reaction of **1** is larger than that with **2** because of crowding in the addition compound T_I^+ formed from **1**; if k_{-I} is larger, a higher concentration of catalyst must be added before the proton-transfer step, k_{cat}, is no longer rate determining.

A larger value of k_{-I} is also expected if there is more effective electron donation to expel the attacking amine. This has been observed by Benkovic and co-workers for the methoxyaminolysis of an amidine, which exhibits a nonlinear Brønsted plot for general-base catalysis that provides evidence for a stepwise mechanism with rate-determining proton transfer.[23] Since there are two nitrogen atoms in the tetrahedral addition compound to provide the driving force for the expulsion of the attacking amine and formation of the resonance-stabilized amidinium ion, the rate constant k_{-I} is considerably larger ($k_{-I} > 10^9$ M^{-1} s^{-1}, with no evidence for a change in rate-determining step up to 0.16 M phosphate buffer, 80% dianion) and K_I is considerably smaller ($K_I = 3.7 \times 10^{-13}$ M^{-1}) than for the transimination of **2**. On the other hand, no general-base catalysis by methoxyamine has been observed for the methoxyaminolysis of N-protonated benzylideneanilines.[26] The value of k_{-I} is expected to be smaller for this reaction because of the relatively small electron-donating ability of the aniline nitrogen atom. The absence of catalysis may therefore reflect a solvent-mediated proton transfer that is faster than k_{-I}, so that buffer-mediated trapping is not significant.

References and Notes

(1) Supported by grants from the National Science Foundation (BMS71-01501 A03) and the National Institute of General Medical Sciences of the National Institutes of Health (GM 20888).
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A Method of Synthesis of β-Methylfurans and α-Methylene and β-Methylene γ-Lactones. Two Menthofuran Syntheses[1]

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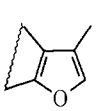
Abstract: The copper-catalyzed thermolysis of α-diazo-β-dicarbonyl compounds, diazoacetylacetone, methyl diazoacetoacetate, and dimethyl diazomalonate, in the presence of enol ethers of an aldehyde and a ketone is described. The first two diazo compounds produce 5-alkoxy-3-acyl-4,5-dihydrofurans, while diazomalonic ester is transformed into a cyclopropane derivative with the first enol ether and into an olefinic equivalent with the second enol derivative. The diazomalonate-derived products are convertible into β-methylfurans or their methylene lactone equivalents by simple reduction, oxidation, and isomerization operations. A method for the regioselective synthesis of one enol ether of β-methylcyclohexanone is introduced and the product converted into menthofuran by the above diazomalonate-initiated scheme as well as by a photolysis of methyl α-diazopropionate in its presence, followed by reduction, oxidation, and acid-induced dealcoholation.

As part of an ongoing program of study of the use of β-oxycyclopropylcarbonyl compounds, prepared by the interaction of diazomethyl ketones and carboxylates with enol ethers or esters, in organic synthesis,[4-6] especially directed toward terpenic natural products,[7] an investigation of the chemistry of functionally more complex α-diazoketo systems was initiated.[8] The present paper deals with α-diazo-β-dicarbonyl compounds and their use in the construction of the β-methylfuran (**1**), α-methylene γ-lactone (**2**), and β-methylene γ-lactone (**3**) units, common to many furanoid terpenes.[9]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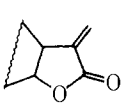
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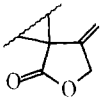
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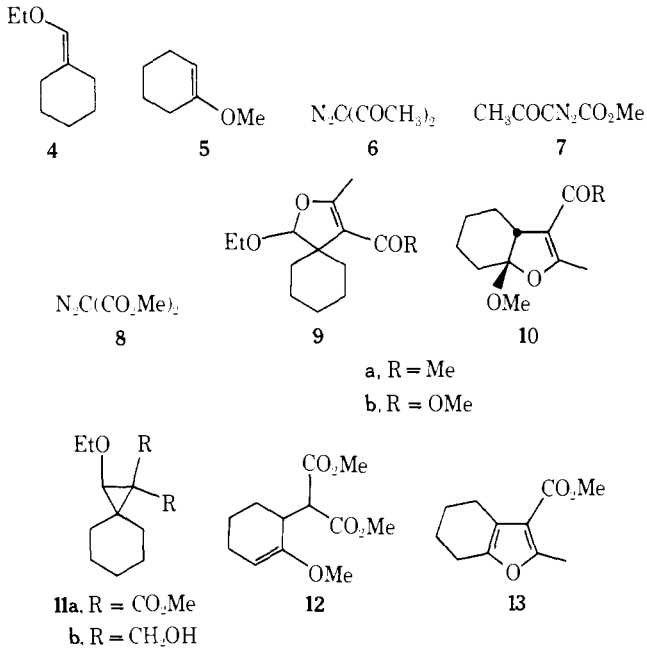
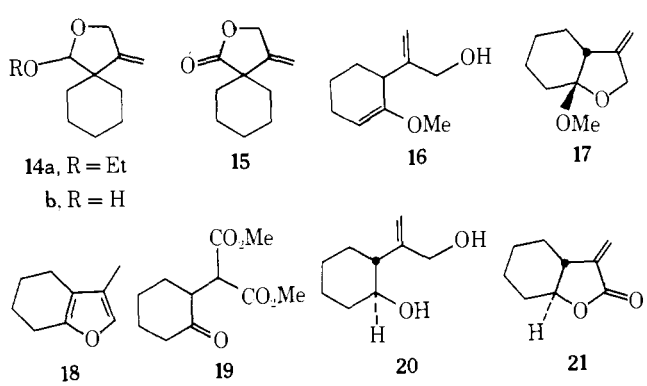
The aldehyde and ketone enol ethers ethoxymethylenecyclohexane (**4**) and 1-methoxycyclohexene (**5**), respectively, served as substrates for 3-diazo-2,4-pentanedione (**6**),[10] methyl 2-diazo-3-oxobutanoate (**7**),[11] and dimethyl diazomalonate



