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QUANTITATIVE STUDIES ON FREE RADICAL REACTIONS WITH THE SCAVENGER 1,1,3,3-TETRAMETHYLISOINDOLINYL-2-OXY

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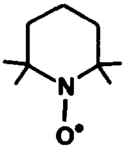
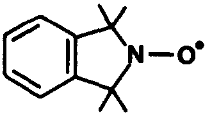
Abstract: Previously unobserved reaction pathways for the attack of *tert*-butoxy radicals on vinyl monomers have been found by a technique which employs the title nitroxide as radical scavenging agent.

A little known feature of the chemistry of stable, di-tertiary alkyl nitroxides (*eg.* 1) is their ability to scavenge alkyl radicals at near diffusion controlled rates ($k = 10^7$–10^9 $M^{-1}S^{-1}$)[1] to give stable alkoxyamine products[2] ($\rangle$N-O$^\bullet$ + R$^\bullet$ $\longrightarrow$ $\rangle$N-O-R) and yet not combine with many oxygen-centred radicals[3]. We have recently begun to exploit this feature to outline the reactions of free radicals with commercially important monomers[4].



(1)



(2)

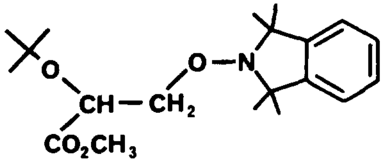
Our technique requires efficient separation of these alkoxyamine products in sufficient quantity to determine their structure by conventional spectroscopic methods. The often complex mixtures can only be resolved by reverse-phase high performance liquid chromatography (HPLC), preferably with the aid of UV detection. The majority of products from readily available (1) have poor UV absorbance which is in the region (215nm), where HPLC solvents begin to absorb strongly.

The detection of products would therefore be improved if instead of (1), we employed a nitroxide with a suitable UV absorbing chromophore. Ideally, such a compound would also be thermally stable, unreactive towards olefins[5], symmetrical (so as to generate a minimum number of isomers and NMR signals in the products) and be relatively inert to free radical attack with the exception of alkyl radical combination at the nitroxide function[6]. These criteria are satisfied most admirably by 1,1,3,3-tetramethylisoindolinyl-2-oxy (2), a new compound. We synthesized (2) from a readily available precursor[7-10] and its use as a radical scavenger has enabled us to outline multiple reaction pathways of free radicals in considerable detail.

For example, tert-butoxy radicals (from di-*tert*-butyl peroxyoxalate $(2\mathrm{x}10^{-2}\mathrm{M})$at 60°) in methyl acrylate containing (2) $(4.4\mathrm{x}10^{-2}\mathrm{M})$ react by several competing pathways (scheme 1). The alkoxyamine products derived from the carbon radicals shown in the scheme were isolated in the percentages indicated[11] and are exemplified by compounds (3), (4) and (5) below[12]. The major pathway is addition of the *tert*-butoxy radical to the unsubstituted terminus of the double bond of the olefin ("tail" addition) (path a). However, smaller amounts of "head" addition (path b, see (3)), H-abstraction (path c, see (5)) and fragmentation of the *tert*-butoxy radical to give methyl radicals and acetone (path e) were also observed.

			%
(a)	$(CH_3)_3CO^\bullet + CH_2{=}CH(CO_2CH_3)$	$\longrightarrow (CH_3)_3COCH_2\dot{C}H(CO_2CH_3)$	62.9
(b)	$(CH_3)_3CO^\bullet + CH_2{=}CH(CO_2CH_3)$	$\longrightarrow (CH_3)_3COCH(CO_2CH_3)CH_2^\bullet$	0.9
(c)	$(CH_3)_3CO^\bullet + CH_2{=}CH(CO_2CH_3)$	$\longrightarrow (CH_3)_3COH + CH_2{=}CHCO_2CH_2^\bullet$	8.8
(d)	$CH_2{=}CHCO_2CH_2^\bullet + CH_2{=}CH(CO_2CH_3)$	$\longrightarrow$ dimer radical	3.4
(e)	$(CH_3)_3CO^\bullet$	$\longrightarrow (CH_3)_2CO + CH_3^\bullet$	12.4
(f)	$CH_3^\bullet + CH_2{=}CH(CO_2CH_3)$	$\longrightarrow CH_3CH_2\dot{C}H(CO_2CH_3)$	5.1
(g)	$(CH_3)_3COCH_2\dot{C}H(CO_2CH_3) + CH_2{=}CH(CO_2CH_3)$	$\longrightarrow$ dimer radical	5.5
(h)	$(CH_3)_3COCH(CO_2CH_3)CH_2^\bullet + CH_2{=}CH(CO_2CH_3)$	$\longrightarrow$ dimer radical	0.4

