3-(*p*-Toluenesulfonyl)butanal (6). Glacial acetic acid (6.0 g, 5.8 mL, 0.10 mol) was added dropwise to a solution of sodium *p*-toluenesulfinate monohydrate (21.4 g, 0.1 mol) in water (100 mL) plus tetrahydrofuran (50 mL) stirred at 0 °C under nitrogen. Freshly distilled crotonal (6.0 g, 8.25 mL, 0.1 mol) in THF (25 mL) was added, and the mixture was stirred for 21 h at room temperature. Water (250 mL) was then added, and the mixture was extracted with methylene chloride, which was dried and stripped to yield an oil. NMR analysis showed the material to be pure sulfone aldehyde **6**, which was used directly in the next step: NMR δ 9.78 (1 H, s), 7.78 (2 H, d, J = 8 Hz), 7.38 (2 H, d, J = 8 Hz), 3.64 (1 H, m), 3.17 (1 H, d of d, J = 19, 4 Hz), 2.60 (1 H, d of d, J = 19, 8 Hz), 2.44 (3 H, s), 1.28 (3 H, d, J = 8 Hz).

2-[2-(*p*-Toluenesulfonyl)propyl]-1,3-dioxolane (7). Crude aldehyde **6** (0.10 mol) was dissolved in dry benzene (200 mL) plus ethylene glycol (6.2 g, 5.6 mL, 0.10 mol) and *p*-toluenesulfonic acid (100 mg) was added as a catalyst. The mixture was refluxed under nitrogen through a Dean–Stark trap for 5 h, then the solution was cooled and washed with aqueous $NaHCO_3$, and the organic phase was dried and stripped. The oil was crystallized by taking it up in hexane/ethyl acetate, cooling in a dry ice/ethanol bath, and scratching briskly with a glass rod. The resulting white crystals were filtered and dried to yield 22.8 g (84%): mp 31–33 °C; NMR δ 7.74 (2 H, d, J = 8 Hz), 7.32 (2 H, d, J = 8 Hz), 4.96 (1 H, t, J = 5 Hz), 3.85 (4 H, m), 3.3 (1 H, m), 2.45 (3 H, s), 2.2 (1 H, m), 1.8 (1 H, m), 1.32 (3 H, d, J = 8 Hz).

2-[(*p*-Toluenesulfonyl)-2-(carboxyethyl)propyl]-1,3-dioxolane (8). Sulfone acetal **7** (19.8 g, 73 mmol) was dissolved in dry THF (200 mL) under nitrogen, to which triphenylmethane (100 mg) had been added as an indicator. Then, a solution of *n*-butyllithium in hexane (43 mL of 1.7 M solution, 73 mmol) was added dropwise and the mixture was stirred for 15 min at room temperature. The temperature was maintained with a water bath as ethyl chloroformate (11.9 g, 9.6 mL, 110 mol) was added over the period of 5 min. The solution was stirred for 21 h, then water was added and the product was extracted with methylene chloride, which was dried and stripped to yield **8** (25 g, 99%) as an oil: NMR δ 7.72 (2 H, d, J = 8 Hz), 7.34 (2 H, d, J = 8 Hz), 5.00 (1 H, d of d, J = 6, 4 Hz), 4.16 (2 H, q, J = 7 Hz), 3.8 (4 H, m), 2.58 (1 H, d of d, J = 14, 6 Hz), 2.45 (3 H, s), 2.20 (1 H, d of d, J = 14, 4 Hz), 1.67 (3 H, s), 1.21 (3 H, t, J = 7 Hz).

3-(*p*-Toluenesulfonyl)-3-(carboxyethyl)butanal (9). Ester **8** (3.42 g, 10 mmol) was dissolved in dioxane (50 mL) and water (8 mL) and cooled to 0 °C under nitrogen as 60% aqueous perchloric acid (42 mL) was added dropwise over 15 min. The mixture stirred at 0 °C for 2 h, then water (200 mL) was added and the product was extracted with methylene chloride. The organic phase was washed with water, dried, and stripped to yield sulfone aldehyde **9**, which was used immediately in the next step: NMR δ 9.74 (1 H, s), 7.72 (2 H, d, J = 8 Hz), 7.32 (2 H, d, J = 8 Hz), 4.12 (2 H, q, J = 7 Hz), 3.54 (1 H, d, J = 18 Hz), 2.94 (1 H, d, J = 18 Hz), 2.45 (3 H, s), 1.84 (3 H, s), 1.17 (3 H, t, J = 7 Hz).

Ethyl β-Formylmethacrylate (10). Aldehyde **9** (10 mmol) was dissolved in ether (50 mL) and trimethylamine gas was bubbled through while cooling in a water bath. An oil formed and precipitated, and the ether solution was decanted. The precipitate was shown by NMR to be trimethylammonium *p*-toluenesulfinate. The ether solution was washed with brine, and the ether was carefully removed under a nitrogen stream. The crude yellow oil was purified by molecular distillation at 100 °C (0.2 mmHg), yielding pure unsaturated ester **10** of undetermined stereochemistry, but with greater than 90% selectivity (presumably the *E* isomer). The yield was 785 mg (56% from **8**): NMR δ 10.28 (1 H, d, J = 8 Hz), 6.84 (1 H, d of q, J = 8, 1 Hz), 4.30 (2 H, q, J = 7 Hz), 2.34 (3 H, d, J = 1 Hz), 1.34 (3 H, t, J = 7 Hz).

