(30 mL). The combined organic layer was washed with water and saturated NaCl solution. Drying ($MgSO_4$) and removal of the solvent under reduced pressure left 58 mg of a yellow-brown solid. Recrystallization from hexane gave 50 mg (77% recovery) of crystalline **8d**: mp 143–144 °C; ^1H NMR (60 MHz, $CDCl_3$) δ 3.82 (s, 1.5 H), 6.8–7.7 (m, 8 H).

Acknowledgment. We gratefully acknowledge support of this work by the Research Corp., the donors of the Petroleum Research Fund, administered by the American Chemical Society, and Hamilton College. We also thank the NIH Resource of Syracuse University for use of the NMR facility.

Registry No. **8d**, 261-40-5; **8e**, 59273-35-7; **8f**, 110458-53-2; **8g**, 59590-82-8; **9a**, 72301-71-4; **9d**, 110458-57-6; **9e**, 110458-58-7; **9f**, 110458-59-8; **9g**, 110458-60-1; **11**, 110458-61-2; **15**, 54086-39-4; $[(Et_2N)_2AsCl]$, 1734-99-2; KNH_2, 17242-52-3; *o*-bromodiphenylmethane, 23450-18-2; *o*-[bis(diethylamino)arsino]diphenylmethane, 110458-54-3; *o*-[bis(chloro)arsino]diphenylmethane, 110458-55-4; diphenylmethane-*o*-arsonic acid, 110458-56-5; acridarsinic acid, 5880-36-4; 9-chloro-9,10-dihydro-9-arsanthracene, 25093-02-1.

Notes

An Efficient Synthesis of Optically Pure (*S*)-(−)-3-Methylcyclohexanone

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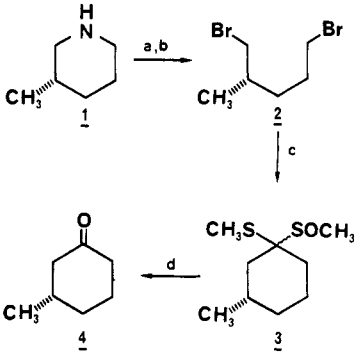
Received February 12, 1987

In connection with our synthetic and pharmacological studies of chiral phencyclidine analogues we required, in high optical purity, large quantities of both enantiomers of 3-methylcyclohexanone. While (+)-3-methylcyclohexanone is commercially available, its antipode is less accessible. Although a variety of synthetic methods for the preparation of the (−)-isomer have been described,[1] it was not clear that any of them could provide the optically pure material in the large quantity we required. Also, the wide range of optical rotations offered in the literature[2] for optically "pure" (+)-3-methylcyclohexanone made it difficult to assess the reliability of any of the sources, although it has been noted by Posner and Frye[3] that optically pure (+)-3-methylcyclohexanone is commercially available.[4] The importance of both (−)- and (+)-3-methylcyclohexanones as synthetic building blocks for drugs and natural products prompts us to describe the preparation of optically pure (*S*)-(−)-3-methylcyclohexanone by a route that appears amenable to large-scale synthesis and provides confirmation for the optical purity of (*R*)-(+)-3-methylcyclohexanone from a commercial source.[4]

Scheme I[a]



[a] Reagents: (a) PhCOCl, NaOH; (b) PBr_3, Br_2; (c) $CH_3SCH_2SOCH_3$, KH; (d) H_3O^+.

Ogura et al.[5] demonstrated that cyclic ketones can be prepared in a two-phase system by the dialkylation of methyl (methylsulfinyl)methyl sulfide[6] with alkyl dihalides. For this method to be applicable to the synthesis of optically active 3-methylcyclohexanones, the corresponding enantiomers of 1,5-dibromo-2-methylpentane would be needed. We prepared these enantiomers by the application of the Von Braun reaction[7] to the easily resolved optical isomers of 3-methylpiperidine.

The route to (−)-3-methylcyclohexanone is shown graphically in Scheme I. (*S*)-(−)-3-Methylpiperidine (**1**) was obtained by resolution of the racemic material according to the procedure of Marwaha et al.[8] Benzoylation and nitrogen abstraction using PBr_3/Br_2 to give (−)-2-methyl-1,5-dibromopentane (**2**) was accomplished in 46% overall yield. The reaction of **2** with methyl (methylsulfinyl)methyl sulfide in the presence of potassium hydride afforded a mixture of dithioketal *S*-oxides **3** in excellent yield. Acid hydrolysis of **3** gave rise to (*S*)-(−)-3-methylcyclohexanone (**4**) with $[\alpha]^{23}_D$ −12.8° (neat) in 83% yield. The optical purity of **4** was established by the ^1H noise-decoupled ^{13}C NMR of the cyclic ketal prepared from **4** and (2*R*,3*R*)-(−)-butane-2,3-diol.[9] It was found to be in

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greater than 98% enantiomeric excess as described below.

