sin $/\lambda$(max), 0.6225 Å^{-1}; 2788 reflections (761 with $I < \sigma(I)$); function minimized, $\sum w\Delta^2$; R, 0.076.

The amount of erigerol available was very small, and it was not possible to prepare large crystals. The only crystal of any practical size (prepared by slow evaporation of a chloroform solution) had dimensions 0.3 × 0.1 × 0.03 mm, and this was used for all X-ray measurements. Since it could not be determined whether radiation damage would cause problems and finding another suitable crystal would be difficult, the intensity data were collected rapidly, allowing a constant time of 30 s for each reflection. In retrospect, a longer counting time would have been possible since there was no evidence of radiation damage, but the data proved adequate for structure solution and refinement. The remainder of the sample was used for spectroscopic experiments, and thus the crystal density was not measured.

The phase problem was solved by the use of programs of MULTAN78[19] and was conducted in parallel by means of the standard convergence method and also by a Monte Carlo method similar to that described by Yao.[20] In contrast to Yao's prescription, all phases generated randomly were given the same weight, and, to avoid prejudicing the course of the calculation, neither the origin nor the enantiomorph were directly specified. As a result of this structure determination and several others, we find ourselves in opposition to Hall and Subramanian[21] who recently stated "it is particularly important that the Monte-Carlo aspects of the multisolution approach are minimized".

The model was refined by using the programs of XRAY72,[22] and all hydrogen atoms were visible in a difference map. The final R factor, using anisotropic parameters, $\exp(-2\pi^2(\sum_i\sum_j U_{ij}a_i^*a_j^*h_ih_j))$, for the heavier atoms and isotropic parameters for the H atoms, was 7.6%. The R factor is quite satisfactory considering the less-than-optimum X-ray intensity data, and, although the esd's of the H atom thermal parameters are fairly large, the results are quite adequate. The atomic parameters for the heavier atoms are given in Table III, and the observed and calculated structure factors were submitted to the referees and may be obtained from J.V.S.

Acknowledgment. This paper is dedicated to Dr. Ulrich Weiss, NIADDK, NIH, on the occasion of his 75th birthday. Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for financial support of this research. We are grateful to Dr. Robert Highet for valuable discussions regarding NMR spectra.

Registry No. 1, 87462-32-6; dihydroerigerol, 87462-33-7; erigerol trimethylsilyl ether, 87507-93-5.

Supplementary Material Available: Tables of atomic parameters for all atoms of erigerol (2 pages). Ordering information is given on any current masthead page.

(19) Main, P.; Hull, S. E.; Lessinger, L.; Germain, G.; Declercg, J. P.; Woolfson, M. M. MULTAN78, a system of computer programs for the solution of crystal structures from X-ray diffraction data, Universities of York and Louvain, 1978.

(20) Yao, J. X. *Acta Crystallogr., Sect. A* **1981**, *37*, 642.

(21) Hall, S. R.; Subramanian, V. *Acta Crystallogr., Sect. A* **1982**, *38*, 598.

(22) Stewart, J. M.; Kruger, G. J.; Ammon, H. L.; Dickinson, C.; Hall, S. R. XRAY72, Computer Center, University of Maryland, College Park, MD, 1972, Report TR-192.

General Method of Synthesis of Cyclopentanoid Terpenic Acids. Stereocontrolled Total Syntheses of (±)-Isocomenic Acid and (±)-Epiisocomenic Acid

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(4β,8α)-1α,2,4β-Trimethyl-9α-carboxytricyclo[6.3.0.0^{4,8}]undec-2-ene (**1**, isocomenic acid) and (4β,8α)-1α,2,4β-trimethyl-9β-carboxytricyclo[6.3.0.0^{4,8}]undec-2-ene (**28**, epiisocomenic acid) were prepared in 10 steps from ester **13**. The internal cyclopropanation of exocyclic acrylates and the subsequent vinylcyclopropane–cyclopentene rearrangement were used in an efficient synthesis of a key intermediate, triquinane **23**, containing all of the contiguous quaternary centers. The utilization of abnormal Reformatsky reaction of 4-bromocrotonates with keto esters served in the preparation of important precursors to the cyclopentene annulation sequence, the lactone **15**, and the dienic acid **19**. Hydrogenation of **23** produced the keto ester **25a**, which was converted in three steps to *either 1 or 28* with complete control of stereochemistry. Carbon-13 data are reported for all intermediates. A total of eight natural products are accessible in a stereocontrolled fashion from keto ester **25a**. The generality of this method is thus addressed in the context of system-oriented design of synthesis of cyclopentanoid terpenes.

Introduction

Terpenoid carboxylic acids containing at least one cyclopentane ring are being isolated in increasing numbers from sources within either the plant or the animal kingdom. Among the better known examples are gibberellic and gascardic acids, zizanoic acid (**2**), retigeranic acid (**3**), and hirsutic acid (**4**). With the exception of sesterterpene **3**, all of these acids became available through the chemical synthesis shortly after their isolation.[2]

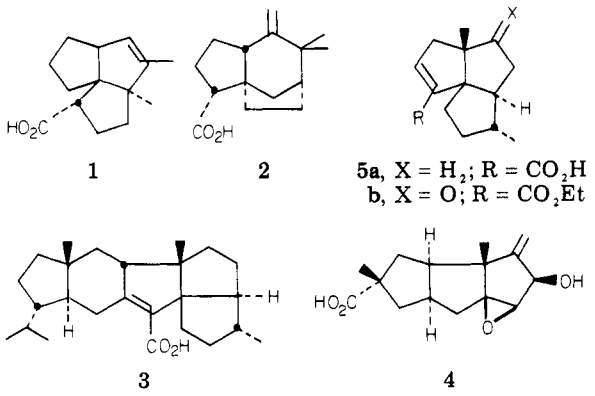
We pursued the design of a method that could be applied not only to the synthesis of all or most of the cyclopentanoid acids but also to the parent hydrocarbon

(1) (a) Fellow of the Alfred P. Sloan Foundation, 1981–3. (b) Work done at I.I.T. Chicago, by J. M. R., on leave from the University of Grenoble, France.

(2) See the following for representative syntheses. **Gibberellic Acid**: Corey, E. J.; Danheiser, R. L.; Chandrasekaran, S.; Keck, G. E.; Gopalan, B.; Larsen, S. D.; Siret, P.; Grass, J. L. *J. Am. Chem. Soc.* **1978**, *100*, 8034. Lombardo, L.; Mander, L. N.; Turner, J. V. *Ibid.* **1980**, *102*, 6626. Hook, J. M.; Mander, L. N.; Urech, R. *Ibid.* **1980**, *102*, 6628. **Gascardic Acid**: Boeckman, R. K., Jr.; Blum, D. M.; Arthur, S. D. *Ibid.* **1979**, *101*, 5060. **Zizanoic acids/khusane-type terpenes**: Oppolzer, W.; Pitteloud, R. *Ibid.* **1982**, *104*, 6478. Liu, H. J. *Can. J. Chem.* **1982**, *60*, 1081. Vettel, P. R.; Coates, R. M. *J. Org. Chem.* **1980**, *45*, 5430. Piers, E.; Banville, J. *J. Chem. Soc., Chem. Commun.* **1979**, 1138. **Retigeranic acid**: The triquinane portion of this molecule has been synthesized. See ref 5 also for compliation of isolation and structure retermination.

0022-3263/83/1948-4453$01.50/0

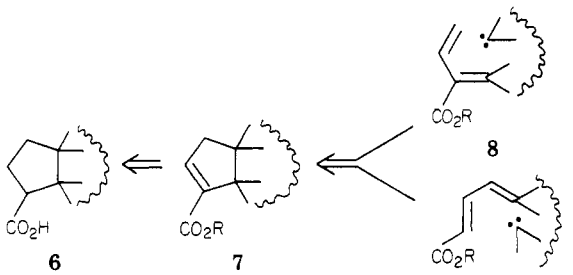
Chart I



1 2 5a, X = H_2; R = CO_2H
b, X = O; R = CO_2Et

3 4

Scheme I



6 7 8

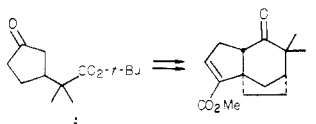
species as well. Since the biogenesis of hydrocarbon terpenes normally precedes the formation of oxygenated species, such method would also provide access to the various reduced forms of the carboxylates and would eventually lead to the parent hydrocarbons. Enzymic systems responsible for the oxidation of zizaene to zizanol, and zizanoic acid, for example, are not understood well enough to allow their ready use in the chemical laboratory. Thus it appears more facile, at least for the moment, to utilize the *reductive* sequence for the synthesis of the parent hydrocarbons.

We chose as targets the various terpenic acids depicted in Chart I for several reasons, the most challenging of which was the presence of multiple quaternary centers in the triquinane skeletons.

In this paper we report the synthesis of isocomenic acids **1** and **28** and compare their preparation[3] with those of zizanoic acid (**2**)[4] and a tricyclic cyclopentene carboxylate **5**, which we prepared as an intermediate in the convergent assembly of retigeranic acid **3**.[5]

(3) These acids have not to date been isolated. We anticipate their existence on the basis of the parallel between hydrocarbons and their oxygenated derivatives found among other classes of terpenes. From such parallels we may expect that only the secondary methyl groups are prone to enzymatic oxidation. The availability of **1** and **28** will facilitate their identification in the extracts of such plant species as *Isocoma Wrightii* and *Berkheya Radula*, the sources of the corresponding sesquiterpene hydrocarbons.

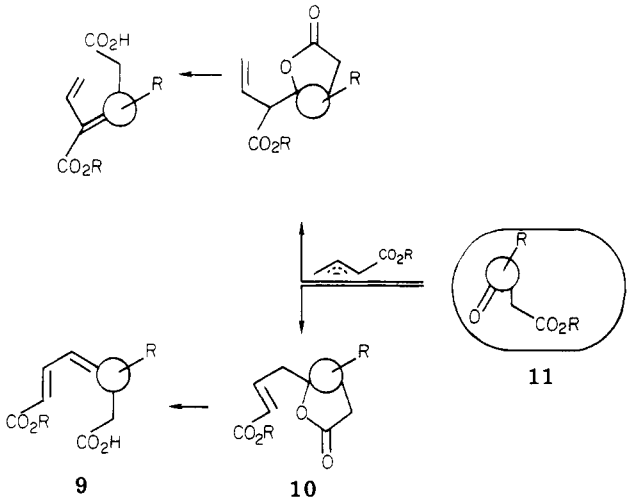
(4) We have recently prepared the tricyclic carboxylate ii as a precursor to zizanoic acids and zizaenes by a route analogous to that employed in the synthesis of **23**. However, this attempt did not prove to be reproducible. In contrast to the synthesis of other fused polycyclic systems, the cyclopropanation–rearrangement sequence leading to bridged structures such as ii is plagued by competing C–H insertions of the carbenoid. Development of a viable alternative is in progress.



i ii

(5) Hudlicky, T.; Short, R. P. *J. Org. Chem.* **1982**, *47*, 1522.

