Table I. Vertical Ionization Potentials (eV)[a] of **3, 4,** and **5**[b]

Cyclopentanone (**3**)	Cyclopenten-2-one (**4**)	Cyclopenten-3-one (**5**)
9.25 (710 and 1220 cm^{-1})	9.34 (663 cm^{-1})	9.44 (1423 cm^{-1})
11.3–15.3[c]	10.10 (1089 and 1417 cm^{-1})	9.98 (1204 cm^{-1})
15.94	11.9–15.3[c]	12.0–15.1[c]
16.56	16.23	16.22

[a] ±0.02 eV. [b] The vibrational spacings are given in parentheses, and are ±40 cm^{-1}. [c] Several ionization potentials measured from adiabatic onset.

cm^{-1} may be associated with the symmetric methylene group wagging or twisting modes which have been assigned in the 1150–1330-cm^{-1} region.[6]

The first ionization of **4** at 9.34 eV is assigned to removal of a n electron, and it has a vibrational spacing of 663 cm^{-1}. In **4**, the n level has been stabilized by 0.09 eV relative to the n level in cyclopentanone. This is probably due to the greater inductive effect of the two sp^2 carbons in **4**. The second band at 10.10 eV is assigned to ionization from a π level. The vibrational progressions of 1089 and 1417 cm^{-1} on this band are probably due to C=C and C=O stretching modes in the ion which occur at 1593 and 1720 cm^{-1} in the neutral molecule.[7] This IP is substantially higher than the π ionization in cyclopentene, 9.18 eV.[8] The inductive effect of the oxygen atom, the additional sp^2 carbon in the ring, and the interaction between the π_{CC} and π_{CO} levels would all tend to lower the π level in **4**. We can estimate the effect of replacing one sp^3 carbon with an sp^2 carbon in the following manner. The average of the two π IP's of cyclopentadiene is 9.66 eV,[8] and hence replacement of two sp^3 carbons with sp^2 carbons in a five-membered ring lowers the average π levels by 0.48 eV relative to cyclopentene. Therefore, the replacement of one sp^3 carbon with an sp^2 carbon should stabilize the π level by *ca.* 0.24 eV. The inductive effect of the oxygen atom is not expected to be large. Thus the dominant effect in the stabilization of the π level in **4** is the conjugative interaction between the π_{CC} and π_{CO} levels. At first this may appear surprising, since one might expect the interaction in an α,β-unsaturated carbonyl system to be analogous to a 1,3-diene where the highest π level is raised.[9] However, simple Hückel calculations[12] and more advanced treatments[13] indicate that, in the case of an α,β-unsaturated ketone, the π_{CC} level is in fact stabilized on conjugation with the π_{CO} levels.[14]

The first pe band of **5**[15] at 9.44 eV with a vibrational spacing of 1423 cm^{-1} is assigned to ionization from the n level which has been stabilized by 0.19 eV relative to **3**. The uv spectrum of **3** has a band at 3001 Å (4.13 eV) assigned to an n → π^* transition[16] and **5** has a band at 2850 Å (4.35 eV)[17] due to an n → π^* transition. Part of this hypsochromic shift of 0.22 eV *may* be ascribed to a stabilization of the n level in **5** rather than only to a shift in the π^* level, as was previously thought[12] (*vide infra*). The second band at 9.98 eV is assigned to ionization from a π level, mainly π_{CC}. Cyclopenten-3-one (**5**) has an ir band at 1605 cm^{-1} which is assigned to the C=C stretch. The corresponding spacing of 1204 cm^{-1} in the second IP of **5** agrees well with the values of 1320 and 1250 cm^{-1} in the π ionizations of cyclopentene[8] and ethylene,[18] respectively. This π_{CC}[14] level in **5** has an IP 0.80 eV greater than the corresponding level in cyclopentene. As in **4**, the most important contribution to this stabilization of the π_{CC} level no doubt is due to the resultant interaction of the π_{CC} with both π_{CO} levels. This interaction may occur directly through space[3,12] or through a σ_{CH_2} level of the appropriate symmetry.[3] If the replacement of an sp^3 carbon by an sp^2 carbon should stabilize the π_{CC} level by 0.24 eV (*vide supra*), then the π_{CC} stabilization due to the π interactions must be *ca.* 0.56 eV. This implies that the π_{CO}^* level has been destabilized.[19]

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(6) (a) C. Sablayrolles, L. Bardet, and G. Fleury, *J. Chim. Phys. Physicochim. Biol.*, **66**, 1139 (1969); (b) M. Rey-Lafon and M.-T. Forel, *Bull. Soc. Chim. Fr.*, 1145 (1967).

