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SYNTHESIS AND REACTIVITY OF NITRO SUGAR-DERIVED SILYL NITRONATES

Olivier R. Martin*, Faiza E. Khamis, and S. Prahlada Rao

Department of Chemistry, S.U.N.Y.-University Center,
Binghamton, New York 13901, U.S.A.

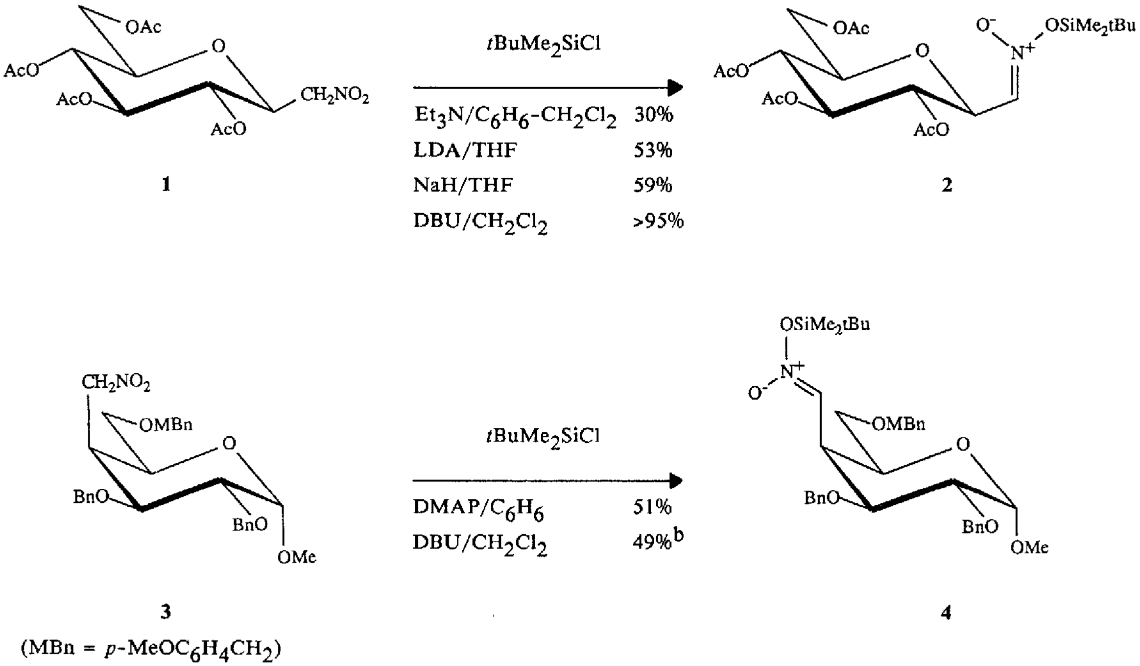
Abstract: Silyl nitronates are readily generated from carbohydrates containing a nitromethyl group; these nitronates participate in F^--catalyzed nitroaldol reactions with aldehydes provided that the nucleophilic carbon atom is sufficiently remote from the cyclic carbohydrate moiety.

As we have shown in the preceding communication,[1] silyl nitronates derived from simple nitro compounds react very effectively with *aldehydo*-sugars under the conditions described by Seebach *et al.*[2] to provide the corresponding chain-extended nitro sugars in high yield. Our intention was to utilize this methodology in the key step of a synthetic approach to *C*-disaccharides, namely for the attachment of two carbohydrate units by way of a carbon-carbon bond and, therefore, we also investigated the formation and reactivity of silyl nitronates derived from sugars containing a primary nitro group. We describe, in this communication, the first examples of such silyl nitronates, their behavior in fluoride-ion catalyzed nitroaldol reactions, and their oxidative cleavage to *aldehydo*-sugars.

Compound **1**, readily available from D-glucose in two steps,[3] constitutes a key building block for the synthesis of *C*-disaccharidic structures; a major advantage of this compound is the fact that it can act as a carbohydrate *C*-nucleophile without concurrent β-elimination. Several bases were examined for the deprotonation of **1** and the silylation of the corresponding nitronate (Scheme I); an essentially quantitative reaction was achieved using DBU in CH_2Cl_2, conditions recently described by Palomo *et al.*[4] Although the highly moisture-sensitive silyl nitronate **2** cannot be purified by conventional methods, its formation is clearly demonstrated by ^1H-NMR spectroscopy and, in particular, by the appearance of a characteristic doublet at low field (δ = 6.15) for the nitronate proton. The *t*-butyldimethylsilyl group was chosen because of the greater stability of *t*-butyldimethylsilyl nitronic esters *vs.* the corresponding trimethylsilyl esters.[2] Similarly, the *t*-butyldimethylsilyl nitronate **4** was prepared from the branched-chain sugar **3**,[5] a potential precursor of 1,4-linked pseudodisaccharides (Scheme I).

