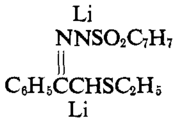
Table II. Deuterium Exchange of Lithium Salts of Tosylhydrazones in Ethylene Glycol-d_2 and in Tetrahydrofuran–D_2O

Tosylhydrazone of	Temp, °C	Time, hr	Number (percentage) of deuterium atoms incorporated
Acetone[a]	71	6.3	0 (5), 1 (17), 2 (31), 3 (30), 4 (17), 5 (<1)
Cyclopentanone[a]	71	6.3	0 (32), 1 (37), 2 (22), 3 (8), 4 (1)
Cyclohexanone[a]	71	6.3	0 (5), 1 (17), 2 (13), 3 (30), 4 (17), 5 (<1)
Diisopropyl[b] ketone	30	115	0 (94), 1 (6), 2 (<1)

[a] Pure lithium salt (0.01 mole) was heated with ethylene glycol-d_2 (0.09 mole, >99% d_2); the tosylhydrazone was regenerated with equivalent amounts of D_2SO_4, converted to its lithium salt by reaction with butyllithium in ether, and pyrolyzed dry to hydrocarbons which were analyzed mass spectrometrically at low voltages. [b] This tosylhydrazone was exchanged in tetrahydrofuran (50 ml)–99.7% D_2O (0.30 mole).

what the details of the mechanics of reaction of excess butyllithium with sulfonylhydrazones are, what we wish to emphasize at present is that sulfonylhydrazones undergo facile deuterium exchange of their α-hydrogens, and such methods in conjunction with decomposition of sulfonylhydrazones *via* cationic, carbenic, and α-elimination processes should be valuable for synthesis of deuterated compounds.



$$\begin{array}{c} \text{Li} \\ \text{NNSO}_2\text{C}_7\text{H}_7 \\ \| \\ \text{C}_6\text{H}_5\text{CCHSC}_2\text{H}_5 \\ \text{Li} \end{array}$$

V

Lithium and sodium salts of aldehyde *p*-tosylhydrazones decompose efficiently at reduced pressures to pure primary diazoalkanes.[7] Salts of *p*-tosylhydrazones of unbranched ketones decompose at higher temperatures than those of aldehydes, and the secondary diazo compounds formed do not survive (~5%) pyrolysis.[7] It has now been found that (1) the decomposition temperatures of lithium salts of *p*-tosylhydrazones as solids, in suspension or in solution, are considerably lower than those of sodium salts, and (2) salts of *p*-tosylhydrazones of α-substituted ketones decompose at lower temperatures (30–40°) than do their unsubstituted analogs. It is now possible to convert lithium salts of *p*-tosylhydrazones of ketones such as 3-methyl-2-butanone and 3,3-dimethyl-2-butanone to 2-diazo-3-methylbutane and 2-diazo-3,3-dimethylbutane in 90–95% yields and >98% purity by vacuum pyrolysis. Highly unstable and involatile diazo compounds such as 2-diazo-1-phenylpropane and 2-diazo-1,3-diphenylpropane can now be prepared by the pyrolytic method at 80–120°. It is suggested that the lower decomposition temperatures of salts of *p*-tosylhydrazones of substituted ketones result primarily from *cis* strain release in conversion to products containing the linear diazo function.

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Received September 5, 1967

glycol-d_2 is being investigated kinetically to determine if sulfonylhydrazone dianions are being generated under these conditions.

(7) G. M. Kaufman, J. A. Smith, G. G. Vander Stouw, and H. Shechter, *J. Am. Chem. Soc.*, 87, 935 (1965).

The Structure of Monensic Acid, a New Biologically Active Compound

Sir:

We wish to report the structure of a biologically active compound produced by a new strain of *Streptomyces cinnamonensis*. This compound, which has been named monensic acid,[1] is a potent inhibitor of alkali metal cation transport into rat liver mitochondria[2] and has broad-spectrum anticoccidial activity.[3]

Monensic acid ($C_{36}H_{62}O_{11}$, mol wt 670)[4] has mp 103–105°, $\nu_{\max}^{CHCl_3}$ 3236 (OH) and 1695 cm^{-1} (C=O), pK_a' = 6.65 (66% DMF), and exhibits no ultraviolet absorption maximum above 210 mμ. The 1695-cm^{-1} band, attributed to the carboxyl group, moved to 1563 cm^{-1} in the sodium salt. The nmr spectrum[5] indicated the presence of a single methoxyl group at δ 3.37 ppm. The acid and its alkali metal salts are only slightly soluble in water (*ca.* 0.1 mg/ml), but are soluble in most organic solvents.

