tions 34–38 and atalaphylline (20 mg), R_f 0.42, from fractions 42–47. The latter fractions furnished a tarry mass which still showed the presence of a number of less polar components.

***N*-Methylbicycloatalaphylline.**—The alkaloid crystallized from benzene as yellow needles: mp 185°; $\lambda_{\max}^{\mathrm{EtOH}}$ 228 nm (log ϵ 4.20), 274 (4.49), 340 (4.07), 420 (3.66); $\lambda_{\max}^{\mathrm{EtOH + alkali}}$ 245 nm (log ϵ 4.24), 308 (4.52), 375 (4.14); $\nu_{\max}$ 3475, 1630, 1560, 1530, 1450 cm^{-1}.

Anal. Calcd for $C_{24}H_{27}NO_4$: C, 73.26; H, 6.92; N, 3.56. Found: C, 73.25; H, 6.46; N, 3.69.

Methylation of *N*-Methylbicycloatalaphylline.—A solution of IV (0.05 g) in MeOH (5 ml) was treated with excess CH_2N_2 and the product was chromatographed over silica gel, and a semisolid mass (V), homogeneous by tlc in several solvent systems, migrated out. It exhibited $\nu_{\max}^{\mathrm{Nujol}}$ 1640, 1600, 1575 cm^{-1} and a molecular ion peak (M^+) at *m/e* 407.

Methylation of *O*-Methylbicycloatalaphylline.—A solution of VI (0.02 g) in acetone (15 ml) was refluxed with MeI (2 ml) and anhydrous K_2CO_3 (0.1 g) over a steam bah for 96 hr. Usual work-up led to a gummy mass containing traces of starting material. Separation by preparative tlc over silica gel gave a semisolid mass which gave a superimposable ir spectrum with that of V.

Registry No.—IV, 35096-35-6.

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Valence Isomerization of 2,4,6-Trimethyl-2*H*-pyran[1]

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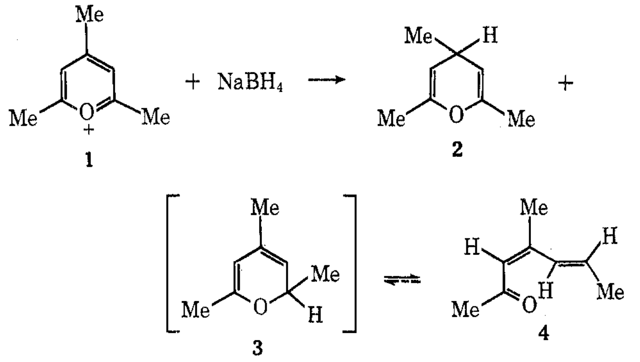
Balaban, Mikai, and Nenitzescu[2] showed that reaction of 2,4,6-trimethylpyryllium perchlorate with sodium borohydride gave two products to which they



assigned the structures 2 and 4 (stereochemistry not given). They made the reasonable assumption that 4 was formed by a rapid valence isomerization from 3. Because of our general interest in electrocyclic reactions, we investigated this reaction somewhat more thoroughly than had the previous workers.[2] The reaction proceeds exactly as they described and the two products were isolated in good yield. The nmr spectra are described in the Experimental Section, and these are in accord with the assigned structures. In addition the spectrum of 4 permits us to assign its stereochemistry. Thus the Δ^5 double bond must be trans, since J_{56} is 15.0 Hz, and the Δ^3 double bond is cis since the shift for H_5 (7.63 ppm) can be accounted for only if the acetyl and C_5H groups have a cis orientation.[3]

We were unable to ascertain satisfactorily whether an observable amount of 3 is in equilibrium with 4 or not. The nmr spectrum of 4 has peaks of low intensity at δ 1.18 (d), 4.77, and 4.85 which might be assigned to 3, but these do not exhibit the expected intensity increase and decrease on heating and cooling. Furthermore, there are a number of other small peaks which could not be associated with 3 which also appear in the spectrum.