SCHEME 1



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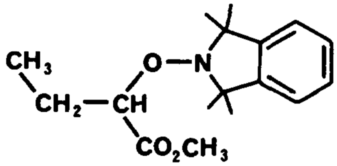

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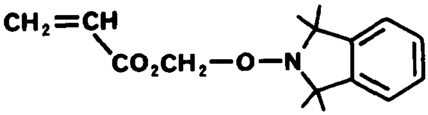

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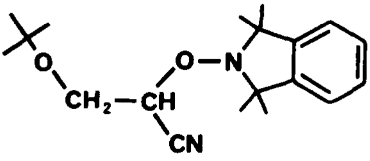

(6)

Due to the high trapping rate of (2), no polymer results from these reactions although under the conditions defined above, the initially formed carbon-centred radicals were observed to escape complete scavenging by (2). These reacted by "tail" addition to monomer to give the adduct (4) (path f) and dimer radicals (path d,g and h) trapped as alkoxyamines.[13]

It is significant that only pathway (a) was detected by the ESR spin trapping technique using nitroso *tert*-butane.[14]

Our technique employing (2) can therefore furnish valuable information about the selectivity of attack of the *tert*-butoxy radical on vinyl monomers and has allowed us to demonstrate for example that "head" addition is a more common process than has been hitherto appreciated (Table 1).

Table 1. Relative orientation of double bond addition by $(CH_3)_3CO\cdot$[a]

Monomer	Tail Addition	Head Addition	Other products
Acrylonitrile	81	- b	Methyl radicals 19%
Styrene[c]	98.7	- b	" " " " " 1.3%
Methyl Acrylate	68.4	1.3	As in scheme 1
Ethyl Vinyl Ether	51.2	5.8	H-abstraction 40%, methyl radicals 1.5%
Vinyl Acetate	65.3	12.0	H-abstraction 5%, methyl radicals 17%

[a] Radicals from di-tert-butyl peroxyoxalate @60° in neat monomer.
[b] Addition to give this radical was not observed.
[c] G. Moad, personal communication.

The only previous report of "head" addition by the tert-butoxy radical is the case of vinylidene fluoride, oddly enough to the exclusion of addition at the unsubstituted end of the monomer.[14] Previous studies on methyl acrylate and vinyl acetate by an ESR spin-trapping technique[15] as well as ethyl vinyl ether by the ESR flow technique[16], have reported only "tail" addition.

The orientation and rate of tert-butoxy radical addition to olefins is controlled by steric, polar and bond strength factors and it is difficult to separate the contributions of each effect.[17] However, the results in the table are consistent with the concept that the steric effect has the greatest overall influence on the orientation of addition to olefins.[17,18] Additionally, resonance stabilization of the product radical by an adjacent π-electron system can contribute to a preferred direction of addition.[17] This can explain the increased selectivity for the first three monomers in the table.

Differently polarised olefins are attacked at different rates by the electrophilic tert-butoxy radical and this is reflected in the relative yield of methyl radical products shown in the table. For example, attack on acrylonitrile is apparently much slower than attack on ethyl vinyl ether and styrene.[19] Nonetheless, double bond addition by the tert-butoxy radical to give (6) is still the dominant reaction (81%). This contradicts an earlier conclusion to the effect that fragmentation of tert-butoxy radicals is faster than addition to the "electron-poor" double bond of acrylonitrile.[20]

The nitroxide (2) does not influence the relative rates of these competing reactions as shown from the results of concentration studies and other evidence.[21] For this reason we are confident that the true interaction of tert-butoxy radicals with these olefins is being observed.

Our improved technique therefore is a valuable tool for the observation and quantitation of many organic reactions involving free radicals. Aspects of this work which are important to an understanding of polymer chemistry are currently being investigated and will be reported elsewhere.

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12. Complete analysis of this mixture is aided by the fact that the alkoxyamine products resulting from (2) have identical molar extinction values (ε1100 @270nm) so that the relative percentage of each pathway is directly and accurately reflected in the peak areas of the HPLC chromatogram.
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21. Varying the concentration of (2) relative to monomer does not change the relative proportions of the reactions occurring, with the obvious exception that the extent of propagation increases with decreasing concentration of (2).
22. We are grateful to Professor A.L.J. Beckwith for the ESR spectrum of (2).

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