Carbohydrate Research, 38 (1974) 189–203

PREPARATION OF ACETYLENIC SUGAR DERIVATIVES BY WAY OF 2-(*N*-NITROSO)ACETAMIDO SUGARS*†

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(Received July 31st, 1974; accepted August 31st, 1974)

ABSTRACT

N-Nitrosation with dinitrogen tetraoxide was used to convert 2-acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-α-D-glucopyranose (**1**) and 2-acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-β-D-galactopyranose (**4**) in high yield into the *N*-nitroso derivatives **2** and **5**, respectively. Similarly, 3-acetamido-1,2,4,6-tetra-*O*-acetyl-3-deoxy-β-D-glucopyranose (**12**) and methyl 2-acetamido-3,4,5,6-tetra-*O*-acetyl-2-deoxy-D-gluconate (**15**) gave their respective, crystalline *N*-nitroso derivatives **13** and **16**. Various other 2-acetamido sugar derivatives were likewise nitrosated. In ethereal solution, compounds **2** and **16** reacted with potassium hydroxide in isopropyl alcohol to give the C_5 acetylene, 1,2-dideoxy-D-*erythro*-pent-1-ynitol, isolated as the known triacetate **3**. By the same procedure, the *galacto* derivative **5** was converted in high yield into the 3-epimeric C_5 acetylene, 1,2-dideoxy-D-*threo*-pent-1-ynitol, isolated as its triacetate **6** and characterized by conversion into the known, crystalline 1,2-dideoxy-3-*O*-(3,5-dinitrobenzoyl)-4,5-*O*-isopropylidene-D-*threo*-pent-1-ynitol (**7**).

INTRODUCTION

The preceding report[1] described the two-step conversion of 2-acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-β-D-glucopyranose in high yield into a C_5 acetylene, 1,2-dideoxy-D-*erythro*-pent-1-ynitol, by the action of dinitrogen tetraoxide on the acetamido sugar followed by treatment of the resultant *N*-nitrosoamide with strong base; the acetylenic product was characterized as a known, crystalline derivative. Results of several related nitrosation experiments are now reported, the relative stabilities of the *N*-nitrosoamides are compared, and the conversion of some of them into acetylenic compounds is described; 2-acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-β-D-galactopyranose (**4**) gives 1,2-dideoxy-D-*threo*-pent-1-ynitol, isolated in high yield as the triacetate **6**, by way of the corresponding nitrosoamide **5**.

*Part XIV of the series "Extension of Sugar Chains Through Acetylenic Intermediates". For Part XIII, see ref. 1. This work was supported, in part, by the National Institute of General Medical Sciences, National Institutes of Health, U. S. Public Health Service Grant No. GM-11976 (The Ohio State University Research Foundation Project 1820).

†Preliminary report: D. Horton and W. Loh, *Abstr. Papers Amer. Chem. Soc. Meeting*, 167 (1974) CARB-2.

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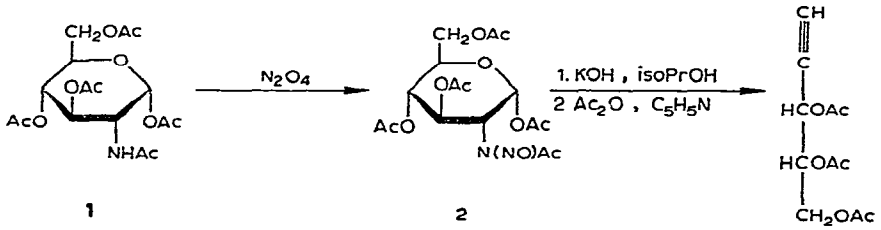
DISCUSSION

By the general procedure already described[1,2], 2-acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-α-D-glucopyranose[3] (**1**) in chloroform was treated at 0° with an excess of dinitrogen tetraoxide in the presence of sodium acetate to give the *N*-nitroso derivative[4] **2** as a yellow syrup in 82% yield. The reaction required considerably more time (~3 h) than that for the β anomer[1]. The properties of **2** corresponded closely with those reported[4] for **2** prepared by the action of nitrosyl chloride on **1**, with characteristic[5] i.r. absorption at 6.55 μm for the N=O group. Although **2** could be stored for several h at −80°, it was much less stable than the (syrupy) β anomer[1], and it decomposed during the recording of its n.m.r. spectrum in chloroform-*d* at ~40°.



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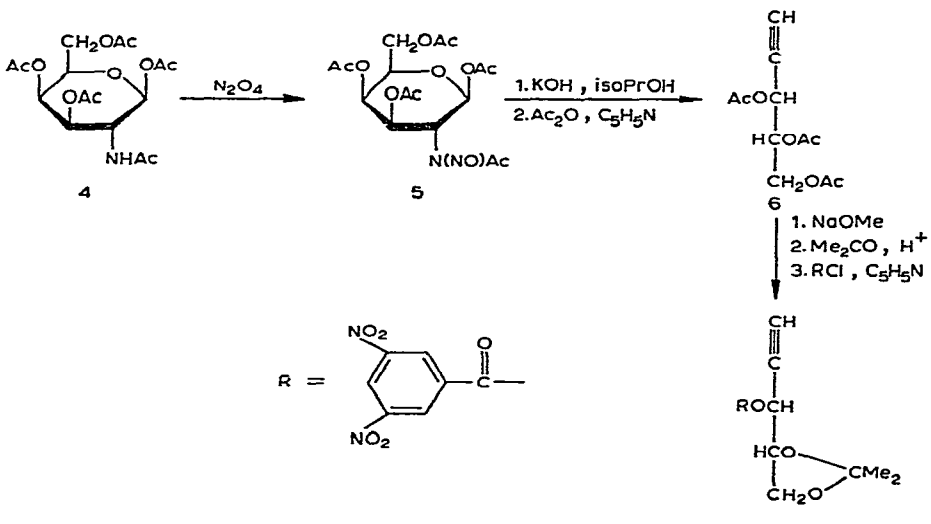
The same procedure was used to convert 2-acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-β-D-galactopyranose[6] (**4**) into the corresponding *N*-nitrosoamide **5**, obtained in 93% yield as a yellow syrup that displayed typical N=O absorption[1,2,5] at 6.55 μm in the i.r. spectrum, and characteristic[1,4] absorptions for the nitroso chromophore at



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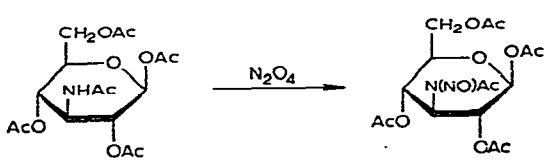
389, 406, and 425 nm in the electronic spectrum. The compound decomposed to a considerable extent if kept for several h at 25°. Its 100-MHz n.m.r. spectrum in benzene-d_6 was first order (see Table I) and indicated that the product was quite homogeneous; no NH signal was present, and the NAc signal was observed at characteristic low field (τ 7.67).

