Five-membered ring annulation via thermal rearrangement of β-cyclopropyl α,β-unsaturated ketones. A formal total synthesis of the sesquiterpenoid (±)-zizaene

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Treatment of the β-iodo enones **7–10** with lithium (phenylthio)(cyclopropyl)cuprate provided excellent yields of the corresponding β-cyclopropyl α,β-unsaturated ketones **11–14**, respectively. When 3-isopropenyl-2-cyclohexen-1-one (**16**) was allowed to react with dimethyloxosulfonium methylide in dimethyl sulfoxide – tetrahydrofuran, 3-(1-methylcyclopropyl)-2-cyclohexen-1-one (**17**) was produced in 59% yield. Although thermal rearrangement (~425–450°C) of compounds **11** and **17** produced high yields of the annulation products **19** and **22**, respectively, similar reactions involving the β-cyclopropyl enones **12** and **13** were not efficient in terms of production of the corresponding bicyclic systems (**23**, **26**, and/or **27**, respectively). In these cases, predominant (**24** + **25** from **12**) or significant (**28** + **29** from **13**) amounts of monocyclic dienones were formed. The annulation product **22** served as a convenient starting material for a new formal total synthesis of the sesquiterpenoid (±)-zizaene (**30**). Conjugate addition of lithium divinylcuprate to **22** afforded the ketone **36** which was converted by standard methods (via **38** and **39**) into the enone **40**. Treatment of the latter substance with thiophenol in the presence of tetra-*n*-butylammonium fluoride gave **41**, which was transformed via ketalization (**41** → **42**), hydroboration (**42** → **43**), tosylation (**43** → **44**), and oxidation (**44** → **45**) into the sulfone **45**. When the latter compound was treated with potassium *tert*-butoxide in hexamethylphosphoramide, the tricyclic ketal sulfone **46** was produced in 85% yield. Reduction of **46** with sodium amalgam afforded the ketal **47**, which upon hydrolysis under mild conditions gave the ketone **32**. Treatment of the latter substance with sodium methoxide in methanol provided a 1:2 mixture of the epimeric ketones **31** and **32**, which had been converted previously by Coates and Sowerby into (±)-zizaene (**30**).

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Les β-iodo énones **7–10** réagissent avec le (phénylthiocyclopropyl) cuprate de lithium en conduisant respectivement avec d'excellents rendements aux cétones α,β-insaturées, β-cyclopropyles correspondantes **11–14**. Si on laisse réagir l'isopropényl-3 cyclohexène-2 one-1 (**16**) avec le méthylure de diméthyloxosulfonium dans le diméthylsulfoxyde – tétrahydrofuranne, on obtient le (méthyl-1 cyclopropyl)-3 cyclohexèn-2 one-1 (**17**) avec un rendement de 59%. Bien que la transposition thermique (~425–450°C) des composés **11** et **17** donne avec de bons rendements respectivement les produits d'annellation **19** et **22**, les réactions analogues impliquant les β-cyclopropylenones **12** et **13** ne sont pas efficaces du point du vue de la formation des systèmes bicycliques correspondants (respectivement **23**, **26** et/ou **27**). Dans ces cas, il se forme des quantités majoritaires de diénones monocycliques (**24** + **25** à partir de **12**) ou des quantités significatives de ces mêmes composés (**28** + **29** à partir de **13**). Le produit d'annellation **22** sert de point de départ pour une nouvelle synthèse formelle et totale du sesquiterpène (±) zizaène (**30**). L'addition conjugué du divinylcuprate de lithium sur le composé **22** conduit à la cétone **36** que l'on transforme par des méthodes normales (via les composés **38** et **39**) en l'énone **40**. Cette dernière réagit avec le thiophénol en présence du fluorure de tétra-*n*-butylammonium pour donner le composé **41** que l'on transforme en sulfone **45** d'après la suite de réactions: la cétalisation (**41** → **42**), l'hydroboration (**42**→**43**), la tosylation (**43** → **44**) et l'oxydation en sulfone **45** à partir du composé **44**. Le sulfone en présence de *tert*-butylate de potassium dans l'hexaméthylphosphoramide conduit au sulfone cétal tricyclique **46** avec un rendement de 85%. La réduction du composé **46** par l'amalgame de sodium conduit au cétal **47** qui par hydrolyse dans des conditions douces fournit la cétone **32**. Cette dernière réagit avec le méthylate de sodium dans le méthanol en donnant un mélange 1:2 de cétones épimères **31** et **32** que Coates et Sowerby ont déjà transformé en (±) zizaène (**30**).

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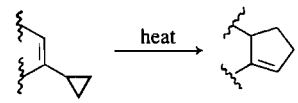
Introduction

The first examples of the thermal vinylcyclopropane to cyclopentene rearrangement, indicated in general terms by eq. [1], were reported more than

[1] 

20 years ago (1, 2). Since that time, this interesting reaction has been studied quite extensively from a mechanistic point of view.[1] More recently, however, the synthetic utility of this type of transformation has received considerable attention, both in connection with methodology and natural product synthesis (10–24). In general, it has been found that, although successful execution of the rearrangement reaction often requires relatively high temperatures (typically in the range 400–600°C),[2] the products are, in many instances, formed cleanly and efficiently.

A recent report (25) from this laboratory de-

[1]For reviews, see refs. 3 and 4. For more recent studies, see refs. 5–9 and citations therein.

[2]An exception to this general statement can be found in the very interesting work of Danheiser and co-workers (20) who found that lithium salts of 2-vinylcyclopropanols rearrange to cyclopentenols at 25°C. For earlier work relating to the effect of substituents on the rate of the vinylcyclopropane to cyclopentene rearrangement, see ref. 21.

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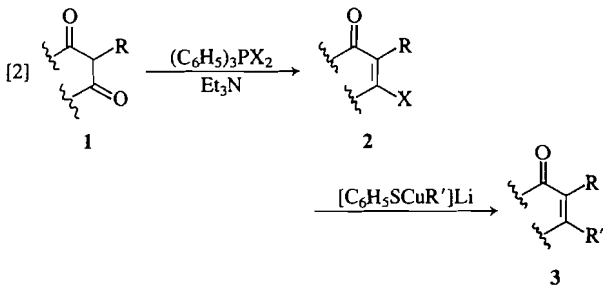
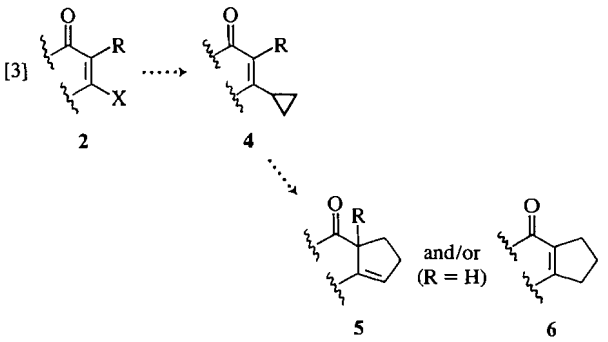
scribed an efficient conversion of cyclic 1,3-diketones **1** into the corresponding β-halo α,β-unsaturated ketones **2** (X = Cl, Br, I). Work reported in a subsequent paper (26) revealed that the latter substances, particularly the bromo and iodo derivatives, react smoothly with a number of lithium (phenylthio)(alkyl)cuprate reagents to provide excellent yields of 3-alkyl- or 2,3-dialkyl-2-cycloalken-1-ones **3** (eq. [2]). Although these transfor-



1 2 3

mations constitute a useful method for the overall conversion of **1** into **3**, we wished to extend this work to include the preparation of compounds **3** in which the R′ group would impart synthetically useful reactivity to these substances. For example, one possibility which we considered to be potentially interesting and useful is outlined in eq. [3].



