Unexpected Products from the Reaction of *tert*-Butoxyl Radicals with Acetylenes in the Presence of an Aminoxyl Radical Scavenger

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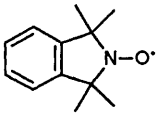
The radical trapping technique employing 1,1,3,3-tetramethyl-2,3-dihydro-1*H*-isoindol-2-yloxyl (**1**) as a scavenger has been used to study the reaction of *tert*-butoxyl radicals with phenylacetylene, methyl acetylenecarboxylate and dimethyl acetylenedicarboxylate. With phenylacetylene, an aromatic ketone (**5**) was formed in which both the *tert*-butoxy group and the radical trap were bound to the same carbon, whereas the acetylenecarboxylates gave vinylamine and vinyloxyamine products. The mechanism of formation of these unexpected products is discussed. Acetylene and diphenylacetylene did not appear to react with *tert*-butoxyl radicals.

In previous papers[1,2] we described the use of the radical scavenger 1,1,3,3-tetramethyl-2,3-dihydro-1*H*-isoindol-2-yloxyl (**1**) to study the complex pattern of reaction of *tert*-butoxyl radicals with alkenes such as allyl methacrylate and diallyl ether. Extensive H-abstraction as well as addition to the double bond(s) was observed. In this paper we report the results of analogous studies with the alkynes acetylene, phenylacetylene, diphenylacetylene, methyl acetylenecarboxylate, dimethyl acetylenedicarboxylate and hept-1-yne.

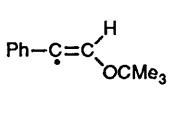
Radical additions to alkynes are of importance in organic synthesis and in polymer chemistry. Polyacetylenes are of considerable current interest as conducting polymers. High molecular weight polyacetylenes may be formed using Zeigler,[3] tungsten or molybdenum[4] catalysts, but the products from free radical initiations are usually of low molecular weight.[5]

It was anticipated that the aminoxyl-radical trapping technique might provide a more detailed understanding of the mechanism of the initiation stage, and provide an explanation for the lack of formation of high molecular weight polymers in the free radical polymerisation of acetylenes. Related studies with alkenic monomers have been very successful in demonstrating the existence of initiation pathways for radical polymerisation other than the 'text-book' tail addition of initiator radical to monomer.[6]

Reaction of phenylacetylene with *tert*-butoxyl radicals could, in principle, give rise to the vinyl radical **2** or (by H-abstraction) the alkyne radical **3**; such radicals might be expected to be trapped efficiently by **1**. The aminoxyl **1** has been shown to trap alkyl radicals at close to diffusion-controlled rates ($k_T \sim 1.2 \times 10^9$ dm^3 mol^{-1} s^{-1})[7] to give stable alkoxyamine products, but trapping of vinyl radicals of type **2** or of alkyne radicals, does not appear to have been studied. The attempted generation and trapping of **2** and/or **3** is described below.



1 ≡ $R_2N{-}O^{\bullet}$



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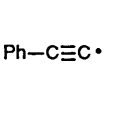

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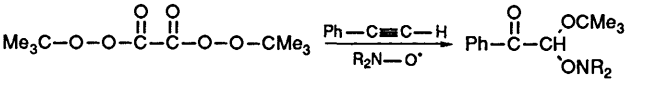
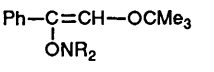
Results and Discussion

tert-Butoxyl radicals were generated by thermolysis of di-*tert*-butyl peroxalate (**4**). Thus, excess aminoxyl (**1**; 0.35 g, 1.84 mmol) and initiator (**4**; 0.1 g, 0.43 mmol) were dissolved in phenylacetylene (6 cm^3). Argon was bubbled through the solution for a few minutes and the reaction mixture was degassed by several freeze–thaw cycles under vacuum ($< 10^{-2}$ mmHg). The sealed reaction vessel was heated in an oil bath at 60 °C for 1 h ($t_{\frac{1}{2}}$ for **4** at 60 °C = 6.8 min).[8] Phenylacetylene was removed under reduced pressure and the residue analysed by reversed-phase HPLC. A single major (>98%) UV-active peak was observed. Preparative HPLC resulted in the isolation of **5** as a solid. Recrystallisation from aqueous methanol gave white needles (0.151 g, 46% based on **4**, m.p. 157–158 °C).



4 **5**



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The structure of **5** was deduced from ^{1}H and ^{13}C NMR, IR (1685 cm^{-1}) and mass spectral data (M + 1 peak, 382), which clearly excluded the expected structure **6**. Structure **5** would also be expected to undergo acid-catalysed hydrolysis to give phenylglyoxal. This was confirmed by treatment of **5** with 2,4-dinitrophenylhydrazine in acidic methanol to produce an orange precipitate [m.p. 295–296 °C (decomp.); (lit.,[9] for phenylglyoxal derivative, 295–297.5 °C) (decomp.)]. As conclusive evidence for **5**, an X-ray structure analysis was carried out. The result is consistent with the formulation given and the structure is shown in Fig. 1; geometrical parameters are as expected.

The mechanism of formation of **5** remains obscure. It was thought initially that the source of the oxygen for the ketone group may be the peroxyoxalate initiator **4**. However, replacement of **4** by di-*tert*-butyl hyponitrite an alternative source of *tert*-butoxyl radicals, gave a virtually identical result. It is possible that the oxygen comes from the aminoxyl and that **2** is a precursor of **5**. Trapping of **2** by **1**, followed by homolysis of the N–O bond would generate an enoxyl radical that could be trapped by further **1** to give **5** (Scheme 1).

