Conversion of Aliphatic and Alicyclic Carboxylic Acids into nor-Hydroperoxides, nor-Alcohols, and nor-Oxo Derivatives using Radical Chemistry

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Radicals generated from esters of *N*-hydroxypyridine-2-thione react smoothly with oxygen in the presence of t-butyl thiol to furnish nor-hydroperoxides, from which the corresponding alcohols and carbonyl derivatives can be readily obtained.

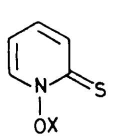
We recently reported[1,2] that the esters of *N*-hydroxypyridine-2-thione (**1**) are a very convenient source of carbon radicals. Since the change from a carboxylic acid (R–CO_2H) to the corresponding nor-alcohol (R–OH) is normally effected in several steps, we have examined an expeditive method for this transformation which exploits this new source of carbon radicals.

We conceived that carbon radicals would be captured by oxygen in the presence of t-butyl thiol (**19**), the latter serving to quench the hydroperoxide radicals formed giving t-butylthiyl radicals which would restart the chain (Scheme 1). Reduction of the hydroperoxides with Me_2S or (better) with trimethyl phosphite would give the nor-alcohols and treatment with toluene-*p*-sulphonyl chloride in the presence of

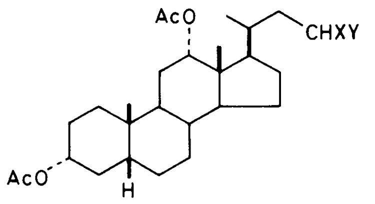
Table 1

Acid chloride	Method	Reaction time[d] with O_2/min	Bu^{t}SH/ mmol	Me_2S/ml	$(MeO)_3P$/ ml	Products[e] yield (%)
(3)[a]	A	10	9	1	-	**(7)** 14, **(4)** 51, **(18)** 80
(3)[a]	A	10	27	1	-	**(6)** 41, **(4)** 35, **(18)** 67
(3)[a]	A	10	4.5	1	-	**(7)** 15, **(4)** 41, **(18)** 42
(3)[a]	C	10	9	2	-	**(7)** 17, **(4)** 57, **(18)** 47
(3)[a]	A	10	9	-	0.25	**(6)** 26, **(4)** 75, **(18)** 68
(3)[a]	C	20	9	-	0.25	**(6)** 23, **(4)** 67, **(18)** 56
(3)[a]	C	15	9	-	0.25	**(5)**[f] 77, **(6)** 13, **(18)** 25, **(4)** 65
(8)[b]	B	60	9	-	0.25	**(9)** 82
(12)[c]	A	20	9	-	0.25	**(13)** 69, **(18)** 65
(16)[c]	A	20	9	-	0.25	**(17)** 97

[a] Redistilled commercial acid chloride. [b] Prepared in essentially quantitative yield from the acid and $SOCl_2$ followed by distillation. [c] Prepared immediately prior to use by treatment of the acid with oxalyl chloride and dimethylformamide in benzene. [d] The rate of flow of oxygen was approximately 0.33 l/min. [e] All new products gave satisfactory spectroscopic and microanalytical data. [f] Estimated by n.m.r. on crude reaction mixture prior to treatment with $(MeO)_3P$, see Method C.



(1) X = H
(2) X = Na



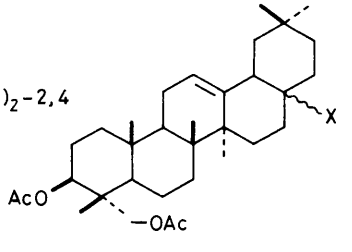
(12) X = COCl, Y = H
(13) X = OH, Y = H
(14) X = OOH, Y = H
(15) X = Y = O / polymer
(20) X = Y = N—NHC$_6$H$_3$(NO$_2$)$_2$-2,4

Me[CH$_2$]$_{13}$CHXY

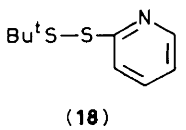
(3) X = COCl, Y = H
(4) X = OH, Y = H
(5) X = OOH, Y = H
(6) X = Y = H
(7) X = Y = O/polymer
(21) X = Y = N—NHC$_6$H$_3$(NO$_2$)$_2$-2,4

