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HOMOLYTIC SUBSTITUTIONS IN INDOLINONE NITROXIDE RADICALS—I

REACTION WITH AROYLOXYL RADICALS

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Abstract—Indolinone nitroxides undergo a homolytic substitution with aroyl oxyl radicals, leading to two isomers, 7-aroyloxy- and 5-aroyloxy-derivative, respectively, whose structures were assigned on the basis of the ESR hfccs and of the ^{1}H NMR spectra of the corresponding amines. The presence of aroyl oxyl radicals in the reaction medium was demonstrated by thermal decomposition of benzoyl peroxide in the presence of aromatic acids.

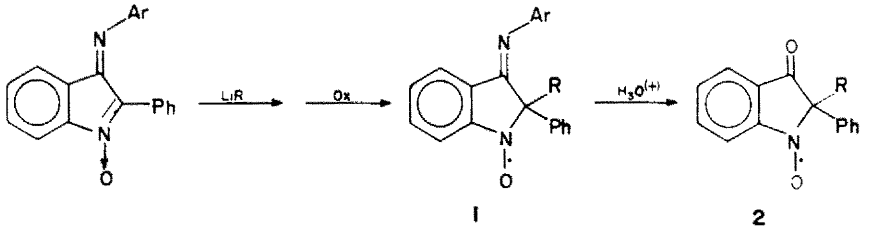
In a previous paper[1] we reported the synthesis of a number of indolinone nitroxide radicals **1** by reaction of organometallic compounds with 2 - phenyl - 3 - aryliminoindolenines N-oxide and subsequent oxidation of the intermediate hydroxylamines; acid hydrolysis of **1** gave radicals **2**.

EPR spectra[1] of **1** and **2** indicate an extended delocalisation of the unpaired electron throughout the molecule, with a relevant spin density on C-5 and C-7 of the aromatic nucleus. This fact, coupled with the unusual, very high stability of radicals **2**, prompted us to study their chemical behaviour; in the present paper we report the reaction of **2** with aroyloxyl radicals.

Wieland *et al.*[2] studied the behaviour of diphenylnitroxide towards a number of inorganic (NO$^\cdot$ and NO$_2^\cdot$) and organic (Ph$_3$C$^\cdot$ and R$^\cdot$) radicals, from which derivatives at the N, O and C atoms were obtained. Treatment of the nitroxides (**2a–c**) with benzoyl peroxide gave in each case a mixture of the isomers (**3** and **4**) (Table 1) in which the former predominated.

Interpretation of their ESR spectra (Figs. 1a and 2a) was easily achieved and confirmed by spectral simulation (Table 2). Comparison of the intensities[3] of their ESR spectra, with that of **2c**, which is a 100% radical,[1] indicated that the purity of the radicals was 80 ± 2%.

