Evaporation gave a residue, which solidified on standing overnight. HPLC analysis of the crude dipeptide (μPorasil, 3.9 × 30 mm) gave a single peak, t_R 5.76 min (85:15 hexane:2-propanol). The D,L-dipeptide prepared analagously had a retention of 6.41 min. In this manner we observed less than 0.2% of the D,L-dipeptide in our sample, thus reflecting >99.8% optical purity for our O-alkylated tyrosine.

Acknowledgment. We are grateful to Edith Reich for microanalyses and optical rotations; D. Staiger, G. Zuber, G. D. Roberts and L. B. Killmer provided NMR and mass spectra. We express appreciation to Monica M. Holmes for her technical assistance.

Registry No. L-1, 3978-80-1; D-1, 70642-86-3; L-2, 1164-16-5; CH_3Br, 74-83-9; CH_3I, 74-88-4; C_2H_5Br, 74-96-4; C_2H_5I, 75-03-6; n-C_3H_7Br, 106-94-5; n-C_3H_7I, 107-08-4; sec-C_4H_9Br, 78-76-2; sec-C_4H_9I, 513-48-4; c-C_5H_9Br, 137-43-9; i-C_3H_7Br, 75-26-3; t-Boc-L-Tyr(OEt)-L-Phe-OMe, 87190-95-2; t-Boc-D-Tyr(OEt)-L-Phe-OMe, 87190-96-3; t-Boc-L-tyrosine methyl ether, 53267-93-9; t-Boc-L-tyrosine ethyl ether, 76757-91-0; t-Boc-D-tyrosine ethyl ether, 76757-92-1; t-Boc-L-tyrosine propyl ether, 76757-93-2; t-Boc-L-tyrosine sec-butyl ether dicyclohexylamine salt, 87190-91-8; t-Boc-L-tyrosine cyclopentyl ether, 82152-22-5; Cbz-L-tyrosine ethyl ether, 66147-90-8; Cbz-L-tyrosine isopropyl ether, 87190-92-9; Cbz-L-tyrosine cyclopentyl ether dicyclohexylamine salt, 87190-94-1; cyclohexyl bromide, 108-85-0; L-phenylalanine methyl ester, 2577-90-4.

Addition of Piperidine to Some 2-Alkylbenzo[*b*]thiophene 1,1-Dioxides

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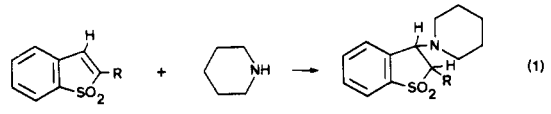
Received March 16, 1983

Within the framework of our systematic studies of the chemistry[1a] and photochemistry[1b] of the benzo[*b*]thiophene system, it was of interest to prepare 3-piperidino-2-methyl-2,3-dihydrobenzo[*b*]thiophene. The addition of piperidine to 2-methylbenzo[*b*]thiophene 1,1-dioxide followed by the reduction of the adduct with lithium aluminum hydride[2] appeared to be the appropriate synthetic sequence. Benzo[*b*]thiophene 1,1-dioxide (**1a**),[3] its 2-bromo derivative **1b**,[4] and the 2-phenyl derivative **1c**[5] undergo addition reactions in a manner comparable to other α,β-unsaturated sulfones. In all these cases, the formation of a carbon–nitrogen bond takes place at the 3-position in the benzo[*b*]thiophene ring (eq 1).



(1)

1a, R = H; **1b**, R = Br; **1c**, R = C_6H_5

2a; **2b**; **2c**

(1) (a) Grandclaudon, P.; Lablache-Combier, A. *J. Org. Chem.* **1978**, *43*, 4379. (b) Grandclaudon, P.; Lablache-Combier, A. *J. Chem. Soc. D* **1971**, 892. Grandclaudon, P.; Lablache-Combier, A.; Párkányi, C. *Tetrahedron* **1973**, *29*, 651. Lablache-Combier, A.; Lerner, D.; Pollet, A. *J. Chem. Res. Synop.* **1978**, 38; *J. Chem. Res., Miniprint* **1978**, 281–286.

