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Chiral Silyl Ketene Acetals from Thioesters: Reaction with Acetals and Peroxyacetals to form 3-Alkoxy- and 3-Peroxyalkanoates

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Abstract—The Lewis acid-mediated reaction of chiral *O*- and *S*-silyl ketene acetals (SKAs) with peroxyacetals and acetals was investigated as an approach to the asymmetric synthesis of 3-peroxy- and 3-alkoxyalkanoates. SKAs derived from chiral *O*-acetates fail to react with peroxyacetals and provide little diastereoselection in reactions of nonperoxidic acetals. Reaction of thioacetate SKAs with peroxyacetals furnishes 3-peroxyalkanoate thioesters in good yield but with poor diastereoselection. In the case of silyl ketene acetals based upon a camphorsulfonamide chiral auxiliary the diastereomeric peroxyalkanoates are easily separated.

Introduction

The 3-peroxycarbonyl and homoallyl peroxide motifs are common substructures within peroxide natural products and their synthetic precursors.[1] Recent work in our group has revealed an efficient approach to these subunits based upon the Lewis acid-mediated reaction of peroxyacetals with electron-rich alkenes (Fig. 1).[2,3] In the course of synthetic studies towards plakinic acids, we required a method for synthesis of enantiomerically enriched 3-peroxyalkanoates.[4] We now report our investigations into the reactions of chiral silyl ketene acetal nucleophiles with prochiral peroxycarbenium ions.

Given the recent advances in methodology for enantioselective addition to prochiral aldehydes, control of stereochemistry in corresponding reactions of peroxyacetals might seem straightforward. However, in analogy to the corresponding reactions of nonperoxidic acetals,[5] the Lewis acid-mediated reactions of alkenes with peroxyacetals appears to involve intermediate peroxycarbenium ion. Given this mechanistic assumption, neither the chirality of the acetal, the Lewis acid, or the leaving group is likely to exert a significant influence on product stereochemistry. We were therefore drawn to the use of chiral nucleophiles, of which chiral silyl ketene acetals (SKAs) appeared to be ideal candidates. Several classes of chiral SKAs undergo highly stereoselective Lewis acid-mediated aldol reactions with prochiral aldehydes; in at least one example, reaction is postulated to proceed via an open transition state.[6–8] In addition, the retention of the auxiliary chiral center in the ester product provides a handle for resolution of stereoisomeric products. Finally, peroxyalkanoates are easily saponified or reduced without destruction of the peroxide.[2,9]

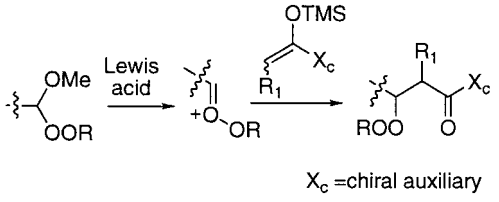

Figure 1.

Results and Discussion

Several substrates were employed for these studies (Fig. 2). A monoperoxyacetal (**1**), prepared via transacetalization of benzaldehyde dimethyl acetal, offered a model for additions to secondary peroxycarbenium ions. Alkoxydioxolane **2**, prepared from 4-methyl-3-pentan-2-one according to a

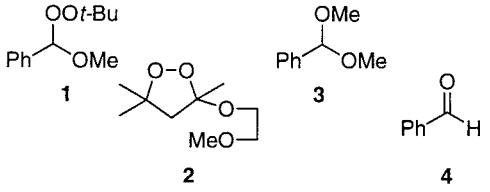

Figure 2.

Keywords: thioester; chiral auxiliary; silyl ketene acetal; peroxide.
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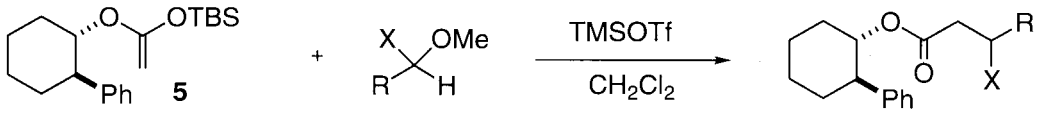
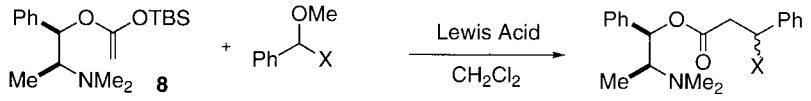
Table 1. Reaction of SKA derived from phenylcyclohexyl acetate

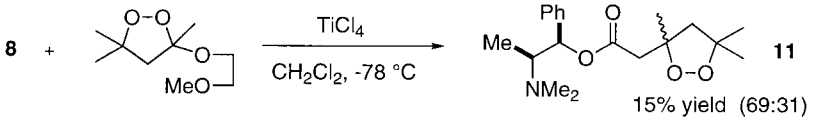


Substrate	R	X	*T* (°C)	Product	Yield (%)	Diast. ratio
1	Ph	OO*t*-Bu	−20	**6**	18	54:46
2	Ph	OMe	−78	**7**	37	56:43
3	Ph	OMe	0	**7**	42	52:48

Table 2. Reactions of SKA derived from ephedrine acetate



Substrate	X	Lewis acid	*T* (°C)	Product	Yield (%)	Diast. ratio
1	OO*t*-Bu	TMSOTf	−20	–	0	–
1	OO*t*-Bu	$TiCl_4$	−78	**9**	14	55:45
3	OMe	$SnCl_4$	−78	–	0	–
3	OMe	TMSOTf	−20	–	0	–
3	OMe	$TiCl_4$	−78	**10**	45	62:38



known procedure,[10] provided a model for approaches to the plakinic acids. Given the lack of data regarding reactions of chiral SKAs with simple acetals we also investigated reactions of benzaldehyde dimethyl acetal (**3**). Finally, benzaldehyde was included to allow direct comparison of the new nucleophiles against more established reagents.

Our initial efforts featured the *t*-butyl dimethyl silyl ketene acetal **5** of *trans*-2-phenyl cyclohexyl acetate,[11] reported to undergo stereoselective addition to benzaldehyde. However, little product was observed for reaction with peroxyacetals, while reaction with benzaldehyde dimethyl acetal proceeded with low chemical yield and minimal diastereoselection (Table 1).

A similar outcome was experienced with SKA **8**, derived from *N*-methyl ephedrine acetate (Table 2). The corresponding *E*- or *Z*-propionate SKAs react with aldehydes to furnish *anti* aldol products in high enantiomeric excess.[8] However, reaction of **8** with peroxyacetals **1** and **2** provided poor yield and low diastereoselection (Table 2). Reaction with acetal **3** proceeded in moderate yield and low diastereoselection.

At this point, unrelated work in our group with achiral esters revealed the superiority of thioacetate SKAs as nucleophiles towards peroxyacetals (Fig. 3).[2] As an added bonus, the thioacetate SKAs are substantially easier to generate and handle than the *O*-ester analogs.[12]

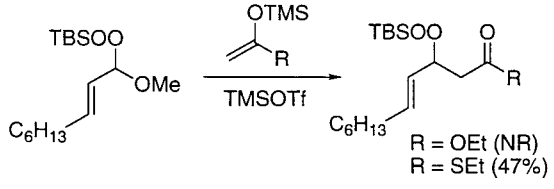


Figure 3.

