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Regiospecific Generation and Alkylation of γ-Oxo α-Ester Enolates. Application to the Synthesis of Polycyclopentanoids[1]

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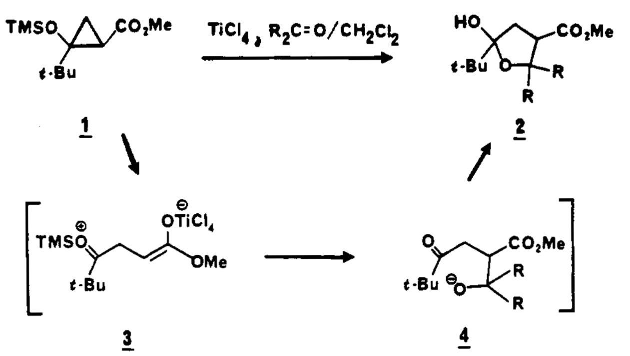
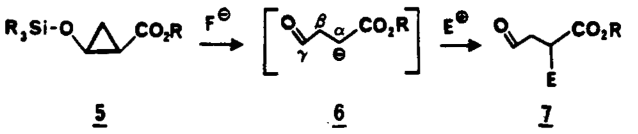
A new strategy for [3 + 2] annulation utilizes the combination of a three-carbon synthon in the form of a γ-oxo α-ester enolate with a two-carbon Michael acceptor. The enolate synthon is derived from the fluoride-induced desilylation of 2-(silyloxy)cyclopropanecarboxylate esters. This new methodology has been applied to the construction of the bicyclo[3.3.0]octane and the tricyclo[6.3.0.0^{2,6}]undecane ring systems using a reiterative process.

(β-Alkoxycyclopropyl)carbonyl derivatives, readily available from enol ethers and α-diazo carbonyl compounds, are valuable synthons in organic chemistry. Their best known reaction is the acid-, base-, or thermal-promoted ring opening, which has been widely utilized to effect many synthetically useful transformations.[2,3] The ease of ring fission is provided by the unique combination of the strain energy inherent in a compound of this type and the complementary electronic effects of its substituents. Precisely, the recognition of this complementarity has led chemists to refer to (β-alkoxycyclopropyl)carbonyl compounds as "donor–acceptor-substituted cyclopropanes".[4] Until recently, however, the high degree of electrophilicity of these synthons and their potential utility for the formation of new chemical bonds, in particular carbon–carbon bonds, had not become apparent. Indeed, Reissig has been among the first to realize the high reactivity of 2-(silyloxy)cyclopropane esters toward electrophilic species, and a few years ago he reported their addition to carbonyl compounds. Thus, treatment of **1** with equimolar amounts of a symmetrical ketone and titanium tetrachloride provided the corresponding γ-lactols **2** after aqueous workup (Scheme I).[5]

Scheme I



Scheme II



A mechanistic rationalization of the transformation in Scheme I has been recently suggested:[6] ring opening of **1** by the Lewis acid would render a ketene acetal intermediate, which would then attack the electrophile to deliver the corresponding γ-lactol **2** after intramolecular hemiketal formation.

Preliminary Results

As a direct consequence of our own involvement with the chemistry of 2-(silyloxy)cyclopropanecarboxylate esters,[7] it was envisioned that fluoride-induced desilylation of these compounds should promote ring opening to generate a discrete γ-oxo α-ester enolate anion (cf., **6**), which,

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[1] A preliminary report of this work has been published: Marino, J. P.; Laborde, E. *J. Am. Chem. Soc.* **1985**, *107*, 734.

[2] Reviews: (a) Wenkert, E. *Acc. Chem. Res.* **1980**, *13*, 27. (b) Wenkert, E. *Heterocycles* **1980**, *14*, 1703. (c) Conia, J. M. *Pure Appl. Chem.* **1975**, *43*, 317. (d) Schollkopf, U. *Angew. Chem., Int. Ed. Engl.* **1968**, *7*, 588.

[3] For the transition-metal-catalyzed rearrangement of β-alkoxycyclopropanecarboxylate esters to vinyl ethers, see: Doyle, M. P.; van Lausen, D. *J. Am. Chem. Soc.* **1981**, *103*, 5917.

[4] Reissig, H.-U.; Hirsch, E. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 813.

[5] Reissig, H.-U. *Tetrahedron Lett.* **1981**, *22*, 2981. For a former example involving a related C alkylation of oxycyclopropane derivatives, see: Makamura, E.; Kuwajima, I. *J. Am. Chem. Soc.* **1977**, *99*, 7360.

[6] Reissig, H.-U.; Reichelt, I. *Tetrahedron Lett.* **1984**, *25*, 5879.

[7] Marino, J. P.; Fernandez de la Pradilla, R.; Laborde, E. *J. Org. Chem.* **1984**, *49*, 5279.

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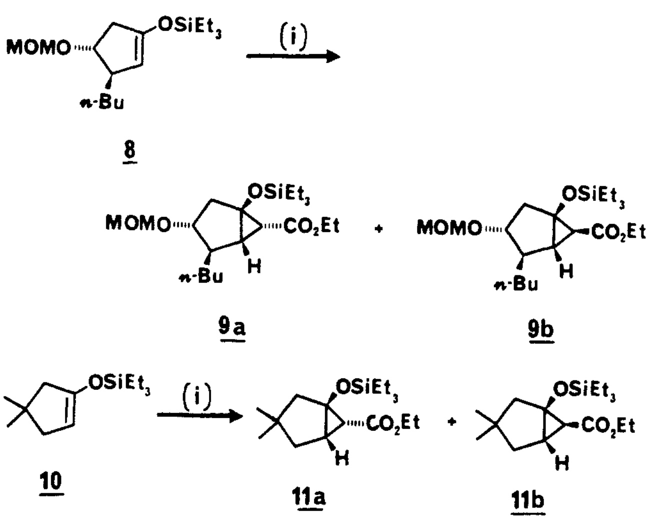
Scheme III[a]



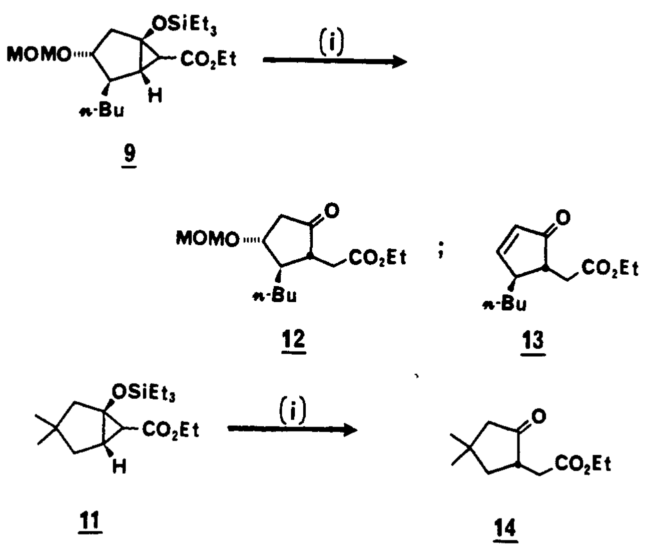
[a] Key: (i) EtO_2C-CHN_2; $CuSO_4$/PhH, Δ.

in principle, could be trapped with different electrophiles (Scheme II). Such a strategy would provide a simple and rather mild method for performing a regiospecific alkylation of an ester enolate in the presence of a ketone moiety, an operation that has heretofore eluded synthetic chemists.

Our study on the chemistry of 2-(silyloxy)cyclopropane esters was carried out on the bicyclic systems **9** and **11**. These compounds were obtained by the copper-catalyzed addition of ethyl diazoacetate onto the corresponding triethylsilyl enol ethers **8** and **10**.[8] Among the catalysts tested for this reaction were copper powder, copper bronze, copper(II) sulfate, copper(II) acetylacetonate, copper(I) acetylacetonate, copper(I) iodide–trimethyl phosphite complex, and rhodium(II) acetate, all of which have been previously used for this type of cycloaddition.[9] An initial screening for the optimal reaction conditions, which essentially involved slow addition of the diazo ester to a refluxing suspension of the catalyst and the enol ether in benzene, showed copper sulfate to be the most suitable catalyst. Not only did this metal salt provide a clean mixture of cycloadducts, but it did so in significantly higher yield than any of the other catalysts employed. Additional experiments established a 3 M concentration of diazo compound and a 200:1 molar ratio of diazo compound and copper sulfate, respectively, as our best set of experimental conditions.

In particular, the reaction of silyl enol ether **8**[10] with carboethoxycarbene afforded a 1:4 mixture of syn and anti carboethoxy isomers **9a** and **9b**, respectively, in 85% combined yield (Scheme III). The stereochemical assignment was based on the ^1H NMR data obtained for each compound. Thus, the coupling constant between H3 and H4 is 0 Hz in **9a** and 1.6 Hz in **9b**, confirming a trans orientation of these two protons in both isomers; the coupling constant between H2 and H3, on the other hand, is 9.8 Hz in **9a** and 4.0 Hz in **9b**, indicating a cis and a trans relationship, respectively.[11] This last conclusion is further supported by the observation that H3 in **9b** appears about 0.5 ppm downfield than in **9a**, which can be attributed to the deshielding effect of the cis carboethoxy group. Finally, it should be mentioned that the observed ratio of syn and anti carboethoxy isomers agrees with the reported anti stereoselectivity of carboethoxycarbenes.[12]

Scheme IV[a]



[a] Key: (i) KF, 18-crown-6/CH_3CN, Δ.

The copper(II) sulfate catalyzed cyclopropanation of 4,4-dimethyl-1-[(triethylsilyl)oxy]cyclopentene (**10**)[10] with carboethoxycarbene, on the other hand, provided a ca. 2:1 mixture of syn and anti carboethoxy isomers **11a** and **11b**, respectively, in 95% combined yield (Scheme III). The ^1H NMR data obtained for each isomer allow for unequivocal assignments of their respective structures. Thus, the values for the coupling constant between H2 and H3 are 13.6 Hz in **11a** and 4.1 Hz in **11b**, which correspond to a cis and a trans relationship, respectively.[11] In addition, H2 in **11a** shows a small (ca. 2.2-Hz) *W*-type coupling constant with H4. The relative chemical shifts of H3 and H4α in each isomer are also very significant. Indeed, H3 is approximately 0.6 ppm downfield in **11b** than in **11a**, as it is expected from the deshielding effect of the cis carboethoxy group.[11] In order to explain the observed syn to anti ratio, it would be necessary to assume that the syn isomer is thermodynamically more stable than the anti isomer. Considering that the steric interaction between the carboethoxy and the (triethylsilyl)oxy groups may be the more important one within this particular system, the above assumption does seem highly probable.

