methylcyclohexyl)piperidine picrate, 53635-33-9; *trans*-*N*-(4-methylcyclohexyl)piperidine picrate, 86822-61-9; *cis*-*N*-(4-methylcyclohexyl)-*N*-phenylbenzamide, 86822-62-0; *trans*-*N*-(4-methylcyclohexyl)-*N*-phenyl-*p*-toluenesulfonamide, 86822-63-1; *cis*-*N*-cyclohexyl-4-methylcyclohexylamine hydrochloride, 86822-64-2; *trans*-*N*-cyclohexyl-4-methylcyclohexylamine, 86822-65-3; *trans*-*N*-(3-methylcyclohexyl)pyrrolidine picrate, 86822-67-5; *cis*-*N*-(3-methylcyclohexyl)pyrrolidine picrate, 86822-69-7; *trans*-*N*-(3-methylcyclohexyl)piperidine picrate, 86822-71-1; *cis*-*N*-(3-methylcyclohexyl)piperidine picrate, 86822-73-3; *cis*-*N*-(2-methylcyclohexyl)pyrrolidine picrate, 86822-74-4; *trans*-*N*-(2-methylcyclohexyl)pyrrolidine picrate, 86822-75-5; *cis*-*N*-(2-methylcyclohexyl)piperidine picrate, 86822-76-6; *trans*-*N*-(2-methylcyclohexyl)piperidine picrate, 86822-77-7; *cis*-*N*-(2-methylcyclohexyl)morpholine picrate, 86822-78-8; *trans*-*N*-(2-methylcyclohexyl)morpholine, 64760-75-4; *cis*-*N*-benzyl-2-methylcyclohexylamine hydrochloride, 86822-79-9; *trans*-*N*-(2-methylcyclohexyl)-*N*-benzyl-*p*-toluenesulfonamide, 86822-80-2; *cis*-*N*-phenyl-2-methylcyclohexylamine, 86822-81-3; *trans*-*N*-(2-methylcyclohexyl)-*N*-phenyl-*p*-toluenesulfonamide, 86822-82-4; *cis*-*N*-cyclohexyl-2-methylcyclohexylamine, 86834-27-7; *trans*-*N*-cyclohexyl-2-methylcyclohexylamine, 59083-13-5; *cis*-*N*-(2-ethylcyclohexyl)morpholine picrate, 86822-84-6; *trans*-*N*-(2-ethylcyclohexyl)morpholine picrate, 86822-86-8; *cis*-*N*-(2-cyclohexylcyclohexyl)pyrrolidine picrate, 86834-29-9; *trans*-*N*-(2-cyclohexylcyclohexyl)pyrrolidine picrate, 86822-88-0; *cis*-*N*-(2-methylcyclopentyl)pyrrolidine picrate, 86822-89-1; *trans*-*N*-(2-methylcyclopentyl)pyrrolidine picrate, 86822-90-4; *cis*-*N*-(2-methylcyclopentyl)piperidine picrate, 86822-92-6; *trans*-*N*-(2-methylcyclopentyl)piperidine picrate, 86822-94-8; *cis*-*N*-(2-methylcyclopentyl)morpholine picrate, 86822-96-0; *trans*-*N*-(2-methylcyclopentyl)morpholine picrate, 86822-98-2; *cis*-*N*-(4-*tert*-butylcyclohexyl)pyrrolidine, 67282-82-0; *cis*-*N*-(4-*tert*-butylcyclohexyl)pyrrolidine picrate, 86822-99-3; *trans*-*N*-(4-*tert*-butylcyclohexyl)pyrrolidine, 67282-90-0; *trans*-*N*-(4-*tert*-butylcyclohexyl)pyrrolidine picrate, 86823-00-9; *cis*-*N*-(4-*tert*-butylcyclohexyl)piperidine picrate, 86823-01-0; *trans*-*N*-(4-*tert*-butylcyclohexyl)piperidine, 16499-27-7; *cis*-*N*-(4-*tert*-butylcyclohexyl)morpholine picrate, 86823-02-1; *trans*-*N*-(4-*tert*-butylcyclohexyl)morpholine picrate, 86823-03-2; *cis*-*N*-benzyl-4-*tert*-butylcyclohexylamine, 67498-84-4; *trans*-*N*-benzyl-4-*tert*-butylcyclohexylamine, 67498-86-6; *cis*-*N*-phenyl-4-*tert*-butylcyclohexylamine hydrochloride, 86823-04-3; *trans*-*N*-phenyl-4-*tert*-butylcyclohexylamine, 16622-85-8; *cis*-*N*-cyclohexyl-4-*tert*-butylcyclohexylamine hydrochloride, 86823-05-4; *trans*-*N*-cyclohexyl-*N*-(4-*tert*-butylcyclohexyl)benzamide, 86823-06-5; *trans*-*N*-benzyl-3,3,5-trimethylcyclohexylamine hydrochloride, 86823-07-6; *cis*-*N*-benzyl-3,3,5-trimethylcyclohexylamine, 86823-08-7; *trans*-*N*-(4-*tert*-butylcyclohexyl)-*p*-toluenesulfonamide, 31023-38-8; *cis*-*N*-(4-*tert*-butylcyclohexyl)-*p*-toluenesulfonamide, 31023-37-7; *trans*-*N*-(2-ethylcyclohexyl)-*p*-toluenesulfonamide, 86823-09-8; *cis*-*N*-(3,3,5-trimethylcyclohexyl)-*p*-toluenesulfonamide, 86823-10-1; 4-*tert*-butylcyclohexanone, 98-53-3; 2-methylcyclohexanone, 583-60-8; 2-methylcyclopentanone, 1120-72-5; 2-methylcyclohexanone oxime, 1122-26-5; 2-cyclohexylcyclohexanone oxime, 4575-20-6; 2-ethylcyclohexanone oxime, 86823-11-2; 4-*tert*-butylcyclohexanone oxime, 4701-98-8; 3,3,5-trimethylcyclohexanone oxime, 37694-11-4; *cis*-2-methylcyclopentylamine, 86823-12-3; *trans*-2-methylcyclopentylamine, 6604-07-5; *cis*-2-methylcyclohexylamine, 2164-19-4; *trans*-2-methylcyclohexylamine, 931-10-2; *cis*-2-cyclohexylcyclohexylamine, 2163-28-2; *trans*-2-cyclohexylcyclohexylamine, 2163-29-3; *cis*-2-ethylcyclohexylamine, 24216-90-8; *trans*-2-ethylcyclohexylamine, 2164-24-1; *cis*-3,3,5-trimethylcyclohexylamine, 32158-56-8; *trans*-3,3,5-trimethylcyclohexylamine, 32958-55-7; *cis*-4-*tert*-butylcyclohexylamine, 2163-33-9; *trans*-4-*tert*-butylcyclohexylamine, 2163-34-0; bis(2-bromoethyl) ether, 5414-19-7; diethylene glycol, 111-46-6; *cis*-*N*-phenyl-4-*tert*-butylcyclohexylamine, 86823-13-4; *p,p'*-dimethoxybenzhydrylamine, 19293-62-0; *cis*-2-*n*-propyl-4-*tert*-butylcyclohexanone 2,4-dinitrophenylhydrazone, 86823-14-5.

Intramolecular Cyclopentene Annulation. 3.[1] Synthesis and Carbon-13 Nuclear Magnetic Resonance Spectroscopy of Bicyclic Cyclopentene Lactones as Potential Perhydroazulene and/or Monoterpene Synthons

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The internal cyclopropanation of several diversely substituted dienic diazo esters is described. Thermolysis of the resulting vinylcyclopropanes yielded cyclopentene-annulated lactones in good yields. Depending on the choice of the dienyl unit, either guaiane or pseudoguaiane substitution patterns of the cyclopentene portion were obtained. Stereochemical assignments based on ^{13}C NMR data are provided for all of these lactones. Subsequent transformations of the bicyclic lactones to differentially functionalized cyclopentenes are described. The potential of these synthons in the synthesis of perhydroazulene sesquiterpenes and several monoterpene cyclopentanoid natural products is addressed.

