The Reaction of Lead Tetra-acetate with Oximes. Part II.¹ Substituted Acetophenone Oximes

By J. W. Lown

In the reaction between lead tetra-acetate and a series of substituted acetophenone oximes in methylene chloride, three types of stable nitrogen free radical are observed. Two of these are unambiguously assigned structures of the iminoxy and acetoxy-phenylethane nitroso radical anions. The reaction between these oximes and lead tetra-acetate is sensitive to substituent and steric hindrance effects.

IN Part I¹ we showed that stable nitrogen free radicals are obtained by the action of lead tetra-acetate in methylene chloride on several aliphatic and alicyclic oximes. We now report on the intermediate free radicals obtained by the action of lead tetra-acetate on substituted acetophenone oximes, which exhibited different behaviour.

Reaction of Acetophenone Oximes with Lead Tetraacetate; Characteristics of E.p.r. Spectra of Free Radicals. —The methods used to generate and observe the free radicals were reported in Part I.¹

When acetophenone oxime is oxidised by ceric salts² in a rapid-flow system, it gives rise to an iminoxy radical showing three lines due to nitrogen hyperfine coupling (1:1:1), $a_N = 30.6$ Oe. When the oxime is treated with lead tetra-acetate in benzene,³ the iminoxy radical is again obtained, $a_N = 31.7$ Oe, but under these conditions showing hyperfine coupling, $a_H = 1.4$ Oe, to five protons, *i.e.*, the three C-CH₃ protons and two from the aromatic ring. Complex, time-variable spectra were observed but no other assignments were possible.

In the present study, by the reaction of substituted acetophenone oximes with lead tetra-acetate in methylene chloride, we have detected three different types of radical, two of which may be assigned unambiguously.

The behaviour of acetophenone is typical. The initial spectrum corresponded to that of the iminoxy PhCMe(:NO), showing in this solvent quartet (1:3:3:1) splitting of each triplet line due to interaction with the methyl protons (proved by deuteriation) $a_N = 31.4$, $a_{\rm H} = 1.7$ Oe). The latter coupling was infrequently observed owing to the lability of the radical during the time taken to scan the spectrum [Figure 1(c)]. This lability probably prevented the resolution of small wing-lines which are expected in view of other results.³ However, since no such additional coupling was resolved in methylene chloride, hyperfine coupling in the iminoxy radicals has been reported as arising only from the C-CH₃ groups.

Within a short time the appearance of the spectrum changed drastically and new lines appeared. Figure 1(a) shows the spectrum after 3 minutes; the methyl proton coupling of the iminoxy radical (large triplet) has disappeared and a new (1:1:1) triplet with a smaller nitrogen hyperfine coupling $(a_N = 13.7 \text{ Oe})$ has appeared. After several minutes the spectrum takes on the appearance of Figure 1(b) or (d), when two radicals may

be distinguished. One of the radicals gives rise to three sets of overlapping quartets (1:3:3:1), clearly arising from three equivalent protons and a nitrogen $(a_{\rm H} = 11\cdot8, a_{\rm N} = 14\cdot8$ Oe). The second radical, consisting of three lines (1:1:1), $a_{\rm N} = 13\cdot70$ Oe, corresponds to that observed earlier. These latter radicals are especially stable in the presence of a small amount of added



FIGURE 1 First derivative e.p.r. spectra from reaction of lead tetra-acetate with (a) acetophenone oxime after 3 min., (b) acetophenone oxime after *ca*. 15 min., (c) 2,3,4,5,6-penta-deuterioacetophenone oxime after 1 min., (d) 2,3,4,5,6-penta-deuterioacetophenone oxime after 15 min., (e) $\alpha\alpha\alpha$ -trideuterioacetophenone oxime, and (f) phenacyl bromide oxime. (The scale in each case represents 30 oersted.)

tertiary base (e.g., triethylamine); however, they are unstable in the presence of an excess of acetic acid.