The stability of the 2-(*N*-nitroso)acetamido sugars seems to be dependent upon the nature of the substituents at C-1, C-3, C-4, and C-6, upon the anomeric configuration, and upon the physical state (crystalline or liquid) of the product. Nitrosation of methyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranoside[7] (**9**) with dinitrogen tetraoxide gave the crystalline nitrosoamide[8] **11**, whose stability was such that it could be kept for several weeks at −10°. In contrast, although the α analog, methyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranoside[9] (**8**), underwent nitrosation with dinitrogen tetraoxide to give the yellow nitrosoamide **10**, this product was so unstable that it decomposed during attempted isolation. Similarly, benzyl 2-acetamido-3,4,6-tri-*O*-acetyl-α-D-glucopyranoside[10] underwent nitrosation, but the nitrosoamide was of low stability; it could be kept long enough for the N=O absorption in the i.r. spectrum and the N(NO)Ac methyl resonance in the n.m.r. spectrum to be observed, but it was of much lower stability than the crystalline β anomer described in the previous paper[1]. Thus, of three anomeric pairs examined, the nitrosoamides of the β series were qualitatively more stable than the α analogues. The two crystalline β-D-nitrosoamides (**11** and its benzyl analogue[1]) showed the highest stability, with the β-D analogue[1] of **2** (a syrup) displaying rather lower stability. The α-D analogues **2**, the benzyl glycoside, and the methyl glycoside **10** were of progressively lower stability. Examination of another anomeric pair, methyl 2-acetamido-3,4,6-tri-*O*-methyl-2-deoxy-α-D-glucopyranoside[11] and its β anomer[12], revealed the same relative behavior, except that the nitrosoamides were of higher overall lability; the β-nitrosoamide could be isolated and kept long enough for its i.r. and n.m.r. spectra to be recorded, but the α-nitrosoamide decomposed before isolation could be accomplished. Apparently, factors contributing to stabilization of the nitrosoamides are electron-withdrawing

8 α anomer
9 β anomer

10 α anomer
11 β anomer



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substituents at the other ring positions and a *trans*-disposition of O-1 to the 2-(*N*-nitroso)acetamido group.

In an extension to a derivative of a 3-amino sugar, 3-acetamido-1,2,4,6-tetra-*O*-acetyl-3-deoxy-β-D-glucopyranose[13] (**12**) was treated with dinitrogen tetraoxide, and the crystalline nitrosoamide **13** was obtained in 89% yield. The product was stable enough for recrystallization, gave an acceptable elemental analysis, and could be kept for some weeks at −10° without any decomposition being evident. Its n.m.r. spectrum in benzene-d_6 was essentially first order (see Table I), and all of the characterizing data (see Experimental) accorded with the structure assigned.

Methyl 2-acetamido-3,4,5,6-tetra-*O*-acetyl-2-deoxy-D-gluconate (**15**), prepared from 2-amino-2-deoxy-D-gluconic acid (**14**) by esterification and subsequent acetylation, reacted with dinitrogen tetraoxide to give the stable, crystalline *N*-nitrosoamide **16** in 92% yield. The data of i.r., u.v., and mass spectra (see Experimental) and of n.m.r. spectra (see Table I) were fully concordant with the assigned structure; the mass spectrum displayed peaks at *m/e* 418 for the $M^{+} - \cdot NO$ fragment and at *m/e* 417 for $M^{+} - \cdot OMe$, together with other characteristic ions. The high stability of this product (**16**) can be attributed to the presence of the electron-withdrawing $-CO_2Me$ group; the high stability of the 2-diazo analogue of **16** has been noted in an earlier report[14].

When the α-nitrosoamide **2** in ethereal solution was treated with an excess (~6 moles per mole) of potassium hydroxide in isopropyl alcohol at room temperature, and the product was acetylated, there was obtained the C_5 acetylene, 3,4,5-tri-*O*-acetyl-1,2-dideoxy-D-*erythro*-pent-1-ynitol (**3**), in 73% yield. This product was