Monensic acid formed a diacetate ($C_{40}H_{66}O_{13}$),[6] pK_a' = 7.60 (66% DMF), $\nu_{\max}^{CHCl_3}$ 3448 (OH) and 1727 cm^{-1} (C=O) with acetic anhydride–pyridine. Treatment of the diacetate with diazomethane in ether gave a crystalline methyl ester ($C_{41}H_{68}O_{13}$, calcd mol wt, 768; found, *m/e* 768), mp 113–114°, $\nu_{\max}^{CHCl_3}$ 3546 (OH) and 1724 cm^{-1} (C=O). That a primary and a secondary hydroxyl had been acetylated was inferred from the presence of an AB quartet centered at δ 4.08 ppm and a partially resolved multiplet at δ 4.72 ppm. Monensic acid reacted with 1 mole of periodate to yield formaldehyde as one of the products. The deshydroxymethyl oxidation product, obtained as an amorphous solid, upon acetylation (acetic anhydride–pyridine) and treatment with diazomethane gave a crystalline monoacetyl methyl ester ($C_{38}H_{62}O_{11}$, calcd mol wt, 694, found, *m/e* 694), mp 130.5–132.5°, $\nu_{\max}^{CHCl_3}$ 1724 cm^{-1} (C=O), partially resolved multiplet at δ 4.72 ppm.

These results suggested that monensic acid contained vicinal primary and tertiary hydroxyl groups and an isolated secondary hydroxyl group, which together with the carboxyl and methoxyl groups accounted for six of the eleven oxygen atoms. The remaining five were assumed to be present as ethers. Since no double

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(1) A detailed report of the discovery and isolation of monensic acid will be published by M. E. Haney, Jr., and M. M. Hoehn.

(2) S. Estrada-O., B. Rightmire, and H. Lardy, to be published.

(3) R. F. Shumard and M. E. Callender, to be published.

(4) The molecular formula of monensic acid is derived from the high-resolution mass spectrum of its sodium salt: calcd mol wt for $C_{36}H_{61}O_{11}Na$, 692.41117; found, *m/e* 692.41375. Mass spectra of the free acid typically exhibit no peak for the molecular ion. The highest mass peak (*m/e* 634) corresponds to the loss of two molecules of water.

(5) The nmr spectra were recorded in $CDCl_3$ solution with TMS as the internal reference unless indicated otherwise.

(6) Satisfactory elemental analyses were obtained for all compounds whose molecular formulas are given.

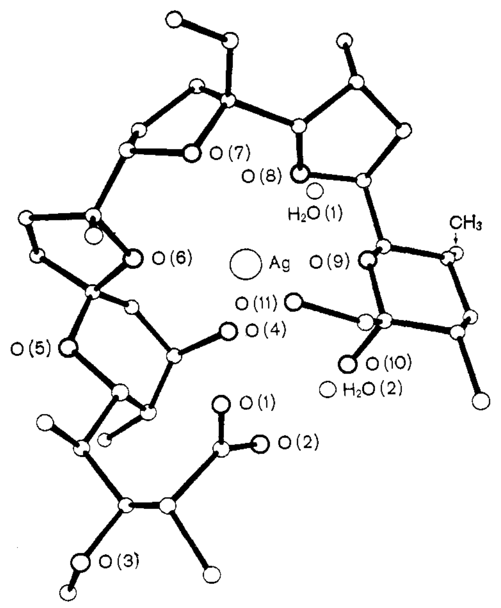
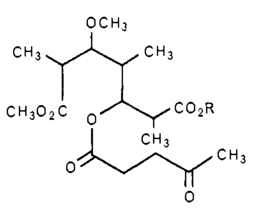


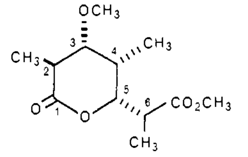
Figure 1.