3-Methyl-5-hydroxy-2(5*H*)-furanone (2-Methyl-4-hydroxybut-2-enolide) (1). Unsaturated ester **10** (785 mg, 5.6 mmol) was heated at 100 °C for 2 h under nitrogen in 10% aqueous sulfuric acid (10 mL). The mixture was then cooled to room temperature, saturated with NaCl, and extracted three times with methylene chloride. The organic phase was dried and carefully stripped to yield the crystalline hydroxy lactone. The material could be purified by sublimation at 100 °C (0.25 mmHg), but was best purified by recrystallization from cyclohexane plus a few drops of ether to give a total of 420 mg (72%) from two crystal crops: mp 69–71 °C (lit.[5] 69–71 °C); NMR δ 6.90 (1 H, m), 6.10 (1 H, q, J = 1 Hz), 3.7 (1 H, s br), 1.90 (3 H, d, J = 1 Hz).

Registry No. 1, 931-23-7; **2**, 616-02-4; **3**, 40834-42-2; **4**, 4170-30-3; **5**, 824-79-3; **6**, 71041-35-5; **7**, 70451-38-6; **8**, 71041-36-6; **9**, 71041-37-7; **10**, 71041-38-8; ethyl chloroformate, 541-41-3.

3-Ethylidenecyclohexyl Acetates from Acetic Acid Treatment of 1-(1-Hydroxyethyl)bicyclo[3.1.0]hexanes

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In the course of studies directed toward the partial synthesis of vitamin D analogues, it became of interest to prepare 3-ethylidenecyclohexanols in which the geometry of the exocyclic double bond could be controlled by the choice of an appropriate synthetic method. Surprisingly, the parent system has not yet been reported, and a general, stereoselective synthesis of such a γ,δ-disubstituted homoallylic system apparently has not been studied.

Of the methods available for the preparation of homoallylic alcohols,[1] we chose to investigate the rearrangement of the cyclopropylcarbinyl system generated from 1-(1-hydroxyethyl)bicyclo[3.1.0]hexane (**1**). This system, which

1a R = H **1b**
c R = α-naphthNHCO **d**
e R = 3,5-$(NO_2)_2C_6H_3CO$ **f**
g R = CH_3CO **h**

2a **2b**

is present in the rigid framework of 6α- and 6β-hydroxy-3α,5α-cyclosteroids, has been found to rearrange selectively and in high yield on acid treatment to give the corresponding steroidal 5-en-3β-ol system.[2] Solvolysis of the closely related bicyclo[3.1.0]hex-1-ylmethyl *p*-nitrobenzoate affords >80% yield of 3-methylenecyclohexanol.[3] Recent studies on the solvolysis of 3,5-cyclovitamin D

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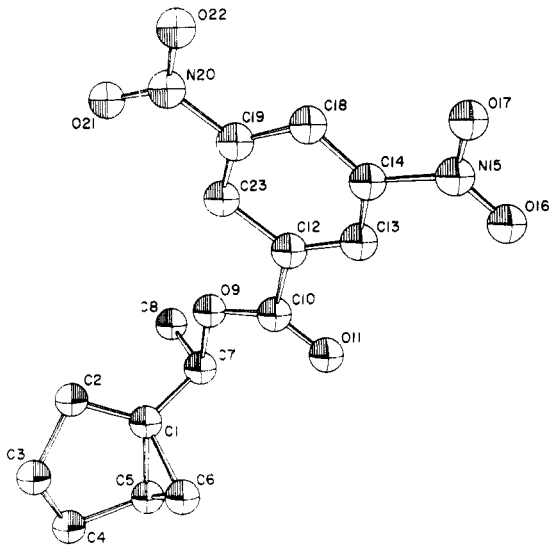

Figure 1. Perspective drawing of the 3,5-dinitrobenzoate **1e**. For clarity, hydrogens have not been included.

derivatives have shown that 3β-hydroxyvitamins of 5*E* and 5*Z* geometry are formed, with the natural 5*Z* isomer being present in higher amounts than would have been predicted with only steric considerations.[4] We thus anticipated that the rearrangement of **1** would likewise be selective to give 3-ethylidenecyclohexanol and that any variation in the geometry of the product olefin would be dependent on the relative orientation of the hydroxyl group to the cyclopropane ring in the two diastereoisomers of **1**.

Racemic **1** was prepared in two steps from 1-acetylcyclopentene[5] by reaction with dimethylsulfoxonium methylide followed by sodium borohydride reduction. The diastereoisomeric alcohols were formed in a ratio of about 2:1 as analyzed by NMR and high-pressure LC. These could be separated by preparative high pressure LC utilizing a recycle feature to give the major, more mobile isomer (**1a**) and a less mobile isomer (**1b**). Each isomer could be distinguished from the other by the NMR shift of the methine hydrogen of the hydroxyl-bearing carbon, the quartet of **1a** being centered at 3.64 ppm and that of 1b at 3.48 ppm. Crystalline derivatives **1c,e** and **1d,f** of each isomer were prepared by reaction with α-naphthyl isocyanate and with 3,5-dinitrobenzoyl chloride, respectively. The structure of the 3,5-dinitrobenzoate (**1e**) of **1a** was determined by X-ray analysis and is depicted in the ORTEP drawing of Figure 1. Acetates (**1g** and **1h**) of each alcohol were also prepared.

