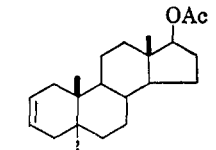
Table I

Compd	Bp, °C (mm)	pK_a	ν, cm^{-1}	Nmr (>N—CH$_2$), τ (J, cps)	Picrate mp, °C	Flavanate mp, °C	n_D (T, °C)
12	65–70 (0.03)		3024, 2987 1227, 1213	6.85, d (11.5) 7.72, d (11.5)	162–164	180 dec	1.5086 (24)
2a	25 (0.2)	8.50	3015, 2997 1219	7.26, d (11.5) 7.47, d (11.5)	158–160	187–189	1.4753 (23)
2b		8.34	3010, 1212		214–217 dec		

Lead tetraacetate in benzene was also found to be an excellent oxidant[6] and converted **3** into **4a** almost quantitatively. With yellow mercuric oxide in ethylene glycol, oxidation was partially successful to give a 21% yield of **4a**. Compound **9** on treatment with either NCS or lead tetraacetate afforded **10** ($C_{22}H_{33}O_2N$; mp 236–240° dec; $[\alpha]^{23}D$ +41.0°; ν_{max} 1725 cm^{-1}) in 71 and 80% yields, respectively.



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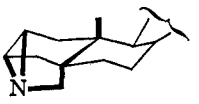
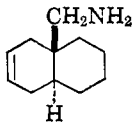
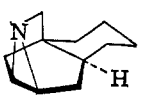


10

Oxidation of **11**, **1a**, and **1b** with NCS yielded fairly stable monochloramines which could not be smoothly changed by pyrolytic decomposition into the aziridines **12**, **2a**, and **2b**.[7] However, oxidation with lead tetraacetate and potassium carbonate gave good results. The bridged aziridines **12**, **2a**, and **2b** were obtained in 55–60% yields. These bridged aziridines are volatile oils and quite unstable.[8] They readily polymerize at room temperature and cannot be distilled without polymerization. On the other hand, the aziridine salts are stable.



11



12

Physical properties are summarized in Table I. Infrared bands at around 3000 and 1220 cm^{-1}, characteristic of the aziridine ring,[9] an AB-type quartet patterns of the methylene group attached to the nitrogen atom in the nmr spectra, and lower pK_a values support the assigned structures. Chemical evidence will be presented in the forthcoming paper.

(6) To our knowledge, aromatic primary amines are oxidized to diazo compounds (K. H. Pausacker and J. G. Scroggie, *J. Chem. Soc.*, 4003 (1954)) and aliphatic primary amines to the corresponding carbonitriles probably through aldimines (M. Lj. Mihailovic, A. Stojikovic, and V. Andrejevic, *Tetrahedron Letters*, 461 (1965)). Our result is quite striking when compared with these results.

(7) It is suspected that cyclization of **11**, **1a**, and **1b** may not be effected because of low rigidity of the molecules; that is, the functionated amidomethyl group cannot always be close to the double bond in the ground state, particularly in **1b**.

(8) The relatively low yields may be partly due to unstability and volatility.

(9) K. C. Tsou, K. Hoegerle, and H. C. F. Su, *J. Med. Chem.*, **6**, 435 (1963); J. B. Patrick, R. P. Williams, W. E. Meyer, W. Fulmor, D. B. Cosulich, R. W. Broschard, and J. S. Webb, *J. Am. Chem. Soc.*, **86**, 1889 (1964).

Acknowledgment. We wish to thank Mr. M. Yoshioka for participation in this work.

Wataru Nagata, Shoichi Hirai, Kyozo Kawata, Tsutomu Aoki
Shionogi Research Laboratory, Shionogi & Co., Ltd.
Fukushima-ku, Osaka, Japan
Received July 6, 1967

A New Method for Isoquinuclidine Synthesis. A Total Synthesis of Desethylibogamine

Sir:

The isoquinuclidine nucleus forms a part of alkaloids such as ibogaine[1] and dioscorine.[2] Most previous methods for preparing the nucleus comprise either internal condensation[3] of a *cis*-4-aminocyclohexanecarboxylic acid ester followed by reduction of the resulting lactam or the Diels–Alder reaction[4] of 1,2-dihydropyridine with a dienophile. Recently, Cava and his co-workers[5] developed a new method consisting of the Diels–Alder reaction of a methyleneurethan with cyclohexadiene.

