Sulfoximine-Mediated Syntheses of Optically Active Alcohols

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Optically active β-hydroxy sulfoximines were prepared, as diastereomeric pairs, by the addition the lithium derivative of optically active *N,S*-dimethyl-*S*-phenylsulfoximine to prochiral ketones and aldehydes. The ketone adducts after separation by medium-pressure chromatography on silica gel were desulfurized with Raney nickel to yield optically active tertiary alcohols. The aldehyde adducts were directly treated with Raney nickel to yield secondary alcohols in optical purities dependent of the asymmetric induction in adduct formation. Optical purities for the various alcohols prepared ranged from 30% to 100%.

In the method (Scheme I) herein described for the production of optically active secondary and tertiary alcohols, the asymmetry emanates from the use of optically active *N*, *S*-dimethyl-*S*-phenylsulfoximine (1)—a compound available in high optical purity from thioanisole in a four-step route described previously.[1]

In a preliminary report we noted that the condensation of (+)-(*S*)-1 with benzaldehyde produced two diastereomers, readily distinguishable by ^{1}H NMR, in a 3:2 ratio. Fractional crystallization gave one of the diastereomers pure; treatment of this material with aluminum amalgam in aqueous THF yielded optically pure (+)-(*R*)-1-phenylethanol.[2] The process is similar to that used by Tsuchihashi in a synthesis of this optically active alcohol based on phenyl methyl sulfoxide.[3]

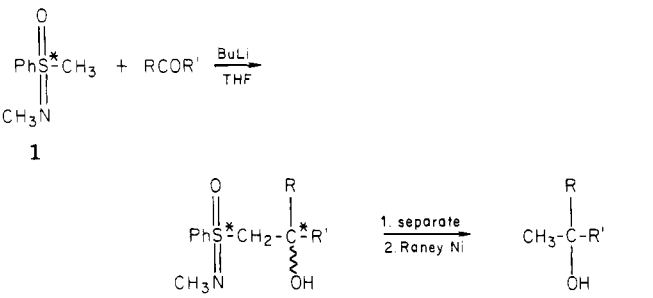
Our design of this study was based on the anticipation that the various diastereomeric β-hydroxy sulfoximines were excellent candidates for separation by preparative medium pressure liquid chromatography. These compounds have hydrogen-bond donating and/or accepting sites intimately associated with two closely situated chiral center.

Results and Discussion

Reaction of (+)-(*S*)-1 as the lithium derivative with 1-phenyl-1-propanone (room temperature, overnight) produced **2** (R = Ph, R′ = Et) in 88% yield as a 60:40 mixture of diastereomers. These diastereomers proved readily separable; an R_f-difference of about 0.25 was observed on silica gel plates with a 3:1 hexane/ethyl acetate mixture as developing solvent. Conditions for preparative scale differed since these β-hydroxy sulfoximines showed a proclivity for crystallization during column chromatography. Decreasing ratios of carbon tetrachloride and ethyl acetate were utilized, beginning with a 10:1 mix. A total recovery of 79% of the pure diastereomers was achieved. The individual diastereomers were crystalline. Their purity could be ascertained by the sharpness of their melting points, by thin-layer chromatography, and by ^{1}H NMR (the *N*-methyl singlets of different chemical shifts).

In our preliminary report of desulfurization of β-hydroxy sulfoximines, aluminum amalgam in aqueous THF was used.[2] With this reagent the desired alcohol is accompanied by considerable amounts of alkene from reductive β-elimination. (The alkene becomes the exclusive product in the presence of acetic acid—the overall process providing a convenient method for the methylenation of aldehydes and ketones.[4]) After considerable experimentation with various dissolving metal reductions, we returned to the classic desulfurization reagent—Raney nickel. In our hands, the highest yields of alcohols were obtained with this reagent.

Scheme I



2a (higher R_f, silica gel)
b (low R_f, silica gel)

optically pure

Raney nickel in ethanol at reflux resulted in the desired bond cleavage, but thin-layer chromatography of the reaction mixture indicated contamination by starting sulfoximine 1 and ketone. It was found that on stirring a mixture of Raney nickel, the β-hydroxy sulfoximine, and *wet* diethyl ether at room temperature the desired hydrogenolysis occurred without production of contaminants. (**Caution**: Failure to use ether which has been saturated with water can result in fires.) Filtration followed by rotary evaporation to remove the ether and bulb-to-bulb distillation yielded the pure alcohol.