2 4 5 6

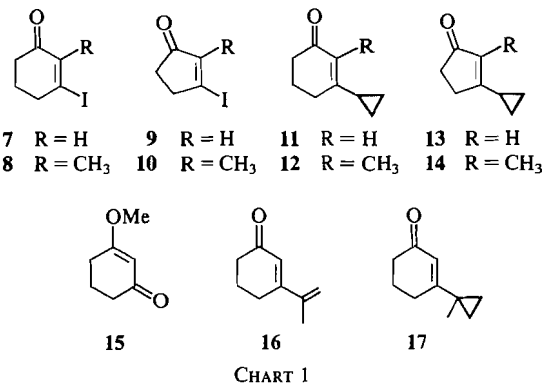
Thus, successful reaction of the β-halo enones **2** with a suitable (cyclopropyl)cuprate reagent would produce the β-cyclopropyl α,β-unsaturated ketones **4**. It is clear that the latter substances incorporate into their structures a vinylcyclopropane moiety and, if these materials were to be successfully subjected to thermal rearrangement, products **5** and/or **6** (if R = H) would be produced. In an overall sense, a new five-membered ring annulation sequence (**1** → **5** and/or **6**) would have been developed.

We report herein (a) the preparation of the β-cyclopropyl enones **11–14** and **17**, (b) the thermal rearrangement of four of these materials (**11–13, 17**), and (c) the use of one of the resultant annulated products (**22**) as a starting material for a new, formal total synthesis of the racemic modification of the tricyclic sesquiterpenoid (+)-zizaene (**30**).[3]

Results and discussion

(a) *Preparation of the β-cyclopropyl α,β-unsaturated ketones 11–14 and 17 (see Chart 1)*

The β-cyclopropyl α,β-unsaturated ketones **11–14** were prepared conveniently by reaction of the corresponding β-iodo enones **7–10** (25) with lithium



7 R = H **8** R = CH_3 **9** R = H **10** R = CH_3 **11** R = H **12** R = CH_3 **13** R = H **14** R = CH_3

15 **16** **17**

CHART 1

(phenylthio)(cyclopropyl)cuprate in ether–tetrahydrofuran (THF). A clear, light-brown solution of the latter reagent was produced by adding freshly prepared ethereal cyclopropyllithium (29)[4] (1 equivalent) to a slurry of phenylthiocopper (31, 32) in cold (−78°C) THF, and allowing the resultant mixture to stir at −20°C for 20 min.[5] Although the conversions **7** into **11** and **9** into **13** could be carried out efficiently (yields 82 and 97%, respectively) at −78°C (2.5 h) using 1.5 equivalents of the cuprate reagent, the transformations involving substrates containing an α methyl group (**8**, **10**) were, not unexpectedly, considerably more sluggish. In these cases, a higher reaction temperature (0°C) and more cuprate reagent (2 equivalents) were required to effect complete conversion of the starting material within the same length of time (2.5 h). However, these transformations were also clean and efficient (the yields of **12** and **14** were 88 and 84%, respectively) and, thus, the reaction of β-iodo enones with lithium (phenylthio)(cyclopropyl)-

[3]For preliminary reports regarding some of the work reported in this paper, see refs. 27 and 28.

[4]The cyclopropyllithium solution was standardized by the method of Gilman and Cartledge (30).

[5]To our knowledge, the first example of the use of a (cyclopropyl)copper reagent for the conjugate addition of a cyclopropyl group to an enone was reported by Hahn and Jones (33). For subsequent reports involving the use of these synthetically versatile reagents, see refs. 34–40.

cuprate appears to be an excellent method for the preparation of β-cyclopropyl enones.

With respect to the preparation of 3-(1-methylcyclopropyl)-2-cyclohexen-1-one (**17**) it is pertinent to point out that this compound was envisaged as being the starting material for a projected synthesis of (±)-zizaene (**30**) (*vide infra*). Therefore, we required fairly large quantities of this material and since we did not have a convenient source of 1-methylcyclopropyllithium, an alternative route to compound **17** was employed. Thus, treatment of 3-methoxy-2-cyclohexen-1-one (**15**) (41) with isopropenylmagnesium bromide, followed by acid hydrolysis of the resultant 1,2-addition product, provided 3-isopropenyl-2-cyclohexen-1-one (**16**) in 84% yield. The latter substance, when allowed to react with dimethyloxosulfonium methylide (42) in a mixture of dimethyl sulfoxide and THF, was converted into the desired β-(1-methylcyclopropyl) enone **17** (59% yield).

(b) *Thermal rearrangement of the β-cyclopropyl α,β-unsaturated ketones 11–13 and 17 (see Chart 2)*

A vertically held Pyrex tube (1.2 × 32 cm), filled with glass helices and surrounded by a vertical, tubular furnace, was washed thoroughly with saturated aqueous sodium bicarbonate, water, acetone, and *n*-hexane. The tube was then heated to 450°C for 3 h, during which time it was thoroughly purged with a stream of nitrogen. While a solution of 3-cyclopropyl-2-cyclohexen-1-one (**11**) in *n*-hexane was added dropwise to the top of the heated column, a slow stream of nitrogen (~3–5 mL/min) was passed through the tube and the thermolysate

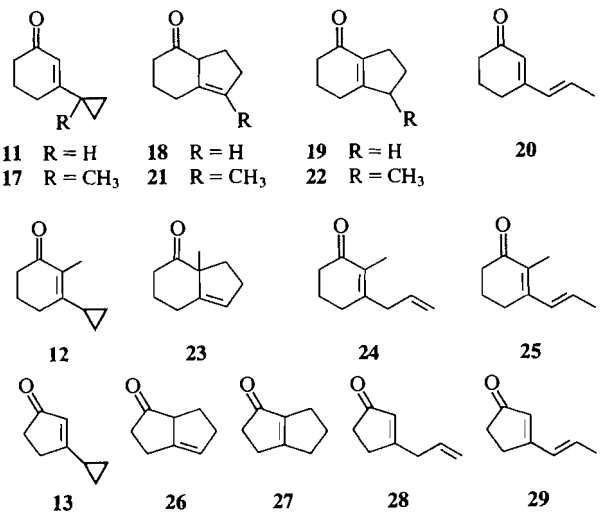


CHART 2

was collected in a two-necked flask equipped with a drying tube and immersed in a cold (−78°C) bath. Gas–liquid chromatographic analysis of the product, a colorless oil obtained in 78% yield, revealed that it consisted of three compounds, **18** (~3%), **19** (43) (~84%), and **20** (44) (~11%), along with a number of very minor unidentified components (~2%). A small sample of each of compounds **18**, **19**, and **20** was obtained by preparative glc and, in each case, the pure material exhibited spectral data in accord with the structural assignment. Furthermore, when a solution of **18** was passed through a short column of basic alumina, it was isomerized cleanly and efficiently to the conjugated enone **19**.

A brief study of the effect of thermolysis temperature on the rearrangement of compound **11** was carried out. For these experiments a longer thermolysis tube (100 cm), wrapped with a heating tape, was employed. The overall procedure used was very similar to that summarized above, although argon was employed as the "carrier gas" instead of nitrogen. The cyclopropyl enone **11** was subjected to thermolysis at 320, 400, 425, and 450°C. It was found that no rearrangement took place at 320°C, since starting material was recovered in essentially quantitative yield. At 400°C, the enone **11** was partially converted into a mixture of **18** and **19** (ratio ~2:1), but a considerable amount (~40%) of the starting material remained. The best result was obtained by carrying out the thermolysis at 425°C, under which conditions **11** was converted in high yield (98%) into an approximately 1:2 mixture of **18** and **19**, respectively, accompanied by < 5% of minor impurities. When a solution of this mixture was eluted through a column of basic alumina, the conjugated enone **19** could be obtained in 88% yield. Thermolysis of **11** at 450°C produced, in a yield (71%) significantly lower than that of the 425°C reaction, a mixture of compounds **18** (~5%), **19** (~90%), and minor impurities (~5%). This result was comparable to that obtained by rearrangement of **11** at ~450°C using the shorter thermolysis tube (*vide supra*), although the amount of the dienone **20** formed was diminished.

