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EPR/Spin-trapping study of free radical intermediates in the photolysis of trifluoromethyl ketones with initiators

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Photolysis of trifluoromethyl ketones (TFMKs) 1a–1e *versus* the non-fluorinated ketones 2a–2b in the presence of radical initiators by electron paramagnetic resonance spectroscopy has been studied for the first time. The transient radicals generated after irradiation of the ketones were identified by trapping with 2-methyl-2-nitrosopropane (MNP) and 2,4,6-tri-*tert*-butylnitrosobenzene (TTBNB) as spin traps. TTBNB is a powerful, particularly useful spin trap in these kinds of processes producing anilino and nitroxyl spin adducts due to the ambivalent reactivity on the N and O atoms. In the presence of *t*-butylperoxide, short-chain TFMKs, such as 1,1,1-trifluoroacetone (1d) and hexafluoroacetone (1e), give rise to detection of the elusive trifluoromethyl radical. In contrast, long-chain TFMKs did not provide clues to prove formation of the trifluoromethyl radical but instead to radicals derived by abstraction of one α-methylene proton to the carbonyl. Although TFMKs are quite stable to photodegradation in the absence of initiator, methyl ketone 2b and phenyl ketone 3 produce radicals resulting from abstraction of a γ-hydrogen to the carbonyl group. Copyright © 2010 John Wiley & Sons, Ltd.

Keywords: irradiation; spin trap; spin adduct; EPR; trifluoromethyl ketones; photolysis

Introduction

The spin-trapping technique can be used to uncover radical mechanisms of many organic reactions through electron paramagnetic resonance (EPR). This technique is particularly useful in processes in which only low steady-state radical concentrations are present.[1–3] Free radicals, as reactive transient intermediates in many organic reactions, are scavenged by spin traps, such as C-nitroso compounds and nitrones, and converted to more stable spin adducts. EPR spectra of these adducts provide valuable information about the structure of the corresponding radical intermediates and therefore to unravel the mechanism of the reactions in which they are involved. Nitroso spin traps have the advantage that the reactive radical attaches directly to the nitroso nitrogen atom, and it is therefore in close proximity to the unpaired electron that is located primarily in the nitroxyl function. This usually results in the detection of additional distinctive hyperfine couplings from magnetic nuclei present in the added radical. In nitrone spin traps, however, the reactive radical adds to the carbon atom adjacent to the incipient nitroxyl group, and it is therefore more distant from the molecular orbital containing the unpaired electron. So, it is often not possible to resolve any hyperfine couplings from the added radical itself. This adduct identification is easier and more definitive when using nitroso spin traps than nitrones.

In the course of our work directed to the inhibition of the chemical communication in insects as a new biorational approach for pest control,[4] we needed to know the stability of trifluoromethyl ketones (TFMKs) in photochemical conditions and in the presence of initiators. It is well known that nucleophilic radicals such as hydroxyl and alcoxyl radicals abstract hydrogen from an α-C–H group in a ketone. Polar effects from the carbonyl group stabilize an unpaired electron on an adjacent carbon atom and, consequently, play an important role in determining the chemo- and regio-selectivity of these hydrogen atom transfer reactions.[5–7] Some of the TFMKs to study, particularly those structurally related to insect sex pheromones, have shown their effectiveness as potential control agents of economically important pests.[8] We describe herein for the first time the stability of TFMKs **1a**–**1e** (Fig. 1) by irradiation in the presence of hydrogen peroxide or di-*tert*-butyl peroxide as initiators. Two nitroso compounds, 2-methyl-2-nitrosopropane (MNP) and 2,4,6-tri-*tert*-butylnitrosobenzene (TTBNB), are used as spin traps of the transient radicals generated in the irradiation processes. The results have been compared with the non-fluorinated ketones **2a**–**2b** and **3.** An important goal of the study was to disclose whether the TFMKs generate the highly elusive trifluoromethyl radicals under the irradiation conditions.

Results and Discussion

Irradiation of ketones: identification of radicals formed in the process

Two spin traps, MNP and TTBNB, were selected to scavenge transient radicals formed in the irradiation of ketones displayed in Fig. 1. Both compounds preferentially trap carbon-centred radicals $R^\bullet$. When MNP is used as spin trap, $R^\bullet$ attacks the nitrogen atom of the nitroso group to form nitroxyl adducts of type (a) (Scheme 1).

