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(7) No loss in stereochemical integrity of C-8 was observed in either the formation or the hydrolysis of the ketal.
(8) Proton NMR, infrared, and high-resolution mass spectral data consistent with the proposed structures of all new compounds except **1a** were obtained.
(9) Dr. P. S. Stotter, University of Texas at San Antonio, has found that comparatively slow Baeyer–Villiger oxidations are accelerated by the presence of bicarbonate (private communication). In the present case, the rate is approximately doubled.
(10) Under identical conditions, the ketoolefin **7** underwent epoxidation to the exclusion of lactone formation.
(11) We are grateful to Professor Miles for an authentic sample and copies of the original spectra of sarracenin.
(12) In a separate series of experiments, the *exo*-methyl ketone **6** was converted to 8-episarracenin and in neither series was there a loss of stereochemical integrity at C-8.

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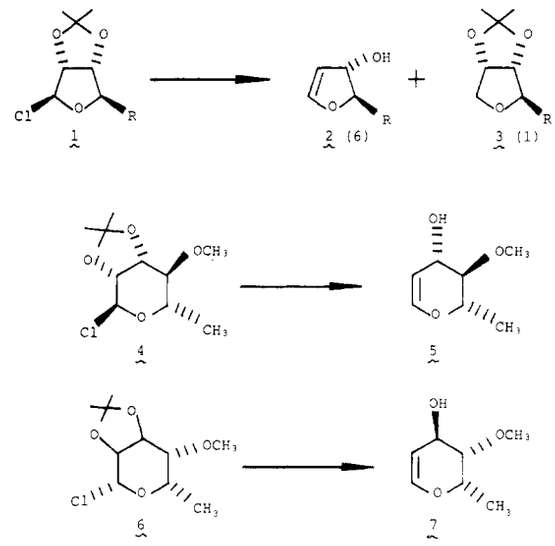
An Efficient Method for the Preparation of Furanoid and Pyranoid Glycals[1]

Summary: The reduction of furanosyl and pyranosyl halides with lithium–ammonia provides an efficient high yielding synthesis of furanoid and pyranoid glycals.

Sir: In connection with a synthetic program underway in these laboratories on the total synthesis of ionophores, it became necessary to prepare both furanoid and pyranoid glycals. While the total synthesis project is not yet complete, a recent report by Eitelman and Jordaan[2] on a similar, but not as efficient and general, method for the formation of furanoid glycals prompts us to report our results on this phase of the work now.

Glycals in general tend to undergo acid-catalyzed allylic rearrangement,[3] particularly as their C-3 hydroxyl derivatives. This tendency is most pronounced in the furanoid system where the C-3 carbon–oxygen bond of either epimer is more nearly coplanar with the π cloud of the enol ether double bond. In order to avoid this undesirable result, the C-3 oxygen substituent must be a poor leaving group[4] and the reaction conditions should be basic rather than acidic. For furanoid glycal formation, particularly, these considerations preclude the use of the classical Fischer–Zach method[5] for pyranoid glycal generation by zinc–acetic acid reduction of acetylated pyranosyl halides. The well-known fragmentation of β-alkoxyethyl halides on treatment with metals in inert solvents suggests a solution to this problem and the prospect for a general glycal formation procedure.

To test this possibility 2,3-*O*-isopropylidene-β-D-erythrofuranosyl chloride [**1**, R = H; mp 60–61.5 °C; $[\alpha]^{24}_D$ −167° ($HCCl_3$, *c* 0.8)] was prepared from D-erythronolactone in 79% overall yield by acetonide formation [CH_3COCH_3, $(CH_3)_2C(OCH_3)_2$, *p*-TSA] and partial reduction (DIBAL, Et_2O, −78 °C) to 2,3-*O*-isopropylidene-D-erythrose [mp 30–32.5 °C, $[\alpha]^{24}_D$ −79.3° ($HCCl_3$, *c* 0.925)] and then chloride formation



[CCl_4, THF, $(C_6H_5)_3P$]. Reduction of this furanosyl chloride **1** (R = H) with lithium in liquid ammonia (4 equiv of Li, NH_3, 2 h; 6 equiv of NH_4Cl; evaporate NH_3; extract Et_2O) resulted in a 60% yield of a 6:1 (NMR) mixture [evaporative distillation 60–70 °C (35 mmHg)] of the glycal **2** (R = H) and the tetrahydrofuran **3** (R = H) from hydride displacement without fragmentation. This mixture was not separated due to the lability of the glycal, and for most preparative purposes the presence of the tetrahydrofuran component is not deleterious.

