Hydroperoxides as Pseudohalides: Oxidation, Oxidative Alkylation, Acylation and Arylation of Acrylonitrile

Silvia Araneo, Francesca Fontana, Francesco Minisci,* Francesco Recupero and Anna Serri
Dipartimento di Chimica del Politecnico, via Mancinelli 7, I-20131 Milano, Italy

New general syntheses, based on free-radical oxidative alkylation, acylation and arylation of acrylonitrile, in the presence of Bu^tO_2H, are reported; the concept of the peroxy group as a pseudohalide is suggested to explain these new reactions.

Aryl and nucleophilic alkyl radicals add rapidly to electron-deficient alkenes.[1,2] Thus, for example, primary alkyl radicals add to acrylonitrile with a rate constant[2a] of 1.1×10^6 dm^3 mol^{-1} s^{-1} at 60 °C, while aryl radicals add to alkenes conjugated with electron-withdrawing groups with rate constants in the range 10^7–10^8 dm^3 mol^{-1} s^{-1} at room temperature.[3,4] This high reactivity has been widely utilized for the reductive alkylation of alkenes conjugated with electron-withdrawing groups by Si, Sn or Ge hydrides (HMR_3) [eqns. (1)–(3)], which already represent a major synthetic methodology in organic synthesis.[5]

$$\underset{\mathbf{1}}{R^1}\text{-}X + {}^{\bullet}MR_3 \rightarrow R^{1\bullet} + X\text{-}MR_3 \qquad (1)$$

$$R^{1\bullet} + CH_2{=}CH\text{-}Y \rightarrow \underset{\mathbf{2}}{R^1\text{-}CH_2\dot{C}H\text{-}Y} \qquad (2)$$

Y = electron-withdrawing group

$$R^1\text{-}CH_2\dot{C}H\text{-}Y + H\text{-}MR_3 \rightarrow R^1\text{-}CH_2\text{-}CH_2\text{-}Y + {}^{\bullet}MR_3 \qquad (3)$$

This synthetic success is related to the fact that, while the initial radical **1** has nucleophilic character, the radical adduct **2** has electrophilic character, and this is favourably reflected in both radical addition to alkenes [eqn. (2)] and hydrogen abstraction from the hydride [eqn. (3)].[1,2] For the same reason it is much more difficult to obtain the oxidative alkylation of the same alkenes, because oxidation of the nucleophilic radical **1** is generally much easier to bring about than that of the electrophilic radical adduct. **2**.[2] Similarly, the free-radical reductive arylation of electron-deficient alkenes has been achieved using diazonium and Ti^{III} salts [eqn. (4)].[4]

$$Ar\text{-}N_2^+ + CH_2{=}CH\text{-}Y + 2\,Ti^{III} + H_2O \rightarrow Ar\text{-}CH_2\text{-}CH_2\text{-}Y + N_2 + 2\,Ti^{IV} + OH^- \qquad (4)$$

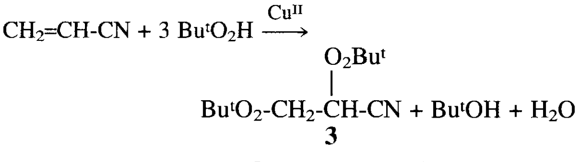
The oxidative arylation of electron-deficient alkenes occurs effectively when a halogen ligand-transfer oxidation is involved [Meerwein reaction, eqn. (5)], owing to the high rate of addition of aryl radicals to the double bond[3,4] and the low sensitivity to the polar effects of the halogen transfer from the $Cu^{II}Cl$ complex to carbon-centred radicals.[6] The free-radical haloalkylation of alkenes[7] is less selective, owing to the fact that the addition of alkyl radicals to the double bond is slower by two orders of magnitude than that of aryl radicals, and that chlorine transfer to radical **1** [eqn. (6)] is always competitive with transfer to the radical adduct **2** [eqn. (7)].

$$Ar\text{-}N_2Cl + CH_2{=}CH\text{-}Y \xrightarrow{Cu^{II}} Ar\text{-}CH_2\text{-}CHCl\text{-}Y + N_2 \qquad (5)$$

$$\mathbf{1} + Cu^{II}Cl \rightarrow R^1\text{-}Cl + Cu^I \qquad (6)$$

$$\mathbf{2} + Cu^{II}Cl \rightarrow R^1\text{-}CH_2\text{-}CHCl\text{-}Y \qquad (7)$$

Now we report new reactions, which allow the obtention of the free-radical oxidative alkylation, acylation and arylation of acrylonitrile by Bu^tO_2H (TBH) with Cu^{II}/Cu^I catalysis. The origin of these new synthetic developments is related to the peroxidation of acrylonitrile by TBH and Cu salt catalysis in benzene solution [eqn. (8)]. We explain the result by the redox chain of eqns. (9)–(12).



