°C; IR (Nujol) 1720, 1660, and 1638 cm^{-1}; UV (dioxane) λ_{max} 307 nm (ϵ 15 400), 289 (18 400), and 229 (10 300); NMR (100 MHz, $CDCl_3$) δ 7.2–7.7 (m, 4), 6.38 (s, 1), 3.62 (s, 3), 3.32 (AB q, 2, J = 16 Hz, $\Delta\nu_{AB}$ = 54 Hz), and 2.0–2.9 (ABCD m, 4). Anal. Calcd for $C_{15}H_{14}O_3$: C, 74.36; H, 5.82. Found: C, 74.38; H, 5.78.

Methyl 9,9a-Dihydro-3-oxo-3*H*-fluorene-9a-carboxylate (20). A solution of 160 mg (0.66 mmol) of (+)-**19**, $[\alpha]^{RT}{}_{578}$ +313° (c 2.0, benzene), and 181 mg (1.63 mmol) of SeO_2 in 14.1 g of *tert*-butyl alcohol was refluxed for 43 h. Evaporation of the *tert*-butyl alcohol at reduced pressure, filtration of the residue through 15 g of neutral Al_2O_3 with toluene, and short-path distillation (160 °C at 0.02 mm) of the eluate yielded 89 mg of impure **20**, $[\alpha]^{RT}{}_{578}$ −191° (c 1.8, benzene). Analytically pure **20** (52 mg, 33%) was obtained by recrystallization from hexane followed by short-path distillation (125 °C at 0.001 mm): mp 106–124 °C; $[\alpha]^{RT}{}_{578}$ −238° (c 0.5, benzene); IR (Nujol) 1730, 1660, 1638, and 1605 cm^{-1}; UV (dioxane) λ_{max} 314 nm (ϵ 15 000) and 247 (13 600); NMR (60 MHz, $CDCl_3$) δ 7.3–7.8 (m, 4), 6.3–7.2 (ABC m, 3), 3.60 (s, 3), and 3.48 (AB q, 2, J = 16 Hz, $\Delta\nu_{AB}$ = 49 Hz). Anal. Calcd for $C_{15}H_{12}O_3$: C, 74.99; H, 5.04. Found: C, 74.69; H, 5.04.

Acknowledgment. K.H. graciously thanks the Stiftung für Stipendien auf dem Gebiete der Chemie of Switzerland for a grant in support of part of this investigation.

Registry No.—**1a**, 1655-07-8; **1b**, 14160-65-7; **1c**, 69881-56-7; **2**, 78-94-4; (*R*)-(+)-**3a**, 69881-57-8; (*S*)-(−)-**3a**, 69881-58-9; **3b**, 69881-59-0; **3c**, 69881-60-3; **4**, 22955-77-7; (*R*)-5, 69881-61-4; (*S*)-5, 69881-62-5; **6**, 130-95-0; **7**, 56-54-2; **8**, 1301-42-4; **9**, 18797-86-9; **10**, 69881-63-6; **11**, 69881-64-7; **12**, 69927-28-2; **13**, 69307-86-4; **14a**, 68235-49-4; **14b**, 69881-65-8; **14c**, 69927-37-3; **15a**, 69979-91-5; **15b**, 69881-66-9; **15c**, 69881-67-0; **19**, 69881-68-1; **20**, 69881-69-2; **21**, 69881-70-5; **22**, 42982-87-6; diethyl 4-oxoheptanedioate, 6317-49-3.

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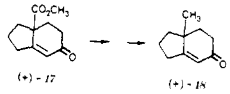

(+)-17 (+)-18

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Reaction of 2,2,4,4-Tetramethylpentane-3-thione *S*-Oxide (Di-*tert*-butylsulfine) with Grignard Reagents

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The reaction of 2,2,4,4-tetramethylpentane-3-thione *S*-oxide with RCH_2MgX gives a thiirane, whereas the reaction with R_2CHMgX affords a sulfide. The reaction with 1,1-dimethylethylmagnesium chloride results in the formation of 2,2,4,4-tetramethylpentane-3-thione. The reactions are interpreted in terms of competitive nucleophilic attack and one-electron-transfer processes: a Grignard reagent from a primary alkylmagnesium halide prefers the nucleophilic attack, whereas a *tert*-alkylmagnesium halide prefers the electron transfer. A *sec*-alkylmagnesium halide is between them in behavior.