Scheme II[a]



9 10 11

[a] R = CH_3, alkyl.

Results and Discussion

A general method of synthesis must address, in as few steps as possible, the construction of a unit common to all members of a given set. The examination of various terpenic acids revealed the carboxylate **6** as a repeating feature (Scheme I). The analysis of biogenetic schemes for these terpenes also informed us that in most cases the substitution patterns are impressed into a 1,2,2,3- or a 1,2,2,3,3-polysubstituted cyclopentane. At times this either central or peripheral carboxylate ring is also functionalized at positions 4 and 5, as in the cases of gibberellic and retigeranic acids for example. The carboxylate in **6** could be manipulated reductively at the completion of the synthesis to methylols, aldehydes or hydrocarbons as desired.

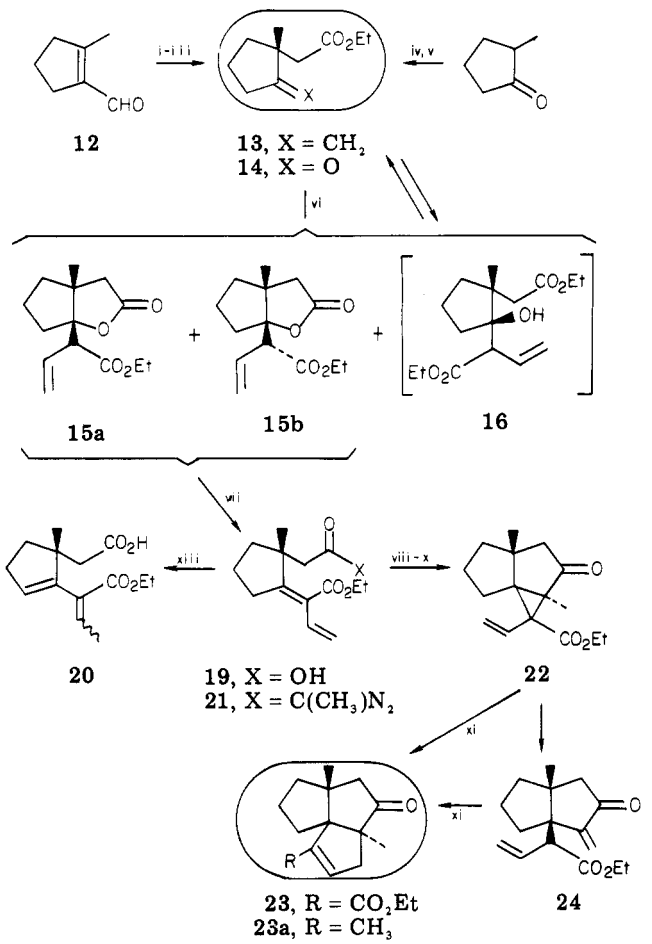
The suitable precursor to **6** is the unsaturated ester **7**, which would impart a control of stereochemistry on the selective formation of the acids. In most structures of type **7** catalytic hydrogenation of the acrylate unit would yield the *less stable* saturated ester due to the approach of hydrogen from the less hindered face of the molecule. The *epimerization* of such an ester should then provide the *more stable* or less hindered carboxylate, therefore allowing controlled access to either diastereomer of **6**.

The cyclopentene carboxylate **7** can in turn be obtained by the well-established cyclopentene annulation sequence involving a suitable dienic diazo ketone possessing either of the regiochemical patterns in **8**.[6] Both patterns, A and B, place the incipient acrylate bond on the unsubstituted periphery of the cyclopentene, thereby simplifying the choice of starting dienes. These dienes can be constructed rapidly and with complete regiochemical control from ketones by utilizing the abnormal (A) or the normal (B) mode of addition of the Reformatsky reagent derived from ethyl 4-bromocrotonate (Scheme II).[7] Since the logical precursor to a diazo ketone is the corresponding acid **9**, both the diene and the acid can be liberated in one operation from a lactone of type **10** that is generated during the Reformatsky reaction of a keto ester **11**.[5] Thus the required key cyclopentene carboxylate **7** is accessible in a few operations from simple starting materials. The

(6) For model studies and applications of this methodology, see, for example: (a) Hudlicky, T.; Koszyk, F. J.; Kutchan, T. M.; Sheth, J. P. *J. Org. Chem.* **1980**, *45*, 5020. (b) Hudlicky, T.; Koszyk, F. J.; Dochwat, D. M.; Cantrell, G. L. *Ibid.* **1981**, *46*, 2911. (c) Hudlicky, T.; Kutchan, T. M.; Wilson, S. R., Mao, D. T. *J. Am. Chem. Soc.* **1980**, *102*, 6351.

(7) For a review of the Reformatsky reaction, see: Rathke, M. W. *Org. React. (N.Y.)* **1975**, *22*, 423.

Scheme III[a]



12 13, X = CH_2; 14, X = O

15a 15b 16

20 19, X = OH; 21, X = $C(CH_3)N_2$ 22

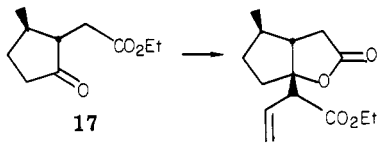
23, R = CO_2Et; 23a, R = CH_3 24

[a] Reagents: (i) $NaBH_4/Et_2O$/MeOH; (ii) $CH_3C(OEt)_3$/$Hg(OAc)_2/CH_3CH_2CO_2H$/220 °C; (iii) O_3, −78 °C, CH_2Cl_2, Zn/HOAc; (iv) Me_3SI/Et_3N; (v) MeLi/$BrCH_2CO_2Et$; (vi) Zn(Cu)/$BrCH_2CH{=}CHCO_2Et/Et_2O$; (vii) DBU/DME/0 °C; (viii) $(COCl)_2$/benzene; (ix) CH_3CHN_2/Et_2O; (x) $CuSO_4/Cu(acac)_2$/benzene/Δ; (xi) Vycor/$PbCO_3$/580 °C; (xii) 450 °C; (xiii) DBU/room temperature.

syntheses performed to date by this method are concerned with the A approach.[5]

We began the synthesis of isocomenic acid with the keto ester **14**,[8] which was obtained via two different routes. The alkylation of an enolate anion derived from the trimethylsilyl enol ether of 2-methylcyclopentanone[9] with ethyl α-bromoacetate gave reasonable yields of **14**, but the product always contained an unknown contaminant that codistilled with the product. Since we had large quantities of aldehyde **12**[10] on hand, we prepared the olefin **13** by a high-yielding orthoester-Claisen rearrangement of the allylic alcohol obtained by the reduction of **12** (Scheme III). The ozonolysis of this olefin provided the keto ester **14** uncontaminated and in an overall yield comparable to or better than that of the alkylation route.

The interaction of keto ester **14** with ethyl 4-bromocrotonate in the presence of the Zn/Cu couple[11] led exclusively to the formation of lactone **15**. Several features of this reaction deserve mention. First, the regiochemical course of the Reformatsky reaction of **14** paralleled that observed in the case of a similar lactone used in the synthesis of **5**.[5] Only the "abnormal" or the "α-mode" of addition took place. We believe that trace amounts of acetic acid remaining on the surface of the catalyst after its preparation render the reaction medium more polar, thus favoring the α-addition of the Reformatsky reagent.[5] The second feature of this reaction was the overall yield of lactone **15**. In the case of lactone **18**, the precursor not only possessed a more available carbonyl but was also optically active. The combination of these two parameters was responsible for the formation of only one diastereomer of **18** in high yield (quantitative reaction, 81% distilled yield).



17 18

The above features were lacking in the keto ester **14**. The highest *reaction yield* of the lactone **15** was 42%, with the remainder of the reaction mixture consisting of the keto ester **14**. From other studies we were aware of the instability of the Reformatsky products containing free hydroxyls.[12] Such compounds decompose to the ketone and ethyl crotonate on workup, on treatment with either acids or bases, or on distillation. No stereoselectivity could be expected in the additions to **14**, since it is likely that an equivalent amount of a trans addition takes place to give hydroxy ester **16**, which does not lactonize and collapses to the starting material during workup. We attempted to acetylate the crude mixtures in order to isolate the corresponding acetates of **16** for precise stereochemical identification but failed, although such acetylations worked quite well on other less hindered substrates.[12] We based the overall yields of lactone on recovered starting material that was recycled after each conversion. The lactone **15** was shown to be a mixture of two diastereomers, **15a** and **15b** (2:1), which were separable by preparative TLC (multiple elutions). Careful, slow addition of DBU to a solution of **15a** and **15b** at 0 °C produced dienic acid **19** as a mixture of *E*/*Z* diastereomers in approximately 1:1 ratio. This ratio was independent of the diastereomeric composition of lactone **15**, each diastereomer giving rise to the identical mixture of acids. If the elimination was carried out at room temperature (or if the base was added in one portion), the isomerized acid **20** could be isolated in varying proportions, again as a mixture of *E*/*Z* isomers (3:1).[13] Prolonged treatment of **19** with base resulted in

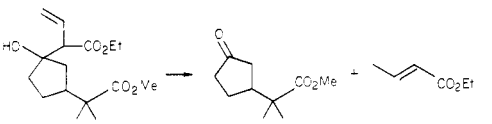
(8) Asselin, A. A.; Humber, L. G.; Dobson, T. A.; Komlosy, J. *J. Med. Chem.* **1976**, *19*, 787.

(9) House, H. O.; Czuba, L. J.; Gall, M.; Olmstead, H. D. *J. Org. Chem.* **1969**, *34*, 2324.

(10) The aldehyde was prepared from 2-methylcyclohexene by using a procedure adapted from: White, J. D.; Ruppert, J. F.; Avery, M. A.; Torii, S.; Nokami, J. *J. Am. Chem. Soc.* **1981**, *103*, 1813.

(11) Santaniello, E.; Manzocchi, A. *Synthesis* **1977**, 698.

