Nitroxide Chemistry. Part XII.[1] Free Radical Formation in the Reactions between Trifluoronitrosomethane and Some 1,3-Diketones

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The 1,3-diketones $RCO{\cdot}CH_2{\cdot}COR'$ ($R = R' = CH_3$ or CF_3, and $R = CH_3$, $R' = CF_3$) react with trifluoronitrosomethane to generate the nitroxide radicals $CF_3{\cdot}N(\dot{O}){\cdot}CH(COR'){\cdot}COR$ and their tautomers $CF_3{\cdot}N(\dot{O}){\cdot}C(COR'){:}C(OH)R$ together with the iminoxy-radicals $(RCO)(R'CO)C{:}N{\cdot}\dot{O}$, all detected by e.s.r. spectroscopy. Diethyl 2-methyl-3-oxosuccinate affords only the radical $CF_3{\cdot}N(\dot{O}){\cdot}CMe(CO_2Et)CO{\cdot}CO_2Et$ under similar conditions. Intermediate hydroxylamine anions $CF_3{\cdot}N(\bar{O}){\cdot}CH(COR){\cdot}COR'$, are proposed as intermediates which can undergo further reaction by two different pathways to give the observed radicals. The e.s.r. parameters of the various nitroxide radicals are given, and these are interpreted in terms of a deviation from planarity at the nitrogen atom.

MUCH use has been made of *C*-nitroso-compounds to 'spin-trap' free radicals,[2] but care must be exercised under conditions where nucleophilic attack on the nitroso-compound is also possible, since the resulting hydroxylamine anions are easily oxidised to the corresponding nitroxide by either traces of oxygen or an excess of the nitroso-compound.[3]

Results are now presented which illustrate the ready formation of nitroxide and iminoxy-radicals *via* initial nucleophilic attack of carbanions on trifluoronitrosomethane, a compound more susceptible to nucleophilic attack than other *C*-nitroso-compounds.[4]

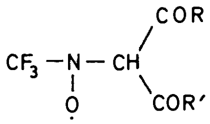
RESULTS

$CH_3{\cdot}CO{\cdot}CH_2{\cdot}CO{\cdot}CH_3 + CF_3NO$.—When mixtures of trifluoronitrosomethane and acetylacetone in carbon tetrachloride solution are allowed to warm up from 77 K to room temperature immediate e.s.r. spectra are obtained. Depending upon the relative amounts of the two reactants present, the spectra show the presence of up to three different radicals whose e.s.r. parameters are shown in Table 1.

When the starting ratio of trifluoronitrosomethane and acetylacetone was between 0.5 : 1 and 3 : 1 only the spectra of radicals (Ia) and (IIa) were observed. When there was an initial deficiency of trifluoronitrosomethane the spectra were observed for only a few hours, and consisted predominantly of radical (IIa). On increasing the amount of trifluoronitrosomethane used, radical (Ia) became predominant, and the spectra were readily observed for at least a day before decay products became important (*vide infra*). On increasing the ratio of trifluoronitrosomethane and acetylacetone above 3 : 1 the spectrum of radical (IIIa) became apparent along with that of radical (Ia). Under these conditions the spectrum of radical (IIa) is not seen. Radical (IIIa), although far from being a transient species, was not as stable as (Ia), since its spectrum decayed over a period of a few hours in contrast to the several days required for the complete disappearance of the spectrum of (Ia).

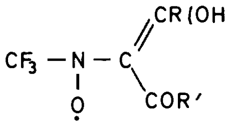
When samples containing an initial excess of trifluoronitrosomethane were kept at room temperature for periods of a day, or longer, a new species (IVa) having the e.s.r. parameters shown in Table 2 began to appear. The spectrum of (IVa) persisted when all the previously observed spectra had disappeared, and under the reaction conditions employed it was found to be stable for periods of at least one month.

