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EVIDENCE AGAINST STRONGLY-BRIDGED BROMONIUM ION INTERMEDIATES IN BROMOCYCLIZATION REACTIONS OF 2-BUTENE DERIVATIVES[1]

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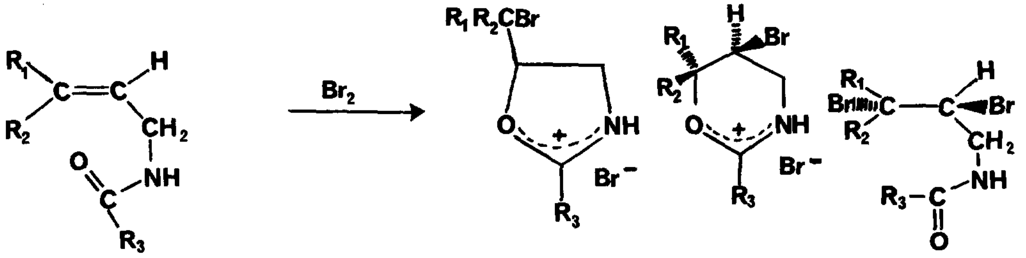
Cyclic bromonium ions have long been considered important species in electrophilic bromination of alkenes[2]. Evidence for their intermediacy in bromination of non conjugated alkenes is abundant,[3-9] and the mechanism[6] of bromine addition is assumed to involve fast, reversible π-complex formation, rate-determining bromonium ion formation, and nucleophilic displacement of the bridged bromine. It is now well-documented[6,9] that styrene and stilbene derivatives, unlike non-conjugated alkenes, may undergo bromination *via* competing mechanisms which involve a benzylic cation intermediate and a bromonium ion intermediate, respectively, depending on substituents.

We recently reported[10] evidence of significant carbocationic character in the product-forming step during bromination of N-cinnamyl-*p*-nitrobenzamide (Ia). The results of that study were assumed to be consistent[11] with the mechanism of the bromination of styrene derivatives as proposed by Yates and McDonald.[6] After an extensive comparative investigation of the isomeric 2-butenes versus styrene derivatives, Rolston and Yates[4] stated that "the marked differences in the behavior of the 2-butene system compared with that of the styrene system. . . leave little doubt that the nature of the reaction intermediates, and hence the mechanisms of bromine addition to these two systems, are quite different". They concluded that the results from their studies of the 2-butene system are consistent with a strongly-bridged bromonium ion intermediate of the type originally proposed by Roberts and Kimball.[2a] Thus, we turned our attention toward investigating bromocyclization reactions of non-conjugated allylic amides. We now wish to report our results of product studies from bromination of some 2-butene derivatives. These results are inconsistent with the mechanism of Yates *et*. *al*.[4,6] in that significant carbocationic character in the product determining step is evident.

The products of bromination of Ia-d are shown in Table I. The reactions of Ia-Ic were



I II III IV

a: $R_1=Ph$, $R_2=H$, $R_3=C_6H_4\text{-}p\text{-}NO_2$

b: $R_1=R_2=Me$, $R_3=C_6H_4\text{-}p\text{-}NO_2$

c: $R_1=Me$, $R_2=H$, $R_3=C_6H_4\text{-}p\text{-}NO_2$

d: $R_1=R_2=H$, $R_3=Ph$ or $C_6H_4\text{-}p\text{-}OMe$

carried out at room temperature in both acetic acid and carbon tetrachloride, and the cyclic products were isolated as the bromo-oxazoline or -oxazine derivatives after treatment of the crude salts with triethylamine. Nmr and mass spectral analysis unequivocally confirmed the structural assignments of all products, and the percentages of IIc, IIIc and IVc from the bromination of Ic were determined both by nmr and gas chromatography. The pure bromo-oxazine (from IIIc) was obtained by column chromatography on alumina.

