next step: IR (neat) 1700 cm^{-1}; ^{1}H NMR (80 MHz, $CDCl_3$) δ 3.72 (t, J = 7 Hz, 2 H, H-1), 2.88 (t, J = 7 Hz, 2 H, H-2), 2.45 (t, J = 7 Hz, 2 H, H-4), 1.5 (m, 4 H, H-5, H-6), 0.91 (t, J = 6 Hz, 3 H, H-7); MS, m/e (relative intensity) 148 (M^+, 18), 113 (15), 108 (18), 106 (54), 91 (20), 85 (100), 57 (80). A solution of this chloro ketone (2.37 g, 15.9 mmol), ethylene glycol (2 mL, 35 mmol), and pyridinium p-toluenesulfonate (0.5 g, 2 mmol) in benzene (50 mL) was stirred at reflux under nitrogen for 2 h in an apparatus equipped with a Dean–Stark trap. The reaction mixture was cooled to room temperature, washed with saturated $NaHCO_3$, dried, and concentrated in vacuo to yield 2.91 g (95%) of the ketal as an oil which was bulb-to-bulb distilled (oven temperature 130–140 °C, 0.1 mm) to give 2.53 g (83%) of colorless oil: IR absence of CO stretching; ^{1}H NMR ($CDCl_3$, 80 MHz) δ 0.9–1.8 (m, 9 H, CH_3 and CH_2), 2.1 (t, J = 8 Hz, 2 H, CH_2CH_2Cl), 3.52 (t, J = 8 Hz, 2 H, CH_2Cl), 3.9 (s, 4 H, ethylenedioxy CH_2). A mixture of the chloro ketal (2.3 g, 12 mmol), potassium iodide (2.5 g, 15 mmol), and 18-crown-6 (150 mg) in dry toluene (30 mL) was heated at reflux for 15 h. The cooled reaction mixture was filtered and evaporated to dryness. The colored residue was then purified by chromatography on a short column of alumina (hexane–CH_2Cl_2, 1:1) to yield the iodo ketal **2** as a colorless oil (2.52 g, 74%): ^{1}H NMR (80 MHz, $CDCl_3$) δ 0.95 (t, J = 7 Hz, 3 H, CH_3), 1.2–1.7 (m, 6 H, CH_2), 2.3 (t, J = 8.5 Hz, 2 H, CH_2CH_2I), 3.2 (t, J = 8.5 Hz, CH_2I), 3.96 (s, 4 H, ethylenedioxy CH_2); MS, m/e (relative intensity) 227 (M^+ – 57, 90), 155 (11), 129 (100), 100 (10).

Preparation of Amino Nitrile 3. Chiral synthon **1** (1.14 g, 5 mmol) was dissolved in dry THF (25 mL) and slowly added under argon atmosphere to a cooled (–70 °C) solution of LDA [from 1.6 mL (10.8 mmol) of diisopropylamine and 7 mL (10.8 mmol) of 1.6 M butyllithium in hexane] in THF (25 mL). The resulting pale yellow solution was stirred at –70 °C for 10 min. Ketal **2** (2 g, 7 mmol) was then added and stirring was continued for 2 h at –70 °C and for 1 h at –50 °C. The reaction was quenched by addition of a phosphate buffer (pH 6.2, 0.5 M, 10 mL). The reaction mixture was then diluted with phosphate buffer (50 mL) and extracted several times with methylene chloride. The combined methylene chloride fractions were dried (Na_2SO_4) and concentrated to give a pale yellow oil. Purification by flash chromatography on silica (hexane–ether 8:2) gave pure **3** as a colorless oil which crystallized upon standing (1.25 g, 65%): mp 48 °C; $[\alpha]^{20}_D$ –101.5° ($CHCl_3$, c 1.21); IR 2150 cm^{-1} (CN); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.83 (t, J = 7 Hz, 3 H, CH_3), 1–2 (m, 16 H, piperidine ring and side chain CH_2), 3.24 and 3.33 (2 m, 2 H, OCH_2CH_2O), 3.66 (m, 2 H, OCH_2CH_2O), 3.75 (dd, J = 4.5 Hz, J' = 8.5 Hz, 1 H, H-8 or H-9), 4.05 (dd, J = 4.5 Hz, J' = 8.5 Hz, 1 H, H-8 or H-9), 4.16 (dd, J = 2.5 Hz, J' = 9.5 Hz, 1 H, H-6), 4.23 (t, J = 8.5 Hz, 1 H, H-8 or H-9), 7.3 (m, 5 H, H Ar); MS, m/e (relative intensity) 384 (M^+, 0.5), 326 (17), 228 (13), 227 (38), 129 (66), 104 (100). Anal. Calcd for $C_{23}H_{32}N_2O_3$: C, 71.83; H, 8.39; N, 7.29; O, 12.49. Found: C, 71.58; H, 8.29; N, 7.40; O, 12.21.

