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NOVEL REARRANGEMENT OF PROP-2-YNYL N-OXIDES TO HYDROXYLAMINE O-ALLENYL ETHERS: MECHANISTIC STUDIES

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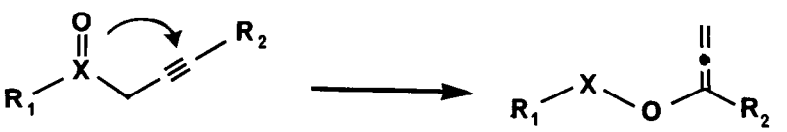
Summary: The novel thermolytic rearrangement of prop-2-ynyl N-Oxides to hydroxylamine O-allenyl ethers has been examined by deuterium labeling. Product analysis by gc-eims and by cims has shown the reaction to proceed by a concerted cyclic transition state.

Concerted [2,3] sigmatropic rearrangements have been reported for propargylic systems (Scheme 1) in which X was S[1], or P[2]. However, in the case of the selenoxide rearrangement (double rearrangement) in which X was Se[3] (Scheme 1), the reaction was shown to be partially intermolecular, since a mixed experiment gave 30% of the crossover product.[3] Moreover, the



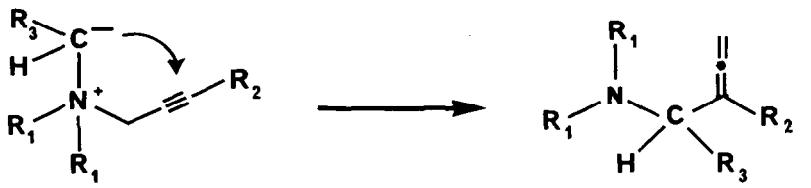
Scheme 1

rearrangement of the closely related propynyl ammonium ylide (Scheme 2) was concluded[4] to occur by a non-concerted pathway via cyclic σ-bonded intermediates rather than by the concerted direct [2,3]sigmatropic mechanism.[4]

We have examined[5] a number of the analogous propargylic N-oxides, obtained from the appropriate tertiary amines and m-chloroperbenzoic acid[6] and converted into their picrate salts using one equivalent of lithium picrate solution. The free N-oxides were freshly liberated from their purified picrates by passing them through basic alumina (1:100) and eluting with 5% methanol in chloroform. We found[5] that thermolysis of the N-oxides (either neat or in DMF) readily gave the hydroxylamine O-allenyl ethers (Scheme 1, X=N). Thus rearrangement of the N-oxides 1 and 2 (Table 1) led to the O-allenyl ethers 3 and 4 in high yield. A single product was obtained in each case, and (though readily hydrolyzed) was stable enough to be distilled and fully characterized by ir and nmr spectroscopy and both low

resolution gc-eims and high resolution cims.

This reaction, a Meisenheimer rearrangement,[7] may be compared with the thermolysis of allylic N-oxides to the corresponding O-allylhydroxylamines investigated by Cope.[7] The present reaction may take place either by a cyclic five-membered ring transition state, by a radical dissociation - recombination pathway, or via carbonium ion intermediates.[7] A carbonium ion intermediate would involve the equilibrium [$^{+}CH_2$-C C-R $\leftrightarrow CH_2$=C=$\overset{+}{C}$R], and since the former is more stable than the latter,[8] the formation of the isomers 5 and 6. In a free radical mechanism, the equilibrium [CH_2-C C-R $\leftrightarrow CH_2$=C=CR] would also favor the former of the two isomers,[9] and would again result in the formation of 5 and 6, as well as the dimer 7. However, nmr analysis confirmed the absence of the $-OCH_2-$ moiety, showing that compounds 5 and 6 were not present in detectable amounts. In addition, the dimer 7 was not detected as a product.



Scheme 2

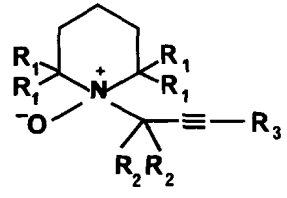
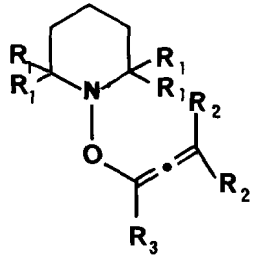
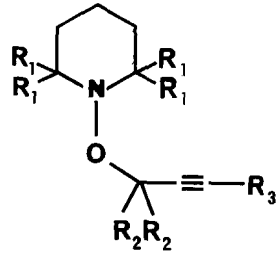
A deuterium labeled variant 8 of the N-oxide 2 was synthesized from the product obtained by reducing N-prop-2-ynylglutarimide with lithium aluminum deuteride. Thermolysis of 8 gave only the allenic product 9, no trace of the propargylic isomer 10 being detected.

$$R_3 - C \equiv C - CH_2CH_2 - C \equiv C - R_3 \qquad 7$$

A mixed reaction of equimolar amounts of 1 and 8 was analyzed by gc-eims using multiple specific ion recording, each of the two gc peaks being scanned simultaneously[10] at the masses corresponding to the molecular ions of the d_0 and d_4 variants of the possible products 3, 4, 9, and 11. Only the two products 3 and 9 were found, in > 97% amount, with only traces (<3%) of the molecular ions corresponding to the "crossover" products 4 and 11 which would result from a free radical mechanism. The nmr spectrum showed no evidence of the propargylic products 5, 6, 10, and 12 which would arise from carbonium ion intermediates.

Because of possible uncertainties regarding the relative reaction rates[11] of 1 and 8, the reaction was reinvestigated using two isotopic variants of the same compound. The d_2-analogue

Table 1

S T R U C T U R E S			Substituents		
			R_1	R_2	R_3
1	3	5	H	H	H
2	4	6	H	H	CH_3
8	9	10	D	H	CH_3
-	11	12	D	H	H
13	14	15	H	D	CH_3
-	16	-	D	D	CH_3

13 was obtained using 1-bromobut-2-yne-1,1-d_2, the corresponding alcohol being readily prepared by lithium aluminum deuteride reduction of methyl tetrolate. The N-oxide 13 thermolyzed to give solely the allene 14; the propargylic product 15 was not detected.

The N-oxides 8 and 13 had identical reaction rates. An equimolar mixture of 8 and 13 gave a product (single gc peak) which was a single chemical compound in which 9 and 14 represented the d_4 and d_2 variants (i.e. the products of intramolecular reaction) while 4 and 16 would be the d_0 and d_6 variants expected from an intermolecular mechanism. In this case it was found that scrambling of the allenyl side chain occurred in the gc-eims process,[12] resulting in the observation of all four products 4, 9, 14, and 16. However, analysis of the same product by direct insertion cims showed the formation of equal amounts of the intramolecular products 9 and 14 to predominate (>95%) with only trace amounts (<5%) of the products of intermolecular reaction.

On the basis of the above evidence, the rearrangement may be considered to proceed by a concerted [2,3]sigmatropic shift, and affords a further instance of the synthetic utility of this type of cyclic intramolecular process.

References and Notes

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12. This cannot be due to scrambling of the label, since no variants of the molecule containing odd numbers of deuterium were observed.

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