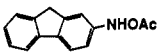
carbons of **5** or **6** (see structures **8** and **10** of eq 2) also suggests that the environment at the reactive sites of **33** is sterically congested. This study provides the first evidence that products such as **20** and **26**, in which bond formation occurs directly at the nitrogen of an ester derivative of an *N*-arylhydroxamic acid, can be formed by an S_N1 process. This is somewhat surprising because all available calculations show that the charge on *N*-acyl-*N*-arylnitrenium ions is predominately delocalized on the ortho and para carbons of the aromatic ring.[18] Studies are now underway on less reactive analogues of **1**, such as **1a** and **29**, to determine if these compounds react with **5** and **6** and, if so, by what mechanism.[11]

The adducts **2** and **3** isolated from the reaction of **1** or **1a** with deoxyguanosine residues of DNA or deoxyguanosine[2] are structurally similar to those obtained in this study. Homogeneous conditions under which guanosine reacts with **1** in yields which are sufficiently high for mechanistic studies have not yet been discovered, but it now appears, based on these results, that this reaction is likely to be an S_N1 process. This is in contrast to the conclusion reached by ourselves[3] and others[19] that deacylated analogues of **1** such as **34** and **35**, which have also



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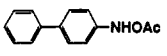

35

been implicated as carcinogens,[20] are likely to react with guanosine via an S_N2 mechanism. Obviously much work remains to be done before a full understanding of the nucleophilic substitution reactions of these species is obtained.

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Registry No. **1**, 138235-69-5; **5**, 62-53-3; **6**, 121-69-7; **12**, 138235-70-8; **13**, 138235-71-9; **14**, 1838-56-8; **15**, 2784-86-3; **16**, 138235-72-0; **17**, 53-95-2; **18**, 138235-73-1; **19**, 138235-74-2; **20**, 138235-75-3; **21**, 138235-76-4; **22**, 138235-77-5; **23**, 138235-78-6; **24**, 138235-79-7; **25**, 53-96-3; **26**, 138235-80-0; **27**, 138235-81-1; **28**, 101-61-1.

Supplementary Material Available: Tabulation of IR and ^1H NMR data for **12**, **13**, **16**, **20–24**, **26**, and **27** and ^{13}C NMR and selected COSY-90 NMR spectra for the same compounds (14 pages). Ordering information is given on any current masthead page.

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Biocatalytic Resolutions of Sulfinylalkanoates: A Facile Route to Optically Active Sulfoxides

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Two methods are presented for kinetic resolutions of compounds containing ester and sulfoxide functionalities (sulfinylalkanoates). In the first a crude lipase preparation from *Pseudomonas* sp. (K10) mediates enantioselective hydrolysis of these esters in an aqueous environment. The second method uses the same lipase preparation to promote enantioselective transesterifications with alcohols in hexane. Both procedures are suitable for preparation of sulfinylalkanoates where the ester and sulfoxide groups are separated by one or two methylene units (sulfinylacetates and sulfinylpropanoates) but compounds with three methylene "spacer groups" (sulfinylbutanoates) are not substrates for the lipase under either set of conditions.

Compounds containing both ester and sulfoxide functionalities are useful reagents for organic synthesis.[1,2] Sulfinylacetate **I**, for instance, can be used in asymmetric aldol reactions providing, after reduction, chiral unsubstituted enolate equivalents (eq 1).[3–5] Knoevenagel condensations of sulfinylacetate **I** with nonenolizable aldehydes afford α,β-unsaturated sulfoxides[6–8] which can be elaborated via conjugate additions, directed by the sulfoxide functionality (eq 2).[9,10] Moreover, sulfinylacetates **I** are reagents for the SPAC reaction with enolizable aldehydes (eq 3),[11] a powerful transformation which creates

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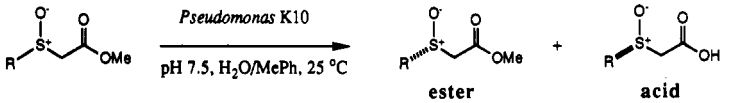
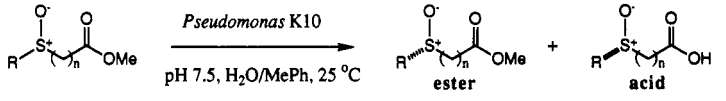
Table I. Hydrolytic Resolutions of Methyl Sulfinylacetates 1–7



			ester		acid	
compd	R	time,[a] h	% yield	% ee[b]	% yield	% ee[c]
1	4-ClC_6H_4	25	48	>95	38	91
2[d]	4-$NO_2C_6H_4$	96	33	>95	22[f]	>95
3	Ph	55	48	>95	17	92
4	4-$MeOC_6H_4$	96	48	>95	34[f]	88
5	2-Nap	27	45	>95	35	80
6	*n*-Bu	96	33	>95	–[e]	–[e]
7	Cy	96	49	>95	18[f]	>95

[a] See Experimental Section for the general procedure applied for these reaction times. [b] Enantiomeric excess from chiral shift experiments with Eu(hfc)$_3$, monitoring the CO_2CH_3 signal; none of the other enantiomer was detected in entries where >95% ee is quoted. [c] The crude acid was esterified with diazomethane, and the optical purity of the ester produced was determined by chiral shift experiments. [d] This substrate is not very soluble in toluene; however, it did react as a suspension under the conditions outlined in the general procedure but with 5 times the amount of toluene. [e] The butyl sulfoxides are appreciably less stable than others in this series; the acid was not isolated in this particular experiment. In another run 40% of the unreacted ester (90% ee) and 19% of the methyl ester derived from the acid with diazomethane (54% ee) were obtained; some racemization of the acid apparently occurred in the workup procedure. [f] These acids were converted to the corresponding methyl esters via treatment with diazomethane prior to isolation from the crude reaction mixture.

