The Hydrolysis of α,α′-Dimethoxydihydrofurans

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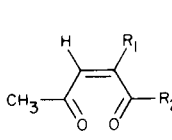
A series of α,α′-dimethoxydihydrofurans have been prepared and subjected to various acidic and neutral hydrolysis conditions in attempts to prepare conjugated enediones in a stereospecific manner. Isomerization of the 3-hexene-2,5-diones and rearrangements of other enediones to β,γ-unsaturated-γ-lactones have been uncovered. Methods of assignment of stereochemical configuration to the enediones are evaluated; reaction with hydrazine hydrate in the absence of acid is proposed as a useful criterion.

No general route has been reported thus far for the preparation of stereochemically pure acyclic conjugated *cis* and *trans*-enedione systems (**1** and **2**, respectively). One route which appears feasible is a sequence involving conversion of the appropriately substituted furan (**3**) to the corresponding α,α′-dimethoxydihydrofuran (**4**) (by either chemical or electrochemical techniques) (3) followed by hydrolysis of dimethoxydihydrofuran (**4**) to the enedione system (**1** and/or **2**). Birkofer and Dutz (4) and Van Duuren and Schmitt (5) have utilized such a sequence to convert sylvan (**3a**) into β-acetylacrolein (**1a** and **2a**) of unknown stereochemistry.

Levisalles (6) prepared several α,α′-dimethoxydihydrofurans with 2- or 2,5-substitution patterns (**4e**, R_1 = ethyl, *n*-propyl, and *n*-butyl, **4b**, and **4d**), but could not isolate several other analogous oxidative methoxylation products, such as the 2-methyl-5-ethyl compound **4f** or any 2,3,5-trialkyl or 2,3,4,5-tetraalkyl system. The dimethoxy compound **4b**, prepared from 2,5-dimethylfuran (**3b**), was converted to the *cis*-enedione **1b** on two minute reflux with aqueous acetic acid (6) and to the *trans*-enedione **2b** on treatment with concentrated hydrochloric acid (6). *Cis*-3-hexene-2,5-dione (**1b**) was isomerized to the *trans* compound **2b** by aqueous hydrobromic acid (6). Proof of stereochemistry for both **1b** and **2b** was based upon ultraviolet spectra (6) and isomerization to the presumably more thermodynamically stable *trans* compound. Levisalles (6) converted all of his isolated dimethoxy compounds (**4b**, **4d**, and **4e**) into the corresponding pyridazines (**5b**, **5c**, and **5d**, respectively) with aqueous acid and hydrazine hydrate, although the pyridazines were obtained in poor yield and somewhat questionable purity. Clauson-Kaas had earlier (7) reported similar problems with the 2-methyl series, **4a** → **5a**. Levisalles (6) also reported that *trans*-3-hexene-2,5-dione (**2b**) yielded



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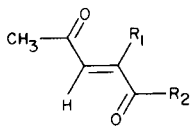
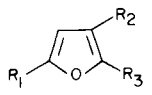


2

a, $R_1 = R_2 = H$
b, $R_1 = H$, $R_2 = CH_3$
c, $R_1 = CH_3$, $R_2 = H$



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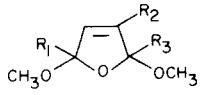
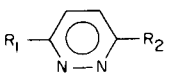


4

a, $R_1 = CH_3$, $R_2 = R_3 = H$
b, $R_1 = R_3 = CH_3$, $R_2 = H$
c, $R_1 = R_2 = CH_3$, $R_3 = H$
d, $R_1 = CH_3$, $R_3 = CH_3CH_2CH_2$, $R_2 = H$
e, R_1 = primary alkyl, $R_2 = R_3 = H$
f, $R_1 = CH_3$, $R_3 = CH_3CH_2$, $R_2 = H$

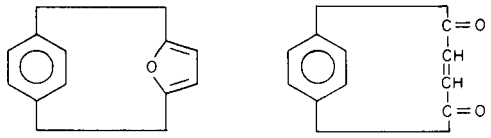


5

a, $R_1 = CH_3$, $R_2 = H$
b, $R_1 = R_2 = CH_3$
c, $R_1 = CH_3$, $R_2 = CH_3CH_2CH_2$
d, R_1 = primary alkyl, $R_2 = H$

only tars when treated with hydrazine hydrate with or without added 10 *N* sulfuric acid.

