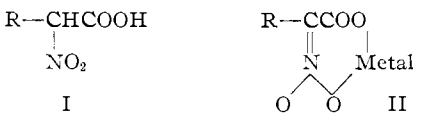
ylate.[1] In stronger alkali the acids form divalent salts such as dipotassium nitroacetate,[2] which does not decarboxylate readily, and which forms typically ionic crystals.[3] The chelate salts (II) have not been characterized, although their existence



I II

was suggested by the effect which many polyvalent metal ions have upon the rate of decarboxylation of nitroacetic acid.[1,4] We have now succeeded in preparing the aluminum and magnesium salts of nitroacetic acid, and have utilized the stability of magnesium salts to provide a remarkably simple synthesis of α-nitro acids from primary nitroalkanes and carbon dioxide.

Aluminum nitroacetate precipitates when aluminum isopropoxide and nitroacetic acid are mixed in ether solution. The white powder has the composition $Al_2(C_2HNO_4)_3 \cdot (solvent)_x$,[5] is insoluble in the common solvents, and is decomposed by aqueous hydrochloric acid to free nitroacetic acid. Magnesium nitroacetate has not been obtained crystalline, but may be prepared in methanol (λ_{max} 272 mμ, log ϵ 4.05) and shown spectroscopically to be a 1:1 complex by the method of continuous variation.[6]

Magnesium methyl carbonate[7] may be prepared by saturating a solution of magnesium methoxide in dimethylformamide with dry carbon dioxide. Treatment of nitromethane with 4 molar equivalents of this solution (2 molar) at 50° for 4–5 hours resulted in quantitative conversion to magnesium nitroacetate as determined spectrophotometrically. Hydrolysis of the solution with ice and hydrochloric acid led to the isolation of nitroacetic acid, m.p. 89–92° (reported 87–89°,[2] 91.5–92°[4]) in 63% yield. This result demonstrates that the well-known decarboxylation of nitroacetic acid is a reversible reaction, the position of equilibrium being completely shifted by chelation.

Other primary nitroparaffins react similarly. Nitroethane is converted to **2-nitropropionic acid** in 49% yield under conditions found best for nitroacetic acid, although these conditions may not be optimum in this and other cases. The following amino acids were prepared by hydrogenating the crude nitro acids, prepared as described above, in acetic acid at room temperature with 10% Pd/C, in the specified over-all yield based on nitroparaffin: **DL-alanine,**[8] dec. 292–294° (46%) from nitroethane; **DL-α-aminobutyric acid,** dec. 283–285° (34%) from 1-nitropropane; and **DL-norvaline,** dec. 290–292° (42%) from 1-nitrobutane.

2-Nitropropane, which could not give rise to a species such as II, fails to undergo the reaction.

The use of magnesium methyl carbonate as a carboxylating agent for other active hydrogen compounds is being investigated.

(1) K. J. Pedersen, *Trans. Faraday Soc.*, **23**, 316 (1927).

(2) W. Steinkopf, *Ber.*, **42**, 3925 (1909).

(3) D. J. Suter, F. J. Llewellyn and H. S. Maslen, *Acta Cryst.*, **7**, 145 (1954).

(4) K. J. Pedersen, *Acta Chem. Scand.*, **3**, 676 (1949).

(5) The atomic ratio of nitrogen to aluminum was 1.43 and 1.42 for two samples prepared by mixing alkoxide and acid in molar ratios of 1.4 and 0.5, respectively. The elemental analyses [Found: C, 33.5; H, 6.0; N, 8.2; Al, 11.1 (former sample) and C, 29.5; H, 4.6; N, 7.7; Al, 10.4 (latter sample)] suggest that the identity and number of solvent molecules in the salt depend upon the details of preparation. Two molecules of ether or isopropyl alcohol are probably involved. (Calcd. for $C_{12}H_{19}O_{14}N_3Al_2$: C, 29.8; H, 4.0; N, 8.7; Al, 11.2; for $C_{14}H_{23}O_{14}N_3Al_2$: C, 32.9; H, 4.5; N, 8.2; Al, 10.6).

(6) A. E. Martell and M. Calvin, "Chemistry of the Metal Chelate Compounds," Prentice-Hall, Inc., New York, 1952, p. 29.

(7) E. Szarvasy, *Ber.*, **30**, 1836 (1897).

(8) The amino acids were identified by comparison of their decomposition temperatures and infrared spectra (Nujol) with those of commercial samples.