Scheme 1 requires two equivalents of aminoxyl to produce one equivalent of product **5**, suggesting that the reaction should be quite sensitive to the concentration of aminoxyl. This was

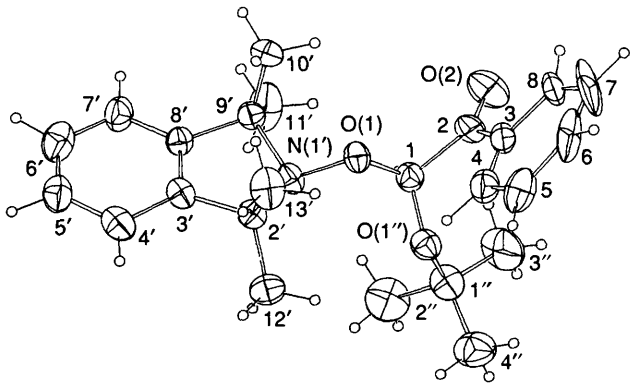

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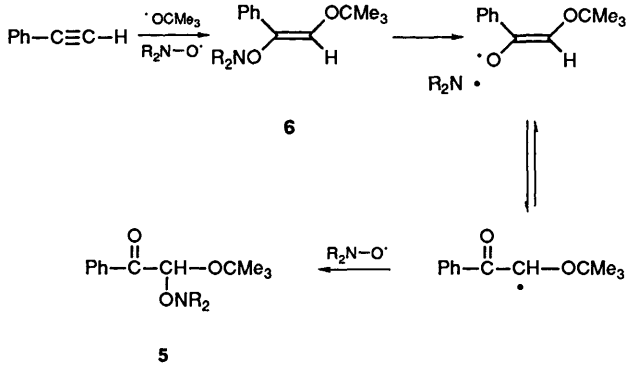
Fig. 1 Projection of a molecule of **5**. 20% Thermal ellipsoids are shown for the non-hydrogen atoms; hydrogen atoms have arbitrary radii of 0.1 Å.



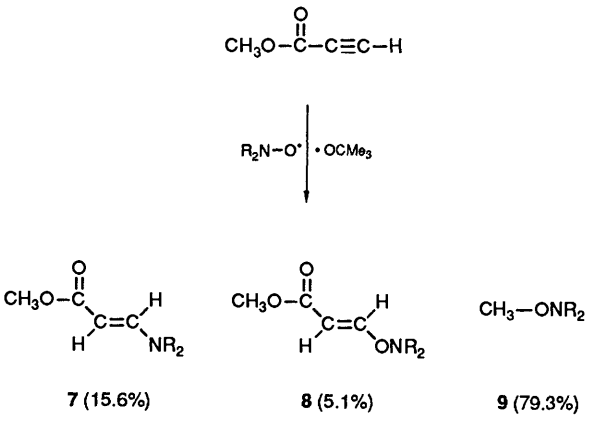
Scheme 1

found to be the case. Halving the aminoxyl concentration halved the amount of product **5** formed. Reduction of the aminoxyl concentration to 25% similarly reduced the yield of **5** with a concomitant increase in a range of minor products being detected by HPLC. We have attempted to isolate the proposed intermediate **6** by carrying out the reaction at a lower temperature (UV initiation at 25 °C was tried) but without success, **5** still being the only product isolated. (Much lower temperatures were not possible using neat phenylacetylene, as the solution solidifies below room temperature, while the use of a cosolvent gives rise to side reactions as illustrated below for acetylene and diphenylacetylene).

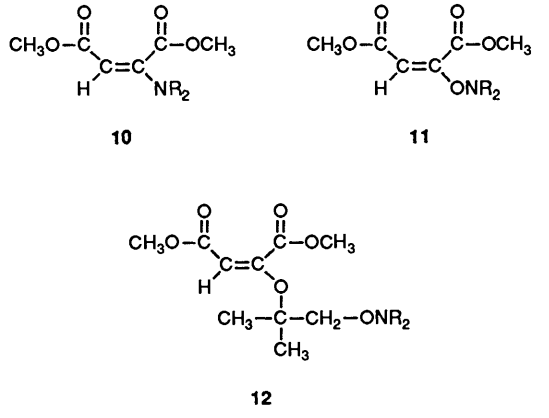
Use of methyl acetylenecarboxylate instead of phenylacetylene gave equally intriguing results. Two major acetylene-derived products were isolated in this case, the enamine **7** and the vinyloxyamine **8** as shown in Scheme 2. There was no product analogous to **5** detected. The methoxyamine **9** is formed by β-scission of *tert*-butoxyl radicals, a process that can serve as a 'radical clock' for this reaction.[10] The fact that **9** is the major product of the reaction (approx. 80%), suggests that reactions such as addition of *tert*-butoxyl radicals to the acetylene or H-abstraction from the methyl group of the ester are kinetically slow relative to the β-scission process.

Dimethyl acetylenedicarboxylate gave the analogous compounds **10** (3.4%) and **11** (1.9%). In addition, the *tert*-butoxyl-derived adduct **12** (6.2%) was formed, as well as **9** (86.9%), once again the major product of the reaction.

The structures of **7**, **8**, **10**, **11** and **12** followed from mass spectral and ^1H and ^{13}C NMR data. The formula of **7** was confirmed by an X-ray structure analysis (Fig. 2); molecular geometries (Tables 3 and 4, see later) are indicative of extensive delocalisation throughout the molecular tail. The arrays



Scheme 2



Scheme 3

N(1)C(2–9) are significantly non-planar (χ^2 1226, 1183), deviations of N(1), C(2,9,11) from the planar (C(3–8) arrays (χ^2 8.7, 11.2) are 0.11, 0.03, 0.04, 0.21 (molecule 1) 0.11, 0.01, 0.02, 0.20 (molecule 2). Compound **9** has been characterised previously.[11]

We suggest that **12** arises via addition of a *tert*-butoxyl radical to the alkyne, followed by a 1,5-hydrogen shift and trapping by the nitroxide (Scheme 3). Analogous 1,5-hydrogen shifts were first reported by Heiba and Dessau[12] in 1967, while Gilbert and Parry *et al.*[13–16] have detected 1,4-, 1-5- and 1,6-hydrogen migrations using EPR methods. The process is attributable to the greater stability of the sp^3 radicals generated relative to the