$CF_3{\cdot}CO{\cdot}CH_2{\cdot}CO{\cdot}CH_3 + CF_3NO$.— Trifluoronitrosomethane reacted similarly with 1,1,1-trifluoropentane-2,4-dione to give a spectrum which showed the presence of up to three different radicals, whose e.s.r. parameters are shown in Table 1. In contrast to the results obtained with acetylacetone, one species (IIb) was observed only in mixtures where the starting ratio of trifluoronitrosomethane and $CF_3{\cdot}CO{\cdot}CH_2{\cdot}CO{\cdot}CH_3$ was less than 0.4 : 1, and then was only seen for periods of up to one hour. At starting ratios of up to 3 : 1 the spectrum of radical (Ib) was easily visible. This radical was stable for periods of up to one day before decay products became apparent (*vide infra*). In all experiments the spectrum due to radical (IIIb) was seen when an excess of trifluoronitrosomethane was employed; this species was stable for periods of up to one week.



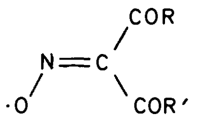
(I)

a ; $R = R' = CH_3$
b ; $R = CH_3$, $R' = CF_3$
c ; $R = R' = CF_3$



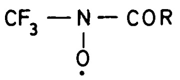
(II)

a ; $R = R' = CH_3$
b ; $R = CH_3$, $R' = CF_3$



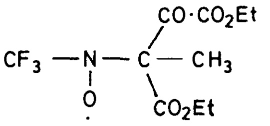
(III)

a ; $R = R' = CH_3$
b ; $R = CH_3$, $R' = CF_3$
c ; $R = R' = CF_3$



(IV)

a ; $R = CH_3$
b ; $R = CF_3$



(V)

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[1] Part XI, B. L. Booth, D. J. Edge, R. G. G. Holmes, and R. N. Haszeldine, *J.C.S. Dalton*, 1976, 2305.

[2] C. M. Camaggi, R. J. Holman, and M. J. Perkins, *J.C.S. Perkin II*, 1972, 501; C. Lagercrantz, *J. Phys. Chem.*, 1971, **75**, 3466.

[3] A. R. Forrester and S. P. Hepburn, *J. Chem. Soc.* (*C*), 1971, 701.

[4] R. E. Banks, M. G. Barlow, and R. N. Haszeldine, *J. Chem. Soc.*, 1965, 4714.

A sample containing an initial excess of CF_3NO, which initially gave the spectrum of radical (Ib), when kept for periods of longer than one day at room temperature, began to show changes in the spectrum consistent with the formation of at least two, and possibly three, extra species. After a further day only one of these new radicals (IVb) remained, and this species was still observable after several weeks. The e.s.r. parameters of this species are given in Table 2. The spectra of the other two species could not be analysed fully.

$CF_3{\cdot}CO{\cdot}CH_2{\cdot}CO{\cdot}CF_3 + CF_3NO$.—Reaction of trifluoronitrosomethane and 1,1,1,5,5,5-hexafluoropentane-2,4-dione under similar conditions gave an e.s.r. spectrum which indicated the presence in solution of only two radical species (Ic) and (IIIc) respectively (Table 1); radical (IIIc), which was stable for over one month in solution, was present for all the ratios of starting materials employed, whereas the less-stable radical (Ic), which decayed after one day, was only observed when the starting ratio of $CF_3NO : CF_3{\cdot}CO{\cdot}CH_2{\cdot}CO{\cdot}CF_3$ was less than 2 : 1. In samples in which there was an excess of trifluoronitrosomethane at the start of the reaction, the initial formation of radical (Ic) was followed by its decay to radical (IVb), the identification of which was rendered difficult by the overlap of the intense spectrum from radical (IIIc).

TABLE 1

E.s.r. Parameters of the radicals obtained initially from solutions of trifluoronitrosomethane and 1,3-diketones in carbon tetrachloride at 293 K

Diketone	Radical product	a_N / gauss	$a_F(3)$ / gauss	a_{other} / gauss	g
$CH_3{\cdot}CO{\cdot}CH_2{\cdot}CO{\cdot}CH_3$	(Ia)	10.50	10.70	2.54 [a]	2.006 33
	(IIa)	9.82	8.88		2.006 68
	(IIIa)	27.36			2.004 10
$CF_3{\cdot}CO{\cdot}CH_2{\cdot}CO{\cdot}CH_3$	(Ib)	11.17	11.17	4.22 [a]	2.006 25
	(IIb)	10.45	10.45		2.006 11
	(IIIb)	28.13	5.06		2.003 54
$CF_3{\cdot}CO{\cdot}CH_2{\cdot}CO{\cdot}CF_3$	(Ic)	9.95	9.95	3.60 [a,b]	2.006 60
	(IIIc)	30.40	4.90	1.14 [c]	2.003 50
$EtO_2C{\cdot}CO{\cdot}CHMe{\cdot}CO_2Et$	(V)	11.01	8.70		2.006 16

[a] One proton. [b] Also six fluorines with h.f.s. = 0.5 gauss. [c] Three fluorines.