Introduction

The preparation of multiply functionalized cyclopentanes remains near the top margin on the list of synthetic priorities today. We have applied the internal cyclopropanation–rearrangement sequence to the synthesis of cyclopentanoid natural products[3] as well as extended its scope to provide access to cyclopentenecarboxylates via a high-yielding internal cyclopropanation of unsaturated esters.[4]

(1) (a) For part 2 see: Hudlicky, T.; Koszyk, F. J.; Dochwat, D. M.; Cantrell, G. L. *J. Org. Chem.* **1981**, *46*, 2911. (b) Presented in part at the Southwest-Southeast Regional Meeting of the American Chemical Society New Orleans, LA, Dec. 10–13, 1980; American Chemical Society: Washington, DC, 1980; Abstr. 466.

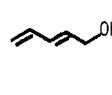
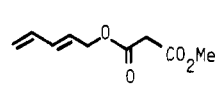
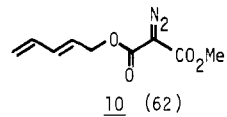
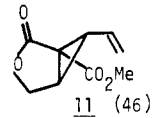
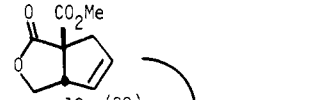
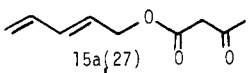
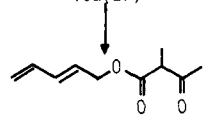
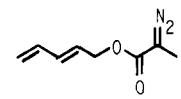
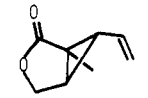
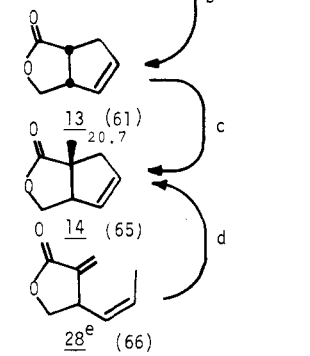
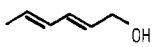
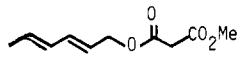
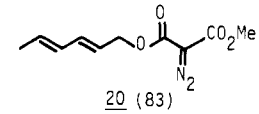
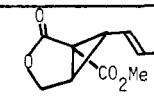
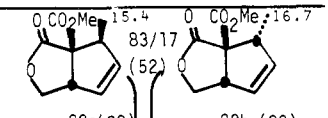
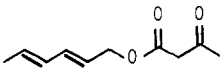
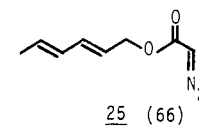
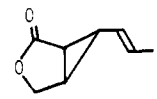
(2) Fellow of the Alfred P. Sloan Foundation, 1981–1983.

(3) Hudlicky, T.; Kutchan, T. M.; Wilson, S. R.; Mao, D. T. *J. Am. Chem. Soc.* **1980**, *102*, 6351.

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

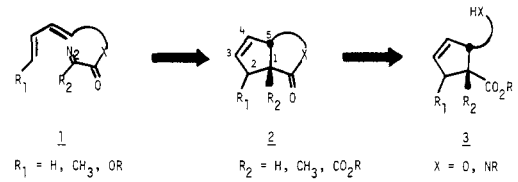
0022-3263/83/1948-3422$01.50/0

Table I

alcohol (%)[a]	ester[f] (%)	diazoester (%)	cyclopropane (%)	cyclopentene lactone (%)[g]
 8	 9 (74)	 10 (62)	 11 (46)	 12 (28)
PSEUDOGUAIANE SERIES	 15a (27)  15 (97)	 16 (42)	 17 (63)	 13 (61) 20.7 14 (65) 28[e] (66)
 18	 19 (60)	 20 (83)	 21 (84)	 22a (30) 22b (22) 23a (42) 23b
GUAIANE SERIES	 24 (72)	 25 (66)	 26 (68)	

[a] Yields represent isolated amounts. [b] LiI/DMF/140 °C/2 h. [c] LDA/THF (−78 to −40 °C)/MeI. [d] 620 °C, Vycor, $PbCO_3$. [e] < 500 °C. [f] The corresponding ethyl ester series was also prepared. [g] ^{13}C NMR shifts of cyclopentenyl methyl groups are indicated (Me_2Si, 0.0 ppm).

The next most logical extrapolation presented itself in the introduction of a heteroatom into the dienic α-diazo carbonyl compound, thereby providing the means of manipulating the resulting annulated systems in a ring-opening manner (eq 1). The first such series chosen for



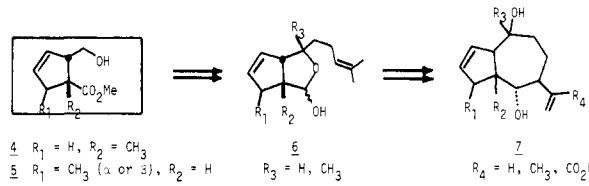
1 2 3

R_1 = H, CH_3, OR; R_2 = H, CH_3, CO_2R; X = O, NR (1)

investigation were the lactones of type **2**.[5] Hydrolytic manipulations of lactones **2** would yield substituted cyclopentenes **3**, which can be transformed into various terpenoid synthons as well as into diversely functionalized cyclopentanes. The advantages of forming compounds such as **3** by this method are clear since no regio- or stereoselectivity could be expected from the *inter*molecular union of a dienic alcohol with the corresponding diazo esters. The formation of lactones **2** imposes certain steric requirements on the system, such as cis ring junction and the relative stereochemistry of substituents at C-1 and C-2. The open forms **3** on the other hand can easily be epimerized to *both* trans-substituted patterns particularly if the oxidation of the C-5 functionality renders the corresponding hydrogen acidic. Furthermore both the carboxylate and the alcohol possess internal delivery capacities and can therefore be used to functionalize the cyclopentene double bond to yield complex substitution patterns on a cyclopentane ring in relatively few steps.

The above potential coupled with the functional topology at C-1 and C-2 thus allows for selective entries into either *guaiane*- or *pseudo*guaiane-type sesquiterpenes possessing either cis- or trans-fused perhydroazulene ring systems. The decision regarding particular structural types can be made at the stage of diazo ester **1** where the C-1 and C-2 substituents are introduced into the *ester* or *alcohol* moieties, respectively.

Keeping the above rationale in mind we describe herein the synthesis and the stereochemical outcome of the first series of lactones **2** aimed at the development of a *general method* of synthesis for perhydroazulene terpenes via synthons **4** and **5**. Equation 2 summarizes the projected



4 R_1 = H, R_2 = CH_3; **5** R_1 = CH_3 (α or β), R_2 = H — **6** R_3 = H, CH_3 — **7** R_4 = H, CH_3, CO_2R (2)

utility of synthons **4** and **5** in the context of perhydroazulene synthesis.

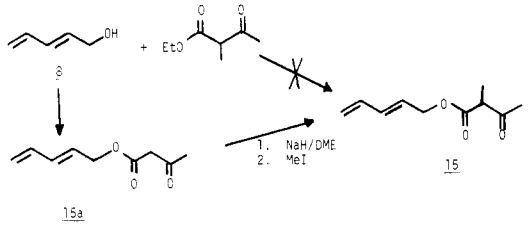
Results and Discussion

We began our investigations by imposing the cyclopropanation conditions developed previously[1,4] on the diazo esters **10**, **16**, **20**, and **25** (Table I). These esters were available in high yields from the transesterification reactions of alcohols **8** and **18**.[6] We prepared **8** from pentadienoic acid[7] by a low-temperature $LiAlH_4$ reduction[8] and

(5) For a review of cyclopropanation of simple olefinic diazo esters see: Burke, S. P.; Grieco, P. A. *Org. React. (N.Y.)* **1979**, *26*, 361. House, H. O.; Blankley, C. *J. Org. Chem.* **1968**, *33*, 53; Kirmse, W.; Dietrich, H. *Chem. Ber.* **1965**, *98*, 4027.