The alcohols **1a** and **1b** proved to be quite stable to glacial acetic acid at room temperature, remaining unaltered after 8 h. Exposure to hot (110 °C) glacial acetic acid resulted in rapid conversion to a mixture of olefinic acetates. Both **1a** and **1b** on heating at 110 °C in this solvent for ≥10 min gave the same major product along with a second component whose relative yield was dependent upon the configuration of the starting alcohol. A third, minor (<3%) component(s) has a retention time on high-pressure LC coincidental with that of the acetates of the starting cyclopropylcarbinols. The major and secondary products were found to be stable to the reaction conditions over a 24-h period; however, the cyclopropyl acetates, **1g** and **1h**, rearranged in a fashion similar to their parent alcohols. From the alcohol **1a** the ratio of major to secondary product in the acetolysis was about 5:1 as measured by NMR vinyl hydrogen peak heights or by refractive index monitoring of high-pressure LC elution. From alcohol **1b** the ratio was slightly greater than 2:1. If either of the cyclopropylcarbinols **1a** or **1b** was heated only briefly (≤5 min) in hot glacial acetic acid, the product mixture contained an appreciable amount (>20%) of a *mixture* of the acetates **1g** and **1h** as well as the olefinic acetate major and secondary products mentioned above.

The major and secondary acetolysis products could be preparatively separated by recycle high-pressure LC on silica gel. The major, less mobile material **2a** has proton NMR shifts at δ 5.23 (1 H, q, J = 8 Hz), 4.72 (1 H, m), 2.02 (s), and 1.57 (d, J = 8 Hz) while the more mobile material **2b** has shifts at δ 5.30 (1 H, q, J = 8), 4.73 (1 H, m), 2.03 (3 H, s), and 1.58 (3 H, d, J = 8 Hz). These spectra along with infrared and mass spectral data are consistent with the assignment of **2a** and **2b** as being geometric isomers of 3-ethylidenecyclohexyl acetates.

The geometry of the double bond in the isomers of **2** was assigned by use of ^{13}C NMR. The assignments are based on the rule that cis α-carbons are shielded in trisubstituted olefins by approximately 8 ppm when compared with the adjacent trans α-carbon.[6] A decision on the relative stereochemistry thus rests on the ability to identify the C2 carbon of the cyclohexane ring in each of the isomers. This was accomplished by obtaining ^{13}C spectra of a 2:1 mixture of isomers obtained from **1b** while simultaneously decoupling the individual allyl equatorial protons at C2. In deuteriobenzene, the ^1H NMR shifts of these protons appear separately and slightly downfield from the aliphatic envelope. The decoupling leads to simplification of ^{13}C resonances at 40.6 and 32.1 ppm for the major and minor isomers, respectively. The major isomer thus has the *E* configuration **2a** and the minor isomer the *Z* configuraton **2b**.

The observation that each diastereomer, **1a** and **1b**, gives the same major isomer but different ratios of products indicates a mixed mechanism of product formation. One would anticipate that if the C–O bond breaking was concerted with breaking of the C1–C5 bond of the bicyclohexane, **1a** would give **2a** and **1b** would give **2b** stereoselectively because of preferred bond overlap in the transition state (see Figure 2).[7] Indeed, the product **2a** which would result from the intermediate with the smaller internal steric interaction is the major product formed and is formed in a higher ratio from **1a** than from **1b**. If a nondelocalized cyclopropylcarbonium ion results as an initial event in this reaction, both **1a** and **1b** would be expected to give the same ratio of products because the expected free rotation about the bond exocyclic to the bicyclohexane ring would make the intermediates equivalent. As the cyclopropyl acetates **1g** and **1h** could be observed in the early stages of the acetolysis of each of **1a** and **1b**, it is clear that at least a portion of the reaction products results from a process where C–O bond breaking and formation occurs prior to rupture of the cyclopropane ring. By the same token, some concerted process involving cyclopropane ring opening must also take place directly via the alcohols, as the increased amount of **2b** in the acetolysis mixture from **1b** can be explained by its direct

(4) (a) M. Sheves and Y. Mazur, *J. Am. Chem. Soc.*, **97**, 6249 (1975); (b) M. Sheves and Y. Mazur, *Tetrahedron Lett.*, 2987 (1976); (c) H. E. Paaren, D. E. Hamer, H. K. Schnoes, and H. F. DeLuca, *Proc. Natl. Acad. Sci. U.S.A.*, **75**, 2080 (1978).

(5) H. O. House, T S. B. Sayer, and C.-C. Yau, *J. Org. Chem.*, **43**, 2153 (1978).

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(7) For an analogous argument see S. F. Brady, M. A. Ilton, and W. S. Johnson, *J. Am. Chem. Soc.*, **90**, 2882 (1968). In our case the methylene group of the cyclopropane seriously eclipses the side chain methyl group of **1b**, thus making the concerted-reaction transition state less favorable.

formation, as shown in Figure 2.