Strained tricycloaziridine and its derivatives reported in a previous paper[6] are highly reactive and useful for the preparation of isoquinuclidines. We wish to report a new method for preparing isoquinuclidines and a total synthesis of desethylibogamine. When the bridged aziridines **1a–c** were treated with an acylating agent such as acyl halide or acid anhydride (RX) in an appropriate solvent such as ether, acetone, or pyridine, facile cleavage[7] of the aziridine ring occurred, giving in excellent yield a 4:1 mixture of the isomeric azabicyclo-[2.2.2]- and -[3.2.1]octane compounds **2** and **3**. Both isomers can be readily differentiated by nmr spectra, since the signal of the bridgehead proton at C_1 and the methyl signal at the other bridgehead (C_4) of isoquinuclidines **2** (in the case of R_1 = CH_3; R_2 = H) appear at higher fields by 10–20 and 12 cps, respectively, than the signals of the azabicyclo[3.2.1]octane ring compound

(1) For a review of the iboga-type alkaloids, see H-G. Boit, "Ergebnisse der Alkaloid Chemie bis 1960," Akademie-Verlag, Berlin, 1961, p 631.

(2) W. A. M. Davies, I. G. Morris, and A. R. Pinder, *Chem. Ind.* (London), **35**, 1410 (1961).

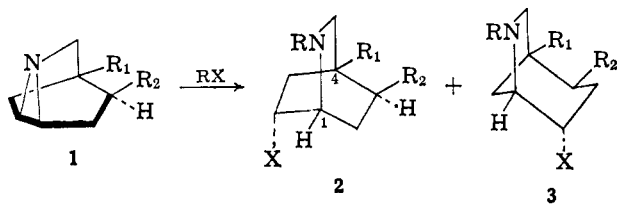
(3) J. W. Huffman, C. B. S. Rao, and T. Kamiya, *J. Org. Chem.*, **32**, 697 (1967); E. Ferber and H. Bruchner, *Ber.*, **75B**, 425 (1952); **76B**, 1019 (1953); L. H. Werner and S. Ricca, Jr., *J. Am. Chem. Soc.*, **80**, 2733 (1958); W. Schneider and R. Dillmann, *Ber.*, **96**, 2377 (1963).

(4) G. Büchi, D. L. Coffen, K. Kocsis, P. E. Sonnet, and F. E. Ziegler, *J. Am. Chem. Soc.*, **88**, 3099 (1966); O. Mumm and J. Diedrichsen, *Ann.*, **538**, 195 (1939); K. Schenker and J. Druey, *Helv. Chim. Acta*, **42**, 1960 (1959); **45**, 1344 (1962); M. Saunders and E. H. Gold, *J. Org. Chem.*, **27**, 1439 (1962); T. Agawa and S. I. Miller, *J. Am. Chem. Soc.*, **83**, 449 (1961).

(5) M. P. Cava, C. K. Wilkins, Jr., D. R. Dalton, and K. Bessho, *J. Org. Chem.*, **30**, 3772 (1965).

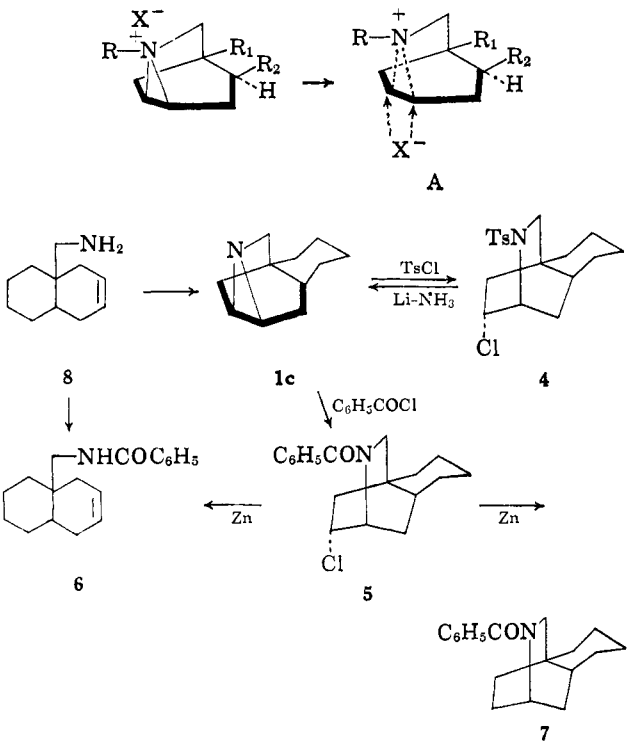
(6) W. Nagata, S. Hirai, K. Kawata, and T. Aoki, *J. Am. Chem. Soc.*, **89**, 5045 (1967).