(6) Bader, A. R.; Cummings, L. O.; Vogel, H. A. *J. Am. Chem. Soc.* **1951**, *73*, 4195.

18 by a similar reduction of sorbic acid *or* aldehyde (Aldrich). The transesterification of these alcohols with the acid chloride of methyl malonate gave the precursory esters 9 and 19, while heating of the alcohols with 2 equiv of ethyl acetoacetate gave the β-keto esters **15a** and **24** necessary for the synthesis of **16** and **25**. The diazo transfer reaction of the above esters gave excellent yields of **10**, **16**, **20**, and **25**. The procedure was adopted from diazotization of β-keto esters, which proceed with the concomitant loss of a terminal acetyl group from **15** and **24** under alkaline conditions.[9,14] Some problems were encountered during the preparation of methyl diazo ester **16** (eq 3). The



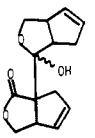
(3)

conventional thermal transesterification of **8** with ethyl acetopropionate did not produce **15** but led instead to extensive polymerization. We bypassed this obstacle by the alkylation of the available keto ester **15a**, the formation of which was problem free.

With the diazo esters in hand we studied the cyclopropanation reactions and discovered that the conditions employed previously for carbon analogues[1] did not produce cyclopropanes in useful yields. Apparently the presence of additional oxygen in the molecule was responsible for the low yields in the reactions where *catalytic* amounts of copper salts were used by interacting with the catalyst, thereby making it unavailable for the crucial complexation with the diene. Since this complexation must precede cyclopropane formation, we decided to depart from the catalytic mode and to utilize the heterogeneous conditions developed during the cyclopropanations of relatively unreceptive dienes.[4] With excess $CuSO_4$ suspended in refluxing benzene, diazo esters **10** and **20** gave excellent yields of cyclopropanes **11** and **21**, which could be isolated as low melting crystalline solids (Table I). The yields of **17** and **26** on the other hand were substantially lower. It therefore appeared that the two-step sequence involving cyclopropanation and LiI-induced decarbomethoxylation could prove more economical provided other factors remained the same. Interestingly such decision was complicated by a surprising reversal of expected steric outcome in the formation of lactones **22** and **23**.

Pseudoguaiane Synthons. The pyrolysis of cyclopropane **11** gave good yield of lactone **12**, which was decarboxymethylated with LiI in DMF to afford the highly volatile lactone **13**. Attempted alkylation of **13** under a variety of experimental conditions[10] gave low yields of **14** at the expense of products derived from ketene formation[3] and/or dimerization to give up to 60% of **27**.

Pyrolysis of **17** under identical conditions gave reasonable yields of **14**. As in the carbocyclic cases, the competing 1,5-shift encountered in the pyrolyses of compounds of this type was only observed at lower temperatures. No product



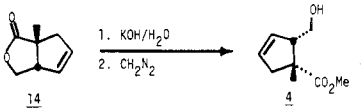
27

corresponding to **28** was isolated from thermolyses above

28

600 °C although such product was produced at lower temperatures[11] (<450 °C) and may prove to be useful in the generation of α-methylene lactones.[12] We have prepared **28** at ~400–450 °C and shown it to be transformable to **14** at 620 °C, again in analogy with the documented carbocyclic cases.[11]

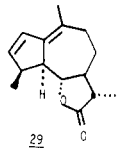
With **14** available rapidly from alcohol **8** via the route depicted in Table I we prepared ester alcohol **4** (eq 4)



(4)

which will eventually be used in a synthesis of pseudoguaiane terpenes as indicated in eq 2. Cyclopentane **4** possesses, in addition to the two differentiated functionalities necessary for further elaboration and annulation of the seven-membered ring, the means of introducing additional substituents at a later stage via various oxidative transformations of the double bond.

Guaiane Synthons. The rearrangement of cyclopropane **21** gave a mixture of two lactones, **22a** and **22b**, in a ratio of 83:17, respectively (as determined by gas chromatography). This was completely unexpected since previous studies with angularly substituted cyclopropanes gave the trans-substituted products predominantly.[1] We were delighted when the pyrolysis of **26** furnished the mixture of **23a** and **23b** in nearly the opposite ratio, namely 28:72.[13] At the moment we have no rational explanation for this remarkable reversal of steric outcome and must await the confirmation of these results by repetition of this work as well as by examining other cases. Since the lactones **22** were easily converted to **23** by their exposure to LiI/DMF, we now had a reasonably selective method of acquisition of *either* **23a** or **23b** depending on which substitution pattern we desired in the future guaiane synthesis. Since our planning was to address the synthesis of perhydroazulenes possessing the configuration of arborescin (**29**) first and since the *overall* yields of **22** superceded those



29

(7) Muskat, I. E.; Becker, B. C.; Lowenstein, J. S. *J. Am. Chem. Soc.* **1930**, *52*, 326.

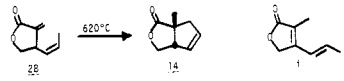
(8) The reduction was carried out either by refluxing ether through a Soxhlet thimble filled with the crystalline acid into a flask containing $LiAlH_4$ in ether or by performing a $LiAlH_4$ reduction in Et_2O at −20 °C. The latter method gave better yields.

(9) Ledon, H. J. *Org. Synth.* **1979**, *59*, 66.

(10) Procedures adapted from alkylations of similar systems: Takano, S.; Chiba, K.; Yonaga, M.; Ogaswara, K. *J. Chem. Soc., Chem. Commun.* **1980**, 616.

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

(12) Lactone **28** was also transformed to bicyclic lactone **14** at >600

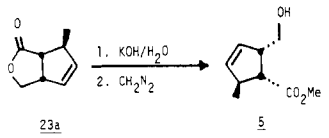


°C in analogy with carbocyclic cases. Lactone **i** was identified as a minor constituent of these transformations.

(13) Hudlicky, T.; Koszyk, F. J.; Kutchan, T. M.; Sheth, J. P. *J. Org. Chem.* **1980**, *45*, 5020.

(14) Hendrickson, J. B.; Wolf, W. A. *J. Org. Chem.* **1968**, *33*, 3610. This procedure involves anhydrous conditions but gives lower yields than the phase transfer conditions.

of **23**, we functionalized **23a** in the same fashion as **14** (eq 5). Once the substitution events have taken place at the



23a 5 (5)

site of a hydroxyl in **5**, the ester will be epimerized to the more stable trans-substitution pattern. If we are successful with the conversion of **5** to arborescin, we may utilize the diastereomer **23b** in similar syntheses of guaianes having bulnesene-type configuration of the secondary methyl group.

The structural assignments of lactones **22** and **23** were made by using shielding arguments in the analyses of their ^{13}C NMR spectra and need not be discussed since they were based on and correspond closely to the assignments made on their carbocyclic counterparts.[1] In addition to the projected use of the cyclopentene lactones in the synthesis of perhydroazulenes, we have converted **13** to sarkomycin **30** via the known ketone **31**[15] and envision the

31 30 32

synthesis of other methylenomycins by functionalization of the olefin in substituted analogues of lactone **13**. We have previously obtained sarkomycin in low yields from **32**.[11,16,17] Thus the second route to **30** provides a useful topological alternative to the synthesis of monoterpenoids by this methodology.

Conclusions

We have completed the synthesis of the first heteroatom containing series of bicyclic cyclopentanoids and indicated their utility as synthons in either sesquiterpene or monoterpene cyclopentanoid preparation.

Our future endeavors may include the synthesis of iridoids via the six-membered homologues of lactones **13** and/or **23** as well as experimentation with both diazo amides and nitrenes as an entry to alkaloids containing a substituted pyrrolidine nucleus.