Compounds **3** and **4** were assigned the reported struc-



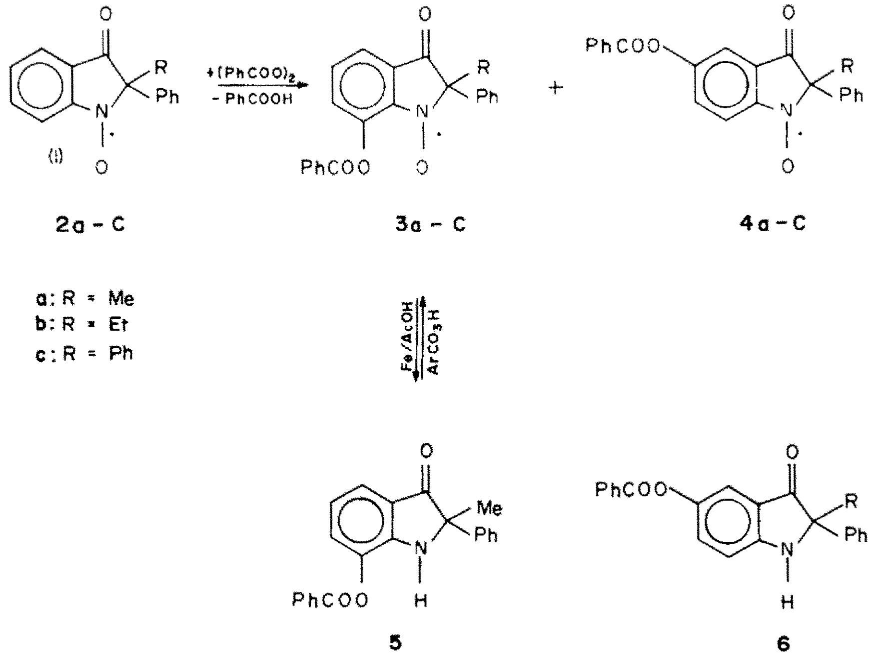


Table 1. Analytical and physical data of compounds **3**, **4**, **5** and **9**

Compound	m.p. °C	Formula	Analysis	Found % Calcd %		IR (ν) cm^{-1}
3a[a]	—	$C_{22}H_{16}NO_4$	C 73.48	H 4.58	N 3.79	1730[c]
			73.73	4.50	3.90	1747[d]
3b[a]		$C_{23}H_{18}NO_4$	C 74.27	H 4.93	N 3.58	1730[c]
			74.17	4.87	3.76	1747[d]
3c[a]		$C_{25}H_{18}NO_4$	C 75.52	H 4.38	N 3.65	1740[e]
			75.74	4.58	3.53	
4a[a]						1735[e]
4b[a]						1730[e]
4c[a]		$C_{25}H_{18}NO_4$	C 76.02	H 5.19	N 3.58	1733[e]
			75.74	4.58	3.53	
5		$C_{22}H_{17}NO_3$	C 76.85	H 5.03	N 4.16	1720[e]
			76.95	4.99	4.08	3430
9	129[b]	$C_{23}H_{17}N_2O_6$	C 66.21	H 4.24	N 6.72	1725[c]
			66.18	4.11	6.71	1753[d]

[a] Isolated as pure incrystallizable oil.

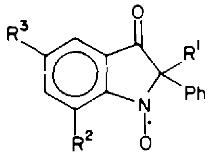
[b] From EtOH.

[c] Ketonic carbonyl.

[d] Ester carbonyl.

[e] Broad.

Table 2. Hffcc values (in Gauss) for radicals **3**, **4** and **9**



Compound	R^1	R^2	R^3	a^{N_1}	a^{H_5}	a^{H_7}	$a^{H_{4,6}}$(2H)	a^{R_1}
3a	Me	$PhCO_2$	H	9.22	3.26	—	1.00	0.18 (3H)
3b	Et	$PhCO_2$	H	9.17	3.27	—	1.02	0.32 (1H)
3c	Ph	$PhCO_2$	H	9.19	3.22	—	1.00	—
4a	Me	H	$PhCO_2$	9.53	—	3.00	1.03	0.16 (3H)
4b	Et	H	$PhCO_2$	9.48	—	2.98	1.04	0.29 (1H)
4c	Ph	H	$PhCO_2$	9.51	—	2.94	1.02	—
9	Ph	p-$NO_2C_6H_4CO_2$	H	9.52	3.41	—	1.05	0.31 (1H)

tures on the basis of their ESR spectra and of the ^1H NMR spectrum of compound **5** (Table 1) obtained by reduction of **3a**. Oxidation of **5** with organic peracids gave the starting compound **3a**. ESR spectra of **3** and **4** indicate the presence of two H atoms with $a^H \cong 1G$ and of only one with $a^H \cong 3G$. The first two coupling constants were assigned to the hydrogens at C-4 and C-6, whilst the third was attributable either to the C-5 or to the C-7 H atom, in agreement with the usual values of the hfccs in such system.[1] Also the a^N and other a^H values are in agreement with the literature data.[1]