(7) H. N. A. Al-Jallo and E. S. Waight, *J. Chem. Soc. B*, 73 (1966).

(8) P. Bischof and E. Heilbronner, *Helv. Chim. Acta*, **53**, 1677 (1970).

(9) In butadiene the first π level IP occurs at 9.06 eV,[10] whereas the corresponding value in propylene is at 10.01 eV.[11]

(10) (a) C. R. Brundle and M. B. Robin, *J. Amer. Chem. Soc.*, **92**, 5550 (1970); (b) M. I. Al-Joboury and D. W. Turner, *J. Chem. Soc.*, 4434 (1964).

(11) D. C. Frost and J. S. Sandhu, to be published.

(12) E. I. Snyder and B. Franzus, *J. Amer. Chem. Soc.*, **86**, 1166 (1964).

(13) H. Suzuki, "Electronic Absorption Spectra and Geometry of Organic Molecules," Academic Press, New York, N. Y., 1967, p 438.

(14) These are not *pure* π_{CC} or π_{CO} levels in the conjugated systems, but are combinations of the two. Unfortunately, the π_{CO} IP in compounds **3–5** is obscured by the σ IP's. For example, the π_{CO} ionization in formaldehyde occurs at 14.09 eV: D. W. Turner, A. Baker, C. Baker, and C. R. Brundle, "Molecular Photoelectron Spectroscopy," Wiley-Interscience, New York, N. Y., 1970, pp 132–163.

(15) (a) H. M. Hess and H. C. Brown, *J. Org. Chem.*, **32**, 4138 (1967); (b) E. L. Allred, J. Sonnenberg, and S. Winstein, *ibid.*, **25**, 26 (1960).

(16) (a) E. M. Kosower and G.-S. Wu, *J. Amer. Chem. Soc.*, **83**, 3142 (1961); (b) A. Udvarhazi and M. A. El-Sayed, *J. Chem. Phys.*, **42**, 3335 (1965), and references therein.

(17) L. D. Hess and J. N. Pitts, Jr., *J. Amer. Chem. Soc.*, **89**, 1973 (1967).

(18) G. R. Branton, D. C. Frost, T. Makita, C. A. McDowell, and I. A. Stenhouse, *J. Chem. Phys.*, **52**, 802 (1970).

(19) We are grateful to the NRC of Canada for financial grants, to Professor C. A. McDowell for advice and encouragement, and to Mr. A. B. Cornford for invaluable experimental assistance. One of us (D. C.) is grateful to the SRC of Great Britain for the award of a NATO fellowship.

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Received June 10, 1971

Conversion of Natural Phthalideisoquinolines into Benzazepine Alkaloids

Sir:

We wish to report the successful conversion of the opium alkaloid nornarceine (**1**) into the benzazepine (±)-11-methyl-2,3-methylenedioxy-4,6,7,8-tetramethoxyrheadan[1] (**2**). Since **1** is derivable from the phthalide alkaloid (−)-α-narcotine[2] (**3**), the following reaction sequence[3] constitutes the first chemical transforma-

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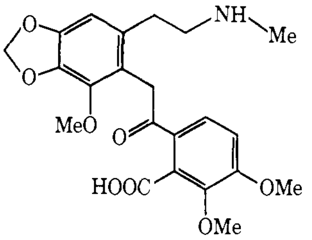
(1) The generic name rheadan is proposed for the basic tetracyclic structure common to rhoeadine and related alkaloids (T. Kametani, "The Chemistry of the Isoquinoline Alkaloids," Elsevier, Amsterdam, 1969, Chapter 14). Our proposal conforms with *Chemical Abstracts* practices and is exemplified by the numbering and lettering shown for the rheadan **2**. It is suggested that the term isorheadan be used when the 4b and 10b hydrogens are in a trans relationship.

