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FREE RADICAL CARBOCYCLIC RING RECONSTRUCTION

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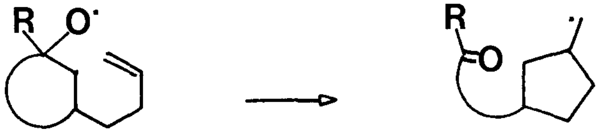
Abstract: Alkenyl radical generated by β-fragmentation of tertiary cyclohexyloxy radical with carbocyclic ring opening, possessing a suitably located olefinic double bond, undergoes to the intramolecular 5-exo-trigonal cyclization and a new carbocyclic ring was formed.

Among a variety of reactions β-fragmentation is one of the preferential mode of stabilisation of tertiary alkoxy radicals[1]. Homopolar nature of β-cleavage reaction of alkoxy radicals is well-established and the carbonyl containing fragment and products derived from the alkyl radical fragment were produced[1-6]. The rate of β-cleavage of alkoxy radicals is independent of the radical precursors but is mainly dependent of the stability of the initialy formed carbon radicals[2,3]. Thereby, intramolecular cyclization of 5-hexenyl radicals to the cyclopentylmethyl radicals are well known reaction for the construction of carbocyclic[7,8] and heterocyclic rings[9].

However, homopolar scission of C-C bond in the alkoxy radical intermediates, followed by radical recombination reaction with a new C-C bond formation in the same molecule have not been investigated together as a sequence of reactions. This radical recombination reactions could involve one ring opening and the other ring closure with a considerable change of the carbon skeleton (Scheme 1.).

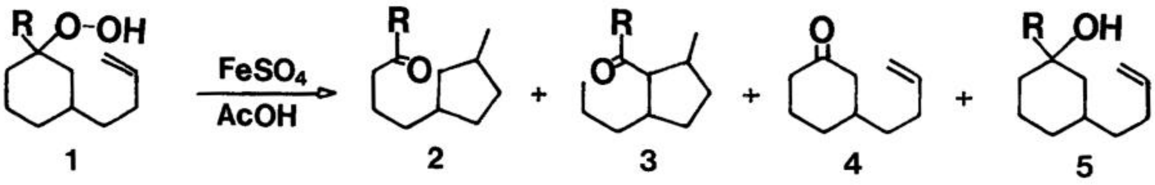


Scheme 1.

We wish to report a new approach to carbocyclic ring reconstruction involving a tertiary alkoxy radical fragmentation and intramolecular addition of arising alkenyl radical onto the suitably located olefinic double bond.

It was found that this free radical fragmentation-cyclization reaction involving a ring reconstruction can be achieved by ferrous ion induced decomposition of 1-alkyl- or 1-aryl-3-(3-alkenyl)-cyclohexyl hydroperoxides 1a-c[10]. Two saturated ketones having a cyclopentane ring 2a-c and 3a-c were obtained as a chief reaction products in 28-38% and 7-30% yields, respectively, in addition to the unsaturated ketones 4a-c (8-30%) and starting alcohols 5a-c (7-20% yields) (Scheme 2.).

In a typical experiment 2.48 g (13.5 mmole) of alkyl hydroperoxide 1a[11] was treated with 3.75 g of powdered crystaline ferrous sulfate in acetic acid as a solvent in inert atmosphere. During 3 hrs hydroperoxide was completly reduced. The reaction mixture was worked up as it was described[12] and products were separated and purified by glc and characterized by ir, nmr and mass spectra[13].

