Tetrahedron Letters No. 38, pp 3427 - 3430, 1976. Pergamon Press. Printed in Great Britain.

SYNTHESIS OF 1 - ISOCYANO SUGARS

Paul BOULLANGER and Gérard DESCOTES.

Université Claude Bernard LYON I, Laboratoire de Chimie Organique II
E. S. C. I. L. 43, Boulevard du 11 Novembre 1918-69621-Villeurbanne

(Received in France 12 May 1976; received in UK for publication 9 August 1976)

The substitution of 1-halogeno sugars with sodium or mercuric cyanide generally yields 1-cyano sugars [1,2,3,4,5,6] or with vicinal participating groups (acetates, benzoates), cyano orthoesters [7,8]. ACTON *et al* [9] assumed in the synthesis of 2,3,5-tri-O-benzyl-1-cyano-1-deoxy-D-arabinofuranose by a similar substitution with silver cyanide, the formation of an isonitrile intermediate, but did not isolate it.

The synthesis of 3,4,6-tri-O-benzyl-D-glucal **1** [10] and halogenated derivatives **2** [11] allowed us to study the reaction of silver cyanide on benzyl halogenated glycosides. Isocyanides **3** are obtained as syrups in good yields (table I) at room temperature in aprotic solvents (toluene, dichloromethane) with a time of reaction of 15 minutes for **2a** two or three days for **2b** and **2d** or a week for **2c** . The substitution is stereospecific for **2a** and gives mainly the β -anomer for the other glycosyl halides.

TABLE I

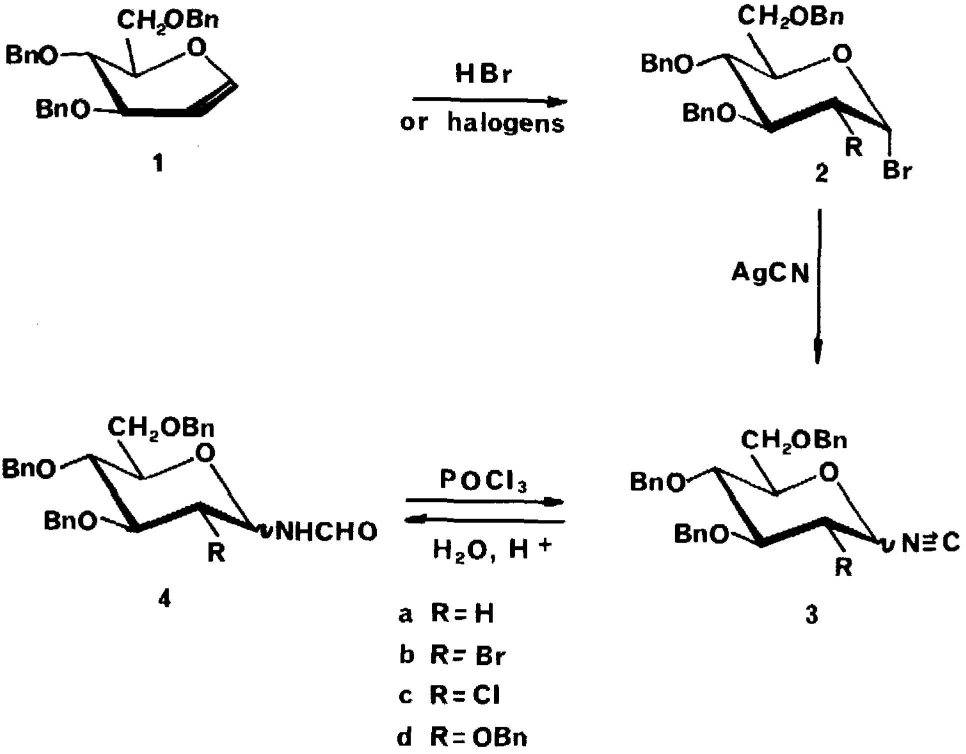
Synthesis of **3** (toluene or CH_2Cl_2 *)