Various other groups have prepared *cis*- and *trans*-enediones in paracyclophane systems. Cram (8) converted [2.2](2,5)-furanoparacyclophane (**6**) to the dimethoxydihydro compound and hydrolyzed the reaction mixture under acidic conditions to the *trans*-enedione (**7a**) and under neutral or basic conditions to the *cis*-enedione (**7b**). The higher-melting *cis* isomer (**7b**) was isomerized to the *trans* isomer (**7a**) thermally at 170° or under acidic conditions. Additional structural information was obtained from the proton magnetic resonance spectra of the Diels-Alder adducts obtained by treatment of **7a** and **7b**, respectively, with 1,3-butadiene at 100°. Cope and Pawson (9) repeated this preparation (8) of the *trans*-enedione **7a**, while Whitesides, Pawson, and Cope (10) prepared deuterated analogs from the corresponding saturated diketoparacyclophane.



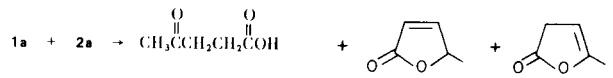
6 7

a, *trans*

b, *cis*

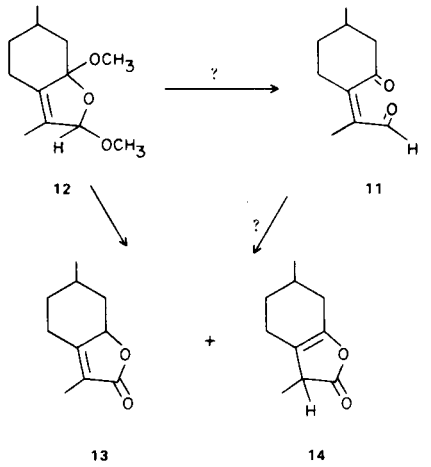
Consideration of the above experiments (3-10) suggests that hydrolysis of α,α′-dimethoxydihydrofurans under conditions involving mineral acids should produce *trans*-enediones, while hydrolysis under neutral or basic conditions should produce *cis*-enediones. More rigorous proof of stereochemical relationships in the enediones would be desirable to place these relationships on a more firm basis, a goal toward which some progress is reported herein.

However, another problem appears to be associated with the hydrolysis reaction other than the stereochemical one. β-Acetylacrolein (**1a** + **2a**) is readily converted into levulinic acid (**8**) (4) and the angelica lactones (**9** and **10**) (11) on treatment with aqueous acid at a reasonably fast rate. Hirsch and Eastman (12) were unable to isolate the



1a + 2a → $CH_3CCH_2CH_2COH$ + + 8 9 10

γ-ketoaldehyde **11** expected on hydrolysis of α,α′-dimethoxydihydromenthofuran (**12**), obtaining only the unsaturated lactones **13** and **14**, presumably by isomerization of **11** prior to isolation. Some way which minimizes such isomerizations must, therefore, be found in order that the hydrolyses might be used to prepare stereochemically pure enediones.



12 11 13 14

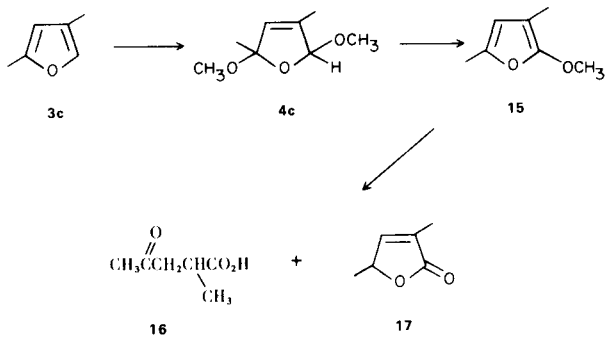
Results and Discussion.

Preparation of α,α′-Dimethoxydihydrofurans.

Freshly distilled sylvan (**3a**) was converted to 2,5-dimethoxy-2,5-dihydrosylvan (**4a**) by electrochemical methoxylation (3) and by treatment with bromine-sodium carbonate in methanol at -10°, the method Levisalles (6) used for other furans. Yields were much higher by the chemical method (65-72% compared to 45-50%). Electrolytic methoxylation yields were not improved by operating at lower temperatures (-40°).

Electrochemical techniques cleanly converted 2,5-dimethylfuran (**3b**) into the α,α′-dimethoxy compound **4b** (3) in 40-63% yield. However, the Levisalles bromine-sodium carbonate-methanol system (6) produced *trans*-3-hexene-2,5-dione (**2b**) directly in 53-55% yield. In contrast, Ross, Finkelstein, and Uebel (13) reported successful production of **4b** using either chemical (6) or electrochemical oxidation conditions. We have no explanation for this discrepancy under the chemical conditions except to note that a poor yield of the desired dimethoxy compound (**4b**) was obtained in one of our reaction mixtures.

