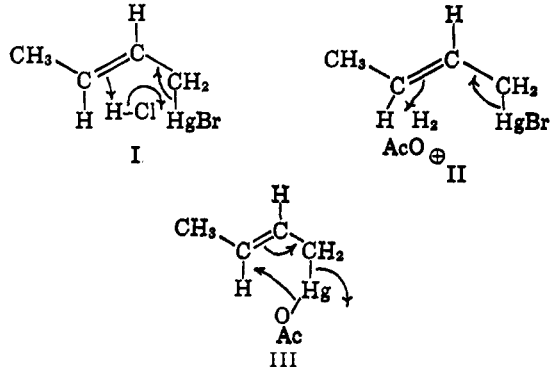
in a few minutes, or by 0.02 *M* perchloric acid in acetic acid solvent in 0.5 hr. Olefin is also the product from crotylmercuric acetate and hydrogen chloride in ethyl acetate, ligand exchange presumably being sufficiently rapid so that crotylmercuric chloride is the species cleaved to yield olefin. On the other hand, treatment of crotylmercuric acetate in acetic acid with dilute perchloric acid gives rise essentially exclusively to solvolysis products, the butenyl acetates, by way of the crotylmercuric ion.

Two noteworthy features of the acid cleavages of the allylic mercurials are the high rates of reaction compared to saturated mercurials and the relatively complete allylic rearrangement which accompanies them. Thus, crotylmercuric bromide reacts with hydrogen chloride more rapidly than does the *n*-butyl analog[7] by a factor which is roughly 10.[7] From this cleavage, as well as from the crotylmercuric acetate cleavage with hydrogen chloride, the butene obtained is very nearly pure 1-butene (Table I). This is true also of the butene from crotylmercuric bromide and perchloric acid in acetic acid solvent. Cinnamylmercuric derivatives behave similarly to the crotylmercuric analogs, hydrogen chloride cleavage leading nearly exclusively to allylbenzene.

TABLE I
OLEFINS FROM RCH=CHCH$_2$HgX

R	X	Solvent	Reagent	% Olefins: RCH$_2$CH=CH$_2$	RCH=CHCH$_3$ *trans*	RCH=CHCH$_3$ *cis*
CH_3	OAc	EtOAc	HCl	>99.2	0.3	<0.5
CH_3	Br	EtOAc	HCl	>99.3	.2	< .5
CH_3	Br	AcOH	$HClO_4$	>98.9	.6	< .5
C_6H_5	OAc	Et_2O	HCl	98.4	.9	.7
C_6H_5	Br	Et_2O	HCl	98.4	1.1	.5

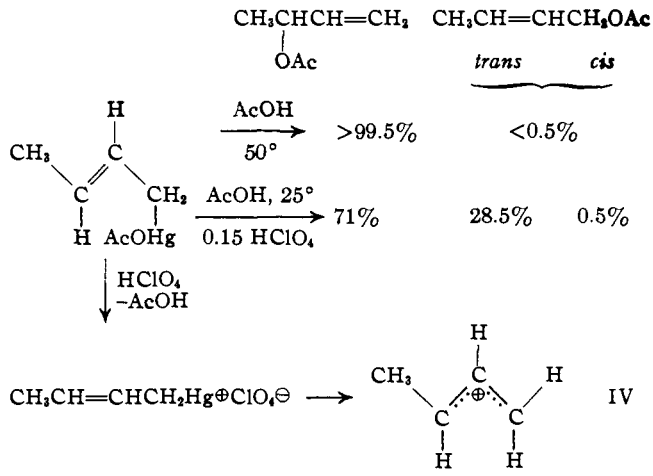
Both the high rate and the complete allylic rearrangement are explained by an S$_E$′ path for the acid cleavages. With hydrogen chloride in ether or ethyl acetate, the S$_{Ei}$′ designation (I) seems most likely, while the S$_E$2′ description (II) seems best for the cleavage with perchloric acid in acetic acid solvent.



Partial neutralization (11–16%) of *ca.* 0.05 *M* crotylmercuric acetate with perchloric acid in acetic acid solvent causes very rapid formation of mercury. The first order rate constant for the crotylmercuric perchlorate is (1.7 ± 0.3) × 10^{-2} sec.$^{-1}$ at 25.0°, some seven powers of ten greater than that for the *n*-butyl analog.[4a] The product of this demercuration is a 71:29 mixture of α-methylallyl and γ-methylallyl acetates, respectively, a result in accord with a carbonium ion description for the solvolysis. It is interesting that the crotyl component of the acetate product is nearly pure *trans*, in line with preservation of the *trans*-configuration by the crotyl cation[8] IV.

