Studies on Stable Free Radicals. X.[1] Photolysis of Hindered *N*-Chloroamines

Toshimasa TODA, Eiko MORI, Hideo HORIUCHI, and Keisuke MURAYAMA
Central Research Laboratories, Sankyo Co., Ltd., Shinagawa-ku, Tokyo

(Received October 5, 1971)

Photolysis of the hindered *N*-Chloroamines, 1-chloro-2,2,6,6-tetramethyl-4-oxopiperidine (IIa), 1-chloro-2,2,6,6-tetramethylpiperidine (IIb), and 1-chloro-2,2,5,5-tetramethyl-4-oxoimidazolidine (IIc), in benzene solution were carried out in an ESR spectrometer cavity. The ESR spectra of the corresponding amino radicals IIIa, IIIb, and IIIc were observed in evacuated solutions. In solutions containing oxygen, it was found that amino radicals IIIb and IIIc readily reacted with oxygen to give the corresponding stable nitroxide radicals IVb and IVc, from the shapes of spectra and *g*-values. Amino radical IIIa did not react with oxygen. Although the amino radicals could not be isolated, their formation was confirmed by the isolation of a coupling product with a benzyl radical generated from dibenzylmercury.

Although syntheses and studies of the properties of stable nitroxide radicals have been carried out extensively,[2] stable amino radicals which can be isolated, analyzed and presented for a long time are scarcely known except for the diphenylpicrylhydrazyl and verdazyl radicals,[3] whose stability seems to result from the delocalization of the unpaired electron. The ESR spectra of diaryl amino radicals generated from corresponding hydrazines by pyrolysis in solution can be observed even at high temperatures,[4] but those of dialkyl amino radicals with no conjugated system for the unpaired electron, obtained by photolysis of tetraalkyltetrazenes in solution can be detected only at low temperatures.[5]

It has been reported that dialkyl amino radicals are relatively poor dehydrogenating agents, *e.g.*, dimethylamino radicals give dimethylamine and *N*-methylformaldimine by disproportionation at high temperatures.[6]

$$2\cdot Me_2N\cdot \rightarrow Me_2NH + CH_2 = NMe$$

Thus, a hindered amino radical lacking hydrogen on the α-carbon of the radical group is expected to be more stable than a dimethylamino radical.

Sholle *et al.* succeeded in observing the ESR spectrum of 2,2,6,6-tetramethyl-4-oxo-1-piperidyl radical (IIIa) at room temperature, but it was also unstable.[7]

Although this amino radical has no hydrogen on the α-carbons of the radical group, the hydrogens at the α-positions of the keto group in piperidine ring are easily abstracted.[8]

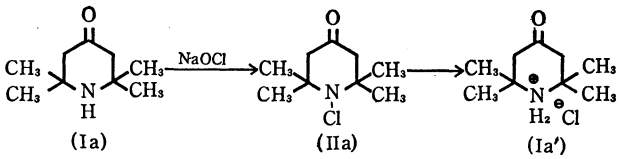
We have prepared hindered *N*-chloroamines containing no easily abstracted hydrogen and observed the ESR spectra of the corresponding amino radicals generated directly by photolysis of the *N*-chloroamines in a cavity of the ESR spectrometer. The amino radicals thus obtained were sensitive to oxygen and gave the corresponding stable nitroxide radicals.

Results and Discussion

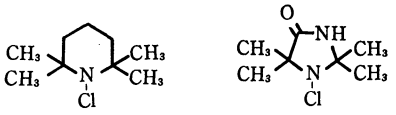
We prepared 1-chloro-2,2,6,6-tetramethyl-4-oxopiperidine (IIa) by the reaction of the corresponding amine (Ia) with sodium hypochlorite,[9] but IIa was unstable. On keeping it to stand 2,2,6,6-tetramethyl-4-oxopiperidine hydrochloride (Ia′) separated as a precipitate.