Electrolytic methoxylation of 2,4-dimethylfuran (**3c**), prepared by the sultone procedure of Morel and Verkade (14), produced a reaction mixture which, after neutralization and removal of inorganic material and solvent, was distilled at 60° and 20 mm Hg. The only product obtained was identified as 2-methoxy-3,5-dimethylfuran (**15**) by spectral and elemental analyses and by conversion to α-methyllevulinic acid (**16**) and a conjugated γ-lactone, **17**, by concentrated hydrobromic acid (15). Cava and coworkers (16) have reported an analogous loss of methanol from 2,5-dimethoxy-2,5-dihydrofuran at 360° under acidic conditions to form 2-methoxyfuran, but this elimination is unprecedented at such low temperatures. Both 2,5-dimethoxy-2,5-dihydrosylvan (**4a**) and 2,5-dimethoxy-2,5-dimethyl-2,5-dihydrofuran (**4b**) were distilled at very similar temperatures and pressures without mishap. The



3c 4c 15

16 17

reaction mixture obtained from the 2,4-dimethylfuran system prior to distillation was found to be the desired dimethoxy compound **4c** in at least 95% purity. This unexpected synthesis of a methoxyfuran does not account for Levisalles' inability to form several α,α′-dimethoxydihydrofurans (6) if the most obvious mechanism, 1,4-elimination of the elements of methanol, is postulated under the pyrolytic conditions.

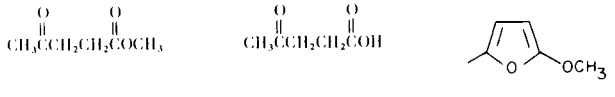
α,α′-Dimethoxydihydromenthofuran (**12**) was prepared as reported by Hirsch and Eastman (12).

All of the α,α′-dimethoxydihydrofurans were used as the synthetic mixtures of *cis* and *trans* isomers. The proton magnetic resonance spectra consistently supported the presence of more or less equal amounts of these two isomers (13,17).

Preparation of Enediones.

Hydrolysis of the methoxy compound formed from 2,5-dimethylfuran, **4b**, in refluxing one percent acetic acid for two minutes (4) produced the expected *cis*-3-hexene-2,5-dione (**1b**) in 66-78% yield. Hydrolysis of 2,5-dimethoxy-2,5-dihydrosylvan (**4a**) under identical conditions produces a 22.6% yield of a compound identified as *cis*-β-acetylacrolein (**1a**). A better yield (43-50%) of **1a** was obtained on hydrolysis of **4a** in the absence of acid under a nitrogen atmosphere.

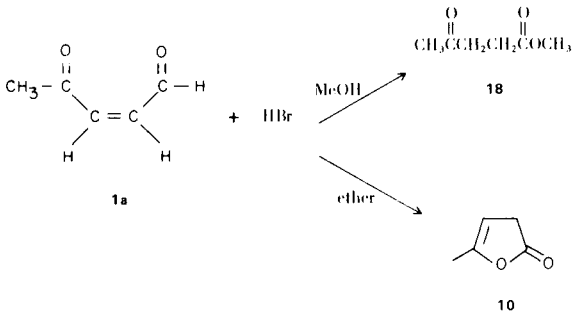
Hydrolysis of **4a** with concentrated hydrochloric acid at room temperature, conditions expected to lead to *trans*-enedione (6), produced methyl levulinate (**18**) as the major product. Higher temperatures with 2 *N* hydrochloric acid were known (4) to convert **4a** to levulinic acid (**8**), presumably by hydrolysis of ester **18**.



18 8 19

An attempt to prepare *trans*-β-acetylacrolein (**2a**) directly from sylvan by the method of Cram (8) (bromine-methanol-sodium acetate at 0° followed by 5% sulfuric acid) produced a complex mixture containing *cis*-β-acetylacrolein (**1a**), methyl levulinate (**18**), α-angelica lactone (**10**), 2-methoxy-5-methylfuran (**19**), three other volatile components, and an extensive amount of polymeric material. The products identified were characterized by chromatographic comparison with authentic samples or by spectral and elemental analysis of purified material.

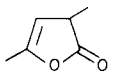
Another method of preparing a *trans*-enedione has been reported by Levisalles (6) - aqueous hydrobromic acid isomerization of the *cis* isomer. Hydrobromic acid in methanol at ambient temperatures converted *cis*-β-acetylacrolein (**1a**) into methyl levulinate (**18**), while use of ether as the solvent instead of methanol yielded α-angelica lactone (**10**) (11,18).



