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STEREOCHEMICALLY MATCHED SULFINYLACETATES FOR DOUBLE DIASTEREOSELECTION IN THE SPAC REACTION

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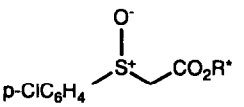
4-Chlorophenylsulfinylacetates of defined stereochemistry at sulfur were prepared from monochiral alcohols: compound **2** from (+)-menthol; **3** and **4** from (-)-8-phenylmenthol; **5** and **6** from (+)-*trans*-2-phenylcyclohexanol; and, **7** and **9** from (-)-10-dicyclohexylsulfamoyl-D-isoborneol. Reagents for which the sulfoxide asymmetry is matched with the inducing effect of the auxiliary give good diastereoselection in SPAC reactions affording γ-hydroxy-α,β-unsaturated alcohols of high optical purity. Asymmetry at the sulfoxide has a greater effect than the auxiliaries on the stereochemical outcome of these reactions.

This paper describes syntheses of diastereomerically and optically pure sulfinylacetates **I** bearing chiral auxiliaries in the ester functionality.



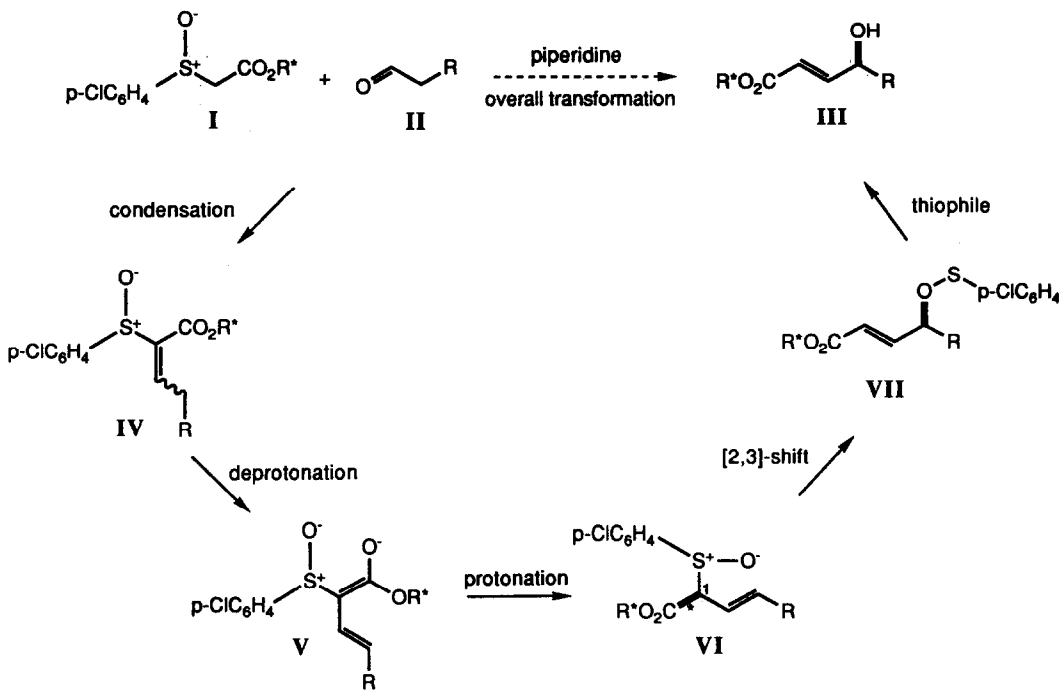
I

R* = chiral auxiliary

These reagents have several potential applications,[1] but we were particularly interested in using them as reagents for asymmetric SPAC reactions (Sulfoxide, Piperidine, And Carbonyl, Scheme 1). Previously, we described asymmetric SPAC reactions of monochiral methyl sulfinylacetates and subsequent biocatalytic resolutions as a route to optically active γ-hydroxy-α,β-unsaturated esters **III**,[2] potential chirons for many different syntheses. This approach is useful when the aldehyde substrate **II** is not valuable, and when the resulting SPAC reaction products can be resolved efficiently in the subsequent biocatalytic resolution; however, an alternative is required when these criteria are not applicable. The latter part of this paper describes asymmetric variants of the SPAC reaction which give good optical yields *without using kinetic resolution procedures on the products.* We advocate this as the method of choice when the aldehyde substrate for the SPAC process is relatively precious, for example one produced in the advanced stages of a total synthesis.

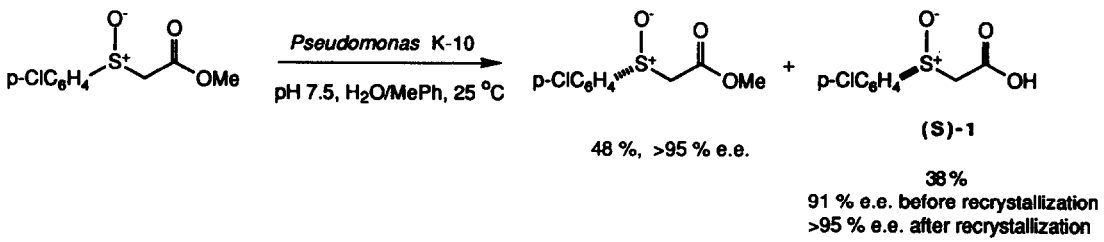
Optically active methyl sulfinylacetates which are chiral just at sulfur, give γ-hydroxy-α,β-unsaturated esters **III** of up to 75 % e.e. in the SPAC reaction. The rationale for expecting improvements with sulfinylacetates functionalized with chiral auxiliaries is as follows. Previous studies have shown attack of the thiophile (piperidine in this case) on intermediate **VII** is faster than the retro-[2,3] shift (Scheme 1),[3,4] consequently we conclude the SPAC reaction of aliphatic aldehydes is probably kinetically controlled. Sulfoxide asymmetry has relatively minor effects on the stereochemical outcome of [2,3]-rearrangements of chiral allylic sulfoxides[5-7]

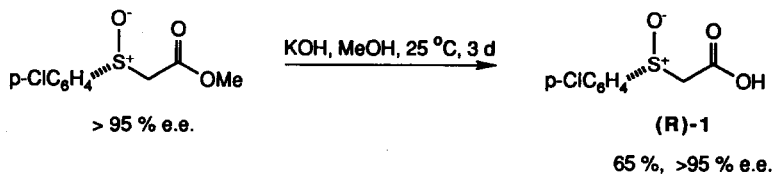
because the sulfoxide rearranges on the face of the double bond which corresponds to minimum 1,3-allylic strain in the transition state.[8,9] Consequently, configurations of alcohols formed in SPAC reactions are determined by the transient asymmetric center C^1 of intermediate **VI**; asymmetry at the sulfoxide is significant in the preceding proton transfer step and thereafter it is unimportant. Consequently, successful asymmetric variants of the SPAC reaction must involve protonation of the intermediate enolate **V** with good diastereofacial selectivity.[8-10] The strategy described here is to control this process with the auxiliaries (R^*) of reagents **I** and, if necessary, enhance the selectivity by matching these auxiliaries with asymmetry at the sulfoxide center. This study should reveal the sense and magnitude of effects that can be obtained from these two inducing groups and optimal reagent stereochemistries for maximum induction.[11]



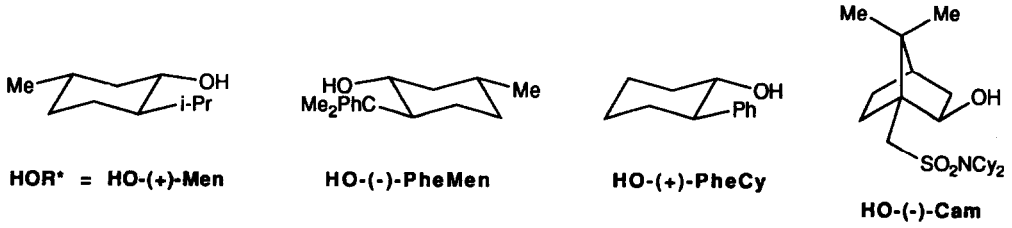
Scheme 1. The SPAC Reaction of 4-Chlorophenylsulfinylacetate **I**.
Stereoselection in this transformation is determined by diastereofacial selectivity in protonation of enolate **V**.

Preparations of Sulfinylacetates Functionalized with a Chiral Auxiliary. Recently we described a hydrolysis of racemic methyl 4-chlorophenylsulfinylacetate mediated by *Pseudomonas* K-10.[12] (S)-4-Chlorophenylsulfinylacetic acid, **(S)-1**, of 91 % e.e. can be isolated via this route and its optical purity is enhanced to greater than 95 % e.e. after a single recrystalization. Furthermore, base catalyzed hydrolysis of (R) methyl 4-chlorophenylsulfinylacetate (recovered from the enzymatic process in greater than 95 % e.e.) affords the corresponding (R)-sulfinylacetic acid, **(R)-1**, without loss of optical activity. Consequently, *both optical antipodes of 4-chlorophenylsulfinylacetic acid are conveniently available in near enantiomerically pure form.*



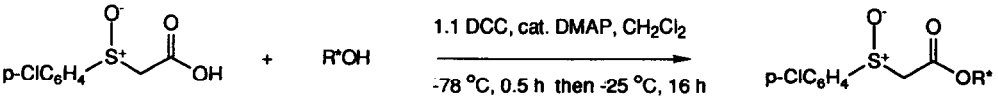


The cheap and convenient kinetic resolution described above is the basis of the easiest synthesis of stereochemically matched sulfinylacetate reagents whereby monochiral samples of the sulfinylacetic acid **1** are esterified with the four chiral alcohols (R*OH) shown below (eq. 1). Three of these auxiliaries, **(-)-PheMen**,[13 - 16] **(+)-PheCy**,[17] and **(-)-Cam**,[18] were chosen because of their proven ability to direct enolate electrophile processes. All four alcohols are commercially available (but **PheCy** is only sold in racemic form and must be resolved).[17]

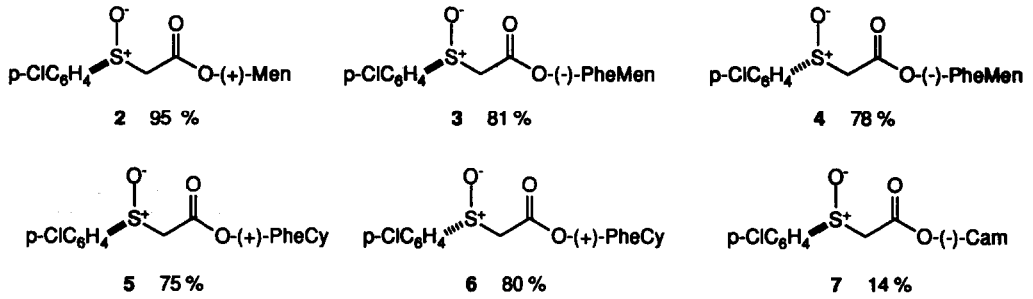


HOR* = HO-(+)-Men **HO-(-)-PheMen** **HO-(+)-PheCy** **HO-(-)-Cam**

These esterifications rely upon selective activation of carboxylic acid functionality, hence mild conditions[19] were chosen to avoid competing sulfoxide activation. Chemoselectivity is not perfect in these reactions since Pummerer rearrangements *are* sometimes observed but the desired esterification predominates in all cases (Scheme 2) except those involving **HO-(-)-Cam**; this alcohol is extremely hindered, hence coupling tends to be slower than competing sulfoxide activation.

