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Enhanced radical delivery from aldoxime esters for EPR and ring closure applications

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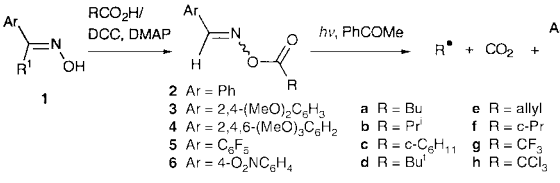
Arylmethaniminyl and alkyl radicals were generated from di- and tri-methoxyphenyl aldoxime esters, by photolysis in the presence of 4-methoxyacetophenone, and were detected by EPR spectroscopy: good yields of cyclised products were isolated from suitably unsaturated alkyl substituents.

Molecules suitable for direct photochemical or thermal generation of free radicals, other than peroxides and azo compounds, are quite limited, and therefore potential alternative types are of special interest. Oxime esters **2** are easily made from aldehyde (or ketone) oximes **1** and carboxylic acids (or acyl halides) (Scheme 1) and are much easier to handle and characterise than peroxides or azo compounds. These esters, which contain weak N–O bonds, appear to be a category of precursors for carbon-centred and iminyl radicals (**7**) with promise of considerable generality, but so far exploitation has been minimal. Thus, benzophenone oxime esters [$Ph_2C{=}NOC(O)R$] were shown to function as photolytic sources of alkyl and diphenylmethaniminyl radicals and used in preparations of alkyl aromatics,[1,2] alkyl chlorides,[2] and alkanes.[2] Radical induced homolysis of oxime benzoates by tributylstannane was found to be a useful method for generating iminyl radicals,[3,4] which were also produced, without the need for toxic organotin compounds, by use of Ni powder and acetic acid.[5,6]

Aldoxime esters **2** (Ar = Ph) displayed strong UV absorption bands at 208 and 254 nm. Inclusion of methoxy substituents in the aryl group (**3**, **4**) induced additional strong absorption bands at longer wavelengths ($\lambda_{\max}$ = 273, 312 nm) and this implied that photo-dissociation to radicals might be more efficient. We tested this prospect by monitoring solution phase photolyses of oxime esters containing a range of aromatic and alkyl substituents by means of 9 GHz EPR spectroscopy. No observable spectra were obtained from photolysis (500 W Hg arc, unfiltered) of degassed solutions of oxime esters **2** to **6** in *tert*-butylbenzene solution in the temperature range 200 to 320 K, except for a very weak spectrum of the allyl radical from **2e**. However, on addition of 4-methoxyacetophenone to the solutions as a photosensitiser ($\geqslant$0.1 equiv.), good quality EPR spectra were obtained, especially from methoxy-substituted oxime esters of types **3** and **4**, but not from types **5** and **6** containing electron-withdrawing substituents. In the sensitised photolyses of **2d**, **3d** and **4d**, for example, the EPR spectra consisted of a superposition of two radicals [see Fig. 1(*a*), (*b*)]. The most prominent signals were due to the *tert*-butyl radical, with EPR parameters identical to those reported in the literature.[7] Two widely spaced groups of nitrogen triplets could also be discerned in the wings of the spectra [from **7** (Ar = Ph): a(H) = 80.5, a(N) = 10.0 G, g = 2.0034 at 250 K]. The exceptionally large a(H) values, as well as the other EPR parameters, are the signatures of rarely observed arylmethaniminyl radicals,[8] *i.e.* **7**. Fig. 1(*b*) shows the well-resolved second-order structure of the individual lines of the *tert*-butyl radical and the partly resolved long range splitting from ring hydrogens in iminyl radical **7** (Ar = Ph). The ratio of the concentrations of the alkyl and iminyl radicals depended on temperature and on the nature of R. For example, from **3e** (R = allyl) very intense spectra mainly of allyl were obtained, particularly for lower power and low modulation amplitude [Fig. 2(*a*), whereas for **4a** (R = Bu) the spectra were dominated by iminyl signals [Fig. 2(*b*)] and in general primary alkyls were difficult to detect. These differences in the concentrations of the two radicals were probably due to minor differences in the rates of their termination reactions. For highly reactive σ-radicals, *e.g.* cyclopropyl, generated from **4f** and trifluoromethyl generated from **4g**, the EPR spectra showed only the 2,4,6-trimethoxy-