Silyl nitronates **2** and **4** were then reacted with a variety of aldehydes in the presence of a catalytic amount of fluoride ion;[2] however, these reactions did not afford more than traces of the expected nitroaldols. The low reactivity of these silyl nitronates can be attributed to steric hindrance at the nucleophilic carbon which is linked to a secondary position in both cases. The importance of steric effects was further supported by the behavior of sugar-derived silyl nitronates in which the reactive site is more remote from the cyclic carbohydrate moiety: silyl nitronates **6a** and **6b**, prepared from terminal nitro

SCHEME I[a]



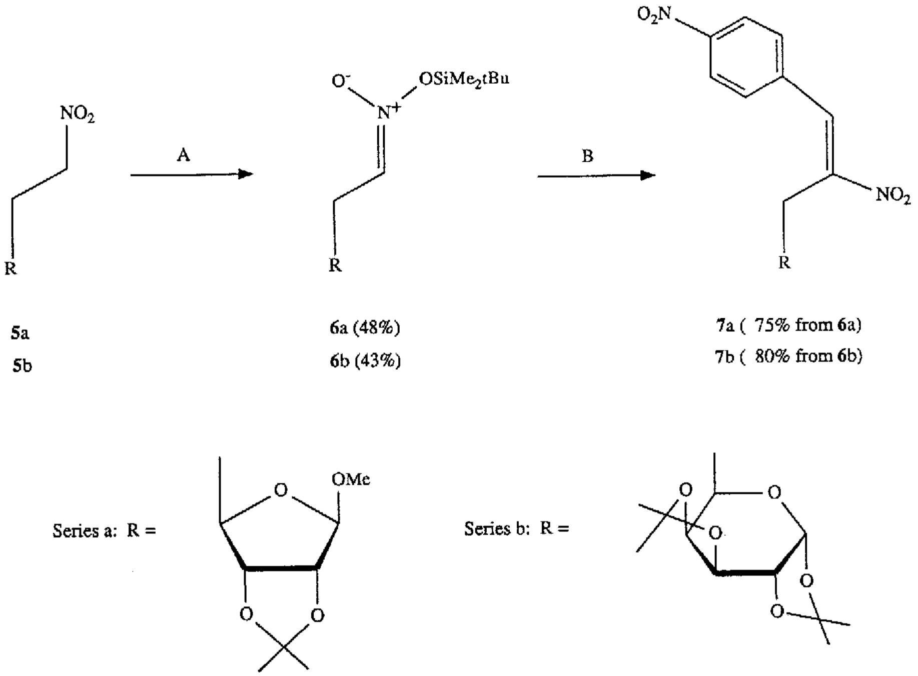
[a] Percent conversion of starting material to silyl nitronate, determined by ^{1}H-NMR immediately after processing (removal of the salts by filtration and of the solvent by evaporation *in vacuo*). In all cases one equivalent of base and a slight excess of silylating agent were used.

[b] Silyl nitronate **4** undergoes a further, yet undetermined, reaction under these conditions.

sugars **5a**[8] and **5b**[8] by the method of Torssell,[9] were found, indeed, to condense effectively with, for example, *p*-nitrobenzaldehyde (Scheme II). The corresponding nitroaldols were dehydrated and characterized as nitroalkenes **7a** and **7b**[10] (*E*-isomers only).

Thus, silyl nitronates derived from sugars bearing a *C*-nitromethyl branch appear to be unsuitable for fluoride-ion catalyzed nitroaldol reactions. These nitronates, however, were found to be readily converted into the corresponding *aldehydes* by ozonolysis at low temperature, a procedure that provides a very convenient and mild alternative to the Nef reaction.[11] For example, the extremely sensitive 2,6-anhydro-*aldehydo*-heptose derivative **8** was generated and reacted immediately after processing with the