(2) The original procedure of P. Rabe (*Chem. Ber.*, 40, 3280 (1907)) has been replaced by a new and improved method which will be reported in the full paper.

(3) The absolute configurations indicated in **2**, **7**, **8**, and **9** represent only one of the two possible enantiomers. All compounds gave acceptable elemental analyses.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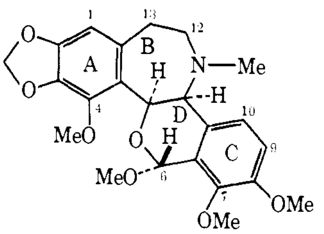
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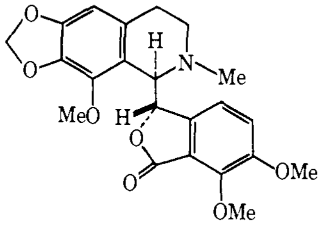
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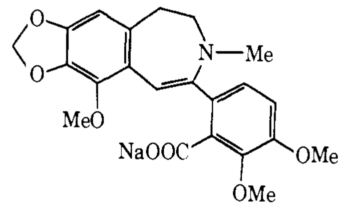
tion of a phthalideisoquinoline into a rheadan derivative.[4,5]

Treatment of nornarceine (**1**) with 2 *N* sodium hydroxide at 95° for 2 hr afforded the crystalline dihydrobenzazepine sodium salt **4** [84% yield; mp 190–195°; $\lambda_{\max}^{\mathrm{EtOH}}$ 210 (ϵ 51,400), 325 (10,600); $\delta^{\mathrm{D_2O}}$ 6.13 (s, vinyl proton)] whose structure was confirmed by an X-ray analysis of the corresponding rubidium salt as the dihydrate [monoclinic crystals, space group $P2_1/a$, $a = 13.065$, $b = 8.661$, $c = 20.659$ Å, $\beta = 92.07°$, $Z = 4$, $d_{\mathrm{obsd}} = 1.51$ g cm^{-3}, μ(Cu Kα) = 36.9 cm^{-1}; $R = 3.9\%$ (all atoms except hydrogens anisotropic)]. In contrast to mineral acid which regenerated **1**, acidification of an aqueous solution of **4** with acetic acid effected cyclization to the spiro lactone **5** [85% yield; mp 169–171°; $\nu_{\max}^{\mathrm{KBr}}$ 1760 cm^{-1}; $\delta^{\mathrm{CDCl_3}}$ 3.15, 3.44 (d, 2 H, CH_2, AB pattern, J = 15 Hz), 2.8–3.25 (m, 4 H, CH_2-CH_2)].

Oxidation of **5** was readily accomplished by exposing an ethanolic solution to air for 10 days to provide the keto lactone **6** [63% yield; mp 186–190°; $\nu_{\max}^{\mathrm{KBr}}$ 1760, 1710 cm^{-1}; Raman (4480 Å, powder) 1750 (vs), 1705 cm^{-1} (s); $\delta^{\mathrm{CDCl_3}}$ 2.8–3.22 (m, 4 H,CH_2CH_2)]. Reduction of **6** with lithium borohydride in tetrahydrofuran followed by neutralization with acetic acid afforded the cis hydroxy acid **7** [70% yield; mp 258–260°; $\nu_{\max}^{\mathrm{KBr}}$ 1690 cm^{-1} (carboxylate); $\delta^{\mathrm{NaOD,D_2O}}$ 4.93, 5.62 (d's, 2 H, J = <1 Hz)]. Treatment of **7** with dilute hydrochloric acid or acetic anhydride effected ring closure to the cis lactone **8** [85% yield; mp 218–220°; $\lambda_{\max}^{\mathrm{EtOH}}$ 292 (ϵ 3700), 308 (3650); $\nu_{\max}^{\mathrm{KBr}}$ 1735 cm^{-1}; $\delta^{\mathrm{CDCl_3}}$ 3.06, 5.90 (d's, 2 H, J = <1 Hz)].