The topological considerations outlined above for the syntheses of sarkomycin portend well for the utility of the various permutations of cyclopentene annulation in a *system-oriented* design of a synthesis of cyclopentanoids.

Experimental Section

Melting and boiling points are uncorrected. All nonhydrolytic reactions were carried out under an inert atmosphere (nitrogen or argon). All solvents were distilled prior to use. Ultra-dry solvents were produced accordingly (THF and DME from benzophenone and potassium, benzene from P_2O_5, Et_2O from $LiAlH_4$, CH_2Cl_2 from BaO). Infrared spectra were recorded on Perkin-Elmer 257 and Pye-Unicam 3-3300 spectrophotometers. ^1H NMR spectra were obtained on Varian T-60, Varian EM 390, or Nicolet 300 instruments while ^{13}C NMR spectra were recorded on JEOL 60, JEOL FX 200, or Varian CFT-20 equipment. In all instances tetramethylsilane was used as a reference.

Chromatography was performed on Brinkman (EM reagents) silica PF 254 (TLC) or Macherey Nagle and Co. (column). The purity of compounds was ascertained by chromatographic and spectral means (gas chromatography on OV-101/flame ionization, analytical TLC, and ^{13}C NMR spectra).

Mass spectral measurements were obtained on a Du Pont 20-491 (low resolution) or Du Pont 21-110C instrument (exact mass).

Methyl 2,4-Pentadien-5-yl Malonate (9). 2,4-Pentadienol (**8**)[5,6] (5.04 g, 0.06 mol) was dissolved in 60 mL of dry methylene chloride and cooled to 0 °C. Methyl malonate monochloride (8.19 g, 0.06 mol) was added, and then 9.17 g (0.09 mol) of triethylamine was added dropwise. The cooling bath was removed and 0.1 g of 4-(*N*,*N*-dimethylamino)pyridine was added. The mixture was stirred at room temperature (22 °C) for 2 h and then quenched with 3 N HCl (30 mL). The aqueous layer was extracted with CH_2Cl_2 (2 × 100 mL), and the combined extracts were rinsed with 3 N HCl, saturated sodium bicarbonate, and brine and dried over Na_2SO_4. Evaporation of solvents followed by distillation afforded 8.2 g (74%) of pure ester **9**, bp, 75–77 °C (0.075 mm); analytical TLC (silica gel, CH_2Cl_2/hexane (80:20) R_f 0.55, a colorless oil; IR (neat) 1750 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.3 (s, 2 H), 3.7 (s, 3 H), 4.62 (d, 2 H, J = 4 Hz), 5.0–6.5 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 41.0 (t), 52.2 (q), 65.3 (t), 118.7 (t), 126.1 (d), 134.9 (d), 135.6 (d), 165.9 (s), 166.6 (s); mass spectrum (70 eV), m/e (relative intensity), 184 (M^+, 0.3), 149 (7.3), 101 (16.2), 85 (20.1), 68 (100), 57 (43.6); calcd for $C_9H_{12}O_4$, 184.0735; found, 184.0743.

Methyl 2,4-Pentadien-5-yl Diazomalonate (10). Keto ester **9** (7.7 g, 0.04 mol), tosyl azide (7.8 g, 0.04 mol), and triethylamine (4.1 g, 0.04 mol) were mixed in 75 mL of dry acetonitrile and stirred at room temperature for 30–36 h. The mixture was diluted with 60 mL of Et_2O and washed with 10% KOH (6 × 15 mL), H_2O (6 × 15 mL), and brine, and the organic layer was dried over Na_2SO_4. Evaporation of the solvent yielded crude diazo ester **10**, 6.5 g (77.3%), suitable for use in the next step. A filtration through silica with hexane/ether (1:1) as an eluent gave pure **10**, analytical TLC (silica gel, hexane/Et_2O (60:40)) R_f 0.4; an oil (5.3 g, 62.2%); IR (neat) 2150, 1750, 1690, 1610 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.8 (s, 3 H), 4.62 (d, 2 H, J = 4 Hz), 5.0–6.5 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 51.7 (q), 64.2 (s), 64.6 (t), 118.3 (t), 125.86 (d), 134.6 (d), 135.2 (d), 159.8 (s), 160.6 (s); mass spectrum (70 eV), m/e (relative intensity) 210 (M^+, 1.7), 137 (4.5), 127 (18.4), 101 (20.7), 83 (42.5), 67 (100), 53 (25.7); calcd for $C_9H_{10}O_4N_2$, 210.0640; found, 210.0637.

1-Oxo-4a-carbomethoxy-1,3,3a,4a-tetrahydro-4-vinylcyclopropa[*c*]furan (11). Diazoester **10** (6.3 g, 0.03 mol) in 50 mL of dry benzene was added over 60 min to a vigorously stirred, refluxing mixture of 15 g of anhydrous $CuSO_4$ and 0.65 g of $Cu(acac)_2$ in 450 mL of benzene. After the addition was completed the mixture was refluxed for 24 h under nitrogen. The reaction mixture was cooled and filtered through a plug of silica gel. Evaporation of solvents yielded 5.3 g (94%) of crude product which was purified by column chromatography (hexane/Et_2O (3:2), silica) to give pure **11**, analytical TLC (silica gel, hexane/Et_2O (60:40)) R_f 0.2; a low-melting, waxy solid (2.56 g, 45.5%); IR (neat) 1780, 1725, 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.15 (dd, 1 H, J_1 = 7 Hz, J_2 = 4 Hz), 2.82 (dt, 1 H, J_1 = 7 Hz, J_2 = 2.5 Hz), 3.8 (s, 3 H), 4.25 (m, 2 H), 5.0–6.0 (m, 3 H); ^{13}C NMR ($CDCl_3$) δ 30.5 (d), 35.7 (s), 37.2 (d), 52.6 (q), 66.8 (t), 120.2 (t), 129.9 (d), 165.1 (s), 169.7 (s); mass spectrum (70 eV), m/e (relative intensity) 183 (M^+ + 1, 2.8), 182 (M^+, 2.2), 150 (23.5), 138 (25.7), 123 (40.8), 107 (10.6), 95 (37.4), 79 (100), 65 (71.5), 59 (78.2), 53 (89.3); calcd for $C_9H_{10}O_4$: 182.0579; found: 182.0583.

1-Oxo-6a-carbomethoxy-1,3,3a,6a-tetrahydrocyclopenta[*c*]furan (12). Cyclopropane **11** (3.3 g, 0.018 mol) was evaporated under vacuum (0.01 mm) at 580–600 °C through a horizontally situated Vycor tube pretreated with $PbCO_3$ as described previously.[1] The condensate was collected in a liquid nitrogen cooled trap and weighed (2.56 g, 77.6% mass recovery). The crude product was chromatographed (silica gel, hexane/Et_2O (1:1)) to give 0.93 g (28.2%) of pure lactone **12**, analytical TLC (silica gel, hexane/Et_2O (1:1)) R_f 0.5; IR (neat) 1780, 1730 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.05 (sextet, 2H), 3.7 (s, 3 H), 4.25 and 4.30 (d of AB q, 1 H each), 5.4 (m, 1 H), 5.8 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 39.9 (t), 52.2 (d), 52.8 (q), 59.2 (s), 70.9 (t), 128.8 (d), 131.5 (d), 161.1 (s), 175.9 (s); mass spectrum (70 eV), m/e (relative int.) 182 (M^+, 35.6), 150 (34.2), 138 (41.1), 137 (38.4), 124 (72.6), 105 (39.7), 79

(15) Wexler, B. A.; Toder, B. H.; Minaskanian, G.; Smith, A. B., III. *J. Org. Chem.* **1982**, *47*, 3333. Marx, J. N.; Minaskanian, G. *Ibid.* **1982**, *47*, 3306.

(16) Low-temperature titration of the CH_2Cl_2 solution of **32** with standard ozone solution gave low yields of sarkomycin (analyzed by its conversion to the methyl ester).