(12) The Reformatsky adduct iii encountered during the synthesis of zizanoic acids dissociated readily on distillation or attempted chromatography.



iii

(13) The acid **20** was produced as a mixture of *E*/*Z* isomers. The major isomer (*E*) had the following spectral properties: IR (neat) 3400–2900, 1700, 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.2 (s, 3 H), 1.38 (t, 3 H, *J* = 7 Hz), 1.78 (d, 3 H, *J* = 6 Hz), 1.7–1.9 (m, 2 H), 2.2–2.3 (m, 2 H), 2.36 (br s, 2 H), 4.15 (q, 2 H, *J* = 7 Hz), 5.55 (t, 1 H, *J* = 2 Hz), 7.04 (q, 1 H, *J* = 6 Hz); ^{13}C NMR ($CDCl_3$) δ 14.2 (q), 16.3 (q), 26.2 (q), 30.6 (t), 37.9 (t), 45.3 (t), 50.5 (s), 61.6 (t), 133.9 (s), 134.4 (d), 142.2 (s), 143.3 (d), 168.8 (s), 175.8 (s); mass spectrum (70 eV) *m*/*e*, (relative intensity) 252 (M^+) (13), 222 (40), 206 (50), 193 (32), 192 (50), 178 (42), 164 (58), 147 (60), 146 (45), 133 (32), 126 (36), 109 (75), 108 (55), 91 (43), 79 (22), 77 (29), 69 (26), 55 (27), 45 (29), 43 (B).

its conversion to **20**, indicating extreme dependence of this reaction on precise experimental conditions. The only reproducible results were obtained by a slow addition of base, minimizing its local excess in the reaction mixture. Although we have initially isolated and identified all of the diastereomers involved in the sequence **15–23** and carried these separately to the stage of tricyclic ketone **23**, we have used the mixtures in all of the subsequent reactions since the diastereomeric centers converged in **23**. This simplification proved especially important in the large-scale preparations of acid **19**, which was obtained by the treatment of *crude* lactone **15** (also containing **16**) with DBU. Workup of the basic mixture yielded the dimer of ethyl crotonate and the starting ketone **14**, which was recovered by distillation, whereupon the acidic workup of the aqueous layer yielded acid **19** (80% from **14**, based on the recovery and recycling of **14**). Acid **19** was converted via its acid chloride to diazo ketone **21**, which consisted of two easily separable diastereomers (R_f 0.6 and 0.7, hexane/Et_2O, 3:1) reflecting the composition of acid **19**. Cyclopropanation was performed by adding a dilute solution of **21** to a refluxing slurry of $CuSO_4$/Cu(acac)$_2$ in benzene.[5] Again, the cyclopropanes **22** were easily separated (R_f 0.7 and 0.8) to facililate their spectral assignments. No diastereomeric scrambling took place during the cyclpropanation of *either* diazo ketone in the pure state, indicating either a carbenoid mechanism or an ylide addition followed by alkylation. The latter process would have to proceed with complete stereospecificity. Flash pyrolysis of **22** at 580 °C over a $PbCO_3$-conditioned Vycor column gave tricyclic ketone **23** in 64% yield (GC). If the column temperature was not most carefully controlled *or* if the pyrolysis was carried out too quickly (optimum conditions involved evaporation of 1-g sample over a 10-min period), the α-methylene ketone **24** was present in the mixtures in up to 30% yield. It was, however, convertible to the tricyclic ketone **23**, by further pyrolysis in analogy with the behavior of similar retro-ene products encountered in previous studies.[6] It is noteworthy that **23** differs from **5b** (the ketone-containing precursor to **5a**) only in the position of an angular methyl group. Thus the synthesis and carbon-13 data of **23** helped us confirm the stereochemistry of **5** (see Stereochemical Assignments).

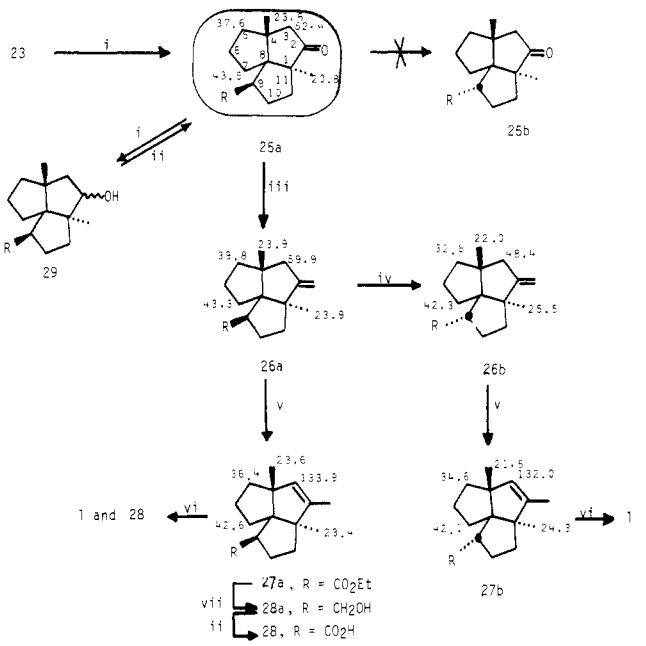
The single diastereomer of acrylate **23** was hydrogenated to **25a** by using PtO_2 as a catalyst (Scheme IV). Although the reaction time was considerably shorter than in the case of Pd(C), the alcohol **29** was sometimes found as a by-product in the hydrogenation mixtures.[14] The amounts of **29** varied (5–50%) and the outcome of the hydrogenation seemed unpredictable. Although the alcohols could be converted to **25a** by an almost quantitative titration with standard Jones reagent, the use of Pd(C) as a catalyst eliminated this extra step at the expense of longer reaction times. No trace of the epimeric ester **25b** could be detected in the hydrogenation product (GC, ^1H and ^{13}C NMR.

This observation contrasted the reported hydrogenation of olefinic ketone **23a**[15] to a saturated ketone with the methyl in the correct β-configuration of isocomene.

The remaining carbon was introduced into the keto ester **25a** via the modified Wittig reaction developed by Conia[16] and recently used by Dauben on a similar carbonyl system.[17] The exposure of **25a** to 2 equiv of methylenetriphenylphosphorane (derived from methyltriphenylphosphonium bromide and sodium *tert*-amylate) in refluxing toluene yielded somewhat surprisingly **26b** as an exclusive product after 2 h. Careful monitoring of the consumption of the starting material revealed formation of another compound (identified by early quenching as **26a**) and its eventual conversion to **26b**. Performing the Wittig reaction at room temperature resulted in a mixture of 26a and **26b** (>9:1 after 6 h) and starting ketone (~30%). The epimeric ratio remained unchanged even after the addition of another equivalent of the Wittig reagent, provided the reaction mixture remained at 25 °C and provided that it was quenched when GC analysis indicated complete consumption of starting ketone. Elevated temperatures or *prolonged* stirring at room temperature led to complete epimerization of **26a** to **26b** through the action of the *tert*-amylate/*tert*-amyl alcohol system present from the generation of the Wittig reagent. In this way **26a** was produced, contaminated by approximately 10% of **26b**. The less stable configuration of the ester group in **26a** was rapidly isomerized (refluxing toluene, sodium *tert*-amylate, *tert*-amyl alcohol; 0.5 h) to **26b**, thereby suggesting that the Wittig reaction preceded epimerization since under identical conditions the ketone **25a** remained inert to equilibration (perhaps a consequence of the presence of another acidic hydrogen in **25a**).

The esters **26a** and **26b** represent the β (or exocyclic) configuration of isocomene terpenes[18] and are convertible not only to the corresponding acids but also to the hydrocarbons.

Scheme IV[a,b]



[a] Reagents: (i) H_2/PtO_2/EtOH; (ii) CrO_3/H^+/acetone; (iii) $-CH_2P^+(Ph)_3$/*tert*-amyl alcohol, sodium amylate/toluene; (iv) sodium amylate/amyl alcohol/toluene/Δ; (v) *p*-TsOH, CH_2Cl_2, room temperature; (vi) KOH/EtOH; (vii) $LiAlH_4/Et_2O$. [b] R = CO_2Et.

(14) Spectral data for alcohols **29**: IR (neat) 3400, 1705 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.96 (s, 3 H), 0.99 (s, 3 H), 1.25 (t, 3 H, J = 7 Hz), 1.4–2.1 (m, 12 H), 2.4 (m, 1 H), 3.42 (dd, 1 H, J = 8 Hz), α-oxomethine), 3.72 (t, 1 H, J = 8 Hz, β-oxomethine), 4.25 (q, 2 H, J = 7 Hz).

(15) Chatterjee, S. *J. Chem. Soc., Chem. Commun.* **1979**, 620.

(16) Conia, J. M.; Limasset, J. C. *Bull Soc. Chim. Fr.* **1967**, *6*, 1936.

(17) Dauben, W. G.; Walker, D. M. *J. Org. Chem.* **1981**, *46*, 1103. We would like to thank Professor Dauben for providing us with a precise and updated experimental for this reaction.

(18) For published syntheses of isocomene, see: ref 15, 17, and 19. Paquette, L. a.; Han, Y. K. *J. Org. Chem.* **1979**, *44*, 4014. Pirrung, M. C. *J. Am. Chem. Soc.* **1979**, *101*, 7130. Paquette, L. A.; Han, Y. K. *Ibid.* **1981**, *103*, 1831 (full paper). Wender, P. A.; Dryer, G. B. *Tetrahedron* **1981**, *37*, 4445. Wenkert, E.; Arrhenius, T. S. *J. Am. Chem. Soc.* **1983**, *105*, 2030.

Either **26a** or **26b** was treated with *p*-TsOH (6 h, CH_2Cl_2, room temperature) and isomerized cleanly to the corresponding α (endocyclic) configurations **27a** and **27b**.[19] It will be at this stage that isocomene and epiisocomene become available by the reduction of the carboxylate.

The ester **27b** was hydrolyzed cleanly to isocomenic acid **1** while **27a** gave a mixture of **1** and its epimer **28**. This epimerization was partially due to the long reaction times necessary for the hydrolysis of the hindered ester moiety in **27a** (6 h, refluxing 20% KOH, EtOH for **27b** vs. 36 h for **27a**). To maintain stereodistinction in the synthesis of **1** and **28**, we reduced **27a** to the alcohol **28a** and then oxidized the alcohol to **28** without any epimerization. In this fashion a complete control of access to either acid was maintained.

