(δ, $CDCl_3$) 135.1, 123.8, 45.8, 35.2, 29.6, 22.8, 17.9, 14.1; high-resolution mass spectrum calcd for $C_{11}H_{20}$ m/e 152.1566, found m/e 152.1566.

(*E*)-4-((*Z*)-1-Propenyl)-2-octene ((*E*,*Z*)-7) obtained by preparative GC was contaminated with ≈50% (*E*,*E*)-7 and had the following properties: IR (neat) 3010 (m), 2970 (s), 2940 (s), 2880 (s), 1450 (m), 1360 (w), 950 (s); NMR (δ, $CDCl_3$) 5.1–5.6 (m, 4 H), 2.97 (app p, 0.47 H, J = 6.5), 2.54 (app p, 0.53 H, J = 6.6), 1.6–1.7 (three overlapping doublets, 6 H), 1.2–1.4 (m, 6 H), 0.88 (br t, 3 H, J = 6.4); ^{13}C NMR (corrected for (*E*,*E*)-7, δ, $CDCl_3$) 134.7, 134.2, 123.4, 122.9, 44.2, 40.2, 25.5, 24.3, 23.3, 22.3, 13.0; determination of the stereoisomer ratio was accomplished by integration of the methine resonances in the ^1H NMR: δ 2.54 ((*E*,*E*)-7) and δ 2.97 ((*E*,*Z*)-7).

(*E*,*Z*)-6-Methyl-2,4-decadiene ((*E*,*Z*)-8): IR (neat) 3010 (m), 3000 (w), 2960 (s), 2930 (s), 2880 (s), 2860 (s), 1420 (m), 1390 (m), 990 (s), 960 (s), 830 (m); NMR spectrum including decoupling experiments led to the assignment of (*E*,*Z*)-8 (δ, $CDCl_3$) 6.31 (dd, 1 H, J = 14.9, 10.9), 5.89 (app t, 1 H, J = 10.9), 5.65 (dq, 1 H, J = 14.9, 6.8), 5.06 (app t, 1 H, J = 10.9), 2.55 (m, 1 H), 1.78 (d, 3 H, J = 6.8), 1.22 (m, 6 H), 0.95 (d, 3 H, J = 6.6), 0.84 (t, 3 H, J = 6.8); high-resolution mass spectrum calcd for $C_{11}H_{20}$ m/e 152.1566, found m/e 152.1566.

(*E*,*E*)-6-Methyl-2,4-decadiene ((*E*,*E*)-8): IR (neat) 3010 (m), 2950 (s), 2920 (s), 2860 (s), 1470 (m), 1460 (m), 1380 (m), 990 (s); NMR including decoupling experiments led to the assignment of (*E*,*E*)-8 (δ, $CDCl_3$) 6.04 (ddd, 1 H, J = 14.1, 10.3, 1.5), 5.96 (dd, 1 H, J = 14.3, 10.3), 5.56 (dq, 1 H, J = 14.1, 6.5), 5.43 (dd, 1 H, J = 14.3, 7.8), 2.10 (m, 1 H), 1.73, (dd, 3 H, J = 6.8, 1.5), 1.27 (m, 6 H), 0.98 (d, 3 H, J = 6.6), 0.87 (t, 3 H, J = 6.8); high-resolution mass spectrum calcd for $C_{11}H_{20}$ m/e 152.1566, found m/e 152.1566.

(*E*,*E*)-4-Phenyl-2,5-heptadiene: IR (neat) 3090 (w), 3070 (w), 3020 (s), 2970 (s), 2940 (s), 2920 (s), 2880 (w), 2860 (m), 1500 (m), 1450 (s), 980 (s), 760 (m), 700 (s); NMR (δ, $CDCl_3$) 7.2–7.4 (m, 5 H), 5.64 (ddq, 2 H, J = 15.2, 6.8, 1.3), 5.47 (dqd, 2 H, J = 15.2, 5.9, 0.6), 3.94 (br t, 1 H, J = 6.8), 1.70 (ddd, 6 H, J = 5.9, 1.3, 0.9); high-resolution mass spectrum calcd for $C_{13}H_{16}$ m/e 172.1253, found m/e 172.1254.

(*E*,*Z*)-6-Phenyl-2,4-heptadiene ((*E*,*Z*)-13): IR (CCl_4) 3070 (w), 3020 (s), 2980 (s), 2940 (s), 2935 (s), 2870 (m), 1500 (s), 1450 (s), 980 (m), 950 (m), 600 (s); NMR (δ, $CDCl_3$) 7.1–7.5 (m, 5 H), 6.44 (dd, 1 H, J = 15.0, 10.4), 5.96 (app t, 1 H, J = 10.4), 5.72 (dq, 1 H, J = 15.0, 6.6), 5.40 (app t, 1 H, J = 10.4), 3.92 (br dq, J = 10.4, 6.9), 1.79 (d, 3 H, J = 6.6), 1.38 (d, 3 H, J = 6.9); high-resolution mass spectrum calcd for $C_{13}H_{16}$ m/e 172.1253, found m/e 172.1254.

Determination of Deuterium Distribution in the Coupling Products Derived from α-D-(*Z*,*E*)-5-OPiv. Reaction of α-D-(*Z*,*E*)-5-OPiv with organocopper reagents was carried out according to the general procedures, and conjugated products (8 or 13) were separated from unconjugated products by preparative GC. Integration of the methine resonances in the ^1H NMR ((*E*,*E*)-8, δ 2.10; (*E*,*Z*)-8, δ 2.55; (*E*,*Z*)-13, δ 3.92) proved a convenient and reproducible method for determining the deuterium distribution. Duplicate runs gave identical (±2%) results, and control experiments indicated that 2% was the lower limit of detection.

Acknowledgment. This work was supported by the National Science Foundation (Grant CHE-8406480).

Registry No. *cis*-2-OPiv, 119819-17-9; *trans*-2-OPiv, 80006-87-7; *cis*-4-OPiv, 119819-13-5; *trans*-4-OPiv, 119819-14-6; (*Z*,*E*)-5-OPiv, 119819-15-7; α-(*Z*,*E*)-5-OH, 84838-74-4; α-D-(*Z*,*E*)-5-OPiv, 119819-16-8; (*E*,*E*)-7, 119819-18-0; (*E*,*Z*)-7, 119819-19-1; (*E*,*E*)-8, 119819-21-5; (*E*,*E*)-8 (α,ε-D), 119819-23-7; (*E*,*Z*)-8, 119819-20-4; (*E*,*Z*)-8 (α,ε-D), 119850-51-0; (*E*,*Z*)-13, 68099-40-1; CuCN, 544-92-3; CuCl, 7758-89-6; BuMgBr, 693-03-8; $LiCuBu_2$, 24406-16-4; BuMgI, 1889-20-9; LiCu(CN)Bu, 41742-63-6; $LiCuPh_2$, 23402-69-9; LiCu(CN)Ph, 41742-64-7; Ph_2CuMgI, 51340-38-6; PhMgBr, 100-58-3; $H_2C{=}CHMgBr$, 1826-67-1; (*Z*,*E*)-$H_3CCH(OH)CH{=}CHCH{=}CHCH_3$, 84838-74-4; (*E*)-$C_6H_5CH{=}CHCH_2Bu$, 10201-58-8; $C_6H_5CH(Bu)CH{=}CH_2$, 40395-23-1; (*Z*)-$C_6H_5CH{=}CHCH_2Bu$, 10201-59-9; (*Z*)-$BuCH_2CH{=}CHCH_3$, 7642-04-8; $H_2C{=}CHCH(Bu)CH_3$, 4810-09-7; (*E*)-$BuCH_2CH{=}CHCH_3$, 13389-42-9; $H_2C{=}CHCH(Bu)CH_3$, 4810-09-7; (*Z*)-$C_6H_5CH{=}CHCH_2C_6H_5$, 1138-83-6; $(C_6H_5)_2CHCH{=}CH_2$, 3542-14-1; (*E*,*E*)-$H_3CCH{=}CHCH(C_6H_5)CH{=}CHCH_3$, 119819-22-6; (*E*,*Z*)-$H_3CCH{=}CHCH{=}CHCD(C_6H_5)CH_3$, 119850-52-1; (*E*,*Z*)-$H_3CCD{=}CHCH{=}CHCH(C_6H_5)CH_3$, 119819-24-8; (*E*)-1-phenyl-1,4-pentadiene, 55666-17-6; (*Z*)-1-phenyl-1,4-pentadiene, 97632-25-2; *trans*-crotyl alcohol, 504-61-0; (*Z*,*E*)-3,5-heptadienone, 4857-17-4; *cis*-crotyl alcohol, 4088-60-2; pivaloyl chloride, 3282-30-2; lithium dimethylcuprate, 15681-48-8.

Asymmetric Alkylation of β-Keto Esters with Optically Active Sulfonium Salts

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Alkylation of the cyclic β-keto ester 2-(methoxycarbonyl)-1-indanone (**2**) with racemic alkylsulfonium salts **1a–h** gave 2-alkylindanones **3** and **4** in 60–96% yields. The relative reactivities of the alkyl substituents of aryldialkylsulfonium salts **1e** and **1f** were quite different from those in S_N2 alkylations. Asymmetric induction occurred upon alkylation of **2** with optically active sulfonium salts. (*R*)-2-Ethyl-2-(methoxycarbonyl)cyclohexanone (**11**) was obtained in up to 16% ee by alkylation of the enolate ion of 2-(methoxycarbonyl)cyclohexanone (**9**) with optically active (*R*)-(+)-(*p*-chlorophenyl)ethylmethylsulfonium *d*-10-camphorsulfonate (**1k**). Alkylation of the enolate ion of **2** with sulfonium salts containing optically active alkyl groups afforded C-alkylated products with inversion of configuration at the asymmetric alkyl carbon atom. These alkylations appear to proceed via an S–O sulfurane intermediate or a tight ion pair with subsequent stereoselective alkyl migration to the enolate.

Introduction

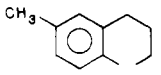
Recently, extensive studies have been published on asymmetric syntheses with enantiomerically pure sulfoxides.[1] However, little has been reported on the use of optically active sulfonium salts in asymmetric syntheses, except for the use of optically active sulfonium ylides prepared by deprotonation of sulfonium salts with strong bases.[2] Moreover, few chiral sulfonium salts have been

(1) (a) Solladie, G. *Synthesis* **1981**, 185. (b) Colonna, S.; Annunziata, R.; Cinquini, M. *Phosphorus Sulfur* **1981**, *10*, 197.

(2) (a) Asymmetric epoxidation: Johnson, C. R.; Schroeck, C. W. *J. Am. Chem. Soc.* **1973**, *95*, 7418 and 7424. (b) Trost, B. M.; Hammen, R. F. *J. Am. Chem. Soc.* **1973**, *95*, 962.

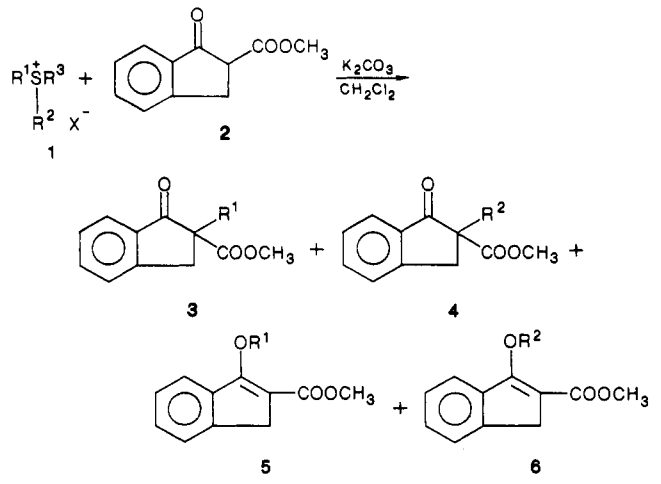
0022-3263/89/1954-2374$01.50/0

Table I. Alkylation of 2 with Racemic Sulfonium Salts 1a–h

entry	sulfonium salts 1					product and yield[a] (%) C-alkylation 3	4	O-alkylation 5	6
		R^1	R^2	R^3	X^-				
1	1a	CH_3	Ph	1-naphthyl	BF_4^-	74		25	
2	1b	C_2H_5	Ph	1-naphthyl	BF_4^-	62		38	
3	1c	C_2H_5	Ph	Ph	ClO_4^-	68		32	
4	1d	CH_3			ClO_4^-	76		13	
5	1e	CH_3	C_2H_5	Ph	ClO_4^-	26	32	7	14
6	1f	CH_3	i-C_3H_7	Ph	ClO_4^-	34	27	6	33
7	1g	CH_3	CH_2Ph	Ph	ClO_4^-	0	86	0	4
8	1h	CH_3	$CH_2CH{=}CH_2$	Ph	ClO_4^-	0	96	0	0

[a] Isolated yields.