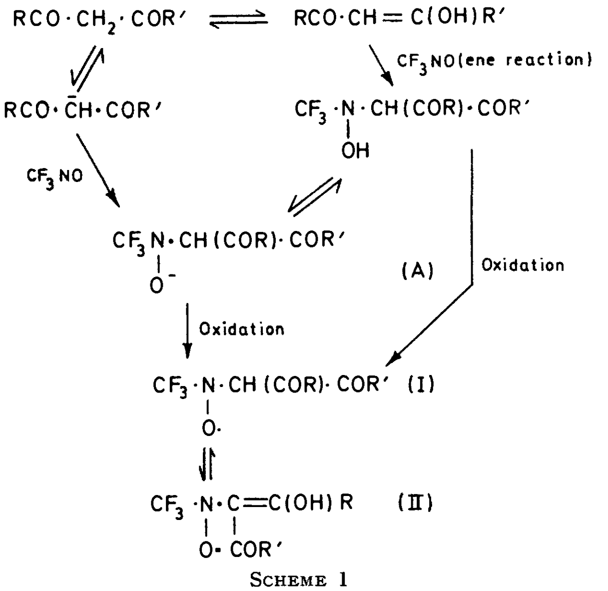
$CH_3{\cdot}CH(CO_2Et)CO{\cdot}CO_2Et + CF_3NO$.—The reaction between CF_3NO and diethyl 2-methyl-3-oxosuccinate gave only one radical species [(V); see Table 1] at all relative concentrations of the reactants. This species was stable for a period of several weeks, and no decay products were observed by e.s.r. spectroscopy over this period.

DISCUSSION

It is clear from the e.s.r. parameters given in Table 1 that the radicals initially observed in this work can be divided into two distinct groups. The radicals (Ia—c), (IIa, b), and (V) are all trifluoromethyl nitroxide derivatives as evidenced by the values of the nitrogen h.f.s. (9—12 gauss) and the g values (2.006 0—2.006 5). The other radicals of type (III) are readily identifiable as iminoxy-radicals by the large nitrogen h.f.s. values and the lower g values.

Initial Radicals.—It is suggested (Scheme 1) that reaction of the diketone with CF_3NO results in the initial formation of a carbanion, which then adds to a further molecule of CF_3NO to form a hydroxylamine anion intermediate (A), a reaction which is somewhat analogous to that postulated as the first step in the base-catalysed reaction between aromatic nitroso-compounds and active methylene compounds.[5] An alternative route to (A) is the ene reaction between CF_3NO and the enol tautomer of the diketone (*cf.* ene reaction of nitrosobenzene and certain alkenes[6]). Oxidation of intermediate (A), or its enol form, either by traces of oxygen present or by an excess of nitroso-compound[3] could give the initially formed nitroxide (I) and its tautomer (II).

The iminoxy-radicals (III) could be formed by one of several routes, which include elimination of CF_3^- from anion (A), or loss of $CF_3{\cdot}$ from nitroxide (I), to give a transient nitroso-compound, $O{:}N{\cdot}CH(COR){\cdot}COR'$, and hence (III) by conventional rearrangement to the oxime $HO{\cdot}N{:}C(COR){\cdot}COR'$ followed by oxidation. Alternatively, direct nitrosation of the diketone would give (III); control experiments have shown that the possible contaminants $(CF_3)_2NO{\cdot}NO$, NO, and $(CF_3)_2N{\cdot}O{\cdot}N(CF_3)_2$ are not involved, but others, including the known[7] nitrosating agent NO_2, could be responsible.



SCHEME 1

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[5] H. Feuer, 'Chemistry of the Nitro and Nitroso Groups,' Interscience, New York, 1969, p. 271.

[6] A. B. Sullivan, *J. Org. Chem.*, 1966, **31**, 2811.