Diastereomer **2a** (R = Ph, R′ = Et) was converted in 48% yield to (+)-2-phenyl-2-butanol, $[\alpha]^{27}_D$ +16.1° (*c* 1.28, EtOH). The second diastereomer **2b** (R = Ph, R′ = Et) was desulfurized to produce the (−)-enantiomer, $[\alpha]^{27}_D$ −15.7° (*c* 0.8, EtOH). The above samples were prepared from optically pure (+)-1. A larger sample of **2a** (R = Ph, R′ = Et) prepared from 97% optically pure 1 gave (+)-2-phenyl-2-butanol of $[\alpha]^{27}_D$ +18.0° (neat) and $[\alpha]^{27}_D$ +15.3° (2.5, EtOH) corresponding to 98% optical purity based on the literature value of +18.4° (neat) (Table I).

Other ketones which were converted to optically active tertiary alcohols are listed in Table I. Chromatographic separations of β-hydroxy sulfoximines derived from prochiral dialkyl ketones proved to be considerably more difficult than those derived for alkyl aryl ketones. For the materials considered in Table I the yields in the condensation reaction ranged from 83% to quantitative, the total recovery of the separated diastereomers ranged from 67% to 94%, and the yields of alcohols by desulfurization with Raney nickel ranged from 43 % to 83%.

The two diastereomers produced in the condensation of 1 with 1-penten-3-one were separated. However, treatment

(1) Johnson, C. R. *Acc. Chem. Res.* **1973**, *6*, 341. Johnson, C. R.; Schroeck, C. W. *J. Am. Chem. Soc.* **1973**, 95, 7418.
(2) Schroeck, C. W.; Johnson, C. R. *J. Am. Chem. Soc.* **1971**, *93*, 5305.
(3) Tsuchihashi, G; Iriuchijima, S; Ishibashi, M. *Tetrahedron Lett.* **1972**, 4605.
(4) Johnson, C. R.; Kirchhoff, R. A. *J. Am. Chem. Soc.* **1979**, *101*, 3602.

0022-3263/82/1947-1193$01.25/0

Table I. Optically Active Tertiary Alcohols from β-Hydroxy Sulfoximines (Scheme I)

adduct 2	R	R′	config of 1	opt purity 1, %	alcohol 3 obsd $[\alpha]_D$	alcohol 3 lit. $[\delta]_D$(max)
a	Ph	Et	S	100	$[\alpha]^{27}_D$ +16.1° (c 1.3, EtOH)	
b			S	100	$[\alpha]^{27}_D$ -15.7° (c 0.8, EtOH)	
a			S	97	$[\alpha]^{22}_D$ +18.0° (neat) $[\alpha]^{27}_D$ +15.4° (c 2.5, EtOH)	18.4[a] (neat)
a	Ph	n-Pr	S	87	$[\alpha]^{25}_D$ +5.59° (c 0.9, acetone)	
b			S	87	$[\alpha]^{25}_D$ -5.14° (c 1.4, acetone)	
a	Ph	n-Bu	S	99	$[\alpha]^{22}_D$ +9.9° (c 3.2, acetone)	
b			S	99	$[\alpha]^{22}_D$ -9.6° (c 3.1, acetone)	
a	Ph	c-C_6H_{11}	S	97	$[\alpha]^{25}_D$ +20.8° (c 2.7, $CHCl_3$)	20.6[b] ($CHCl_3$)
b			S	97	$[\alpha]^{25}_D$ -20.7° (c 2.1, $CHCl_3$)	
a	$PhCH_2$	Et	S	99	$[\alpha]^{31}_D$ -8.61° (c 2.6, EtOH)	4.8[c] (EtOH)
b			S	99	$[\alpha]^{31}_D$ +7.79° (c 2.3, EtOH)	
a	i-Bu	Et	R	66	$[\alpha]^{21}_D$ -1.86° (neat) $[\alpha]^{21}_D$ -3.36° (c 3.3, acetone)	2.72[d] (neat)
b			R	66	$[\alpha]^{21}_D$ +3.6° (c 3.3, acetone)	

[a] Davies, A. G.; Kenyon, J.; Salami, L. *J. Chem. Soc.* **1957**, 3148. [b] Inch, T. D.; Lewis, G. J.; Sainsburg, G. L.; Sellers, D. J. *Tetrahedron Lett.* **1969**, 3657. [c] Thakev, K. A.; Dave, N. S.; Potel, S. H.; Vase, I. G. *J. Sci. Ind. Res., Sect. B.*, **1962**, *21*, 210. Doering, W. v.E.; Zeiss, H. A. *J. Am. Chem. Soc.* **1950**, 72, 147.