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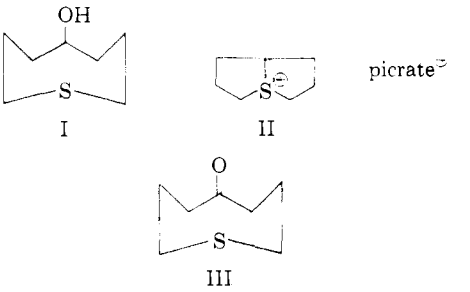
RECEIVED DECEMBER 4, 1958

A TRANSANNULAR REACTION IN AN EIGHT-MEMBERED RING SULFIDE

Sir:

We wish to report a novel transannular reaction in a cyclic 8-membered ring sulfide. The carbinol (I), 5-hydroxythiacycloöctane, on treatment with phosphoric anhydride and then treatment of the purified solution (ion exchange) with picric acid, gave the bicyclic sulfonium salt II, 57%, bicyclo-[3,3,0]octane-1-thianium picrate, m.p. 262–264° (microblock, corr.) C, 43.55; H, 4.23; N, 11.75.



I II III

This sulfonium picrate was identical (infrared spectrum) with the same compound prepared by R. H. Eastman[1] and G. Kritschevsky, m.p. 261–263°, mixed m.p. 261–264 (micro-block, corr.)

The eight-membered ring ketone (III),[2] 5-oxothiacycloöctane, b.p. 120–123 (19 mm.), m.p. 50–52°; C, 58.26; H, 8.39; (2,4-dinitrophenylhydrazone, m.p. 194–195°, N, 17.34) was prepared by the Dieckmann cyclization of ethyl thio-di-*n*-butyrate with subsequent hydrolysis and decarboxylation (31%). The infrared spectrum (0.01 *M* in CCl_4) showed a strong normal carbonyl absorption for this compound at 1707 cm.$^{-1}$, with a shoulder at 1690 cm.$^{-1}$. We had reported previously a single absorption for the 7-membered

(1) We are indebted to Dr. R. Eastman for a sample of this picrate; Gene Kritschevsky, Ph.D. Thesis, Stanford University, September 1955; prepared from 3-(2-tetrahydrofuryl)-propyl chloride (from the corresponding alcohol by reaction with thionyl chloride) by conversion of the latter into the isothiuronium salt and then by treatment with ammonium hydroxide to yield the mercaptan, which then was treated with concd. hydrochloric acid at 100° (74% yield) to give the bicyclo[3,3,0]octane-1-thianium chloride—isolation was then carried out by the formation of the picrate.

(2) This product was identical with a sample of the same material kindly forwarded to us by Dr. N. J. Leonard of the University of Illinois and described in the accompanying communication by N. J. Leonard, T. L. Brown and T. W. Milligan.

ring homolog (1710 cm.$^{-1}$).[3] This is an indication of interaction of the sulfur electrons with the carbonyl increasing the dipolar character of the carbonyl and is similar to what has been observed in the nitrogen system.[4] III was reduced with lithium aluminum hydride to give I, 80%; b.p. 78–80° (2 mm.), n^{20}D 1.5379, m.p. 29–29.5; *m*-nitrobenzenesulfonate, C, 46.97; H, 5.34; 5-acetoxythiacycloöctane-1,1-dioxide, C, 49.12; H, 7.35; S, 14.49.

Work is in progress to determine the scope of these novel transannular effects with sulfur.

(3) C. G. Overberger and A. Katchman, THIS JOURNAL, **78**, 1965 (1956).

(4) N. J. Leonard, M. Oki, J. Broder and H. Boaz, *ibid.*, **77**, 6237 (1955), and earlier papers.

(5) A portion of thesis submitted by A. Lusi in partial fulfillment of the degree of Master of Science in the Graduate School of the Polytechnic Institute of Brooklyn.