Scheme I



assigned absolute configurations.[3] There have been a few reports on the alkylation of oxygen nucleophiles such as carboxylate and phenolate ions,[4] nitrogen nucleophiles such as amines,[4] and carbon nucleophiles such as enolate ions of β-keto esters[5] with racemic alkylsulfonium salts. (*S*)-Adenosyl-L-methionine is an important biological methylating agent, and many natural O- and N-methylated compounds derive their methyl groups from (*S*)-adenosyl-L-methionine.[6]

Meerwein's reagent (triethyloxonium or trimethyloxonium tetrafluoroborate) is a potent alkylating agent for alcohols, phenols, carboxylic acids, and amines.[7] However, it is not possible to make an optically active oxonium salt as an asymmetric alkylating agent. In contrast, sulfonium salts possess a chiral center at the sulfonium group and may be expected to act as chiral alkylating agents for carbon nucleophiles under weakly basic conditions that do not produce a sulfonium ylide from the salt. We here report on the asymmetric alkylation of a cyclic β-keto ester with optically active sulfonium salts.[8]

Table II. Solvent Effect in the Alkylation of 2 with (*p*-Chlorophenyl)ethylmethylsulfonium Perchlorate (1i)

solvent	E_T,[a] kcal/mol (25 °C)	C-alkylation	(3, 4),[b] %	O-alkylation	(5, 6),[b] %
C_6H_6	34.5	31	(13,18)	67	(22,45)
THF	37.4	42	(19,23)	57	(19,38)
CH_2Cl_2	41.1	73	(30,43)	25	(8,17)
acetone	42.2	62	(24,38)	36	(12,24)
DMF		70	(29,41)	28	(9,19)
CH_3CN	46.0	85	(32,53)	13	(4,9)
CH_3OH	55.5	93	(36,57)	6	(2,4)

[a] Reichardt, C. *Lösungsmittel Effekt in der organischen Chemie*; Verlag Chemie, 1969. [b] Determined by GC.

Results and Discussion

Alkylation of 2-(Methoxycarbonyl)-1-indanone (2) with Racemic Sulfonium Salts. A mixture of a racemic sulfonium salt (**1a–h**), 2-(methoxycarbonyl)-1-indanone (**2**), and anhydrous potassium carbonate was stirred in dichloromethane at room temperature to give 2-alkyl-2-(methoxycarbonyl)-1-indanones **3**, **4**, and 1-alkoxy-2-(methoxycarbonyl)-1-indenes **5**, **6** (Scheme I, Table I).

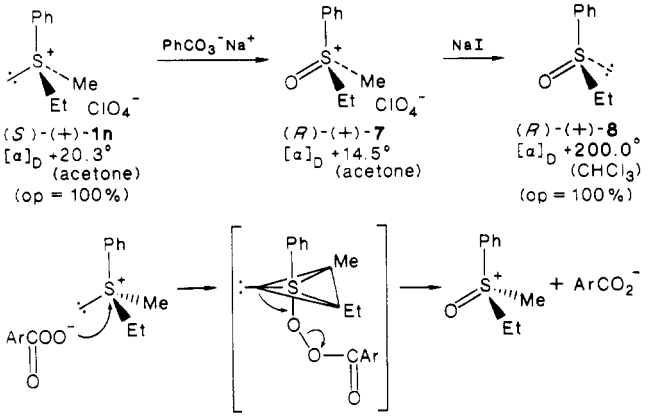
C-Alkylation to give **3** and **4** is the main reaction in all cases. The reaction of **2** with alkyldiarylsulfonium salts **1a–c** or the cyclic sulfonium salt **1d** gives C-alkylation product **3** and O-alkylation product **5** without accompanying arylation (entries 1–4). The reaction of **2** with ethylmethylphenylsulfonium perchlorate (**1e**) or isopropylmethylphenylsulfonium perchlorate (**1f**) gives C-methylated product **3e** (or **3f**) and C-ethylated product **4e** (or C-isopropylated product **4f**). The ratios of **3** to **4** are close to 1 in entry 5 (**3e**:**4e** = 26:32; $R^2 = C_2H_5$) and entry 6 (**3f**:**4f** = 34:27, $R^2 = i\text{-}C_3H_7$). These results are quite different from the relative reactivities expected for ordinary S_N2 alkylation reactions on carbon. For instance, the relative reactivities of alkylmethylphenylsulfonium perchlorates with iodide anion in acetone at 50 °C (known to proceed by an S_N2 mechanism) are CH_3 (1.0) > C_2H_5 (0.20) > $i\text{-}C_3H_7$ (0.05).[9]

The effect of solvent on C- vs O-alkylation in the reaction of **2** with (*p*-chlorophenyl)ethylmethylsulfonium perchlorate (**1i**) is quite different from that in the alkylation of ethyl acetoacetate with alkyl halides (Table II).[10]

The C-alkylation of enolate ions of β-keto esters with alkyl halide decreases and O-alkylation increases in more polar solvents.[10] On the other hand, the C-alkylation of the enolate ion of **2** with sulfonium salt **1i** increased (31% in benzene; 62% in acetone; 70% in DMF), and O-alkyl-

(3) Andersen, K. K.; Caret, R. L.; Ladd, D. L. *J. Org. Chem.* **1976**, *41*, 3096.
(4) (a) Badet, B.; Julia, M.; RamiRez-Muñoz, M. *Synthesis* **1980**, 926. (b) Yamauchi, K.; Tanabe, T.; Kinoshita, M. *J. Org. Chem.* **1979**, *44*, 638.
(5) (a) McBride, B. J.; Garst, M. E.; Hopkins, M. *J. Org. Chem.* **1984**, *49*, 1824. (b) Garst, M. E.; McBride, B. *J. Org. Chem.* **1983**, *48*, 1362.
(6) For a review of (*S*)-adenosyl-L-methionine: Maw, G. A. *The chemistry of the sulfonium group*; Stiring, C. J. M., Patai, S., Eds.; John Wiley & Sons: New York, 1981; pp 703–770.
(7) Meerwein, H. *Organic Syntheses*; Wiley: New York, 1973; Collect. Vol. 5, pp 1080 and 1096.
(8) (a) Kobayashi, M.; Umemura, K.; Watanabe, N.; Matsuyama, H. *Chem. Lett.* **1985**, 1067. (b) Kobayashi, M.; Umemura, K.; Matsuyama, H. *Chem. Lett.* **1987**, 327.
(9) Matsuyama, H.; Minato, H.; Kobayashi, M. *Bull. Chem. Soc. Jpn.* **1975**, *48*, 3287.
(10) House, H. O. *Modern Synthetic Reactions*, 2nd ed.; W. A. Benjamin: Menlo Park, CA, 1972; pp 492–628.

Scheme II



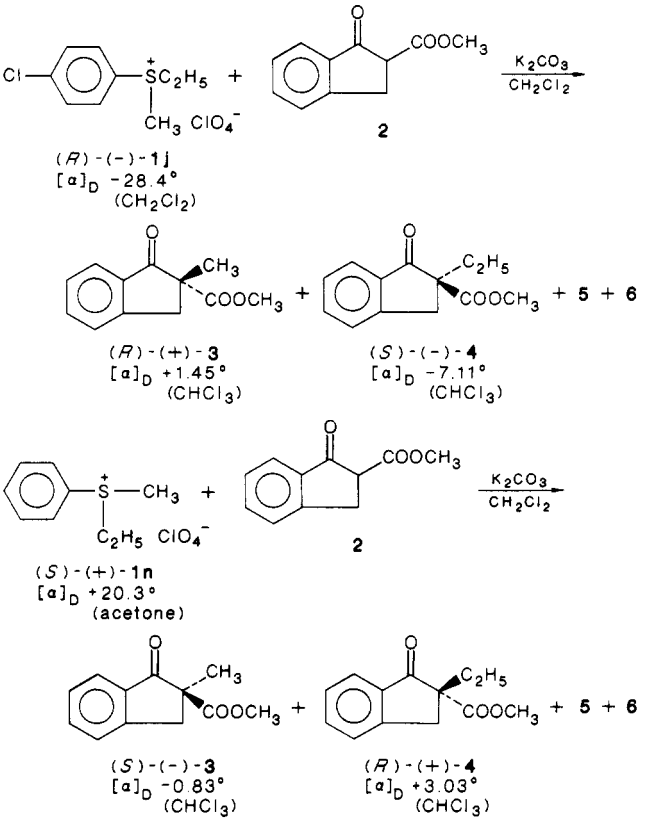
ation decreased (67% in benzene; 36% in acetone; 28% in DMF), with increasing solvent polarity.

Preparation and Absolute Configuration of Optically Active Sulfonium Salts. Optically active sulfonium salts have been synthesized previously by treating alkoxysulfonium salts, derived from sulfoxides by alkylation, with organocadmium or Grignard reagents.[3] Andersen et al.[3] established that the absolute configuration of (+)-ethylmethyl-*p*-tolylsulfonium tetrafluoroborate was *S*. We obtained optically pure sulfonium salts **1j–p** by fractional crystallization of the diastereomeric *d*-10-camphorsulfonate salts. Their absolute configurations were determined by their circular dichroism spectra, and optical purity was determined by the procedure shown in Scheme II.

The absolute configuration of (+)-ethylmethylphenylsulfonium perchlorate [(+)-**1n**] was determined as *S* because circular dichroism showed a strong positive Cotton effect at 223 nm and a weak negative Cotton effect at 266 nm.[3] The 100% optical purity of sulfonium salt (*S*)-(+)-**1n** was determined as shown in Scheme II. The absolute configuration of (+)-**7** was determined by converting it into **8** with an optical purity of 100%.[11] The sulfoxide **8** was assigned the *R* configuration because Mislow et al.[12] established that (+)-alkyl aryl sulfoxides have the *R* configuration. Since demethylation of the ethylmethylphenyloxosulfonium ion proceeds by S_N2 attack of iodide ion on the methyl group, the stereochemistry of the sulfur atom is retained during demethylation. Therefore, (+)-**7** is assigned the *R* absolute configuration.[13] These findings establish that oxidation of sulfonium salt (*S*)-(+)-**1n** with sodium perbenzoate proceeds with retention of configuration around the sulfur atom. The peracid anion may attack the sulfur atom of (*S*)-(+)-**1n** to form a sulfurane intermediate, and then acid anion may be eliminated to produce the oxosulfonium salt (*R*)-(+)-**7**. The optical purities of sulfonium salts **1j–m** and **1o,p** were assumed to be 100% by analogy with **1n**.

Alkylation of Cyclic β-Keto Ester 2 (or 9) with Optically Active Sulfonium Salts. The alkylation of **2** with optically active (*R*)-(−)-**1j** in the presence of anhydrous potassium carbonate in dichloromethane gave the C-methylated product (*R*)-(+)-**3** (30%, 6.8% ee) and the C-ethylated product (*S*)-(−)-**4** (44%, 10% ee) accompanied by O-methylated product 1-methoxy-2-(methoxycarbonyl)-1-indene (**5**) (8%) and O-ethylated product 1-ethoxy-2-(methoxycarbonyl)-1-indene (**6**) (16%).

Scheme III



On the other hand, the alkylation of cyclic β-keto ester **2** with optically active (*S*)-(+)-**1n** produced the C-methylated product (*S*)-(−)-**3** (26%, 3.9% ee) and the C-ethylated product (*R*)-(+)-**4** (32%, 4.1% ee) accompanied by O-methylated product **5** (7%) and O-ethylated product **6** (14%) (Scheme III).