Table II. Optically Active Secondary Alcohols (Scheme I, without Separation of Diastereomers)

2 (R = H), R′	(+)-(S)-1 opt purity	alcohol 2, opt purity, %
Ph	85	37[a]
n-hexyl	85	25[b]
i-Bu	92	30[c]
t-Bu	95	46[d]

[a] Based on $[\alpha]_D$ (cyclopentane) concentration dependence studies by Reich, C. J. Ph. D. Dissertation, Stanford University, Stanford, CA, 1976. [b] Based on $[\alpha]^{17}_D$ +9.8° (ethanol) (Pickard, R. H.; Kenyon, J. *J. Chem. Soc.* **1970**, 2058). [c] Based on $[\alpha]^{30}_D$ 20.3° (neat) (Pickard, R. H.; Kenyon, J. *J. Chem. Soc.* **1911**, 45). [d] Based on $[\alpha]^{20}_D$ +3.31° (c 10.3, benzene) (Mosher, H. S.; Yamaguchi, S. *J. Org. Chem.* **1973**, *38*, 1870).

of the diastereomers with Raney nickel affected not only carbon–sulfur hydrogenolysis but also hydrogenation of the double bond which resulted in the production of achiral 3-methyl-3-pentanol.

Pairs of diastereomeric β-hydroxy sulfoximines were prepared from resolved **1** and aldehydes. Separation of the diastereomers followed by hydrogenolysis would result in optically active secondary alcohols. Separation of the diastereomers by preparative-scale medium-pressure liquid chromatography on silica gel proved impractical due to poor resolution. However, it was found that moderate optical yields of secondary alcohols could be realized by cleavage of the carbon–sulfur bonds of the unresolved mixtures of β-hydroxy sulfoximines formed by the addition of **1**, as the lithium derivative, to aldehydes at −78 °C. Adduct yields ranged from 55% to 79% and alcohols yields ranged from 31% to 79%. Results are summarized in Table II.

The methodology described above results in a trade-off of a resolved sulfur center for a resolved carbon center. The disadvantage of lack of recyclibility of the reagent is apparent. This disadvantage is offset by the ease of resolution of methylphenylsulfoximine.[5] In cases of secondary and tertiary methylcarbinols where separation of the β-hydroxy sulfoximine adducts by chromatography can be realized, the present scheme may be superior with respect to optical yields of *both* enantiomers, material yields, and time invested to schemes based on conventional resolution techniques (e.g., brucine salts of half phlthalate esters) or asymmetric synthesis (e.g., chiral hydride reagents or Grignard reactions mediated by chiral ligands).

Work is continuing aimed at the development of sulfoximines—the adducts of which will be more generally responsive to resolution by column chromatography—and improved methods for acheiving reductive removal of the sulfonimidoyl group.

Experimental Section

General Procedures. Melting points were determined with a Thomas-Hoover melting-point apparatus and are uncorrected. Optical rotations were measured on a Perkin-Elmer 141 polarimeter. Nuclear magnetic resonance spectroscopy was achieved through the use of a Varian T-60 instrument or a JEOLCO 100-MHz instrument. Infrared spectra were recorded on a Perkin-Elmer Model 267 spectrophotometer. Microanalytical analyses were carried out by Midwest Microlabs, Indianapolis, IN; those noted were within ±0.3% of theory.

Analytical thin-layer chromatography (TLC) was done on microscope slides coated with silica gel GF-254 supplied by EM Reagents. Preparative thick-layer chromatography was carried out by using 20 × 20 cm glass plates coated with silica gel GF-254 with a thickness of 2 mm. Column chromatography was done with either silica gel H (Applied Science Lab., Inc.) or silica gel 60 (230–400 mesh) (EM Reagents) as absorbent and Michel-Miller (Ace glass) columns. THF was distilled from Na/benzophenone.