A general drawback observed with the use of MNP as spin trap is the presence of an intense and very persistent EPR signal

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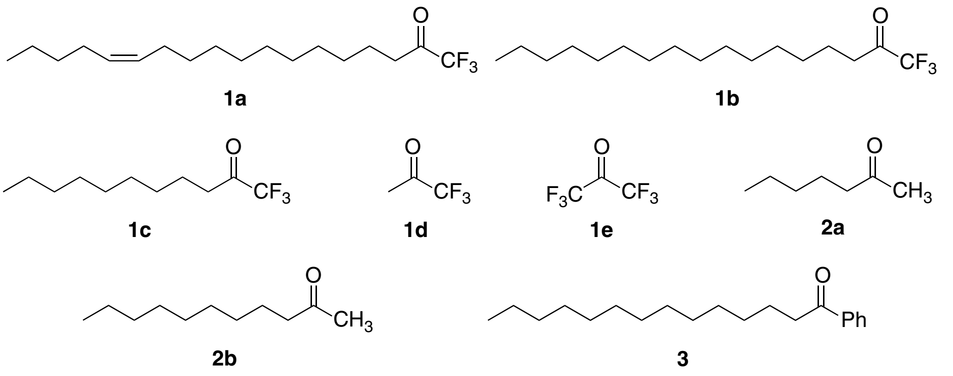
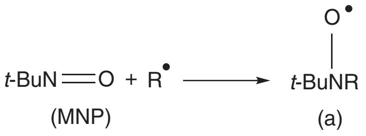
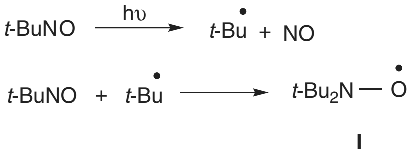


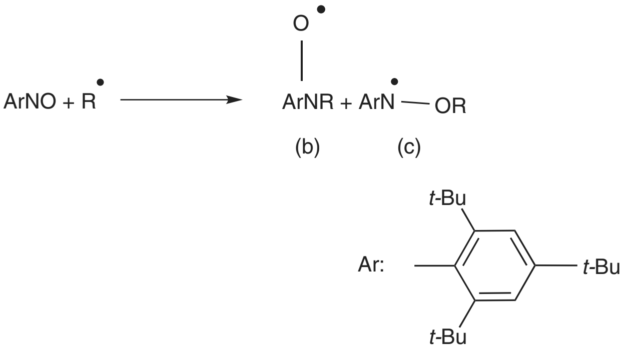
Figure 1. Structures of the ketones considered for the photodegradation study.



Scheme 1. Radical adduct from MNP as spin trap.



Scheme 2. Radical adduct from photolysis of MNP.



Scheme 3. Radical adducts from TTBNB as spin trap.

corresponding to the di-*tert*-butylnitroxide radical (**I**), resulting from reaction of the initially formed *tert*-butyl radical with unreacted MNP[9] (Scheme 2). Radical **I** appears as a triplet corresponding to the N hyperfine splitting ($a^N = 16.00$ G), often masking the signals of other expected spin adducts (Scheme 2).

TTBNB is also an excellent spin trap.[10] It has two trapping sites: the nitrogen atom to form nitroxyl radical as spin adduct (b) and the oxygen to form the anilino adduct (c) if R• is bulky[11,12] (Scheme 3). Generally, primary alkyl radicals form nitroxides (b), tertiary radicals give rise to anilino radicals (c), and secondary radicals may produce both types of radicals.

In order to study systematically the nature of the spin adducts formed in the irradiation of TFMKs **1a–1c** in the presence of a hydrogen scavenger and MNP or TTBNB as spin traps, we proceeded first to study the transient radicals resulting from irradiation of more simple fluorinated ketones, such as 1,1,1-trifluoroacetone (**1d**) and hexafluoroacetone (**1e**), and the non-fluorinated acetone, 2-heptanone (**2a**), 2-undecanone (**2b**) and tridecylphenyl ketone (**3**). The hyperfine splittings of all radical adducts were easily derived by simulation[13] and are summarized in Tables 1 and 2.

Using MNP as spin trap

When ketones **1d, 1e** and acetone were irradiated in the presence of MNP and in the absence of a hydrogen scavenger only a very strong triplet corresponding to the di-*tert*-butylnitroxide radical (**I**) was observed. However, in the presence of hydrogen peroxide as initiator, irradiation of acetone showed a new spin adduct in addition to radical **I**. This new radical ($a^N = 14.90$ G; $a^{2H} = 8.70$ G; $g = 2.0059 \pm 0.0005$) was assigned as adduct **II** as previously described,[15] and its formation can be explained by abstraction of one hydrogen atom of acetone by the hydroxyl radical generated by photolysis of hydrogen peroxide, followed by reaction with MNP (Scheme 4).