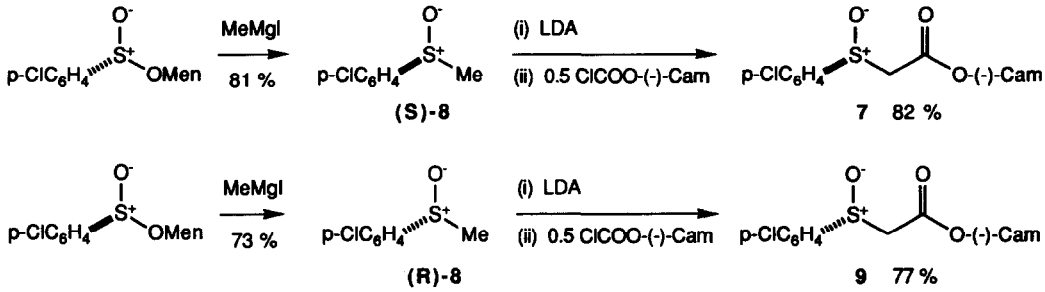


1 **2 - 7** eq. 1



Scheme 2 Preparations of Sulfinylacetates **2** - **7**. (Isolated yields in parentheses)

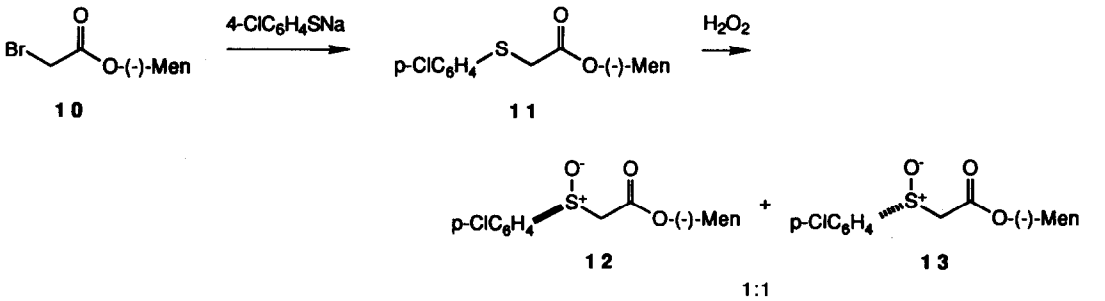
Sulfinylacetates containing **(-)-Cam** were prepared as shown in Scheme 3 since the previous route (eq. 1) did not work well with this auxiliary. Thus, menthyl sulfinates were resolved via fractional crystalization and transformed into the corresponding methyl sulfoxides;[20] deprotonation and reaction with 10-dicyclohexylsulfamoyl-D-isoborneol chloroformate (formed from phosgene plus the monochiral alcohol, and used without purification) gave the sulfinylacetates **7** and **9**. Conversion in the last step of this process is limited to 50 % because the product is more acidic than the starting material, nevertheless yields based on the auxiliary component of the reaction are good.

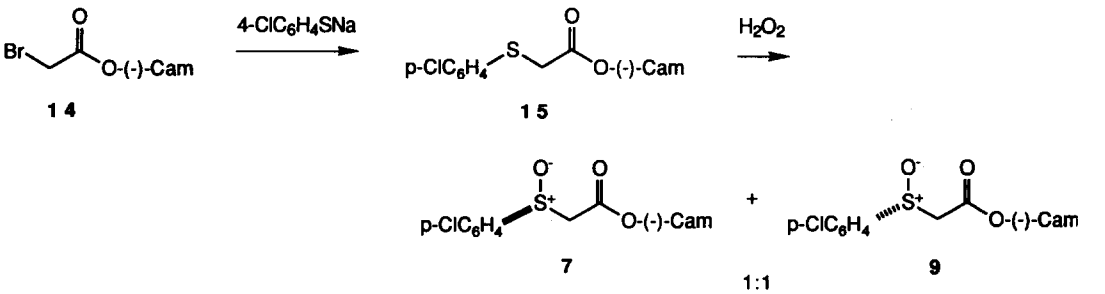


Scheme 3. Preparation of Sulfinylacetates **7** and **9**.

Preparations of sulfinylacetates **7** and **9** via asymmetric oxidation of sulfide **15** were also investigated; these efforts gave poor diastereoselection, but were interesting nonetheless. Under standard conditions[21 - 23] {1 eq. $Ti(O^iPr)_4$, 1 eq. H_2O, 2 eq. t-BuOOH, at -20 °C in dichloromethane, in the presence of 2 eq. DET (diethyl tartrate)}, sulfide **15** was oxidized with a diastereomeric excess of 55 % of **9** over **7** using (+)-DET, whereas (-)-DET gave 49 % d.e. *in the same sense*. This implies that the oxidation is controlled by the chiral auxiliary with minimal influence from the catalyst. Attempts to enhance asymmetric induction in this reaction were fruitless. For instance, reasoning the ester functionality could fulfill the role of water as a ligand in these reactions and enhance selectivity, we performed the oxidations under anhydrous conditions; however, the selectivity decreased.

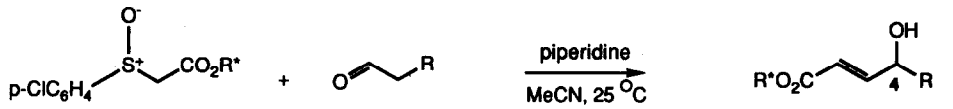
Finally, sulfinylacetates of undefined configuration at the sulfoxide center were easily prepared. Treatment of **HO-(-)Men** and **HO-(-)-Cam** with bromoacetyl bromide gave the corresponding bromoesters **10** and **14**, which were converted to sulfides, **11** and **15** respectively, and oxidized to the desired products; however, we were unable to separate the diastereomeric products via flash chromatography[24] or fractional crystalization.





Diastereoselective SPAC Reactions. The Table shows results obtained for SPAC reactions of sulfinylacetates **3** - **7**, **9**, **12**, and **13** with a range of aldehydes. Entry 1 describes a SPAC reaction utilizing a mixture of menthyl sulfinylacetates of undefined configuration at sulfur (i.e. a 1:1 mixture of **12** and **13**); low diastereoselection is obtained indicating menthyl is a poor stereodirecting group for this process. Entry 7 indicates the camphor based system is better but the induction is still less than that which can be obtained using a sulfoxide of defined configuration and an achiral ester.[3,10,25 - 27] Consequently, matched and mismatched combinations[28] of the sulfoxide center with the auxiliaries were investigated. Poor to moderate diastereoselection results when **(-)-PheMen**, **(+)-PheCy** and **(-)-Cam** are paired with (S)-sulfoxide asymmetry (entries 2, 5 and 6), indicative of destructive stereochemical pairing. However, incorporating these auxiliaries with (R)-configuration at sulfur gives appreciable diastereoselectivities in the SPAC transformation. The camphor-based ligand, **(-)-Cam**, and **(-)-PheMen** are comparable in this process, and significantly more effective than **(+)-PheCy** (entries 3, 4, and 8 - 14). Matched reagents **4** and **9** give high diastereoselection with pentanal in the SPAC reaction (entries 3 and 10); **9** was also reacted with six other aldehydes and good diastereoselection was obtained in each case (entries 8, 9 and 11 - 14). Furthermore, the products containing the camphor-based auxiliary tend to be solids so their stereoisomeric purity can be enhanced by recrystallization.

Table. Constructive and Destructive Stereochemical Pairing in the SPAC Reaction.



entry	R*	R	configuration at sulfoxide (reagent)	yield %[a]	ratio of diastereomers R:S (at C^4)[b]
1	(-)-Men	Me	1:1 mixture (12) + (13)	69	54:46
2	(-)-PheMen	n-Pr	S (3)	82	42:58
3	(-)-PheMen	n-Pr	R (4)	98	88:12
4	(+)-PheCy	n-Pr	R (6)	60	75:25
5	(+)-PheCy	n-Pr	S (5)	66	29:71
6	(-)-Cam	Me	S (7)	83	25:75
7	(-)-Cam	Me	1:1 mixture (7) + (9)	78	64:36
8	(-)-Cam	Me	R (9)	69	88:12
9	(-)-Cam	Et	R (9)	89	87:13
10	(-)-Cam	n-Pr	R (9)	93	91:09
11	(-)-Cam	phalCH_2	R (9)	59[c]	88:12
12	(-)-Cam	i-Pr	R (9)	98	82:18
13	(-)-Cam	CyCH_2	R (9)	86	82:18
14	(-)-Cam	Me_2ThexSiO$(CH_2)_2$	R (9)	98	78:22

[a] Isolated yields after flash chromatography. [b] Determined from ^{1}H NMR of (MPTA) Mosher's ester derivatives. SPAC reactions of methyl (R)-sulfinylacetates give (R)-4-hydroxy-2-enoates. In this work the sulfoxide dominates over the chiral auxiliary hence the same relationship is assumed; ^{1}H NMR analysis of Mosher's ester derivatives of the product supports this assignment. [c] Unoptimized yield, 39 % of the sulfoxide reagent recovered.

