(–), 138.50 (–), 123.00 (–), 107.65 (+), 106.99 (+), 101.40 (+), 57.99 (+), 42.74 (–), 39.16 (+), 38.14 (+), 29.96 (–), 28.99 (–), 26.27 (–), 23.77 (–); IR (CCl_4) 2935 (s), 1650 (s), 1613 (s), 1504 (s), 1478 (s), 1461 (s), 1411 (s), 1392 (m), 1355 (s), 1320 (m), 1282 (m), 1248 (s), 1042 (s), 943 (m), 804 (s), 797 (s) cm^{-1}, MS (EI, 70 eV) m/z (rel int) 271 (M^+, 2.5), 270 ($M^+ - 1$, 2.4), 242 (0.4), 228 (1.0), 203 (1.0), 189 (1.1), 123 (3.4), 121 (32.2), 119 (97.3), 117 (100.0), 86 (2.7), 84 (16.6), 82 (25.1), 49 (11.0), 47 (34.0); HRMS calcd for $C_{16}H_{17}NO_3$ 271.1208, found 271.1196. These data matched the literature data.[6e]

Acknowledgment. We thank the National Institutes of Health (GM-35572) and the University of Michigan (Sokol Predoctoral Fellowship to J.M.S.) for support of this research.

Supplementary Material Available: Improved experimental procedures for the preparation of **8** and **32** and ^{1}H NMR and ^{13}C NMR spectra of the compounds which had no elemental analysis: **3** (γ-lycorane), **14**, **26–31**, and *N*-hydroxy **29** (21 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

Asymmetric Synthesis of Alkane- and Arenesulfinates of Diacetone-D-glucose (DAG): An Improved and General Route to Both Enantiomerically Pure Sulfoxides

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Received April 29, 1992

Diacetone-D-glucose (DAG), a commercially available, sugar-derived secondary alcohol, was found to react with alkane- and arenesulfinyl chlorides in the presence of a tertiary amine in a very useful manner. When i-Pr_2NEt is used as the base, (–)-(*S*)-alkane- and arenesulfinates are obtained in 50–90% yield with 89–≥95% de. Simply changing the base from i-Pr_2NEt to Py affords (+)-(*R*)-alkane- and arenesulfinates in 56–87% yield with 70–≥95% de. The de's were determined by ^{1}H NMR. Optically pure alkane- and arenesulfinates are obtained either by recrystallization or by column chromatography. These sulfinates were transformed into various enantiomerically pure sulfoxides (alkyl alkyl and alkyl aryl) by reaction with different Grignard reagents. This new methodology is cheap, quick, and very convenient when both enantiomers of a given sulfoxide are needed enantiomerically pure. The influence of the solvent, as well as the effect of other types of bases, on the stereochemical course of the reaction has been evaluated, and a possible origin of the diastereoselectivity is discussed. Other optically pure secondary alcohols are used in the same reaction, and the comparison of their behavior with that of DAG is also reported.

Introduction

Optically active sulfoxides have proven themselves to be powerful auxiliaries in highly efficient asymmetric syntheses.[1-8] Additionally, molecules bearing a sulfinyl function (such as sparsomycin[9] and oxisurane[10] and their analogs,[11] carpetomycin A,[12] RP49356,[13] and several methyl vinyl sulfoxides[14]) are of great biological interest. For these reasons, the preparation of sulfoxides with high enantiomeric purity has received considerable attention over the years.

Nowadays, practically all types of optically pure sulfoxides can be prepared by combining the different methods described in the literature. Nevertheless, a simple and general protocol that permits quick access to the desired sulfoxide is still greatly needed. Up to now, there have been two basic approaches to the synthesis of optically pure (op) sulfoxides: (i) the asymmetric oxidation of prochiral sulfides[15] and (ii) the nucleophilic addition of alkyl or aryl ligands to an electrophilic sulfur with established chirality and the subsequent displacement of the sulfoxide. Because of the limited generality of the former

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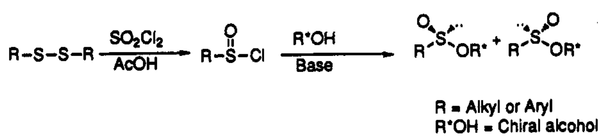
Scheme I



method, especially for the synthesis of sulfoxides bearing two alkyl groups, the nucleophilic displacement seems to be the most convenient approach.

The widely used Andersen method[16] is the most popular adaptation of the latter strategy. The method is based on the conversion of chiral sulfinates into sulfoxides with various types of organometallics. The starting sulfinic ester is generally obtained from a chiral alcohol, usually (−)-menthol, as a mixture of epimeric sulfinates, which have to be separated.[1,2,6,17] This technique provides ready access to only one enantiomeric series of sulfoxides because generally only one diastereomer of the intermediate menthol sulfinate ester is crystalline. The Andersen method has allowed the synthesis of optically pure diaryl and aryl alkyl sulfoxides, but the preparation of enantiomerically pure dialkyl sulfoxides is not possible by this method. The starting alkanesulfinates have not been available epimerically pure at sulfur; e.g., the menthyl methanesulfinates are oils, and attempts to separate the epimers have not succeeded.

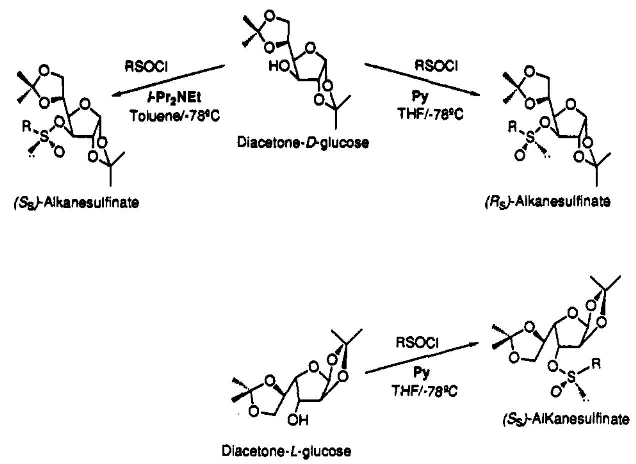
Andersen and Mikolajczyk[18] overcame this problem by using (−)-cholesterol instead of (−)-menthol as the chiral alcohol. Cholesteryl (−)-(*S*)- and (+)-(*R*)-methanesulfinates were obtained diastereomerically pure by fractional recrystallization, although in very poor chemical yields (3.5% and 0.7%, respectively). Additionally, some optically pure chiral sulfoxides have been obtained from 1,2,3-oxathiazolidine with ephedrine as the chiral auxiliary.[19] Recently, Kagan's group reported a more efficient route, using chiral sulfites, that permits the preparation of some op dialkyl sulfoxides.[20]

In this paper, we describe a short, efficient, and general protocol for the preparation of optically pure alkane- and arenesulfinates. Both epimers at sulfur can be obtained using DAG as a unique inducer of chirality, and by choosing the appropriate base, we can predict the configuration at the sulfur atom. The efficiency of this methodology has been demonstrated by the preparation of optically active alkyl aryl and dialkyl sulfoxides with high ee (up to 100%).