When 1,1,1-trifluoroacetone (**1d**) was irradiated in the presence of hydrogen peroxide, abstraction of a hydrogen in the α position to the carbonyl yielded the trifluoroacetylmethyl radical ($^{\bullet}CH_2COCF_3$), which could decompose to ketene and trifluoromethyl radical. This latter and elusive radical was trapped by MNP to generate spin adduct **III** (Scheme 5). Trifluoromethyl radical was first trapped from photolysis of trifluoroiodomethane in benzene in the presence of phenyl-*tert*-butylnitrone (PBN).[14,16] A similar

Table 1. EPR spectral parameters of spin adducts generated by irradiation of ketones **1a, 1c, 1d, 1e, 2a, 2b** in the presence of hydrogen peroxide and MNP as spin trap

Ketones	Radical adducts	Spectral parameters
1a	**VI**	$a^N = 15.40$ G; $a^{2H} = 2.40$ G; $g = 2.0067 \pm 0.0005$
1c	**VII**	$a^N = 15.50$ G; $a^{2H} = 2.60$ G; $g = 2.0060 \pm 0.0005$
1d	**III**[a]	$a^N = 13.50$ G; $a^{3F} = 12.90$ G; $g = 2.0060 \pm 0.0005$
1e	**III**[a]	$a^N = 13.50$ G; $a^{3F} = 12.90$ G; $g = 2.0060 \pm 0.0005$
2a	**IV**	$a^N = 14.80$ G; $a^{2H} = 2.00$ G; $g = 2.0058 \pm 0.0005$
2b	**V**	$a^N = 15.00$ G; $a^{2H} = 2.00$ G; $g = 2.0063 \pm 0.0005$

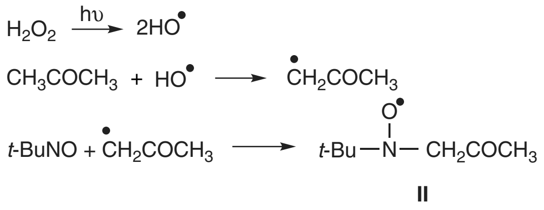
[a] Parameters from literature[14] do not distinguish between N- and F-couplings ($a^N = a^{3F} = 12.24$ G in acetone).

Table 2. EPR spectral parameters of spin adducts generated by irradiation of ketones **1a, 1b, 1d, 1e, 2b** and **3** in the presence of hydrogen peroxide in acetone or di-*tert*-butyl peroxide (neat) and TTBNB as spin trap

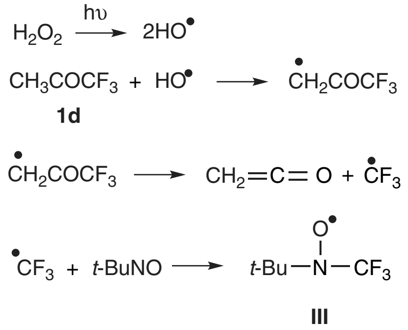
Ketones	Radical adducts	Spectral parameters
1a	**XV**	$a^N = 11.13$ G; $a^{3H} = 1.75$ G; $g = 2.0048 \pm 0.0005$
	XVI	$a^N = 13.75$ G; $a^{1H} = 21.75$ G; $g = 2.0063 \pm 0.0005$
1b	**XVII**	$a^N = 10.75$ G; $a^{3H} = 1.88$ G; $g = 2.0048 \pm 0.0005$
	XVIII	$a^N = 13.75$ G; $a^{1H} = 23.25$ G; $g = 2.0066 \pm 0.0005$
1d	**IX**	$a^N = 10.25$ G; $a^{3F} = 9.4$ G; $a^{2H} = 0.75$ G; $g = 2.0069 \pm 0.0005$
1e	**IX**	$a^N = 10.25$ G; $a^{3F} = 9.4$ G; $a^{2H} = 0.75$ G; $g = 2.0069 \pm 0.0005$
2b	**X**	$a^N = 10.75$ G; $a^{3H} = 1.88$ G; $g = 2.0046 \pm 0.0005$
	XI	$a^N = 13.88$ G; $a^{1H} = 23.13$ G; $g = 2.0061 \pm 0.0005$
3	**XII**	$a^N = 10.63$ G; $a^{3H} = 1.88$ G; $g = 2.0047 \pm 0.0005$
	XIII	$a^N = 13.75$ G; $a^{1H} = 23.25$ G; $g = 2.0060 \pm 0.0005$

result was obtained upon irradiation of hexafluoroacetone (**1e**). It is worthwhile to note that for the first time the trifluoromethyl radical has been trapped with MNP by irradiation of TFMKs in solution and in the presence of radical initiators. The hyperfine splittings of radical **III** are depicted in Fig. 2 and Table 1.