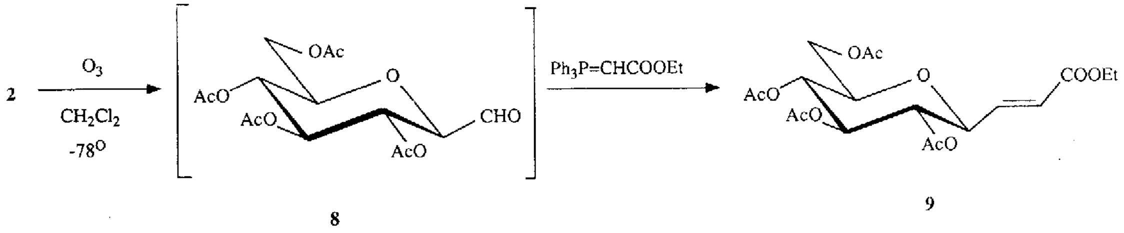
SCHEME II



Conditions: A: tBuMe$_2$SiCl, Et$_3$N/C$_6$H$_6$

B: (i) p-O$_2$NC$_6$H$_4$CHO, nBu$_4$NF(cat); aqueous processing; (ii) Ac$_2$O, DMAP/Et$_2$O

appropriate Wittig reagent to give the unsaturated nononate **9** (m.p. 112 - 113°) in essentially quantitative yield from **1**. This is a particularly remarkable result since three steps are involved in the conversion of **1** to **9**! This new procedure should prove very useful for the synthesis of both branched-chain and chain-extended sugars. Furthermore, silyl nitronates derived from C-glycosyl nitromethanes such as compound **1** should constitute convenient starting materials for the synthesis of C-nucleosides by way of a cycloaddition process.



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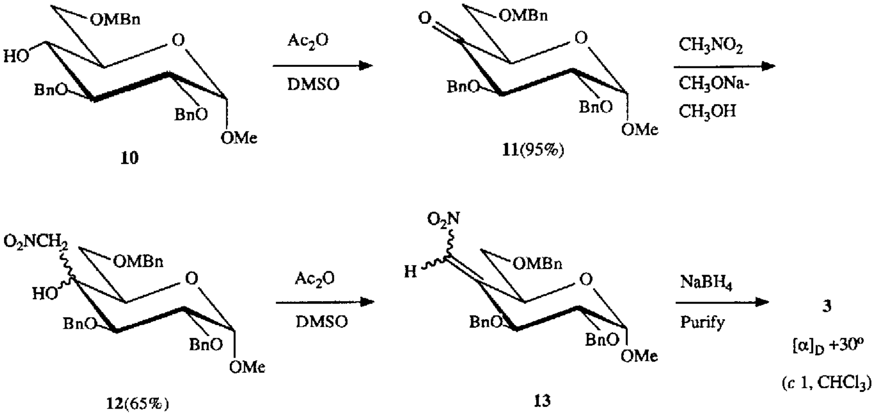
2. E. W. Colvin, A. K. Beck, and D. Seebach, *Helv. Chim. Acta* **1981**, *64*, 2264; D. Seebach, A. K. Beck, T. Mukhopadhyay, and E. Thomas, *Helv. Chim. Acta* **1982**, *65*, 1101.
3. L. Petrus, S. Bystricky, T. Sticzay, and V. Bilik, *Chem. Zvesti.* **1982**, *36*, 103; A. Förtsch, H. Kogelberg, and P. Köll, *Carbohydr. Res.* **1987**, *164*, 391.
4. J. M. Aizpurua, M. Oiarbide, and C. Palomo, *Tetrahedron Lett.* **1987**, *28*, 5361.
5. Compound **3** was prepared from **10** (ref. 6) as follows:



The conversion of **11** to **12** by reversible addition of nitromethane reached a limit of ~65%. As it could not be separated from the nitro alcohols **12**, the residual keto sugar was carried through the following steps and separated, as a mixture of epimers at C-4, from the final product **3**, after $NaBH_4$-reduction. The dehydration of **12** was performed according to the procedure of Moffatt.[7] The reduction of the nitroalkene function of **13** led to the *galacto* isomer exclusively.

6. R. Johansson and B. Samuelsson, *J. Chem. Soc., Perkin Trans. I* **1984**, 2371.
7. H. P. Albrecht and J. G. Moffatt, *Tetrahedron Lett.* **1970**, 1063.
8. For the preparation of compound **5b**, see: Y. Fukuda, H. Kitasato, H. Sasai, and T. Suami, *Bull. Chem. Soc. Jpn.* **1982**, *55*, 880; compound **5a** was prepared from methyl 2,3-*O*-isopropylidene-α-D-*ribo*-pentodialdofuranoside by the same procedure.
9. K. Torssell and O. Zeuthen, *Acta Chem. Scand.* **1978**, *B32*, 118.
10. All new stable compounds were characterized by spectral data and microanalysis or mass spectrometry.
11. While our work was in progress, the oxidative cleavage of silyl nitronates to ketones with *m*-chloroperbenzoic acid was reported: see ref. 4.

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