(17) Govindan, S. V.; Hudlicky, T.; Koszyk, F. J., note in this issue.

(100), 77 (64.4), 65 (67.1), 39 (91.8), 34 (60); calcd for $C_9H_{10}O_4$, 182.0579; found, 182.0584.

1-Oxo-1,3,3a,6a-tetrahydrocyclopenta[*c*]furan (13). To a solution of 0.170 g (0.93 mmol) of ester **12** in 2.5 mL of dry DMF was added 0.401 g (0.0028 mol) of anhydrous LiI and the mixture refluxed for 2.5 under nitrogen. After cooling it was diluted with ether and washed with 3 N HCl. The organic layer was rinsed with H_2O (6 × 1 mL) and brine, dried, and evaporated to give 0.103 g (88.95%) of crude product. Analytically pure material could be obtained by preparative TLC (hexane/ether, 1:1) to give 0.070 g (60.5%) of **13**, analytical TLC (silica gel, hexane/Et_2O (1:1)) R_f 0.6; IR (neat) 1760, 1610 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.7 (m, 2 H), 3.05 (m, 1 H), 3.5 (m, 1 H), 4.25 (m, 2 H), 5.6–5.8 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 36.6 (t), 41.7 (d), 46.5 (d), 71.5 (t), 130.6 (d), 132.45 (d), 180.6 (s); mass spectrum (70 eV), *m/e* (relative intensity) 124 (M^+, 45.2), 123 (31.5), 79 (49.3), 66 (100), 39 (24.7); calcd for $C_7H_8O_2$, 124.0524; found, 124.0526.

Attempted Alkylation of 13. The corresponding enolate anion from **13** was generated by using LDA, lithium dicyclohexylamide, lithium tetramethylpiperidide, potassium *tert*-amylate, or potassium *tert*-butoxide in THF, DME, or *t*-BuOH. The reactions were performed on a scale of 0.001 mol of **13** at various temperatures (−78 °C to room temperature). In all instances trace amounts of **14** were produced, with the major product always being a mixture of diastereomers of **27** (isolated by preparative TLC, hexane/Et_2O, 1:1); IR (neat) 3520, 1780, 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.6 (m, 4 H), 3.2–3.6 (m, 3 H), 4.1–4.4 (m, 4 H), 5.6 (bm, 4 H); ^{13}C NMR ($CDCl_3$) δ 33.8 (t), 36.6 (t), 38.9 (t), 40.2 (t), 41.7 (t), 46.0 (d), 47.3 (d), 48.8 (d), 49.5 (d), 51.6 (d) 52.2 (d) 60.5 (s), 61.0 (s), 71.5 (t), 72.7 (t) 107.6 (s), 107.8 (s), 130.8 (d), 131.2 (d), 132.5 (d), 133.5 (d), 180.9 (s), 181.2 (s); mass spectrum (70 eV), *m/e* (relative intensity) 230 ($M^+ - H_2O$, 55), 218 (40), 124 (52), 79 (100).

2,4-Pentadien-1-yl α-Methylacetoacetate (15). 2,4-Pentadienol (2.5 g) and ethyl acetoacetate (7.8 g (2 equiv)) were heated at 115 °C under aspirator pressure (~50 mm) for 15 h. The mixture was distilled to afford 1.3 g (26.6%) of 2,4-pentadienyl acetoacetate **15a** and 4.3 g of recovered ethyl acetoacetate. The distilled ester **15a** (3.6 g, 21.4 mmol) in 10 mL of dry dimethoxyethane was added to a suspension of NaH (896 mg, 60% dispersion, 22.6 mmol) in 30 mL DME and the mixture stirred at room temperature for 30 min, whereupon 2.7 mL of MeI (43.4 mmol) was added at once and the stirring continued for 18 h. The solvent was removed under reduced pressure and the residue taken up in water and extracted with ether (4 × 25 mL). Solvent removal afforded 3.7 g (96.8%) of **15** suitable for use in the next step; IR (neat) 1740, 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.3 (d, 3 H, J = 7 Hz), 2.2 (s, 3 H), 3.4 (q, 1 H, J = 7 Hz), 4.6 (d, 2 H, J = 6 Hz), 5.0–6.3 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 12.7 (q), 28.4 (q), 53.5 (d), 65.3 (t), 118.9 (t), 126.4 (d), 135.3 (d), 135.8 (d), 170.1 (s), 203.1 (s); mass spectrum (70 eV), *m/e* (relative intensity) 182 (M^+ 0.6), 149 (15.6), 95 (15.1), 81 (40.8), 69 (100), 55 (61.5); calcd for $C_{10}H_{14}O_3$, 182.0943; found, 182.0937.

2,4-Pentadien-1-yl α-Diazopropionate (16). Methylated ester **15** (1.04 g, 5.73 mmol) in 3 mL of dry tetrahydrofuran was added over 5 min to a stirred suspension of NaH (60% dispersion, 450 mg, 11.2 mmol) in 7.5 mL of THF. The mixture was cooled in an ice bath, stirred for 10 min at 0 °C, and treated with a solution of 1.78 g (9 mmol) of tosyl azide in THF. The reaction was stirred for 2 h at room temperature under argon. At the end of this period it was diluted with 100 mL of hexane and the precipitate filtered off and rinsed with hexane. The combined hexane extracts were washed with H_2O and brine and dried over Na_2SO_4. Evaporation gave a dark red oil containing tosyl azide. Chromatography on silica (hexane/Et_2O, 9:1) gave pure diazo ester **16**, analytical TLC (silica gel, hexane/Et_2O (1:1)) R_f 0.7; 0.395 g (42%); IR (neat) 2080, 1660, 1595 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.0 (s, 3 H), 4.7 (d, 2 H, J = 6 Hz), 5.0–6.4 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 8.4 (q), 64.7 (t), 118.6 (t), 127.4 (d), 134.5 (d), 135.9 (d), 167.5 (s); mass spectrum (70 eV), *m/e* (relative intensity) 166 (M^+, 0.8), 138 (8.4), 108 (77.1), 93 (30.7), 79 (100), 67 (78.2), 55 (45.8); calcd for $C_8H_{10}N_2O_2$, 166.0742; found, 166.0745.

1-Oxo-4a-methyl-1,3,3a,4a-tetrahydro-4-vinylcyclopropa[*c*]furan (17). Diazo ester **16**, (900 mg, 0.0054 mol) in 10 mL of dry benzene was added over 15 min to a stirred and refluxing mixture of anhydrous $CuSO_4$ (3.8 g) and $Cu(acac)_2$ (0.15 g) in 40 mL of benzene. After the evolution of nitrogen subsided, the reaction was refluxed for 2 h, cooled, and filtered with suction. The bed of inorganic salts was washed well with benzene, the solvent evaporated, and the oil taken up in 50 mL of ether. The precipitated $Cu(acac)_2$ was filtered off and the filtrate concentrated to an oil, which was chromatographed (silica, hexane) to afford 470 mg (63%) of pure cyclopropane **17**, analytical TLC (silica gel, hexane/Et_2O (1:1)) R_f 0.3; IR (neat) 1750, 1620 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.35 (s, 3 H), 1.8 (dd, 1 H, J = 4.5 Hz, 7.5 Hz), 2.1 (br t, 1 H, J = 4.5 Hz), 4.2 (AB q, 1 H), 4.25 (br s, 1 H), 5.0–5.6 (m, 3 H); ^{13}C NMR ($CDCl_3$) δ 9.6 (q), 28.5 (d), 31.8 (d), 48.7 (s), 68.1 (t), 118.2 (t), 132.1 (d), 171.0 (s); mass spectrum (70 eV), *m/e* (relative intensity) 138 (M^+, 3.4), 108 (14.5), 97 (11.2), 93 (10.1), 79 (100), 65 (14.0), 53 (24.0); calcd for $C_8H_{10}O_2$, 138.0681; found, 138.0686.