Results and Discussion

The condensation of a chiral secondary alcohol with an alkane- or arenesulfinyl chloride in the presence of a base (usually Py) is a general method for the asymmetric synthesis of sulfinate esters. The starting sulfinyl chlorides are readily accessible by oxidation of the corresponding disulfide according to the Herrmann methodology[21] (Scheme I). In the pool of enantiomerically pure chiral alcohols, besides the widely used (−)-menthol, there are other chiral secondary alcohols that have been used as inducers of chirality in this reaction, with some good results but with no general synthetic utility.[18,22] Sugar derivatives have been employed in the preparation of chiral sulfinic esters.[23] Carbohydrates are cheap starting materials that possess an ample body of hydroxylic functions in many configurations, and the hydroxyl groups can be selectively protected and manipulated in order to obtain a specific secondary alcohol. Carbohydrates could be successfully used in the preparation of chiral, op sulfinates either by kinetic resolution of the racemic sulfinyl chloride or by a good physical separation of the two possible sulfinic ester diastereomers created by the chiral centers of the sugar matrix. Accordingly, our utilization of DAG as the chiral alcohol was dictated by the hope that the two diastereomeric sulfinates formed could be easily separated by column chromatography or by recrystallization. Moreover, DAG is a cheap, commercially available starting material in which the secondary hydroxylic function is flanked by two functionalities that are very different from both a steric and a stereoelectronic point of view; that is, the OH at C-3 in DAG is surrounded by a hydrogen at C-2 and by the D-glyceraldehyde chiral backbone at C-4.

Scheme II



R= Me, Et, Pr, *i*-Pr, *p*-Tol.

In a preliminary paper,[24] we reported that DAG reacted with methanesulfinyl chloride in the presence of a base in a very useful manner. When Py was used as base, op (*R*)-methanesulfinate 1 was obtained in 87% yield after flash chromatography of the reaction mixture (which contained 7% of the (*S*)-methanesulfinate). Simply changing the base from Py to $i\text{-}Pr_2NEt$ afforded diastereomerically pure (*S*)-sulfinate 2 in 90% yield after purification by crystallization from hexane (Scheme II, R = Me).

Because of its importance and novelty, we now report a systematic study of this reaction and the generalization of the reaction to the asymmetric synthesis of both epimerically pure alkane- and arenesulfinates.

The drastic and spectacular change in the stereochemistry of the reaction caused by changing the base used prompted us to carry out a systematic study of the effect of the base. Different bases were used in the reaction of DAG with methanesulfinyl chloride in various solvents at −78 °C. The results of the study confirmed that the

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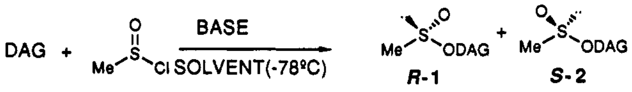
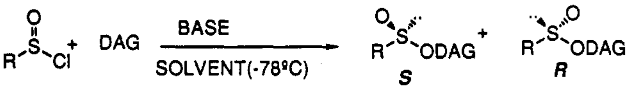
Table I. Influence of the Base and Solvent on the Stereochemistry of the Reaction of DAG with Methanesulfinyl Chloride



base	solvent	(*R*)-1/(*S*)-2
pyridine	THF	93/7
	toluene	83/17
	Et_2O	84/16
	CH_2Cl_2	76/24
	CH_3CN/THF	73/27
DMAP	THF	78/22
imidazole	THF	82/18
i-Pr_2NEt	toluene	≤2/≥98[a]
	THF	≤2/≥98[a]
	CH_2Cl_2	≤2/≥98[a]
collidine	THF	37/63
	toluene	17/83
Me_2NPh (DMA)	THF	42/58
	toluene	37/63
NEt_3	THF	17/83
	toluene	≤2/≥98[a]

[a] Only one isomer was detected by ^1H NMR. The conversion of the crude sulfinate into sulfoxide by treatment with *p*-TolMgBr gave 11 with ee ≈98%.[24]

Table II. Reaction of DAG with Different Sulfinyl Chlorides



entry	R	base	solvent	*R*/*S*	yield,[a] %
1	Me	pyridine	THF	93/7	87
2	Me	*i*-Pr_2NEt	toluene	≤2/≥98[b]	90
3	Et	pyridine	THF	86/14	85
4	Et	*i*-Pr_2NEt	toluene	≤2/≥98[b]	90
5	*n*-Pr	pyridine	THF	85/15	75
6	*n*-Pr	*i*-Pr_2NEt	toluene	4/96	80
7	*i*-Pr	pyridine	THF	≥98/≤2[b]	56[c]
8	*i*-Pr	*i*-Pr_2NEt	toluene	≤2/≥98[b]	50[c]
9	*p*-Tol	pyridine	THF	86/14	84
10	*p*-Tol	*i*-Pr_2NEt	toluene	6/94	87

[a] Diastereomerically pure compounds after purification of the major isomers by cc or recrystallization. [b] Only one isomer was detected by ^1H NMR. [c] The low yield is due to decomposition during the purification step (cc).

stereocourse of this reaction is tightly tied to the nature of the base (Table I). The differences in chemical shifts allow the determination of the ratio of sulfinates 1 and 2 by ^1H NMR analysis of the reaction mixture. The anomeric proton H-1 is a doublet (J = 3.5 Hz) with a chemical shift of 5.91 ppm for both 1 and 2. For sulfinate 2, H-2 is also a doublet (J = 3.5 Hz, 4.62 ppm). For sulfinate 1, H-2 is at 4.78 ppm together with H-3 of both sulfinates.

Based on the major sulfinate formed in this reaction, the base can be classified as one of two types: (*i*) *"type A or pyridine-like bases,"* which include Py, DMAP, and imidazole, give principally the (*R*)-methanesulfinate with 56–86% de and (ii) *"type B or i-Pr₂NEt like-bases,"* which include *i*-Pr_2NEt, Et_3N, collidine, and DMA, give mainly the (*S*)-methanesulfinate with 16–≥95% de. Thus, aliphatic amines, including very hindered tertiary amines, behave like *i*-Pr_2NEt, and bases having a nonhindered heterocyclic nitrogen act like pyridine. There is no good correlation between the strength of the base and its behavior in the reaction, and the only meaningful factor seems to be the bulkiness of the amine.

The de is also dependent on the solvent. *Py-like bases* give the highest de in THF, while the de obtained with *i-Pr₂NEt-like bases* is highest in toluene.

To our knowledge, this is the first report that the stereocourse of formation of sulfinate esters depends not only on the chiral alcohol but also on the nature of the base. With the same inducer of chirality, DAG, simply changing the base from Py to *i*-Pr_2NEt affords optically pure (*S*)-methanesulfinate instead of the *R* diastereomer. Using DAG and *i*-Pr_2NEt is equivalent to using Py and changing the inducer of chirality from cheap and commercially available DAG to the diacetone derivative of expensive, nonnatural (–)-L-glucose (Scheme II, R = Me).

Encouraged by the good results obtained with the methanesulfinates, we extended the methodology to other alkane- and arenesulfinates. For this purpose, several sulfinyl chlorides (alkane and arene) were synthesized from the corresponding disulfide.[21] The reactivity of each sulfinyl chloride with DAG was checked using the optimal conditions previously determined for each base: (1) *i*-Pr_2NEt in toluene at –78 °C and (2) Py in THF at –78 °C. The results obtained are summarized in Table II. Fortunately, all the sulfinyl chlorides show behavior similar to that of methanesulfinyl chloride:

(i) In all cases, the stereochemistry of the final sulfinate ester is determined by the base used. Sulfinates of *S* configuration at the sulfur atom are obtained as the main isomer (de 89–≥95%) when *i*-Pr_2NEt is used, and sulfinates with *R* configuration at sulfur are predominantly obtained (de 70–≥95%) when Py is used as the base.