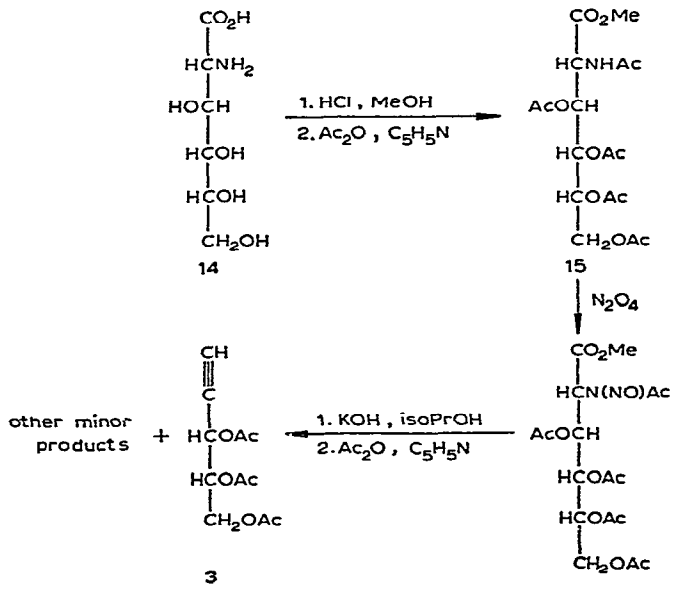


TABLE I

100-MHz N.M.R. SPECTRAL DATA[a] FOR COMPOUNDS **2, 3, 5, 6, 11, 13, 15,** AND **16**

Compound	*Solvent*	*Chemical shifts in τ values (first-order couplings in Hz in parentheses)*								
		H-1	H-2	H-3	H-4	H-5	H-6	H-6′	NAc	Other
1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-(*N*-nitroso)-acetamido-α-D-gluco-pyranose[b] (2)	$CDCl_3$	4.15d ($J_{1,2}$ 3)		3.70dd (J 9, 11)					7.32s	7.93s, 7.95s 7.99s, and 8.12s (OAc)
3,4,5-Tri-*O*-acetyl-1,2-dideoxy-D-*erythro*-pent-1-ynitol (3)	$CDCl_3$	7.44d ($J_{1,3}$ 2.2)		4.34dd ($J_{3,4}$ 4.2)	4.70dt ($J_{4,5}$ 4.2, $J_{4,5'}$ 6.8)	5.56dd ($J_{5,5'}$ 11.8)				5.73dd (H-5′), 7.89s[c] (OAc), 7.93s (OAc)
1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-(*N*-nitroso)-acetamido-β-D-galacto-pyranose (5)	C_6D_6	3.42d ($J_{1,2}$ 8)	4.49dd ($J_{2,3}$ 11)	4.10dd ($J_{3,4}$ 3.5)	4.63dd ($J_{4,5}$ ~1)	6.26–6.48m (dt?)	5.85dd[d] ($J_{5,6}$ 7, $J_{6,6'}$ 11)	6.00dd ($J_{5,6'}$ 6)	7.67s	8.32s, 8.37s, 8.48s, and 8.58s (OAc)
3,4,5-Tri-*O*-acetyl-1,2-dideoxy-D-*threo*-pent-1-ynitol (6)	$CDCl_3$	7.51d ($J_{1,3}$ ~2.5)		4.47dd ($J_{3,4}$ 6.5)	4.78dt ($J_{4,5}$ ~3.8, $J_{4,5'}$ 6)	5.59dd ($J_{5'5'}$ 12.5)				5.84dd (H-5′), 7.94s[c], 7.98s (OAc)
Methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-(*N*-nitroso)-acetamido-β-D-gluco-pyranoside (11)	$CDCl_3$	4.80d ($J_{1,2}$ 8)	5.13dd (J 8, 10)	4.88dd (J 9.5) and 4.40dd (J 9, 10)[e]		6.21 (8-line pattern, ($J_{4,5}$ 10)	5.64dd[f] ($J_{5,6}$ 5, $J_{6,6'}$ 12.2)	5.85dd ($J_{5,6'}$ 2.5)	7.32s	6.64s (OMe), 7.94s, 8.02s, and 8.19s (OAc)

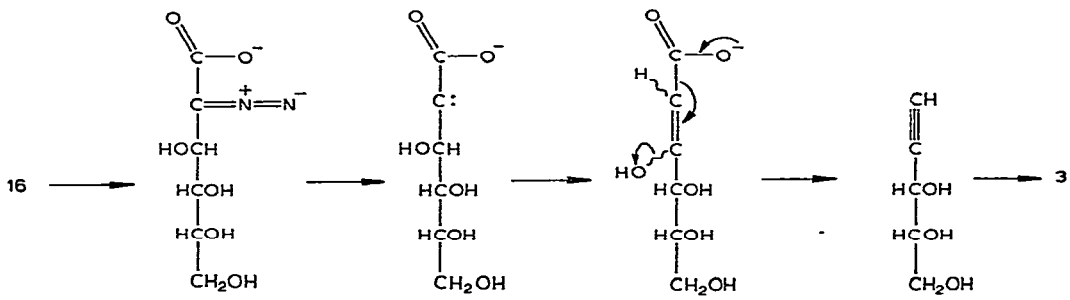
TABLE I (*Continued*)

Compound	*Solvent*	*Chemical shifts in τ values (first-order couplings in Hz in parentheses)*								
		H-1	H-2	H-3	H-4	H-5	H-6	H-6′	NAc	Other
Methyl 3,4,6-tri-*O*-methyl-2-(*N*-nitroso)acetamido-2-deoxy-β-D-gluco-pyranoside[b]	$CDCl_3$	5.14d ($J_{1,2}$ 8)							7.24s	6.50s, 6.59s, and 6.69s[c] (OMe)
1,2,4,6-Tetra-*O*-acetyl-3-deoxy-3-(*N*-nitroso)-acetamido-β-D-gluco-pyranose (13)	C_6D_6	4.20d ($J_{1,2}$ 8)	4.03dd ($J_{2,3}$ 9.5)	4.72t ($J_{3,4}$ 9.5)	4.19t ($J_{4,5}$ 9.5)	6.52 (8-line pattern)	5.79dd[f] ($J_{5,6}$ 4.5, $J_{6,6'}$ 12.7)	6.01dd ($J_{5,6'}$ 2.5)	7.54s	8.32s, 8.40s, 8.48s[c]
Methyl 2-acetamido-3,4,5,6-tetra-*O*-acetyl-2-deoxy-D-gluconate (15)	$CDCl_3$		4.99dd ($J_{2,3}$ 5)		4.49t (J 5) and 4.61t (J 5)[e]	4.73–4.92m	5.70dd[f] ($J_{5,6}$ 4, $J_{6,6'}$ 12.2)	5.92dd ($J_{5,6'}$ 5)		3.70d (NH, J 9), 6.32s (CO_2Me), 7.84–8.10m[g] (Ac)
Methyl 3,4,5,6-tetra-*O*-acetyl-2-deoxy-2-(*N*-nitroso)acetamido-D-gluconate (16)	$CDCl_3$		4.53–4.71m	——4.05–4.29m——		4.93 (8-line pattern)	5.68dd[f] ($J_{5,6}$ 3, $J_{6,6'}$ 12.2)	5.85dd ($J_{5,6'}$ 4.3)	7.27s	6.30s (CO_2Me), 7.78s, 7.93s, 7.95s, and 8.12s (OAc)

[a]First-order couplings are given in Hz; peak multiplicities: d, doublet; dd, doublet of doublets; dt, doublet of triplets; m, multiplet; s, singlet; t, triplet. [b]Decomposition occurred during the measurements (at a probe temperature of ~40°). [c]Integrated intensity, 6 protons. [d]AB portion of an ABX system; $J_{5,6}$ 7.1, $J_{5,6'}$ 5.9 (calculated by ABX analysis). [e]Signals for H-3 and H-4 are not specifically differentiated. [f]AB portion of an ABX system; measured (first-order) spacings and chemical shifts are given. [g]Integrated intensity, 15 protons.

