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-acetoxythiacyclooötane-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.

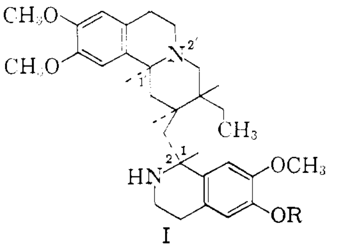
DEPARTMENT OF CHEMISTRY C. G. OVERBERGER
POLYTECHNIC INSTITUTE OF BROOKLYN
BROOKLYN, NEW YORK AINO LUSI[5]

RECEIVED DECEMBER 4, 1958

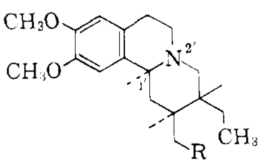
THE STEREOCHEMISTRY OF THE IPECAC ALKALOID EMETINE

Sir:

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



I



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

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]

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF WISCONSIN EUGENE E. VAN TAMELEN
MADISON, WISCONSIN JACKSON B. HESTER, JR.

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.