trans-1-(1′,1′-Dimethylpentyl)-2-methylcyclopropan-1-ol (**22**): ir (CCl_4) 3630, 3410, 2967, 1346, 1230 cm^{-1}; nmr (CCl_4) δ 0.5–2.1 (mult, 22 H); ms *m/e* (%) 170 (1), 152 (1), 128 (36), 101 (24), 100 (10), 86 (53), 70 (92), 58 (100). *Anal.* Calcd for $C_{11}H_{22}O$: 170.16706. Found: 170.16791.

A Eu(fod)$_3$ shift study on a 70:30 mixture of **22**:**23** produced a 50-Hz shift of the methyl doublet of the major isomer **22**.

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New Synthetic Methods. Spiropentanes

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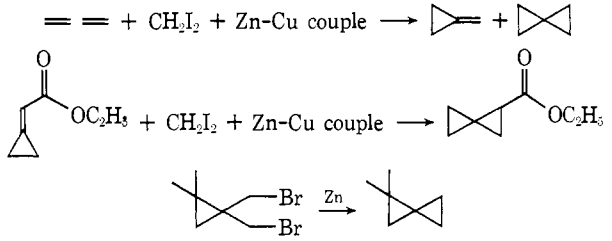
Abstract: The facile conjugate addition of diphenylsulfonium cyclopropylide to chalcone, carvomenthone, and methyl acrylate constitutes a new useful spiropentane synthesis. Even utilizing the potassium hydroxide reversible ylide generation technique, the sensitive ester remained intact although excess base allows isolation of the corresponding acid. Use of the 2-methylcyclopropylide with chalcone leads to the four possible isomers possessing phenyl and benzoyl trans. The isomer ratio reflects the stereochemistry of the starting ylide mixture, demonstrating that in conjugate addition reactions, like carbonyl addition reactions, no loss of configuration at ylidic carbon occurs.

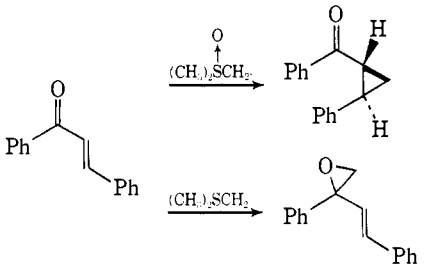
Sulfur ylides have been utilized as a convenient source of cyclopropanes from α,β-unsaturated carbonyl compounds.[2] A novel approach to the synthesis of an unusual class of cyclopropanes, spiropentanes, may be derived from a suitable sulfur ylide. The relative difficulties associated with spiropentane synthesis led us to explore this route which starts with readily available α,β-unsaturated carbonyl compounds and diphenylsulfonium cyclopropylide.[3]

Previously, spiropentanes have been prepared from allenes or alkylidene cyclopropanes *via* a Simmons–Smith or diazoalkane cyclopropanation reaction.[4] Other cyclopropane syntheses such as 1,3 elimination



reactions also have been utilized to form spiropentanes. Usually the yields of spiropentanes are at best moderate.

The ambient nature of α,β-unsaturated ketones toward sulfur ylide attack enables cyclopropanation to occur. One of the earliest examples of this duality of pathways available to sulfur ylides is the cyclopropanation of chalcone with dimethylsulfoxonium methylide as contrasted to the epoxide formation with dimethylsulfonium methylide.[2]



The stability of the ylide carbanion and the rate of 1,3 elimination usually govern how the molecule will react with α,β-unsaturated ketones. With highly reactive anions, they undergo carbonyl addition, whereas with stabilized anions they undergo conjugate addition. Alternatively, if the rate of 1,3 elimination in the betaine derived from carbonyl addition is slowed, as in the case of the isopropylide,[5] again products from conjugate addition prevail. However, the α,β-unsaturated carbonyl compound may also influence the course of reaction: either bulky substituents on the β carbon or higher relative reactivity of the carbonyl (*i.e.*, aldehyde > ketone > ester) leads to carbonyl addition.