Conclusions

Sulfinylacetates functionalized with chiral auxiliaries and with defined sulfoxide configuration can be conveniently synthesized. Both enantiomers of the sulfoxide component can be derived from biocatalytic resolutions or Andersen syntheses, and both optical antipodes of the chiral auxiliaries are commercially available in optically pure form {**HO-Men**, **HO-Cam**, and **HO-PheMen**} or easily resolved {**HO-PheCy**}.

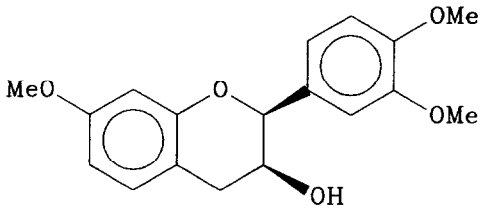
This research proves sulfoxide asymmetry has the dominant inducing effect in SPAC reactions of sulfinylacetates prepared from optically active alcohols, but auxiliaries can have an appreciable influence. The electronic directing effects of the α-sulfoxide functionality and steric blocking characteristics of auxiliaries can be coupled to effect diastereoselective protonation of enolate **V**, hence good selectivity in the SPAC process. Dominance of the sulfoxide chirality in the diastereoselective protonation of enolate **V** (Scheme 1) may be a reflection of the powerful influence of a sulfoxide group on α-carbanion reactivity (c.f. carbanions adjacent to sulfoxides which are otherwise unstabilized tend to be tetrahedral and configurationally stable).[29,30]

The most effective auxiliaries for the purposes outlined above {**Cam** and **PheMen**} are also powerful directing groups for other reactions, so further manipulations of these γ-hydroxy-α,β-unsaturated esters should prove interesting and synthetically useful.[31]

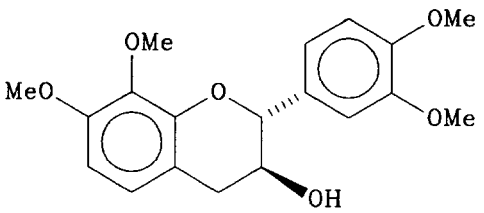
densed tannin derivatives (*vide infra*).

The yields of the oxygenation products of the (+)-catechin and (-)-epicatechin derivatives are thus comparable for DDQ and $K_2S_2O_8$[8] but are substantially increased with these reagents in comparison to those for $Pb(OAc)_4$[5-7]. Utilization of DDQ and $K_2S_2O_8$ as oxidant offers the additional advantage of reduced reaction times compared to those for $Pb(OAc)_4$ hence minimizing side reactions[a], *e.g.* excessive anthocyanidin formation and also condensations to form procyanidin oligomers. Such improved yields and reduced reaction times achieved with DDQ relative to those of acetoxylation with $Pb(OAc)_4$ are dependent on the double molar excess of DDQ for rapid hydride ion abstraction (*vide infra*), and on the complete reduction of the excess of DDQ with sodium borohydride immediately after the specified reaction times.

Application of the optimized conditions to 3-*O*-acetyl-trimethyl-(-)-fisetinidol 11 (5 days) and 3',4'-di-*O*-methyl-(-)-fisetinidol 12 (3 h) afforded the corresponding dihydroflavonols 13 and 14 in *ca.* 20% yields following acetylation of the crude reaction mixtures. Similar low yields and extended times were also observed for trimethyl-(+)-epifisetinidol 17 and tetramethyl-(+)-mesquitol[11] 18 hence limiting the utility of DDQ as oxidant for the benzylic functionalization of 5-deoxy flavan-3-ols. (+)-Mollisacacidin tri-*O*-methyl ether 15 was, however, oxidized in 2 hours with 1 molar equivalent of DDQ to tri-*O*-methyl-(+)-fustin 16 in 69% yield. Such an approach usefully complements existing methodology[12] for the selective oxidative conversion of flavan-3,4-diol to dihydroflavonol with conservation of the integrity of absolute configuration at C-2 and C-3 (*cf.* Experimental).



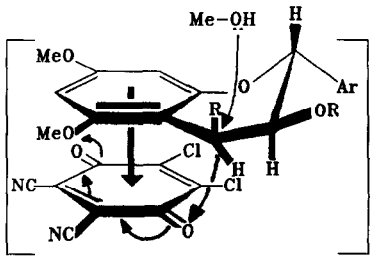
(17)



(18)

The functionalizations involving the (+)-catechin and (-)-epicatechin derivatives are characterized by a high degree of regio- and stereoselectivity. Both these features are presumably explicable in terms of the ability of DDQ to form charge-transfer complexes with aromatic substrates[13,14]. Owing to the higher electron density of the phloroglucinol-type A-ring compared to that of the pyrocatechol-type B-ring in *e.g.* 1, such a charge-transfer complex will preferentially involve the former ring hence explaining the selective oxygenation at C-4 *vs.* possible competing functionalization at C-2 *via* B-ring/DDQ complexes. Repulsive steric interactions between the axial H-2 and the bulky oxidant would facilitate association of DDQ from the α-face hence permitting the selective removal of the pro-*R* diastereotopic benzylic hydrogen as hydride ion within a

[a] These side reactions as were evidenced by strong coloration and the formation of highly polar compounds respectively, contributed significantly to the observed 'loss' of material.



(19) **R = H**

(20) **R = 2,4-dihydroxyphenyl**

(21) **R = 2,4,6-trihydroxyphenyl**

(22) **R = (2*R*,3*S*)-2,3-*trans*-3',4',5,7-tetramethoxy-3-*O*-acetylflavan-8-yl**

tightly bound complex 19. The incipient carbocationic species is then attacked simultaneously by the nucleophile (MeOH) from the opposite side, *i.e.* in an S_N2 fashion with the exclusive formation of 2,4-*trans* products. An intense green coloration which appeared when the reagents were first mixed and which disappeared as the reaction progressed was indicative of a charge-transfer interaction[14]. Additional evidence for the formation of the charge-transfer complex was derived from the observation that (+)-catechin tetramethyl ether 1 was functionalized in chloroform/methanol in 50% yield, *vs.* the 20% yield in methanol only, chloroform being capable of assisting the initial formation of the complex[10] 19.

The alignment of reactants in the intermediate complex may presumably be depicted as in formulation 19. Such a conformation permits the simultaneous abstraction of hydride ion at C-4 and the minimization of repulsive steric interactions by eclipsing H-6 and H-8 of the flavan-3-ol A-ring and the bulky chloro and cyano substituents (or *vice versa*) of DDQ.

The conjecture that steric interactions between the axial H-2 and the bulky oxidant inhibits its association from the β-face of the substrate, was demonstrated by subjecting the 4α- and 4β-arylflavan-3-ol derivatives 23, 24 and 25, 26 separately to reaction with DDQ under similar conditions. Thus, only the 4β-analogues 25 and 26 were stereoselectively oxygenated at C-4 to give the 4β-methoxy-4α-arylflavan-3-ol derivatives 27 (35%) and 28 (20%) presumably *via* the intermediate complexes 20 and 21. In the case of the 4β-(2,4,6-trimethoxyphenyl)-analogue 26, the 4β-methoxy derivative 28 was accompanied by the flav-3-en-3-ol derivative 29 in 15% yield. Substitution of H-4(C) in 25 and 26 by a methoxy group in 27 and 28 was evident from ^{1}H NMR data which indicated an AB-system (J10.5 Hz) for the heterocyclic protons (δ 5.50, 6.06; δ 5.56, 6.09: H-2 and -3 for 27 and 28 respectively) and a three-proton singlet (δ 3.19, 3.13 for 27 and 28 respectively) for the C-4 methoxy protons. A pronounced n.O.e. association (5.8 and 6.1% for 27 and 28 respectively) between these protons and H-2(C) strongly indicated a 4β-methoxy group and hence 4*S* absolute configuration for 27 and 4*R* for 28. The structure of the flav-3-en-3-*O*-acetyl derivative 29 was verified by ^{1}H NMR analysis which indicated the presence of a single deshielded and secondary coupled heterocyclic proton at δ 6.06 [H-2(C)].

The formation of the flavan-3-en-3-ol derivative 29 constitutes an important feature of the oxygenation reactions. Its generation may represent the first step towards the formation of an anthocyanidin derivative of type 30 hence explaining the considerable degree of reddening observed in all these oxidations. In the (+)-catechin derivatives the axial H-3(C) would facilitate rapid and concerted loss of a proton either in the

(C), 136.9 (C), 129.4 (CH/CH_3), 124.8 (CH/CH_3), 43.7 (CH/CH_3); IR ($CHBr_3$) 3500 (br md), 3090 (md), 3075 (md), 3040 (md), 3920 (wk), 1650 (wk), 1580 (md), 1480 (st), 1425 (md), 1410 (md), 1390 (st) cm^{-1}; MS (EI, 70 eV) m/z (%) 176 {36, $M(Cl^{37})+$}, 174 {93, $M(Cl^{35})+$}, 161(30), 159 (100); HRMS calcd for C_7H_7ClOS 173.99061, found 173.99087.

(R)(+)-(4-Chlorophenyl)methyl Sulfoxide {(R)-8}. Procedure as for **(S)-8** except (1R,2S,5R)-menthyl (S)(-)-4-chlorophenylsulfinate was used.

10-Dicyclohexylsulfamoyl-D-isobornyl (S)(-)-4-Chlorophenylsulfinylacetate (7). 10-Dicyclohexylsulfamoyl-D-isobornyl chloroformate was formed by reaction of 1.99 g (5.00 mmol, 1.00 eq.) of 10-dicyclohexylsulfamoyl-D-isoborneol with excess phosgene in the presence of 0.710 g (5.50 mmol, 1.10 eq.) of quinoline in 40 mL of toluene at 0 °C for 52 h; this solution was then filtered and the solvent removed on a vacuum line (solvents/excess phosgene removed *should be disposed with care*) and used as is.

