trans configuration. This assignment is in accord with that made previously on the basis of infrared, nmr, glpc, and chemical reactivity data. The latter criteria may now be used with more confidence for making stereoisomer assignments.

The assignments recently used[9] in speculations on a new mechanism for ozonide formation are also the correct ones; thus this hypothesis gains additional support.

Apart from its importance for the ozonide stereoisomer assignment problem, this appears to be the first example of partial resolution of a *dl*-ozonide. The fact that the active ozonide can be rerun through the gas chromatograph and retain its activity is an initial indication of its stability toward racemization.

Acknowledgment. We are very grateful to Mr. F. P. Hood, III, for his valuable assitance in making the ORD measurements, and to Dr. E. A. Chandross for helpful discussions.

(15) On leave of absence from the Weizmann Institute of Science, Rehovoth, Israel.

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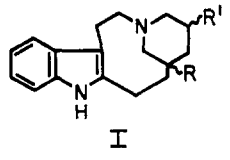
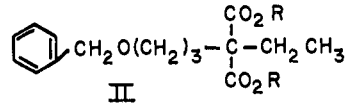
A New Total Synthesis of *dl*-Quebrachamine and *dl*-Aspidospermidine. A General Entry into the Aspidosperma Alkaloids

Sir:

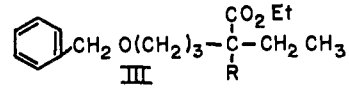
In previous communications[1-3] we described novel transannular cyclizations which provided a synthetic entry into the Aspidosperma, Vinca, and Iboga alkaloids. The complete stereospecificity of these reactions[4,5] has revealed that the compounds such as quebrachamine (I, R = Et; R′ = H), dihydrocleavamine (I, R = H; R′ = Et), and their ester derivatives occupy a central position in providing synthetic pathways to a considerable variety of alkaloids in the above classes. We now report a new total synthesis of *dl*-quebrachamine[6-8] *via* a sequence which we believe to be completely general in its application to the preparation of other nine-membered ring systems.



I



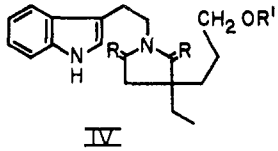
II



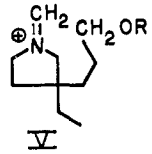
III

Ethyl γ-benzyloxypropylmalonate[9] on treatment with sodium ethoxide and ethyl iodide gave ethyl γ-benzyloxypropylethylmalonate (II, R = Et), bp 220–222° (1.5 mm), which on alkaline hydrolysis gave the diacid[10] (II, R = H), mp 117–120°. This compound was decarboxylated to the monoacid and the latter esterified to give ethyl α-(γ-benzyloxypropyl)butyrate (III, R = H), bp 156–159° (0.25 mm). Alkylation of this ester with triphenylmethylsodium and ethyl bromoacetate gave ethyl α-(γ-benzyloxypropyl)-α-ethylsuccinate (III, R = CH_2CO_2Et) as a viscous liquid.

Condensation of the succinate with tryptamine provided the succinimide (IV, R = O; R′ = $CH_2C_6H_5$), $C_{26}H_{30}N_2O_3$, which showed the following spectral properties: λ_{max}^{MeOH} 221, 275 (sh), 283, and 291 mμ; ν_{CHCl_3} 5.67 and 5.91 μ; nmr signals[11] 3.06 (doublet, α-proton on indole), 5.88 (singlet, $C_6H_5CH_2O$), 6.25 (triplet, CH_2N), 6.68 (triplet, OCH_2CH_2), 7.0 (triplet, CH_2CH_2N), 7.6 (singlet, CH_2CO), 9.27 (triplet, CH_3). Lithium aluminum hydride reduction of the latter yielded the amine (IV, R = H; R′ = $CH_2C_6H_5$) which still exhibited a normal indole absorption in the ultraviolet but had lost the characteristic imide absorption in the infrared spectrum. The molecular formula, $C_{26}H_{34}N_2O$, was established by high-resolution mass spectrometry, which provided the value 390.269 (calculated 390.267). The mass spectrum also revealed the expected fragmentation of the molecule under electron impact to provide the base peak at *m/e* 260 due to the stable ion V (R = $CH_2C_6H_5$).