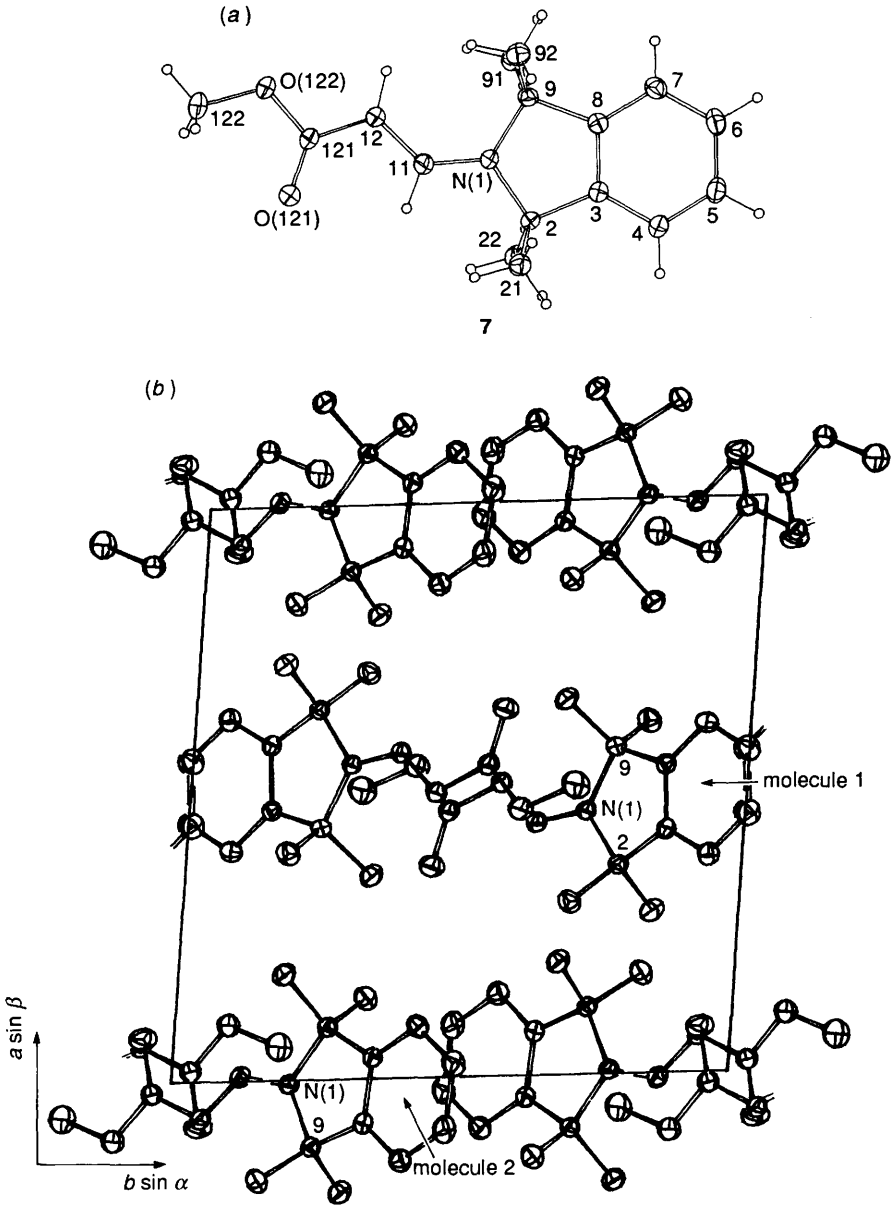
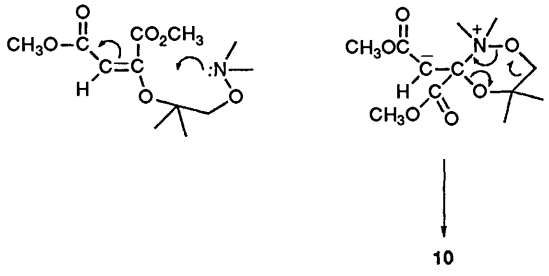


Fig. 2 (*a*) Projection of molecule 1 of **7**; molecule 2 is pseudosymmetrically related and similar in conformation. (*b*) Unit-cell contents of **7** projected down the *c* axis, showing the pseudosymmetry and alignment of the independent molecular arrays.

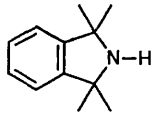
sp^2 (vinyl) radicals and is reflected in the greater bond strength for the C–H bond in alkenes compared with alkanes.[17] Since the aminoxyl **1** scavenges carbon-centred radicals at close to diffusion-controlled rates,[7] the 1,5-hydrogen transfer must be very fast. No adduct could be isolated correspondinging to **13**.

An attractive hypothesis is that **12** may undergo an internal Michael addition with subsequent ejection of formaldehyde and acetone, thereby forming enamine **10** (Scheme 4). The methyl acetylenecarboxylate, being less hindered sterically, is completely converted into the enamine **7** with no detection of the intermediate analogous to **12** in this case. However, **12** was quite stable under the reaction conditions. Moreover, it was isolated unchanged after being heated in glacial acetic acid at 120 °C or in a sealed tube at 140 °C for 18 h. Clearly another mechanism must be involved.