Assignment of Free Radical Structures.—The secondary radicals are not products of decomposition, since the acetophenone carbon skeleton remains intact, as shown by preparative-scale oxidation of several substituted acetophenone oximes, when, after acid hydrolysis, the acetophenone, isolated as the 2,4-dinitrophenylhydrazone, is obtained as the only organic product, in excellent yield. The preparative-scale reactions were run under conditions as close as possible to those used in the observation of the e.p.r. spectra. Acetophenone oxime

³ M. Bethoux, H. Lemaire, and A. Rassat, Bull. Soc. chim. France, 1964, 1485.

¹ Part I, J. W. Lown, J. Chem. Soc. (B), 1966, 441.

² J. R. Thomas, J. Amer. Chem. Soc., 1960, 82, 5955.

completely deuteriated in the aromatic ring gives rise to the same e.p.r. spectra in the same sequence [see Figures 1(c) and (d)], confirming that, under the present reaction and solvent conditions, none of the ring hydrogens is detectably involved in coupling. Acetophenone oxime completely deuteriated in the *C*-methyl group gave rise initially to the iminoxy radical $(a_N =$ 31.4 Oe), which was converted within a short time into two new radicals. One radical, on deuteration in the *C*-methyl group, gave, as expected, only nitrogen hyperfine coupling $(a_N = 13.7$ Oe), as observed previously. By analogy with the aliphatic acetoxynitroso radical anions,¹ we assign structure (I) to this radical and confirm it as follows.

Preparative-scale reaction of aliphatic and alicyclic oximes with lead tetra-acetate affords fairly stable α -acetoxy-nitroso compounds as blue oils.⁴ The corresponding α -acetoxy-nitrosoalkane radical anions were specifically generated from these compounds by the action of base, and these radicals showed characteristic nitrogen hyperfine couplings of 12·10—13·80 Oe.¹ They did not participate, however, in the reaction between these oximes and lead tetra-acetate.

An attempt was made to isolate the corresponding acetoxy-nitroso-compound from acetophenone oxime. A deep blue oil was obtained which, however, was very sensitive to heat and decomposed readily, yielding acetophenone with the evolution of acetic acid and nitrous fumes on attempted distillation. The α -acetoxy-nitrosoderivatives like (II) have highly characteristic visible

absorption maxima in the region of 660 mµ ($\varepsilon \sim 20$).¹ Examination of the blue material from acetophenone oxime showed maximum absorption at 663 m μ . Therefore, we assign to this material, which is produced together with acetophenone, the analogous nitrosoacetate structure (II). The e.p.r. spectrum of the blue solution in methylene chloride treated with base (e.g., triethylamine) showed a strong triplet (1:1:1) whose nitrogen hyperfine coupling $(a_N = 13.7 \text{ Oe})$ coincided with that of one of the triplets observed previously (see Figures 1 and 2). The specific generation of this radical from (II) by the action of base, and its instability on the addition of acetic acid, confirm our assignment as the radical anion (I). Of the other substituted acetophenone oximes studied in the present work, a total of seven were treated similarly, *i.e.*, isolation on the preparative scale and treatment of the blue oil with base. In all cases, the e.p.r. hyperfine coupling of the radical anion coincided (see Tables 1 and 2, and Figure 2) Visible absorption maxima of 1-acetoxy-1-nitroso-phenylalkanes, and e.p.r. hyperfine coupling constants of 1-acetoxy-1-nitroso-phenylalkane radical anions in methylene chloride

		Nitrogen hyperfine coupling (Oe) of radical
	$\lambda_{max}(m\mu)$	anion
PhC(Me)(O·COMe)N=O	663	13.60
p-MeO·C _e H ₄ C(Me)(O·COMe)N=O	660	13.65
p-Me·C.H. C(Me)(O·COMe)N=O	659	13.65
p-Cl·C, H, C(Me)(O·COMe)N=O	658	$13 \cdot 10$
p-F·C.H. C(Me)(O·COMe)N=O)	660	13.61
3.4-Me.C.H. C(Me)(O COMe)N=O	660	13.60
p-MeO·C.H. C(Et)(O·COMe)N=O	660	13.80