Treatment of an acetonitrile solution of (silyloxy)cyclopropanecarboxylate esters **9** and **11** with anhydrous potassium fluoride at room temperature resulted in no reaction. The addition of a catalytic amount of 18-crown-6 and the use of higher temperatures, however, provided a quantitative yield of γ-keto esters **12** and **14** after aqueous workup (Scheme IV). It should be mentioned that the use of more acidic desilylating agents such as $(n\text{-}Bu)_4NF$ was deleterious to the reaction of **9**, since the intermediate γ-oxo ester enolate equilibrated with the ketone enolate

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(8) The triethylsilyl (TES) enol ethers exhibited greater stability than the corresponding trimethylsilyl (Me_3Si) analogues.

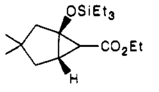
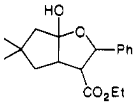
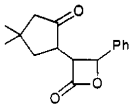
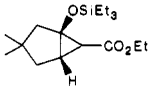
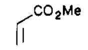
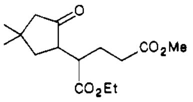
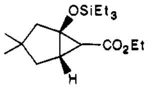
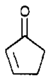
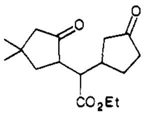
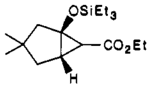
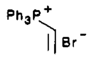
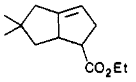
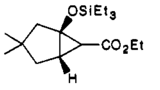
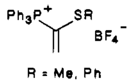
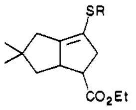
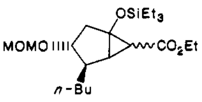
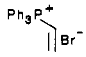
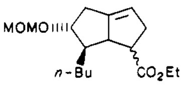
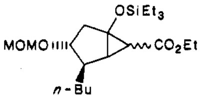
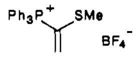
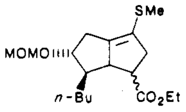
(9) (a) Dave, V.; Warnhoff, E. W. *Org. React.* **1970**, *18*, 217. (b) Kirmse, W. *Carbene Chemistry*, 2nd ed.; Academic: New York, 1971. (c) Moser, W. R. *J. Am. Chem. Soc.* **1969**, *91*, 1135 and references therein.

(10) **8**. See footnote 9 of: Marino, J. P.; Laborde, E. *J. Am. Chem. Soc.* **1985**, *107*, 734. **10**. Exon, C.; Nobbs, M.; Magnus, P. *Tetrahedron* **1981**, *37*, 4515.

(11) Gaudemer, A. In *Stereochemistry: Fundamentals and Methods*; Kagan, H. B., Ed.; Georg Thieme: Stuttgart, 1977; Vol. 1.

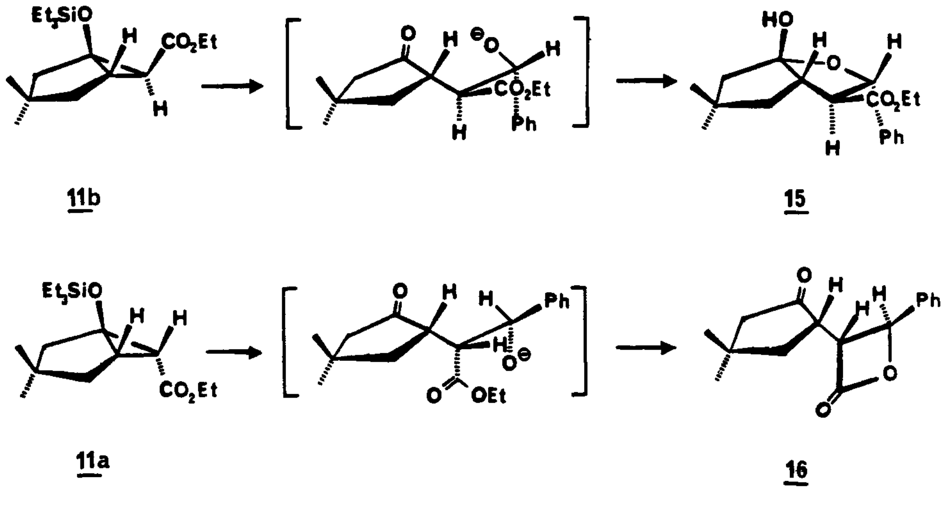
(12) For reviews on the stereochemistry of carbene and carbenoids additions to double bonds, see: (a) Moss, R. A. In *Selective Organic Transformations*; Thyaragajan, B. S., Ed.; Wiley-Interscience: New York, 1970; Vol. 1, pp 35ff. (b) Closs, G. L. *Structures of Carbenes and the Stereochemistry of Carbene Additions*; Eliel, E. L., Allinger, N. L., Eds.; Interscience: New York, 1968; Vol. 3, pp 193 ff. (c) Jones, M., Jr.; Ando, W.; Hendrick, M. E.; Kulczycki, A., Jr.; Howley, P. M.; Hummell, K. F.; Malament, D. S. *J. Am. Chem. Soc.* **1972**, *94*, 7469. (d) Dave, V.; Warnhoff, E. W. *Org. React.* **1970**, *18*, 217.

Table I[a]

entry	(silyloxy)cyclopropane ester	electrophile	product(s) (yield, %)
1	 **11**	PhCHO	 **15** (10)  **16** (15)
2	 **11**		 **17** (42)
3	 **11**		 **18** (33)
4	 **11**		 **19** (80)
5	 **11**		 **20**, R = Me (91) **21**, R = Ph (80)
6	 **9**		 **22** (75)
7	 **9**		 **23** (80)

[a] The 2-(silyloxy)cyclopropanecarboxylate esters **9** and **11** were used as mixtures of diastereoisomers.

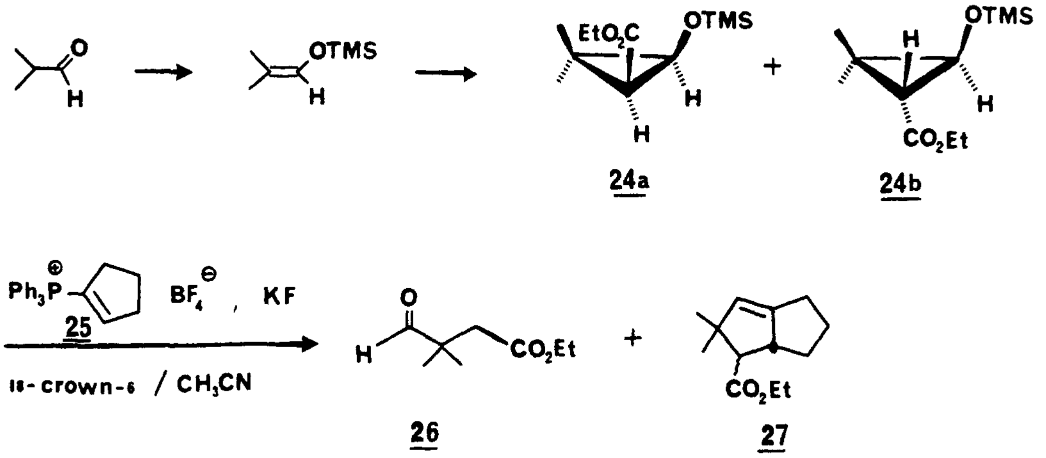
Scheme V



that, in turn, underwent β-elimination to afford the corresponding cyclopentenone **13**.

Our first prediction, then, had been proven true. Under conditions that increase its solubility in organic solvents, potassium fluoride cleanly effects desilylation with concomitant opening of the cyclopropane ring. The next step in confirming the intermediacy of a γ-oxo α-ester enolate in this process required the trapping of such an enolate with a suitable electrophile. The results obtained to this end are summarized in Table I. The reaction of **11** (2:1 mixture of **11a** and **11b** respectively) with benzaldehyde afforded a ca. 1:1.5 mixture of the expected γ-lactol **15** and the unusual β-lactone **16**. The latter is derived from the attack of the intermediate alkoxide ion onto the ester instead of the ketone carbonyl. Only one isomer of each product was observed on the ^{1}H NMR, indicating that the reaction is highly stereoselective. The spectroscopic data, however, do not allow for unequivocal stereochemical as-

Scheme VI



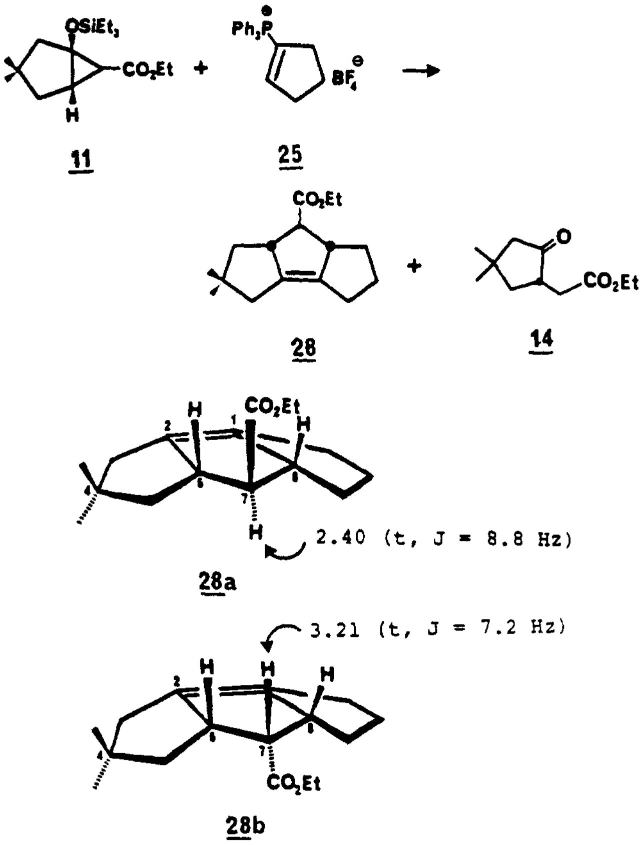
signments but strongly support the structures given below for **15** and **16** (Scheme V).

The product distribution and the observed stereoselectivity of the reaction correlate with the thermodynamic stabilities of the lactol products. Thus, while lactol **15** has the carboethoxy group in a preferred pseudoequatorial position, the isomeric lactol derived from **11a** would require such a group to adopt a hindered pseudoaxial arrangement. Consequently, in the latter case the alkoxide prefers to attack the ester carbonyl to form the β-lactone **16**.

As expected, the reaction of **11** with methyl acrylate (entry 2) and 2-cyclopentenone (entry 3) showed a clean preference for 1,4 addition, which may be attributed to the "soft" nature of the enolate involved. No product arising from a subsequent aldol-type reaction was detected in either case. In entries 4–7, the specific activated alkenes (i.e., vinylphosphonium salts) were chosen so as to generate in situ a Wittig reagent that could react intramolecularly with the ketone carbonyl.[13] This time, the bicyclo[3.3.0]octenes **19–23** were obtained in high yield. In all cases, the products were 1:2 mixtures of α- and β-carboethoxy isomers, respectively, indicating that there is scrambling in the configuration of the carbanionic center during the reaction. The observed ratio, consequently, must reflect the relative stabilities of the two isomeric products. From a synthetic point of view, such a stereochemical outcome is not totally unfortunate, for the less thermodynamically stable α isomer could be epimerized to the β isomer. Alternatively, the carbon atom bearing the ester group could be further elaborated into a carbonyl group.[14]

The potential of this strategy for the construction of bicyclo[3.3.0]octenes led us to examine the reaction of 2-(silyloxy)cyclopropane esters **24** with the cyclic phosphonium salt **25**. The cyclopropane esters were obtained from the addition of carboethoxycarbene onto the trimethylsilyl enol ether of isobutyraldehyde, while the phosphonium salt was prepared according to the procedure given by Minami[15] for the analogous perchlorate salt. The major product of the reaction, however, was the ring-opened γ-oxo ester **26**, derived from protonation of the ester enolate; only a small amount of the bicyclo[3.3.0]octene **27** was obtained (Scheme VI). The low yield of annulated product has been attributed to both the instability of the [(trimethylsilyl)oxy]cyclopropane esters **24** and the somewhat lower reactivity of the cyclic phosphonium salt **25**.