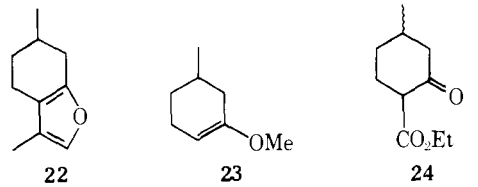
(8).[12] In contrast to the cyclopropanation behavior of simple α-diazocarbonyl compounds toward such enol derivatives the decomposition of the diazoacetylacetone (**6**) in **4** and **5** over cupric acetylacetonate afforded dihydrofurans **9a** and **10a**, respectively, albeit in low yield. Similarly, the thermal decomposition of the diazoacetoacetic ester (**7**) over trimethoxyphosphinecopper(I) iodide led to dihydrofurans **9b** and **10b**, respectively (also in low yield).[13] On the other hand, the catalyzed thermolysis of diazomalonic ester (**8**) in **4** yielded the expected cyclopropane ester **11a** (85%), whereas decomposition of the diazo compound in **5** produced a cyclopropane isomer, the enol ether 12 in 56% yield.[15,16] Treatment of **10b** with acid afforded the β-furoic ester **13** (54%).

The diazomalonate-derived diesters **11a** and **12** serve as excellent intermediates en route to the natural furanoid systems **1**, **2**, and **3**. Lithium aluminum hydride reduction of **11a** yielded diol **11b** (97%), whose exposure to acid produced acetal **14a**. Longer acid treatment of **11b** gave hemiacetal **14b** (86%),



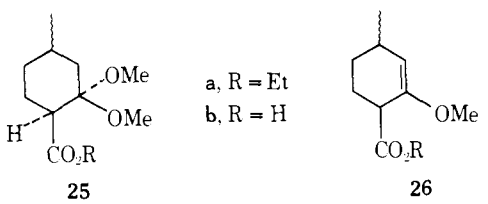
whose Collins oxidation afforded the spiro-β-methylene γ-lactone **15** (82%).[17] Lithium aluminum hydride reduction of the sodio enolate of diester **12**[18] led to acid-labile alcohol **16** (90%), which even on short exposure to acid was converted into ketal **17**. Further mild acid treatment produced furan **18** (up to 80%). Finally, mild acid hydrolysis of diester **12** yielded keto ester **19** (94%), whose sequential treatments with sodium hydride and lithium aluminum hydride[18] produced diol **20**, a compound which has been transformed previously into the α-methylene γ-lactone **21**.[19,20]

With a facile, new β-methylfuran synthesis in hand it was of interest to apply it to the synthesis of a furanoid terpene and menthofuran (**22**) was chosen as the goal. For this purpose the



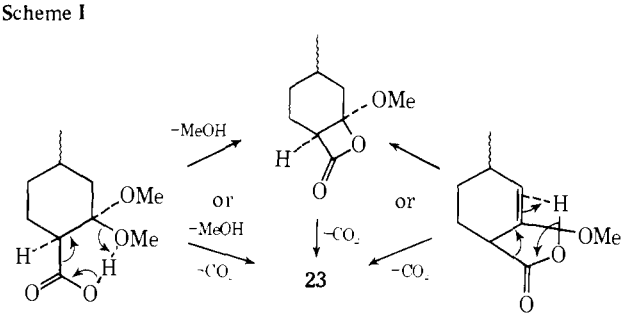
enol ether **23** of β-methylcyclohexanone was needed as starting material. Unfortunately, it could not be obtained readily by acid-induced demethanolation of β-methylcyclohexanone dimethyl ketal, since this process gave a difficultly separable mixture of the two possible enol ethers.[21] As a consequence a study of a regioselective synthesis of **23** of conceivably general applicability was undertaken.

Base-catalyzed condensation of β-methylcyclohexanone with diethyl oxalate has been shown to be regioselective, permitting a ready two-step synthesis of keto ester **24**.[22] Exposure of the latter to trimethyl orthoformate in methanolic acid led to ketal ester **25a** (85%) or enol ether **26a** (94%), depending

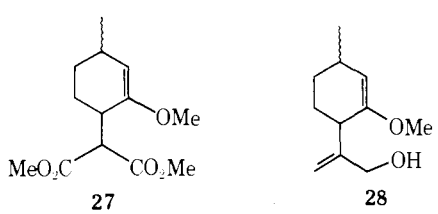


on the reaction conditions (see Experimental Section).[23] Mild, alkaline hydrolysis of the esters gave labile acids **25b** and **26b**, respectively, whose pyrolysis yielded enol ether **23** (58 and 76%, respectively) in over 95% purity. The formation of a single enol ether had been anticipated on the basis of the mechanistic reasoning outlined in Scheme I.