IV



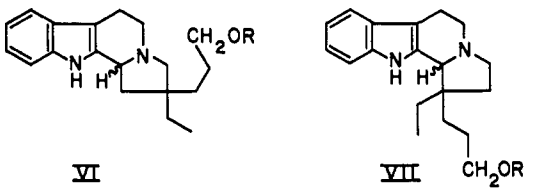
V

The benzyloxyamine was then treated with excess mercuric acetate in methanol–acetic acid and the crude product, without isolation, reduced immediately with sodium borohydride to give the cyclized amine (VI, R = $CH_2C_6H_5$), $C_{26}H_{32}N_2O$ (Found: mol wt, 388.251. Calcd: mol wt, 388.251): λ_{max}^{MeOH} 273 (sh), 284, and 292 mμ; no nmr signal for the α-proton on the indole ring and a two-proton singlet at τ 8.05 (N–CH_2–C<). This latter datum eliminates the alternative, sterically less favored structure VII for the cyclization product, since this compound must exhibit a multiplet for the methylene protons attached to the basic nitrogen atom. The mass spectrum of VI was completely different from that of the amine IV, and intense peaks at *m/e* 198, 184, 170, 156, etc., were noted. The fragments attributed to these peaks are well known in the mass spectra of indole alkaloids.[12]

Removal of the benzyl group was accomplished by brief treatment of VI (R = $CH_2C_6H_5$) with boron tri-

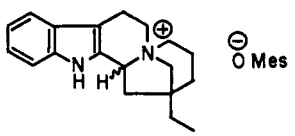
(1) J. P. Kutney and E. Piers, *J. Am. Chem. Soc.*, 86, 953 (1964).
(2) J. P. Kutney, R. T. Brown, and E. Piers, *ibid.*, 86, 2286 (1964).
(3) J. P. Kutney, R. T. Brown, and E. Piers, *ibid.*, 86, 2287 (1964).
(4) A. Camerman, N. Camerman, J. P. Kutney, E. Piers, and J. Trotter, *Tetrahedron Letters*, 637 (1965).
(5) J. P. Kutney, R. T. Brown, and E. Piers, *Can. J. Chem.*, 44, 637 (1966).
(6) G. Stork and J. E. Dolfini, *J. Am. Chem. Soc.*, 85, 2872 (1963).
(7) Y. Ban, Y. Sato, I. Inoue, M. Nagai, T. Oishi, M. Terashima, O. Yonemitsu, and Y. Kanaoka, *Tetrahedron Letters*, 2261 (1965).
(8) M. E. Kuehne and C. Bayha, *ibid.*, 1311 (1966).
(9) L. C. Cheney and J. R. Piening, *J. Am. Chem. Soc.*, 67, 2213 (1945).
(10) Satisfactory elemental analyses were obtained for all new compounds reported. In addition, high-resolution mass spectrometry using an AEI, MS9 mass spectrometer was employed in most instances to establish the molecular formulas.
(11) All nmr spectra were measured in deuteriochloroform with tetramethylsilane as the internal standard with a Varian A-60 spectrometer. All signals are reported in τ units.
(12) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Structure Elucidation of Natural Products by Mass Spectrometry," Vol. I, Holden-Day, Inc., San Francisco, Calif., 1964, p 77.

bromide in dichloromethane at 0° to provide the amino alcohol (VI, R = H) which still retained the normal indole ultraviolet spectrum while the nmr spectrum indicated a complete absence of the typical benzyl ether proton signals mentioned above. The molecular formula, $C_{19}H_{26}N_2O$, was again established by high-resolution mass spectrometry (Found: mol wt, 298.204. Calcd: mol wt, 298.204) and the mass spectrum also indicated fragments at *m/e* 184, 170, 156, etc., as mentioned above.



VI

VII CH_2OR



VIII

The total synthesis of *dl*-quebrachamine was completed when the quaternary mesylate (VIII), formed directly from the reaction of the amino alcohol with methanesulfonyl chloride in pyridine, was reduced with sodium and liquid ammonia.[13,14] The reaction product was identical with an authentic sample of (−)-quebrachamine obtained from natural sources (infrared, thin layer chromatography, mass spectrometry).

This synthesis also completes a total synthesis of *dl*-aspidospermidine.[4] Since there is little doubt that tryptamine derivatives bearing functional groups (OCH_3, for example) on the aromatic ring will react similarly, the above sequence can be extended to other Aspidosperma alkaloids.

The obvious extension of this synthesis to the Vinca alkaloids, the dihydrocleavamine series, and, in turn, to the Iboga alkaloids is now under investigation.

Acknowledgment. Financial aid from the National Cancer Institute of Canada and the National Research Council of Canada is gratefully acknowledged.

(13) E. Wenkert, S. Garratt, and K. G. Dave, *Can. J. Chem.*, 42, 489 (1964).

(14) J. P. Kutney, E. Piers, and T. Inaba, unpublished results.

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β-Lactams Containing an Exocyclic Double Bond[1]

Sir:

We wish to report that symmetrically and unsymmetrically substituted allenes[2] react with chlorosulfonyl isocyanate (CSI)[3] to form β-lactams containing an exocyclic double bond and 2-carboxamido-1,3-butadiene derivatives.