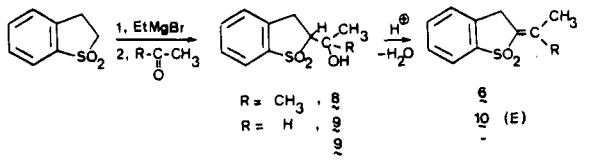
(2) Van Zyl, G.; de Jongh, D. C.; Heasley, V. L.; Van Dyke, J. W. *J. Org. Chem.* **1961**, *26*, 4946.

(3) Bordwell, F. G.; McKellin, W. H. *J. Am. Chem. Soc.* **1950**, *72*, 1985.

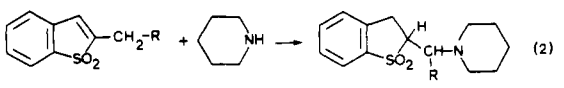
(4) Bordwell, F. G.; Lampert, B. B.; MeKellin, W. H. *J. Am. Chem. Soc.* **1949**, *71*, 1702.

(5) Centre d'Etudes pour l'Industrie Pharmaceutique, Ger. Offen. 1973, 2341894; *Chem. Abstr.* **1974**, *80*, 146007*f*.

Scheme I



However, reaction of the 2-alkylbenzo[*b*]thiophene 1,1-dioxides **1d** or **1e** with piperidine resulted in the formation of the unexpected adducts **3** and **4**, respectively, in which the amino group is bonded to the α-carbon atom of the side chain (eq 2). The addition reaction is slow, but the conversion of the starting sulfone is nearly quantitative within 100 h.[6]



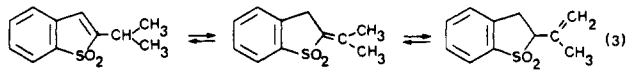
(2)

1d, R = H; **1e**, R = CH_3

3; **4**

Two adjacent centers of asymmetry are present in the compound **4**, resulting in erythro and threo diastereoisomers. The VPC and TLC analyses and ^1H and ^{13}C NMR spectra confirmed the formation of only one diastereoisomer but do not allow an unequivocal assignment of configuration. Compound **4** was subsequently identified as the threo diastereoisomer by single-crystal X-ray analysis.[7]

Treatment of 2-isopropylbenzo[*b*]thiophene 1,1-dioxide (**1f**) with piperidine or triethylamine gave a mixture of isomeric olefins in which the major product was the exocyclic olefin **6** (eq 3). Attempted isomerization of **1d** and **1e** in refluxing triethylamine resulted in a quantitative recovery of the starting material even after 2 weeks.



(3)

1f; **6**; **7**

We suggest that a rapid base-catalyzed isomerization of the sulfones **1d** and **1e** precedes the slow addition of the amine to the most reactive exocyclic olefins. The failure of the hindered **6** to add piperidine is consistent with the results of Stirling et al.[8] who have clearly shown the effect of the substitution in decreasing the reactivity of the double-bond toward amines. Because it cannot be obtained by isomerization, it was of interest to prepare the exocyclic olefin **10** by an alternate route. This was accomplished by the sequence depicted in Scheme I.

The metalation of 2,3-dihydrobenzo[*b*]thiophene 1,1-dioxide has been achieved with ethylmagnesium bromide[3] or n-butyllithium[9] with the same results. Condensation with acetaldehyde gave a 50:50 mixture of the threo[10] and erythro β-hydroxy sulfones **9**. Compound **8** was readily converted into **6** in a high yield by acid-catalyzed dehydration. The differences in the behavior of the threo and erythro β-hydroxy sulfones observed by Truce and Klinger[9] were also found in the case of **9**. The erythro isomer was converted into **10**, but the threo isomer was recovered

(6) Addition of cyclohexylamine is much slower[13] but leads to similar adducts.

(7) Abraham, F.; Trehoux, J.; Grandclaudon, P. *Acta Crystallogr., Sect C* **1983**, *39*, 483.

(8) McDowell, S. T.; Stirling, C. J. M. *J. Chem. Soc. B* **1967**, 351.

(9) Truce, W. E.; Klinger, T. C. *J. Org. Chem.* **1970**, *35*, 1834.