Sulfines belong to a class of heterocumulenes and are available by several syntheses.[1,2] Since sulfines have three potentially reactive centers (carbon, sulfur, and oxygen), we can expect a variety of reactions with them. Reactions of aromatic sulfines with dienes,[3] 1,3-dipoles,[4–7] and nucleophiles[8] give sulfoxides. Aryl arylthiosulfines[9] and aryl arylsulfonylsulfines[10] behave similarly. On the other hand, substitution on the sulfinyl carbon is known for chlorosulfines.[9a,11]

Sulfines have also been the subject of interest from the viewpoint of theoretical calculations.[12–17] van Lierop and his co-workers have proposed, based on the ab initio INDO calculations on sulfine and halogenated sulfines, that regardless of the substituent(s) the charges on sulfur and oxygen were almost constant, keeping the S–O grouping as a whole almost neutral.

To extend our understanding on the chemistry of sulfines, it is desirable to study their reactions systematically. The reactions of aliphatic sulfines have been especially ignored,

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Table I. Reaction of 2,2,4,4-Tetramethylpentane-3-thione *S*-Oxide with Grignard Reagents[a]

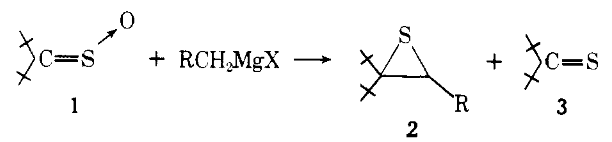
alkyl halide	reaction time, h	products and yields (%) $t\text{-Bu}_2\text{C=S}$	sulfide	other
CH_3I	3	8	**2a**, $t\text{-Bu}_2\overline{\text{C–S–C}}\text{H}_2$ (78)	
C_2H_5I	3	12[b]	**2b**, $t\text{-Bu}_2\overline{\text{C–S–C}}\text{HCH}_3$ (68)[b]	
$CH_2{=}CHCH_2Cl$	4	4	**2c**, $t\text{-Bu}_2\overline{\text{C–S–C}}\text{HCH=CH}_2$ (74)	
$PhCH_2Cl$	2	12	**2d**, $t\text{-Bu}_2\overline{\text{C–S–C}}\text{HPh}$ (62)	
$(CH_3)_2CHCl$	4	5	**4a**, $t\text{-Bu}_2\text{CHSCH(CH}_3)_2$ (81)	$(CH_3)_2CHOH$ (5)
$(c\text{-}C_6H_{11})Cl$	3	9[c]	**4b**, $t\text{-Bu}_2\text{CHS(c-C}_6\text{H}_{11})$ (84)[c]	$(c\text{-}C_6H_{11})OH$ (5) $c\text{-}C_6H_{10}$ (35)
$(CH_3)_3CCl$	12	47		$(CH_3)_3COH$ (20)

[a] Reaction in ether at room temperature. [b] In the presence of 10% CuI, the yields of **2b** and **3** were 59 and 15%, respectively. [c] In the presence of 10% CuI, the yields of **3** and **4b** were 13 and 81%, respectively.

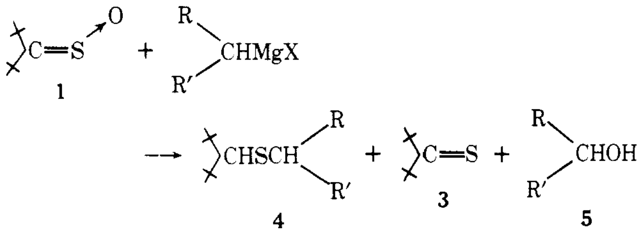
and we have now studied the reactions of 2,2,4,4-tetramethylpentane-3-thione *S*-oxide (di-*tert*-butylsulfine, **1**) with three types of Grignard reagents.

Results

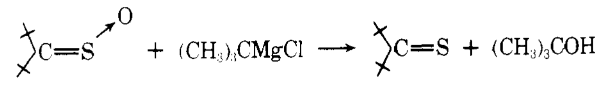
When a Grignard reagent derived form a primary alkyl or aralkyl halide reacted with **1** in ether at room temperature, a thiirane (**2**) was produced with a small amount of 2,2,4,4-tetramethylpentane-3-thione (di-*tert*-butyl thioketone, **3**). No sulfoxide was detected from the reaction mixture even when the Grignard reagent was added dropwise to a solution of excess **1**.