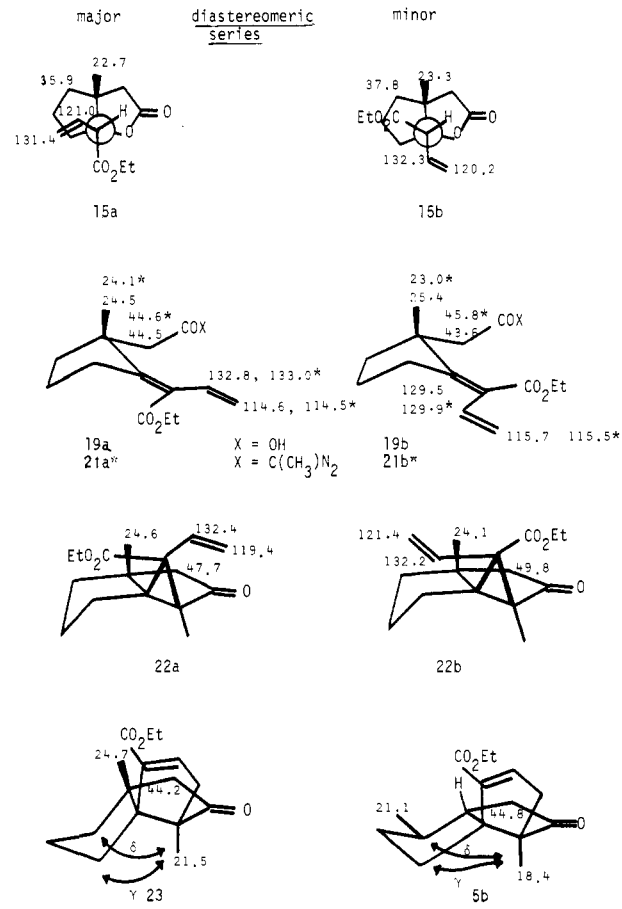
The isocomenic acids synthesized by the above procedure could be reduced to the corresponding methylols or aldehydes at the stage of esters **27**, thus providing access to all or most derivatives at isocomene terpenes.[18] It is probable that only *secondary* methyl groups in isocomene and other sesquiterpenes are subject to oxidation since all combinations of oxidation levels and of their diastereomers are found in other classes of compounds (khusanes, acoranes, cedranes, guaianes) and since it is unlikely that the parent hydrocarbons are produced as diastereomeric mixtures during their biogenesis. It will be illustrative to ascertain the existence of isocomenic acids in the isocomene-producing genera of plants.

Stereochemical Assignments

Carbon-13 chemical shifts of relevant substituents were relied upon in assignment of any diasteromers. Although the diasteromers in the sequence **15–23** converged, we attempted a complete assignment since we may encounter similar compounds in diastereomeric purity during future endeavors. The assignments of threo and erythro epimers of lactones **15** and *E*/*Z* isomers of acids **19**, diazo ketones **21**, and cyclopropanes **22** are based on the shifts of vinyl carbons and of cyclopentane methylenes. The relevant shifts for all compounds are indicated in Chart II and Scheme IV. In each instance the terminal carbon of the vinyl group rests either above a methylene or within the deshielding cone of a carbonyl group. The corresponding average chemical shift difference (~2 ppm) is indicative of *relative* stereochemistry. In the case of acids **19** and diazo ketones **21** and *E*/*Z* assignment becomes difficult, unless an analysis of ^1H NMR is performed. In the *Z* isomer (pictured in Scheme III), the angular methyl group is *deshielded* by the acrylate carbonyl to the extent of 0.5 ppm. This trend remains constant also for the diazo ketones **21**.

The chemical shifts observed in the carbon-13 spectrum of **23** served to further confirm the earlier stereochemical assignment of **5b**.[5] Both angular methyls next to the carbonyls are shielded by the eclipsed methylenes (see arrows in Chart II). In **5b** the methyl group is also *deshielded* by the methine (the combination of these two effects explains why this methyl is not found at ~15–16 ppm as are its counterparts in the model studies).[6c] In **23**, this deshielding interaction is attributed to the methylene, which is even closer to a perfect 1,3-synaxial configuration due to the increased rigidity (and concavity) of the angularly substituted pentalene nucleus. Thus the carbonyl methyl group is displaced by an additional 3 ppm downfield. The shifts of the secondary methyl in **5b** and of the angular methyl in **23** are influenced by the proximity of the ethyl carboxylate (again this effect is more pronounced in **23**).

Chart II



The hydrogenation forces the carboxylate inside the ring system. This compression results in a remarkable deshielding of the α-keto methylene in **25a**. Replacement of carbonyl by exocyclic methylene in **26a** shifts the allylic methylene to 59.9 ppm! (Its signal overlaps that of the ethoxy methylene.) The isomerization of ester **26a** removes this deshielding interaction and results instead in the mutual deshielding of the carboxylate and the angular allylic methyl group in **26b** through a 1,3-synaxial interaction. The methylenes at C-3, C-5, and C-7 as well as the C-4 methyl are shifted upfield as a consequence of the removal of deshielding influence of the carboxylate. The above arguments hold also for the series of endocyclic olefins **27a** and **27b** as well as the acids. The ultimate proof of stereochemistry will become available upon the conversion of **27b** to isocomene by the reduction of the carboxylate entity.

Conclusions

The controlled synthesis of isocomenic acids provides the access to and concludes the synthetic design for most sesquiterpenes related to the isocomene nucleus. Any member of this class can be synthesized from tricyclic ketone **23** as long as the functional diversity involves rings B and C, which are differentiated by the ketone and acrylate moieties. Should ring A be found oxidized (a remote possibility at best, since such oxidation would have to take place at an unactivated carbon *after* the initial closure to the proto-illudane system), the starting keto ester can be functionalized accordingly. Thus the approach to sesquiterpene carboxylates can impart generality to the

(19) Oppolzer, W.; Battig, K.; Hudlicky, T. *Helv. Chim. Acta* **1979**, *62*, 1493; *Tetrahedron* **1981**, *37*, 4359 (full paper).

synthesis of entire classes of cyclopentanoid terpenes. We hope to demonstrate such system-oriented design by repeating the above synthesis on a large scale and by converting the olefinic ester **26a** into the four acids and the four hydrocarbons associated with isocomene, as well as any intermediate oxidation levels that may be of interest in the future.

Experimental Section

Melting and boiling points are uncorrected. ^1H NMR spectra were determined at 90 MHz (Varian EM-390), 200 MHz (JEOL-FX 200), and 300 MHz (Nicolet 300). ^{13}C NMR spectra were recorded at 20 MHz (Varian CFT-20), 15 MHz (JEOL-FX60Q), and 50 MHz (JEOL-FX 200). Chemical shifts are reported in parts per million relative to internal tetramethylsilane or chloroform-*d*. Infrared spectra were obtained on Perkin-Elmer 257, Pye-Unicam 3-300, and Beckman IR 20A-X spectrophotometers. Mass spectra were recorded on a Du Pont 20-491 or a Varian MAT-112 instrument (low resolution) or on a double-focusing Du Pont 21-110C instrument (high resolution and exact mass data).

Gas chromatography was performed on a Varian 3700 instrument (FID, 5% OV-101 on Chromosorb, 50 cm at 30 mL/min N_2).

All solvents were distilled from usual drying agents (Et_2O/$LiAlH_4$; THF, benzene, toluene, DME/K, and benzophenone). All nonhydrolytic reactions were performed under an inert atmosphere and in previously flame-dried glassware.

Chromatography was performed on J. T. Baker Alumina, Macherey Nagle Co. silica gel 60, or silica PF 254 by EM reagents (TLC). Flash chromatography utilized Kiesel gel 60 (230–400 mesh) by EM reagents.

Purity of all compounds was ascertained by GC, TLC, TLC on $AgNO_3$-impregnated silica, and carbon-13 spectra, with emphasis on the latter.

2-Methyl-2-(carbethoxymethyl)methylenecyclopentane (13). 2-Methylcyclopent-1-ene-1-carboxaldehyde (**12**)[10] (6.0 g, 0.054 mol) was dissolved in 50 mL of ethyl ether and cooled to 0 °C. Sodium borohydride (3.0 g, 0.079 mol) was added followed by 5 mL of absolute methanol. The reaction mixture was allowed to attain room temperature and stirred for 12 h (or until complete by TLC), whereupon it was poured into 100 mL of H_2O and 50 mL of CH_2Cl_2 and *carefully* acidified with 3 M HCl until the evolution of hydrogen ceased. The aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL), and the combined organic layer was washed with brine and dried (Na_2SO_4). Evaporation of the solvent in vacuo gave 5.2 g (85%) of clear oil, which was suitable for use in the next step. An analytically pure sample was obtained by distillation: bp 54–60 °C (1.5 mm); IR (neat) 330 cm^{-1}, ^1H NMR ($CDCl_3$) δ 1.7 (br s, 3 H), 1.8 (m, 2 H), 2.3 (m, 4 H), 4.1 (br s, 2 H); ^{13}C NMR ($CDCl_3$) δ 13.2 (q), 21.1 (t), 33.7 (t), 38.3 (t), 58.1 (t), 134.1 (s), 134.6 (s); mass spectrum 70 eV) *m/e*, (relative intensity) 112 (M^+) (50), 97 (80), 81 (80), 79 (B), 67 (45), 55 (50); calcd for $C_7H_{12}O$ 112.0888, found 112.0891.

The above alcohol (3 g, 0.026 mol) was dissolved in 10 mL of triethyl orthoacetate. Propionic acid (150 mg) and $Hg(OAc)_2$ (100 mg) were added, and the mixture was degassed with nitrogen, sealed in a thick-walled Pyrex tube, and heated at 220 °C for 5 h (cooling of the tube to room temperature required an additional 3 h). The crude mixture was taken up in 20 mL of ether and washed with 50% HCl (2 × 15 mL).

The aqueous layer was extracted with ether (2 × 20 mL), and the combined organic extracts were neutralized with $NaHCO_3$, washed with brine, and dried over Na_2SO_4. Evaporation gave 4.3 g (89%) of **13**, which was 94% pure (GC, 140 → 200 °C, 20° min^{-1} OV-101) and could be used in the next step. Distillation gave 3.5 g of pure **13** (bp 70–80 °C (0.5 mm), Kugelrohr) at the expense of extensive polymerization.