Diphenylsulfonium cyclopropylide (**1**) behaves like dimethyloxosulfonium methylide in reactions with α,β-unsaturated carbonyl compounds. Thus, irreversible generation of ylide **1** *via* treatment of cyclopropyldiphenylsulfonium fluoroborate (**2**) with sodium methylsulfinyl carbanion in dimethoxyethane at −40°

(1) Camille and Henry Dreyfus Teacher–Scholar Grant Recipient.

(2) For reviews, see E. J. Corey and M. Chaykovsky, *J. Amer. Chem. Soc.*, **87**, 1353 (1965).

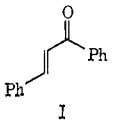
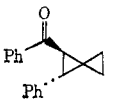
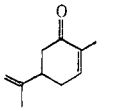
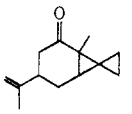
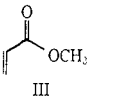
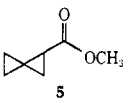
(3) B. M. Trost and M. J. Bogdanowicz, *ibid.*, **93**, 3773 (1971). The present contribution represents part VIII in our series on new synthetic reactions.

(4) D. E. Applequist and G. F. Fanta, *ibid.*, **82**, 6393 (1960); D. E. Applequist, G. F. Fanta, and B. W. Henrikson, *ibid.*, **82**, 2368 (1960); E. F. Ullman and W. J. Fanshawe, *ibid.*, **83**, 2379 (1961); L. M. Konzelman and R. T. Conley, *J. Org. Chem.*, **33**, 3828 (1968); H. E. Simmons, E. P. Blanchard, and H. D. Hartzler, *ibid.*, **31**, 295 (1966); R. Noyori, H. Takaya, Y. Nakanisi, and H. Nozaki, *Can. J. Chem.*, **47**, 1242 (1969); J. J. Gajewski and L. T. Burka, *J. Org. Chem.*, **35**, 2190 (1970).

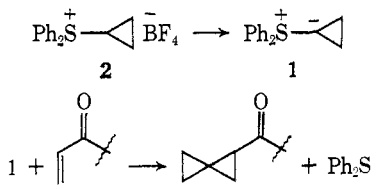
(5) E. J. Corey, M. Jautelat, and W. Oppolzer, *Tetrahedron Lett.*, 2325 (1967); E. J. Corey and M. Jautelat, *J. Amer. Chem. Soc.*, **89**, 3912 (1967).

or reversible generation of **1** from **2** in dimethyl sulfoxide with potassium hydroxide leads to spiropentanes upon reaction with unsaturated carbonyl compounds. The examples in Table I illustrate the procedure. In

Table I. Preparation of Spiropentanes

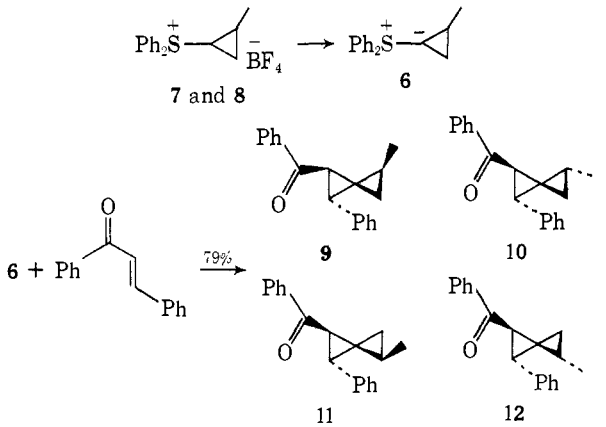
Carbonyl compd	Spiropentane	% yield	Method[a]
 I	 3	55	A
		79	B
 II	 4	67	A
		75	B
 III	 5	41	A
		83	B[b]

[a] Method A, irreversible generation of ylide **1** with dimsylsodium in dimethoxyethane at −40°. Method B, reversible generation of ylide **1** with potassium hydroxide in dimethyl sulfoxide at 25°. [b] Utilization of 5 equiv of potassium hydroxide led to *in situ* hydrolysis of **5** to spiropentylcarboxylic acid in 89% overall yield.



general, the reversible ylide generation procedure, method **B**, is the easiest to carry out experimentally and offers the higher isolated yields of spiropentanes.