2-Oxo-3-methylene-4-(1-*cis*-propenyl)tetrahydrofuran (28). Cyclopropane **17** (500 mg, 0.0036 mol) was evaporated at ~450 °C (0.1 mm) through a horizontally situated Vycor tube pretreated with a slurry of $PbCO_3$. The condensate collected in a trap cooled with liquid nitrogen was shown to consist of predominantly **28**; GC (5% OV-101 on Chromosorb, FID, 140–180 °C (10 °C/min)) retention time was 0.8 min at a flow of 30 cm^3/min; isolated by filtration through silica gel (hexane/ether, 9:1) in 66% yield; IR (neat) 1780, 1670 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.7 (d, 3 H, J = 6 Hz), 3.8–4.5 (m, 3 H), 5.2 (m, 1 H), 5.5 (d, 1 H, J = 3 Hz), 5.7 (m, 1 H), 6.25 (d, 1 H, J = 3 Hz); mass spectrum (70 eV), *m/e* (relative intensity) 138 (M^+, 5.0), 108 (57.0), 93 (16.8), 79 (100), 65 (10.6), 53 (16.8); calcd for $C_8H_{10}O_2$, 138.0681; found, 138.0683.

1-Oxo-6a-methyl-1,3,3a,6a-tetrahydrocyclopenta[*c*]furan (14). A. By Pyrolysis of Vinylcyclopropane 17. The pyrolysis was carried out as described at 620 °C. At this temperature, 65% yield of lactone **14** was obtained (purified on silica, hexane:ether (9:1)).

B. By Pyrolysis of α-Methylene Lactone 28. A sample of **28** (200 mg) was subjected to the pyrolytic conditions at 630 °C. The product of this pyrolysis was shown to consist of 53% of **14** and 45% of unreacted **28**.[12] A second pass of this crude mixture resulted in a 65% yield of bicyclic lactone **14**, GC (OV-101/Chromosorb, 140–180 °C (10 °C/min)) retention time 0.67 min; IR (neat) 1750, 1610 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.4 (s, 3 H), 2.7 (ABX q of quartets, 2 H), 3.15 (m, 1 H), 4.2 (AB q, 2 H), 5.6 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 20.7 (q), 44.4 (t), 49.0 (s), 52.9 (d), 70.2 (t), 130.8 (d), 132.4 (d), 177.0 (s); mass spectrum (70 eV), *m/e* (relative intensity) 138 (M^+, 16.8), 108 (6.7), 93 (37.4), 80 (100), 77 (36.3), 65 (13.4), 53 (16.8); calcd for $C_8H_{10}O_2$, 138.0681; found, 138.0682.

1-Methyl-1-carbomethoxy-2-(hydroxymethyl)cyclopent-3-ene (4). Bicyclic lactone **14** (70 mg) was dissolved in ether (5 mL) and added to 3 mL of 0.5 N NaOH in H_2O. The mixture was stirred at room temperature for 3 h, acidified, and extracted with ether. The crude hydroxy acid (IR (neat) 3400, 3200–2700, 1690, 1610 cm^{-1}) was immediately esterified with ethereal diazomethane to afford 35 mg of hydroxy ester **4**: IR (neat) 3400, 1710, 1610 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.35 (s, 3 H), 2.2 (m, 2 H), 3.0 (m, 1 H), 3.6 (m, 2 H), 3.65 (s, 3 H), 5.6 and 5.7 (bm, 1 H each); mass spectrum (70 eV), *m/e* (relative intensity) 152 (M − 18, 0.6), 138 (14.5), 108 (15.1), 93 (50.3), 79 (100), 65 (23.5), 53 (30.2); calcd for $C_9H_{14}O_3$, 170.0943; found, 170.0947.

2,4-Hexadienyl Methyl Malonate (19). Sorbyl alcohol (13.97 g, 0.14 mol) and (methoxycarbonyl)acetyl chloride (19.4 g, 0.142 mol) were mixed in 140 mL of dichloromethane and chilled to 0 °C. Triethylamine (21.7 g, 0.21 mol) was added dropwise to the reaction mixture over ~15 min. The ice bath was removed and 0.375 g of 4-(*N,N*-dimethylamino)pyridine was added, whereupon the mixture was stirred at room temperature for 1.5–2 h. The reaction was quenched in 3 N HCl (75 mL) and extracted with dichloromethane (2 × 100 mL). Neutralization ($NaHCO_3$), washing (NaCl), drying (Na_2SO_4), and evaporation of the organic layer gave crude ester which was distilled (Kügelrohr, 75–78 °C (0.05 mm)) to give 16.9 g (60%) of pure **19**, analytical TLC (silica gel, CH_2Cl_2/hexane (80:20)) R_f 0.5; IR (neat) 1740, 1650 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.8 (d, 3 H, J = 6 Hz), 3.3 (s, 2 H), 3.72 (s, 3 H), 4.6 (d, 2 H, J = 6 Hz), 5.0–6.5 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 17.5 (q), 40.8 (t), 51.9 (q), 65.4 (t), 122.7 (d), 130.0 (d), 130.9 (d), 134.8 (d), 165.8 (s), 166.4 (s); mass spectrum (70 eV), *m/e* (relative

intensity) 198 (M^+, 2.2), 101 (54.2), 97 (47.5), 81 (100), 79 (58.1), 69 (27.4), 59 (70.4), 53 (35.8); calcd for $C_{10}H_{14}O_4$, 198.0892; found, 198.0897.

2,4-Hexadienyl Methyl α-Diazomalonate (20). Dienyl malonate **19** (13.7 g, 0.069 mol), tosyl azide (13.6 g, 0.069 mol), and triethylamine (7.05 g, 0.069 mol) were stirred in 130 mL of dry acetonitrile for 48–60 h (completion indicated by TLC). The reaction mixture was diluted with 100 mL of ether, and the solution was washed with 10% KOH (6 × 25 mL), water (6 × 25 mL), and saturated NaCl (3 × 25 mL) and dried with Na_2SO_4. Removal of solvents in vacuo afforded 12.7 g (83%) of **20** as an oil suitable for use in the next step, analytical TLC (silica gel, hexane/Et_2O (1:1)) R_f 0.45; IR (neat) 2150, 1740, 1720, 1695, 1610 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.8 (d, 3 H, J = 6 Hz), 3.9 (s, 3 H), 4.76 (d, 2 H, J = 6 Hz), 5.4–6.3 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 17.4 (q) 51.7 (q), 65.2 (t), 65.5 (s), 122.5 (d), 129.8 (d), 134.9 (d), 130.9 (d), 159.8 (s), 160.6 (s); mass spectrum (70 eV), m/e (relative intensity) 224 (M^+, 7.8), 200 (11.2), 181 (19.6), 164 (17.9), 155 (29.0), 149 (22.3), 145 (8.9), 137 (54.7), 127 (7.8), 97 (40.2), 91 (15.0), 81 (100), 69 (21.2), 53 (40.2); calcd for $C_{10}H_{12}O_4N_2$, 224.0797; found, 224.0801.

1-Oxo-4a-carbomethoxy-4-prop-1-en-1-yl-1,3,3a,4a-tetrahydrocyclopropa[*c*]furan (21). Diazoester **20** (12.26 g, 0.054 mol) in 100 mL of dry benzene was added to a refluxing slurry of 12 g of anhydrous $CuSO_4$ and 1.2 g $Cu(acac)_2$ in 800 mL of benzene during 1 h. After the addition was complete, the mixture was refluxed for 24 h. Filtration of this solution through silica and removal of solvent afforded 8.9 g of **21** (84%) as a clear oil, analytical TLC (silica gel, CH_2Cl_2/hexane (75:25)) R_f 0.2; IR (neat) 1775, 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.85 (d, 3 H, J = 6 Hz), 2.4 (dd, 1 H, J = 8 Hz, 2 Hz), 2.9 (br t, 1 H), 3.95 (s, 3 H), 4.4 (br dd, 2 H), 5.4–6.2 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 17.5 (q), 30.0 (d), 35.2 (s), 36.8 (d), 52.0 (q), 66.5 (t), 122.5 (d), 131.3 (d), 164.9 (s), 169.5 (s); mass spectrum (70 eV), m/e (relative intensity) 196 (M^+, 1.7), 164 (15.6), 137 (60.3), 119 (8.9), 107 (24.6), 91 (74.9), 85 (18.4), 81 (55.3), 77 (100), 65 (31.3), 59 (65.9); calcd for $C_{10}H_{12}O_4$, 196.0735; found, 196.0739.

