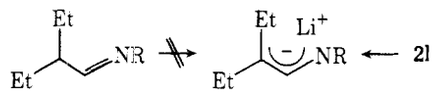
Transformation of the *N*-alkenylimine into the corresponding metalloenamine is readily performed by reaction of the former with *tert*-butyllithium. The efficiency of this process, as determined by trapping of the metalloenamine with various electrophiles, is illustrated by the entries in Table II. Several features of this tabulation are noteworthy. First, the overall yields are moderate to excellent, even in cases, such as entry 5, where the conjunction of a sterically encumbered nucleophile and electrophile is required in the alkylation step. Secondly, the process is regiocontrolled: imines **1c** and **1d** are converted into imines **6** (>99.5% VPC isomeric purity) and **7** (R = Me, >99.5% VPC isomeric purity), respectively, without evidence of crossover (i.e., metalloenamine equilibration). Similarly, imine **1e** regiospecifically provides the alkylated imine **8** (>99.5% VPC isomeric purity). By contrast, the metalloenamine generated in this process (**1e** → **8**) cannot be prepared from the corresponding methyl ketimine using conventional deprotonation, since such methodology is restricted to metalation "on the methyl group only".[4] Finally, the process is not subject to the steric constraints encountered in imine deprotonation. For example, Wittig[1b] reported that imine **12** (R = c-C_6H_{11}) was not deprotonated by lithium di-

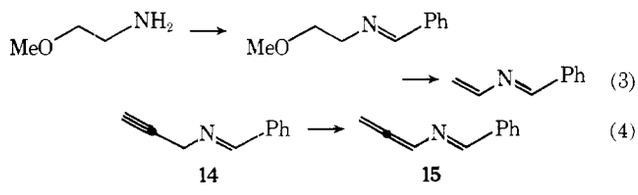


12 **13**

isopropylamide (2 h), tritylsodium, or tritylpotassium (for periods exceeding 4 weeks). Using the present method, the related metalloenamine **13** (R = CH(*t*-Bu)PhOMe-*p*) was efficiently generated from **2l** and converted to **11** (R = Bz) in an overall yield of 83% (isolated).

The *N*-allylic imines used in the present study were formed in >91% yield through condensation of the allylic amine[11] with benzaldehyde and converted to the corresponding metalloenamines using commercially available reagents. The following procedure is representative. Imine **1a** (16.5 mmol, ~1 M THF) was added to a solution of *t*-BuOK (3.4 mmol) in THF (42 mL). The resulting solution was stirred at ambient temperature (10 min), cooled to −78 °C, and transferred via cannula to a well-stirred solution (−78 °C) of *t*-BuLi (25 mmol) in pentane (14.8 mL). After 15 min, *n*-butyl iodide (33.5 mmol) was added. The resulting solution was stirred for 1 h at −78 °C, 1 h at ambient temperature, and treated with an equivalent volume of water. The mixture was extracted with methylene chloride and the combined organic phase was dried (Na_2SO_4) and concentrated. Distillation of the crude oil provided imine **4** (R = Bu, bp 119–129 °C (0.2 mm), 95%).[12] The alkylated imines are readily converted into the carbonyl derivatives by hydrolysis with 2 N hydrochloric acid or by distillative hydrolysis using aqueous oxalic acid.

In addition to the transformations of allylic imines and unsaturated imines into alkylated imines (and thence ketones and aldehydes) noted above, several further consequences of this chemistry are noteworthy. For example, the allylic imine isomerization involves a transient species which is functionally equivalent to a homoenolate. Thus, the method can be used to prepare β-deuteriocarbonyl derivatives (vide supra).[13] Furthermore, the imine functionality can be used to facilitate elimination reactions (eq 3) and, as such, this strategy can be employed as an alternative method for the preparation of alkenylimines.[14] Finally, in vitro analogy for suicide enzyme inhibition has been demonstrated in the conversion of propargylimine **14** into the novel allenylimine **15** (eq 4). Further studies are in progress.



14 **15**

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(7) For a review on this subject, see R. H. Abeles and A. L. Maycock, *Acc. Chem. Res.*, **9**, 313 (1976).