Partial reduction of a pyridine solution of **8** at 4° with sodium bis(2-methoxyethoxy)aluminum hydride in a mixture of benzene and tetrahydrofuran afforded the 6-hydroxy rheadan **9** [62% yield; mp 224–226°; $\lambda_{\max}^{\mathrm{EtOH}}$ 282 (ϵ 3700); $\nu_{\max}^{\mathrm{KBr}}$ 3160 cm^{-1} (bonded OH); $\delta^{\mathrm{CDCl_3}}$ 3.84, 5.31 (d's, $H_{4b,10b}$, J = <1 Hz)] whose relative configuration was established by an X-ray analysis of the corresponding methiodide [monoclinic crystals, space group $P2_1/c$, $a = 8.941$, $b = 18.030$, $c = 15.370$ Å, $\beta = 107.16°$, $Z = 4$, $d_{\mathrm{obsd}} = 1.53$ g cm^{-3}, μ(Cu Kα) = 112.2 cm^{-1}; $R = 7.2\%$ (all atoms anisotropic, no hydrogens)]. Etherification of a suspension of **9** in methanol with trimethyl orthoformate catalyzed by sulfuric acid provided the desired 6-methoxy rheadan **2** [80% yield; mp 137–138°; $\lambda_{\max}^{\mathrm{EtOH}}$ 283 (ϵ 3800); $\delta^{\mathrm{CDCl_3}}$ 3.51, 5.89 (d's, $H_{4b,10b}$, J = 4.0 Hz), 5.79 (s, 1, H_6)] which could be reconverted into **9** with dilute hydrochloric acid at 25°.

This X-ray determination showing the cis relationship of the 4b and 10b hydrogens and the configuration at the 6 position supports the nmr evidence advanced by Šantavý and coworkers[6] and Shamma and Weiss,[7] respectively, for related rheadans.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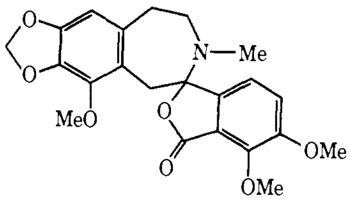
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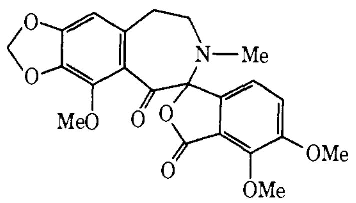
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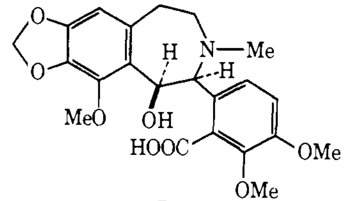
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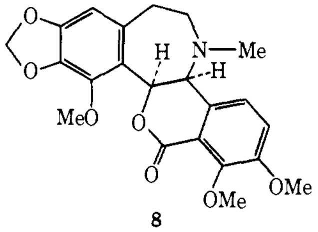
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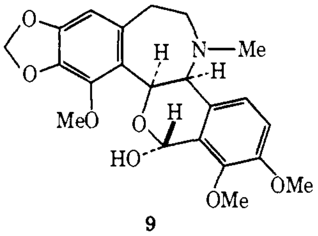
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The above transformations demonstrate a facile entry into the synthesis of the rheadan class of alkaloids. Studies are now in progress to prepare naturally occur-

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(4) The aromatic substitution pattern present in the rheadan derivative **2** has thus far not been found in nature. This suggests that the naturally occurring rheadans may not be biogenetically derived from the phthalide alkaloids.

(5) A partial synthesis of a (±)-rheadan utilizing a spiroisoquinoline derived from unnatural sources has been reported by H. Irie, S. Tani, and H. Yamane, *Chem. Commun.*, 1713 (1970).

(6) F. Šantavý, J. L. Kaal, L. Hruban, L. Dolejš, V. Hanuš, K. Bláha, and A. D. Cross, *Collect. Czech. Chem. Commun.*, **30**, 3479 (1965).