A methyl-substituted cyclopropylide **6** generated *via* method **B** from a mixture of 20:80 *cis*- (**7**) and *trans*- (**8**) 2-methylcyclopropyldiphenylsulfonium fluoroborate reacts in a similar fashion with chalcone to yield a mixture of *trans*-1-benzoyl-2-phenyl-3-methylspiropentanes **9–12**.



Analysis of the mixture of spiropentanes **9–12** by a europium(III) shift nmr study resulted in the separation of four distinct pairs of doublets, one of each spiropentane. These doublets are due to the two methine protons on the cyclopropane ring next to the benzoyl and phenyl groups. The coupling constants for these doublets are all identical, *i.e.*, 4 Hz, indicative of trans

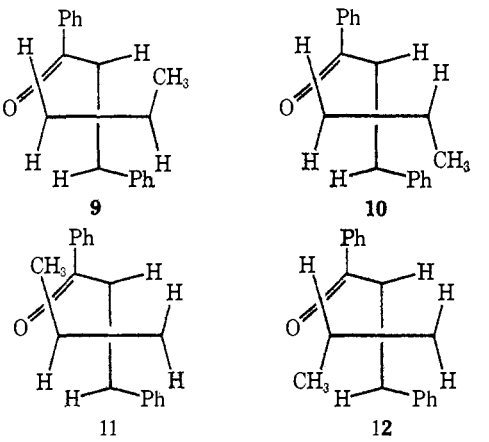
Table II. Europium(III) (30 mol %) Shift Data on a Mixture of **9–12**

Spiropentane	$\Delta\delta(H_\alpha)^a$	$\Delta\delta(H_\beta)^b$	$\delta(H_\alpha)^a$	$\delta(H_\beta)^b$	Rel %[c]
12	0.96	0.33	4.06	3.43	13
11	1.33	0.59	4.43	3.69	37
10	2.26	2.10	5.36	4.20	17
9	2.41	1.42	5.51	4.52	33

[a] H_α is the proton α to the carbonyl group. [b] H_β is the proton β to the carbonyl group. [c] Relative per cent of each isomer was determined by integration of the pairs of doublets in the nmr spectrum.

hydrogens on a cyclopropane ring. Table II summarizes the relative shifts of the protons and structural assignments of the doublet pairs.

A rationalization for the structural assignments is based on the attenuation of the effect of europium(III) by steric interactions of the molecule in the area of the carbonyl group. A molecule whose conformation prohibits close association of the europium atom will exhibit less of a shift phenomenon for the closest hydrogens. Thus, the conformations illustrated for spiropentanes **9–12** appear in the order of increasing

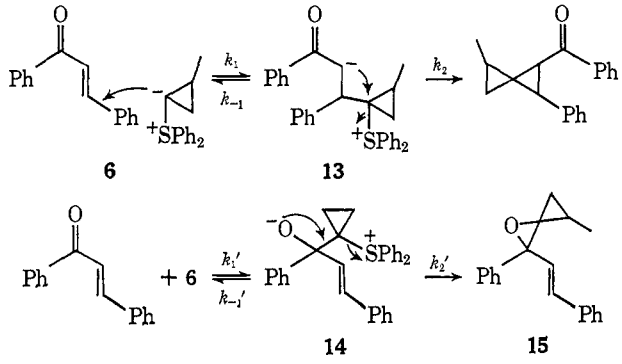


steric interaction for approach of the europium atom. If the europium(III) complexes with the carbonyl from the underface of the molecule, the molecule which has the methyl group cis,trans (**12**) will exhibit the greatest steric interaction with the europium and the cis,cis molecule (**11**) would be the next most hindered spiropentane. The cis–trans relationship about the first cyclopropane ring is the most important factor determining the magnitude of the shifts observed. The stereochemistry of the second ring is less important; however, its effect is observable in the shifts in the direction predicted.