(8) The alkenylimines and alkylated imines prepared in this study gave IR and NMR data completely in accord with the assigned structures. The latter compounds were additionally characterized by conversion to the known carbonyl compounds, which were further characterized by transformation to previously reported derivatives.

(9) The *E* and *Z* isomers of the d_1 alkenylimine were formed in approximately equal amounts.

(10) In the case of **1g** isomerization gave exclusively the unsaturated imine as expected from the general preference for *endo*- over *exo*-olefin in such systems: A. H. Dickens, W. E. Hugh, and G. A. R. Kon, *J. Chem. Soc.*, 1630 (1928); J. C. Aumiller, and J. A. Whittle, *J. Org. Chem.*, **41**, 2959 (1976).

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(15) National Science Foundation Predoctoral Fellow, 1975–1977.

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Total Synthesis of (±)-Sarracenin

Summary: The synthesis of the iridoid monoterpene sarracenin is described.

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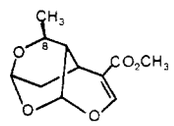
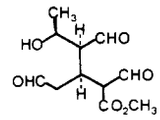
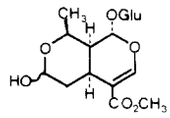
Sir: In 1976, Miles[1] reported the isolation and single-crystal x-ray structural determination of the monoterpene sarracenin (**1**), obtained from the roots and leaves of the insectivorous golden trumpet (*sarracenin flavia*) growing in the Okefenokee swamp. The structural similarity between sarracenin and other secoiridoid terpenes [e.g., morroniside (**2**)][2] is evident from inspection of the trialdehyde **1a** resulting from "unzipping" the novel bisacetal–enol ether system present in sarracenin.



1



1a



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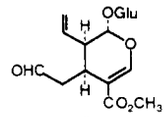
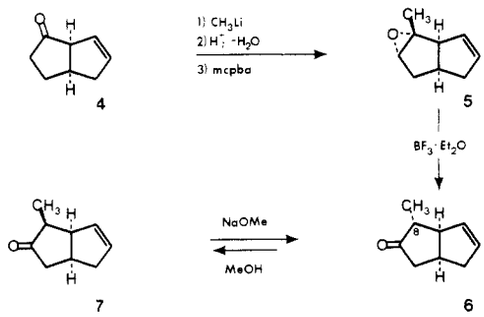


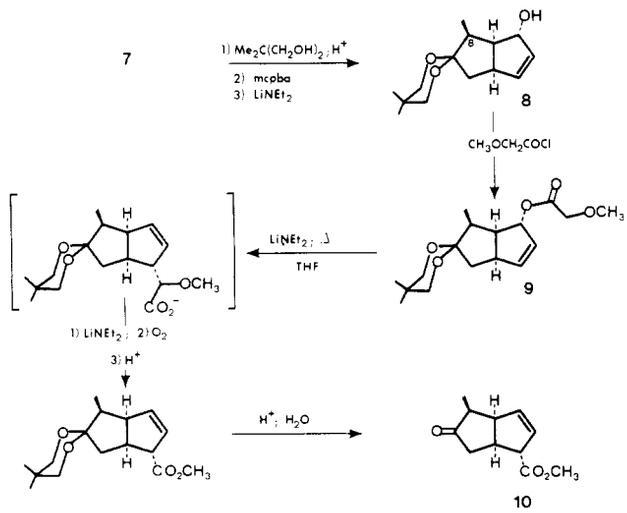
3

The biosynthetic pathway leading from mevalonic acid through the cyclopentanoid monoterpenes to the indole alkaloids has been traced as far as secologanin (**3**).[3] Miles has postulated that sarracenin may play an important role in this sequence by supplementing or possibly supplanting the route through secologanin. This hypothesis is intriguing in that sarracenin displays the same absolute configuration at C-8 (absent in secologanin) that is present in many of the indole alkaloids (e.g., reserpinine and ajmalicine). We thus undertook

Scheme I



Scheme II



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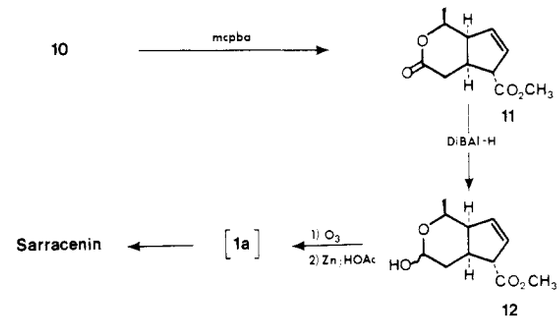
Scheme III



the total synthesis of sarracenin in order to set the stage for the preparation of radiochemically double-labeled material that could be used for feeding–incorporation studies.