(7) J. Keller, Thesis, U.C.L.A., 1948.

(8) W. G. Young, S. H. Sharman and S. Winstein, *J. Am. Chem. Soc.*, **82**, 1376 (1960).



The behavior of crotylmercuric acetate in neutral acetic acid makes an interesting contrast with that in the presence of perchloric acid. In neutral acetic acid, slow solvolysis occurs along with some butene formation[9] (*ca.* 16% at 50°.) The kinetics of this reaction are not well behaved,[9] the solvolysis rate constant at 50° being *ca.* 5 × 10^{-6} sec.$^{-1}$. This figure is at least 10^6 times a value for *n*-butylmercuric acetate which can be deduced from data reported by Jensen.[4a] The product from neutral acetolysis of crotylmercuric acetate at 50° is entirely the rearranged secondary acetate, at least 99.5% pure.

The strict S$_N$i′ type result in the neutral acetolysis of crotylmercuric acetate suggests that this type of demercuration is another example in the whole spectrum of merging ion pair and non-ionic cyclic mechanisms of allylic rearrangements (see III). The present example is reminiscent of allylic azide,[10a] thiocyanate[10b] and thionbenzoate[10c] isomerizations.[11]

(9) This and other features of the neutral reaction have not yet been clarified.

(10) (a) A. Gagneux, S. Winstein and W. G. Young, *J. Am. Chem. Soc.*, **82**, 5956 (1960); (b) A. Iliceto, A. Fava and U. Mazzuceto, *Tetrahedron Letters*, **No. 11**, 27 (1960); (c) S. Smith, *J. Am. Chem. Soc.*, **83**, 4285 (1961).

(11) Allylmercuric acetate in neutral acetic acid yields more propylene than allyl acetate, the rate of the latter reaction being slower than the corresponding one for the crotyl analog by a factor of *ca.* 4–5 at 75°. If one assesses carbonium ion character of the transition state by the effect of the γ-methyl group on reactivity, neutral demercuration may be judged comparable to the above-mentioned isomerizations as regards ionic character.

(12) Standard Oil Company of California Fellow in Chemistry, 1959–1962.

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF CALIFORNIA
LOS ANGELES 24, CALIFORNIA
PAUL D. SLEEZER[12]
S. WINSTEIN
W. G. YOUNG

RECEIVED APRIL 24, 1963

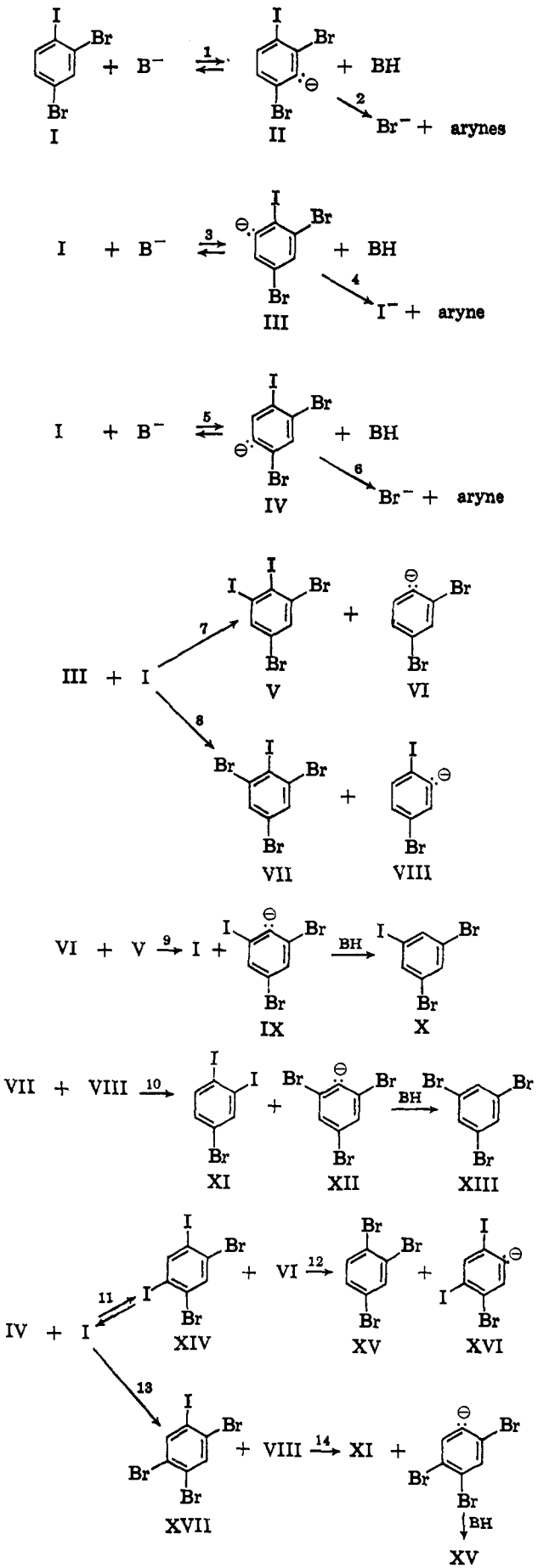
Base-Catalyzed Isomerization of Trihalobenzenes