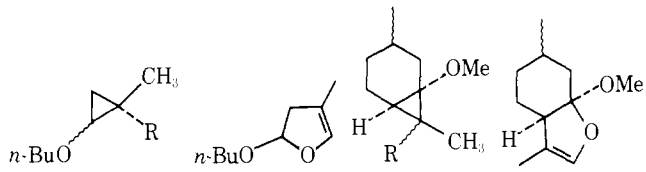
Scheme I



The synthesis of menthofuran (**22**) from **23** followed the procedure of the **5** → **18** conversion. The thermal interaction of enol ether **23** with dimethyl diazomalonate over trimethoxyphosphinecopper(I) iodide afforded the malonic ester **27** (39%), whose treatment with sodium hydride and subsequently with lithium aluminum hydride gave diol **28** (90%). Exposure of the latter to acid yielded menthofuran (**22**) (72%).



Finally, an alternate β-methylfuran (**1**) synthesis, also involving β-oxycyclopropylcarbonyl compounds as intermediates, was developed and a model study, based on *n*-butyl vinyl ether and ethyl α-diazopropionate,[24] undertaken. Thermal decomposition of the diazo compound in the enol ether over copper bronze produced ester **29a** (66%), whose reduction with lithium aluminum hydride yielded alcohol **29b** (99%). Fétizon oxidation (silver carbonate/Celite) of the latter led to a dihydrofuran



29a, R = CO_2Et **30** **31a**, R = CO_2Me **32**
b, R = CH_2OH **b**, R = CH_2OH

(**30**) (91%),[25] the oxidation state equivalent of β-methylfuran.

This reaction sequence was put to good use in an alternate menthofuran synthesis. A benzophenone-sensitized photolysis of methyl α-diazopropionate[24] in enol ether **23**[26] yielded ester **31a** (46%), whose lithium aluminum hydride reduction produced alcohol **31b** (98%). Fétizon oxidation of the latter gave dihydrofuran **32** (62%), whose acid treatment led to menthofuran (**22**) (91%).[27]

Experimental Section

Uncorrected melting points were determined on a Reichert micro hot stage. Infrared spectra were recorded on Perkin-Elmer Model 137 and 167 spectrophotometers and high-resolution mass spectra were registered on an A.E.I. MS-9 spectrometer. ^1H NMR spectra were run on $CDCl_3$ or CCl_4 solutions with Me_4Si as internal standard (δ = 0 ppm) and recorded on Varian A-60 and HR-220 spectrometers.

4-Acetyl-2-ethoxy-5-methyl-3,3-pentamethylene-2,3-dihydrofuran (9a). A solution of 2.00 g of diazoacetylacetone (**6**) in 5 mL of hexane was added slowly over a 2-h period to a refluxing mixture of 4.00 g of ethoxymethylenecyclohexane (4)[28] and 100 mg of bis(acetoacetonato)copper(II) and refluxing continued for 34 h. The mixture was filtered, the solvent evaporated under vacuum, and the residue distilled, affording 800 mg (27%) of **9a:** bp 128 °C (2.3 Torr); IR (neat) C=O 1720 (s), C=C 1610 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.24 (t, 3, J = 7 Hz, Me of Et), 2.18, 2.22 (s, 3 each, Me, Me of Ac), 3.61 (q, 2, J = 7 Hz, OCH_2), 5.06 (s, 1, OCH); *m/e* (calcd for $C_{14}H_{22}O_3$: 238.1568) 238.1572.

3-Acetyl-7a-methoxy-2-methyl-3a,4,5,6,7,7a-hexahydrobenzofuran (10a). A mixture of 11.00 g of 1-methoxycyclohexene (**5**) and 100 mg of bis(acetoacetonato)copper(II) was warmed at 60 °C under nitrogen for 1 h, a solution of 4.89 g of diazoacetylacetone (**6**) in 6.00 g of **5** was added slowly over a 3-h period, and the heating was continued for 5 days. The mixture was filtered, the excess enol ether removed from the filtrate by vacuum distillation, and the residue chromatographed on neutral alumina (activity I). Elution with 5:1 hexane-ether and distillation of the major eluate yielded 500 mg (6%) of liquid ketone **10a:** bp 93 °C (0.55 Torr); IR (neat) C=O 1720 (s), C=C 1625 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.13, 2.22 (s, 3 each, Me, Me of Ac), 3.13 (s, 3, OMe); *m/e* (calcd for $C_{12}H_{18}O_3$: 210.1255) 210.1248.