Irradiation of neat 2-heptanone (**2a**) and 2-undecanone (**2b**) in the presence of hydrogen peroxide and MNP yielded two new radicals in the form of a triplet of doublets, which were attributed to spin adducts **IV** and **V**, respectively, in addition to radical **I** (Table 1). In these new ketones, the hydroxyl radical preferentially abstracts one methylene hydrogen in the α-position to the carbonyl over one of the methyl group, in accordance with previous results[15] (Scheme 6).



Scheme 4. Photolysis of acetone in the presence of H_2O_2 and MNP as spin trap.



Scheme 5. Photolysis of 1,1,1-trifluoroacetone in the presence of H_2O_2 and MNP as spin trap.

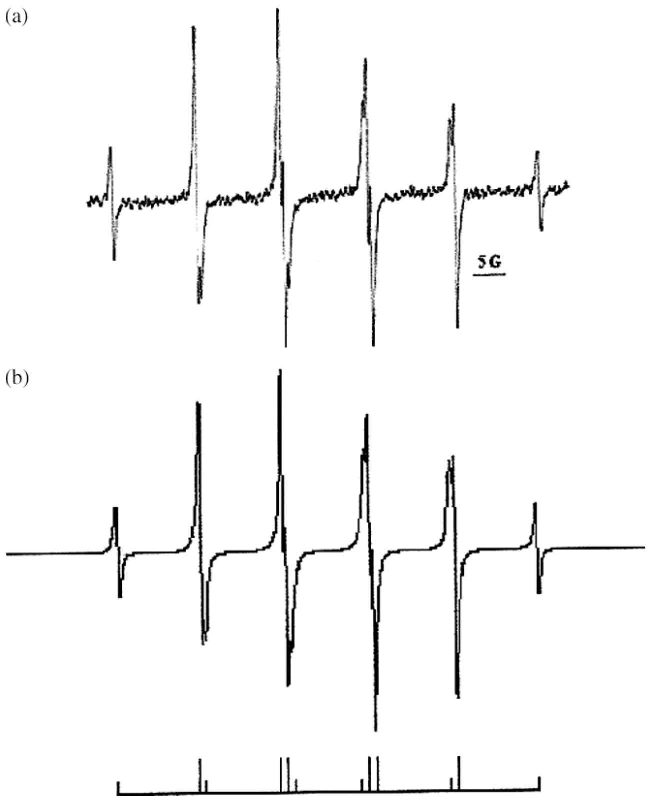
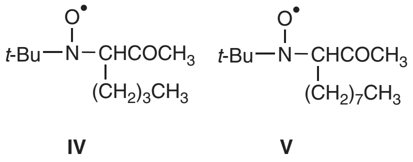
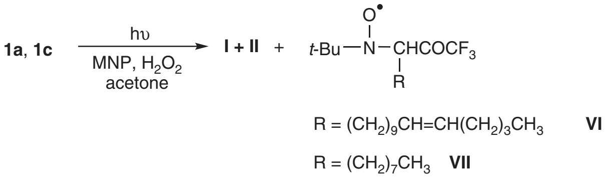


Figure 2. (a) EPR spectrum of spin adduct **III** after irradiation of ketones **1d** and **1e** with hydrogen peroxide as initiator and MNP as spin trap. (b) Computer simulation of **III** using the parameters given in Table 1.

Similarly, when TFMKs **1a** and **1c** were irradiated in acetone in the presence of hydrogen peroxide and MNP, we detected spin adducts **VI** and **VII**, respectively, by abstraction of one methylene proton in the α-position to the carbonyl by the initiator. In addition, adducts **I** and **II** from the MNP and the acetone present in the sample were also detected (Scheme 7, Table 1). It is worth noting that in no case, however, the spin adduct **III** corresponding to trapping of the $CF_3{}^\bullet$ radical was detected.



Scheme 6. Radical adducts from photolysis of 2-heptanone (**2a**) and 2-undecanone (**2b**) in the presence of H_2O_2 and MNP as spin trap.



Scheme 7. Photolysis of trifluoromethylketones **1a** and **1c** in the presence of H_2O_2 and MNP as spin trap.