Sir:

The unprecedented isomerization of 1,2,4-tribromobenzene to 1,3,5-tribromobenzene, in 33% yield through the action of sodium amide in liquid ammonia, was reported by Wotiz and Huba.[1] A 24% yield of 3,4-dibromoaniline was also reported.

Using potassium amide as the base and with careful attention to the purity and identity of reactant and product, we have been able to confirm that this unusual isomerization does occur, although conversions were only about 12% in our hands. However, when potassium anilide was employed instead of potassium amide, conversions of 1,2,4- to 1,3,5-tribromobenzene of 50–80% were observed. Rearrangement was never complete, and some products presumed to be diphenylamine derivatives were formed.

(1) J. H. Wotiz and F. Huba, *J. Org. Chem.*, **24**, 595 (1959).



It was found that 1-bromo-2,4-dichlorobenzene rearranges to 1-bromo-3,5-dichlorobenzene (33%) under similar conditions. However, 1,2,4-trichlorobenzene and 1,2,4-triiodobenzene did not isomerize. Nor was reversion of 1,3,5- to 1,2,4-tribromobenzene observable, even to a slight extent.

An elimination–addition mechanism, involving formation of 3,5-dibromobenzyne, reacquisition of bromide ion at the 1-position and finally proton recapture, was considered. Halide ion addition to benzyne has been demonstrated,[2] and by Roberts' rule[3] should go to the 1-position of 3,5-dibromobenzyne. However, no dibromochlorobenzenes or dibromoiodobenzenes were obtained when 1,2,4-tribromobenzene was isomerized in the presence of large amounts of potassium chloride or iodide, respectively.

Experiments with 1-iodo-2,4-dibromobenzene (I) have been illuminating as to reaction mechanism. When this substrate (0.02 *M*) reacted for 30 min. with potassium anilide (0.01 *M*) in refluxing liquid ammonia, the following were produced (percentages based on I): unrearranged I, 30.1%; 1-iodo-3,5-dibromobenzene (X), 28.5%; 1,2,4-tribromobenzene (XV), 11.7%; 1-bromo-3,5-diiodobenzene, 3.9%; 1,3,5-tribromobenzene (XIII), trace; Br^-, 9.9%; I^-, 14.5%; total, 98.6%. Several less abundant organic products are as yet unidentified. Organic products were determined by gas–liquid chromatography. Identities of all products were established by retention time analysis and by infrared spectra of effluent fractions condensed on powdered potassium bromide and then compressed into pellets. I, X and XV were isolated and further identified by melting point and mixture melting point. Halide ions were determined by potentiometric titration. In the presence of a large excess of potassium bromide, tribromobenzene formation was no greater than in the absence of external bromide ion.

Apart from the ineffectuality of external halide ions, the elimination–addition mechanism is contraindicated by the fact that 1,2,4-tribromobenzene overshadows its 1,3,5-isomer as a product from I. A more satisfactory account of the reaction is given by a mechanism comprising a series of nucleophilic displacements by phenyl anions on halogen atoms, as sketched. Such steps find analogy in the familiar halogen–lithium interchange reaction.[4]

It is considered that the 2-halogen of a 1,2,3,5-tetrahalobenzene is most apt to be captured by a phenyl anion, that a 2,6-dihalophenyl anion is unlikely to capture halogen, and that, other things being equal, an iodine is more apt to be captured than a bromine. The formation of X is accounted for by steps 3, 7 and 9, of XIII by steps 3, 8 and 10, and of XV either by 5, 11 and 12 or by 5, 13 and 14. Other alternative aryl anion intermediates and capture steps are conceivable, including some leading from XI or XVI to 3,5-diiodobromobenzene, and evaluation of the relative importance of the alternatives is not now attempted. It is possible that product–reactant pairs such as V + VI or XIV + VI remain partially in a charge transfer complex until they react further.