It would appear that the conditions of the reaction, although providing ethylidenecyclohexyl acetate in good yield, do not afford sufficient geometric selectivity of olefin formation to make this a good method for controlling double bond configuration in γ,δ-disubstituted homoallylic alcohols. It has been found in other studies that the rearrangement for 16α,17α-methylenepregnene-20α- and -20β-diols by this method gives as the only isolable product the corresponding *D*-homosteroid with the ethylidene group at C17a being in the *E* configuration.[8] This would indicate that steric interactions in the transition state to a large extent govern product formation. It is likely that one could change the product ratio by modifying the conditions to those which might be less acidic and thus would not favor initial carbonium ion formation. An active ester solvolysis in a buffered medium might be expected to give a product mixture which would indicate more accurately the degree of direct cyclopropane participation and the attendant stereoselectivity related to this process.

Experimental Section

General Methods. Melting points and boiling points are uncorrected. Infrared spectra were determined with a Perkin-Elmer Infracord, Model 137. ^{1}H NMR spectra were obtained on Varian T-60 and SC-300 spectrometers. ^{13}C NMR spectra were recorded on a Varian SC-300 spectrometer. Mass spectra were obtained from a LKB model 9000 spectrometer equipped with GC and direct inlet systems. Analytical high-pressure LC separations were made on a Waters Associates ALC200 series chromatograph equipped with a Model 6000A pump, a 3.9 mm × 30 cm μPorasil column, and a Series 400 refractometer detector. Preparative high-pressure LC separations were made on a Waters Associates Prep 500 chromatograph equipped with one or two Prep-Paks (325 g of silica gel each). X-ray data were collected on a Syntex $P2_1$ diffractometer.

1-Acetylbicyclo[3.1.0]hexane. Sodium hydride from 3.0 g of a 56% suspension in mineral oil was washed free of the oil by repeated rinsings with petroleum ether. To the dry hydride under nitrogen was added successively 50 mL of freshly distilled dimethyl sulfoxide and 21.0 g (0.095 mol) of anhydrous trimethyloxosulfonium iodide. When hydrogen evolution ceased (~20 min), 1-acetylcyclopentene[5] (7.0 g, 0.063 mol) was added with stirring at room temperature. After 3 h the reaction was poured into 125 mL of water and the product extracted with ether. The organic layer was washed with water (2×), dried ($MgSO_4$), and concentrated to a pale yellow liquid. Distillation afforded 4.92 g (60%) of colorless liquid: bp 26–27 °C (0.1 mm Hg); IR (film) 5.92, 7.29, 7.86, 8.80, 8.94 μm; ^{1}H NMR ($CDCl_3$, 60 MHz) 2.08 (3 H, s, CH_3), 1.4–1.8 (6 H, m, CH_2), 0.85–1.0 ppm (2 H, m, cyclopropyl CH_2); mass spectrum, *m/e* 124 (M^+), 109, 96, 81, 43.

Diastereoisomers of 1-(1-Hydroxyethyl)bicyclo[3.1.0]-hexane. A solution of 7.56 g (0.061 mol) of 1-acetylbicyclo-[3.1.0]hexane in 100 mL of methanol was treated at −10 °C over a period of 1.5 h with 15 g of sodium borohydride. After being stirred an additional 30 min at room temperature, the reaction mixture was diluted with water, and the product was extracted with ether. The organic layer was washed with water, dried ($MgSO_4$), and concentrated to leave about 7 g of liquid. After elution through a short column of silica gel (E. Merck) with 1:1 hexane–ethyl acetate to remove polar materials, the mixture of alcohols was separated by preparative, recycle high-pressure LC eluting through two Paks with 20% ethyl acetate in hexane. Five passages of the desired peaks through the Paks with trimming sufficed to separate the fast and slow isomers cleanly. The fast-moving isomer **1a** amounted to 4.23 g of a colorless liquid: IR (film) 2.9 (br), 3.38, 3.47, 6.91, 7.34, 9.76, 9.98, 10.17, 10.70, 10.91, 11.39 μm; ^{1}H NMR ($CDCl_3$, 300 MHz) 3.64 (1 H, q, J = 7 Hz, C*H*CH_3), 1.55–1.75 (6 H, m, CH_2), 1.17 (3 H, d, J = 7 Hz, CH_3), 1.05–1.15 (1 H, m, CH), 0.35–0.47 ppm (2 H, m, cyclopropyl CH_2); mass spectrum, *m/e* 126 (M^+), 108, 93, 91, 82, 80, 67 (base).

The slow-moving isomer **1b** amounted to 2.89 g of a colorless liquid: IR 2.9 (br), 3.35, 3.45, 6.90, 7.32, 9.80, 10.0, 10.47, 10.62, 10.93, 11.39 μm; ^{1}H NMR ($CDCl_3$, 300 MHz) 3.48 (1 H, q, J = 7 Hz, C*H*CH_3), 1.6–1.9 (6 H, m, CH_2), 1.20 (3 H, d, J = 7 Hz, CH_3), 1.1–1.3 (1 H, m, CH), 0.35–0.45 ppm (2 H, m, cyclopropyl CH_2); mass spectrum, *m/e* 126 (M^+), 108, 93, 91, 82, 79, 67 (base).