The reaction of a secondary alkylmagnesium halide, on the other hand, resulted in the formation of a sulfide, **4**, with small amounts of **3** and a secondary alcohol, **5**. No thiirane was formed. In order to elucidate the origin of a hydrogen on the methine carbon of the 2,2,4,4-tetramethylpent-3-yl group in **4**, the reaction mixture was quenched by deuterium oxide, and it was found that only 21% of the deuterium was incorporated in the methine position. That is, about 80% of the hydrogen came from the solvent ether.

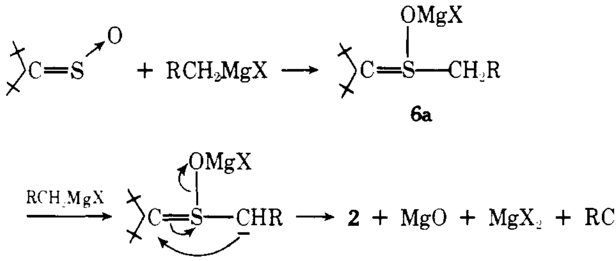


tert-Butylmagnesium chloride did not afford an addition compound. Instead, the reaction with **1** yielded **3** and *tert*-butyl alcohol in 47 and 20% yields, respectively. The results are summarized in Table I.

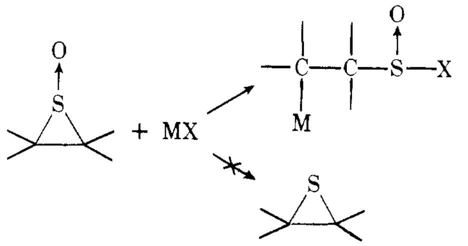


Discussion

Despite the difference in the type of the reaction products, we suggest that all the Grignard reactions reported herein occur by the (primary) interaction between the sulfur–oxygen bond and a Grignard reagent. Namely, the reaction with a primary alkylmagnesium halide can be rationalized by eq 1. The fact that no sulfoxide was isolated even from the reaction mixture with excess **1** indicates that the abstraction of a proton from an intermediate, **6a**, by the second molecule of Grignard reagent takes place quite smoothly. It is known that the attack of a nucleophile or an electrophile on a thiirane *S*-oxide results in the opening of the thiirane ring without extruding the oxygen.[18] The reaction of a primary alkyl Grignard reagent with **3** afforded entirely different products as exemplified by eq 3 and 4.[19] Thus, it seems reasonable to anticipate that the formation of the three-membered ring and the extrusion of oxygen take place simultaneously. Another possibility that **2** is formed by initial attack of a Grignard reagent on the sulfinyl carbon of **1**, proton abstraction, and cyclization (eq 5) is unreasonable, because the proton to be abstracted does not have enough acidity.



(1)



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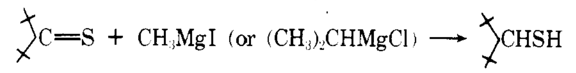

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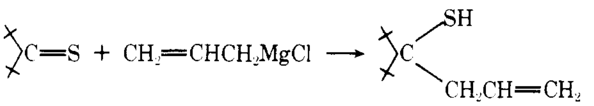

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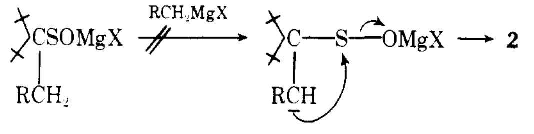