1a 18 10

Isomerization of *cis*-3-hexene-2,5-dione (**1b**) to the *trans* isomer could be effected with iodine in ether at room temperature for 30 minutes. No *trans* → *cis* isomerization could be observed under these conditions. Iodine treatment of *cis*-β-acetylacrolein (**1a**) produced impure α-angelica lactone (**10**) and large amounts of polymeric material, with no evidence of the desired *trans* isomer **2a**.

Hydrolysis of slightly impure 2,5-dimethoxy-2,4-dimethyl-2,5-dihydrofuran (**4c**) using one percent acetic acid at reflux for four minutes produced a lactone, **20**, analogous to α-angelica lactone. This prevalent formation of the unconjugated unsaturated lactone had previously been noted in the menthofuran system (12).



20

Treatment of α,α′-dimethoxydihydromenthofuran (**12**) with aqueous acetic acid at reflux for two minutes or with concentrated hydrochloric acid at room temperature for ten minutes produced only the unsaturated lactones **13** and **14** previously observed (12) from less acidic and neutral hydrolyses.

In summary, hydrolytic conditions to convert α,α′-dimethoxydihydrofurans into *cis* enediones are readily available. Preparation of *trans* enediones may often be accomplished using iodine-catalyzed isomerization of *cis* isomers or using reactions performed directly on the furan itself without the intermediacy of the dimethoxydihydro

compound. Neither of these techniques proved to be amenable when one of the carbonyl groups of the enedione was an aldehyde.

Enediones containing an aldehydic carbonyl and alkylated α to this aldehyde group rearrange to unsaturated lactones at a rate apparently faster than hydrolysis of the relevant α,α′-dimethoxydihydrofuran, precluding easy isolation of the enedione. If this rearrangement is viewed as an intramolecular process (19), formation of the β,γ-unsaturated lactone may be readily rationalized. Increased electron density in the carbon-carbon double bond when alkyl groups are present would enhance the nucleophilicity of the keto carbonyl and promote the rearrangement process. An attempt to prove the intramolecular nature of this rearrangement using deuterium labelling (20) provided evidence for an intermediate such as the enedione capable of undergoing extensive deuterium exchange with solvent molecules and for the retention of some deuterium during the rearrangement. However, the results were not sufficiently conclusive to establish the nature of the rearrangement process.

Nevertheless, on the basis of the products isolated from the various hydrolysis reactions, it seems reasonable to propose that hydrolysis of α,α′-dimethoxydihydrofurans leads to enediones under all hydrolytic reaction conditions. These enediones rearrange to β,γ-unsaturated γ-lactones, which may themselves isomerize to α,β-unsaturated γ-lactones. Either of these unsaturated lactones may be hydrolyzed to appropriately substituted levulinic acids or esters.

Stereochemical Configuration of Enediones.

Preparation of two geometrical isomers of 3-hexene-2,5-dione (**1b** and **2b**) presents the opportunity to develop techniques for distinguishing between such enedione stereoisomers. These techniques may then be applied to the problem of identifying the single isomer of β-acetylacrolein (**1a** or **2a**) obtained.

For reasons of symmetry, the vinyl hydrogens are equivalent in both isomers of 3-hexene-2,5-dione. Application of proton magnetic resonance to β-acetylacrolein is informative, but not unequivocal. Olefinic coupling constants fall in the range of 7-12 Hz for *cis* hydrogens and 13-18 Hz for *trans* hydrogens (21). The observed value of 12 Hz suggests the *cis*-β-acetylacrolein structure (**1a**), but is uncomfortably close to the area of possible ambiguity. The absorption of the aldehyde hydrogen at 10.1 δ is consistent with that reported for *cis* α,β-unsaturated aldehydes (22) and distinctly different from the 9.3-9.6 δ values reported for *trans* systems (22,23).

Ultraviolet spectra data also support a *cis* assignment for the β-acetylacrolein isomer obtained, but are dependent on Levisalles' (6) somewhat arbitrary assignments to the 3-hexene-2,5-diones (**1b** and **2b**) (Table I).

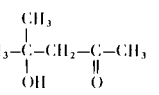
TABLE I

Ultraviolet Spectra of Enediones (a)

Compound	λ max (ε)	Reference
trans-3-hexene-2,5-dione (**2b**)	228 (14,600), 324 (70)	6
	227 (14,220), 328 (67)	this work
cis-3-hexene-2,5-dione (**1b**)	223 (6,600), 282 (175)	6
	221 (3,825), 284 (100)	this work
β-acetylacrolein isomer	218 (2,084), 301 (553)	this work

(a) Spectra obtained as solutions in absolute ethanol.