[7] W. H. Wolodasky and J. K. S. Wan, *Spectroscopy Letters*, 1973, **6**, 429.

The reaction with diethyl 2-methyl-3-oxosuccinate gives only the nitroxide radical (V), since there is no possibility here of tautomerism to a radical of type (II), and no way in which oxime formation can occur leading to a radical of type (III).

The radicals (Ia—c) are identified by the fact that they all show a β-methine proton splitting in addition to the splitting from the trifluoromethyl group and the nitrogen atom. The structures of the radicals (IIa and b) are assigned on the basis of the lower trifluoromethyl and nitrogen h.f.s. values compared with those of the nitroxy-radicals of type (I). This lowering of the h.f.s. values is attributed to delocalisation into the double-bond as noted for other substituted vinyl nitroxides.[8]

TABLE 2

E.s.r. parameters of the radicals obtained as decay products from the reactions of trifluoronitrosomethane and 1,3-diketones in carbon tetrachloride at 293 K

Diketone	Radical product	a_N gauss	$a_F(3)$ gauss	a_{other} gauss	g
$CH_3{\cdot}CO{\cdot}CH_2{\cdot}CO{\cdot}CH_3$	(IVa)	7.16	8.27	0.35 [a]	2.006 65
$CF_3{\cdot}CO{\cdot}CH_2{\cdot}CO{\cdot}CH_3$	(IVb)	6.96	8.43	0.45 [a]	2.006 62
$CF_3{\cdot}CO{\cdot}CH_2{\cdot}CO{\cdot}CF_3$	(IVc)	7.00	8.40	0.40 [a]	2.006 60

[a] Three protons or three fluorines.

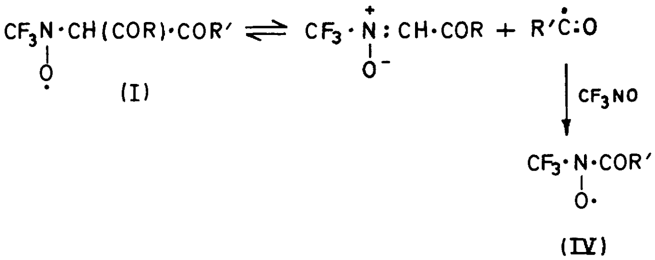
The iminoxy-radicals (IIIa—c) are identified by the close similarity of their parameters with those previously reported for similar species.[7,9]

Two points arising from these assignments require some further comment. Firstly, the direction of enolisation in radical (IIb) cannot be deduced from the e.s.r. parameters, but since enolisation of radical (Ia) from acetylacetone occurs readily, while radical (Ic) from $CF_3{\cdot}CO{\cdot}CH_2{\cdot}CO{\cdot}CF_3$ does not apparently enolise, it seems probable that the enol of (Ib) will contain a :CMe(OH) group as in (IIb). Secondly, two geometrical isomers are possible for the iminoxy-radical (IIIb). A comparison of the h.f.s. values for this radical with those observed for the *syn*- and *anti*-groups of the symmetric iminoxy-radical (IIIc) suggests that in (IIIb) the acetyl group is *anti* to the oxygen atom bearing the unpaired electron; a similar structure for radical (IIIb), obtained by nitrosation of $CF_3CO{\cdot}CH_2{\cdot}COMe$ with NO_2, has been proposed previously.[7]

Decay of Initial Radicals.—The structures of the secondary species formed by decay of the initial radicals are readily assigned as the acyl nitroxides (IVa and b) on the basis of their low nitroxy nitrogen h.f.s. values. Their e.s.r. parameters (Table 2) are very similar, and are identical in all respects to those of the radicals formed by reaction of trifluoronitrosomethane with the aldehydes $CH_3{\cdot}CHO$ or $CF_3{\cdot}CHO$ (80 °C for 30 min, then cool to 20 °C). The radicals (IVa and b) are only observed as decay products when radicals of type (I) are formed initially in the presence of an excess of trifluoronitrosomethane, and this suggests that (I) is either in equilibrium with acyl radical plus nitrone or decays to these, with trifluoronitrosomethane acting as a radical trap for the acyl radical (Scheme 2). The lack of any decay product with diethyl 2-methyl-3-oxosuccinate can be attributed to the added stability of a tertiary alkyl nitroxide over a secondary alkyl nitroxide.