β-Hydroxy Sulfoximines from the Reaction of *N*,*S*-Dimethyl-*S*-phenylsulfoximine with Ketones. A known quantity of *N*,*S*-dimethyl-*S*-phenylsulfoximines, **1**, was added to a flame-dried flask fitted with a stirring bar, an inlet, and an outlet for nitrogen. THF was added to dissolve the sulfoximine and the solution was cooled to 0 °C. An equivalent of butyllithium was added slowly while the solution was stirred. The cooling bath was removed and the mixture allowed to stir for 15 min; a yellow suspension formed.[8] A THF solution of an equimolar amount of the ketone was added dropwise at room temperature. The mixture was allowed to stir under a positive nitrogen pressure

(5) A new method for the direct resolution of the *N*-methyl derivative is under development in our laboratory and will be described in due course.

(6) For a compilation, see Wilen, S. H. "Tables of Resolving Agents and Optical Resolutions"; University of Notre Dame Press: Notre Dame, IN 1972.

(7) Morrison, J. D.; Mosher, H. S. "Asymmetric Organic Reactions"; American Chemical Society: Washington, DC, 1976.

(8) Homogeneous solutions of the lithium derivative may also be used (ref 4). By using 1 g of **1** in 30 mL of THF, the lithium derivative will remain in solution at −78 °C.

overnight. An equal volume of aqueous 6 N H_2SO_4 was then added. The mixture was stirred for 15 min and then transferred to a separatory funnel. The aqueous layer was removed and the THF layer was extracted once with a small portion of aqueous 6 N H_2SO_4. (If a third oily layer forms, it should be combined with the aqueous layer.) The aqueous layers were combined and shaken twice with hexane; the hexane and THF layers were discarded. Aqueous 10% NaOH was added to the combined aqueous layers until a permanent turbidity was produced. The turbid solution was then extracted several times with dichloromethane. The organic extracts were washed once with saturated aqueous $NaHCO_3$, dried ($MgSO_4$), and concentrated on a rotary evaporator to yield the pure β-hydroxy sulfoximines as mixtures of diastereomers.

(*SS*,2*S*)- and (*SS*,2*R*)-1-(*N*-Methylphenylsulfonimidoyl)-2-phenyl-2-propanol were obtained as a mixture (76%) from the reaction of (+)-(*S*)-1 with acetophenone. The diastereomers were separated by silica gel chromatography with a 2:1 hexane/ethyl acetate mixture as eluent (85% combined recovery). The diastereomer that eluted first displyed the following characteristics: mp 107–109 °C; IR ($CHCl_3$) 3200 (br), 1250–1200 cm^{-1} (br); ^1H NMR ($CDCl_3$) δ 8.0–7.1 (m, 10, Ph), 3.6 (s, 2, SCH_2), 2.5 (s, 3, NCH_3), 1.5 (s, 3, CCH_3). The more slowly moving diastereomer exhibited an IR similar to the first diastereomer but had mp 103–105 °C: ^1H NMR ($CDCl_3$) δ 8.0–6.8 (br m, 10, Ph), 3.8–3.2 (q, 2, SCH_2), 2.7 (s, 3, NCH_3), 1.8 (s, 3, CCH_3). Anal. ($C_{16}H_{19}NO_2S$) C, H.

(*SS*,2*S*)- and (*SS*,2*R*)-1-(*N*-Methylphenylsulfonimidoyl)-2-phenyl-2-butanol were obtained as a mixture (89%) from the reaction of (+)-(*S*)-1 with 1-phenyl-1-propanone. The diastereomers were separated by silica gel chromatography with a carbon tetrachloride/ethyl acetate mixture as eluent. The total recovery of separated diastereomers was 79%. The diastereomer that eluted first had the following characteristics: mp 88–89 °C; IR (neat) 3500–2700 (br), 1250–1200 cm^{-1} (br); $_1H$ NMR ($CDCl_3$) δ 7.7–7.1 (m, 10, Ph), 6.8–6.5 (brs, 1 OH), 3.6 (s, 2, SCH_2), 2.5 (s, 3, NCH_3), 2.0–1.5 (m, 2, CH_2CH_3), 0.9–0.5 (t, 3, CH_2CH_3). The slower moving diastereomer displayed a similar IR but had mp 105 °C; ^1H NMR ($CDCl_3$) δ 7.5–7.0 (br m, 10, Ph), 3.5 (s, 2, SCH_2), 2.6 (s, 3, NCH_3), 2.6–1.4 (m, 2, CH_2CH_3), 0.9–0.5 (t, 3, CH_2CH_3). Anal. ($C_{17}H_{21}NO_2S$) C, H.