Hydrazine hydrate in non-acidic medium might be utilized as a chemical method for unambiguously solving this stereochemical problem. Both *cis*-3-hexene-2,5-dione (**1b**) and the β-acetylacrolein isomer were converted under non-acidic conditions into the corresponding (hygroscopic) pyridazines **5b** and **5a** in 45 and 39% yields, respectively. All other products were polymeric. The *trans*-3-hexene-2,5-dione (**2b**) under the same reaction conditions yielded 15.8% of pyridazine **5b** and about equal amounts of three other components, one of which has been isolated by preparative vapor-phase chromatography (23% yield) and identified as 4-hydroxy-4-methyl-2-pentanone (**21**).



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EXPERIMENTAL

Melting points and boiling points are uncorrected. Nmr spectra were recorded on a Varian A-60A instrument using 10% solutions of deuteriochloroform and are reported in parts per million downfield from tetramethylsilane as an internal standard. Only distinct absorptions will be reported herein. Infrared spectra were determined with a Beckman IR 10 spectrophotometer on 5% solutions in chloroform. Only major absorptions are listed herein. Ultraviolet spectra were measured with Beckman DK-2 spectrophotometer in absolute ethanol. Elemental analysis were performed by Alfred Bernhardt Mikroanalytisches Laboratorium, Elbach, West Germany.

Methoxylation.

Method I (Electrolytic).

Electrolysis (3) of 0.1 mole of furan compound in 140 ml. of absolute methanol containing 0.05 mole of ammonium bromide using platinum electrodes (one annular cylindrical electrode, height 5 cm, diameter 3.5 cm; one spiral electrode, height 4.5 cm, diameter 1 cm) at temperature below 0° with magnetic stirring at 0.5-1.0 amp for 6.5-9.5 hours produced a yellow solution. To this solution was added 50 ml. of methanolic sodium methoxide which contained base equivalent to the ammonium bromide used. The product was concentrated on a steam bath with periodic filtration to remove the solid material which separated. After all

solvent and solids had been removed, the dark, liquid residue was vacuum-distilled.

Method 2 (Chemical).

The bromine-sodium carbonate method of Levisalles (6) was followed. Bromine, 0.5 mole, in 150 ml. of absolute methanol was added slowly with stirring to a solution of 0.5 mole of furan compound and 1.0 mole of sodium carbonate in 400 ml. of absolute methanol cooled to -10°. The reaction mixture was poured into a saturated sodium chloride solution, extracted with methylene chloride and dried (magnesium sulfate). The solvent was removed and the product vacuum-distilled.

2,5-Dimethoxy-2,5-dihydrosylvan (**4a**).

Method 1 (Electrolytic).

This compound was prepared from freshly distilled sylvan (**3a**) in 46.4% yield by the method of Clauson-Kaas (3); b.p. 61° (21 mm); n_D 1.4290 (lit. (4) 60-65° (20 mm), n_D^{20} 1.4290); nmr δ 1.50, 1.56 (2s, 3), 3.13, 3.20, 3.42, 3.50, (4s, 6), 5.50, 5.76 (broad d, 1), 5.97 (s, 2).

Method 2 (Chemical).

The same compound was obtained in 72% yield using the bromine-sodium carbonate method of Levisalles (6).

2,5-Dimethyl-2,5-dimethoxydihydrofuran (**4b**).

Method 1 (Electrolytic).

This compound was prepared from **3b** in 62.6% yield by the method of Clauson-Kaas (3): b.p. 57° (15 mm); n_D^{20} 1.4375 (lit. (6) 59° (16 mm), n_D^{16} 1.4312); nmr δ 1.46, 1.58 (2s, 3), 3.22, 3.31 (2s, 6), 5.90 (s, 2).

Method 2 (Chemical).

An attempt to prepare this compound by the bromine method led, after the described work up, to *trans*-3-hexene-2,5-dione (**2b**) in 53.5% yield. A sample recrystallized from cyclohexane exhibited m.p. 76-77° (lit. (6) 76-77°), ir 1685, 1625, 1365, 985 cm^{-1}; nmr δ 2.33 (s, 6) 6.71 (s, 2); uv Table I.

Anal. Calcd. for $C_6H_8O_2$: C, 64.27; H, 7.19. Found: C, 64.16; H, 7.18.