Scheme VII



Synthetic Approaches to Tricyclo[6.3.0.0]undecanes

In an effort to construct a tricyclo[6.3.0.0^{2,6}]undecane ring system as a model for the synthesis of hirsutene type molecules, we examined the reaction of **11** with **25**. Unfortunately, only a 10% yield of tricycloundecene **28** was obtained; the ring-opened cyclopentanone **14** accounted for most of the remaining product (Scheme VII).

The low yield of annulated products, in this particular case, may be rationalized in terms of the unfavorable steric interactions in the *syn*-betaine **29** required for elimination to the alkene. On this basis, the ring fusion in **28** has been assigned as being cis-syn rather than the cis-anti, characteristic of the naturally occurring triquinanes.[16] In-

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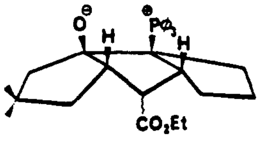
(13) For a related use of vinylphosphonium salts, see: (a) Hewson, A. T. *Tetrahedron Lett.* **1978**, 3267. (b) Hewson, A. T.; MacPherson, D. T. *Ibid.* **1983**, *24*, 5807. (c) Cameron, A. G.; Hewson, A. T. *J. Chem. Soc., Perkin Trans. 1* **1983**, 2979.

(14) Trost, B. M.; Tamaru, Y. *J. Am. Chem. Soc.* **1975**, *97*, 3528.

(15) Minami, T.; Sako, H.; Ikehira, T.; Hanamoto, T.; Hirao, I. *J. Org. Chem.* **1983**, *48*, 2569.



29

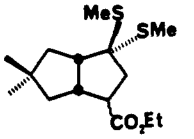
terestingly, both possible isomers of **28** were produced in the reaction. The structural assignments have been made on the recognition that an α orientation of the H7 proton should result in an upfield shift with respect to the other isomer, for in the former case such a proton would be cis to the substituents at C6 and C8 (i.e., the other two five-membered rings).[11]

The above disappointing results, in terms of both yield and stereochemistry of the annulated product, prompted us to investigate an alternative route for the construction of the desired cis-anti tricyclo[6.3.0.0^{2,6}]undecane ring system. Thus, the bicyclooctenyl sulfides **20** were readily hydrolyzed with trifluoroacetic acid in refluxing chloroform[17] to the corresponding bicyclooctanones **30**, which were used as the starting material for a second pentannulation sequence (Scheme VIII). Regiospecific generation of the kinetic enolate of **30** and subsequent trapping with triethylsilyl chloride at low temperature afforded the enol ethers **31** (2:1 mixture of β- and α-carboethoxy isomers, respectively) in 90% yield. Addition of carboethoxycarbene as described before provided the novel oxycyclopropane diesters **32**. These esters were subjected to the [3 + 2] annulation with [(methylthio)vinyl]triphenylphosphonium tetrafluoroborate, to produce the tricyclic vinyl sulfides **33** (mixture of all four isomers) in ca. 45% overall yield from **31**. Finally, hydrolysis of **33** led to the functionalized tricyclo[6.3.0.0^{2,6}]undecanones **34** in 90% yield.

The stereochemical outcome of the above carbene addition deserves some comment. Of the eight possible isomeric tricyclic diesters **32** (four for each arrangement of the three rings; i.e., cis-anti and cis-syn), only two isomers accounted for more than 90% of the product obtained. These two isomers, in turn, were formed in a ca. 2:1 ratio. From their respective ^{1}H NMR spectra, we have determined that the major isomer bears a trans relationship (J = 3.9 Hz) between the cyclopropane protons, while for the minor isomer these two protons are cis oriented (J = 9.8 Hz). Considering the stereochemistry of the starting enol ethers **31** and the preferred approach of the carbene from the less sterically hindered β face of the bicyclic ring system, we have assigned structure **32a** to the major product of the carbene addition and **32b** to the minor one. These assignments, in turn, led to a cis-anti ring fusion of the final products **34**. The present strategy, then, provides a mild and expeditious route for the construction of functionalized tricyclo[6.3.0.0^{2,6}]undecanes, which should prove useful in the synthesis of suitable precursors to the naturally occurring compounds.

The availability of highly functionalized bicyclo[3.3.0]octenes via the fluoride-induced [3 + 2] annulation of 2-(silyloxy)cyclopropane esters with vinylphosphonium salts led us to also consider their application for the construction of the more challenging tricyclo[6.3.0.0^{4,8}]undecane ring system. A recent report[18] on the successful cycloaddition of dichloroketene to vinyl sulfides seemed to offer an expeditious route to the "bent" triquinane system. Thus, it was envisioned that a [2 + 2] cycloaddition of dichloroketene onto vinyl sulfides **20** could provide the tricyclic ketones **35**. Regiospecific one-carbon expansion of the cyclobutanone ring with diazomethane[19] would then set the desired tricyclopentanoid system **36** (Scheme IX).

A major concern regarding the outcome of the cycloaddition came to our attention upon the observation that the examples reported in the literature did not include a trisubstituted vinyl sulfide such as **20**. However, a closer inspection of the reaction showed that the unfavorable steric effects, intrinsic in a compound such as **20**, could be compensated by the known[20] tendency of the bridgehead carbon to undergo rehybridization, presumably leading to a corresponding decrease in the ring strain at this center. In fact, treatment of an ethereal suspension of zinc–copper couple and **20** with trichloroacetyl chloride at reflux afforded the tricyclodecanones **35** (ca. 1.5:1 mixture of β- and α-carboethoxy isomers) in 85% combined yield. It should be mentioned that the use of dichloroketene generated by the dehydrohalogenation method (i.e., from dichloroacetyl chloride and triethylamine) also provided **35**, albeit in a more modest yield (ca. 50%). Interestingly, the thioketal **37** was isolated from the last reaction as a minor product.



37

The next step of the strategy proved to be our Achilles heel. Indeed, treatment of **35** with ethereal diazomethane (ca. 0.1 M generated from Diazald), followed by addition of methanol (5% v/v), resulted in recovery of the starting material as indicated by the infrared absorption at ca. 1800 cm^{-1}, characteristic of the dichlorocyclobutanones. The introduction of a catalytic amount of boron trifluoride to activate the ketone carbonyl toward nucleophilic attack did not change the above result. Such a lack of reactivity of the dichlorocyclobutanones **35** has been attributed to the hindered position of the ketone carbonyl carbon. Indeed, it became apparent not only that this is a bis neopentylic carbon but also that nucleophilic attack from the rear face of the molecule (the less hindered one) would place the oxygen atom on top of the fused cyclopentane rings, developing serious steric interactions with their β substituents in the transition state. In order to alleviate the steric congestion around the ketone carbonyl and, therefore, facilitate the attack by the nucleophile, it was decided to remove the chlorine atoms even at the recognized risk of losing regiocontrol in the subsequent ring expansion step. Thus, a small sample of **35** was reacted with excess zinc–copper couple in refluxing aqueous tetrahydrofuran.[21] Workup and purification provided a mixture of the corresponding cyclobutanones **38** (carbonyl absorptions at 1775 and 1725 cm^{-1}) in 90% yield. Treatment of these with ethereal diazomethane in the presence of boron trifluoride etherate, followed by addition of methanol, afforded four unseparable products. The

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[16] For excellent reviews on polyquinane chemistry, see: (a) Paquette, L. *Top. Curr. Chem.* **1984**, 119. (b) Trost, B. M. *Chem. Soc. Rev.* **1982**, *11*, 141. (c) Demuth, M.; Schaffner, K. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 820. (d) Eaton, P. E. *Tetrahedron* **1979**, *35*, 2189.

[17] Grayson, J. I.; Warren, S. *J. Chem. Soc., Perkin Trans. 1* **1977**, 2263.

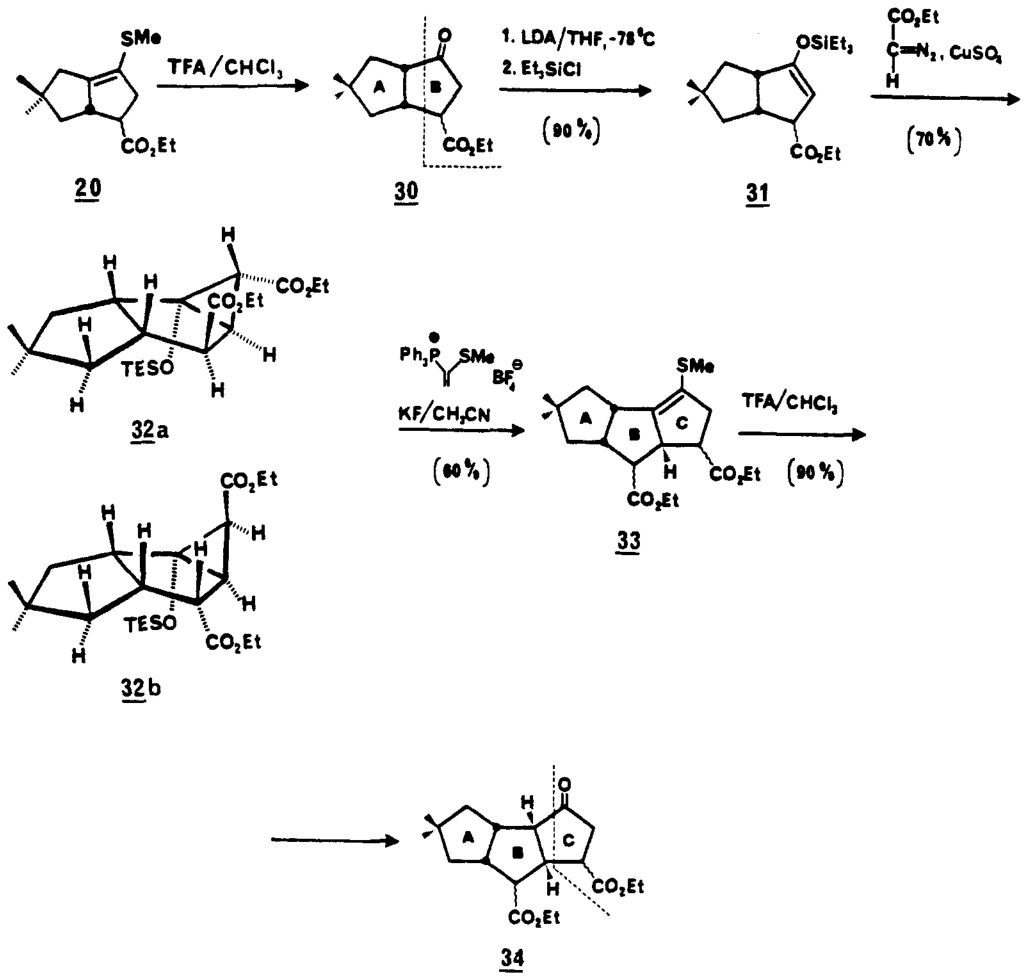
[18] Liebeskind, L. S.; Baysdon, S. L. *Tetrahedron Lett.* **1984**, *25*, 1747.