TABLE 2

Hyperfine couplings (Oersteds) of free radicals from oxidation of oximes *

	Radical type †	Radical	Radical
Oxime of	PhCMe(:NO)	type (11)	type R
Acetophenone	$a_{\rm N} = 31.4$ (3) $a_{\rm H} = 1.7$	$a_{\rm N}=13.7$	$a_{\rm N} = 14.8$ (3) $a_{\rm H} = 11.8$
2,3,4,5,6-Penta- deuterioaceto- phenone	$a_{ m N} = 31.5$ (3) $a_{ m H} = 1.7$	$a_{\rm N} = 13.7$	$a_{\rm N} = 14.8$ (3) $a_{\rm H} = 11.8$
aaa-Trideuterio- acetophenone	$a_{\rm N}=31\cdot4$	$a_{\rm N}=13.7$	$a_{\rm N} = 14.8$ (3) $a_{\rm D} = 1.8$
4-Methoxyaceto- phenone	$a_{\rm N}=32.0$	$a_{\rm N}=13.6$	
4-Methylaceto- phenone	$a_{ m N}=32{\cdot}5$	$a_{\rm N}=13.7$	$a_{\rm N} = 14.6$ (3) $a_{\rm H} = 11.9$
4-Bromoaceto- phenone	$a_{\mathrm{N}}=32.0$	$a_{\rm N} = 13.4$	$a_{\rm N} = 14.5$ (3) $a_{\rm H} = 11.6$
4-Chloroacetophenone	$a_{ m N} = 31.8$ (3) $a_{ m H} = 1.42$	$a_{\rm N} = 13.2$	$a_{\rm N} = 14.6$ (3) $a_{\rm H} = 11.9$
4-Fluoroacetophenone	$a_{ m N} = 30.8$ (3) $a_{ m H} = 1.42$	$a_{\mathrm{N}} = 13.6$	$a_{ m N} = 14.6$ (3) $a_{ m H} = 11.8$
4-Nitroacetophenone	$a_{ m N} = 31 \cdot 2 \ (3) \ a_{ m H} = 1 \cdot 5$		
3-Bromoacetophenone	$a_{\rm N}=30.8$	$a_{\rm N}=13\cdot 2$	$a_{\rm N} = 14.7$ (3) $a_{\rm H} = 11.7$
4-Methoxypropio- phenone	$a_{\mathrm{N}}=31.0$	$a_{\rm N}=13.9$	
Isobutyrophenone	$a_{ m N}=31{\cdot}6$	$a_{\rm N}=13\cdot 8$	
ααα-Trideuterio-4- bromoacetophenone	$a_{\rm N}=32\cdot 0$	$a_{\mathrm{N}} = 13.4$	$a_{\rm N} = 14.6$ (3) $a_{\rm D} = 1.7$
ααα-Trideuterio-4- chloroacetophenone	$a_{\rm N}=31.8$	$a_{\rm N} = 13 \cdot 2$	$a_{\rm N} = 14.6$ (3) $a_{\rm D} = 1.8$
Phenacyl bromide	$a_{ m N}=31{\cdot}6$	$a_{\rm N} = 13.4$	$a_{ m N} = 13.8$ (2) $a_{ m H} = 16.9$
2,5-Dimethylaceto- phenone	$a_{ m N}=31{\cdot}5\ (4)a_{ m H}=1{\cdot}5$		
3,4-Dimethylaceto- phenone	$a_{\rm N}=31.6$	$a_{\rm N}=13.5$	
2,5-Dichloroaceto- phenone	$a_{N} = 32.8$ (3) $a_{H1} = 1.6$ (1) $a_{N2} = 3.2$		

* The number in parentheses next to proton hyperfine couplings signifies the number of equivalent protons or deuterons. Radicals generated from the oximes in methylene chloride at 0° with lead tetra-acetate. † The radical types refer to those discussed in the text.

⁴ D. C. Iffland and G. X. Criner, Chem. and Ind., 1965, 751.

with that of one of the radicals generated by the action of lead tetra-acetate on the oxime in methylene chloride. Therefore, there is no doubt that here the acetoxy-nitrosophenylalkane radical anion participates as an intermediate in the reaction. The isolated products all exhibited visible absorption maxima characteristic of the parent acetoxy-nitroso-compound (Table 1).