It is interesting that the C-methylated product **3** and the C-ethylated product **4** have opposite configurations. The absolute configuration of the major enantiomers was tentatively assigned by comparison with their oxobutyl analogues.[14] The ee was determined by ^1H NMR analysis in the presence of Eu(hfc)$_3$ and by HPLC using an optically active column. The CD spectra of both (−)-**4** and (2*S*)-(−)-2-(methoxycarbonyl)-2-(3-oxobutyl)indanone[14] show a negative Cotton effect for the n → π* transition at about 320 nm.

In a similar manner, asymmetric alkylation reactions were conducted by using optically active sulfonium salts (*R*)-**1k**, (*R*)-**1l**, (*S*)-**1m**, and (*S*)-**1o** (Table III).

The stereochemistries of **3** and **4** depend on the stereochemistry of the optically active sulfonium salts **1** used as alkylating agents. No change in the absolute configurations of **3** and **4** was observed when the counterion was changed from perchlorate to *d*-10-camphorsulfonate (Table III, entries 1, 2, and 5, 6).[15]

(11) Holland et al. synthesized optically active (*R*)-(+)-ethyl phenyl sulfoxide ([α]D +154° ($CHCl_3$); 86% ee by NMR) by biotransformation of ethyl phenyl sulfide by *M. isabellina*: Holland, H.; Popperl, H.; Ninniss, R. W.; Chenchaiah, P. C. *Can. J. Chem.* **1985**, *63*, 1118.

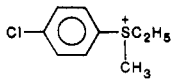
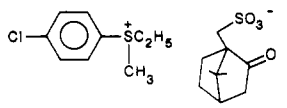
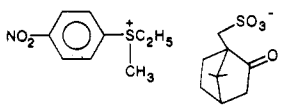
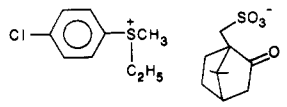
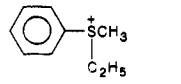
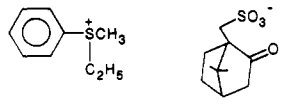
(12) Mislow, K.; Green, M. M.; Laur, P.; Melillo, J. T.; Simmons, T.; Ternarg, A. L. *J. Am. Chem. Soc.* **1965**, *87*, 1958.

(13) (a) Kobayashi, M.; Kamiyama, K.; Minato, H.; Oishi, Y.; Takada, Y.; Hattori, Y. *Chem. Commun.* **1971**, 1577. (b) Kobayashi, M.; Kamiyama, K.; Minato, H.; Oishi, Y.; Takada, Y.; Hattori, Y. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 3703. (c) Kamiyama, K.; Minato, H.; Kobayashi, M. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 3895.

(14) Herman, H.; Wynberg, H. *J. Org. Chem.* **1979**, *44*, 2238.

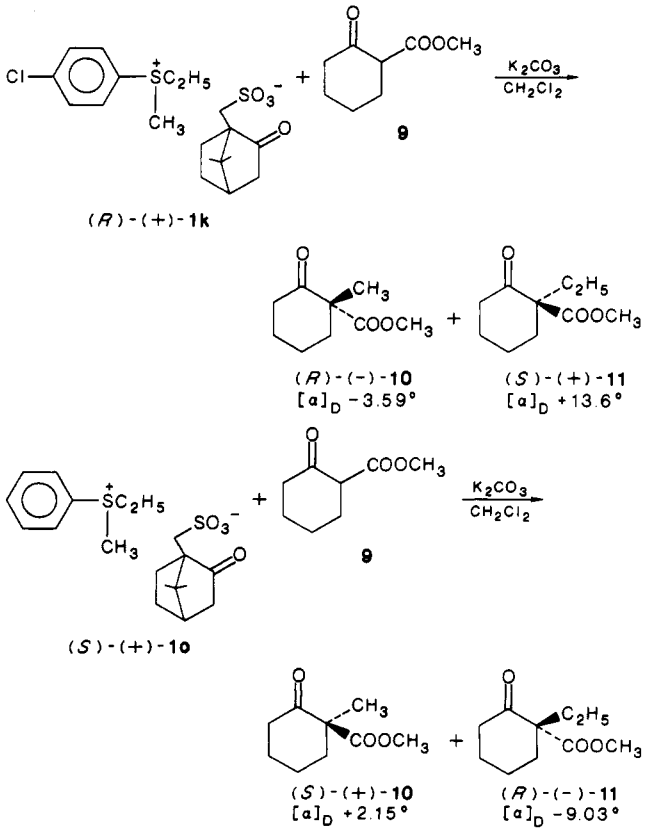
(15) A blank run using the *d*-10-camphorsulfonate salt [α]D +22.6° (c 4.3, MeOH) of an unresolved sulfonium salt (PhEtMeS$^+$) was examined for comparison. However, no asymmetric induction was observed for the alkylated products **3** and **4**. So far, it is not clear why the use of a chiral anion influences the asymmetric induction for **3** and **4** (Table III).

Table III. Asymmetric Alkylation of 2 with Optically Active Sulfonium Salts 1[a]

entry	sulfonium salts 1	(confn)	isolated yield, %	$[\alpha]_D$/deg ($CHCl_3$)	ee/%[b] (confn)[c]	CD $[\theta]_{320}$[d]
1		((*R*)-**1j**)	**3** 30.0 **4** 43.9	+1.45 -7.11	6.8 (*R*) 10.0 (*S*)	+61 -154
2		((*R*)-**1k**)	**3** 25.9 **4** 33.3	+2.59 -8.17	12.2 (*R*) 11.0 (*S*)	+108 -246
3		((*R*)-**1l**)	**3** 28.2 **4** 38.5	+1.60 -6.41	7.5 (*R*) 8.7 (*S*)	+67 -140
4		((*S*)-**1m**)	**3** 25.5 **4** 32.0	-2.90 +6.21	13.6 (*S*) 8.3 (*R*)	-120 +135
5		((*S*)-**1n**)	**3** 25.7 **4** 31.6	-0.83 +3.03	3.9 (*S*) 4.1 (*R*)	-34 +64
6		((*S*)-**1o**)	**3** 23.0 **4** 32.0	-1.44 +8.37	6.7 (*S*) 11.3 (*R*)	-60 +180

[a] Reaction conditions: base and solvent; K_2CO_3 in CH_2Cl_2 (entries 1, 2, 3, and 5); potassium enolate of **2** in DMF (entries 4 and 6). [b] The ee of **4** in entry 2 was determined by LIS-NMR technique ($Eu(hfc)_3$) and in entries 1, 3, 4, 5, and 6, the ee of **4** was calculated by comparison with the optical rotations of entry 2. The ee of **3** in entry 2 was determined by HPLC (using optically active column; Daicel Chemical CA-1) and in entries 1, 3, 4, 5, and 6, the ee of **3** was calculated by comparison with the optical rotations of entry 2. [c] Absolute configuration was estimated by correlating **3** and **4** with (2*S*)-(−)-2-(methoxycarbonyl)-2-(3-oxobutyl)indanone: ref 14. [d] CD spectra were taken in $CHCl_3$ (entry 2) and methanol (entries 1, 3, 4, 5, and 6).

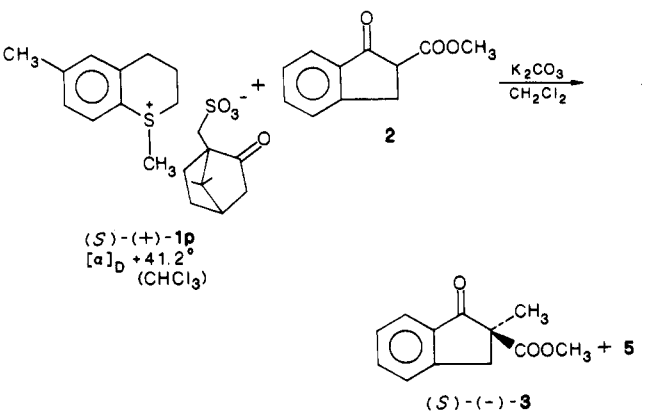
Scheme IV



Alkylation of the cyclic β-keto ester **9** with (R)-(+)-**1k** gave the C-methylated product (*R*)-(−)-**10** (21%, 3.3% ee)[16] and the C-ethylated product (*S*)-(+)-**11** (12%, 16.3% ee).[17] The degree of asymmetric induction and the absolute configurations of **10** and **11** were determined by comparison with known compounds[16] and also by the LIS-NMR technique using $Eu(hfc)_3$. The configurations of **10** and **11** are opposite (Scheme IV).

In a similar manner, alkylation of **9** with (*S*)-(+)-**1o** gave the C-methylated product (*S*)-(+)-**10** (24%, 2.0% ee) and the C-ethylated product (*R*)-(−)-**11** (14%, 10.8% ee) (Scheme IV).

Scheme V

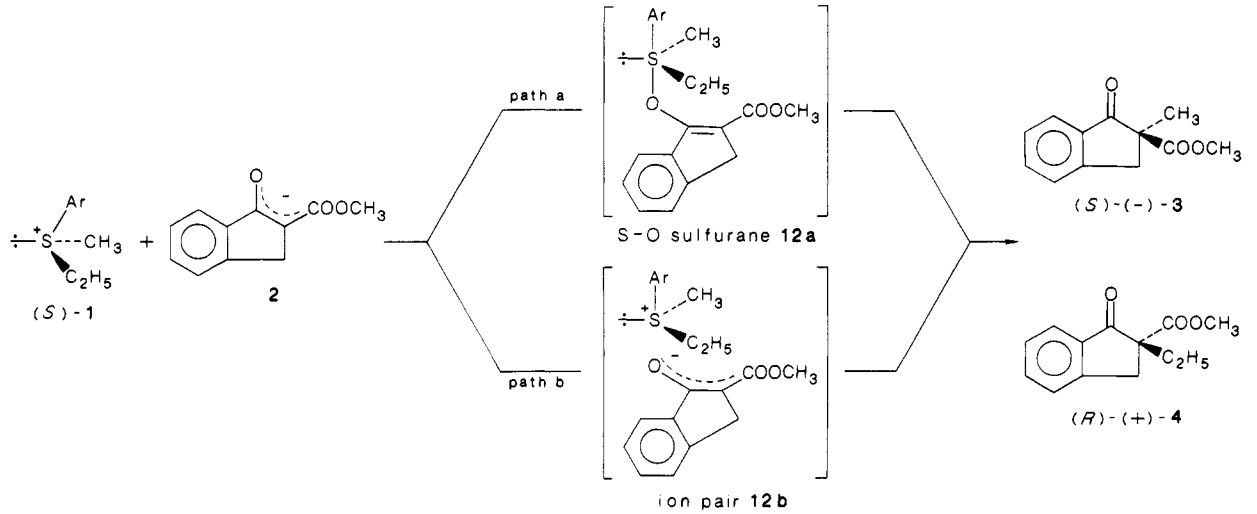


The effect of reaction temperature on the degree of asymmetric induction was studied in the alkylation of **2** with the cyclic sulfonium salt (*S*)-(+)-**1p** (Scheme V). The C-methylated product (*S*)-(−)-**3** was formed in 4.5% ee [80%, $[\alpha]_D$ −0.95° ($CHCl_3$)] at 25 °C and in 8.9% ee [49%, $[\alpha]_D$ −1.88° ($CHCl_3$)] at −28 °C. Thus asymmetric induction is slightly greater at the lower temperature.

(16) The asymmetric synthesis of (*R*)-(−)-**10** ($[\alpha]_D$ −108° (EtOH); >99% ee) was reported by Tomioka et al.: Tomioka, K.; Ando, K.; Takamasa, Y.; Koga, K. *J. Am. Chem. Soc.* **1984**, *106*, 2718.