(10) The threo diastereoisomer of **9** was identified by single-crystal X-ray analysis. Trehoux, J.; Abraham, F.; Grandclaudon, P. *Acta Crystallogr., Sect C*, in press.

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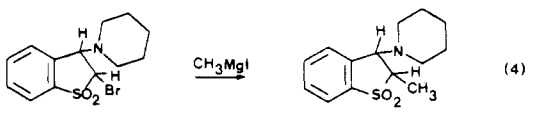
unchanged after 1 h or else underwent decomposition after a longer time. Compound **10** was shown to be the *E* olefin by comparison of its ^1H NMR spectrum with that of **6**. The methyl group of **10** has a chemical shift of 1.90 ppm, similar to that of methyl group trans to the sulfone group in **6**, i.e., 1.95 ppm (the other methyl group cis to the sulfone group is deshielded[11]). The complete isomerization of **10** into **1e** has been readily achieved with piperidine together with formation of a small amount of the adduct **4**.[12] This is consistent with a fast isomerization and a slow addition of the amine. The formation of the threo diastereoisomer of **4** as the only isomer may proceed through a cis addition of the amine to *E*-exocyclic olefin **10**, resulting from the isomerization of **1e**. This is compatible with the concerted process of addition suggested earlier[4,13,14] in which two molecules of an amine are involved.

The synthesis of one of the desired adducts **5** was accomplished by the reaction of methylmagnesium iodide with the bromo derivative **2b**[4] (eq 4). The adduct **5** was obtained in a poor yield together with the dehydrohalogenation product.



(4)

2b 5

Experimental Section

All melting points are uncorrected. ^1H NMR spectra were recorded in $CDCl_3$ with Me_4Si as an internal standard on a Brucker WP 60 spectrometer, and ^{13}C NMR spectra on a Brucker WP 80 spectrometer. Mass spectra were determined on a Ribermag 10.10 spectrometer. VPC analyses were performed on a Girdel 300 Chromatograph (column packed with 3% SE-30 on Chromosorb W).

Starting Materials. Alkylbenzo[*b*]thiophenes were synthesized and oxidized to the corresponding sulfones according to standard procedures: 2-methyl (**1d**);[15,16] 2-ethyl (**1e**);[16,17] 2-isopropyl (**1f**).[18]

2-(Piperidinomethyl)-2,3-dihydrobenzo[*b*]thiophene 1,1-Dioxide (3). A solution of the sulfone **1d** (1.1 g, 6 mmol) in piperidine (15 mL) was refluxed for 100 h. Evaporation of the amine and dilution with water gave a solid residue. Compound **3** was obtained by crystallization in acetone–water: 1.45 g (90%); mp 84–85 °C; ^1H NMR ($CDCl_3$)[19] δ 1.5 (m, 6 H), 2.45 (m, 4 H), 2.7 (dq, 1 H, $J_{2,3}$ = 6 Hz, $J_{3,3'}$ = 13 Hz, C_3 H), 3.0 (dq, 1 H, $J_{2,3'}$ = 9 Hz, $J_{3,3'}$ = 13 Hz, C_3 H), 3.2 (dq, 1 H, $J_{1,2}$ = 7.5 Hz, $J_{1,1'}$ = 16.5 Hz, CH_2N), 3.5 (dq, 1 H, $J_{1',2}$ = 7.5 Hz, $J_{1,1'}$ = 16.5 Hz, CH_2N), 3.7 (m, 1 H, C_2 H), 7.3–7.7 (m 4 H, aromatic H); ^{13}C NMR ($CDCl_3$) 31.3 (C_3), 58.9 (C_2), 56.3 (CN) ppm; mass spectrum, *m/e* (relative intensity) 265 (M^+, 10), 98 (100).

Anal. Calcd for $C_{14}H_{19}NO_2S$: C, 63.36; H, 7.21; N, 5.27; O, 12.06; S, 12.09. Found: C, 63.35; H, 7.23; N, 5.40; O, 11.98; S, 11.88.