Thermolysis of 3-(1-methylcyclopropyl)-2-cyclohexen-1-one (**17**) at 450°C under conditions similar to those employed for compound **11** gave a mixture of two products, the ratio of which varied somewhat from one experiment to another. The spectral data derived from this mixture indicated that the two components were the positionally isomeric enones **21** and **22** and, therefore, these substances were not separated. Instead, a solution of this mixture in methanol containing sodium

methoxide was stirred at 0°C for 1 h. Under these conditions, compound **21** was completely converted into the conjugated enone **22**[6] and the latter substance was isolated in 87% yield. It should be noted that, in general, the thermal rearrangement of **17** was cleaner and less "temperamental" than that of the demethyl analog **11**. Furthermore, thermolysis of **17** could readily be carried out on preparative scale, thus providing a very convenient synthesis of appreciable quantities of the enone **22**.

An investigation of the thermal rearrangement of the cyclopropyl enones **12** and **13** showed that, with respect to the formation of annulated products, these reactions are not as synthetically useful as those employing compounds **11** and **17** as substrates. Not unexpectedly (3, 4), the presence of an α methyl substituent *cis* to the cyclopropyl group (substrate **12**) and the requirement of having to form a fairly strained bicyclo[3.3.0]octenone ring system **26** (rearrangement of **13**), have deleterious effects on the efficiency of ring formation. Thus, thermolysis of 3-cyclopropyl-2-methyl-2-cyclohexen-1-one (**12**) at 450°C (conditions similar to those employed for **11** and **17**) gave a mixture of products (73% yield) containing only a minor amount (~10%) of the desired annulation product **23**. The remainder of the mixture consisted of the dienones **24** (~20%) and **25** (~50%) along with a number of minor unidentified components (gas–liquid chromatographic analysis). Pure samples of compounds **23–25** were collected by preparative glc and, in each case, the substance exhibited spectral data in accord with the structural assignment.

Analysis (glc) of the product obtained (80% yield) from thermal rearrangement of the β-cyclopropyl cyclopentenone **13** showed that it consisted of four major components, **26** (~46%), **27** (~14%), **28** (~20%), and **29** (~18%), along with minor impurities (~2%). Again, a small sample of each of the major products, obtained by preparative glc, exhibited the expected spectral properties. Furthermore, the enone **26** and the dienone **28** were readily isomerized (basic alumina) into the corresponding conjugated isomers **27** and **29**, respectively.

Although the investigation summarized above was not extensive, it is clear that from a synthetic point of view, the results are mixed. Although thermolyses of the β-cyclopropyl enones **11** and **17** provide excellent methods for preparing the bicyclic enones **19** and **22**, similar reactions involving compounds **12** and **13** are, with respect to formation of annulation products, much less efficient. Finally, it is perhaps pertinent to point out that recent work, particularly that of Hudlicky and co-workers (16–19), has shown that product distribution in the vinylcyclopropane → cyclopentene rearrangement can vary considerably with reaction conditions and that this type of transformation can be carried out successfully on structurally quite complex substrates.

(c) *A formal total synthesis of (±)-zizaene (30)*

The structurally interesting sesquiterpenoid (+)-zizaene (**30**),[7] the parent hydrocarbon of a small number of zizaane-type natural products isolated from vetiver oil, contains the tricyclo[6.2.1.$0^{1,5}$]undecane carbon skeleton.[8] One possible route which might be employed for the total synthesis of (±)-zizaene is revealed by the retrosynthetic analysis outlined in Scheme 1. Thus, removal of the two methyl groups from C-7 of **30** and replacement of the exocyclic olefinic double bond at C-6 with a carbonyl group provides the tricyclic ketone **31**. In fact, at the time that we were planning our work, the latter substance (or an equilibrium mixture of **31** and the epimer **32**) had already been employed by Coates and Sowerby (49) as an intermediate in their total synthesis of racemic zizaene. Therefore, in our work, the ketones **31** and/or **32** became the synthetic targets.[9]

Heterolytic disconnection of the C-8—C-9 bond in **31** or **32** so as to leave C-8 as a donor atom and C-9 as an acceptor site gives the bicyclic synthon **33**. A synthetic equivalent to the latter species would have to contain functional groups at C-8 and C-9 which would render these positions nucleophilic and electrophilic, respectively. Since C-8 is β to the carbonyl group in **33**, it would, in terms of normal reactivity patterns, be considered as a potential electrophilic site and, therefore, reactivity umpolung[10] would have to be employed in effecting the synthetic conversion of **33** into **31** and/or **32**. Further disconnection involving the C-1—C-10 bond in **33** would provide the synthons **34** and **35**. It is clear that a potential synthetic equivalent to the synthon **34** would be the bicyclic enone **22**. Furthermore, on the basis of steric

[6]For an alternative preparation of this compound, see ref. 45.

[7]Other names for this natural product which can be found in the literature are tricyclovetivene, khusinene, and khusene.

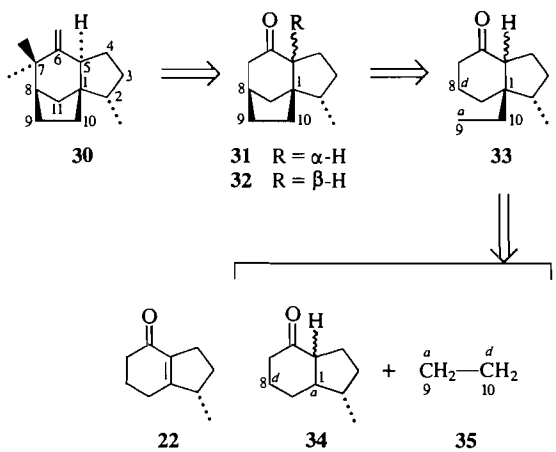
[8]For previous synthetic work on zizaane-type sesquiterpenoids and for literature citations regarding the isolation and structural elucidation of members of this family of natural products, see refs. 46–52, inclusive.

[9]Very recently, an alternative preparation of (±)-**31** has been reported by Barker and Pattenden (53).

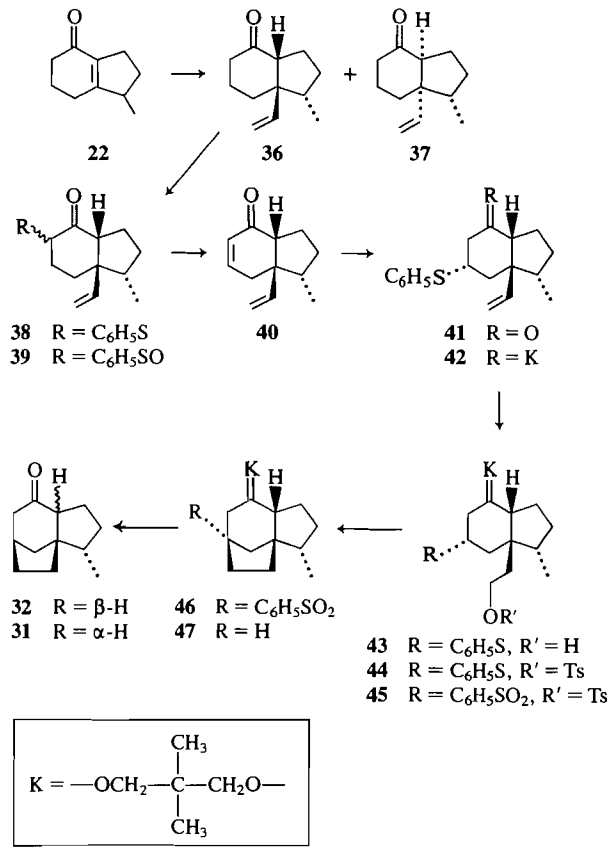
[10]For an excellent, stimulating article on methods of reactivity umpolung, see ref. 54.

considerations, conjugate addition of a suitable two-carbon species to the enone system in **22** would be expected to take place stereoselectively from the side opposite the adjacent secondary methyl group, thus producing a product which would be synthetically equivalent to **33**. Therefore, since a very convenient synthesis of the enone **22** was available (*vide supra*), we wished to investigate the possibility of employing this substance as the starting material in a projected synthesis of (±)-zizaene (**30**) via the general plan summarized in Scheme 1.