(ii) All the sulfinates are obtained in high chemical yields, and the de's are easily determined as before on the basis of the ^1H NMR chemical shifts of H-1 and H-2 (see Table III).

(iii) Purification of sulfinates is, in general, easily achieved by column chromatography (cc) (3:7, ether–hexane). The only exceptions are the *p*-toluenesulfinates, where the two isomers are not sufficiently resolved for a convenient chromatographic separation (entry 9, Table II). Fortunately, the (*S*)-*p*-toluenesulfinate (10) is a solid, and it can be obtained optically pure in 87% yield by a recrystallization from hexane. It is interesting to note that

Table III. Specific Rotation and ^1H NMR Data of Alkane- and Arenesulfinates, RS(O)ODAG

compd	R	config at S	$[\alpha]_D$	H-1 (ppm)	H-2 (ppm)
1	Me	*R*	+17 (*c* 4.4, Me_2CO)	5.91	4.73–4.80
2	Me	*S*	–60 (*c* 2.7, Me_2CO)	5.91	4.62
3	Et	*R*	+12 (*c* 1.8, Me_2CO)	5.89	4.65–4.82
4	Et	*S*	–63 (*c* 4.3, Me_2CO)	5.88	4.64
5	*n*-Pr	*R*	+6.4 (*c* 1.1, Me_2CO)	5.91	4.67–4.83
6	*n*-Pr	*S*	–33 (*c* 0.5, Me_2CO)	5.88	4.85
7	*i*-Pr	*R*	+11 (*c* 2.9, Me_2CO)	5.89	4.78
8	*i*-Pr	*S*	–50 (*c* 0.3, Me_2CO)	5.90	4.60
9	*p*-Tol	*R*	+10 (*c* 1.7, Me_2CO)	5.86	4.7
10	*p*-Tol	*S*	–125 (*c* 0.4, Me_2CO)[a]	5.92	4.84

[a] Diastereomeric mixture containing 86/14 of (*S*)-10/(*R*)-9.

Table IV. Synthesis of Optically Active Methyl Sulfoxides, MeS(O)R, from DAG Methanesulfinates and R′MgX

methanesulfinates				sulfoxide				
entry	compd	(config at S)	R′in R′MeX[a]	compd	yield,[b] %	$[\alpha]_D$[c]	config (ee %)[d]	lit. $[\alpha]_D$[ref]
1	**1**	*R*	*p*-Tol	**11**	84	+145 (*c* 8.3, Me_2CO)	*R* (100)	+146[26]
2	**1**	*R*	Ph	**12**	78	+149 (*c* 2.0, EtOH)	*R* (100)	+146[27]
3	**1**	*R*	$PhCH_2$	**13**	83	−105 (*c* 6.0, EtOH)	*R* (100)	−106[18]
4	**1**	*R*	*n*-Pr	**14**	66	−137 (*c* 6.0, EtOH)	*R* (100)	−139[18]
5	**1**	*R*	*t*-Bu	**15**	62	+4.3 (*c* 1.64, Me_2CO)	*S* (100)	+4.2[20,28]
6	**2**	*S*	*p*-Tol	**16**	90	−145 (*c* 1.0, Me_2CO)	*S* (100)	−146[26]
7	**2**	*S*	Ph	**17**	80	−143 (*c* 1.0, Me_2CO)	*S* (100)	−146[27]
8	**2**	*S*	$PhCH_2$	**18**	83	+104 (*c* 0.15, EtOH)	*S* (100)	+106[18]
9	**2**	*S*	*n*-Pr	**19**	69	+136 (*c* 0.31, EtOH)	*S* (100)	+139[18]
10	**2**	*S*	*t*-Bu	**20**	50	−4.3 (*c* 3.83, Me_2CO)	*R* (100)	−4.2[20,28]
11	**2**	*S*	vinyl	**21**	37	+229 (*c* 0.41, $CHCl_3$)	*S* (100)	

[a] All reactions were carried out by adding 1.2–1.3 equiv of the Grignard reagent to a 0.05 M solution of the DAG methanesulfinate adduct in toluene at 0 °C. [b] Yield after flash chromatography. [c] All the $[\alpha]_D$ were taken in the same solvent as those given in the literature. [d] Measured by ^1H NMR with $Eu(hfc)_3$ and by comparison with maximum specific rotation given in the literature.

Table V. Synthesis of Optically Active Sulfoxides, RS(O)R′, from DAG Alkane- or Arenesulfinates, RS(O)ODAG, and R′MgX

sulfinate				sulfoxide				
compd	R	config at S	R′in R′MgX[a]	compd	yield,[b] %	$[\alpha]_D$[c]	config (ee %)[d]	lit$[\alpha]_D$[ref]
1	Me	*R*	*p*-Tol	**11**	84	+145 (*c* 8.3, Me_2CO)	*R* (100)	+146[26]
2	Me	*S*	*p*-Tol	**16**	90	−145 (*c* 1.0, Me_2CO)	*S* (100)	−146[26]
3	Et	*R*	*p*-Tol	**22**	96	+195 (*c* 4.0, Me_2CO)	*R* (99)	−198[29]
4	Et	*S*	*p*-Tol	**23**	90	−195 (*c* 2.9, Me_2CO)	*S* (99)	−198[29]
5	*n*-Pr	*R*	*p*-Tol	**24**	88	+203 (*c* 1.2, EtOH)	*R* (100)	+201[30]
6	*n*-Pr	*S*	*p*-Tol	**25**	89	−200 (*c* 0.4, EtOH)	*S* (100)	−201[30]
7	*i*-Pr	*R*	*p*-Tol	**26**	98	+188 (*c* 4.0, EtOH)	*R* (100)	+173[29]
8	*i*-Pr	*S*	*p*-Tol	**27**	89	−187 (*c* 2.4, EtOH)	*S* (100)	−173[29]
9	*p*-Tol	*R*	Et	**23**	87	−137 (*c* 5.0, Me_2CO)	*S* (70)[e]	−198[29]
10	*p*-Tol	*S*	Et	**22**	80	+196 (*c* 0.3, Me_2CO)	*R* (100)	+198[29]

[a] All reactions were carried out by adding 1.2–1.3 equiv of the Grignard reagent to a 0.05 M solution of the sulfinate in toluene at 0 °C. [b] Yield after flash chromatography. [c] All the $[\alpha]_D$ were taken in the same solvent as those given in the literature. [d] Measured by ^1H NMR with $Eu(hfc)_3$ and by comparison with maximum specific rotation given in the literature. [e] Obtained from a crude sulfinate with 72% de.

the stereochemistry at sulfur for **10** is the same as that of (−)-menthyl (−)-(*S*)-*p*-toluenesulfinate, which was the first sulfinate prepared by Phillips in a pure state[25] and is widely used in the Andersen method.

All the sulfinates of DAG prepared are stable and can be stored for several days in the refrigerator without any decomposition. An interesting common feature of all these sulfinates is the sign of the specific rotation: (*R*)-sulfinates are dextrorotatory, and (*S*)-sulfinates are levorotatory.