(*SS*,2*S*)- and (*SS*,2*R*)-1-(*N*-Methylphenylsulfonimidoyl)-2-phenyl-2-pentanol were obtained as amixture (93%) from the reaction of (+)-1 with 1-phenyl-1-butanone. The diastereomers were separated (67%) by silica gel chromatography with a 5:1 pentane/ether mixture as eluent. The diastereomer that eluted first displayed the following characteristics: mp 77 °C; IR ($CHCl_3$) 3180 (br), 1250–1210 cm^{-1} (br); ^1H NMR ($CDCl_3$) δ 7.4–6.9 (m, 10, Ph), 3.4 (s, 2, SCH_2), 2.5 (s, 3, NCH_3), 2.3–0.4 (m, 7, *n*-Pr). Anal. ($C_{18}H_{23}NO_2S$) C, H. The more slowly moving diastereomer exhibited an IR similar to the more rapidly moving one but had mp 141–142 °C: ^1H NMR ($CDCl_3$) δ 7.8–6.9 (m, 10, Ph), 6.7 (br s, 1, OH), 3.6 (s, 2, SCH_2), 2.5 (s, 3, NCH_3), 2.0–0.4 (m, 7, *n*-Pr).

(*SS*,2*S*)- and (*SS*,2*R*)-1-(*N*-Methylphenylsulfonimidoyl)-2-phenyl-2-hexanol were obtained as a mixture (96%) from the reaction of (+)-(*S*)-1 with 1-phenyl-1-pentanone. The diastereomers were separated by silica gel chromatography with an 8:1 hexane/ethyl acetate mixture as eluent (95%). The more rapidly eluting diastereomer displayed the following characteristics: mp 66–68 °C; IR 3200 (br), 1260–1210 cm^{-1} (br); ^1H NMR ($CDCl_3$) δ 7.6–6.9 (m, 11, Ph and OH), 3.6 (s, 2, SCH_2), 2.7 (s, 3, NCH_3), 2.5–0.5 (m, 9, *n*-Bu). The more slowly eluting diastereomer exhibited an IR similar to the first but had mp 62–64 °C: ^1H NMR ($CDCl_3$) 7.8–7.0 (m, 10, Ph), 6.7 (br s, 1, OH), 3.7 (s, 2, SCH_2), 2.6 (s, 3, NCH_3), 3.2–0.4 (m, 9, *n*-Bu). Anal. ($C_{19}H_{25}NO_2S$) C, H.

(*SS*,1*S*)- and (*SS*,1*R*)-1-Cyclohexyl-2-(*N*-methylphenylsulfonimidoyl)-1-phenylethanol were obtained as a mixture of diastereomers (92%) from the condensation of (+)-(*S*)-1 with cyclohexyl phenyl ketone. The diastereomers were separated by silica gel chromatography, using a 10:1 hexane/ethyl acetate mixture as eluent (67%). The rapidly eluting diastereomer displayed the following characteristics: mp 119–120 °C; IR (CCl_4) 3200 (br), 1250 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.7–6.7 (m, 10, Ph), 4.0–3.4 (q, 2, SCH_2), 2.6 (s, 3, NCH_3), 2.3–0.6 (br m, 11, cyclohexyl). Anal. ($C_{21}H_{27}NO_2S$) C, H. The more slowly moving diastereomer displayed an IR similar to the faster moving one but had mp 135 °C: ^1H NMR ($CDCl_3$) δ 7.8–7.0 (m, 10, Ph), 6.7 (s, 1, OH), 4.0–3.5 (q, 2, SCH_2), 2.5 (s, 3, NCH_3), 2.1–0.6 (br m, 11, cyclohexyl).

(*SS*,2*S*)- and (*SS*,2*R*)-1-(*N*-Methylphenylsulfonimidoyl)-2-benzyl-2-butanol were pepared as a mixture (83%) from the reaction of (+)-(*S*)-1 with 1-phenyl-2-butanone. The diasteromers were separated with difficulty by silica gel chromatograpy with decreasing ratios of a benzene/ethyl acetate mixture as eluent, beginning with a 15:1 mixture. The percent recovery of separated diastereomers was 55%. The more rapidly eluting diastereomer exhibited the following characteristics: mp 137–139 °C; IR ($CHCl_3$) 3200 (br), 1250, 1150 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.1–7.3 (m, 5, Ar), 7.2 (s, 5, Ar), 6.6 (brs, 1, OH), 3.4–3.0 (q, 2, SCH_2), 2.8 (s, 2, CH_2Ph), 2.6 (s, 3, NCH_3), 2.3–1.8 (q, 2, CH_2CH_3), 1.3–0.9 (t, 3, CH_3CH_3). The more slowly eluting diastereomer displayed an IR similar to the former diastereomer but had mp 105–110 °C: ^1H NMR ($CDCl_3$) δ 8.1–7.1 (m, 10, Ar), 6.8 (br s, 1, OH), 3.6–2.9 (m, 4, $PhCH_2CCH_2S$), 2.7 (s, 3, NCH_3), 1.6–1.2 (m, 2, CH_2CH_3), 1.0–0.6 (t, 3, CH_2CH_3). Anal. ($C_{18}H_{23}NO_2S$) C, H.