(7) M. Shamma and J. A. Weiss, *Chem. Commun.*, 212 (1968).

ring rheadans from appropriate phthalideisoquinoline alkaloids.

Acknowledgment. We are indebted to our Physical Chemistry Department, under the direction of Dr. R. P. W. Scott, for the spectral and analytical data. We are grateful to Mr. J. Borgese and Mrs. J. Cheung for technical assistance and to Professor G. Büchi, Massachusetts Institute of Technology, for fruitful discussions.

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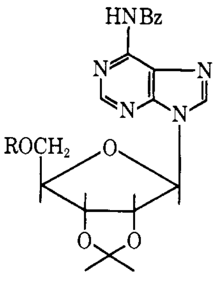
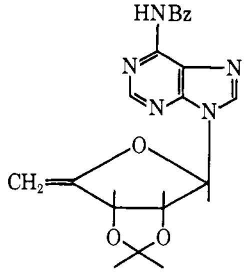
Synthesis of the Nucleoside Antibiotic Nucleocidin

Sir:

Nucleocidin, a fairly broad spectrum antibacterial and antitrypanosomal agent elaborated by *Streptomyces calvus*,[1] has been shown to have the structure 4'-fluoro-5'-*O*-sulfamoyladenosine (**8**) although the D-ribo configuration has never been unequivocally proved.[2] This structure is of particular interest since nucleocidin is the first naturally occurring derivative of a fluoro sugar. We now wish to report a synthesis of this compound which also confirms the proposed structure.

Reaction of N^6-benzoyl-2',3'-*O*-isopropylideneadenosine (**1a**)[3] with methanesulfonyl chloride gave the 5'-*O*-mesyl derivative **1b** which was not purified but rather directly treated with potassium *tert*-butoxide in tetrahydrofuran to give 6-benzamido-9-(5-deoxy-2,3-*O*-isopropylidene-β-D-*erythro*-pent-4-enofuranosyl)purine (**2**)[4] in a yield of 60% from **1a**: mp 151–153° (benzene); λ_{max}^{MeOH} 230 (ϵ 13,700), 279 nm (ϵ 21,400); nmr ($CDCl_3$) 4.53 (d, 1, J_{gem} = 2.5 Hz, $C_{5'a}H$), 4.67 (q, 1, J_{gem} = 2.5 Hz, $J_{3',5'b}$ = 1 Hz, $C_{5'b}H$), 6.31 (s, 1, $C_{1'}H$), 8.05 and 8.77 ppm (s, 1, C_2H and C_8H). Treatment of **2** with benzoyl chloride in pyridine gave the dibenzoyl olefin **3** as a homogeneous foam isolated by chromatography on silicic acid in 90% yield: $\lambda_{max}^{dioxane}$ 249 (ϵ 21,900), 276 nm (ϵ 16,900); nmr ($CDCl_3$) 4.49 (d, 1, J_{gem} = 2.5 Hz, $C_{5'a}H$), 4.64 (q, 1, J_{gem} = 2.5 Hz, $J_{3',5'b}$ = 1 Hz, $C_{5'b}H$), 6.33 (s, 1, $C_{1'}H$), 8.12 and 8.68 ppm (s, 1, C_2H and C_8H). The addition of iodine (4 equiv) to a vigorously stirred solution of **3** (1 equiv) in nitromethane, tetrahydrofuran, or methylene chloride in the presence of freshly ground silver fluoride (5 equiv) led to a mixture of the epimeric 5'-deoxy-4'-fluoro-5'-iodonucleosides **4** and **5** in a combined yield of 80–90%.[5,6] The ratio of the β-D-ribo (**4**) and α-L-lyxo (**5**) isomers varied between 3:2 and 1:9 depending upon the solvent, temperature, and rate of addition of iodine. Slow addition of solid iodine to a dilute solution of **3** in nitromethane at 0–10° gave good results. Separation of **4** and **5** was achieved by chromatography on a column of silicic acid using 2.5% acetone in chloroform and preparative tlc using 4% acetone in chloroform.


