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Experimental and Theoretical (AM1) Studies on Photoaddition Reactions of 3-Nitro-2-enopyranoside Derivatives

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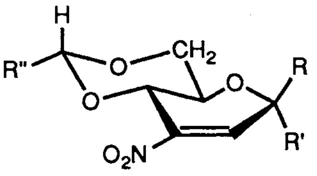
Irradiation of 3-nitro-α- and β-D-*erythro*-hex-2-enopyranoside derivatives in methanol, ethanol, and isopropanol with high pressure Hg lamp gave the adducts in moderate yields. The stereoselectivities calculated by AM1 calculation by the use of model compounds with 1,3-dioxolan-2-yl radical are not conflict with those observed in similar photoreaction in 1,3-dioxolane as well as the present results .

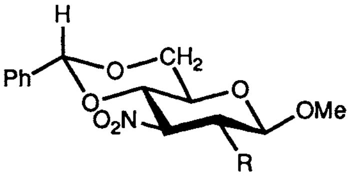
Although nucleophilic addition reactions to 2-enopyranoside derivatives having such an electron-withdrawing group as a nitro function are extensively studied,[1)] the corresponding radical reactions are limited. Recently we have performed the photoaddition reactions of 3-nitro-2-enopyranoside derivatives in 1,3-dioxolane.[2,3)]

In this communication[4)] we report the results of photoaddition reactions of methyl 3-nitro-β- **1** and α-D-*erythro*-hex-2-enopyrnoside derivatives **2** in methanol, ethanol, and isopropanol and those of semiempirical (AM1 method[5)]) molecular orbital calculation.

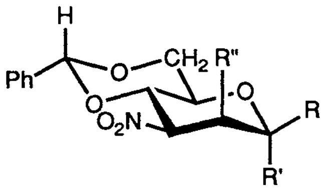
When compound **1**[6)](500 mg) was irradiated in methanol (200 mL) by high pressure Hg lamp in the presence of small amount of benzophenone (50 mg, added as a sensitizer) at 8 °C for 2.5 h, almost equal amounts of the *gluco* **5** {mp 167-168°, $[\alpha]^{25}_D$ -21° (*c*, 0.5, $CHCl_3$)} and *manno* products **10** {mp 135.5-136.0°, $[\alpha]^{25}_D$ -72° (*c*, 1.0, $CHCl_3$)} were obtained in 64% yield, together with the 2-*O*-methyl derivative[7)] **8** (5%). Similar photoreaction of **1** in ethanol afforded the *gluco* isomers **6** (55%), a 1 : 1 mixture due to the chiral carbon atom at 1-hydroxyethyl moiety, together with the oxime[8)] **15** (4%). Oxidation of the crude alcohols **6** with pyridinium chlorochromate (PCC) gave almost quantitatively the 2-*C*-acetyl derivative **9** {mp 156-157°, $[\alpha]^{25}_D$ -79° (*c*, 0.5, $CHCl_3$)} with the *gluco* configuration. Similar photoreaction in 2-propanol provided the β-D-*gluco* product **7** (33%) {mp 130-131° $[\alpha]^{25}_D$ -91° (*c*, 1.0, $CHCl_3$)} and the oxime **15** (30%). A similar photoaddition reactions of **2**[9)] in methanol afforded the α-D-*manno* products **11** (68%) {mp 117-119°, $[\alpha]^{25}_D$ +36° (*c*, 0.3, $CHCl_3$)}. In contrast with the case of the β-anomer **1**, no evidence for formation of the *gluco* product was obtained in the case of the α-anomer **2**. Similar photoaddition reaction in ethanol and isopropanol gave the *manno* products **12** (ca. 1 : 1 mixture owing to the chiral center generated) and **13**[10)] (ca.25%), respectively, together with the oxime[8)] **16** (20%) in the latter reaction. The *manno* configurations for **12** are again confirmed by its conversion into the 2-*C*-acetyl derivative **14** (37% yield from **2**) {mp 233-234.5°, $[\alpha]^{25}_D$ +32° (*c*, 0.5, $CHCl_3$)} by oxidation with PCC. The *manno* configuration for **13** was supported by transformation into **17** {mp 167-169, $[\alpha]^{25}{}_D$ -109° (*c*, 0.6, $CHCl_3$)} by treatment with acetic anhydride, triethylamine, and dimethylaminopyridine.



