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NOVEL CARBON–CARBON BOND CLEAVAGE REACTIONS OF α-AZOHYDROPEROXIDES

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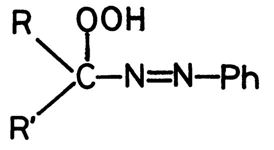
1-Phenylazo-1-hydroperoxycyclohexanes, easily prepared by the autoxidation of cyclohexanone phenyl hydrazones, have been found to undergo C(1)–C(2) bond cleavages when treated with acids, bases, or reducing reagents under mild conditions. Thus 6-oxoalkanoic acids and their derivatives have been obtained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

α-Azohydroperoxides **1**, easily obtained by the autoxidation of phenylhydrazones,[1] 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-phenyl-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**–**4**[6] formed from the corresponding hydrazones[7] (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 rearrangement[8] is



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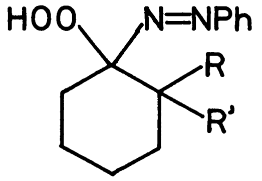
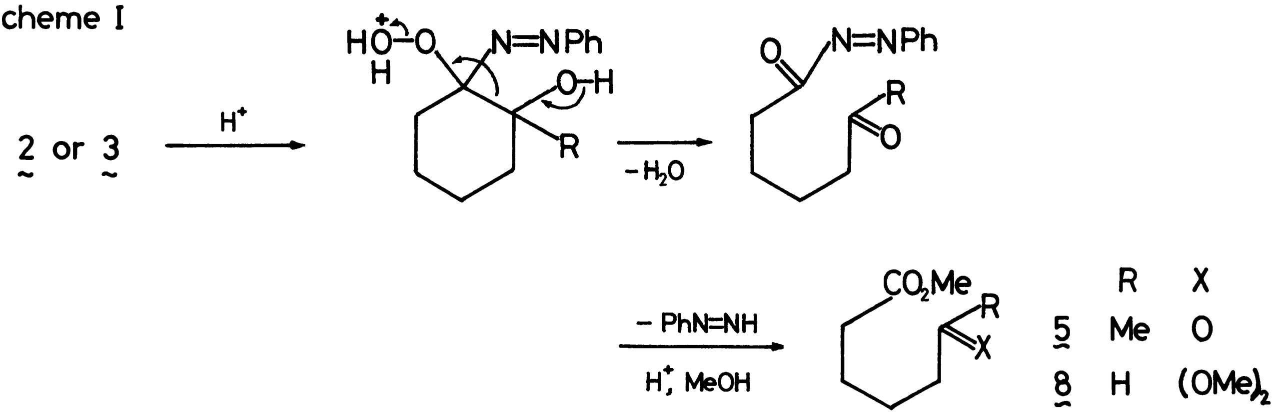
R = alkyl or aryl, R' = H