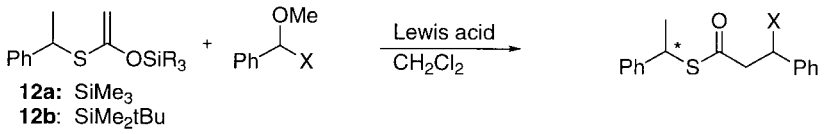
As illustrated in Table 3, the SKA of 1-phenylethanethiol acetate underwent Lewis acid-mediated reaction with peroxyacetals and acetal **3** to provide good yields of 3-peroxy- and 3-alkoxyalkanoate thioesters. Unfortunately, no diastereoselection was observed in either case.

We next investigated SKAs derived from camphorsulfonamide esters.[6] The *O*-acetate SKAs have been reported to achieve high stereoselection in acetate aldol reactions through a transition state relevant to the peroxycarbenium ion chemistry (Scheme 1).

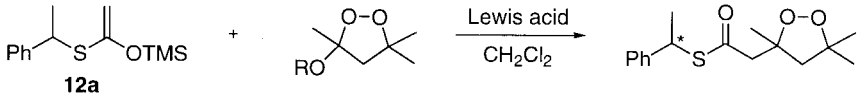
Given the low reactivity of *O*-acetate SKAs towards peroxyacetals, we elected to synthesize the thioacetate analog of Oppolzer's camphorsulfonamide (Scheme 2). The known camphorsulfonamide[13] was converted to the corresponding thione using Lawesson's reagent.[14] Reduction with sodium borohydride selectively produced the *exo* thiol, which was easily converted to the corresponding thioacetate. Enolization, followed by trapping with trialkylsilyl chlorides, furnished the TMS, TBS and TIPS silyl ketene acetals. The crude SKAs obtained after extraction and concentration were stable as refrigerated solutions in CH_2Cl_2 for periods of up to several weeks.

Reaction of the trimethylsilyl SKA **17a** with an acetal, the two peroxyacetals, and benzaldehyde occurred in poor, moderate, and good yield, respectively (Table 4). However, diastereoselection was nonexistent. The bulkier triisopropyl SKA **17c** failed to react with peroxyacetal **1** but showed high reactivity and moderate diastereoselection with benzaldehyde. The TBS SKA **17b** provided good reactivity but no

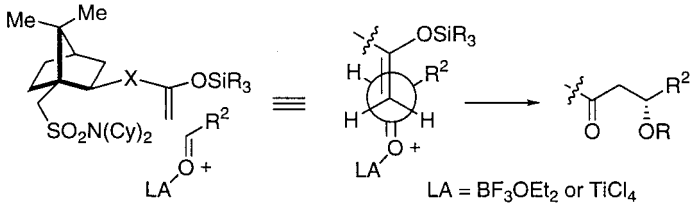
Table 3. Reactions of SKAS from 1-phenethyl thioacetate



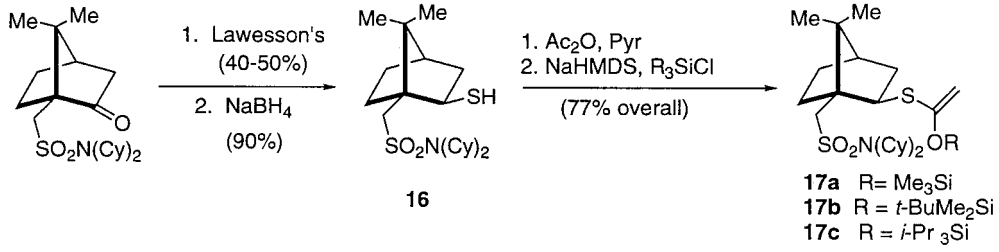
Substrate	SKA	Lewis acid	X	*T* (°C)	Product	Yield (%)	Diast. ratio
1	**12a**	TMSOTf	OO*t*-Bu	−20	**13**	40	50:50
1	**12b**	TMSOTf	OO*t*-Bu	−20	–	0	–
3	**12a**	TMSOTf	OMe	−20	**14**	68	50:50
3	**12b**	TMSOTf	OMe	−78	–	0	–
3	**12b**	$SnCl_4$	OMe	−78	**14**	33	50:50



2a		TMSOTf	R=Me	−20	**15**	0	–
2a		$SnCl_4$	R=Me	−78	**15**	0	–
2b		$TiCl_4$	R=MeOEt	−78	**15**	64	50:50

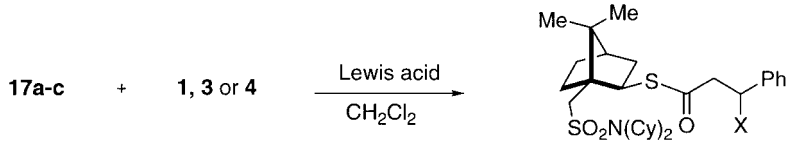


Scheme 1.

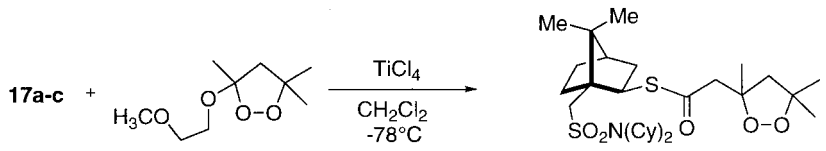


Scheme 2.

Table 4. Reactions of SKAs from camphorsulfonamide thioacetate



SKA	Substrate	Lewis acid	*T* (°C)	Product	X	Yield (%)	Diast. ratio
17a	**1**	TMSOTf (0.1)	−20	**18**	OO*t*-Bu	54	50:50
17c	**1**	TMSOTf	−20	**18**	OO*t*-Bu	0	–
17b	**1**	TMSOTf	−20	**18**	OO*t*-Bu	50	50:50
17a	**4**	$TiCl_4$	−78	**19**	OH	70	50:50
17b	**4**	$TiCl_4$	−78	**19**	OH	58	37:63
17c	**4**	$TiCl_4$	−78	**19**	OH	52	29:71
17a	**3**	TMSOTf (0.1)	−20	**20**	OMe	28	50:50



17a				**21**		52	50:50
17c				**21**		0	–
17b				**21**		26	50:50

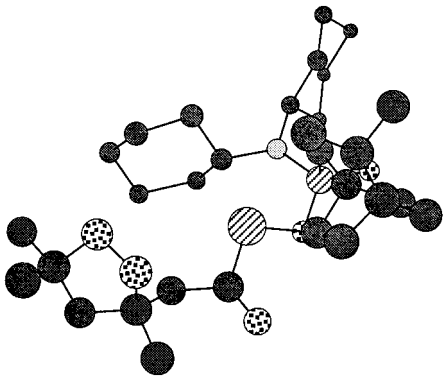


Figure 4.

diastereoselectivity in reaction with peroxyacetal **1**; intermediate diastereoselection (63:37) was achieved for reaction with benzaldehyde. The correlation between aldol diastereoselection and steric bulk of the silyl group (TMS<TBS<TIPS) presumably reflects steric bias in the transition state. The 3-hydroxyalkanoate thioester derived from reactions of benzaldehyde product was easily separable by flash chromatography, while the 3-methoxyalkanoate thioesters from benzaldehyde dimethyl acetal were not easily separated.