Alternatively, a stainless steel autoclave equipped with a glass liner was used for large-scale preparation of **13**. Thus 25 g of alcohol, 100 mL of triethylorthoacetate, 2 mL of propionic acid, and 500 mg of $Hg(OAc)_2$ were heated at 220 °C for 6 h. Workup as above followed by Kugelrohr distillation gave 28 g (68%) of pure **13**: IR (neat) 1730, 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.2 (s, 3 H), 1.28 (t, 3 H, J = 7 Hz), 1.5–2.2 (m, 6 H), 2.4 (s, 2 H), 4.1 (q, 2 H, J = 7 Hz), 4.75 and 4.86 (dt, J = 1.5 Hz); ^{13}C NMR ($CDCl_3$) δ 14.3 (q), 22.4 (t), 26.8 (q), 33.1 (t), 38.8 (s), 39.4 (t), 45.3 (t), 59.9 (t), 104.2 (t), 160.0 (s); mass spectrum (70 eV), *m/e* (relative intensity) 182 (M^+) (2), 180 (6), 153 (9), 139 (14), 125 (10), 111 (25), 109 (71), 108 (30), 95 (29), 93 (39), 79 (40), 67 (30), 55 (38), 43 (B); calcd for $C_{11}H_{18}O_2$; 182.1307, found 182.1301.

2-Methyl-2-(carbethoxymethyl)cyclopentanone (14). A. By Ozonolysis of Ether 13. Either crude or distilled ester **13** (28 g) was dissolved in 200 mL of CH_2Cl_2 and ozonized at −78 °C. The blue color, indicating a saturated solution, persisted after approximately 2 h (Model 03V10-0, OREC Inc., 1.5 L/min). The solution was transfered into an Erlenmeyer flask. Zinc dust (10 g) and glacial acetic acid (20 mL) were added, and the mixture was stirred at room temperature for 2 h. It was filtered, washed with $NaHCO_3$ and brine, dried (Na_2SO_4), and evaporated to give crude **14** as an oil. Distillation gave 21 g (74%) of **14** (bp 78 °C (0.5 mm)).

The concentration of olefin in CH_2Cl_2 did not alter the yield of ketone. However, the customary workup of the ozonides with Me_2S gave ketone **14** in lower yields (<50%). Distillation of those crude mixtures worked up with Me_2S left approximately 50% of the total mass as a polymer.

B. By Alkylation of 2-Methylcyclopentanone. To a suspension of potassium iodide (18.6 g, 0.11 mol) in 100 mL of dry (P_4O_{10}) acetonitrile was added freshly distilled chlorotrimethylsilane (14.2 mL, 0.11 mol), and the mixture was stirred in the dark for 1 h. 2-Methylcyclopentanone[20] (10 g, 0.10 mol) was added followed by triethylamine (15.6 mL, 0.11 mol), and the cloudy brown solution was refluxed in the dark for 2 h.[21]

The cooled mixture was diluted with 200 mL of pentane, washed rapidly with two 100-mL portions of ice-cold saturated aqueous sodium bicarbonate, and dried ($MgSO_4$).

Solvent was removed by distillation at atmospheric pressure, and the residue distilled through a 15-cm Vigreux column at reduced pressure to give 13.9 g (80%) of the silyl enol ether; bp 73–74 °C (27 mm) [lit.[9] bp 78 °C (34 mm)].

Freshly distilled trimethylsilyl enol ether (13.9 g, 0.082 mol) was dissolved in 250 mL of dry tetrahydrofuran and cooled to ice temperature. Methyllithium (1.4 *M* solution in Et_2O, 65 mL, 0.091 mol) was added, and the solution was stirred at ice temperature for 2 h.[24]

The solution was cooled to dry ice–2-propanol temperature, and ethyl bromoacetate (10 mL, 0.90 mol) was added over a 15-min period. Stirring was continued at ca. −70 °C for 1 h, and the mixture was brought to room temperature over 3 h. An additional portion of ethyl bromoacetate was added (1 mL), and after a further 12 h of stirring at room temperature, the mixture was partitioned between 100 mL of ethyl ether and 200 mL of dilute aqueous HCl. The aqueous layer was extracted three times with ethyl ether, and the combined organic extracts were washed successively with water and saturated aqueous sodium bicarbonate and dried ($MgSO_4$).

Solvent was removed in vacuo, and the residue was distilled through a short-path column to give 12.9 g (69% from 2-methycyclopentanone) of keto ester **14**: bp 78 °C (0.5 mm) [lit.[8] bp 63–65 °C (0.5 mm)]; IR (neat) 1730, 1720 (br) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.98 (s, 3 H), 1.1 (t, 3 H, J = 7 Hz), 1.6–2.3 (m, 6 H), 2.37 (AB q, 2 H, J_1 = 12, J_2 = 10 Hz), 4.05 (q, 2 H, J = 7 Hz); ^{13}C NMR ($CDCl_3$ δ 13.7 (q), 18.2 (t), 22.0 (q), 34.4 (t), 36.6 (t), 41.0 (t), 45.6 (s), 64.8 (t), 170.2 (s), 220.7 (s).

Ethyl 2-(Hexahydro-2-oxo-3aα-methyl-2*H*-cyclopenta[*b*]furan-6aα-yl)but-3-enoate (15). Zinc powder (20 g) was stirred at room temperature for 0.5 h in 10 mL of a previously prepared stock solution of copper(II) diacetate monohydrate ($Cu(OAc)_2 \cdot H_2O$, 16 g in 300 mL of acetic acid).[11]

The acetic acid was decanted, and the Zn–Cu couple was washed thoroughly with anhydrous ethyl ether and then covered

(20) House, H. O.; Kramer, V. *J. Org. Chem.* **1963**, *28*, 3362.
(21) This procedure was used to generate trimethylsilyl iodide in situ. For the preparation and the use of this reagent for synthesis of silyl enol ethers, see ref 22 and 23, respectively.
(22) Olah, G. A.; Harang, S. C.; Gupta, B. G. B.; Walhotra, R. *J. Org. Chem.* **1979**, *44*, 1247.
(23) Miller, R. D.; McKean, D. R. *Synthesis* **1979**, 730.
(24) Adapted from: Snitman, D. L.; Tsai, M. Y.; Watt, D. S. *J. Org. Chem.* **1979**, *44*, 2838.

with 10 mL of the same solvent. To this stirred suspension was added keto ester **14** (5.0 g, 0.27 mol) in one portion. Ethyl 4-bromocrotonate (10.5 g, 0.054 mol) was added neat in the following manner: 2.5 g in one portion, followed by iodine crystals (ca. 0.1 g), which initiated a vigorous reaction, 8.0 g, dropwise over 10–12 h via a slow additional funnel. After the addition was complete, the mixture was warmed at reflux for 10–12 h, cooled to room temperature, and partioned between 100 mL of ethyl ether and 200 mL of 3 M HCl. The aqueous layer was extracted three times with 50 mL of ethyl ether, and the combined organic extracts were washed with brine and dried (Na_2SO_4). Solvent was removed in vacuo to give 11.3 g of an oil shown by GC (OV-101, Chromosorb 180–240 °C, 20° min^{-1}) to contain both lactones **15a** and **15b** (42%) as well as ketone **14** (~40%). Analytical samples of **15a** and **15b** were obtained by column chromatography (silica, hexane/Et_2O (3:1)) followed by preparative thin-layer chromatography of the mixture of **15a** and **15b** (six to eight elutions, hexane/Et_2O (3:1)) to give prue analytical samples.

15a (major diastereomer): R_f 0.4; IR (neat) 1770, 1720, 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.25 (s, 3 H), 1.3 (t, 3 H, J = 7 Hz), 1.3 (t, 3 H, J = 7 Hz), 1.8 (m, 4 H), 2.1 (m, 2 H), 2.56 (AB q, 2 H, J_1 = 14, J_2 = 8 Hz), 3.42 (d, 1 H, J = 8 Hz), 4.2 (q, 2 H, J = 7 Hz), 5.35 (d, 1 H, J = 4 Hz), 5.4 (s, 1 H), 6.0 (dd, 1 H, J = 4 Hz); ^{13}C NMR ($CDCl_3$) δ 14.0 (q), 21.9 (t), 22.8 (q), 35.9 (t), 43.0 (t), 44.3 (t), 48.8 (s), 55.0 (d), 61.6 (t), 94.1 (s), 121.0 (t), 131.4 (d), 170.7 (s), 175.8 (s).

15b (minor diastereomer): R_f 0.35; IR (neat) 1170, 1720, 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.2 (s, 3 H), 1.24 (t, 3 H, J = 7 Hz), 1.6–1.9 (m, 4 H), 2.1 (m, 2 H), 2.56 (AB q, 2 H, J_1 = 16, J_2 = 8 Hz), 3.22 (d, 1 H, J = 7 Hz), 4.2 (q, 2 H, J = 7 Hz), 5.3 (d, 1 H, J = 6 Hz), 5.4 (d, 1 H, J = 4 Hz), 6.0 (dd, 1 H, J = 4 Hz); ^{13}C NMR ($CDCl_3$) δ 13.9 (q), 21.8 (t), 23.3 (q), 37.8 (t), 44.2 (t), 44.6 (t), 45.9 (s), 54.8 (d), 61.0 (t), 96.8 (s), 120.2 (t), 132.3 (d), 170.2 (s), 175.1 (s); mass spectrum (70 eV), m/e (relative intensity) 252 (M^+) (40), 236 (35), 208 (70), 207 (70), 139 (B), 111 (40), 83 (30), 69 (25), 54 (B); calcd for $C_{14}H_{20}O$ 252.1361, found 252.1369.

[1α-Methyl-2-(vinylcarbethoxymethylene)cyclopentyl]-acetic Acid (19). A. From Purified Lactones. Lactone **15** (either diastereomer, 3.0 g, 0.012 mol) was dissolved in 30 mL of dry dimethoxyethane, and the stirred solution was cooled to 0 °C. 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU, 2.0 g, 0.013 mol) in 10 mL of DME was added dropwise over a 5-min period, and the dark reddish brown mixture was stirred for an additional 40 min, with constant cooling. *Ice-cold* 1 N HCl (ca. 50 mL) was added in one portion, followed by 100 mL of methylene chloride, and the light yellow mixture was stirred for 10 min. and then poured into 100 mL of 3 N HCl. The organic layer was separated, and washed three times with 50 mL of 3 N HCl, and dried (Na_2SO_4). Solvent was removed in vacuo to give 2.75 g (92%) of crude acids **19**. For analytical samples, this mixture was chromatographed (flash chromatography, silica, EtOAc) and furnished pure diastereomers.