[19] For example, see: Greene, A. E.; Depres, J.-P. *J. Am. Chem. Soc.* **1979**, *101*, 4003.

[20] Danishefsky, S.; Zamboni, R.; Kahn, M.; Etheredge, S. J. *J. Am. Chem. Soc.* **1981**, *103*, 3460.

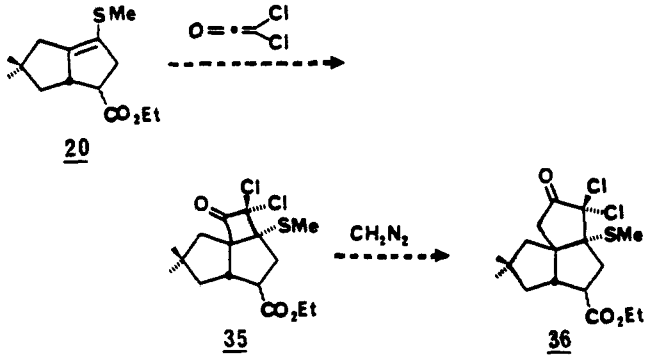
[21] Blankenship, R. M.; Burdett, K. A.; Swenton, J. S. *J. Org. Chem.* **1974**, *39*, 2300.

Scheme VIII[a]

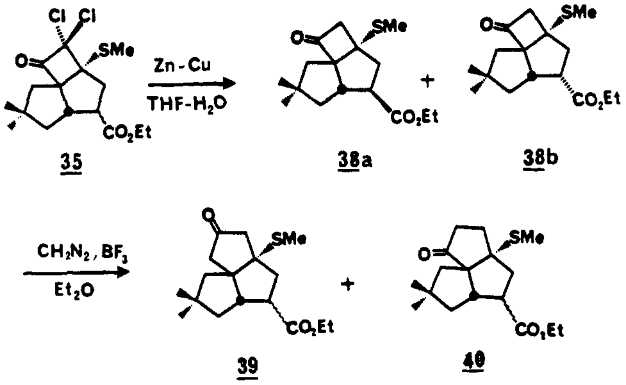


[a] TES = Et$_3$Si.

Scheme IX



Scheme X



GC–MS analysis of this mixture revealed three peaks with M = 310, one more intense than the other two, while its infrared spectrum showed a single and broad carbonyl absorption at ca. 1730 cm^{-1}. These results indicated that the ring expansion had indeed taken place but, not totally unexpected, without regioselectivity (Scheme X).

Concluding Remarks

The fluoride-induced ring opening of 2-(silyloxy)cyclopropanecarboxylate esters, then, provides a simple access to γ-oxo α-ester enolate anions, which can be alkylated with a variety of electrophiles. When the electrophile is an α,β-unsaturated carbonyl compound, there is a clear preference for 1,4 over 1,2 addition, preference that is rationalized in terms of the soft nature of the potassium enolate involved in the reaction. The trapping of such an enolate with a vinylphosphonium salt, on the other hand, allows for a subsequent intramolecular Wittig reaction, affording functionalized cyclopentenes in very good yield. This new strategy for [3 + 2] annulation allows the introduction of the three-carbon synthon as a nucleophile, thus complementing previous approaches to cyclopentenes involving electrophilic cyclopropanes.[22]

Experimental Section

All reactions were conducted under a positive atmosphere of dry nitrogen. Diethyl ether and tetrahydrofuran were distilled from lithium aluminum hydride; dichloromethane and acetonitrile, from calcium hydride. All other commercially available reagents

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[22] (a) Marino, J. P.; Landick, R. C. *Tetrahedron Lett.* **1975**, *4531*. (b) For a review see: Danishefsky, S. *Acc. Chem. Res.* **1979**, *12*, 66.

were used without further purification unless otherwise noted.

Flash chromatography was performed on Baker 40-μm particle diameter silica gel. Other column chromatography was done on Merck 70–230-mesh, Grace 100–200-mesh, or Baker 40–140-mesh silica gel.

Infrared spectra were recorded on either a Perkin-Elmer 727B or 457 grating spectrophotometer; band positions are reported in wavenumbers.

Proton nuclear magnetic resonance (^{1}H NMR) spectra were obtained in CDCl$_3$ solution at 360 MHz on a Bruker WM-360 FT NMR spectrometer; the 7.24 ppm resonance of residual chloroform was used as internal reference. Carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra were measured at 22.5 MHz on a JEOL FX90Q or at 90.4 MHz on a Bruker WM-360 FT NMR spectrometer, in chloroform-*d* solution; the CDCl$_3$ resonance at 77.00 ppm was used as internal reference. In both, ^{1}H NMR and ^{13}C NMR, chemical shifts are reported in δ units downfield from tetramethylsilane. The followed abbreviations are used to described peak patterns when appropriate: br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet.

Low- and high-resolution mass spectra (MS) were obtained on a Finnigan 4021 GCMS/DS and VG 70-250S instruments, respectively. Masses are reported in units of mass over charge (*m/z*); the molecular and base peaks are indicated by (M) and (100%), respectively.

Elemental analyses were performed by Spang Microanalytical Laboratories, Eagle Harbor, MI, or Galbraith Laboratories, Knoxville, TN.

(1α,3α)-4β-*n*-Butyl-2α(β)-carboethoxy-5α-[(methoxymethyl)oxy]-1β-[(triethylsilyl)oxy]bicyclo[3.1.0]hexanes 9a and 9b. A 50-mL round-bottomed flask fitted with a Claisen head bearing a reflux condenser and an addition funnel was charged with 4.90 g (15.6 mmol) of silyl enol ether **8** (10) and 20 mg (0.12 mmoL) of anhydrous copper(II) sulfate. The suspension was heated at 90 °C, and a solution of 2.74 g (24.0 mmoL) of ethyl diazoacetate in 10 mL of anhyrous benzene was added dropwise over a 5-h period. After addition was complete, the reaction mixture was stirred at ca. 30–40 °C for an additional 12 h. The excess solvent was removed under reduced pressure and the residue taken up in petroleum ether and filtered through 50 g of neutral alumina (activity grade III). Concentration of the filtrate afforded a pale yellow oil, which was chromatographed on silica gel (hexane–ethyl acetate, 25:1) to give 0.49 g (10%) of unreacted silyl enol ether, 4.20 g (67%) of **9b**, and 1.15 g (18%) of **9a**.

9a: R_f 0.27 in hexane–ethyl acetate (9:1); IR (CHCl$_3$) 1110, 1180, 1470, 1720; ^{1}H NMR δ 0.62 (6 H, q, J = 7.9 Hz), 0.87 (3 H, t, J = 7.0 Hz), 0.93 (9 H, t, J = 7.9 Hz), 1.26 (3 H, t, J = 7.1 Hz), 1.30–1.39 (6 H, m), 1.58 (1 H, dd, J = 9.8, 1.6 Hz), 2.06 (1 H, dd, J = 9.8, 1.1 Hz), 2.08–2.14 (1 H, m), 2.33 (1 H, dd, J = 13.7, 8.9 Hz), 2.44 (1 H, dd, J = 13.7, 6.7 Hz), 3.32 (3 H, s), 4.04 (1 H, dt, J = 8.9, 6.7 Hz), 4.09–4.18 (2 H, m), 4.56 (2 H, AB, J_{AB} = 6.8 Hz); ^{13}C NMR δ 5.11, 6.57, 13.94, 14.27, 22.72, 30.41, 33.99, 35.01, 35.77, 38.70, 43.63, 55.22, 59.88, 68.17, 85.18, 95.53, 169.58; MS for $C_{17}H_{30}O_5Si$ ($M^+ - C_2H_5$), *m/z* obsd 371.2254, calcd 371.2254.

9b: R_f 0.41 in hexane–ethyl acetate (9:1); IR (CDCl$_3$) 980, 1160, 1465, 1720; ^{1}H NMR δ 0.59 (6 H, q, J = 7.9 Hz), 0.88 (dist t, J = 7.1 Hz), 0.93 (9 H, t, J = 7.9 Hz), 1.24 (3 H, t, J = 7.1 Hz), 1.28–1.37 (6 H, m), 1.84–1.87 (1 H, m), 2.06 (1 H, dd, J = 4.0, 1.3 Hz), 2.12 (1 H, d, J = 4.0 Hz), 2.21 (1 H, dd, J = 14.2, 0.7 Hz, 2.30 (1 H, dd, J = 14.2, 6.8 Hz), 3.28 (3 H, s), 3.78 (1 H, br d, J = 6.8 Hz), 4.10 (2 H, q, J = 7.1 Hz), 4.49 (2 H, s); ^{13}C NMR δ 5.33, 6.63, 13.83, 14.27, 22.61, 29.71, 31.98, 33.50, 35.88, 40.65, 47.85, 55.11, 59.99, 70.66, 80.14, 94.71, 169.64; MS, *m/z* 400 (M), 309, 207, 151, 116, 88, 76, 59 (100%). Anal. Calcd for $C_{21}H_{40}O_5Si$: C, 62.96; H, 10.06. Found: C, 63.06; H, 9.91.

(1α,3α)-2α(β)-Carboethoxy-5,5-dimethyl-1β-[(triethylsilyl)oxy]bicyclo[3.1.0]hexanes 11a and 11b. From 11.1 g (49 mmoL) of silyl enol ether **10** (10), 80 mg (0.50 mmoL) of anhydrous copper(II) sulfate, and 14.0 g (123 mmoL) of ethyl diazoacetate, the above procedure provided 14.5 g (95%) of a 2:1 mixture of **11a** and **11b**, respectively.

11a: R_f 0.40 in hexane–ether (25:1); IR (CDCl$_3$) 1080, 1140, 1290, 1715; ^{1}H NMR δ 0.57 (6 H, q, J = 7.9 Hz), 0.90 (9 H, t, J = 7.9 Hz), 0.98 (3 H, s), 1.14 (3 H, s), 1.23 (3 H, t, J = 7.1 Hz), 1.49–1.56 (2 H, m), 1.73 (1 H, dd, J = 13.6, 2.2 Hz), 1.94 (1 H, d, J = 9.4 Hz), 2.01 (1 H, ddd, J = 9.4, 7.0, 2.4 Hz), 2.27 (1 H, d, J = 13.5 Hz), 4.10 (2 H, complex ABX$_3$); ^{13}C NMR δ 5.16, 6.57, 14.43, 26.24, 31.28, 34.80, 35.99, 37.78, 46.82, 59.50, 73.91, 170.56; MS, *m/z* 313, 312 (M), 228, 151, 115, 91, 87 (100%). Anal. Calcd. for $C_{17}H_{32}O_3Si$: C, 65.33; H, 10.32. Found: C, 65.48; H, 10.44.