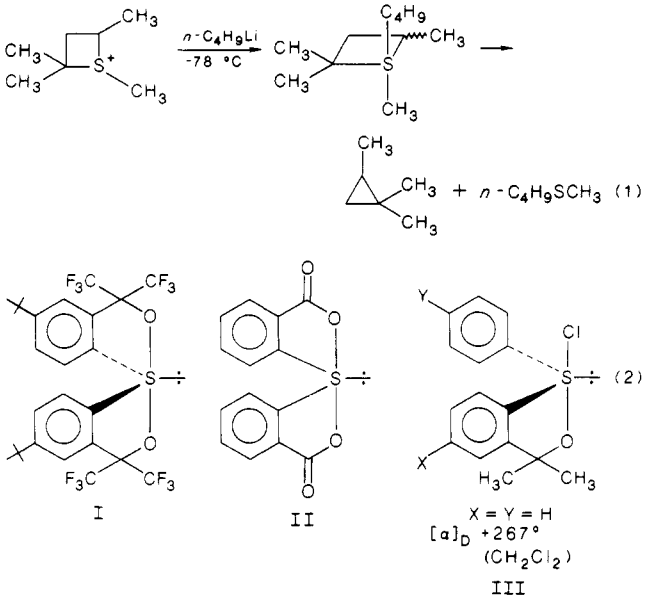
(17) The ee value for **11** was determined by LIS-NMR technique using the chiral shift reagent $Eu(hfc)_3$.

Scheme VI



Mechanism

A number of papers describe synthetically important reactions of sulfonium compounds involving sulfurane intermediates. For example, treatment of 1,2,2,4-tetramethylthietanonium fluoroborate with *n*-butyllithium at −78 °C affords *n*-butyl methyl sulfide and 1,1,2-trimethylcyclopropane by way of a "σ-sulfurane" or tetracoordinated sulfur intermediate[18] (eq 1). σ-Sulfuranes in which sulfur is bonded to one or more fluorine atoms or oxygen groups in addition to carbon are reasonably stable, and such sulfuranes as I,[19] II,[19] and III[20] can be isolated (eq 2).



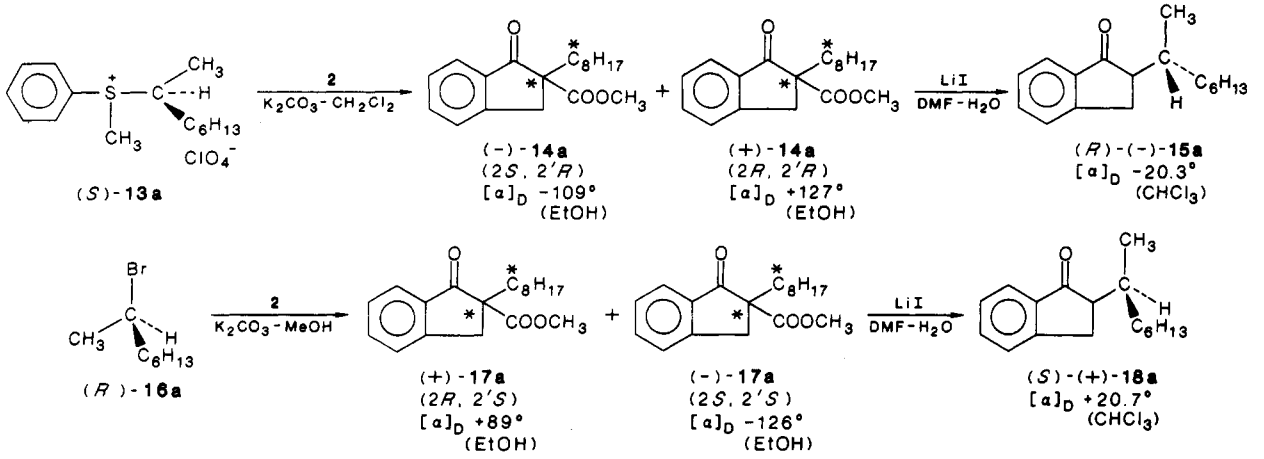
It is difficult to explain the asymmetric alkylation of **2** with optically active sulfonium salts **1** by a simple S_N2 mechanism for the following reasons. (i) The yield of C-ethylated product **4** was greater than that of C-methylated product **3**. (ii) The solvent effects on C- vs O-alkylation of **2** with sulfonium salt **1i** are quite different from those in S_N2 alkylation with alkyl halides. (iii) The configurations of C-methylated product (*S*)-(−)-**3** and C-ethylated product (*R*)-(+)-**4** are opposite. Accordingly, we propose that the reaction proceeds via sulfurane intermediate **12** (Scheme VI, path a). First the enolate ion of **2** attacks the cationic sulfur atom of (*S*)-ethylmethylarylsulfonium salt **1** to form S–O sulfurane intermediate **12a**. In the alkylation stage, the methyl group may exist in the bottom (*re*) face of the enolate π face (SOC=C) of sulfurane **12a**, with C-methylation taking place preferentially from the *re* face to give the C-methylated product (*S*)-(−)-**3**. Accordingly, C-ethylation takes place preferentially from the top (*si*) face of sulfurane **12a** to yield the C-ethylated product (*R*)-(+)-**4** (Scheme VI).[21]

A reviewer has suggested the alternative path b (Scheme VI), in which (*S*)-**1** and **2** form tight ion pair **12b**, which could partition to give the products. Such an ion pair might be affected differently by different solvents and give different product ratios than those reported in the literature for alkylations.[10] The sulfonium salt could be the counterion and the electrophile for the enolate. Both the enolate and the salt are very soft and therefore well-matched. Neither of these ions should be solvated by water or alcohol as smaller ions are.[10] To explain the ratio of Et to Me products, one might postulate a transition state with some S–C bond breaking before enolate alkylation (i.e., some carbonium character).

Stereochemical Outcome in the Alkylation of Enolate Ions with Unresolved Sulfonium Salts Containing Optically Active Alkyl Groups. Scheme VI does not address the question of whether the steric configuration of the entering alkyl group is retained or inverted. We therefore examined the reaction between the enolate ion of **2** and unresolved sulfonium ions **13a**, **13b** containing the optically active alkyl groups (*S*)-2-octyl and (*S*)-2-butyl. Unresolved (*S*)-**13a**, $[\alpha]_D$ −4.5° (EtOH), was prepared by methylation of phenyl (*S*)-2-octyl sulfide, $[\alpha]_D$ +1.7° ($CHCl_3$), which was obtained from (*R*)-2-octyl bromide (**16a**), $[\alpha]_D$ −34.1° (EtOH), and sodium benzenethiolate in ethanol. Alkylation of **2** with sulfonium salt **13a** in the presence of anhydrous potassium carbonate in dichloromethane gave C-octylated product **14a** (8.3%) as a mixture of diastereoisomers together with O-octylated (50.7%), C-methylated (35.7%), and O-methylated (5.3%)

(18) Trost, B. M.; Schinsk, . L.; Chen, F.; Mantz, I. B. *J. Am. Chem. Soc.* **1971**, *93*, 676.
(19) (a) Martin, J. C.; Perozzi, E. F. *J. Am. Chem. Soc.* **1974**, *96*, 3155. (b) Kapovits, I.; Kalman, A. *Chem. Commun.* **1971**, 649.
(20) Martin, J. C.; Balthazer, T. M. *J. Am. Chem. Soc.* **1977**, *99*, 152.
(21) It is not clear why the ee values for **3** and **4** are very low although the proposed mechanism accounts for the slight excess of one product over another. Presumably free rotation around the S–O bond axis and pseudorotation of sulfurane **12** may take place in the alkylation stage (Scheme VI). For pseudorotation: (a) Martin, J. C.; Perozzi, E. F. *Science* **1976**, *191*, 154. (b) Astrologes, G. W.; Martin, J. C. *J. Am. Chem. Soc.* **1976**, *98*, 2895.

Scheme VII



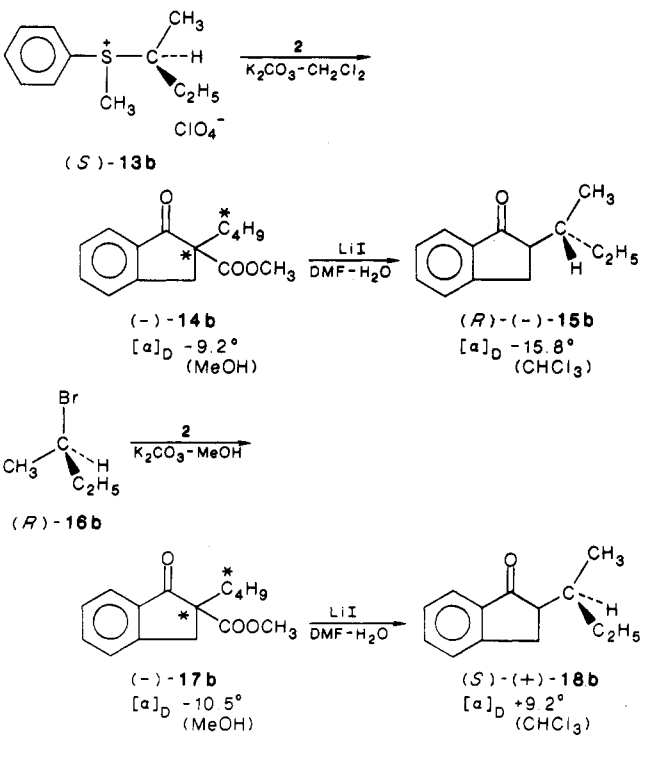
products. The C-octylated products (2*S*,2′*R*)-(−)-**14a** and (2*R*,2′*R*)-(+)-**14a** were transformed into (−)-**15a** by demethoxycarbonylation[22] (LiI, DMF–H_2O, 9:1, reflux for 3 days), using their enolates to remove asymmetry induced at the quaternary carbon atom of **14a**.

Authentic (*S*)-(+)-**18a** was obtained by alkylation of **2** with (*R*)-2-octyl bromide [**16a**, $[\alpha]_D$ −34.1° (EtOH)] and subsequent demethoxycarbonylation of the diastereoisomers (2*R*,2′*S*)-(+)-**17a** and (2*S*,2′*S*)-(−)-**17a** (Scheme VII). Since the configuration at the 2-octyl carbon atom inverts during this S_N2 alkylation, the 2-octyl carbon atom of authentic **18a** was assigned the *S* configuration. From the optical rotation and configuration of (+)-**18a**, the 2-octyl carbon atom of (−)-**15a** derived from sulfonium salt **13a** was assigned the *R* configuration (Scheme VII). (*R*)-(−)-**15a** and (*S*)-(+)-**18a** have opposite chirality but the same ee. This result shows that a stereospecific inversion of configuration takes place at the 2-octyl carbon atom of **13a** and **16a**.

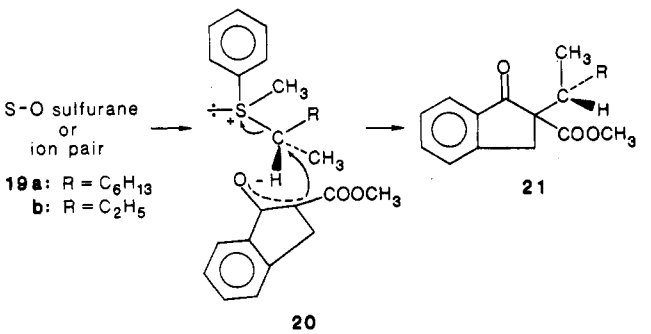
In a similar manner, **2** was alkylated with unresolved (*S*)-**13b**, $[\alpha]_D$ +3.3° (MeOH), to afford **15b** by demethoxycarbonylation of the diastereoisomers (−)-**14b**. The 2-butyl carbon atom of **15b** was also assigned the *R* configuration by comparison with authentic (*S*)-**18b**, which was prepared by alkylation of **2** with (*R*)-2-butyl bromide [**16b**, $[\alpha]_D$ −22.9° (EtOH)] and subsequent demethoxycarbonylation of (−)-**17b** (Scheme VIII).[23]

Thus the optically active 2-alkyl groups of sulfonium salts **13a** and **13b** are transferred to the enolate ion of **2** with inversion of configuration. We propose that the reaction proceeds as shown in Scheme IX. The enolate ion of **2** attacks the cationic sulfur atom of sulfonium salt **1** to form S–O sulfurane intermediate or tight ion pair **19**. Cleavage of the S–O bond of **19** forms **20**, and the enolate attacks the alkyl group from the rear to give **21**.[24]

Scheme VIII



Scheme IX



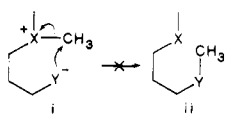
Experimental Section

Melting points were determined on a Yamato Model MP-21 melting point apparatus and are uncorrected. ^1H NMR spectra were recorded on a JEOL PMX 60 SI spectrometer (60 MHz) in $CDCl_3$, unless otherwise indicated, with Me_4Si as an internal standard. Chemical shifts and coupling constants were recorded in δ (ppm) and Hertz units. IR spectra were recorded on a Hitachi

(22) Lane, S.; Ouick, S.; Taylor, R. J. K. *J. Chem. Soc., Perkin Trans. I* **1985**, 893.