$$CH_2{=}CH\text{-}CN + 3\,Bu^tO_2H \xrightarrow{Cu^{II}} \underset{\mathbf{3}}{Bu^tO_2\text{-}CH_2\text{-}\overset{O_2Bu^t}{\overset{|}{C}}H\text{-}CN} + Bu^tOH + H_2O \qquad (8)$$

$$Bu^tO_2H + Cu^I \rightarrow Bu^tO^{\bullet} + Cu^{II} + OH^- \qquad (9)$$

$$Bu^tO^{\bullet} + HO_2Bu^t \rightarrow Bu^tOH + Bu^tO_2^{\bullet} \qquad (10)$$

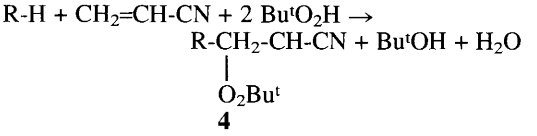
$$Bu^tO_2^{\bullet} + CH_2{=}CH\text{-}CN \rightarrow Bu^tO_2\text{-}CH_2\text{-}\dot{C}H\text{-}CN \qquad (11)$$

$$Bu^tO_2\text{-}CH_2\text{-}\dot{C}H\text{-}CN + Cu^{II}O_2Bu^t \rightarrow \mathbf{3} + Cu^I \qquad (12)$$

Since no polymer is formed, it is clear that the reaction [eqn. (12)] is faster than the propagation rate of acrylonitrile polymerization. The reaction has a quite close resemblance to the diazidation of alkenes[8] [eqn. (13)], which is explained by a similar redox chain,[8] from this point of view the peroxy group appears to behave like a halide or pseudohalide.

$$Me_2C{=}CMe_2 + 2\,HN_3 + H_2O_2 \rightarrow Me_2(N_3)C\text{–}C(N_3)Me_2 + 2\,H_2O \qquad (13)$$

When the reaction was carried out under the same conditions in the presence of hydrogen donors (R-H), the oxidative alkylation of acrylonitrile occurred [eqn. (14)]. A variety of substrates (cyclohexane, adamantane, toluene, dioxane, benzaldehyde, butanal, *etc.*) has been used, as reported in Table 1. The redox chain of eqns. (9), (10) and (15)–(17) explains these results. The mixed peroxide can be easily converted into the corresponding α-ketonitrile by alkaline catalysis [eqn. (18)].



$$R\text{-}H + CH_2{=}CH\text{-}CN + 2\,Bu^tO_2H \rightarrow \underset{\mathbf{4}}{R\text{-}CH_2\text{-}\underset{O_2Bu^t}{\underset{|}{C}}H\text{-}CN} + Bu^tOH + H_2O \qquad (14)$$

$$R\text{-}H + Bu^tO^{\bullet}\ (Bu^tO_2^{\bullet}) \rightarrow \underset{\mathbf{5}}{R^{\bullet}} + Bu^tOH\ (Bu^tO_2H) \qquad (15)$$

Table 1 Free-radical oxidation and oxidative alkylation, acylation and arylation of acrylonitrile according to eqns. (8), (14) and (19)

R	Procedure[a]	Amount of R-H	Yields (%)[b] 3	4
Cyclohexyl	A	25 ml	12	36
$PhCH_2$[c]	A	25 ml	10	16
Bu^tO_2	B	—	55	—
1-Adamantyl	C	25 mmol	—	44
Dioxanyl	C	5 ml	10	13
α-Tetrahydrofuranyl	C	5 ml	—	80
Ph-CO	C	5 mmol	—	43
$n\text{-}C_3H_7\text{-}CO$	C	5 mmol	—	40
Ph	D	—	—	15

[a] *Procedures.* A: 25 mmol of substrate (cyclohexane or toluene), 5 mmol of TBH, 10 mmol of acrylonitrile, 0.25 mmol of $Cu(OAc)_2$ were warmed at 50 °C for 18 h; B : 5 mmol of TBH, 25 mmol of acrylonitrile, 0.25 mmol of $Cu(OAc)_2$ in 25 ml of benzene were warmed at 50 °C for 18 h; C : as B with the amount of R-H reported in the table; D : 1 mmol of $(PhCOO)_2$, 2 mmol of acrylonitrile, 1 mmol of TBH, 0.1 mmol of $Cu(OAc)_2$ in 7 ml of acetone were heated under reflux for 21 h. [b] Yields based on TBH. [c] 35% of $Ph\text{-}CH_2\text{-}O_2Bu^t$ is also formed.