11b: R_f 0.20 in hexane–ether (25:1): IR (CDCl$_3$) 1010, 1280, 1370, 1410, 1725; ^{1}H NMR δ 0.56 (6 H, q, J = 8.0 Hz), 0.88 (3 H, s), 0.90 (9 H, t, J = 8.0 Hz), 1.06 (3 H, s), 1.21 (3 H, t, J = 7.1 Hz), 1.33 (1 H, br d, J = 13.5 Hz), 1.64 (1 H, d, J = 4.1 Hz), 1.93 (1 H, dd, J = 13.5, 5.7 Hz), 1.96 (2 H, AB, J_{AB} = 13.5 Hz), 2.17 (1 H, br t, J = 4.4 and 4.7 Hz), 4.06 (2 H, ABX$_3$); ^{13}C NMR δ 5.33, 6.63, 14.27, 30.84, 33.06, 34.36, 36.04, 38.75, 43.14, 51.70, 59.99, 72.99, 169.42; MS, *m/z* 313, 312 (M), 228, 151, 131, 115, 87 (100%), 75, 59. Anal. Calcd. for $C_{17}H_{32}O_3Si$: C, 65.33; H, 10.32. Found: C, 65.12; H, 10.25.

2α(β)-Carboethoxy-3,3-dimethyl-1β-[(trimethylsilyl)oxy]cyclopropanes 24a and 24b. From 9.0 g (62 mmoL) of 2-methyl-1-[(trimethylsilyl)oxy]propene, 112 mg (0.7 mmoL) of anhydrous copper(II) sulfate, and 14.1 g (124 mmoL) of ethyl diazoacetate was obtained 7.0 g (50%) of 2-(silyloxy)cyclopropanecarboxylate esters **24** (2:1 mixture of trans and cis isomers, respectively) as pale yellow oils.

24a: IR (CDCl$_3$) 860, 1045–1100 (br), 1165, 1730; ^{1}H NMR δ 0.09 (9 H, s), 1.02 (3 H, s), 1.21 (3 H, t, J = 7.1 Hz), 1.28 (3 H, s), 1.32 (1 H, d, J = 6.8 Hz), 3.39 (1 H, d, J = 6.8 Hz), 4.05 (2 H, q, J = 7.1 Hz); ^{13}C NMR δ −0.36, 13.18, 14.37, 24.78, 26.18, 30.41, 59.50, 61.99, 169.20; MS, *m/z* 230 (M), 185, 157 (100%), 97, 73. Anal. Calcd. for $C_{11}H_{22}O_3Si$: C, 57.35; H, 9.63. Found: C, 57.06; H, 9.44.

24b: IR (CDCl$_3$) 860, 1150, 1310, 1440, 1725; ^{1}H NMR δ 0.12 (9 H, s), 1.14 (3 H, s), 1.18 (3 H, s), 1.22 (3 H, t, J = 7.1 Hz), 1.41 (1 H, d, J = 3.2 Hz), 3.62 (1 H, d, J = 3.2 Hz), 4.09 (2 H, complex ABX$_3$, J_{AB} = 7.1 Hz); ^{13}C NMR δ −0.41, 14.37, 18.11, 19.74, 29.06, 34.31, 59.99, 63.94, 171.59; MS, *m/z* 230 (M), 185, 157 (100%), 97, 73. Anal. Calcd. for $C_{11}H_{22}O_3Si$: C, 57.35; H, 9.63. Found: C, 57.51; H, 9.83.

General Procedure for the Reaction between 2-(Silyloxy)cyclopropane Esters and Electrophiles. A flame-dried round-bottomed flask fitted with a magnetic stirring bar and a Claisen head bearing a reflux condenser and a pressure-equalizing dropping funnel was charged with 5.0 equiv of anhydrous potassium fluoride, 0.20–0.25 equiv of vacuum-dried 18-crown-6 (1,4,7,10,13,16-hexaoxacyclooctadecane), and 20–25 mL of dry acetonitrile/mmoL of (silyloxy)cyclopropane. The above suspension was heated at reflux in an oil bath, and a solution of 1.5–2.0 equiv of the electrophile and the 2-(silyloxy)cyclopropane carboxylate ester in 10–15 mL of dry acetonitrile/mmoL of the latter was added dropwise from the addition funnel. After the addition was complete, the reaction mixture was stirred under reflux for an additional 12–24 h. The solvent was then removed on a rotary evaporator and the crude product subjected to column chromatography on silica gel using mixtures of hexane and ether as the eluent.

(a) Reaction of 11 with Benzaldehyde. From 313 mg (1.0 mmoL) of **11** and 212 mg (0.20 mL, 2.0 mmoL) of benzaldehyde was obtained 30 mg (10%) of γ-lactol **15** and 39 mg (15%) of butyrolactone **16**.

15: IR (CDCl$_3$) 1020–1060, 1180, 1605, 1725, 3400–3540, 3600; ^{1}H NMR δ 0.79 (3 H, s), 1.12 (3 H, s), 1.20–1.30 (4 H, t and m, J = 7.1 Hz), 1.43 (1 H, m), 2.20 (1 H, dd, J = 16.1, 6.1 Hz), 2.50–2.70 (3 H, m), 4.17 (2 H, q, J = 7.1 Hz), 4.65 (1 H, d, J = 5.8 Hz), 7.28–7.40 (5 H, m); MS for $C_{18}H_{22}O_3$ ($M^+ - H_2O$), *m/z* obsd 286.1570, calcd 286.1569.

16: IR (CDCl$_3$) 1150, 1185, 1735, 1780, 3040–3080; ^{1}H NMR δ 0.89 (3 H, s), 1.00 (3 H, s), 1.89 (1 H, d, J = 17.0 Hz), 2.13–2.22 (1 H, m), 2.20 (1 H, d, J = 17.0 Hz), 2.50–2.59 (1 H, m), 2.64 (1 H, d, J = 15.0 Hz), 3.12 (1 H, d, J = 15.0 Hz), 5.60 (1 H, s), 7.10–7.40 (5 H, m); MS for $C_{16}H_{18}O_3$ (M^+), *m/z* obsd 258.1263, calcd 258.1256.

(b) Reaction of 11 with Methyl Acrylate. From 313 mg (1.0 mmoL) of **11** and 172 mg (2.0 mmoL) of methyl acrylate was obtained 120 mg (42%) of **17** as a pale yellow oil: IR (CDCl$_3$) 1035, 1180, 1740 (br), 2900–3050; ^{1}H NMR δ 1.11 (3 H, s), 1.17 (3 H, s), 1.21 (3 H, t, J = 7.1 Hz), 1.75 (1 H, d, J = 13.9 Hz), 1.83–1.95 (2 H, m), 2.03 (1 H, d, J = 13.9 Hz), 2.30–2.44 (4 H, m), 2.47 (2 H s), 3.63 (3 H, s), 4.08 (2 H, q, J = 7.1 Hz); ^{13}C NMR δ 14.25, 29.16, 31.31, 32.80, 32.93, 40.54, 48.19, 50.11, 51.74, 52.80, 60.66, 171.13, 173.46, 220.58 (one carbon unaccounted for); MS, m/z 285, 284 (M), 197, 165, 151, 83 (100%), 55. Anal. Calcd for $C_{15}H_{24}O_5$: C, 63.36; H, 8.51. Found: C, 63.48; H, 8.47.

(c) Reaction of 11 with 2-Cyclopentenone. From 313 mg (1.0 mmoL) of **11** and 123 mg (1.5 mmoL) of 2-cyclopentenone were obtained 70 mg (35%) of γ-keto ester **14** and 90 mg (33%) of **18** as a pale yellow oil.

18: IR ($CDCl_3$) 1000–1080 (br), 1140, 1250, 1730; ^{1}H NMR δ 1.04–1.23 (7 H, m), 1.24 (3 H, t, $J = 7.1$ Hz), 1.56 (1 H, m), 1.61–1.70 (1 H, m), 1.80–1.92 (1 H, m), 2.06–2.40 (7 H, m), 2.52–2.60 (2 H, m), 4.11 (2 H, q, $J = 7.1$ Hz); MS, m/z 281, 280 (M), 193, 152, 109, 83, 55, 41 (100%). Anal. Calcd for $C_{16}H_{24}O_4$: C, 68.54; H, 8.63. Found: C, 68.60; H, 8.62.

(d) 4α(β)-Carboethoxy-7,7-dimethylbicyclo[3.3.0]oct-1-ene (19). From 313 (1.0 mmoL) of **11** and 738 mg (2.0 mmoL) of triphenylvinylphosphonium bromide was obtained 166 mg (80%) of bicyclooctenecarboxylate esters **19** (2:1 mixture of anti and syn isomers, respectively) as pale yellow oils: IR ($CDCl_3$) 1160, 1190, 1725, 3070; ^{1}H NMR (major isomer) δ 0.90–1.01 (1 H, m), 0.993 and 1.039 (6 H, 2 s), 1.21 (3 H, t, $J = 7.1$ Hz), 1.50 (1 H, dd, $J = 11.9, 7.5$ Hz), 1.88–2.10 (2 H, m), 2.64–2.74 (1 H, m), 2.86–2.93 (1 H, m), 3.15 (1 H, ddd, $J = 9.7, 7.8, 2.0$ Hz), 3.41–3.52 (1 H, m), 4.11 (2 H, q, $J = 7.1$ Hz), 5.16–5.19 (1 H, m), (minor isomer) δ 0.90–1.01 (1 H, m), 1.018 and 1.039 (6 H, 2 s), 1.22 (3 H, t, $J = 7.1$ Hz), 1.73 (1 H, dd, $J = 12.2, 7.9$ Hz), 1.88–2.10 (2 H, m), 2.64–2.74 (2 H, m), 2.76–2.86 (1 H, m), 3.14–3.34 (1 H, m), 4.01 (2 H, q, $J = 7.1$ Hz), 5.12–5.14 (1 H, m); ^{13}C NMR (major isomer) δ 14.37, 30.36, 30.68, 39.13, 39.51, 42.60 (2 C), 44.06, 53.33, 59.93, 117.25, 150.30, 174.57, (minor isomer) δ 14.37, 30.36, 30.68, 40.11, 40.43, 43.14, 46.28, 52.13, 53.76, 60.15, 116.17, 152.19, 175.32; MS, m/z 209, 208 (M), 119, 93, 79 (100%), 55. Anal. Calcd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68. Found: C, 74.89; H, 9.68.

