Communications TO THE EDITOR

A New Fructose Anhydride

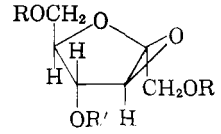
Sir:

Nitrates of ketohexoses, in contrast to aldohexoses, have not yet been obtained in the monomeric form. Schwager and Leibowitz[1] have recently shown that the nitration of fructose by means of a nitric-sulfuric acid mixture[2] affords a mixture of nitrates of difructose dianhydrides along with other dimeric derivatives of fructose. In a course of a study designed toward the formation of monomeric fructose nitrates we found that this could be achieved by using aprotic nitration agents.[3]

Nitration of fructose by means of N_2O_5 in chloroform according to the method of Caesar and Goldfrank[4] yielded a mixture of monomeric fructose nitrates. Fractional crystallization of this mixture afforded in 30% yield, long crystalline needles of a trinitrate (I), melting at 80.5° (from methanol). $[\alpha]_D^{25}$ = +34.5 (ethanol). *Anal.* Calcd. for $C_6H_7O_{11}N_3$: N, 14.14; mol. wt., 297. Found: N, 14.02; mol.wt., 300 (in benzene). In the infrared spectrum I shows three absorption bands at 1665 cm.$^{-1}$; 1306 cm.$^{-1}$ and 2180 cm.$^{-1}$ (O–NO_2). λ_{max}^{EtOH} 220 mμ, log ϵ, 3.28.

Catalytic reduction of I with palladium-charcoal (10%) in ethanol, according to Kuhn[5] resulted in complete denitrification, yielding a colorless sirup (II), $[\alpha]_D^{25}$ = +79.4 (ethanol). Infrared: 3366 cm.$^{-1}$, 3306 cm.$^{-1}$ (OH), 1064 cm.$^{-1}$ (C-O ethers) and 1263 cm.$^{-1}$ (epoxide). It did not respond to the Fehling test, but underwent facile acid hydrolysis in cold *N* hydrochloric acid solution affording fructose in quantitative yield, identified by its optical rotation, chromatographic R_f value and by its osazone (m.p. 207°). Acetylation of II by means of acetic anhydride–pyridine gave a crystalline triacetate (III), m.p. 112° (from ethanol), $[\alpha]_D^{25}$ = +57.4 (ethanol). *Anal.* Calcd. for $C_{12}H_{16}O_8$: C, 50.00, H, 5.59; mol. wt., 288. Found: C, 49.93, H, 5.1; mol. wt., 289. Infrared: 1751 cm.$^{-1}$ (C=O), 1230 cm.$^{-1}$ (C—O ether) 1264 cm.$^{-1}$ (epoxide). II resisted oxidation by means of potassium periodate even after prolonged standing. Exhaustive methylation of II followed by acid hydrolysis afforded a sirup which failed to produce an osazone. Tritylation of II by means of trityl chloride–pyridine[6] afforded a ditrityl derivative (IV) as colorless crystals (from ethanol) melting at 207°. *Anal.* Calcd. for $C_{44}H_{38}O_5$: C, 81.88; H, 5.88. Found: C, 81.74; H, 5.74. Infrared: 3410 cm.$^{-1}$, 3370 cm.$^{-1}$ (OH), 3030 cm.$^{-1}$ (C-H), 1262 cm.$^{-1}$ (epoxide). Tosylation of I by tosyl chloride–pyridine[7] gave exclusively a ditosyl derivative (V) as colorless crystals melting at 156° (from ethanol). *Anal.* Calcd. for $C_{20}H_{22}O_9S_2$: C, 51.48; H, 4.68; S, 12.86. Found: C, 51.52; H, 4.86, S, 12.5. Infrared: 3546 cm.$^{-1}$ (OH), 1373 cm.$^{-1}$, 1184 cm.$^{-1}$ (O–SO_2) 1265 cm.$^{-1}$ (epoxide). Heating a solution of V in acetone and sodium iodide at 100° produced two molar equivalents of sodium *p*-toluenesulfonate in quantitative yield along with an iodide derivative. Nitration of II by means of N_2O_5 in $CHCl_3$ resulted in the re-formation of I while nitration by means of HNO_3–H_2SO_4 caused polymerization.

The series of reactions clearly permits the assignment of 2,3-*anhydro*-fructofuranose structure for II. For absolute configuration assignment, we studied the mechanism of formation of I and the information now at hand suggests that the epoxide ring is oriented above the furanose ring,[3] as formulated below.



I. R=R′=No$_2$. II. R=R′=H. III. R=R′=Ac. IV. R=Tr; R′=H. V. R=Ts; R′=H.

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(1) A. Schwager and J. Leibowitz, *Bull. Res. Counc. of Israel*, 5*A*, 266 (1956); A. Schwager-Shamgar, Ph.D. Thesis, Hebrew University (1958).

(2) W. Will and F. Lenze, *Ber.*, **31**, 68 (1898).

(3) M. Sarel-Imber, Ph. D. Thesis, Hebrew University (1958).