1-Oxo-6a-carbomethoxy-6-methyl-1,3,3a,6a-tetrahydrocyclopenta[*c*]furan (22). Cyclopropane **21** (1.5 g, 0.008 mol) was evaporated through a horizontally situated Vycor tube pretreated with $PbCO_3$ at 580 °C (0.02 mmHg); the crude pyrolystate was collected in a trap cooled with liquid nitrogen. The trap and the tube were washed with CH_2Cl_2 and the solution filtered through neutral alumina. Evaporation of the solvent gave an oil composed of 22a:22b/83:17 (OV-101, 140–180 °C (10°/min), 30 cc N_2/min), which was chromatographed on silica (hexane/ether, 6:4) to give 450 mg of pure **22a** (30%); IR (neat) 1780, 1720, 1640 cm^{-1}; ^1H NMR ($CDCl_3$) 1.3 (d, 3 H, J = 7 Hz), 2.2 (m, 1 H), 2.8 (m, 1 H), 3.8 (s, 3 H), 4.0–4.4 (m, 2 H), 5.7 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 15.4 (q), 45.9 (d), 52.8 (d), 53.1 (q), 61.7 (s), 70.2 (t), 127.3 (d), 137.7 (d), 169.7 (s), 171.5 (s). In addition to pure **22a** 320 mg of a mixture of **22a** and **22b** was isolated (22%). Repeated purification yielded **22b**; IR (neat) 1780, 1730, 1620 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.1 (d, 3 H, J = 7 Hz), 1.9–2.6 (m, 2 H), 3.9 (s, 3 H), 4.1–4.3 (m, 2 H), 5.8 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 16.7 (q), 47.4 (d), 48.7 (d), 52.9 (q), 62.8 (s), 70.2 (t), 128.2 (d), 137.4 (d), 169.7 (s), 171.2 (s); mass spectrum (70 eV), m/e (relative intensity) 196 (M^+, 1.1), 178 (8.4), 164 (12.3), 152 (8.9), 146 (6.7), 136 (12.3), 119 (25.1), 105 (26.8), 91 (82.7), 77 (100), 65 (31.3); calcd for $C_{10}H_{12}O_4$: 196.0735; found: 196.0741.

2,4-Hexadien-1-yl Acetoacetate (24). Sorbyl alcohol (**18**) (4.5 g, 0.046 mol) and ethyl acetoacetate (11.9 g, 0.092 mol) were heated at 120 °C under ~70 mmHg for 12 h. The mixture was distilled to recover excess ethyl acetoacetate and to afford 6 g (72%) of keto ester **24** as a clear oil, bp 75–80 °C (0.05 mm) (Kügelrohr); analytical TLC (silica gel, hexane/CH_2Cl_2 (1:1)) R_f 0.55; IR (neat) 1720, 1710 1660 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.8 (d, 3 H, J = 6 Hz), 2.1 (s, 3 H), 3.2 (s, 2 H), 4.65 (d, 2 H, J = 6 Hz), 5.4–6.2 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 18.0 (q), 30.0 (q), 49.9 (t), 65.7 (t), 123.1 (d), 130.4 (d), 131.5 (d), 135.4 (d), 166.9 (s), 200.4 (s); mass spectrum (70 eV), m/e (relative intensity) 182 (M^+, 0.3), 149 (7.3), 111 (11.2), 99 (18.4), 95 (14.0), 85 (100), 69 (62.0), 58 (45.8), 55 (34.6); calcd for $C_{10}H_{14}O_3$, 182.0943; found, 182.0937.

2,4-Hexadienyl α-Diazoacetate (25). Keto ester **24** (9.1 g, 0.05 mol), tosyl azide (9.86 g 0.05 mol), and tetrabutylammonium bromide (0.386 g, 0.0012 mol) were stirred in 200 mL of dichloromethane for 30 min, whereupon 10 mL of 10 N NaOH solution was added and the mixture stirred for 12 h at room temperature. The mixture was washed with 10% KOH (3 × 25 mL), water (3 × 25 mL), and brine (3 × 25 mL) and dried with Na_2SO_4. Removal of solvents gave a reddish oil, which was chromatographed (silica, hexane/ether (3:2)) to afford 5.49 g (66%) of pure diazo ester **25**, analytical TLC (silica gel, hexane/CH_2Cl_2 (1:1)) R_f 0.6; IR (neat) 2150, 1700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.8 (d, 3 H, J = 6 Hz), 4.7 (d, 2 H, J = 6 Hz), 4.8 (s, 1 H, diazo H), 5.2–6.2 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 18.0 (q), 46.2 (d), 65.2 (t), 123.7 (d), 130.5 (d), 131.3 (d), 135.0 (d), 166.7 (s); mass spectrum (70 eV), m/e (relative intensity) 166 (M^+, 2.2), 148 (0.6), 134 (2.8), 119 (4.5), 105 (5.0), 93 (24.6), 91 (12.8), 81 (100), 79 (93.9), 77 (37.8), 69 (38.0); calcd for $C_8H_{10}O_2N_2$, 166.0742; found, 166.0745.

1-Oxo-4-prop-1-en-1-yl-1,3,3a,6a-tetrahydrocyclopropa[*c*]furan (26). Diazo ester **25** (5 g, 0.03 mol) in 50 mL of dry benzene was added to a refluxing slurry of 11.6 g of anhydrous $CuSO_4$ and 0.32 g of $Cu(acac)_2$ in 400 mL of dry benzene over 30 min. The resulting mixture was refluxed further for 2 h. Filtration through a bed of Celite, removal of solvents, and a bulb-to-bulb distillation afforded 2.85 g (68%) of pure cyclopropane **26**, analytical TLC (silica gel, hexane/Et_2O (60:40)) R_f 0.25; bp 60–80 °C (Kügelrohr (0.05 mmHg)); IR (neat) 1780, 1660 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.7 (d, 3 H, J = 6 Hz), 1.8 (m, 1 H), 2.0 (dd, 1 H), 2.2 (m, 1 H), 4.3 (m, 4 H); 5.1 (dd, 1 H), 5.6 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 17.4 (q), 24.0 (d), 24.5 (d), 27.8 (d), 69.0 (t), 126.8 (d), 126.9 (d), 174.9 (s); mass spectrum (70 eV) m/e (relative intensity) 138 (M^+, 3.9), 123 (8.9), 94 (24.0), 91 (10.6), 81 (20.7), 79 (100), 77 (36.9), 65 (13.4), 55 (12.3), 53 (29.0); calcd for $C_8H_{10}O_2$, 138.0681; found, 138.0678.

1-Oxo-6-methyl-1,3,3a,6a-tetrahydrocyclopenta[*c*]furan (23). A. From Pyrolysis of 26. Cyclopropane **26** (1.5 g, 0.011 mol) was evaporated through a Vycor tube preconditioned with $PbCO_3$ at 600 °C (0.05 mm). The pyrolysate was collected in a trap cooled with liquid nitrogen. The crude product (0.84 g, 56%) was shown to consist of **23a** and **23b** (28:72) (OV-101, 140–180 °C (10°/min), 30 cc/min N_2). It was chromatographed (silica, hexane/ether, 6:4) to afford **23b** (42%); IR (neat) 1770, 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.1 (d, 3 H, J = 7 Hz), 1.8 (m, 1 H), 3.0 (m, 2 H), 4.1–4.4 (m, 2 H), 5.8 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 15.7 (q), 41.9 (d), 44.4 (d), 46.8 (d), 71.2 (t), 129.2 (d), 138.1 (d), 168.0 (s); mass spectrum (70 eV), m/e (relative intensity) 138 (M^+, 7.3), 123 (8.4), 110 (3.9), 93 (53.6), 91 (16.8), 80 (76.0), 79 (100), 77 (62.6), 65 (19.0), 53 (34.6); calcd for $C_8H_{10}O_2$, 138.0681; found, 138.0683.

