the band to ensure purity. Each plate was spotted with 40 mg of product and a total of 34 mg of 2*E*,4*Z* and 26 mg of 2*E*,4*E* was obtained. A silver nitrate (20% by weight) coated silica gel column failed to produce any separation of the isomers. 2*E*,4*Z* isomer: ^{1}H NMR (CCl_4) δ 7.43 (dd, J = 10, 15 Hz, 1 H), 6.03 (t, J = 10 Hz, 1 H), 5.55–5.95 (m, 1 H), 5.71 (d, J = 15 Hz, 1 H), 4.12 (q, J = 7 Hz, 2 H), 2.15–2.50 (m, 2H), 1.10–1.70 (m, 6 H), 1.24 (t, J = 7 Hz, 3 H), and 0.75–1.10 (m, 3 H). 2*E*,4*E* isomer: ^{1}H NMR (CCl_4) δ 7.10 (ddd, J = 15, 6, 3 Hz, 1 H), 5.95–6.20 (m, 2 H), 5.62 (d, J = 15 Hz, 1 H), 4.09 (q, J = 7 Hz, 2 H), 1.95–2.30 (m, 2 H), 1.10–1.65 (m, 6 H), 1.24 (t, J = 7 Hz, 3 H), and 0.70–1.10 (m, 3 H).

Ethyl (*E*)-2,4-Pentadienoate. Reconjugation of allene 4 under the same conditions as described above gave essentially a single product as indicated by GLC analysis. Although TLC did give a very faint indication of a higher R_f spot, no other product could be isolated. The reduced yield (50%) resulted from the volatility of the product: ^{1}H NMR (CCl_4) δ 7.14 (dd, J = 15, 11 Hz, 1 H), 6.39 (dt, J = 17, 10 Hz, 1 H), 5.10–5.95 (m, 3 H), 4.10 (q, J = 7 Hz, 2 H), and 1.27 (t, J = 7 Hz, 3 H); IR 1720 (C=O), 1647, 1605, 1010, and 925 (C=C) cm^{-1}; mass spectrum *m/e* (rel intensity) 126 (M^+, 17), 111 (2), 98 (20), 97 (12), 81 (100), 70 (8), 53 (58), and 43 (10). Anal. Calcd for $C_7H_{10}O_2$: C, 66.65; H, 7.99. Found: C, 66.77; H, 8.05.

Acknowledgments. Support for this research through grants from the National Institutes of Health (PHS GM 17061) and the National Science Foundation (NSF MPS 73-08691 and 76-10037) is gratefully acknowledged. J.A.K. is a Camille and Henry Dreyfus Teacher-Scholar and R.A.A. was supported by fellowships from the University of Illinois, Procter and Gamble, Eli Lilly, and Johnson and Johnson.

Registry No.—**1a,** 106-96-7; **1b,** 16156-58-4; **2a,** 56579-97-6; **2b,** 64706-02-1; **3,** 63093-41-4; **4,** 30332-99-1; **5a,** 818-72-4; **5b,** 64706-03-2; **6,** 36186-28-4; **12,** 64714-94-9; **13,** 64706-04-3; *E*-14 Methyl ester, 64706-05-4; *Z*-14 Methyl ester, 64706-06-5; (2*E*,4*Z*)-**16,** 3025-30-7; (2*E*,4*E*)-**16,** 7328-34-9; (2*Z*,4*E*)-**16,** 3025-31-8; ethyl bromide, 74-96-4; hexanal, 66-25-1; methanesulfonyl chloride, 124-63-0; propargyl alcohol, 107-19-7; ethyl (*E*)-2,4-pentadienoate, 13369-23-8.

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An Efficient Synthesis of γ-Methylene-γ-butyrolactone (α′-Angelicalactone). Application to the Synthesis of Deoxyobtusilactone and Deoxyisoobtusilactone

Richard A. Amos and John A. Katzenellenbogen*

Roger Adams Laboratory, Department of Chemistry, University of Illinois, Urbana, Illinois 61801

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The mercury(II)-catalyzed cyclization of 4-pentynoic acid proceeds efficiently to give γ-methylene-γ-butyrolactone (α′-angelicalactone). The enolate of this lactone reacts with 11-dodecenal producing separable diastereomeric β-hydroxylactones. The corresponding methanesulfonate derivatives undergo partially selective elimination to afford deoxyobtusilactone and deoxyisoobtusilactone.