The relative ratios of **9–12** reflect closely the stereochemistry of the ylide precursors **7** and **8**. Spiropentanes **9** and **11** account for 70% while **10** and **12** account for 30% of the spiropentanes obtained. Sulfonium salts **7** and **8** do not lose their stereochemical integrity when reacted with simple ketones to form oxaspiropentanes.[6] Therefore, as in simple carbonyl additions, the ylide **6** attacks the α,β-unsaturated carbonyl compound with retention of configuration at ylide carbon and subsequently loses diphenyl sulfide with inversion at the cyclopropyl ring (Scheme I). The

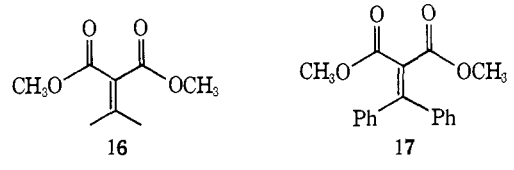
(6) B. M. Trost and M. J. Bagdanowicz, *J. Amer. Chem. Soc.*, **95**, 5311 (1973).

Scheme I. Rationalization for Spiropentane Formation



initial attack of an ylide on an α,β-unsaturated carbonyl is most assuredly on the carbonyl anion, $k_1' > k_1$.[7] Thus, whether a spiropentane or an oxaspiropentane is produced depends upon the relative rates of betaine (**14**) decomposition, k_{-1}' and k_2' and/or 1,3 elimination, k_2 and k_2'. To produce an oxaspiropentane, betaine decomposition k_2' must be fast relative to reversion, k_{-1}'. Conversely, if k_{-1}' is large relative to k_2' the products are those of conjugate addition, the result of thermodynamic control. The decomposition pathway k_{-1}' will increase relative to k_2' with ylides of increasing anionic stability. Furthermore, sulfonium ylides in which the rate of 1,3 elimination (k_2') is decreased (*e.g.*, cyclopropylides) also result in spiropentane formation.

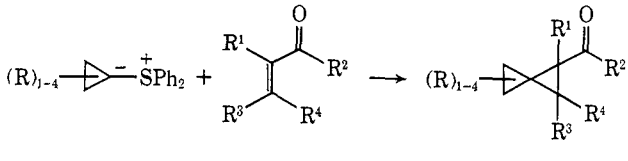
Interestingly, ylide **6** does not cyclopropanate the alkylidene malonates **16** or **17**. Isopropylidene dimethyl malonate (**16**) undergoes proton removal with

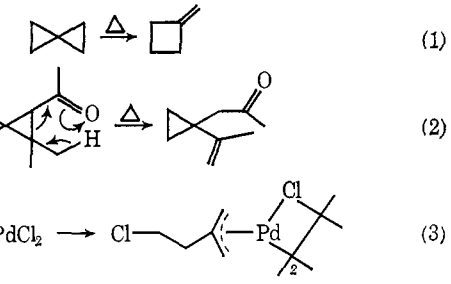


the ylide to form the vinyl malonate anion resulting in isolation of both starting materials upon protonation. Diphenyl methylidenedimethyl malonate (**17**) does not react with **6** at all; starting malonate was recovered unchanged.

Even in light of the limitations of ylide **6** toward Michael acceptor systems as described above, the total synthetic utility of this spiropentane synthesis is evident. In an independent investigation Johnson and coworkers reported the use of an oxosulfonium cyclopropylide to achieve spiropentane formation.[8] Their reagent requires a six-step synthesis in an overall yield of 41.7%; whereas, cyclopropyldiphenylsulfonium fluoroborate is available in 68.8% yield in two steps.

The overall process forms spiropentanes from readily available α,β-unsaturated carbonyl compounds with the ability to easily vary the substitution pattern. The ease of synthesis of spiropentanes may provide materials to explore some of their known and possibly new reactions (eq 1,[9] 2,[8] and 3[10]).





Experimental Section

General. Melting points were taken on a Thomas-Hoover melting point apparatus and are uncorrected. Unless otherwise stated, infrared spectra were determined in carbon tetrachloride solution on a Beckman IR-8 spectrophotometer; ultraviolet spectra were determined in 95% ethanol on a Cary Model 15 spectrometer. Nmr spectra were determined in carbon tetrachloride solution on Varian A60 or A60A spectrometers; chemical shifts are given in δ with TMS as the internal standard. Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; bs, broad singlet; mult, multiplet. Coupling constants are given in hertz. Mass spectra were taken on the AEI MS 902 high resolution mass spectrometer or a Consolidated Electronic Corporation 103C mass spectrometer at an ionizing voltage of 70 eV and an ionizing current of 98 mA. All exact mass determinations were obtained on the MS-902 instrument. Analyses were performed by Spang Microanalytical Laboratories, Ann Arbor, Mich. Vpc analyses were formed on an Aerograph Model 90G instrument with a helium flow rate of 60 ml/min.