The enamines **7** and **10** and the alkoxyamines **8** and **11** all appear to be Michael-addition products of the respective acetylenes with the isoindoline **14** or the hydroxylamine **15**, respectively. Thus, treatment of methyl acetylenecarboxylate



Scheme 4



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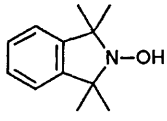

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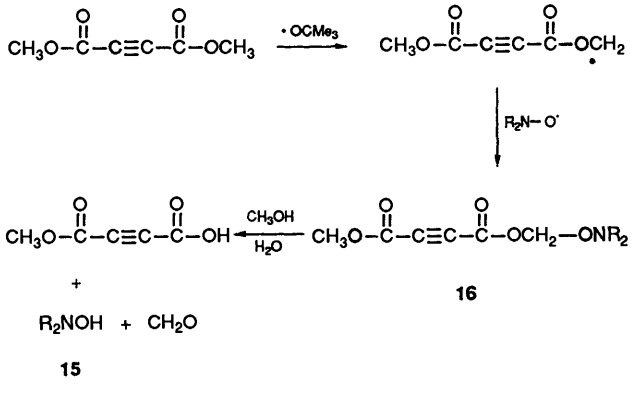
with the hydroxylamine **15** at room temperature for 5 min gave a quantitative yield of **8**. Analogous results were obtained with dimethyl acetylenedicarboxylate, **11** being obtained cleanly after only a few minutes at room temperature. This is in accord with the known susceptibility of acetylenecarboxylates to Michael additions with hydroxylamines.[18,19] There was no reaction when either acetylene was heated with the aminoxyl **1** in the absence of the initiator **4**.

Simple Michael addition of the isoindoline **14** to methyl acetylenecarboxylate was much slower than that for the corresponding addition of the hydroxylamine **15**. Thus, after 5 min at room temperature, there was no **7** detected by HPLC. Compound **7** was detected, however, after 2 h of heating at 60 °C, but another, longer retention time component of about equal peak magnitude (at 270 nm) was also present. This latter material was not evident in the reaction of methyl acetylenecarboxylate with *tert*-butoxyl radicals and the aminoxyl **1**, thus precluding a mechanism of formation of **7** involving simple Michael addition of **14**. Instead, we believe that **7** is formed by a radical-catalysed Michael addition of **14**. Thus, when methyl acetylenecarboxylate and **14** were heated at 60 °C for 1 h with the initiator **4**, HPLC showed the clean formation of **7**. The longer retention time component observed under non-radical conditions was not present. Analogous results were obtained with dimethyl acetylenedicarboxylate, with **14** adding cleanly to give **11**.

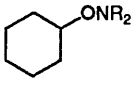
The source of **14** and of **15** is not clear. The isoindoline **14** may be formed by a mechanism analogous to that in Scheme 1, however, we were unable to detect any acetylenecarboxylate products analogous to **5**.

The most likely source of the hydroxylamine **15** is from **16**, the product formed by hydrogen abstraction from the methyl ester.



There is good precedent for hydrogen-abstraction from methyl esters by *tert*-butoxyl radicals[6] and product **16** would be expected to be very labile in the methanol–water mixtures used for HPLC work-up. Similar acetal-like compounds have been shown to be unstable under these conditions.[20] Once formed, the hydroxylamine **15** would readily add to the unchanged acetylene still present to generate **8** and **11**. Our inability to detect products such as **16** does not mean that they were not present in the reaction mixture. We have only attempted to isolate the major products (> 1%) in all of these reactions. There were other very minor (< 1%) products present but these were not isolated.

The large proportion of methoxyamine product **9** formed in the acetylenecarboxylate reactions contrasts with the very small amount (< 1%) formed with phenylacetylene. This presumably reflects the 'electrophilic' nature[21] of *tert*-butoxyl radicals. The acetylenecarboxylates, being electron-poor, are less reactive towards the *tert*-butoxyl radical which therefore undergoes the kinetically more favoured β-scission process. Strangely, both diphenylacetylene and acetylene itself were quite unreactive towards *tert*-butoxyl radicals. Thus, when diphenylacetylene was melted with **1** and **4** and kept at 60 °C for an hour, the only product isolated was the methoxyamine **9** (> 95%). When cyclohexane was used as a solvent, in addition to **9**, the hydrogen-abstraction product **17** was also isolated.



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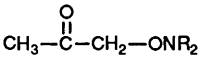
Reaction with acetylene was carried out in acetone in which the gas is quite soluble.[22] Thus, the aminoxyl **1** (270 mg, 1.4 mmol) and initiator **4** (75 mg, 0.32 mmol) were dissolved in acetone (10 cm^3) in a Parr hydrogenation apparatus. The reaction vessel was flushed several times with Argon, and the acetylene gas was introduced. The reaction vessel was heated at 50 °C and 60 psi* of acetylene for 2 h. Acetone was removed under vacuum and the reaction mixture separated by HPLC. Only two products were detected: the methoxyamine **9** (30%) and the hydrogen-abstraction product **18** (70%).



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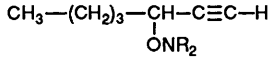
The reaction was also carried out in benzene as solvent. There were several compounds detected by HPLC, however, all of these products also occurred when benzene, **1** and **4** were heated in the absence of acetylene. Clearly, addition of *tert*-butoxyl radicals to acetylene is not favoured compared with the competing β-scission reaction or reaction with the solvent. This is supported by the results of Giese[23,24] who showed that radicals add more slowly to alkynes than to similar alkenes. Bloodworth *et al.*[25] have also demonstrated that no addition of *tert*-butoxyl radicals to alkynes could be detected by EPR spectroscopy.

Finally, the reaction of *tert*-butoxyl radicals with hept-1-yne was briefly examined. Reversed-phase HPLC analysis of the reaction mixture showed two components: the methoxyamine **9** (11.4%) and another, longer retention time product, tentatively assigned the structure **19** (88.6%).



19

Compound **19** was very unstable and decomposed upon HPLC work-up using either methanol–water or acetonitrile–water eluents. It was also unstable to silica gel chromatography. A ^1H NMR spectrum of a rapidly isolated fraction was consistent with the assigned structure **19**, however. The absence of any *tert*-butyl signal in the spectrum eliminated any possibility of this longer retention product arising from addition of *tert*-butoxyl radicals. Given the high reactivity of allylic hydrogens towards abstraction by *tert*-butoxyl radicals[1,2] the formation of **19** is not surprising.