Methyl 2-Ethoxy-5-methyl-3,3-pentamethylene-2,3-dihydrofuran-4-carboxylate (9b). A mixture of 4.00 g of 4 and 100 mg of trimethoxyphosphinecopper(I) iodide was heated at 120 °C under nitrogen for 1 h, 3.80 g of diazoacetoacetic ester (**7**) was added dropwise over a 2-h period at 80 °C, and the mixture was stirred at this temperature for 34 h. The mixture was filtered through an infusorial earth pad and the excess enol ether removed by vacuum distillation. The residue was distilled and the distillate, 1.65 g, chromatographed on neutral alumina (activity 1). Elution with 4:1 hexane-ether yielded 1.55 g of liquid whose redistillation afforded liquid ester **9b** (25%): bp 125 °C (0.7 Torr); IR (neat) C=O 1690 (s), C=C 1632 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.22 (t, 3, J = 7 Hz, Me of OEt), 2.13 (s, 3, Me), 3.63 (s, 3, OMe), 3.77 (q, 2, J = 7 Hz, OCH_2), 5.10 (s, 1, OCH). Anal. ($C_{14}H_{22}O_4$) C, H.

Methyl 7a-Methoxy-2-methyl-3a,4,5,6,7,7a-hexahydrobenzofuran-3-carboxylate (10b). A mixture of 4.00 g of **5** and 100 mg of trimethoxyphosphinecopper(I) iodide was refluxed under nitrogen for 1 h, 1.50 g of diazoacetoacetic ester (**7**) was added dropwise over a 2-h period at 80 °C, and the mixture was stirred at this temperature for 24 h. The mixture was filtered, the excess enol ether distilled off under vacuum, and the residue distilled. Chromatography of the distillate, 1.20 g, on neutral alumina (activity 1) and elution with 4:1 hexane-ether gave 1.00 g of liquid ester **10b:** bp 100 °C (0.2 Torr); IR (neat) C=O 1700 (s), C=C 1640 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.20 (d, 3, J = 1 Hz, Me), 3.23 (s, 3, OMe), 3.67 (s, 3, ester OMe); *m/e* (calcd for $C_{12}H_{18}O_4$: 226.1204) 226.1214.

Dimethyl 2-Ethoxyspiro[2.5]octane-1,1-dicarboxylate (11a). A mixture of 4.00 g of 4 and 100 mg of trimethoxyphosphinecopper(I) iodide in 30 mL of hexane was refluxed under nitrogen for 1 h, a solution of 3.00 g of diazomalonic ester (**8**) in 5 mL of hexane was added slowly, and the mixture was refluxed for 10 h. Filtration of the mixture and crystallization of the residue gave 100 mg of tetramethyl ethylenetetracarboxylate, mp 119-120 °C (lit.[12] mp 119-120 °C). Distillation of the filtrate removed the excess enol ether and yielded 4.50 g of liquid ester **11a:** bp 89-90 °C (0.2 Torr); IR (neat) C=O 1725 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.16 (t, 3, J = 7 Hz, Me of OEt), 3.66 (q, 2, J = 7 Hz, OCH_2), 3.67 (s, 6, $(OMe)_2$), 3.80 (s, 1, OCH); *m/e* (calcd for $C_{14}H_{22}O_5$: 270.1466) 270.1472. Anal. ($C_{14}H_{22}O_5$) C, H.

Dimethyl 2-Methoxy-2-cyclohexenylmalonate (12). A mixture of 20.0 g of **5** and 200 mg of trimethoxyphosphinecopper(I) iodide was refluxed under nitrogen for 1 h, a solution of 10.00 g of dimethyl diazomalonate (**8**) in 10.00 g of **5** was added dropwise over a 2-h period at 80 °C, and the mixture was kept at this temperature for 48 h. The mixture was filtered, the excess enol ether recovered by distillation of the filtrate, and the resultant residue chromatographed on neutral alumina (activity I). Elution with 5:1 hexane-ether gave 8.60 g of an oil, whose distillation produced liquid ester **12:** bp 120 °C (0.8 Torr); IR (neat) C=O 1763 (s), 1748 (s), C=C 1675 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.5-1.8 (m, 4, $(CH_2)_2$), 1.9-2.2 (m, 2, allyl CH_2), 2.8-3.0 (m, 1, allyl CH), 3.42 (s, 3, OMe), 3.57 (d, 1, J = 4 Hz, COCH), 3.72 (s, 3, ester OMe), 4.65 (t, 1, J = 2 Hz, olefinic H). Anal. ($C_{12}H_{18}O_5$) C, H.

Methyl 2-Methyl-4,5,6,7-tetrahydrobenzofuran-3-carboxylate (13). A mixture of 500 mg of ester **10b** and 3 g of Amberlite IR-120-H cation exchange resin, previously washed with anhydrous methanol and ether, in 20 mL of dry methylene chloride was stirred at room temperature for 12 h and then filtered. The filtrate was evaporated under vacuum and the resultant residue, 260 mg, chromatographed on silica gel. Elution with 4:1 hexane-ether furnished 250 mg of liquid ester **13:** IR (neat C=O, C=C 1740 (s), 1710 (s), 1630 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.32 (s, 3, Me), 3.69 (s, 3, OMe); *m/e* (calcd for $C_{11}H_{14}O_3$: 194.0942) 194.0947.