A solution of 1.75 g (10.0 mmol, 2.00 eq.) of **(S)-8** in 12 mL of THF was added to 11.0 mmol (2.20 eq.) of LDA in 31 mL of THF and 6 mL of hexane at -78 °C under N_2. The resulting deep yellow solution was stirred at -78 °C for 30 min. A solution of 1.50 mmol (1.00 eq.) of the chloroformate in 22 mL of THF was added dropwise to the solution of the deprotonated sulfoxide at -78 °C. The resulting orange solution was stirred at -78 °C for 45 min.then stored at -23 °C for 45 h. The reaction was quenched by cautious addition of 20 mL of saturated aq. NH_4Cl solution. The organic layer was collected and the aqueous fraction extracted with 3 x 100 mL of CH_2Cl_2. After drying the combined organic fractions ($MgSO_4$) and removal of the volatiles in vacuo, purification by flash chromatography (20 % EtOAc in hexane) gave sulfinylacetate **7** (2.46 g, 82 %) as colorless crystals (recrystallized from EtOAc/hexane); mp 161-162 °C; R_f 0.4 (20 % EtOAc in hexane); $[\alpha]^{25}_D$ -71 °; ^1H NMR δ 7.68 (d, J = 8.4 Hz, 2 H), 7.50 (d, J = 8.4 Hz, 2 H), 4.96 (m, 1 H),3.91 (d, J = 12.9 Hz, 1 H), 3.57 (d, J = 12.9 Hz, 1 H), 3.23 (m, 3 H), 2.65 (d, J = 13.3 Hz; 1 H), 0.86 - 1.95 (m, 27 H), 0.90 (s, 3 H), 0.86 (s, 3 H); ^{13}C NMR δ 162.7 (C), 141.6 (C), 138.1 (C), 129.7 (CH/CH_3), 125.8 (CH/CH_3), 80.3 (CH/CH_3), 61.9 (CH_2), 57.5 (CH/CH_3), 53.8 (CH_2), 49.5 (C), 49.2 (C), 44.3 (CH/CH_3), 39.4 (CH2), 32.9 (CH2), 32.6 (CH2), 30.5 (CH2), 26.9 (CH_2), 26.4 (CH_2), 25.1 (CH_2), 20.3 (CH/CH_3), 19.8 (CH/CH_3); IR ($CHBr_3$) 2940 (st), 1725 (st), 1320 (st), 1270 (br st), 1045 (st) cm^{-1}; MS (EI, 70 eV) m/z (%) 298 (3), 244 (1), 180 (100). Anal: Calcd for $C_{30}H_{44}NClO_5S_2$: C, 60.23; H, 7.41; N, 2.34. Found: C, 60.10; H, 7.54; N, 2.32.

10-Dicyclohexylsulfamoyl-D-isobornyl (R)(+)-4-Chlorophenylsulfinylacetate (9). Procedure as for **7** except 1.75 g (10.0 mmol, 2.00 eq.) of **(R)-8** was used. Purification by flash chromatography (20 % EtOAc in hexane) gave sulfinylacetate **9** (2.30 g, 77 %) as colorless crystals (recrystallized from EtOAc/hexane): mp 111-113 °C; R_f 0.4 (20 % EtOAc in hexane); $[\alpha]^{25}_D$ +45 °; ^1H NMR δ 7.61 (d, J = 8.1 Hz, 2 H), 7.48 (d, J = 8.1 Hz, 2 H), 5.02 (m, 1 H), 3.72 (d, J = 14.5 Hz, 1 H), 3.61 (d, J = 14.5 Hz, 1 H), 3.21 (m, 2 H), 3.20 (d, J = 13.3 Hz, 1 H), 2.61 (d, J = 13.3 Hz; 1 H), 0.84 - 2.01 (m, 27 H), 0.97 (s, 3 H), 0.84 (s, 3 H); ^{13}C NMR δ 163.9 (C), 142.2 (C), 137.8 (C), 129.8 (CH/CH_3), 125.5 (CH/CH_3), 80.5 (CH/CH_3), 62.5 (CH_2), 57.6 (CH/CH_3), 54.0 (CH_2), 49.8 (C), 49.2 (C), 44.5 (CH/CH_3), 39.4 (CH2), 32.8 (CH2), 32.7 (CH2), 30.5 (CH2), 27.0 (CH_2), 26.5 (CH_2), 25.2 (CH_2), 20.4 (CH/CH_3), 20.1 (CH/CH_3); IR ($CHBr_3$) 2940 (st), 1725 (st), 1320 (st), 1270 (br st), 1045 (st) cm^{-1}; MS (EI, 70 eV) m/z (%) 298 (3), 244 (1), 180 (100). Anal.: Calcd for $C_{30}H_{44}NClO_5S_2$: C, 60.23; H, 7.41; N, 2.34. Found: C, 58.97; H, 7.59; N, 2.33.

(1R,2S,5R)-Menthyl 4-Chlorophenylsulfinylacetate {1:1 epimeric mixture of (12) and (13)}. Procedure to synthesize crude (1R,2S,5R)(-)-menthyl 4-chlorophenylsulfenylacetate **(11)** as for **15** except **10** was used. {(1R,2S,5R)-menthyl bromoacetate **(10)** was synthesized in the same way as **14**, except (1R,2S,5R)(-)-menthol and only 1.05 equivalents of bromoacetyl bromide were used. Purification by vacuum-distillation gave **10** (57 %) as a colorless oil.} **11**, without further purification, was oxidized to the 1:1 epimeric mixture of **12** and **13** in the same way as for the 1:1 epimeric mixture of **7** and **9** except 1.20 eq. of 30.8 % aq. H_2O_2 was used. Purification by flash chromatography (20 % acetone in hexane) gave the 1:1 epimeric mixture of **12** and **13** (3.57 g, 100 %) as a yellow oil: R_f 0.4 (20 % EtOAc in hexane); ^1H NMR δ 7.62 (d, J = 8.50 Hz, 2 H), 7.48 (d, J = 7.94 Hz, 2 H), 4.65 (m, 1 H), 3.84 (d, J = 13.8 Hz, 1 H - first diastereomer), 3.83 (d, J = 13.6 Hz, 1 H - second diastereomer), 3.65 (d, J = 13.8 Hz, 1 H -first diastereomer), 3.64 (d, J = 13.6 Hz, 1 H - second diastereomer), 0.62-1.86 (m, 18 H); ^{13}C NMR δ 164.1 (C), 141.7 (C), 138.1 (C), 129.7 (CH/CH_3), 126.0 (CH/CH_3), 76.6 (CH/CH_3), 61.8 (CH_2), 61.7 (CH_2), 46.7 (CH/CH_3), 40.7 (CH_2), 40.6 (CH_2), 34.0 (CH_2), 31.4 (CH/CH_3), 26.1 (CH/CH_3), 26.0 (CH/CH_3), 23.2 (CH_2), 21.9 (CH/CH_3), 20.8 (CH/CH_3), 20.7 (CH/CH_3), 16.1 (CH/CH_3); IR ($CHBr_3$) 2950 (st), 2870 (st), 1715 (st), 1570 (wk), 1050 (st) cm^{-1}; MS (EI, 70 eV) m/z (%) 358 {0.7, $M(Cl^{37})+$}, 356 {0.7, $M(Cl^{35})+$}, 159 (100); HRMS calcd for $C_{18}H_{25}ClO_3S$ 356.1213, found 356.1205.

10-Dicyclohexylsulfamoyl-D-isobornyl 4-Chlorophenylsulfenylacetate (15). Solutions of 0.642 g (4.44 mmol, 1.00 eq.) of 4-chlorothiophenol in 6.0 mL of benzene and 2.30 g (4.44 mmol, 1.00 eq.) of **14** {10-Dicyclohexylsulfamoyl-D-isobornyl bromoacetate **(14)** was synthesized by addition of 3.21 g (15.9 mmol, 2.0 eq.) of bromoacetyl bromide to a solution of 3.12 g (7.90 mmol, 1.00 eq.) of (-)-10-dicyclohexylsulfamoyl-D-isoborneol, 0.751 g (9.50 mmol, 1.20 eq.) of pyridine and a catalytic amount of 4-DMAP in 50 mL of CH_2Cl_2 at 0 °C under N_2. The resulting yellow suspension was stirred for 1 h at 0 °C and 24 h at 25 °C then 60 mL of CH_2Cl_2 and 30 mL of 2M HCL were added. The organic layer was collected and washed with 30 mL of 2M HCl, 30 mL of saturated aq. $NaHCO_3$ solution and 30 mL of H_2O and then dried (Na_2SO_4). Removal of the volatiles in vacuo gave brown crystals. These were recrystallized from 90-110 °C petroleum ether to give colorless crystals of **14** (1.05 g, 94 %)}.in 6.0 mL of benzene were added to an emulsion of 2.88 g (4.44 mmol, 1.00 eq.) of 40 % aq. tetrabutylammonium hydroxide in 9.0 mL of benzene under N_2. The resultant mixture was stirred at 25 °C for 3 h, then 150 mL of EtOAc and 100 mL of 2 M HCl were added. The organic layer was collected and washed with 100 mL of saturated aq. $NaHCO_3$ and 100 mL of H_2O. After drying ($MgSO_4$), the volatiles were removed in vacuo to give an orange oil. The oil crystallized when stirred under petroleum ether for several hours to give sulfenylacetate **15** (1.96 g, 76 %) as colorless crystals (recrystallized from 90-110 °C petroleum ether): mp 119-121 °C; R_f 0.4 (10 % EtOAc in hexane); $[\alpha]^{25}_D$ -55 ° (c 1.6, $CHCl_3$); ^1H NMR δ 7.26 (m, 4 H), 4.97 (m, 1 H), 3.64 (d, J = 15.4 Hz, 1 H), 3.58 (d, J = 15.4 Hz, 1H), 3.24 (d, J = 13.3 Hz, 1 H), 3.24 (m, 2 H), 2.63 (d, J = 13.3 Hz,1 H), 1.01 - 1.98 (m, 33 H), 0.86 (s, 3 H), 0.85 (s, 3 H); ^{13}C NMR δ 167.6 (C), 133.8 (C), 132.8 (C), 130.6 (CH/CH_3), 129.2 (CH/CH_3), 79.9 (CH/CH_3), 57.5 (CH/CH_3), 53.8 (CH_2), 44.5 (CH/CH_3), 39.3 (CH_2), 36.8 (CH_2), 33.0 (CH_2), 32.7 (CH_2), 30.4 (CH_2), 27.0 (CH_2), 26.5 (CH_2), 26.2 (CH_2), 20.4 (CH/CH_3), 19.2 (CH/CH_3); IR ($CHBr_3$) 2940 (st), 2860 (st),1720 (st), 1320 (st), 1275 (st), 1045 (st) cm^{-1}; MS (EI, 70 eV) m/z (%) 583 {46, $M(Cl^{37})+$}, 581 {100, $M(Cl^{35})+$}; HRMS calcd for $C_{30}H_{44}ClNO_4S_2$ 581.24000, found 581.23926.