Conclusions

The radical-trapping technique has shown that, in general, alkynes are much less reactive towards *tert*-butoxyl radicals than are alkenes. The products of reaction with phenylacetylene

* 1 psi ≈ 6.895 × 10^3 Pa.

and with acetylenecarboxylates are not the expected products arising from the trapping of vinyl radicals, but are products formed by unusual rearrangement, fragmentation or redox processes. The mechanisms of formation of these products and their significance for the usefulness of the radical-trapping technique in the study of acetylenic systems, are not yet clear.

Experimental

Phenylacetylene (Merck) was fractionally distilled before use. Diphenylacetylene was obtained from Aldrich and not further purified. Dimethylacetylenedicarboxylate was obtained from Fluka and used without further purification. Methyl acetylenecarboxylate was prepared from propynoic acid, methanol and concentrated sulphuric acid and purified by distillation through a Vigreux column, b.p. 99–102 °C (lit.,[26] 102 °C at 740 mmHg). Acetylene gas was industrial grade from CIG and used as received. Hept-1-yne (Aldrich) was distilled under reduced pressure before use.

^1H and ^{13}C NMR spectra (proton-noise decoupled; off-resonance decoupled) were recorded on either a Bruker CXP-300 spectrometer (at 300.06 and 75.46 MHz), or a Bruker WM-250 spectrometer (at 250.12 and 62.80 MHz). Spectra were run for compounds in deuteriated chloroform (unless otherwise stated) with tetramethylsilane as the internal standard. Mass spectra were recorded at the Australian National University on a VG7070F spectrometer (Dr. J. K. McLeod). Microanalyses were carried out by the Microanalytical Service, University of Queensland or by the Australian Microanalytical Service, AMDEL, Melbourne.

Analytical HPLC studies were carried out with either an analytical Ranin Instruments Dynamax-60A 8 mm 250 × 4.6 mm C_{18} or a semi-preparative Whatman Partisil 10-ODS-3 500 × 10 mm C_{18} column using an ETP Kortec K35M Dual Piston HPLC pump and either a Soma S-310A-11 or an ETP Kortec K95 variable wavelength UV detector set at 270 nm. The columns were protected with Uptight 2 cm guard columns filled with Whatman 30–38 mm glass beads coated with C_{18} groups.

Peak areas were determined by integration of the HPLC chromatogram. Allowance for differing chromophores was made either by determining the extinction coefficients, at 270 nm, of the isolated products, or by the re-injection of solutions of known concentration to assess peak response ratios for the UV detector. The adjusted peak areas were converted into relative product yields and normalised to 100%.

The reaction products were isolated using preparative reversed-phase HPLC on a Ranin Instruments Dynamax-60A 8 mm 250 × 21.4 mm C18 preparative column. Compounds were detected by the Soma detector fitted with a 1 mm preparative cell. Solvent flow rates were variable depending upon the methanol–water ratio and the back pressure developed. The solvents were pumped at pressures less than 2000 psi by a Gilson 330 pump fitted with a 25 cm^3 min^{-1} preparative head and an 803C manometric module.

In some instances two preparative columns were linked together with a coupling piston effectively to make a 500 × 21.4 mm column.

Final purification of the isolated products was achieved with a Whatman semi-preparative column.

Di-*tert*-butyl peroxalate was prepared from oxalyl chloride and *tert*-butyl hydroperoxide by the method of Bartlett *et al.*,[8] m.p. 51–52 °C (decomp.). 1,1,3,3-Tetramethyl-2,3-dihydro-1*H*-isoindol-2-yloxyl (**1**) was prepared, by the method of Griffiths *et al.*,[27] m.p. 128–129 °C. 1,1,3,3-Tetramethyl-2,3-dihydro-1*H*-isoindole **14** was an intermediate *en route* to **1**. 2-Methoxy-1,1,3,3-tetramethyl-2,3-dihydro-1*H*-isoindole (**9**) was identified by HPLC and ^1H and ^{13}C NMR comparison with an authentic sample.[11] It can most easily be prepared by reaction of **1** with H_2O_2 and ferrous sulphate in dimethyl sulphoxide at room temperature.[28] 2-Cyclohexyloxy-1,1,3,3-tetramethyl-2,3-dihydro-1*H*-isoindoline (**17**) was identical by ^1H NMR and HPLC with an authentic sample.[29] 1-(1,1,3,3-Tetramethyl-2,3-dihydro-1*H*-isoindol-2-yloxy)propanone (**18**) was identical by m.p. 84–85 °C and ^1H NMR spectroscopy to an authentic sample.[11] 2-Hydroxy-1,1,3,3-tetramethyl-2,3-dihydro-1*H*-isoindole (**15**) was prepared by hydrogenation of **1** in pentane using Adam's catalyst at room temperature and pressure for 20 min. It was identical by HPLC and ^1H NMR spectroscopy to an authentic sample.[30]

The general procedure for the radical-trapping experiments was the same as that employed for phenylacetylene. The initiator concentration was kept below 25% of the aminoxyl concentration to ensure efficient scavenging of all carbon-centred radicals. New compounds isolated were characterised by the spectroscopic data listed below. The substitution pattern for all carbons was confirmed by either DEPT or off-resonance spectra for all compounds isolated. T denotes the isoindoline moiety of the aminoxyl trap.