The 80 MHz ^1H NMR spectrum of **5** exhibits a complex pattern in the aromatic hydrogen region, but a quartet corresponding to one H atom is clearly distinguishable at 6.82 δ, well separated from the remaining signals. This quartet constitutes an AB system from which two very similar J values can be obtained, $J_1 = 8.3$ and $J_2 = 8.4$ Hz, respectively. These values led us to assign compounds **3** the reported structure of 7-benzoyloxy derivatives and to exclude the isomeric one of 5-benzoyloxy derivatives. In fact, compound **5** must present in the ^1H NMR spectrum two *ortho* and one *meta* coupling constant, whilst the isomeric compound **6** must present one *ortho*, one *meta* and one *para* coupling constant. The experimental values 8.3 and 8.4 Hz, attributable to $J_{H_4-H_5}$ and to $J_{H_5-H_6}$, respectively, are both in the usual range for the *ortho* J values and are by far too great to be attributable to a J^{meta}.

The structure of the other radicals **3b,c** and **4b,c** was assigned on the basis of the similarity of their hfcc values (Table 2) with the corresponding values for compounds **3a** and **4a**.

It is worthy to note that in 7-benzoyloxy derivatives **3** the a^N value is always lower than the corresponding value for 5-benzoyloxy derivatives **4** (9.2 against 9.5 G.

Table 3. Yields in the reaction between **2a–c** and $(PhCOO)_2$

Products Reagents	2†	3	4
2a	50%	30%	traces
2b	55%	17%	traces
2c	60%	16%	3–4%

†Recovered unchanged after 72 hr.

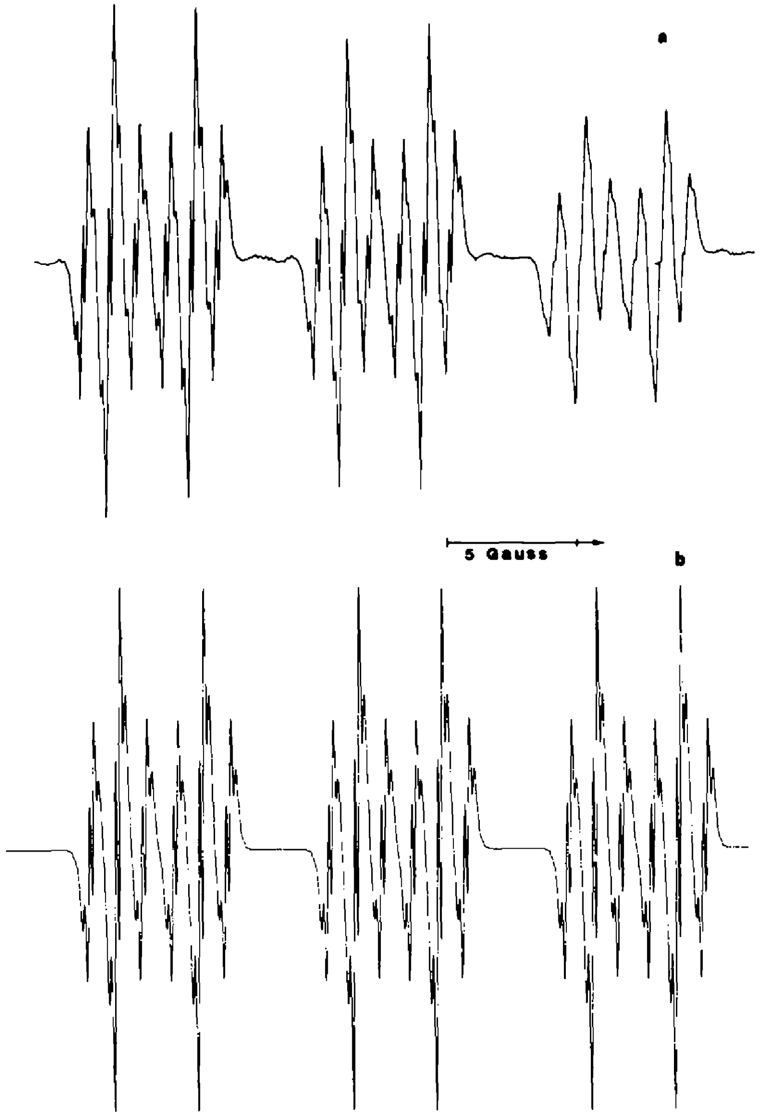
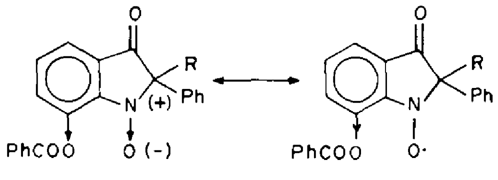