19a (major diastereomer): R_f 0.8; IR (neat) 3400–2800, 1710, 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.28 (s, 3 H), 1.32 (t, 3 H, J = 7 Hz), 1.6–1.9 (m, 4 H), 2.0–2.2 (m, 2 H), 2.6 (AB q, 2 H, J_1 = 14, J_2 = 8 Hz), 4.26 (q, 2 H, J = 7 Hz), 4.98 (d, 1 H, J = 8 Hz), 5.12 (br s, 1 H), 6.32 and 6.52 (dd, 1 H, J = 8 Hz); ^{13}C NMR ($CDCl_3$) δ 14.0 (q), 21.6 (t), 24.5 (q), 32.1 (t), 40.2 (t), 41.5 (t), 44.7 (s), 60.9 (t), 114.6 (t), 126.5 (s), 132.8 (d), 152.8 (s), 169.2 (s), 177.1 (s).

19b (minor diastereomer): R_f 0.75; IR (neat) 3400–2900, 1710, 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.3 (t, 3 H, J = 7 Hz), 1.4 (s, 3 H), 1.6–2.2 (m, 6 H), 2.5 (m, 2 H), 4.22 (q, 2 H, J = 7 Hz), 5.08 (d, 1 H, J = 8 Hz), 5.15 (d, 1 H, J = 2 Hz), 6.58 and 6.74 (dd, 1 H, J = 8 Hz); ^{13}C NMR ($CDCl_3$) δ 14.0 (q), 22.9 (t), 25.4 (q), 34.6 (t), 42.4 (t), 43.6 (t), 44.4 (s), 60.5 (t), 115.7 (t), 126.5 (s), 129.5 (d), 153.7 (s), 170.2 (s), 178.1 (s); mass spectrum (70 eV), m/e (relative intensity) 252 (M^+) (30), 207 (85), 193 (40), 165 (B), 146 (50), 139 (65), 119 (80), 118 (40), 91 (90), 79 (40), 55 (50); calcd for $C_{14}H_{20}O_4$ 252.1361, found 252.1362.

B. From Keto Ester 14. In practice the crude mixture of lactones, starting ketone, and the dimer of ethyl crotonate was treated with DBU, the acids were isolated by extraction, and the neutral layer was subjected to recovery and recycling of keto ester **14**. A representative procedure is given below.

A 10.4-g sample of the crude mixture (from 4.5 g of ketone) containing lactones **15a** and **15b** was dissolved in 100 mL of dry dimethoxyethane and cooled to 0 °C. To this stirred solution was added 5.0 g of DBU in 25 mL of DME, dropwise over a 10-min period, and the dark brown mixture was stirred an additional 40 min with constant cooling. Ice-cold 1 N HCl (ca. 100 mL) was added in one portion, followed by 200 mL of methylene chloride, and the stirring was continued for 10 min. The light yellow mixture was poured into 200 mL of 3 N HCl, and the organic layer was separated, washed three times with dilute aqueous acid, and then dried (Na_2SO_4). Solvent was removed in vacuo and the residue was dissolved in 100 mL of ethyl ether. The ethereal solution was extracted five times with 50 mL of 5% aqueous NaOH, and the combined basic extracts were washed twice with 50 mL of ether and acidified with concentrated HCl. This aqueous solution was extracted five times with CH_2Cl_2, and the combined extracts were dried (Na_2SO_4) and solvent was removed in vacuo to give 2.55 g of acids **19a** and **19b** (41% from keto ester **14**).

The combined ethereal extracts were washed twice with dilute aqueous acid and then brine and dried (Na_2SO_4). Solvent was removed in vacuo to give 7.5 g of an oil, fractional distillation of which yielded 2.16 g of keto ester **14** (bp 78 °C (0.5 mm)); the yield of acids based on recovered ketone is 80%.

3-Diazo-1-[1α-methyl-2-(vinylcarbethoxymethylene)-cyclopent-1-yl]butan-2-one (21). Dienic acids **19** (2.15 g, 0.0085 mol) were dissolved in 40 mL of dry benzene. Freshly distilled oxalyl chloride (1.5 mL, 0.017 mol) was added in one portion, and the mixture was stirred at room temperature for 2.5 h. Completion of reaction was ascertained by concentrating an aliquot in vacuo and examining its IR spectrum. Acid chloride: IR (neat) 1800, 1715, 1620 cm^{-1}.

Ethereal diazoethane was prepared by the slow addition (at 0 °C) of *N*-nitrosomethylurea (4.0 g, 0.034 mol) to a two-phase system consisting of 15 mL of 50% aqueous potassium hydroxide and 40 mL of ethyl ether. The solution was swirled as addition proceeded, and after 15 min the ethereal layer was decanted onto KOH pellets for drying at 0 °C. After 0.5 h, the solution was again decanted into a precooled flask, and 1 mL of dry triethylamine was added.

To this mixture was added dropwise with cooling and stirring acid chloride (2.15 g, 0.08 mol) in 20 mL of anhydrous ether. The resulting cloudy suspension was stirred an additional 0.5 h at 0 °C and filtered with suction through a medium frit. The clear filtrate was concentrated in vacuo, diluted with 3:1 hexane/Et_2O, and filtered through basic alumina (10 g, 60–200 mesh, Brockman activity I), eluting with the same solvent. Concentration of the eluent in vacuo gave 2.38 g (96%) of mixed diazo ketones suitable for use in the next step. The two diastereomers could be separated by either column chromatography or preparative TLC (hexane-/Et_2O, 3:1) for identification.

Note that the preparation of diazo ketones proved to be extremely sensitive to precise experimental conditions. The purity of the starting acid and acid chloride and the reaction time as well as the time of filtration all contributed to variations in yields (75–95%) upon repetition of this work.

21a (major diastereomer): R_f 0.6; IR (neat) 2080, 1710, 1620 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.31 (s, 3 H), 1.40 (t, 3 H, J = 7 Hz), 1.6–2.0 (m, 4 H), 2.0 (s, 3 H), 2.0–2.2 (m, 2 H), 2.8 (AB q, 2 H, J_1 = 18, J_2 = 8 Hz), 4.28 (q, 2 H, J = 7 Hz), 5.0 (d, 1 H, J = 8 Hz), 5.2 (d, 1 H, J = 2 Hz), 6.5 (dd, 1 H, J = 8 Hz); ^{13}C NMR ($CDCl_3$) δ 8.3 (q) 14.1 (q), 21.8 (t), 24.1 (q), 32.1 (t), 40.3 (t), 44.6 (t), 52.8 (s), 46.2 (s), 60.7 (t), 114.5 (t), 126.0 (s), 133.0 (d), 153.8 (s), 169.2 (s), 192.8 (s).

21b (minor diastereomer): R_f 0.5; IR (neat) 2240, 2080, 1750, 1710, 1620 cm^{-1}; ^{H} NMR ($CDCl_3$) δ 1.26 (t, 3 H, J = 7 Hz), 1.4 (s, 3 H), 1.6–2.0 (m, 4 H), 1.85 (s, 3H), 2.0–2.2 (m, 2 H), 2.7 (m, 2 H), 4.15 (q, 2 H, J = 7 Hz), 5.0 (d, 1 H, J = 8 Hz), 5.3 (m, 1 H), 6.6 (dd, 1 H, J = 8 Hz); ^{13}C NMR ($CDCl_3$) δ 8.4 (q), 14.3 (q), 21.9 (t), 23.0 (q), 34.7 (t), 40.3 (t), 44.3 (s), 45.8 (t), 54.2 (s), 60.2 (t), 115.5 (t), 126.0 (s), 129.9 (d), 151.0 (s), 171.0 (s), 192.0 (s); mass spectrum (70 eV), m/e (relative intensity) 290 (M^+) (10), 272 (60), 234 (50), 216 (b), 205 (70), 139 (50), 97 (60), 73 (40), 55 (B); calcd for $C_{16}H_{22}N_2O_3$ 290.1630, found 290.1642.

(1α,6α)-1α,4β-Dimethyl-5β-carbethoxy-5α-vinyltricyclo-[4.3.0.0^{4,6}]nonan-3-one (22a) and Its 5α,5β Isomer (22b). A solution of diazo ketones **21** (2.0 g, 0.0069 mol) in 25 mL of dry benzene was added over a 10-min period to 200 mL of refluxing benzene containing 8 g of anhydrous cupric sulfate and 0.3 g of

copper(II) acetoacetonate. The mixture was kept at reflux for 2.0 h, cooled to room temperature and filtered with suction through a medium glass frit. The filtrate was concentrated in vacuo and dissolved in anhydrous ethyl ether, and the resulting suspension was filtered through a plug of basic alumina. This filtrate was concentrated in vacuo to give 1.7 g (94%) of crude vinylcyclopropanes. Distillation (Kugelrohr 110–160 °C bath temperature (0.07 mm)) gave 1.1 g (61%) of vinylcyclopropanes as a clear oil, suitable for use in pyrolysis. An arduous separation using preparative TLC (hexane/Et_2O, 3:1, multiple elution) furnished analytical samples of vinylcyclopropanes.

22a (major diastereomer): R_f 0.8; IR (neat) 1710 (br), 1610 cm^{-1}; ^1H NMR ($CDCl_3$) δ (t, 3 H, J = 7 Hz), 1.05 (s, 3 H), 1.12 (s, 3 H), 1.25, 1.6–2.4 (m, 6 H), 2.18 (m, 2 H), 4.15 (q, 2 H, J = 7 Hz), 5.2–5.4 (m, 3 H); ^{13}C NMR ($CDCl_3$) δ 8.6 (q), 13.9 (q), 20.9 (t), 23.2 (t), 24.6 (q), 37.4 (s), 40.4 (s), 41.9 (t), 45.2 (t), 47.7 (t), 54.6 (s), 61.4 (t), 119.2 (t), 132.4 (d), 168.6 (s), 214.0 (s); mass spectrum (70 eV), m/e (relative intensity) 262 (M^+) (B), 234 (50), 217 (22), 205 (27), 189 (42), 178 (22), 173 (20), 161 (65), 160 (28), 159 (23), 149 (42), 147 (36), 139 (54), 133 (56), 119 (40), 105 (75), 91 (54), 77 (37), 69 (36), 55 (72), 43 (61), 41 (74); calcd for $C_{16}H_{22}O_3$ 262.1569, found 262.1574.

22b (minor diastereomer): R_f 0.7; ^1H NMR ($CDCl_3$) δ 1.18 (t, 3 H, J = 7 Hz), 1.19 (s, 3 H), 1.20 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 9.3 (q), 14.1 (q), 20.8 (t), 21.3 (t), 24.1 (q), 30.9 (s), 36.9 (s), 42.2 (t), 45.5 (s), 49.8 (t), 57.0 (s), 60.9 (t), 121.4 (t), 132.2 (d), 167.0 (s).