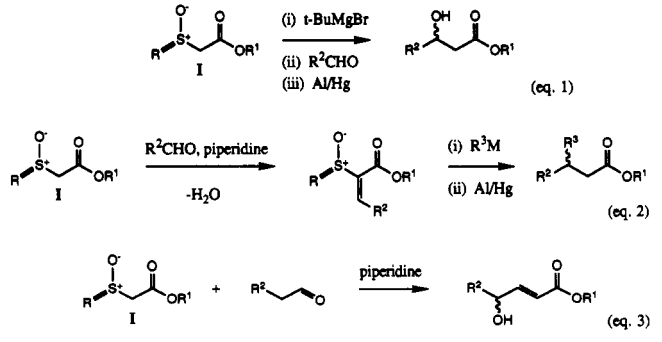
Table II. Hydrolytic Resolutions of Methyl Sulfinylalkanoates



				ester		acid	
compd	R	*n*	time,[a] h	% yield	% ee[b]	% yield	% ee[c]
1	4-ClC_6H_4	1	25	48	>95	38	91
8	4-ClC_6H_4	2	37	30	>95	29	63
9	4-$NO_2C_6H_4$	2	66	44	>95	35	82
10	Ph	2	38	48	>95	24	91
11	4-ClC_6H_4	3	54	no reaction	–	–	–
12	Ph	3	36	no reaction	–	–	–

[a] See Experimental Section for the general procedure. [b] From chiral shift experiments with Eu(hfc)$_3$, monitoring the CO_2CH_3 signal; none of the other enantiomer was detected in entries where >95% ee is quoted. [c] The crude acid was esterified with diazomethane and the optical purity of the ester produced was determined by chiral shift experiments.

a C=C bond and converts a methylene group to a hydroxymethine in a single step. Interest in the latter reaction[12–15] led us to investigate asymmetric syntheses of sulfoxide esters. Our initial studies in this area indicated that biocatalytic hydrolyses could be used for large-scale preparations of optically active sulfoxides.[16] Here we outline the scope of this methodology and different approaches that can be used to effect these kinetic resolutions.



Hydrolyses

Screening experiments with methyl [(4-chlorophenyl)sulfinyl]acetate [(±)-1] revealed crude lipase preparations from *Pseudomonas* sp. (K–10, and AK, Amano), and porcine pancreatic lipase (Sigma) catalyzed enantioselective hydrolyses of this substrate. Lipase from *Candida cylindracea* (Sigma) gave optically enriched material but contaminated with other products, and racemic ester 1 was recovered from the experiment using *Mucor meihei*. All the enzymes that mediated enantioselective hydrolysis of ester (±)-1 preferentially hydrolyzed the *S* isomer.

The crude lipase preparation *Pseudomonas* sp. K-10 was selected for further studies of these enzymatic hydrolyses.[17] Table I shows data for hydrolyses of methyl sulfinylacetates. These resolutions were performed using approximately equal masses of the crude lipase preparation and substrate. There seem to be no obvious restrictions on the nature of the sulfur alkyl or aryl substitutent except that the *tert*-butyl substituted compound is not processed.[16] However, the aliphatic compounds are less stable than the aromatic ones presumably due to β-elimination reactions and, possibly, more facile degradation via free-radical pathways.

Optically active samples of esters 1 and 3 have been prepared by other routes,[18] hence the absolute configura-

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(12) Burgess, K.; Henderson, I. *Tetrahedron Lett.* **1989**, *30*, 4325.
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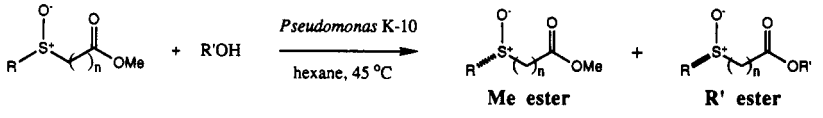
(17) This lipase preparation is only marginally superior to *Pseudomonas* sp. AK and porcine pancreatic lipase; it may not be the best enzyme for enantioselective hydrolyses of other sulfinylalkanoates.

Table III. Resolution of Methyl Sulfinylalkanoates via Transesterification



						Me ester		R′ ester	
compd	R	R′	n	time,[a] h	conversion, %	yield, %	ee,[b] %	yield, %	ee,[c] %
2	4-ClC_6H_4	n-Bu	1	27	44	50	79	42	>95
5	2-Nap	n-Bu	1	28	49	24	85	30	91
8	4-ClC_6H_4	n-Bu	2	55	50	25	>95	33	90[d]
11	4-ClC_6H_4	n-Bu	3	7 days	no reaction	–	–	–	–
2	4-ClC_6H_4	$CH_2CH(CH_2)_9$	1	35	not determined	55	59	13	>95

[a] See Experimental Section for the general procedure applied for these reaction times. [b] From chiral shift experiments with $Eu(hfc)_3$, monitoring the CO_2CH_3 signal; none of the other enantiomer was detected in entries where >95% ee is quoted. [c] The enantiomeric purities of these materials were assessed by converting small samples of the methyl esters using methanol/$NaHCO_3$; these were subjected to chiral shift NMR experiments in the usual way. [d] This material decomposed under the transesterification conditions described in note c; consequently, the optical purity of this material was assessed directly via chiral shift experiments (a racemic sample of this ester was prepared for comparison).

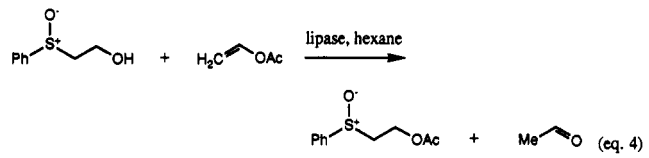
tion of recovered starting materials in these resolutions was established by correlation. Resolved samples of esters from the biocatalytic resolutions of 1–7 all have positive rotations and give the same enantiomer in a SPAC reaction with butanal.[13,15] Consequently, the absolute configurations of the resolved esters 2 and 4–7 are tentatively assigned to be as shown in Table I.