Formation of Ia′ is plausible, if IIa decomposes into amino radical IIIa and Cl· by homolysis, and both radicals abstract hydrogens from keto α-methylene group in IIa or IIIa to give amine (Ia) hydrogen chloride. The assumption seems reasonable from the consideration that 2,2,6,6-tetramethyl-4-oxopiperidine-1-oxyl (IVa) abstracted hydrogens from keto α-methylene group of IVa to give 1-hydroxy-2,2,6,6-tetramethyl-4-oxopiperidine and phorone under reflux in benzene, while 2,2,6,6-tetramethylpiperidine-1-oxyl (IVb) was recovered unchanged under the same reaction conditions.[8]

We therefore prepared 1-chloro-2,2,6,6-tetramethylpiperidine (IIb) and 1-chloro-2,2,5,5-tetramethyl-4-oxoimidazolidine (IIc) which have no ketonic α-methylene hydrogens, by the reaction of these amines with sodium hypochlorite. Chloroamines IIb and IIc were more stable than IIa.



(Ia) (IIa) (Ia′)



(IIb) (IIc)

1) Part IX: Ref. 16.

2) a) A. R. Forrester, J. M. Hay, and R. H. Thomson, "Organic Chemistry of Stable Free Radicals," Academic Press, New York, N. Y. (1968), pp. 180—238. b) E. G. Rozantsev, "Free Nitroxyl Radicals" Plenum Press, New York, N. Y. (1970), Translated from Russian.

3) R. Kuhn and H. Trischmann, *Angew Chem.*, **75**, 294 (1963).

4) P. H. H. Fischer and F. A. Neugebauer, *Chem. Ber.*, **98**, 844 (1965).

5) W. C. Danen and T. T. Kensler, *J. Amer. Chem. Soc.*, **92**, 5235 (1970).

6) D. Mackay and W. A. Waters, *J. Chem. Soc. C*, **1966**, 813.

7) V. Sholle, E. G. Rozantsev, A. I. Prokof'ev, and S. P. Solodovnikov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, **1967**, 2504.

8) K. Murayama and T. Yoshioka, This Bulletin, **42**, 2307 (1969).

9) G. H. Coleman, *J. Amer. Chem. Soc.*, **55**, 3001 (1933).

The ESR spectra of the radicals generated directly from the chloroamines by photolysis in an ESR spectrometer cavity were recorded at room temperature under two conditions, *viz.*, in the presence and absence of oxygen.

Photolysis of Chloroamine IIa. The radical generated by UV irradiation of IIa in evacuated benzene solution gave the spectrum shown in Fig. 1a. Triplet lines, due to the interaction of a ^{14}N nucleus and supplementary splitting of each component of the triplet caused by the interaction with 12 protons of four methyl substituents in amino radical IIIa, were observed. The radicals generated by UV irradiation of IIa in benzene (containing oxygen) and in toluene (containing or not containing oxygen), gave the same spectrum as that of Fig. 1a. After cessation of UV irradiation, the spectra remained observable for a certain period and then disappeared gradually.

Photolysis of Chloroamine IIb. The radical generated by photolysis of IIb in an evacuated benzene solution gave the spectrum shown in Fig. 1b. Supplementary splittings resulting from 12 protons of four methyl substituents in amino radical IIIb were observed. The spectrum disappeared immediately when UV irradiation was terminated. In an evacuated toluene solution, photolysis of IIb gave no spectrum.