All experiments were carried out under an atmosphere of dry nitrogen unless noted otherwise. In experiments requiring dry solvents, ether, tetrahydrofuran, and dimethoxyethane were distilled from sodium–benzophenone. Methylene chloride and dimethyl sulfoxide were distilled from calcium hydride. Apparatus for experiments requiring dry conditions were dried either by flaming under reduced pressure or in a nitrogen stream, or drying in an oven at 120° for 12 hr.

During work-up of the reactions, general drying of the solvent was performed over anhydrous magnesium sulfate unless otherwise stated.

Thin layer or preparative thick layer plates were made of E. Merck AG Darmstadt silica gel PF-254 activated by drying for 2 hr at 140°. The general eluent was 10% ether in hexane unless described in the text. Removal of material from the silica gel was accomplished by successive washings with ether.

Preparation of Sodium Methylsulfinyl Carbanion (Dimsylsodium) in Dimethyl Sulfoxide.[11] Sodium hydride (2.4 g, 0.10 mol) was washed with pentane to remove the mineral oil and was mixed with 100 ml of distilled dimethyl sulfoxide. The mixture was stirred at 50° for 3.5 hr at which time hydrogen evolution was complete. After cooling, the solution was transferred to dry bottles for storage. Addition of 0.5 ml of mineral oil to each bottle provides a protective layer toward air oxidation. Titration with 0.01 *N* hydrochloric acid to a phenolphthalein endpoint for total base indicated 1.105 *M*. With triphenylmethane as an indicator and cyclohexanone as the proton source, the methylsulfinyl carbanion concentration was 1.06 ± 0.03 *M*. Refrigeration of the solution at 0° resulted in solidification which enhanced its shelf life.

Generation of Diphenylsulfonium Cyclopropylide (1) with Dimsylsodium in Dimethoxyethane. Reaction with α,β-Unsaturated Carbonyl Compounds. A suspension of cyclopropyldiphenylsulfonium fluoroborate (314 mg, 1.00 mmol) in 10 ml of dry dimethoxyethane was cooled in a Dry Ice–chlorobenzene slush (*ca.* −40°). (It is important that the temperature not be lower than −45° for ylide generation. If it is, the dimethyl sulfoxide solution of dimsylsodium freezes with formation of chunks and precludes ylide formation.) Dimsylsodium (1.0 ml of 1.06 *M* dimethyl sulfoxide solution, 1.16 mmol) was added rapidly and a deep orange-yellow

(7) C. R. Johnson and C. W. Schroeck, *J. Amer. Chem. Soc.*, **93**, 5303 (1971).
(8) C. R. Johnson, G. F. Katekar, R. F. Huxoland, and E. R. Janiga, *J. Amer. Chem. Soc.*, **93**, 3771 (1971).
(9) J. P. Chesick, *J. Phys. Chem.*, **65**, 2170 (1961).
(10) A. D. Ketley and J. A. Braatz, *Chem. Commun.*, 959 (1969).
(11) E. J. Corey and M. Chaykovsky, *J. Amer. Chem. Soc.*, **87**, 1345 (1965).

color developed. The suspended sulfonium salt was no longer present; the mixture appeared homogeneous. The resultant orange-yellow solution was mixed for 4 min at which time the desired ketone was added (1 mmol). This mixture was stirred for 15 min at −40° and then allowed to warm to room temperature over 30 min. Then 5.0 ml of aqueous 1 *M* tetrafluoroboric acid was added. This solution was extracted with 2 × 10 ml portions of ether. The ether was evaporated to yield the mixture for analysis. The aqueous layer was extracted with methylene chloride (10 ml) which resulted in less than 2% of starting sulfonium salt. The results are listed in Table III.