2	Time	% **3**α	$[\alpha]_D^{22}$ **	% **3**β	$[\alpha]_D^{22}$ **	yield % **3**
a	15 mn	100	+64°	-	-	80
b ***	2 days	15	-	85	-	75
c ***	1 week *	35	-	65	-	60
d	3 days	40	+52,4°	60	+ 22,5°	75

** C = 2,5 , chloroform

*** α and β anomers are not separated

SCHEME I



The ^1H nmr spectra gives the configurations of the anomeric isocyanides **3** (**3a** : $\underline{J}_{1,2a}$ = 1,6Hz and $\underline{J}_{1,2e}$ = 3,4Hz ; **3**α : $\underline{J}_{1,2}$ = 3,4 to 3,7Hz , **3**β : $\underline{J}_{1,2}$ = 8,4 to 8,7Hz). The ^{13}C nmr spectra shows the carbon of the isocyano group at 139,05 ± 0,1 ppm, whereas the carbon of the nitrile group appears between 114,5 and 117 ppm.

The infrared spectra of isocyanides **3** shows a very intense band composed of two peaks, one at 2123 cm^{-1} to the α -anomer and the other at 2142 cm^{-1} (β -anomer).

Chemical transformation of **3** confirmed the isocyanide structure. Acidic hydrolysis of **3** gives the formamide **4** with preferential precipitation of the β -anomer ; nmr(acetone d_6): 8,25 (1, m, NHC$\underline{H}$O) , 7,9 (1,m, N$\underline{H}$CHO). This structure was confirmed by dehydrating **4** to the starting material **3** (β -anomer) with phosphoryl chloride.

The synthesis of a new class of compounds in the field of carbohydrates is of particular interest because of the potential reactivity of the isocyano group. The well-known reactions of α -metallation [12], α -addition [13] and the uses of isonitriles as ligands [14] could be the principal synthetic applications of these compounds in carbohydrate series.

TYPICAL EXPERIMENT :

To a solution of **1** (1g, 2 mmol.) in 50 ml of dry toluene at 0° and in darkness was added hydrogen bromide until saturation. After fifteen minutes of reaction, the solvent was removed in vacuo. The crude product **2** was stirred with freshly prepared silver cyanide (800 mg , 6 mmol.) in 25 ml of toluene for thirty minutes. The precipitate was removed by filtration and the filtrate evaporated in vacuo. The isocyanide **3** was obtained after chromatography (TLC) on silica gel (eluent : ether - benzene - hexane 1 : 2 : 2).

BIBLIOGRAPHY :

1 A. KOLB, T. HUYNH DINH and J. IGOLEN, Bull. Soc. Chim. Fr., 1973, p. 3447.

2 M. W. WINKLEY, Carbohydr. Res., 1973, 31, 245.

3 B. HELFERICH and K. L. BETTIN, Ber. Dtsch. Chem. Ger., 1961, 94, 1159.

4 B. HELFERICH and W. OST, Ber. Dtsch. Chem. Ger., 1962, 95, 2612.

5 M. BOBEK and J. FARKAŠ, Collect. Czech. Chem. Comm., 1969, 34, 247.

6 B. COXON, Tetrahedron, 1966, 22, 2281.

7 B. COXON and H. G. FLETCHER Jr., J. Am. Chem. Soc., 1963, 85, 2637.

8 G. BARNATHAN, T. HUYNH DINH, A. KOLB and J. IGOLEN, Eur. J. Med. Chem. Chim. Ther., 1976, 11, 67.

9 E. M. ACTON, A. N. FUJIWARA, L. GOODMAN and D. W. HENRY Carbohydr. Res., 1974, 33, 135.

10 P. BOULLANGER, G. DESCOTES and J. C. MARTIN, J. Heterocyclic. Chem., 1975, p. 91.

11 P. BOULLANGER and G. DESCOTES, Carbohydr. Res., 1976 (in press)

12 D. HOPPE, Angew. Chem., Int. Ed., 1974, 13, 789.

13 G. E. NIZNIK, W. H. MORRISON and H. M. WALBORSKY, J. Org. Chem., 1974, 39, 600.

14 T. SAEGUSA and Y. ITO, Synthesis, 1975, p. 291.