10-Dicyclohexylsulfamoyl-D-isobornyl 4-Chlorophenylsulfinylacetate (1:1 epimeric mixture of (7) and (9)). 0.552 g (5.00 mmol, 2.00 eq.) of 30. % aq. H_2O_2 was added to a solution of 1.46 g (2.50 mmol, 1.00 eq.) of 10-dicyclohexylsulfamoyl-D-isobornyl 4-chlorophenylsulfenylacetate **(15)** in 35 mL of glacial acetic acid cooled in a water bath. The resulting pale yellow solution was stirred at 25 °C for 24 h then 100 mL of Et_2O was added and the solution washed (CAREFULLY!) with 3 x 100 mL of saturated aq. $NaHCO_3$ solution followed by 100 mL of saturated aq. sodium bisulfite solution and 100 mL of H_2O. After drying ($MgSO_4$), and removal of volatiles in vacuo, purification by flash chromatography (15 - 30 % EtOAc in hexane) gave the 1:1 epimeric mixture of **7** and **9** (1.38 g, 92 %) as colorless crystals (recrystallized from EtOAc/hexane): R_f 0.4 (20 % EtOAc in hexane); ^1H NMR δ 7.43 - 7.67 (m, 4 H), 5.02 (m, 1 H - first diastereomer), 4.94 (m, 1 H - second diastereomer), 3.89 (d, J = 12.9 Hz, 1 H - second diastereomer), 3.73 (d, J = 14.6 Hz, 1H - first diastereomer), 3.58 (m, 1 H), 3.21 (m, 3H); 2.62 (m, 1 H), 0.83 - 2.14 (m, 33 H); ^{13}C NMR δ 163.9 (C), 162.8 (C), 142.2 (C), 141.8 (C), 138.2 (C), 137.8 (C), 129.8 (CH/CH_3), 129.7 (CH/CH_3), 125.9 (CH/CH_3), 125.5 (CH/CH_3), 80.5 (CH/CH_3), 80.4 (CH/CH_3), 62.5 (CH2), 62.0 (CH_2), 57.6 (CH/CH_3), 54.0 (CH_2), 49.8 (C),49.6 (C), 49.2 (C), 44.5 (CH/CH_3), 44.4 (CH/CH_3), 39.5 (CH_2), 39.4 (CH_2), 33.0 (CH_2), 32.9 (CH_2), 32.8 (CH_2), 32.7 (CH_2), 30.5 (CH_2), 27.0 (CH_2), 26.5 (CH_2), 25.2 (CH_2), 20.4(CH/CH_3), 20.1 (CH/CH_3), 19.9 (CH/CH_3); IR ($CHBr_3$) 2940 (st), 1725 (st), 1320 (st), 1270 (st), 1045 (st) cm^{-1}; MS (EI, 70 eV) m/z (%) 298 (3), 244 (1), 180 (100). Anal.: Calcd for $C_{30}H_{44}NClO_5S_2$: C, 60.23; H, 7.41; N, 2.34. Found: C, 58.97; H, 7.59; N, 2.33.

General Procedure for the Preparation of γ-Hydroxy-α,β-unsaturated Esters (Table 1). A 0.5 M solution of the aldehyde in acetonitrile was added over ~ 1 hour to a stirred solution of piperidine (5.0 eq.) and a 0.5 M solution of the sulfinylacetate (1.0 eq.) in acetonitrile under N_2. The resulting solution was stirred at 25 °C for the time specified below. Removal of the volatiles in vacuo gave the crude product which was purified by flash chromatography (0 - 40 % EtOAc in hexane).

E-(1R,2S,5R)-Menthyl 4-Hydroxypent-2-enoate (R = Me, R* = (-)-Men) (entry 1). Using 0.070 g (1.2 mmol, 1.2 eq.) of propionaldehyde and 0.36 g (1.0 mmol, 1.0 eq.) of the 1:1 mixture of **12** and **13**. Stirred for 3 d. The product (0.18 g, 69 %) was obtained as a yellow oil: R_f 0.4 (20 % EtOAc in hexane); 8 % d.e. (from ^1H NMR of MTPA ester); ^1H NMR δ 6.91 (dd, J = 15.6 and 4.62 Hz, 1 H), 5.97 (dd, J = 15.6 and 1.45 Hz, 1 H), 4.71 (dt, J = 10.9 and 4.3 Hz, 1 H), 4.45 (m, 1 H), 2.86 (br. s, 1 H), 0.68-2.10 (m, 15 H), 1.26 (d, J = 6.6 Hz, 3 H), 0.69 (d, J = 6.9 Hz, 3 H); ^{13}C NMR δ 166.4 (C), 151.0 (CH/CH_3), 119.8 (CH/CH_3), 74.3 (CH/CH_3), 67.0 (CH/CH_3), 47.0 (CH/CH_3), 40.9 (CH_2), 34.2 (CH_2), 31.3 (CH/CH_3), 26.2 (CH/CH_3), 23.5 (CH_2), 22.6 (CH/CH_3), 22.0 (CH/CH_3), 20.7 (CH/CH_3), 16.4 (CH/CH_3); IR ($CHBr_3$) 3430 (br st), 2950 (st), 2920 (st), 2860 (st), 1695 (st), 1645 (md), 1265 (st), 1030 (md) cm^{-1}; MS (EI, 70 eV) m/z (%) 221 (7), 219 (17), 81 (100); HRMS calcd for $C_{15}H_{26}O_3$ 254.18818, found 254.18810.

E-(1R,2S,5R)-8-Phenylmenthyl 4-Hydroxyhept-2-enoate (R = n-Pr, R* = (-)-8-PheMen) (entry 2). Using 0.043 g (0.50 mmol, 5.0 eq.) of pentanal and 0.043 g (0.10 mmol, 1.0 eq.) of **3**. Stirred for 49 h. The product (0.029 g, 82 %) was obtained as an orange oil: R_f 0.4 (20 % EtOAc in hexane); 17 % d.e. (from ^1H NMR); ^1H NMR δ 7.09 - 7.32 (m, 5 H), 6.56 (dd, J = 15.8 and 5.15 Hz, 1 H - minor diastereomer), 6.44 (dd, J = 15.7 and 4.74 Hz, 1 H - major diastereomer), 5.45 (d, J = 15.7 Hz, 1 H - major diastereomer), 5.40 (d, J = 15.8 Hz, 1 H - minor diastereomer), 4.84 (dt, J = 10.6 and 4.27 Hz, 1 H), 4.17 (m, 1 H), 0.84 -

2.08 (m, 25 H); ^{13}C NMR δ 165.7 (C), 151.8 (C), 149.6 (CH/CH_3), 149.4 (CH/CH_3), 128.0 (CH/CH_3), 125.5 (CH/CH_3), 124.9 (CH/CH_3), 120.7 (CH/CH_3), 120.3 (CH/CH_3), 74.4 (CH/CH_3), 71.0 (CH/CH_3), 70.8 (CH/CH_3), 50.5 (CH/CH_3), 41.7 (CH2), 39.8 (C), 38.7 (CH2), 38.6 (CH_2), 34.6 (CH_2), 31.3 (CH/CH_3), 28.0 (CH/CH_3), 27.8 (CH/CH_3), 26.6 (CH_2), 25.2 (CH/CH_3), 25.0 (CH/CH_3), 21.9 (CH/CH_3), 18.5 (CH_2), 14.0 (CH/CH3); IR (neat) 3475 (br md), 2980 (st), 2930 (st), 1710 (st), 1660 (md) cm^{-1} MS (EI, 70 eV) m/z (%) 238 (1), 213 (9), 119 (100); HRMS calcd for $C_{23}H_{34}O_3$ 358.25078, found 358.25043.

E-(1R,2S,5R)-8-Phenylmenthyl 4-Hydroxyhept-2-enoate (R = n-Pr, R* = (-)-8-PheMen) (entry 3). Using 0.043 g (0.50 mmol, 5.0 eq.) of pentanal and 0.043 g (0.10 mmol, 1.0 eq.) of **4**. Stirred for 50 h. The product (0.030 g, 83 %) was obtained as an orange oil: R_f 0.4 (20 % EtOAc in hexane); 75 % d.e.(from ^1H NMR); ^1H NMR δ 7.09 - 7.26 (m, 5 H), 6.56 (dd, J = 15.8 and 5.15 Hz, 1 H - major diastereomer), 6.44 (dd, J = 15.7 and 4.74 Hz, 1 H - minor diastereomer), 5.45 (d, J = 15.7 Hz, 1 H - minor diastereomer), 5.40 (d, J = 15.8 Hz, 1 H - major diastereomer), 4.84 (dt, J = 10.6 and 4.27 Hz, 1 H), 4.17 (m, 1 H), 0.84 - 2.08 (m, 25 H); ^{13}C NMR δ 165.7 (C), 151.8 (C), 149.6 (CH/CH_3), 149.4 (CH/CH_3), 128.0 (CH/CH_3), 125.5 (CH/CH_3), 124.9 (CH/CH_3), 120.7 (CH/CH_3), 120.3 (CH/CH_3), 74.4 (CH/CH_3), 71.0 (CH/CH_3), 70.8 (CH/CH_3), 50.5 (CH/CH_3), 41.7 (CH2), 39.8 (C), 38.7 (CH2), 38.6 (CH2), 34.6 (CH2), 31.3 (CH/CH_3), 28.0 (CH/CH_3), 27.8 (CH/CH_3), 26.6 (CH_2), 25.2 (CH/CH_3), 25.0 (CH/CH_3), 21.9 (CH/CH_3), 18.5 (CH_2), 14.0 (CH/CH_3); IR (neat) 3475 (br md), 2980 (st), 2930 (st), 1710 (st), 1660 (md) cm^{-1}; MS (EI, 70 eV) m/z (%) 238 (1), 213 (9), 119 (100); HRMS calcd for $C_{23}H_{34}O_3$ 358.25078, found 358.25043.