2-(1-Piperidinoethyl)-2,3-dihydrobenzo[*b*]thiophene 1,1-Dioxide (4). Reaction of **1e** (1.15 g, 6 mmol) with piperidine and separation of the adduct **4** as previously described: 1.6 g (96%); mp 177–178 °C; ^1H NMR ($CDCl_3$)[19] δ 1.1 (d, 3 H, J_{1,CH_3} = 6.8 Hz, CH_3), 1.5 (m, 6 H), 2.55 (m, 4 H), 2.95 (dq, 1 H, $J_{2,3}$ = 7.5 Hz, $J_{3,3'}$ = 16 Hz, C_3 H), 3.2 (dq, 1 H, $J_{2,3'}$ = 10.5 Hz, $J_{3,3'}$ = 16 Hz, C_3 H), 3.3 (m, 1 H, C_2 H), 3.65 (dq, 1 H, $J_{1,2}$ = 10.5 Hz, J_{1,CH_3} = 6.8 Hz, CHN), 7.2–7.7 (m, 4 H, aromatic H); ^{13}C NMR ($CDCl_3$) 10.3 (CH_3), 30.6 (C_3), 58.9 (C_2), 64.6 (CN) ppm; mass spectrum, *m/e* (relative intensity) 279 (M^+, 15), 112 (100).

Anal. Calcd for $C_{15}H_{21}NO_2S$: C, 64.48; H, 7.57; N, 5.01; O, 11.45; S, 11.46. Found: C, 64.32; H, 7.50; N, 5.06; O, 11.91; S, 11.62.

3-Piperidino-2-methyl-2,3-dihydrobenzo[*b*]thiophene 1,1-Dioxide (5). To a Grignard reagent prepared from 0.18 g (7.5 mmol) of magnesium turnings and 1.07 g (7.5 mmol) of methyl iodide in anhydrous THF (25 mL) was added with stirring 1.9 g (6 mmol) of **2b**[4] in THF (50 mL). After being stirred for 6 h, the solution was poured into water and the organic phase separated and dried. The solvent was removed and the residue submitted to chromatography (SiO_2, toluene–ethyl acetate, 2:1). 3-Piperidinobenzo[*b*]thiophene 1,1-dioxide and numerous byproducts were discarded, and **5** was recrystallized in heptane–toluene: 0.175 g (11%); mp 111–113 °C; ^1H NMR ($CDCl_3$) δ 1.5 (m, 6 H), 1.55 (d, 3 H, CH_3), 2.55 (m, 4 H), 3.6 (m, 1 H, C_2 H), 4.1 (dq, 1 H, C_3 H), 7.5–7.9 (m, 4 H, aromatic H).

Anal. Calcd for $C_{14}H_{19}NO_2S$: C, 63.36; H, 7.21; N, 5.27; O, 12.06; S, 12.09. Found: C, 63.21; H, 7.40; N, 5.29; O, 11.99; S, 12.10.

Isomerization of 1f. Compound **1f** (1.25 g, 6 mmol) was refluxed in piperidine or triethylamine (15 mL) for 100 h. The ratio of **1f**:6:7 was estimated by VPC analysis as 15:75:10. After evaporation of the amine, the mixture (1.20 g) was hydrogenated in the presence of 5% Pd/C to furnish only 2-isopropyl-2,3-dihydrobenzo[*b*]thiophene 1,1-dioxide (**11**): 1.12 g (93%); recrystallization in toluene–cyclohexane; mp 132–133 °C; ^1H NMR ($CDCl_3$) δ 1.15 (d, 3 H, CH_3), 1.25 (d, 3 H, CH_3), 2.3 (m, 1 H, $CH(CH_3)_2$), 2.9–3.5 (m, 3 H, C_2 H and C_3 H), 7.3–7.8 (m, 4 H, aromatic H); mass spectrum, *m/e* (relative intensity) 210 (M^+, 8), 91 (100).

Anal. Calcd for $C_{11}H_{14}O_2S$: C, 62.83; H, 6.71; O, 15.22; S, 15.25. Found: C, 62.54; H, 6.71; O, 15.48; S, 15.25.