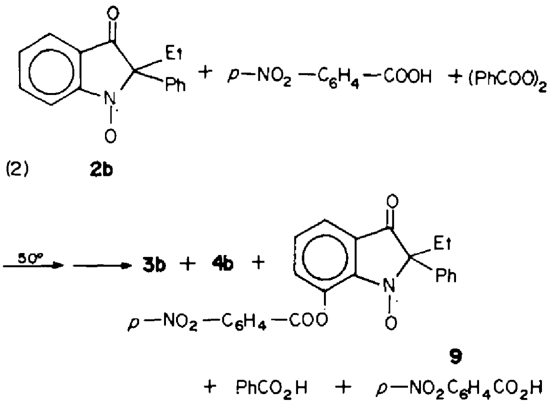
Fig. 1. (a) ESR first-derivative spectrum of the nitroxide **3a**: observed spectrum in $CHCl_3$ solution. (b) Calculated spectrum of nitroxide **3a** with Lorentzian line width of 0.12 gauss.

approx), whilst the $a^{5\text{-}H}$ value is greater than the $a^{7\text{-}H}$ one (3.2 vs 3.0 G. approx). This may be rationalised considering that in compounds **3** the polarised $C_7 \rightarrow$—OBz bond is parallel to the $N \rightarrow O$ bond, the mutual repulsion between these two dipoles being reduced if the lesser polar limit form **8** is favoured against the more polar one **7**, so reducing the spin density at the N atom.[4]



7 **8**

When the reaction between radical **2b** and benzoyl peroxide was carried out in the presence of p-NO_2-benzoic acid, the new nitroxide radical **9** (Tables 1 and 2 and Fig. 3) was obtained in low yield besides the usual products.



Only one isomer bearing the p-nitrobenzoyloxy group in the aromatic nucleus was isolated from the reaction mixture and it was assigned the structure **9** of 7-substituted derivative on the basis of the analogy with the benzoyl peroxide reaction, in which case the 7-substituted isomer always considerably predominates over