The reagent which served as a convenient source of the required two-carbon unit (cf. synthon **35**) was lithium divinylcuprate, readily prepared by addition of two equivalents of ethereal vinyllithium (55) to a solution of cuprous bromide – dimethylsulfide complex (56, 57) in a mixture of ether and dimethyl sulfide. Reaction of the enone **22** with 1.1 equivalents of the cuprate reagent afforded, after suitable work-up, a product which contained a number of minor, unidentified components with relatively short retention times (gas–liquid chromatographic analysis), along with two ketones in a ratio of ~98:2. Purification of this material by column chromatography on silica gel provided a small sample of the minor ketone and allowed for the isolation of the major product in 72% yield. As mentioned previously, the conjugate addition reaction was expected to be stereoselective in the desired sense, with transfer of the vinyl group occurring preferentially to the side of the enone opposite to the secondary methyl group. Therefore, with respect to the relative orientation of the vinyl and methyl groups, the major and minor ketonic products were assigned structures **36** and **37**, respectively (see Scheme 2). Furthermore,



SCHEME 1



SCHEME 2

examination of molecular models, along with the knowledge that *cis*-hydrindan-4-one is more stable than the corresponding *trans* isomer (58), led to the conclusion that each of these compounds possesses a *cis*-fused ring system.[11] Although these latter assignments were not crucial in terms of the overall synthesis, the conclusion regarding the stereochemistry of the required isomer **36** was later shown to be correct.

When the keto olefin **36** was treated with three equivalents of lithium diisopropylamide in THF–hexamethylphosphoramide (HMPA) and the resultant enolate anion was trapped with diphenyl disulfide (59), the α-sulfenylated ketone **38** was obtained in 91% yield. The latter material, a mixture of epimers, was oxidized (sodium periodate in aqueous methanol) to the corresponding sulfoxide **39** which, upon heating (120°C/0.3 Torr) with direct distillation of the product, gave the enone **40** in 64% yield.

[11]Treatment of **36** and **37** with sodium methoxide in methanol showed that both were stable to epimerization conditions and that they were not interconvertible.

Bearing in mind the synthetic plan (Scheme 1), it was necessary at this stage of the synthesis to add an appropriate functional group to the β carbon atom of the α,β-unsaturated ketone system in **40**. The nature of this group had to be such that it would be capable of imparting nucleophilic character to the β carbon atom (cf. C-8 in synthon **33**), presumably by enhancing the acidity of the proton attached to this center. Furthermore, after having served its purpose, the group would have to be amenable to ready removal by a suitable chemical transformation. It appeared that a sulfur-containing moiety would adequately fulfil these requirements.

Treatment of the enone **40** with thiophenol in acetone containing tetra-*n*-butylammonium fluoride (60) afforded a single crystalline conjugate addition product in 95% yield. On the basis of an examination of molecular models of **40**, it seemed highly likely that the nucleophile would approach the β carbon of the enone system from the side opposite the angular vinyl group. Therefore, although conclusive evidence regarding this point was not sought, the conjugate addition product was assigned the stereochemistry shown in **41**. After ketalization of the latter substance, the vinyl group of the resultant product **42** was functionalized by hydroboration with borane – dimethyl sulfide (61). The crude product thus obtained consisted of a mixture of the starting material **42** and the desired ketal alcohol **43**. However, since the latter compound was quite unstable (interaction of the hydroxyl group and the ketal function?), this mixture was treated immediately with *p*-toluenesulfonyl chloride in pyridine. Separation of the resultant mixture by column chromatography on silica gel gave the desired tosylate **44** in 86% yield, based on unrecovered **42**.

Oxidation (*m*-chloroperbenzoic acid, dichloromethane, 0°C) of the sulfide linkage in **44** afforded a quantitative yield of the crystalline sulfone **45** and the stage was now set for effecting the closure of the five-membered ring to provide the required tricyclo[6.2.1.$0^{1,5}$]undecane ring system. Thus, when freshly prepared, dry potassium *tert*-butoxide was added to a solution of the sulfone tosylate **45** in HMPA, and the resultant solution was stirred at room temperature for 1.5 h, the crystalline tricyclic product **46** was produced in 85% yield. The phenyl sulfone moiety, having effectively served its required function, was removed cleanly and efficiently by reduction of **46** with sodium amalgam in methanol–benzene containing disodium hydrogen phosphate (62). The desired tricyclic ketal **47** was obtained in 90% yield. Treatment of compound **47** with oxalic acid in THF–methanol–water at room temperature gave the tricyclic ketone **32** (93% yield), containing none of the epimeric substance **31**. However, when a solution of **32** in methanol containing sodium methoxide was stirred at room temperature for 24 h, a 2:1 mixture of the epimers **32** and **31** was obtained. This mixture was spectrally identical[12] with a 2:1 mixture of the same two compounds which had been prepared previously by Coates and Sowerby (49) and which had been converted by these workers into (±)-zizaene (**30**). Therefore, the acquisition of this material completed, in a formal sense, a new total synthesis of the racemic sesquiterpenoid.

Experimental

General

Melting points, which were taken on a Fisher–Johns melting point apparatus, and boiling points (or distillation temperatures) are uncorrected. Ultraviolet (uv) spectra were recorded on a Cary 15 spectrophotometer, while infrared (ir) spectra were taken on Perkin–Elmer models 710 or 710 B spectrophotometers. Proton magnetic resonance (^{1}H nmr) spectra (deuterochloroform solution unless otherwise noted) were measured using Varian Associates spectrometers, models T-60 and/or HA-100 or XL-100. Tetramethylsilane was employed as the internal standard. High resolution mass spectrometric measurements were recorded on a Kratos MS-50 mass spectrometer. Gas–liquid chromatography (glc) was carried out with a Hewlett–Packard model 5832 A gas chromatograph (analytical) or with a Varian Aerograph model 90-P instrument (preparative). Microanalysis were performed by Mr. P. Borda, Microanalytical Laboratory, University of British Columbia, Vancouver, B.C.

3-Cyclopropyl-2-cyclohexen-1-one (11)

To a cold (−78°C), stirred slurry of phenylthiocopper (32) (779 mg, 4.5 mmol) in dry THF (30 mL), under an atmosphere of argon, was added a solution of freshly prepared cyclopropyllithium (29, 30) (4.5 mmol) in ether. The mixture was warmed to −20°C and stirred at this temperature for 20 min. The resulting clear, light-brown solution was cooled to −78°C and a solution of 3-iodo-2-cyclohexen-1-one (7) (25) (666 mg, 3 mmol) in 6 mL of dry THF was added. After the reaction mixture had been stirred at −78°C for 2.5 h, methanol (2 mL) and ether (20 mL) were added, the mixture was allowed to warm to room temperature, and then was filtered through a short column of Florisil (30 g, 80–100 mesh). The column was eluted with a further 300 mL of ether. Removal of the solvent from the combined eluate, followed by distillation (air bath temperature 62–75°C/0.3 Torr) of the crude oil afforded 335 mg (82%) of the desired β-cyclopropyl enone **11** (33) as a colorless oil; uv (methanol) λ_{max}: 254 nm (ε 17100); ir (film): 1660, 1625, 1610 cm^{-1}; ^{1}H nmr δ: 0.66–2.50 (m, 11H), 5.81 (s, 1H).

3-Cyclopropyl-2-cyclopenten-1-one (13)

The conversion of 3-iodo-2-cyclopenten-1-one (**9**) (25) into the corresponding β-cyclopropyl enone **13** was carried out via a procedure identical with that described above. From 624 mg (3 mmol) of **9** there was obtained 355 mg (97%) of crystalline product **13**; distillation temperature ~65°C (air bath)/0.2 Torr;

[12]We are very grateful to Professor R. M. Coates for his assistance in making this comparison.

mp 31–33°C; uv (methanol) λ_{max}: 244 nm (ε 16270); ir ($CHCl_3$): 1700, 1670, 1600 cm^{-1}; ^1H nmr δ: 0.74–1.22 (m, 4H), 2.00–2.68 (m, 1H), 3.26–3.60 (m, 4H), 5.88 (t, 1H, J = 1.8 Hz). *Exact Mass* calcd. for $C_8H_{10}O$: 122.0731; found: 122.0733.