2-(2-Hydroxyisopropyl)-2,3-dihydrobenzo[*b*]thiophene 1,1-Dioxide (8). A solution of 2.5 g (15 mmol) of 2,3-dihydrobenzo[*b*]thiophene 1,1-dioxide[3] in 70 mL of dry benzene was added with stirring to a Grignard reagent prepared from 0.49 g (20 mmol) of magnesium turnings and 2.22 g (20 mmol) of ethyl bromide. The mixture was refluxed for 2 h and then cooled. Acetone (0.87 g, 15 mmol) was added, and stirring was continued for 2 h. After hydrolysis, extraction, and evaporation of the solvent, **8** was recrystallized in toluene–CCl_4: 2.2 g (65%); mp 90–91 °C; ^1H NMR ($CDCl_3$) δ 1.25 (s, 3 H, CH_3), 1.65 (s, 3 H, CH_3), 3.0–3.7 (m, 3 H, C_2 H and C_3 H), 7.3–7.7 (m, 4 H, aromatic H).

Anal. Calcd for $C_{11}H_{14}O_3S$: C, 58.38; H, 6.23; O, 21.21; S, 14.17. Found: C, 58.43; H, 6.20; O, 21.02; S, 13.86.

2-(1-Hydroxyethyl)-2,3-dihydrobenzo[*b*]thiophene 1,1-Dioxide (9). Prepared from 2,3-dihydrobenzo[*b*]thiophene 1,1-dioxide and ethanal as previously described. A yield of 2.25 g (71%) of an oily mixture of the threo and erythro diastereoisomers was obtained (ratio estimated by VPC analysis to be 50:50). TLC separation (SiO_2, toluene–ethyl acetate, 3:1) gave *threo*-**9** [mp 148–149 °C (recrystallization in toluene–cyclohexane); ^1H NMR ($CDCl_3$) δ 1.5 (d, 3 H, CH_3), 3.1 (s, 1 H, OH), 3.3–3.6 (m, 3 H, C_2 H and C_3 H), 4.3 (m, 1 H, CHO), 7.4–7.9 (m, 4 H, aromatic H); X-ray analysis[10]] and *erythro*-**9** [oil; ^1H NMR ($CDCl_3$) δ 1.35 (d, 3 H, CH_3), 3.35 (m, 3 H, C_2 H and C_3 H), 3.4 (s, 1 H, OH), 4.5 (m, 1 H, CHO), 7.4–7.9 (m, 4 H, aromatic H)].

Anal. Calcd for $C_{10}H_{12}O_3S$: C, 56.60; H, 5.66; O, 22.64; S, 15.09. Found: C, 56.65; H, 5.80; O, 22.61; S, 15.05.

2-Isopropylidene-2,3-dihydrobenzo[*b*]thiophene 1,1-Dioxide (6). A solution of 0.57 g (25 mmol) of **8** in xylene was refluxed with 1 drop of H_2SO_4 for 3 h, poured into ice–water, and extracted with CH_2Cl_2. Recrystallization in heptane–toluene gave **6**: 0.31 g (60%); mp 213–214 °C; ^1H NMR ($CDCl_3$) δ 1.95 (t, 3 H, ^5J = 2 Hz, CH_3 trans/SO_2), 2.3 (s, 3 H, CH_3 cis/SO_2), 3.85 (m, 2 H, C_3 H), 7.3–7.9 (m, 4 H, aromatic H); mass spectrum, *m/e* (relative intensity) 208 (M^+, 42), 129 (100).

Anal. Calcd for $C_{11}H_{12}O_2S$: C, 63.43; H, 5.81; O, 15.36; S, 15.40. Found: C, 63.37; H, 5.91; O, 15.13; S, 15.47.

(*E*)-2-Ethylidene-2,3-dihydrobenzo[*b*]thiophene 1,1-Dioxide (10). Dehydration of *erythro*-**9** as above: 0.29 g (60%); mp 118–119 °C; ^1H NMR ($CDCl_3$) δ 1.9 (dt, 3 H, ^3J = 7 Hz, ^5J = 1.7 Hz, CH_3), 3.85 (m, 2 H, C_3 H), 6.7 (m, 1 H, ^3J = 7 Hz, ^4J

