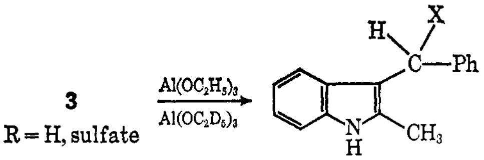
Scheme IV



9a, X = H
b, X = D

obtained in 10–15% yield[10] when the free base of **3**, prepared in methylene chloride with triethylamine under a stream of nitrogen, was heated with freshly prepared aluminum alkoxide in methylene chloride for 30 min. The solvent was then replaced by toluene and refluxed for several hours. The formation of acetaldehyde in the case of aluminum ethoxide was proved using the 2,4-dinitrophenylhydrazone. Further evidence for the hydrogen transfer from the ethanol was demonstrated by the reduction of **3** with deuterated aluminum ethoxide[11] under similar reaction condition. 3-Benzyl-2-methylindole (**9b**) obtained by using deuterated aluminum ethoxide showed the presence of a deuterium at the benzylic position by nmr ($\delta_{\text{TMS}}^{\text{CDCl}_3}$ 2.30 (s, 3 H), 4.00 (s, 1 H)) and mass spectra (*m/e* 222 (M^+)). The deuterated acetaldehyde was obtained as its 2,4-dinitrophenylhydrazone, mp 150–152°, *m/e* 228 (M^+), 227, 226, 225. Although the yield of the reaction was low, the results support the dehydrogenase mechanism proposed by Schellenberg. It is interesting to note that the conjugated double bond has been reduced by aluminum alkoxides.

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[10] Crystalline by-products were obtained from the reaction mixture; none of them was found to be a biindolylmethane derivative. The details will be reported in a full paper.

[11] The reagent was prepared from ethanol-d_6 and aluminum thin foil following the procedure in A. H. Blatt, "Organic Syntheses," Coll. Vol. 2, John Wiley & Sons, Inc., New York, N. Y., 1943, p 598.

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Miserotoxin, a New Naturally Occurring Nitro Compound

Sir:

Livestock poisoning due to the ingestion of various *Astragalus* (Leguminosae) species (locoweeds, poison vetches) has been known for many years. These plants can be divided[1] into three groups based upon fundamentally different properties: (1) selenium toxicity caused by selenium accumulation, (2) the chronic, true "loco" symptoms particularly observed with horses, and (3) an acute poisoning caused by several botanically related species and typified by that due to timber milkvetch (*Astragalus miser*).

We report here the isolation and characterization of miserotoxin, the first isolated poison from the third group of plants.

Above-ground parts of *A. miser* Dougl. var. *oblongifolius* (Rydb.) Cronq., collected near Logan, Utah, were dried and ground, and the powder was extracted with hot ethanol. The ethanol solution was cooled and decanted from a solid residue. The ethanol was evaporated to dryness and the residue was dissolved in water and washed several times with chloroform and then with *n*-butyl alcohol. The resulting aqueous solution was purified by automatic countercurrent distribution between water and *n*-butyl alcohol. All fractions were tested by chick bioassay[2] and the only poisonous material was found to be concentrated in several consecutive fractions. Only the poisonous fractions gave a positive test[2] for a nitro group and gave identical nmr spectra. These fractions were combined to give a homogeneous oil (dubbed miserotoxin), $[\alpha]^{25}\text{D}$ −22° (*c* 2.0, H_2O), corresponding to about 3% by weight of the dried plant material. All attempts at crystallization of miserotoxin failed.

The 60-MHz nmr spectrum (in D_2O with added DCl to displace the HDO peak) showed a quintet (2 H, J = 6 cps, $\text{-CH}_2\mathit{CH}_2\text{CH}_2\text{NO}_2$) centered at 2.34 ppm (from external TMS), a triplet (2 H, J = 6 cps, $\text{-}\mathit{CH}_2\text{-NO}_2$) at 4.68 ppm, and a doublet (1 H, J = 7.5 cps, anomeric α proton of a pyranose sugar) at 4.51 ppm. Double irradiation[3] at 100 MHz of the quintet reduced the triplet to a singlet, and irradiation of the triplet reduced the quintet to a triplet. The only other absorptions were in the 3.0–4.2-ppm range, and the complex multiplet was not successfully analyzed even at 100 MHz. The mass spectrum of miserotoxin did not show an identifiable molecular ion, but mainly showed fragments explicable as arising from a glucopyranose derivative. However, a high-resolution mass spectrum[4] identified a large *m/e* 88 peak as $C_3H_6NO_2$, which, along with the above nmr analysis, the chemical tests, and an infrared spectrum showing typical NO_2 group absorptions at 1380 and 1520 cm^{-1}, indicated the presence of a $\text{-CH}_2\text{CH}_2\text{CH}_2\text{NO}_2$ group in miserotoxin. Miserotoxin thus appeared to be a β-D-glucoside of 3-nitro-1-propanol. However, treatment of miserotoxin with acetic anhydride and sodium acetate produced in high yield a hexaacetyl derivative (mol wt 519, $C_{21}H_{29}NO_{14}$, by mass spectrum[4]) rather than the expected tetraacetate. Studies on model primary nitro compounds showed, however, that oxidative diacetylation of such compounds is in general a high yield reaction,[5] and hence all data now indeed point to I as the structure of miserotoxin. The correctness of this conclusion was proven by hydrolysis of miserotoxin to D-glucose (identified by nmr, tlc, and an osazone derivative) and 3-nitro-1-propanol (identified by comparison with an authentic sample synthesized from 3-bromo-1-propanol). Oral treatment of a 140-kg calf with 8 g of