(23) The optical rotation of authentic (*S*)-(+)-**18b** is smaller than that of (*R*)-(−)-**15b** obtained from sulfonium salt (*S*)-**13b**. A partial racemization of (*R*)-2-butyl bromide may take place under these alkylation conditions (in methanol), because no optical rotation was observed for **17b**, which was prepared from the reaction of **16b** and **2** in DMF.

(24) Nucleophiles in onium salts do not undergo the superficially reasonable reaction i → ii because of the requirement for colinearity in the transition state of the S_N2 displacement. Tenud, L.; Farooq, S.; Seibl,



J.; Eschenmoser, A. *Helv. Chim. Acta* **1970**, *53*, 2059.

Model 260-10 spectrometer. Optical rotations were measured in a 1.0-dm or 0.5-dm cell on a JASCO DIP-140 polarimeter. Circular dichroism (CD) spectra were measured on a JASCO Model J-40A CD spectrometer. Low resolution mass spectra were obtained on a JEOL JMS-DX 300 mass spectrometer at 70 eV with sample introduction via direct probe or through a 1-m GC column containing 10% SE-30. UV spectra were recorded on a Hitachi Model 220-A spectrometer.

2-(Methoxycarbonyl)-1-indanone (2) was prepared by a standard procedure:[25] 79.4% yield; mp 49.0–55.0 °C (hexane–ether); bp 128–130 °C (2 mmHg); IR (KBr) 1723, 1703 cm^{-1}; MS m/z 190 (M^+), 158, 147, 130, 118; ^1H NMR ($CDCl_3$) δ 3.2–3.8 (3 H, m), 3.73 (3 H, s), 7.2–7.8 (4 H, m), 10.3 (0.1 H, br s).

2-(Methoxycarbonyl)cyclohexanone (9) was prepared by a standard procedure:[26] 89.2% yield; bp 68.0 °C (1 mmHg); IR (film) 1745, 1715, 1660, 1615 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.62 (4 H, m), 2.22 (4 H, m), 3.37 (0.25 H, t, J = 7.0 Hz), 3.74 (3 H, s), 12.10 (0.75 H, s); MS m/z 156 (M^+).

2-Methyl-2-(methoxycarbonyl)-1-indanone (3). A mixture containing 2-(methoxycarbonyl)-1-indanone (**2**) (380 mg, 2.00 mmol) and anhydrous potassium carbonate (829 mg, 6.0 mmol) in 50 mL of dry acetone was stirred and heated to reflux. After the addition of methyl iodide (567 mg, 4.00 mmol), the solution was again refluxed overnight. Acetone was removed under vacuum and the product was extracted three times with ether. The combined organic extracts were washed with water and dried over $MgSO_4$, and the solvent was removed in vacuo. The resulting crude product was purified by silica gel column chromatography (hexane/ether, 5:1) to give 2-methyl-2-(methoxycarbonyl)-1-indanone (**3**) (402 mg, 98.5%): mp 57.5–58.0 °C (from hexane–ether); MS m/z 204 (M^+), 190, 176, 161, 145; ^1H NMR ($CDCl_3$) δ 1.45 (3 H, s), 2.95 (1 H, d, J = 17.0 Hz), 3.59 (1 H, d, J = 17.0 Hz), 3.62 (3 H, s), 7.16–7.80 (4 H, m); HRMS, calcd for $C_{12}H_{12}O_3$ 204.0786, found 204.0779.

2-Methyl-2-(methoxycarbonyl)cyclohexanone (10) was prepared by the procedure described above: 99% yield; MS m/z 170 (M^+), 155, 139, 127, 123; ^1H NMR ($CDCl_3$) δ 1.33 (3 H, s), 1.67 (4 H, m), 2.43 (4 H, m), 3.67 (3 H, s); HRMS, calcd for $C_9H_{14}O_3$ 170.0942, found 170.0963.

2-(Methoxycarbonyl)-1-indanone, Potassium Salt (K Enolate).[27] 2-(Methoxycarbonyl)-1-indanone (**2**) (554 mg, 2.91 mmol) was added with stirring to a cooled (5–10 °C) mixture of H_2O–MeOH (1:6, 7 mL) and potassium hydroxide (235 mg), keeping the temperature below 20 °C. After 2 min, ether (10 mL) was added and the pasty precipitate formed was filtered under suction immediately and washed with ice-cold methanol (2 mL) and then with ether (10 mL). The solid obtained was pressed damp-dry on filter paper and then dried in vacuo for 8 h to give the white solid potassium enolate (524 mg, 78.4%).

General Procedure for Alkylation of Cyclic β-Keto Esters 2 with Racemic Sulfonium Salts 1a–h. A mixture of racemic sulfonium salt **1a–h** (1 mmol), cyclic β-keto ester (1 mmol), and anhydrous potassium carbonate (1.3 mmol) was stirred in dry dichloromethane (10 mL) at room temperature for 2 days. After filtration of insoluble materials, the alkylated products were purified by preparative TLC (Merck Kieselgel $60F_{254}$) and medium pressure column chromatography. The results are listed in Table I.

2-Ethyl-2-(methoxycarbonyl)-1-indanone (4e): ^1H NMR ($CDCl_3$) δ 0.87 (3 H, t, J = 7.6 Hz), 1.98 (2 H, q, J = 7.6 Hz), 2.95 (1 H, d, J = 17.0 Hz), 3.69 (3 H, s), 3.63 (1 H, d, J = 17.0 Hz), 7.16–7.80 (4 H, m); MS m/z 218 (M^+), 203, 190, 175, 158; HRMS, calcd for $C_{13}H_{14}O_3$ 218.0942, found 218.0937.

2-Isopropyl-2-(methoxycarbonyl)-1-indanone (4f): ^1H NMR ($CDCl_3$) δ 0.74 (3 H, d, J = 6.8 Hz), 0.96 (3 H, d, J = 6.8 Hz), 2.86 (1 H, q, J = 6.8 Hz), 2.98 (1 H, d, J = 18.0 Hz), 3.73 (1 H, d, J = 18.0 Hz), 3.97 (3 H, s), 7.30–7.89 (4 H, m); MS m/z 232 (M^+), 201, 190, 172, 157; HRMS, calcd for $C_{14}H_{16}O_3$ 232.1099, found 232.1079.

2-Benzyl-2-(methoxycarbonyl)-1-indanone (4g): ^1H NMR ($CDCl_3$) δ 3.08 (1 H, d, J = 18.0 Hz), 3.33 (2 H, d, J = 4.0 Hz), 3.62 (1 H, d, J = 18.0 Hz), 3.63 (3 H, s), 7.20–7.47 (9 H, m); MS m/z 280 (M^+), 262, 249, 221, 189, 157; HRMS, calcd for $C_{18}H_{16}O_3$ 280.1099, found 280.1126.

2-Allyl-2-(methoxycarbonyl)-1-indanone (4h): ^1H NMR ($CDCl_3$) δ 2.69 (1 H, d, J = 6.4 Hz), 2.80 (1 H, d, J = 6.4 Hz), 3.11 (1 H, d, J = 18.0 Hz), 3.63 (3 H, s), 3.69 (1 H, d, J = 18.0 Hz), 4.87–6.00 (3 H, m), 7.23–7.83 (4 H, m); MS m/z 230 (M^+), 212, 199, 187, 171; HRMS, calcd for $C_{14}H_{14}O_3$ 230.0942, found 230.0947.

1-Methoxy-2-(methoxycarbonyl)-1-indene (5a): ^1H NMR ($CDCl_3$) δ 3.77 (3 H, s), 3.62 (2 H, s), 4.21 (3 H, s), 7.15–7.56 (4 H, m); MS m/z 204 (M^+), 189, 173, 157, 145; HRMS, calcd for $C_{12}H_{12}O_3$ 204.0786, found 204.0876.

1-Ethoxy-2-(methoxycarbonyl)-1-indene (5b): ^1H NMR ($CDCl_3$) δ 1.41 (3 H, t, J = 7.6 Hz), 3.62 (2 H, s), 3.74 (3 H, s), 4.59 (2 H, q, J = 7.6 Hz), 7.11–7.56 (4 H, m); MS m/z 218 (M^+), 187, 175, 159, 145; HRMS, calcd for $C_{13}H_{14}O_3$ 218.0942, found 218.0936.

1-(Isopropyloxy)-2-(methoxycarbonyl)-1-indene (6f): ^1H NMR ($CDCl_3$) δ 1.36 (6 H, d, J = 6.4 Hz), 3.62 (2 H, s), 3.73 (3 H, s), 5.17 (1 H, q, J = 6.4 Hz), 7.23–7.57 (4 H, m); MS m/z 232 (M^+), 204, 190, 158, 130; HRMS, calcd for $C_{14}H_{16}O_3$ 232.1099, found 232.1126.

2-Ethyl-2-(methoxycarbonyl)cyclohexanone (11): ^1H NMR ($CDCl_3$) δ 0.83 (3 H, t, J = 8.0 Hz), 1.50–2.73 (10 H, m), 3.70 (3 H, s); MS m/z 184 (M^+), 169, 161, 156, 152; HRMS, calcd for $C_{10}H_{16}O_3$ 184.1099, found 184.1078.

General Procedure for Asymmetric Alkylation of Cyclic β-Keto Esters 2 (or 9) with Optically Active Sulfonium Salts. A mixture of optically active sulfonium salts **1j–o** (1 mmol), cyclic β-keto ester **2** (or **9**) (1 mmol), and anhydrous potassium carbonate (1.3 mmol) was stirred in dry dichloromethane (10 mL) at room temperature for 2 days (entries 1, 2, 3, and 5). Alternatively, the potassium enolate of **2** was reacted with the sulfonium salt **1l** (or **1n**) in DMF (entries 4 and 6) at room temperature. After filtration of insoluble materials, the alkylated products were purified by preparative TLC (Merck Kieselgel $60F_{254}$) and medium pressure column chromatography. The absolute configuration was determined by comparison with known compounds,[14,16] and the enantiomeric excess (ee) was determined by ^1H NMR analysis for compounds **4** and **11** in the presence of the chiral shift reagent tris(3-(heptafluoropropyl)(hydroxymethylene)-*d*-camphorate)-europium(III) ($Eu(hfc)_3$) and by HPLC for compound **3** (using an optically active column; Daicel Chemical Chiralcel CA-1; methanol as eluent). Asymmetric alkylation of cyclic β-keto ester **2** with optically active sulfonium salts **1j–o**: the results are listed in Table III.

Asymmetric Alkylation of Cyclic β-Keto Ester 9 with Optically Active 1k and 1o. (a) Alkylation of 9 with 1k. (*R*)-(−)-2-Methyl-2-(methoxycarbonyl)cyclohexanone (10): $[\alpha]_D$ −3.59° (*c* 0.65, EtOH); 3.3% ee; CD $[\Theta]_{298}$ −92 (EtOH); 21.3%; ^1H NMR ($CDCl_3$) δ 1.33 (3 H, s), 1.67 (4 H, m), 2.43 (4 H, m), 3.67 (3 H, s); MS m/z 170 (M^+), 155, 139, 127, 123; HRMS, calcd for $C_9H_{14}O_3$ 170.0942, found 170.0963. **(*S*)-(+)-2-Ethyl-2-(methoxycarbonyl)cyclohexanone (11)**: $[\alpha]_D$ +13.6° (*c* 0.41, EtOH); 16.3% ee; CD $[\Theta]_{293}$ +560 (EtOH); 12.1% chemical yield; ^1H NMR ($CDCl_3$) δ 0.83 (3 H, t, J = 8.0 Hz), 1.50–2.73 (10 H, m), 3.70 (3 H, s); MS m/z 184 (M^+), 169, 161, 156, 152; HRMS, calcd for $C_{10}H_{16}O_3$ 184.1099, found 184.1078. 1-Methoxy-2-(methoxycarbonyl)-1-cyclohexene, 37.4%; 1-ethoxy-2-(methoxycarbonyl)-1-cyclohexene; 11.5%.