R = alkyl, R' = alkyl



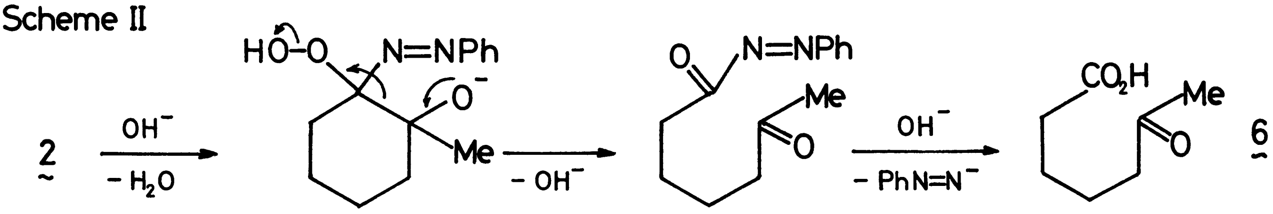
	R	R'
2	Me	OH
3	H	OH
4	Me	H

Scheme I

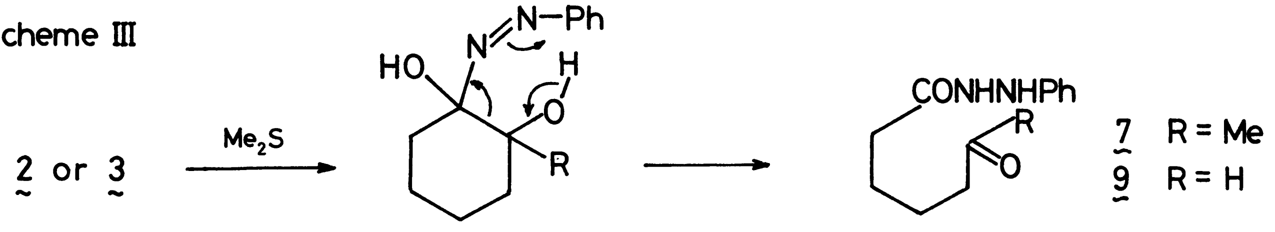


	R	X
5	Me	O
8	H	(OMe)$_2$

Scheme II



Scheme III



10 R = Me **11** R = H

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 alkyl-group migration[8] 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 methanolysis[9] 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 product[13] (entry 3). Another diol 11 was gradually rearranged to 9, although stable enough to permit the acquisition of ^{13}C NMR spectrum[14] (entry 5). The rearrangements 10→7 and 11→9 are best accounted for by six-membered intramolecular acid catalysis, being driven by the unstable α-hyroxyalkyl azo function[1c,15] (Scheme III).

Table I. Carbon–Carbon Bond Cleavage Reactions of α-Azohydroperoxides in Methanol[a]

entry	hydroperoxide	conditions reagent	 temp, °C	 time, h	product (% yield)
1	2	H_2SO_4[b]	12	5	5 (70)
2	2	NaOH[c]	12	5	6 (56)[d]
3	2	Me_2S[e]	12	1.5	7 (80)
4	3	H_2SO_4[b]	12	4	8 (40)
5	3	Me_2S[e]	0	0.5	9 (70)
6	4	H_2SO_4[b]	65[f]	1	5 (26)
7	4	NaOH[c]	30	6	6 (23)[d]

[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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5) Schulz, M.; Somogyi, L. *Angew. Chem. Internat. Edit.* 1967, 6, 168.
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 ^{13}C NMR spectra in $CDCl_3$. 2–4: UV max (MeOH) 273 nm (ε 11000).
7) The ketones reacted with one equivalent of phenylhydrazine in the absence of solvent. The water formed in the reaction mixtures was removed in vacuo to give the hydrazones quantitatively.
8) Ref 1a, pp 65–70.
9) Hoffmann, R. W. *Chem. Ber.* 1964, 97, 2772–2778.
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11) Acetal 8 isolated by preparative TLC and identified by elemental and spectral analyses (IR, ^1H and ^{13}C NMR).
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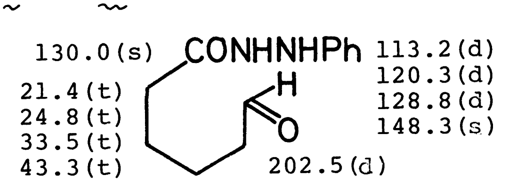
13) Carbohydrazide 7 recrystallized from CCl_4 (mp 88.5–89.0 °C) and identified by elemental and spectral analyses (IR, ^1H and ^{13}C NMR).
14) The conversion 11 → 9 was completed within 11 h at 55 °C. The ^{13}C NMR spectra for 9 and 11 are shown below:



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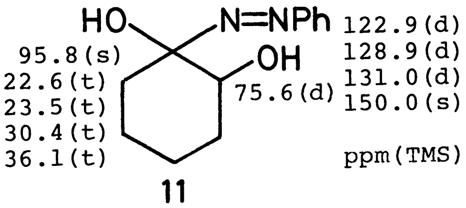

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