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Ozonolysis of Uracils in Water

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The ozonolysis of uracils unsubstituted at the 1-position gave new 1-acyl-5-hydroxyhydantoins and 5-hydroxyhydantoins in water, while that of 1-substituted uracils gave the corresponding 5-hydroxyhydantoins in low yields. The structure of 1-acetyl-5-hydroxy-5-methylhydantoin was determined by X-ray crystallography.

The study on the ozonization reaction of cellular substances is one of the most important subjects in ozone chemistry. Though the reaction of DNA and RNA with ozone (O_3) is of interest in connection with the damage of biological systems, the reaction has received only limited attention.[1,2] With pyrimidine nucleotides, O_3 preferentially attacks the base moieties.[3] This report clarifies the reaction of uracils with O_3.

In a general procedure, uracil (1a) (2 mmol) was ozonized with an O_3-O_2 mixture (O_3: 0.22 mmol min^{-1}, O_2: 200 ml min^{-1}) in water (100 ml) at 37 °C. After the reaction, the products were chromatographed on preparative TLC (SiO_2, EtOAc: Me_2CHOH:H_2O=75:16:9). In all cases, the unidentified products were detected on the original spot in TLC. The products, 1-acyl-5-hydroxyhydantoins, gave pertinent spectral data with the structures.[4,5] In order to determine the structure of new 1-acyl-5-hydroxyhydantoins definitely, X-ray crystallography of 1-acetyl-5-hydroxy-5-methylhydantoin (2d) recrystallized from EtOAc was carried out.[6] The result is shown in Fig. 1. The reactions of uracils with O_3 are summarized in Table 1. The reaction of uracil (1a) in water gave 1-formyl-5-hydroxyhydantoin (2a) and 5-hydroxyhydantoin (3a) in 32 and 31% yields, respectively. While that of 1a

Table 1. Reaction of Uracils with Ozone

Run	Substrate	Substituent				Time	Yield / %[a)]	
		R^1	R^2	R^3	R^4	min	2	3
1	1a	H	H	H	H	120	32	31
2	1a	H	H	H	H	20[b)]	29	0
3	1b	H	H	Me	H	90	23	27
4	1c	H	H	H	Me	120	34	18
5	1d	H	H	Me	Me	120	27	26
6	1e	H	Me	H	H	120	44	9
7	1f	Me	H	H	H	120	0	14[c)]
8	1g	Me	Me	H	H	120	0	21[d)]

a) determined by HPLC (SS-10, EtOAc: Me_2CHOH:H_2=75:16:9. b) in AcOH. c) N-Methylparabanic acid was also obtained in a 3% yield. d) N,N-Dimethylparabanic acid was also obtained in a 21% yield.

in acetic acid preferentially gave 2a in a 29% yield. The reaction of uracils 1b-e also gave both the corresponding 1-acyl-5-hydroxyhydantoins 2 and 5-hydroxyhydantoins 3. With 1-methyluracils 1f,g, the reaction gave 5-hydroxhydantoins 3f,g in low yields accompanied by the formation of parabanic acids. A mechanism is proposed in Scheme 1.

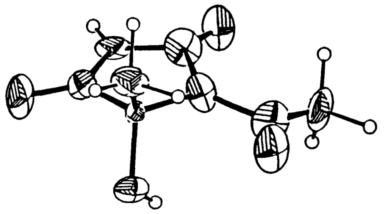
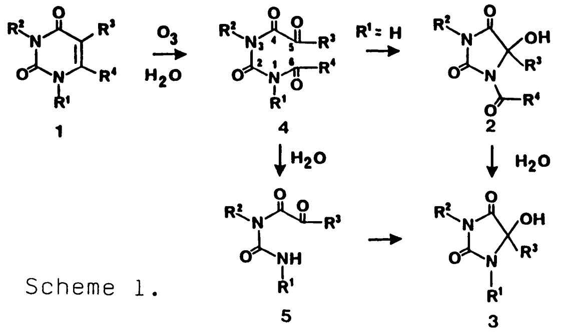


Fig. 1. ORTEP view of 2d.



Scheme 1.

References

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2) K. J. Kolonko, R. H. Shapiro, R. M. Barkley, and R. E. Sievers, J. Org. Chem., 44, 3769 (1979).

3) K. Ishizaki, N. Shinriki, A. Ikehata, and T. Ueda, Chem. Pharm. Bull., 29, 868 (1981).

4) 2a: mp 153-155 °C; ^{1}H NMR δ_H 5.47 (d, J=8 Hz, 1H), 7.56 (d, J=8 Hz, 1H), 8.95 (s, 1H), and 11.70 (br.s, 1H); ^{13}C NMR δ_C 75.8 (d), 154.2 (s), 158.9 (d), and 171.1 (s); MS (70 eV) m/z 144 (M^+); Found m/z 144.0175. Calcd for $C_4H_4N_2O_4$: M, 144.0171. 2b: mp 182-184 °C; ^{1}H NMR δ_H 1.67 (s, 3H), 7.30 (s, 1H), 8.94 (s, 1H), and 11.80 (br.s, 1H); ^{13}C NMR δ_C 20.4 (q), 84.4 (s), 153.8 (s), 158.7 (d), and 173.1 (s); MS (70 eV) m/z 158 (M^+); Found m/z 158.0343. Calcd for $C_5H_6N_2O_4$: M, 158.0328. 2c : mp 139-143 °C; ^{1}H NMR δ_H 2.62 (s, 3H), 5.61 (d, J=8 Hz, 1H), 7.53 (d, J=8 Hz, 1H), and 11.65 (br.s, 1H); ^{13}C NMR δ_C 24.7 (q), 77.5 (d), 153.4 (s), 168.7 (s), and 170.2 (s); MS (70 eV) m/z 158 (M^+); Found m/z 158.0298. Calcd for $C_5H_6N_2O_4$: M, 158.0328. 2d; mp 179-182 °C; ^{1}H NMR δ_H 1.68 (s, 3H), 2.39 (s, 3H), 7.18 (s, 1H), and 11.63 (br.s, 1H); ^{13}C NMR (acetone-d_6) δ_C 22.2 (q), 26.2 (q), 87.6 (s), 153.5 (s), 170.2 (s), and 172.3 (s); MS (70 eV) m/z 172 (M^+); Found m/z 172.0478. Calcd for $C_6H_8N_2O_4$: M, 172.0484. 2e: mp 142-146 °C; ^{1}H NMR δ_H 2.92 (s, 3H), 5.54 (s, 1H), 7.60 (br.s, 1H), and 9.01 (s, 1H); ^{13}C NMR δ_C 24.4 (q), 75.2 (d), 158.9 (d), 159.4 (s), and 169.8 (s); MS (70 eV) m/z 158 (M^+); Found m/z 158.0301. Calcd for $C_5H_6N_2O_4$: M, 158.0328. All the NMR spectra were measured in DMSO-d_6 solutions, otherwise stated.

5) E. B. Henson, P. M. Gallop, and P. V. Hauschka, Tetrahedron, 37, 2561 (1981).

6) Crystal data for 2d: $C_6H_8N_2O_4$, triclinic, a=8.425 (9), b=12.042 (9), c=8.419 (4) Å, space group P_1, α=106.52 (5)°, β=96.72 (7)°, γ=106.61 (7)°, Z=4, 2079 unique reflections, D_c=1.49 g cm^{-1}. Intensities were measured on a Rigaku AFC-5 diffractmeter with Mo-K_α radiation. The structure was solved by direct method (MULTAN 78) and refined by block diagonal least-squares calculations to R=0.088.

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