(b) Alkylation of 9 with 1o. (*S*)-(+)-2-Methyl-2-(methoxycarbonyl)cyclohexanone (10): $[\alpha]_D$ +2.15° (*c* 2.0, EtOH); 2.0% ee; CD $[\Theta]_{293}$ +55 (EtOH); 24.0%. **(*R*)-(−)-2-Ethyl-2-(methoxycarbonyl)cyclohexanone (11)**: $[\alpha]_D$ −9.30° (*c* 1.19, EtOH); 10.0% ee; CD $[\Theta]_{293}$ −370 (EtOH); 14.0%. 1-Methoxy-2-(methoxycarbonyl)-1-cyclohexene, 20%; 1-ethoxy-2-(methoxycarbonyl)-1-cyclohexene, 15%.

Asymmetric Alkylation of Cyclic β-Keto Ester 2 with Optically Active Cyclic Sulfonium Salt 1p. (a) Reaction of 2 with 1p at 25 °C. (*S*)-(−)-3: $[\alpha]_D$ −0.95° (*c* 1.3, $CHCl_3$); 4.5% ee; CD $[\Theta]_{320}$ −40 (MeOH); 79.5%. **1-Methoxy-2-(methoxycarbonyl)-1-indene (5)**: 19.3%. **(b) Reaction of 2 with 1p at −28 °C. (*S*)-(−)-3**: $[\alpha]_D$ −1.88° (*c* 0.60, $CHCl_3$); 8.9% ee; CD $[\Theta]_{320}$ −80 (MeOH); 48.6%. **1-Methoxy-2-(methoxycarbonyl)-1-indene (5)**: 16.0%.

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Racemic alkylsulfonium salts **1a–i** were prepared from an alkyl aryl sulfide, an alkyl iodide, and silver perchlorate in acetonitrile in 74 to 100% yields.[28]

Ethylmethylphenylsulfonium perchlorate (1e): mp 84.5 °C (acetone–ether; ^{1}H NMR (acetone-d_6) δ 1.40 (3 H, t, J = 7.2 Hz), 3.52 (3 H, s), 3.92 (2 H, q, J = 7.2 Hz), 7.76–8.33 (5 H, m).

Isopropylmethylphenylsulfonium perchlorate (1f): ^{1}H NMR (acetone-d_6) δ 1.31 (3 H, d, J = 7.0 Hz), 1.58 (3 H, d, J = 7.0 Hz), 3.28 (3 H, s), 4.20 (0.5 H, q, J = 7.0 Hz), 4.30 (0.5 H, q, J = 7.0 Hz), 7.53–8.00 (5 H, m).

Benzylmethylphenylsulfonium perchlorate (1g): mp 115–117 °C (acetone–ether); ^{1}H NMR (acetone-d_6) δ 3.41 (3 H, s), 5.10 (2 H, d, J = 4.4 Hz), 7.25 (5 H, br s), 7.57–8.00 (5 H, m).

Allylmethylphenylsulfonium perchlorate (1h): ^{1}H NMR (acetone-d_6) δ 3.41 (3 H, s), 4.52 (2 H, d), 5.30–6.00 (3 H, m), 7.63–8.18 (5 H, m).

Methylnaphthylphenylsulfonium tetrafluoroborate (1a): mp 139–140 °C (acetone); ^{1}H NMR (acetone-d_6) δ 4.00 (3 H, s), 7.50–8.54 (12 H, m).

Ethylnaphthylphenylsulfonium tetrafluoroborate (1b): mp 117–118 °C (acetone); ^{1}H NMR (acetone-d_6) δ 1.60 (3 H, t, J = 7.4 Hz), 4.62 (2 H, q, J = 7.4 Hz), 7.56–8.60 (12 H, m).

Ethyldiphenylsulfonium perchlorate (1c): mp 81.0–81.5 °C (acetone–ether); ^{1}H NMR (acetone-d_6) δ 1.51 (3 H, t, J = 7.8 Hz), 4.41 (2 H, q, J = 7.8 Hz), 7.60–8.23 (10 H, m).

1,6-Dimethyl-3,4-dihydro-2*H*-1-benzothiopyranium perchlorate (1d): mp 89–91 °C (acetone–ether); ^{1}H NMR (acetone-d_6) δ 2.17–2.16 (2 H, m), 2.37 (3 H, s), 2.93–3.20 (2 H, m), 3.27 (3 H, s), 3.77–4.07 (2 H, m), 7.10–7.57 (3 H, m).

(*p*-Chlorophenyl)ethylmethylsulfonium perchlorate (1i): mp 87.5–88.5 °C (acetone–ether); ^{1}H NMR (acetone-d_6) δ 1.41 (3 H, t, J = 7.2 Hz), 3.47 (3 H, s), 3.88 (2 H, q, J = 7.2 Hz), 7.74 and 8.14 (4 H, AA′BB′, 8.4 Hz).

General Procedure for Synthesizing Optically Active Aryldialkylsulfonium Salts 1j–p. The counter anion of the racemic sulfonium perchlorate **1** was exchanged with chloride anion on an ion exchange column (IRA-400). To an acetonitrile solution of silver *d*-10-camphorsulfonate, which was prepared from *d*-10-camphorsulfonic acid and silver oxide in acetonitrile, was added an acetonitrile solution of aryldialkylsulfonium chloride at room temperature. Silver chloride was filtered off and the solvent was evaporated to give racemic aryldialkylsulfonium *d*-10-camphorsulfonate. After fractional recrystallization of diastereoisomers of sulfonium *d*-10-camphorsulfonate from acetone–ether several times, an optically pure aryldialkylsulfonium *d*-10-camphorsulfonate was obtained. The sulfonium salt was added to an aqueous solution of sodium perchlorate and the separated oil was extracted with dichloromethane. Evaporation of the solution gave the optically active sulfonium perchlorate, and the salt was recrystallized from acetone–ether. The absolute configuration and optical purity were determined by their circular dichroism spectra[3] and oxidation method[13] ((*S*)-(+)-**1n**, (*R*)-(+)-**7**, (*R*)-(+)-**8**) as shown in Scheme II.

(+)-Ethylmethylphenyloxosulfonium Perchlorate (7). (+)-Ethylmethylphenylsulfonium perchlorate (**1n**) was prepared from ethyl phenyl sulfide by methylation with methyl iodide in the presence of silver perchlorate. Sulfonium salt **1n** (3.00 g, 11.9 mmol) ([α]$_D$ +20.3° (*c* 1.3, acetone)) (op 100%) was oxidized with a 0.2 M aqueous solution of sodium *m*-chloroperbenzoate (180 mL, 35.6 mmol). (*R*)-(+)-Ethylmethylphenyloxosulfonium perchlorate (**7**): 2.91 g (91%); mp 79.0–79.5 °C; IR (KBr) 1220 cm^{-1}; [α]$_D$ +14.5° (*c* 20.5, acetone); ^{1}H NMR (acetone-d_6) δ 1.55 (3 H, t, J = 7.2 Hz), 4.39 (3 H, s), 4.54 (1 H, q, J = 7.2), 4.57 (1 H, q, J = 7.2 Hz), 7.95–8.50 (5 H, m). Anal. Calcd for $C_9H_{13}O_5SCl$: C, 40.23; H, 4.88. Found: C, 40.21, H, 4.75.

(+)-Ethyl Phenyl Sulfoxide (8). A mixture of (+)-ethylmethylphenyloxosulfonium perchlorate (**7**) ([α]$_D$ +14.5° (*c* 20.5, acetone)) (0.276 g, 1.09 mmol) and NaI (0.327 g, 2.18 mmol) in 5 mL of acetone was refluxed for 1 h. Water was added to the mixture, and the sulfoxide was extracted with ether. After the ethereal extracts were dried over $MgSO_4$ and the ether was removed under reduced pressure, (+)-ethyl phenyl sulfoxide was obtained: 86.7 mg (51.3%); [α]$_D$ +200.0° (*c* 1.68, $CHCl_3$); [α]$_D$ +185.6° (*c* 0.71, acetone) (op 100%);[11] ^{1}H NMR ($CDCl_3$) δ 1.14 (3 H, t), 2.70 (2 H, q) 7.49 (5 H, m).

(*R*)-(−)-(*p*-Chlorophenyl)ethylmethylsulfonium perchlorate (1j): [α]$_D$ −23.3° (*c* 1.2, MeOH); mp 93–94.5 °C (MeOH–ether); ^{1}H NMR (acetone-d_6) δ 1.42 (3 H, t), 3.50 (3 H, s), 3.73–4.10 (2 H, m), 7.85–8.23 (4 H, AA′BB′, J = 8.4 Hz); CD (MeOH) [Θ]$_{232}$ −9400, [Θ]$_{255}$ +1200, [Θ]$_{261}$ +2200. Anal. Calcd for $C_9H_{12}Cl_2O_4S$: C, 37.64; H, 4.21. Found: C, 37.68; H, 4.31.

(*R*)-(+)-(*p*-Chlorophenyl)ethylmethylsulfonium *d*-10-camphorsulfonate (1k): [α]$_D$ +7.52° (*c* 1.94, MeOH); mp 128–130 °C (acetone–ether); ^{1}H NMR (acetone-d_6) δ 0.83 (3 H, s), 1.14 (3 H, s), 1.33 (3 H, t, J = 7.2 Hz), 1.33–2.15 (4 H, m), 2.33–3.33 (5 H, m), 3.57 (3 H, s), 4.07 (2 H, q, J = 7.2 Hz), 7.68–8.36 (4 H, AA′BB′, J = 8.0 Hz); CD (MeOH) [Θ]$_{233}$ −6200, [Θ]$_{293}$ +5400. Anal. Calcd for $C_{19}H_{27}ClO_4S_2$: C, 54.46; H, 6.51. Found: C, 54.17; H, 6.68.

(*S*)-(+)-Ethylmethylphenylsulfonium perchlorate (1n): [α]$_D$ +20.3° (*c* 1.03, acetone); mp 104–105.5 °C (acetone–ether); ^{1}H NMR (acetone-d_6) δ 1.40 (3 H, t, J = 7.2 Hz), 3.52 (3 H, s), 3.91 (1 H, q, J = 7.2 Hz), 3.93 (1 H, q, 7.2 Hz), 7.76–8.33 (5 H, m); CD (MeOH) [Θ]$_{223}$ +2200, [Θ]$_{266}$ −260. Anal. Calcd for $C_9H_{13}ClO_4S$: C, 42.77; H, 5.18. Found: C, 42.83; H, 5.31.

(*S*)-(+)-Ethylmethylphenylsulfonium *d*-10-camphorsulfonate (1o): [α]$_D$ +44.57° (*c* 2.8, MeOH); mp 113–115 °C (MeOH–ether); ^{1}H NMR (acetone-d_6) δ 0.81 (3 H, s), 1.10 (3 H, s), 1.40 (3 H, t, J = 7.2 Hz), 1.12–2.10 (4 H, m), 2.33–3.30 (5 H, m), 3.52 (3 H, s), 3.91 (1 H, q, J = 7.2 Hz), 3.93 (1 H, q, J = 7.2 Hz), 7.76–8.33 (5 H, m); CD (MeOH) [Θ]$_{273}$ +3900, [Θ]$_{292}$ +5760. Anal. Calcd for $C_{19}H_{28}O_4S_2$: C, 59.33; H, 7.35. Found: C, 58.91; H, 7.64.

(*S*)-(+)-(*p*-Chlorophenyl)ethylmethylsulfonium *d*-10-camphorsulfonate (1m): [α]$_D$ +46.6° (*c* 1.1, MeOH); mp 135.5–136.5 °C (acetone–MeOH); ^{1}H NMR (acetone-d_6) δ 0.83 (3 H, s), 1.14 (3 H, s), 1.33 (3 H, t, J = 7.2 Hz), 1.33–2.15 (4 H, m), 2.33–3.33 (5 H, m), 3.57 (3 H, s), 4.05 (2 H, q, J = 7.2 Hz), 7.76–8.36 (4 H, AA′BB′); CD (MeOH) [Θ]$_{276}$ +5540, [Θ]$_{295}$ +6850. Anal. Calcd for $C_{19}H_{27}O_4ClS_2$: C, 54.46; H, 6.51. Found: C, 54.20; H, 6.91.