Introduction

γ-Methylene-γ-butyrolactone or α′-angelicalactone (**1**) forms the basic ring structure of two newly described classes of natural products, the obtusilactones (**2a–f**)[1] and the fimbrolides (**3**).[2,3] Obtusilactone (**2a**) was the first-discovered member of a series of cytotoxic natural products (**2b–f**) isolated from the plant *Lindera obtusiloba* by Yamamura and co-workers.[1] The fimbrolides are marine natural products with antimicrobial (including antifungal) activity that have been isolated from the red alga *Delisea fimbriata* by Wells[2] and Sims.[3] Because of the demonstrated biological activity of these compounds, the synthesis of γ-methylene-γ-butyrolactones is of interest. In this report, we describe a method for the facile synthesis of γ-methylene-γ-butyrolactone and the application of this method to the preparation of the deoxy analogs of obtusilactone (**2a**) and isoobtusilactone (**2b**).

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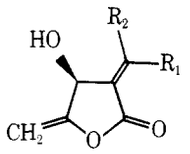
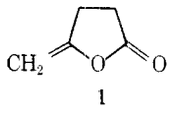


2a, $R_1 = -(CH_2)_9CH{=}CH_2$; $R_2 = H$
b, $R_1 = H$; $R_2 = -(CH_2)_9CH{=}CH_2$
c, $R_1 = -(CH_2)_{12}CH_3$; $R_2 = H$
d, $R_1 = H$; $R_2 = -(CH_2)_{12}CH_3$
e, $R_1 = -(CH_2)_5CH{=}CH(CH_2)_7CH_3$; $R_2 = H$
f, $R_1 = H$; $R_2 = -(CH_2)_5CH{=}CH(CH_2)_7CH_3$



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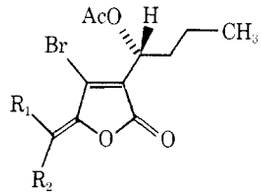
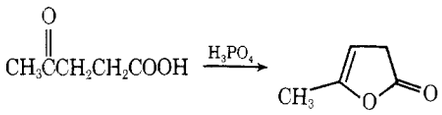


3, R_1R_2 = H,Cl,Br,I

Results and Discussion

Routes to Angelicalactones. The preparation of enol lactones has been well studied, with some of the work dating back to the late 1800's. Two major routes exist to these compounds, cyclization of either a keto acid or an acetylenic acid. The acid-catalyzed cyclization of levulenic acid to give α-angelicalactone (**4**) was first observed by Wolff[4] and further



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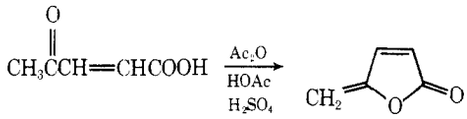
explored by Helberger.[5] The only reported case of formation of the exocyclic double bond by this approach is the synthesis of protoanemonin (**5**) by a similar cyclization of acetylacrylic



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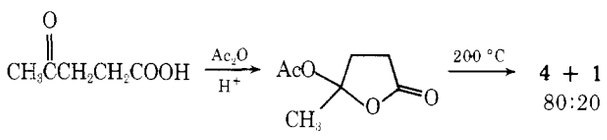
acid.[6] In this case, however, the presence of the conjugated double bond ensures the formation of the exocyclic enol ester. It is apparent that acid-catalyzed cyclization of keto acids is not an appropriate method for the preparation of γ-methylene-γ-butyrolactones since isomerization to the more stable endocyclic olefin would be expected under the acidic conditions.

Swern[7] has recently modified this procedure by trapping the intermediate lactol **6**; subsequent pyrolytic elimination



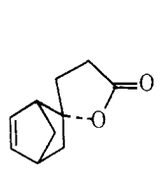
6

4 + 1
80:20

gave unfavorable mixtures of the α- and α′-angelicalactones.

Other pyrolytic approaches recently reported involve the retro-Diels–Alder reaction of **7** to give **1**[8] and the rearrangement of **8** to a substituted analog of **1**.[9]

The well-precedented Markownikoff addition of carboxylic acids across terminal acetylenes[10] would appear to provide ready access to γ-methylene-γ-butyrolactones. In fact, the iodolactone corresponding to **1** is formed upon treatment of



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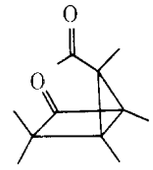