Table II summarizes experiments designed to probe the response of the enzyme to increased separation between the hydrolysis site (the methyl ester) and the chiral center (the sulfoxide).[19] The ester functionality becomes less hindered, and the probability of simultaneous binding of the ester and sulfoxide fragments diminishes as the number of methylene "spacer groups" increases. Consequently, we expected increased reaction rate and decreased enantioselectivity for compounds with a larger separation between the ester and the asymmetric center. When these are separated by two methylene groups (i.e. the propanoates 8–10), the enantioselectivity of the enzyme is high, giving results comparable with those obtained for the methyl sulfinylacetates. Surprisingly, the compounds with three methylene groups between the sulfoxide and ester center (i.e. the butanoates 11 and 12) give no hydrolysis product after several days under our standard reaction conditions. Perhaps the diminished water solubility of these longer chain substrates, relative to the sulfinylacetates and propanoates, retards their hydrolyses. Results presented in the next section, however, indicate these compounds are genuinely inferior substrates for biocatalytic resolutions mediated by lipase from *Pseudomonas* sp. K-10.

Transesterifications

Lipase-mediated transesterifications in organic solvents[20] were also investigated as a route to optically active sulfinylalkanoates (Table III).[19] We reasoned that if these reactions were effective they would facilitate incorporation of alkoxide functionality with simultaneous resolution. In the event, lipase from *Pseudomonas* sp. K-10 was found to promote enantioselective transesterification. These reactions are similar to the hydrolyses described above in two respects: (i) the lipase discriminates against the same absolute configuration of substrate under both sets of reaction conditions, and (ii) only those compounds with one or two methylene groups between the sulfoxide and the ester functionality are processed; sulfinylbutanoates do not react. The latter feature indicates that the active enzyme(s) in the *Pseudomonas* K-10 is/are unable to accommodate extended substrates. These substrates dissolve under the conditions used for these transesterifications; consequently, we infer that the failure of these same compounds to react under the hydrolytic conditions (vide supra) probably is not due to poor water solubility. These transesterifications can be used to prepare sulfinylalkanoates of functionalized alcohols, as demonstrated in the acyl transfer to 10-undecen-1-ol (Table III, final entry).

Experiments in which the sulfoxide constitutes the *alcohol* component in transesterification reactions were less successful. Irreversible acylations[21–23] of sulfinyl alcohols (eq 4) proceed rapidly at room temperature but with poor enantiodiscrimination (E values <10)[24,25] for each of the lipases screened (*Pseudomonas* sp. K10, *Pseudomonas* sp. AK, porcine pancreatic lipase, and *C. cylindracea*).



Conclusions

Enantiomerically pure sulfoxides are useful reagents for asymmetric syntheses, but they are not particularly easy to prepare. Optically active sulfinylacetates are usually obtained via resolutions of menthyl sulfinate esters[26,27] followed by displacement of menthoxide with an ester enolate[1] (eq 5) or transformation of these menthyl sulfinate esters into methyl sulfoxides and alkoxycarbonylation (eq 6).[4,28,29] Three disadvantages of these approaches are as follows: (i) they involve tedious and time-consuming fractional crystallizations of diastereomeric menthyl sulfinate esters; (ii) displacement of menthoxide from sulfi-

(18) Ohta, H.; Kato, Y.; Tsuchihasi, G. *Chem. Lett.* **1986**, 217.
(19) Absolute configurations indicated in Tables II and III are assigned either by correlation or by the sign of the rotation. It is encouraging that the known R stereoisomer of the sulfinylbutanoic acid (4-MeC_6H_4)SO-$(CH_2)_3CO_2H$ has, as expected, a positive rotation.[48]
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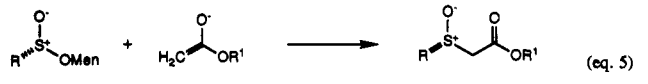
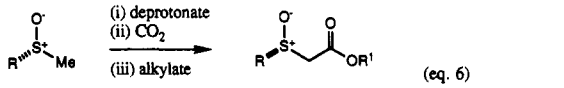
nate esters by enolates can only proceed in 50% yield based on the enolate since the product is more acidic than the starting material; and (iii) many compounds that might be required are not amenable to the fractional crystlization and/or the displacement steps.



(eq. 5)



(eq. 6)

Other routes to optically active sulfoxides include enantioselective oxidation using catalytic tartrate diester/*tert*-butyl hydroperoxide/titanium tetraisopropoxide/water, but this only gives products of >90% ee if one large and one small substituent are attached to the sulfoxide.[30-34] Similar restrictions apply to enantioselective oxidations by chiral oxaziridines.[35,36] Furthermore, they are unsuitable for large-scale preparations because stoichiometric quantities of the reagents are required, and appreciable quantities of byproducts therefore must be separated from the product at the end of the reaction. Oxidation of sulfides equipped with chiral auxiliaries[37] generally is not a useful approach because the chiral auxiliary must be incorporated into, then cleaved from, the substrate. Oxidation of sulfides [38] via biological[39-43] and biomimetic[44,45] systems have been investigated extensively, but the enantiomeric excesses obtained are often low, and the necessary materials are not readily available. Successive displacements of oxygen or nitrogen groups via reactions of cyclic, optically active oxathiazolidines,[46] and sulfites,[47] are apparently useful for preparation of *tert*-butyl-substituted sulfoxides,[47] but few others. The closest precedent to the resolutions presented in this paper are enantioselective hydrolyses of sulfoxide esters by a relatively inaccessible microorganism.[18]