(4) G. V. Caesar and M. Goldfrank, *J. Am. Chem. Soc.*, **68**, 372 (1946).

(5) L. P. Kuhn, *J. Am. Chem. Soc.*, **68**, 1761 (1946).

(6) B. Helferich, *J. prakt. Chem.*, **147**, 60 (1936).

(7) J. Compton, *J. Am. Chem. Soc.*, **60**, 395 (1938).

(8) M. Sarel-Imber and J. Leibowitz, unpublished results.

Azomethine and α-Bromoamine Formation in the Aralkylation of Certain Weak Aromatic Amines in Dimethyl Sulfoxide[1]

Sir:

Alkylation of weak aromatic amines with alkyl bromides (*e.g.*, 2-aminofluorenone with ethyl bro-

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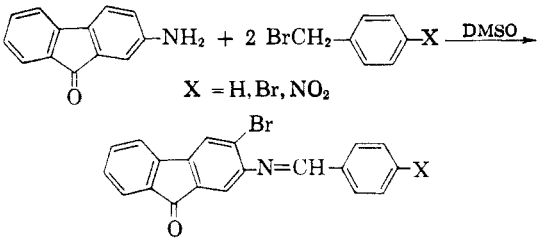
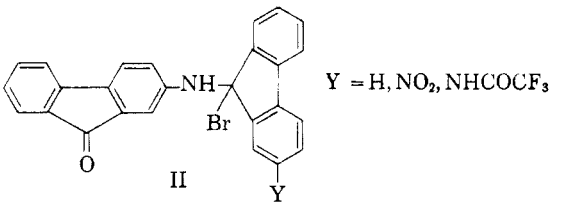
mide) in dimethyl sulfoxide gave ring brominated *N*-alkyl derivatives.[2] However, aralkylation of 2-aminofluorenone with aralkyl bromides, such as benzyl and *para* substituted benzyl bromides, in dimethyl sulfoxide (1.5 hours; 100°) leads to azomethines as main products (when X is Br or NO_2, the yield of I is 80%). The reaction of 2-



N-benzylaminofluorenones with 48% hydrobromic acid (2 equivalents) in dimethyl sulfoxide (1.5 hours; 100°) also gives I in high yields. Therefore, it appears that both the fluorene nucleus and the aliphatic carbon attached to the nitrogen of the aralkylamino intermediate (—NH—CH_2—Ar) are brominated. Dehydrobromination leads to the formation of I.

Oxidation of the aralkyl bromides to aldehydes in dimethyl sulfoxide[3] followed by condensation with the amine does not seem to take place, at least to any appreciable extent, because we find that aralkylation of the amine takes place more readily than oxidation of the aralkyl bromide. For example, 2-aminofluorenone and *p*-bromobenzyl bromide in dimethyl sulfoxide at room temperature for 5 or 8 days yields neither *p*-bromobenzaldehyde nor the azomethine. The main products are the *N*-monoaralkylated-3-bromo- and diaralkylated 2-aminofluorenones.

The reaction of 2-aminofluorenone and some substituted 9-bromofluorenes in dimethyl sulfoxide at 100° gives intermediates of type II in high yields. The bromine is aliphatic, is not detectable in alcoholic solution with starch-iodide or alcoholic silver nitrate, but is removed with hot alcoholic potassium hydroxide (*anal.*, for example with Y = $NHCOCF_3$, found for $C_{28}H_{16}BrF_3H_2O_2$: C, 60.88; H, 2.96; N, 4.82 Br, 14.82). *p*-Nitroaniline similarly gives *N*-9′-(9′-bromofluorenyl)-*p*-nitroaniline.



II

Bromination of 2-*N*-(9′-fluorenyl)aminofluorenones with 48% hydrobromic acid in dimethyl sulfoxide or with *N*-bromosuccinimide (UV) gives II. 2-*N*-(9′-Fluorenyl)amino-3-bromofluorenone and *N*-bromosuccinimide (UV) gives 2-amino-3-bromofluorenone hydrobromide, which indicates that bromination of the carbon α to the amine, followed by formation of an azomethine by oxidative dehydrobromination is, in turn, followed by cleavage to give the 2-amino-3-bromo compound.

We have found, therefore, a new type of oxidation (to azomethines) of certain secondary amines by way of a brominated intermediate. The secondary amine may be used as such or it may be formed as a first step in the reaction. With some types we can isolate this intermediate, brominated on the same carbon atom from which bromine was removed in the formation of the secondary amine.

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(2) T. L. Fletcher and H. L. Pan, *J. Am. Chem. Soc.*, **78**, 4812 (1956); T. L. Fletcher, M. J. Namkung, and H. L. Pan, *Chem. & Ind. (London)*, 660 (1957).

(3) N. Kornblum, J. W. Powers, G. J. Anderson, W. J. Jones, H. O. Larson, O. Levand, and W. M. Weaver, *J. Am. Chem. Soc.*, **79**, 6562 (1957).