While no diastereoselection was seen with the peroxide substrate, the 3-peroxyalkanoate thioester products were easily separated by semipreparative HPLC. In the case of the 1,2-dioxolane adduct **21**, an X-ray structure was obtained for the first eluting isomer (Fig. 4).

Conclusions

The SKA derived from *N*-methyl ephedrine furnishes low yields and stereoselection in reactions with peroxyacetals, and moderate yields and stereoselection with acetals. The 1-phenylethanethiol SKA provides moderate yields with both acetals and peroxyacetals, but no stereoinduction. The camphor-derived thioacetate displays good reactivity with both peroxyacetals and acetals, but no stereoinduction. The *O*-ester analog of **17b** has been reported to react with Lewis acid/aldehyde complexes through an open transition state. However, the results obtained for reactions of **17b** suggest that, at least for the thioacetate SKA, the transition states for reactions of aldehydes and acetals are quite different. The ease of separation of the diastereomeric peroxyalkanoates, combined with the synthetic versatility of thioesters, make the camphor thioacetate an excellent candidate for applications to peroxide natural product synthesis. Further investigation of this methodology is under way and will be reported in due course.

Experimental

All reagents and solvents were used as supplied commercially, except THF and CH_2Cl_2, which were distilled from Na/Ph_2CO and CaH_2, respectively. Compounds **1** and **2**[4] were prepared using reported procedures. ^1H and ^{13}C spectra were recorded at 300 and 75 MHz, respectively, in $CDCl_3$ unless otherwise specified; individual peaks are reported as (multiplicity, number of hydrogens, coupling constant in Hz). Unless otherwise indicated, IR spectra were recorded as neat films; only selected absorbances are reported. Progress of reactions involving peroxides were monitored by TLC, using an *N,N′*-dimethyl-*p*-phenylenediamine indicator; hydroperoxides and peracids yield an immediate reddish-pink spot while perketals or peresters exhibit a pink or green-red color after mild charring.[15] TLC plates were also monitored with a handheld UV light source or after staining/charring with a solution of 1% ceric sulfate/2.5% ammonium molybdate in 10% sulfuric acid. Hydroperoxides were stabilized with a few drops of 1% solution of BHT in CH_2Cl_2 prior to concentration. Much of the chromatography was performed with ethyl acetate/hexane (EA/hex) recycled and quantitated by a reported procedure.[16] Elemental analyses were obtained from Desert Analytics in (Tucson, Arizona, USA), or Quantitative Technologies, Inc. (New Jersey, USA). Silyl ketene acetals of *O*- and *S*-acetates were prepared using reported procedures.[17]

Safety: No problems were experienced in the course of these studies. However, caution should always be observed in the preparation and handling of peroxides.

General procedure for reaction of acetals and peroxyacetals with silyl ketene acetals of *trans*-2-phenylcyclohexyl acetate

To a 0.1 M solution of peroxyacetal (1 equiv.) in methylene chloride was added the silyl ketene acetal[11] (1.5 equiv.) followed by TMSOTf (1 equiv.). The reaction mixture was stirred until TLC indicated the reaction was complete. The reaction mixture was then quenched with saturated aqueous $NaHCO_3$ solution and the aqueous layer was extracted twice with methylene chloride. The combined organic layers were washed with brine and water and dried with anhydrous Na_2SO_4 prior to concentration. The crude mixture was purified by flash chromatography (5% EA/hex).

3-(*t*-Butyldioxy)benzenepropanoic acid, *trans*-2-phenylcyclohexyl ester (6). R_f =0.47 (10% EtOAc/hexanes); ^1H NMR δ 7.20 (m, 5H), 5.17 (dd, 0.63H, J=7.7, 6.0 Hz), 5.08 (apt. t, 0.37H, J=6.9 Hz), 4.94 (td, 0.63H, J=10.5, 4.4 Hz), 4.89 (td, 0.36, J=10.9, 4.4 Hz), 2.78 (dd, 0.37H, J=14.9, 6.9 Hz), 2.76 (dd, 0.63H, J=15.7, 7.7 Hz), 2.64 (m, 1H), 2.41 (dd, 0.37H, J=14.9, 7.3 Hz), 2.31 (dd, 0.63H, J=15.7, 6.0 Hz), 2.09 (m, 0.63H), 1.98 (m, 0.37H), 1.91 (m, 1H), 1.75–1.85 (m, 2H), 1.20–1.585 (m, 4H), 1.12 (s, 5.7H), 1.15 (s, 3.3H); ^{13}C NMR (75 MHz) 170.0, 169.6, 143.1, 143.0, 139.4, 128.3, 128.2, 128.2, 128.0, 128.0, 127.5, 127.4, 127.1, 127.0, 126.4, 81.8, 81.8, 76.4, 76.2, 49.7, 49.5, 39.8, 33.8, 33.7, 32.2, 26.4, 25.8, 24.7, 24.7; IR 1733 cm^{-1}.

3-Methoxy-3-phenyl propionic acid, *trans*-2-phenylcyclohexyl ester (7). R_f=0.47 (10% EtOAc/hexanes); ^1H NMR) δ 7.23 (m, 10H), 5.03 (td, J=10.5, 4.4 Hz), 5.00 (td, 0.55H, J=10.9, 4.4 Hz), 4.37 (dd, 0.55H, J=7.6, 6.0 Hz), 4.32 (dd, 0.45H, J=9.7, 4.0 Hz), 3.08 (s, 1.65H), 2.98 (s, 1.35H), 2.71 (td, 0.45H, J=11.3, 3.6 Hz), 2.69 (td, 0.55H, J=11.3, 3.6 Hz), 2.57 (dd, 0.55H, J=14.9. 8.0 Hz), 2.55 (dd, 0.45H, J=15.3, 9.7 Hz), 2.37 (dd, 0.55H, J=14.9,

6.0 Hz), 2.26 (dd, 0.45H, J=15.3, 4.0 Hz), 2.20 (m, 0.45H), 2.06 (m, 0.55H), 1.77–1.96 (m, 3.3H), 1.29–1.66 (m, 4.6H); ^{13}C NMR 170.1, 169.9, 143.2, 143.1, 140.7, 140.6, 128.4, 128.3, 128.2, 128.16, 127.8, 127.5, 127.4, 126.5, 126.4, 126.35, 126.3, 79.9, 79.8, 76.1, 76.0, 56.5, 56.48, 49.6, 49.5, 43.6, 43.5, 34.0, 33.96, 32.3, 32.1, 25.8, 25.77, 24.7, 24.65; IR 1731 cm^{-1}.