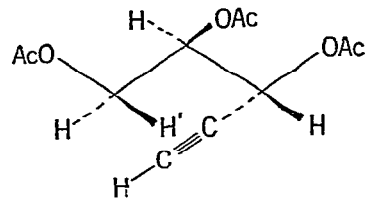
identical in all respects with **3** obtained[1] by the same sequence from the β analogue of **2**. This reaction sequence, proceeding from either anomer of the acetylated amino sugar by way of the nitrosoamides, to afford the acetylene **3** in high yield through a one-carbon chain descent, is thus a preparatively useful route to this acetylenic sugar; it compares favorably with the previous route[15] *via* chain ascent, in that it gives, exclusively, the one diastereoisomer. In contrast, the chain-ascent route requires a tedious separation of epimers and their stereochemical identification.

Application of the same, base-catalyzed, decomposition sequence to the acyclic nitroso derivative **16** also gave the C_5 acetylene **3**. The yield (30%) was lower than that obtained from the aldose derivative **2** or its β anomer[1], and the mechanism of the reaction has not yet been investigated. A probable course would involve conversion of the 2-substituent into a diazo group (compare ref. 14) and saponification of the ester groups; loss of nitrogen, and hydride migration in the incipient carbenoid species, would generate an enolate that could suffer C-1–C-2 cleavage with expulsion of HO^- and loss of CO_2 to generate **3**.



The β-D-*galacto* nitrosoamide **5** was subjected to the action of potassium hydroxide in isopropyl alcohol at ~25°. Acetylation of the reaction product gave a 74% yield of a colorless, levorotatory oil identified as 3,4,5-tri-*O*-acetyl-1,2-dideoxy-D-*threo*-pent-1-ynitol (**6**), the 3-epimer of **3**. The product gave an acceptable elemental analysis, and showed ≡C–H and C≡C absorption in the i.r. spectrum, and its mass spectrum displayed $M^+ - 59$ and $M^+ - 73$ fragments, corresponding to the loss of an acetate and an acetoxymethyl group, respectively. The reaction course **5**→**6** presumably follows a mechanism analogous to that suggested[1] for the conversion of **2** into **3**. The i.r. and mass-spectral data were similar to those observed with the 3-epimer **3**. The n.m.r. spectrum showed, in addition to the anticipated acetate-group signals, a high-field (τ 7.51) narrow doublet[15,16] for the acetylenic proton H-1 coupled to H-3. The $J_{3,4}$ and $J_{4,5'}$ couplings, of 6.5 and 6 Hz respectively, indicate[14–19] that H-3 and H-4, and also H-4 and H-5′, are preponderantly antiparallel (see Fig. 1).

The stereochemistry assigned to **6** is based on the known stereochemistry of the precursor **5** and the assumption that the configuration at C-4 and C-5 is retained during the conversion of **5** into **6**; a classical proof of the structure of **6** was provided by successive Zemplén deacetylation (conditions under which the chiral, propargylic



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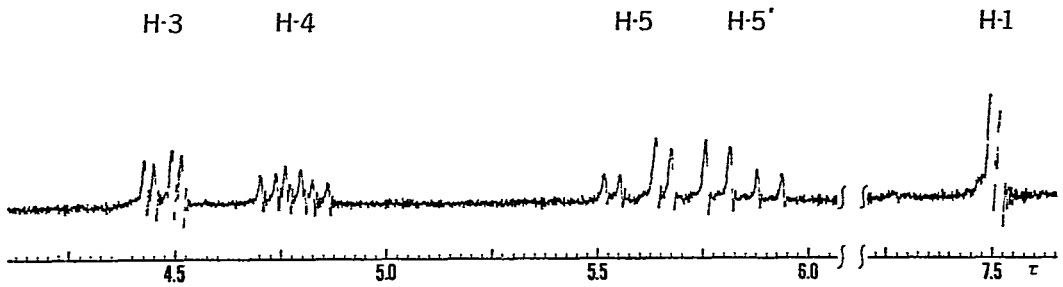

Fig. 1. The 100-MHz n.m.r. spectrum of 3,4,5-tri-*O*-acetyl-1,2-dideoxy-D-*threo*-pent-1-ynitol (**6**) in chloroform-*d* (acetate resonances omitted).

alcohol group can be expected[1,20] to be stereochemically stable), acetonation to give the anticipated dioxolane incorporating the primary alcohol group, and (3,5-dinitrobenzoyl)ation to yield the known[15] 1,2-dideoxy-3-*O*-(3,5-dinitrobenzoyl)-4,5-*O*-isopropylidene-D-*threo*-pent-1-ynitol **7**. The latter was earlier prepared in this laboratory[15] from 2,3-*O*-isopropylidene-D-glyceraldehyde by ethynylation, separation of the 3-epimers, and subsequent (3,5-dinitrobenzoyl)ation. The crystalline product **7** was identical with the independently prepared material in all respects, including the X-ray powder diffraction pattern.

It is possible to correlate[15,16,19] the $J_{3,4}$ coupling constants with the configuration at C-3 in the two pentyne derivatives **3** and **6**. The *threo*-ynitol **6** shows a larger $J_{3,4}$ coupling (6.5 Hz) than the corresponding *erythro*-ynitol **3** ($J_{3,4}$ 4.2 Hz), indicating that the stereoelectronic requirements of the ester group exceed those of the ethynyl group[16]. The observed $J_{3,4}$ couplings reflect a population-weighted time-average of three rotamer states; the larger value for **6** indicates a major contribution from the rotamer having H-3 and H-4 antiparallel, and the small value for **3** indicates a large contribution from one (or both) rotamers having H-3 and H-4 gauche.

As acetylenic sugar derivatives are versatile intermediates in synthetic sugar chemistry[21], improved routes for their preparation are of considerable interest. The simple, high-yielding procedure leading to the C_5 acetylenes **3** and to **6** from corresponding hexosamine precursors offers considerable advantage over the chain-ascent route, as single, stereochemically defined products are obtained. The method may be of general utility whenever suitable 2-amino sugar precursors are available.