3,5-Dinitrobenzoate (1e) of the Fast-Moving Alcohol. A mixture of **1a** (126 mg, 1.0 mmol), 3.0 mL of anhydrous pyridine, and 230 mg (1.0 mmol) of 3,5-dinitrobenzoyl chloride was stirred under a nitrogen atmosphere at 0 °C for 20 min and then at 25 °C for 24 h. The reaction mixture was added to water and extracted with ether. The organic layer was washed successively with saturated $NaHCO_3$ solution (3×), water, 1% HCl solution (3×), water, and saturated NaCl solution. The solution was dried ($MgSO_4$) and concentrated to a white solid. Two crystallizations from 2-propanol afforded **1e**: mp 110–112 °C; ^{1}H NMR ($CDCl_3$, 60 MHz) 9.10–9.35 (3 H, m, aromatic CH), 5.25 (1 H, q, J = 7 Hz, CHO), 1.1–2.1 (6 or 7 H, m, CH_2), 1.37 (3 H, d, J = 7 Hz), CH_3), 0.4–0.8 ppm (2 H, m, cyclopropane CH_2); mass spectrum, *m/e* 195, 149, 108 (base).

Anal. Calcd for $C_{15}H_{16}N_2O_6$: C, 56.23; H, 4.99; N, 8.75. Found: C, 56.15; H, 5.09; N, 8.53.

X-ray Crystallographic Study of the 3,5-Dinitrobenzoate 1e. Thin crystalline needles of **1e** were formed by evaporation from 2-propanol. Preliminary diffraction experiments indicated that the symmetry of the crystal lattice was $P2_1/c$ with a = 9.453 (5), b = 6.044 (3), and c = 27.080 (9) Å and β = 94.74 (4)°. Since the crystal used for the data collection was quite small, only 710 (34%) of the reflections measured with $2\theta \leq 114°$ (λ = 1.5418 Å) were considered observed ($I \geq 3\sigma_I$). The structure was solved by using a multisolution tangent formula approach[9] and subsequently

Table I. Bond Distances (Å) of the 3,5-Dinitrobenzoate of 1a[a]

C1-C2	1.448 (26)	C12-C13	1.309 (23)
C1-C5	1.512 (29)	C12-C23	1.431 (24)
C1-C6	1.605 (33)	C13-C14	1.410 (23)
C1-C7	1.484 (24)	C14-N15	1.509 (26)
C2-C3	1.508 (41)	C14-C18	1.374 (27)
C3-C4	1.515 (42)	N15-O16	1.176 (27)
C4-C5	1.528 (36)	N15-O17	1.173 (23)
C5-C6	1.581 (32)	C18-C19	1.344 (23)
C7-C8	1.468 (27)	C19-N20	1.451 (22)
C7-O9	1.450 (21)	C19-C23	1.397 (23)
O9-C10	1.321 (24)	N20-O21	1.202 (22)
C10-O11	1.200 (25)	N20-O22	1.254 (20)
C10-C12	1.563 (24)		

[a] Standard deviations of the least significant figures of each distance are given in parentheses.

Table II. Bond Angles (deg) of the 3,5-Dinitrobenzoate of 1a[a]

C2-C1-C5	109.8 (16)	O11-C10-C12	117.9 (17)
C2-C1-C6	112.9 (17)	C10-C12-C13	119.1 (15)
C2-C1-C7	125.5 (18)	C10-C12-C23	118.6 (14)
C5-C1-C6	60.9 (14)	C13-C12-C23	122.2 (15)
C5-C1-C7	115.0 (16)	C12-C13-C14	118.3 (15)
C6-C1-C7	115.1 (18)	C13-C14-N15	114.7 (16)
C1-C2-C3	103.3 (21)	C13-C14-C18	123.0 (15)
C2-C3-C4	103.5 (20)	N15-C14-C18	122.3 (15)
C3-C4-C5	104.8 (21)	C14-N15-O16	119.6 (17)
C1-C5-C4	103.7 (18)	C14-N15-O17	112.7 (18)
C1-C5-C6	62.4 (15)	O16-N15-O17	127.6 (20)
C4-C5-C6	104.3 (20)	C14-C18-C19	116.2 (15)
C1-C6-C5	56.7 (13)	C18-C19-N20	120.1 (15)
C1-C7-C8	113.9 (17)	C18-C19-C23	124.3 (16)
C1-C7-O9	106.9 (13)	N20-C19-C23	115.5 (15)
C8-C7-O9	102.9 (15)	C19-N20-O21	121.2 (15)
C7-O9-C10	114.8 (14)	C19-N20-O22	116.3 (15)
O9-C10-O11	128.5 (18)	O21-N20-O22	122.6 (16)
O9-C10-C12	113.6 (15)	C12-C23-C19	115.5 (14)

[a] Standard deviations of the least significant figures are given in parentheses.

(8) N. G. Steinberg, G. H. Rasmusson, and R. A. Reamer, *J. Org. Chem.*, **44**, 2294 (1979).

refined with Fourier and least-squares methods[10] by minimizing $\sum w(|F_o| - |F_c|)^2$ with $w = 1$ for all observed reflections. A number of weighting schemes were tried with σF and F^2; however, these were judged quite unsatisfactory because of proportionally large counting errors relative to the weak observed reflections. The final unweighted R factor is 0.114 with anisotropic temperature parameters for nonhydrogen atoms and calculated positions for hydrogens. Figure 1 contains a perspective drawing of **1e**[11] while Tables I and II contain bond distances and bond angles, respectively. Some bond distances and angles are slightly distorted from expected values because of the small number of intensities observed. A table of fractional coordinates and thermal factors is included as supplementary material.