1a, R = H
b, R = SO_2Me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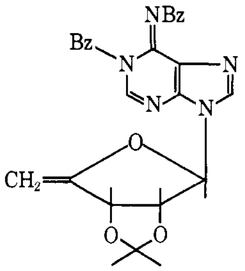
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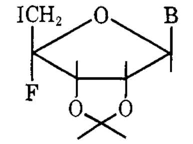
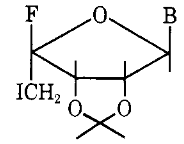
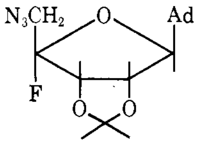

4a, B = N^1,N^6-Bz_2adenine
b, B = adenine


5a, B = N^1,N^6-Bz_2adenine
b, B = adenine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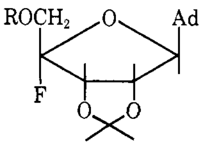
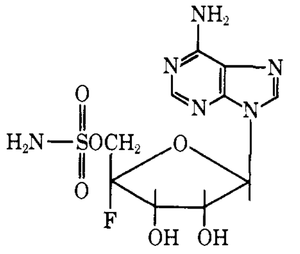

7a, R = H
b, R = $SnBu_3$
c, R = SO_2NH_2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The more polar β-D isomer (**4a**) was a homogeneous foam: $\lambda_{max}^{dioxane}$ 249 (ϵ 21,600), 275 nm (ϵ 17,000); ORD (dioxane) positive Cotton effect with $[\Phi]_{280}^{pk}$ +9700°, $[\Phi]_{248}$ 0°; $[\Phi]_{235}^{tr}$ −9800°; nmr $CDCl_3$ 5.41 (q, 1, $J_{2',3'}$ = 7 Hz, $J_{3'F}$ = 12 Hz, $C_{3'}H$), 6.35 (br s, 1, $J_{1',2'} \simeq$ 1 Hz, $C_{1'}H$), 8.15 and 8.67 ppm (s, 1, C_2H and C_8H). The less polar α-L-lyxo isomer **5a** was also a foam: $\lambda_{max}^{dioxane}$ 249 (ϵ 22,500), 275 nm (ϵ 17,900); nmr ($CDCl_3$) 5.08 (t, 1, $J_{2',3'}$ = $J_{3',F}$ = 5.5 Hz, $C_{3'}H$), 6.48 (q, 1, $J_{1',2'}$ = 0.5 Hz, $J_{1',F}$ = 2.5 Hz, $C_{1'}H$), 8.24 (br s, $W_{1/2}$ = 2 Hz, C_8H), 8.70 ppm (s, 1, C_2H). It is to be noted that the D-ribo isomer **4a** shows a larger $C_{3',F}$ coupling (trans) than does **5a** and that **5a** (but not **4a**) shows long-range coupling of the 4'-fluorine to both $C_{1'}H$ and one of the adenine ring protons (probably C_8H).[7] Confirmation of the structure of **4a** came from

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(1) (a) E. J. Backus, H, D. Tresner, and T. H. Campbell, *Antibiot. Chemother.*, 7, 532 (1957); (b) S. O. Thomas, V. L. Singleton, J. A. Lowery, R. N. Sharpe, M. Pruess, J. N. Porter, J. H. Mowat, and N. Bohonos, *Antibiot. Ann.*, 716 (1956–1957).

(2) G. O. Morton, J. E. Lancaster, G. E. VanLear, W. Fulmor, and W. E. Meyer, *J. Amer. Chem. Soc.*, **91**, 1535 (1969).

(3) S. Chladek and J. Smrt, *Collect. Czech. Chem. Commun.*, **29**, 214 (1964).

(4) All new compounds gave satisfactory elemental analyses and nmr spectra.

(5) Addition of iodine monofluoride to glycals is known to lead to glycosyl fluorides: see, *e.g.*, L. D. Hall and J. F. Manville, *Chem. Commun.*, 35 (1968).

(6) Satisfactory addition of iodine fluoride to **2** was also achieved, but in this case separation of the isomeric products was difficult.

(7) The nmr spectra of these compounds will be considered in detail in a later paper.