Reaction of acetals and peroxyacetals with silyl ketene acetals derived from *N*-methyl ephedrine

Silyl ketene acetals were prepared from *N*-methyl ephedrine[18] using a reported procedure[19] and were used without purification. To a −78°C 0.1 M solution of acetal or peroxyacetal (1 equiv.) in CH_2Cl_2 was added $TiCl_4$ (1 equiv. of a 1 M solution in CH_2Cl_2), followed, after 3 min, by the silyl ketene acetal (1.5 equiv.) The reaction mixture was stirred until reaction was complete according to TLC. The reaction was then quenched with 5% aqueous $NaHCO_3$ and 1.5N aqueous NaOH and filtered through Celite. The aqueous layer was then extracted with CH_2Cl_2 (2×10 mL) and the combined organic layers were dried over anhydrous Na_2SO_4 and concentrated. The crude product was purified by flash chromatography (49:49:2 EA/hexane/methanol). The diastereomeric products were separated by semi-preparative HPLC (20% ethanol/hexane, Rainin Dynamax 8 μm Si).

3-(*t*-Butyldioxy)-3-phenyl propionic acid, 2-(dimethylamino)-1-phenylpropyl ester (9). *First eluting:* R_f=0.33 (49:49:2 EA/hexanes/MeOH); ^{1}H NMR (500 MHz) δ 7.34 (m, 10H), 6.04 (d, 1H, J=4.9 Hz), 5.48 (apt. t, J=7.0 Hz), 3.24 (dd, 1H, J=15.7, 7.5 Hz), 2.99 (m, 1H), 2.88 (dd, 1H, J=15.5, 6.2 Hz), 2.39 (s, 6H), 1.29 (s, 9H), 1.13 (d, 3H, J=6.8 Hz); ^{13}C NMR (125 MHz) 128.17, 127.15, 126.09, 81.74, 77.10. 75.58, 63.52, 57.06, 48.99, 42.44, 41.13, 40.19, 35.55, 27.68, 26.68, 26.20, 25.74, 24.61, 23.69, 9.25; IR (Neat) 1745 cm^{-1}.

Second eluting: ^{1}H NMR (500 MHz) δ 7.23 (m, 10H), 5.87 (d, 1H), 5.34 (apt. t, J=7.0 Hz), 3.14 (dd, 1H, J=15.7, 7.2 Hz), 2.87 (m, 1H), 2.77 (dd, 1H, J=15.2, 6.8 Hz), 2.19 (s, 6H), 1.11 (s, 9H), 0.96 (d, 3H, J=6.7 Hz); ^{13}C NMR (125 MHz) 128.26, 127.26, 126.47, 81.81, 75.71, 63.35, 40.95, 26.10, 9.10; (IR (Neat) 1742 cm^{-1}.

3-Methoxy-3-phenyl propionic acid, 2-(dimethylamino)-1-phenylpropyl ester (10). R_f=0.10 (2% MeOH/CH_2Cl_2); ^{1}H NMR δ 7.47 (m, 10H), 5.94 (d, 1H, J=5.0 Hz), 4.61 (dd, 1H, J=9.1, 4.8 Hz), 3.17 (s, 2H), 2.89 (dd, 1H, J=15.3, 9.1 Hz), 2.88 (q, 1H, J=6.7 Hz), 2.64 (dd, 1H, J=15.3, 4.8 Hz), 2.24 (s, 6H), 1.00 (d, 3H, J=6.7 Hz); ^{13}C NMR 170.0, 140.5, 139.9, 128.6, 128.2, 128.16, 128.11, 128.06, 127.4, 80.1, 75.7, 63.6, 56.7, 43.8, 41.3, 9.3; IR (Neat) 1738 cm^{-1}.

3,5,5-Trimethyl-1,2-dioxolane acetic acid, 2-(dimethylamino)-1-phenypropylester (11). *First eluting:* R_f=0.25 (49:49:2 EA/hexanes/MeOH) ^{1}H NMR δ 7.30 (m, 5H), 5.92 (d, 1H, J=5.5 Hz), 2.93 (apt. quintet, 1H, J=6.2 Hz), 2.84 (d, 1H, J=14.8 Hz), 2.71 (d, 1H, J=14.8 Hz), 2.46 (d, 1H, J=12.4 Hz), 2.28 (s, 6H), 2.14 (d, 1H, J=12.8 Hz), 1.44 (s, 3H), 1.35 (s, 3H), 1.28 (s, 3H), 1.08 (d, 3H, J=6.7 Hz); ^{13}C NMR 169.7, 139.8, 128.2, 127.6, 126.5, 84.2, 84.1, 76.0, 63.4, 56.5, 44.3, 41.2, 27.0, 25.7, 23.9, 9.3. *Second eluting:* R_f=0.25 (2% MeOH/(50 % EtOAc/hexanes); ^{1}H NMR δ 7.31 (m, 5H), 5.94 (d, 1H, J=4.5 Hz), 2.94 (apt. quintet, 1H, J=6.4 Hz), 2.85 (d, 1H, J=14.8 Hz), 2.70 (d, 1H, J=14.8 Hz), 2.54 (d, 1H, J=12.6 Hz), 2.31 (s, 6H), 2.15 (d, 1H, J=12.4 Hz), 1.38 (s, 3H), 1.37 (s, 3H), 1.34 (s, 3H), 1.09 (d, 3H, J=6.7 Hz); ^{13}C NMR 169.7, 139.7, 128.3, 127.6, 126.4, 84.3, 84.1, 75.9, 63.5, 56.6, 44.4, 41.3, 27.0, 25.7, 23.9, 9.3.

Silyl ketene acetal of 1-phenylethanylthioacetate (12a). Into a solution of thioacetate (16.6 mmol, 2.98 g) and TMSOTf (16.6 mmol, 3.2 mL) in CH_2Cl_2 (20 mL) under N_2 in a dry 250 mL flask at 0°C was slowly added Et_3N (19.9 mmol, 2.8 mL). The reaction was stirred for 2 h and then concentrated. The residue was dissolved in hexane and filtered though Celite. The crude product was used without further purification: ^{1}H NMR δ 7.34 (m, 5H), 4.76 (q, 1H, J=7.2 Hz), 4.42 (d, 1H, J=1.6 Hz), 4.38 (d, 1H, J=1.5 Hz), 4.33 (q, 1H, J=7.2 Hz), 1.63 (d 3H, J=7.2 Hz), 0.24 (s, 9H; TMS); ^{13}C NMR 152.5, 143.2, 128.4, 127.1, 127.0, 96.1, 44.2, 22.3, −0.1.

General procedure for reaction with thioacetate silyl ketene acetals

To a −20°C 0.1 M solution of acetal or peroxyacetal (1 equiv.) in CH_2Cl_2 was added the silyl ketene acetal (1.5 equiv.) followed by TMSOTf (0.1 equiv.). The reaction mixture was stirred until complete according to TLC. The reaction mixture was then quenched with saturated aqueous $NaHCO_3$ and the aqueous layer extracted twice with CH_2Cl_2 and the organic layers were washed with brine and water, dried with Na_2SO_4, concentrated and purified by flash chromatography (5% EA/hex).