bonds were detected, monensic acid was considered to be pentacyclic. While it is stable in basic solution, monensic acid is sensitive to acid. Under appropriate conditions, a product of acid treatment can be isolated as an amorphous solid which has $\lambda_{\max}^{\text{EtOH}}$ 281 mμ ($E_{1\text{ cm}}^{1\%}$ 319), $\nu_{\max}^{\text{CHCl}_3}$ 3356 (OH), 1718 (C=O), 1661 (C=O), 1631 (C=C), and 1603 (C=C) cm^{-1}, δ 1.78 (broad singlet), 3.47 (singlet), 5.95 (doublet, J = 9 cps), 6.12 (doublet, J = 16 cps), and 7.26 ppm (doublet, J = 16 cps), pK_a' = 7.35 (66% DMF); reduction with sodium borohydride moved the ultraviolet absorption maximum to 235 mμ. These data were interpreted as indicating the presence of an α,β,γ,δ-unsaturated ketone moiety, substituted by a methyl group in the γ position.[7] Periodate–permanganate oxidation[8] of the dienone yielded, among other products, a crystalline, tetracyclic dilactone (calcd mol wt for $C_{23}H_{36}O_6$, 408.24747; found, m/e 408.24671), mp 89–91°, $\nu_{\max}^{\text{CHCl}_3}$ 1765 (C=O, γ-lactone) and 1735 cm^{-1} (C=O, δ-lactone), pK_a's of the corresponding diacid 4.6 and 5.0 (H_2O). The 100-Mc nmr spectrum[9] showed methyl groups (acetone-d_6) at δ 0.91 (triplet), 0.96 (doublet), 1.06 (doublet), 1.17 (doublet), 1.27 ppm (singlet); no methoxyl group.

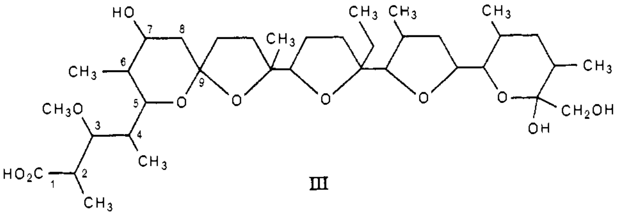
Oxidation of methyl diacetylmonensate with chromic acid in aqueous acetic acid produced, among other products, (+)-monomethyl α,α′-dimethyl-β-methoxyglutarate [isolated as the dimethyl ester, calcd mol wt for $C_{10}H_{18}O_5$, 218.11523; found, m/e 218.11542; $[\alpha]_D$ +26° (c 0.77, MeOH)] and the fragment Ia, which contained the methoxyl group and the carbomethoxy group of the parent compound. The acid Ia was isolated as the crystalline methyl ester Ib ($C_{18}H_{30}O_8$), mp 39–40°, $\nu_{\max}^{\text{CHCl}_3}$ 1727 cm^{-1} (C=O), $\lambda_{\max}^{\text{MeOH}}$ 272 mμ (ε 26), δ 0.92 (3 H, doublet, J = 7 cps), 1.11 (3 H, doublet, J = 7 cps), 1.17 (3 H, doublet, J = 7 cps), ~1.7 (1 H, multiplet), 2.18 (3 H, singlet), 2.68 (6 H, multiplet), 3.28 (3 H, singlet), 3.40 (1 H, doublet of doublets, J = 4 and 8 cps), 3.66 (3 H, singlet), 3.70 (3 H, singlet), and 5.45 ppm (1 H, doublet of doublets, J = 3 and 9 cps); 2,4-dinitrophenylhydrazone ($C_{24}H_{34}N_4O_{11}$) mp 126–127°. Treatment of Ib with base followed by acid gave the lactone II (calcd mol wt for $C_{12}H_{20}O_5$, 244.12902; found, m/e 244.13107), mp 105–106°, $\nu_{\max}^{\text{CHCl}_3}$ 1724 cm^{-1} (C=O). The 100-Mc nmr spectrum had δ 0.88 (3 H, doublet, J = 7 cps), 1.36 (3 H, doublet, J = 7 cps), 1.38 (3 H, doublet, J = 7 cps), ~2.3 (H-4, multiplet), ~2.5 (H-2, multiplet), 2.82 (H-6, multiplet), 3.26 (H-3, doublet of doublets, $J_{3,4}$ = 4, $J_{2,3}$ = 10 cps), 3.34 (3 H, singlet), 3.71 (3 H, singlet), and 4.19 ppm (H-5, doublet of doublets, $J_{4,5}$ = 2, $J_{5,6}$ = 10 cps) (the results of spin decoupling were in agreement with structure II). The lactone II was obtained also from the chromic acid oxidation of monensic acid along with the C_{23}-dilactone described above. The presence of a levulinate moiety in I was confirmed by reaction of Ib with hydrazine to give 4,5-dihydro-6-methyl-3-pyridazone,[10] mp 87–88°.