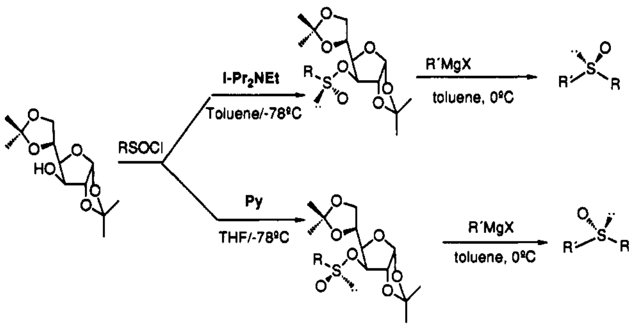
The availability of all the starting materials and the unusual "base effect" make this methodology a simple, general, and powerful route to both optically pure epimers of alkane- and arenesulfinates (Scheme II).

Determination of the Absolute Configuration. The absolute configuration of each sulfinate was assigned by transforming it into a known sulfoxide. The ee was determined from the specific rotation of a purified sample and by ^1H NMR using $Eu(hfc)_3$ as a chiral shift reagent.

The condensation of the methanesulfinates with 1.2 equiv of an alkyl or aryl Grignard reagent gives the corresponding enantiomers at sulfur of alkyl methyl or aryl methyl sulfoxides, respectively, with 100% ee and in high yield (Table IV). In the same way, the rest of alkanesulfinates were transformed to *p*-tolyl, alkyl sulfoxides in high yield and high optical purity (Table V). In these reactions, inversion of configuration leads from the (*R*)-alkanesulfinate to the (*R*)-sulfoxide, and retention of configuration results in a change in the CIP conventions, i.e., (*R*)-sulfinate goes to (*S*)-sulfoxide (Tables IV and V).

The fact that the absolute configurations of the final sulfoxides are known[18,26–30] (Tables IV and V) allowed us to assign the absolute configuration of our sulfinates. Assuming that the displacement step occurs with complete inversion of configuration at sulfur[2,17,31] (Scheme III), we can conclude that the sulfinates predominantly obtained with *i*-Pr_2NEt as the base have the *S* configuration at sulfur and the predominant sulfinates obtained with Py as base have the *R* configuration.

Scheme III



In the case of the *p*-toluenesulfinates of DAG, treatment of pure *S* isomer **10** with EtMgBr gave (*R*)-*p*-TolSOEt (**22**) in 80% yield and 100% ee. The preparation of optically pure (*S*)-*p*-TolSOEt (**23**) from (*R*)-*p*-toluenesulfinate **9** was

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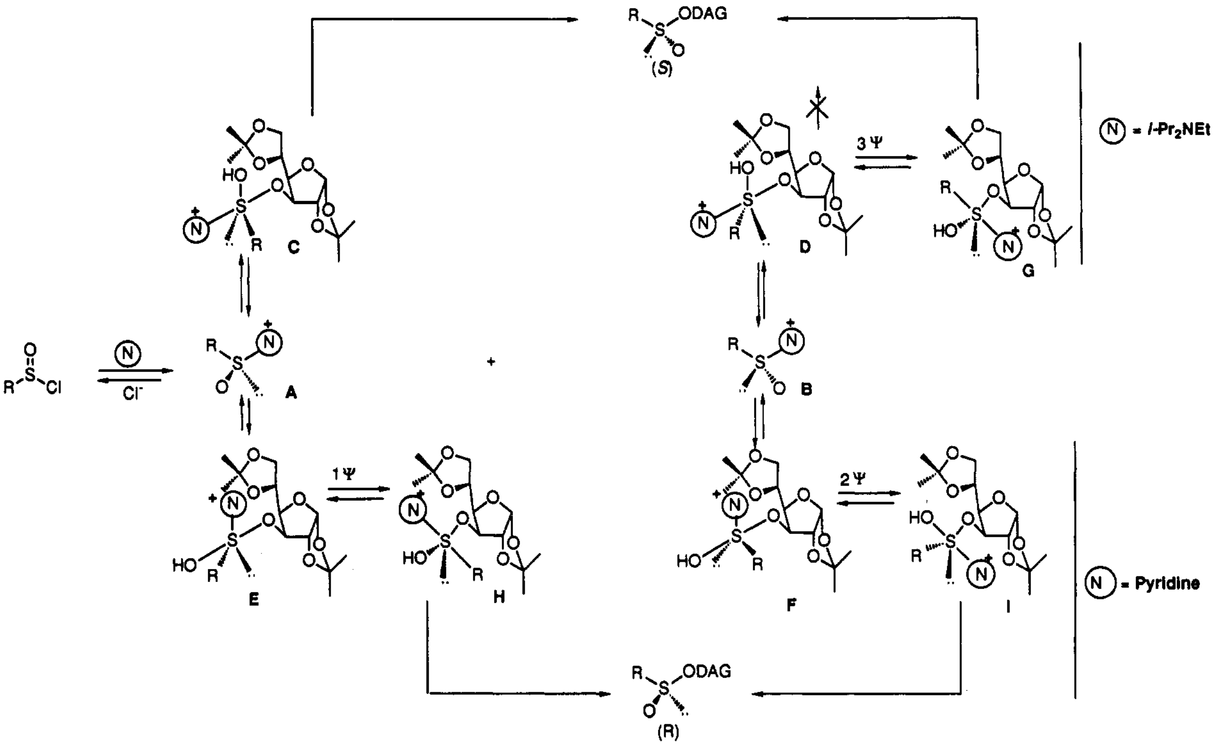
Scheme IV



not possible. As mentioned before, this sulfinate was not well separated by column chromatography.[32] Nevertheless, sulfoxide **23** is easily obtained in 90% yield and 99% ee by condensation of *p*-TolMgBr with the (*S*)-ethanesulfinate of DAG (**4**).

Entries 5 and 10 in Table IV show that the reaction of *t*-BuMgCl with (*R*)- and (*S*)-methanesulfinates gave (*S*)- and (*R*)-*t*-BuSOMe, respectively, in 62% and 50% yield with total retention of configuration. This result is in concordance with the recent work of Mikolajczyk and Drabowicz.[17]

All the sulfoxides obtained by our methodology have specific rotations comparable to the highest ones reported in the literature (see Tables IV and V), indicating the high optical purity of the starting sulfinates.

Possible Orgin of the Diastereoselectivity. The experimental data unambiguously demonstrates that the diastereoselective formation of a sulfinate is base dependent. Therefore, the proposed mechanism has to include the influence of the base on the stereocourse of the reaction. Some additional premises have to be taken into account:

(i) The reaction of sulfinyl chlorides with alcohols in the presence of bases does not proceed via a sulfine intermediate.[33]

(ii) Mislow and his group have demonstrated that the reaction of chiral alcohols with sulfinyl chlorides in the presence of a base is kinetically controlled.[34]

(iii) Upon first inspection, one could imagine the extreme case where DAG, under the influence of the base, reacts with only one of the enantiomeric sulfinyl chlorides. However, this is not the case because the same yield and ee are obtained when 1.2 or 2 equiv of MeSOCl are used. Accordingly, the first step of the process could be an equilibrium reaction involving the sulfinyl chloride and the base. The racemic sulfinamide formed would be the *active sulfur species* that interacts with the sugar derivative.