(7) J. E. Dolfini and D. M. Dolfini, *Tetrahedron Letters*, 2053 (1965).



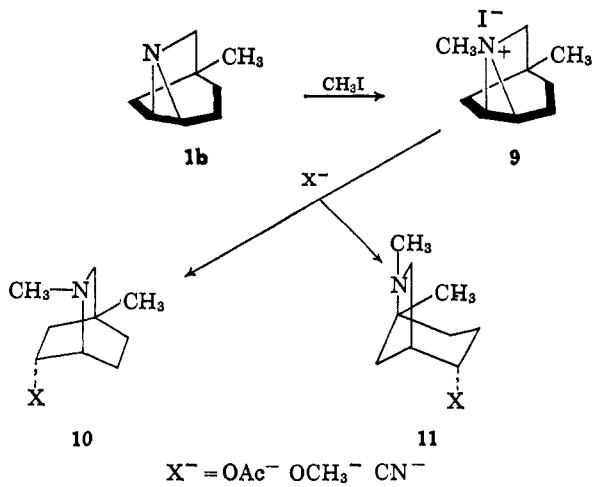
a, $R_1=R_2=H$
b, $R_1=CH_3$; $R_2=H$
c, $R_1R_2=-CH_2(CH_2)_2CH_2-$

3. The structural proof of both **2** and **3** was made by independent synthesis of them performed in an unequivocal manner.[8] The *endo* orientation of the functional group X is assigned on the basis of the mode of reaction and from the following chemical evidence.[9] Compound **1c** on treatment with *p*-toluenesulfonyl chloride gave the isoquinuclidine **4** which was reconverted almost quantitatively into the aziridine **1c** by Birch reduction. Compound **5** was subjected to fragmentation by treatment with zinc in ethanol giving **6** (which was identical with the N-benzoate of the primary amine **8**) together with the normal dechlorinated product **7**.

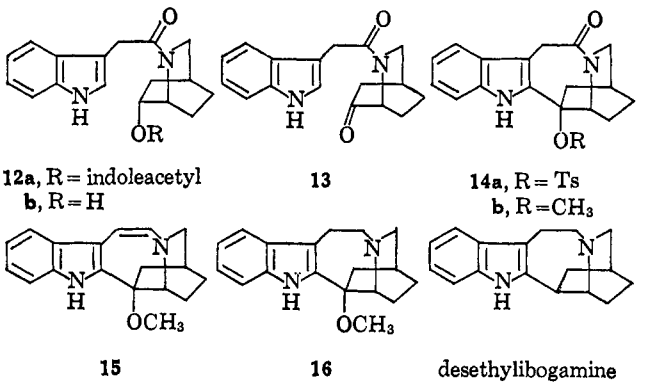


Aziridine **1b** reacted with methyl iodide at −50° to give in good yield the methiodide **9** which was smoothly attacked by various nucleophiles such as acetate, methoxide, and cyanide to yield the substituted isoquinuclidines **10** and the isomers **11** in about 2:1 ratio.

Almost exclusive formation of the isoquinuclidines was effected by catalytic hydrogenation of both the bridged aziridines **1** and their quaternary salts **9**, enhancing the value of this method for isoquinuclidines synthesis. Aziridines **1** were reduced to the isoquinuclidines **2** (R = H; X = H). Likewise, hydrogenation of the methiodide **9** gave the N-methylisoquinuclidine **10** (X = H).