Preparation of 4. Amino nitrile **3** (488 mg, 1.27 mmol) was dissolved in anhydrous THF (45 mL) and stirred under argon at room temperature. Silver tetrafluoroborate (492 mg, 2.5 mmol) in THF (2 mL) was added via syringe to the solution of **3**, producing a white precipitate which was stirred for 5–10 min. The mixture was then cooled to –50 °C followed by slow addition of a 0.1 M ether solution of $Zn(BH_4)_2$[14] (10 mL, 1 mmol). The resulting reaction mixture was stirred at –50 °C for 2 h, after which time water (2–3 mL) was added via syringe and the temperature was allowed to rise to room temperature. More water (25 mL) was then added and the black mixture was filtered through a Celite bed. The clear solution was extracted with methylene chloride. The methylene chloride extracts were washed with water, dried (Na_2SO_4), and concentrated in vacuo to give an oily product which was purified by flash chromatography on silica (hexane–ether, 6:4) to yield **4** as colorless oil (384 mg, 84%). **4** was an epimeric mixture (not observable on TLC analysis) as determined by spectral analysis: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.85 (t, J = 7 Hz, 0.6 × 3 H, CH_3), 0.87 (t, J = 7 Hz, 0.4 × 3 H, CH_3), 1–2.05 (m, 16 H, CH_2), 2.25 (tt, J = 10 Hz, J' = 3 Hz, 0.6 × 1 H, H-2), 2.53 (m, 0.4 × 1 H, H-2), 3.15 and 3.4 (2 m, 2 H, OCH_2CH_2O), 3.6–3.9 (m, 4.2 H, OCH_2CH_2O, major product H-6, H-8 and H-9, minor product H-8 or H-9), 4.16 (t, J = 8 Hz, 0.6 × 1 H, H-8 or H-9), 4.32 (t, J = 7.5 Hz, 0.4 × 1 H, H-8 or H-9), 4.42 (dd, J = 7.5 Hz, J' = 4 Hz, 0.4 × 1 H, H-8 or H-9), 4.55 (t, J = 3 Hz, 0.4 × 1 H, H-6); MS, m/e (relative intensity) 359 (M^+, 2), 358 (3), 302 (16), 203 (14), 202 (100), 129 (20); exact mass 359.2448 (calcd for $C_{22}H_{33}NO_3$, 359.2451).

Preparation of 5. In an experiment similar to the preceding one (preparation of **4**) an aliquot (5 mL, ≃ 0.14 mmol) was removed via syringe from the reaction mixture at –50 °C and allowed to rise to room temperature. Stirring was continued for 1 h at room temperature and the reaction was quenched by addition of water. The black mixture was filtered through a Celite bed and the clear solution was extracted with methylene chloride. The methylene chloride extracts were washed with water, dried (Na_2SO_4), and concentrated in vacuo to give an oil which was purified by filtration on silica (CH_2Cl_2–MeOH, 9:1). Alcohol **5** (41 mg, 82%) was obtained pure as a colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.85 (t, J = 7 Hz, 3 H, CH_3), 1.2–1.8 (m, 16 H, CH_2), 2.55 (m, 2 H, H-6), 2.82 (m, 1 H, H-2), 3.75 (m, 7 H, H-8, H-9 and ethylenedioxy CH_2), 7.3 (m, 5 H, Ar); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 14.1 (CH_3), 20.0, 20.8, 23.0, 25.1, 26.1, 28.2, 34.4, 37.0, 43.3 (piperidine ring and side chain CH_2), 57.8 (C-2), 62.3 (C-8), 64.9 (2 ethylenedioxy CH_2), 67.3 (C-9), 111.9 (>C(–O–)–), 127.4, 128.4, 128.7, 140.9 (Ar); MS, m/e (relative intensity) 361 (M^+, 0.5), 330 (100), 304 (10), 204 (38), 137 (20), 135 (20).

Preparation of 6 and 7. An ether solution of CH_3MgI (2 mL, 7 mmol, 3.5 M) was added slowly via syringe to a cooled (–70 °C) solution of oxazolidine **4** (359 mg, 1 mmol) in dry ether (50 mL), and the resulting mixture was stirred at –70 °C for 3 h. The reaction was stopped by addition of saturated NH_4Cl solution (10 mL) and the mixture was allowed to warm to room temperature. The layers were decanted and the aqueous layer was extracted with methylene chloride. The organic layers were joined, dried (Na_2SO_4), and evaporated to dryness. The pale yellow oil was purified by chromatography on silica (CH_2Cl_2–CH_3OH, 97:3); three pure products were obtained: unreacted oxazolidine **4** (75 mg, 21%), *cis*-dialkyl alcohol **6** (208 mg, 55%), and *trans*-dialkyl alcohol **7** (46 mg, 12%) as colorless oils.