E-(1S,2R)-2-Phenylcyclohexanyl 4-Hydroxyhept-2-enoate (R = n-Pr, R* = (+)-PheCy) (entry 4). Using 0.043 g (0.50 mmol, 5.0 eq.) of pentanal and 0.038 g (0.10 mmol, 1.0 eq.) of **5**. Stirred for 24 h. The product (0.020 g, 66 %) was obtained as an orange oil: R_f 0.6 (20 % EtOAc in hexane); 42 % d.e.(from ^1H NMR of MTPA ester); ^1H NMR δ 7.12 - 7.38 (m, 5 H), 6.68 (dd, J = 4.85 and 15.6 Hz, 1 H - major diastereomer), 6.77 (m, 1 H - minor diastereomer), 5.76 (dd, J = 1.60 and 15.6 Hz, 1 H - major diastereomer), 5.75 (dd, J = 1.43 and 15.6 Hz, 1 H - minor diastereomer), 5.00 (dt, J = 4.51 and 10.6 Hz, 1 H), 4.16 (m, 1 H), 2.68 (dt, J = 3.72 and 12.0 Hz, 1 H), 1.22 - 2.18 (m, 13 H), 0.89 (t, J = 7.29 Hz, 3 H); ^{13}C NMR δ 165.8 (C), 149.9 (CH/CH_3), 149.7 (CH/CH_3), 143.2 (C), 128.3 (CH/CH_3), 127.5 (CH/CH_3), 126.4 (CH/CH_3), 120.4 (CH/CH_3), 120.1 (CH/CH_3), 76.2 (CH/CH_3), 71.0 (CH/CH_3), 70.8 (CH/CH_3), 49.8 (CH/CH_3), 38.6 (CH_2), 34.0 (CH_2), 32.4 (CH_2), 29.8 (CH_2), 25.9 (CH_2), 24.8 (CH_2), 18.4 (CH_2), 13.9 (CH/CH_3); IR ($CHCl_3$) 3445 (br md), 2920 (st), 2855 (st), 1715 (st), 1660 (md) cm^{-1}; MS (EI, 70 eV) m/z (%) 157 (100), 126 (50), 90 (67).

E-(1S,2R)-2-Phenylcyclohexanyl 4-Hydroxyhept-2-enoate (R = n-Pr, R* = (+)-PheCy) (entry 5). Using 0.043 g (0.50 mmol, 5.0 eq.) of pentanal and 0.038 g (0.10 mmol, 1.0 eq.) of **6**. Stirred for 24 h. The product (0.018 g, 60 %) was obtained as an orange oil: R_f 0.6 (20 % EtOAc in hexane); 50 % d.e.(from ^1H NMR of MTPA ester); ^1H NMR δ 7.12 - 7.38 (m, 5 H), 6.68 (m, 1 H - minor diastereomer), 6.77 (dd, J = 5.32 and 15.6 Hz, 1 H - major diastereomer), 5.76 (dd, J = 1.60 and 15.6 Hz, 1 H - minor diastereomer), 5.75 (dd, J = 1.43 and 15.6 Hz, 1 H - major diastereomer), 5.00 (dt, J = 4.51 and 10.6 Hz, 1 H), 4.16 (m, 1 H), 2.68 (dt, J = 3.72 and 12.0 Hz, 1 H), 1.22 - 2.18 (m, 13 H), 0.89 (t, J = 7.29 Hz, 3 H); ^{13}C NMR δ 165.8 (C), 149.9 (CH/CH_3), 149.7 (CH/CH_3), 143.2 (C), 128.3 (CH/CH_3), 127.5 (CH/CH_3),

126.4 (CH/CH_3), 120.4 (CH/CH_3), 120.1 (CH/CH_3), 76.2 (CH/CH_3), 71.0 (CH/CH_3), 70.8 (CH/CH_3), 49.8 (CH/CH_3), 38.6 (CH_2), 34.0 (CH_2), 32.4 (CH_2), 29.8 (CH_2), 25.9 (CH_2), 24.8 (CH_2), 18.4 (CH_2), 13.9 (CH/CH_3); IR ($CHCl_3$) 3445 (br md), 2920 (st), 2855 (st), 1715 (st), 1660 (md) cm^{-1}; MS (EI, 70 eV) m/z (%) 157 (100), 126 (50), 90 (67).

E-10-Dicyclohexylsulfamoyl-D-isobornyl 4-Hydroxypent-2-enoate (R = Me, R* = (-)-Cam) (entry 6). Using 0.029 g (0.50 mmol, 5.0 eq.) of propionaldehyde and 0.060 g (0.10 mmol, 1.0 eq.) of **7**. Stirred for 57 h. The product (0.041 g, 83 %) was obtained as colorless crystals (recrystallized from EtOAc/hexane): R_f 0.2 (20 % EtOAc in hexane); 50 % d.e.{from ^1H NMR of MTPA ester using Eu(III)}; ^1H NMR δ 6.94 (dd, J = 15.6 and 4.10 Hz, 1 H), 5.99 (dd, J = 15.6 and 1.74 Hz, 1 H), 5.03 (m, 1 H), 4.45 (m, 1 H), 3.25 (d, J = 13.3 Hz, 1 H), 3.19 (m, 2 H), 2.66 (d, J = 13.3 Hz, 1 H), 0.97 (s, 3 H), 0.86 (s, 3 H), 0.85 - 2.03 (m, 31 H); ^{13}C NMR δ 165.1 (C), 151.0 (CH/CH_3), 150.8 (CH/CH_3), 119.8 (CH/CH_3), 119.4 (CH/CH_3), 78.4 (CH/CH_3), 67.1 (CH/CH_3), 67.0 (CH/CH_3), 57.5 (CH/CH_3), 53.6 (CH_2), 49.4 (C), 49.2 (C), 44.5 (CH/CH_3), 39.5 (CH_2), 32.9 (CH_2), 32.7 (CH_2), 29.9 (CH_2), 27.0 (CH_2), 26.5 (CH_2), 25.2 (CH_2), 23.0 (CH/CH_3), 22.7 (CH/CH_3), 20.5 (CH/CH_3), 20.1 (CH/CH_3); IR ($CHBr_3$) 3520 (st), 2940 (br st), 2860 (st), 1705 (st), 1650 (md), 1310 (st), 1275 (st), 1045 (st) cm^{-1}; MS (EI, 70 eV) m/z (%) 495 (5, M+), 98 (100); HRMS calcd for $C_{27}H_{45}NO_5S$ 495.30182, found 495.30181. Anal.: Calcd for $C_{27}H_{45}NO_5S$: C, 65.42; H, 9.15; N, 2.83. Found: C, 65.67; H, 9.37; N, 2.81.

E-10-Dicyclohexylsulfamoyl-D-isobornyl 4-Hydroxypent-2-enoate (R = Me, R* = (-)-Cam) (entry 7). Using 0.035 g (0.60 mmol, 1.2 eq.) of propionaldehyde and 0.30 g (0.50 mmol, 1.0 eq.) of the 1:1 mixture of **7** and **9**. Stirred for 22 h. The product (0.19 g, 78 %) was obtained as colorless crystals (recrystallized from EtOAc/hexane): R_f 0.2 (20 % EtOAc in hexane); 27 % d.e. {from ^1H NMR of MTPA ester using chiral Eu(III)}; ^1H NMR δ 6.94 (m, 1 H), 5.99 (m, 1 H), 5.03 (m, 1 H), 4.45 (m, 1 H), 3.25 (d, J = 13.3 Hz, 1 H), 3.19 (m, 2 H), 2.66 (d, J = 13.3 Hz, 1 H), 0.97 (s, 3 H), 0.86 (s, 3 H), 0.85 - 2.03 (m, 31 H); ^{13}C NMR δ 165.1 (C), 151.0 (CH/CH_3), 150.8 (CH/CH_3), 119.8 (CH/CH_3), 119.4 (CH/CH_3), 78.4 (CH/CH_3), 67.1 (CH/CH_3), 67.0 (CH/CH_3), 57.5 (CH/CH_3), 53.6 (CH_2), 49.4 (C), 49.2 (C), 44.5 (CH/CH_3), 39.5 (CH_2), 32.9 (CH_2), 32.7 (CH_2), 29.9 (CH_2), 27.0 (CH_2), 26.5 (CH_2), 25.2 (CH_2), 23.0 (CH/CH_3), 22.7 (CH/CH_3), 20.5 (CH/CH_3), 20.1 (CH/CH_3); IR ($CHBr_3$) 3520 (st), 2940 (br st), 2860 (st), 1705 (st), 1650 (md), 1310 (st), 1275 (st), 1045 (st) cm^{-1}; MS (EI, 70 eV) m/z (%) 495 (5, M+), 98 (100); HRMS calcd for $C_{27}H_{45}NO_5S$ 495.30182, found 495.30181. Anal.: Calcd for $C_{27}H_{45}NO_5S$: C, 65.42; H, 9.15; N, 2.83. Found: C, 65.67; H, 9.37; N, 2.81.