Next, we applied our reaction to the synthesis of desethylibogamine. Compound **1a** was cleaved readily with indoleacetic anhydride in acetone to give amorphous **12a** which upon hydrolysis with aqueous potassium carbonate in methanol afforded the hydroxy derivative **12b** (mp 195–196°; $C_{17}H_{22}N_2O_2$). The Oppenauer oxidation of **12b** followed by cyclization with 1.2 equiv of *p*-toluenesulfonic acid in benzene yielded the lactam tosylate **14a** which was then treated with sodium methoxide in boiling methanol to give the methoxy lactam **14b** (mp >290°; $C_{18}H_{20}N_2O_2$). Unexpectedly, this compound on treatment with lithium aluminum hydride gave the conjugated enamine **15** (mp 216–218°; $C_{18}H_{20}N_2O$). The structural assignment was based upon ultraviolet absorptions at 235 (ε 23,200) and 283 mμ (ε 12,500) in alcohol which are shifted to 222 (ε 33,800) and 281 mμ (ε 8720) by addition of hydrochloric acid, and also upon the nmr spectrum (AB-type quartet at τ 3.78 and 3.94 with a coupling constant of 8 cps ascribable to the conjugated *cis*-olefinic protons). This enamine **15** was hydrogenated readily on palladium, giving the methoxy base **16** (mp 193–195°; $C_{18}H_{22}N_2O$). Reductive elimination of the 18-methoxy group was accomplished smoothly by lithium aluminum hydride reduction performed in an analogous way to reduction of methoxyibogaine to ibogaine.[10] Thus, there was finally obtained desethylibogamine [mp 184–186°; $C_{17}H_{20}N_2$; λ_{max} 226 (ε 33,600), 284 (ε 7250), and 291 mμ (ε 6860)], physical



(8) The synthetic pathway will be described in a full paper.

(9) It is noteworthy that in the cleavage reaction of the bridged aziridines with an acylating agent in an alkaline medium, none of the solvent anion incorporated externally in this reaction. This fact clearly indicates intermediate formation of an ion pair such as A and the ion-pair return from the opposite side of nitrogen to give the ring opening compounds.

(10) G. Büchi and R. E. Manning, *J. Am. Chem. Soc.*, **88**, 2532 (1966).

properties of which are in good accord with those reported by Huffman[11] and his associates.

Acknowledgment. We wish to thank Mr. M. Murakami for his technical assistance.

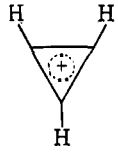
(11) We thank Professor Huffman for sending a copy of the infrared spectrum of desethyligogamine.

Wataru Nagata, Shoichi Hirai, Kyozo Kawata, Tamotsu Okumura
Shionogi Research Laboratory, Shionogi & Co., Ltd.
Fukushima-ku, Osaka, Japan
Received July 6, 1967

Cyclopropenyl Cation

Sir:

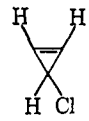
Following the synthesis of triphenylcyclopropenyl cation,[1] a number of other derivatives of this simplest aromatic system have been prepared.[2] The properties of these species, particularly in comparison with related compounds,[3] show clearly that the two π-electron cyclopropenyl cation is strongly stabilized by conjugation and meets other criteria of aromaticity. However, the properties of the parent cyclopropenyl cation (I) are still of considerable interest. We wish to report the synthesis of this cation as an isolable salt and some evidence on its stability.



I

We have previously reported[4] that the reduction of tetrachlorocyclopropene with tri-*n*-butyltin hydride affords a mixture of mono-, di-, and trichlorocyclopropenes; the dichlorocyclopropenes were converted to cyclopropenone.[4] Under appropriate conditions one can produce a mixture of mono- and dichlorocyclopropenes from which 3-chlorocyclopropene (II) is isolated by preparative glpc (5-ft 3% SE-30 on Chromosorb G at 22°) in 22% over-all yield. The mass spectrum shows the parent ion at *m/e* 74 (and 76), chlorocyclopropenyl cation at *m/e* 73 (and 75), and a very strong peak (85% of total intensity) for cyclopropenyl cation at *m/e* 39. The infrared spectrum (CCl_4 solution) has bands at 3080, 2970, 1615, 1245, 1155, 1120, 1025, and 865 cm^{-1}. In the nmr, II (in CCl_4 at 40°) shows a two-proton doublet at δ 7.57 and a one-proton triplet at δ 4.23 (J = 1.5 cps). In SO_2 (−40°) the chlorine rapidly moves from one carbon to another, presumably by reversible ionization to I, and a single sharp nmr line appears at δ 6.72, the weighted average position. In acetonitrile solution, the exchange rate is intermediate and lines from II are broadened beyond detection; the $\Delta H^{\pm}$ for this process must be quite small since the spectrum is unresolved from −40 to +40°.