2,4-Dimethylfuran (**3c**).

The sultone of mesityl oxide was prepared by the method of Morel and Verkade (14) in 40.7% yield. Pyrolysis of the sultone at 230-235° using calcium oxide with a catalytic amount of quinoline gave **3c** in 42.9% yield: b.p. 94° (lit. (14) 93-97°); ir 1620, 1555 cm^{-1}; nmr δ 1.96 (s, 3), 2.20 (s, 3), 5.78 (s, 1), 6.95 (s, 1).

2-Methoxy-3,5-dimethylfuran (**15**).

2,4-Dimethylfuran (**3c**) (38.6 g.) was methoxylated by method 1. After adding the required amount of sodium methoxide, the reaction mixture was concentrated on a steam bath, poured into a saturated sodium chloride solution and extracted with methylene chloride. The extract was dried (magnesium sulfate), the solvent removed under vacuum and the product distilled to yield 18.4 g. (36.3% yield) of **15**: b.p. 65° (36 mm); n_D^{25} 1.4476; ir 1660, 1595 cm^{-1}; nmr δ 1.79 (s, 3), 2.12 (s, 3), 3.78 (s, 3), 5.62 (s, 1); uv max (ethanol) 213 mμ (ε, 2,100).

Anal. Calcd. for $C_7H_{10}O_2$: C, 66.65; H, 7.99. Found: C, 66.85; H, 7.92.

Cleavage of 2-Methoxy-3,5-dimethylfuran (**15**).

To 5.96 g. of methoxyfuran **15** was added 40 ml. of 48% hydrobromic acid (15), with an exothermic reaction occurring on mixing. The reaction mixture was refluxed for 2 hours, diluted with water and extracted with methylene chloride and dried (magnesium sulfate). The solvent was removed and the product distilled to yield 2.69 g. (50.8%) of lactone **17**: b.p. 89° (6.2 mm); ir 1805, 1745, 1655 cm^{-1}; nmr δ 1.31 (d, 3, J = 6.5 Hz), 1.79 (m, 3), 4.78 (m, 1), 6.76 (m, 1); uv max (ethanol) 207 mμ (ε, 11,100).

Anal. Calcd. for $C_6H_8O_2$: C, 64.27; H, 7.19. Found: C, 64.32; H, 7.07.

The residue after distillation was treated with aqueous sodium hydroxide solution and washed with ether. The aqueous layer was acidified with hydrochloric acid, extracted with ether and dried (magnesium sulfate). The solvent was removed to yield 1.52 g. (26.5%) of acid **16**: ir 1750, 1725-1705 cm^{-1}; nmr δ 1.16 (d, 3, J = 6.5 Hz), 2.04 (s, 3), 10.06 (broad s, 1, COOH).

Anal. Calcd. for $C_6H_{10}O_3$: C, 55.37; H, 7.74. Found: C, 55.29; H, 7.66.

2,4-Dimethyl-2,5-dimethoxydihydrofuran (**4c**).

Method 1 (Electrolytic).

This compound was prepared from 16 g. of **3c** by the method of Clauson-Kaas (3). When the electrolysis was completed and a sodium methoxide solution had been added, most of the methanol was removed at reduced pressure using a water bath heated to 35°. The residue was washed (water), extracted with ether, and the ethereal extract was dried (magnesium sulfate) and concentrated to yield 17.1 g. (67.6% yield) of **4c**. Gas chromatographic analysis (24) indicated the product to be at least 95% pure **4c**: ir 1675 cm^{-1}; nmr δ 1.44, 1.48 (2s, 3), 1.75 (s, 3), 3.06, 3.12, 3.33, 3.43 (4s, 6), 5.16, 5.45 (2 broad s, 2).

Anal. Calcd. for $C_8H_{14}O_3$: C, 60.74; H, 8.92. Found: C, 60.49; H, 8.75.

α,α′-Dimethoxydihydromenthofuran (**12**).

Method 1 (Electrolytic).

This compound was prepared from menthofuran in 82.7% yield as described by Hirsch and Eastman (12) (spectra as reported (12)).

Hydrolysis.

Method A (6).

To 0.1 mole of the dimethoxydihydrofuran compound was added 20 ml. of aqueous 1% acetic acid. The reaction mixture was refluxed for 2 minutes, neutralized with 50 ml. aqueous 2% sodium bicarbonate, saturated with sodium chloride and extracted with methylene chloride. The extract was dried (magnesium sulfate), the solvent removed under vacuum and the product vacuum-distilled.