(e) 4α(β)-Carboethoxy-7,7-dimethyl-2-(methylthio)bicyclo[3.3.0]oct-1-ene 20. From 313 mg (1.0 mmoL) of **11** and 844 mg (2.0 mmoL) of [1-(methylthio)vinyl]triphenylphosphonium tetrafluoroborate was obtained 230 mg (90%) of vinyl sulfides **20** (2:1 mixture of anti and syn isomers, respectively) as colorless oils: IR ($CDCl_3$) 1175, 1250–1285, 1725; ^{1}H NMR (major isomer) δ 0.97–1.15 (1 H, hidden dd), 1.05 and 1.06 (6 H, 2 s), 1.24 (3 H, t, $J = 7.1$ Hz), 1.73 (1 H, dd, $J = 11.8, 7.3$ Hz), 1.92–2.12 (2 H, m), 2.24 (3 H, s), 2.73 (1 H, dt, $J = 10.0, 8.7, 8.7$ Hz), 2.81–2.87 (1 H, m), 2.97–3.06 (1 H, m), 3.33–3.41 (1 H, m), 4.13 (2 H, q, $J = 7.1$ Hz), (minor isomer) δ 0.95–1.10 (1 H, m), 1.04 and 1.05 (6 H, 2 s), 1.23 (3 H, t, $J = 7.1$ Hz), 1.51 (1 H, dd, $J = 11.7, 7.1$ Hz), 1.86–1.96 (2 H, m), 2.26 (3 H, s), 2.80–2.88 (1 H, m), 3.08 (1 H, complex d, $J = 15.2$ Hz), 3.17 (1 H, ddd, $J = 9.6, 7.8, 1.8$ Hz), 3.50–3.60 (1 H, m), 4.09 (2 H, ABX_3, $J_{AB} = 7.1$ Hz); ^{13}C NMR (major isomer) δ 14.27, 15.19, 30.08, 30.52, 39.78, 43.03, 43.68, 46.34, 50.51, 54.79, 60.37, 121.85, 147.21, 174.57, (minor isomer) δ 14.27, 15.06, 30.08, 30.52, 39.40, 41.52, 42.60, 43.00, 43.03, 54.03, 60.10, 123.26, 145.91, 174.08. Anal. Calcd for $C_{14}H_{22}O_2S$: C, 66.10; H, 8.72; S, 12.60. Found: C, 65.94; H, 8.71; S, 12.70.

(f) 4α(β)-Carboethoxy-7,7-dimethyl-2-(phenylthio)bicyclo[3.3.0]oct-1-ene (21). From 2.41 g (7.7 mmoL) of **11** and 4.84 g (10.0 mmoL) of [1-(phenylthio)vinyl]triphenylphosphonium tetrafluoroborate was obtained 1.95 g (80%) of vinyl sulfides **21** (2:1 mixture of anti and syn isomers, respectively) as pale yellow oils: IR ($CDCl_3$) 1170, 1280, 1600, 1735, 2900–3100; ^{1}H NMR (more polar isomer) δ 1.09 (6 H, s), 1.18 (1 H, dd, $J = 12.2, 10.2$ Hz), 1.22 (3 H, t, $J = 7.1$ Hz), 1.82 (1 H, dd, $J = 12.2, 7.9$ Hz), 1.97 (1 H, complex d, $J = 18.0$ Hz), 2.10 (1 H, complex d, $J = 18.0$ Hz), 2.70–2.81 (1 H, m), 2.97–3.04 (1 H, m), 3.43–3.52 (1 H, m), 4.11 (2 H, q, $J = 7.1$ Hz), 7.14–7.20 (1 H, m), 7.22–7.29 (4 H, m); ^{13}C NMR (more polar isomer) δ 14.27, 30.19, 30.63, 39.94, 43.47 (2 C), 46.28, 50.89, 54.46, 60.48, 119.53, 126.30, 128.90 (2 C), 129.60 (2 C), 134.80, 155.39, 174.46; MS (more polar isomer), m/z 318, 317, 316 (M), 207, 187, 133 (100%), 91, 77. Anal. Calcd for $C_{19}H_{24}O_2S$: C, 72.11; H, 7.64; H, 7.64; S, 10.13. Found: C, 72.12; H, 7.54; S, 10.10.

(g) 6β-*n*-Butyl-4α(β)-carboethoxy-7α-[(methoxymethyl)oxy]bicyclo[3.3.0]oct-1-ene (22). From 400 mg (1.0 mmoL) of **9** and 740 mg (2.0 mmoL) of triphenylvinylphosphonium bromide was obtained 221 mg (74.6%) of bicyclooctenes **22** (2:1 mixture of anti and syn isomers, respectively).

Major isomer: IR ($CDCl_3$) 1060, 1170, 1680 (small sh), 1730; ^{1}H NMR δ 0.86 (3 H, dist t, $J = 7.0$ Hz), 1.24 (3 H, t, $J = 7.1$ Hz), 1.21–1.60 (7 H, m), 2.36 (1 H, complex ddd, $J = 16.8, 6.4, 1.6$ Hz), 2.57 (1 H, complex ddd, $J = 16.9, 8.3, 2.7$ Hz), 2.76–2.87 (4 H, m), 3.35 (3 H, s), 3.96 (1 H, ddd, $J = 8.3, 6.6, 5.0$ Hz), 4.13 and 4.14 (2 H, 2 q, $J = 7.1$ Hz), 4.60 (2 H, AB, $J_{AB} = 6.8$ Hz), 5.17–5.18 (1 H, m); ^{13}C NMR of 13.94, 14.27, 23.10, 29.49, 31.82, 32.14, 41.24, 50.94, 51.86, 55.44, 57.44, 60.31, 85.50, 95.85, 116.68, 147.91, 175.59; MS, m/z 296 (M), 234, 119, 105, 91, 79, 45 (100%). Anal. Calcd for $C_{17}H_{28}O_4$: C, 68.89; H, 9.52. Found: C, 68.77; H, 9.44.

Minor isomer: IR ($CDCl_3$) 1045, 1155, 1690 (small sh), 1730; ^{1}H NMR δ 0.89 (3 H, br t, $J = 7.0$ Hz), 1.24 (3 H, t, $J = 7.2$ Hz), 1.22–1.38 (5 H, m), 1.48–1.54 (2 H, m), 1.63–1.70 (1 H, m), 2.18 (1 H, complex ddd, $J = 14.6, 6.0, 1.9$ Hz), 2.60 (1 H, complex ddd, $J = 14.9, 8.3, 2.0$ Hz), 2.74–2.87 (3 H, m), 3.15 (1 H, ddd, $J = 8.7, 6.7, 2.0$ Hz), 3.35 (3 H, s), 3.98 (1 H, dt, $J = 6.0, 7.9, 7.9$ Hz), 4.10 (2 H, complex ABX_3), 4.61 (2 H, AB, $J_{AB} = 6.8$ Hz), 5.27–5.30 (1 H, m); MS for $C_{17}H_{28}O_4$ (M^+), m/z obsd 296.1989, calcd 296.1987.

(h) 6β-*n*-Butyl-4α(β)-carboethoxy-7α-[(methoxymethyl)oxy]bicyclo[3.3.0]oct-1-ene (23). From 400 mg (1.0 mmoL) of **9** and 634 mg (1.5 mmoL) of [1-(methylthio)vinyl]triphenylphosphonium tetrafluoroborate was obtained 273 mg (80%) of vinyl sulfides **23** (2:1 mixture of anti and syn isomers, respectively) as slightly yellow oils. Column chromatography on silica gel using hexane–ether (10:1) provided an analytically pure sample of the major isomer: IR ($CDCl_3$) 1045, 1115, 1725, 2800–3000; ^{1}H NMR δ 0.85 (3 H, dist t, $J = 6.9$ Hz), 1.25 (3 H, t, $J = 7.1$ Hz), 1.20–1.58 (7 H, m), 2.23 (3 H, s), 2.14–2.28 (1 H, m), 2.59 (1 H, ddd, $J = 17.2, 8.5, 2.1$ Hz), 2.81–2.99 (4 H, m), 3.36 (3 H, s), 3.97 (1 H, dt, $J = 5.8, 8.0, 8.0$ Hz), 4.13 (2 H, 2 q, $J = 7.1$ and 7.2 Hz), 4.61 (2 H, AB, $J_{AB} = 6.8$ Hz); ^{13}C NMR δ 14.00, 14.27, 15.02, 23.10, 29.60, 32.47, 36.48, 48.61, 49.32, 51.65, 55.33, 57.55, 60.58, 83.23, 95.80, 114.97, 146.67, 174.30. Anal. Calcd for $C_{18}H_{30}O_4S$: C, 63.12; H, 8.83; S, 9.36. Found: C, 62.85; H, 8.86; S, 9.24.

4α(β)-Carboethoxy-3,3-dimethylbicyclo[3.3.0]oct-1-ene (27). From 2.3 g (10.0 mmoL) of (silyloxy)cyclopropane esters **24** and 6.4 g (15.4 mmoL) of phosphonium salt **25** were obtained 103 mg (65%) of ethyl 3,3-dimethyl-4-oxobutanoate (**26**) and 200 mg (10%) of bicyclooctenes **27** as a mixture of diastereoisomers.

26: ^{1}H NMR δ 1.01 (3 H, s), 1.88 (3 H, t, $J = 7.1$ Hz), 1.24 (3 H, s), 2.52 (2 H, 2 s), 4.07 (2 H, ABX_3, $J_{AB} = 7.1$ Hz), 9.51 (1 H, s). Anal. Calcd for $C_8H_{14}O_3$: C, 60.78; H, 8.93. Found: C, 60.75; H, 9.01.

27: ^{1}H NMR δ 1.19–1.23 (10 H, t and m, $J = 7.1$ Hz), 2.33–2.60 (7 H, m), 4.08 (2 H, q, $J = 7.1$ Hz), 5.36 (1 H, br s). Anal. Calcd for $C_{13}H_{20}O_2$: C, 75.02; H, 9.68. Found: C, 74.98; H, 9.70.

***cis*,*syn*-7α(β)-Carboethoxy-4,4-dimethyltricyclo[6.3.0.0^{2,6}]undec-1-enes 28a and 28b.** From 313 mg (1.0 mmoL) of (silyloxy)cyclopropanecarboxylate esters **11** and 832 mg (2.0 mmoL) of phosphonium salt **25** were obtained 140 mg (71%) of γ-keto ester **14** and 25 mg (10%) of a mixture of epimeric tricycloundecenes **28**.

28a: R_f 0.15 in hexane–ether (40:1): IR ($CDCl_3$) 1380, 1470, 1725, 2860–3020; ^{1}H NMR δ 1.026 (3 H, s), 1.033 (3 H, s), 1.11 (1 H, dd, $J = 12.2, 9.5$ Hz), 1.19 (1 H, dd, $J = 8.7, 3.1$ Hz), 1.24 (3 H, t, $J = 7.1$ Hz), 1.68 (1 H, dd, $J = 12.2, 7.9$ Hz), 1.79–2.10 (7 H, m), 2.40 (1 H, t, $J = 8.8$ Hz), 3.39–3.50 (1 H, m), 3.60–3.73 (1 H, m), 4.12 (2 H, q, $J = 7.1$ Hz). Anal. Calcd for $C_{16}H_{24}O_2$: C, 77.43; H, 9.75. Found: C, 77.37; H, 9.68.