3-Cyclopropyl-2-methyl-2-cyclohexen-1-one (12)

The procedure used for the preparation of compound **12** was identical with that employed for the conversion of **7** into **11**, except that 2 equiv. (6 mmol) of lithium (phenylthio)(cyclopropyl)cuprate were used, and the reaction was carried out for 2.5 h at 0°C instead of at −78°C. From 708 mg (3 mmol) of 3-iodo-2-methyl-2-cyclohexen-1-one (**8**) (25) there was obtained 396 mg (88%) of an oil (distillation temperature 65–85°C (air bath)/0.35 Torr) which crystallized in a refrigerator. Recrystallization of a small sample of this material from ether–hexanes provided pure **12** (63); mp 36–37°C; uv (methanol) λ_{max}: 262 nm (ε 14950); ir ($CHCl_3$): 1660, 1610 cm^{-1}; ^1H nmr δ: 0.70–1.00 (m, 4H), 1.70–2.60 (m, 7H), 1.90 (s, 3H). *Exact Mass* calcd. for $C_{10}H_{14}O$: 150.1044; found: 150.1032.

3-Cyclopropyl-2-methyl-2-cyclopenten-1-one (14)

This compound was obtained via a procedure identical with that described for the preparation of the β-cyclopropyl enone **12** (see above). From 666 mg (3 mmol) of the iodo enone **10** (25) there was obtained a crude oil which upon distillation (air bath temperature ~50°C/0.1 Torr) gave 343 mg (84%) of the cyclopentenone **14** (63) as a colorless oil; uv (methanol) λ_{max}: 254 nm (ε 18580); ir (film): 1698, 1637 cm^{-1}; ^1H nmr δ: 0.80–1.15 (m, 4H), 1.77 (t, 3H, J = 1.2 Hz), 1.90–2.40 (m, 5H). *Exact Mass* calcd. for $C_9H_{12}O$: 136.0887; found: 136.0888.

3-Isopropenyl-2-cyclohexen-1-one (16)

A stirred, cold (0°C) solution of isopropenylmagnesium bromide (29.04 g, 0.20 mol) in 50 mL of dry THF, under an atmosphere of nitrogen, was diluted with 75 mL of dry ether. A solution of 3-methoxy-2-cyclohexen-1-one (**15**) (41) (12.61 g, 0.10 mol) in 20 mL of dry ether was added dropwise and the resultant mixture was stirred at room temperature for 4 h. After the solution had been cooled to 0°C, 100 mL of 5% aqueous sulfuric acid was added slowly and the mixture was stirred for a few minutes. The organic phase was separated, washed successively with dilute aqueous sodium carbonate and water, and dried over anhydrous sodium sulfate. Removal of the solvent, followed by distillation of the residual oil gave 11.46 g (84%) of 3-isopropenyl-2-cyclohexen-1-one (**16**) as a clear colorless liquid; bp 60–63°C/0.3 Torr; uv (methanol) λ_{max}: 267 nm (ε 22000); ir (film): 2980, 1666, 1626, 1586, 1256, 878 cm^{-1}; ^1H nmr (CCl_4) δ: 1.77–2.60 (m, 6H), 1.97 (s, 3H), 5.17 (broad s, 1H), 5.33 (s, 1H), 5.83 (s, 1H). *Anal.* calcd. for $C_9H_{12}O$: C 79.39, H 8.88; found: C 79.53, H 9.04.

3-(1-Methylcyclopropyl)-2-cyclohexen-1-one (17)

A solution of dimethyloxosulfonium methylide (42) (0.082 mol) in 90 mL of dry dimethyl sulfoxide, kept under an atmosphere of nitrogen, was diluted with 40 mL of dry THF and cooled to 0°C. A solution of 3-isopropenyl-2-cyclohexen-1-one (11.0 g, 0.081 mol) in 10 mL of dry THF was added dropwise and the resultant reddish reaction mixture was stirred overnight at room temperature. The solution was poured into 500 mL of cold water and the resultant mixture was extracted with six 75 mL portions of ether. The combined extract was washed with water and brine and dried over anhydrous sodium sulfate. Removal of the solvent, followed by distillation of the residual oil, yielded 7.2 g (59%) of 3-(1-cyclopropyl)-2-cyclohexen-1-one (**17**) as a colorless oil which exhibited one peak by gas–liquid chromatographic analysis; bp 72–76°C/0.3 Torr; uv (methanol) λ_{max}: 253 nm (ε 16600); ir (film): 1665, 1610 cm^{-1}; ^1H nmr (CCl_4) δ: 0.4–1.08 (m, 4H), 1.15 (s, 3H), 1.67–2.35 (m, 6H), 5.70 (broad s, 1H). *Exact Mass* calcd. for $C_{10}H_{14}O$: 150.1044; found: 150.1039.

Thermal rearrangement of 3-cyclopropyl-2-cyclohexen-1-one (11)

(a) *Procedure A*

A vertically held Pyrex tube (1.2 × 32 cm), filled with glass helices and placed inside a vertical, tubular furnace, was washed successively with saturated aqueous sodium bicarbonate, water, acetone, and *n*-hexane. The tube was heated to 450°C and kept at this temperature for 3 h. During this time, the column was thoroughly purged with a stream of nitrogen. A solution of 3-cyclopropyl-2-cyclohexen-1-one (**11**) (200 mg) in *n*-hexane (20 mL) was added dropwise, over a period of 1.5 h, to the top of the heated tube. During this time, a slow flow of nitrogen (~3–5 mL/min) was passed through the column. The thermolysate was passed through a water condensor into a cold (−78°C) two-necked flask equipped with a drying tube. After the solution of **11** had been added, the hot tube was treated with an additional 30 mL of *n*-hexane. Removal of the solvent from the combined thermolysate, followed by distillation (air bath temperature ~110°C/16 Torr) of the residual material gave 156 mg (78%) of a colorless oil. Gas–liquid chromatographic analysis of this material showed that it consisted of a mixture of the ketones **18** (~3%), **19** (~84%), and **20** (~11%), along with a number of very minor unidentified components (~2%). A pure sample of each of compounds **18**, **19**, and **20** was obtained by preparative glc.

Ketone **18**: ir (film): 1718, 1665 cm^{-1}; ^1H nmr δ: 1.7–2.7 (diffuse m, 10H), 3.37 (m, 1H), 5.43 (m, 1H). When an ethereal solution of **18** was passed through a short column of basic alumina, compound **18** was isomerized cleanly into the conjugated isomer **19** (identification by glc, ir, and ^1H nmr).

Ketone **19**: ir (film): 1660, 1630 cm^{-1}; ^1H nmr δ: 1.7–2.8 (diffuse m). The 2,4-dinitrophenylhydrazone derivative exhibited mp 252°C (dec.) (lit. (43) mp 251.5°C (dec.)).

Ketone **20** (44): ir (film): 1670, 1642, 1590 cm^{-1}; ^1H nmr δ: 1.86 (d, 3H, J = 5 Hz), 1.8–2.6 (diffuse m, 6H), 5.84 (s, 1H), 6.18 (m, 2H).

(b) *Procedure B*

This procedure was identical with that described above, except that the thermolysis tube was longer (100 cm), the tube was heated by means of a heating tape rather than a furnace, the "carrier gas" was argon instead of nitrogen, and the thermolysis temperature was 425°C rather than 450°C. From 200 mg of the β-cyclopropyl enone **11** there was obtained 196 mg (98%) of a distilled oil which, on the basis of analysis by glc, consisted very largely of the ketones **18** (~31%) and **19** (~67%). An ether solution of this mixture was passed through a short column of basic alumina, and the column was eluted with further volumes of ether. Removal of the solvent from the combined eluate, followed by bulb-to-bulb distillation of the residual oil, gave 176 mg (88%) of the enone **19**.