Alcohol **7**: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.81 (t, J = 7 Hz, CH_3), 1–1.75 (m with d (J = 7 Hz) at 1.15, 17 H, piperidine ring and side chain CH_2, and CH_3), 2.97 (m, 1 H, H-2), 3.25 (m, 1 H, H-6), 3.36 (dd, J = 10.5 Hz, J' = 5 Hz, 1 H, H-8 or H-9), 3.75 (t, J = 10.5 Hz, H-8 or H-9), 3.86 (s, 4 H, ethylenedioxy CH_2), 4.1 (dd, J = 10.5 Hz, J' = 5 Hz, 1 H, H-8 or H-9), 7.25 (m, 5 H, Ar); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 14.1 (CH_3), 20.6 (CH_3), 20.3, 23.0, 26.0, 26.6, 26.8, 30.2, 34.6, 37.1 (piperidine ring and side chain CH_2), 48.7 (C-6), 52.9 (C-2), 59.4 (C-9), 60.8 (C-8), 65.0 (ethylenedioxy), 111.9 (>C(–O–)–), 127.5, 128.4, 129.3, 141.3 (Ar); MS, m/e (relative intensity) 375 (M^+ 1), 345 (20), 344 (100), 318 (10), 300 (8), 218 (15), 129 (25).

Alcohol **6**: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.92 (t, J = 7 Hz, 3 H, CH_3), 1.09 (d, J = 7 Hz, 3 H, CH_3), 1.1–1.75 (m, 14 H, piperidine and side chain CH_2), 2.85 (m, 1 H, H-2), 3.04 (m, 1 H, H-6), 3.72

(13) Brown, E.; Touet, J.; Ragault, M. *Bull. Soc. Chim. Fr.* **1972**, 212.

(14) Prepared according to Gensler, W. J.; Johnson, F. A.; Sloan, A. B. D. *J. Am. Chem. Soc.* **1960**, *82*, 6074.

(dd, J = 5 Hz, J' = 10.5 Hz, 1 H, H-8 or H-9), 3.83 (dd, J = 7.5 Hz, J' = 10.5 Hz, 1 H, H-8 or H-9), 3.93 (m, 4 H, ethylenedioxy), 4.04 (dd, J = 7.5 Hz, J' = 5 Hz, 1 H, H-8 or H-9), 7.33 (m, 5 H, Ar); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 14.1 (CH_3), 16.0 (CH_3), 20.3, 23.1, 26.1, 26.8, 28.2, 31.4, 35.4, 37.0 (piperidine ring or side chain CH_2), 50.8 (C-6), 53.7 (C-2), 62.2 (C-8), 65.0 (ethylenedioxy), 65.5 (C-9), 111.9 (>C(-O-)-), 127.6, 128.4, 128.6, 130.0 (Ar); MS, m/e (relative intensity) 375 ($M^{+\cdot}$, 1), 360 (1), 344 (100), 318 (14), 218 (68), 144 (12), 129 (17), 98 (30), 91 (6). Anal. Calcd for $C_{23}H_{37}NO_3$: C, 73.54; H, 9.94; N, 3.73. Found: C, 73.17; H, 10.05; N, 3.83.

Preparation of (-)-Monomorine I (9 and 10a). A solution of alcohol **6** (75 mg, 0.2 mmol) in methanol (10 mL) containing HCl (0.1 mL, 1 M) was hydrogenated over 10% Pd/C at atmospheric pressure for 6 days. The reaction mixture was then filtered through a Celite bed and the filtrate evaporated in vacuo to give a white solid which was washed several times with ether to eliminate phenylethanol. The product was recrystallized from CH_2Cl_2 to give 43 mg (93%) of the epimeric mixture of **9**·HCl and **10a**·HCl. The mixture of bases was separated by a short column chromatography on alumina (hexane-ether, 9:1) which afforded monomorine I **9**·HCl (32 mg as hydrochloride, 70%) and the epimer **10a**·HCl (5 mg as hydrochloride, 10%).