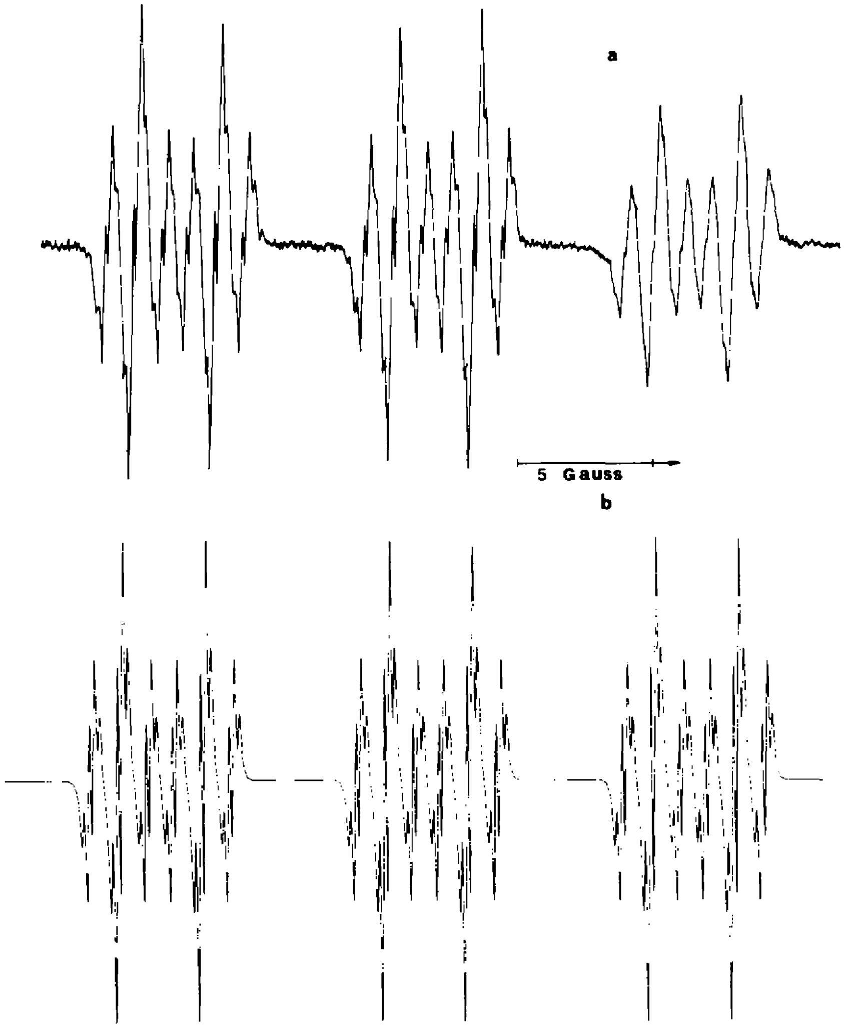


Fig. 2. (a) ESR first-derivative spectrum of nitroxide **4a**: observed spectrum in $CHCl_3$ solution. (b) Calculated spectrum of nitroxide **4a** with Lorentzian line width of 0.10 gauss.

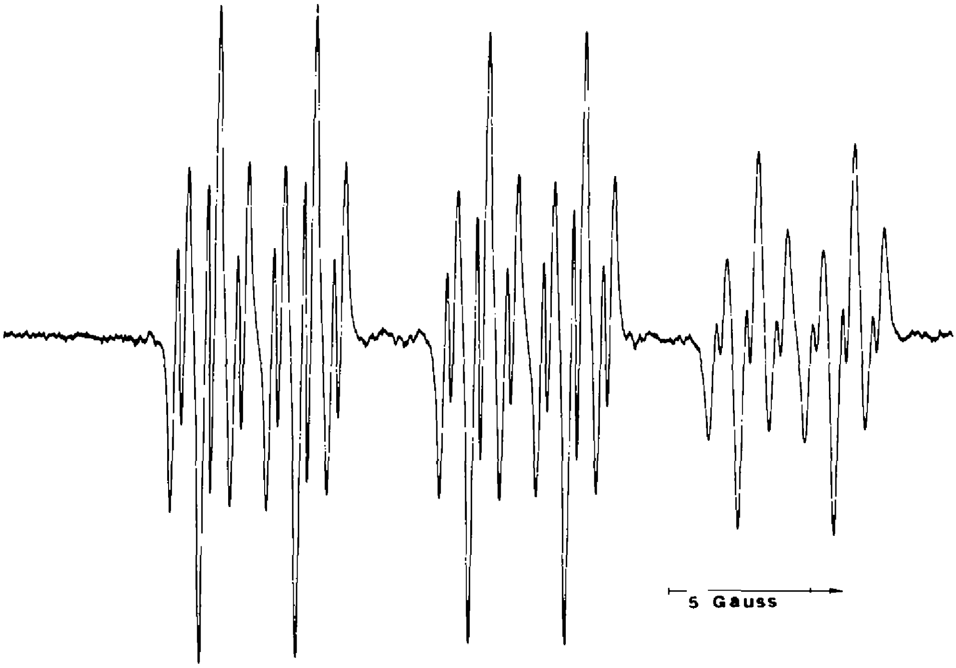


Fig. 3. ESR first-derivative spectrum of nitroxide **9**: observed spectrum in $CHCl_3$ solution.

the 5-isomer. In the present case, the 5-isomer of **9** was not isolated.