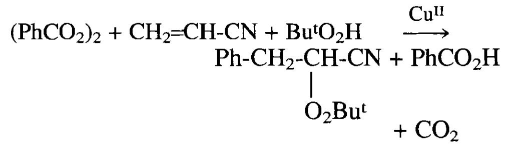
$$\mathbf{5} + CH_2{=}CH\text{-}CN \rightarrow \underset{\mathbf{6}}{R\text{-}CH_2\text{-}\dot{C}H\text{-}CN} \quad (16)$$

$$\mathbf{6} + Cu^{II}O_2Bu^t \rightarrow \mathbf{4} + Cu^I \quad (17)$$

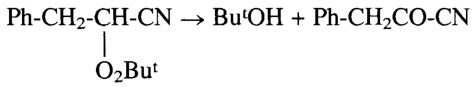
$$\mathbf{4} \xrightarrow{Et_3N} R\text{-}CH_2\text{-}CO\text{-}CN + Bu^tOH \quad (18)$$

The success of the new synthesis is related to the fact that the addition of radical **5** to acrylonitrile is faster than its oxidation by Cu^{II} salt, which is anyway present in low amounts, while the oxidation of the radical adduct **6** is faster than the propagation rate of the polymerization. Thus, the transfer of the peroxy group [eqn. (17)] appears to be more selective than the transfer of other halide or pseudohalide groups [eqns. (6) and (7)]. With benzyl radical, which reacts somewhat more slowly with acrylonitrile,[9] its oxidation by $Cu^{II}(O_2Bu^t)$, however, competes with reaction (16), and significant amounts of $Ph\text{-}CH_2\text{-}CO_2Bu^t$ are formed.

The thermal decomposition of benzoyl peroxide in the presence of TBH and Cu^{II} salt leads to the oxidative arylation of acrylonitrile [eqn. (19)] by a mechanism similar to that of eqns. (16) and (17). Under the same reaction conditions the peroxide is decomposed to the corresponding α-ketonitrile [eqn. (20)].



$$(PhCO_2)_2 + CH_2{=}CH\text{-}CN + Bu^tO_2H \xrightarrow{Cu^{II}} Ph\text{-}CH_2\text{-}\underset{O_2Bu^t}{\underset{|}{C}H}\text{-}CN + PhCO_2H + CO_2 \quad (19)$$



$$Ph\text{-}CH_2\text{-}\underset{O_2Bu^t}{\underset{|}{C}H}\text{-}CN \rightarrow Bu^tOH + Ph\text{-}CH_2CO\text{-}CN \quad (20)$$

This result bears a close resemblance to the above-mentioned Meerwein reaction, whose mechanism[6] is similar to that of eqns. (16) and (17). According to these results, hydroperoxides can be considered as pseudohalides, unlike other hydroxy derivatives such as alcohols and carboxylic acids. Like the other halide and pseudohalide ions, peroxy groups coordinated to metal salts also appear to be particularly suitable for the ligand-transfer oxidation of carbon-centred radicals [eqns. (12) and (17)], and seem even more selective, while the alcoholates and carboxylates of Cu^{II} appear to be much more suitable for electron-transfer than for ligand-transfer oxidation of carbon-centred radicals, because of the higher sensitivity to polar effects.

Received, 7th April 1995; Com. 5/02272J

References

1. F. Minisci, T. Caronna, M. Cecere, R. Galli and V. Malatesta, *Tetrahedron Lett.*, 1968, 5609; F. Minisci, P. Zammori, R. Bernardi, M. Cecere, R. Galli and V. Malatesta, *Tetrahedron*, 1970, **26**, 4153.
2. (*a*) A. Citterio, F. Minisci and A. Arnoldi, *J. Org. Chem.*, 1979, **44**, 2674; (*b*) A. Citterio, F. Minisci and M. Serravalle, *J. Chem. Res.*, 1981, (*S*), 198; (*M*), 2174; (*c*) F. Minisci, in *Fundamental Research in Homogeneous Catalysis*, ed. M. Graziani, Plenum, New York, 1984, p. 173.
3. J. C. Scaiano and L. C. Stewart, *J. Am. Chem. Soc.*, 1983, **105**, 3609.
4. A. Citterio, F. Minisci and E. Vismara, *J. Org. Chem.*, 1982, **47**, 81.
5. B. Giese, in *Radicals in Organic Syntheses: Formation of Carbon–Carbon Bonds*, ed. J. E. Baldwin, Pergamon, Oxford, 1986.
6. J. K. Kochi, *J. Am. Chem. Soc.*, 1955, **77**, 5090; 5270; 1956, **78**, 1228; 4815; 1957, **79**, 2942.
7. F. Minisci and U. Pallini, *Gazz. Chim. Ital.*, 1961, **91**, 1030.
8. F. Minisci, *Acc. Chem. Res.*, 1975, **8**, 165; *La Chimica e l'Industria*, 1967, **49**, 706; *Tetrahedron Lett.*, 1962, 533; 1963, 357.
9. H. Fischer, personal communication.