B. From Decarbomethoxylation of 22. A mixture of **22a** and **22b** (83:17) (235 mg, 0.0012 mol), anhydrous lithium iodide (482 mg, 0.0036 mol), and 3 mL of dry DMF was refluxed under nitrogen for 2 h. It was then cooled, quenched with 3 N HCl, and extracted with ether (4 × 50 mL). The ethereal layer was thoroughly washed with H_2O (6 × 1 mL) and brine (3 × 1 mL). Drying (Na_2SO_4) and removal of solvent yielded 150 mg (91%) of a mixture of **23a** and **23b** in the unchanged ratio of 83:17 (GC, OV-101). Chromatography gave **23a**; IR (neat) 1760, 1610 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.0 (d, 3 H, J = 7 Hz), 1.8 (m, 1 H), 3.0 (m, 2 H), 4.4 (m, 2 H), 5.8 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 20.7 (q), 42.5 (d), 45.2 (d), 48.1 (d), 71.3 (t), 129.3 (d), 138.4 (d), 168.1 (s); mass spectrum (70 eV), m/e (relative intensity) 138 (M^+, 3.9), 123 (5.0), 93 (39.1), 91 (11.7), 79 (100), 77 (47.5), 66 (15.1), 53 (22.9); calcd for $C_8H_{10}O_2$, 138.0681; found, 133.0679.

1-Carbomethoxy-2-(hydroxymethyl)-5-methylcyclopent-3-ene (5). Lactones **23** (150 mg, 0.001 mol) were refluxed in 3 mL of 30% alcoholic KOH for 3 h. The mixture was cooled and extracted with hexane (2 × 10 mL). The aqueous layer was acidified and extracted with $CHCl_3$ (4 × 20 mL). Drying and removal of solvents gave a mixture of hydroxy acids; IR 3400–2700, 1700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.0 and 1.1 (two doublets, 3 H, α- and β-methyls). This mixture (70 mg) was esterified with ethereal diazomethane to give 55 mg of esters **5** (74%). Purification of these esters was effected by preparative TLC (silica, hexane:ether, 3:2). **5a**: R_f 0.5 (hexane/Et_2O (1:1)); IR (neat) 3300, 1740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.1 (d, 3 H, J = 7 Hz), 1.8 (m, 1 H), 2.8–3.0 (m, 2 H), 3.6 (m, 2 H); 3.7 (s, 3 H), 5.6 (m, 2 H). **5b**: IR (neat) 3400, 1740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.0 (d, 3 H, J = 7 Hz), 1.8 (m, 1 H), 3.0 (m, 2 H), 3.6 (m, 2 H), 3.65 (s, 3 H), 5.6 (m, 2 H); mass spectrum (70 eV), m/e (relative intensity) 170 (M^+, 2.8), 152 (31.8), 139 (38.0), 120 (17.3), 111 (27.9), 107 (39.1), 95 (19.6),

92 (100), 91 (81.6), 85 (35.8), 81 (79.9), 77 (89.4), 67 (57.5), 59 (92.2), 55 (79.9); calcd for $C_9H_{14}O_3$, 170.0943; found, 170.0948.

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Studies Directed toward the Total Synthesis of Securinega Alkaloids

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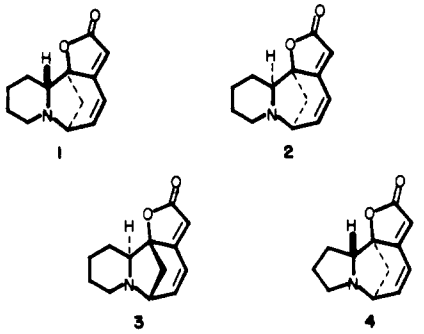
An approach to the synthesis of securinega alkaloids is reported. Reductive amination of ethyl 2-thienylacetoacetate (**12**) with methyl (*S*)-prolinate gives a mixture of diastereomeric amino diesters **6** and **13** in a ratio of 44:56. Dieckmann cyclization of the mixture followed by treatment of the product with acid affords the crystalline (±)-**10** in 64% yield. Separation of **6** and **13** prior to cyclization provides samples of the enantiomers (−)-**10** and (+)-**10**, respectively. Attempts to open the thiophene ring of **10** were not successful. Treatment of (±)-**10** with excess *n*-butyllithium and trimethylsilyl chloride results in a novel fragmentation, leading to the benzothiophene **18**.

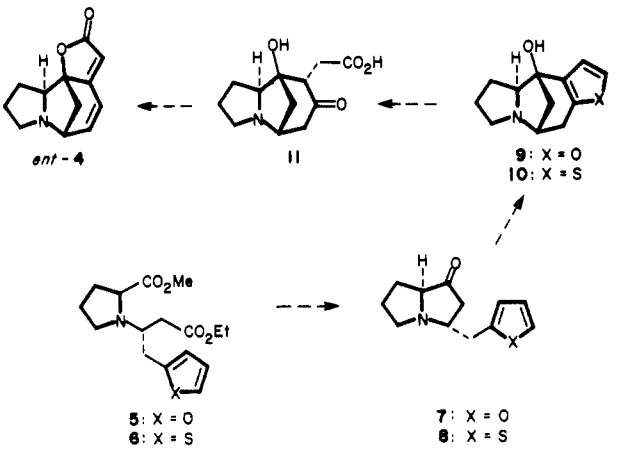
The securinega alkaloids are a group of compounds found in the *Securinega* and *Phyllanthus* genera of the *Euphorbiaceae* family of plants.[1] The most abundant representative, and the first to be isolated and characterized, is securinine (**1**). Other naturally occurring



members of the group are the securinine stereoisomers allosecurinine (**2**) and virosecurinine (**3**) and the *A*-nor compound norsecurinine (**4**). In this paper, we report a simple approach to construction of the skeleton of **4**. Although the approach, which utilizes an intramolecular Friedel–Crafts reaction of a 3-(arylmethyl)pyrrolizid-1-one, has been abandoned for both chemical and stereochemical reasons, some interesting chemistry has emerged from the project. In addition, the current work has led to a more successful approach to norsecurinine, which will be communicated separately.

Our retrosynthetic analysis is summarized in Scheme I. At the outset, we elected to develop a synthesis of *ent*norsecurinine (*ent*-**4**), rather than norsecurinine itself, so that we could employ methyl (*S*)-prolinate, rather than the less readily available methyl (*R*)-prolinate. The decision to mask the γ-keto acid moiety (e.g., in **11**) as a

Scheme I



heteroaromatic ring was made because it was believed that some form of protection would be necessary in any event and that by employing an aromatic ring for this purpose, we would make available a greater range of options for formation of ring C (e.g., **7** or **8** to **9** or **10**). Although some of our exploratory work was done with the furan series (**5**, **7**, **9**), difficulties in working with these exceedingly acid-sensitive compounds encouraged us to concentrate on the thiophene series at an early stage.

Ethyl 2-thienylacetoacetate (**12**) has previously been prepared from (2-thienyl)acetyl chloride and *tert*-butyl ethyl malonate, albeit in only 22% yield.[2] We prepared β-keto ester **12** by the Yonemitsu method[3] in 73% yield. Reductive amination of **12** with methyl (*S*)-prolinate and sodium cyanoborohydride[4] provides a mixture of diaste-

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