In order to explain the diastereoselectivity observed in this process, we propose the formation of an intermediate sulfurane that can undergo pseudorotation during the reaction[35] (Scheme IV). This mechanism is similar to that proposed by Mikolajczyk for the reaction of chiral sulfinamides with alcohols.[36]

As shown in Scheme IV, the bulky, electronegative i-Pr_2NEt and the incoming alcohol occupy the apical positions to form sulfuranes **C** and **D**. Sulfurane **C** evolves directly into the (*S*)-sulfinate. The formation of sulfurane **D** is less favorable because of a destabilizing interaction between the alkyl or aryl group (R) and C-5 of the sugar ring. Alternatively, the formation of (*S*)-sulfinate as the sole isomer can be explained by the simultaneous formation of sulfuranes **C** and **D**. By three consecutives pseudorotations, sulfurane **D** gives sulfurane **G**, which evolves into the (*S*)-sulfinate (Scheme IV).

When Py is used as the base, sulfuranes **E** and **F** are formed; the incoming alcohol is in an apical position and the less bulky base in an equatorial position. Sulfurane **E** is less favorable because of the interaction between the alkyl or aryl group (R) and C-5 of the sugar ring. By two successive Berry pseudorotations, the more favorable sulfurane **F** gives sulfurane **I**, where the leaving group is in an apical position, and **I** evolves into the (*R*)-sulfinate (Scheme IV). As in the case of i-Pr_2NEt, it is also possible that sulfuranes **E** and **F** are formed simultaneously and that, by one single pseudorotation, sulfurane **E** gives sulfurane **H**, which yields the (*R*)-sulfinate (Scheme IV).

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[32] (*S*)-*p*-TolSOEt (**23**) was obtained from the crude reaction in 70% ee in good agreement with the de calculated for sulfinate **9** by ^{1}H-NMR.

[33] Heering, A.; Jaspers, M.; Schwermann, I. *Chem. Ber.* **1979**, *112*, 2903.

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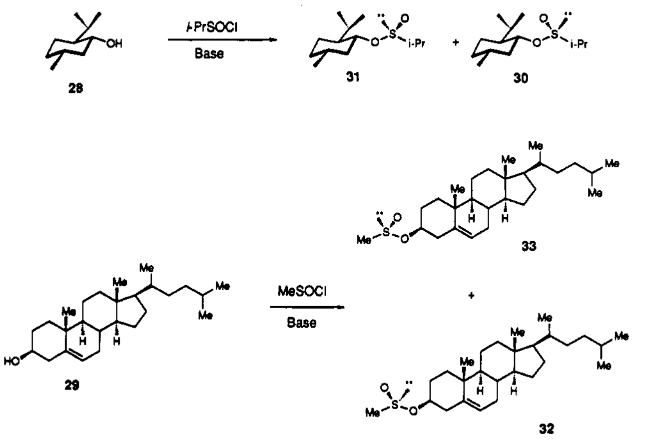
Table VI. Behavior of Other Chiral Secondary Alcohols in the Reaction with Sulfinyl Chlorides

		sulfinate			sulfoxide RSO-*p*-Tol		
alcohol	base	compd	R	config at S (de %)	compd	$[\alpha]_D$	config (ee %)
menthol **28**	pyridine	**30**	*i*-Pr	*R* (44)	**26**	+83 (*c* 6.0, EtOH)	*R* (44)
	$i\text{-Pr}_2\text{NEt}$	**31**	*i*-Pr	*S* (43)	**27**	−81 (*c* 2.5, EtOH)	*S* (43)
cholesterol **29**	pyridine	**32**	Me	*S* (4)	**12**	−6 (*c* 1.8, Me_2CO)	*S* (4)
	$i\text{-Pr}_2\text{NEt}$	**33**	Me	*R* (6)	**11**	+8 (*c* 2.1, Me_2CO)	*R* (6)

Scheme V



Although the present experimental data do not allow us to confirm the exact mechanism, there is a good qualitative agreement between experimental data and the mechanism proposed in Scheme IV.

It is interesting to compare the behavior of other secondary chiral alcohols with that of DAG under the same conditions. For this purpose, we chose widely used menthol (**28**) and cholesterol (**29**). For each alcohol, the corresponding sulfinates were prepared under the two different conditions indicated above (Scheme V). The results are summarized in Table VI.

The ^1H NMR determination of the de for (−)-cholesteryl and (−)-menthyl sulfinates was not possible because the two diastereomeric sulfinates, epimeric at sulfur, have identical ^1H NMR spectra. The de, as well as the absolute configuration at sulfur for the major diastereomer, was determined by transforming the sulfinate to a known sulfoxide.

(−)-Menthol behaves in the same way as DAG: with $i\text{-Pr}_2\text{NEt}$ (*S*)-2-propanesulfinate **30** is obtained with 44% de, and with Py the (*R*)-sulfinate **31** is obtained with 43% de. These results indicate that the effect of the base is not exclusive to DAG but can be generalized to other chiral alcohols.

When cholesterol is the chiral alcohol, a small base effect is observed, but the de are two low (4–6%) to be significant.

Conclusions

We have studied in detail the reactivity of DAG with alkane- and arenesulfinyl chlorides in the formation of the corresponding sulfinates. From this study, we found that the identity of the base is crucial to the outcome of the reaction. With $i\text{-Pr}_2\text{NEt}$, mainly (−)-(*S*)-alkane- and arenesulfinates are formed. When the same inducer of chirality is used and the base is changed from $i\text{-Pr}_2\text{NEt}$ to Py, predominantly (+)-(*R*)-alkane- and -arenesulfinates are obtained.

In addition to having high stereoselectivity and chemical yield, this new methodology, which affords both epimers at sulfur of alkane- and arsenesulfinates, presents other advantages:

(i) The reaction is cheap, quick (1–3 h), and very easy to carry out.

(ii) All the sulfinates formed are stable and easy to handle.

(iii) Optically pure alkane- and arenesulfinates are easily obtained either by recrystallization or by column chromatography.

(iv) The stereochemistry at sulfur can be predicted.

(v) The de are easily determined by ^1H NMR and agree with the ee calculated for the sulfoxide obtained upon treatment of the sulfinate with a Grignard reagent.[24,31]

(vi) Condensation of op sulfinates with Grignard reagents is an easy method to obtain both epimers at sulfur of various enantiomerically pure sulfoxides.

This new methodology, together with the Kagan's method,[20] affords access to most types of sulfoxides.

Besides working on determining the exact mechanism of the reactions with the two types of bases, we are now applying this methodology to the synthesis of biologically active molecules bearing a sulfinyl moiety in their structure.

Experimental Section

General Methods. Melting points were determined in open capillary tubes on a Gallenkamp apparatus and are not corrected. Routine monitoring of reactions was performed using Merck 60 F254 silica gel, glass supported TLC plates. For flash chromatography, silica gel 60 (230–400 mesh ASTM, E. Merck) was used. Columns were eluted with positive air pressure. Infrared spectra were recorded on a Bomem, Michelson 100, FTIR spectrophotometer, either neat or in $CDCl_3$, as indicated. ^1H NMR spectra were recorded at 80 or 200 MHz and ^{13}C NMR spectra at 20 or 50 MHz, on Bruker instruments. Chemical shifts are reported in ppm, and coupling constants are reported in Hz. High-resolution mass spectra were recorded on a Kratos MS-80-RFA spectrometer. Optical rotations were taken on a Perkin-Elmer 241-MC apparatus. All reactions were run under an atmosphere of dry argon using flame-dried glassware and freshly distilled and dried solvents. The organic extracts were dried over anhydrous sodium sulfate and concentrated in vacuo.