1,1-Bis(hydroxymethyl)-2-ethoxyspiro[2.5]octane (11b). A mixture of 2.50 g of lithium aluminum hydride and 5.10 g of diester **11a** in 100 mL of dry ether was stirred at room temperature under nitrogen for 8 h. Water, 12 mL, was added carefully and the stirring continued for 1 h. The mixture was filtered, the precipitate washed exhaustively with ether, and the combined organic solutions dried (Na_2SO_4) and evaporated under vacuum. Chromatography of the residue, 3.93 g, on silica gel and elution with ether gave 3.85 g of viscous, liquid diol **11b:** IR (neat) OH 3450 (broad m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.17 (t, 3, J = 7 Hz, Me), 2.87 (s, 1, OCH), 3.47 (q, 2, J = 7 Hz, OCH_2), 3.90 (s, 4, $(CH_2OH)_2$); *m/e* (calcd for $C_{12}H_{22}O_3$: 214.1568) 214.1574.

2-Ethoxy-4-methylene-3,3-pentamethylenetetrahydrofuran (14a). A mixture of 1.26 g of diol **11b** and 10 mL of 5% sulfuric acid in 15 mL of tetrahydrofuran was refluxed for 0.5 h. It was poured into 100 mL of water and extrated with 60 mL of ether. The extract was washed with 20 mL of saturated sodium bicarbonate solution and with 20 mL of water, dried (Na_2SO_4), and evaporated under vacuum, leaving 1.00 g of liquid **14a:** IR (neat) C=C 1660 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.30 (t, 3, J = 7 Hz, Me), 3.65 (q, 2, J = 7 Hz, OCH_2 of OEt), 4.33, 4.78 (t, 2 each, J = 2 Hz, OCH_2, olefinic CH_2), 4.90 (m, 1, OCH); *m/e* (calcd for $C_{12}H_{20}O_2$: 196.1463) 196.1464.

2-Hydroxy-4-methylene-3,3-pentamethylenetetrahydrofuran (14b). A mixture of 1.00 g of diol **11b** and 30 mL of 5% sulfuric acid in 5 mL of tetrahydrofuran was refluxed for 24 h and worked up as for **14a** above. Chromatography of the residue, 675 mg, on silica gel and elution with 6:1 hexane-ether yielded 668 mg of solid whose crystallization from cold hexane afforded 630 mg of crystalline **14b:** mp 47-48 °C; IR ($CHCl_3$) OH 3410 (m), C=C 1660 (m) cm^{-1}; ^1H NMR ($CDCl_3$) 4.50, 4.90 (t, 2 each, J = 2 Hz, OCH_2, olefinic CH_2), 5.40 (s, 1, OCH); *m/e* ($M^+ - OH$) (calcd for $C_{10}H_{15}O$: 151.1122) 151.1129. Anal. ($C_{10}H_{16}O_2$) C, H.

β-Methylene-α,α-pentamethylene-γ-butyrolactone (15). A mixture of 300 mg of chromium trioxide and 500 mg of dry pyridine in 8 mL of methylene chloride was stirred for 15 min, whereupon a solution of 80 mg of **14b** in 2 mL of methylene chloride was added and the

stirring continued for 10 min. The mixture was poured into 20 mL of ether, washed with 30 mL of 5% sodium hydroxide solution and with 30mL of 10% cupric sulfate solution, dried ($MgSO_4$), and evaporated. Crystallization of the solid residue, 65 mg, mp 43 °C, from cold hexane yielded crystalline lactone **15:** mp 46 °C; IR ($CHCl_3$) C=O 1770 (s), C=C 1665 (m) cm^{-1}; ^1H NMR ($CDCl_3$) 4.67 (t, 2, J = 2 Hz, OCH_2), 5.04 (d of t, 2, J = 6, 2 Hz, olefinic CH_2); *m/e* (calcd for $C_{10}H_{14}O_2$: 166.0993) 166.1015. Anal. ($C_{10}H_{14}O_2$) C, H.

3-Methyl-4,5,6,7-tetrahydrobenzofuran (18). A mixture of 6.00 g of sodium hydride, 7.60 g of diester **12,** and 100 mg of ethanol in 100 mL of anhydrous 1,2-dimethoxyethane was stirred under nitrogen at room temperature for 8 h. A mixture of 3.00 g of lithium aluminum hydride in 150 mL of anhydrous ether was added and the stirring continued for 5 h. After the addition of 12 mL of water and further stirring for 1 h the mixture was filtered. The filter cake was washed with ether and the combined organic solutions evaporated, leaving 4.70 g of liquid alcohol **16:** IR (neat) OH 3400 (br m), C=C 1675 (m) cm^{-1}; ^1H NMR (CCl_4) δ 3.42 (s, 3, OMe), 3.99 (s, 2, OCH_2), 4.7-5.2 (m, 3, olefinic Hs). Chromatography of the latter on silica gel and elution with 4:1 hexane-ether liberated liquid ketal **17:** IR (neat) C=C 1680 (m) cm^{-1}; ^1H NMR (CCl_4) δ 3.13 (s, 3, OMe), 4.30 (m, 2, OCH_2), 4.81 (m, 2, olefinic CH_2).

A mixture of 1.20 g of alcohol **16** and 5 g of Amberlite IR-120-H resin, previously washed with anhydrous methanol and ether, in 30 mL of dry ether was stirred at room temperature for 12 h. Filtration and evaporation of the filtrate at 10 °C gave 778 mg of a pale yellow oil whose chromatography on neutral alumina (activity I) and elution with pentane furnished 760 mg of colorless, liquid normenthofuran (**18**): IR (neat) C=C 1640 (m), 1560 (m) cm^{-1}; ^1H NMR (CCl_4) δ 1.86 (s, 3, Me), 6.90 (br s, 1, aromatic H); *m/e* (calcd for $C_9H_{12}O$: 136.0888) 136.0896.