The second radical (R) observed on complete C-methyl deuteriation showed septet coupling from three equivalent deuterium atoms [see Figure 1(e)] $(a_N = 14.8, a_D = 1.8 \text{ oe})$. The reduction in coupling constant upon



FIGURE 2 First derivative e.p.r. spectra of (a) 1-acetoxy-1-p-fluorophenyl-1-nitrosoethane radical anion, (b) 1-acetoxy-1-p-methylphenyl-1-nitrosoethane radical anion, (c) 1-acetoxy-(3,4-dimethylphenyl)1-nitrosoethane radical anion, (d)1acetoxy-1-phenyl-1-nitrosoethane radical anion, all in methylene chloride. (The scale in each case represents 30 oersted.)

deuteriation from 11.8 Oe by a factor of 6.5 (equal to the theoretical isotopic ratio ⁵), and the equality of the nitrogen hyperfine couplings, show this latter radical to be the deuteriated analogue of that observed previously $(a_{\rm N} = 14.8, a_{\rm H} = 11.8$ Oe). This confirms that the large quartet coupling arises from the *C*-methyl protons in this radical. The assignment receives added support from examination of the analogous free radical generated from the oxime of phenacyl bromide. As can be seen from Figure 1(f), the expected 1:1:1 triplet of 1:2:1 triplets is observed.

The magnitude of the coupling must reflect a high spin-density on the carbon atom (corresponding to the carbonyl group in the product acetophenone), and is consistent only with a $\cdot N$ -CH₃ or $\cdot C$ -CH₃ arrangement. Also, the isolation of only acetophenone indicates no change in the carbon skeleton. A structure (III), corresponding to diacetoxylation of the C=N bond, is unacceptable since such structures reasonably proposed

for the stable free radicals obtained from certain aliphatic oximes do not display large α -proton coupling.¹ Coupling from a proton directly bonded to nitrogen is



well documented ⁶ in the case of substituted hydroxylamine radicals, and can be observed in methylene chloride when present.¹ Consequently, structures such as (IV) are also eliminated.

Alternative structures such as (V), which could arise from the oxidation of the product of acetylation of the

$$\begin{array}{ccc} PhCMe & PhCMe \\ \parallel & & \parallel \\ N \cdot O \cdot COMe & & + N \cdot O \cdot COMe \end{array} (V)$$

oxime, are unlikely since experimentally it was shown that acetophenone oxime acetate is completely unreactive towards lead tetra-acetate. (The author is grateful to a referee for this suggestion.)

Therefore, it is not at present possible to arrive at a satisfactory assignment of structure for this type of secondary radical (R) produced in the reaction.

Substituent Effects on the Course of the Reaction.— The order of effectiveness of ring substituents to promote conversion of the iminoxy radical into either radical was qualitatively in the order: p-MeO > p-Me > H > F, Cl, and Br $\gg p$ -NO₂.

The first two substituted acetophenone oximes of those listed above gave iminoxy-radicals initially which were very unstable with respect to the secondary radicals and reacted very rapidly. The behaviour of acetophenone oxime has been described. The p-Br, p-Cl, and p-F compounds gave iminoxy radicals showing much greater stability, and in which C-methyl coupling could be clearly resolved. A small proportion of the secondary radicals could be observed in each case in equilibrium with the iminoxy radical and slowly developed. The rate of production of these radicals was considerably enhanced by the addition of a small quantity of a tertiary amine, resulting in a shift of the equilibrium until eventually, clearly resolved spectra like that in Figure 1(d) were obtained. The 4-nitroacetophenone iminoxy radical was stable under all conditions and was not accompanied by any other radicals.

Steric Hindrance Effects.—In view of the proposed free-radical structure of (I), the interconversion of radicals would be expected to be sensitive to steric hindrance effects. 2,5-Dimethylacetophenone oxime gave rise to an iminoxy radical stable under all conditions. 2,5-Dichloroacetophenone oxime exhibited similar

⁵ J. A. Pople, W. G. Schneider, and H. J. Berstein, "High Resolution Nuclear Magnetic Resonance," McGraw-Hill, New York, 1959, p. 163.