E-10-Dicyclohexylsulfamoyl-D-isobornyl 4-Hydroxypent-2-enoate (R = Me, R* = (-)-Cam) (entry 8). Using 0.035 g (0.60 mmol, 5.0 eq.) of propionaldehyde and 0.072 g (0.12 mmol, 1.0 eq.) of **9**. Stirred for 53 h. The product (0.041 g, 69 %) was obtained as colorless crystals (recrystallized from EtOAc/hexane): R_f 0.2 (20 % EtOAc in hexane); 76 % d.e. rising to 86 % d.e. after recrystallization from EtOAc/hexane {from ^1H NMR of MTPA ester using Eu(III)}; ^1H NMR δ 6.93 (dd, J = 4.1 Hz and 15.6 Hz, 1 H); 5.99 (d, 15.6 Hz, 1 H); 5.04 (m, 1 H); 4.44 (m, 1 H); 3.62 (s, 1 H); 3.25 (d, 13.3 Hz, 1 H); 3.20 (m, 2 H); 2.66 (d, 13.3 Hz, 1 H); 2.02 - 0.83 (m, 30 H); 0.98 (s,3 H); 0.87 (s, 3 H); ^{13}C NMR δ 165.1 (C); 151.0 (CH/CH_3); 150.7 (CH/CH_3); 119.8 (CH/CH_3); 119.5 (CH/CH_3); 78.5 (CH/CH_3); 70.6 (CH_2); 67.2 (CH/CH_3); 57.5 (CH/CH_3); 53.7 (CH_2); 49.5 (C); 49.2 (C); 44.6 (CH/CH_3); 39.5 (CH_2); 32.9 (CH_2); 32.7

(CH_2); 30.0 (CH_2); 27.1 (CH_2); 26.5 (CH_2); 25.2 (CH_2); 23.0 (CH/CH_3); 22.8 (CH/CH_3); 20.5 (CH/CH_3); 20.1 (CH/CH_3); IR ($CHBr_3$) 3520 (st), 2940 (br st), 2860 (st), 1705 (st), 1650 (md), 1310 (st), 1275 (st), 1045 (st) cm^{-1}; MS (EI, 70 eV) m/z (%) 495 (5, M+), 98 (100); HRMS calcd for $C_{27}H_{45}NO_5S$ 495.30182, found 495.30181. Anal.: Calcd for $C_{27}H_{45}NO_5S$: C, 65.42; H, 9.15; N, 2.83. Found: C, 65.67; H, 9.37; N, 2.81.

E-10-Dicyclohexylsulfamoyl-D-isobornyl 4-Hydroxyhex-2-enoate (R = Et, R* = (-)-Cam) (entry 9). Using 0.036 g (0.50 mmol, 5.0 eq.) of butyraldehyde and 0.060 g (0.10 mmol, 1.0 eq.) of **9**. Stirred for 53 h. The product (0.045 g, 88 %) was obtained as colorless crystals (recrystallized from EtOH): R_f 0.3 (20 % EtOAc in hexane); 74 % d.e. rising to > 95 % d.e. after recrystallization from ethanol {from ^1H NMR of MTPA ester using Eu(III)}; ^1H NMR δ 6.95 (dd, J = 4.4 Hz and 15.5 Hz, 1 H); 6.02 (d, J = 15.5 Hz, 1 H); 5.05 (m, 1 H); 4.22 (m, 1 H); 3.26 (d, J = 13.3 Hz, 1 H); 3.21 (m, 2 H); 2.67 (d, J = 13.3 Hz, 1 H); 2.03 - 0.81 (m, 33 H); 0.98 (s, 3 H); 0.87 (s, 3 H); ^{13}C NMR δ 165.1 (C); 149.7 (CH/CH_3); 120.5 (CH/CH_3); 120.3 (CH/CH_3); 78.5 (CH/CH_3); 72.4 (CH/CH_3); 57.5 (CH/CH_3); 53.7 (CH_2); 49.5 (C); 49.2 (C); 44.6 (CH/CH_3); 39.5 (CH_2); 32.9 (CH_2); 32.7 (CH_2); 30.0 (CH_2); 29.9 (CH_2); 27.1 (CH_2); 26.5 (CH_2); 25.3 (CH_2); 20.5 (CH/CH_3); 20.2 (CH/CH_3); 9.6 (CH/CH_3); IR ($CHBr_3$) 3520 (st), 2940 (br st), 2860 (st), 1710 (st), 1655 (md), 1310 (st), 1275 (st), 1050 (st) cm^{-1}; MS (EI, 70 eV) m/z (%) 509 (5, M+), 112 (100); HRMS calcd for $C_{28}H_{47}NO_5S$ 509.31747, found 509.31800. Anal.: Calcd for $C_{28}H_{47}NO_5S$: C, 65.98; H, 9.29; N, 2.75. Found: C, 65.98; H, 9.47; N, 2.80.

E-10-Dicyclohexylsulfamoyl-D-isobornyl 4-Hydroxyhept-2-enoate (R = n-Pr, R* = (-)-Cam) (entry 10). Using 0.034 g (0.41 mmol, 5.0 eq.) of pentanal and 0.048 g (0.081 mmol, 1.0 eq.) of **9**. Stirred for 56 h. The product (0.040 g, 93 %) was obtained as colorless crystals (recrystallized from EtOH): R_f 0.3 (20 % EtOAc in hexane); 81 % d.e.{from ^1H NMR of MTPA ester using Eu(III)}; ^1H NMR δ 6.95 (dd, J = 15.6 and 4.58 Hz, 1 H), 6.01 (dd, J = 15.6 and 1.58 Hz, 1 H), 5.05 (m, 1 H), 4.28 (m, 1 H), 3.25 (d, J = 13.3 Hz, 1 H), 3.20 (m, 2 H), 2.66 (d, J = 13.3 Hz, 1 H), 0.98 (s, 3 H), 0.87 (s, 3 H), 0.85 - 2.02 (m, 35 H); ^{13}C NMR δ 165.2 (C), 150.1 (CH/CH_3), 120.2 (CH/CH_3), 78.5 (CH/CH_3), 71.0 (CH/CH_3), 57.5 (CH/CH_3), 53.7 (CH_2), 49.5 (C), 49.2 (C), 44.6 (CH/CH_3), 39.5 (CH_2),39.0 (CH_2), 32.9 (CH_2), 32.7 (CH_2), 30.0 (CH_2), 27.1 (CH_2), 26.5 (CH_2), 25.3 (CH_2), 20.5 (CH/CH_3), 20.2 (CH/CH_3), 18.6 (CH_2), 14.0 (CH/CH_3); IR ($CHBr_3$) 3510 (st), 2940 (br st), 2860 (st), 1710 (st), 1655 (md), 1315 (st), 1275 (st), 1045 (md) cm^{-1}; MS (EI, 70 eV) m/z (%) 523 (3, M+), 126 (100); HRMS calcd for $C_{29}H_{49}NO_5S$ 523.33312, found 523.33417. Anal.: Calcd for $C_{29}H_{49}NO_5S$: C, 66.50; H, 9.43; N, 2.67. Found: C, 66.00; H, 9.55; N, 2.66.

E-10-Dicyclohexylsulfamoyl-D-isobornyl 4-Hydroxy-5-phthalimidopent-2-enoate (R = phalCH_2, R* = (-)-Cam) (entry 11). Using 0.016 g (0.19 mmol, 1.2 eq.) of 3-phthalimidopropionaldehyde (synthesized by ozonolysis of 4-phthalimidobut-1-ene) and 0.096 g (0.16 mmol, 1.0 eq.) of **9**. Stirred for 48 h. The product (0.060 g, 59 %) was obtained as colorless crystals: R_f 0.2 (20 % EtOAc in hexane); 75 % d.e.(from ^1H NMR of MTPA ester); ^1H NMR δ 7.80 (m, 4 H), 6.97 (dd, J = 15.5 and 3.87 Hz, 1 H - major diastereomer), 6.94 (dd, J = 15.5 and 3.66 Hz, 1 H - minor diastereomer), 6.22 (dd, J = 15.5 and 1.91 Hz, 1 H - minor diastereomer), 6.19 (dd, J = 15.5 and 1.87 Hz, 1 H - major diastereomer), 5.07 (m, 1 H), 4.60 (m, 1 H), 3.93 (m, 1 H), 3.81 (dd, J = 14.4 and 8.16 Hz, 1 H), 3.25 (d, J = 13.3 Hz, 1 H), 3.20 (m, 2 H), 2.67 (d, J = 13.3 Hz, 1 H), 0.97 (s, 3 H), 0.91 - 2.02 (m, 28 H), 0.87 (s, 3 H); ^{13}C NMR δ 168.8 (C), 164.6 (C), 145.7 (CH/CH_3), 134.4 (CH/CH_3), 131.8 (C), 123.7 (CH/CH_3), 122.7 (CH/CH_3),

78.6 (CH/CH_3), 70.1 (CH/CH_3), 57.5 (CH/CH_3), 53.6 (CH_2), 49.5 (C), 49.2 (C), 44.6 (CH/CH_3), 43.6 (CH_2), 39.4 (CH_2), 32.9 (CH_2), 32.7 (CH_2), 29.9 (CH_2), 27.1 (CH_2), 26.5 (CH_2), 25.2 (CH_2), 20.5 (CH/CH_3), 20.2 (CH/CH_3); IR ($CHBr_3$) 3480 (br st), 2935 (st), 1715 (st), 1665 (wk) cm^{-1}; MS (EI, 70 eV) m/z (%) 640 (1, M+), 159 (100); HRMS calcd for $C_{35}H_{48}N_2O_7S$ 640.31818, found 640.31736.