(1) R. Breslow, *J. Am. Chem. Soc.*, 79, 5318 (1957).
(2) (a) R. Breslow and H. W. Chang, *ibid.*, 83, 2367 (1961); (b) R. Breslow, J. Lockhart, and H. W. Chang, *ibid.*, 83, 2375 (1961); (c) D. G. Farnum and M. Burr, *ibid.*, 82, 2651 (1960); (d) R. Breslow, H. Höver, and H. W. Chang, *ibid.*, 84, 3168 (1962); (e) R. West, A. Sadô, and S. Tobey, *ibid.*, 88, 2488 (1966); (f) for a review see A. W. Krebs, *Angew. Chem. Intern. Ed. Engl.*, 4, 10 (1965).
(3) R. Breslow, W. Bahary, and W. Reinmuth, *J. Am. Chem. Soc.*, 83, 1763 (1961); R. Breslow and P. Dowd, *ibid.*, 85, 2729 (1963).
(4) R. Breslow and G. Ryan, *ibid.*, 89, 3073 (1967).



II

On mixing solutions of II and $SbCl_5$ in CH_2Cl_2, cyclopropenyl hexachloroantimonate (I-$SbCl_6^-$) is precipitated as a white solid in quantitative yield and almost analytical purity (*Anal.* Found: C, 10.37; H, 1.42). The compound is stable for long periods at −20° and for several hours at room temperature, but on heating it darkens with no well-defined decomposition (or melting) point. Exposure to atmospheric moisture causes rapid blackening. The infrared spectrum[5] (mulls in Nujol or in CCl_4) shows only four bands in the usual region: 3105, 1276, 908, and 738 cm^{-1}. The first and third are C–H stretching and bending frequencies, while the second and fourth correspond to the two skeletal E′ bands reported[2e] for trichlorocyclopropenyl cation in this region. The nmr spectrum (in CH_3CN with $SbCl_5$) shows a single peak at δ 11.1 with singlet (half-width 0.75 cps) ^{13}C satellites ($J_{^{13}C-H}$ = 265 cps). The ^{13}C coupling constant is larger than those[4] for cyclopropenes or cyclopropenone, as in the case of other[6] carbonium ions. The satellites should be triplets, but the H–H coupling constant is expected to be small. In FSO_3H this salt has its signal at δ 10.87.[7] When II is treated with $AgBF_4$ in CH_3CN or SO_2 at −40°, AgCl precipitates and solutions of I-BF_4^- are produced identical in nmr with the above.

The observations on the stability of I, and in particular the fact that it is readily prepared but that II is covalent even in SO_2, are consistent with our previous[2b] extrapolations from substituted derivatives. Further work will be required to determine thermodynamic quantities of interest for I, and these must be interpreted[2a,d] in terms of both the conjugative and the strain factors which are involved. However, the fact that a salt of I can be prepared under such mild conditions is further evidence for the aromatic character of this system.[8]

(5) These bands disappear on exposure to atmospheric moisture in favor of a complex new spectrum.
(6) *Cf.* G. Olah, E. Baker, J. Evans, W. Tolgyesi, J. McIntyre, and I. Bastien, *J. Am. Chem. Soc.*, 86, 1360 (1964).
(7) *Cf.* D. G. Farnum, G. Mehta, and R. S. Silberman, *ibid.*, 89, 5048 (1967).
(8) This work was supported by the National Institutes of Health, through GM-13651 and a predoctoral fellowship for J. T. G.

Ronald Breslow, John T. Groves, Gordon Ryan
Department of Chemistry, Columbia University
New York, New York 10027
Received July 31, 1967

Ester Decarbonylation as a Route to Cyclopropenium Ion and Its Mono- and Dimethyl Derivatives

Sir:

Some years ago we reported the decarbonylation of 1,2-diphenylcyclopropene-3-carboxylic acid (Ia) in perchloric acid to give diphenylcyclopropenium ion (IIa).[1] The simultaneous application of this technique to the synthesis of dipropylcyclopropenium ion (IIb) by

(1) D. G. Farnum and M. Burr, *J. Am. Chem. Soc.*, 82, 2651 (1960).