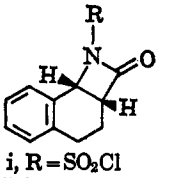
In general, the allenes are added slowly to CSI in ether solution, after which the mixture is added to ice and the whole extracted with water. Thus, 3-methyl-1,2-butadiene (**1**),[4] on treatment with CSI, gave 1-chlorosulfonyl-3-methylene-4,4-dimethyl-2-azetidinone (**3**, 21%) from the ether solution and, from the aqueous extract, 2-carboxamido-3-methyl-1,3-butadiene (**4**, 36%). A third, as yet unidentified, product was obtained in 22% yield.[5] Compound **3** was obtained as white plates from pentane, mp 51–52°; $\lambda_{max}^{CCl_4}$ 5.51 μ (C=O). *Anal.* Found: C, 34.61; H, 4.03; N, 6.80. The nmr spectrum (CCl_4) displayed absorptions at δ 1.79 (6 H, singlet), 5.57, and 6.05 (2 H, two identical vinyl doublets, J = 2.5 cps). Reduction of **3** with benzenethiol and pyridine in acetone[6] led to 3-methylene-4,4-dimethyl-2-azetidinone (**5**, 55%) as long white needles from pentane, mp 64–65° (sublimed 50° (1 mm)); $\lambda_{max}^{CS_2}$ 5.63 and 5.69 μ (C=O);[7] $\lambda_{max}^{CHCl_3}$ 3.24 μ (=CH_2, Raman). *Anal.* Found: C, 65.15; H, 8.42; N, 12.59. Ozonolysis of **3** and **5** furnished formaldehyde, identified as its 2,4-DNP derivative. Butadiene **4** was obtained as long white needles from ether–petroleum ether (bp 30–60°), mp *ca.* 70° (rapid heating); λ_{max}^{KBr} 6.09 (C=O), 6.18, and 6.32 μ; $\lambda_{max}^{CH_3OH}$ 223 mμ (ε 7800). *Anal.* Found: C, 64.90; H, 8.24; N, 12.27. The nmr ($CDCl_3$) consisted of absorptions at δ 1.92 (3 H, multiplet), 5.11 (2 H, multiplet, β =CH_2), 5.28, 5.52 (2 H, two unresolved singlets, peak width at half-height 4 cps, α =CH_2), and *ca.* 6.30 (2 H). Treatment of **4** with maleic anhydride yielded the Diels–Alder adduct, white plates, mp 160–161°.[8]

The β-lactam **5** was identified by hydrolytic cleavage to the unsaturated amino acid hydrochloride (**6**),[8] reduction of which produced 3-amino-2,3-dimethylbutanoic acid hydrochloride (**7**).[8,9] The identity of butadiene **4** was established by stepwise reduction to

(1) For a review of available methods of β-lactam synthesis, see J. C. Sheehan and E. J. Corey, *Org. Reactions*, 9, 388 (1958). Two new syntheses have recently been reported: E. J. Corey and A. M. Felix, *J. Am. Chem. Soc.*, 87, 2518 (1965); R. B. Woodward, K. Heusler, J. Gosteli, P. Naegeli, W. Oppolzer, R. Ramage, S. Ranganathan, and H. Vorbrüggen, *ibid.*, 88, 852 (1966).

(2) A recent review of allene chemistry is available: A. A. Petrov and A. V. Fedorova, *Russ. Chem. Rev.*, 33, 1 (1964).

(3) H. Ulrich, *Chem. Rev.*, 65, 369 (1965), summarizes the chemistry of CSI to July 1964. We have recently reported on the reaction of 1,2-dihydronaphthalene with CSI to prepare i, and therefrom, ii [E. J. Moriconi and P. H. Mazzocchi, *J. Org. Chem.*, 31, 1372 (1966)]. CSI is



i, R = SO_2Cl
ii, R = H

now commercially available from American Hoechst Corp., New York, N. Y.

(4) W. J. Bailey and C. R. Pfeifer, *J. Org. Chem.*, 20, 95 (1955).

(5) This compound seems to be an adduct of two equivalents of CSI with one of **1**.

(6) R. Graf, *Ann.*, 661, 111 (1963).

(7) The infrared spectrum of **5** showed marked and reversible changes with concentration suggestive of a monomer ⇄ (dimer) ⇄ polymer equilibrium, probably involving intermolecular hydrogen bonding between N—H and O=C bonds. Thus in dilute solution, the main, monomeric C=O peak appeared at 1777 cm^{-1}, with a weak secondary at 1757 cm^{-1} (dimer or polymer C=O); with increasing concentration these intensities reversed. Similarly the N–H stretching band of the monomer at 3430 cm^{-1} is progressively displaced at higher concentration by the typical broad N–H stretching band at 3240 cm^{-1} of the bonded species.

(8) Satisfactory elemental analytical data and nmr, ultraviolet, and infrared spectra have been obtained for this compound.

(9) Compound 7 was identical by all the usual criteria with the acid hydrolysis product of 3,4,4-trimethyl-2-azetidinone.[6]