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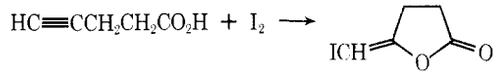
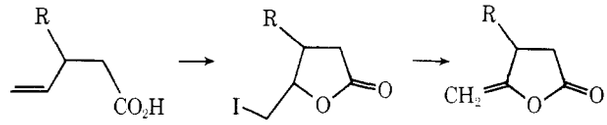
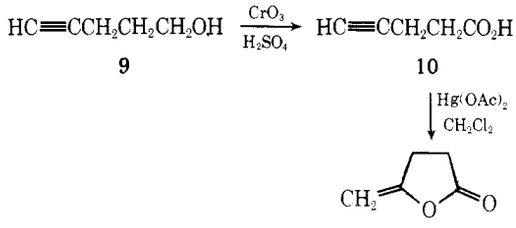
4-pentynoic acid with iodine.[11] Two other reported cyclizations have given endocyclic double bond isomers of the parent compound, however.[12,13]



A very recent report of Jäger and Günther[14] describes a selective preparation of γ-methylene-γ-butyrolactones by iodolactonization of 4-pentenoic acids, followed by dehydroiodination.[15]



Selective Preparation of α′-Angelicalactone. We have found that treatment of 4-pentynoic acid (**10**) in dichloromethane with a catalytic amount of mercuric acetate (4.5 mol %) gave the desired cyclization product γ-methylene-γ-butyrolactone (**1**) in 74% yield. This compound was the sole



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isolable product from the reaction with no evidence of either α- or β-angelicalactones or the corresponding δ-lactone that would result from an anti-Markownikoff addition. As 4-pentynoic acid is prepared in good yield by chromic acid oxidation of commercial 4-pentyn-1-ol (**9**),[16] this two-step synthesis represents a very short and efficient route to a compound that has been prepared only with difficulty by most previous routes.

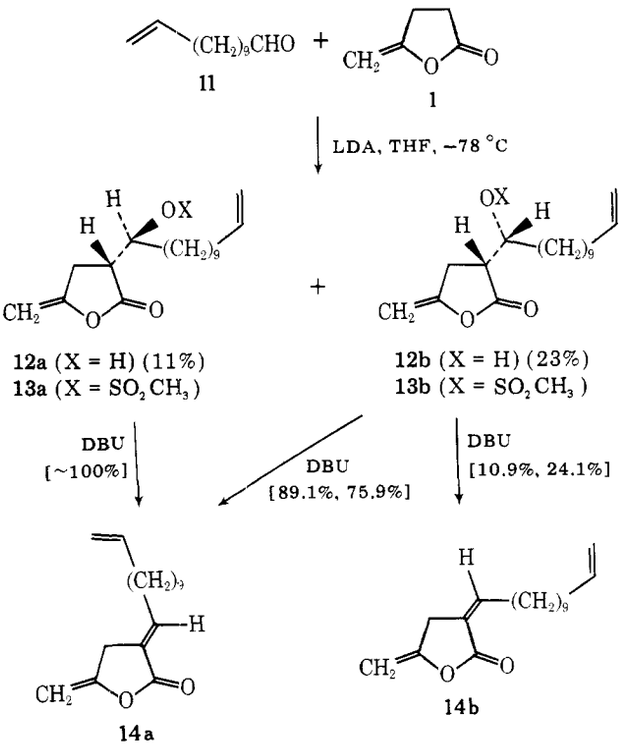
Synthesis of Deoxyobtusilactone and Deoxyisoobtusilactone. The approach we have taken to the deoxyobtusilactones is outlined in Scheme I.

Although the required aldehyde **11** is not commercially available, the lower homologous alcohol 10-undecen-1-ol (**15a**) is available. Homologation of **15a** was effected by displacement of the methanesulfonate **15b** (prepared from **15a** and used without purification) with sodium cyanide in dimethyl sulfoxide (92% yield), followed by controlled reduction with diisobutylaluminum hydride in benzene at room temperature, to give the aldehyde **11** (75% yield).[17] Homologation of the corresponding tosylate **15d** was equally efficient.

Several methods have been developed for condensing carbonyl compounds with lactones, although most of these represent syntheses of α-methylene lactones[18] rather than α-alkylidene lactones; phosphonium ylides,[19] α-silyl carbanions,[20] or α-thiomethylene intermediates[21] have been utilized. These approaches give predominantly or exclusively the *E*-alkylidene isomers and thus are not suitable for generating the *Z* geometry in obtusilactone.