Next we attempted to determine whether 3 could be identified as a transient intermediate. The presence of a transient intermediate was readily shown by spectral means. If the reduction is carried out under an overlayer of pentane at 0°, a diluted aliquot of the pentane layer has $\lambda_{\max}$ 277 nm, which disappears rapidly at room temperature, leaving the $\lambda_{\max}$ 272 nm of 4. The 277-nm band is quite reasonable for the α-pyran 3, since Hinnen and Dreux[4] have found $\lambda_{\max}$ (CH_3OH) 282 nm for 2,2,4,6-tetramethyl-α-pyran. Additional evidence to support a structural assignment for the intermediate was obtained from the nmr spectrum of a solution obtained by reducing 1 with an underlayer of carbon tetrachloride. At $-22°$ the spectrum shows (in addition to bands due to 2 and 4) resonances at δ 1.18 (d, J = 6.5 Hz), 1.56 (s), 1.76 (s), 4.6 (m), 4.8 (broad s), and 4.9 (broad s). When the solution is warmed to 35°, these bands rapidly disappear and the final spectrum matches that of the crude reduction product obtained from the normal reaction procedure. These data provide strong support for the assignment of structure 3 to the transient intermediate.

An estimate of the rate of conversion of 3 to 4 was obtained by following the change in absorbance at 253.5 nm where the intermediate showed no absorption. With the assumption that 3 goes directly to 4 with no intermediate, the rate of disappearance of 3 can be calculated. The reaction shows good first-order kinetics with k (13°) $\cong 3 \times 10^{-3}$ sec^{-1}. More recently we have shown[5] that the rate of ring opening of 2,2,4,6-tetramethyl-α-pyran is 1.6×10^{-4} sec^{-1} at 14.6°. Since 3 is lacking the cis methyl group on the terminal carbon present in 2,2,4,6-tetramethyl-α-pyran, which is expected to reduce the rate of the latter, the rate difference of *ca.* 20-fold seems quite reasonable.

Experimental Section

2,4,6-Trimethyl-4*H*-pyran (2) and 4-Methyl-*cis*-3-*trans*-5-heptadien-2-one (4).—An aqueous solution of 1 was reduced with sodium borohydride according to the procedure of Balaban, Mikai, and Nenitzescu.[2] The two products were separated by fractional distillation using a Nester and Faust 30-cm spinning band column. The pyran 2, bp 30° (6 mm), nmr (CCl_4) δ 0.98 (d, J = 6.5 Hz, 3 H), 1.71 (d, J = 0.8 Hz, 3 H), 2.79 (m,

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(1) Support of this study by the National Science Foundation under Grant GP-4985 is gratefully acknowledged.

(2) A. T. Balaban, G. Mikai, and C. D. Nenitzescu, *Tetrahedron*, **18**, 257 (1962).

(3) L. M. Jackman and R. H. Wiley, *J. Chem. Soc.*, 2881, 2886 (1960).

(4) A. Hinnen and J. Dreux, *C. R. Acad. Sci., Ser. C*, **255**, 1747 (1962).

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1 H), 4.38 (d, J = 3.8 Hz, 2 H), constituted about $^1/_8$ to $^1/_4$ of the distillate. The dienone **4**, bp 53–54° (6 mm), nmr (CCl_4) δ 1.81 (d of d, J = 6.7, 1.0 Hz, 3 H), 1.91 (d, J = 1.0 Hz, 3 H), 2.1 (s, 3 H), 5.98 (s, 1 H), 6.17 and 7.63 (AB part of ABX pattern, J_{AB} = 15.0, $J_{AX} \cong 1.0$, J_{BX} = 6.7 Hz), was the major product.

2,4,6-Trimethyl-2*H*-pyran (3) as Transient Intermediate.—A mixture of 0.5 g (2.1 mmol) of **1**, 100 ml of pentane, and 10 ml of water was cooled in an ice bath. To this was added 0.2 g (53 mmol) of sodium borohydride and the mixture was stirred vigorously for 20–30 sec. About 25 ml of the pentane layer was decanted into a test tube stored in a Dry Ice bath. The pentane solution had λ_{max} 277 nm, which disappeared rapidly (10 min at 25°), giving λ_{max} 272 nm for **4**. The rate of change of the spectrum at 253.5 nm followed first-order kinetics, since a plot of 2.3 log $(A_\infty - A_t)/A_\infty$ *vs.* time gave a straight line.

Reduction was carried out as described above except that spectral grade carbon tetrachloride was used in place of the pentane. The organic layer was pipetted into a cold test tube and was dried briefly ($MgSO_4$). A nmr spectrum at −22° gave a complex spectrum containing, in addition to bands associated with **2** and **4**, new bands at δ 1.18 (d, J = 6.5 Hz), 1.56 (s), 1.76 (s), 4.6 (m), 4.8 (s), and 4.9 (s). All of these bands disappear rapidly when the solution is warmed to 35°.

Registry No.—**2**, 35030-93-4; **3**, 35030-94-5; **4**, 29178-98-1.