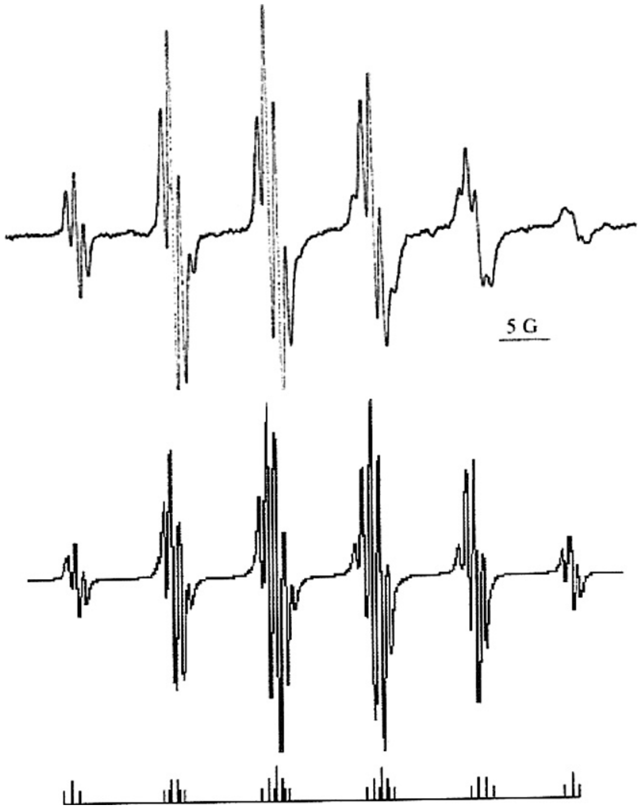
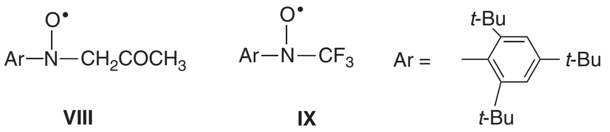


Figure 3. (a) EPR spectrum of spin adduct **IX** from irradiation of ketones **1d** and **1e** with hydrogen peroxide as initiator and TTBNB as spin trap. (b) Computer simulation using the parameters given in Table 2.



Scheme 8. Radical adducts from photolysis of acetone (radical adduct **VIII**) and of ketones **1d** and **1e** (radical adduct **IX**) in the presence of H_2O_2 and TTBNB as spin trap.

Using TTBNB as spin trap

As cited above, this nitroso compound gives rise to two different kinds of spin adducts, the nitroxyl and anilino adducts[10,12] and both can be distinguished by their *g*-values and nitrogen splittings. Usually, the *g*-values of the anilino adducts are slightly lower than those of the corresponding nitroxyl adducts. An important advantage of TTBNB over MNP is its photostability: the former is transparent in EPR upon irradiation in benzene. Unfortunately, this solvent could not be used in our experiments due to the partial solubility of some of the substrates, particularly TFMKs **1a** and **1b**. Long irradiation ($\sim$40 min) of TTBNB in acetone in the presence of hydrogen peroxide as radical initiator led to the detection of spin adduct **VIII** ($a^N = 13.94$ G; $a^{2H} = 14.52$ G; $a^{1H} = 1.0$ G; $g = 2.0058 \pm 0.0005$), derived from reaction of the acetylmethyl radical with the spin trap (Scheme 8). The spectral parameters of **VIII** (Table 2) are in close agreement with those reported previously.[12] Irradiation of ketones **1d** and **1e** in acetone in the presence of the initiator and TTBNB yielded indistinctly radical **IX** by trapping, as with MNP, the nascent trifluoromethyl radical (Scheme 8) (Fig. 3, Table 2). The absence of the anilino adducts in these spectra is surprising. No spectral signals appeared in the absence of the initiator.

Photolysis of neat (absence of solvent) ketones **2b** and **3** in the presence of di-*tert*-butyl peroxide as radical initiator allowed detection of the pairs **X, XI** and **XII, XIII**, respectively, along with the simple adduct **XIV** in both processes (Scheme 9). Adducts **X, XI, XII** and **XIII** were formed by trapping the transient radicals derived from abstraction of one α-methylene hydrogen to the carbonyl group of the ketones, whereas adduct **XIV** resulted by trapping the hydrogen atom.[17] As an example, the EPR spectrum of the adducts detected in the photolysis of ketone **2b** is shown in Fig. 4. The spectral parameters of radicals are shown in Table 2.

These experiments allowed us also to establish the higher stability of the nitroxyl adducts with regard to the anilino adducts. Thus, although the predominant spin adducts first generated upon irradiation were those of an anilino nature (**X, XII**), when the solutions were left in the dark for 24 h more, the only detected adducts were then the corresponding nitroxides **XI, XIII** (Fig. 4).

