Propellane Type Derivatives of Uric Acid. *X*-Ray Structure of 9-Acetyl-4,5-(1-methoxyethylidenedioxy)-4,5-dihydrouric Acid

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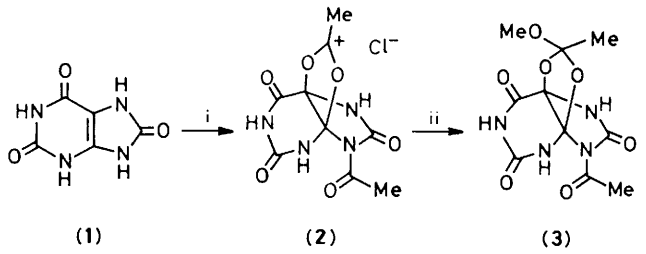
The chlorination of uric acid (**1**) in acetic anhydride yields an acetoxonium chloride (**2**), previously formulated as 5-acetoxy-9-acetyl-4-chloro-4,5-dihydrouric acid, which on methanolysis affords the corresponding cyclic orthoacetate (**3**); new structures were established by chemical, spectroscopic, and *X*-ray methods.

Recent investigations into oxidative transformations of uric acid (**1**) have led to the discovery of new β-cytotoxic compounds which could conceivably play a part in the aetiology of diabetes mellitus.[1-3] In extending the study of preparations, properties, and structures of alloxan-type derivatives of (**1**) we have re-investigated the reaction of (**1**) with chlorine in acetic anhydride (Scheme 1).[4]

Repetition of Biltz's procedure gave an unstable crystalline product $C_9H_9ClN_4O_6$, m.p. (decomp.) 300—302 °C, which was originally assigned the 5-acetoxy-9-acetyl-4-chloro-4,5-dihydrouric acid structure.[4] Our decision in favour of the acetoxonium chloride structure (**2**) was made by consideration of the course of methanolysis. Treatment of (**2**) (3 g) with methanol (15 ml) at room temperature gave (**3**) ($C_{10}H_{12}N_4O_7$, m.p. (decomp.) 222—223 °C, 90%) as the sole product on work-up and crystallization from water [ν_{max} (KBr) 3290, 3200, 3100, 1777, 1735—1690, 1463, 1445, 1370, 1307, 1280, 1242, 1190, 1175, 1151, 1043, 1020, 980, 931, and 896 cm^{-1}; ^1H n.m.r. ($CDCl_3$), δ 11.32 (N-1-H), 10.19 (N-3-H), 8.75 (N-7-H), 3.18 (OMe), 2.39 (COMe), and 1.56 (Me-orthoacetate); ^{13}C n.m.r. ($CDCl_3$), δ 169.0 (N*C*OMe), 162.3 (C-6), 151.3 (C-8), 147.8 (C-2), 123.9 (C-orthoacetate), 97.0 (C-4), 83.3 (C-5), 49.4 (OMe), 24.2 (CO*Me*), and 23.5 p.p.m. (Me-orthoacetate)].†



Scheme 1. *Reagents:* i, Cl_2, Ac_2O; ii, MeOH.

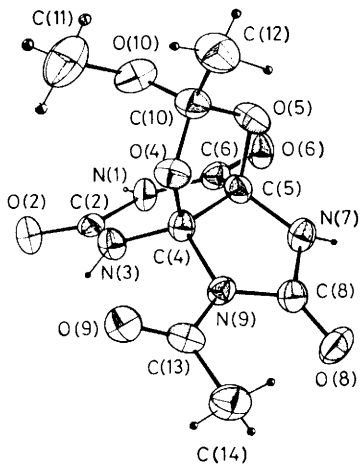


Figure 1. ORTEP view of the molecule (**3**). The nitrogen systems (C_3N_2 and C_4N_2) are planar, and the dioxolan ring (C_3O_2) has an envelope conformation (Δ 34.3°); dihedral angles in the Y-shaped molecule: C_3N_2/C_4N_2 124.5, C_3N_2/C_3O_2 116.7, and C_3O_2/C_4N_2 118.8°. Hydrogen bonds: intramolecular N(3)···O(9) 2.738(5), H(3)···O(9) 2.062(3) Å, N(3)–H(3)···O(9) 131.8(2)°; intermolecular N(1)···O(6) 2.894(4), H(1)···O(6) 1.838(3) Å, N(1)–H(1)···O(6) 168.3(2)° and N(7)···O(2) 2.802(3), H(7)···O(2) 1.856(3) Å, N(7)–H(7)···O(2) 154.5(3)°.

Although (**3**) does not show a molecular ion in the electron-impact spectrum it shows the ion corresponding to $(M - MeO)^+$. Reaction of (**3**) with diazomethane in diethyl ether followed by reductive deacetylation of the resulting trimethyl derivative ($C_{13}H_{18}N_4O_7$, m.p. 112 °C), afforded 1,3,7-trimethyluric acid.[4] These data clearly establish the orthoacetate structure for (**3**) and the position of substitution, leading to the hetero[4.3.3]propellane skeleton shown. The relative configuration of (**3**) was determined by *X*-ray analysis (Figure 1).

Crystal data: $C_{10}H_{12}N_4O_7$, M = 300.23, monoclinic, space group $P2_1/c$, a = 10.738(5), b = 9.000(6), c = 13.023(7) Å, β = 91.54(3)°, U = 1257.29 Å^3, D_c = 1.565 g cm^{-3}, Z = 4, Mo-K_α radiation, λ = 0.7107 Å, μ = 1.46 cm^{-1}. The structure was solved by direct methods[5] and the least-squares refinement gave a final R = 0.043 (R_w = 0.049) (Philips PW 1100 diffractometer, 1116 reflections, 5.5° < 2θ < 58.9°).‡

The structure of (**3**) (Figure 1) is yet another example of a new and unique array reminiscent of the structure of tetrodotoxin.[6]

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References

1 M. Poje and B. Ročić, *Tetrahedron Lett.*, 1979, 4781.
2 M. Poje, E. F. Paulus, and B. Ročić, *J. Org. Chem.*, 1980, **45**, 65.
3 M. Poje and B. Ročić, *Experientia*, 1980, **36**, 78.
4 H. Biltz and H. Pardon, *J. Prakt. Chem.*, 1934, **140**, 209.
5 G. Germain, P. Main, and M. M. Woolfson, *Acta Crystallogr., Sect. A.*, 1971, **27**, 368.
6 R. B. Woodward, *Pure Appl. Chem.*, 1964, **9**, 49.

† There is also some evidence for the formation of the epimeric orthoester (signals at δ_c 124.3, 50.4, and 22.1 p.p.m.) when the reaction is carried out at 0 °C. Reaction of (**2**) with hot methanol (50—60 °C) gave 5-methoxy-5-ureido-(1*H*,3*H*,5*H*)-pyrimidine-2,4,6-trione, in agreement with earlier findings.[4]

‡ The atomic co-ordinates for this work are available from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Rd., Cambridge, CB2 1EW. Any request should be accompanied by the full literature citation for this communication. The structure factor table is available as Supplementary Publication No. SUP 23515 (10 pp) from the British Library Lending Division. For details of how to obtain this material, see Notice to Authors No. 7, *J. Chem. Soc., Dalton* or *Perkin Trans.*, Index Issues.