for the first time, and its structure was proved with the aid of the earlier work on the hypoxanthines.[6] 6-Methoxy-9-β-D-ribofuranosylpurine, (II) the product of *O*-methylation, was also shown to be an important product of the reaction.

EXPERIMENTAL[8,9]

The method of Bredereck and Martini[4] was followed in allowing diazomethane to react with tri-*O*-acetylinosine[10] in solution in methanol and acetone.[5] The product isolated by precipitation with ether, as described, appeared to melt from ~110–120° and could not be crystallized from any of a number of different solvents. Paper chromatography in solvent system A showed two main spots at R_f 0.44 and 0.70 with some quenching material below 0.44.

In order to obtain a partial resolution of the mixture, 1 g. of the reaction product was dissolved in 1-butanol saturated with water and chromatographed on 100 g. of potato starch, using the same solvent for elution. Fractions of approximately 10 ml. were collected and the development of the column was followed by paper chromatography and ultraviolet spectroscopy.

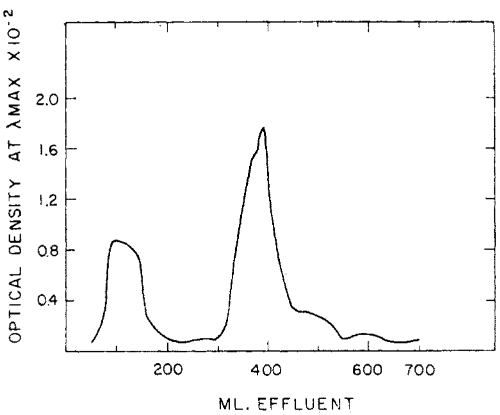

Figure 1

The elution curve is shown in Fig. 1. The first and second large peaks contained primarily the 6-methoxy and 1-methyl compounds, respectively, as demonstrated below. In addition, there was a small amount of material of λ_{max} 257 and R_f 0.55 at ~ 380 ml. of effluent, and, beginning with the trailing edge of the second large peak, material of λ_{max} 261 mμ and λ_{min} 240 mμ was eluted. These other components were not investigated further.

1-Methylinosine. The tubes from 320–460 ml. contained 400 mg. of a material of R_f 0.44. Evaporation yielded a crystalline compound of m.p. 200–205°, and recrystallization for analysis raised this value to 211–212°. The absorption spectrum had a maximum at 251 mμ (ϵ 10,400) and minimum at 227 mμ.

Anal. Calcd. for $C_{11}H_{14}N_4O_5$: C, 46.81; H, 5.00; N, 19.85; OCH_3, 0.00; NCH_3, 5.32. Found: C, 46.89; H, 4.95; N, 19.95; OCH_3, 0.0; NCH_3, 5.52.

As the analytical values showed that a single N—CH_3 group had been introduced, the compound had to be either 1-methyl- or 3-methylinosine. To distinguish between the two possibilities, the crystalline material was heated for 1 hr. at 100° in 5% sulfuric acid and then neutralized with barium hydroxide. The ultraviolet spectra of the hydrolysis product were measured at three *p*H values and compared with the spectra of authentic 1-methyl- and 3-methyl hypoxanthine, reported previously by Elion.

ULTRAVIOLET ABSORPTION MAXIMA (mμ)

*p*H	Acid Hydrolysis Product	1-Methyl-hypoxanthine	3-Methyl-hypoxanthine
7	251	251	264
1	249	249	253
11	260	260	265

Further confirmation of the identity of the purine was provided by a comparison of the R_f values of the hydrolysis product with those of authentic samples of 1-methylhypoxanthine and 3-methylhypoxanthine. Thus, the hydrolysis product and 1-methylhypoxanthine both moved with an R_f of 0.59 in solvent A, whereas 3-methylhypoxanthine had an R_f of 0.46. In system B, and R_f values were 0.30, 0.30, and 0.15, respectively.

It is therefore clear that the hydrolysis product is 1-methylhypoxanthine, not 3-methylhypoxanthine, and hence that the nucleoside is 1-methylinosine.

6-Methoxy-9-β-D-ribofuranosylpurine (II). The tubes from 80 to 190 ml. were pooled and found to contain a single ultraviolet-absorbing material. The R_f value (0.70 in system A) and the ultraviolet maximum (248 mμ) were the same as those of an authentic sample of II.[11] Acid hydrolysis of authentic II and of the present material gave products having the same R_f as hypoxanthine (0.49 in system A; 0.19 in system B). On the basis of the ϵ value reported earlier[11] these tubes contained 190 mg. of the *O*-methyl compound, or about 20% of the total material.

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(8) Microanalyses by Joseph Alicino, Metuchen, N. J.

(9) Solvent A: 1-butanol–water–acetic acid (160:40:75). The R_f values decreased with age of solvent as esterification proceeded; solvent B: butanol saturated with water and exposed to the vapor of 3% aqueous ammonia.

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2,2-Dimethyl-1,3-dioxepane

L. B. WEISFELD AND J. R. LITTLE

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The preparation of higher ketals from 2,2-dimethoxypropane by acid catalyzed interchange has recently been described in detail.[1] In these laboratories, we had attempted to prepare the polymeric ketal by the reaction of equimolar amounts of 1,4-butanediol and acetone dimethyl ketal through similar methods. Instead, the heretofore undescribed cyclic ketal, 2,2-dimethyl-1,3-dioxepane, resulted in about a 75% yield.