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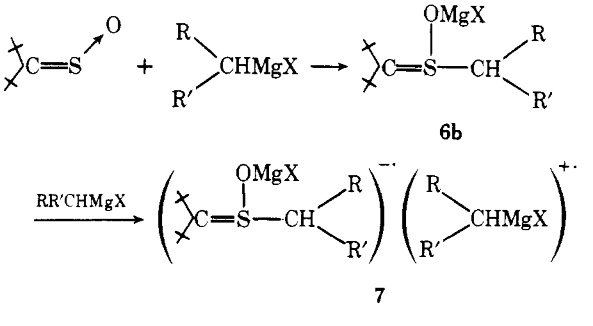
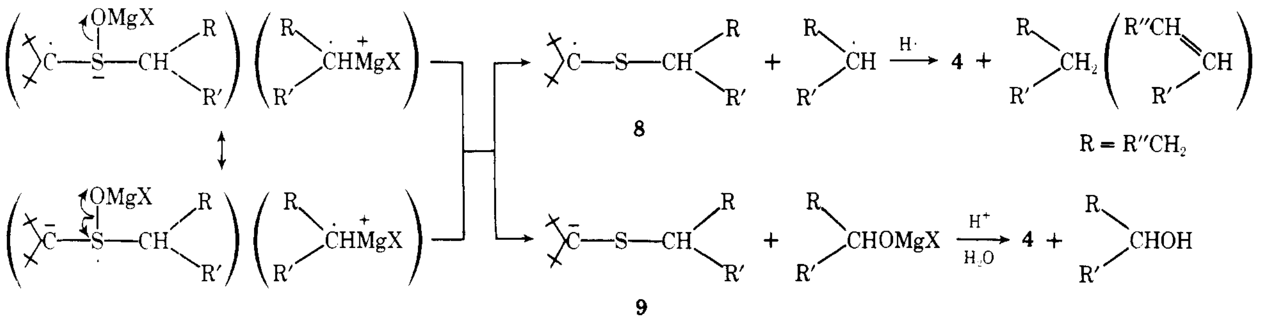


(6)

Scheme I



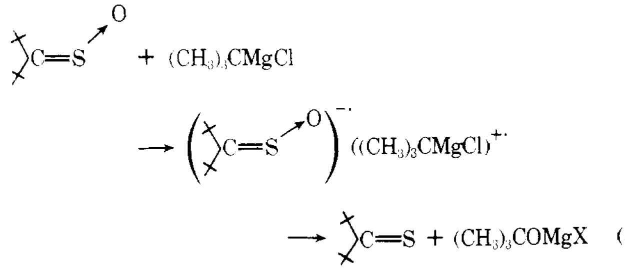
(7a)

(7b)

In the reaction with a secondary alkylmagnesium halide, proton abstraction from an intermediate, **6b**, by the Grignard reagent to afford a thiirane is a reaction between secondary reaction centers, which is a sterically hindered process. Furthermore, a secondary carbanion is less stable than a primary carbanion, and one-electron transfer from the second molecule of the Grignard reagent to **6b** may proceed more easily (eq 6). The tracer experiment with deuterium oxide proves that a carbon radical, **8**, is formed as a major intermediate of the reaction (eq 7a, Scheme I). The formation of cyclohexene in 35% yield in the reaction with cyclohexylmagnesium chloride also supports the radical process. At the same time, the formation of a carbanion intermediate, **9**, can be recognized by the production of alcohol and deuterated **4** (eq 7b). The existence of these intermediates is consistent with the idea of initial formation of a radical–ion pair, **7**. The major formation of **8** from **7** is a reasonable result from the difference in electronegativity of carbon and (oxygen-substituted) sulfur.

It is reported that certain sulfoxides are reduced to the corresponding sulfides by ethylmagnesium bromide containing 10% cuprous iodide, whereas ethylmagnesium bromide by itself does not result in the reduction.[20] Although the mechanism of the reduction has not been confirmed, it is well-known that the addition of transition metal salt to a Grignard reagent promotes the reaction with an electron transfer.[21] Thus, the reduction of **6b** through an electron-transfer process is highly probable.

tert-Butylmagnesium chloride is an efficient reagent for one-electron transfer,[22] and the carbon–magnesium bond in this reagent is less ionic than those in primary and secondary alkylmagnesium halides. Therefore, it is not surprising that the reaction of this reagent with **1** proceeds through a one-electron-transfer process instead of a nucleophilic attack on sulfur (eq 8). The formation of **3** by the reaction with other



(8)

Grignard reagents suggests that one-electron transfer and nucleophilic attack are competitive processes. Although not appreciable, the presence of 10% cuprous iodide in the reaction of **1** with ethylmagnesium iodide or cyclohexylmagnesium chloride shows the tendency to increase the yield of **3** at the sacrifice of the yield of a sulfide.