(*SR*,3*S*)- and (*SR*,2*R*)-5-Methyl-3-[(*N*-methylphenylsulfonimidoyl)methyl]-3-hexanol were prepared in essentially quantitative yield from (−)-(*R*)-1 and 5-methyl-3-hexanone, following the procedure described below for aldehydes. The diastereomers were separated on silica gel with an 8:1 hexane/ethyl acetate mixture as eluent; total recovery of separated diastereomers was 79%. The more rapidly moving diastereomer exhibited the following characteristics: IR ($CHCl_3$) 3250 (br), 1250–1210 (br), 1150 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.0–7.2 (m, 5, Ph), 6.4 (s, 1, OH), 3.5–2.9 (q, 2, SCH_2), 2.6 (s, 3, NCH_3), 2.3–0.4 (m, 14). The more slowly eluting diastereomer displayed a similar IR but had mp 69–71 °C; ^1H NMR ($CDCl_3$) δ 8.0–7.3 (m, 5, Ph), 7.3 (br s, 1, OH), 3.5–2.9 (q, 2, SCH_2), 2.65 (s, 3, NCH_3), 2.3–0.5 (m, 14). Anal. ($C_{15}H_{25}NO_2S$) C, H.

Production of β-Hydroxy Sulfoximines from the Reaction of *N*, *S*-Dimethyl-*S*-phenylsulfoximine with Aldehydes. A known quantity of *N*, *S*-dimethyl-*S*-phenylsulfoximine, 1, was added to a flame-dried flask fitted with a stirring bar, an inlet, and an outlet for nitrogen. THF was added to dissolve the sulfoximine and the solution was cooled to 0 °C. An equivalent of butyllithium was added slowly while the solution was stirred. The cooling bath was removed and the mixture allowed to stir for 15 min; during this time a yellow suspension formed. This mixture was then cooled to −78 °C and an equimolar amount of the aldehyde, dissolved in THF, was added dropwise. The mixture was allowed to stir for 1 h at −78 °C and then 1 h at ambient temperature. After this time, the reaction mixture was added to an equal volume of 6 N H_2SO_4. Isolation of the pure β-hydroxy sulfoximine (obtained as a mixture of stereoisomers) proceeded in a fashion analogous to that described for the isolation of hydroxy sulfoximines obtained from ketones.

(*SS*,2*S*)- and (*SS*,1*R*)-2-(*N*-Methylphenylsulfonimidoyl)-1-phenylethanol were obtained (78%) as a mixture from the reaction of resolved (+)-1 with benzaldehyde. The diastereomeric ratio (ca. 3:1) was determined from the ^1H NMR spectrum by integration of the areas for the methine protons of the two structures. The spectral properties compared favorably to those reported by Schroeck.[9]

(*SS*,2*S*)- and (*SS*,2*R*)-1-(*N*-Methylphenylsulfonimidoyl)-2-octanol were obtained (70%) as a mixture from the reaction of resolved 1 with heptanal. An approximate diastereomeric ratio (3:2) was determined from the ^1H NMR spectrum by integration of the areas for the NCH_3 protons of the two structures. The spectral properties compared favorably to those reported by Schroeck.[9]

(*SS*,2*S*)- and (*SS*,2*R*)-4-Methyl-1-(*N*-methylsulfonimidoyl)-2-pentanol were obtained (69%) as a mixture from the reaction of (+)-1 with 3-methylbutanal. The diastereomeric ratio (ca. 5:2) was determined from the ^1H NMR spectrum by integration of the areas for the NCH_3 protons of the two structures. The material was isolated as a colorless oil and displayed the following characteristics: IR (neat) 3350 (br), 1250 (br), 1140, 1100,

(9) Schroeck, C. W. Ph.D. Dissertation, Wayne State University, Detroit, MI, 1972.

