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Studies on Stable Free Radicals. IV.*1 Decomposition of Stable Nitroxide Radicals

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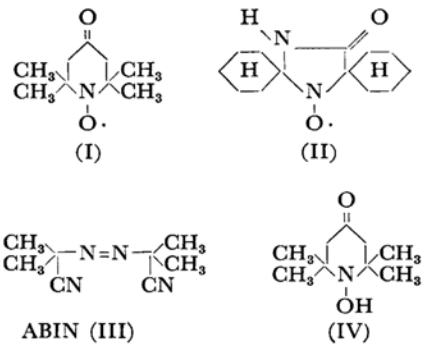
Decomposition studies of extremely stable free radicals such as 2,2,6,6-tetramethyl-4-oxopiperidine-1-oxyl (I), 2,2,6,6-tetramethylpiperidine-1-oxyl (VIII) and 2,2,6,6-tetramethyl-4-hydroxypiperidine-1-oxyl (IX) were carried out: although radical I decomposed to give 1-hydroxy-2,2,6,6-tetramethyl-4-oxopiperidine (IV) both in the light and dark, radicals VIII and IX were more stable under these reaction conditions. Therefore it was confirmed that i) a source of hydrogen was the ketonic α-methyene hydrogens, ii) a radical which could give a thermodynamically stable conjugated product by a cycloelimination was easily decomposed and iii) the decomposition of radical I was only accelerated by heating and was independent of the action of light.

In a previous study on reactivity of extremely stable free radicals,[1] it was reported that the reaction of stable free radicals such as 2,2,6,6-tetramethyl-4-oxopiperidine-1-oxyl (I) and cyclohexane-1-spiro-2'-(4'-oxoimidazolidine-1'-oxyl)-5'-spiro-1''-cyclohexane (II) with a *C*-radical derived from α,α'-azo-bis(isobutyronitrile) (ABIN) (III) gave the corresponding coupled products. Although the reaction of II with III proceeded in a high yield, the reaction of I with III only gave a coupled product in a poor yield and a by-product, 1-hydroxy-2,2,6,6-tetramethyl-4-oxopiperidine (IV), in 38.4% yield.[1] We wish to explain the differences in the mechanism in the case of I and II in this paper.



Results and Discussion

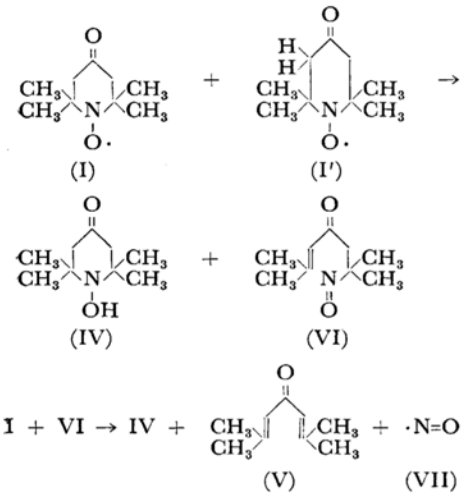
It appears that the by-product (IV) arose from a hydrogen abstraction reaction of I. *A priori* following sources of hydrogen would be possible: i) hydrogen from the solvent (MeOH), ii) a trace of water, iii) a methyl-hydrogen in ABIN (III), iv) that in radical I, v) a methylene-hydrogen in I. In order to exclude the possibilities i) ii) and iii), a solution of radical I in anhydrous benzene was refluxed for 30 hr under a dry nitrogen atmosphere. Under these conditions radical I afforded the >N–O–H (IV) and a polymeric substance[2] in 60% and 30% yields, respectively. A trace of 2,6-dimethyl-2,5-heptadien-4-one (phorone) (V) was also isolated and identified by comparison of melting point, IR and NMR spectra and vpc retention time with those of an authentic sample. Furthermore heating of radical I at 105—110°C in the absence of solvent for 3 hr under a

*1 Part III: K. Murayama and T. Yoshioka, This Bulletin, **42**, 1942 (1969).

1) K. Murayama, S. Morimura and T. Yoshioka, This Bulletin, **42**, 1640 (1969).

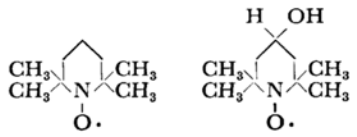
2) The structure of a polymeric substance was uncertain.

dry nitrogen atmosphere, gave the same results. These observations would suggest the following mechanism. The stable radical I abstracts a hydrogen atom from an α-methylene of the ketone in another radical I (=I') to give a reactive intermediate (VI). A second stable radical I abstracts a hydrogen atom from the intermediate VI to give a second >N–O–H (IV), a thermodynamically stable conjugated ketone (phorone) (V) and nitric oxide (VII).[3] Thus three moles of I give two moles of IV and therefore the theoretical yield of IV is 66.6% based on the weight of the starting material. This supposition is therefore compatible with our observation. Phorone (V) prepared from I may be further polymerized by nitric oxide (VII).[4]



Thus : 3·(I) → 2·(IV)

The following additional argument was made for the sake of confirming the action of a hydrogen atom on a α-carbon of the ketone group in the piperidine ring. If such α-methylene hydrogens were effective, 2,2,6,6-tetramethylpiperidine-1-oxyl (VIII) and 2,2,6,6-tetramethyl-4-hydroxypiperidine-1-oxyl (IX), which had no ketone group, should be more stable than radical I.