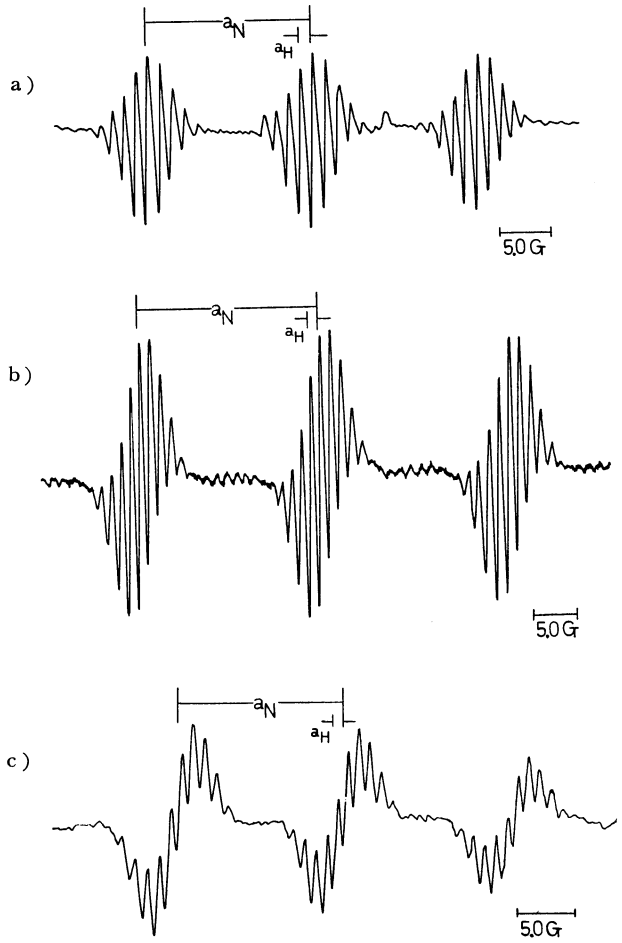


Fig. 1. ESR spectra of Amino Radicals genrated by the photolysis of *N*-chloroamines in degassed benzene solution at room temperature: a) from IIa. b) from IIb. c) from IIc.

The spectrum of the radical generated by photolysis of IIb in benzene (containing oxygen) is given in Fig. 2. Only triplet lines due to a ^{14}N nucleus were observed. The spectrum remained observable for a long time after cessation of UV irradiation. In toluene (containing oxygen), photolysis of IIb gave a spectrum of triplet lines similar to that in Fig. 2.

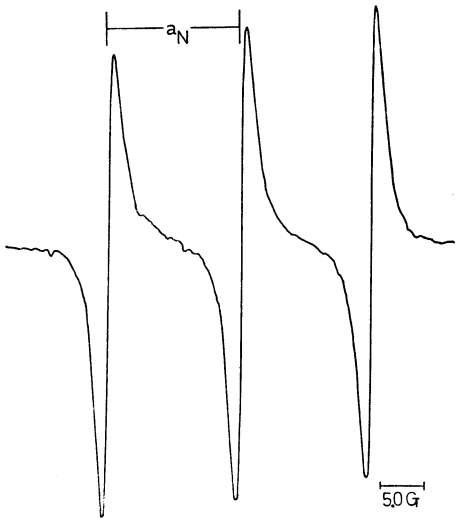
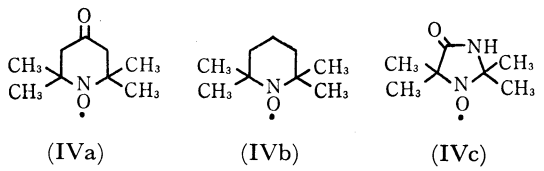


Fig. 2. ESR spectrum of Nitroxide Radical IVb generated by the photolysis of IIb in undegassed benzene solution at room temperature.

Photolysis of Chloroamine IIc. The spectrum of the radical obtained from IIc in an evacuated benzene solution is shown in Fig. 1c. Triplet lines due to a ^{14}N nucleus and further splittings caused by the interaction with 12 protons of four methyl substituents in the amino radical IIIc were observed. The interaction with another ^{14}N at the 3-position in IIIc was not observed (Fig. 1c). When UV irradiation was stopped, the spectrum as well as that given in Fig. 1b disappeared immediately. No spectrum was observed in an evacuated toluene solution. The spectra of the radicals generated from IIc in benzene and in toluene (each containing oxygen) gave triplet lines as the spectrum in Fig. 2.

