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FORMATION OF QUATERNARY CARBON CENTRES FROM TERTIARY ALCOHOLS BY FREE RADICAL METHODS

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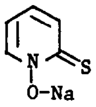
Abstract: The deoxygenation of tertiary alcohols via the radical decomposition of their mixed oxalate esters with N-hydroxypyridine-2-thione in the presence of electron deficient olefins leads to the formation of quaternary carbon centres in reasonable yield.

The formation of carbon-carbon bonds from derivatives of alcohols by free radical pathways is a relatively new synthetic method.[1] To the best of our knowledge the formation of quaternary carbon centres from tertiary alcohols by a free radical pathway is an unknown process.[1]

Tertiary alcohols have been quaternised with both trimethylaluminium[2] and titanium^{IV} reagents.[3] Quaternary carbon centres can be formed in a free radical manner in both the aliphatic[4] and aromatic[5] $S_{RN}1$ reactions as well as by our own decarboxylation proceedures.[6,7] The extension of the method of Giese[8] (treatment of a derived xanthate or thiocarbonylimidazolide with tri-n-butylstannane in the presence of a Michael acceptor) and the method of Keck[9] (reaction of a derived thiocarbonylimidazolide with allyltributylstannane) to tertiary alcohols is barred by the instability of the required thiocarbonylesters. Thioformylated tertiary alcohols would be suitable[10] but we considered that the combination of our recent method for the free radical deoxygenation of tertiary alcohols[11] with either of our two free radical methods for the formation of carbon-carbon bonds[6,7] should result in an easier method for the formation of quaternary carbon centres. Thus the addition of the half oxalate of 1-adamantanol (1 mmol) in benzene to a stirred suspension of reagent 1 (1.2 mmol) and of fumarodinitrile (1.1 mmol) under nitrogen at reflux in benzene resulted, after 1 h, in the formation of the derivative 3 (Table, entry 1) by the known free radical chain mechanism.[7,11] Likewise the radical derived from the half oxalate of tertiary butanol (Table, entry 2) was added to methylacrylate giving the derivative 5.

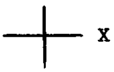
A more efficient and cleaner process was carbethoxyallylation.[7] In chlorobenzene, at reflux, the half oxalate of 1-adamantanol (1 mmol) furnished the 1-adamantyl radical which added efficiently to the olefin 15 (1.5 mmol) with concomitant expulsion of the t-butylthiyl radical (Table, entry 3). As expected[7] t-butyl-2-pyridyldisulphide 17 was also formed. Similarly the half oxalate derived from 3α-methyl-3β-trimethylsilyloxy-5αH-cholestane 7 afforded the product 8 (Table, entry 4) on reaction with reagent 1 and olefin 15 at reflux in chlorobenzene.

Finally we turned our attention to radical allylation. The ready availability of allyl-t-butylsulphide[12], its ease of removal from the reaction mixture[13] as compared to allyltributylstannane and the evident efficiency of the t-butyl thiyl radical as a chain carrier in our systems were the main factors in our choice of this reagent. Indeed the reaction of tertiary alcohol half oxalates (1 mmol) with reagent 1 (1.2 mmol) in the presence of an excess of olefin 16 (Table, entries 5 and 6) resulted in the formation of the allyl compounds 10 and 12.

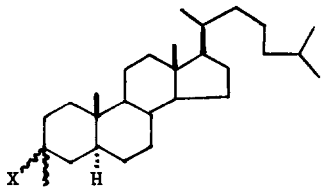


1

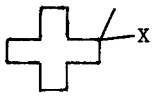
2 X = OH
3 X = CH(CN)CH(CN)-2-pyridylthio
6 X = CH_2-C(=CH_2)CO_2Et



4 X = OH
5 X = $CH_2CH(CO_2CH_3)$-2-pyridylthio
17 X = 2-pyridyldithio



7 X = β-O-Si$(CH_3)_3$
8 X = αβ-CH_2-C(=CH_2)CO_2Et



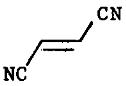
9 X = OH

10 X = $CH_2CH{=}CH_2$

$CH_3(CH_2)_{16}C(CH_3)_2\text{-}X$

11 X = OH

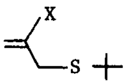
12 X = $CH_2CH{=}CH_2$



13

$CH_2{=}CH\text{-}CO_2CH_3$

14



15 X = CO_2Et

16 X = H

Table

Entry	Substrate	Olefin (eq.)	Products[a,b] (% Yield)
1	2	13 (1,1)	3[c] (32)
2	4	14 (2,2)	5 (32)
3	2	15 (1,5)	6 (53) + 17 (55)
4	7	15 (1,2)	8[c] (52)
5	9	16 (30)	10 (49) + 17 (51)
6	11	16 (15)	12 (54)

a) Products were isolated by chromatography after filtration and concentration to dryness of the crude reaction mixture.

b) All new products gave satisfactory spectroscopical and microanalytical data.

c) Isolated and characterised as a mixture of diastereoisomers.

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13. The excess olefin is simply distilled off together with the reaction solvent in the rotary evaporator.

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