Preparation of *trans*-2,3-*trans*-5,6-dioxane-d_4. Use of a Hindered Base to Prevent Acid-Catalyzed Side Reactions

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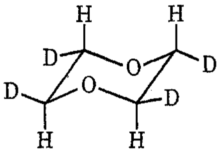
In the course of another investigation[1] it became necessary to synthesize a 1,4-dioxane, substituted with deuterium such that a definite geometric isomer, *trans*-2,3-*trans*-5,6-dioxane-d_4 (I), was obtained. The usual preparations of 1,4-dioxane (*e.g.*, the acid-catalyzed self-condensation of ethylene glycol) were not expected to lead to pure geometric isomers, and preliminary results were in accord with this expectation.



I

A double displacement on an appropriately deuterated ethane, with leaving groups in the 1 and 2 positions, by the oxygens of an appropriately deuterated ethylene glycol, would be expected to give I.

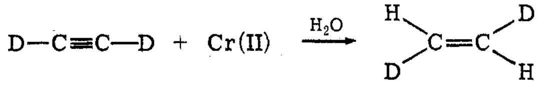
An attempt to displace the tosylate groups of ethylene glycol ditosylate with the dilithium salt of ethylene glycol in hexamethylphosphoramide yielded no 1,4-dioxane. Heating ethylene glycol directly with ethylene glycol ditosylate in p-dimethoxybenzene to 210° also yielded no 1,4-dioxane. When ethylene glycol and ethylene glycol ditosylate were heated together to 180°, without solvent, 1,4-dioxane was obtained in 20% yield. This dioxane may have arisen in part from the acid-catalyzed self-condensation of ethylene glycol (toluenesulfonic acid is obtained from the desired reaction and from decomposition of the tosylate). To test this possibility, 1,1,2,2-ethylene glycol-d_4 was synthesized and reacted with undeuterated ethylene glycol ditosylate. Mass spectral analysis of the dioxane product revealed parent peaks at 92 (dioxane-d_4) and 96 (dioxane-d_8), and none at 88 (dioxane-d_0). In the course of a reaction, the amount of the acid-catalyzed self-condensation product (dioxane-d_8) formed depended on the extent of conversion and varied between 25–50%.

It thus became necessary to eliminate the formation of the ethylene glycol self-condensation product. Since this undesired reaction apparently was acid-catalyzed, various bases were added to the reaction mixture. With quinoline as the added base, heating produced only a red tar and no volatiles. Evidently, base-catalyzed side reactions took precedence over the desired reaction.

Brown and Kanner[2] have reported that hindered pyridines, such as 2,6-di-*tert*-butylpyridine, act as normal bases toward free protons, but do not act as nucleophiles. Base-catalyzed eliminations would also be expected to be minimal with such a hindered base. When two equivalents of this base were heated with one equivalent each of ethylene glycol and ethylene glycol ditosylate, the yield of 1,4-dioxane went up dramatically to 70%. After removing the volatiles, the 2,6-di-*tert*-butylpyridinium-p-toluenesulfonate salt in the residue was recovered and recrystallized from acetone–carbon tetrachloride. When ethylene glycol-d_4 was substituted for the undeuterated ethylene glycol, mass spectral analysis of 1,4-dioxane product showed only dioxane-d_4 and no dioxane-d_8 or dioxane-d_0. As little as 2 or 3% of these side products could have been detected. When a less hindered base (2,6-lutidine) was used, a lower yield of 1,4-dioxane (20%) was obtained, although deuterium labeling experiments indicated that no or minimal self-condensation reactions had occurred.

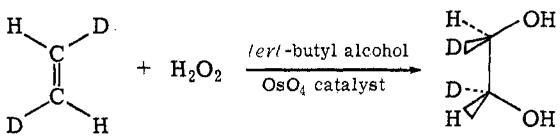
The reaction employing 2,6-di-*tert*-butylpyridine is therefore suitable for the preparation of geometric isomers of 1,4-dioxane. Synthesis of *dl*-1,2-ethylene glycol-d_2 and its ditosylate was accomplished by the following sequence of reactions.

Acetylene-d_2 was reduced to *trans*-1,2-ethylene-d_2 (eq 1) by water–chromium(II) chloride in a trans fashion.[3]



(1)

Cis hydroxylation of *trans*-1,2-ethylene-d_2, using the osmium tetroxide catalyzed hydrogen peroxide–*tert*-butyl alcohol reagent (eq 2) of Milas and Sussman,[4] gave



(2)

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