The splitting constants and *g*-values of the radicals obtained in this study were determined from the spectra and are listed in Table 1.

The ESR spectra of the corresponding nitroxide radicals IVa,[10] IVb[10], and IVc[11] were also measured. Each spectrum showed triplet lines as in Fig. 2. Values for their splitting constants and *g*-values are listed in Table 2.



(IVa) (IVb) (IVc)

10) E. G. Rozantsev and M. B. Neiman, *Tetrahedron*, **20**, 131 (1964).

11) T. Toda, S. Morimura, E. Mori, H. Horiuchi, and K. Murayama, This Bulletin, **44**, 3445 (1971).

Table 1. Values of hyperfine splitting constants and *g*-values of the radicals generated by photolysis on *N*-chloroamines[a]

Chloro-amine	Amino radical[b]			Nitroxide radical[c]		
	a_N[d]	a_H[d]	*g*-value[e]	a_N[d]	a_H[d]	*g*-value[e]
IIa	15.0	1.2	2.0027	15.0[g]	1.2[g]	2.0043[g]
IIb	14.3	0.78	2.0041	15.0	f)	2.0056
IIc	14.3	1.2	2.0038	14.0	f)	2.0053

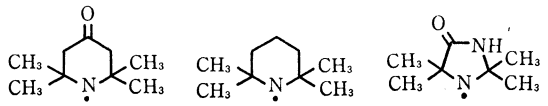
a): measured in benzene solution at room temperature. b): in degassed solution. c): in undegassed solution. d): unit in gauss. accuracy ±0.1 gauss. e): accuracy ±0.0001. f): not resolved. g): corresponding amino radical.

Table 2. The values of hyperfine splitting constants and *g*-values of the nitroxide radicals[a]

Radical	a_N[b]	a_H	*g*-value[c]
IVa	14.3	d)	2.0055
IVb	15.0	d)	2.0056
IVc	14.0	d)	2.0052

a): measured in benzene at room temperature. The two values obtained in degassed and undegassed solutions were the same. b): unit in gauss. accuracy ±0.1 gauss. c): accuracy ±0.0001. d): not resolved.

The radicals obtained in the absence of oxygen appear to be amino radicals IIIa, IIIb, and IIIc from the following considerations.



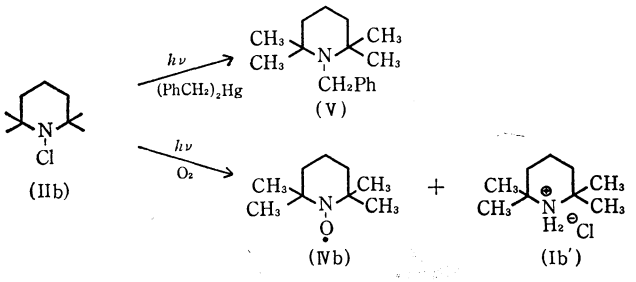
(IIIa) (IIIb) (IIIc)

Supplementary splittings were observed besides the triplet lines in each ESR spectrum as shown in Fig. 1 a-c, while only triplet lines were observed for the corresponding nitroxide radicals. Values for the coupling constants of a ^{14}N nucleus in the amino radicals IIIa and IIIc are larger than those for the corresponding nitroxide radicals (except for radical IIIb). This can be accounted for by the consideration that the density of each unpaired electron is almost entirely localized on the nitrogen atom, while in the corresponding nitroxide radical, each unpaired electron can be delocalized, $>N-O\cdot \leftrightarrow >\overset{\oplus}{N}-\overset{\ominus}{O}$.[12] *g*-Values for the amino radicals are smaller than those for the corresponding nitroxide radical as shown in Tables 1 and 2. This might be due to the difference in the spin-orbit coupling constants and has been pointed out in the cases of the di-*p*-tolyl-amino radical[4] and the di-*p*-tolyl nitroxide radical.[13]

In the presence of oxygen, the radicals obtained from IIb and IIc appear to be nitroxide radicals IVb and IVc, because splittings resulting from protons of the methyl substituents in these compounds were not observed in the ESR spectra, and g-values agreed with those of the corresponding nitroxide radicals. The radicals obtained from IIa in benzene or in toluene (each containing or not containing oxygen) appear to be amino radical IIIa, because their ESR spectra agreed with the spectrum of amino radical IIIa as shown in Fig. 1a.