E-10-Dicyclohexylsulfamoyl-D-isobornyl 4-Hydroxy-5-methylhex-2-enoate (R = i-Pr, R* = (-)-Cam) (entry 12). Using 0.043 g (0.50 mmol, 5.0 eq.) of 3-methylpropionaldehyde and 0.060 g (0.10 mmol, 1.0 eq.) of **9**. Stirred for 43 h (a colorless precipitate gradually formed). The product (0.051 g, 98 %) was obtained as colorless crystals: R_f 0.4 (20 % EtOAc in hexane); 64 % d.e. (from ^1H NMR of MTPA ester); ^1H NMR δ 6.98 (dd, J = 15.6 and 4.38 Hz, 1 H - major diastereomer), 6.96 (m, 1 H - minor diastereomer), 6.03 (d, J = 15.6 Hz, 1 H), 5.05 (m, 1 H), 4.09 (m, 1 H), 3.26 (d, J = 13.3 Hz, 1 H), 3.21 (m, 2 H), 2.67 (d, J = 13.3 Hz, 1 H), 0.87 - 2.03 (m, 41 H); ^{13}C NMR δ 165.1 (C), 148.8 (CH/CH_3), 121.2 (CH/CH_3), 78.5 (CH/CH_3), 76.0 (CH/CH_3), 57.5 (CH/CH_3), 53.7 (CH_2), 49.5 (C), 49.2 (C), 44.6 (CH/CH_3), 39.6 (CH_2), 33.9 (CH/CH_3), 32.9 (CH_2), 32.7 (CH2), 30.0 (CH_2), 27.1 (CH_2), 26.5 (CH_2), 25.3 (CH_2), 20.6 (CH/CH_3), 20.2 (CH/CH_3), 18.4 (CH/CH_3), 17.3 (CH/CH_3); IR ($CHBr_3$) 3530 (md), 2935 (st), 2860 (st), 1720 (st), 1670 (md) cm^{-1}; MS (EI, 70 eV) m/z (%) 523 (9, M+), 126 (100); HRMS calcd for $C_{29}H_{49}NO_5S$ 523.33312, found 523.33417.

E-10-Dicyclohexylsulfamoyl-D-isobornyl 4-Hydroxy-5-cyclohexylpent-2-enoate (R = $CyCH_2$, R* = (-)-Cam) (entry 13). Using 0.017 g (0.50 mmol, 5.0 eq.) of 3-cyclohexylpropionaldehyde and 0.060 g (0.10 mmol, 1.0 eq.) of **9**. Stirred for 48 h (a colorless precipitate gradually formed). The product (0.049 g, 86 %) was obtained as colorless crystals: R_f 0.3 (20 % EtOAc in hexane); 63 % d.e.{from ^1H NMR of MTPA ester using Eu(III)}; ^1H NMR δ 6.96 (dd, J = 15.6 and 4.44 Hz, 1 H), 6.02 (d, J = 15.6 Hz, 1 H), 5.05 (m, 1 H), 4.39 (m, 1 H), 3.26 (d, J = 13.3 Hz, 1 H), 3.21 (m, 2 H), 2.67 (d, J = 13.3 Hz, 1 H), 0.88 (s, 3 H), 0.98 (s, 3 H), 0.81 - 2.03 (m, 41 H); ^{13}C NMR δ 165.2 (C), 150.8 (CH/CH_3), 150.6 (CH/CH_3), 119.9 (CH/CH_3), 119.6 (CH/CH_3), 78.4 (CH/CH_3), 78.5 (CH/CH_3), 68.7 (CH/CH_3), 68.6 (CH/CH_3), 57.5 (CH/CH_3), 53.7 (CH_2), 49.5 (C), 49.2 (C), 44.7 (CH_2), 44.6 (CH/CH_3), 39.5 (CH_2), 34.1 (CH_2), 33.9 (CH/CH_3), 32.9 (CH_2), 32.7 (CH_2), 29.9 (CH_2), 29.8 (CH_2), 27.0 (CH_2), 26.5 (CH_2), 26.3 (CH_2), 26.1 (CH_2), 25.3 (CH_2), 20.5 (CH/CH_3), 20.1 (CH/CH_3); IR ($CHBr_3$) 3500 (br st), 3425 (st), 2925 (st), 1710 (st), 1675 (wk), 1650 (wk) cm^{-1}; MS (EI, 70 eV) m/z (%) 577 (3, M+), 98 (100); HRMS calcd for $C_{33}H_{55}NO_5S$ 577.38007, found 577.37882.

E-10-Dicyclohexylsulfamoyl-D-isobornyl 4-Hydroxy-6-(dimethylthexylsilyl)hex-2-enoate (R = $Me_2ThexSiO(CH_2)_2$, R* = (-)-Cam) (entry 14). Using 0.028 g (0.12 mmol, 1.2 eq.) of 4-dimethylthexylsilylbutyraldehyde (synthesized by Swern oxidation of 4-dimethylthexylsilylbutan-1-ol) and 0.060 g (0.10 mmol, 1.0 eq.) of **9**. Stirred for 48 h. The product (0.067 g, 100 %) was obtained as a yellow oil: R_f 0.6 (20 % EtOAc in hexane); 55 % d.e.(from ^1H NMR of MTPA ester); ^1H NMR δ 6.95 (dd, J = 15.4 and 3.54 Hz, 1 H - major diastereomer), 6.93 (dd, J = 15.2 and 3.25 Hz, 1 H - minor diastereomer), 6.12 (dd, J = 15.4 and 1.89 Hz, 1 H), 5.06 (m, 1 H), 4.51 (m, 1 H), 3.83 (m, 2 H), 3.28 (d, J = 13.3 Hz, 1 H), 3.21 (m, 2 H), 2.67 (d, J = 13.3 Hz, 1 H), 0.66 - 2.03 (m, 49 H), 0.06-0.12 (m, 6 H); ^{13}C NMR δ 165.3 (C), 149.8 (CH/CH_3), 149.7 (CH/CH_3), 120.3 (CH/CH_3), 119.7 (CH/CH_3), 78.4 (CH/CH_3), 78.2 (CH/CH_3), 71.5 (CH/CH_3), 71.2 (CH/CH_3), 62.7 (CH_2), 62.0 (CH_2), 57.5 (CH/CH_3), 53.6 (CH_2), 49.5 (C), 49.2 (C), 44.6

(CH/CH_3), 39.5 (CH_2), 37.5(CH_2), 37.1 (CH_2), 34.1 (CH/CH_3), 32.9 (CH_2), 32.7 (CH_2), 29.9 (CH_2), 27.1 (CH_2), 26.5 (CH_2), 25.2 (CH_2), 25.0 (CH_2), 20.5 (CH/CH_3), 20.2 (CH/CH_3), 20.1 (CH/CH_3), 18.5 (CH/CH_3), 18.4 (CH/CH_3), -3.6 (CH/CH_3), -3.7 (CH/CH_3); IR ($CHBr_3$) 3500 (br md), 2940 (st), 2870 (st), 1720 (st), 1675 (md) cm^{-1}.

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REFERENCES AND NOTES

1 Posner, G. H. in "Chemistry of Sulfones and Sulfoxides"; S. Patai, Z. Rappoport, and C. J. M. Stirling, Ed.; Wiley: New York, 1988; pp 823.
2 Burgess, K.; Cassidy, J.; Henderson, I. *J. Org. Chem.* **1991** *56*, in the press.
3 Annunziata, R.; Cinquini, M.; Cozzi, F.; Raimondi, L.; Restelli, A. *Gazz. Chim. Ital.* **1985** *115*, 637.
4 Tanikaga, R.; Kaji, A. *Chemistry Lett.* **1988** 677.
5 Bickart, P.; Carson, F. W.; Jacobus, J.; Miller, E. G.; Mislow, K. *J. Am. Chem. Soc.* **1968** *90*, 4869.
6 Tang, R.; Mislow, K. *J. Am. Chem. Soc.* **1970** *92*, 2100.
7 Evans, D. A.; Andrews, G. C. *Acc. Chem. Res.* **1974** *7*, 147.
8 Hoffmann, R. W. in "Organic Sulfur Chemistry"; R. K. Freidlina, andA. E. Skorova, Ed.; Pergamon Press: New York, 1981; pp 69.
9 Hoffmann, R. W. *Chem. Rev.* **1989** *89*, 1841.
10 Kosugi, H.; Kitaoka, M.; Takahashi, A.; Uda, H. *J. Chem. Soc. Chem. Commun.* **1986** 1268.
11 Burgess, K.; Henderson, I. *Tetrahedron Lett.* **1989** *30*, 4325.
12 Burgess, K.; Henderson, I. *Tetrahedron Lett.* **1989** *30*, 3633.
13 Corey, E. J.; Ensley, H. *J. Am. Chem. Soc.* **1975** *97*, 6908.
14 Kipphardt, H.; Enders, D. *Merck Kontakte* **1985** *(2)*, 37.
15 Herzog, H.; Scharf, H. *Synthesis* **1987** 420.
16 Ort, O. *Org. Synth.* **1987** *65*, 203.
17 Whitesell, J. K.; Chen, H.; Lawrence, R. M. *J. Org. Chem.* **1985** *50*, 4663.
18 Oppolzer, W. *Tetrahedron* **1987** *43*, 1969.
19 Ihara, M.; Takahashi, M.; Taniguchi, N.; Yasui, K.; Fukumoto, K. *J. Chem. Soc. Perkin Trans 1* **1989** 1989.
20 Solladie, G.; Hutt, J.; Girardin, A. *Synthesis* **1987** 173.
21 Pitchen, P.; Deshmukh, M.; Dunach, E.; Kagan, H. B. *J. Am. Chem. Soc.* **1984** *106*, 8188.
22 Dunach, E.; Kagan, H. B. *Nouveau J. Chim.* **1985** *9*, 1.
23 Zhao, S. H.; Samuel, O.; Kagan, H. B. *Org. Synth.* **1989** *68*, 49.
24 Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978** *43*, 2923.
25 Nokami, J.; Mondai, T.; Imakura, Y.; Nishiuchi, K.; Kawada, M.; Wakabayashi, S. *Tetrahedron Lett.* **1981** *22*, 4489.
26 Burgess, K.; Jennings, L. *J. Org. Chem.* **1990** *55*, 1138.
27 Burgess, K.; Henderson, I. *Tetrahedron Asymmetry* **1990** *1*, 57.
28 Masamune, S.; Choy, W.; Peterson, J. S.; Sita, L. R. *Angew. Chem. Int. Ed. Engl.* **1985** *24*, 1.
29 Marsch, M.; Massa, W.; Harms, K.; Baum, G.; Boche, G. *Angew. Chem. Int. Ed. Engl.* **1986** *25*, 1011.
30 Wolfe, S.; Stolow, A.; LaJohn, L. A. *Tetrahedron Lett.* **1983** *24*, 4071.
31 This methodology may prove to be most valuable for elaboration of precious aldehydes. Most of the experiments reported here were performed with volatile, cheap aldehydes; five equivalents were used for convenience. However, such large excesses are not essential, as illustrated in the procedures corresponding to entries 11 and 14 of the Table.