28b: R_f 0.30 in hexane–ether (40:1); IR ($CDCl_3$) 1370, 1460, 1725, 2840–3000; ^{1}H NMR δ 1.02 (3 H, s), 1.08 (3 H, s), 1.22 (3 H, t, $J = 7.1$ Hz), 1.34 (2 H, d, $J = 9.1$ Hz), 1.38–1.50 (1 H, m), 1.86–2.20 (7 H, m), 3.21 (1 H, t, $J = 7.2$ Hz), 3.42–3.54 (1 H, m), 3.67–3.80 (1 H, m), 4.06 (2 H, m). Anal. Calcd for $C_{16}H_{24}O_2$: C, 77.43; H, 9.75. Found: C, 77.51; H, 9.70.

4α(β)-Carboethoxy-7,7-dimethylbicyclo[3.3.0]octan-2-one (30). A solution of 1.8 g (7.0 mmoL) of vinyl sulfide **20** in 70 mL of chloroform was treated with 50 mL of trifluoroacetic acid. The resulting mixture was stirred at room temperature for 24 h and then quenched with saturated aqueous sodium bicarbonate. The aqueous layer was decanted and extracted with chloroform. The combined organic extracts were dried over anhydrous magnesium sulfate and concentrated under reduced pressure to provide a yellow oil. Column chromatography on silica gel [hexane–ether (10:3)] afforded a total of 1.26 g (80%) of bicyclooctanones **30** as colorless oils.

Less Polar Isomer: R_f 0.22 in hexane–ether (10:3); IR ($CDCl_3$) 1030, 1195 (br), 1265, 1305, 1730 (br); ^{1}H NMR δ 0.95 and 1.03 (6 H, 2 s), 1.25 (3 H, t, J = 7.1 Hz), 1.20–1.35 (1 H, m), 1.49 (1 H, dd, J = 13.2, 7.3 Hz), 1.78 (1 H, ddd, J = 13.2, 9.8, 1.8 Hz), 1.84 (1 H, ddd, J = 12.9, 7.9, 1.5 Hz), 2.58 (1 H, d, J = 8.2 Hz), 2.59 (1 H, dd, J = 5.8, 1.3 Hz), 2.81–2.88 (2 H, m), 3.02 (1 H, ddd, J = 17.1, 9.3, 3.7 Hz), 4.14 (2 H, q, J = 7.1 Hz); ^{13}C NMR δ 14.31, 27.96, 29.03, 40.29, 41.54, 43.45, 44.52, 44.88, 47.80, 51.32, 60.97, 173.30, 219.24; MS, m/z 210, 179, 163, 151, 114 (100%), 95. Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.64; H, 9.09.

More Polar Isomer: R_f 0.20 in hexane–ether (10:3); IR ($CDCl_3$) 1030, 1370, 1460, 1730 (br), 2860–3000; ^{1}H NMR δ 0.91 and 0.99 (6 H, 2 s), 1.11–1.20 (1 H, m), 1.24 (3 H, t, J = 7.1 Hz), 1.40 (1 H, br dd, J = 12.2, 6.0 Hz), 1.49 (1 H, dd, J = 13.5, 6.0 Hz), 1.79 (1 H, ddd, J = 13.5, 10.3, 1.9 Hz), 2.35 (1 H, complex dd, J = 19.6, 7.3 Hz), 2.65–2.74 (1 H, m), 2.80 (1 H, dd, J = 18.9, 11.0 Hz), 3.16–3.25 (2 H, m), 4.14 (2 H, q, J = 7.1 Hz); ^{13}C NMR 14.25, 27.90, 28.97, 37.55, 40.71, 41.07, 42.32, 43.03, 43.75, 53.22, 60.67, 172.70, 220.02; MS for $C_{13}H_{20}O_3$ (M$^+$), m/z obsd 224.1405, calcd 224.1412.

4α(β)-Carboethoxy-7,7-dimethyl-2-[(triethylsilyl)oxy]bicyclo[3.3.0]oct-2-ene (31). To a magnetically stirred solution of 0.64 g (0.9 mL, 6.3 mmoL) of dry *N*,*N*-diisopropylamine in 120 mL of anhydrous THF, at 0 °C, was added 2.23 mL of *n*-BuLi (2.59 M in hexane, 5.8 mmoL). After 30 min the solution was cooled to −78 °C and 1.18 g (5.3 mmoL) of bicyclooctanone **30** (mixture of anti and syn isomers) dissolved in 10 mL of anhydrous THF was added dropwise. After 1 h at −78 °C, the enolate was quenched with 0.95 g (6.3 mmoL) of triethylsilyl chloride and the reaction mixture allowed to warm to room temperature over 6 h. The solvent was removed on a rotary evaporator and the residue taken up in petroleum ether and filtered through a short column of Florisil. Concentration of the filtrate under reduced pressure provided 1.61 g (90%) of triethylsilyl enol ether **31** as a slightly yellow oil. The ^{1}H NMR of this crude product showed a 2:1 mixture of epimers at C4 as determined by the relative integration of the corresponding vinylic protons. Column chromatography on silica gel [hexane–ether (50:1)] afforded a pure sample of the major isomer: IR ($CDCl_3$) 1185, 1240, 1415, 1450, 1640, 1725; ^{1}H NMR δ 0.67 (6 H, q, J = 7.9 Hz), 0.91 (3 H, s), 0.95 (9 H, t, J = 7.9 Hz), 1.02 (3 H, s), 1.17 (1 H, dd, J = 12.1, 10.2 Hz), 1.22 (3 H, t, J = 7.1 Hz), 1.28–1.34 (1 H, m), 1.60 (1 H, ddd, J = 12.7, 9.0, 2.0 Hz), 1.75 (1 H, ddd, J = 12.1, 8.0, 2.0 Hz), 2.88–2.93 (1 H, m), 3.03 (1 H, dist q, J = 2.4 Hz), 3.06–3.13 (1 H, m), 4.09 (2 H, complex ABX_3), 4.42 (1 H, dist t, J = 2.0 Hz). (note the vinylic proton of the minor isomer that appears at 4.44 ppm); MS for $C_{19}H_{34}O_3Si$ (M$^+$), m/z obsd 338.2273, calcd 338.2277.

***cis*,*anti*-3,5-Di(carboethoxy)-8,8-dimethyl-2-[(triethylsilyl)oxy]tricyclo[4.3.0.0^{2,4}]nonane 32.** The (silyloxy)cyclopropane esters **32** were obtained from 1.55 g (4.6 mmoL) of enol ethers **31**, 11 mg (0.07 mmoL) of copper(II) sulfate, and 1.40 g (12.3 mmoL) of ethyl diazoacetate following essentially the same procedure described for **9**. After chromatographic purification on silica gel [hexane–ether (10:1)] were obtained 200 mg (13%) of starting enol ether, 450 mg (23%) of **32b**, 780 mg (40%) of **32a**, and 115 mg (6%) of a complex mixture of the last two products and at least one other isomer, as determined by ^{1}H NMR.

32b: R_f 0.29 in hexane–ether (15:1); IR ($CDCl_3$) 1160–1200, 1310, 1410, 1725; ^{1}H NMR δ 0.59 (6 H, q, J = 7.9 Hz), 0.88 (3 H, s), 0.90 (9 H, t, J = 7.9 Hz), 1.01 (3 H, s), 1.11 (1 H, dd collapsed to a t, J = 11.4 Hz), 1.21 (3 H, t, J = 7.1 Hz), 1.23 (3 H, t, J = 7.1 Hz), 1.35–1.47 (2 H, m), 1.76 (1 H, dd, J = 12.2, 9.6 Hz), 2.02 (1 H, d, J = 9.8 Hz), 2.40 (1 H, dd, J = 9.8, 0.9 Hz), 2.90 (1 H, dd, J = 17.5, 8.6 Hz), 3.05 (1 H, ddd, J = 8.4, 18.7, 8.0 Hz), 3.15 (1 H, dd, J = 9.6, 0.9 Hz), 4.00–4.18 (4 H, m); ^{13}C NMR δ 5.32, 6.72, 14.28, 14.38, 26.51, 28.84, 32.41, 35.68, 40.61, 42.89, 44.40, 47.68, 48.92, 59.88, 60.14, 73.21, 169.82, 173.88 (one carbon unaccounted for); MS, m/z 424 (M), 378, 321, 191, 115, 91, 87 (100%), 75, 59. Anal. Calcd for $C_{23}H_{40}O_5Si$: C, 65.05; H, 9.49. Found: C, 64.94; H, 9.57.

32a: R_f 0.23 in hexane–ether (15:1); ^{1}H NMR δ 0.59 (6 H, q, J = 7.9 Hz), 0.86–0.95 (12 H, m), 1.04 (3 H, s), 1.22 (6 H, 2 t, J = 7.1 Hz for each), 1.51 (2 H, m), 1.61 (1 H, dd, J = 4.0 Hz), 1.72–1.80 (1 H, m), 2.42 (1 H, m), 2.53 (1 H, d, J = 3.9 Hz), 3.00–3.16 (3 H, m), 4.08 (2 H, q, J = 7.1 Hz), 4.12 (2 H, q, J = 7.1 Hz); ^{13}C NMR δ 5.54, 6.72, 14.17, 14.24, 27.30, 29.74, 33.75, 38.61, 42.06, 43.74, 44.60, 47.51, 50.30, 52.24, 60.56, 60.65, 75.46, 170.79, 175.45; MS, m/z 425, 424 (M), 378, 351 (100%), 191, 115, 75, 59.

5,7-Di(carboethoxy)-10,10-dimethyl-3-(methylthio)tricyclo[6.3.0.0^{2,6}]undec-2-ene (33). This compound was prepared from 380 mg (0.89 mmoL) of (silyloxy)cyclopropanecarboxylate esters **32** and 752 mg (1.78 mmoL) of [1-(methylthio)vinyl]triphenylphosphonium tetrafluoroborate according to the general procedure. Column chromatography of the crude product on silica gel [hexane–ether (10:1)] afforded 196 mg (60%) of the tricyclic vinyl sulfides **33** as a mixture of diastereoisomers: IR ($CDCl_3$) 1000–1120 (br), 1180, 1600, 1720; ^{1}H NMR δ 0.88 (3 H, s), 1.00 (3 H, s), 1.10–1.30 (8 H, m), 1.60–1.80 (2 H, m), 2.20 (3 H, s), 2.24–2.30 (1 H, m), 2.40–3.20 (5 H, m), 3.80–3.86 (1 H, m), 4.05–4.20 (4 H, m); MS for $C_{20}H_{30}O_4S$ (M$^+$), m/z obsd 366.1851, calcd 366.1865.