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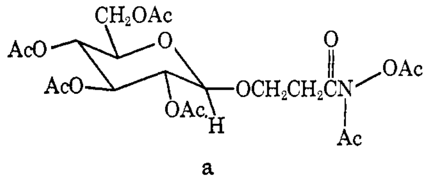
[1] J. M. Kingsbury, "Poisonous Plants of the United States and Canada," Prentice-Hall, Inc., Englewood, Cliffs, N. J., 1964, p 306.

[2] M. C. Williams and F. A. Norris, *Weed Sci.* **17**, 236 (1969).

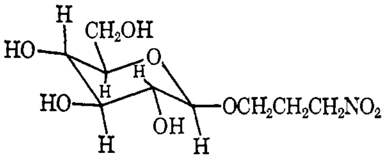
[3] We are indebted to Dr. D. A. Nelson of the University of Wyoming for performing this experiment.

[4] High-resolution spectra were obtained from the Purdue Mass Spectrometry Center which is supported under U. S. Public Health Service Grant FR-00354.

[5] Thus, 1-nitropropane is converted readily to $\text{CH}_3\text{CH}_3\text{CON(OAc)(Ac)}$ and miserotoxin to a. This reaction will be discussed more fully elsewhere.



a



I

3-nitro-1-propanol (which would correspond to a toxic dose of the original plant material) caused death with symptoms identical with those of *A. miser* poisoning.[6] Miserotoxin was rapidly metabolized to 3-nitro-1-propanol in livestock rumen fluid.[7]

Miserotoxin is a new addition to the small number of known aliphatic nitro compounds and is most closely related to the endecaphyllins,[8] which are glucose derivatives of 3-nitropropanoic acid (hiptagenic acid) and are constituents of *Indigofera* (Leguminosae) species. We did not find 3-nitropropanoic acid or any of its derivatives in *A. miser*, although the structural closeness to miserotoxin and 3-nitro-1-propanol might indicate a similar biogenesis.[9]

(6) M. C. Williams, K. R. Van Kampen, and F. A. Norris, *Am. J. Vet. Res.*, in press.

(7) M. C. Williams, F. A. Norris, and K. R. Van Kampen, *ibid.*, in press.

(8) A. Cooke, *Arch. Biochem. Biophys.*, **55**, 114 (1955); R. A. Finnegan and W. H. Mueller, *J. Pharm. Sci.*, **54**, 1136 (1965); R. A. Finnegan and R. A. Stephani, *ibid.*, **57**, 353 (1968).

(9) P. D. Shaw and J. A. McCloskey, *Biochemistry*, **6**, 247 (1967); P. D. Shaw, *ibid.*, **6**, 2253 (1967).

(10) National Aeronautics and Space Administration Predoctoral Fellow.

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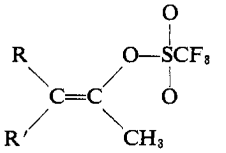
Preparation and Solvolysis of Vinyl Trifluoromethanesulfonates. I. Evidence for Simple Alkylvinyl Cation Intermediates

Sir:

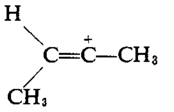
Few vinyl cations have been generated by direct solvolysis of suitable vinyl precursors, and in each known case either an aromatic ring,[1] a neighboring double bond,[2] or a cyclopropyl ring[3] was attached to the carbon bearing the leaving group, resulting in delocalization and special stabilization of the cation observed. We wish to report the preparation and solvolysis of vinyl trifluoromethanesulfonates (triflates) and present evidence for a simple alkylvinyl cation intermediate.