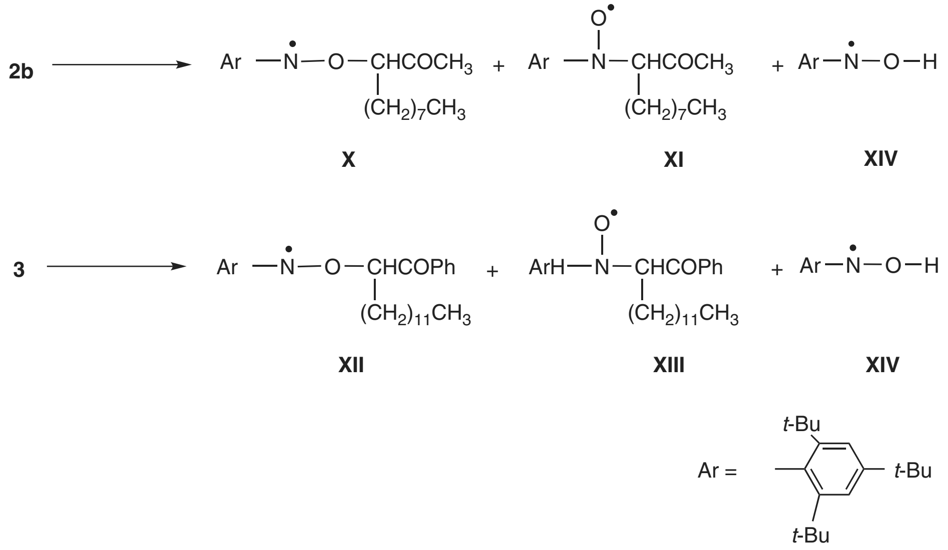
Similarly, when fluorinated ketones **1a** and **1b** were irradiated in the presence of di-*tert*-butyl peroxide and TTBNB a mixture of anilino and nitroxyl radicals, assigned as **XV** and **XVI** from ketone **1a** and **XVII** and **XVIII** from ketone **1b**, respectively, were detected (Scheme 10). The radicals were again assigned by their splittings and *g*-values (Table 2) and only the nitroxyl adducts were stable in the dark after 24 h, in a similar manner to the irradiation of the non-fluorinated ketones **2b** and **3**.

The different behavior in the photodegradation in the presence of an initiator of acetone **1d** and ketones **1a, 1b** and **1c** could proceed from the differences in the relative stability of the radical intermediates generated by an αH-abstraction reaction, that is a primary carbon radical in **1d** and a secondary radical in the others. In acetone **1d**, the intermediate methyl radical leads by an intramolecular electronic rearrangement to trifluoromethyl radical which is scavenged by the spin trap to give the final spin adduct, as shown in Scheme 5. In ketones **1a, 1b** and **1c**, the intermediate methylene radicals are stable enough to give the expected spin adducts.

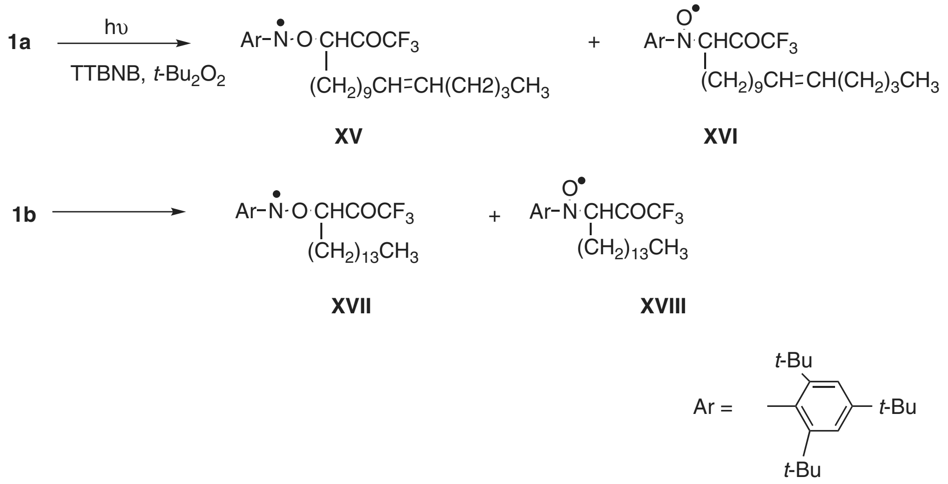
Photolysis in the cavity of the EPR spectrometer of ketones containing γ-hydrogens to the carbonyl could produce the spin adducts resulting from trapping the radicals derived by abstraction of a γ-hydrogen, according to a Norrish type II mechanism.[18] However, photolysis of TFMKs **1a** and **1b** in the absence of initiator and in the presence of TTBNB gave no detectable EPR signals except those of adduct **XIV**. In the same way, irradiation of ketone **2b** under identical conditions did yield the nitroxide **XIX** ($a^N = 13.75$ G; $a^{1H} = 22.75$ G; $g = 2.0067 \pm 0.0005$) by abstraction of a γ-hydrogen of the ketone and carbonyl reduction to the secondary alcohol (Fig. 5, Scheme 11). In the same line, irradiation of the aromatic ketone **3** led to both anilino- and nitroxyl adducts **XX** ($a^N = 10.60$ G; $a^{2H} = 1.75$ G; $a^{1H} = 1.0$ G; $g = 2.0048 \pm 0.0005$) and **XXI** ($a^N = 14.0$ G; $a^{1H} = 23.25$ G; $g = 2.0060 \pm 0.0005$), respectively, following analogous Norrish type II degradation (Fig. 5, Scheme 11). In both cases, radical **XIV** appeared also superimposed on the main radical adducts. In no case radicals derived from cleavage of the α-CC bonds of the carbonyl were trapped (Norrish type I mechanism).[18]