The biocatalytic resolutions we have described are the most convenient route to optically active sulfinylalkanoates yet reported, and constitute a valuable starting point for preparations of other sulfoxides. Crude *Pseudomonas* sp. K-10 is currently available for under $1 per gram, and consequently these resolutions are extremely economical. The experimental procedures are simple, and the hydrolytic route involves no chromatography and can be performed on a large scale. We have exploited these resolutions in our studies of the SPAC reaction,[14,15] and optically active 3-sulfinylpropanoic acids (from hydrolyses of esters **8-10**) are useful for asymmetric syntheses of saturated and α,β-unsaturated, γ-substituted γ-lactones.[48] It is evident that these nonracemic sulfoxides and their derivatives could be exploited in many branches of asymmetric syntheses.[49]

Experimental Section

General Procedures. Melting points were uncorrected. High-field NMR spectra were recorded on 300- or 250-MHz instruments using $CDCl_3$ solvent. In cases where abbreviated DEPT sequence experiments were carried out during ^{13}C NMR experiments, the carbon multiplicities are listed as (C) quaternary, (CH_2) methylene, and (CH/CH_3) methine/methyl. The purity of all products was assessed as >95% via ^1H and ^{13}C NMR analyses. The ee's of the methyl sulfinylalkanoates were determined via ^1H NMR spectroscopy using the chiral shift reagent (+)-Eu(hfc)$_3$. Enantiomeric excesses of the other sulfinylalkanoates and sulfinylalkanoic acids were determined via the corresponding methyl esters (formed using $MeOH/NaHCO_3$ and CH_2N_2, respectively). Thin-layer chromatography was performed on silica gel 60 F_{254} plates from Whatman. Flash chromatography was performed on SP silica gel 60 (230-400-mesh ASTM).

The racemic methyl sulfinylacetates **1-7** were prepared as described in the literature.[11] **(±)-Methyl [(4-Chlorophenyl)-sulfinyl]acetate [(±)-1].**[11,18] **(±)-Methyl [(4-Nitrophenyl)-sulfinyl]acetate [(±)-2].**[11] **(±)-Methyl (Phenylsulfinyl)-acetate [(±)-3].**[11,18] **(±)-Methyl [(4-methoxyphenyl)-sulfinyl]acetate [(±)-4]**: obtained as an oil; R_f 0.1 (40% EtOAc in hexane); ^1H NMR δ 7.62 (d, J = 8.73 Hz, 2 H), 7.03 (d, J = 8.73 Hz, 2 H), 3.87 (d, J = 13.4 Hz, 1 H), 3.85 (s, 3 H), 3.62 (d, J = 13.4 Hz, 1 H); ^{13}C NMR δ 164.9 (C), 162.0 (C), 133.3 (C), 125.9 (CH/CH_3), 114.4 (CH/CH_3), 61.0 (CH_2), 55.1 (CH/CH_3), 52.2 (CH/CH_3); IR (neat) 2955 (md), 1735 (st), 1595 (st), 1580 (md), 1495 (st), 1440 (md), 1255 (st), 1175 (st), 1090 (st), 1050 (st) cm^{-1}; MS (EI, 70 eV) m/z (%) 228 (13, M$^+$), 156 (100); HRMS calcd for $C_{10}H_{12}O_4S$ 228.04561, found 228.04565. **(±)-Methyl (2-naphthylsulfinyl)acetate [(±)-5]**: obtained as colorless crystals (recrystallized from acetone/hexane); R_f 0.3 (25% acetone in hexane); mp 42-43 °C; ^1H NMR δ 8.24 (s, 1 H), 7.93 (m, 3 H), 7.62 (m, 3 H), 3.91 (d, J = 13.7 Hz, 1 H), 3.75 (d, J = 13.7 Hz, 1 H), 3.70 (s, 3 H); ^{13}C NMR δ 165.5 (C), 141.0 (C), 134.8 (C), 133.0 (C), 129.7 (CH/CH_3), 128.6 (CH/CH_3), 128.1 (CH/CH_3), 128.1 (CH/CH_3), 127.5 (CH/CH_3), 125.0 (CH/CH_3), 119.6 (CH/CH_3), 61.5 (CH_2), 52.8 (CH/CH_3); IR ($CHBr_3$) 3450 (br), 1740 (st), 1595 (md), 1420 (md), 1275 (md), 1150 (st), 825 (md), 775 (md) cm^{-1}; MS (EI, 70 eV) m/z (%) 248 (5, M$^+$), 17 (100); HRMS calcd for $C_{13}H_{12}O_3S$ 248.0507, found 248.0509. **(±)-Methyl (*n*-butylsulfinyl)acetate [(±)-6]**: obtained as an oil: R_f 0.2 (60% EtOAc in hexane); this compound decomposed slowly at room temperature hence only limited spectral data was obtained; ^1H NMR δ 3.79 (s, 3 H), 3.68 (s, 2 H), 2.86 (m, 2 H), 1.78 (m, 2 H), 1.49 (m, 2 H), 0.96 (t, J = 7.30 Hz, 3 H); ^{13}C NMR δ 165.4 (C), 55.0 (CH_2), 52.5 (CH/CH_3), 51.9 (CH_2), 24.0 (CH_2), 21.5 (CH_2), 13.3 (CH/CH_3); IR (neat) 2960 (st), 1740 (st), 1440 (md), 1380 (md), 1280 (st) 1100 (st) cm^{-1}. **(±)-Methyl (cyclohexylsulfinyl)-acetate [(±)-7]**: obtained as an oil; R_f 0.1 (40% EtOAc in hexane); this compound decomposed slowly at room temperature, hence, only limited spectral data was obtained; ^1H NMR δ 3.79 (s, 3 H), 3.69 (d, J = 13.7 Hz, 1 H), 3.59 (d, J = 13.7 Hz, 1 H), 2.73 (m, 1 H), 1.22-2.11 (m, 10 H); ^{13}C NMR δ 165.8 (C), 58.6 (CH_2), 52.4 (CH/CH_3), 26.0 (CH/CH_3), 24.9 (CH_2), 24.6 (CH_2), 23.7 (CH_2); IR (neat) 2935 (st), 2855 (st), 1735 (st), 1450 (st), 1270 (st), 1040 (st) cm^{-1}; MS (EI, 70 eV) m/z (%) 204 (2, M$^+$), 82 (100).