Scheme 1

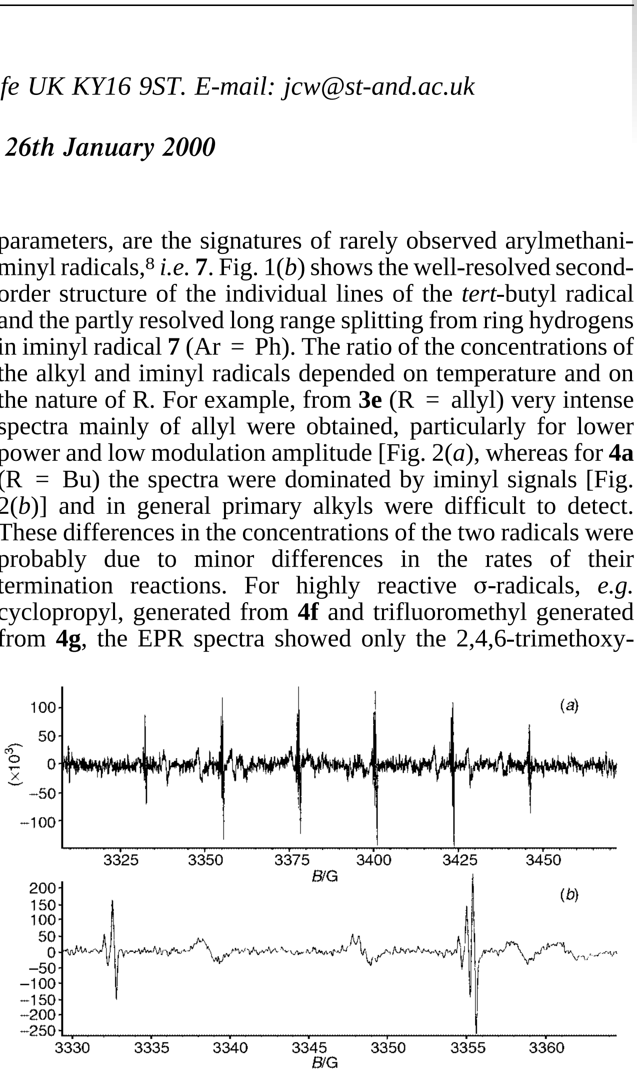


Fig. 1 (*a*) 9.4 GHz EPR spectrum obtained from photolysis of a solution of **2d** and MAP in *tert*-butylbenzene at 225 K showing the *tert*-butyl and iminyl radicals. (*b*) Scale expansion of a section of the above spectrum at 250 K showing the second order structure on the *tert*-butyl radical and partly resolved long range splittings on the iminyl radical **7** (Ar = Ph).

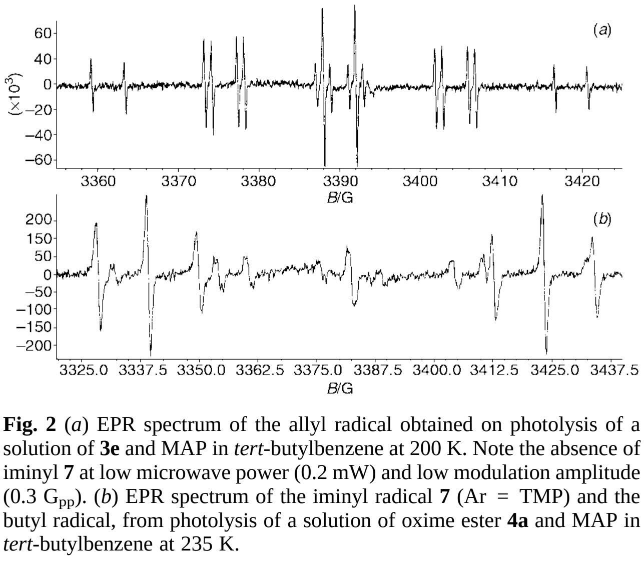


Fig. 2 (*a*) EPR spectrum of the allyl radical obtained on photolysis of a solution of **3e** and MAP in *tert*-butylbenzene at 200 K. Note the absence of iminyl **7** at low microwave power (0.2 mW) and low modulation amplitude (0.3 G_{pp}). (*b*) EPR spectrum of the iminyl radical **7** (Ar = TMP) and the butyl radical, from photolysis of a solution of oxime ester **4a** and MAP in *tert*-butylbenzene at 235 K.

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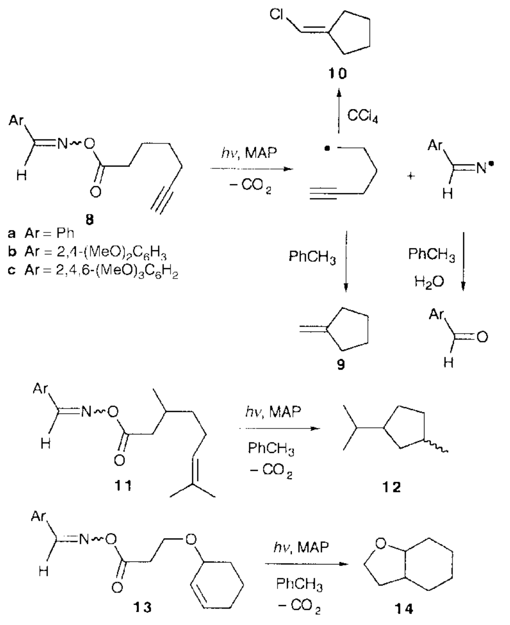