(4β,8α)-1α,4β-Dimethyl-9-carbethoxytricyclo[6.3.0.0^{4,8}]undec-9-en-2-one (23). A. From Vinylcyclopropanes 22. A sample of **22** (1 g, 0.0038 mol) was evaporated (590 °C (0.05 mm)) through a horizontally situated Vycor tube (1 m, 1-cm i.d.) that was thoroughly cleaned (nitric acid; 50% KOH) and pretreated with a slurry of $PbCO_3$. The pyrolysate was condensed in a trap cooled with liquid nitrogen. The pyrolysis on this scale took approximately 10 min. Faster evaporation or lower *local* temperature resulted in the production of **24** (see below). The apparatus was thoroughly washed with CH_2Cl_2; the solution filtered to remove inorganic impurities, and the solvent evaporated to give 940 mg (94% mass balance) of orange oil shown to consist of **23** (64%), some dienone byproducts (25%), and small volatile fragments (10%). The mixture was chromatographed (silica, hexane/Et_2O, 3:1) to obtain pure **23** (a single diastereomer) as an oil: 570 mg, 57%; IR (neat) 1730, 1705, 1620 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.06 (s, 3 H), 1.18 (s, 3 H), 1.3 (t, 3 H, J = 7 Hz), 1.6–2.2 (m, 6 H), 2.26 (m, 2 H), 2.6 (m, 2 H), 4.2 (q, 2 H, J = 7 Hz), 6.7 (t, 1 H, J = 2 Hz); ^{13}C NMR ($CDCl_3$) δ 14.2 (q), 21.5 (q), 24.5 (t), 24.7 (q), 30.6 (t), 40.9 (t), 44.2 (t), 49.5 (s), 51.7 (t), 59.9 (s), 60.1 (t), 68.9 (s), 139.5 (s), 141.8 (d), 165.3 (s), 221.3 (s); mass spectrum (70 eV); m/e (relative intensity) 262 (M^+) (96), 234 (10), 217 (23), 216 (27), 206 (22), 189 (40), 188 (29), 178 (B), 166 (54), 165 (35), 161 (42), 160 (29), 149 (23), 145 (24), 138 (17), 119 (40), 105 (60), 93 (43), 91 (71), 77 (40); calcd for $C_{16}H_{22}O_3$ 262.1569, found 262.1576.

At times the oven temperature fluctuated slightly, thereby lowering the *local* oven temperature sufficiently to produce varying amounts of the retro-ene product **24**. These compounds are normally formed from *cis*-methylvinylcyclopropanes in the range 450–520 °C.[25] The exocyclic α-methylene ketone **24** could be isolated (up to 30% yield in some mixtures) by flash chromatography or preparative TLC. (R_f in hexane/Et_2O (3:1), **23** 0.7; **24** 0.77).

24: IR (neat) 1710, 1690, 1610 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.15 (s, 3 H), 1.22 (t, 3 H, J = 7 Hz), 1.6–2.2 (m, 6 H), 1.8 (d, 3 H, J = 7 Hz), 2.52 (AB q, J_1 = 18, J_2 = 12 Hz), 4.05 (q, 2 H, J = 7 Hz), 5.15 (s, 1 H), 5.9 (s, 1 H), 6.56 (q, 1 H, J = 7 Hz); ^{13}C NMR ($CDCl_3$) δ 14.2 (q), 16.2 (q), 24.2 (t), 25.8 (q), 42.9 (t), 45.2 (t), 48.0 (s), 53.3 (t), 60.3 (s), 60.6 (t), 117.3 (t), 135.5 (d), 139.4 (s), 157.2 (s), 170.5 (s), 207.1 (s); mass spectrum (70 eV), m/e (relative intensity) 262 (M^+) (B), 247 (15), 234 (14), 216 (28), 169 (29), 168 (26), 175 (20), 174 (17), 173 (16), 147 (21), 145 (20), 119 (16), 108 (22), 91 (28), 79 (16), 77 (17), 55 (15); calcd for $C_{16}H_{22}O_3$ 262.1569, found 262.1564.

B. By Pyrolysis of Ketone 24. A sample of pure **24** (collected over several experiments) 0.300 g, 0.011 mol) was evaporated at 590 °C through the Vycor tube under the conditions described above. The pyrolysate contained ~60% of tricycle **23**, which was isolated by preparative TLC.

(4β,8α)-1α,4β-Dimethyl-9β-carbethoxytricyclo[6.3.0.0^{4,8}]undecan-2-one (25a). Unsaturated ester **23** (0.262 g, 0.001 mol) was dissolved in 10 mL of absolute ethanol, 50 mg of PtO_2 was added, and the mixture was agitated on a Parr hydrogenator under 50 psi of H_2 for 10 h. Filtration and evaporation of the solvent gave 0.264 g (100%) of **25a** as a clear oil. Distillation (Kuglerohr, 110–130 °C (0.05 mm)) gave 0.248 g (94%) of pure **25a** as a single diastereoisomer; IR (neat) 1730 (br) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.05 (s, 3 H), 1.15 (s, 3 H), 1.28 (t, 3 H, J = 7 Hz), 1.6–2.2 (m, 10 H), 2.3 (br s, 2 H), 2.8 (t, 1 H, J = 6 Hz), 4.2 (q, 2 H, J = 7 Hz); ^{13}C NMR ($CDCl_3$) δ 14.1 (q), 20.8 (q), 23.1 (t), 23.6 (q), 27.1 (t), 34.4 (t), 37.6 (t), 43.5 (t), 46.9 (s), 52.4 (t), 53.3 (d), 60.3 (t), 61.9 (s), 64.3 (s), 173.9 (s), 221.1 (s); mass spectrum (70 eV), m/e (relative intensity) 264 (M^+) (19), 222 (75), 218 (20), 180 (38), 163 (37), 107 (56), 106 (33), 95 (24), 93 (25), 91 (21), 79 (23), 40 (B); calcd for $C_{16}H_{24}O_3$ 264.1725, found 264.1735.

(4β,8α)-1α,4β-Dimethyl-9β-carbethoxy-2-methylenetricyclo[6.3.0.0^{4,8}]undecane (26). Keto ester **25a** (130 mg, 0.0005 mol) was added to a suspension of methylenephosphorane generated in a manner described below for the preparation of **26b**.[17,26] The reaction mixture was stirred at room temperature for 6 h (GC analysis showed 7% of **26b**, 60% of **26a**, and 30% of starting material). Another 2 equiv of the Wittig reagent (from 0.357 g of methyltriphenylphosphonium bromide and 0.8 mL of a 1.5 M solution of sodium *tert*-amylate) were prepared and *added to* the reaction mixture. Stirring was continued at ambient temperature for precisely 2.5 h (at this time the GC spectrum of an aliquot indicated complete consumption of **25a**). The reaction was worked up as described below for **26b** and the crude oil likewise chromatographed. The eluents corresponding to **26a** were treated with methyl iodide to give after filtration 105 mg (81%) of **26a** as an oil, which later solidified to waxy crystals. The only contaminant was **26b** (10–15%): IR (neat) 1720, 1650, 910, 810, 760, 740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.04 (s, 3 H), 1.08 (s, 3 H), 1.28 (t, 3 H, J = 7 Hz), 1.5–2.1 (m, 10 H), 2.2 (br AB q, 2 H); ^{13}C NMR ($CDCl_3$) δ 14.1 (q), 23.9 (q), 23.9 (q), 27.1 (t), 35.0 (t), 39.8 (t), 43.6 (t), 49.4 (t), 51.5 (s), 52.6 (d), 56.5 (s), 59.9 (t), 59.9 (t), 66.2 (s), 101.4 (t), 160.2 (s), 174.6 (s); mass spectrum (70 eV), m/e (relative intensity) 262 (M^+) (40), 220 (70), 189 (80), 147 (B), 133 (60), 119 (65), 115 (70), 95 (80); calcd for $C_{17}H_{26}O_2$ 262.1933, found 262.1938.

(4β,8α)-1α,4β-Dimethyl-9α-carbethoxy-2-methylenetricyclo[6.3.0.0^{4,8}]undecane (26b). A. From Ketone 25a. Methyltriphenylphosphonium bromide (357 mg, 0.001 mol) was suspended in 1 mL of dry toluene under argon in a previously flame-dried apparatus. A toluene solution of freshly prepared sodium *tert*-amylate (0.8 mL of a 1.5 M solution) was added and the resulting yellow suspension stirred at room temperature for 20 min. Keto ester **25a** (130 mg, 0.0005 mol) in 1 mL of toluene was added dropwise over period of 2 min. The yellow-brown reaction mixture was brought to reflux over the next 5 min and maintained so for 2 h, whereupon it was cooled and quenched with 3 mL of saturated NH_4Cl solution and extracted with ether (3 × 10 mL). The combined organic extracts were washed once with saturated NH_4Cl and dried with $MgSO_4$. Evaporation of solvents yielded a viscous oil, which was immediately filtered through silica gel (1 × 25 cm) with hexane/Et_2O (97:3). The eluent was evaporated to give 129 mg of an oil, which was dissolved in 1 mL of hexane. Methyl iodide (1 mL) was added and the mixture allowed to stand at room temperature for 1 h. Filtration removed the precipitated methyltriphenylphosphonium iodide and the filtrate was concentrated in vacuo to give 108 mg (83%) of pure **26b** as a single diastereomer: IR (neat) 1715, 1640, 790, 745, cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.10 (s, 3 H), 1.16 (s, 3 H), 1.28 (t, 3 H, J = 7 Hz), 1.7–2.1 (m, 10 H), 2.28 (AB q, 2 H, J_1 = 11, J_2 = 16 Hz),

(25) Hudlicky, T.; Koszyk, F. J. *Tetrahedron Lett.* **1980**, *21*, 2487.

(26) The toluene solution of sodium *tert*-amylate was prepared as follows: *tert*-amyl alcohol (100 mL) containing sodium (2 g) was refluxed until all of the metal dissolved. The alcohol was then distilled from this mixture. Excess sodium (4 g) was placed in freshly distilled (potassium benzophenone) toluene (100 mL), and the dry amyl alcohol (17.2 g, 0.2 M) was added. The mixture was refluxed 12 h and cooled and the sodium shot allowed to settle. Titration of this solution gave amylate concentrations of 1.9–2.1 M. The solution darkened over a few days even when stored under N_2 but retained its concentration of base.