The reactions of methyllithium and ethyllithium with **1** also afforded the corresponding thiirane in 84 and 88% yields, respectively. All reactions of **1** reported herein have revealed that the sulfur–oxygen bond is attacked by the carbon nucleophiles forming an oxygen anion. The observation is in marked contrast to that in the reaction of aromatic sulfines,[8–10] where the corresponding sulfoxide is formed by the reaction of the sulfur–carbon bond. The difference can be accounted for by the stability of an intermediate: when the sulfinyl carbon is substituted by two aromatic groups or their equivalents,[23] the intermediate anion can be stabilized with a large electron density on the sulfinyl carbon. Whereas, when the sulfinyl carbon is substituted by two alkyl groups as in the case of **1**, the resulting carbanion is destabilized by substituents, and the formation of the oxygen anion is energetically more favored.

Experimental Section

Materials. 2,2,4,4-Tetramethylpentane-3-thione[24] and 2,2,4,4-tetramethylpentane-3-thione *S*-oxide[25] were prepared according to literature procedures. Ether was dried over sodium wires and distilled prior to use. Deuterium oxide (99.8% D) was purchased from Merck & Co., Inc.

General Procedure. All reactions were carried out under a nitrogen atmosphere at room temperature (about 25 °C) with stirring. To 4 mmol of a Grignard reagent in 10 mL of ether was added 2 mmol of **1** in 10 mL of ether, or vice versa. No difference was recognized in the result by the change of the addition order. At the end of the reaction, 6 N hydrochloric acid was added to the reaction mixture. The ether layer was separated from the aqueous layer and washed with water. The combined ethereal solution was dried over sodium sulfate. After the solvent was evaporated in vacuo, the residue was subjected to column chromatography over silica gel with hexane–benzene (4:1 v/v) as an eluent. Analytically pure products were obtained by means of preparative VPC on a Varian Aerograph 920. The yields listed in Table I are isolated yields. Yields for alcohols were determined on VPC (Yanagimoto G-1800, PEG 20%, 60–75 °C) with ethylbenzene as an internal standard.

The reactions with ethylmagnesium iodide and cyclohexylmagnesium chloride were also carried out in the presence of 0.4 mmol of cuprous iodide. The yields of products from these reactions were determined on VPC (Yanagimoto G-1800, OV-17 5%, 1.5 m, 150 °C).

The structures of products were confirmed by the identity of spectral data with those of authentic samples (except for **2b** and **2c**). Thiiranes **2a** and **2d** were prepared from 2,2,4,4-tetramethylpentane-3-thione with trimethylsulfoxonium iodide in the Wittig reaction[26] and with phenyldiazomethane, respectively. Sulfides **4a** and **4b** were obtained by the reaction of 2,2,4,4-tetramethylpentane-3-thiol with the corresponding alkyl chloride.

Physical Properties. 2a: yellow liquid; NMR (CDCl$_3$, Me$_4$Si) δ 1.16 (s, 18 H) and 2.38 (s, 2 H); MS (M$^+$) *m/e* 172. **2b:** yellow liquid; NMR δ 1.17 (s, 9 H), 1.27 (s, 9 H), 1.67 (d, 3 H), and 3.13 (q, 1 H); MS 186. **2c:** yellow liquid; NMR δ 1.22 (s, 9 H), 1.26 (s, 9 H), 3.57 (d, 1 H), 5.06–5.62 (m, 2 H), and 5.94–6.49 (m, 1 H); MS 198. **2d:** mp 67 °C (uncorrected); NMR δ 1.00 (s, 9 H), 1.21 (s, 9 H), 4.27 (s, 1 H), and 7.20–7.50 (m, 5 H); MS 248. **4a:** colorless liquid; NMR δ 1.16 (s, 18 H), 1.32 (d, 6 H), 1.84 (s, 1 H), and 2.41–2.96 (m, 1 H); MS 202. **4b:** colorless liquid; NMR δ 1.16 (s, 18 H), 2.24 (s, 1 H), and 0.72–2.67 (m, 11 H); MS 242.

Anal. Calcd for $C_{10}H_{20}S$ (**2a**): C, 69.70; H, 11.70. Found: C, 69.48; H, 11.51. Calcd for $C_{11}H_{22}S$ (**2b**): C, 70.89; H, 11.90. Found: C, 70.47; H, 12.14. Calcd for $C_{12}H_{22}S$ (**2c**): C, 72.66; H, 11.18. Found: C, 72.51; H, 11.40. Calcd for $C_{16}H_{24}S$ (**2d**): C, 77.36; H, 9.68. Found: C, 77.48; H, 9.91. Calcd for $C_{12}H_{26}S$ (**4a**): C, 71.21; H, 12.95. Found: C, 71.42; H, 13.04. Calcd for $C_{15}H_{30}S$ (**4b**): C, 74.93; H, 11.74. Found: C, 74.77; H, 11.70.