Dimethyl 2-Oxocyclohexylmalonate (19). A solution of 2.00 g of ester **12** and 20 mL of 10% hydrochloric acid in 5 mL of methanol was stirred at room temperature for 1 h, then poured into 150 mL of water, and extracted with ether. The extract was washed with water, dried ($MgSO_4$), and evaporated. Distillation of the residue gave 1.70 g of liquid ester **19:** bp 112 °C (0.15 Torr); IR (neat) C=O 1760 (s), 1740 (s), 1710 (s) cm^{-1}; ^1H NMR (CCl_4) δ 3.56 (d, 1, J = 9 Hz, $(CO)_2CH$), 3.68 (s, 6, $(OMe)_2$); *m/e* (calcd for $C_{11}H_{16}O_5$: 228.0997) 228.0991.

2-(*trans*-2-Hydroxycyclohexyl-)2-propenol (20). A mixture of 843 mg of sodium hydride, 4.00 g of keto ester **19,** and 100 mg of ethanol in 100 mL of dry 1,2-dimethoxyethane was stirred under nitrogen at room temperature for 5 h. A mixture of 2.00 g of lithium aluminum hydride in 150 mL of anhydrous ether was added and the stirring continued for 1 h. Workup as for **16** above and crystallization of the solid product, 1.08 g, from hexane-ether gave crystalline alcohol **20:** mp 65-66 °C; mp, IR, and ^1H NMR spectral data identical with those reported;[19] *m/e* (calcd for $C_9H_{16}O_2$: 156.1149) 156.1143.

1-Methoxy-5-methyl-1-cyclohexene (23).[29] A solution of 49.00 g of keto ester **24,** 71 g of methyl orthoformate, and 2.8 mL of concentrated sulfuric acid in 550 mL of methanol was stirred at room temperature for 48 h. After neutralization with methanolic sodium methoxide the solvent was removed under vacuum. The residue was washed with 5% sodium bicarbonate solution and water and extracted with ether. The extract was dried (Na_2SO_4) and evaporated. Distillation of the residue furnished 58.50 g of a 3:1 mixture of ester **25a** and its methyl ester equivalent (^1H NMR integration). A solution of 14.98 g of the mixture and 35 mL of 0.070 M sodium hydroxide in 35 mL of methanol and 25 mL of ethanol was refluxed gently for 18 h and stripped to dryness under vacuum at room temperature. A water solution (80 mL) of the residue was extracted with ether, 4.39 g of starting ester mixture being recovered from the extract, and evaporated under vacuum at room temperature. The residual solid was dissolved in 75 mL of methanol and 24.96 mL of a tetrahydrofuran solution of 0.943 N sulfuric acid added dropwise to neutralize the unreacted sodium hydroxide. The solvents were removed under vacuum at room temperature and the residual solid salt dried on a steam bath under vacuum and then suspended in 75 mL of anhydrous tetrahydrofuran. A solution of 49.63 mL of tetrahydrofuranic 0.943 N sulfuric acid was added dropwide to the stirring mixture at 0 °C and the stirring continued for 2 h. Filtration through a coarsely fritted filter funnel and evaporation of the filtrate under vacuum yielded crystalline acid **25b:** IR ($CHCl_3$) C=O 1742 (s), 1706 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.91 (d, 3, J = 6 Hz, Me), 2.92 (m, 1, COCH), 3.10, 3.24 (s, 3 each, OMe), 10.32 (s, 1, OH). Anal. ($C_{10}H_{18}O_4$) C, H.

A solution of the dry acid **25b** in 20 mL of dry tetrahydrofuran was added dropwise to a dry flask heated at 150 °C (400 Torr), connected to a trap cooled to −78 °C, and containing some solid potassium carbonate. Filtration of the trap contents and distillation of the filtrate yielded 3.43 g of enol ether **23:** bp 156-160 °C (760 Torr), 63 °C (35 Torr); IR (neat) C=C 1670 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.95 (d, 3, J = 6 Hz, Me), 3.44 (s, 3, OMe), 4.52 (t, 1, J = 4 Hz, olefinic H). Anal. ($C_8H_{14}O$) C, H.