EXPERIMENTAL

General methods. — Melting points are uncorrected. Optical rotations were measured with a Perkin–Elmer Model 141 recording polarimeter. I.r. spectra were recorded with a Perkin–Elmer Model 457 grating i.r. spectrophotometer. N.m.r. spectra were recorded by using a Varian HA-100 spectrometer, with tetramethylsilane as the internal standard. Chemical shifts are given on the τ scale and the J values recorded are first-order spacings. U.v. spectra were recorded with a Cary Model 14 recording spectrophotometer. T.l.c. was performed with 0.25-mm layers of Silica Gel G (E. Merck, Darmstadt, Germany); plates were activated at 110°. Components were detected by spraying the plates with 5% (v/v) sulfuric acid in ethanol, and then heating. Column chromatography was conducted with Merck silica gel No. 7734. X-Ray powder diffraction data give interplanar spacings, Å, for CuKα radiation. Relative intensities were estimated visually: m, moderate; s, strong; v, very; w, weak. The strongest lines are numbered in order (1, strongest). The camera diameter was 114.59 mm. Mass spectra were recorded by C. R. Weisenberger with an AEI MS-902 instrument operating at an ionization potential of 70 eV and an accelerating potential of 8 kV; the source temperature (direct-inlet system) was 150°. Elemental analyses were performed by W. N. Rond. G.l.c. was performed on a Beckman GC-5 dual-column instrument with columns (2 mm × 1.98 m) of 10% of SE-30 on Chromosorb Q, and helium as the carrier gas at a flow rate of 50 ml.min^{-1}. The injection-port temperature was 250°.

*1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-*(N-*nitroso*)*acetamido-*α*-*D*-glucopyranose* (**2**). — To a stirred mixture of 2-acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-α-D-glucopyranose[3] (**1**, 1.167 g, 3.0 mmoles) and anhydrous sodium acetate (740 mg, 9.0 mmoles) in chloroform (10 ml) at 0° was added dinitrogen tetraoxide[1,2] (1.65 g, 1.10 ml, 18 mmoles) in chloroform (10 ml) during 5 min at 0°. The mixture was stirred for an additional 2.75 h at 0°, chloroform (10 ml) was then added, and the mixture was purged with nitrogen for 1 h at 0°. Additional chloroform was added at intervals during the passage of nitrogen to keep the volume of the mixture constant. The resulting solution was successively washed with water (10 ml), 2% aqueous sodium carbonate (10 ml), and water (10 ml), all washings being performed at 0°. The organic phase was dried (magnesium sulfate) and evaporated at 0° to give the *N*-nitrosoamide **2** as a yellow syrup (t.l.c. showed only a minute trace of material migrating at the rate of the starting material); yield 1.040 g (83%); R_F 0.75 (1:1 chloroform–ethyl acetate); λ_{max}^{film} 5.68 (C=O) and 6.55 μm (N=O)[1,2,5]; λ_{max}^{EtOH} 390, 406, and 425 nm (typical values[4] for *N*-nitrosoamides, $\lambda_{max}^{CHCl_3}$ 389, 405, and 424 nm); for n.m.r. data, see Table I. Decomposition occurred during the n.m.r. measurements (at a probe temperature of ~40°), and the product was not sufficiently stable to permit elemental analysis.

Conversion of **2** *into 3,4,5-tri-*O*-acetyl-1,2-dideoxy-*D*-*erythro*-pent-1-ynitol* (**3**). — A solution of **2** (1.040 g, 2.5 mmoles) in ether (20 ml) was stirred magnetically at ~25°. Potassium hydroxide (790 mg, 14.1 mmoles) dissolved in isopropyl alcohol (20 ml) was added during 2 min, while efficient stirring was maintained. The mixture was

stirred for an additional 10 min at ~25° and, after evaporation of the solvents at 35–40° under diminished pressure, pyridine (10 ml) and acetic anhydride (5 ml) were added, and the mixture was stirred overnight at ~25°. Ice and water (50 ml) were added, and the solution was extracted with three 15-ml portions of chloroform. The dark-brown extract was washed with water (10 ml), dried (anhydrous magnesium sulfate), and evaporated. T.l.c. revealed minute traces of unidentified materials having R_F 0.67 and 0.00 (1:1 chloroform–ethyl acetate). The main component (**3**, R_F 0.84) was separated by chromatography on a column of silica gel by using the t.l.c. solvent. Evaporation of the solvent gave **3** as a clear syrup; yield 442 mg (73%). An analytical sample (380 mg) was obtained by distillation onto a cold finger at 55–60° (bath)/10 μtorr; $[\alpha]_D^{24}$ +64±1° (*c* 1.3, chloroform); λ_{max}^{film} 3.06 (C≡CH), 4.72 (C≡C), 5.74 (C=O), 6.98 (weak), 7.30, 8.20 (broad), and 9.58 μm; for n.m.r. data, see Table I.

Anal. Calc. for $C_{11}H_{14}O_6$: C, 54.55; H, 5.79. Found: C, 54.47; H, 5.79.

The product was identical with an authentic sample of **3** by comparative i.r. and n.m.r. spectra. For mass-spectral data, see ref. 1.

*1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-*(N*-nitroso)acetamido-β-*D*-galactopyranose* (**5**). — A mixture of 2-acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-β-D-galactopyranose[6] (**4**, 778 mg, 2.0 mmoles) and anhydrous sodium acetate (492 mg, 6.0 mmoles) in dichloromethane (20 ml) was stirred at 0° while dinitrogen tetraoxide[1,2] (1.10 g, 0.73 ml, 12.0 mmoles) in dichloromethane (10 ml) was added during 5 min at 0°. The mixture was stirred for 1 h at 0°; additional dinitrogen tetraoxide (0.40 g, 0.27 ml, 4.4 mmoles) in dichloromethane (5 ml) was then added, and the mixture was stirred for 1.25 h at 0°. The subsequent procedure for isolation was similar to that for the *N*-nitrosoamide **2**. Evaporation of the solvent at 0° gave the *N*-nitrosoamide **5** as a yellow syrup; yield 775 mg (93%), $[\alpha]_D^{19}$ +12±1° (*c* 2.3, ethanol); R_F 0.78 (1:1 chloroform–ethyl acetate, t.l.c. indicated a minute trace of starting material); λ_{max}^{film} 5.75 (C=O) and 6.55 μm (N=O)[1,2,5]; λ_{max}^{EtOH} 389 (ε 40), 406 (70), and 425 nm (79); for n.m.r. data, see Table I.