2-tert-*Butoxy*-1-*phenyl*-2-(1,1,3,3-*tetramethyl*-2,3-*dihydro*-1H-*isoindol*-2-*yloxy*)*ethan*-1-*one* (**5**).—δ_C 25.1, 25.7, 29.6, 29.9 (Me), 28.6 (Me_3C), 67.7, 68.1 (C-1, C-3 T), 75.2 (Me_3CO), 105.1 (C-2), 121.5, 121.7 (C-4, C-7 T), 127.4 (C-5, C-6 T), 128.0, 130.7, 133.0, 133.8 (Ph), 145.0 (C-3a, C-7a T) and 196.0 (C=O); δ_H 1.0 (s, 12 H, Me_3C and Me T), 1.20, 1.38, 1.50 (s, 9 H, 3 × MeT), 5.30 (s, 1 H, 2-H), 6.8–7.4 (m, 7 H, Ar-H) and 8.1 (m, 2 H, Ar-H) (Found: C, 78.1; H, 5.4; N, 3.8. $C_{24}H_{31}NO_3$ requires C, 78.1; H, 5.2; N, 3.8%).

(E)-*Methyl* 3-(1,1,3,3-*Tetramethyl*-2,3-*dihydro*-1H-*isoindol*-2-*yl*)*propenoate* (**7**).—Pale yellow crystals, m.p. 156–157 °C; δ_C 28.7 (Me), 50.3 (OMe), 67.2 (C-1, C-3 T), 85.9 (C-2), 121.4 (C-4, C-7 T), 128.1 (C-5, C-6 T), 143.5 (C-3), 143.6 (C-3a, C-7a T) and 170.0 (C=O); δ_H 1.59 (s, 12 H, Me T), 3.68 (s, 3 H, OMe), 4.94

Table 1 Non-hydrogen atom coordinates for **5**

Atom	*x*	*y*	*z*
C(1)	0.0908(4)	0.8945(8)	−0.020(1)
O(1)	0.1503(2)	0.8925(4)	0.0499(7)
C(2)	0.0622(4)	0.994(1)	0.076(1)
O(2)	0.0206(4)	0.9671(7)	0.153(1)
C(3)	0.0831(5)	1.1086(9)	0.059(1)
C(4)	0.1277(5)	1.1383(8)	−0.036(1)
C(5)	0.1458(5)	1.2547(9)	−0.045(2)
C(6)	0.1132(9)	1.323(1)	0.067(2)
C(7)	0.070(1)	1.298(3)	0.162(3)
C(8)	0.0576(5)	1.192(1)	0.159(1)
N(1′)	0.1779(3)	0.7858(5)	0.0166(8)
C(2′)	0.2396(4)	0.8044(7)	−0.041(1)
C(3′)	0.2685(4)	0.7012(7)	0.023(1)
C(4′)	0.3254(4)	0.657(1)	−0.020(1)
C(5′)	0.3439(5)	0.561(1)	0.060(2)
C(6′)	0.3100(7)	0.5123(8)	0.167(2)
C(7′)	0.2553(5)	0.5556(8)	0.207(1)
C(8′)	0.2360(4)	0.6509(7)	0.132(1)
C(9′)	0.1799(4)	0.7169(7)	0.166(1)
C(10′)	0.1854(5)	0.784(1)	0.310(1)
C(11′)	0.1235(4)	0.6424(8)	0.166(2)
C(12′)	0.2376(4)	0.8123(9)	−0.214(1)
C(13′)	0.2713(4)	0.9102(6)	0.026(1)
O(1″)	0.0960(2)	0.9210(5)	−0.1742(8)
C(1″)	0.0518(4)	0.8727(9)	−0.276(1)
C(2″)	0.0647(5)	0.753(1)	−0.305(2)
C(3″)	−0.0083(5)	0.897(1)	−0.225(2)
C(4″)	0.0628(5)	0.937(1)	−0.429(1)

Table 2 Non-hydrogen atom coordinates for **7**

Atom	Molecule 1			Molecule 2		
	x	*y*	*z*	*x*	*y*	*z*
N(1)	0.4547(1)	0.7143(1)	0.5370(2)	−0.0063(1)	0.2126(1)	0.0372(2)
C(2)	0.3577(2)	0.7788(2)	0.4667(2)	0.0923(2)	0.2753(2)	−0.0289(2)
C(21)	0.2956(2)	0.6953(2)	0.4166(2)	0.1834(2)	0.1908(2)	−0.0778(2)
C(22)	0.2774(2)	0.8450(2)	0.5497(2)	0.1401(2)	0.3397(2)	0.0563(2)
C(3)	0.4184(2)	0.8609(2)	0.3616(2)	0.0374(2)	0.3596(2)	−0.1359(2)
C(4)	0.3715(2)	0.9395(2)	0.2602(2)	0.0898(2)	0.4377(2)	−0.2342(2)
C(5)	0.4425(2)	1.0071(2)	0.1725(2)	0.0240(2)	0.5072(2)	−0.3251(2)
C(6)	0.5566(2)	0.9986(2)	0.1849(2)	−0.0906(2)	0.4991(2)	−0.3165(2)
C(7)	0.6031(2)	0.9205(2)	0.2871(2)	−0.1425(2)	0.4224(2)	−0.2181(2)
C(8)	0.5327(2)	0.8518(2)	0.3741(2)	−0.0771(2)	0.3515(2)	−0.1275(2)
C(9)	0.5653(2)	0.7605(2)	0.4891(2)	−0.1161(2)	0.2606(2)	−0.0145(2)
C(91)	0.6097(2)	0.8173(2)	0.5838(2)	−0.1943(2)	0.3178(2)	0.0784(2)
C(92)	0.6509(2)	0.6650(2)	0.4505(2)	−0.1718(2)	0.1672(2)	−0.0559(2)
C(11)	0.4363(2)	0.6266(2)	0.6373(2)	0.0084(2)	0.1246(2)	0.1383(2)
C(12)	0.5069(2)	0.5587(2)	0.7189(2)	−0.0645(2)	0.0580(2)	0.2169(2)
C(121)	0.4602(2)	0.4675(2)	0.8139(2)	−0.0192(2)	−0.0333(2)	0.3154(2)
O(121)	0.3636(1)	0.4435(1)	0.8303(2)	0.0787(1)	−0.0552(2)	0.3364(2)
O(122)	0.5396(1)	0.4042(1)	0.8879(2)	−0.0993(1)	−0.0968(1)	0.3844(2)
C(122)	0.4997(2)	0.3078(3)	0.9829(3)	−0.0592(2)	−0.1905(2)	0.4856(3)

