A Convenient High Yielding Synthesis of Nor-alcohols from Carboxylic Acids

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Esters (mixed anhydrides) of carboxylic acids and thiohydroxamic acid (**2**) react with tris(phenylthio)antimony in the presence of oxygen and water to give high yields of nor-alcohols.

We recently invented a convenient method for the generation of carbon radicals from carboxylic acids *via* their esters (mixed anhydrides) (**1**) with suitable thiohydroxamic acids such as (**2a**) or (**2b**).[1] As part of our continuing study of this system, we have examined the production of organometallic species (**3**) by addition of the carbon radical to metallic thiophenoxides *e.g.* (**4**) (Scheme 1). The choice of thiophenoxides was dictated by the need for a good chain propagator (the phenylthiyl radical) in order for the process to be efficient.[1] We now report the results obtained using the readily prepared tris(phenylthio)antimony (**4**).

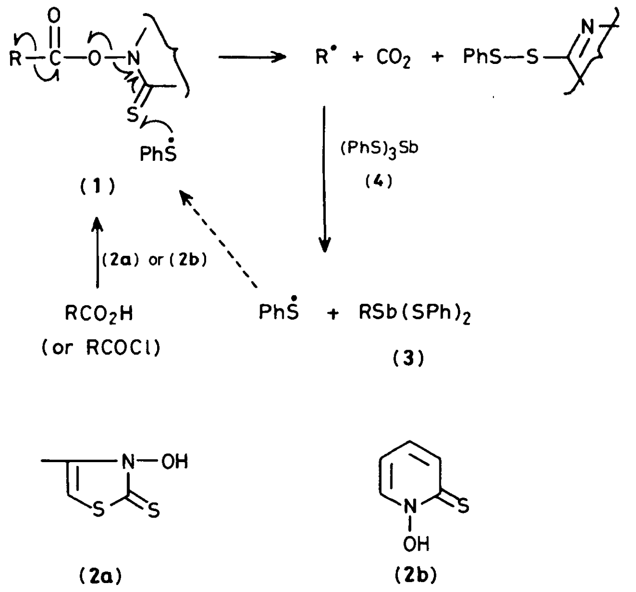
When the palmitic acid derivative (**5**) was heated with two equivalents of (**4**) in chlorobenzene at 90 °C under an inert atmosphere for 3 h, pentadecanol (**6**) was isolated in 65—70% yield (after an aqueous work-up) along with a little (8%) of the sulphide (**7**). The mixed disulphide (**8**) (20%), thiol (**9**) (55%), and diphenyl disulphide are also produced. Essentially all the antimony is recovered as the trioxide, Sb_2O_3 (Scheme 2). The $Sb(SPh)_3$ must be free from thiophenol, otherwise the hydrocarbon (**11**) is formed by the conventional[1a] hydrogen atom transfer reaction.

The formation of the alcohol by aerial oxidation of an intermediate organometallic species, presumably (**10**), is supported by the following observations. When the same experiment is conducted with rigorous exclusion of oxygen and part of the reaction mixture is quenched with concen-

Table 1.

Entry	Ester	Temperature	Solvent	Time/h	Alcohol	Isolated yield/%
1	(**5**)	90 °C[a]	PhCl	3	(**6**)	65—70
2	(**5**)	room temp.[b]	Et_2O	4	(**6**)	85
3	(**15**)	room temp.	PhCl	12	(**16**)	85
4	(**17**)	room temp.	PhCl	12	(**18**)	90
5	(**19**)	room temp.	PhCl	12	(**20**)	91
6	(**19**)	room temp.	Et_2O	12	(**20**)	85
7	(**21**)	room temp.	Et_2O	12	(**22**)	93
8	(**23**)	room temp.	Et_2O	0.5	(**24**)	91
9	(**25**)	room temp.	CH_2Cl_2	12	(**26**)	91
10	(**27**)	room temp.	Et_2O	2	(**28**)	82
11	(**29**)	room temp.	$Et_2O + CH_2Cl_2$	12	(**30**)	81

[a] Under inert atmosphere followed by normal work-up. [b] All room temperature reactions were performed in air.