(*R*)-(+)-Ethylmethyl(*p*-nitrophenyl)sulfonium *d*-10-camphorsulfonate (1l): [α]$_D$ +11.3° (*c* 1.47, MeOH); mp 142–143 °C (acetone–MeOH); ^{1}H NMR (MeOH-d_4) δ 1.00 (3 H, s), 1.27 (3 H, s), 1.55 (3 H, t, J = 8.0 H), 1.61–3.40 (9 H, m), 3.57 (3 H, s), 3.97 (2 H, q, J = 8.0 Hz), 8.43–8.70 (4 H, AA′BB′); CD (MeOH) [Θ]$_{212}$ −730, [Θ]$_{220}$ −400, [Θ]$_{294}$ +7300. Anal. Calcd for $C_{19}H_{27}O_6NS_2$: C, 53.12; H, 6.35. Found: C, 52.74; H, 6.72.

(*S*)-(+)-1,6-Dimethyl-3,4-dihydro-2*H*-1-benzothiopyranium *d*-10-camphorsulfonate (1p): [α]$_D$ +26.4° (*c* 1.3, MeOH); mp 135–136 °C (acetone–ether); ^{1}H NMR ($CDCl_3$) δ 0.81 (3 H, s), 1.08 (3 H, s), 1.17–2.30 (6 H, m), 2.37 (3 H, s), 2.43–3.33 (7 H, m), 3.33 (3 H, s), 3.90–4.30 (2 H, m), 7.10 (1 H, s), 7.17 (1 H, d, J = 8.0 Hz), 7.56 (1 H, d, J = 8.0 Hz); CD (MeOH) [Θ]$_{296}$ +6130. Anal. Calcd for $C_{21}H_{30}O_4S_2$: C, 61.42; H, 7.34. Found: C, 61.33; H, 7.60.

(*R*)-(−)-2-Octyl Bromide (16a).[29] Phosphorus tribromide (21.0 g, 77 mmol) was added slowly to 10.1 g (77 mmol) of (*S*)-(+)-2-octanol ([α]$^{20}_{546}$ +11 ± 1°) (Fluka) at 0 °C, and the mixture was stirred for 8 h at room temperature, then allowed to warm to 50 °C. The mixture was poured into a mixture of ether and saturated aqueous $NaHCO_3$. The aqueous phase was extracted with ether and the combined organic extracts were dried ($MgSO_4$) and concentrated in vacuo to afford (*R*)-(−)-2-octyl bromide (**16a**) (13.2 g, 88.5%): [α]$_D$ −34.1° (*c* 8.7, EtOH) (lit.[29] [α]$_D$ −44.9° (EtOH)); ^{1}H NMR ($CDCl_3$) δ 0.67 (13 H, br s), 1.66 (3 H, d, J = 7.0 Hz), 3.80–4.33 (1 H, m).

Unresolved Methyl-(*S*)-2-octylphenylsulfonium Perchlorate (13a). To a mixture of silver perchlorate (1.09 g, 5.26 mmol) and (*S*)-(+)-2-octyl phenyl sulfide ([α]$_D$ +1.72° (*c* 4.97, $CHCl_3$)) (1.19 g, 5.35 mmol) in 5 mL of acetonitrile, which was prepared from (*R*)-(−)-2-octyl bromide ([α]$_D$ −34.1° (*c* 8.7, EtOH)) and thiophenol, was added slowly a solution containing of methyl

(28) For a review of synthesis of sulfonium salts: Lowe, P. A. *The Chemistry of the Sulfonium Group*; Stiring, C. J. M., Patai, S. Eds.; John Wiley & Sons: New York, 1981; pp 267–312.

(29) (a) Hsueh, C. M.; Marvel, C. S. *J. Am. Chem. Soc.* **1928**, *50*, 856. (b) Preparation of optically pure isomers of octyl bromide: Coulson, E. J.; Gerrard, W.; Hudson, H. R. *J. Chem. Soc.* **1965**, 2364. *l* form [α]$^{20}_D$ −44.91°.

iodide (2.51 g, 17.7 mmol) in 5 mL of acetonitrile at 0 °C and the mixture was stirred for 1 day at room temperature. After the insoluble materials were filtered off, the solvent was evaporated and the residue was washed with ether to give methyl-(*S*)-2-octylphenylsulfonium perchlorate (**13a**) (1.8 g, 100%): $[\alpha]_D$ −4.52° (*c* 2.71, EtOH); ^{1}H NMR (MeOH-d_4) δ 0.90–1.40 (13 H, m), 1.55 (3 H, d, *J* = 7.0 Hz), 3.30 (3 H, s), 3.42–4.13 (1 H, m), 7.63–8.10 (5 H, m).

Optically Active 2-(2-Octyl)-2-(methoxycarbonyl)-1-indanone (14a). A mixture of sulfonium salt **13a** (1.46 g, 3.35 mmol) ($[\alpha]_D$ −4.52° (*c* 2.71, EtOH)), cyclic β-keto ester **2** (743 mg, 3.91 mmol), and anhydrous potassium carbonate (813 mg, 5.88 mmol) was stirred in dichloromethane (15 mL) at room temperature for 2 days. After filtration of insoluble materials, the alkylated product was purified by silica gel column chromatography to give a mixture of two C-octylated diastereoisomers **14a** (51.8 mg, 8.3%; $[\alpha]_D$ +24.8° (*c* 1.03, EtOH)), which were separated by medium pressure column chromatography (hexane/AcOEt, 25:1) to give the fast eluted diastereoisomer, (2*S*,2′*R*)-(−)-2-(2-octyl)-2-(methoxycarbonyl)-1-indanone ((−)-**14a**) ($[\alpha]_D$ −109.4° (*c* 1.32, EtOH); CD (EtOH) $[\Theta]_{340}$ −1490), and the slow eluted diastereoisomer, (2*R*,2′*R*)-(+)-2-(2-octyl)-2-(methoxycarbonyl)-1-indanone ((+)-**14a**) ($[\alpha]_D$ +127.4° (*c* 1.39, EtOH; CD (EtOH) $[\Theta]_{340}$ +1740): ^{1}H NMR ($CDCl_3$) δ 0.66–1.50 (16 H, m), 2.45–2.88 (1 H, m), 3.04 (1 H, d, *J* = 18.4 Hz), 3.67 (3 H, s), 3.72 (1 H, d, *J* = 18.4 Hz), 7.17–7.83 (4 H, m); MS *m*/*z* 302 (M^+), 284, 271, 243, 190; HRMS, calcd for $C_{19}H_{26}O_3$ 302.1881, found 302.1859.

(*R*)-(−)-2-(2-Octyl)-1-indanone (15a). A solution containing the two C-octylated diastereoisomers (**14a**) (51.7 mg, 0.171 mmol) and lithium iodide (240 mg, 1.42 mmol) in 7 mL of DMF–H_2O (9:1) was heated under gentle reflux for 4 days.[22] After cooling the solution to room temperature, the product was extracted with ether to give (*R*)-(−)-2-(2-octyl)-1-indanone (**15a**) (32.5 mg, 77.8%): $[\alpha]_D$ −20.4° (*c* 1.60, $CHCl_3$); ^{1}H NMR (CCl_4) δ 0.63–1.50 (16 H, m), 2.38–3.15 (3 H, m), 4.07–4.15 (1 H, m), 7.13–7.67 (4 H, m); MS *m*/*z* 244 (M^+), 229, 159, 145, 132; HRMS, calcd for $C_{17}H_{24}O$ 244.1826, found 244.1841.

2-(2-Octyl)-2-(methoxycarbonyl)-1-indanone (17a). A mixture containing 2-(methoxycarbonyl)-1-indanone (**2**) (307 mg, 1.62 mmol), anhydrous potassium carbonate (468 mg, 3.39 mmol), and 18-crown-6-ether (68.9 mg, 0.28 mmol) in dry methanol (10 mL) was stirred at room temperature. After the addition of (*R*)-(−)-2-octyl bromide (**16a**)[30] (499 mg, 2.59 mmol) ($[\alpha]_D$ −34.1° (*c* 8.7, EtOH)) to the solution, the reaction mixture was refluxed for 2 days. Methanol was removed under vacuum and the product was extracted with ether. The crude product was purified by preparative TLC to give a mixture of two C-octylated diastereoisomers **17a** (106.6 mg, 21.0%; $[\alpha]_D$ −11.6° (*c* 1.99, EtOH)), which were separated by medium pressure column chromatography (hexane/AcOEt, 25:1) to give the slow eluted diastereoisomer, (2*S*,2′*S*)-(−)-2-(2-octyl)-2-(methoxycarbonyl)-1-indanone ((−)-**17a** ($[\alpha]_D$ −126.4° (*c* 1.54, EtOH); CD (EtOH) $[\Theta]_{340}$ −1760), and the fast eluted diastereoisomer, (2*R*,2′*S*)-(+)-2-(2-octyl)(2-methoxycarbonyl)-1-indanone ((+)-**17a**) ($[\alpha]_D$ +89.2° (*c* 1.86, EtOH) (CD (EtOH) $[\Theta]_{340}$ +1400); MS *m*/*z* 302 (M^+), 284, 271, 243, 190; HRMS, calcd for $C_{19}H_{26}O_3$ 302.1881, found 302.1952.

(*S*)-(+)-2-(2-Octyl)-1-indanone (18a). A solution containing the C-octylated diastereoisomer **17a** (62.4 mg, 0.206 mmol) and lithium iodide (192 mg, 1.13 mmol) in 6 mL of DMF–H_2O (9:1) was heated under gentle reflux for 4 days. After cooling the solution to room temperature, the product was extracted with ether to give (*S*)-(+)-2-(2-octyl)-1-indanone (**18a**) (45.0 mg, 89.3%); $[\alpha]_D$ +20.7° (*c* 2.08, $CHCl_3$); ^{1}H NMR (CCl_4) δ 0.63–1.50 (16 H, m), 2.38–3.15 (3 H, m), 4.07–4.15 (1 H, m), 7.13–7.67 (4 H, m); MS *m*/*z* 244 (M^+), 229, 159, 145, 132; HRMS, calcd for $C_{17}H_{24}O$ 244.1826, found 244.1826.

(*R*)-(−)-Butyl Bromide (16b).[31] Phosphorus tribromide (20.0 g, 77 mmol) was added slowly to 5.23 g (70.6 mmol) of (*S*)-(+)-2-butanol ($[\alpha]_D$ +12.9° (*c* 1.0, MeOH)) (Nakarai Chemicals, LTD) at 0 °C. After 24 h, the reaction mixture was allowed to warm to 50 °C and poured into a mixture of ether and saturated aqueous $NaHCO_3$. The aqueous phase was extracted with ether, and the combined organic extracts were dried ($MgSO_4$) and concentrated to afford (*R*)-(−)-2-butyl bromide (**16b**) (7.65 g, 79.1%); $[\alpha]_D$ −22.9° (*c* 4.91, EtOH); ^{1}H NMR (CCl_4) δ 1.10 (3 H, t, *J* = 7.2 Hz), 1.66 (3 H, d, *J* = 7.0 Hz), 3.31 (q, 2 H, *J* = 7.2 Hz), 3.94 (1 H, q, *J* = 7.0 Hz).

Unresolved Methyl-(*S*)-2-butylphenylsulfonium Perchlorate (13b).[32] To a mixture containing silver perchlorate (1.93 g, 9.31 mmol) and (*S*)-(+)-2-butyl phenyl sulfide ($[\alpha]_D$ +11.8° (*c* 5.2, MeOH)) (1.54 g, 9.27 mmol) in 5 mL of acetonitrile, which was prepared from (*R*)-(−)-2-butyl bromide ($[\alpha]_D$ −22.9° (*c* 4.91, EtOH)) and thiophenol, was added slowly a solution of methyl iodide (12.1 g, 85.2 mmol) in acetonitrile (5 mL) at 0 °C and the mixture was stirred for 1 day at room temperature. After the insoluble materials were filtered, the solvent was evaporated and the residue was washed with ether to give methyl-(*S*)-2-butylphenylsulfonium perchlorate (**13b**) (1.70 g, 95.1%): $[\alpha]_D$ +3.29° (*c* 4.18, MeOH); ^{1}H NMR (acetone-d_6) δ 1.31 (3 H, t, *J* = 7.2 Hz), 1.31 (1.5 H, d, *J* = 7.2 Hz), 1.58 (1.5 H, d, *J* = 7.2 Hz), 1.62 (2 H, q, *J* = 7.2 Hz), 3.43 (1.5 H, s), 3.47 (1.5 H, s), 4.11 (1 H, q, *J* = 7.2 Hz), 7.67–8.25 (5 H, m).