The following experiments were carried out in order to confirm the formation of the amino radical and the nitroxide radical in photolysis of the chloroamine.

We obtained 1-benzyl-2,2,6,6-tetramethylpiperidine (V) by the photolysis of a mixture of IIb and dibenzylmercury[14] in benzene with bubbling argon gas. The reaction did not proceed in dark. Photodecomposition of IIb in benzene with bubbling oxygen gas gave 2,2,6,6-tetramethylpiperidine-1-oxyl (IVb) and 2,2,6,6-tetramethylpiperidine hydrochloride (Ib′).



Thus, the photolysis of the hindered *N*-chloroamine would proceed as shown in Chart 1.

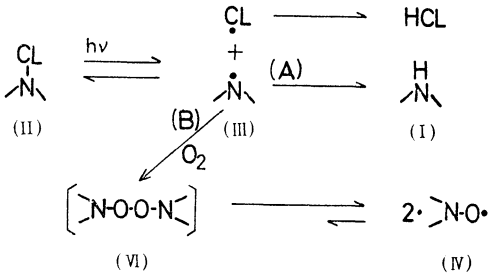


Chart 1

Processes A and B are considered to be competitive reactions for the following reasons. (1) the photodecomposition of IIb in benzene with bubbling oxygen gas gave nitroxide radical IVb and salt Ib′; and (2) no ESR spectra were observed in the photolyses of IIb and IIc in evacuated toluene solutions and the radicals obtained from IIb and IIc in toluene containing oxygen were the corresponding nitroxide radicals IVb and IVc, respectively.

Amino radical IIIa does not react with oxygen and would mainly abstract hydrogens to give corresponding amine Ia, because the radical obtained by photolysis of IIa even in the presence of oxygen was the amino radical IIIa. Salt Ia′ was obtained on keeping IIa to stand.

From the fact that amino radicals IIIb and IIIc are converted into nitroxide radicals IVb and IVc in the presence of oxygen, it seems reasonable to assume

12) see Ref. 1b. p. 127.

13) F. A. Neugebauer and P. H. H. Fischer, *Z. Naturforsch.* **19a**, 1514 (1964).

14) W. J. Pope and C. S. Gilson, *J. Chem. Soc.*, **101**, 735 (1912).

the existence of peroxide (VI), precursor of the nitroxide radical as shown in Chart 1. Such a peroxide has been suggested in the photolysis of perfluoro-*N*-fluoropiperidine.[15] We consider that there may be an equilibrium between peroxide VI and nitroxide radical IV in solution[16], but the equilibrium lies far on the side of the radical.

The results suggest that even hindered amino radicals cannot be isolated, because they are sensitive towards oxygen to give the corresponding nitroxide radicals and readily abstract a hydrogen from media or another radical to give the amines, even though these radicals have no hydrogen on the α-carbon in the radical group.

Table 1 shows that the nitrogen coupling constant of IIIb is smaller than that of the corresponding nitroxide radical IVb. This seems to be correlated with the result that amino radical IIIa does not react with oxygen, which would be caused by the effect of 4-oxo group in piperidine ring.

Experimental

Melting points and boiling points are uncorrected. IR spectra were determined by means of Nujol mulls and liquid films. NMR spectra were obtained with a Varian A-60 NMR spectrometer using tetramethylsilane as an internal standard at 32°C. Mass spectra were obtained with a JEOL-JMS-OIS spectrometer at 75 eV.