⁶ C. J. W. Gutch and W. A. Waters, J. Chem. Soc., 1965, 751.

behaviour. It is interesting that, in these two iminoxy radicals, through-space coupling of 1.5 and 3.2 Oe, respectively, occurs to one ring proton at the 6-position, indicating a structure such as (VII) for these radicals.



A similar example of such 1,6-through-space coupling in iminoxy radicals has been reported previously.⁷ In contrast, 3,4-dimethylacetophenone oxime readily gives an iminoxy, then an acetoxy radical anion resulting from addition of an acetate anion to the unobstructed oximino group. Consistent with this interpretation in terms of steric hindrance, a number of substituted benzophenone oximes afforded only iminoxy radicals under all conditions.

EXPERIMENTAL

Visible spectra were recorded in methylene chloride solutions on a Beckman DB recording spectrophotometer, and n.m.r. spectra (by R. N. Swindlehurst of this laboratory) on a Varian A-60 analytical spectrometer for ca. 10% (w/v) carbon tetrachloride solutions using tetramethylsilane as internal standard.

The purification of the methylene chloride, and preparation and purification of the lead tetra-acetate, have been described.¹ Oximes were prepared by the pyridine procedure.¹

 $\alpha\alpha\alpha$ -Trideuterioacetophenone.—A solution of acetophenone (5·14 g.) and anhydrous potassium carbonate (0·356 g.) in deuterium oxide (6 ml.) and sodium-dried dioxan (15 ml.) was refluxed for 10 hr., cooled, and extracted with dry benzene (5 × 7 ml.). The extract was evaporated to a small volume *in vacuo*, and the residual oil subjected to a second similar exchange. The exchanged acetophenone (3·7 g.) was isolated by benzene extraction and fractionation, b. p. 87°/10 mm. The n.m.r. spectrum showed complete absence of the singlet at τ 7·52 characteristic of the *C*-methyl group in acetophenone. The ketone was converted into the oxime (70%) by the method given above.

aaa-Trideuterio-4-chloro- and 4-bromo-acetophenone.— These and the corresponding oximes were obtained by similar procedures.

2,3,4,5,6-Pentadeuterioacetophenone.— Freshly distilled AnalaR acetyl chloride $(3\cdot3 \text{ g.})$ was added dropwise with stirring to a cooled and stirred suspension of finely powdered aluminium chloride $(4\cdot5 \text{ g.})$ in hexadeuteriobenzene (10 g.) during 20 min. After complete addition of the acetyl chloride the mixture was warmed to 50° for 1 hr. and poured on to ice. The pentadeuterioacetophenone was isolated by extraction with ether and fractionation, b. p. 89°/10 mm., in 70% yield on the basis of unrecovered deuteriobenzene. The n.m.r. spectrum showed complete absence of lines characteristic of aryl protons. The ketone was immediately converted into the oxime as described above.

Preparation of Solutions for the Recording of E.p.r. Spectra.—An ice-cold solution of lead tetra-acetate or lead tetrabenzoate in methylene chloride was added dropwise to a 5% solution of the oxime in methylene chloride at 0° . An immediate cloudy blue or green colour of the radicals developed, with formation of a precipitate of lead acetate. When required, two drops of trimethylamine or pyridine were added, which cleared the solution. The solution was transferred to an e.p.r. tube which was stoppered and transferred immediately to the spectrometer cavity.

For recording of the spectra of the acetoxy-nitroso radical anions, the blue liquid was simply diluted with methylene chloride and treated with triethylamine.

