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OXIDATIONS WITH ACYLNITROXYLS

S.Altaf Hussain, Terence C.Jenkins and M.John Perkins

Department of Chemistry, Chelsea College, University
of London, Manresa Road, London SW3 6LX

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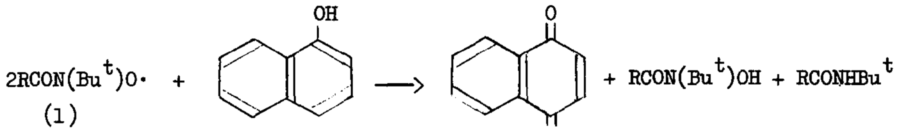
Many nitroxide radicals are sufficiently stable to be isolated. Of these, the di-t-alkyl nitroxides are sufficiently unreactive to permit the spin labelling technique; their low reactivity is further reflected in a rate constant for reaction with ethylbenzene of _ca._ 2×10^{-7} l mol^{-1} sec^{-1} at 75°.[1] Negatively substituted nitroxides such as Fremy's radical $[(K^{+-}O_3S)_2NO\cdot]$[2] and bistrifluoromethyl nitroxide[3] are more reactive, the former having been extensively studied as an oxidising agent, in particular for the conversion of monohydric phenols to quinones(the Teuber reaction).

We have recently isolated stable acyl t-butyl nitroxyls (1)[4] which have a relatively high spin density on oxygen[5] and are more reactive than dialkyl nitroxides. It is now reported that these radicals may have some value as homolytic oxidising agents. Thus, like Fremy's radical, they oxidise phenols to quinones, apparently by a similar mechanism;[6] the reaction is however effected in an organic solvent, in contrast to the normal Teuber procedure. In most cases yields are good, and are generally superior to those obtained with other organic nitroxides,[7] although the reaction is unsatisfactory with certain simple phenols including phenol itself. In this case, using (1,R=Ph), t-butylbenzamide is obtained in high yield (90%), but the oxidation products of phenol have not been characterised.

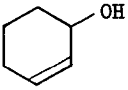
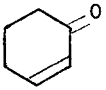
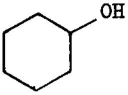
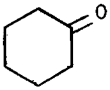


Dihydric phenols are oxidised to quinones though the procedure has no special merit over conventional alternatives.

Also of potential value is the efficient oxidation of allylic and benzylic alcohols to the corresponding aldehydes and ketones. Because the α-CH bond is much weaker in these than in saturated alcohols, selective oxidations are possible. Slow formation of ketones is observed with saturated secondary alcohols,[8] but the aldehydes formed from saturated primary alcohols are rapidly oxidised further.

Of interest is the oxidation of meso-dihydrobenzoin to benzil without oxidative fission.

Table : Oxidations by Acylnitroxyls[a]

Substrate	Radical (1) R	Product (yield[b])	
2,5-Dimethylphenol	Ph	2,5-Dimethyl-p-benzoquinone	(42%)
2,6-Dimethylphenol	"	2,6-Dimethyl-p-benzoquinone	(86%)
3,5-Dimethoxyphenol	"	2,6-Dimethoxy-p-benzoquinone	(60%)
2,6-Dichlorophenol	"	2,6-Dichloro-p-benzoquinone	(46%)
2-t-Butylphenol	"	2-t-Butyl-p-benzoquinone	(60%)
3-t-Butylphenol	"	4-t-Butyl-o-benzoquinone[c]	(70%)
4-t-Butylphenol	"	4-t-Butyl-o-benzoquinone	(51%)
2,4-Di-t-butylphenol	"	3,5-Di-t-butyl-o-benzoquinone	(87%)
3,5-Di-t-butylcatechol	"	3,5-Di-t-butyl-o-benzoquinone	(97%)
p-Dihydroxybenzene	"	p-Benzoquinone	(95%)
α-Naphthol	"	α-Naphthoquinone	(72%)
β-Naphthol	"	β-Naphthoquinone	(84%)
9-Anthranol	"	Anthraquinone	(93%)
Ph_2CHOH	"	Ph_2CO	(95%)
PhCHOHCHOHPh	"[d]	PhCOCOPh	(89%)
$PhCH_2OH$	$3,5-(O_2N)_2C_6H_3$ [e]	PhCHO	(65%)
$PhCH{=}CHCH_2OH$	"	PhCH=CHCHO	(83%)
PhCHOHMe	"	PhCOMe	(90%)
	"		(93%)
	"		(51%)

(a) Experiments normally employed 0.05 mmol of substrate and 0.1 mmol radical in 1-2 ml solvent (CH_2Cl_2 or ether at room temperature for the phenols, warm benzene for the alcohols).

(b) Isolated for solid products: by g.l.c for liquids. No attempt to optimise these yields has been made.

(c) 2-t-Butyl-p-benzoquinone not detected.

(d) Four equivalents of radical employed.

(e) The hydroxamic acid $[(O_2N)_2C_6H_3CON(Bu^t)OH]$ separated from these reactions and could be reoxidised to nitroxyl.

Examples of the above reactions are collected in the Table. Reactions with phenols employed the benzoylnitroxyl (1, R=Ph), but for most of the alcohols the more reactive 3,5-dinitro-derivative (1, R = $3,5\text{-}(O_2N)_2C_6H_3$) was the reagent of choice.[9] Diphenylamine gives N-phenyl-p-benzoquinoneimine with (1, R=Ph), but separation of the product from the accompaying N-t-butylbenzamide proved difficult; this problem could be overcome by using the undecanoylnitroxyl (1, R=$C_{10}H_{21}$) which gave hexane-soluble by-products readily separated from the imine. This exemplifies the possibility of tailoring the reagent to solve particular oxidation problems.

The acylnitroxyls react with a variety of C-H bonds. Thus (1, R=Ph) slowly reacts with excess ethylbenzene ($k = 3.0 \times 10^{-4}\ l\ mol^{-1}\ sec^{-1}$ at 75° ; compare ref. 1) to give a quantitative yield of (2):

$$\underset{(1)}{RCON(Bu^t)O\cdot} + PhCH_2Me \xrightarrow{R=Ph} PhCON(Bu^t)OH + Ph\dot{C}HMe$$

$$Ph\dot{C}HMe \xrightarrow{(1,\ R=Ph)} \underset{(2)}{PhCON(Bu^t)OCH(Me)Ph}$$

The selectivity of the same radical is quite high, as revealed in the relative reactivities of alkylbenzenes ($MeCH_3$: $PhCH_2Me$: $PhCHMe_2$:: 1 : 22 : 70 per benzylic hydrogen at 75°). As expected, the radical shows electrophilic character in these reactions;[10] the rates of reactions with substituted toluenes (p-MeO to p-O_2N) correlate well with σ^+ ($\rho = -0.99$ at ca. 90°).

Reactions of (1, R = Ph) with saturated hydrocarbons are much slower, and the self-reaction of the radical ($\rightarrow Bu^tNO + PhCON(Bu^t)OCOPh$) competes. However the 3,5-dinitro-derivative gives a good yield of $3,5\text{-}(O_2N)_2C_6H_3CON(Bu^t)OC_6H_{11}$ with excess cyclohexane.

The high yields obtained in reactions using isolable nitroxides can be attributed to the efficient scavenging of the substrate-derived radical by a second molecule of nitroxide. Furthermore, the site of attack on a given substrate is largely dependent on the relative strengths of different bonds to hydrogen in the substrate, and these can usually be estimated with confidence.[11]

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