Thermal rearrangement of 3-(1-methylcyclopropyl)-2-cyclohexen-1-one (17)

Thermolysis of compound **17** was accomplished via a procedure very similar to that described under Procedure A, above, except that the thermolysis tube was 40 cm in length and the reaction was done on a much larger scale. Thus, from 12.3 g of **17** (added to the heated column as a solution in 30 mL of *n*-hexane) there was obtained a distilled oil which was shown by analysis (glc, ir, ^1H nmr) to consist of a mixture of the two ketones **21** and **22**, in a ratio of approximately 7:3, respectively.[13] This mixture was dissolved in 100 mL of methanol containing a small amount of sodium methoxide and the resultant solution was stirred at 0°C for 1 h. The methanol was removed under reduced pressure and the residue was taken up

[13]The ratio of the two products varied somewhat from one thermolysis experiment to another.

in ether. The ether solution was washed with brine and dried over anhydrous magnesium sulfate. Removal of the ether, followed by distillation of the residual material gave 10.7 g (87%) of the conjugated enone **22** as a clear oil which exhibited one peak by gas–liquid chromatographic analysis; bp 55–58°C/0.3 Torr; uv (methanol) λ_{max}: 247 nm (ε 12 100); ir (film): 1670, 1638 cm^{-1}; ^1H nmr δ: 1.08 (d, 3H, J = 6.5 Hz), 1.1–1.7 (m, 2H), 1.7–3.0 (diffuse m, 9H). *Exact Mass* calcd. for $C_{10}H_{14}O$: 150.1044; found: 150.1032.

Thermal rearrangement of 3-cyclopropyl-2-methyl-2-cyclohexen-1-one (12)

Thermolysis of **12** was carried out via a procedure very similar to Procedure A, above. From 175 mg of **12** (added to the hot tube as a solution in 17.5 mL of *n*-hexane) there was obtained a crude thermolysate which upon distillation (air bath temperature ~110°C/12 Torr) gave 128 mg (73%) of a clear oil. Analysis of this material by glc showed that it consisted of a mixture of the ketones **23** (~10%), **24** (~20%), and **25** (~50%), along with a number of minor, unidentified components. A small sample of each of the major products was obtained by preparative glc.

Ketone **23**: ir (film): 1715, 1660 cm^{-1}; ^1H nmr δ: 1.23 (s, 3H), 1.4–2.8 (diffuse m, 10H), 5.30 (m, 1H). *Exact Mass* calcd. for $C_{10}H_{14}O$: 150.1044; found: 150.1039.

Ketone **24**: uv (methanol) λ_{max}: 243 nm (ε 9400); ir (film): 1665, 1635 cm^{-1}; ^1H nmr δ: 1.54–2.58 (diffuse m, 6H), 1.75 (t, 3H, $J \approx$ 1 Hz), 2.95 (d, 2H, J = 6.5 Hz), 4.9–5.04 (m, 1H), 5.06–5.16 (m, 1H), 5.54–6.0 (m, 1H). *Exact Mass* calcd. for $C_{10}H_{14}O$: 150.1044; found: 150.1041.

Ketone **25**: uv (methanol) λ_{max}: 281 nm (ε 19 050); ir (film): 1660, 1630, 1585 cm^{-1}; ^1H nmr δ: ~1.8–2.08 (m, 2H), 1.86 (s, 3H), 1.91 (d, 3H, J = 6 Hz), 2.32–2.58 (m, 4H), 5.96–6.36 (d of q, 1H, J = 15, 6 Hz), 6.60 (broad d, 1H, J = 15 Hz). *Exact Mass* calcd. for $C_{10}H_{14}O$: 150.1044; found: 150.1038.

Thermal rearrangement of 3-cyclopropyl-2-cyclopenten-1-one (13)

From 200 mg of compound **13**, thermolyzed as described under Procedure A, above, there was obtained a crude mixture of products which, upon distillation (air bath temperature 100–110°C/16 Torr), gave 160 mg (80%) of a clear oil. Analysis of this material by glc showed that it consisted very largely of four components: **26** (~46%), **27** (~14%), **28** (~20%), and **29** (~18%). A pure sample of each of these compounds was obtained by preparative glc.

Ketone **26**: ir (film): 1740, 1660 cm^{-1}; ^1H nmr δ: 1.57–2.84 (diffuse m, 8H), 3.12–3.43 (m, 1H), 5.42–5.60 (m, 1H). *Exact Mass* calcd. for $C_8H_{10}O$: 122.0731; found: 122.0730. When an ethereal solution of **26** was eluted through a short column of basic alumina, it was isomerized to the α,β-unsaturated ketone **27**.

Ketone **27**: uv (methanol) λ_{max}: 237 nm (ε 11 370); ir (film): 1690, 1630 cm^{-1}; ^1H nmr δ: 2.20–2.90 (diffuse m). *Exact Mass* calcd. for $C_8H_{10}O$: 122.0731; found: 122.0734.

Ketone **28**: uv (methanol) λ_{max}: 226 nm (ε 14 090); ir (film): 1705, 1610 cm^{-1}; ^1H nmr δ: 2.2–2.8 (diffuse m, 4H), 3.12 (d, 3H, J = 6.5 Hz), 5.00–5.12 (m, 1H), 5.14–5.26 (m, 1H), 5.64–6.08 (m, 1H), 5.93 (t, 1H, J = 1.5 Hz). *Exact Mass* calcd. for $C_8H_{10}O$: 122.0731; found: 122.0728. When an ethereal solution of **28** was eluted through a short column of basic alumina, it was isomerized to the conjugated dienone **29**.

Ketone **29**: uv (methanol) λ_{max}: 268 nm (ε 18 630); ir (film): 1640, 1570 cm^{-1}; ^1H nmr δ: 1.89 (d, 3H, J = 6 Hz), 2.2–2.8 (diffuse m, 4H), 5.91 (broad s, 1H), ~6.30 (d of q, 1H, J = 16, 6 Hz), 6.56 (d, 1H, J = 16 Hz). *Exact Mass* calcd. for $C_8H_{10}O$: 122.0731; found: 122.0732.

Reaction of the enone 22 with lithium divinylcuprate

A stirred solution of cuprous bromide – dimethyl sulfide complex (56, 57) (10.99 g, 53.4 mmol) in a mixture of dimethyl sulfide (53 mL) and ether (72 mL) was cooled to −60°C under an atmosphere of nitrogen. During this cooling, some of the complex crystallized from the solution. A solution of vinyllithium (55) in ether (121 mL, 0.92 *M*, 115 mmol) was added dropwise while the temperature of the reaction mixture was maintained at −50°C to −60°C. To the resulting dark-brown solution was added dropwise a solution of the bicyclic enone **22** (7.9 g, 49.3 mmol) in 30 mL of anhydrous ether. After the reaction mixture had been stirred at −50°C for 20 min and at room temperature for 1 h, it was diluted with ether (200 mL) and then treated with saturated aqueous ammonium chloride. The resulting mixture was filtered and the collected solid material was washed thoroughly with ether. The combined filtrate was washed successively with aqueous ammonium chloride and brine and dried over anhydrous magnesium sulfate. Removal of the solvent, followed by distillation (air bath temperature 60–70°C/0.3 Torr) of the residual oil, gave a clear liquid. Analysis of this material by glc showed that it contained, in addition to a number of minor unidentified components with very short retention times, two products in a ratio of about 98:2.