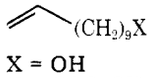
The reaction of lactone enolates with various electrophiles has constituted an important route to α-methylene lactones.[22]

Scheme I[a]



[a] Yields in parentheses are isolated; yields in brackets are product ratios. Where two numbers are given, the first is from reaction in ether, the second in hexane (see text).

Application of this method to aldehydes other than formaldehyde has not been well studied, but Zimmer[23] has reported the condensation of both alkyl and aryl aldehydes with lac-



15a, X = OH
b, X = OSO_2CH_3
c, X = CN
d, X = $OSO_2C_6H_4CH_3$

tones using weak bases, diethylamine or sodium methoxide. To minimize self-condensation of the aldehyde, we considered it desirable to modify Zimmer's procedure by preforming the lactone enolate stoichiometrically.

As indicated in Scheme I, the enolate of α'-angelicalactone (**1**) was generated by the addition of the lactone to a tetrahydrofuran solution of lithium diisopropylamide (LDA) at −78 °C. The aldehyde **11** was then added at low temperature, giving complete consumption of starting material within 10 min. Two major products were formed having substantially different R_f's on thin layer chromatography. The isolated compounds had essentially identical mass and infrared spectra and elemental analyses, and their spectra differed only in the resonances assigned to the hydrogens α to the carbonyl and on the carbon bearing the hydroxyl; thus, they appeared to be the diastereomeric β-hydroxy lactones **12a** and **12b**. The pronounced chromatographic separation between these species is presumably due to differences in intramolecular hydrogen bonding, although construction of models of **12a** and **12b** does not allow any definite conclusion as to why one diastereomer should show more effective intramolecular bonding than the other. Nevertheless, it was possible to assign structures to the more and less polar components based on the stereochemistry of their elimination products (vide infra).

The conventional method for the elimination of α-hydroxymethyl lactones is conversion of the alcohol to the methanesulfonate, followed by elimination in refluxing pyridine. This method was applied to a model compound, the condensation product between the enol lactone **1** and hexanal, and was found to proceed quite slowly. To avoid these rather strenuous conditions, we used the stronger base 1,5-diazabicyclo[5.4.0]undec-5-ene (DBU). Compared to bases such as pyridine, these amidine bases (DBU and DBN) are particularly effective in promoting elimination reactions.[24]

The methanesulfonates **13a** and **13b** were formed by treatment of the corresponding alcohols with excess methanesulfonyl chloride in a triethylamine–dichloromethane solvent. Isolated but not purified, the methanesulfonates were treated with DBU in an ether solvent, giving an immediate reaction at 0 °C as evidenced by a rapid clouding of the solution and an eventual (2–3 min) precipitation of a viscous oil.

Methanesulfonate **13a**, derived from the less polar diastereomer **12a**, gave the deoxyisoobtusilactone **14a** in 75% yield with only faint traces of the other olefin isomer present by thin layer chromatography. The *E* configuration for the trisubstituted double bond was assigned on the basis of the lower field ^{1}H NMR resonance at δ 6.61 for the vinyl proton β to the carbonyl.[19a] Methanesulfonate **13b**, derived from the more polar diastereomer **12b**, gave a mixture of 63% of **14a** and 8% of **14b** (deoxyobtusilactone), the latter being assigned the *Z* configuration on the basis of the higher field ^{1}H NMR resonance at δ 6.12 for the vinyl proton β to the carbonyl.[19a]

The eliminations are not highly stereoselective. Presumably, this results from the fact that the elimination is proceeding by both ElcB and E2 mechanisms. Under the ElcB mechanism, both methanesulfonates undergo predominant elimination to the more stable *E* isomer (**14a**), with **13a** giving only this isomer. However, since **13b** does give small amounts of the *Z* isomer (**14b**), some of this isomer must react by an E2 mechanism; otherwise, if the distribution of *E* and *Z* isomers from **13b** were thermodynamic, then **13a** would be expected to produce some **14b**. Thus, from the antiperiplanar geometry of the E2 mechanism, we can assign the stereochemistries of **12a** (less polar diastereomer) and **12b** (more polar diastereomer) as shown in Scheme I.

As the E2 and ElcB mechanisms appear to be operating in competition, it was anticipated that a change to a less polar solvent, one less capable of stabilizing the intermediate carbanion, might increase the extent of E2 elimination and improve reaction stereoselectivity. Indeed, when **13b** was treated with DBU in hexane at 0 °C, the yields of **14b** and **14a** were 16.0% and 50.4%, as compared to 7.7% and 63.2% from the ether reaction. The stereoselectivity expressed in terms of the isomeric composition of the alkylidene lactone products is even better; hexane as solvent afforded 24.1% and 75.9% of **14b** and **14a**, respectively, while ether gave 10.9% and 89.1%.