(d, 1 H, ^3J = 13.5 Hz, 2-H), 7.1–7.3 (m, 4 H, ArH) and 7.69 (d, 1 H, ^3J = 13.5 Hz, 3-H); ν_{max}/cm^{-1} 1680 (C=O) (Found: C, 74.0; H, 8.0; N, 5.1%; M^+, 259.1572. $C_{16}H_{21}NO_2$ requires C, 74.1; H, 8.2; N, 5.4%; *M*, 259.1572).

(E)-*Methyl* 3-(1,1,3,3-*Tetramethyl*-2,3-*dihydro*-1H-*isoindol*-2-*yloxy*)*propenoate* (**8**).—δ_C 24.9, 29.2 (Me), 51.0 (OMe), 68.3 (C-1, C-3 T), 95.8 (C-2), 121.6 (C-4, C-7 T), 127.8 (C-5, C-6 T), 143.8 (C-3a, C-7a T), 167.1 (C-3) and 168.7 (C=O); δ_H 1.32 (br s, 6 H, Me T), 1.43 (br s, 6 H, Me T), 5.67 (d, 1 H, ^3J = 12.4 Hz, 2-H), 7.04–7.24 (m, 4 H, ArH) and 7.85 (d, 1 H, ^3J = 12.4 Hz, H-3); ν_{max}/cm^{-1} 1705 (C=O) (Found: $M^+ - CH_3$ 260.1292. $C_{16}H_{21}NO_3 - CH_3$ requires *m*/*z* 260.1287).

(E)-*Dimethyl* 2-(1,1,3,3-*Tetramethyl*-2,3-*dihydro*-1H-*isoindol*-2-*yl*)*butenedioate* (**10**).—δ_C 28.8 (Me), 50.3, 52.6 (OMe), 69.4 (C-1, C-3 T), 89.7 (C-3), 121.1 (C-4, C-7 T), 128.1 (C-5, C-6 T), 145.0 (C-3a, C-7a T), 150.6 (C-2), 166.4 and 167.8 (C=O); δ_H 1.68 (s, 12 H, Me T), 3.64 (s, 3 H, OMe), 3.92 (s, 3 H, OMe), 5.18 (s, 1 H, 3-H) and 7.07–7.31 (m, 4 H, ArH); ν_{max}/cm^{-1} 1755 and 1705 cm^{-1} (C=O) (Found: M^+, 302.1394. $C_{17}H_{20}NO_4$ requires *M*, 302.1392).

(E)-*Dimethyl* 2-(1,1,3,3-*Tetramethyl*-2,3-*dihydro*-1H-*isoindol*-2-*yloxy*)*butenedioate* (**11**).—δ_C 25.1, 29.3 (Me), 51.3, 52.7 (OMe), 69.3 (C-1, C-3 T), 95.4 (C-3), 121.6 (C-4, C-7 T), 128.0 (C-5, C-6 T), 143.9 (C-3a, C-7a T, C-2), 165.5 and 167.3 (C=O); δ_H 1.4 (s, 6 H, Me T), 1.50 (s, 6 H, MeT), 3.67 (s, 3 H, OMe), 3.90 (s, 3 H, OMe), 6.00 (s, 1 H, 3-H), 7.08–7.28 (m, 4 H, ArH) (Found: M^+, 318.1340. $C_{17}H_{20}NO_5$ requires *M*, 318.1341).

(E)-*Dimethyl* 2-[2-(1,1,3,3-*Tetramethyl*-2,3-*dihydro*-1H-*isoindol*-2-*yloxymethyl*)*propan*-2-*yloxy*]*butenedioate* (**12**).—δ_C 23.2 (Me); 25.0 (Me T), 31.0 (Me T), 51.3 (OMe), 52.5 (OMe), 67.6 (C-1, C-3 T), 83.0 (CH_2), 84.1 (C-2^1, 97.7 (C-3), 121.5 (C-4, C-7 T), 127.3 (C-5, C-6 T), 145.1 (C-3a, C-7a T, C-2), 159.0, 166.6 (C=O); δ_H 1.34 (br s, 12 H, Me T), 1.49 (s, 6 H, Me), 3.81 (s, 3 H, OMe), 3.96 (s, 3 H, OMe), 5.41 (s, 1 H, 3-H), 7.00–7.19 (s, 4 H, ArH) (Found: M^+, 405.2110. $C_{22}H_{31}NO_6$ requires *M*, 405.2151).

3-(1,1,3,3-*Tetramethyl*-2,3-*dihydro*-1H-*isoindol*-2-*yloxy*)*hept*-1-*yne* (**19**).—Unstable compound (see the text), tentative assignment based on the ^{1}H NMR spectrum: δ_H 0.92 (t, 3 H, ^3J = 3 Hz, CH_3), 1.2–1.9 (m, 18 H, 4 Me T, 4-H, 5-H, 6-H), 2.41 (d, 1 H, ^3J = 2.1 Hz, H-1), 4.44 (ddd, 1 H, ^3J = 2.1, 5.8, 7.2 Hz, H-3), 7.00–7.26 (m, 4 H, ArH).