The racemic methyl sulfinylpropanoates **8-10** were prepared as follows. The thiol (1.00 equiv) followed by methyl acrylate (1.10 equiv) were added dropwise to a suspension of sodium hydride (0.100 equiv) in MeOH (0.33 M with respect to the thiol). The resultant solution was refluxed for 2 h. The volatiles were then

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removed in vacuo, and the residue which was redissolved in ether and washed with saturated aqueous NH_4Cl and H_2O and then dried ($MgSO_4$). Removal of the volatiles gave the methyl sulfenylpropanoate. To a 2.0 M solution of the methyl sulfenylpropanoate in glacial acetic acid at 0 °C was added 30% hydrogen peroxide (1.10 equiv). The resulting solution was stirred at 25 °C for 24 h. Removal of the volatiles and purification by flash chromatography gave the product. **(±)-Methyl 3-[(4-chlorophenyl)sulfinyl]propanoate [(±)-8]**: obtained as colorless crystals (recrystallized from acetone/hexane); R_f 0.3 (50% EtOAc in hexane); mp 69–70 °C; ^1H NMR δ 7.55 (m, 4 H), 3.65 (s, 3 H), 3.27 (m, 1 H), 2.95 (m, 2 H), 2.58 (m, 1 H); ^{13}C NMR δ 171.5 (C), 141.3 (C), 137.4 (C), 129.6 (CH/CH_3), 125.4 (CH/CH_3), 52.2 (CH/CH_3), 51.5 (CH_2), 25.8 (CH_2); IR ($CHBr_3$) 3020 (st), 1735 (st), 1576 (md), 1475 (st), 1143 (st), 1044 (st), 665 (st) cm^{-1}; MS (EI, 70 eV) *m/z* (%) 246 (10, M^+), 159 (100); HRMS calcd for $C_{10}H_{11}O_3ClS$ 246.0117, found 246.0117. **(±)-Methyl 3-[(4-nitrophenyl)sulfinyl]propanoate [(±)-9]**: obtained as colorless crystals (recrystallized from acetone/hexane); R_f 0.1 (33% acetone in hexane); mp 78–80 °C; ^1H NMR δ 8.39 (d, J = 8.6 Hz, 2 H), 7.82 (d, J = 8.6 Hz, 2 H), 3.67 (s, 3 H), 3.30 (m, 1 H), 2.94 (m, 2 H), 2.61 (m, 1 H); ^{13}C NMR δ 171.3 (C), 150.6 (C), 149.5 (C), 125.2 (CH/CH_3), 124.4 (CH/CH_3), 52.3 (CH/CH_3), 51.2 (CH_2), 25.8 (CH_2); IR ($CHBr_3$) 3020 (st), 1734 (st), 1603 (md), 1526 (st), 1437 (md), 1345 (st), 1142 (st), 658 (st) cm^{-1}; MS (EI, 70 eV) *m/z* (%) 221 (5), 159 (67), 28 (100); HRMS calcd for $C_{10}H_{11}NO_5S$ 257.0358, found 257.0358. **(±)-Methyl 3-(Phenylsulfinyl)-propanoate [(±)-10].**[18]

