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PREPARATION OF THE THERMODYNAMICALLY LESS STABLE ALTROPYRANOSIDE FROM A NITRO-SUGAR WITH ACETYLACETONE

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The Michael reaction of the 3-nitro-2-enopyranoside **1** with ethyl malonate in THF or with acetone in the presence of small amounts of NaOH gave the mannopyranoside **2** or **3**, respectively, whereas the similar reaction with acetylacetone afforded a mixture of the mannopyranoside **4** and the altropyranoside **5**.

Our recent findings[1)] that phase transfer catalyzed heterogeneous reactions of **1** with active methylene compounds give the thermodynamically less stable mannopyranosides prompted us to carry out similar reactions in a homogeneous system. We wish to report the preparation of the altropyranoside **5** from **1** with acetylacetone; this is the first example where not only the nucleophilic addition but also subsequent protonation was controlled kinetically in the Michael reaction of nitroolefin derivatives.

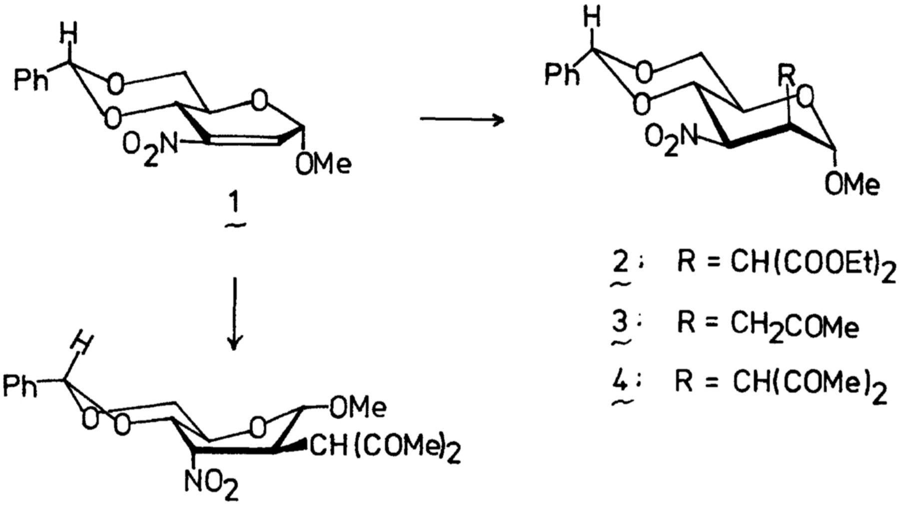
Treatment of **1**[2)] (0.1 mmol) with ethyl malonate (0.15 mmol) in THF (2 ml) in the presence of 0.05N-NaOH (0.2 ml) or 5.0N-NaOH (0.2 ml) at room temperature for 1 h resulted in the recovery of **1** or afforded many products, from which isolation of **2** was failed, respectively. However, similar reaction with 1.0N-NaOH (0.2 ml) exclusively yielded methyl 4,6-*O*-benzylidene-2-*C*-bis(ethoxycarbonyl)methyl-2,3-dideoxy-3-nitro-α-*D*-mannopyranoside (**2**) ; this result is the same as the phase transfer catalyzed reaction.[1)]

Though in the heterogeneous system the reaction of **1** with acetone resulted in the introduction of a hydroxyl group instead of an acetonyl group at the C-2 position, homogeneous reaction of **1** with acetone smoothly proceeded to give the desired mannopyranoside **3** in a high yield.

Similar treatment of **1** (0.1 mmol) in THF (2 ml) with acetylacetone (0.2 mmol) in the presence of 0.2N-NaOH (0.1 ml) afforded a new compound **5** [mp 163-164°C, $[\alpha]_D^{20}$ + 26.8° (*c*1, Me_2CO)] besides the expected mannopyranoside **4**[1)] in a ratio of 3 : 1. When this reaction was stopped after 10 min, **5** was isolated in 82 % yield (quantitatively on tlc and by NMR spectroscopy). The reaction was monitored by NMR spectroscopy ; the ratio of **4** to **5** increased along with reaction time as 0.3 (1 h), 0.5 (2 h), 1.0 (4 h), and finally only **4** was detected (1 day). The *manno* isomer **4** did not epimerize to the *altro* isomer **5** under the above conditions. These results suggest that **5** is a thermodynamically less stable epimer of **4**, namely, the altropyranoside. Generally nucleophilic addition reaction to nitroolefin in a six-membered ring system afforded only the products with the equatorial nitro group because of strong tendency of the nitro group to occupy the equatorial orientation.$^{3)}$ The *altro* structure for **5** was supported by NMR data, of which assignment was carried out with the help of INDOR method and confirmed in comparision with the spectrum of 3-deuterated derivative of **5** ; i) $J_{1,2}$=10.5 Hz indicates the diaxial relationship between H-1 and H-2, ii) $J_{2,3}$=2.5 and $J_{3,4}$=4.5 Hz suggest the equatorial orientation of H-3, iii) $J_{4,5}$=10.0, $J_{5,6e}$=5.0, and $J_{5,6a}$=10.0 Hz show the benzylidene acetal ring having normal chair conformation. An acceptable structure for these values is limitted to the *altro* configuration with a slightly twisted boat form. The structure of **5** is very interesting because, to our knowledge, there are few examples$^{4)}$ that transfusion of a benzylidene acetal ring at the C-4 and C-6 position of a hexopyranose system adopts the boat form.$^{5)}$

It is particularly noteworthy that as seen from NMR spectrum the more stable *manno* isomer **4** epimerized partially to the less stable *altro* isomer **5**, when **4** was treated with 0.2N-NaOH in DMSO-d_6, but not at all in THF.

More detail of such solvent effects and application of this system to other acive methylene compounds are on progress.



1

2; R = CH(COOEt)$_2$

3; R = CH$_2$COMe

4; R = CH(COMe)$_2$

5

References and Note

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