The distilled material was subjected to column chromatography on silica gel (400 g). Elution of the column with benzene gave a mixture of unidentified compounds which exhibited no carbonyl absorption in the ir spectrum. Further elution with benzene – ethyl acetate (9:1) gave the minor ketonic product **37**, contaminated with a small amount of the major product **36**. A small sample of **37** was obtained by preparative glc; ir (film): 3100, 1710, 1630, 900 cm^{-1}; ^1H nmr (CCl_4) δ: 0.77 (d, 3H, J = 6.0 Hz), 2.56 (d of d, 1H, J = 8, 5 Hz), 4.94 (d of d, 1H, J = 18, 1.5 Hz), 5.07 (d of d, 1H, J = 11, 1.5 Hz), 5.72 (d of d, 1H, J = 18, 11 Hz). *Exact Mass* calcd. for $C_{12}H_{18}O$: 178.1358; found: 178.1369.

Further elution of the above chromatography column with benzene – ethyl acetate (9:1) gave the pure bicyclic ketone **36** (6.28 g, 72%) as a colorless oil which exhibited bp 65°C/0.1 Torr; ir (film): 3100, 1705, 1630, 910 cm^{-1}; ^1H nmr (CCl_4) δ: 0.90 (d, 3H, J = 6.0 Hz), 4.89 (d of d, 1H, J = 18, 1.5 Hz), 5.01 (d of d, 1H, J = 11, 1.5 Hz), 5.67 (d of d, 1H, J = 18, 11 Hz). *Anal.* calcd. for $C_{12}H_{18}O$: C 80.85, H 10.18; found: C 80.77, H. 10.20. *Exact Mass* calcd.: 178.1358; found: 178.1354.

Treatment of either of the two ketones **36** and **37** with sodium methoxide in methanol clearly showed that the two compounds were not interconvertible. In each case, only starting material was recovered.

Preparation of the bicyclic α,β-unsaturated ketone 40

To a cold (−25°C) solution of diisopropylamine (3.06 g, 30.2 mmol) in dry THF (40 mL) under an atmosphere of nitrogen was added a solution of *n*-butyllithium in hexane (11.6 mL, 2.6 *M*, 30.16 mmol) and the resulting solution was stirred for 30 min. A solution of the bicyclic ketone **36** (1.80 g, 10.1 mmol) in a mixture of dry THF (20 mL) and dry HMPA (20 mL) was added dropwise over a period of 10 min. After the reaction mixture had been stirred for 30 min at −25°C, for 1 h at 0°C, and for 15 min at room temperature, a solution of diphenyl disulfide (6.59 g, 30.18 mmol) in 20 mL of dry THF was added rapidly and the solution was stirred at room temperature for 2 h. Hydrochloric acid (10%) was added and the resultant mixture was extracted thoroughly with ether. The combined ether extract was washed successively with saturated aqueous sodium bicarbonate and brine and dried over anhydrous magnesium sulfate. Removal of the solvent afforded an oil which was subjected to column chromatography on silica gel (300 g). Elution of the column with benzene gave 2.634 g (91%) of the α-phenylthio ketone **38**.

Analysis of this material by tlc and ^{1}H nmr showed that it was a mixture of two diastereomers. *Exact Mass* calcd. for $C_{18}H_{22}OS$: 286.1391; found: 286.1392.

To a cold (0°C) solution of the crude α-phenylthio ketone **38** (3.386 g, 11.8 mmol) in 50 mL of methanol was added dropwise a solution of sodium periodate (2.72 g, 12.7 mmol) in water (20 mL). After the resultant cloudy reaction mixture had been stirred at room temperature for 16 h, it was filtered and the solid collected material was washed with methanol. The combined filtrate was concentrated under reduced pressure and the residue was diluted with ether. The resultant solution was washed with brine and dried over anhydrous magnesium sulfate. Removal of the solvent gave the crude sulfoxide **39** as a yellow oil, to which was added ~20 mg of solid calcium carbonate. The resultant mixture was heated (air bath temperature 120°C) under reduced pressure (0.3 Torr) and the collected distillate was subjected to column chromatography on silica gel (100 g). Elution of the column with benzene–ether (95:5) afforded an oil which upon distillation (air bath temperature 80°C/0.3 Torr) gave 1.34 g (64%) of the pure bicyclic enone **40**; uv (methanol) λ_{max}: 228 nm (ε 7900); ir (film): 3100, 1670, 900 cm^{-1}; ^{1}H nmr (CCl_4) δ: 0.89 (d, 3H, J = 6.0 Hz), 1.12–2.64 (diffuse m, 8H), 4.91 (d of d, 1H, J = 18, 1 Hz), 5.03 (d of d, 1H, J = 11, 1 Hz), 5.69 (d of d, 1H, J = 18, 11 Hz), 5.84 (broad d, 1H, J = 10 Hz), 6.73 (d of d of d, 1H, J = 10, 5, 3 Hz). *Anal.* calcd. for $C_{12}H_{16}O$: C 81.77, H 9.15; found: C 81.45, H 9.40. *Exact Mass* calcd.: 176.1202; found: 176.1207.

*Preparation of the phenylthio ketone **41***

To a stirred solution of the bicyclic enone **40** (0.17 g, 0.96 mmol) and tetra-*n*-butylammonium fluoride (0.013 g) in 1.5 mL of dry acetone under an atmosphere of nitrogen was added, dropwise, 0.117 g (1.06 mmol) of thiophenol. After the reaction mixture had been stirred for 3 h at room temperature, it was diluted with ether (100 mL) and the resultant solution was washed successively with saturated aqueous sodium bicarbonate and brine and then dried over anhydrous magnesium sulfate. Removal of the solvent gave 0.263 g (95%) of a crystalline material which was homogeneous by tlc. An analytical sample of the phenylthio ketone **41**, obtained by recrystallization of this material from pentane, exhibited mp 76–77°C; ir ($CHCl_3$): 3100, 1700, 1635, 1580, 915 cm^{-1}; ^{1}H nmr δ: 0.86 (d, 3H, J = 5.5 Hz), 1.4–2.2 (diffuse m, 7H), 2.45 (d, 2H, J = 8 Hz), ~2.62 (m, 1H), 3.18–3.56 (m, 1H), 4.86 (d, 1H, J = 17 Hz), 5.03 (d, 1H, $J \approx$ 11 Hz), 5.66 (d of d, 1H, J = 17, 11 Hz), 7.30 (m, 5H). *Anal.* calcd. for $C_{18}H_{22}OS$: C 75.48, H 7.68; found: C 75.42, H 7.76. *Exact Mass* calcd.: 286.1391; found: 286.1368.

*Preparation of the ketal **42***

A solution of the phenylthio ketone **41** (0.247, 0.86 mmol) and 2,2-dimethyl-1,3-propanediol (0.269 g, 2.6 mmol) in 12 mL of benzene containing 0.01 g of *p*-toluenesulfonic acid was refluxed under a Dean–Stark water separator for 3 h. After a small amount of solid sodium bicarbonate had been added to the cooled solution, the latter was diluted with 100 mL of benzene and the resultant solution was washed successively with saturated aqueous sodium bicarbonate and brine and then dried over anhydrous magnesium sulfate. Removal of the solvent gave 0.317 g (99%) of the ketal **42** as a clear oil which was homogeneous by tlc; ir ($CHCl_3$): 3100, 1635, 1590, 1100, 910 cm^{-1}; ^{1}H nmr δ: 0.69 (d, 3H, J = 6.0 Hz), 0.80, 0.96 (s, s, 3H each), 1.06–1.96 (diffuse m, 8H), 2.19 (m, 1H), 2.57 (broad t, 1H), 3.2–3.6 (diffuse m, 5H), 4.74 (d of d, 1H, J = 17, 1 Hz), 4.95 (d of d, 1H, J = 11, 1 Hz), 5.58 (d of d, 1H, J = 17, 11 Hz), 7.14–7.50 (m, 5H). *Exact Mass* calcd. for $C_{23}H_{32}O_2S$: 372.2123; found: 372.2149.