For a given diketone the amount of trifluoronitrosomethane used determined the relative amount of the radicals of types (I), (II), and (III) formed initially. On increasing the relative amount of trifluoronitrosomethane used the amounts of the enol nitroxides (II) decreased at the expense of the keto nitroxides (I), suggesting that the CF_3NO inhibits the enolisation process.

The relative proportions of the radicals of type (I), (II), and (III) observed in these reactions also depends upon the structure of the diketone. This is most noticeable at low relative concentrations of trifluoronitrosomethane. Only the nitroxide radicals (Ia) and (IIa) were observed from acetylacetone, whereas 1,1,1-trifluoropentane-2,4-dione gave the nitroxide radicals (Ib) and (IIb) and the iminoxy-radical (IIIb), except when the concentration of CF_3NO was very low. The iminoxy-radical (IIIc) from the hexafluoropentanedione was detected under all conditions, whereas the oxo nitroxide (Ic) could only be observed when the concentration of trifluoronitrosomethane was low; no enol nitroxide was detected at all.



SCHEME 2

When these reactions between CF_3NO and diketones were carried out using perfluorohexane or hexafluorobenzene as solvent rather than carbon tetrachloride, the same initial radical species were observed, and their decay products were identical. This appears to rule out any possibility that the observed primary radicals or their acyl nitroxide decay products are derived from trichloromethyl radicals adventitiously formed from the solvent.

E.s.r. Parameters.—The e.s.r. spectrum of bis(trifluoromethyl) nitroxide is well known[10] and from a

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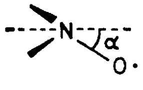
[8] H. G. Aurich and F. Baer, *Tetrahedron Letters*, 1965, 3879.

[9] C. Lagercrantz and K. Torssell, *Arkiv. Kemi.*, 1968, **29**, 203.

[10] W. D. Blackley and R. R. Reinhard, *J. Amer. Chem. Soc.*, 1965, **87**, 802.

study of the temperature dependence of the h.f.s. values [11] and INDO calculations [12] it has been deduced that the angle α at nitrogen is *ca.* 30°, in contrast to the planar structure ($\alpha = 0°$) of the corresponding dimethyl nitroxide.[13]



The results of temperature-dependence studies for other fluorinated nitroxides are far from being well defined,[14] but it has been found that the replacement of one trifluoromethyl group by a SO_3^- group leads to a temperature-independent e.s.r. spectrum, suggesting planarity at the radical centre.[15] The e.s.r. spectra of some of the nitroxide radicals reported in this present work have been obtained over a range of temperatures, and the results for radicals (Ia) and (IVa) are summarised in Tables 3 and 4 respectively. Very similar variations were found for the other dioxo and acyl nitroxides of type (I) and (IV) respectively, while the e.s.r. spectra of the enol nitroxides (II) were found to be temperature independent over the range studied.

TABLE 3

Temperature dependence of the h.f.s. values of radical (Ia) in carbon tetrachloride

T/K	a_N/gauss	a_{CF_3}/gauss	$a_H(1)$/gauss
293	10.50	10.70	2.54
273	10.49	10.79	2.50
253	10.45	10.80	2.44
233	10.43	10.87	2.39
223	10.41	10.89	2.37
213	10.39	10.91	2.34

TABLE 4

Temperature dependence of the h.f.s. values of radical (IVa) in carbon tetrachloride

T/K	a_N/gauss	a_{CF_3}/gauss	a_{CH_3}/gauss
313	7.225	8.255	0.35
303	7.185	8.260	0.35
293	7.155	8.270	0.35
273	7.055	8.405	0.35
253	6.955	8.515	0.35
233	6.855	8.635	0.35

The temperature dependence of the parameters of the nitrogen atom and the trifluoromethyl group in (Ia) is very similar to that reported for bis(trifluoromethyl) nitroxide,[11] and assuming that a correlation exists between the two radicals it suggests that there is a deviation from planarity at the nitrogen atom of radical (Ia). The variation in the h.f.s. value of the β-methine proton does not give any useful information about the conformation of the diacetylmethyl group. The observed decrease with decreasing temperature is to be expected since the amplitude of the oscillations of the methine group will follow the same trend.