The racemic methyl sulfinylbutanoates **11** and **12** were prepared in the same way as the methyl sulfinylacetates (vide supra)[11] but using methyl halobutanoate in place of methyl chloroacetate. **(±)-Methyl 4-[(4-chlorophenyl)sulfinyl]butanoate [(±)-11]**: obtained as an oil; R_f 0.1 (33% acetone in hexane); ^1H NMR δ 7.53 (m, 4 H), 3.65 (s, 3 H), 2.81 (m, 2 H), 2.45 (t, J = 7 Hz, 2 H), 2.14 (m, 2 H); ^{13}C NMR δ 173.0 (C), 143.0 (C), 137.5 (C), 129.5 (CH/CH_3), 125.4 (CH/CH_3), 55.9 (CH_2), 52.1 (CH/CH_3), 32.4 (CH_2), 17.5 (CH_2); IR (neat) 3447 (br), 2952 (md), 1734 (st), 1636 (wk), 1477 (md), 1214 (md), 1175 (md), 1046 (md), 825 (md), 742 (md) cm^{-1}; MS (EI, 70 eV) *m/z* (%) 101 (100), 28 (92); HRMS calcd for $C_{11}H_{13}O_3ClS$ 260.0273, found 260.0274. **(±)-Methyl 4-(Phenylsulfinyl)butanoate [(±)-12].**[18] **General Procedure for the Resolutions of Methyl Sulfinylalkanoates via Hydrolyses Catalyzed by *Pseudomonas* sp. K-10 (Tables I and II).** To a 1.0 M solution of the racemic methyl sulfinylalkanoate in toluene was added 8 times the volume of a 0.05 M solution of phosphate buffer (pH 7.5) and 1.0 mass equiv of *Pseudomonas* sp. K-10 (Amano). The heterogeneous mixture was stirred at 25 °C for the time indicated. The reaction was filtered through Celite (washing with Et_2O and H_2O) to remove the enzyme and then extracted with several portions of Et_2O. The aqueous fraction was retained and treated as described below. The combined organic fractions were dried, and removal of the volatiles gave the optically active unreacted ester. The aqueous layer was acidified with glacial acetic acid (2 times the original toluene volume), and the sulfinylalkanoic acid was extracted with $CHCl_3$. The combined organic fractions were dried, and removal of the volatiles gave the optically active acid. Alternatively the H_2O was removed in vacuo from the aqueous layer, and the residue obtained was partially dissolved in $CHCl_3$. Excess diazomethane was then added, and the reaction mixture was stirred for 12 h. The remaining diazomethane was quenched with glacial acetic acid. Removal of the volatiles and purification by flash chromatography gave the optically active methyl sulfinylalkanoate (derived from the sulfinylalkanoic acid). **(*R*)-(+)-Methyl [(4-chlorophenyl)sulfinyl]acetate [(*R*)-(+)-1]**:[16,18] using 1.16 g (5.00 mmol, 1.00 equiv) of (±)-**1**. The resulting suspension was stirred at 25 °C for 25 h. (*R*)-(+)-**1** (0.56 g, 48%) was recovered from the organic layer of as colorless crystals: $[\alpha]^{25}_D$ +201° (*c* 0.32, EtOH) [lit.[18] +193° (*c* 1–2, EtOH), 97% ee]; >95% ee. (*S*)-(−)-[(4-Chlorophenyl)sulfinyl]acetic acid[16,50] (0.42 g 38%) was also obtained from the aqueous layer of as colorless crystals (recrystallized from EtOAc/hexane): mp 125–127 °C; 91% ee. **(*R*)-(+)-Methyl [(4-nitrophenyl)sulfinyl]acetate [(*R*)-(+)-2]**: using 0.729 g (3.00 mmol, 1.00 equiv) of (±)-**2** in 30 mL of toluene (this substrate is significantly less soluble in toluene, hence the larger volume). The resulting suspension was stirred at 25 °C for 3 d. (*R*)-(+)-**2** (0.24 g, 33%) was recovered from the organic layer as colorless crystals: $[\alpha]^{25}_D$ +179° (*c* 0.46, $CHCl_3$); >95% ee. (*S*)-(−)-**2** (0.16 g, 22%) derived from the (*S*)-(−)-[(4-nitrophenyl)sulfinyl]acetic acid in the aqueous layer was also obtained after flash chromatography (50–60% EtOAc in hexane) as colorless crystals (recrystallized from methanol): $[\alpha]^{25}_D$ −174° (*c* 0.49, $CHCl_3$); >95% ee. **(*R*)-(+)-Methyl (phenylsulfinyl)acetate [(*R*)-(+)-3]**:[18,31] using 0.990 g (5.00 mmol, 1.00 equiv) of (±)-**3**. The resulting suspension was stirred at 25 °C for 55 h. (*R*)-(+)-**3** (0.48 g 48%) was recovered from the organic layer as an