Experimental Section

General. Analytical thin layer chromatography was performed using 0.25-mm silica gel glass-backed plates with F-254 indicator (Merck). Visualization was by ultraviolet light, iodine, or phosphomolybdic acid. Preparative TLC plates were from Merck or were prepared using Merck silica gel 60 PF-254 + 366.

Proton magnetic resonance ^{1}H NMR spectra were recorded on Varian Associates spectrometers, Models T-60, A-60, EM-390, and HR-220; chemical shifts are reported in ppm downfield from a tetramethylsilane internal standard (δ scale). The ^{1}H NMR data are presented in the form: δ value of signal (peak multiplicity, coupling constant (if any), integrated number of protons). Infrared spectra were recorded on either a Perkin-Elmer Model 137 spectrometer or a Beckman Model IR-12 instrument. Unless otherwise noted, spectra were obtained on neat compounds held between sodium chloride plates. Data are presented in cm^{-1} and only the important diagnostic bands are reported.

Mass spectra were obtained from a Varian MAT CH-5 spectrometer

and were at 70 eV ionization voltage unless otherwise indicated. Data are presented in the form: *m/e* (intensity relative to base peak). Elemental analyses were provided by the microanalytical service laboratory of the University of Illinois.

Chemicals were obtained from the following sources: Aldrich Chemical Co., tetrahydrofuran, triethylamine, diisopropylamine, 10-undecen-1-ol, methanesulfonyl chloride, *p*-toluenesulfonyl chloride, 1,5-diazabicyclo[5.4.0]undec-5-ene; Fisher Scientific Co., dichloromethane; J. T. Baker Chemical Co., mercuric acetate; Chem. Samples, 4-pentyn-1-ol; Mallinckrodt, dimethyl sulfoxide, diethyl ether, chromium trioxide; Ventron, *n*-butyllithium, diisobutylaluminum hydride.

Tetrahydrofuran was distilled from sodium benzophenone by use of a recirculating still, maintaining a deep blue coloration at all times. Diisopropylamine and triethylamine were refluxed over calcium hydride and then distilled to ensure dryness. The organolithium reagents were titrated periodically to determine the organic base present, using either the double titration method[25] or the single titration method[26] with 1,10-phenanthroline as an indicator. All values used were the average of at least three separate determinations.

Reaction products were dried over anhydrous magnesium sulfate unless otherwise stated. All yields reported are isolated products after purification unless indicated otherwise. Silica gel chromatography was performed using 0.05–0.2 mm silica gel with weight ratios usually in the range 30:1 to 50:1 silica gel–crude product. Close separations required ratios as high as 200:1. Elution solvent mixtures are given as volume percentages.

4-Pentynoic Acid (10). This was prepared in 74% yield from 4-pentyn-1-ol according to the method of Holland and Gilman.[16] Recrystallization from hexane–THF gave white crystalline plates: mp 53–55 °C; lit.[16] 54.5–56.5 °C; ^{1}H NMR ($CDCl_3$) δ 11.30 (s, 1 H), 2.45–2.70 (m, 4 H), 1.99 (t, *J* = 2 Hz, 1 H).

Anal. Calcd for $C_5H_6O_2$: C, 61.22; H, 6.16. Found: C, 60.95; H, 6.07.

Dihydro-5-methylene-2(3*H*)-furanone (γ-Methylene-γ-butyrolactone; α′-Angelicalactone) (1). 4-Pentynoic acid (**10**), 1.47 g (15 mmol), was dissolved in 100 mL of dichloromethane, followed by 0.21 g (0.66 mmol) of mercuric acetate. Initially, the mixture was cloudy but it cleared during the course of the reaction. After 24 h at room temperature, TLC showed the complete consumption of starting material with a single spot of R_f slightly higher than the acid. The product was stirred with saturated sodium bicarbonate for 5 to 10 min and was then extracted thoroughly and dried. Silica gel chromatography (40% ether–hexane) removed the remaining mercury salts and gave 1.08 g (74%) of pure product: ^{1}H NMR (CCl_4) δ 4.55–4.75 (m, 1 H), 4.15–4.30 (m, 1 H), 2.35–3.10 (m, 4 H); IR 1815 (C=O), 1675 (C=C), 1130 (CO), and 885 (C=CH_2) cm^{-1}; mass spectrum (10 eV) *m/e* (rel intensity) 98 (M^+, 100), 70 (32), 56 (48), 55 (10), 42 (30), 28 (23).