A mixture of 4.15 g of keto ester **24,** 5.2 g of methyl orthoformate, and 1 g of Amberlite IR-120-H resin, previously washed with methanol, in 7 mL of anhydrous methanol was stirred at room temperature for 20 h and at 60 °C for 1 h. The mixture was filtered and the filtrate evaporated. Distillation of the residue yielded 4.18 g of ester **26b:** bp 73 °C (0.2 Torr); IR (neat) C=O 1735 (s), C=C 1665 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.05, 1.11 (d, ca. 1.5 each, J = 6 Hz, Me), 1.31 (t, 3, J = 7 Hz, Me of Et), 3.68 (s, 3, OMe), 3.84 (d, 1, J = 3 Hz, COCH), 4.35 (q, 2, J = 7 Hz, OCH_2), 4.81 (d, 1, J = 4 Hz, olefinic H). A solution of 5.33 g of the latter in 30.00 mL of a 1.655 M methanolic solution of potassium hydroxide and 5 mL of water was refluxed for 1 h and then poured onto a mixture of 200 mL of water, 200 mL of methylene chloride, and 1 drop of phenolphthalein. A solution of 49.59 mL of cold 1.00 M hydrochloric acid was added dropwise to the vigorously stirring two-phase mixture, while the methylene chloride layer was withdrawn and constantly replenished with fresh organic solvent. The combined methylene chloride solutions were washed with saturated brine, dried ($MgSO_4$), and evaporated, leading to 4.50 g of acid **26b** (solid on cooling): IR (Nujol) OH 3190 (br s), C=O 1705 (s), C=C 1660 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.01, 1.09 (d, ca. 1.5 each, J = 6 Hz, Me), 3.71 (s, 3, OMe), 4.83 (d, 1, J = 4 Hz, olefinic H), 13.20 (s, 1, OH). A solution of the latter in 15 mL of liquid poly(ethylene glycol), previously degassed under vacuum, was added dropwise over a 2-h period to 25 mL of liquid poly(ethylene glycol) at 120-135 °C (2 Torr) in a flash distillation apparatus equipped with two traps cooled by a dry ice-acetone bath and thereafter the heating was continued for 30 min. Redistillation of the distillate, 2.53 g, yielded 2.48 g of enol ether **23:** spectra were identical with those above.

Dimethyl 2-Methoxy-4-methyl-2-cyclohexenylmalonate (27). A mixture of 2.90 g of **23** and 80 mg of trimethoxyphosphinecopper(I) iodide was heated at 120 °C under nitrogen for 0.5 h, 2.50 g of dimethyl diazomalonate (**8**) was added dropwise over a 2-h period at 100 °C, and the temperature was maintained for an additional 6 h. Distillation of the mixture yielded 2 g of crude product whose chromatography on neutral alumina (activity I) and elution with 6:1 hexane-ether gave 1.6 g of liquid. Distillation of the latter furnished 1.50 g of liquid ester **27:** bp 120-121 °C (0.3 Torr); IR (neat) C=O 1760 (s), 1740 (s), C=C 1670 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.92, 1.02 (d, ca. 1.5 each, J = 6 Hz, Me), 3.20 (m, 1, OCCH), 3.45 (s, 3, OMe), 3.50 (d, 1, J = 4 Hz, COCH), 3.75 (s, 6, ester $(OMe)_2$), 4.58, 4.61 (d, ca. 0.5 each, J = 2 Hz, olefinic H). Anal. ($C_{13}H_{20}O_5$) C, H.

2-(2-Methoxy-4-methyl-2-cyclohexenyl-)2-propenol (28). A mixture of 2.00 g of sodium hydride, 1.40 g of diester **27,** and 100 mg of ethanol in 40 mL of anhydrous 1,2-dimethoxyethane was stirred under nitrogen at room temperature for 5 h. A mixture of 2.00 g of lithium aluminum hydride in 50 mL of dry ether was added and the stirring continued for 1 h. Workup as for **16** above gave 900 mg of colorless, liquid alcohol **28:** IR (neat) OH 3400 (br m), C=C 1670 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.41 (s, 3, OMe), 4.10 (s, 2, OCH_2), 4.65 (m, 1, OC=CH), 4.9-5.2 (m, 2, olefinic Hs); *m/e* (calcd for $C_{11}H_{18}O_2$: 182.1306) 182.1310.

(±)-Methofuran (22). A mixture of 213 mg of **28** and 3 g of Amberlite IR-120-H resin, previously washed with dry methanol, in 30 mL of dry ether was stirred at room temperature for 3 h. Workup as for **18** above yielded 120 mg of (±)-menthofuran (**22**): IR and ^1H NMR spectral data and GC retention time identical with those of an authentic specimen.

A mixture of 119 mg of **32** (vide infra) and 0.5 g of Amberlite IR-120-H resin, previously washed with methanol and ether, in 6 mL of dry ether was stirred at room temperature for 1.5 h. Filtration and careful evaporation of the filtrate at 10 °C yielded 111 mg of pale yellow oil, whose chromatography on 4 g of neutral alumina (activity III) and elution with pentane furnished 108 mg of (±)-menthofuran (**22**); IR and ^1H NMR spectra identical with those of the authentic monoterpene.

Ethyl 2-n-Butoxy-1-methylcyclopropanecarboxylate (29a). A so-

lution of 3.00 g of methyl α-diazopropionate in 15 mL of methylcyclohexane was added dropwise over a 6-h period to a stirring, refluxing suspension of 800 mg of copper bronze in 50 mL of *n*-butyl vinyl ether and the refluxing continued for 1.5 h. Filtration and distillation of the filtrate yielded 3.10 g of ester **29a:** bp 44–46 °C (0.025 Torr); IR (neat) C=O 1730 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.90 (t, 3, J = 7 Hz, Me of *n*-Bu), 1.22 (t, 3, J = 7 Hz, ester Me), 1.30 (s, 3, Me), 3.4–3.6 (m, 3, OCH, OCH_2), 4.06 (q, 2, J = 7 Hz, ester OCH_2). Anal. ($C_{11}H_{20}O_3$) C, H.