Table 3 Non-hydrogen bond lengths in **7**/Å. Values are for molecules 1 and 2

Atoms	Distances	
N(1)–C(2)	1.496(2)	1.494(3)
N(1)–C(9)	1.485(3)	1.486(3)
N(1)–C(11)	1.340(3)	1.340(3)
C(2)–C(21)	1.524(4)	1.524(3)
C(2)–C(22)	1.519(3)	1.519(4)
C(2)–C(3)	1.501(3)	1.506(3)
C(3)–C(4)	1.393(3)	1.387(3)
C(3)–C(8)	1.380(3)	1.377(3)
C(4)–C(5)	1.379(3)	1.387(3)
C(5)–C(6)	1.377(4)	1.378(4)
C(6)–C(7)	1.395(3)	1.377(3)
C(7)–C(8)	1.378(3)	1.389(3)
C(8)–C(9)	1.509(3)	1.507(3)
C(9)–C(91)	1.524(4)	1.523(3)
C(9)–C(92)	1.530(3)	1.523(4)
C(11)–C(12)	1.352(3)	1.341(3)
C(12)–C(121)	1.428(3)	1.437(3)
C(121)–O(121)	1.208(3)	1.206(3)
C(121)–O(122)	1.355(3)	1.341(3)
O(122)–C(122)	1.438(3)	1.449(3)

Structure Determination.—Unique data sets were measured within the specified $2\theta_{max}$ limit (Enraf-Nonius CAD-4 diffractometer, monochromatic Mo-Kα radiation (λ = 0.7106$_9$ Å), $2\theta/\theta$ scan mode, $T \sim 295$ K). *N* Independent reflections were measured, N_o with $I > 3\sigma(I)$ being used in the full-matrix least-squares refinements without absorption correction, the structures being solved by direct methods; statistical weights derivative of $\sigma^2(I) = \sigma^2(I_{diff}) + 0.0004\sigma^4(I_{diff})$ were used. Residuals on $|F|$,*R*,*R*′ are quoted. Neutral-atom complex scattering factors were used;[31] computation used the XTAL 2.4 program system[32] implemented by Hall. Pertinent results are presented in Figs. 1 and 2 and Tables 1–4. Thermal parameters, hydrogen-atom coordinates and molecular non-hydrogen geometries have been deposited at the Cambridge Crystallographic Data Centre.*

* For details of the CCDC deposition scheme see 'Instructions for Authors' (1991), *J. Chem. Soc., Perkin Trans. 2*, issue 1.

Table 4 Non-hydrogen interbond angles 7/°

Atoms	Angle	
C(2)–N(1)–C(9)	114.2(1)	114.5(1)
C(2)–N(1)–C(11)	119.8(2)	119.8(2)
C(9)–N(1)–C(11)	125.9(2)	125.6(2)
N(1)–C(2)–C(21)	111.0(2)	111.1(2)
N(1)–C(2)–C(22)	110.7(2)	111.2(2)
N(1)–C(2)–C(3)	100.8(2)	100.8(2)
C(21)–C(2)–C(22)	110.8(2)	110.8(2)
C(21)–C(2)–C(3)	111.4(2)	111.1(2)
C(22)–C(2)–C(3)	111.8(2)	111.5(2)
C(2)–C(3)–C(4)	127.3(2)	127.2(2)
C(2)–C(3)–C(8)	112.0(2)	111.5(2)
C(4)–C(3)–C(8)	120.7(2)	121.3(2)
C(3)–C(4)–C(5)	118.3(2)	118.3(2)
C(4)–C(5)–C(6)	121.2(2)	120.4(2)
C(5)–C(6)–C(7)	120.3(2)	121.2(2)
C(6)–C(7)–C(8)	118.6(2)	118.8(2)
C(3)–C(8)–C(7)	120.8(2)	120.0(2)
C(3)–C(8)–C(9)	111.8(2)	112.5(2)
C(7)–C(8)–C(9)	127.3(2)	127.5(2)
N(1)–C(9)–C(8)	100.8(2)	100.4(1)
N(1)–C(9)–C(91)	111.5(2)	111.4(2)
N(1)–C(9)–C(92)	111.3(2)	111.5(2)
C(8)–C(9)–C(91)	110.7(2)	110.9(2)
C(8)–C(9)–C(92)	110.1(2)	110.4(2)
C(91)–C(9)–C(92)	111.9(2)	111.7(2)
N(1)–C(11)–C(12)	131.6(2)	132.1(2)
C(11)–C(12)–C(121)	117.4(2)	117.7(2)
C(12)–C(121)–O(121)	127.3(2)	126.3(2)
C(12)–C(121)–O(122)	111.8(2)	112.2(2)
O(121)–C(121)–O(122)	120.9(2)	121.5(2)
C(121)–O(122)–C(122)	115.0(2)	115.0(2)

Crystal and Refinement Data.—Compound **5**. $C_{24}H_{31}NO_3$, M = 381.5. Orthorhombic, space group $P2_12_12_1$ (D_2^4, No. 19), a = 22.447(9), b = 11.937(5), c = 8.601(4) Å, U = 2305 Å^3. D_c (Z = 4) = 1.10 g cm^{-3}; $F(000)$ = 824. μ_{Mo} = 0.4 cm^{-1}. $2\theta_{max}$ = 45°, N = 1715, N_o = 1215; R = 0.073, R' = 0.076.

Abnormal features. Data was of poor quality with wide linewidths and high thermal motion in the resulting model.

Compound **7**. $C_{16}H_{21}NO_2$, M = 259.4. Triclinic, space group $P\bar{1}$ (C_i^1, No. 2), a = 11.971(7), b = 11.746(13), c = 10.937(9) Å, α = 76.74(8), β = 83.73(6), γ = 83.28(8)°, U = 1481 Å^3. D_c (Z = 4) = 1.16 g cm^{-3}; $F(000)$ = 560. μ_{Mo} = 0.1 cm^{-1}. $2\theta_{max}$ = 50°, N = 5191, N_o = 3732; R = 0.048, R' = 0.057.

Abnormal features. Two independent molecules, pseudo-symmetrically related [Fig. 2(*b*)] comprise the asymmetric unit of the structure.

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