The conformation of the five-membered ring in the solid state can best be described as midway between an envelope and a half-chair conformation with torsional angles of C1–C2–C3–C4 = –38°, C2–C3–C4–C5 = 35°, C3–C_4–C_5–C1 = –17°, C4–C5–C1–C_2 = –7°, and C5–C1–C2–C3 = 28°. In addition, the torsional angle delineated by O9–C7–C1–C5 is –160°.

3,5-Dinitrobenzoate (1f) of the Slow-Moving Alcohol. Reaction of **1b** (126 mg, 1.0 mmol) with 3,5-dinitrobenzoyl chloride as described above for **1a** gave a mixture (NMR, 4:1) of the desired dinitrobenzoate and starting alcohol. Crystallization from methanol and then 2-propanol afforded 113 mg of **1f**: mp 130–131 °C; ^{1}H NMR ($CDCl_3$, 60 MHz) 9.10–9.30 (3 H, m, aromatic CH), 5.06 (1 H, q, J = 7 Hz, CHO), 0.98–2.10 (6 or 7 H, m, CH_2), 1.45 (3 H, d, J = 7 Hz, CH_3), 0.45–0.68 (2 H, m, cyclopropane CH_2); mass spectrum, m/e 195, 149, 108 (base).

Anal. Calcd for $C_{15}H_{16}N_2O_6$: C, 56.23; H, 4.99; N, 8.75. Found: C, 56.19; H, 4.98; N, 8.57.

***N*-α-Naphthylcarbamates** were prepared from each isomer of **1** by reaction of equal molar quantities of the alcohol and α-naphthyl isocyanate (1 mmol/4 mL) in refluxing benzene for 24 h. The crude carbamates were purified by preparative thin-layer chromatography (silica gel, 1:1 hexane–ethyl acetate) followed by crystallization from methanol and then 2-propanol. The product **1c** from the fast-moving alcohol **1a** had mp 266–268 °C: ^{1}H NMR (Me_2SO-d_6, 60 MHz) 7.12–8.0 (7 H, m, aromatic CH), 4.92 (1 H, q, J = 7 Hz, CHO), 0.95–1.95 (6 or 7 H, m, CH_2), 1.30 (3 H, d, J = 7 Hz, CH_3), 0.42–0.75 (2 H, m, cyclopropyl CH_2); mass spectrum, m/e 295 (M^+), 251, 187, 143, 109 (base). The product **1d** from the slow-moving alcohol **1b** had mp 259–260 °C; ^{1}H NMR (Me_2SO-d_6, 60 MHz) 7.43–8.40 (7 H, m, aromatic CH), 4.75 (1 H, q, J = 7 Hz, CHO), 1.20–2.00 (6 or 7 H, m, CH_2), 1.34 (3 H, d, J = 7 Hz, CH_3), 0.42–0.76 (2 H, m, cyclopropane CH_2); mass spectrum, m/e 295 (M^+), 251, 187, 143, 109 (base).

Acetates of each isomer of **1** were prepared by reaction of 126 mg of the alcohol with 102 mg of acetic anhydride in 3 mL of pyridine at 25 °C for 18 h. The reaction mixture was added to water and extracted with ether. The organic layer was washed successively with 5% HCl (3×) and water and then dried ($MgSO_4$) and concentrated to the liquid product. Chromatography (silica gel, 1:1 hexane–ether) afforded the acetate free of starting material. The liquid acetate **1g** from the fast-moving alcohol had ^{1}H NMR ($CDCl_3$, 300 MHz) 4.84 (q, J = 7 Hz, CHO), 2.03 (s, CH_3CO), 1.56–1.84 (m, CH_2), 1.22 (d, J = 7 Hz, CH_3), 0.42 and 0.48–0.54 ppm (t, J = 5 Hz and dd, cyclopropane CH_2). The liquid acetate **1h** from the slow-moving alcohol had ^{1}H NMR ($CDCl_3$, 300 MHz) 4.73 (q, J = 7 Hz, CHO), 2.03 (s, CH_3CO), 1.51–1.84 (m, CH_2), 1.23 (t, J = 7 Hz, CH_3), 0.38–0.46 ppm (m, cyclopropane CH_2).