Conclusions

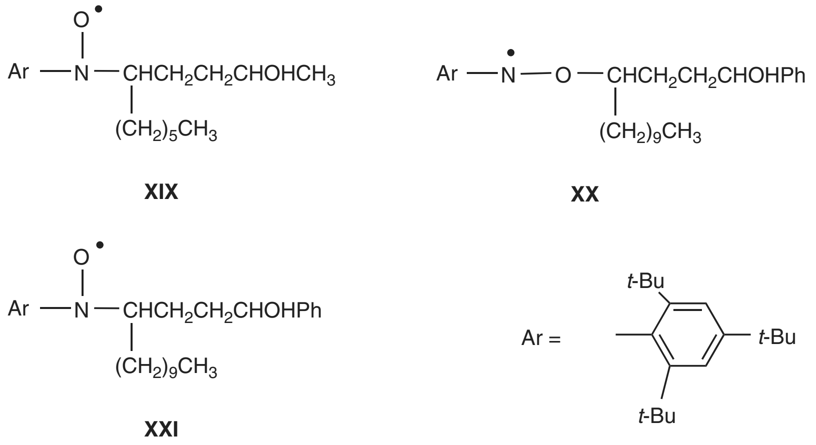
In the presence of a radical initiator (hydrogen peroxide or di-*tert*-butyl peroxide), irradiation of TFMKs and methyl ketones give



Scheme 9. Photolysis of ketones **2b** and **3** in the presence of di-*tert*-butyl peroxide and TTBNB as spin trap.



Scheme 10. Photolysis of ketones **1a** and **1b** in the presence of di-*tert*-butyl peroxide and TTBNB as spin trap.



Scheme 11. Photolysis of ketone **2b** (radical adduct **XIX**) and ketone **3** (radical adducts **XX** and **XXI**) in the presence of TTBNB as spin trap.

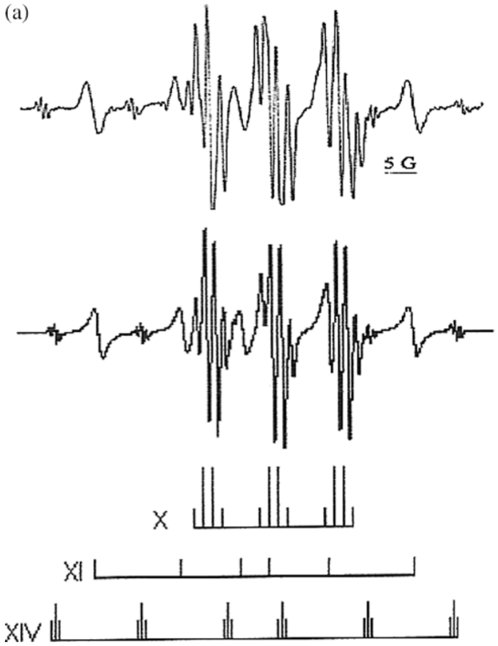


Figure 4. (a, above) EPR spectrum of the mixture of spin adducts **X,XI** and **XIV**, upon irradiation of ketone **2b** with di-*tert*-butylperoxide as initiator and TTBNB as spin trap. (a, below) Computer simulation using the parameters given in Table 2. (b, above) EPR spectrum after 24 h in the dark. (b, below) Computer simulation.