Tracer Experiment. 2,2,4,4-Tetramethylpentane-3-thione *S*-oxide and 2-propylmagnesium chloride were reacted in ether as described above. The reaction mixture was poured into a saturated deuterium oxide solution of ammonium chloride and the ether layer was worked up as described above. The deuterium content in **4a** was analyzed on a Varian T-60 NMR and Shimadzu LKB-9000S GC–MS spectrometers to be 21 ± 1%.

Reaction of 2,2,4,4-Tetramethylpentane-3-thione with Alkylmagnesium Halide. A Grignard reagent made from methyl iodide or 2-propyl chloride was reacted with the thioketone, **3,** under the same condition as described above. After the usual workup, 2,2,4,4-tetramethylpentane-3-thiol[25] was isolated in 82 or 74% yield, respectively. The Grignard reaction of **3** with allylmagnesium chloride afforded 2,2-dimethyl-3-(1′,1′-dimethylethyl)hex-5-ene-3-thiol in 92% yield as a yellow liquid: NMR ($CDCl_3$, Me_4Si) δ 1.16 (s, 9 H), 1.19 (s, 9 H), 1.34 (s, 1 H), 2.50–2.77 (m, 2 H), 4.84–5.13 (m, 1 H), and 5.92–6.37 (m, 2 H); MS (M^+) *m/e* 200.

Anal. Calcd for $C_{12}H_{24}S$: C, 71.93; H, 12.07. Found: C, 71.94; H, 12.05.

Reaction of 2,2,4,4-Tetramethylpentane-3-thione *S*-Oxide with Alkyllithium. The reactions were carried out similarly to the Grignard reactions described above. The products were identical with those obtained from the reactions of the corresponding Grignard reagents.

Registry No.—**1**, 56956-24-3; **2a,** 69912-55-6; **2b,** 69912-52-3; **2c,** 69912-53-4; **2d,** 69912-54-5; **3,** 54396-69-9; **4a,** 65566-46-3; **4b,** 69543-45-9; 2,2-dimethyl-3-(1′,1′-dimethylethyl)hex-5-en-3-thiol, 65566-36-1; methyl iodide, 74-88-4; ethyl iodide, 75-03-6; allyl chloride, 107-05-1; benzyl chloride, 100-44-7; 2-propyl chloride, 75-29-6; cyclohexyl chloride, 542-18-7; *tert*-butyl chloride, 507-20-0; 2-propanol, 67-63-0; cyclohexanol, 108-93-0; cyclohexene, 110-83-8; *tert*-butanol, 75-65-0; trimethylsulfoxonium iodide, 1774-47-6; phenyldiazomethane, 766-91-6; 2,2,4,4-tetramethylpentane-3-thiol, 57602-97-8.

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Separation of Diastereomers Using a Low Cost Preparative Medium-Pressure Liquid Chromatograph

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A series of diastereomeric oxazolines (**2** and **5**) derived from asymmetric addition of organometallics to the prochiral oxazolines **1** and **4** have been examined on an efficient preparative liquid chromatograph. The pure diastereomers were readily obtained using this component system, and enantiomerically pure acids **3** and **6** were isolated. It is suggested that $[\alpha]_D$ values for pure chiral products be recorded only after this separation scheme is employed. Details for the construction of the liquid chromatograph and its operation are given.

In the course of studying and developing new methodology for asymmetric syntheses, the efficiency of the asymmetric induction is usually evaluated by comparing the specific rotation of the synthetic product with that reported by others, mainly from resolution methods. The tedious procedures associated with repeated crystallization of diastereomeric precursors has, in the main, restricted the scope of asymmetric methodology to those compounds whose specific rotations have been described in the literature, and this has had a regressive effect upon this area of study. Furthermore and probably more significant is the tendency of workers in asymmetric synthesis to rely heavily upon the extent of enantiomeric purity based on optical rotation data. The inherent danger of using *only* optical rotations has already been described by Valentine and Scott,[1] who urged investigators to consider "direct methods to determine the enantiomeric excess of many typical asymmetric synthesis products". The advent of chiral shift reagents and chiral solvents has done much to facilitate enantiomeric determination of chiral products, but this is limited to certain structural features

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