Ia (R=H)
Ib (R=CH₃)



II



III

The complete structure of monensic acid (III) was obtained by X-ray crystallographic analysis of its silver salt (Figure 1).[11] The investigation of the structure by X-ray crystallography was carried out on crystals of the silver salt of monensic acid obtained from a mixture of water and acetone. Approximately 2900 independent reflections were collected with filtered molybdenum radiation using the Supper-Pace autodiffractometer. Application of the Patterson superposition and heavy atom syntheses readily gave the complete structure, which was then refined by least squares using anisotropic temperature factors when necessary, and from the final Fourier synthesis most of the hydrogen atoms were located. With hydrogens included the final R was 8.1%.

The crystal structure (Figure 1) can be described as the monensic acid ion being wrapped around the cation and held in this conformation by two very strong hydrogen bonds between the carboxyl group and the two alcohol groups of the terminal six-membered ring. Six oxygen atoms are within 2.7 A of the silver, but the

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(7) This chromophore is present in tylosin, a macrolide antibiotic (R. B. Morin and M. Gorman, *Tetrahedron Letters*, 2339 (1964)).

(8) J. T. Edward, D. Holder, W. H. Lunn, and I. Puskas, *Can. J. Chem.*, 39, 599 (1961).

(9) We wish to thank W. Jankowski and R. Ettinger for the 100-Mc nmr spectra and H. Boaz for helpful discussions.

(10) W. G. Overend and L. F. Wiggins, *J. Chem. Soc.*, 239 (1947).

(11) It is interesting to note the similarity of the C_1–C_9 portion of monensic acid and the corresponding segment of the nonpolyene macrolide antibiotics: W. D. Celmer, *J. Am. Chem. Soc.*, **88**, 5028 (1966). The name monensic acid has been changed to monensin upon the recommendation of the USAN Council.

carboxyl group is 3.8 A away. The exterior is almost completely hydrocarbon-like, which could account for the low solubility of monensic acid salts in water.

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Structure, Isomerization, and Cleavage of 1,2-Bis(dichloroboryl)ethylene

Sir:

Recent interest[1-3] in the stereochemistry of the addition of tetrachlorodiborane(4) to unsaturated organic compounds prompts us to report results obtained in this laboratory on the structure, isomerization, and cleavage reactions of the 1:1 addition product of B_2Cl_4 with acetylene. This compound was of interest in connection with a study[4] of the relative reactivities of a series of unsaturated organometallic derivatives with B_2Cl_4, for which materials of known stereochemistry were required.

The previously known[5] 1:1 addition product (I) was obtained in 88% yield from the reaction of B_2Cl_4 with excess C_2H_2 at room temperature and an initial pressure of about 2 atm. The proton magnetic resonance spectrum of the pure liquid at 60 MHz consisted of a broad single line at −6.57 ppm (external tetramethylsilane reference) which narrowed significantly when the sample was simultaneously irradiated at 19.25 MHz to decouple the ^{11}B nuclei. In addition, when the spectrum was sharpened by $^1H-\{^{11}B\}$ double resonance, two satellite doublets ($J = 17.5$ Hz), centered at 73.5 Hz on either side of the principal peak, could be observed.

The presence of a single line in the principal spectrum and the simplicity of the satellite spectrum suggested strongly that the addition product I is a single isomer. The doublet structure of the satellites is attributable to H–H coupling, observable in the spectrum of a 1,2-disubstituted ethylene containing one ^{13}C atom because of the magnetic nonequivalence of the protons.[6] Thus, the possibility that I is the asymmetric isomer, 1,1-bis(dichloroboryl)ethylene, must be eliminated, since the satellite lines in the spectrum of that compound would be singlets.