3-(*t*-Butyldioxy)-benzenepropanoic acid, 1-phenylethyl thioester (13). R_f=0.20 (3% EtOAc/hexanes); ^{1}H NMR δ 7.29 (m, 10H), 5.39 (dd, 0.5H, J=8.3, 5.5 Hz), 5.37 (dd, 0.5H, J=8.1, 6.2 Hz), 4.74 (q, 0.5H, J=7.2 Hz), 4.73 (q, 0.5H, J=7.2 Hz), 3.19 (dd, 1H, J=15.0, 8.3 Hz), 2.83 (dd, 0.5H, J=14.5, 6.0 Hz), 2.81 (dd, 0.5H, J=15.3, 5.7 Hz), 1.65 (d, 1.5H, J=7.2 Hz), 1.21 (s, 4.5H1.13 (s, 4.5H); ^{13}C NMR 195.5, 142.4, 142.3, 139.1, 128.6, 128.5, 128.2, 128.1, 127.3, 127.2, 127.1, 126.9, 126.8, 82.1, 80.9, 80.8, 49.3, 49.2, 42.9, 42.8, 26.3, 26.2, 22.1, 21.9; IR (Neat) 1683 cm^{-1}.

3-Methoxy-3-phenyl propanoic acid, 1-phenylethyl thioester (14). R_f=0.39 (5% EtOAc/hexanes); ^{1}H NMR δ 7.31 (m, 10H), 4.78 (q, 0.5H, J=7.2 Hz), 4.77 (q, 0.5H, J=7.2 Hz), 4.66 (dd, 0.5H, J=9.1, 4.0 Hz), 4.65 (dd, 0.5H, J=9.1, 5.0 Hz), 3.21 (s, 1.5H), 3.19 (s, 1.5H), 3.02 (dd, 0.5H, J=14.8, 9.1 Hz), 3.01 (dd, 0.5H, 15.3, 9.3 Hz), 2.74 (dd, 0.5H, J=14.5, 4.8 Hz), 2.69 (dd, 0.5H, J=14.1, 5.0 Hz), 1.66 (d, 1.5H, J=7.4 Hz), 1.61 (d, 1.5H, J=7.2 Hz); ^{13}C NMR 196.7, 141.0, 129.3, 129.2, 128.7, 127.9, 127.8, 127.2, 127.1, 80.7, 80.6, 57.6, 57.5, 52.8, 43.5, 22.8, 22.7; IR (Neat) 1683 cm^{-1}.

3,5,5-Trimethyl-1,2-dioxolane acetic acid, 1-phenylethyl thioester (15). R_f=0.18 (3% EtOAc/hexanes); ^{1}H NMR δ

7.32 (m, 5H), 4.73 (q, 1H, J=7.2 Hz), 2.97 (d, 0.5H, J=14.3 Hz), 2.94 (d, 0.5H, J=14.3 Hz), 2.85 (d, 0.5H, J=14.3 Hz), 2.81 (d, 0.5H, J=14.3 Hz), 2.57 (d, 0.5H, J=12.4 Hz), 2.50 (d, 0.5H, J=12.4 Hz), 2.15 (d, 0.5H, J=12.4 Hz), 2.14 (d, 0.5H, J=12.4 Hz), 1.65 (d, 3H, J=7.2 Hz), 1.44 (s, 1.5H), 1.39 (s, 1.5H), 1.36 (s, 1.5H), 1.35 (s, 1.5H), 1.34 (s, 1.5H), 1.29 (s, 1.5H); ^{13}C NMR 195.8, 142.4, 142.3, 128.57, 127.3, 127.2, 84.4, 84.3, 84.2, 84.1, 56.4, 56.2, 52.5. 43.1, 27, 25.6, 24.1, 24.0, 22.2, 22.1; IR (Neat) 1693 cm^{-1}.

***N,N*-Dicyclohexyl-7,7-dimethyl bicyclo[2.2.1]heptane-1-methanesulfonamide-2-thiol (16).** A solution of 4-methoxyphenylthionophosphine sulfide, (12.28 g, 30.63 mmol) and camphor-10-(*N,N*-dicyclohexyl)sulfonamide (10.1 g, 25.34 mmol) in anhydrous toluene (40 mL) was refluxed under nitrogen. After 30 min pyridine (1.0 mL, 12.9 mmol) was added, and the mixture was refluxed for an additional 2 days, at which time TLC indicated consumption of starting material. The reaction was quenched with sat. aq. $NaHCO_3$, (200 mL), and diluted with ether (200 mL). The aqueous layer was extracted with ether (2×150 mL). The combined organic layers were washed with sat. aq. NaCl, dried over sodium sulfate, filtered, concentrated, and purified by flash chromatography (7–15% EA/hex). The residue was recrystallized (50% EA/hex), to afford the thione (5.86 g, 55.6%), as a bright orange solid: R_f 0.61 (10% EA/hex); mp 145–150°C; $[\alpha]_D$=+94.1° (c=1.04, $CHCl_3$); ^{1}H NMR δ 3.88 (d, 1H, J=14.5 Hz), 3.33 (m, 2H), 2.90 (d, 1H, J=14.5 Hz), 2.85–2.62 (m, 2H), 2.47 (d, 2H, J=21.0 Hz), 2.23–2.05 (2H), 1.89–1.70 (12H), 1.62 (m, 2H), 1.46 (m, 2H), 1.40–1.26 (3H), 1.25 (s, 3H), 1.13 (m, 2H), 1.00–0.94 (1H), 0.84 (s, 3H) ^{13}C NMR 69.8, 57.6, 54.9, 49.7, 45.1, 33.1, 32.5, 29.7, 27.0, 26.5, 25.2, 19.8; FT-IR (KBr) 1733 cm^{-1}; HRMS calcd for $C_{22}H_{37}S_2O_2N$ (M^+) 411.2266, found 411.2275.

To a stirred 0°C solution of the thione (0.839 g, 2.04 mmol), in THF (10 mL) and isopropanol (10 mL) was added $NaBH_4$ (765 mg, 20.2 mmol. After 20 min the reaction was brought to rt and stirred an additional 20 min at which time TLC indicated consumption of thione. The reaction was slowly diluted with H_2O and 10% aq HCl was added until bubbling subsided. The reaction was partitioned with ether (40 mL), and the aqueous layer was extracted with ether (2×40 mL). The combined organic layers were washed with sat. aq. NaCl, H_2O (2×), and then dried over MgSO4. The filtered solution was concentrated, and purified by flash chromatography (5% EA/hex) to afford the thiol (0.70 g, 83.0%) as a white flaky crystal: R_f 0.62 (10% EA/hex); mp 105–110°C; $[\alpha]_D$=−31.4° (c=1.04, $CHCl_3$); ^{1}H NMR 3.72 (AB, 1H, J=13.4 Hz), 3.44 (m, 1H), 3.30 (m, 2H), 2.71 (AB_2, 1H, J=13.4 Hz), 2.56 (d, 1H, SH), 2.02 (m, 2H), 1.87–1.69 (12H), 1.67–1.52 (4H), 1.39–1.2 (5H), 1.11 (m, 4H), 0.95 (s, 3H), 0.87 (s, 3H); ^{13}C NMR 58.2, 56.1, 50.6, 50.3, 45.9, 44.8, 40.8, 34.2, 34.0, 33.0, 27.9, 27.2, 25.9, 21.7, 20.7; FT-IR 2361, 2336 cm^{-1}; HRMS calcd for $C_{22}H_{39}S_2O_2N$ (M^+) 413.2422, found 413.2417.