(PhCH$_2$)$_2$CXY

(8) X = COCl, Y = H
(9) X = OH, Y = H
(10) X = OOH, Y = H
(11) X = Y = O



(16) X = β-COCl
(17) X = OH



(18)

Bu^{t}SH

(19)

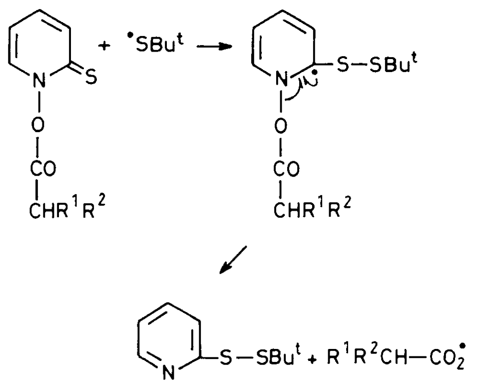
Me[CH$_2$]$_{13}$CH$_2$OH

(22)

pyridine would afford the nor-oxo compounds (aldehydes, R^1 or R^2 = H; ketones, R^1 and R^2 ≠ H).

In practise we have been able to realise these reactions with promising yields of the desired products.

Table 1 lists a number of acids which have been converted into nor-alcohols in the yields indicated. In every case toluene saturated with a vigorous stream of oxygen has been used as solvent. Three different methods have been developed for carrying out the reaction. *Method A:* the acid chloride (1 mmol) in toluene (10 ml) and t-butyl thiol (see Tables 1 and 2) in toluene (10 ml) were added simultaneously to a stirred suspension of **(2)** (1.2 mmol) and 4-dimethylaminopyridine (0.1 mmol) in toluene (10 ml) at 80 °C through which oxygen was passed (see Table 1) *via* a sintered frit. When the reaction was complete (decolouration) Me_2S or $(MeO)_3P$ (see Table 1) were added. *Method B:* here the ester was prepared at room temperature (filtration) and then added to the toluene containing the t-butyl thiol at 80 °C as above. *Method C:* method B was followed except that all operations were at room temperature with irradiation by a 300 W tungsten lamp. After completion of the reaction (decolouration) the excess of t-butyl thiol was washed out with water, the solution dried and the solvent evaporated *in vacuo* at room temperature. This gave the hydroperoxide (Table 2) without alcohol (n.m.r. spectroscopy). Addition of toluene-*p*-sulphonyl chloride (1.1—1.5 mmol) in pyridine (3 ml) for 2—3 h gave the oxo-derivatives characterised, where appropriate as their 2,4-dinitrophenylhydrazones (Table 2, last column).



$$R^1R^2CH{-}CO_2^{\bullet} \longrightarrow CO_2 + R^1R^2CH^{\bullet} \xrightarrow{O_2} R^1R^2CH{-}O_2^{\bullet}$$

$$R^1R^2CH{-}O_2^{\bullet} \xrightarrow{Bu^tSH} R^1R^2CHO_2H + Bu^tS^{\bullet}$$

Scheme 1

The synthesis of hydroperoxides, especially primary and secondary hydroperoxides is not an easy reaction. The method

Table 2

Acid chloride	Method	Reaction time[d] with O_2/min	Bu^tSH/ mmol	Hydroperoxide[f] yield (%)	Products[e] yield (%)
(3)[a]	C	10	9	**(5)** 89	**(7)** 53 [→ **(21)** 37]
(12)[c]	C	15	9	**(14)** 80	**(20)** 57
(12)[c]	C	10	9	**(14)** 74	**(15)** 56
(8)[b]	C	10	9	**(10)** 85	**(11)** 62
(3)[a,g]	C	15	9	**(5)** 84	**(7)** 18, **(5)** 45, **(18)** 84, **(22)** 9

[a] See footnote a, Table 1. [b] See footnote b, Table 1. [c] See footnote c, Table 1. [d] See footnote d, Table 1. [e] See footnote e, Table 1. [f] See footnote f, Table 1. [g] In this case the crude extracts were treated with 2,4-dinitrophenylhydrazine reagent without prior treatment with toluene-*p*-sulphonyl chloride–pyridine.

of Walling and Buckler[3] using carbanion oxygenation is well known. Carbon radicals formed by reduction of organomercury compounds with sodium borohydride give good yields of hydroperoxides.[4] Our own method has generality and with suitable pressure equipment should give good yields on a larger scale.

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References

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