9: $[\alpha]^{20}_D$ -35.8° (*n*-hexane, *c* 1.35);[10] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.47 (t, J = 7 Hz, 3 H, CH_3), 1.69 (d, J = 6.5 Hz, 3 H, CH_3), 1.75-2.35 (m, 22 H, CH_2), 2.53 (m, 1 H, H-3 or H-9), 2.66 (m, 1 H, H-5), 2.9 (m, 1 H, H-3 or H-9); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 14.2 (CH_3), 22.9 (CH_3), 23.0, 25.1, 29.4, 29.8, 30.5, 31.1, 36.1, 39.8 (CH_2), 60.3 (C-5), 63.0 (C-3), 67.3 (C-9); MS, m/e (relative intensity) 195 ($M^{+\cdot}$, 3), 194 (2), 180 (3), 139 (11), 138 (100), 98 (15). Anal. Calcd for $C_{13}H_{25}N$·HCl: C, 67.35; H, 11.30; N, 6.04. Found: C, 66.89; H, 11.11; N, 6.34.

10a·HCl: $[\alpha]^{20}_D$ -69.2° (MeOH, *c* 0.55); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.91 (t, J = 7 Hz, 3 H, CH_3), 1.1-2.4 (m with d (J = 7 Hz) at 1.48, 22 H, CH_2 and CH_3), 2.97 (m, 2 H, H-5 and H-9), 3.83 (m, 1 H, H-3); MS, m/e (relative intensity) 195 ($M^{+\cdot}$, 3), 194 (2), 180 (6), 138 (100); exact mass 195.1986 (calcd fo r $C_{13}H_{25}N$ 195.1980).

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Registry No. 1, 88056-92-2; 2, 94458-71-6; 3, 94458-72-7; 4 (isomer 1), 94458-73-8; 4 (isomer 2), 94535-29-2; 5, 94458-74-9; 6, 94458-75-0; 7, 94535-26-9; 9, 94535-27-0; 9·HCl, 94595-24-1; 10a·HCl, 94535-28-1; valeryl chloride, 638-29-9; ethylene, 74-85-1; 1-chloro-3-heptanone, 94458-76-1; 1-chloro-3-heptanone ethylene ketal, 94458-77-2; (+)-monomorine I, 53447-44-2; (-)-phenylglycinol, 56613-80-0; glutaraldehyde, 111-30-8.

Electrochemical Reduction of Unsymmetrically Substituted Diphenyliodonium Salts at Mercury Cathodes in Dimethylformamide

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A study has been made of the electrochemistry of five unsymmetrically substituted diphenyliodonium salts at mercury cathodes in dimethylformamide containing tetramethylammonium perchlorate. Polarograms indicate that the iodonium cations undergo reduction in three stages: (1) one-electron reduction to yield either (a) iodobenzene and a substituted phenylmercury radical or (b) a substituted iodobenzene and a phenylmercury radical, (2) two-electron reduction of the iodobenzene or substituted iodobenzene, and (3) one-electron reduction of the substituted or unsubstituted phenylmercury radical. When electrolyses are performed at potentials corresponding to the first stage of reduction, electron-withdrawing substituents induce the production of more iodobenzene than substituted iodobenzene, whereas electron-releasing groups favor the formation of less iodobenzene than substituted iodobenzene; the other major products (diphenylmercury and symmetrically disubstituted diphenylmercury) arise via disproportionation of adsorbed phenylmercury radicals. At potentials corresponding to the second stage of reduction, electrolyses yield benzene, substituted benzene, and diorganomercury compounds; at potentials corresponding to the third stage of reduction, benzene and substituted benzene are formed.

In a recent investigation[1] we examined the polarographic and electrolytic behavior of diphenyliodonium bromide in dimethylformamide containing tetramethylammonium perchlorate. Depending on the concentrations of the supporting electrolyte and the diphenyliodonium cation, either three or four pulse polarographic waves are observed; for a solution containing 0.1 M tetramethylammonium perchlorate and greater than 0.74 mM diphenyliodonium bromide, four waves (Ia, Ib, II, and III) are seen. Large-scale controlled-potential electrolyses yield equal quantities of diphenylmercury and iodobenzene at potentials corresponding to either wave Ia or Ib, comparable amounts of benzene and diphenylmercury at potentials corresponding to wave II, and mostly benzene with some diphenylmercury at potentials corresponding to wave III.

Only two previous publications have dealt with the electrochemistry of unsymmetrically substituted iodonium salts. Colichman and Maffei[2] studied, as part of a larger survey, the polarography of (β-chlorovinyl)phenyliodonium chloride in an aqueous medium. In a later report Bachofner, Beringer, and Meites[3] probed the effects of size, electronegativity, charge, and reducibility of substituents on the polarographic waves for symmetric and unsymmetric diphenyliodonium compounds in an ethanol-water system. None of the preceding work concerned the behavior of unsymmetrically substituted diphenyliodonium salts in a nonaqueous solvent, nor were any results published pertaining to the influence of substituents on

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