When the *N*-nitrosoamide **5** was kept for 10 h at 25°, considerable decomposition was observed by t.l.c.

Conversion of the nitrosoamide **5** *into 3,4,5-tri-*O*-acetyl-1,2-dideoxy-*D*-threo-pent-1-ynitol* (**6**). — A solution of the *galacto* derivative **5** (560 mg, 1.3 mmoles) in ether (10 ml) was stirred magnetically at ~25°, and potassium hydroxide (420 mg, 7.5 mmoles) dissolved in isopropyl alcohol (10 ml) was added during 2 min. The brown mixture was stirred for an additional 10 min at ~25° and, after evaporation of the solvents at 35–40° under diminished pressure, pyridine (10 ml) and acetic anhydride (3 ml) were added, and the mixture was stirred overnight at ~25°. The subsequent procedure for isolation was similar to that for **3**. A solution of the product in chloroform was passed through a short column of silica gel. Evaporation of the solvent gave **6** as a clear syrup; yield 241 mg (74%). An analytical sample was obtained by distillation onto a cold finger at 55° (bath)/10 μtorr; $[\alpha]_D^{20}$ −39 ±1° (*c* 1.0, chloroform); R_F 0.86 (1:1 chloroform–ethyl acetate); λ_{max}^{film} 3.06 (C≡CH), 4.72 (C≡C), 5.75 (C=O), 7.30, 8.20 (broad), and 9.61 μm; for n.m.r. data, see Table I; *m/e* (relative intensities and probable assignments given in parentheses): 183 (0.2, $M^+ - \cdot OAc$), 182 (0.3,

$M^+ - AcOH$), 169 (0.4, $M^+ - \cdot CH_2OAc$), 158 (0.2, $M^+ - HC{\equiv}COAc$), 145 {15, Ac_3O^+ and $[CH(OAc)CH_2OAc]^+$}, 103 [13, $(Ac_2OH)^+$ and $145 - CH_2CO$ (*m** 73.2, calc. 73.2)], 98 [14, $(C_5H_6O_2)^+$], and 43 (100, Ac^+).

Anal. Calc. for $C_{11}H_{14}O_6$: C, 54.55; H, 5.79. Found: C, 54.80; H, 5.91.

*1,2-Dideoxy-3-O-(3,5-dinitrobenzoyl)-4,5-O-isopropylidene-*D-threo*-pent-1-ynitol* (**7**). — A solution of the triacetate **6** (240 mg, 1 mmole) in abs. methanol (20 ml) was treated with a catalytic amount of sodium, and the mixture was stirred for 6 h at room temperature. The base was neutralized with Dry Ice, and methanol was removed at ~30° under diminished pressure. The residue was shaken for 6 h at room temperature with anhydrous copper(II) sulfate (200 mg) in acetone (20 ml) containing a catalytic amount of concentrated sulfuric acid. The acid was then neutralized by stirring the mixture with anhydrous sodium carbonate (400 mg), the mixture was filtered, and the filtrate evaporated. To the residue were added dry pyridine (10 ml) and freshly prepared 3,5-dinitrobenzoyl chloride (400 mg), and the mixture was stirred for 6 h at room temperature. Ice and water (100 ml) were then added, and, after 1 h, the solid product was filtered off, washed with water, and dried. A solution of the product in chloroform was passed through a short column (6 × 2 cm) of silica gel. Evaporation of the effluent, and crystallization of the product from abs. methanol (twice), gave the acetylenic ester **7** as colorless needles; yield 153 mg (43%), m.p. 132–133°, $[\alpha]_D^{25}$ −30 ±1° (*c* 1.9, chloroform) [lit.[15] m.p. 133.5–134.5°, $[\alpha]_D^{24}$ −31.5 ±1° (*c* 1.5, chloroform)]; λ_{max}^{KBr} 3.06 (C≡CH), 4.71 (C≡C), 5.78 (C=O), 6.15 (weak), 6.46, 6.86 (weak), 7.43, 7.83, 8.58, 9.34, 10.4, 11.8, and 13.9 μm.

The product gave an acceptable elemental analysis, and was identical with an authentic sample[15] of **7** by mixed m.p., comparative i.r. spectrum, and X-ray powder diffraction pattern.

*Methyl 3,4,6-tri-O-acetyl-2-deoxy-2-(N-nitroso)acetamido-β-*D*-glucopyranoside* (**11**). — To methyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranoside[7] (**9**, 1.810 g, 5.0 mmoles) and anhydrous sodium acetate (1.230 g, 15.0 mmoles) in dichloromethane (15 ml) at 0° was added dinitrogen tetraoxide (2.760 g, 1.86 ml, 30.0 mmoles) in dichloromethane (15 ml) during 5 min at 0°. After the mixture had been stirred for an additional 90 min at 0°, dichloromethane (15 ml) was added, and the mixture was purged with nitrogen for 1 h at 0°. The subsequent procedure for isolation was identical to that for the *N*-nitrosoamide **2**. The solvent was evaporated at 0° to give the pure *N*-nitrosoamide **11** as a syrup that spontaneously solidified; yield 1.820 g (92%). Recrystallization from ethanol–hexane gave **11** as large, yellow prisms, m.p. 87–88° (dec.) (lit.[8] m.p. 87.5–88.5°), $[\alpha]_D^{24}$ −38 ±1° (*c* 0.8, chloroform); R_F 0.81 (1:1 chloroform–ethyl acetate); λ_{max}^{KBr} 5.71 (C=O), 6.58 (N=O), 7.22, 7.32, 8.10 (doublet), 9.50 (broad), 10.70, and 11.05 μm; λ_{max}^{EtOH} 391 (ε 48), 407 (77), and 427 nm (79) [lit.[8] λ_{max} 393 (ε 53), 408 (84), and 428 nm (86)]; for n.m.r. data, see Table I; X-ray powder diffraction data: 10.39 vs (1), 9.02 w, 7.43 m, 6.91 vw, 6.46 s, 6.02 s, 5.50 w, 5.12 w, 4.79 vw, 4.50 w, 4.25 vw, 3.91 s, 3.75 w, 3.56 s, 3.41 w, 3.25 m, 3.15 m, and 2.99 m.