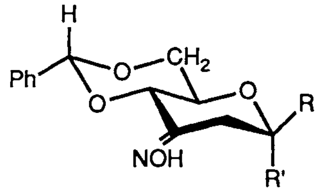
1 R = OMe, R' = H, R" = C_6H_5
2 R = H, R' = OMe, R" = C_6H_5
3 R = OH, R' = R" = H
4 R = R" = H, R' = OH



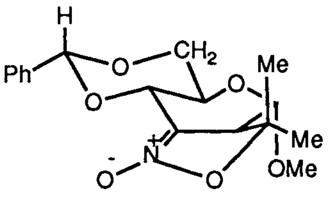
5 R = CH_2OH
6 R = CHMeOH
7 R = CMe_2OH
8 R = OMe
9 R = COMe



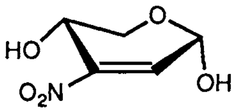
10 R = OMe, R' = H, R" = CH_2OH
11 R = H, R' = OMe, R" = CH_2OH
12 R = H, R' = OMe, R" = CHMeOH
13 R = H, R' = OMe, R" = CMe_2OH
14 R = H, R' = OMe, R" = COMe



15 R = OMe, R' = H
16 R = H, R' = OMe



17



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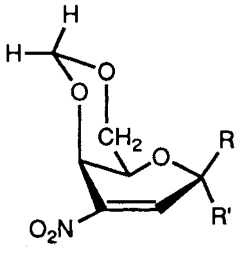

19 R = OH, R' = H
20 R = H, R' = OH

To our best knowledge, there is no example to apply molecular orbital calculation in photoaddition reactions to unsaturated sugars. Then we have performed AM1 method whether or not the stereoselectivities could be reproduced or not. 1,3-Dioxolan-2-yl radical chosen as a radical reagent, because we had already performed the photoaddition reactions in 1,3-dioxolane using *all possible four isomers* as methyl 4,6-O-benzylidene-3-C-nitro-D-hex-2-enopyranoside derivatives.

As an equatorial attack, an optimized 1,3-dioxolan-2-yl radical was put on just below the C-2 of an optimized **18**, used as a model compound for **2**. The distance was fixed at 2.0 Å and others were full optimized.11) This model was, however, found not to be suitable. The optimized structure calculated has a $^{O,3}B$-like conformation, derived by the movement of C-2, C-3, and C-4 atoms, in which both the hydroxyl groups occupy the axial positions. This conformation should be favorable, because of anomeric effect,12) but in the 4,6-*O*-benzylidene derivative such a movement gives rise to a strain to the dioxane ring. Therefore, 4,6-*O*-methylene derivative **4** was used as a model compound. The optimized structure by equatorial attack has expectedly a $B_{2,5}$-like conformation, generated by the movement of C-1, C-2, and C-3. The axial attack is more favorable than the equatorial one by 9.2 J/mol at 2.0 Å, as judged from heat of formation. The distance between C-2 of the 1,3-dioxolan-2-yl radical and C-2 of the sugar moiety makes a reaction coordinate (r) and others (except the dihedral angle of the hydrogen atom of the anomeric hydroxyl group13)) were optimized. As shown in Figure 1, the calculation revealed that the axial attack is always more favorable than the equatorial attack. Similar calculations of 3-nitro-β-D-*erythro*- (**3**), -β-D-*threo*- (**19**), and -α–D-*threo*-hex-2-enopyranoside derivatives (**20**) could also qualitatively reproduce the experimental results as shown in Fig. 1.

It is noteworthy that in the case of β-D-*erythro* derivative **3**(Fig.1,b)), the lines crossed at around 2.4 Å, suggesting that if the distance becomes long in a transition state, the amount of the β-D-*manno* product should be increased. If one assumes that the more reactive radical, the longer the reaction distance (r) in a transition state on the basis of Hammond's postulate, the present results observed in the β-anomer **1** is acceptable, because the reactivity of radicals increases through the sequence of $Me_2\dot{C}OH < Me\dot{C}HOH < \dot{C}H_2OH$. The results observed