Similarly, the nitrogen and trifluoromethyl h.f.s. values of (IVa) show the same type of temperature dependence, and again non-planarity at the nitrogen atom is indicated. The lower values of these h.f.s. values compared to those of other nitroxides can be explained in terms of conjugation of the carbonyl group with the nitroxide function.[16] However, the value is still higher than might have been expected by analogy with the non-fluorinated analogues.* This relatively higher value of a_N for the acyl nitroxides studied in this work is paralleled by results obtained for sulphonyl nitroxides, $RN(\dot{O}){\cdot}SO_2Ar$,[18] where the nitrogen h.f.s. values are *ca.* 11 gauss, compared with *ca.* 8 gauss for the corresponding acyl nitroxides.[16] This higher value has been attributed to differences in configuration of the respective nitrogen atoms,[18,19] the sulphonyl nitroxides being more pyramidal. A similar argument can be used to explain the relatively higher value of a_N in the acyl nitroxides observed in this work, the assumption being that they assume a more pyramidal configuration around the nitrogen atom than does bis(trifluoromethyl) nitroxide, thus reducing the amount of conjugation between the nitroxide system and the carbonyl group.†

No temperature variation was found for the h.f.s. values of the iminoxy-radicals observed in this study. This is in contrast to the quite marked temperature dependence of the h.f.s. values of $(CF_3)_2C{:}N{\cdot}\dot{O}$, which also shows characteristic geometric isomerism.[20] This difference may well be due to a difference in spin transmission in these 'σ' type radicals; this type of interaction varies with the distance from the electron-bearing orbital.[21]

EXPERIMENTAL

E.s.r. spectra were obtained using a Varian E-9 spectrometer using 10 kHz modulation, and equipped with a Varian E-257 variable-temperature accessory. Splitting constants were measured to within ±0.05 gauss, the field sweep being calibrated against an aqueous solution of Fremy's salt ($a_N = 13.01$ gauss), which also served as a g-value standard ($g = 2.005\,5$) when the dual-cavity configuration was employed. Carbon tetrachloride was dried

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* In $Bu^tN(\dot{O}){\cdot}CH_3$ $a_N = 16.4$ gauss,[17] and in $Bu^tN(\dot{O}){\cdot}CO{\cdot}CH_3$ $a_N = 8.0$ gauss,[16] whereas in $CF_3{\cdot}N(\dot{O}){\cdot}CF_3$ $a_N = 9.4$ gauss,[10] and in $CF_3{\cdot}N(\dot{O}){\cdot}CO{\cdot}CF_3$ $a_N = 7.0$ gauss.

† Preliminary INDO calculations have confirmed this assumption, but optimisation of the bond lengths and hence the amount of conjugation is at present incomplete.

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[14] K. J. Klabunde, *J. Amer. Chem. Soc.*, 1970, **92**, 2427.

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[16] A. Macker, Th. A. J. W. Wajer, and Th. J. de Boer, *Tetrahedron*, 1968, **24**, 1623.

[17] G. Chapelet-Letourneux, H. Lemaire, and A. Rassat, *Bull. Soc. chim. France*, 1965, 3283.

[18] Th. A. J. W. Wajer, H. W. Geluk, J. B. F. N. Engberts, and Th. J. de Boer, *Rec. Trav. chim.*, 1970, **89**, 696.

[19] G. Rawson and J. B. F. N. Engberts, *Tetrahedron*, 1970, **26**, 653.

[20] D. R. Choudhury, D. J. Edge, and R. N. Haszeldine, unpublished observations.

[21] B. C. Gilbert and R. O. C. Norman, *J. Chem. Soc.* (*B*), 1966, 86.

over molecular sieves (type 4A) and de-oxygenated by bubbling dry, oxygen-free nitrogen through it.

The standard procedure for carrying out the reactions was to make up a 0.1M-solution of the diketone in carbon tetrachloride, and a 0.5 cm^3 aliquot of this solution was then placed into a thin-walled glass tube. The required amount of trifluoronitrosomethane was then distilled into this tube from a vacuum system, before the tube was sealed under vacuum. The e.s.r. spectrum of the sample was then recorded.

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