Anal. Calcd for $C_5H_6O_2$: C, 61.22; H, 6.16. Found: C, 61.25; H, 6.19.

***p*-Toluenesulfonate of 10-Undecen-1-ol (15d).** Alcohol **15a**, 17.03 g (0.10 mol), was added to a solvent mixture of 12.14 g (0.12 mol) of triethylamine in 50 mL of dichloromethane. After cooling to 0 °C, 20.02 g (0.105 mol) of *p*-toluenesulfonyl chloride was added. A precipitate of the amine hydrochloride salt appeared rapidly, but 4 days at 0 °C was required for consumption of the alcohol. When TLC indicated the reaction to be essentially complete, it was diluted with 200 mL of ether, stirred over saturated sodium bicarbonate for 4 h at 25 °C, washed with brine and 3 N hydrochloric acid, and dried. Removal of the solvent gave an essentially quantitative yield of **15d** sufficiently pure for the subsequent reactions. The analytical sample was purified by silica gel chromatography (30% ether–hexane): ^{1}H NMR (CCl_4) δ 7.72 (d, *J* = 8 Hz, 2 H), 7.28 (d, *J* = 8 Hz, 2 H), 5.78 (ddt, *J* = 9.5, 17, 6 Hz, 1 H), 4.75–5.10 (m, 2 H), 3.95 (t, *J* = 6 Hz, 2 H), 2.43 (s, 3 H), 1.80–2.20 (m, 2 H), 1.25 (broad s, 14 H).

Anal. Calcd for $C_{18}H_{28}O_3S$: C, 66.63; H, 8.70; S, 9.88. Found: C, 66.69; H, 8.65; S, 9.87.

The corresponding methanesulfonate (**15b**) was prepared by this procedure but was not purified and characterized.

11-Dodecenenitrile (15c). Sodium cyanide, 0.74 g (15 mmol), was added to 15 mL of dry dimethyl sulfoxide with only a portion dissolving in the solvent. Tosylate **15d**, 3.24 g (10 mmol), was then added dropwise. The mixture was stirred 24 h at room temperature during which time the crystals of sodium cyanide gradually dissolved. The mixture was diluted with 200 mL of water and extracted several times with ether. These extracts were washed with saturated brine and dried. Silica gel chromatography (30% ether–hexane) afforded 1.75 g (98%) of product.

The compound was also prepared on a larger scale (8.24 g of product) by reaction of the sodium cyanide with the corresponding methanesulfonate, **15b**. The methanesulfonate appeared to be less reactive than the *p*-toluenesulfonate but afforded an overall yield of 92% for the two steps: ^{1}H NMR (CCl_4) δ 5.71 (ddt, *J* = 17, 10, 7 Hz, 1 H), 4.75–5.10 (m, 2 H), 2.23 (t, *J* = 6 Hz, 2 H), 1.80–2.20 (m, 2 H), 1.20–1.80 (m, 14 H); IR 3080 (C=CH_2), 2245 (C≡N), 1640, 990, 910 (C=CH_2) cm^{-1}; mass spectrum (10 eV) *m/e* (rel intensity) 179 (M^+, 2.2), 178 (4), 164 (6), 150 (34), 136 (89), 122 (100), 108 (30), 94 (31).

Anal. Calcd for $C_{12}H_{21}N$: C, 80.38; H, 11.81; N, 7.81. Found: C, 80.35; H, 11.88; N, 8.00.

11-Dodecenal (11). Nitrile **15c**, 8.07 g (45 mmol), was added to 90 mL of dry benzene, followed by the dropwise addition of diisobutylaluminum hydride, 9.12 mL (7.11 g, 50 mmol). The addition required 15 min, during which time the reaction temperature was maintained at 20–25 °C by means of a water bath. After 1 h at room temperature, TLC showed no evidence of starting material. The mixture was cooled to 0 °C, and methanol was added slowly until all foaming ceased. The product was diluted with ether and 3 N hydrochloric acid was added with cooling until the aqueous layer was just acid. The organic layer was then separated and dried. Silica gel chromatography (10% ether–hexane) gave 6.15 g (75%) of pure aldehyde: ^{1}H NMR (CCl_4) δ 9.64 (t, *J* = 1 Hz, 1 H), 5.70 (ddt, *J* = 17, 10, 6 Hz, 1 H), 4.75–5.05 (m, 2 H), 2.33 (t, *J* = 6 Hz, 2 H), 1.80–2.20 (m, 2 H), 1.15–1.80 (m, 14 H). IR 3080 (C=CH_2), 2720 (CHO), 1730 (C=O), 1640, 990, 910 (C=CH_2) cm^{-1}; mass spectrum (10 eV) *m/e* (rel intensity) 182 (M^+, 2.5), 180 (4), 164 (35), 153 (4), 139 (9), 135 (35), 125 (15), 121 (60), 98 (100).