We planned our synthetic strategy around the concept of sequentially cleaving both rings of an appropriately constituted bicyclo[3.3.0]octyl skeleton, ultimately forming the trialdehyde **1a** (as some cyclic, hemiacetal form).[4] The sequence outlined in Scheme I was used to refunctionalize the left-hand ring of the readily available bicyclic ketone **4** in preparation for eventual oxidative cleavage.[5] The methyl ketone **6** obtained from the rearrangement of epoxide **5** had predominantly the incorrect relative stereochemistry at C-8; however, equilibration with base gave a 1.3:1 exo/endo mixture from which the desired endo-isomer **7** was easily separated using a Waters Prep 500 System liquid chromatograph.

The regioselective introduction of the allylic carbomethoxy group was accomplished as outlined in Scheme II.[6] Regiospecific formation of the allylic alcohol **8** was accomplished, after protection of the carbonyl group as the ketal,[7] via a dialkylamide initiated rearrangement of the epoxide.[8] The new carbon–carbon bond was then established by an ester enolate Claisen rearrangement of the α-methoxyacetate **9.** Oxidation of the resulting carboxylate as the dianion using molecular oxygen followed by decarboxylation–dehydration removed the superfluous carbon and produced the desired carbomethoxy group. The entire sequence from ketone **7** to ketone **10** was carried out with an overall yield of 25%.

Baeyer–Villiger oxidation of ketone **10** with *m*-chloroperbenzoic acid in methylene chloride in the presence of heterogeneous bicarbonate[9] proceeded cleanly and afforded the lactone **11** essentially uncontaminated by epoxides (Scheme III).[10] Partial and selective reduction of the lactone carbonyl, accomplished with diisobutylaluminum hydride, afforded the crude lactol **12** as mixture of anomers in 72% yield. Without purification, **12** was subjected to ozonolytic cleavage followed by reduction with zinc in acetic acid. Dehydrative cyclization of the penultimate intermediate **1a** was accomplished simply by warming the acetic acid solution resulting from reduction of the ozonide. After chromatographic purification, racemic sarracenin was obtained in 15% yield with mp 107–108 °C (mp 127–128 °C dec for the (−)-enantiomer) and with infrared, ^{1}H and ^{13}C nuclear magnetic resonance, and mass spectral data identical with authentic material.[11,12] We are proceeding now with the preparation of optically active sarracenin as well as radiochemically labeled material.

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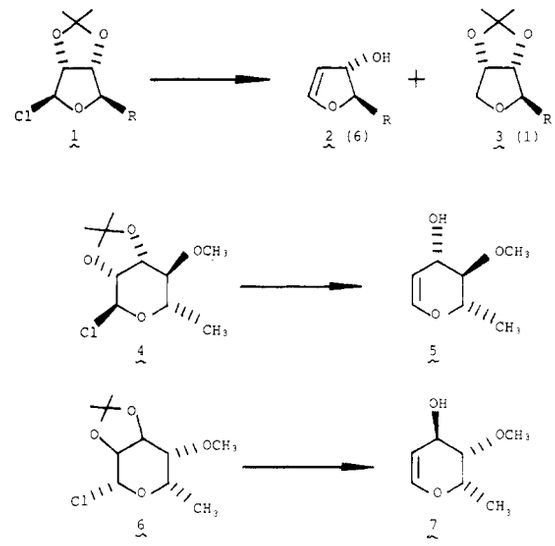
An Efficient Method for the Preparation of Furanoid and Pyranoid Glycals[1]

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;

0022-3263/78/1943-0786$01.00/0