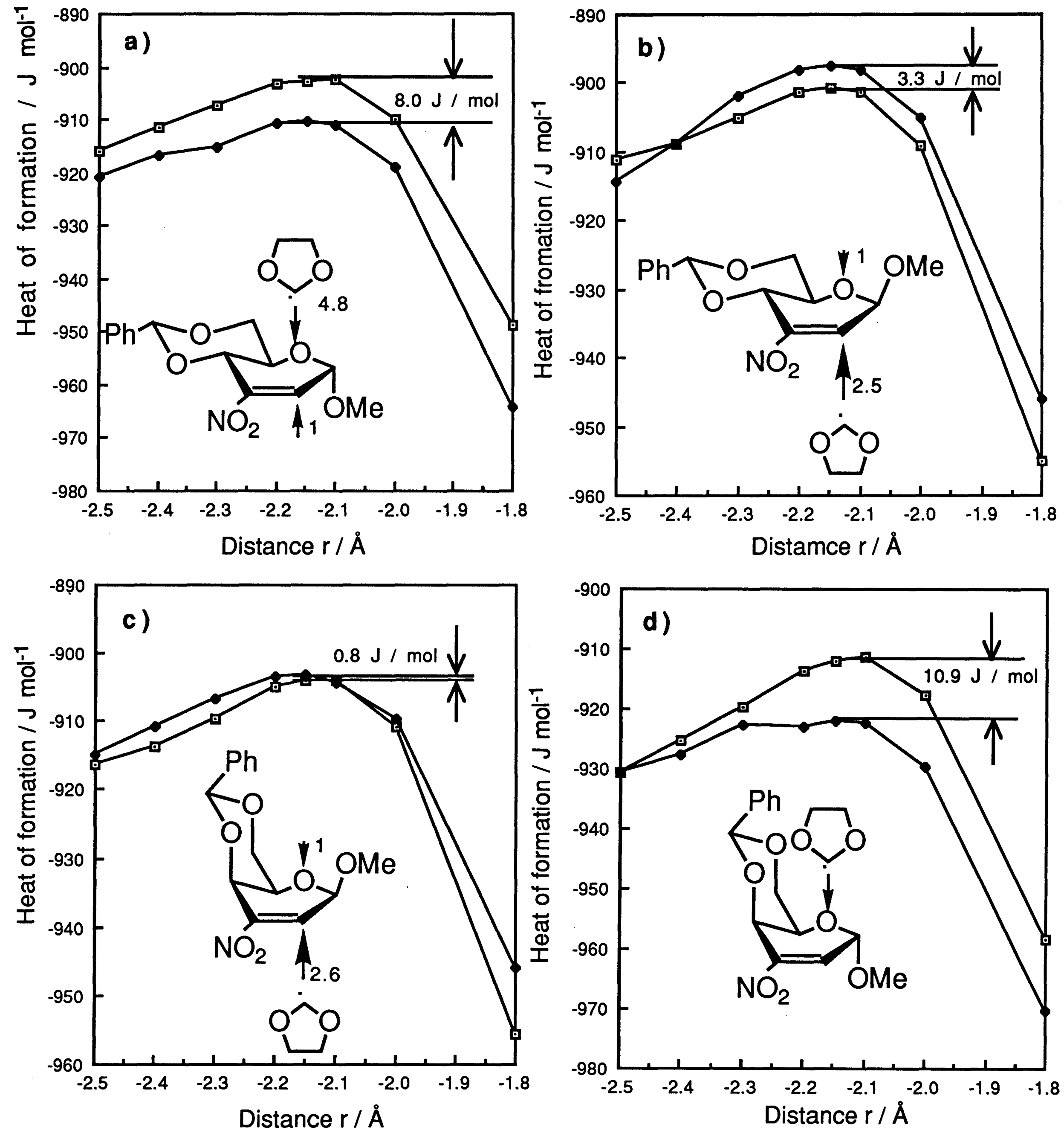

Fig.1. Heat of formation vs reaction coordinate (r) calculated by AM1 method in the approach of 1,3-dioxolan-2-yl radical to the model compounds **3** (b), **4** (a), **19** (c), and **20** (d). Stereoselectivities observed by experiments are also shown and-□-and-◆-indicate the equatorial and axial attacks, respectively.

in the α-anomer **2**, in which radicals always added from the axial side of **2**, is again good agreement with the calculation.

The present work should be one of examples illustrating the versatility of semiempirical molecular orbital calculation in carbohydrate realm.

Molecular orbital calculation was performed with a FACOM M-360AP computer center at the Education Center for Information Processing of Yokohama City University, and we thank its staff for their kind help for the calculations.

References

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3) T. Sakakibara, A. Takaide, and A. Seta, submitted for publication in Carbohydr. Res..
4) Part of the work was presented in Ist Keisan Kagaku Symposium, Tokyo, May, 1991.
5) Quantum Chemistry Program Exchange, # 464 (MOPAC, Ver. 3.0), Chemistry Department, Indiana University, Bloomington, Indiana.
6) H. H. Baer and T. Neilson, Can. J. Chem., **43**, 840 (1965).
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10) Although complete purification of **17** was under progress.
11) Molecular orbital calculation was performed with a FACOM M-360AP computer at the Education Center for Information Precessing of Yokohama City University.
12) For example, A. J. Kirby, " The Anomeric Effect and Related Stereoelectronic Effects at Oxygen," Springer-Verlag, Berlin, 1983.
13) In order to avoid potential hydrogen bonding the dihedral angle of H-O - C-1-C-2 is fixed to -170° for these model compounds. These values were derived by calculation (STO-3G, full optimization) of the corresponding 2,3-dideoxy-3-*C*-nitro-pent-2-enopyranoses; T. Sakakibara and T. Nishitani, unpublished data.

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