oil: >95% ee. (*S*)-(−)-(Phenylsulfinyl)acetic acid[51] (0.15 g, 17%) was also obtained from the aqueous layer as an oil: 92% ee. **(*R*)-(+)-Methyl [(4-methoxyphenyl)sulfinyl]acetate [(*R*)-(+)-4]**: using 0.770 g (3.38 mmol, 1.00 equiv) of (±)-**4**. The resulting suspension was stirred at 25 °C for 3 d. (*R*)-(+)-**4** (0.37 g, 48%) was recovered from the organic layer as an oil: $[\alpha]^{26}_D$ +126° (*c* 1.5, $CHCl_3$); >95% ee. (*S*)-(−)-**4** (0.26 g, 34%) derived from the (*S*)-(−)-[(4-methoxyphenyl)sulfinyl]acetic acid in the aqueous layer was also obtained after flash chromatography (65% EtOAc in hexane) as an oil: $[\alpha]^{25}_D$ −117° (*c* 1.5 $CHCl_3$); 88% ee. **(*R*)-(+)-Methyl (2-naphthylsulfinyl)acetate [(*R*)-(+)-5]**: using 0.124 g (0.5 mmol, 1.00 equiv) of (±)-**5**. The resulting suspension was stirred at 25 °C for 27 h. (*R*)-(+)-**5** (0.056 g, 45%) was recovered from the organic layer as colorless crystals: $[\alpha]^{26}_D$ +124° (*c* 0.8, EtOH); >95% ee. (*S*)-(−)-(2-Naphthylsulfinyl)acetic acid[52] (0.041 g, 35%) was also obtained from the aqueous layer as colorless crystals: 80% ee. **(*S*)-(+)-Methyl (*n*-butylsulfinyl)acetate [(*S*)-(+)-6]**: using 0.178 g (1.00 mmol, 1.00 equiv) of (±)-**6**. The resulting suspension was stirred at 25 °C for 4 d. (*S*)-(+)-**6** (0.074 g, 42%) was recovered from the organic layer as an oil: 89% ee. (*R*)-(−)-**6** (0.038 g, 21%) derived from the (*R*)-(−)-(*n*-butylsulfinyl)acetic acid in the aqueous layer was also obtained after flash chromatography (70% EtOAc in hexane) as an oil: 54% ee (some racemization of the acid apparently occurred in the work-up procedure). **(*R*)-(+)-Methyl (cyclohexylsulfinyl)acetate [(*R*)-(+)-7]**: using 0.380 g (1.86 mmol, 1.00 equiv) of (±)-**7**. The resulting suspension was stirred at 25 °C for 3 d. (*R*)-(+)-**7** (0.19 g, 49%) was recovered from the organic layer as an oil: >95% ee. (*S*)-(−)-**7** (0.067 g, 18%) derived from the (*S*)-(−)-(cyclohexylsulfinyl)acetic acid in the aqueous layer was also obtained after flash chromatography (50–60% EtOAc in hexane) as an oil: >95% ee. **(*R*)-(+)-Methyl 3-[(4-chlorophenyl)sulfinyl]propanoate [(*R*)-(+)-9]**: using 0.123 g (0.5 mmol, 1.00 equiv) of (±)-**8**. The resulting suspension was stirred at 25 °C for 37 h. (*R*)-(+)-**8** (0.037 g, 30%) was recovered from the organic layer as colorless crystals: $[\alpha]^{26}_D$ +143° (*c* 0.4, EtOH); >95% ee. (*S*)-(−)-3-[(4-Chlorophenyl)sulfinyl]propanoic acid (0.033 g, 29%) was obtained from the aqueous layer as an oil: 63% ee. The sulfinylalkanoic acid was characterized as the methyl ester (formed by reaction with CH_2N_2). **(*R*)-(+)-Methyl 3-[(4-nitrophenyl)sulfinyl]propanoate [(*R*)-(+)-9]**: using 0.129 g (0.5 mmol, 1.00 equiv) of (±)-**9**. Resulting suspension was stirred at room temperature for 66 h. (*R*)-(+)-**9** (0.057 g, 44%) was recovered from the organic layer as colorless crystals: $[\alpha]^{26}_D$ +64° (*c* 0.4, EtOH); >95% ee. (*S*)-(−)-3-[(4-nitrophenyl)sulfinyl]-propanoic acid (0.050 g, 35%) was also obtained from the aqueous layer as colorless crystals: 82% ee. The sulfinylalkanoic acid was characterized as the methyl ester (formed by reaction with CH_2N_2). **(*R*)-(+)-Methyl 3-(phenylsulfinyl)propanoate [(*R*)-(+)-10]**:[18] using 0.106 g (0.5 mmol, 1.00 equiv) of (±)-**10**. The resulting suspension was stirred at 25 °C for 38 h. (*R*)-(+)-**10** (0.051 g, 48%) was recovered from the organic layer as an oil: $[\alpha]^{26}_D$ +99° (*c* 1.2, EtOH) [lit.[18]+ 87° (*c* 1–2, EtOH), 96% ee]; >95% ee. (*S*)-(−)-3-(phenylsulfinyl)propanoic acid (0.024 g, 24%) was also obtained from the aqueous layer as an oil: 91% ee. The sulfinylalkanoic acid was characterized as the methyl ester (formed by reaction with CH_2N_2).