Reaction (2) can be explained by a competitive reaction towards **2b** of benzoyloxyl and *p*-nitro-benzoyloxyl radicals, the latter being formed via hydrogen abstraction from *p*-nitrobenzoic acid by benzoyloxyl radicals:

$$p\text{-NO}_2\text{–C}_6\text{H}_4\text{–COOH} + \text{C}_6\text{H}_5\text{–COO}^{\cdot} \rightleftarrows p\text{-NO}_2\text{–C}_6\text{H}_4\text{–COO}^{\cdot} + \text{C}_6\text{H}_5\text{COOH} \qquad (3)$$

To demonstrate the actual occurrence of reaction (3), benzoyl peroxide was refluxed in benzene in the presence of *p*-methyl- and *p*-methoxy-benzoic acid; in the reaction mixture 4-methyl- and 4-methoxy-biphenyl were isolated, respectively, in addition to biphenyl, and were identified by gas-chromatography; the subsequent scheme may be postulated to rationalise the reaction pathway:

$$(\text{PhCOO})_2 \xrightarrow{80^\circ} 2\text{PhCOO}^{\cdot} \xrightarrow{80^\circ} 2\text{Ph}^{\cdot} + 2\text{CO}_2$$

$$\text{Ph}^{\cdot} + \text{C}_6\text{H}_6 \xrightarrow{\text{H}} \text{Ph–Ph}$$

$$\text{Ph}^{\cdot} + p\text{-X–C}_6\text{H}_4\text{–COOH} \longrightarrow \text{C}_6\text{H}_6 + p\text{-X–C}_6\text{H}_4\text{–COO}^{\cdot} \xrightarrow{80^\circ} \longrightarrow p\text{-X–C}_6\text{H}_4^{\cdot} + \text{CO}_2$$

$$p\text{-X–C}_6\text{H}_4^{\cdot} + \text{C}_6\text{H}_6 \xrightarrow{-\text{H}} p\text{-X–C}_6\text{H}_4\text{–C}_6\text{H}_5$$

X = Me; OMe

On the other hand an analogous reaction is already known for persulphuric acid.[5]

As far as the mechanism of reactions **1** and **2** is concerned, a homolytic aromatic substitution can be postulated[6] according to the following scheme (and a similar one for compound **4**).

The predominance of compounds **3** over **4** suggests that a cyclic transition state interesting the nitroxide group may be involved in the reaction pathway.

The intermediate addition product **10** can either rearrange to the hydroxylamine **11** (which is easily oxidised in the reaction medium), or it can be directly oxidised at radical **3** via a hydrogen abstraction by a radical R· present in the reaction medium. A slight modification to the proposed mechanism could arise from a catalytic effect of our nitroxides on the decomposition of benzoyl peroxide;[7] so far, however, we have no experimental data supporting this hypothesis; in fact no reaction was observed when the reaction was carried out at room temperature, where benzoyl peroxide does not decompose. Further studies are under way to confirm this reaction mechanism.

EXPERIMENTAL

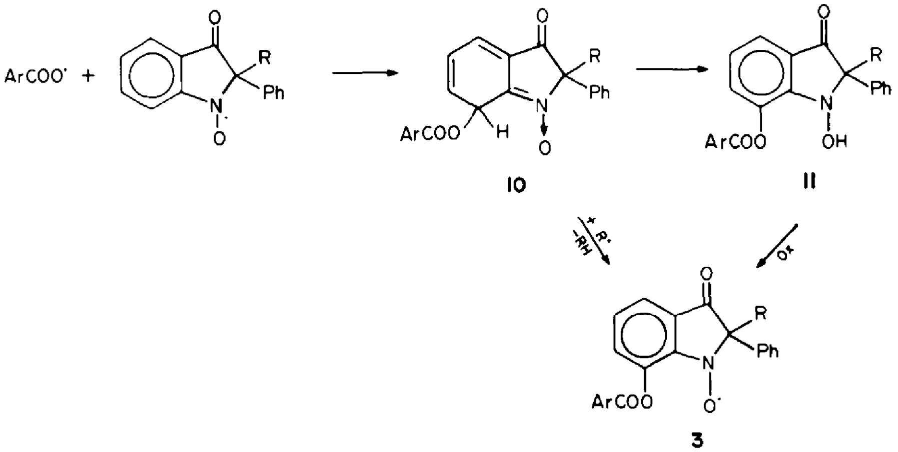
M.ps were not corrected. The IR spectra were recorded in $CHCl_3$ solution using a Perkin–Elmer 257 apparatus; the ESR spectra were recorded in $CHCl_3$ solution using a Varian E4 apparatus; the ^1H NMR spectrum was recorded on a Varian 80 MHz apparatus. Gas chromatographic measures were carried out on a Varian 1400 apparatus. Nitroxides **2a–c** were prepared as described in literature.[1]