DEPARTMENT OF CHEMISTRY C. G. OVERBERGER
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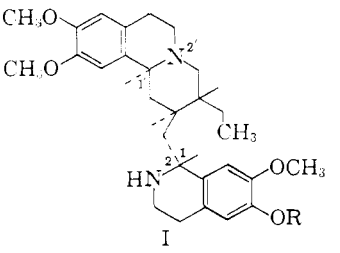
RECEIVED DECEMBER 4, 1958

THE STEREOCHEMISTRY OF THE IPECAC ALKALOID EMETINE

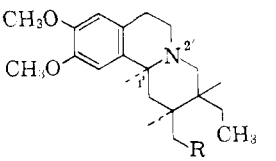
Sir:

The original proposal[1] of stereoformula Ia (I, $\Delta^{1,2}$) for emetine (I, R = CH_3) and related ipecac



I

alkaloids was challenged recently by Brossi, Cohen, Osbond, Plattner, Schnider and Wickens,[2] who advanced an alternative structure in which C-1′ possesses the epimeric, less stable configuration. The modification was occasioned by the belief of Brossi, *et al.*, that Bischler–Napieralski cyclization and reduction of the tricyclic amide IIa led to *two diastereoisomers of emetine;* this report contradicts that of the earlier Russian investigators,[3] whose statement that *emetine* resulted from this reaction sequence provided part of the basis for our proposal. Reinvestigation of the pertinent reactions reveals that (i) catalytic hydrogenation of the $\Delta^{1'}$ precursor (IIb) gives rise to a high yield of saturated tricyclic ester IIc, the only detectable stereoisomer,



IIa, R = $CO\text{-}NHCH_2CH_2C_6H_3\text{-}3,4(OCH_3)_2$
IIb, R = $COOCH_2$, $\Delta^{1',2'}$
IIc, R = $COOCH_3$
IId, R = CH_2OH
IIe, R = CH_3

and (ii) in agreement with the results of Preobrazhenskii, *et al.*,[3] and, more recently, Battersby and Turner,[4a] but contrary to those of Brossi, *et al.*[2] IIa is convertible to emetine and isoemetine (C-1 epimer of emetine). Further, the assigment of stereochemistry of IIa and IIc, originally made[2] only by analogy to certain reduction results obtained in this Laboratory,[1a] now has been validated: lithium aluminum hydride reduction of IIc produced an alcohol (IId) identical with that obtained through another route by Burgstahler and Bithos,[5,6] who related their material to the oxygen-free base IIe; the stereochemistry (II) of the latter had been established previously.[1a] These findings complement those of Battersby[4b] and fully corroborate the original proposal Ia.

Despite inferences to the contrary,[2] the *relative* configuration of C-1 in emetine has not been assigned, and so far there has not appeared any evidence bearing on this point. A simple approach to this unwieldy problem is based upon the structural similarity of the two tetrahydroisoquinoline rings, each with an asymmetric center in the proximity of an ultraviolet chromophore.[7] In the stereoisomer where C-1 and C-1′ are "antipodal" (I), the optical contributions of the two asymmetric centers might be expected approximately to cancel each other and cause a negligible rotational change in the range 300–700 mμ. In the case where the absolute configurations are the same, the optical effects should be reinforced, and the normal change of rotation with wave length should prevail. Experimentally, in the region 350–700 mμ, the slightly positive rotation of *emetine* hydrobromide remains virtually constant, falling off to negative values below 350 mμ; in contrast, *isoemetine* hydrobromide exhibits gradually increasing positive rotation down to 300 mμ, followed by a sharp decline to negative rotations below 300 mμ.[8]

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RECEIVED DECEMBER 8, 1958

(1) (a) E. E. van Tamelen, P. E. Aldrich and J. B. Hester, Jr., THIS JOURNAL, **79**, 4817 (1957); (b) *cf.* A. R. Battersby, R. Binks, D. Davidson, G. C. Davidson and T. P. Edwards, *Chem. and Ind.*, 982 (1957); A. R. Battersby and S. Cox, *ibid.*, 983 (1957).

(2) A. Brossi, A. Cohen, J. M. Osbond, Pl. A. Plattner, O. Schnider and J. C. Wickens, *ibid.*, 491 (1958).

(3) N. A. Preobrazhenskii, R. P. Evstigneeva, R. S. Livshits and K. M. Fedyuohkina, *Doklady Acad. Nauk, USSR*, **81**, 421 (1951).

(4) (a) A. R. Battersby and J. C. Turner, *Chem. and Ind.*, 1324 (1958); (b) A. R. Battersby, *ibid.*, 1324 (1958).

(5) The authors are indebted to Professor Burgstahler for his cooperation in carrying out the identification of this substance.

(6) A. W. Burgstahler and Z. J. Bithos, THIS JOURNAL, **81**, 503 (1959).

(7) See C. Djerassi, *Bull. soc. chim. France*, 741 (1957).

(8) We are grateful to Professor Carl Djerassi for supplying the optical rotatory dispersion data.