5,7-Di(carboethoxy)-10,10-dimethyltricyclo[6.3.0.0^{2,6}]undecan-3-one (34). This compound was prepared from 170 mg (0.46 mmoL) of the tricyclic vinyl sulfides **33** and 4.5 mL of TFA according to the procedure described earlier for **30**. Column chromatography on silica gel [hexane–ether (3:1)] provided 140 mg (90%) of the tricyclo[6.3.0.0^{2,6}]undecanones **34** (mixture of diastereoisomers) as colorless oils: IR ($CDCl_3$) 1040–1100 (br), 1190, 1730; ^{1}H NMR δ 0.90 (3 H, s), 1.04 (3 H, s), 1.18–1.33 (6 H, m), 1.70–1.84 (2 H, m), 2.31–2.94 (7 H, m), 2.97–3.06 (2 H, m), 3.44 (1 H, dist q, J = 7.8 Hz), 3.99–4.21 (4 H, m); MS, m/z 337, 336 (M), 195, 161, 128 (100%), 91, 79, 55, 41. Anal. Calcd for $C_{19}H_{28}O_5$: C, 67.83; H, 8.39. Found: C, 67.91; H, 8.36.

6α(β)-Carboethoxy-3,3-dichloro-9,9-dimethyl-4-(methylthio)tricyclo[5.3.0.0^{14}]decan-2-one (35). A 50-mL round-bottomed flask equipped with a magnetic sitrring bar and a Claisen head bearing a reflux condenser and an addition funnel was charged with 196 mg (3.0 mmoL) of zinc–copper couple, 509 mg (2.0 mmoL) of vinyl sulfides **20** (2:1 mixture of anti and syn isomers, respectively), and 16 mL of anhydrous ether. To the above suspension was added a solution of 473 mg (2.6 mmoL) of freshly distilled trichloroacetyl chloride in 6 mL of anhydrous ether over a 30-min period. After the addition was complete, the reaction mixture was stirred at room temperature for 17 h and then gently refluxed for an additional 6 h. Upon cooling, the mixture was filtered through a pad of Celite and the filtrate concentrated under reduced pressure to give an orange oil. This oil was chromatographed on silica gel [hexane–ether (20:1)] to afford 620 mg (85%) of dichlorocyclobutanones **35** as a 1.5:1 mixture of β- and α-carboethoxy isomers, respectively.

Major Isomer: IR ($CDCl_3$) 1000–1050, 1175, 1730, 1800; ^{1}H NMR δ 1.04 (3 H, s), 1.07 (3 H, s), 1.24 (3 H, t, J = 7.1 Hz), 1.27 (1 H, dd, J = 12.3, 9.0 Hz), 1.68 (1 H, dd, J = 13.7, 1.9 Hz), 1.82 (1 H, ddd, J = 12.6, 8.0, 1.9 Hz), 1.92 (1 H, d, J = 13.7 Hz), 2.27 (3 H, s), 2.51 (1 H, dd, J = 14.2, 12.8 Hz), 2.69 (1 H, dd, J = 14.2, 5.4 Hz), 2.96 (1 H, ddd, J = 12.7, 9.6, 5.3 Hz), 3.17 (1 H, dt collapsed to a q, J = 9.4, 8.2, 9.3 Hz), 4.12 (2 H, q, J = 7.1 Hz).

Minor Isomer: IR ($CDCl_3$) 1035, 1265, 1730, 1800; ^{1}H NMR δ 1.05 (3 H, s), 1.09 (3 H, s), 1.25 (3 H, t, J = 7.1 Hz), 1.36–1.42 (2 H, m), 1.79 (1 H, d, J = 14.8 Hz), 2.07 (1 H, d, J = 14.8 Hz), 2.28 (3 H, s), 3.03 (2 H, 2 d, J = 9.7 Hz), 3.20 (1 H, dd, J = 9.7, 7.1 Hz), 3.24–3.31 (1 H, m), 4.13 (2 H, q, J = 7.1 Hz); ^{13}C NMR δ 13.64, 14.32, 29.26 (2 C), 40.55, 41.13, 42.95, 43.48, 45.45, 55.13, 60.98, 67.08, 83.08, 93.50, 171.63, 200.79; MS, m/z 366 (M), 365, 364, 254, 179, 133, 91 (100%), 79, 55, 41. Anal. Calcd for $C_{16}H_{22}O_3SCl_2$: C, 52.60; H, 6.07; S, 8.78; Cl, 19.41. Found: C, 52.47; H, 5.80; S, 8.77; Cl, 19.72.

6α(β)-Carboethoxy-9,9-dimethyl-4-(methylthio)tricyclo[5.3.0.0^{1,4}]decan-2-one (38). A 25-mL round-bottomed flask equipped with a magnetic stirring bar and a reflux condenser was charged with 115 mg (0.3 mmoL) of the dichlorocyclobutanones **35** (mixture of isomers), 392 mg (6.0 mmoL) of zinc–copper couple, 5 mL of THF, and 0.2 mL of water. The above suspension was refluxed for 17 h. Upon cooling, the reaction mixture was filtered through a pad of Celite with ether as the eluent. The filtrate was concentrated on a rotary evaporator to give a cloudy yellow oil that was chromatographed on silica gel [hexane–ether (3:1)] to afford 80 mg (90%) of a mixture of cyclobutanones **38** as a colorless oil.

38a: IR ($CDCl_3$) 1030, 1190, 1725, 1770; ^{1}H NMR δ 1.04 (3 H, s), 1.07 (3 H, s), 1.23 (3 H, t, J = 7.1 Hz), 1.20–1.26 (1 H, m), 1.69–1.81 (3 H, m), 2.07 (3 H, s), 2.51 (1 H, dd, J = 14.0, 9.1 Hz), 2.67 (1 H, dd, J = 14.0, 3.5 Hz), 2.90 (1 H, dt, J = 9.1, 3.3 Hz), 3.03 (1 H, dd, J = 17.1, 0.7 Hz), 3.18 (1 H, d, J = 18.4 Hz), 3.29 (1 H, ddd, J = 11.0, 7.5, 3.3 Hz), 4.12 (2 H, q, J = 7.1 Hz); ^{13}C NMR δ 12.79, 14.14, 27.39, 28.70, 41.72, 42.60, 43.17, 48.05, 49.92, 51.79, 53.72, 56.07, 61.06, 84.55, 174.66, 210.71; MS, m/z 281, 221, 179, 147 (100%), 133, 91, 77, 55, 41. Anal. Calcd for $C_{16}H_{24}O_3S$: C, 64.83; H, 8.16; S, 10.82. Found: C, 64.83; H, 8.25; S, 10.86.

38b: IR (CDCl$_3$) 1035, 1200 (br), 1250, 1730, 1775; ^{1}H NMR δ 1.00 (3 H, s), 1.06 (3 H, s), 1.24 (3 H, t, J = 7.1 Hz), 1.21–1.28 (1 H, m), 1.36 (1 H, dd, J = 12.0, 6.5 Hz), 1.77 (2 H, s), 2.07 (3 H, s), 2.33 (1 H, dd, J = 13.3, 6.5 Hz), 2.48 (1 H, dd, J = 13.3, 12.1 Hz), 3.06–3.20 (4 H, m), 4.13 (2 H, q, J = 7.1 Hz); ^{13}C NMR δ 12.49, 14.25, 27.65, 28.81, 39.18, 40.66, 42.60, 42.71, 44.31, 50.39, 52.13, 55.31, 60.66, 83.44, 172.03, 210.17. Anal. Calcd for $C_{16}H_{24}O_3S$: C, 64.83; H, 8.16; S, 10.82. Found: C, 64.96; H, 8.18; S, 10.75.

Reaction of Cyclobutanones 38 with Diazomethane. A 25-mL round-bottomed flask fitted with a magnetic stirring bar was charged with a solution of 36 mg (0.12 mmoL) of cyclobutanones **38** (mixture of isomers) in 1 mL of anhydrous ether. The above solution was treated dropwise with 6 mL of ethereal diazomethane (ca. 0.1 M, generated from Diazald); no evolution of gas was observed. Addition of 1 drop of freshly distilled $BF_3\cdot Et_2O$ produced a vigorous evolution of gas and concomitant decolorization of the yellow solution. An additional 10 mL of diazomethane was added followed by 2 drops of methanol. After the reaction mixture was stirred for 48 h, the solvent was removed to give 32 mg of a yellow oil which, when subjected to TLC [hexane–ether (3:1)], showed four spots with very similar R_f values. Column chromatography on silica gel [hexane–ether (3:1)] was ineffective in separating the above-mentioned compounds. The ^{1}H NMR of the mixture was, consequently, too complicated to assign. On the other hand, the IR and MS of the mixture provided the following data: IR (CDCl$_3$) 1040, 1180–1210, 1250–1280, 1730; MS, GLC trace showed three peaks with m/z 310, one of them with higher intensity than the other two. The MS patterns of these three peaks, given in order on increasing retention times, are as follows: (a) 311, 310 (M), 263, 262, 217, 205, 189 (100%), 161, 147, 133, 119, 91, 77, 55, 41; (b) 311, 310 (M), 263, 262, 235, 221, 217, 189, 175, 147 (100%), 133, 190, 105, 91, 79, 55, 41; (c) 311, 310 (M), 263, 234, 219, 189, 161, 147 (100%), 131, 119, 105, 77, 55, 41.

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Zinc Salt Catalyzed Rearrangement of Acetals of Optically Active Aryl 1-Chloroethyl Ketones: Synthesis of Optically Active 2-Arylpropionic Acids and Esters[1]

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The preparation of (*S*)-2-(4′-isobutylphenyl)propionic acid ((*S*)-Ibuprofen) (82% optical purity) and (*S*)-2-(6′-methoxy-2′-naphthyl)propionic acid (Naproxen) (96% optical purity) has been accomplished by starting from optically pure (*S*)-2-chloropropionyl chloride. The investigation for finding the best experimental conditions and minimizing racemization phenomena is presented.

2-Arylalkanoic acids and derivatives are pharmaceutically[2] and agriculturally[3] useful products. Most of them contain a chiral carbon atom and one enantiomer usually shows higher biological or pharmaceutical activity. Well-known examples are 2-(6′-methoxy-2′-naphthyl)propionic acid, whose *S* isomer (Naproxen),[2,4] is 28 times as active as the *R* isomer as an antinflammatory agent, 2-(2′-(*p*-fluorophenyl)-5′-benzoxazolyl)propionic acid, whose *S* isomer (Flunoxaprofen)[5] is a new and interesting example of the same class of antiinflammatory drugs, and (*S*)-2-(4′-chlorophenyl)-3-methylbutanoic acid that is an intermediate for the synthesis of the insecticide Fenvalerate.[3,6]

For the preparation of optically active 2-arylalkanoic acids and/or their convenient precursors many different synthetic strategies have been reported as, for example, the use of (a) optically active bases for resolving racemates;[7a] (b) a second-order resolution of diastereomeric derivatives as salts,[7b] esters, anhydrides, amides, or oxazolines;[7c,d,e] (c) biochemical methods (asymmetric hydrolysis of esters[8a] or oxidation of aromatic hydrocarbons[8b]); (d) optically active catalysts in the asymmetric hydrogenation of prochiral unsaturated 2-aryl carboxylic

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