Irradiation of I for 17 hr at room temperature with a medium-pressure mercury lamp (85%, 2537 A) gave, in addition to other products, a 50% yield of a new compound, II. Examination of the proton magnetic resonance spectrum of II indicated that the photochemically produced product contained less than 5% of unconverted I. Analysis for chloride liberated on hydrolysis with water (72.1% found; 75.2% calcd)[7] and molecular weight (vapor density: 180 found; 188 calcd) were consistent with the formulation of II as an isomer of I. The $^1H-\{^{11}B\}$ spectrum of II was similar to that of I, with a strong singlet in the olefinic proton region at −7.07 ppm. Satellite doublets ($J = 19.6$ Hz) at 76.0 Hz above and below the principal peak confirmed that this compound is also a 1,2-disubstituted olefin.

The infrared spectrum of I is essentially identical with that reported by Rudolph[2] and assigned by him to *cis*-1,2-bis(dichloroboryl)ethylene on the basis of coincidences between the infrared and Raman spectra. The infrared spectrum of II is considerably simpler than that of I. Frequencies (cm^{-1}) and relative intensities of principal bands in the gas-phase spectrum are as follows: 3010 w, 1580 w, 1275 s, 1135 s, 1092 vs, 1015 m, 985 s, 835 vw, 810 vw, 560 m. The weak band at 1580 cm^{-1} is believed to be due to the presence of the small amount of I mentioned above. We have assigned *cis* and *trans* structures to I and II, respectively, on the basis of the considerably simpler spectrum of the latter and the presence of a band of medium intensity in the C=C stretching region in the spectrum of I.

Cleavage of the deuterated analog of I (obtained by the reaction of B_2Cl_4 with C_2D_2) with silver oxide in ammonium hydroxide gave exclusively *cis*-C_2H_2D, identified from the infrared spectrum.[8] The infrared spectrum of the irradiation product of the deuterated compound showed that isomerization of *cis*-$Cl_2BCD{=}CDBCl_2$ (under the conditions used for the undeuterated material) was incomplete, and the resulting *trans* compound was not separable from the *cis* isomer by vacuum-line fractionation. Silver cleavage of the impure product consequently gave both *cis*- and *trans*-$C_2D_2H_2$. Treatment of I with glacial CH_3COOD at 80° for 24 hr gave a mixture of *cis*- and *trans*-$C_2H_2D_2$. The total amount of ethylene recovered was approximately 50% of that expected for complete cleavage. At lower temperatures, smaller amounts of ethylene, containing both isomers, were obtained.

The results obtained in this work are in accord with the recent findings of Rudolph[2] and of Wartik and his co-workers[3] which indicate that the reaction of B_2Cl_4 with acetylenic compounds is predominantly a *cis* addition. A sample of I isolated from a reaction of B_2Cl_4 with C_2H_2 in 2:1 molar ratio (which gave principally the 2:1 addition product) contained a small amount of material with a proton chemical shift identical with that of the *trans* isomer, II. This may indicate that the reaction is not completely stereospecific or that isomerization of the product may occur under the conditions of our experiments.

Protonolysis of alkenylboranes derived from the hydroboration of internal acetylenes has been shown to yield *cis*-olefins,[9] and the acetic acid cleavage reaction has been used to infer the stereochemistry of unsaturated organoboron compounds from that of the resulting

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[1] H. K. Saha, L. J. Glicenstein, and G. Urry, *J. Organometal. Chem.* (Amsterdam), **8**, 37 (1967).

[2] R. W. Rudolph, *J. Am. Chem. Soc.*, **89**, 4216 (1967).

[3] M. Zeldin, A. R. Gatti, and T. Wartik, *ibid.*, **89**, 4217 (1967).

[4] T. D. Coyle and J. J. Ritter, to be published.

[5] C. Chambers and A. K. Holliday, *J. Chem. Soc.*, 3459 (1965).

[6] The complete satellite spectrum of a 1,2-disubstituted ethylene consists of *four* pairs of doublets. In the compounds studied here, the two inner pairs, being obscured by the strong line from the $^{12}C_2$ species, were not observed. The intensity of each line in the satellite spectrum is approximately 0.28% of that of the principal line.

[7] Analyses were performed by Mr. Rolf Paulson of the Microchemical Analysis Section of the National Bureau of Standards.

[8] B. L. Crawford, J. E. Lancaster, and R. G. Inskeep, *J. Chem. Phys.*, **21**, 678 (1953).

[9] H. C. Brown and G. Zweifel, *J. Am. Chem. Soc.*, **81**, 1512 (1959).