***N,N*-Dicyclohexyl-7,7-dimethyl-bicyclo[2.2.1]heptane-1-methanesulfonamide-2-thioacetate.** Into a 0°C solution of the camphorsulfonamide thiol (0.504 g, 1.22 mmol), pyridine (0.16 mL, 2.4 mmol), and DMAP (spatula tip) in CH_2Cl_2 (3.0 mL) was dropwise added of acetic anhydride (0.19 mL, 2.4 mmol). The reaction was stirred for 2 h at 0°C and then allowed to warm to rt overnight. The residue obtained upon concentration was directly subjected to flash chromatography (5–15% EA/hex) to afford the thioacetate (0.423 g, 77.3%) as white powdery crystals: R_f 0.37 (10% EA/hex); $[\alpha]_D$=+79.1° (c=1.38, $CHCl_3$); mp 172–175°C; ^{1}H NMR δ 4.05 (dd, 1H, J=8.2, 5.1 Hz), 3.25 (m, 2H), 3.21 (AB_1, 1H, J=13.6 Hz), 2.73 (AB_2, 1H, J=13.8 Hz), 2.31 (s, 3H), 2.09 (m, 2H), 1.87–1.68 (15H), 1.65–1.57 (2H), 1.35–1.20 (5H), 1.11 (m, 3H), 0.89 (s, 3H) 0.87 (s, 3H) ^{13}C NMR δ 192.9, 57.3, 55.6, 50.5, 49.3, 48.0, 45.5, 40.8, 33.4, 33.2, 32.4, 30.4, 27.2, 26.5, 25.2, 20.4, 20.2; FT-IR 1738, 1694 cm^{-1}; HRMS calcd for $C_{24}H_{41}S_2O_3N$ (M^+) 455.2528, found 455.2512.

General procedure for the formation of silyl ketene acetals 17a–c

To a −78°C solution of NaHMDS (1.2 equiv., 0.5 M in THF), in a oven dried flask under nitrogen, was added dropwise a −78°C solution of camphor thioacetate (1 equiv.) in THF (2.5 mL per mmol). After 10 min a −78°C solution of trialkylsilyl chloride (5 equiv., 2.5 M in THF), was added via cannula. (TMSCl was added directly as the supernatant from centrifugation of 75% TMSCl and 25% triethylamine). If after 30 min TLC still showed starting material additional NaHMDS (0.5 equiv.) and trialkylsilyl chloride (0.5 equiv.) were added by syringe to drive the reaction to completion. After 4 h, the reaction was brought to rt and concentrated to an oil. The residue was mixed with pentane. The pentane solution was filtered through Celite, and concentrated to a viscous yellow oil. The crude SKA was re-dissolved in methylene chloride (1 M) and subsequently used without further purification.

Trimethyl silyl ketene acetal (17a). 500 MHz ^{1}H NMR δ 4.35 (dd, 2H, J=37.0, 1.4 Hz), 3.56 (t, 1H, J=7.3 Hz), 3.47 (AB_1, 1H, J=13.8 Hz), 3.35 (2H), 2.76 (AB_2, 1H, J=13.8 Hz), 2.24 (m, 1H), 2.00 (m, 2H), 1.90–1.64 (15H), 1.63–1.55 (4H), 1.42–1.21 (5H), 1.20–1.07 (m, 2H), 0.92 (s, 3H), 0.89 (s, 3H), 0.26 (s, 9H); 125 MHz; ^{13}C NMR δ 154.3, 91.6, 57.0, 55.7, 50.8, 50.7, 49.2, 45.6, 41.9, 33.6, 33.4, 32.1, 27.4, 26.4, 25.3, 20.8, 20.5.

***t*-Butyl dimethyl silyl ketene acetal (17b).** 500 MHz ^{1}H NMR δ 4.33 (dd, 2H, J=33.9, 1.2 Hz), 3.60 (t, 1H, J=7.3 Hz), 3.46 (AB_1, 1H, J=13.8 Hz), 3.32 (2H), 2.75 (AB_2, 1H, J=13.8 Hz), 2.24 (m, 2H), 2.00 (m, 2H), 1.87–1.65 (15H), 1.63–1.57 (3H), 1.40–1.20 (5H), 1.17–1.02 (2H), 0.94 (s, 9H), 0.91 (s, 3H), 0.88 (s, 3H), 0.23 (s, 3H), 0.21 (s, 3H); 125 MHz ^{13}C NMR δ 154.3, 91.2, 57.0, 55.5, 50.6, 50.3, 49.1, 45.5, 41.7, 33.5, 33.3, 32.1, 27.4, 26.4, 25.6, 25.6, 25.2, 20.7, 20.4, 18.1, 17.9.

Triisopropyl silyl ketene acetal (17c). 360 MHz ^{1}H NMR δ 4.36 (dd, 1H, J=8.3, 2.0 Hz), 3.66 (t, 1H, J=7.8 Hz), 3.46 (AB_1, 1H, J=12.0 Hz), 3.36 (2H), 2.80 (AB_2, 1H, J=12.5 Hz), 2.24 (m, 1H), 2.0 (m, 2H), 1.87–1.70 (15H), 1.65–1.55 (4H), 1.42–1.21 (5H), 1.13 (m, 23H), 0.95 (s, 3H), 0.91 (s, 3H).

Procedure A: reaction of silyl ketene acetals with acetals or peroxyacetals

To a −20°C solution of the acetal or peroxyacetal (1 equiv.) in CH_2Cl_2 (0.1 M) was added the silyl ketene acetal (1.5 equiv.) followed by TMSOTf (0.2 equiv.). The reaction mixture was stirred until TLC indicated consumption of the acetal. The reaction was quenched with sat. aq. $NaHCO_3$ and the aqueous layer was extracted twice with CH_2Cl_2. The combined organic layers were washed with brine and water, dried with Na_2SO_4, concentrated and purified by flash chromatography (5% EA/hex). The diastereomeric mixture of peroxyacetals were separated by semipreparative HPLC (10% EA/hex, Rainin Dynamax 8 μm Si).