2-*n*-Butoxy-1-hydroxymethyl-1-methylcyclopropane (29b). A mixture of 1.00 g of ester **29a** and 500 mg of lithium aluminum hydride in 30 mL of dry ether was stirred at room temperature for 12 h. Moist sodium sulfate was added and the mixture shaken and filtered. The filtrate was dried (Na_2CO_3) and evaporated, yielding 793 mg of alcohol **29b:** bp 44–46 °C (0.020 Torr); ^1H NMR ($CDCl_3$) δ 0.44, 0.68 (m, 1 each, c-Pr CH), 0.84 (t, 3, J = 7 Hz, Me of *n*-Bu), 1.03 (s, <3, Me of minor isomer), 1.19 (s, <3, Me of major isomer), 1.2–1.6 (m, 4, $(CH_2)_2$), 3.03 (d of d, 1, J = 8, 3 Hz, OCH), 3.25 (q, 2, J = 12 Hz, CH_2OH), 3.42 (t, 2, J = 7 Hz, OCH_2). Anal. ($C_9H_{18}O_2$) C, H.

2-*n*-Butoxy-4-methyl-2,3-dihydrofuran (30). Water was removed azeotropically from a stirring suspension of 9 g of Fétizon reagent in 70 mL of benzene. A solution of 150 mg of alcohol **29b** in 5 mL of benzene was added and the mixture refluxed for 2.5 h. Filtration and evaporation of the filtrate yielded 127 mg of liquid **30:** IR (neat) C=C 1684 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.95 (t, 3, J = 7 Hz, Me), 1.19 (s, 3, allyl Me), 1.2–1.6 (m, 4, $(CH_2)_2$), 1.95 (d, 1, J = 7 Hz, allyl H), 2.37 (d of d, 1, J = 7, 2 Hz), 3.15 (d d of t, 2, J = 17, 3, 3 Hz, OCH_2), 4.77 (d, 1, J = 2 Hz, OCH), 6.29 (s, 1, olefinic H); *m/e* (calcd for $C_9H_{16}O_2$: 156.11502) 156.11497.

Methyl 3,7-Dimethyl-1-methoxybicyclo[4.1.0]heptane-7-carboxylate (31a). A solution of 2.00 g of methyl α-diazopropionate, 6 mL of enol ether **23,** and 4 g of recrystallized benzophenone was irradiated by a 250-W Hanovia lamp with Pyrex filter for 24 h (until total disappearance of the 2120-cm^{-1} infrared band characteristic of the diazo group). Distillation of the pale yellow solution under moderate vacuum in a 5-in. Vigreux column led to the recovery of 4.2 mL of **23.** Distillation of the oily residue under high vacuum yielded several fractions of which the 60–90 °C (0.2 Torr) fraction gave 3.40 g of material consisting of 60% desired product and ca. 30% of benzophenone. Redistillation produced 1.30 g of >95% ester **31a:** bp 65–73 °C (0.3 Torr); IR (neat) C=O 1735 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.90 (d, 3, J = 6 Hz, Me), 1.21 (s, <3, c-Pr Me of one isomer), 1.22 (s, <3, c-Pr Me of other isomer), 3.12 (s, <3, OMe of one isomer), 3.15 (s, <3, OMe of other isomer), 3.66 (s, 3, ester OMe); *m/e* (calcd for $C_{12}H_{20}O_3$: 212.1413) 212.1412.

3,7-Dimethyl-7-hydroxymethyl-1-methoxybicyclo[4.1.0]heptane (31b). A mixture of 1.00 g of ester **31a** and 500 mg of lithium aluminum hydride in 35 mL of dry ether was refluxed for 3 h and kept at room temperature for 12 h. Workup as for **29b** above gave 850 mg of colorless oil whose preparative TLC on Merck alumina Oxide PF-254 and elution with 1:1 ether–acetone gave **31b:** ^1H NMR ($CDCl_3$) δ 0.89 (d, 3, J = 6 Hz, Me), 1.04 (s, 3, c-Pr Me), 3.16 (s, <3, OMe of one isomer), 3.21 (s, <3, OMe of the other isomer), 3.4–3.7 (m, 2, OCH_2). Anal. ($C_{11}H_{20}O_2$) C, H.

3,6-Dimethyl-7a-methoxy-3a,4,5,6,7,7a-hexahydrobenzofuran (32). A mixture of 800 mg of alcohol **31b** and 10 g of Fétizon reagent (17.5 mmol of Ag_2CO_3) in 100 mL of benzene was refluxed for 12 h and then filtered. Evaporation of the filtrate gave 760 mg of pale yellow oil whose chromatography on 6 g of neutral alumina and elution with 4:1 pentane–ether furnished 132 mg of **32:** IR (neat) C=C 1675 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.91 (d, 3, J = 6 Hz, Me), 1.57 (s, 3, olefinic Me), 3.26 (s, 3, OMe), 5.97 (s, 1, olefinic H); *m/e* (calcd for $C_{11}H_{18}O_2$ 182.1333) 182.1350.

Elution with 5:1 ether–pentane afforded 613 mg of starting alcohol whose recycling increased the total yield of **32** to 62%.

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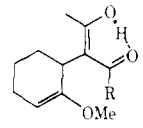

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