Reaction of nitroxide radicals **2a–c** *with* $(PhCOO)_2$. Nitroxides **2a–c** (3 mmoles) and $(PhCOO)_2$ (3 mmoles) in 50 ml C_6H_6 were heated at 50° for 72 hr under stirring, then the mixture was treated with Na_2CO_3aq. The C_6H_6 layer dried on Na_2SO_4 was evaporated to dryness and the residue was chromatographed on SiO_2 using petrolether/EtOAc 9:1 as an eluent. The starting nitroxides **2** and a mixture of two monosubstitued nitroxide radicals were isolated. The mixture of radicals **3** and **4** was resolved by means of preparative TLC on SiO_2 using the same eluent mentioned above; the analytical and spectroscopic data of the compounds **3a–c** and **4a–c** are set out in Tables 1 and 3; the yields are set out in Table 3.

Reaction between nitroxide **2b** *and* $(PhCOO)_2$ *in the presence of* p-NO_2–C_6H_4–COOH. The reaction was carried out and worked as described using a molar 1:2 ratio between $(PhCOO)_2$ and *p*-NO_2–C_6H_4–COOH. The isolated products were **2b** (starting material), **3b**, **4b** and **9**. The analytical and spectroscopic data of **9** are set out in Tables 1 and 2. In this reaction an exact valuation of the yields was impossible because of the difficulty in separating the products.

Decomposition of $(PhCOO)_2$ in C_6H_6 *in the presence of aromatic acids.* Aromatic acid (*p*-CH_3–C_6H_4–COOH or *p*-OCH_3–C_6H_4–COOH) (6 mmoles) and $(PhCOO)_2$ (3 mmoles) in 50 ml C_6H_6 were refluxed for 5 hr, then the mixture was treated with Na_2CO_3aq and washed with H_2O. The C_6H_6 layer dried on Na_2SO_4 was evaporated to dryness, and the residue taken up with Et_2O was analysed by gas chromatography. *p*-Me-diphenyl and *p*-OMe-diphenyl were observed in the reaction from *p*-Me-C_6H_4–COOH and *p*-OMe–C_6H_4–COOH, respectively, and they were identified by comparison with authentic samples. In both cases a large amount of diphenyl was obtained.

Reduction of **3a** *to* **5**. Compound **3a** (0.45 g) and Fe powder (1 g) in 25 ml AcOH were refluxed for 10 min. After cooling the inorganic ppt was filtered off and solid Na_2CO_3 was added to the filtrate until a solid mixture was obtained. This mixture was then extracted with benzene and the extract evaporated to dryness gave **5** in 60% yield; the product was purified by preparative TLC



on SiO_2 using benzene/acetone 9:1 as an eluent; the analytical data of **5** are set out in Table 1 and its ^1H NMR spectrum is discussed in the text.

Assessment of the percentage of radical in **3,4** *and* **9**. The percentage of radical in compound **3**, **4** and **9** was determined by comparing their ESR signals in approx 10^{-3} M benzene soln with the ESR signal of benzene solns of **2c** in approx the same concentration. Double integration of the signal was carried out numerically according to Wyard[3] and the radical content proved to be about 80%.

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