The Non-catalytic Fusion Reaction of Acylated Sugars with Some Purines and Phenols[1]

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The authors wish to report on a new type of non-catalytic fusion of ordinary acylated sugars with some purines and phenols.

Helferich and Gootz[2] have reported that 1-*O*-trichloroacetyl-2, 3, 4, 6-tetra-*O*-acetyl-β-D-glucopyranose (I) is reactive enough in the non-catalytic fusion reaction with phenol to give phenyl 2′, 3′, 4′, 6′-tetra-*O*-acetyl-β-D-glucopyranoside.

When 2, 6-dichloropurine (II)[3] and theophylline (III) are applied to the reaction, only II gave 2, 6-dichloro-9-(2′, 3′, 4′, 6′-tetra-*O*-acetyl-β-D-glucopyranosyl)-purine (in a 57% yield) under the same conditions.[4] Moreover, II gave the corresponding 2′, 3′, 5′-tri-*O*-acetyl-β-D-ribofuranoside in a good yield[5] by the reaction with 1, 2, 3, 5-tetra-*O*-acetyl-β-D-ribofuranose (IV) in the presence of any catalyst, even though the reaction period was very short.[4]

These facts suggest that the non-catalytic reaction might be caused not only by the activation on the $C_{(1)}$-*O*-acyl group, as in the case of I, but also by that of the acidic hydrogen which is attached to the reaction center of such purines as II, as a result of the polar effect of the electron-withdrawing substituents, and that, therefore, the reactivity of purine derivatives can not simply be ascribed to their fusibility[1b] in the reaction with acylated sugars, as has been reported before.

6-Chloro-(V),[6] 6-iodo-,[6] 6-cyano-,[6] II, 2(6)-chloro-6(2)-iodo-,[6] and 2, 6, 8-trichloro-purine,[7] by non-catalytic fusion reaction with IV at 150—155°C in vacuo, gave the corresponding ribonucleosides in yields of 10,[8] 12,[8] 21,[9] 50,[10] 67,[10] and 64%[10] respectively. On the other hand, 6-methoxypurine[11] gave no corresponding product by the same reaction. In these cases, the fusibility of purine derivatives and their thermostability seem also to exert a considerable effect.

p-Nitrophenol, whose p*K*a value is almost the same as that of V,[12] also gave *p*-nitrophenyl 2′, 3′, 4′, 6′-tetra-*O*-acetyl-β-D-glucopyranoside[14] (in a 65% yield) by reaction with 1, 2, 3, 4, 6-penta-*O*-acetyl-β-D-glucopyranose at 175—195°C in vacuo. Similarly, IV gave two kinds of *p*-nitrophenyl tri-*O*-acetyl-D-ribofuranosides: *m*-Nitophenol gave *m*-nitrophenyl 2′, 3′, 4′, 6′-tetra-*O*-acetyl-β-D-glucopyranoside (m. p. 138—139.5°C, $[\alpha]_{578}^{27}$ −38.1°, $[\alpha]_{546}^{27}$ −40.1° in chloroform) in 47% yield, but neither *o*-nitro- nor 2, 4-dinitrophenol gave a corresponding product.

In view of these facts, the interpretation[15] of the polar effects of substituents on the reaction center requires further study. The fusion reaction of deoxy- and unsaturated-sugar derivatives with these purines and phenols is also under investigation.

A kinetic study of this reaction has been carried out by means of ultraviolet absorption spectroscopy; it has been found that the reaction of II with IV is of the second order. Detailed results will be published in the near future.

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1) A portion of this paper was presented at 18th Annual Meeting of the Chemical Society of Japan, Osaka, April, 1965. Previous papers: a) Y. Ishido, A. Hosono, S. Isome, A. Maruyama and T. Sato, This Bulletin, **37**, 1389 (1964); b) Y. Ishido, Y. Kikuchi and T. Sato, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zasshi*), **86**, 240 (1965).

2) B. Helferich and R. Gootz. *Ber.*, **62**, 2788 (1929).

3) J. A. Montgomery, *J. Am. Chem. Soc.*, **78**, 1928 (1956).

4) Y. Ishido, Doctoral Thesis, Tokyo Institute of Technology, Japan, March, 1963.

5) The yields range approximately from 50—80% of the theoretical yields.

6) G. B. Elion and G. H. Hitchings, *J. Am. Chem. Soc.*, **78**, 3508 (1956).

7) J. Davoll and B. A. Lowy, ibid., **73**, 2936 (1951).

8) Both products were isolated as adenosine by treating the acetylated products with methanolic ammonia (saturated at 0°C) in a sealed tube at 100°C.

9) The product was isolated as an equimolar adduct of ammonia by the deacetylation with methanolic ammonia mentioned above; m. p. 210—213°C.

10) These products were isolated as 2′, 3′, 5′-tri-*O*-acetate.

11) G. B. Brown and U. S. Welikey, *J. Biol. Chem.*, **204**, 1019 (1953).

12) A. Bendich, P. J. Russel, Jr., and J. J. Fox, *J. Am. Chem. Soc.*, **76**, 6073 (1954).

13) E. Glaser and W. Wulwek, *Biochem. Z.*, **145**, 514 (1934).

14) Y. Ishido, T. Matsuba, and T. Sato, *The Abstract of 17th Annual Meeting of the Chemical Society of Japan*, 253; (1964) quoted in Ref. 1b.