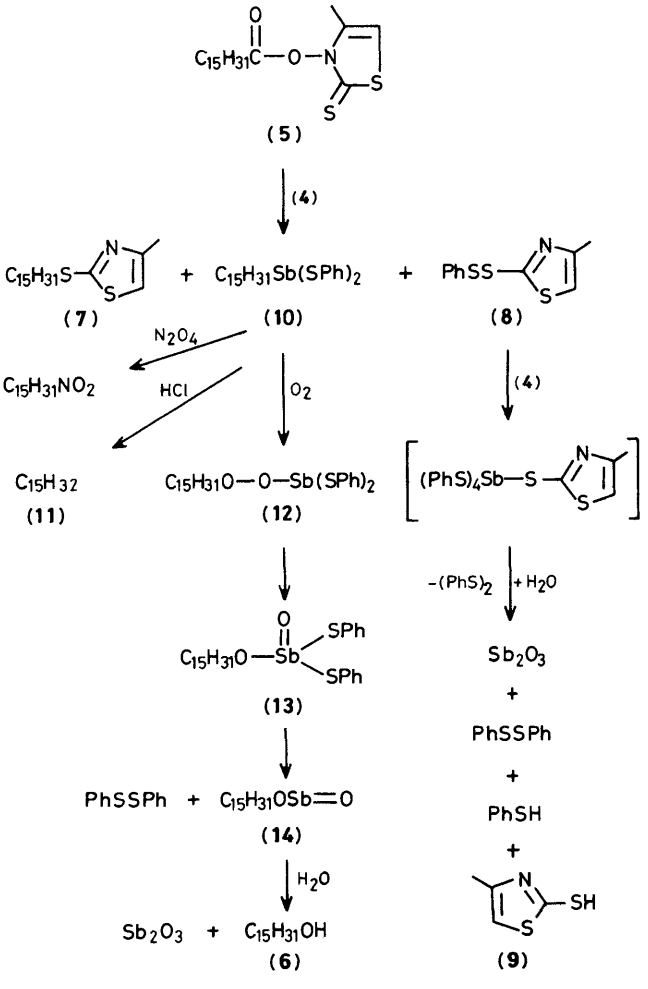
Scheme 1

trated hydrochloric acid, very little alcohol (8%) is produced. The major product is pentadecane (**11**) (85%) as expected from protonolysis of (**10**). Exposure of the remainder to air gives pentadecanol as the main product (70%). If dinitrogen tetroxide is used to decompose (**10**), 1-nitropentadecane is formed, albeit in low yield (26%) (Scheme 2).

Similar organoantimony compounds have been previously prepared by other routes[2] and observed to be air sensitive, although the nature of the autoxidation products was not reported. If, by analogy with other organometallic species,[3] the autoxidation of the organoantimony intermediate (**10**) proceeds *via* a peroxide (**12**), then rearrangement to (**13**) followed by reductive elimination of diphenyl disulphide[4,5] would give the alkoxide (**14**) (probably as a polymer). Hydrolysis finally produces the alcohol and antimony trioxide (confirmed by analysis for Sb^{III}) (Scheme 2).

The thiol (**9**) is formed by reduction of the mixed disulphide (**8**) by unreacted tris(phenylthio)antimony (**4**) in the presence of water[4] as can be shown by separate blank experiments.

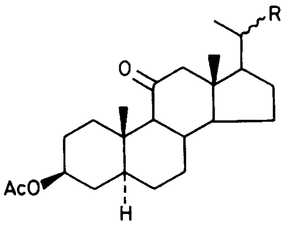
In view of the relatively high yield of alcohol produced, we examined the process in more detail. A synthetically useful method for the conversion of a carboxylic acid into the corresponding nor-alcohol has been invented. Simply stirring the ester (**1**) with tris(phenylthio)antimony (**4**) at room temperature in an open flask affords excellent yields of nor-alcohols derived from a variety of primary, secondary, or tertiary carboxylic acids (Table 1).



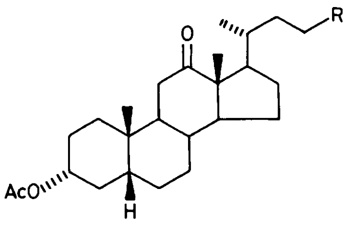
Scheme 2

At this low temperature, the radical chain reaction depicted in Scheme 1 is initiated by the slow decomposition of (**5**) by oxygen.[5]

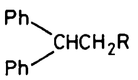
Indeed, no reaction occurs at room temperature in the absence of oxygen and the ester (**5**) *alone* is stable to the



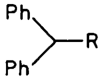
(**15**) R = A (20-*S* configuration)
(**16**) R = OH



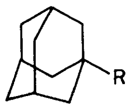
(**17**) R = A
(**18**) R = OH

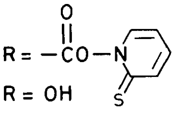


(**19**) R = A
(**20**) R = OH

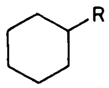


(**21**) R = A
(**22**) R = OH

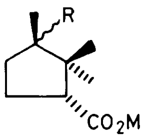




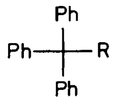
(**23**) R =
(**24**) R = OH



(**25**) R = A
(**26**) R = OH

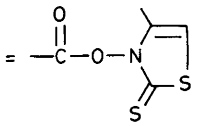


(**27**) R = A(α-configuration)
(**28**) R = OH



(**29**) R = A
(**30**) R = OH

A =



reaction conditions. In contrast to the initial high temperature experiments, practically no sulphide [*e.g.* (**7**)] is produced at room temperature. Yields in alcohol are consequently higher.

For reactions carried out in air, the possibility that some of the carbon radicals are trapped by triplet oxygen (an exceedingly fast reaction[6]) is probable. However, the peroxy radicals produced would react with the antimony reagent, $Sb(SPh)_3$, to give the same intermediate (**10**) and a phenylthiyl radical which would carry the chain (Scheme 3). The production of alcohol is therefore not affected. Appropriate blank experiments showed that the disappearance of the starting ester (**1**) at room temperature was much faster than the rate of diffusion of air into the flask.

$$C_{15}H_{31}^{\bullet} + O_2 \longrightarrow C_{15}H_{31}{-}O{-}O^{\bullet}$$

$$C_{15}H_{31}{-}O{-}O^{\bullet} + Sb(SPh)_3 \longrightarrow C_{15}H_{31}{-}O{-}O{-}Sb(SPh)_3 + {}^{\bullet}SPh$$

Scheme 3

The conversion of carboxylic acids into nor-alcohols by conventional methods involves several steps. We have previously shown[1d] that hydroperoxides (and hence derived alcohols) could be obtained in our carbon radical generating system by interception with triplet oxygen in the presence of a thiol. The reaction that we now report is easier to carry out and better adapted to large scale work.

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