Recently, Peterson and Indelicato reported the first preparation and investigation of cyclic and acyclic alkylvinyl arenesulfonates.[4] However, both the cyclohexenyl and the *cis*-2-buten-2-yl sulfonates were found to react in formic acid *via* an addition–elimination mechanism rather than unimolecular ionization and vinyl cations. Furthermore, the *cis*-2-buten-2-yl tosylate and brosylate were found to be unreactive in 50% aqueous methanol at 59.8° for 18 days. It therefore seems that even such excellent leaving groups as a tosylate and brosylate are unreactive when attached to a trigonal carbon substituted with only alkyl groups. Yet there is no reason to believe that simple alkylvinyl cations are inherently unstable; gas-phase data indicate that the heat of formation of $CH_3CH{=}CH^+$ is in between those of methyl and ethyl cations.[5] Since trifluoromethanesulfonates are known to be at least 10^4–10^5 more reactive[6] under solvolytic conditions than the corresponding arenesulfonates, we undertook an investigation of the preparation and reactivity of the alkylvinyl triflates.

Addition of an equimolar amount of trifluoromethanesulfonic acid to methylacetylene at −78° and subsequent warming to room temperature in a sealed tube afforded, upon distillation, isopropenyl triflate (**1**): 60–80% (bp 25–27° (12 mm)), nmr (CCl_4) δ 2.03 (s, 3, CH_3), 4.88 (m, 1), 5.00 (d, 1). Addition to allene gave the identical product. Addition[7] to dimethylacetylene gave a two-component product (bp 36–37° (12 mm)) in a 65:35 ratio, which was readily separated by preparative gas chromatography (5 ft × 0.25 in., 15% FFAP, 40°) into the *trans* isomer **2** [nmr (CCl_4) δ 1.31 (doublet of quartet, 3, CH_3), 1.66 (broad quintet, 3, CH_3), 4.98 (quartet of quartet, 1, H)] and the *cis* isomer **3** [nmr (CCl_4) δ 1.22 (doublet of quartet, 3, CH_3), 1.68 (multiplet, 3, CH_3), 5.27 (quartet, 1, H)], respectively.[8]



1, R = R′ = H
2, R = CH_3; R′ = H
3, R = H; R′ = CH_3



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The rates[9] of solvolyses of vinyl triflates **1** through **3** are summarized in Table I. Compound **2** in 80% aqueous ethanol at 76° gave 98 ± 3% dimethylacetylene as the only product, measured by gas chromatography utilizing an internal standard; the *cis* isomer **3** at 100° gave 58% dimethylacetylene, 33% 2-butanone, and

(1) C. A. Grob and G. Cseh, *Helv. Chim. Acta*, **47**, 194 (1964); G. Cappozzi, G. Melloni, G. Modena, and M. Piscitelli, *Tetrahedron Letters*, 4039 (1968); L. L. Miller and D. A. Kaufman, *J. Am. Chem. Soc.*, **90**, 7282 (1968).

(2) C. A. Grob and R. Spaar, *Tetrahedron Letters*, 1439 (1969).

(3) S. A. Sherrod and R. G. Bergman, *J. Am. Chem. Soc.*, **91**, 2115 (1969); M. Hanack and T. Bässler, *ibid.*, **91**, 2117 (1969).

(4) P. E. Peterson and J. E. Indelicato, *ibid.*, **90**, 6515 (1968).

(5) J. L. Franklin, "Carbonium Ions," Vol. I, G. A. Olah and P. von R. Schleyer, Ed., Interscience Publishers, New York, N. Y., 1968, pp 85–88.

(6) (a) A. Streitwieser, Jr., C. L. Wilkins, and E. Kiehlmann, *J. Am. Chem. Soc.*, **90**, 1598 (1968); (b) P. von R. Schleyer, T. M. Su, and W. Sliwinski, *ibid.*, in press.

(7) In analogy to similar electrophilic additions to triple bonds (R. C. Fahey, in "Topics in Stereochemistry," Vol. 3, E. Eliel and N. L. Allinger, Ed., Interscience Publishers, New York, N. Y., 1968), this reaction probably proceeds *via* vinyl cations, although this has not yet been investigated.

(8) Stereochemistry was assigned on the basis of chemical shifts and coupling constants. In the *trans* isomer **2**, the vicinal coupling is J = 7.4 Hz and the long-range coupling between the two methyl groups is J = 1.6 Hz and between the hydrogen and methyl is J = 1.1 Hz; in the *cis* isomer **3**, the values are J = 7.6 Hz, J = 1.3 Hz, and $J \leqq 1$ Hz, respectively. See S. Sternhell, *Rev. Pure Appl. Chem.*, **14**, 15 (1964), and G. P. Newsoroff and S. Sternhell, *Tetrahedron Letters*, 6117 (1968), for long-range allylic coupling in substituted ethylenes.

(9) Rates were determined in duplicate or triplicate either conductometrically or by titration with NaOH using phenolphthalein as an indicator. In all cases good first-order rates were observed for more than 90% reaction.