(11) Elvidge, J. A. *J. Chem. Soc. C* **1967**, 2656.
(12) Three hours in refluxing piperidine.
(13) McDowell, S. T.; Stirling, C. J. M. *J. Chem. Soc. B* **1967**, 343.
(14) Shenhav, H.; Rappoport, Z.; Patai, S. *J. Chem. Soc. B* **1970**, 469.
(15) Shirley, D. A.; Cameron, M. D. *J. Am. Chem. Soc.* **1952**, *74*, 664.
(16) Karaulova, E. N.; Meilanova, D. Sh.; Gal'pern, G. D. *Dokl. Akad. Nauk. SSSR* **1958**, *123*, 99; *Chem. Abstr.* **1959**, *53*, 5229.
(17) Royer, R.; Demerseman, P.; Cheutin, A. *Bull. Soc. Chim. Fr.* **1961**, 1534.
(18) Bedell, S. F.; Spaeth, E. C.; Bobbitt, J. M. *J. Org. Chem.* **1962**, *27*, 2026.
(19) The 250-MHz NMR spectrum was recorded on a Cameca TSN 250 spectrometer.

= 2.5 Hz, =CH), 7.5–8.0 (m, 4 H, aromatic H); mass spectrum, *m/e* (relative intensity) 194 (M^+, 100).

Anal. Calcd for $C_{10}H_{10}O_2S$: M_r, 194.0373. Found (high-resolution mass spectrum) M_r, 194.0401.

Registry No. **1d**, 6224-55-1; **1e**, 17347-06-7; **1f**, 87071-05-4; **2b**, 87071-06-5; **3**, 87071-07-6; *threo*-**4**, 87071-08-7; **5**, 78583-20-7; **6**, 87071-09-8; **7**, 87071-10-1; **8**, 87071-11-2; *threo*-**9**, 87071-12-3; *erythro*-**9**, 87071-13-4; (*E*)-**10**, 87071-14-5; 2,3-dihydrobenzo[*b*]-thiophene 1,1-dioxide, 14315-13-0; piperidine, 110-89-4.

Copper(I)-Catalyzed Reactions of β,γ-Epoxy Alcohols with Grignard Reagents

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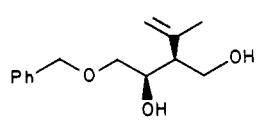
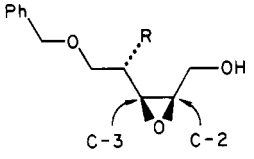
Received May 19, 1983

An ongoing synthetic project required the synthesis of diol **1**. A general procedure for the directed cleavage of



1



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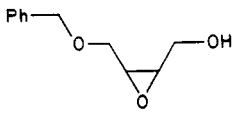
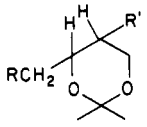


3

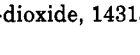
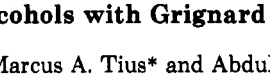


6

sterically unbiased epoxy alcohols with copper(I)-catalyzed Grignard reagents will be described. The regiospecific ring opening of epoxy alcohols has been used to great advantage by Kishi and others.[1] Attack on **2** (R = CH_3) by lithium dimethylcuprate takes place specifically and in excellent yield at C-2. The regiochemical preference observed in this case appears to be steric in origin because treatment of **2** (R = H) under identical conditions leads to an indiscriminate reaction in which equal amounts of 1,2- and 1,3-diol are formed.[2] We will show that regioselective reactions at C-2 of **2** and related epoxy alcohols can be observed by judicious choice of reaction conditions.

The effect of temperature upon the reaction of **3** with lithium dimethylcuprate in ether was examined. Modest regioselectivity in the desired sense was observed at −20 °C (Table I). Lowering the temperature led to an increase in regioselectivity while greatly diminishing the reaction rate. Diisopropenylcuprate (entry 2) was a more sluggish reagent than dimethylcuprate. An acceptable rate could only be achieved by conducting the reaction at −20 °C. Selectivity and yield were poor. The complex derived from diisobutylaluminum chloride and 2 equiv of 2-propenyllithium[3] (entry 3) showed no selectivity. We were disappointed to find that the higher order cyanocuprate[4] (entry 4) in our hands produced only intractable mixtures of products.