Anal. Calc. for $C_{15}H_{22}N_2O_{10}$: C, 46.15; H, 5.64; N, 7.17. Found: C, 46.16; H, 5.61; N, 7.06.

*Nitrosation of methyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-*D*-glucopyranoside*[9] (**10**). — The established procedure[1] for *N*-nitrosation was applied to compound **10** (903 mg, 2.5 mmoles). A yellow color developed, indicating formation of the nitrosoamide **12**, but the isolated product (710 mg) contained at least five components [R_F 0.66, 0.57 (major), 0.34, 0.18, and 0.00–0.07 (streak)] by t.l.c. (3:1 chloroform–ether). Evolution of gas was observed during the evaporation of the last traces of solvent, and an n.m.r. spectrum recorded on the resultant product in chloroform-*d* did not show a significant peak for the N(NO)Ac group at $\tau \sim 7.30$.

*Nitrosation of benzyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-*D*-glucopyranoside.* — The established procedure for *N*-nitrosation was applied to benzyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranoside[10] (656 mg, 1.5 mmoles). T.l.c. revealed at least 3 components in the product mixture [R_F 0.85 (major), 0.61–0.73 (minor), 0.39 (minor, starting material) with 1:1 chloroform–ethyl acetate]; λ_{max}^{film} 6.53 μm (N=O; this absorption disappeared immediately after the first scan); n.m.r. data (100 MHz, $CDCl_3$): τ 7.38 [N(NO)Ac; this singlet appeared as a weak signal, and disappeared as a result of decomposition at the probe temperature of ~40°]. Evolution of gas (presumably nitrogen) was observed in the n.m.r. tube.

After 12 h at ~25°, t.l.c. (1:1 chloroform–ethyl acetate) of the product mixture indicated a minimum of 5 components as a result of self-decomposition [R_F 0.90 (minor), 0.82 (major), 0.52–0.71 (streak, v. minor), 0.37 (minor), and 0.30 (minor)].

*Methyl 3,4,6-tri-*O*-methyl-2-(*N*-nitroso)acetamido-2-deoxy-β-(and α)-*D*-glucopyranoside.* — To methyl 2-acetamido-2-deoxy-3,4,6-tri-*O*-methyl-β-D-glucopyranoside[12] (277 mg, 1.0 mmole) and anhydrous sodium acetate (246 mg, 3.0 mmoles) in dichloromethane (5 ml) was added dinitrogen tetraoxide (675 mg, 0.45 ml, 7.3 mmoles) in dichloromethane (5 ml) during 5 min at 0°, and the mixture was stirred for 75 min at 0°. The subsequent procedure for isolation was identical to that for the *N*-nitrosoamide **2**. Evaporation of the solvent under high vacuum at 0° afforded a yellow syrup; yield 222 mg (73%); R_F 0.72 (1:1 chloroform–ethyl acetate), R_F 0.55 (3:1 chloroform–ether); λ_{max}^{film} 5.73 (C=O) and 6.52 μm (N=O); for n.m.r. data, see Table I.

Decomposition of the product in chloroform during 30 days at ~25° gave a minimum of 6 components, as indicated by t.l.c. [1:1 chloroform–ethyl acetate, R_F 0.60 (major), 0.52 (major), 0.35, 0.29, 0.09, and 0.00].

Application of the same *N*-nitrosation procedure to the α anomer[11] gave a yellow syrup, λ_{max}^{film} 6.60 μm (N=O). This i.r. absorption disappeared immediately after the first scan, indicating that the *N*-nitrosoamide was unstable. The syrup was allowed to warm to room temperature, to complete the decomposition, and g.l.c. then showed a minimum of eight components, T_R 0.05, 0.07, 0.09, 0.12, 0.16, 0.20, 0.25, and 0.32 (T_R relative to that of methyl 2-acetamido-2-deoxy-3,4,6-tri-*O*-methyl-α-D-glucopyranoside = 1.00, at 150°.)

*1,2,4,6-Tetra-*O*-acetyl-3-deoxy-3-(*N*-nitroso)acetamido-β-*D*-glucopyranose* (**13**). — To a stirred mixture of 3-acetamido-1,2,4,6-tetra-*O*-acetyl-3-deoxy-β-D-glucopyranose[13] (**12**, 973 mg, 2.5 mmoles) and anhydrous sodium acetate (615 mg, 7.5 mmoles) in dichloromethane (10 ml) at 0° was added dinitrogen tetraoxide[1,2] (1.38 g,

0.93 ml, 15 mmoles) in dichloromethane (10 ml) during 5 min at 0°. After the mixture had been stirred for an additional 2 h at 0°, dichloromethane (10 ml) was added, and the mixture was purged with nitrogen for 1 h at 0°. The procedure for isolation was similar to that described for the *N*-nitrosoamide **2**. Evaporation of the solvent at 0° gave the pure *N*-nitrosoamide **13** as a yellow syrup that spontaneously solidified; yield 925 mg (89%). Recrystallization from methanol–hexane–ether gave **13** as large, yellow prisms, m.p. 89–90°, $[\alpha]_D^{20}$ +11° (*c* 0.77, chloroform); R_F 0.75 (1:1 chloroform–ethyl acetate); λ_{max}^{KBr} 5.69 (C=O), 5.76 (C=O), 6.53 (N=O)[1,2,5], 7.33, 8.12, 8.24, 9.39, 9.72, 10.8, and 11.0 μm; λ_{max}^{EtOH} 390 (ε 46), 407 (75), and 426 nm (77); for n.m.r. data, see Table I; X-ray powder diffraction data: 8.93 m, 7.96 vw, 7.31 s (2), 6.75 w, 6.23 m, 5.15 vs (1), 4.62 s (3), 4.46 w, 4.33 m, 4.09 m, 3.93 m, 3.78 m, 3.69 s, 3.54 m, 3.37 w, 3.29 m, 3.21 m, 3.05 w, 3.00 w, 2.93 w, 2.87 w, 2.62 vw, 2.54 vw, 2.49 vw, 2.39 vw, and 2.33 vw.