Table III. Preparation of Spiropentanes

Carbonyl compd[a]	Wt, mg (1.0 mmol)	Internal standard, cycloheptanone, mg	Calcd wt, mg	% yield
I	208	70.8	136	55
II	150	55.1	127	67
III	86	70.6	51.5	41

[a] From Table I.

trans-**1-Benzoyl-2-phenylspiropentane (3)** was purified on a silica gel tlc plate for spectral analysis: ir (CCl_4) 3075, 3042, 1672, 1575, 1493, 1449, 1335, 1389, 1212, 1176, 1142, 1026, 1001, 935, 703, 694, 685, 665 cm^{-1}; nmr (CCl_4) δ 1.05 (d (A_2B_2), 4 H), 3.04 (dd, J = 5.0 and 3.5, 2 H), 7.13 (s, 5 H), 7.16–7.50 (mult, 3 H), 7.65–7.91 (mult, 2 H); ms *m/e* (%) 248 (31), 233 (9), 220 (7), 208 (6), 171 (5), 157 (7), 143 (11), 128 (18), 105 (100), 77 (53). *Anal.* Calcd for $C_{18}H_{16}O$: 248.12011. Found: 248.11967.

1-Methyl-4-isopropenylbicyclo[4.1.0^{1,6}]-7-spirocyclopropylheptan-2-one (4) was purified on a silica gel tlc plate for spectral analysis: ir (CCl_4) 3085, 2985, 2933, 2870, 1686, 1645, 1445, 1377, 1335, 1299, 1266, 1103, 1012, 954, 892 cm^{-1}; nmr (CCl_4) δ 0.51–1.08 (mult, 4 H), 1.13 (s, 3 H), 1.67 (s, 3 H), 1.47–2.84 (mult, 6 H), 4.66 (bs, 2 H); ms *m/e* (%) 190 (5), 175 (14), 149 (8), 147 (25), 121 (36), 105 (30), 95 (11), 94 (38), 93 (38), 91 (33), 79 (100), 77 (30). *Anal.* Calcd for $C_{13}H_{18}O$: 190.13576. Found: 190.13511.

Carbomethoxyspiropentane (5) was collected from a 5 ft × 0.25 in. 5% SE-30 on Chromosorb W vpc column at 90°, retention time 15 min, for spectral analysis: ir (CCl_4) 3086, 3003, 2959, 2849, 1726, 1433, 1364, 1316, 1297, 1190, 1164, 1111, 1093, 1008 cm^{-1}; nmr (CCl_4) δ 0.87 (s (degenerate A_2B_2), 4 H), 1.00–2.58 (mult, 3 H), 3.50 (s, 3 H); ms *m/e* (%) 126 (10), 95 (7), 93 (81), 79 (72), 67 (12), 59 (64). *Anal.* Calcd for $C_7H_{10}O_2$: 126.06807. Found: 126.06413.

Generation of Spiropentanes from α,β-Unsaturated Carbonyl Compounds and Diphenylsulfonium Cyclopropylide Generated in Dimethyl Sulfoxide with Potassium Hydroxide. Cyclopropyldiphenylsulfonium fluoroborate (1.57 g, 5.0 mmol) was dissolved in 30 ml of dimethyl sulfoxide at 25°. Then 5.0 mmol of the desired α,β-unsaturated carbonyl compound was added. The resulting solution was stirred under nitrogen and powdered potassium hydroxide was added rapidly to the reaction mixture. After the designated time (see Table IV) the dimethyl sulfoxide mixture was poured into a 1:1 (v/v) pentane–water mixture (200 ml). The pentane layer was separated, washed with a saturated aqueous sodium bicarbonate solution (50 ml), and dried over anhydrous magnesium sulfate. The pentane was evaporated *in vacuo* resulting in an oil. The oil was purified by separation of its two components (the spiropentane and diphenyl sulfide) on a silica gel thick layer plate eluted with hexane. The diphenyl sulfide had an R_f value of 0.6, while the spiropentane had an R_f of *ca.* 0.1. The results are listed in Table IV.

Preparation of *trans*-1-Benzoyl-2-phenyl-3-methylspiropentane (9–12). A solution of chalcone (2.08 g, 10 mmol) and 2-methylcyclopropyldiphenylsulfonium fluoroborate (3.28 g, 10 mmol) in 40 ml of dimethyl sulfoxide was stirred under nitrogen at 25°.