Preparation of Alkane- and Arenesulfinyl Chlorides. All the sulfinyl chlorides were prepared, according to the methodology of Herrmann,[21] by treating the corresponding disulfide with sulfuryl chloride in acetic acid.

General Procedure for the Preparation of Chiral Alkane- and Arenesulfinates. Method A. To a solution of the chiral alcohol (1 mmol) and pyridine (1.2 equiv) in THF (5 mL) at −78 °C, a solution of the corresponding sulfinyl chloride (1.2 equiv)[37] was added dropwise with vigorous stirring. After being stirred for 1–3 h at −78 °C, the reaction mixture was quenched with water and diluted with CH_2Cl_2. The organic phase was washed with 5% HCl solution, 2% $NaHCO_3$ solution, and saturated NaCl solution and dried over Na_2SO_4. After the solvent was removed in vacuo, the sulfinate obtained was purified by recrystallization or by flash chromatography.

Method B. The methodology is similar to that described for method A, but $i\text{-Pr}_2\text{NEt}$ is used as the base and toluene as the solvent.

1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranosyl (+)-(*R*)-Methanesulfinate (1). The reaction of DAG and MeSOCl

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[37] For compounds **3–8**, it was necessary to use up to 2.5 equiv of the corresponding sulfinyl chloride because of the partial formation of sulfines (Zwanenburg, B. *Recl. Trav. Chim. Pays-Bas* **1982**, *101*, 1).

according to method A afforded 1 as an oil after flash chromatography (*i*-PrOH–hexane (1:15)) in 87% yield: $[\alpha]^{25}_{D}$ +17 (*c* 4.4, acetone); IR ($CHCl_3$) 2990, 2955, 2900, 1377, 1217, 1143, 1073, 1022, 939, 837 cm^{-1}; ^1H NMR ($CDCl_3$, 80 MHz), δ 1.31, 1.33, 1.42, 1.50 (4s, 12 H, $OCMe_2O$), 2.70 (s, 3 H, CH_3S), 4.03–4.18 (m, 4 H, H-4, H-5 and H-6), 4.73–4.80 (m, 2 H, H-2 and H-3), 5.91 (d, 1 H, *J* = 3.5 Hz, H-1); ^{13}C NMR ($CDCl_3$, 20 MHz) δ 112.50, 108.96, 105.49, 84.09, 82.94, 80.95, 72.46, 67.73, 44.95, 26.83 (2 C), 26.27, 25.33. Anal. Calcd for $C_{13}H_{22}O_7S$: C, 48.43; H, 6.88. Found: C, 48.63; H, 7.11.

1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranosyl (−)-(*S*)-Methanesulfinate (2). The reaction of DAG and MeSOCl according to method B afforded 2 in 90% yield after purification by recrystallization from hexane: mp 92–94 °C; $[\alpha]^{25}_{D}$ (*c* 1, acetone); IR (film) 2991, 2930, 2900, 2880, 1376, 1217, 1136, 1045, 825, cm^{-1}; ^1H NMR ($CDCl_3$, 80 MHz) δ 1.32, 1.34, 1.43, 1.52 (4s, 12 H, $OCMe_2O$), 2.70 (s, 3 H, CH_3S), 4.00–4.40 (m, 4 H, H-4, H-5 and H-6), 4.62 (d, 1 H, *J* = 3.5 Hz, H-2), 4.78 (d, 1 H, *J* = 1.8 Hz, H-3), 5.91 (d, 1 H, *J* = 3.5 Hz, H-1); ^{13}C NMR ($CDCl_3$, 20 MHz) δ 112.45, 109.29, 105.17, 83.98, 80.51, 78.33, 72.46, 67.03, 44.47, 26.77 (2 C), 26.31, 25.29. Anal. Calcd for $C_{13}H_{22}O_7S$: C, 48.43; H, 6.88. Found: C, 48.15; H, 7.05.

1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranosyl (+)-(*R*)-Ethanesulfinate (3). The reaction of DAG and EtSOCl according to method A afforded 3 as an oil in 85% yield after purification by flash chromatography (ether–hexane (3:7)): $[\alpha]^{25}_{D}$ +12 (*c* 1.8, acetone); IR (film) 2989, 2952, 2895, 1456, 1377, 1218, 1164, 1136, 1074, 1021, 838 cm^{-1}; ^1H NMR ($CDCl_3$, 80 MHz) δ 1.31–1.55 (m, 15 H, $OCMe_2O$ and $\mathit{CH_3}CH_2S$), 2.80 (q, 2 H, *J* = 7.2 Hz, $CH_3\mathit{CH_2}S$), 3.85–4.22 (m, 4 H, H-4, H-5 and H-6), 4.66–4.82 (m, 2 H, H-2 and H-3) and 5.89 (d, 1 H, *J* = 3.5 Hz, H-1); ^{13}C NMR ($CDCl_3$, 20 MHz) δ 112.38, 109.33, 105.48, 83.60, 82.60, 81.12, 72.34, 67.79, 51.56, 26.82 (2 C), 25.31, 25.00, 4.85; HRMS calcd for $C_{14}H_{24}O_7S$ 336.1242, found 336.1251 (2.5 ppm). Anal. Calcd for $C_{14}H_{24}O_7S$: C, 49.99; H, 7.19. Found: C, 50.30; H, 7.24.

1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranosyl (−)-(*S*)-Ethanesulfinate (4). The reaction of DAG and EtSOCl according to method B afforded 4 in 90% yield as an oil after purification by flash chromatography (ether–hexane (3:7)): $[\alpha]^{25}_{D}$ −63 (*c* 4.3, acetone); IR (film) 2980, 2952, 1457, 1378, 1217, 1143, 1075, 1024, 834 cm^{-1}; ^1H NMR ($CDCl_3$, 80 MHz) δ 1.15–1.48 (m, 15 H, $OCMe_2O$ and CH_3S), 2.77 (q, 2 H, *J* = 7.4 Hz, $CH_3\mathit{CH_2}S$), 3.83–4.40 (m, 4 H, H-4, H-5 and H-6), 4.64 (d, 1 H, *J* = 7.3 Hz, H-2), 4.72 (d, 1 H, *J* = 4 Hz, H-3) and 5.88 (d, 1 H, *J* = 7.3 Hz, H-1); ^{13}C NMR ($CDCl_3$, 20 MHz) δ 112.38, 109.17, 105.05, 83.70, 80.60, 79.24, 72.45, 66.82, 51.07, 26.67 (2 C), 26.24, 25.20, 5.07; HRMS calcd for $C_{14}H_{24}O_7S$ 336.1242, found 336.1233 (2.9 ppm).