Acetic Acid Treatment of 1b: Separation and Identification of Ethylidenecyclohexyl Acetates 2a and 2b. A solution of 300 mg of the minor cyclopropyl alcohol **1b** in 3.0 mL of glacial acetic acid was heated at 119–120 °C under nitrogen for 15 min. After cooling to room temperature, the solution was poured carefully into an excess of saturated sodium bicarbonate solution. The product was extracted with ether and was washed successively with water (3×) and saturated sodium chloride solution. After being dried ($MgSO_4$), the ether solution was concentrated under reduced pressure at room temperature to a clear liquid which by thin-layer chromatographic analysis contained no starting material. This liquid was eluted through 18 g of silica gel with 4:1 hexane–ethyl acetate. The forerun was discarded, and fractions containing the product were combined and concentrated to leave 248 mg of a 2:1 mixture of olefinic acetates as determined by 300 MHz ^{1}H NMR analysis and analytical high-pressure LC chromatography. In deuteriobenzene two sets of doublet of doublets in a ratio of 1:2 were located outside the aliphatic envelope, and these were centered at 2.66 (J = 13.5, 3.5 Hz) and 2.44 (J = 12.5, 4.5 Hz) ppm. These were assigned to the equatorial allylic hydrogens at C2 of the minor and major isomers, respectively, as they collapsed to doublets upon decoupling of the acetate bearing methine hydrogen. ^{13}C NMR analyses were carried out in deuteriobenzene and deuteriochloroform. Gated and off-resonance decoupling studies allowed the assignment of shifts for each of the carbon atoms in both the major and minor isomers as follows: ^{13}C NMR ($CDCl_3$, 300 MHz), **2a**, 11.4 (CH_3C=C), 19.8 (CH_3C=O), 22.2 (C5), 25.7 (C4), 30.4 (C6), 40.6 (C2), 71.7 (C1), 117.7 (CH=C), 134 (C3), 169.1 ppm (C=O); **2b**, 11.3 (CH_3C=C), 19.8 (CH_3CO), 23.0 (C5), 30.4 (C6), 32.1 (C2) 34.4 (C4), 71.2 (C1), 117.6 (HC=C), 134.2 (C3), 169.1 ppm (C=O). A portion (70 mg) of this mixture was eluted with 10% ether in hexane through a column, $^3/_8$ in. × 4 ft, packed with Porosil A. For preparative resolution the product was cycled through the column three times. The minor, first-eluted material amounted to 17 mg, and after an overlap fraction was discarded, 27 mg of the major product was isolated. In addition to absorption due to traces of acetate **1h**, the first-eluted material had a ^{1}H NMR spectrum [($CDCl_3$, 300 MHz) 5.30 (1 H, q, J = 8 Hz, HC=C), 4.73 (1 H, m, CHO), 2.66 (1 H, dd, J = 4, 13 Hz equatorial 2-CH), 2.03 (3 H, s, CH_3CO), 1.57 ppm (3 H, d, J = 8 Hz, CH_3CH)] corresponding to that of the Z isomer, **2b**, the minor component of the reaction mixture as analyzed prior to separation. The major product has a ^{1}H NMR spectrum [($CDCl_3$, 300 MHz) 5.23 (1 H, q, J = 8 Hz, HC=C), 4.72 (1 H, heptet, CHO), 2.02 (3 H, s, CH_3CO), 1.57 ppm (3 H, d, J = 8 Hz, CH_3CH)] corresponding to the E isomer **2a** and the major component of the above mixture.

Acetic Acid Treatment of 1a. A solution of 309 mg of the cyclopropyl alcohol **1a** in 3 mL of glacial acetic acid was heated at 125 °C under nitrogen for 15 min. When worked up as described above, 296 mg of liquid **2** was obtained after initial chromatographic cleanup. By measurement of peak heights in the vinyl region of the NMR spectrum and by peak measurement (refractive index detector) of the high-pressure LC chromatogram, the E isomer, **2a**, predominated over the Z isomer, **2b**, by a factor of at least 5:1. A very minor component (<3%) had a retention time on high-pressure LC identical with that of acetate **1h** and gives barely discernible cyclopropyl absorption in the NMR spectrum of the mixture. These components were separated on the $^3/_8$ in. × 4 ft column described above using 70 mg or less per pass. Obtained were 140 mg of **2a**, 28 mg of **2b**, and 7 mg of what is probably a mixture of **1g** and **1h**. The spectra of **2a** and **2b** so isolated are identical with those obtained previously.

Acetic Acid Treatment of Acetates 1g and 1h. Solutions of 10 μL each of **1g** and **1h** in 30 μL of glacial acetic acid were heated at 114–116 °C for 1 h in a capped tube. The solutions were neutralized with aqueous $NaHCO_3$ solution and then ether extracted. After being washed with water and dried ($MgSO_4$), the organic solutions were concentrated. The product mixtures obtained were analyzed by 300-MHz ^{1}H NMR. The spectra from each isomer are essentially identical, indicating a mixture of **2a** and **2b** with no evidence of the original acetates being present.

Five-Minute Treatment of Alcohols 1a and 1b at 110 °C. Solutions of 127 mg each of **1a** and **1b** in 1.5 mL of glacial acetic acid were heated at 110–111 °C for 5 min. In each case the workup was as described above. The crude product was eluted through 8 g of silica gel with 1:1 hexane–ether to separate the acetate mixture from starting alcohol. From **1a** was obtained 95 mg of acetates and from **1b** 42 mg. The acetate mixtures were further separated by recycle chromatography (10% ether in hexane) on a Porosil A packed $^3/_8$ in. × 4 ft column. In this way acetate **2a**

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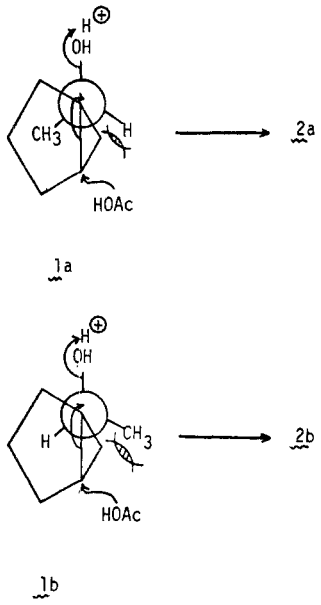

Figure 2. Newman projections of a concerted reaction.

could be separated from an almost equal quantity of an inseparable mixture of **2b** and acetates **1g** and **1h**. The 300-MHz ^1H NMR analyses clearly showed that >50% of the mixed fraction obtained from **1a** and ≤50% of the mixed fraction from **1b** were cyclopropyl acetates **1g** and **1h**.