ESR Measurements. ESR spectra were recorded on a Hitachi MES 4001 type X-band spectrometer employing 100 kHz modulation at room temperature. Degassed samples were prepared in the usual manner. Samples containing *ca.* 5% of dissolved *N*-chloroamine were irradiated with an USIO projector equipped with xenon 2 kw lamp. Splitting constants and *g*-values were measured relative to the aqueous solution of Fremy's salt.

Preparation of N-Chloroamines. The solution of aqueous sodium hypochlorite was prepared by passing chlorine gas (24 g) into a cold solution of sodium hydroxide (36 g) in 300m*l* of water at 0°C.[9]

1-Chloro-2,2,6,6-tetramethyl-4-oxopiperidine (IIa). To a stirred solution of 31.0 g (0.2 mml) of 2,2,6,6-tetramethyl-4-oxopiperidine (Ia)[6,17] and 20 g of aqueous solution of hydrogen chloride (35%) in 200 m*l* of water was added slowly 250 m*l* of aqueous sodium hypochlorite at 0—5°C. After the addition was completed, stirring was continued for 10 min at 0—5°C. The solution was shaken with 300 m*l* of ether. The ether layer was dried over sodium sulfate and evaporated under reduced pressure at room temperature. The residual oil was distilled to give 19.0 g (50.0%) of IIa: bp 63—64°C/0.3 mmHg. Found: C, 56.80; H, 8.61; N, 7.34; Cl, 18.62%. Calcd for $C_9H_{16}ONCl$: C, 56.99; H, 8.50; N, 7.38; Cl, 18.69%. IR(cm^{-1}): $\nu_{C=O}$ 1728. 2,2,6,6-Tetramethyl-4-oxopiperidine hydrochloride (Ia') was precipitated from the distilled oil on standing at room temperature. This was confirmed by comparison of the melting point and IR spectrum with those of the authentic sample prepared by the reaction of Ia with hydrogen chloride in ethanol. Recrystallization from ethanol gave a pure sample: mp 197°C (decomposition). Found: C, 56.41; H, 9.45; N, 7.33; Cl, 18.46%. Calcd for $C_9H_{18}ONCl$: C, 56.39; H, 9.47; N, 7.31; Cl, 18.49%.

1-Chloro-2,2,6,6-tetramethylpiperidine (IIb). In the same way as mentioned above, 34.0 g (96.5%) of IIb was obtained from 28.0 g (0.2 mml) of 2,2,6,6-tetramethylpiperidine (Ib)[10]: bp 65°C/7 mmHg. Found: C, 61.52; H, 10.34; N, 8.23; Cl, 19.69%. Calcd for $C_9H_{18}NCl$: C, 61.52; H, 10.34; N, 8.23; Cl, 19.69%. Calcd for $C_9H_{18}NCl$: C, 61.52; H, 10.32; N, 7.97; Cl, 20.18%. NMR (τ) (in CCl_4): 8.41, broad (6H). 8.80, siglet (12H).

1-Chloro-2,2,5,5-tetramethyl-4-oxoimidazolidine (IIc). To a stirred solution of 1.4 g (10 mmol) of 2,2,5,5-tetramethyl-4-oxoimidazolidine (Ic)[11] in 20 m*l* of water was added slowly 20 m*l* of aquoeus sodium hypochlorite at 0—5°C. The solution was stirred for additional 20 min at 0—5°C, and extracted with 100 m*l* of ether. The ethereal solution was dried over sodium sulfate and evaporated under reduced pressure to give 1.7 g of IIc. Recrystallization from benzene gave an analytically pure sample: mp 153—154°C. Found: C, 48.06; H, 7.66; N, 15.83; Cl, 20.05%. Calcd for $C_7H_{13}ON_2Cl$: C, 47.60; H, 7.42; N, 15.86; Cl, 20.07%. IR(cm^{-1}): $\nu_{C=O}$ 1678 and 1730, ν_{NH} 3150.