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Although cyclic ketals from 1,2- and 1,3-glycols are well known[2] only the unsubstituted and mono-2-substituted dioxepanes have been characterized.[3] These may be easily polymerized in the presence of acid, with a small amount of alcohol or diol to control molecular weights.[4] An attempt to open the ketal dioxepane with 0.025 mole per cent 1,4-butanediol and 0.085 weight per cent *d,l*-camphorsulfonic acid led to only the cracking products, acetone and tetrahydrofuran, in equimolar amounts (87%). Substitution of boron trifluoride etherate for the sulfonic acid caused much faster rearrangement to the same products.

While cyclization to the dioxepane is not remarkable in view of the *gem*-dimethyl substitution,[5] the acid catalyzed rearrangement is noteworthy. This phenomenon, which occurs under relatively mild conditions, is apparently intramolecular since no polytetramethylene oxide was obtained. Mechanistically, it is considered as induced by electron delocalization from one ketal oxygen, yielding a four atom $S_{N}i$ type extrusion process.

EXPERIMENTAL

2,2-Dimethyl-1,3-dioxepane. 2,2-Dimethoxypropane, supplied by the Dow Chemical Co. (98%), was used as received. 1,4-Butanediol was distilled and stored over Linde 4A molecular sieves. Dry 1,4-butanediol (90 g., 1.0 mole) and 104 g. (1.0 mole) of the acetone dimethyl ketal were mixed with 300 ml. of anhydrous benzene. The two phase system became homogeneous upon addition of 0.02 g. of *d,l*-camphorsulfonic acid (Eastman Kodak Co.). The mixture was heated with stirring, and 198 ml. of distillate (mostly b.p. 59°) was collected; the final head temperature reading 80°. The distillate contained approximately the theoretical amount of methanol.

The reaction mixture was neutralized by stirring 3 hr. with 5 g. of sodium bicarbonate, then filtered. The clear benzene solution was distilled, yielding 95.5 g. of a fraction boiling at 136° (yield, 73.5%). A total of 11 g. of residue (nonviscous) was discarded. The clear, pleasant smelling liquid was tentatively assigned the structure of 2,2-dimethyl-1,3-dioxepane; redistillation gave b.p. 136–137° (uncorrected), n_D^{25} 1.4253, d_4^{25} 0.8934.

Anal. Calcd. for $C_7H_{14}O_2$: C, 64.58; H, 10.78; mol. wt., 130.18. Found: C, 64.85; H, 10.95; mol. wt., 131.

Rearrangement of 2,2-dimethyl-1,3-dioxepane: A mixture of 51.73 g. of dimethyldioxepane, 1.186 g. of 1,4-butanediol, and 0.045 g. of *d,l*-camphorsulfonic acid was refluxed for 16 hr., during which time the pot temperature dropped from 137° to 111°. The reaction mixture was then distilled (55–68°), leaving a pot residue (oily) of 6.9 g. (13%). Gas chromatographic analysis showed that the distillate consisted principally of an equimolar mixture of acetone and tetrahydrofuran with about a 20% carry over of unrearranged dimethyldioxepane.

The experiment was repeated, using 3 drops of boron trifluoride etherate to 50 g. of 2,2-dimethyldioxepane, and no butanediol. As the pot temperature approached 125°, violent ebullition occurred and the temperature dropped to 100° within 10 min. After refluxing for 6 hr., the final pot temperature was 85°.

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UNITED STATES RUBBER CO.
WAYNE, N. J.

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Solvolysis of Methylmaleic Anhydrides

OWEN H. WHEELER AND ELSIE E. GRANELL RODRÍGUEZ

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While maleic and methylmaleic (citraconic) acids are known as both their acids and anhydrides, dimethylmaleic acid is only stable as its anhydride.[1] This anhydride usually crystallizes on acidification of solutions of salts of the corresponding acid. This evidence does not necessarily require that the acid cyclizes spontaneously to its anhydride, as if the anhydride were very much less soluble than the acid it would crystallize preferentially. However, Koskikallio[2] has recently prepared dimethylmaleic acid by careful neutralization at 0° of a solution of its sodium salt, and found that the acid was converted into its anhydride at immeasurably high rates in nonaqueous solvents, although at measurable rates in aqueous acetone and methanol. This publication describes a comparative study of the rates of solvolysis of maleic, citraconic and dimethylmaleic anhydrides in aqueous dioxane, to interrelate rate data of these three anhydrides.

The rates of solvolysis (Table I) were determined by measuring the change in conductivity with time.[3] The differences in rate found for maleic and citraconic anhydrides are of the same order as those found in water (11.5 and 7.65×10^{-3} sec.$^{-1}$, respectively.)[3] The rate of hydrolysis of dimethylmaleic anhydride is lower than those of the other two, although the differences are small and consistent with the inductive (−I) effect of the methyl groups which will decrease the positive charge on the carbonyl carbon atom. However whereas the solvolysis was essentially complete in the cases of maleic and citraconic anhydrides, the same final conductance being obtained with solutions of the same molar concentrations of the corresponding acids, the changes in conductance of solutions of dimethylmaleic anhydride were very small (less then 10% of the other two anhydrides). No further change

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