1070 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.0–7.3 (m, 5, Ph), 5.8 (br s, 1, OH), 4.8–2.8 (m, 3, SCH_2CHO), 2.7 (s) 2.6 (s; 3, NCH_3 for both diastereomers), 2.2–0.6 (m, 9, *i*-Bu). Anal. ($C_{13}H_{21}NO_2S$) C, H, N.

(*SS*,2*S*)- and (*SS*,2*R*)-3,3-Dimethyl-1-1-(*N*-methylphenylsulfonimidoyl)-2-butanol were obtained (65%) as a mixture (ca. 2.8:1 by integration of the areas for the *tert*-butyl protons of the two structures) from the reaction of (+)-1 with 2,2-dimethylpropanal. The mixture was a pale yellow oil at room temperature and displayed the following spectral characteristics: IR (neat) 3300 (br), 1250 (br), 1150 cm^{-1} (sh at 1100 and 1080); ^1H NMR ($CDCl_3$) δ 8.1–7.4 (m, 5, Ph), 5.7 (br s, 1, OH), 4.2–2.8 (m, 3, SCH_2CHO), 2.7 (s), 2.6 (s; 3, NCH_3 signals for the diastereomers), 0.9 (s), 0.8 (s; 9, $C(CH_3)_3$ signals of the diastereomers).

Hydrogenolysis of β-Hydroxy Sulfoximines with Raney Nickel W-2. The β-hydroxy sulfoximine was added to a two-neck flask fitted with a mechanical stirrer and dissolved in a minimal amount of water-saturated diethyl ether. **(Caution**: Failure to use water-saturated ether can result in fires.) Twenty equivalents of Raney nickel W-2 (measured as per directions in "Organic Syntheses")[10] were transferred to the sulfoximine soluton. The reaction mixture was vigorously stirred at room temperature and the progress of the reaction was monitored by TLC. When no starting material remained, stirring was stopped and the solvent was carefully decanted. The residue was washed twice by suspension, and the organic layers were combined. The combined organic layers were dried ($MgSO_4$), filtered through Celite, and concentrated by distillation. The product alcohol was obtained from the residue in high purity by short-path distillation or chromatography.

(10) Mozingo, R., "Organic Syntheses", Collect. Vol. 3; Wiley: New York, 1955; p 181.

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Registry No. (+)-(*S*)-1, 33993-53-2; (−)-(*R*)-1, 80482-67-3; (*S*,*S*,2*S*)-2 (R = Ph; R′ = Me), 80441-25-4; (*SS*,2*R*)-2 (R = Ph; R′ = Me), 80441-26-5; (*SS*,2*S*)-2 (R = Ph; R′ = Et), 73798-17-1; (*SS*,2*R*)-2 (R = Ph; R′ = Et), 73798-18-2; (*SS*,2*S*)-2 (R = Ph; R′ = Pr), 80441-27-6; (*SS*,2*R*)-2 (R = Ph; R′ = Pr), 80441-28-7; (*SS*,2*S*)-2 (R = Ph; R′ = Bu), 80441-29-8; (*SS*,2*R*)-2 (R = Ph; R′ = Bu), 80441-30-1; (*SS*,1*S*)-2 (R = Ph; R′ = cyclohexyl), 80441-31-2; (*SS*,1*R*)-2 (R = Ph; R′ = cyclohexyl), 80441-32-3; (*SS*,2*S*)-2 (R = CH_2Ph; R′ = Et), 80441-33-4; (*SS*,2*R*)-2 (R = CH_2Ph; R′ = Et), 80441-34-5; (*SR*,3*S*)-2 (R = Et; R′ = Bu-*i*), 80441-35-6; (*SR*,3*R*)-2 (R = Et; R′ = Bu-*i*), 80441-36-7; (*SS*,1*S*)-2 (R = H; R′ = Ph), 33903-51-4; (*SS*,1*R*)-2 (R = H; R′ = Ph), 72174-41-5; (*SS*,2*S*)-2 (R = H; R′ = hexyl), 80422-48-6; (*SS*,2*R*)-2 (R = H; R′ = hexyl), 80422-49-7; (*SS*,2*S*)-2 (R = H; R′ = Bu-*i*), 80422-50-0; (*SS*,2*R*)-2 (R = H; R′ = Bu-*i*), 80422-51-1; (*SS*,2*S*)-2 (R = H; R′ = Bu-*t*), 78742-30-0; (*SS*,2*R*)-2 (R = H; R′ = Bu-*t*), 78742-34-4; (+)-3 (R = Ph; R′ = Et), 1006-06-0; (−)-3 (R = Phf R′ = Et), 53777-08-5; (+)-3 (R = Ph; R′ = Pr), 52992-90-2; (−)-3 (R = Ph; R′ = Pr), 52992-91-3; (+)-3 (R = Ph; R′ = Bu), 73464-88-7; (−)-3 (R = Ph; R′ = Bu), 19641-54-4; (+)-3 (R = Ph; R′ = hexyl), 80441-37-8; (−)-3 (R = Ph; R′ = hexyl), 80441-38-9; (+)-3 (R = CH_2Ph; R′ = Et), 56640-51-8; (−)-3 (R = CH_2Ph; R′ = Et), 55016-95-0; (+)-3 (R = Bu-*i*; R′ = Et), 80513-04-8; (−)-3 (R = Bu-*i*; R′ = Et), 19113-77-0; (±)-3 (R = H; R′ = Ph), 13323-81-4; (±)-3 (R = H; R′ = hexyl), 4128-31-8; (±)-3 (R = H; R′ = Bu-*i*), 20281-88-3; (±)-3 (R = H; R′ = Bu-*t*), 20281-91-8; acetophenone, 98-86-2; 1-phenyl-1-propanone, 93-55-0; 1-phenyl-1-butanone, 495-40-9; 1-phenyl-1-pentanone, 1009-14-9; cyclohexyl phenyl ketone, 712-50-5; 1-phenyl-2-butanone, 1007-32-5; 5-methyl-3-hexanone, 623-56-3; benzaldehyde, 100-52-7; heptanal, 111-71-7; 3-methylbutanal, 590-86-3; 2,2-dimethylpropanal, 630-19-3.