Anal. Calcd for $C_{12}H_{22}O$: C, 79.06; H, 12.16. Found: C, 78.96; H, 11.94.

3-(1-Hydroxy-11-dodecenyl)dihydro-5-methylene-2(3*H*)-furanone (Diastereomers 12a and 12b). The diisopropylamine, 0.81 g (8 mmol), was added to 50 mL of dry tetrahydrofuran and cooled to −10 °C. *n*-Butyllithium, 3.23 mL of a 2.30 M solution (7.44 mmol), was then added. After 10 min, the mixture was cooled to −78 °C and 0.73 g (7.44 mmol) of lactone **1** was added dropwise. The homogeneous mixture was stirred 30 min at −78 °C, and then 1.36 g (7.44 mmol) of aldehyde **11** was added dropwise. The reaction was stirred 30 min at −78 °C (TLC indicated the reaction was essentially complete within 10 min) and then was quenched with saturated ammonium chloride. The solvent was removed under reduced pressure, and the product was extracted into ether, washed with saturated ammonium chloride, and dried. Silica gel chromatography (25% ether–hexane) yielded two pure components: 239 mg (11%) of a nonpolar material (**12a**) ($R_f \approx$ 0.4 in 50% ether–hexane) and 489 mg (23%) of a polar material (**12b**) ($R_f \approx$ 0.2); nonpolar diastereomer (**12a**): ^{1}H NMR (CCl_4) δ 5.70 (ddt, *J* = 17, 10, 7 Hz, 1 H), 4.75–5.05 (m, 2 H), 4.55–4.70 (m, 1 H), 4.14–4.30 (m, 1 H), 3.90–4.14 (m, 1 H), 2.60–3.10 (m, 4 H, 1 D_2O exchangeable), 1.80–2.20 (m, 2 H), 1.10–1.75 (m, 16 H); IR 3500 (OH), 3085 (C=CH_2), 1805 (C=O), 990, 910, 840 (C=CH_2) cm^{-1}; mass spectrum (10 eV) *m/e* (rel intensity) 280 (M^+, 15), 262 (2), 235 (3), 219 (4), 205 (2), 191 (2), 177 (3), 163 (3), 149 (3), 98 (100).

Anal. Calcd for $C_{17}H_{28}O_3$: C, 72.82; H, 10.06. Found: C, 73.09; H, 10.11.

Polar diastereomer (**12b**): ^{1}H NMR (CCl_4) δ 5.70 (ddt, *J* = 17, 10, 7 Hz, 1 H), 4.75–5.05 (m, 2 H), 4.55–4.75 (m, 1 H), 4.15–4.30 (m, 1 H), 3.50–3.80 (m, 1 H), 3.07 (broad s, 1 H, D_2O exchangeable), 2.50–2.95 (m, 3 H), 1.75–2.20 (m, 2 H), 1.10–1.70 (m, 16 H); IR 3500 (OH), 3080 (C=CH_2), 1800 (C=O), 980, 910, 840 (C=CH_2) cm^{-1}; mass spectrum (10 eV) *m/e* (rel intensity) 280 (M^+, 9), 262 (3), 235 (15), 219 (5), 205 (3), 191 (3), 177 (5), 163 (6), 149 (4), 98 (100).

Anal. Calcd for $C_{17}H_{28}O_3$: C, 72.82; H, 10.06. Found: C, 73.10; H, 10.10.