2-*sec*-Butyl-2-(methoxycarbonyl)-1-indanone (14b). A mixture of sulfonium salt **13b** (1.70 g, 6.06 mmol) ($[\alpha]_D$ +3.29° (*c* 4.18, MeOH)), cyclic β-keto ester **2** (924 mg, 4.86 mmol), and potassium carbonate (1.57 g, 11.3 mmol) in dichloromethane (15 mL) was stirred at room temperature for 2 days. After filtration of insoluble materials, the alkylated product was purified by silica gel column chromatography to give C-butylated diastereoisomers **14b**: $[\alpha]_D$ −9.2° (*c* 1.56, MeOH); ^{1}H NMR (CCl_4) δ 0.73 (3 H, t, *J* = 9.0 Hz), 0.92 (3 H, d, *J* = 9.0 Hz), 2.33–2.73 (2 H, m), 2.94 (1 H, d, *J* = 18.0 Hz), 3.59 (3 H, s), 3.98 (1 H, d, *J* = 18.0 Hz), 3.83–4.13 (1 H, m), 7.18–7.73 (4 H, m); MS *m*/*z* 246 (M^+), 228, 215, 203, 190; HRMS, calcd for $C_{15}H_{18}O_3$ 246.1255, found 246.1230.

(*R*)-(−)-2-*sec*-Butyl-1-indanone (15b). A mixture of diastereoisomers **14b** (31.3 mg, 0.12 mmol) and lithium iodide (240 mg, 1.42 mmol) in 5 mL of DMF–H_2O (9:1) was heated under gentle reflux for 3 days.[22] After cooling the solution to room temperature, the product was extracted with ether to give (*R*)-(−)-2-*sec*-butyl-1-indanone (**15b**) (23.9 mg, 100%): $[\alpha]_D$ −15.8° (*c* 0.98, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.74 (3 H, t, *J* = 6.4 Hz), 0.99 (3 H, dd, *J* = 6.0 and 4.0 Hz), 1.40 (2 H, q, *J* = 6.4 Hz), 2.40–2.77 (1 H, m), 2.83–3.17 (2 H, m), 4.07–4.15 (1 H, m), 7.08–7.67 (4 H, m); MS *m*/*z* 188 (M^+), 173, 159, 145, 133; HRMS, calcd for $C_{13}H_{16}O$ 188.1200, found 188.1153.

2-*sec*-Butyl-2-(methoxycarbonyl)-1-indanone (17b). A mixture of 2-(methoxycarbonyl)-1-indanone (**2**) (357 mg, 1.88 mmol) and anhydrous potassium carbonate (602 mg, 1.88 mmol) in 8 mL of methanol was stirred at room temperature. After the addition of a methanol solution of (*R*)-(−)-2-butyl bromide (**16b**) (5 mL) ($[\alpha]_D$ −22.9° (*c* 4.19, EtOH)), the reaction mixture was warmed to 40 °C and stirred for 5 days. After methanol was removed under vacuum, the product was extracted with ether and purified by preparative TLC to give C-butylated diastereoisomers **17b** (77.4 mg, 16.7%): $[\alpha]_D$ −10.51° (*c* 1.5, MeOH); ^{1}H NMR (CCl_4) δ 0.73 (3 H, t, *J* = 9.0 Hz), 0.92 (3 H, d, *J* = 9.0 Hz), 2.33–2.73 (2 H, m), 2.94 (1 H, d, *J* = 18.0 Hz), 3.59 (3 H, s), 3.98 (1 H, d, *J* = 18.0 Hz), 3.83–4.13 (1 H, m), 7.18–7.73 (4 H, m); MS *m*/*z* 246 (M^+), 228, 215, 203, 190; HRMS, calcd for $C_{15}H_{18}O_3$ 246.1255, found 246.1225.

(*S*)-(+)-2-*sec*-Butyl-1-indanone (18b). A solution containing C-butylated diastereoisomers **14b** (31.3 mg, 0.127 mmol) and lithium iodide (165 mg, 9.70 mmol) in 5 mL of DMF–H_2O (9:1) was heated under gentle reflux for 3 days.[22] After cooling the solution to room temperature, the product was extracted with ether to give (*S*)-(+)-2-*sec*-butyl-1-indanone (**18b**) (23.5 mg, 98.7%): $[\alpha]_D$ +9.18° (*c* 0.92, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.74 (3 H, t, *J* = 6.4 Hz), 0.99 (3 H, dd, *J* = 6.0 Hz, and *J*′ = 4.0 Hz), 1.40 (2 H, q, *J* = 6.4 Hz), 2.40–2.77 (1 H, m), 2.83–3.17 (2 H, m),

(30) The ee of **16a** ($[\alpha]_D$ −34.1°) is probably high since the bromide produced by bromination of the optically active alcohol has a rotation close to that ($[\alpha]_D$ −34.3°) of (*R*)-(−)-2-octyl bromide in ref 29. The ee of **18a,b** could not be determined. The starting bromide **16b** might undergo partial racemization during alkylation of the enolate of **2** (see ref 23).

(31) Goodwin, D. G.; Hudson, H. R. *J. Chem. Soc. B* **1968**, 1333. *d* form $[\alpha]^{20}_D$ +42.64°; *l* form $[\alpha]^{20}_D$ −43.7°.

(32) There is no chiral induction in the formation of **13b** since its ^{1}H NMR spectrum showed that the methyl groups on the sulfonium sulfur atom were observed at δ 3.43 (1.5 H, s) and 3.47 (1.5 H, s) and the ratio of diastereomeric methyl groups is 1:1.

4.07–4.15 (1 H, m), 7.08–7.67 (4 H, m); MS m/z 189 (M^+), 173, 159, 145, 133; HRMS, calcd for $C_{13}H_{16}O$ 188.1200, found 188.1210.

Registry No. **1a**, 100461-72-1; **1b**, 119695-44-2; **1c**, 10504-65-1; **1d**, 119695-46-4; **1e**, 100569-75-3; **1f**, 100461-68-5; **1g**, 100461-70-9; **1h**, 119695-48-6; **1i**, 119785-62-5; (*R*)-**1j**, 100461-74-3; (*R*)-**1k**, 100569-99-1; (*R*)-**1l**, 119816-10-3; (*S*)-**1m**, 119695-50-0; (*S*)-**1n**, 51210-64-1; (*S*)-**1o**, 113083-01-5; (*S*)-**1p**, 119785-64-7; **,2**, 22955-77-7; **2**·K, 119742-72-2; **3**, 72181-95-4; (*R*)-(+)-**3**, 100461-82-3; (*S*)-(−)-**3**, 100461-84-5; **3b**, 119785-60-3; (*S*)-(−)-**4**, 100461-83-4; (*R*)-(+)-**4**, 100461-85-6; **4f**, 119695-41-9; **4g**, 53110-84-2; **4h**, 119695-42-0; **5a**, 100461-78-7; **5b**, 100461-79-8; **6f**, 100461-80-1; **6g**, 100461-81-2; (*R*)-(+)-**7**, 35188-22-8; (*R*)-(+)-**8**, 51207-25-1; **9**, 41302-34-5; **10**, 7500-91-6; (*R*)-(−)-**10**, 89656-82-6; (*S*)-(+)-**10**, 89656-83-7; (*S*)-(+)-**11**, 100461-86-7; (*R*)-(−)-**11**, 119695-51-1; (±)-**11**, 119785-65-8; **13a** (isomer 1), 119785-67-0; **13a** (isomer 2), 119785-76-1; **13b** (isomer 1), 119785-72-7; **13b** (isomer 2), 119785-80-7; (−)-**14a**, 111170-63-9; (+)-**14a**, 111170-60-6; **14b** (isomer 1), 119695-52-2; **14b** (isomer 2), 119695-54-4; (−)-**15a** (isomer 1), 119785-68-1; (−)-**15a** (isomer 2), 119785-77-2; **15b** (isomer 1), 119785-73-8; **15b** (isomer 2), 119785-81-8; **16a**, 5978-55-2; **16b**, 5787-33-7; (−)-**17a**, 111189-00-5; (+)-**17a**, 111170-62-8; **17b** (isomer 1), 119695-53-3; **17b** (isomer 2), 119720-83-1; (+)-**18a** (isomer 1), 119785-69-2; (+)-**18a** (isomer 2), 119785-78-3; **18b** (isomer 1), 119785-74-9; **18b** (isomer 2), 119785-82-9; ethyl phenyl sulfide, 622-38-8; (*S*)-(+)-2-octanol, 6169-06-8; thiophenol, 108-98-5; (*S*)-(+)-2-octylphenyl sulfide, 111265-18-0; (*S*)-(+)-2-butanol, 4221-99-2; (*S*)-(+)-2-butylphenyl sulfide, 119785-70-5.

Alkylmetal Asymmetric Reduction. 20.[1] A Reinvestigation on the Stereochemistry of Ketone Reductions by Optically Active Alkylmetal Compounds

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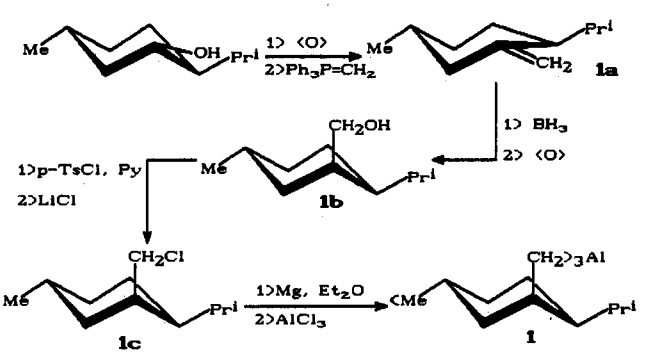
New chiral organometallic reagents, derived from (−)-menthol, tris[[(1*S*,2*S*,5*R*)-2-isopropyl-5-methylcyclohex-1-yl]methyl]aluminum, and from (+)-camphor, [[(1*R*,3*R*)-2,2-dimethylbicyclo[2.2.1]hept-3-yl]methyl]beryllium chloride and bis[[(1*R*,3*R*)-2,2-dimethylbicyclo[2.2.1]hept-3-yl]methyl]beryllium, have been devised as reducing agents. These compounds exhibit a good enantioface-differentiating ability in the reduction of prochiral ketones. The stereochemical results are discussed in the light of additional data on the reduction of ketones by other alkylmetal compounds. The mechanism proposed is consistent with previous reports, and the overall results have shown that, when alicyclic organometallic derivatives are involved in this kind of reduction, the interpretation of the stereochemistry of the processes should include consideration of the particular conformational freedom of each system.

In recent years, a variety of approaches to enantioselective reduction of carbonyl compounds have resulted in systems showing high enantiomeric purities in the reaction products.[2] In this context we have employed a number of chiral organometallic species, especially alkylaluminum compounds, derived from naturally occurring terpenoids, for asymmetric reduction of ketones with varying degrees of enantioselectivity.[3–5] Although some systems have been described that provide useful enantioselectivity,[3,5] our knowledge of reagent structure and mode of reduction has remained at a primitive level, limiting both application and further development. However, in earlier reports,[6,7] we have drawn a simple rule that seemed useful for prediction of the absolute configuration of the carbinol products. In an effort to obtain a greater understanding of the stereochemical outcome of this kind of alkylmetal enantioselective reduction and to confirm the stereochemical model proposed, we have undertaken a thorough investigation of the stereochemical outcome of the reduction of prochiral ketones by some chiral organometallic compounds having alkyl groups of different conformational homogeneity. Therefore we report here the results obtained by using tris[[(1*S*,2*S*,5*R*)-2-isopropyl-5-methylcyclohex-1-yl]-methyl]aluminum and some rigid, highly hindered, organometallic reagents of beryllium and magnesium.

Scheme I



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