Time and Temperature Studies of the Acetolysis Reaction. Solutions of 3 μL of compound in 10 μL of glacial acetic acid were submitted to various temperature and time intervals. They were then quenched in aqueous sodium bicarbonate solution, extracted, and analyzed by thin-layer chromatography or analytical high-pressure LC using a suitable hexane–ether elution system. In this way it was found that at 25 °C **1a** and **1b** were stable to glacial acetic acid for up to 8 h.

The product ratio of acetates obtained by heating either **1a** or **1b** in glacial acetic acid at 110–11 °C over intervals between 10 min and 16 h were not significantly different.

The products **2a** and **2b** were not interchanged significantly over a period of 24 h at 110 °C in glacial acetic acid.

(*E*)-3-Ethylidenecyclohexanol 3,5-Dinitrobenzoate. A solution of 290 mg of **2a** and 180 mg of potassium hydroxide in 4 mL of methanol was refluxed under nitrogen for 1.5 h. The reaction mixture was concentrated to dryness and treated with water. The product was extracted into ether, washed with water (4×), dried ($MgSO_4$), and isolated as a liquid. This material was eluted through 18 g of silica gel to give 88 mg of 3-ethylidenecyclohexanol: ^1H NMR ($CDCl_3$, 60 MHz) 5.24 (1 H, q, J = 7 Hz, HC=C), 3.69 (1 H, heptet, CHO), 2.55 (1 or 2 H, narrow m, allylic CH), 1.60 ppm (3 H, d, J = 7 Hz, CH_3CH).

A solution of this material in 3.0 mL of pyridine was treated with 175 mg of 3,5-dinitrobenzoyl chloride at −5 °C for 20 min and then stirred at 25 °C for 24 h. Water was added and the mixture extracted with ether. The organic layer was washed successively with aqueous $NaHCO_3$ solution (3×), water, 1% hydrochloric acid, water, and saturated NaCl. After being dried ($MgSO_4$) and concentrated, the resulting heavy oil was eluted through silica gel with 1:1 hexane–ether. The product crystallized from ethyl acetate to give 39 mg: mp 56–57 °C; mass spectrum, *m/e* 195, 149, 108 (base), 93, 79.

Registry No. (±)-**1a**, 71129-81-2; (±)-**1b**, 71183-85-2; (±)-**1c**, 71129-82-3; (±)-**1d**, 71183-86-3; (±)-**1e**, 71129-83-4; (±)-**1f**, 71183-87-4; (±)-**1g**, 71129-84-5; (±)-**1h**, 71183-88-5; (±)-**2a**, 71129-85-6; (±)-**2b**, 71129-86-7; (±)-1-acetylbicyclo[3.1.0]hexane, 71129-87-8; 1-acetylcyclopentene, 16112-10-0; (±)-(*E*)-3-ethylidenecyclohexanol 3,5-dinitrobenzoate, 71129-88-9; (±)-(*E*)-3-ethylidenecyclohexanol, 71129-89-0; α-naphthyl isocyanate, 86-84-0.

Supplementary Material Available: A table of fractional coordinates and thermal factors (1 page). Ordering information is given on any current masthead page.

Synthesis of Naturally Occurring Furan Fatty Acids

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Several years ago a novel group of fatty acids with a furan ring in their structure was reported from lipids of fish[1] and, very recently, also from latex of *Hevea brasiliensis*.[2] In contrast to an earlier reported furan fatty acid from *Exocarpus* seed oil,[3] these acids are tri- and tetrasubstituted furan compounds. In fish lipids, 11-(5-pentyl-3,4-dimethyl-2-furyl)undecanoic acid (**8**) and 11-(5-pentyl-3-methyl-2-furyl)undecanoic acid (**14**) are prominent examples. The furan fatty acids of fish may also vary in chain lengths of alkyl and alkylcarboxyl substituents. With furan being the common structural feature, the abbreviations F_1, F_2, . . . were used for them, with F_6 and F_5, respectively, being those named above.[1b]

The widespread occurrence and often high levels of F acids in liver and testes lipids of fish, their preferential esterification to cholesterol, and the apparent correlation of amounts to reproduction[1a,c] make desirable further biochemical and biological investigations. For such a purpose, syntheses of F_6 and of F_5 were undertaken. The syntheses verify the structures of the biological materials which had been deduced by degradation and spectrometric methods.[1b] They open the way to a variety of these tri- and tetrasubstituted furan compounds, including minor components in the group of F acids which so far have been identified only by GLC–MS.[4]

Syntheses of furan-type acids with an alkylcarboxyl and an alkyl group in ring positions 2 and 5, respectively, have been reported. However, the synthetic acids were either lacking the methyl group(s) at the furan ring[5] or were isomers with regard to the natural furan acids.[5d]

For the synthesis of F_6 **8** (Scheme I), 3,4-bis(acetoxymethyl)furan (**1**) was chosen as the starting material. Condensation with valeric acid anhydride[6] yielded the butyl ketone **2**, and its reduction with hydrazine gave the pentylfuran diol **3**. Conversion of the hydroxymethyl to

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