Recording and Calibration of E.p.r. Spectra.—Spectra were obtained on a Varian V-2503 spectrometer and calibrated by comparison with a peroxyamine disulphonate solution according to procedures given in Part I.¹

Preparative-scale Reaction of Acetophenone Oxime with Lead Tetra-acetate.-- A chilled solution of lead tetraacetate (22 g.) in methylene chloride (50 ml.) was added dropwise to a mechanically stirred solution of acetophenone oxime (6.65 g.) in methylene chloride (140 ml.) at 0° . Stirring at 0° was continued for 1 hr. after complete addition of the lead tetra-acetate. The precipitated lead acetate (16.5 g., 94%) was filtered off, and the filtrate shaken with water. The precipitated brown lead dioxide was filtered off and the filtrate separated. The organic layer was washed with saturated sodium hydrogen carbonate solution (100 ml.) and water, and dried (MgSO₄). The filtered solution was evaporated to a small volume under a 12-in. Dufton column under reduced pressure. Part of this blue solution was used to measure the visible absorption maximum $(\lambda_{max}, 663 \text{ m}\mu)$ of the 1-acetoxy-1-nitroso-phenylethane, and to record the e.p.r. spectrum of the corresponding nitroso radical anion $(a_N = 13.70 \text{ Oe})$. The original residual blue oil was made up to 50 ml. with methanol. An aliquot (10 ml.) of this solution was treated with a solution of 2,4-dinitrophenylhydrazine (2.0 g.) and sulphuric acid (20 ml.)in methanol (50 ml.). The precipitated acetophenone 2,4-dinitrophenylhydrazone was dried, and recrystallised from ethyl acetate, to give 2.5 g., m. p. 238° (lit., 8a 238°), representing an 85% overall yield of acetophenone. It had previously been determined that acetophenone was the major product before treatment with the strongly acidic reagent.

Preparative-scale Oxidation of 4-Bromoacetophenone Oxime with Lead Tetra-acetate.—A reaction between 4-bromoacetophenone oxime (7.14 g.) and lead tetra-acetate (15 g.) in methylene chloride was carried out under similar conditions, and the 4-bromoacetophenone produced estimated as the 2,4-dinitrophenylhydrazone, m. p. 237° (lit.,^{8b} 237°), in an overall yield of 92%.

Preparative-scale Oxidation of 4-Nitroacetophenone with Lead Tetra-acetate.—A reaction between 4-nitroacetophenone oxime (10 g.) and lead tetra-acetate (25 g.) in methylene chloride was carried out according to the method described above. Owing to the low solubility of the oxime at 0° , $1 \cdot 0$ g. of unreacted oxime was recovered. The yield of 4-nitroacetophenone was estimated, as the 2,4-dinitrophenylhydrazone, as 85%, on the basis of unrecovered oxime.

Control Reaction between 4-Bromoacetophenone Oxime and Acetic Acid in Methylene Chloride.—A solution of 4 bromoacetophenone oxime (5 g., 0.023 mole) and glacial acetic acid (4.2 g., 0.023 mole) in methylene chloride (160 ml.) was

⁸ N. D. Cheronis and J. B. Entriken, "Semimicro Qualitative Organic Analysis," Interscience, New York, 1961, (a) p. 664; (b) p. 666.

⁷ B. C. Gilbert, R. O. C. Norman, and D. C. Price, *Proc. Chem. Soc.*, 1965, 234.

cooled in ice and mechanically stirred for 4 hr., then set aside at room temperature for 24 hr. The solution was washed with saturated sodium hydrogen carbonate solution and water, and dried (MgSO₄). Evaporation of the filtered solution afforded 4.9 g. (98%) of recovered 4-bromoacetophenone oxime, m. p. 128° (lit., 80 128°).

Attempted Oxidation of Acetophenone Oxime Acetate with Lead Tetra-acetate.-An ice-cold solution of acetophenone oxime acetate (6·1 g., 0·035 mole) in methylene chloride (100 ml.) was treated with a solution of lead tetra-acetate (15.3 g., 0.035 mole) in methylene chloride (75 ml.), and the colourless mixture stirred for 6 hr. Work-up in the usual manner afforded unchanged oxime acetate (5.7 g., 94%). Acetophenone oxime acetate did not give rise to paramagnetic species when treated with lead acetate.

This research was supported by a National Research Council of Canada grant-in-aid.

DEPARTMENT OF CHEMISTRY, UNIVERSITY OF ALBERTA, EDMONTON, ALBERTA, [5/904 Received, August 19th, 1965] CANADA.