Experimental Section

Nuclear magnetic resonance spectra were recorded on a Varian XL300 spectrometer. Infrared spectra were recorded on a Beckman 3001 instrument. Chemical ionization (CI) mass spectra were run on a Finnigan Mat-10150 spectrometer and high-resolution mass spectra on a VG 7070F spectrometer. Gas chromatographic analysis utilized a Hewlett-Packard 5880A instrument with a carbowax capillary. Melting points were obtained with a Thomas-Hoover Unimelt apparatus and are uncorrected.

(*S*)-(+)-3-Methylpiperidine. A slurry of 45.64 g (0.3 mol) of (+)-mandelic acid in 300 mL of ethyl acetate was heated to solution and treated with 29.75 g (0.3 mol) of 3-methylpiperidine in one portion. The mixture was allowed to come to room temperature before filtration. The crystalline material was washed with 400 mL of 1:1 ethyl acetate/ether and dried to give 31.38 g of optically impure salt. Two recrystallizatons of this salt from ethyl acetate gave 24.65 g (64%) of (*S*)-(+)-3-methylpiperidine mandelate, mp 122–123 °C (lit.[8] mp 122–124 °C).

(+)-*N*-Benzoyl-3-methylpiperidine. (*S*)-3-Methylpiperidine mandelate (19.3 g, 76.8 mmol) was dissolved in 200 mL of 1.0 N sodium hydroxide solution. The solution was cooled to 3 °C, and 11.25 g (80.0 mmol) of benzoyl chloride was added dropwise over 10 min. After the addition was complete, the mixture was transferred to a separatory funnel and extracted with ether (2 × 100 mL). The combined extracts were dried ($MgSO_4$) and concentrated to give 14.65 g (94%) of analytically pure amide: mp 72 °C; $[\alpha]^{23}_D$ +49.5° (*c* 1.00, CH_3OH); ^1H NMR (C_6D_6, 70 °C) δ 7.30 (d, *J* = 6 Hz, 2 H), 7.08 (m, 3 H), 4.0 (br, 2 H), 2.58 (ddd, *J* = 13.2, 10.2, 4.1 Hz, 1 H), 2.30 (dd, *J* = 12.9, 9.9 Hz, 1 H), 1.2–1.5 (m, 4 H), 0.8 (m, 1 H), 0.6 (d, *J* = 6.5 Hz, 3 H); IR (neat) 3075, 3000, 1680 cm^{-1}; mass spectrum (CI, NH_3) *m/e* 204 (M + 1). Anal. Calcd for $C_{13}H_{17}NO$: C, 76.80; H, 8.43; N, 6.89. Found: C, 76.73; H, 8.44; N, 6.79.

(−)-2-Methyl-1,5-dibromopentane (2). A 500-mL flask holding 45.1 g (222.2 mmol) of powdered (+)-*N*-benzoyl-3-methylpiperidine was cooled to 5 °C. Phosphorus tribromide (60.1 g, 222.2 mmol) was added from a dropping funnel over 1 h with vigorous stirring. A bright yellow oily crystalline mass was formed. After the addition was complete, the cooling bath was removed, and the mixture became homogeneous upon warming to room temperature. A new dropping funnel containing 11 mL of Br_2 (222.2 mol) was attached, and the Br_2 was added dropwise over 20 min. The resulting mixture was stirred for an additional 3 h. The addition funnel was replaced with a distillation head, and the mixture was distilled under vacuum (1.0 mm) until the pot residue was sticky black. The distillate was dissolved in 100 mL of isooctane and washed successively with water (50 mL), concentrated sulfuric acid (4 × 10 mL), water (50 mL), 1.0 N NaOH solution (2 × 100 mL), and finally water (50 mL). The isooctane solution was dried ($NaSO_4$) and concentrated. The resulting oil was distilled under reduced pressure to give 26.6 g (49.9%) of (−)-2-methyl-1,5-dibromopentane: bp 111 °C (10 mm); $[\alpha]^{23}_D$ −2.99° (neat); ^1H NMR ($CDCl_3$) δ 3.41 (dt, *J* = 6.9, 1.5 Hz, 2 H), 3.35 (dt, *J* = 10.0, 5.9 Hz, 2 H), 1.8–1.95 (m, 3 H), 1.62 (m, 1 H), 1.41 (m, 1 H), 1.04 (d, *J* = 6.5 Hz, 3 H); IR (neat) 2980, 2860, 1450, 1430, 1370, 1250, 1225 cm^{-1}. Anal. Calcd for $C_6H_{12}Br_2$: C, 29.54; H, 4.96. Found: C, 29.80; H, 5.02.