Method B (12).

Approximately 0.1 mole of the dimethoxydihydrofuran compound was stirred with 30 ml. of water under nitrogen at room temperature for 24 hours. The reaction mixture was extracted with ether, dried (magnesium sulfate), the solvent removed and the product vacuum-distilled.

Method C (6).

Approximately 3 g. of the dimethoxydihydrofuran compound was stirred with 0.3 ml. of hydrochloric acid for 10 minutes at room temperature. The reaction was quenched with 25 ml. of a saturated sodium bicarbonate solution and extracted with methylene chloride. The extract was dried (magnesium sulfate), the

solvent removed under vacuum, and the product vacuum-distilled.

Hydrolysis of 2,5-dimethyl-2,5-dimethoxydihydrofuran (**4b**).

Hydrolysis of 17.3 g. of **4b** gave 9.6 g. (78.4% yield) of **1b** by the procedures of Levisalles (6): b.p. 91° (10.7 mm); $n_D^{24.5}$ 1.4541 (lit. (6) 92° (16 mm), n_D^{16} 1.4571); ir 1700, 1615 cm^{-1}; nmr δ 2.23 (s, 6) 6.22 (s, 2); uv Table I.

Anal. Calcd. for $C_6H_8O_2$: C, 64.27; H, 7.19. Found: C, 64.18; H, 7.03.

Hydrolysis of 2,5-Dimethoxydihydrosylvan (**4a**).

Method A.

Hydrolysis of 17.4 g. of **4a** gave 2.68 g. (22.6% yield) of **1a**: b.p. 79° (20 mm) (lit. (4) 67-68° (11 mm)); ir 1685, 1600 cm^{-1}; nmr δ 2.34 (s, 3), 6.09 (q, 1, J = 12, 7 Hz), 6.99 (d, 1, J = 12.0 Hz), 10.1 (d, 1, J = 7 Hz); uv Table I.

Anal. Calcd. for $C_5H_6O_2$: C, 61.22; H, 6.16. Found: C, 61.11; H, 6.29.

Method B.

Hydrolysis of 9.68 g. of **4a** gave 2.87 g. (43.7% yield) of identical **1a**.

Method C.

Hydrolysis of 3.49 g. of **4a** with 0.3 ml. of hydrochloric acid (25) gave 1.13 g. (36% yield) of methyl levulinate (**18**): b.p. 97° (22 mm); n_D^{25} 1.4226 (lit. (26) 85-86° (14 mm), n_D^{20} 1.4233); ir 1710-1750 cm^{-1}; nmr δ 2.15 (s, 3), 2.63 (m, 4), 3.62 (s, 3).

Attempted Preparation of *trans*-β-Acetylacrolein (**2a**).

The method described by Cram (8) was followed. A solution containing 80 g. of bromine in 150 ml. of absolute methanol was added slowly with stirring to 41 g. of sylvan (**3a**) and 82 g. of sodium acetate in 600 ml. of absolute methanol cooled to 0°. The reaction mixture was poured into 600 ml. of 5% sulfuric acid, stirred for 16 hours under nitrogen, extracted with methylene chloride, washed with water and saturated solutions of sodium bicarbonate and sodium chloride, and dried (magnesium sulfate). The solvent was removed at reduced pressures. Gas chromatographic analysis (27) of the crude product mixture indicated the presence of seven components. Three of the components were shown to be *cis*-β-acetylacrolein (**1a**), α-angelica lactone (**10**), and methyl levulinate (**18**), by comparison with authentic samples. Distillation gave only one fraction with one major component. Purification by preparative gas chromatography (27) gave 2-methoxy-5-methylfuran (**19**): b.p. 44° (25 mm); ir 1625, 1600 cm^{-1}; nmr δ 2.13 (s, 3), 3.73 (s, 3), 4.92 (d, 1, J = 3 Hz), 5.71 (m, 1).

Anal. Calcd. for $C_6H_8O_2$: C, 64.27; H, 7.19. Found: C, 64.16; H, 7.27.

Isomerization of *cis*-β-Acetylacrolein (**1a**) in Methanol.

The isomerization of this compound was attempted by the method of Levisalles (6). To 0.73 g. of **1a** in 2 ml. of absolute methanol was added 2 drops of 48% hydrobromic acid and the reaction mixture was stirred at room temperature for 1 hour. The reaction mixture was poured into water and extracted with methylene chloride. The extract was dried (magnesium sulfate) and the solvent removed under vacuum to give 0.62 g. (63.9% yield) of methyl levulinate (**18**).