Table I. Reactions of 3 with Carbon Nucleophiles

entry	reagent	conditions	ratio[a] of 1,3-diol:1,2-diol
1	$(CH_3)_2CuLi$	3 equiv, ether; −20 °C, 10 min	1.5:1
		3 equiv, ether; −60 °C, 2 h	2.5:1[b]
2		4 equiv, ether; −20 °C, 4 h; 0 °C, 1 h	2:1
3		4 equiv, hexane; −20 °C, 1 h	1:1[3]
4		4 equiv, THF; −20 °C, 2 h	*c*, ref 4

[a] Ratios were determined by HPLC with a refractive index detector. The ratios determined by product isolation agreed closely with the HPLC ratios. [b] More than 50% of unreacted starting material was also recovered. [c] Complex mixture of products was obtained.

An encouraging result was obtained with the reagent derived from 2-propenylmagnesium bromide and 0.1 equiv of cuprous iodide (Table II). For determination of the scope of the copper-catalyzed Grignard reaction, a series of epoxy alcohol benzyl ethers, **2** (R = H), **4**, and **5**, was prepared, and their reactions with four Grignard reagents were investigated.[5] The choice of epoxy alcohols was made to test the limits of the reaction. All four compounds lack any stereochemical bias for attack of the epoxide and all have potentially troublesome benzyl ethers that could direct the incoming nucleophile to C-3. In all instances the 1,3-diol resulting from nucleophilic attack at C-2 was the major product. The highest selectivity was 7:1, the lowest was 2.2:1. Even in the least selective case the isolated yield of 1,3-diol was 58% so that the method remained preparatively useful. Although it was reasonable to assume inversion of configuration at C-2, alternative mechanisms could not be ruled out.[6] All 1,3-diols were converted to their acetonides **6**.[7] As expected, diols derived from epoxy alcohols **4** and **5** formed acetonides more rapidly than diols derived from **2** and **3**. The vicinal coupling constants for the methine protons were measured by irradiating the exocyclic methylene group of the acetonides in the 300-MHz NMR spectra. All acetonides derived from (*Z*)-epoxy alcohols **2** and **3** had coupling constants of ca. 3 Hz whereas the acetonides derived from **4** and **5** had coupling constants of ca. 10 Hz.[8] These results are consistent with an inversion of configuration at C-2. It seems likely that the epoxy alcohol directs nucleophilic attack at C-2.[1a]

The selectivity of the reaction is maintained only within a narrow range of conditions. Lower temperatures clearly favor the 1,3-diol but diminish the reaction rate. A compromise between selectivity and an acceptable rate is reached by conducting reactions with vinylic Grignard reagents at −20 to −25 °C and reactions with alkyl Grignard

(1) (a) Johnson, M. R.; Nakata, T.; Kishi, Y. *Tetrahedron Lett.* **1979**, 4343. (b) Johnson, M. R.; Kishi, Y. *Ibid.* **1979**, 4347. (c) Nagaoka, H.; Rutsch, W.; Schmid, G.; Iio, H.; Johnson, M. R.; Kishi, Y. *J. Am. Chem. Soc.* **1980**, *102*, 7962. (d) Katsuki, T.; Lee, A. W. M.; Ma, P.; Martin, V. S.; Masamune, S.; Sharpless, K. B.; Tuddenham, D.; Walker, F. J. *J. Org. Chem.* **1982**, *47*, 1373. (e) Finan, J. M.; Kishi, Y. *Tetrahedron Lett.* **1982**, *23*, 2719.

(2) Treatment of **2** (R = H) with dimethylcuprate in ether at −40 °C produces a 1:2 ratio of 1,3- and 1,2-diols.

(3) Ashby, E. C.; Laemmle, J. T. *Chem. Rev.* **1975**, *75*, 521.

(4) Lipshutz, B. H.; Kozlowski, J.; Wilhelm, R. S. *J. Am. Chem. Soc.* **1982**, *104*, 2305.

(5) For the preparation of the Grignard reagents, see: Luche, J. L.; Damiano, J. C. *J. Am. Chem. Soc.* **1980**, *102*, 7926.

(6) Equilibration of the epoxy alcohol by base prior to attack by the nucleophile could not be ruled out.[1d]

(7) All compounds gave satisfactory ^1H NMR, IR, and mass spectra.

(8) Jackman, L. M.; Sternhell, S. "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry", 2nd ed.; Pergamon Press: New York, 1969; pp 286–289, and references cited therein.

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