Scheme 2

Table 1 Results of irradiation of oxime esters

Oxime ester	Ar[a]	Solvent	MAP/equiv.	Product (%)[b]
8a	Ph	$PhCH_3$	—	**9** (6)
8a	Ph	$PhCH_3$	1	**9** (28)
8b	DMP	$PhCH_3$	—	**9** (39)
8b	DMP	$PhCH_3$	1	**9** (77)
8c	TMP	CCl_4	1	**10** (60)
11c	TMP	$PhCH_3$	1	**12** (34)
13c	TMP	CH_2Cl_2	1	**14** (72)

[a] DMP = 2,4-dimethoxyphenyl, TMP = 2,4,6-trimethoxyphenyl. [b] Yields determined by NMR.

phenylmethaniminyl radical [**7**, Ar = 2,4,5-$(MeO)_3C_6H_2$] except at low temperatures [< *ca.* 220 K], where cyclohexadienyl radicals from addition of cyclopropyl (or CF_3) to the *tert*-butylbenzene solvent were also visible.[9]

The large doublet H-hfs and comparatively few lines of the methaniminyl radicals provide a 'window' of *ca.* 60 G in the centre of the EPR spectrum which minimises overlap with the co-radical. Furthermore, the iminyl spectra act as useful standards with known *g*-factors so that spectral analysis of the co-radical is facilitated. Thus, these oxime esters constitute a convenient new class of radical precursors suitable for spectroscopic studies. Unlike the alternative diacyl peroxides, reagents **2** are innocuous and convenient to handle.

The EPR spectral results indicated that use of di- and trimethoxy oxime esters, in conjunction with a photosensitiser, could enhance their efficiency in preparative reactions. Accordingly, several ring closure reactions of oxime esters **8**, **11** and **13** were investigated. (Scheme 2).

Solutions of individual oxime esters (*ca.* 0.13 mol dm^{-3}) in a hydrogen donor solvent ($PhCH_3$, CH_2Cl_2) were photolysed with light from a 400 W medium pressure Hg lamp for *ca.* 3 h. Table 1 shows that for **8a** yields of the cyclised product, methylenecyclopentane (**9**), were low, but improved on inclusion of photosensitiser. Best yields of **9** were, however, obtained from the dimethoxy oxime ester **8b** when photosensitiser was included. Variation of the photosensitiser concentration showed that as little 0.1 equiv. could be used before serious loss of efficiency was experienced. The bicyclic ether **14** was obtained in good yield from photolysis of the trimethoxy oxime ester **13**, but the yield of 1-isopropyl-3-methylcyclopentane (**12**) from **11** was moderate, possibly because of poor hydrogen donation to the tertiary cyclised radical by the solvent.[10] No uncyclised products from direct reduction of the initial unsaturated alkyl radicals were detected. This is an advantage in that by-products are minimised, but indicates that, as expected, hydrogen donation is slow. An advantage of the method is that halogen-donor solvents can also be used for the preparation of functionalised rings. For example, photolysis of **8c** in CCl_4 afforded a good yield of chloromethylenecyclopentane (**10**). The main products derived from the iminyl radicals were the corresponding aldehydes, probably formed from intermediate imines, ArCH=NH, which are known to be highly susceptible to hydrolysis.

These results demonstrate that di- and tri-methoxy substitution of aryl oxime esters enhances their performance as photolytic sources of carbon-centred and iminyl radicals and that further improvement can be achieved by inclusion of a photosensitiser. These compounds are promising radical precursors of use in spectroscopic studies and as 'cleaner' tin-free reagents for preparative decarboxylative cyclisations of unsaturated carboxylic acids.

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Notes and references

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9 EPR experiments with **2g** were also carried out in liquid cyclopropane which enables lower temperatures to be accessed. However, due partly to poor solubility at low temperatures, only weak spectra of **7** (Ar = 2,4,6-$(MeO)_3C_6H_2$ were observed.

10 For example: oxime ester **13c** (0.25 g, 0.69 mmol) and MAP (0.12 g, 0.8 mmol) in CH_2Cl_2 (5 cm^3) were photolysed in a quartz tube for 3 h at 50 °C with light from a 400 W medium pressure Hg lamp. The solvent was evaporated and the solid remaining was extracted several times with Et_2O. Concentration and microdistillation at ambient temperature/0.01 Torr gave bicyclic ether **14** (ref. 11) (0.01 g, 12%) (ref. 12), δ_H(300 MHz, $CDCl_3$) 1.15–1.30 (2H, m), 1.39–1.68 (6H, m), 1.83–2.04 (3H, m), 3.77–3.87 (2H, m), 3.96 (1H, q, *J* 8).

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12 Low yield due to small scale reaction and volatile product: see final row Table 1 for a better measure of the true yield.

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