It is well known[12,13] that under solvolytic conditions cyclization to a five-membered ring occurs about 10-100 times faster than cyclization to a six-membered ring. Thus, if the allylic amides undergo bromocyclization through a strongly-bridged bromonium ion intermediate, the five-membered derivatives IIa-d should be formed as the major cyclic product in all cases. Only in the case of Id is the five-membered ring the predominant cyclic product and, in that example, it is the sole cyclic product. In fact, the results follow the order of cation stability; Ia and Ib would form the stable benzylic and tertiary carbocations, respectively, and they cyclize solely to six-membered rings upon bromination. Because of the electron-withdrawing amide group, the vinylic carbon away from the amide group in Ic could best accommodate a positive charge, thus a slight preference for six-membered ring formation exists if carbocation stability is important.

Clearly then, strongly-bridged bromonium ions are of minor importance in bromocyclization reactions in polar solvents. Until our kinetic studies are complete on these systems we cannot speculate as to whether the amide group is anchimerically assisting addition.[14] Even if this is

Table I. Products of Bromination of Alkenylamides (a)

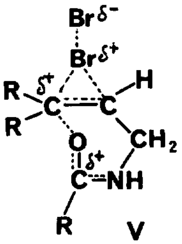
Alkene		Solvent	Cyclization Yield (b)	Ratio II:III	Yield of IV
Ia:	*trans*-N-Cinnamyl-*p*-nitrobenzamide	HOAc	76%	0:100	22%
		CCl_4	36%	0:100	64%
Ib:	N-(3-Methyl-2-buten-1-yl)-*p*-nitrobenzamide	HOAc	65±15%(c)	0:100	35±15%
		CCl_4	45±15%(c)	0:100	55±15%
Ic:	*trans*-N-Crotyl-*p*-nitrobenzamide	HOAc	60%	21:79	35%
		CCl_4	33%	48:52	58%
Id:	N-Allylbenzamide (d)	HOAc	45%	100:0	49%
		$HCCl_3$	42%	100:0	55%

(a) For Ia, Ib, and Ic, the $[Br_2] \cong 0.2M$; for Id, $[Br_2] = 0.94$ M in HOAc and 1.56M in $HCCl_3$; (b) Isolated yields; (c) the uncertainty results from the lability of IVb; refined values will be reported later; (d) Data from L. Goodman and S. Winstein, *J. Amer. Chem. Soc.*, **79**. 4788 (1957).

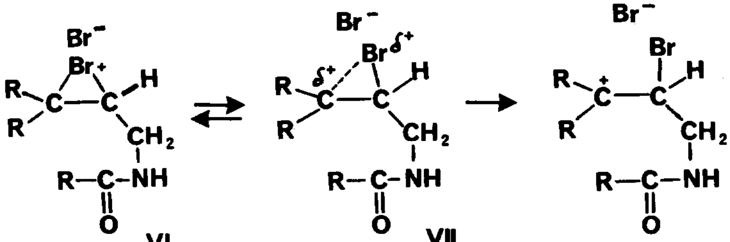
the case, these results are significant, since, to our knowledge, carbocationic character in a synchrous process such as this has not previously been defined.[15] An alternative explanation is that symmetrically-bridged[16] bromonium ions are not long-lived intermediates in unsymmetrical systems under these conditions; that is, the products derive from the most stable partially-bridged or open cation intermediate. Although we are not certain that the mechanism is the same in both solvents, the second explanation accommodates the change in product percentages with a change in solvent. It is likely that the species with the charge (or partial charge) on carbon is more sensitive to solvation effects than is the bromonium ion; thus, in non-polar solvents, there is more bromonium ion character.

The transition state *for an anchimerically assisted bromocyclization* consistent with our product studies, is depicted in V. *If anchimeric assistance is not occurring*, the bromonium ion VI must rapidly equilibrate, especially in polar solvents, to the most stable partially-bridged ion (VII) or, if the resulting cation is sufficiently stable,to an open cation (VIII), a process resembling an S_N1 reaction. With a neighboring group appropriately positioned,cyclization would occur prior to the unencumbered formation of VIII. Since bromide is a better nucleophile than the neighboring group, more dibromide should result from attack on VI. Additionally,if VI becomes important in non-polar solvents the kinetically favorable S_N2-like cyclization pathway (five-membered ring formation) becomes more important.

Assuming a non-concerted addition-cyclization, these results demonstrate the non-limiting nature of some electrophilic bromination reactions. The cmr studies of ethylenebromonium ions[5d] offer a precedent for the behavior observed.



V



VI VII VIII

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