Diastereoselective Reductions of β-Keto Sulfoximines

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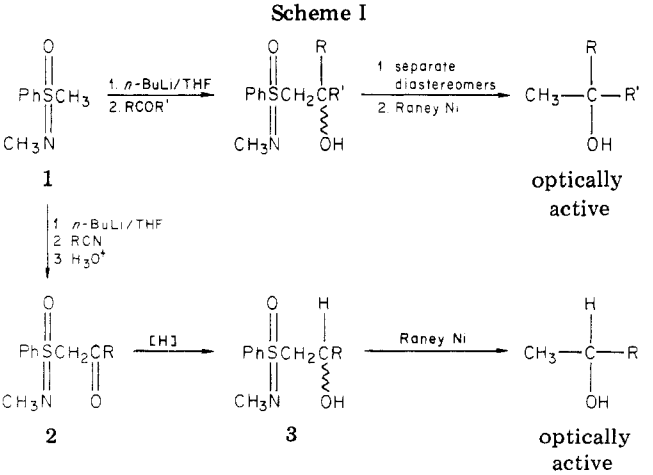
(*S*)-β-Keto sulfoximines have been prepared by butyllithium-mediated condensation of (+)-(*S*)-*N*,*S*-dimethyl-*S*-phenylsulfoximine with nitriles. The β-keto sulfoximines on treatment with a variety of reducing agents afforded β-hydroxy sulfoximines with varying diastereomeric ratios. Highest asymmetric inductions were observed with gaseous diborane. A sulfoximine–borane complex is suggested as an intermediate. Raney nickel desulfurization of the β-hydroxy sulfoximines afforded secondary alcohols with optical purities in the 18–69% range.

The addition of optically active *N*,*S*-dimethyl-*S*-phenylsulfoximines (1) to prochiral ketones followed by chromatographic separation of the diastereomeric adducts and desulfurization has been shown to be a viable route to optically active tertiary alcohols (Scheme I).[1] A similar scheme applied to aldehydes and resulting in optically active secondary alcohols was less successful due to difficulties in chromatographic resolution of the adducts.[1,2] Diastereoselective reduction of β-keto sulfoximines derived from 1 was envisioned as an alternate approach to requisite β-hydroxy sulfoximines (Scheme I). It was anticipated that steric and/or chelation control would lead to significant asymmetric induction at the carbinol site.

Since the completion of this work, a similar study has appeared by Cinquini and co-workers.[3] They prepared keto sulfoximines 2 in 49–69% yields by condensation of the lithium reagent derived from (+)-(*S*)-1 with esters and examined reduction of these substances with sodium bo-

Scheme I



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