NOVEL CARBON-CARBON BOND CLEAVAGE REACTIONS OF α-AZOHYDROPEROXIDES

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1-Phenylazo-1-hydroperoxycyclohexanes, easily prepared by the autoxidation of cyclohexanone phenyl hydrazones, have been found to undergo C(1)-C(2) bond cleavages when treated with acids, bases, or reducing reagents under mild conditions. Thus 6-oxoalkanoic acids and their derivatives have been obtained in good yields from 2hydroxycyclohexanone derivatives. The 2-hydroxyl group seems to play an important role for the cleavage.

 α -Azohydroperoxides], easily obtained by the autoxidation of phenylhydrazones, have been reported to undergo a variety of reactions: the regeneration of original ketone when treated with potassium iodide in acidic media,² the catalytic hydrogenation to afford 1-pheny1-2-benzohydrazide, ^{1c} the decomposition with cuprous or ferrous ion to generate phenyl radical, nitrogen, and the original ketone,³ and the photolysis or thermolysis in anhydrous media to form hydroxyl radical, aryl radical, nitrogen, and the original ketone. 4 Thus, except for the only report focused on the one-carbon degradation of carbohydrate derivatives,⁵ no work has been reported about the cleavage or rearrangement of the carbon framework of the original carbonyl component in α -azohydroperoxides. We report herein an unprecedented C-C bond cleavage α to the carbon bearing a perhydroxyl group by mild reagents.

 α -Azohydroperoxides 2-4⁶ formed from the corresponding hydrazones⁷ (1 mmol) in methanol (20 ml) with one equivalent of oxygen absorbed were treated as such with acids, bases, or reducing reagents under a nitrogen atmosphere. The C-C bond was cleaved under mild conditions to give 6-oxoalkanoic acids or their derivatives 5-9

as the major products. The results are shown in Table I.

The observation for 2 and 3 that the starting ketone was not recovered suggests that the C-C bond cleavage is essential for the reactions (entries 1-5). Nitrogen was not evolved in appreciable amounts. Thus the acid-catalyzed rearrangement⁸ is



expected to generate a positive oxygen which is supplied with a pair of electrons by a neighboring C-C bond. Here the C-C bond cleavage rather than the usual alkylgroup migration⁸ seems more likely owing to the presence of a hydroxyl group which assists the cleavage by releasing a pair of electrons (Scheme I). The resulting N-acyl-N'-phenyldiazene undergoes acid-catalyzed methanolysis⁹ to give 5^{10} and 8^{11} . The electron-withdrawing phenylazo group is capable of becoming a good leaving group as phenyldiazene,¹² the fate of which remains obscure.

The base-catalyzed bond cleavage for 2 seems to be initiated by the attack of hydroxide ion at the hydroxyl hydrogen (entry 2). The reaction path (Scheme II) is similar to that proposed by Schulz et al. 5

The action of dimethyl sulfoxide on 2 and 3 is expected to give the corresponding diols 10 and 11. However, 10 was not isolated, 7 being obtained as the major product¹³ (entry 3). Another diol 11 was gradually rearranged to 9, although stable enough to permit the acquisition of ¹³C NMR spectrum¹⁴ (entry 5). The rearrangements $10 \rightarrow 7$ and $11 \rightarrow 9$ are best accounted for by six-membered intramolecular acid catalysis, being driven by the unstable α -hyroxyalkyl azo function^{1c,15} (Scheme III).

entry	hydroperoxide	reagent	conditions temp, ^O C	time, h	product	(% yield)
1	2~	H ₂ SO ₄ ^b	12	5	5	(70)
2	2~	NaOH	12	5	6	(56) ^d
3	2~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	Me2s	12	1.5	Z	(80)
4	3	H ₂ SO ₄	12	4	8	(40)
5	3	Me ₂ s ^e	0	0.5	9	(70)
6	4	$H_2 SO_4^b$	65 ^f	1	5	(26)
7	4	NaOH ^C	30	6	6 ~	(23) ^d

Table I. Carbon-Carbon Bond Cleavage Reactions of α -Azohydroperoxides in Methanol^a

^{*a*}2-4 derived from 1 mmol of the corresponding hydrazones in 20 ml of methanol were used for the reactions under nitrogen. ^{*b*}0.2 ml (3.8 ml) of concd sulfuric acid was added. Perchloric acid catalyzed the cleavage similarly. ^{*c*}1.6 g of sodium hydroxide in 5 ml of water was added. ^{*d*}Distilled yield as methyl ester. ^{*e*}0.31 g (5 mmol) of dimethyl sulfide was added. Triphenyl phosphine reacted with 2 and 3 as well, but the workup was tedious. ^{*f*}Refluxed.

It is noteworthy that 4 having no hydroxyl group on the β -carbon has been cleaved to 5 or 6 by acid or base catalysis (entries 6 and 7). The mechanism of the C-C bond cleavage for 4 is currently being investigated with an aim to improve the yield. Considering the importance of the cleavage of C-C bonds in organic synthesis, the present cleavage reaction is expected to introduce a promising new method with advantages of mildness and ease. Further work in this area will be reported in due course.

References

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- 6) α -Azohydroperoxides 2-4 are unstable and soon deteriorate at room temperature to a dark oil, especially, when the solvent is removed. However, 4 is stable enough to allow measuring ¹H and ¹³C NMR spectra in CDCl₃. 2-4: UV max (MeOH) 273 nm (ϵ 11000).
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- 13) Carbohydrazide 7 recrystallized from CCl₄ (mp 88.5–89.0 $^{\rm O}$ C) and identified by elemental and spectral analyses (IR, $^{1}{\rm H}$ and $^{13}{\rm C}$ NMR).
- 14) The conversion $11 \rightarrow 9$ was completed within 11 h at 55 °C. The ¹³C NMR spectra for 9 and 11 are shown below:



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1610