General Procedure for the Resolutions of Methyl Sulfinylalkanoates via Transesterifications with *n*-BuOH

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Catalyzed by *Pseudomonas* sp. K-10 (Table III). To a 0.01 M solution of the (±)-methyl sulfinylalkanoate in hexane was added 1-butanol (10.0 equiv) and 1.0 mass equiv of *Pseudomonas* sp. K10. The resulting suspension was stirred at 45 °C for the time indicated. The reaction was then filtered through celite to remove the enzyme (washing with Et_2O). Removal of the volatiles and separation of the crude mixture by flash chromatography gave the pure optically active methyl and *n*-butyl sulfinylalkanoates.

(*S*)-(−)-*n*-Butyl [(4-chlorophenyl)sulfinyl]acetate: using 0.116 g (0.500 mmol) of (±)-**2**. The resulting suspension was stirred at 45 °C for 27 h. After flash chromatography (30% EtOAc in hexane), 0.059 g (50%) of (*R*)-(+)-**2** was obtained as colorless crystals: 79% ee. Also obtained was 0.057 g (42%) of (*S*)-(−)-*n*-butyl [(4-chlorophenyl)sulfinyl]acetate as colorless crystals: R_f 0.7 (50% EtOAc in hexane); $[\alpha]^{25}_D$ −49° (*c* 0.20, EtOH); >95% ee; ^{1}H NMR δ 7.63 (d, *J* = 8.52 Hz, 2 H), 7.51 (d, *J* = 8.52 Hz, 2 H), 4.09 (t, *J* = 6.6 Hz, 2 H), 3.85 (d, *J* = 13.64 Hz, 1 H), 3.65 (d, *J* = 13.64 Hz, 1 H), 1.33 (m, 2 H), 0.90 (t, *J* = 7.27 Hz, 3 H); ^{13}C NMR δ 175.8 (C), 164.5 (C), 141.7 (C), 129.7 (CH/CH_3), 125.7 (CH/CH_3), 66.0 (CH_2), 61.7 (CH_2), 30.4 (CH_2), 19.0 (CH_2), 13.6 (CH/CH_3); IR ($CHBr_3$) 3020 (st), 1730 (st), 1570 (wk), 1470 (md), 1290 (md), 1150 (st), 1050 (md), 1070 (md) cm^{-1}; MS (EI, 70 eV) *m*/*z* (%) 207 (15), 81 (43), 28 (100); HRMS calcd for $C_{12}H_{15}O_3ClS$ 274.0430, found 274.0431. **(*S*)-(−)-*n*-Butyl (2-naphthylsulfinyl)acetate**: using 0.124 g (0.500 mmol) of (±)-**5**. The resulting suspension was stirred at 45 °C for 28 h. After flash chromatography (25% acetone in hexane), 0.030 g (24%) of (*R*)-(+)-**5** was obtained as colorless crystals: 85% ee. Also obtained was 0.044 g (30%) of (*S*)-(−)-*n*-butyl (2-naphthylsulfinyl)aceate as colorless crystals: R_f 0.5 (25% acetone in hexane); $[\alpha]^{25}_D$ −68° (*c* 0.60, EtOH); 91% ee; ^{1}H NMR δ 8.23 (s, 1 H), 7.93 (m, 3 H), 7.62 (m, 3 H), 4.09 (t, *J* = 6.6 Hz, 2 H), 3.92 (d, *J* = 13.58 Hz, 1 H), 3.75 (d, *J* = 13.58 Hz, 1 H), 1.48 (m, 2 H), 1.24 (m, 2 H), 0.90 (t, *J* = 7.27 Hz, 3 H). **(*S*)-(−)-*n*-Butyl 3-[(4-chlorophenyl)sulfinyl]propanoate**: using 0.123 g (0.500 mmol) of (±)-**8**. The resulting suspension was stirred at 45 °C for 55 h. After flash chromatography (25% EtOAc in hexane), 0.031 g (25%) of (*R*)-(+)-**8** was obtained as colorless crystals: >95% ee. Also obtained was 0.047 g (33%) of (*S*)-(−)-*n*-butyl 3-[(4-chlorophenyl)sulfinyl]propanoate as colorless crystals (recrystallized from acetone/hexane): R_f 0.6 (50% EtOAc in hexane); mp 60–61 °C; $[\alpha]^{25}_D$ −62° (*c* 0.40, EtOH); 90% ee; ^{1}H NMR δ 7.53 (m, 4 H), 4.05 (t, *J* = 6.5 Hz, 2 H), 3.19 (m, 1 H), 2.89 (m, 2 H), 2.55 (m, 1 H), 1.58 (m, 2 H), 1.52 (m, 2 H), 0.91 (t, *J* = 7.3 Hz, 3 Hz, 3 H); ^{13}C NMR δ 172.0 (C), 156.0 (C), 142.0 (C), 129.6 (CH/CH_3), 125.5 (CH/CH_3), 65.1 (CH_2), 51.3 (CH_2), 30.5 (CH_2), 26.1 (CH_2), 19.1 (CH_2), 13.7 (CH/CH_3); IR ($CHBr_3$) 3020 (st), 1730 (st), 1600 (md), 1470 (md), 1150 (st), 1050 (md), 1020 (md) cm^{-1}; MS (EI, 70 eV) *m*/*z* (%) 288 (1, M^+), 28 (100); HRMS calcd for $C_{13}H_{17}O_3ClS$ 288.0587, found 288.0587. **(*S*)-(−)-10-Undecen-1-yl [(4-Chlorophenyl)sulfinyl]acetate.** The transesterification procedure described above was used with 2.00 g (8.60 mmol, 1.00 equiv) (±)-**2**, 4.31 mL (21.5 mmol, 2.50 equiv) of 10-undecen-1-ol in place of the *n*-BuOH and only 2.0 mass equiv of *Pseudomonas* sp. K10. The resulting suspension was stirred at 45 °C for 35 h. After flash chromatography (20% EtOAc in hexane) 1.1 g (55%) of (*R*)-(+)-**2** was obtained as colorless crystals: 59% ee. The (*S*)-(−)-10-undecenyl [(4-chlorophenyl)sulfinyl]acetate and the excess 10-undecen-1-ol were not separated by the flash chromatography. Thus the 10-undecen-1-ol was transformed into its tetrahydropyranyl derivative to facilitate its removal. To a solution of the mixture in CH_2Cl_2 (50 mL) were added 3.92 mL (43.0 mmol, 5.00 equiv) of 3,4-dihydro-2*H*-pyran and a catalytic amount of *p*-toluenesulfonic acid monohydrate. The reaction was stirred at 25 °C for 5 h. Removal of the volatiles in vacuo and purification by flash chromatography (10% acetone in hexane) gave 0.42 g (13%) of (*S*)-(−)-10-undecenyl [(4-chlorophenyl)sulfinyl]acetate as an oil: R_f 0.14 (10% acetone in hexane); $[\alpha]^{25}_D$ −58° (*c* 0.45, EtOH); >95% ee; ^{1}H NMR δ 7.64 (d, *J* = 8.5 Hz, 2 H), 7.51 (d, *J* = 8.5 Hz, 2 H), 5.80 (m, 1 H), 4.94 (m, 2 H), 4.07 (t, *J* = 6.8 Hz, 2 H), 3.85 (d, *J* = 13.6 Hz, 1 H), 3.66 (d, *J* = 13.6 Hz, 1 H), 2.03 (m, 2 H), 1.57 (m, 2 H), 1.10–1.40 (m, 12 H); ^{13}C NMR δ 177.0 (C), 164.5 (C), 141.6 (C), 139.1 (CH/CH_3), 129.7 (CH/CH_3), 125.7 (CH/CH_3), 114.1 (CH_2), 66.3 (CH_2), 61.6 (CH_2), 33.8 (CH_2), 29.4 (CH_2), 29.1 (CH_2), 29.0 (CH_2), 28.9 (CH_2), 28.3 (CH_2), 25.7 (CH_2); IR (neat) 3500 (md), 1732 (st), 1650 (md), 1276 (md), 1090 (md), 1055 (md), 1011 (md) cm^{-1}; MS (EI, 70 eV) *m*/*z* (%) 370 (0.4, M^+), 159 (100); HRMS calcd for $C_{19}H_{27}O_3ClS$ 370.1369, found 370.1369.

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Supplementary Material Available: ^{1}H and ^{13}C NMR spectra for selected compounds (20 pages). Ordering information is given on any current masthead page.

Acylal Hydrolysis. The pH-Independent Breakdown of 7-Oxo-6,8-dioxabicyclo[3.2.1]octane

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The hydrolysis of the bicyclic acylal 7-oxo-6,8-dioxabicyclo[3.2.1]octane in water is rapid and pH independent from pH 1–12 (k_0 = 6.0 × 10^{-3} s^{-1} at 20 °C). This reaction proceeds at nearly the same rate in D_2O as in H_2O (k_{H_2O}/k_{D_2O} = 1.1) and is uncatalyzed by buffer. Therefore, the reaction is a unimolecular breakdown to a resonance-stabilized oxocarbonium ion; i.e., the acylal is hydrolyzing like an acetal with a good leaving group and not like an ester. The ^{1}H and ^{13}C NMR spectra indicate a diaxial conformation for the substituents at C-1 and C-5 with moderate distortion of the tetrahydropyran ring. There is a large upfield shift for carbon at C-3 as compared with the corresponding carbon (C-4) of tetrahydropyran (8.8 ppm) or 2-ethoxytetrahydropyran (3.8 ppm). The rapid pH-independent unimolecular breakdown reaction is due to a relatively favorable ΔS* (−2.6 eu) and the lack of effective reversibility of that reaction.

The hydrolysis of both cyclic and acyclic acylals has been extensively studied.[1-5] These compounds combine the structural features of both acetals and esters and can therefore hydrolyze by mechanisms typical of either type

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