Table IV. Preparation of Spiropentanes

α,β-Unsaturated carbonyl compd[a]	Wt, g (mmol)	KOH, g (mmol)	Time, hr	Spiropentane Wt, g (mmol)	Spiropentane % yield
I	1.04 (5.0)	0.56 (10.0)	5	0.98 (3.95)	79
II	0.75 (5.0)	1.40 (25.0)	17	0.71 (3.75)	75

[a] From Table I.

Powdered potassium hydroxide (0.56 g, 10 mmol) was added rapidly and the mixture stirred for 1 hr at 25°. The reaction mixture was then mixed with 100 ml of water and extracted with 2 × 100 ml of ether. The ether was washed with 100 ml of water, dried over anhydrous magnesium sulfate, and evaporated *in vacuo* to yield an oil. The oil was eluted with hexane on a silica gel thick layer plate to remove diphenyl sulfide. The base line which was some starting material and mostly spiropentane, was spread on another silica gel thick layer plate and eluted with 10% ether in hexane resulting in the product eluting slightly faster than chalcone. The recovered spiropentane, 1.96 g (79%), was used for spectral analysis. The amount of chalcone recovered was 0.21 g (10%): ir (CCl_4) 3106, 3077, 3040, 3003, 2967, 2933, 2870, 1669, 1600, 1582, 1493, 1446, 1359, 1335, 1213, 1176, 1124, 1076, 1032, 1018, 705, 695, 686, 660 cm^{-1}; nmr (CCl_4) δ 0.5–1.7 (mult, 6 H), 2.9–3.3 (mult, 2 H), 7.25 (s, 5 H), 7.2–8.2 (mult, 5 H); ms *m/e* (%) 262 (30), 247 (14), 233 (9), 115 (11), 105 (100), 91 (11), 77 (55), 51 (12). *Anal.* Calcd for $C_{19}H_{18}O$: 262.13576. Found: 262.13492.

Preparation of Carbomethoxyspiropentane (5). Cyclopropyldiphenylsulfonium fluoroborate (1.57 g, 5.0 mmol) was dissolved in 30 ml of dimethyl sulfoxide at 25°. The resulting solution was stirred under nitrogen and powdered potassium hydroxide (0.28 g, 5.0 mmol) was added rapidly to the reaction mixture. Methyl acrylate (0.43 g, 5.0 mmol) was dissolved in 10 ml of dimethyl sulfoxide and this solution was added to the reaction mixture over a 10-min period. The solution was mixed for 1.25 hr then poured into a 1:1 (v/v) pentane–water mixture (200 ml). The pentane was separated and washed with 50 ml of a saturated aqueous sodium bicarbonate solution. The pentane was dried over anhydrous magnesium sulfate and evaporated *in vacuo* to yield an oil. The oil, 1.053 g, had a sweet smell unlike methyl acrylate. Nmr analysis of the oil showed 50% diphenyl sulfide and 50% carbomethoxyspiropentane from the integration of phenyl protons to aliphatic protons. Thus, the yield of carbomethoxyspiropentane is 0.52 g (83%). The carbomethoxyspiropentane was separated from the diphenyl sulfide on a silica gel thick layer plate by elution with pentane. Diphenyl sulfide had the higher R_f value, 0.6, while carbomethoxyspiropentane remained near the base line with an R_f value of 0.1. The material recovered from the plate, diphenyl sulfide (0.48 g) and carbomethoxyspiropentane (0.31 g, 49%), reflects a poor mass balance due to the high volatility of the spiropentyl ester.

Upon utilization of 5 equiv of potassium hydroxide, the initially formed carbomethoxyspiropentane was hydrolyzed *in situ* to an acid. The reaction mixture was poured into a 1:1 (v/v) water–ether mixture (200 ml). Hydrochloric acid was added until the mixture was acid (litmus). The ether layer was removed, dried over anhydrous magnesium sulfate, and evaporated to yield 0.98 g (89%) of an oil, spiropentanecarboxylic acid: ir (CCl_4) 3400–2800 broad absorption due to a carboxylic acid, 1703, 1418, 1282, 1214 cm^{-1}; nmr (CCl_4) δ 0.97 (bs, 4 H), 1.1–2.5 (mult, 3 H), 11.73 (s, 1 H).

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