Reaction of IIb. a). A solution of 7.75 g (44 mmol) of IIb and 8.45 g (22 mmol) of dibenzylmercury[14] in 170 m*l* of dry benzene with bubbling argon gas was irradiated with a high pressure mercury lamp (Hanovia, 450 W) for 8 hr at 0—5°C. After cessation of UV irradiation, the solution was decanted into a separatory funnel, shaken with 80 m*l* of 10% hydrochloric acid and separated. The aqueous layer was concentrated to half volume under reduced pressure, neutralized with aqueous solution of potassium hydroxide (40%), extracted with 100 m*l* of benzene and dried over potassium carbonate. After evaporating the solvent, the resulting oil was chromatographed on 50 g of aluminum oxide. Eluting with petroleum ether afforded 1.2 g of 1-benzyl-2,2,6,6-tetramethylpiperidine (V). Recrystallization from petroleum ether gave a pure sample: mp 39—40°C. Found: C, 82.91; H, 11.07; N, 5.87%. Calcd for $C_{16}H_{25}N$: C, 83.05; H, 10.89; N, 6.05%. NMR (τ) (in CCl_4): 2.5—3.0 (5H), 6.20 singlet (2H), 8.45 broad (6H), 8.97 singlet (12H). mass spectrum: M^+=231 (231). Picrate: mp 170—171°C (from ethanol). Found: C, 57.10; H, 6.14; N, 11.91%. Calcd for $C_{22}H_{28}O_7N_4$: C, 57.38; H, 6.13; N, 12.17%. The benzene layer was concentrated in a vacuum to give 2.5 g of crystallline solids. Recrystallization from ethanol gave dibenzyl melting at 52—53°C (mp 52°C).

b). A solution of 17.6 g (0.1 mol) of IIb in 140 m*l* of dry benzene with bubbling oxygen gas was irradiated with a high pressure mercury lamp (Hanovia, 450 W) for 2 hr at 0—5°C. After cessation of UV irradiation, 5.0 g of 2,2,6,6-tetramethylpiperidine hydrochloride (Ib') was separated from the solution by filtration. This was confirmed by comparison of the melting point and IR spectrum with those of the sample prepared by the reaction of Ib with hydrogen chloride in ethanol. Recrystallization from ethanol gave a pure sample: mp 295°C (decomposition). Found: C, 60.78; H, 11.40; N, 7.85; Cl, 19.91%. Calcd for for $C_9H_{20}NCl$: C, 60.83; H, 11.34; N, 7.88; Cl, 19.95%. The filtrate was concentrated under reduced pressure. The oily residue was chromatographed on a column of aluminum oxide and the column eluted successively with petroleum ether, benzene, and methanol. From petroleum ether eluates, 3.5 g of the starting

15) R. E. Banks, K. Mullen, and G. E. Williamson, *J. Chem. Soc. C*, **1968**, 2608.

16) T. Toda, E. Mori and K. Murayama, This Bulletin, **45**, 1904 (1972).

17) K. Murayama, S. Morimura, O. Amakasu, T. Toda, and E. Yamao, *Nippon Kagaku Zasshi*, **90**, 296 (1969).

material was recovered. This was confirmed by IR and NMR spectra. From benzene eluates, 1.0 g of 2,2,6,6-tetramethylpiperidine-1-oxyl (IVb) was obtained. This was confirmed by comparison of the melting point and IR spectrum with those of an authentic sample.[10] An analytically pure sample was given by sublimation in a vacuum: mp 38—39°C. Found: C, 68.76; H, 11.48; N, 8.96%. Calcd for $C_9H_{18}ON$; C, 69.18; H, 11.61; N, 8.96%. ESR (in benzene): $a_N=15.0$ gauss, g-value=2.0056. From methanol eluates, 3.0 g of unknown tarry materials were obtained.

We would like to thank Prof. Makoto Okawara, the Tokyo Institute of Technology, for his valuable comments, Dr. Genshun Sunagawa, the director of these laboratories, for his encouragement and Mr. Susumu Higashida for his technical assistance.