Reaction of I with a twofold excess of potassium amide in ammonia liberated 96.7% of bromide ion and 21.1% of iodide ion, a Br^-/I^- ratio of 4.58 in contrast to 0.68 with potassium anilide as reported above. Thus potassium anilide favors expulsion of iodide rather than bromide ion, as well as isomerization. A reasonable hypothesis is that steps 1, 3 and 5, forward, are largely rate determining with NH_2^-, and lead predominantly to formation of bromide ion (and

(2) G. Wittig and R. W. Hoffmann, *Chem. Ber.*, **95**, 2729 (1962).
(3) J. D. Roberts, C. W. Vaughan, L. A. Carlsmith and D. A. Semenow, *J. Am. Chem. Soc.*, **78**, 611 (1956).
(4) R. G. Jones and H. Gilman, *Org. Reactions*, **6**, 339 (1951).

substitution products) because the 3-hydrogen is the most acidic. With anilide ion, these steps approximate equilibria because aniline is a faster proton donor than ammonia. The rates of Br^- and I^- formation then depend on the respective equilibrium constants and on the rates of steps 2, 4 and 6. In the two cases, different factors determine which halide is expelled.

Acknowledgment.—We thank Professor John Neumer for stimulating discussions and the National Science Foundation and Army Research Office (Durham) for financial support.

METCALF CHEMICAL LABORATORY CHARLES E. MOYER, JR.
BROWN UNIVERSITY J. F. BUNNETT
PROVIDENCE 12, RHODE ISLAND

RECEIVED APRIL 3, 1963

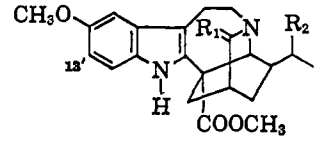
Voacamine

Sir:

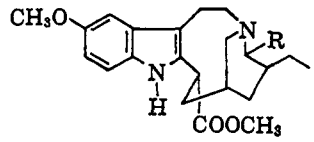
The indole alkaloid voacamine was first isolated from *Voacanga africana* Stapf.[1,2] Researches concerned with its structure established the presence in the molecule of one methoxy, one N-methyl and two carbomethoxy groups.[3,4] Molecular weight determinations indicated a molecule containing approximately twice as many atoms as the common indole alkaloids. Two of the four nitrogen atoms were found to be tertiary and basic whereas the remaining two were readily placed as components of two indole rings. Alkaline treatment furnished a dicarboxylic acid salt which on esterification with methanolic hydrochloric acid gave decarbomethoxy *epi*-voacamine (X). Esterification with diazomethane, however, yielded *epi*-voacamine (XI).[5] The facile decarboxylation of the dicarboxylic acid led to the suggestion[4] that voacangine (I) might be a moiety of the voacamine molecule and this was established by acid-catalyzed cleavage of the dimer to voacangine (I).[6] We now present further observations which establish structure IX for voacamine.

Cleavage of voacamine with 4 *N* hydrochloric acid in CH_3OD/D_2O (23 hr.) at reflux yielded, after recrystallization from methanol, trideuteriovoacangine identical with the product obtained by similar treatment of voacangine (I). All three deuterium atoms were located on the aromatic ring (mass spectra).[7] To exclude part structure IV, dihydrovoacamine,[5] m.p. 212–214° dec., was oxidized with iodine[8] to the corresponding lactam, m.p. 242–244° dec., convertible to voacangine lactam (II), m.p. 252–254°; $\nu_{max}^{CHCl_3}$ 1660, 1725 $cm.^{-1}$ by acid cleavage. The n.m.r. spectrum of voacamine (all in $CDCl_3$; chemical shifts in p.p.m. from tetramethylsilane) shows indole–NH signals at 7.48 and 7.70 δ, shifted to 9.03 and 9.23 δ in acetone-d_6. The voacangine proton at high field disappeared on exchange in D_2O whereas deuteration of the hydrogen bonded proton required acid catalysis. Clearly, the as yet obscure moiety in voacamine is linked to the aromatic ring of an intact voacangine (I) molecule.

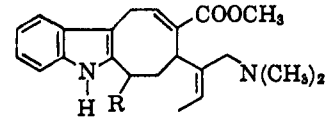
Proton spectra of voacamine did reveal only six aromatic protons and, furthermore, provided the first clue concerning the nature of the second moiety. Signals at 1.66 (doublet, J = 7 c.p.s.), 5.20 (quartet, J = 7 c.p.s.), 2.58 (singlet) and 2.44 δ (singlet) could be assigned to ethylidene, carbomethoxy and N-methyl groupings. In *epi*-voacamine (XI) the methyl ester protons appear at 3.57 δ. Substantially identical chemical shifts for these functionalities are found in the spectra of vobasinol (V)[9,10] and *epi*-vobasinol (VI)[11] and suggested the presence of these structural units in voacamine and *epi*-voacamine, respectively.