3-(11-Dodecenylidene)dihydro-5-methylene-2(3*H*)-furanone (*E* and *Z* Isomers, 14a and 14b, Respectively, or Deoxyisoobtusilactone and Deoxyobtusilactone, Respectively). The enol lactone **12b**, 486 mg (1.73 mmol), was added to 10 mL of dichloromethane, followed by 228 mg (2.25 mmol) of triethylamine. After cooling to 0 °C, 238 mg (2.08 mmol) of methanesulfonyl chloride was added dropwise, followed by stirring for 3 h at 0 °C. The reaction was quenched with saturated sodium bicarbonate, diluted with ether, washed again with the bicarbonate, and dried. After removal of solvents, the crude product was added to 10 mL of ether, cooled to 0 °C, and then 343 mg (2.25 mmol) of 1,5-diazabicyclo[5.4.0]undec-5-ene (DBU) was added dropwise. Formation of an oily precipitate was immediate, and TLC after 15 min showed complete consumption of starting material. The product was diluted with ether, washed with brine, and dried. Silica gel chromatography (5% ether–hexane) gave 35 mg (8%) of **14b** and 287 mg (63%) of **14a**.

A similar procedure on 239 mg of **12a** afforded 167 mg (75%) of **14a** with only faint traces of **14b**. Compound **14b**: ^{1}H NMR (CCl_4) δ 6.12

(tt, J = 7, 2 Hz, 1 H), 5.70 (ddt, J = 17, 10, 7 Hz, 1 H), 4.75–5.05 (m, 2 H), 4.55–4.68 (m, 1 H), 4.05–4.15 (m, 1 H), 3.30–3.50 (m, 2 H), 2.50–2.80 (m, 2 H), 1.80–2.20 (m, 2 H), 1.15–1.70 (m, 14 H); IR 3080 (C=CH_2), 1788 (C=O), 968, 910, 835 (C=C) cm^{-1}; mass spectrum m/e (rel intensity) 262 (M^+, 9), 219 (5), 205 (3), 191 (2), 177 (4), 163 (3), 110 (72), 43 (100).

Anal. Calcd for $C_{17}H_{26}O_2$: C, 77.82; H, 9.99. Found: C, 77.53; H, 10.14.

Compound **14a:** ^1H NMR (CCl_4) δ 6.61 (tt, J = 7, 2.5 Hz, 1 H), 5.70 (ddt, J = 17, 10, 7 Hz, 1 H), 4.74–5.03 (m, 2 H), 4.60–4.74 (m, 1 H), 4.10–4.20 (m, 1 H), 3.25–3.45 (m, 2 H), 1.70–2.35 (m, 4 H), 1.15–1.70 (m, 14 H); IR 3080 (C=CH_2), 1795 (C=O), 955, 910, 837 (C=C) cm^{-1}; mass spectrum m/e (rel intensity) 262 (M^+, 11), 234 (4), 219 (7), 205 (7), 191 (5), 177 (9), 163 (9), 110 (78), 41 (100).

Anal. Calcd for $C_{17}H_{26}O_2$: C, 77.82; H, 9.99. Found: C, 77.97; H, 10.07.

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Thermolysis and Photolysis of Unsaturated Ketones. 26. Preparation of Bicyclo[2.2.2]octan-2-ones and Bicyclo[2.2.1]heptan-2-ones by Thermal Cyclization of Unsaturated Ketones. A Facile Synthesis of (+)-Camphor from (+)-Dihydrocarvone[1]

Jean M. Conia

Laboratoire des Carbocycles, Université de Paris-Sud, 91405 Orsay, France

Gordon L. Lange*

Department of Chemistry, University of Guelph, Guelph, Ontario, N1G 2W1 Canada

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Bicyclo[2.2.2]octan-2-ones **4a** and **4b** have been synthesized in yields of 85 and 50%, respectively, by the thermal cyclization of the appropriate 3-alkenylcyclohexanone at 390 °C. The monoterpene (+)-camphor (**10**) has been prepared in 55% yield and 90% optical purity by cyclization of (+)-dihydrocarvone (**9**) at 400 °C. An explanation for the formation in these thermolyses of a number of side products such as 2-cyclohexenones and alkylbenzenes is offered. Thermal fragmentation of bicyclo[2.2.2]octan-2-ones via a retro-Diels–Alder reaction gives an alkene and a 2-cyclohexenone, which is then converted into an alkylbenzene. It is suggested that these latter transformations may be related to the formation of some petroleum hydrocarbons from terpenoid precursors.

The thermal cyclization of unsaturated ketones has been used to prepare a wide variety of cycloalkyl ketones and cycloalkanones.[2] Bridged systems such as bicyclo[3.2.1]- and -[3.3.1]alkanes have been prepared in high yield using this technique.[2] In this report we describe the preparation of two bicyclo[2.2.2]octan-2-ones and a strained bicyclo[2.2.1]heptan-2-one, the monoterpene (+)-camphor, using this cyclization procedure. The formation of side products in these

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