Procedure B: for reaction of benzaldehyde and 3-alkoxy-1,2-dioxolane with silyl ketene acetals

To a −78°C solution of benzaldehyde or 3-alkoxy-1,2-dioxolane (1 equiv.) in methylene chloride (0.1 M) was added $TiCl_4$ (1 equiv. of a 1 M solution), followed in 3 min by silyl ketene acetal (1.5 equiv. of a 1 M solution). The reaction mixture was stirred until TLC indicated completion and then quenched with saturated aqueous $NaHCO_3$. The aqueous layer was extracted twice with methylene chloride, and the combined layers were washed with brine and water, dried with $MgSO_4$, filtered through Celite, concentrated and purified by flash chromatography (5% EA/hex). The diastereomeric alcohols or peroxides could be separated by semipreparative HPLC (10% EA/hex, Rainin Dynamax 8 μm Si).

3-(*t*-Butyldioxy)-3-phenylpropionic acid, *N*,*N*-dicyclohexyl-7,7-dimethyl-bicyclo[2.2.1]heptane-1-methanesulfonamide-2-thiyl ester (18). FT-IR 1740, 1693 cm^{-1}; HRMS calcd for $C_{35}H_{55}S_2O_5N$ (M^+) 633.3522, found 633.3499. *1st eluting:* oil, R_f 0.35 (10% EA/hex); $[\alpha]_D$=+83.3° (*c*=0.93, $CHCl_3$); ^1H NMR δ 7.31 (5H), 5.40 (dd, 1H, *J*=7.8, 6.3 Hz), 4.01 (dd, 1H, *J*=9.2, 5.1 Hz), 3.33 (ABX_1, 1H, *J*=15.1, 6.3 Hz), 3.28 (m, 2H), 3.14 (AB_1, 1H, *J*=13.6 Hz), 2.91 (ABX_1, 1H, *J*=15.1, 7.7 Hz), 2.72 (AB_2, 1H, *J*=13.8 Hz), 2.03 (m, 2H), 1.89–1.67 (15H), 1.62 (m, 3H), 1.38–1.25 (3H), 1.22 (s, 9H), 1.20–1.08 (4H), 0.86 (s, 3H), 0.80 (s, 3H); ^{13}C NMR δ 193.3, 138.9, 128.3, 128.2, 127.1, 82.1, 80.8, 57.3, 55.8, 50.3, 49.5, 49.0, 48.0, 45.4, 40.8, 33.4, 33.3, 32.3, 27.2, 26.6, 26.5, 26.3, 25.2, 20.4, 20.2.

2nd Eluting: crystalline; R_f 0.35 (10% EA/hex); $[\alpha]_D$=+158.7° (*c*=1.17, $CHCl_3$); mp 118° C; ^1H NMR δ 7.32 (5H), 5.49 (dd, 1H, *J*=9.2, 3.9 Hz), 4.10 (dd, 1H, *J*=9.1, 5.3 Hz), 3.18 (AB_1, 1H, *J*=13.6 Hz), 3.18 (m, 2H), 3.10 (ABX_1, 1H, *J*=15.3, 9.1 Hz), 2.80 (ABX_2, 1H, *J*=15.3, 9.1 Hz), 2.73 (AB_2, 1H, *J*=13.6 Hz), 2.14 (m, 2H), 1.95–1.55 (15H), 1.55–1.5 (3H), 1.38–1.25 (3H), 1.21 (s, 9H), 1.15–0.97 (4H), 0.902 (s, 3H), 0.895 (s, 3H); ^{13}C NMR δ 193.5, 139.6, 128.4, 128.0, 126.6, 81.9, 57.3, 55.7, 50.5, 49.6, 49.5, 48.1, 45.5, 40.9, 33.5, 33.2, 32.3, 27.2, 26.5, 26.47, 26.3, 25.2, 25.1, 20.5, 20.2.

3-Hydroxy-3-phenyl propionic acid, *N*,*N*-dicyclohexyl-7,7-dimethyl-bicyclo[2.2.1]heptane-1-methanesulfonamide-2-thiyl ester (19). FT-IR 3508, 1738, 1689 cm^{-1}; HRMS calcd for $C_{31}H_{47}S_2O_4N$ (M^+) 561.2946, found 561.2926. *1st Eluting:* oil; R_f 0.37 (10% EA/hex); $[\alpha]_D$=−45.6° (*c*=1.25, $CHCl_3$); ^1H NMR δ 7.31 (5H), 5.25 (AB*X*, 1H, *J*=10.0, 2.6 Hz), 4.13 (dd, 1H, *J*=9.3, 5.0 Hz), 3.42 (br s, 1H, O*H*), 3.23 (m^+AB_1, 3H, *J*=13.6 Hz), 2.92 (*A*BX, 1H, *J*=15.1, 10.0 Hz), 2.88 (A*B*X, 1H, *J*=15.1, 2.6 Hz), 2.68 (AB_2, 1H, *J*=13.8 Hz), 2.08 (m, 2H), 1.96–1.83 (14H), 1.82–1.78 (2H), 1.40–1.20 (6H), 1.12 (m, 2H), 0.94 (d, 1H, *J*=6.7 Hz), 0.87 (s, 3H), 0.85 (s, 3H); ^{13}C NMR) δ 196.4, 142.5, 128.4, 127.5, 125.6, 70.7, 57.4, 55.6, 53.7, 50.7, 49.6, 47.3, 45.4, 40.7, 33.9, 33.2, 32.3, 27.3, 26.5, 25.1, 22.6, 20.4, 20.1.

2nd eluting: crystalline, mp 120° C; R_f 0.37 (10% EA/hex); $[\alpha]_D$=+38.4° (*c*=1.25, $CHCl_3$); ^1H NMR δ 7.33 (5H), 5.25 (AB*X*, 1H, *J*=10.1, 2.4 Hz), 4.11 (dd, 1H, *J*=9.2, 5.1 Hz), 3.33 (br s, 1H, O*H*), 3.19 (m^+AB_1, 3H, *J*=13.6 Hz), 2.95 (*A*BX, 1H, *J*=15.4, 10.1 Hz), 2.92 (A*B*X, 1H, *J*=15.4, 2.4 Hz), 2.70 (AB_2, 1H, *J*=13.6 Hz), 2.10 (m, 2H), 1.97–1.62 (15H), 1.60–1.50 (2H), 1.40–1.15 (6H), 1.06 (m, 3H), 0.87 (s, 3H), 0.86 (s, 3H); ^{13}C NMR δ 196.1, 142.3, 128.5, 127.6, 125.5, 70.9, 57.5, 55.7, 53.0, 50.7, 49.6, 47.6, 45.5, 40.9, 33.9, 33.2, 32.4, 27.3, 26.6, 26.5, 25.1, 20.5, 20.2. (Note: The chemical shifts and coupling constants for the strongly coupled ABX spin systems were analyzed using spin-simulation within Nuts software from Acorn NMR, Inc.)