Isomerization of *cis*-β-acetylacrolein (**1a**) was repeated using ether as solvent. After the described work up, the product was distilled to yield 0.33 g. (17.4% yield) of α-angelica lactone (**10**): b.p. 85° (22 mm) (lit. (17) 52° (10 mm)); ir 1795, 1729, 1684 cm^{-1} (as reported (13)); nmr δ 1.96 (m, 3), 3.12 (m, 2), 5.08 (m, 1) (as reported (13)).

Isomerization of *cis*-3-Hexene-2,5-dione (**1b**).

A few crystals of iodine were added to 0.5 g. of **1b** in 10 ml. of ether and stirred at room temperature for 0.5 hour. The reaction mixture was washed with an aqueous sodium thiosulfate solution. The ethereal solution was dried (magnesium sulfate) and the solvent removed under vacuum to yield 0.35 g. of *trans*-3-hexene-2,5-dione (**2b**). Nmr analysis showed the absence of the *cis* isomer **1b**.

The *trans* isomer **2b** remained unchanged under the same reaction conditions.

Hydrolysis of 2,4-Dimethyl-2,5-dimethoxydihydrofuran (**4c**).

Method A.

Hydrolysis of 9.86 g. of **4c** gave after the described work up (6) 0.28 g. of lactone **20**: b.p. 53° (6 mm); ir 1790, 1725, 1685 cm^{-1}; nmr δ 1.32 (d, 3, J = 7.5 Hz), 2.00 (m, 3), 3.23 (m, 1), 5.21 (m, 1).

Anal. Calcd. for $C_6H_8O_2$: C, 64.27; H, 7.19. Found: C, 64.07; H, 7.25.

Hydrolysis of α,α′-Dimethoxydihydromenthofuran (**12**).

Method A.

Hydrolysis of 5.0 g. of **12** by the method of Levisalles (6) gave 2.57 g. (66% yield) of lactones **17** and **18**, spectra as reported (12).

Method B.

Hydrolysis of 3.06 g. of **12** by the method of Levisalles (6) gave 1.77 g. (74.4% yield) of the α,β-unsaturated lactone **13**, spectra as reported (12).

Reaction of Enediones with Hydrazine.

To 0.02-0.05 mole of enedione in 10 ml. of water a 10% excess of hydrazine hydrate was added dropwise while stirring, with an exothermic reaction occurring on mixing. The reaction mixture was refluxed for 1 hour, extracted with methylene chloride and dried (magnesium sulfate). The solvent was removed under vacuum and the product vacuum-distilled.

3,6-Dimethylpyridazine (**5b**).

This hygroscopic compound was prepared from **1b** in 45% yield: b.p. 104-107° (11.25 mm) (lit. (6) 100-110° (15 mm)); ir 1640, 1595 cm^{-1}; nmr δ 2.61 (s, 6), 7.20 (s, 2).

Anal. Calcd. for $C_6H_8N_2$: C, 66.64; H, 7.46. Found: C, 66.52; H, 7.54.

3-Methylpyridazine (**5a**).

This hygroscopic compound was prepared from **1a** in 38.7% yield: b.p. 98° (7 mm); ir 1605 cm^{-1}; nmr δ 2.67 (s, 3), 7.25, 7.29 (2s, 2), 8.94 (t, 1, J = 3.2 Hz).

Anal. Calcd. for $C_5H_6N_2$: C, 63.81; H, 6.43; N, 29.76. Found: C, 63.68; H, 6.48; N, 29.61.

Trans-3-Hexene-2,5-dione (**2b**) with Hydrazine.

Using the procedure for **5a** and **5b**, 5 g. of **2b** was refluxed with hydrazine hydrate. Work up of the reaction mixture gave 3.52 g. of a four component mixture. The products were separated by column chromatography on silica gel (Woelm). One component was identified as 3,6-dimethylpyridazine (**5b**) in 15.8% yield. A second component, obtained in 23% yield, was identified as 4-hydroxy-4-methyl-2-pentanone (**21**): ir 1705, 1615 cm^{-1};

nmr δ 1.18 (s, 6), 2.11 (s, 3), 2.55 (s, 2), 3.58 (broad s, 1); mass spectrum, molecular ion m/e 116, base peak m/e 43.

Anal. Calcd. for $C_6H_{12}O_2$: C, 62.04; H, 10.41. Found: C, 62.03; H, 10.27.

Two other nitrogen-containing compounds were obtained in an impure state in slightly smaller yields and have not been identified.

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