3-Methylcyclohexanone Dimethyl Dithioketal *S*-Oxide (3). Potassium hydride (8.00 g, 50% in oil) was placed in a dry argon-filled 250-mL three-neck flask fitted with rubber septum, argon inlet, and thermometer. The reagent was washed twice with 20 mL of isooctane to remove carrier oil and then covered with 70 mL of dry THF. After cooling the reaction flask to −10 °C, a solution of methyl (methylsulfinyl)methyl sulfide (5.08 g, 41 mmol) in THF (5 mL) was added via cannula over 2 min. After 10 min, a solution of (−)-2-methyl-1,5-dibromopentane (10 g) in THF (30 mL) was added via cannula over 5 min, keeping the reaction temperature below 20 °C. After the addition was complete, the reaction was stirred for an additional 1 h, absolute ethanol (3 mL) was carefully added, and the reaction was poured into a 500-mL separatory funnel containing water (50 mL) and ether (150 mL). The organic layer was removed, dried with $MgSO_4$, and concentrated. The crude material was filtered through a short pad of silica gel using 30% EtOAc/hexane as the eluant, and the filtrate was concentrated to give 6.09 g (78%) of the two diastereomeric dithioketals (ratio 3:5 by GC analysis): ^1H NMR ($CDCl_3$) δ 2.72 (m, 2 H), 2.67 (s, 3 H, SMe), 2.34 and 2.33 (s, 3 H, SMe), 1.6–2.2 (m, 6 H), 1.48 (dd, *J* = 13.0, 12.2 Hz, 1 H), 1.02 and 0.90 (d, *J* = 6.4 Hz, 3 H); IR (neat) 2935, 1445, 1290, 1050 cm^{-1}; mass spectrum (CI, NH_3), *m/e* 143 (M − SOMe); high-resolution mass spectrum, calcd for $C_8H_{15}S$ 143.0891, found 143.0894.

(*S*)-(−)-3-Methylcyclohexanone (4). Concentrated hydrochloric acid (6 mL) was added to a solution of **3** (8.4 g, 40.8 mmol) in methanol (35 mL) and the resulting mixture was refluxed for 15 min. The mixture was then poured into a separatory funnel containing 70 mL of 1 N NaOH solution and extracted with two 25-mL portions of ether. The combined extracts were dried ($MgSO_4$) and filtered. After removal of the solvent by distillation through a Vigreux column, the product was obtained by short-path distillation, bp 169 °C (3.8 g, 83%). The ketone obtained was in all respects (^1H NMR, MS, IR) identical with the commercially available (+)-3-methylcyclohexanone except for optical rotation [$[\alpha]^{23}_D$ −12.8° (neat)] and odor. Anal. Calcd for $C_7H_{12}O$: C, 74.95; H, 10.79. Found: C, 75.02; H, 10.81.

Determination of Optical Purity. Derivatization of commercial (*R*)-(+)-4 and the synthetic (*S*)-(−)-4 with (2*R*,3*R*)-butane-2,3-diol by the method of Plattner and Rapoport,[10] gave the corresponding diastereomeric ketals. ^{13}C NMR analysis, according to Hiemstra and Wynberg,[9] of the ketal derivative of (−)-4 revealed no diastereomeric impurity. Our sample of commercial (+)-4 was also revealed to be optically pure by this method. Addition of 1% of the (+)-4 to our sample of (−)-4, followed by derivatization and ^{13}C NMR analysis clearly showed the presence of the diastereomeric impurity. Thus, both (+)- and (−)-4 were >98% enantiomerically pure.

Acknowledgment. A.T. was supported by the National Institute on Drug Abuse through National Research Service Award No. 5F32 DA05287-02. We thank N. F. Whittaker, LAC, NIDDK, NIH, for the mass spectral data.

Registry No. **2**, 81155-94-4; **3**-(*R*), 109152-47-8; **3**-(*S*), 109278-47-9; **4**, 24965-87-5; Br_3P, 7789-60-8; Br_2, 7726-95-6; (*S*)-(−)-3-methylpiperidine mandelate, 109152-46-7; 3-methylpiperidine, 626-56-2; (+)-*N*-benzoyl-3-methylpiperidine, 109152-48-9; (methylthio)methyl ethyl sulfone, 109152-49-0.

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Metal Catalysis in Oxidation by Peroxides.[1] Anionic Molybdenum-Picolinate *N*-Oxido-Peroxo Complex: An Effective Oxidant of Primary and Secondary Alcohols in Nonpolar Solvents

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Received December 30, 1986

Anionic molybdenum–peroxo complexes are useful reagents in alcohol oxidations.[2] In a preliminary report

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