Under the same reaction conditions, as expected, radicals VIII and IX were almost recovered, and additionally no ketonic compound I was detected by the vpc technique, although the ketone I was anticipated to be prepared from the corresponding secondary alcohol IX by the attack of the *N*-oxyl radical IX just as acetone was prepared from isopropyl alcohol by the attack of the free radicals derived from diacetyl peroxide.[5] Similarly, no formation of acetone was observed during the hydrogen abstraction reaction by the radical IX from isopropyl alcohol.

A similar cycloelimination has been reported by Keana *et al.*[6] They have attempted a photolysis of the stable free radical, *e.g.* 3-carbamoyl-2,2,5,5-tetramethylpyrroline-1-oxyl, to obtain the thermodynamically stable conjugated corresponding ketone and nitric oxide (VII). This fact suggests that the stable free radical I may decompose photochemically. In order to investigate the possibility of photocycloelimination of radical I, a solution of I in anhydrous benzene was refluxed in the dark for 30 hr under a dry nitrogen atmosphere. Thus radical I converted into the >N–O–H (IV) in a high yield just as in the light. Accordingly, the photocycloelimination observed in the study of 3-carbamoyl-2,2,5,5-tetramethylpyrroline-1-oxyl[6] was excluded in a case of the

TABLE 1. REACTION CONDITIONS AND PROPERTIES OF PRODUCTS

Entry	Solvent	Reaction time (hr)	Reaction temperature	Light	Product
i	b	15	reflux	light	IR-OH
ii	b	30	reflux	light	crystal
iii	b	15	reflux	dark	IR-OH
iv	b	30	reflux	dark	crystal
v	non	4	95—100°C	light	crystal
vi	non	4	95—100°C	dark	crystal
vii	non	3	105—110°C	light	crystal
viii	non	3	105—100°C	dark	crystal

b: in a benzene solution; non; without solvent; light: under a room light; IR-OH: detected ν_{O-H} (IR) in a crude oil: crystal: isolated as crystals (mp 90—91°C).

3) No attempt was made to isolate and identify this gas VII as well as in a case of Ref. 6.

4) Polymerization of phorone (V) with nitric oxide (VII) was not attempted in this work.

5) M. S. Kharasch, J. L. Rowe and W. H. Urry, *J. Org. Chem.*, **16**, 905 (1951).

6) J. F. W. Keana and F. Baitis, *Tetrahedron Letters*, **1968**, 365.

stable free radical I. Table 1 shows reaction conditions and properties of products.

It was therefore confirmed that i) a source of hydrogen was the α-methylene hydrogen of the ketone group in the piperidine ring (I), ii) a stable radical which could give a thermodynamically stable conjugated product by a cycloelimination was easily decomposed and iii) the decomposition of radical I was only accelerated by heating and was independent of the action of light.

Experimental

Melting points were uncorrected.

The NMR spectra were obtained with a Varian A-60 NMR spectrometer, using tetramethylsilane as an internal standard at 32°C.

The IR spectra were determined by means of Nujol mull and liquid film.

Materials. 2,2,6,6,-Tetramethyl-4-oxopiperidine-1-oxyl (I) was prepared by the oxidation of the corresponding amine by hydrogen peroxide in the presence of sodium tungstate and ethylenediaminetetraacetic acid (EDTA).[7] 2,2,6,6-Tetramethylpiperidine-1-oxyl (VIII) and 2,2,6,6-tetramethyl-4-hydroxypiperidine (IX) were derived from I.[8,9]

General Procedure for the Decomposition of the Extremely Stable Free Radicals. a) A solution of 17.0 g (0.10 mol) of radical I in anhydrous benzene was refluxed for several hours under a dry nitrogen atmosphere. After the solvent was evaporated under reduced pressure and the IR spectrum of the residue was taken, the residue was distilled under reduced pressure at low temperature (below 80°C). The distillate ($bp_{0.05}$ 75—80°C) was scratched to induce crystallization and the solid obtained was filtered and recrystallized from petroleum benzine to give an analytically pure sample which was identified by comparison of a melting point, IR and NMR spectrum and vpc retention time with that of an authentic 1-hydroxy-2,2,6,6-tetramethyl-4-oxopiperidine (IV),[10] mp 90—91°C. A mixed melting point with the authentic IV was undepressed. Found: C, 63.47; H, 10.19; N, 7.98%. Calcd for $C_9H_{17}NO_2$: C, 63.16; H, 10.04; N, 8.19%.

b). After heating radical I at 110°C for 3 hr under a dry nitrogen atmosphere, the oil was distilled under reduced pressure below the reaction temperature, 105—110°C. In the same manner as a), 1-hydroxy-2,2,6,6-tetramethyl-4-oxopiperidine (IV) was obtained, mp 90—91°C. A mixed melting point with the authentic sample was undepressed.

The Detection and the Identification of a Trace of 2,6-Dimethyl-2,5-heptadien-4-one (Phorone) (V). Phorone (V) was detected from the first distillate (bp_5 60—70°C) both in the general procedure a) and b), and was identical with the authentic V (mp 28°C, IR, NMR, vpc retention time). A mixed melting point with the authentic V was undepressed.

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7) M. B. Neiman, Yu. G. Madedova and E. G. Rozantzev, *Azerb. Khim. Zh.*, **1962**, 37.

8) E. G. Rozantzev and M. B. Neiman, *Tetrahedron*, **20**, 131 (1964).

9) E. G. Rozantzev, *Izv. Akad. Nauk SSSR, Ser. Khim.*, **1966**, 770.

10) E. G. Rozantzev and V. A. Golubev, *ibid.*, **1966**, 891.