2.93 (t, 1 H, J = 4 Hz), 4.1 (q, 2 H, J = 7 Hz), 4.7 (br s, 2 H); ^{13}C NMR ($CDCl_3$) δ 14.3 (q), 22.0 (q), 24.1 (t), 25.5 (q), 29.4 (t), 32.8 (t), 43.3 (t), 42.8 (t), 48.4 (t), 49.3 (s), 51.5 (d), 55.6 (s), 59.9 (t), 67.6 (s), 101.9 (t), 160.6 (s), 175.8 (s); mass spectrum (70 eV), m/e (relative intensity) 262 (M^+) (B), 246 (20), 220 (25), 189 (95), 180 (40), 147 (60), 133 (60), 119 (55), 106 (60), 104 (50), 95 (80); calcd for $C_{17}H_{26}O_2$, 262.1933, found 262.1933.

B. By Isomerization of **26a**. A sample of **26a** (10 mg) was added to excess sodium *tert*-amylate in toluene (1 mL of a 2.1 M solution). The mixture was refluxed for 2 h and worked up as above to give 85 mg (85%) of pure **26b**.

(4β,8α)-1α,2,4β-Trimethyl-9β-carbethoxytricyclo-[6.3.0.0^{4,8}]undec-2-ene (27a). The exocyclic olefin **26a** (100 mg, 0.00038 mol) was dissolved in 3 mL of dry CH_2Cl_2 containing 10 mg of *p*-TsOH as a catalyst. The reaction mixture was stirred at room temperature for 8 h, quenched with 2 mL of saturated $NaHCO_3$ solution, and extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were dried (Na_2SO_4), filtered through a plug of silica gel (4 × 2 cm), and evaporated to give 88 mg (88%) of pure **27a** as an oil: IR (neat) 1735, 810 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.00 (s, 3 H), 1.01 (s, 3 H), 1.28 (t, 3 H, J = 7 Hz), 1.72 (d, 3 H, J = 1 Hz), 1.6–2.2 (m, 10 H), 2.5 (m, 1 H), 4.15 (q, 2 H, J = 7 Hz), 4.85 (br s, 1 H); ^{13}C NMR ($CDCl_3$) δ 12.8 (q) 14.0 (q), 23.4 (q), 23.6 (q), 26.9 (t), 29.5 (t), 35.2 (t), 36.4 (t), 42.6 (t), 52.1 (d), 56.0 (s), 59.8 (t), 61.1 (s), 67.1 (s), 133.9 (d), 142.1 (s), 174.7 (s); mass spectrum (70 eV), m/e (relative intensity) 262 (M^+) (20), 220 (68), 189 (40), 147 (B), 133 (15), 119 (20), 95 (25); calcd for $C_{17}H_{26}O_2$ 262.1933, found 262.1928.

(4β,8α)-1α,2,4β-Trimethyl-9α-carbethoxytricyclo-[6.3.0.0^{4,8}]undec-2-ene (27b). An identical procedure was applied to **26b** (30 mg, 3 mL of CH_2Cl_2, 8 mg of *p*-TsOH). Filtration as described above yielded 28 mg (93%) of pure **27b** as an oil: IR (neat) 1725, 850, 800 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.05 (s, 3 H), 1.06 (s, 3 H), 1.2 (t, 3 H, J = 7 Hz), 1.6–2.1 (m, 10 H), 1.52 (d, 3 H8 J = 1 Hz), 2.8 (br m, 1 H), 4.0 (q, 2 H, J = 7 Hz), 4.8 (br s, 1 H); ^{13}C NMR ($CDCl_3$) δ 13.1 (q), 14.3 (q), 21.5 (q), 2490 (t), 24.3 (q), 28.4 (t), 34.1 (t), 38.4 (t), 42.1 (t), 52.4 (d), 57.3 (s), 59.7 (t), 60.5 (s), 64.1 (s), 132.0 (d), 143.8 (s), 175.9 (s); mass spectrum (70 eV), m/e (relative intensity) 262 (M^+) (20), 246 (10), 220 (70), 189 (25), 172 (15), 147 (B), 133 (15), 119 (20), 95 (20); calcd for $C_{17}H_{26}O_2$ 262.1933, found 262.1948.

(4β,8α)-1α,2,4β-Trimethyl-9α-carboxytricyclo[6.3.0.0^{4,8}]-undec-2-ene (1, Isocomenic Acid). Ester **27b** (68 mg, 0.26 mmol) was refluxed in 5 mL of 20% KOH/EtOH for 6 h. The reaction mixture was diluted with water and extracted with ether to remove traces of unreacted ester. Acidification of the aqueous layer and extraction with CH_2Cl_2, drying, and evaporation gave 40 mg (66%) of acid **1** as a waxy solid. Alternatively, a mixture of esters **27a** and **27b** was treated with 20% NaOMe/MeOH at reflux for 8 h (this process resulted in a quantitative epimerization of **27a** to **27b**), whereupon 5 mL of a 20% KOH solution was added to the reaction mixture and the hydrolysis completed as above to give **1**: IR ($CHCl_3$) 3200–2800, 1705 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.10 (s, 3 H), 1.11 (s, 3 H), 1.2–2.0 (m, 10 H), 1.6 (d, 3 H, J = 1 Hz), 2.86 (t, 1 H, J = 5 Hz), 4.84 (br s, 1 H); ^{13}C NMR ($CDCl_3$) δ 13.2 (q), 21.58 (q), 24.1 (t), 24.3 (q), 28.5 (t), 34.2 (t), 38.4 (t), 42.1 (t), 52.2 (d), 57.5 (s), 60.6 (s), 64.0 (s), 132.1 (d), 143.3 (s), 182.2 (s); calcd for $C_{15}H_{22}O_2$ 234.1620, found 234.1623.

(4β,8α)-1α,2,4β-Trimethyl-9β)carboxytricyclo[6.3.0.0^{4,8}]-undec-2-ene (28, Epiisocomenic Acid). To a stirred solution of lithium aluminum hydride (20 mg, 0.5 mmol) in 7 mL of diethyl ether was added 22 mg (0.08 mmol) of ester **27a** in 3 mL of ether. The reaction mixture was stirred at room temperature for 1 h, refluxed for 2 h, cooled and decomposed with cold water, and extracted with ether (6 × 10 mL). The ethereal layer was washed with saturated NaCl solution, dried (Na_2SO_4), and evaporated to give 18 mg (90%) of alcohol **28a**: IR (neat) 3450 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.0 (s, 3 H), 1.06 (s, 3 H), 1.56 (s, 3 H), 1.2–2.2 (m, 11 H), 3.82 (m, 2 H), 4.7 (br s, 1 H). The alcohol **28a** (18 mg, 0.076 mmol) was dissolved in acetone (5 mL); and a standard solution of the Jones reagent (prepared according to Fieser) was added until the color of the reagent persisted. After 1 h any excess reagent was destroyed with methanol and the reaction mixture partitioned between water and methylene chloride. Extraction with methylene chloride (6 × 10 mL), drying, and evaporation gave a waxy solid, which was chromatographed on silica gel (hexane/Et_2O, 1:1) to give 12 mg (63%) of acid **28** as a semisolid; IR ($CHCl_3$) 3500–2800, 1700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.02 (s, 3 H), 1.12 (s, 3 H), 1.2–2.0 (m, 10 H), 1.57 (s, 3 H), 2.35 (m, 1 H), 4.82 (br s, 1 H); ^{13}C NMR ($CDCl_3$) δ 12.9 (q), 22.7 (q), 23.4 (t), 23.8 (q), 29.6 (t), 35.1 (t), 36.4 (t), 42.5 (t), 51.7 (d), 57.3 (s), 61.2 (s), 63.2 (s), 133.9 (d), 147.6 (s), 179.3 (s).

(4β,8α)-1α-Methyl-9-carboxytricyclo[6.3.0.0^{4,8}]undec-9-ene (5a). The tricyclic acrylate **5b**[5] (82 mg, 0.00033 mmol) was dissolved in 2 mL of absolute EtOH. 40% KOH (2 mL) was added and the mixture refluxed for 4 h. The cooled reaction mixture was extracted once with hexane, and the aqueous layer was acidified and extracted with CH_2Cl_2 (5 × 15 mL). The combined organic layers were dried (Na_2SO_4) and evaporated to give 65 mg (90%) of pure **5a**: mp IR ($CHCl_3$, 5%) 3200–2800, 1690, 1620 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.05 (d, 3 H, J = 6 Hz), 1.15 (s, 3 H), 1.6–2.1 (m, 10 H), 2.36 (br t, 2 H), 6.7 (br t, 1 H, J = 2 Hz); ^{13}C NMR ($CDCl_3$) δ 19.5 (q), 25.1 (q), 28.7 (t), 30.7 (t), 36.2 (t), 40.4 (t), 41.5 (d), 47.1 (t), 52.7 (s), 59.7 (d), 68.5 (s), 141.5 (s), 144.5 (d), 170.6 (s); mass spectrum (70 eV), m/e (relative intensity) 220 (M^+) (40), 205 (20), 191 (15), 175 (30), 164 (20), 139 (40), 138 (55), 133 (40), 119 (42), 105 (60), 91 (B), 77 (72)), 55 (70); calcd for $C_{14}H_{20}O_2$ 220.1463, found 220.1469.

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Registry No. (±)-**1**, 87372-13-2; (±)-**5a**, 87372-14-3; (±)-**5b**, 87420-72-2; **12**, 81328-61-2; 12-ol, 81328-62-3; (±)-**13**, 87372-15-4; (±)-**14**, 87372-16-5; (±)-**15a**, 87372-17-6; (±)-**15b**, 87420-73-3; (±)-**19a**, 87372-18-7; (±)-**19a** (acid chloride), 87393-12-2; (±)-**19b**, 87372-29-0; (±)-**19b** (acid chloride), 87372-30-3; (*E*)-(±)-**20**, 87372-31-4; (*Z*)-(±)-**20**, 87393-30-4; (±)-**21a**, 87372-19-8; (±)-**21b**, 87372-20-1; (±)-**22a**, 87372-21-2; (±)-**22b**, 87420-74-4; (±)-**23**, 87372-22-3; (±)-**24**, 87372-23-4; (±)-**25a**, 87372-24-5; (±)-**26a**, 87372-25-6; (±)-**26b**, 87372-26-7; (±)-**27a**, 87372-27-8; (±)-**27b**, 87420-75-5; (±)-**28**, 87420-76-6; (±)-**28a**, 87372-28-9; (±)-**29** (α-OH), 87372-32-5; (±)-**29** (β-OH), 87420-77-7; $CH_3C(OEt)_3$, 78-39-7; $BrCH_2CH{=}CHCO_2Et$, 6065-32-3.