1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranosyl (+)-(*R*)-Propanesulfinate (5). The reaction of DAG and PrSOCl according to method A afforded 5 as an oil in 75% yield after purification by flash chromatography (ether–hexane (3:7)): $[\alpha]^{25}D$ +6.4 (*c* 1.1, acetone); IR (film) 2995, 2925, 2850, 1456, 1377, 1321, 1227, 1133, 1075, 1000, 954, 841, 753 cm^{-1}; ^1H NMR ($CDCl_3$, 80 MHz) δ 1.06 (t, 3 H, *J* = 7 Hz, $\mathit{CH_3}CH_2CH_2S$), 1.31, 1.32, 1.42, 1.50 (4s, 12 H, $OCMe_2O$), 1.79 (sext, 2 H, *J* = 7 Hz, $CH_3\mathit{CH_2}CH_2S$), 2.82 (m, 2 H, $CH_3CH_2\mathit{CH_2}S$), 3.87–4.22 (m, 4 H, H-4, H-5, H-6), 4.67–4.83 (m, 2 H, H-2, H-3), 5.91 (d, 1 H, *J* = 3.5 Hz, H-1); ^{13}C NMR ($CDCl_3$, 20 MHz) δ 112.46, 109.49, 105.47, 84.09, 83.00, 81.18, 72.33, 67.85, 60.04, 26.80 (2 C), 26.27, 25.30, 14.84, 13.33; HRMS calcd for $C_{15}H_{26}O_7S$ 350.1399, found 350.1398 (0.3 ppm).

1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranosyl (−)-(*S*)-Propanesulfinate (6). The reaction of DAG and PrSOCl according to method B afforded 6 as an oil in 80% yield after purification by flash chromatography (ether–hexane ((3:7)): $[\alpha]^{25}_{D}$ −33 (*c* 0.54, acetone); IR (film) 2975, 2954, 1455, 1377, 1230, 1220, 1142, 1137, 1074, 1021, 839 cm^{-1}; ^1H NMR ($CDCl_3$, 80 MHz) δ 1.05 (t, 3 H, *J* = 7 Hz, $\mathit{CH_3}CH_2CH_2S$), 1.30, 1.33, 1.41, 1.49 (4s, 12 H, $OCMe_2O$), 1.75 (sext, 2 H, *J* = 7 Hz, $CH_3\mathit{CH_2}CH_2S$), 2.75 (t, 2 H, *J* = 7 Hz, $-CH_2S$), 3.87–4.37 (m, 4 H, H-4, H-5 and H-6), 4.85 (d, 1 H, *J* = 3.6 Hz, H-2), 4.72 (d, 1 H, *J* = 2.1 Hz, H-3), 5.88 (d, 1 H, *J* = 3.6 Hz, H-1); ^{13}C NMR ($CDCl_3$, 20 MHz) δ 112.38, 109.17, 105.05, 83.78, 80.57, 79.19, 72.51, 66.82, 59.48, 26.70 (2 C), 26.29, 25.20, 15.02, 13.27; HRMS calcd for $C_{15}H_{26}O_7S$ 350.1399, found 350.1433 (9.6 ppm).

1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranosyl (+)-(*R*)-2-Propanesulfinate (7). The reaction of DAG and *i*-PrSOCl according to method A afforded 7 in 56% yield after purification by flash chromatography (ether–hexane (3:7)): $[\alpha]^{25}_{D}$ +11 (*c* 2.9, acetone); IR (film) 2980, 2935, 1459, 1377, 1240, 1225, 1145, 1136, 1075, 1000, 840 cm^{-1}; ^1H NMR ($CDCl_3$, 80 MHz) δ 1.13–1.55 (m, 18 H, $(\mathit{CH_3})_2CHS$, $OCMe_2O$), 2.80 (sept, 1 H, *J* = 7 Hz, $(CH_3)_2\mathit{CH}S$), 3.82–4.24 (m, 4 H, H-4, H-5, H-6), 4.69 (broad signal, 1 H, H-3), 4.78 (d, 1 H, *J* = 3.5 Hz, H-2), 5.89 (d, 1 H, *J* = 3.5 Hz, H-1); ^{13}C NMR ($CDCl_3$, 20 MHz) δ 112.38, 109.40, 105.47, 83.96, 82.80, 81.30, 72.21, 67.91, 56.22, 26.78 (2 C), 26.28, 24.33, 13.66, 13.33; HRMS calcd for $C_{15}H_{26}O_7S$ 350.1399, found 350.1390 (2.7 ppm).

1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranosyl (−)-(*S*)-2-Propanesulfinate (8). The reaction of DAG and *i*-PrSOCl according to method B afforded 8 as an oil in 50% yield after purification by flash chromatography (ether–hexane (3:7)): $[\alpha]^{25}_{D}$ −50 (*c* 0.3, acetone); IR (film) 2985, 2936, 1459, 1377, 1226, 1150, 1136, 1075, 1022, 836 cm^{-1}; ^1H NMR ($CDCl_3$, 80 MHz) δ 1.15–1.51 (m, 18 H, $(\mathit{CH_3})_2CHS$, $OCMe_2O$), 2.80 (sept, 1 H, *J* = 7 Hz, $(CH_3)_2\mathit{CH}S$), 3.90–4.41 (m, 4 H, H-4, H-5, H-6), 4.60 (d, 1 H, *J* = 3.7 Hz, H-2), 4.71 (d, 1 H, *J* = 2.2 Hz, H-3), 5.90 (d, 1 H, *J* = 3.7 Hz, H-1); ^{13}C NMR ($CDCl_3$, 20 MHz) δ 112.43, 109.19, 104.78, 83.78, 83.24, 80.08, 79.73, 72.32, 66.48, 55.51, 26.58 (2 C), 26.18, 25.02, 13.78; HRMS calcd for $C_{15}H_{26}O_7S$ 350.1399, found 350.1404 (1.5 ppm). Anal. Calcd for $C_{15}H_{26}O_7S$: C, 51.41; H, 7.48. Found: C, 51.61; H, 7.80.

1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranosyl (+)-(*R*)-*p*-Toluenesulfinate (9). The reaction of DAG and *p*-TolSOCl according to method A afforded 9 as an oil in 84% yield and 72% de: $[\alpha]^{25}_{D}$ +10.5 (*c* 1.7, acetone); IR (film) 2985, 2945, 2905, 1453, 1376, 1216, 1141, 1074, 1020, 827 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.30, 1.41, 1.48, 1.51 (4s, 12 H, $OCMe_2O$), 2.43 (s, 3 H, $-C_6H_4\mathit{CH_3}$), 3.82–4.37 (m, 4 H, H-4, H-5, and H-6), 4.73 (d, 1 H, *J* = 3.3 Hz, H-2), 4.95 (d, 1 H, *J* = 2.7 Hz, H-3), 5.86 (d, 1 H, *J* = 3.3 Hz, H-1), 7.33 (d, 2 H, *J* = 8.2 Hz, $-C_6\mathit{H_4}CH_3$), 7.68 (d, 2 H, *J* = 8.2 Hz, $-C_6\mathit{H_4}CH_3$); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 143.12, 140.01, 129.45 (2 C), 125.68 (2 C), 111.93, 108.65, 104.89, 83.99, 80.06, 77.52, 71.86, 66.68, 26.45 (2 C), 26.06, 25.02, 21.38; HRMS calcd for $C_{18}H_{23}O_7S$ ($M^+ - CH_3$) 383.1163, found 383.1164 (0.1 ppm).