*Preparation of the ketal tosylate **44***

To a cold (0°C), stirred solution of the olefinic ketal **42** (0.96 g, 2.57 mmol) in 3 mL of dry THF was added 0.30 mL (3.0 mmol) of borane – dimethyl sulfide complex. The reaction mixture was stirred at 0°C for 2 h, slowly warmed to room temperature over a period of 1 h, and then stirred at this temperature for 1 h. After the mixture had been cooled to 0°C, it was treated successively with methanol (0.6 mL) 3 *N* sodium hydroxide (0.6 mL), and 30% hydrogen peroxide (0.6 mL). The resultant mixture was warmed to 45–50°C, maintained at this temperature for 1 h, diluted with 20 mL of aqueous sodium bicarbonate, and then extracted thoroughly with dichloromethane. The combined extract was washed with brine and dried over anhydrous magnesium sulfate. Removal of the solvent afforded a viscous oil which was dissolved immediately in dry pyridine (4 mL). The solution was treated with *p*-toluenesulfonyl chloride (0.54 g, 2.8 mmol), allowed to stand at room temperature overnight, and then poured into ice-cold water. The resultant mixture was extracted with dichloromethane. The combined extract was washed with brine and dried over anhydrous magnesium sulfate. Removal of the solvent gave a viscous oil which was subjected to column chromatography on silica gel (60 g). Elution of the column with benzene – ethyl acetate (97.5:2.5) gave 0.325 g (34%) of the starting material (olefinic ketal **42**) and 0.80 g (86%, based on unrecovered starting material) of the ketal tosylate **44**. The latter substance was obtained as a clear oil which was homogeneous by tlc and exhibited ir ($CHCl_3$): 1600, 1590, 1195, 1100, 955 cm^{-1}; ^{1}H nmr δ: 0.70 (d, 3H, J = 5.5 Hz), 0.79, 0.85, (s, s, 3H each), 1.1–2.5 (diffuse m, 12H), 2.38 (s, 3H), 3.04–3.46 (diffuse m, 5H), 3.86–4.30 (m, 2H), 7.12–7.44 (m, 7H), 7.74 (d, 2H, J = 8 Hz). *Exact Mass* calcd. for $C_{30}H_{40}O_5S_2$: 544.2317; found: 544.2312.

*Preparation of the sulfone tosylate **45***

To a cold (0°C), stirred solution of the sulfide tosylate **44** (0.25 g, 0.46 mmol) in 3 mL of dry dichloromethane was added, over a period of about 2 min, 0.204 g of 85% *m*-chloroperbenzoic acid and the resultant solution was stirred at 0°C for 2 h. The solution was diluted with 50 mL of saturated aqueous sodium bicarbonate and the resultant mixture was extracted thoroughly with dichloromethane. The combined extract was washed with brine and dried over anhydrous magnesium sulfate. Removal of the solvent afforded a semicrystalline material which was subjected to column chromatography on silica gel (20 g). Elution of the column with benzene – ethyl acetate (9:1) gave 0.264 g (100%) of a crystalline compound which was homogeneous by tlc. An analytical sample of compound **45**, obtained by recrystallization of a small amount of this material from ether–hexane, exhibited mp 145–146°C; ir ($CHCl_3$): 1600, 1365, 1305, 1175, 1150, 1087, 960 cm^{-1}; ^{1}H nmr δ: 0.75 (d, 3H, J = 6 Hz), 0.82, 0.90 (s, s, 3H each), 1.10–2.56 (diffuse m, 12H), 2.44 (s, 3H), 2.94–3.54 (diffuse m, 5H), 3.94–4.32 (m, 2H), 7.30–8.00 (diffuse m, 9H). *Anal.* calcd. for $C_{30}H_{40}O_7S_2$: C 62.47, H 6.99, S 11.12; found: C 62.47, H 7.09, S 11.01.

*Preparation of the tricyclic ketal sulfone **46***

To a solution of the sulfone tosylate **45** (0.235 g, 0.41 mmol) in 3 mL of dry HMPA under an atmosphere of nitrogen was added, over a period of 2 min, freshly prepared dry potassium *tert*-butoxide (2.0 mmol) and the resultant solution was stirred at room temperature for 1.5 h. The reaction mixture was diluted with benzene (150 mL), washed 5 times with brine, and dried over anhydrous magnesium sulfate. Removal of the solvent, followed by column chromatography (10 g silica gel, elution of the column with 9:1 benzene – ethyl acetate) of the residue gave 0.139 g (85%) of the crystalline tricyclic sulfone **46**. An analytical

sample, obtained by recrystallization of a small amount of this material from ether, exhibited mp 168–169°C; ir ($CHCl_3$): 1305, 1150, 1110 cm^{-1}; ^1H nmr δ: 0.88 (d, 3H, J = 6 Hz), 0.86, 0.88 (s, s, 3H each), 1.1–2.5 (diffuse m, 14H), 3.20–3.56 (diffuse m, 4H), 7.40–7.96 (diffuse m, 5H). *Anal.* calcd. for $C_{23}H_{32}O_4S$: C 68.28, H 7.97, S 7.92; found: C 68.06, H 8.09, S 7.80. *Exact Mass* calcd.: 404.2021; found: 404.2015.

Preparation of the tricyclic ketal **47**

To a stirred solution of the ketal sulfone **46** (0.130 g, 0.32 mmol) in a mixture of dry methanol (2.5 mL) and benzene (1.0 mL)[14] was added 0.91 g (6.4 mmol) of anhydrous disodium hydrogen phosphate and 2.4 g of pulverized 6% sodium amalgam and the resultant mixture was stirred at room temperature for 1.5 h. The reaction mixture was diluted with benzene and decanted. The residual solid material was washed with several portions of benzene. The combined organic phase was washed successively with aqueous sodium bicarbonate and brine and dried over anhydrous magnesium sulfate. Removal of the solvent gave an oil which was filtered through a short column of silica gel (2 g). Elution of the column with benzene – ethyl acetate (9:1) gave 0.076 g (90%) of the tricyclic ketal **47** which was homogeneous by tlc and glc. This material exhibited ir (film): 1470, 1100 cm^{-1}; ^1H nmr δ: 0.84 (d, 3H, J = 6 Hz), 0.90, 0.97 (s, s, 3H each), 1.10–2.34 (diffuse m, 15H), 3.40, 3.52 (s, s, 2H each). *Anal.* calcd. for $C_{17}H_{28}O_2$: C 77.22, H 10.67; found: C 77.02, H 10.65.

Preparation of the tricyclic ketone **32**

To a solution of the ketal **47** (75 mg, 0.28 mmol) in a 5:3:2 mixture of THF, methanol, and water (2 mL) was added 76 mg (85 mmol) of oxalic acid and the resultant solution was stirred at room temperature for 45 min. The reaction mixture was diluted with 50 mL of benzene and then was washed successively with saturated aqueous sodium bicarbonate and brine. The organic phase was dried over anhydrous magnesium sulfate. Removal of the solvent, followed by distillation (air bath temperature 85°C/0.3 Torr) of the residual oil, afforded 47 mg (93%) of the ketone **32** as a clear colorless oil which was homogeneous by tlc and glc; ir (film): 1705 cm^{-1}; ^1H nmr δ: 0.89 (d, 3H, J = 6 Hz), 1.16–2.58 (diffuse m, 15H). *Exact Mass* calcd. for $C_{12}H_{18}O$: 178.1357; found: 178.1366.

Equilibration of the tricyclic ketone **32**

A solution of the ketone **32** (12 mg) in methanol (1 mL) containing 20 mg of sodium methoxide was stirred at room temperature for 24 h. Ammonium chloride was added, the methanol was removed under reduced pressure, and the residual material was taken up in a mixture of ether and water. The aqueous layer was washed with additional volumes of ether and the combined extract was dried over anhydrous magnesium sulfate. Removal of the solvent, followed by distillation (air bath temperature 85–90°C/0.4 Torr) of the residual material, gave 10 mg of a clear colorless oil. Analysis of this oil by glc showed that it was a mixture of two compounds, ketones **31** and **32**, in a ratio of 1:2, respectively. The ir and ^1H nmr spectra of this mixture were identical with those of an equilibrated mixture of the same two compounds previously prepared by Coates and Sowerby (49).[12]

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[14]Compound **46** was quite insoluble in methanol. Therefore, benzene was added to increase the solubility.

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