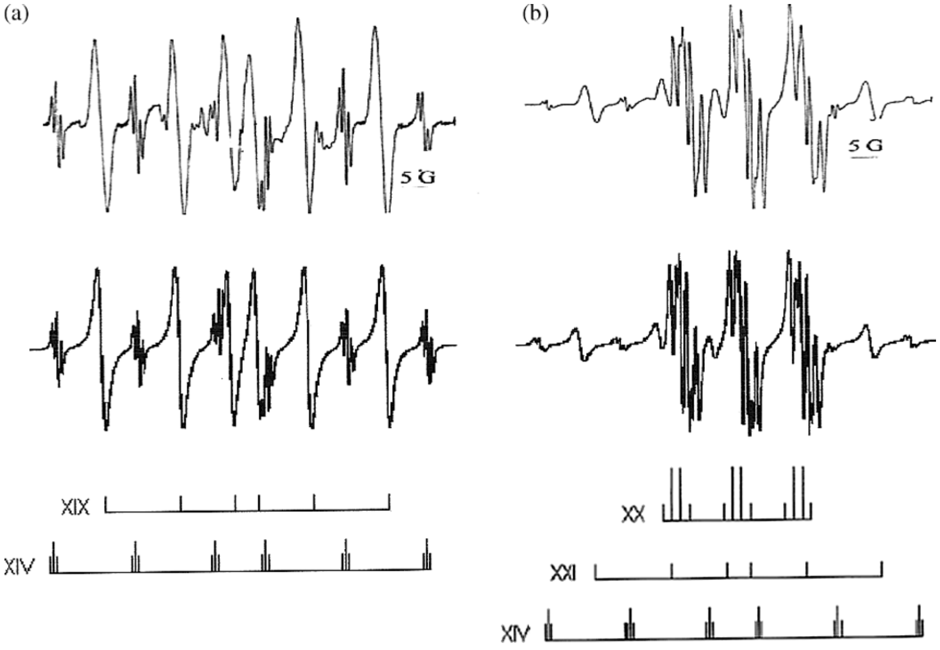


Figure 5. (a, above) EPR spectrum of spin adducts **XIX** and **XIV** upon photodegradation of ketone **2b** with TTBNB as spin trap in the absence of initiator. (a, below) Computer simulation using the parameters given in Table 2. (b, above) EPR spectrum of spin adducts **XX, XXI** and **XIV** upon photodegradation of ketone **3** with TTBNB as spin trap in the absence of initiator. (b, below) Computer simulation using the parameters given in Table 2.

rise to radicals derived by abstraction of an α-methylene proton to the carbonyl. The elusive trifluoromethyl radical has been indirectly detected for the first time upon irradiation of 1,1,1-trifluoroacetone (**1d**) and hexafluoroacetone (**1e**) in the presence of hydrogen peroxide and MNP or TTBNB as spin trap. However, photolysis of long-chain TFMKs, such as **1a, 1b** and **1c,** yields mainly α-carbonylmethylene radicals instead of trifluoromethyl radical.

Experimental

Chemicals

(*Z*)-1,1,1-Trifluoro-13-octadecen-2-one (**1a**) was prepared in a four-step process from (*Z*)-11-hexadecen-1-ol, as previously described.[8] 1,1,1-Trifluoro-2-heptadecanone (**1b**) was obtained from hexadecanoic acid, TFAA and pyridine,[19] 1,1,1-trifluoro-2-undecanone (**1c**) was prepared from decanoic acid as previously shown.[20] 1,1,1-Trifluoroacetone (**1d**), hexafluoroacetone (**1e**), 2-

heptanone (**2a**), 2-undecanone (**2b**) and tridecylphenyl ketone (**3**) were purchased from Aldrich.

EPR spin trapping experiments

The EPR experiments were conducted on a Varian E-109 spectrometer at 9.5 GHz (X-band) using 100 kHz field modulation at room temperature. *g*-Values of the radicals were determined with Mn^{2+} as standard ($g = 2.0054$). The samples, neat or dissolved in benzene or acetone, containing a spin trap and in the presence or not of hydrogen peroxide or di-*tert*-butyl peroxide as initiator, were irradiated in the cavity of the spectrometer with an Oriel high-pressure mercury lamp (500 W). When necessary, blank experiments were also run under the same conditions. EPR simulations were carried out using the WinSim program.[13]

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