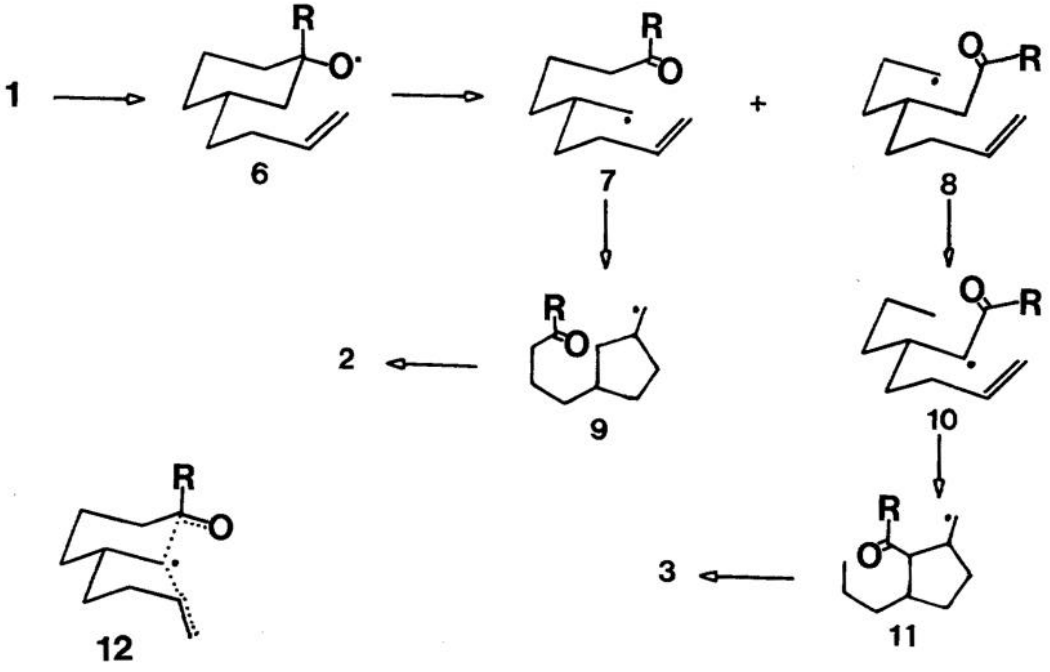


	2	3	4	5
a. R = Me	38%	30%	8%	18%
b. R = Et	28	18	17	20
c. R = Ph	32	7	30	7

Scheme 2.

For example, by decomposition of 1-methyl-3-(3-butenyl)cyclohexyl hydroperoxide 1a by ferrous ion 5-(3-methylcyclopentyl)-pentan-2-one 2a (38%) and methyl (2-methyl 5-n-propyl)-cyclopentyl ketone 3a (30%) were obtained as a products of ring reconstruction reactions.

Tertiary 1-alkylcycloalkyloxy radicals, regardless of its precursors, undergo to the β-cleavage reaction and 5-carbonylpentyl radical was formed as an intermediate[4-6]. By possessing an alkenyl group in position 3 of cyclohexane ring the alkoxy radical 6 is not symmetrical and two possibilities for C_α-C_β bond scission exist, thus two fragmented carbon centered radicals 7 and 8 were generated as intermediates (Scheme 3.). Ratio of ketones 2 and 3, derived from fragmented carbon

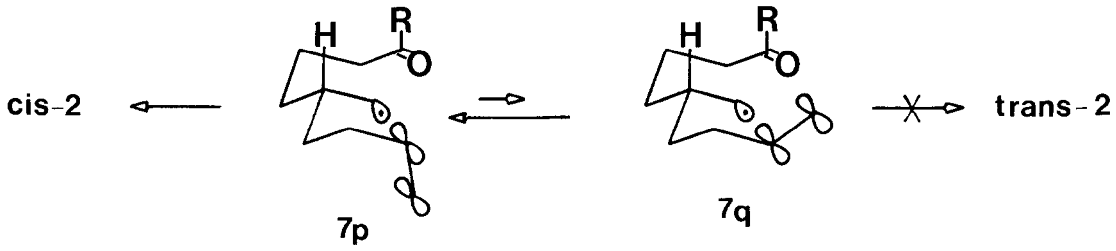


radicals 7 and 8, respectively, indicates that a small long range participation of olefinic double bond on the course of β-cleavage reaction exists. Participation of olefinic bond on the course of β-scission reaction can be explained by involving transition state 12. Although, a litle lower yields of ketone 3 in respect to ketone 2 may be due to side reactions of radicals 8, 10 and 11.

The further reaction of these two primary, fragmented, carbon radicals 7 and 8 are considerably different. By possessing an olefinic bond in position 5 radical 7 undergoes almost exclusively to the intramolecular 5-exo-trigonal cyclization, thus producing a cyclopentylmethyl radical 9. Termination process for radical 9 is hydrogen abstraction and ketone 2 was formed as a final product of radical recombination reactions. Products of 5-endo-trigonal cyclization, coupling dicarbonyl compounds and hydrogen abstraction products, which could be derived from fragmented radical 7, were not observed.

However, fragmented primary carbon radical 8 undergoes to the 1,5-hydrogen abstraction from the methylene group adjacent to carbonyl group and a secondary radical 10 was generated (Scheme 3.). This radical rearrangement is energetically favourable for about 6 kcal/mole[14]. The fate of α-carbonyl radical 10 with an olefinic bond in position 5, as it was expected, it undergoes to the intramolecular cyclization reaction and a new cyclopentylmethyl radical 11 arising which affords a ketone 3 as a final product[15].

Saturated ketone 2 was obtained as a pure cis-isomer, what is in agreement with greater stability of cis-1,3-dialkylcyclopentane derivatives[16], as well as more favourable conformation of butenyl group in carbon radical 7p (Scheme 4.), with quasi-endo-orientation of olefinic bond leading to cis-isomer 2. While the conformation 7q which is requested for trans-isomer formation with quasi-exo-orientation of alkenyl group is less favourable.



Scheme 4.

Investigation of other type of alkoxy radical precursors and other type of rings reconstructions are in progress.

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