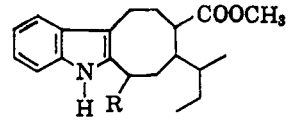
I. $R_1 = H_2$; R_2 = H
II. R_1 = O=; R_2 = H
III. $R_1 = H_2$; R_2 = OH



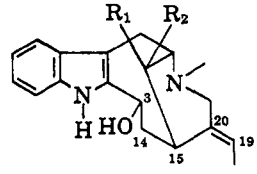
IV



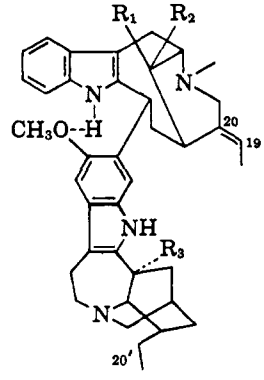
VII. R = voacangine



VIII. R = voacangine



V. R_1 = $COOCH_3$; R_2 = H
VI. R_1 = H; R_2 = $COOCH_3$



IX. $R_1 = R_3 = COOCH_3$; R_2 = H
X. $R_2 = COOCH_3$; $R_1 = R_3$ = H
XI. R_1 = H; $R_2 = R_3 = COOCH_3$

Sodium methoxide-catalyzed Hofmann degradation of voacamine monomethiodide gave the methine (VII),[5] m.p. 216–218° dec., $\gamma_{max}^{CHCl_3}$ 1710 $cm.^{-1}$, λ_{max}^{EtOH} 225, 286, 294 mμ (ϵ 62,700, 19,200, 19,400). In the deuterated methine, prepared from hexadeuteriovoacamine, the new vinyl proton became visible in the n.m.r. spectrum at 7.4 δ (multiplet) and the multiplet due to the adjacent methylene group appeared at 4.5 δ. The spectrum of the hydrogenolysis product (VIII), m.p. 252–255°, prepared by catalytic reduction of the methine over platinum in acetic acid revealed *three* C–methyl groups. Consequently, the carbon–carbon bond linking the two monomers can originate only at C-3, C-14 or C-15 of the vobasine fragment. Structure IX appeared most likely because the n.m.r. spectra of, *e.g.*, dihydrovoacamine (19,20-dihydro-IX) and *epi*-voacamine (XI) contained broad doublets due to a single proton at 5.00 and 4.74 δ, respectively. Condensation of equimolar amounts of dregaminol (19,20-dihydro-V)[9,10] and voacangine (I) in 1% HCl–CH_3OH (reflux, 1 hr.) yielded 50% of dihydrovoacamine (19,20-dihydro-IX), m.p. 213–215° dec., identical (infrared spectrum, R_f values, mixture melting point not depressed) with a sample prepared from natural (?) voacamine (IX). Mannich condensation occurred at the C-13′ position of voacangine (I) since the spectrum of

(1) M.-M. Janot and R. Goutarel, *Compt. rend. acad. sci.*, **240**, 1719 (1955).
(2) J. LaBarre and L. Gillo, *Bull. acad. roy. med. Belg.*, **20**, 194 (1955).
(3) R. Goutarel, F. Percheron and M.-M. Janot, *Compt. rend. acad. sci.*, **243**, 1670 (1956).
(4) F. Percheron, *Ann. chim.* (Paris), [13] **4**, 303 (1959).
(5) U. Renner and D. A. Prins, J. R. Geigy, S. A., Basel, private communication.
(6) W. Winkler, *Naturwiss.*, **48**, 694 (1961).
(7) K. Biemann and M. Friedmann-Spiteller, *J. Am. Chem. Soc.*, **83**, 4805 (1961).
(8) Method of M. F. Bartlett, D. F. Dickel and W. I. Taylor, *ibid.*, **80**, 126 (1958).
(9) U. Renner and D. A. Prins, *Experientia*, **17**, 209 (1961).
(10) U. Renner and D. A. Prins, *Chimia* (Basel), **15**, 321 (1961).
(11) The diamagnetically shifted carbomethoxy protons in vobasine were the subject of a recent communication by M. P. Cava, S. K. Talapatra, J. A. Weisbach, B. Douglas and G. O. Dudek, *Tetrahedron Letters*, **2**, 53 (1963).