Turning to the more functionalized pentose series D-ribonic acid δ-lactone was converted to its acetonide [CH_3COCH_3, $(CH_3)_2C(OCH_3)_2$, *p*-TSA, 12 h, room temperature], O-methylated at C-5 (Ag_2O, CH_3I, CH_3CN, 18 h, 50 °C), and then reduced (DIBAL, Et_2O, 1 h, −78 °C) to the blocked sugar [bp 82.5 °C (0.03 mmHg); $[\alpha]^{26}_D$ −18.75° ($HCCl_3$, *c* 1.68)] in 90% overall yield. Chloride formation (CCl_4, THF, $(C_6H_5)_3P$; 90%) resulted in the furanosyl chloride **1** [R = CH_2OCH_3; evaporative distillation 60–70 °C (0.03 mmHg); $[\alpha]^{27}_D$ −71° ($HCCl_3$, c = 1.80)] which on reduction with lithium in ammonia as above afforded a 75% yield of a 6:1 (NMR) mixture [evaporative distillation 80–90 °C (0.2 mmHg)] of the glycal **2** (R = CH_2OCH_3) and the corresponding tetrahydrofuran derivative[7] **3** (R = CH_2OCH_3). An analytical sample of the glycal **2** [R = CH_2OCH_3; $[\alpha]^{22}_D$ +318° ($HCCl_3$, *c* 0.83)] was obtained with significant material loss (70% recovery) by chromatography on silica gel or Florisil, and the mass spectrum of this monomeric glycal showed only methyl furfuryl ether (*m/e* calcd 112.053, found 112.052). Despite the lability of this furanoid glycal that results in poor recovery after purification, pure glycal is available by this procedure and in most instances the mixture itself may be used directly in subsequent synthetic transformations. These results contrast with those of Eitelman and Jordaan[2] who obtained similar furanoid glycals in no more than 11% yield together with significant amounts of dimeric products as a result of coupling when furanosyl bromides were reduced with sodium or potassium in dry tetrahydrofuran.

Application of this reduction procedure to the pyranose series was even more rewarding. By a similar series of blocking reactions starting with methyl α-L-rhamnopyranoside[8] and methyl 6-deoxy-α,β-L-gulopyranoside,[9] the pyranosyl chlorides **4** [evaporative distillation 95 °C (1.0 mmHg); $[\alpha]^{23}_D$ −114.5° ($HCCl_3$, *c* 1.56)] and **6** [evaporative distillation 65 °C (0.05 mmHg); $[\alpha]^{23}_D$ +45.3° ($HCCl_3$, *c* 1.23)] were prepared in 65 and 71% overall yields, respectively. Reduction of these halides with lithium in liquid ammonia as above led in 90% yields to the corresponding pyranosyl glycals **5** [mp 76–77 °C;

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$[\alpha]^{24}_D$ −0.24° ($HCCl_3$, c 1.25)] and **7** [evaporative distillation 95 °C (1.0 mmHg); $[\alpha]^{23}_D$ −121° ($HCCl_3$, c 1.43)]. In the pyran series only reductive fragmentation was observed and none of the products from direct hydride displacement was observed. While these glycals can be prepared by the Fischer–Zach method, the high yield of this process together with the generation of the glycal itself rather than the more labile ester derivative offers significant advantages. It should be noted that while the acetonide blocking group is used early in the synthetic sequence to achieve functional group selectivity, it is also a requisite of the lithium–ammonia reduction process and serves two useful roles.[10]

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(1) This work was made possible through a grant from the National Institutes of Health, Grant No. HL21367-01.
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(10) All new compounds had satisfactory microanalytical and spectral properties.

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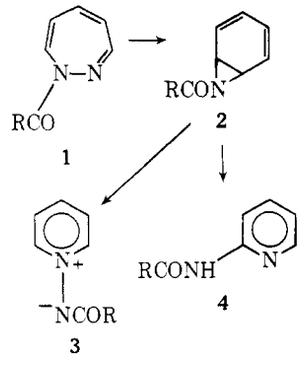
Heterocyclic Studies. 45. Thermal Isomerization of a 1,2-Diazepine to a 1,3-Diazepine

Summary: The 1,2-diazepine **5** at 110 °C gives a mixture of the 6-benzamidopyridine **6** and the 1-benzoyl-1,3-diazepine **7**.