1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranosyl (−)-(*S*)-*p*-Toluenesulfinate (10). The reaction of DAG and *p*-TolSOCl according to method B afforded 10 as a solid in 87% yield after purification by recrystallization from hexane: mp 95–96 °C; $[\alpha]^{25}_{D}$ −125 (*c* 0.42, acetone); IR ($CDCl_3$) 2980, 2958, 2910, 1596, 1454, 1377, 1216, 1139, 1076, 1021, 824 cm^{-1}; ^1H NMR ($CDCl_3$, 50 MHz) δ 1.25, 1.31 and 1.46 (s, 12 H, $OC\mathit{Me_2}O$), 2.45 (s, 3 H, $-C_6H_4\mathit{CH_3}$), 3.89–4.12 (m, 4 H, H-4, H-5, and H-6), 4.50 (d, 1 H, *J* = 2.6 Hz, H-3), 4.84 (d, 1 H, *J* = 3.6 Hz, H-2), 5.92 (d, 1 H, *J* = 3.6 Hz, H-1), 7.3 (d, 2 H, *J* = 7 Hz, $-C_6\mathit{H_4}CH_3$) and 7.6 (d, 2 H, *J* = 7 Hz, $-C_6\mathit{H_4}CH_3$); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 143.34, 140.16, 129.63 (2 C), 125.81 (2 C), 112.18, 108.87, 105.07, 84.11, 80.23, 77.72, 72.06, 66.87, 26.64, 26.59, 26.24, 25.20, 21.56; HRMS calcd for $C_{18}H_{23}O_7S$ ($M^+ - CH_3$) 383.1163, found 383.1162 (0.5 ppm).

(−)-Menthyl [(*R*) and (*S*)]-2-Propanesulfinate (30) and (31).

The reaction of (−)-menthol and *i*-PrSOCl according to method A afforded both diastereomeric sulfinates in quantitative yield. (*R*)-Sulfinate 30 was obtained in 44% de.

Method B yielded a mixture of both epimeric sulfinates in quantitative yield. (*S*)-2-Propanesulfinate 31 was obtained in 43% de.

Both diastereomeric sulfinates have the same proton spectrum: ^1H NMR (200 MHz, $CDCl_3$) δ 0.7–2.3 (m, 19 H, protons of the menthyl skeleton and $(\mathit{CH_3})_2CHS$), 2.7 (m, 1 H, $Me_2\mathit{CH}S$), 3.9 (m, 1 H, *H*CSOOMe).

(−)-Cholesteryl [(−)-(*S*) and (−)-(*R*)]-Methanesulfinates (32) and (33).

The reaction of (−)-cholesterol and MeSOCl according to method A afforded a mixture of both diastereomeric sulfinates in quantitative yield. (−)-(*S*)-Methanesulfinate 32 was obtained with 4% de: $[\alpha]^{25}_{D}$ −30 (*c* 1.1, benzene).

Method B afforded the two methanesulfinates, epimeric at sulfur, in quantitative yield. (+)-(*R*)-Diastereomer 33 was obtained with 6% de: $[\alpha]^{25}_{D}$ −20 (*c* 1.5, benzene).

Both diastereomeric sulfinates have the same proton spectrum: ^1H NMR (200 MHz, $CDCl_3$) δ 0.7–2.5 (m, 45 H, protons of the cholesteryl skeleton), 2.6 (s, 3 H, CH_3S), 4.1 (m, 1 H, *H*COSOMe), 5.4 (broad signal, 1 H, HC=C–).

General Procedure for Preparation of Chiral Sulfoxides 11–27. Sulfoxides were obtained in quantitative yield by the addition of 1.2 equiv of RMgX or ArMgX to a solution of sulfinate in toluene at 0 °C. The mixture was then stirred for 1 h, quenched with saturated aqueous NH_4Cl solution, extracted with CH_2Cl_2, and purified by flash chromatography. Yields, ee's, specific rotations, absolute configurations, and comparison with literature data are collected in Tables IV and V.

Acknowledgment. This work was supported by the "Ministerio de Educación y Ciencia" (Spain) under DGICYT Project No. PB91-0620 and a postdoctoral grant awarded to N.K.

Supplementary Material Available: ^1H NMR spectra for compounds 1–10 and 30–32 (12 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

Regioselectivity in the Reaction of Tantalum–Unsymmetrical Acetylene Complexes with Carbonyl Compounds. Stereoselective Preparation of 1-Alkenyl Sulfides, α,β-Unsaturated Esters, and Amides

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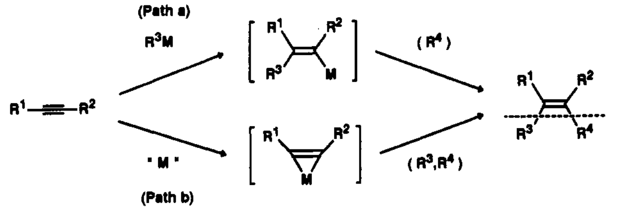
Received May 19, 1992

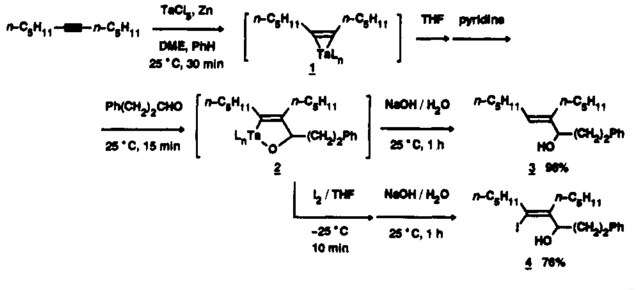
Tantalum–alkyne complexes, derived by treatment of alkynes with low-valent tantalum ($TaCl_5$ and zinc), react in situ with carbonyl compounds to give (*E*)-allylic alcohols stereoselectively. When unsymmetrical acetylenes are employed in the reaction, two regioisomeric allylic alcohols are produced. The regioselectivity of the reaction depends on the steric and electronic effects of the substituents on the acetylenes. For example, treatment of tantalum–alkyne complexes derived from methyl alkynyl sulfides with carbonyl compounds yields (*E*)-3-hydroxy-1-propenyl methyl sulfides in a regioselective manner. Tantalum–alkyne complexes derived from acetylenic esters react with carbonyl compounds regioselectively at the α-position of the esters to give *Z*-isomers of trisubstituted α,β-unsaturated esters. In contrast, tantalum–alkyne complexes derived from acetylenic amides react with carbonyl compounds predominantly at the β-position of the amides. The regioselectivity of the reaction between acetylenic amides and aldehydes, however, cannot be explained solely in terms of the steric and electronic effects of the substituents. Strong coordination of the amide group to the tantalum center could also be responsible for the observed selectivity, which is opposite to that observed with tantalum–acetylenic ester complexes.

The construction of carbon–carbon double bonds in a stereoselective manner is a fundamental but still challenging problem facing chemists, particularly in the case of tetra- and trisubstituted ethenes.[1] One attractive approach involves the introduction of two substituent units onto a readily accessible acetylene as shown in Scheme I. Carbometalation[2] or hydrometalation,[3] followed by treatment with electrophiles (path a), is a typical solution which uses this approach. Insertion of unsaturated compounds into a metal–carbon bond of a metallacyclopropene[4] (path b) provides another approach to substituted ethenes. In both cases, an unavoidable problem is control of the regiochemistry of the reaction when unsymmetrical alkynes ($R^1 \neq R^2$) are employed as starting materials. Electronic effects can be a controlling factor in the regioselectivity of the reaction. The carbometalation of acetylenic esters proceeds selectively to yield β-substituted α,β-unsaturated esters after aqueous workup.[5] Heteroatom substituents on acetylenic triple bonds can also play an important role in directing the regiochemistry. For example, hydroalumination of alkynyl sulfoxides produces α-aluminum-substituted alkenyl sulfoxides because of the strong electron-withdrawing effect of the sulfinyl group.[6] Similar effects are observed in analogous

Scheme I



Scheme II



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