3-Methoxy-3-phenyl propionic acid, *N*,*N*-dicyclohexyl-7,7-dimethyl-bicyclo[2.2.1]heptane-1-methanesulfonamide-2-thiyl ester (20). (mixture of diastereomers); ^1H NMR δ 7.31(5H), 4.75 (dd, 0.5H, *J*=9.9, 2.9 Hz), 4.68 (dd, 0.5H, *J*=7.6, 6.0 Hz), 4.10 (dd, 0.5H, *J*=9.2, 5.4 Hz), 4.02 (dd, 0.5H, *J*=9.2, 5.1 Hz), 3.27 (m, 2H), 3.22 (s, 1.5H), 3.21 (s, 1.5H), 3.04 (m, 2H), 2.73 (m, 2H) 2.11 (m, 2H), 1.95–1.67 (15H), 1.65–1.50 (3H), 1.40–1.20 (4H), 1.08 (m, 3H), 0.88 (s, 3H), 0.87 (s, 1.5H), 0.80 (s, 1.5H); ^{13}C NMR (300 MHz) δ 194.1, 194.0, 140.8, 128.6, 128.5, 127.9, 127.8, 126.6, 126.3, 79.9, 79.6, 57.3, 57.27, 57.1, 56.9, 55.9, 55.6, 52.4, 52.3, 50.6, 50.3, 49.5, 49.4, 48.1, 48.05, 45.5, 40.9, 40.8, 33.6, 33.5, 33.4, 33.2, 32.4, 32.3, 27.3, 27.2, 26.6, 26.5, 26.47, 26.4, 25.2, 25.1, 20.5, 20.4, 20.3, 20.2; FT-IR 1743, 1694 cm^{-1}; HRMS calcd for $C_{32}H_{49}S_2O_4N$ (M^+) 575.3103, found 575.3091.

3,5,5-Trimethyl-1,2-dioxolane-3-acetic acid, *N*,*N*-dicyclohexyl-7,7-dimethyl-bicyclo [2.2.1]heptane-1-methanesulfonamide-2-thiyl ester (21). FT-IR 1738, 1692 cm^{-1}; HRMS calcd for $C_{30}H_{51}S_2O_5N$ (M^+) 569.3209, found 569.3183. *1st Eluting* (crystalline); R_f 0.37 (10% EA/hex); $[\alpha]_D$=+155.6° (*c*=0.5, $CHCl_3$); mp 119–121°C; ^1H NMR δ 4.03 (dd, 1H, *J*=9.2, 5.1 Hz), 3.27 (m, 2H), 3.19 (AB_1, 1H, *J*=13.8 Hz), 2.94 (dd, 2H, *J*=34.1, 14.8 Hz), 2.71 (AB_2, 1H, *J*=13.8 Hz), 2.66 ($A'B_1$, 1H, *J*=12.6 Hz), 2.20 ($A'B_2$, 1H, *J*=12.4 Hz), 2.10 (m, 2H), 1.90–1.71 (15H), 1.70–1.55 (3H), 1.41 (s, 3H), 1.36 (s, 3H), 1.32 (s, 3H), 1.30–1.02 (7H), 0.88 (s, 6H); ^{13}C NMR δ 194.2, 84.5, 84.2, 57.4, 56.8, 55.6, 52.8, 50.6, 49.5, 48.0, 45.5, 41.0, 33.7, 33.3, 32.4, 27.3, 27.0, 26.6, 25.8, 25.2, 23.6, 20.5, 20.2.

2nd Eluting (oil); R_f 0.37 (10% EA/hex); $[\alpha]_D$=+34.3° (*c*=0.95, $CHCl_3$); ^1H NMR δ 4.02 (dd, 1H, *J*=8.8, 5.0 Hz), 3.25 (m, 2H), 3.15 (AB_1, 1H, *J*=13.6 Hz), 2.92 (dd, 2H, *J*=53.8, 14.7 Hz), 2.70 (AB_2, 1H, *J*=13.6 Hz),

2.60 ($A'B_1$, 1H, J=12.4 Hz), 2.18 ($A'B_2$, 1H, J=12.4 Hz), 2.10 (m, 1H), 1.90–1.70 (16H), 1.68–1.57 (3H), 1.47 (s, 3H), 1.36 (s, 3H), 1.33 (s, 3H), 1.32–1.00 (7H), 0.89 (s, 6H, $C(CH_3)_2$); ^{13}C NMR δ 57.3, 56.1, 55.5, 52.8, 50.4, 49.6, 48.1, 45.8, 41.1, 33.9, 33.3, 32.3, 27.3, 27.1, 26.6, 26.5, 26.47, 25.7, 25.2, 24.3, 20.6, 20.2. Crystallographic coordinates for this compound have been deposited with the Cambridge Crystallographic Data Centre.

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References

1. Casteel, D. A. *Nat. Prod. Rep.* **1999**, *16*, 55–73.
2. Dussault, P. H.; Lee, R. L.; Schultz, J. A.; Suh, Y. S. *Tetrahedron Lett.* **2000**, *41*, 5457–5460.
3. Dussault, P. H.; Lee, I. Q. *J. Am. Chem. Soc.* **1993**, *115*, 6458–6459.
4. Dussault, P. H.; Liu, X. *Org. Lett.* **1999**, *1*, 1391–1393.
5. Sammakia, T.; Smith, R. S. *J. Am. Chem. Soc.* **1994**, *116*, 7915–7916.
6. Oppolzer, W.; Marco-Contelles, J. *Helv. Chim. Acta* **1986**, *69*, 1699–1703.
7. Gennari, C.; Beretta, M. G.; Bernardi, A.; Moro, G.; Scolastico, G.; Todeschini, R. *Tetrahedron* **1986**, *42*, 893–909.
8. Gennari, C. In *Comprehensive Organic Synthesis*, Trost, B. M., Fleming, I. Eds.; 1988; Vol. 2, pp 629–660.
9. Schultz, J. A. PhD Thesis, University of Nebraska, 1999.
10. Rieche, A.; Schmitz, E.; Gründemann, E. *Chem. Ber.* **1960**, *93*, 2443–2448.
11. Vasconcellos, M. L.; Desmaële, D.; Costa, P. R. R.; d'Angelo, J. *Tetrahedron Lett.* **1992**, *33*, 4921–4924.
12. Fujita, Y.; Otera, J.; Fukuzumi, S. *Tetrahedron* **1996**, *52*, 9419.
13. Oppolzer, W. *Tetrahedron* **1987**, *43*, 1969–2004.
14. Lawesson, S. O.; Pedersen, B. S.; Scheibye, S.; Nilsson, N. H. *Bull. Soc. Chim. Belg.* **1978**, *87*, 223–228.
15. Smith, L. L.; Hill, F. L. *J. Chrom.* **1972**, *66*, 101–109.
16. Dussault, P.; Woller, K. *The Chem. Educator* **1996**, *1*, 1–6.
17. Otera, J.; Fujita, Y.; Fukuzumi, S. *Synlett* **1994**, 213–214.
18. Spasov, S.; Auramova, P.; Palamareva, M. *J. Prakt Chem.* **1981**, *323*, 793–800.
19. Gennari, C.; Colombo, L.; Bertolini, G. *J. Am. Chem. Soc.* **1986**, *108*, 6394–6395.