Sir: 1-Acyl- and 1-alkoxycarbonyl-1,2-diazepines, readily available by photoisomerization of 1-iminopyridinium ylides,[1] undergo a variety of reactions on heating. 1-Benzoyl-1,2-diazepines[2] and 1-acyl-3,5,7-triaryldiazepines[3] give 1-acyliminopyridinium ylides **3**, and this path is also observed on treatment of 1-alkoxycarbonyl-1,2-diazepines **1** (R = OR′) in hot acetic acid.[4] 2-Aminopyridine derivatives **4** are formed in low yields, together with acyclic dienaminonitriles, on heating 1-alkoxycarbonyldiazepines at 150–170 °C neat or in refluxing



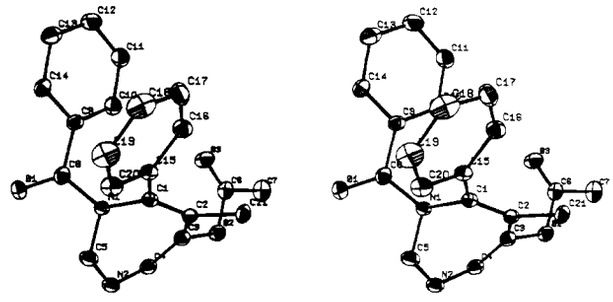
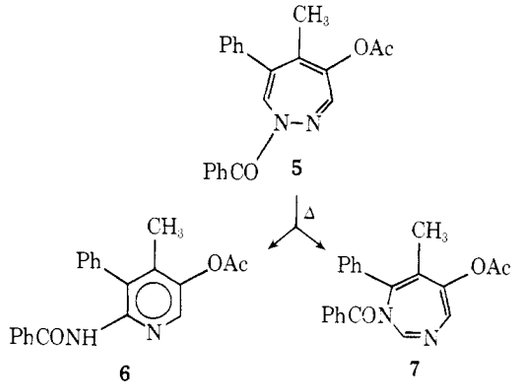


Figure 1. ORTEP stereoprojection of **7** (hydrogens omitted).

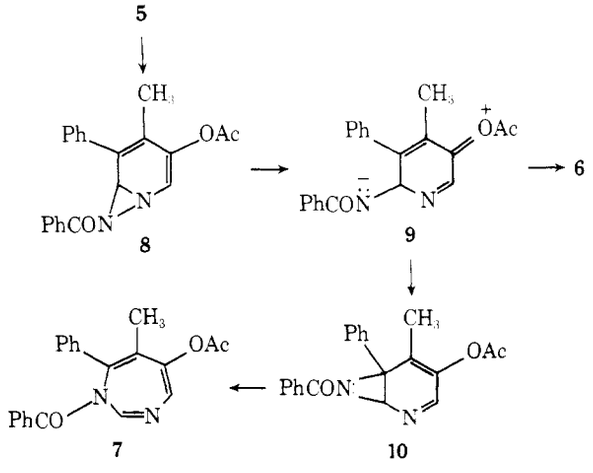
xylene.[4,5] The pyridine products from these reactions have been suggested to arise via 1,7-diazabicyclo[4.1.0]heptadiene valence isomers, but the factors that determine the product distribution are not well defined.

We have now found an additional pathway for the thermal isomerization of 1,2-diazepines. 1-Benzoyl-4-acetoxy-5-methyl-6-phenyl-1,2-diazepine (**5**), prepared by O-acetylation of the 1,5-dihydrodiazepinone,[6] undergoes a very facile thermal reaction to give the 3-acetoxy-6-benzamidopyridine **6** in 50% yield. A second product, isolated in 16% yield, is the 1-benzoyl-1,3-diazepine **7**, in which the positions of carbon and nitrogen in the seven-membered ring have been interchanged. Fully unsaturated 1,3-diazepines such as **7** are little known compounds, although the corresponding 1,3-oxazepines are well characterized.[7,8] The structure of **7** was established by x-ray crystallography.



Several other 1-acyl-4-acyloxydiazepines gave similar mixtures of products (as seen by NMR) on heating in chlorobenzene at 120 °C. In each case the 6-acylamido-3-acyloxypyridines were isolated and characterized as the major products; the minor products have not been isolated but are presumed to be the corresponding 1,3-diazepines.

Scheme I



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