Anal. Calc. for $C_{16}H_{22}N_2O_{11}$: C, 45.93; H, 5.30; N, 6.70. Found: C, 45.95; H, 5.38; N, 6.49.

*Methyl 2-acetamido-3,4,5,6-tetra-*O*-acetyl-2-deoxy-*D*-gluconate* (**15**). — A slurry of 2-amino-2-deoxy-D-gluconic acid[22] (**14**, 12.7 g, 65 mmoles) in dry methanol (100 ml) was saturated with hydrogen chloride. The resultant, hot solution was shaken vigorously for 10 min, and then concentrated to ~30 ml. Dry methanol was several times added to and evaporated from the solution to remove the excess of hydrogen chloride. A solution of the resulting syrup in dry pyridine (50 ml) and acetic anhydride (30 ml) was stirred overnight at room temperature, ice–water (500 ml) was added, and the solution was extracted with three 150-ml portions of dichloromethane. The extracts were combined, washed with water (200 ml), dried (magnesium sulfate), and evaporated to a thick syrup. Crystallization from methanol–ether (twice) gave **15** as colorless crystals; yield 14.7 g (54%) in two crops, m.p. 112–113°, $[\alpha]_D^{25}$ −15.8 ±0.3° (*c* 2.0, chloroform) [lit.[14] m.p. 113.5–114°, $[\alpha]_D^{23}$ −16.6° (*c* 1.0, dichloromethane)]; λ_{max}^{KBr} 2.95 (NH), 5.74 (broad), 5.79, 5.94, 6.53, 6.85 (weak), 6.99, 7.30, 7.62, 7.86, 8.07, 8.22, 8.71 (weak), 9.27, 9.60, and 10.4 μm; for n.m.r. data, see Table I.

Anal. Calc. for $C_{17}H_{25}NO_{11}$: C, 48.69; H, 6.01; N, 3.34. Found: C, 48.79; H, 5.82; N, 3.35.

The product gave an X-ray powder diffraction pattern identical with that of a sample previously isolated[14].

*Methyl 3,4,5,6-tetra-*O*-acetyl-2-deoxy-2-(*N*-nitroso)acetamido-*D*-gluconate* (**16**). — To compound **15** (2.514 g, 6.0 mmoles) and anhydrous sodium acetate (1.476 g, 18.0 mmoles) in dichloromethane (20 ml) at 0° was added dinitrogen tetraoxide[1,2] (3.31 g, 2.20 ml, 36 mmoles) in dichloromethane (20 ml) during 5 min at 0°, and the mixture was stirred for an additional 75 min at 0°. The procedure for isolation was similar to that described for the *N*-nitrosoamide **2**. Evaporation of the solvent at 0° gave the pure *N*-nitrosoamide **16** as a yellow syrup that spontaneously solidified; yield 2.477 g (92%). Recrystallization from methanol–hexane–ether gave **16** as large, yellow prisms, m.p. 108–109°, $[\alpha]_D^{23}$ +133.5° (*c* 1.65, chloroform); R_F 0.75 (1:1 chloroform–ethyl acetate); λ_{max}^{KBr} 5.68, 5.75, 6.65 (N=O)[1,2,5], 7.26, 7.69 (w), 7.80 (w), 8.06, 8.23,

8.80 (w), 9.30 (w), and 9.70 μm; λ_{max}^{EtOH} 3.87 (ε 47), 403 (83), and 422 nm (84); for n.m.r. data, see Table I; *m/e* (relative intensities and probable assignments given in parentheses): 418 (0.04, $M^{+} - \cdot NO$), 417 (0.1, $M^{+} - \cdot OMe$), 388 (0.03, $M^{+} - 60$), 376 (0.1), 375 (0.1, $M^{+} - \cdot CH_2OAc$), 362 (0.1), 361 (0.1), 360 (0.1), 346 (0.03), 334 (0.03), 327 (0.05), 318 (0.3), 302 (2.0), 216 (1.4), 200 (1.5), 187 (1.1), 173 (1.3), 158 (3.6), 145 (4.7), 129 (3.2), 115 (3.7), 103 (3.6), 97 (3.3), 85 (1.2), 73 (0.8), 60 (10), and 43 (100); X-ray powder diffraction data: 11.04 w, 7.89 s (2), 7.31 m, 6.83 s (1), 6.34 m, 5.82 s (3), 5.14 m, 4.80 w, 4.67 w, 4.05 w, 3.94 w, 3.71 m, 3.57 w, 3.42 w, 3.14 m, and 1.99 m.

Anal. Calc. for $C_{17}H_{24}N_2O_{12}$: C, 45.54; H, 5.39; N, 6.25. Found: C, 45.83; H, 5.39; N, 6.31.

Conversion of **16** *into 3,4,5-tri-*O*-acetyl-1,2-dideoxy-*D-erythro*-pent-1-ynitol* (**3**). — A mixture of **16** (448 mg, 1.0 mmole) with ether (50 ml) was stirred magnetically, and potassium hydroxide (280 mg, 5.0 mmoles) dissolved in isopropyl alcohol (10 ml) was added portionwise, with efficient stirring, during 1 h. The solvents were removed at ~35° under diminished pressure (15 min), and then pyridine (10 ml) and acetic anhydride (2 ml) were added, and the mixture was stirred for 12 h at ~25°. The subsequent procedure for isolation was similar to that for **3** obtained from the *N*-nitrosoamide **2**. A solution of the product in dichloromethane was passed through a short column of silica gel. Evaporation of the effluent gave crude **3**, yield 110 mg. T.l.c. revealed minute traces of unidentified materials having R_F 0.51 and 0.36 (3:1 chloroform–ether). Purification by the procedure described for the conversion of **2** into **3** gave 73 mg (30%) of **3**, identical with an authentic sample[1] by comparative i.r. and n.m.r. spectra.

ACKNOWLEDGMENTS

The authors thank Mr. S. J. Eitelman for recording the 100-MHz n.m.r. spectra, and Dr. J. D. Wander for helpful discussions.

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