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ON THE STABILITY AND RADICAL DEOXYGENATION OF TERTIARY XANTHATES.

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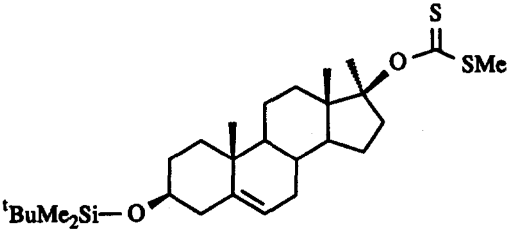
Abstract: Xanthates of tertiary alcohols were isolated and properly characterized. Radical deoxygenation reactions under various conditions to the corresponding alkanes were successfully carried out. Comparative data of various initiatiors and hydrogen atom donors for xanthate deoxygenation are reported.

Since the advent of the Chugaev reaction[1] and more recently the invention of radical deoxygenation[2] of alcohols, *O*-alkyl xanthates have proven to be an invaluable class of compounds for a variety of synthetic transformations.[3] Though there are a plethora of *O*-alkyl xanthates of primary and secondary alcohols reported in the literature[4], xanthates of tertiary alcohols to the best of our knowledge, have seldom been properly characterized. This is in part due to the fact that tertiary xanthates tend to eliminate (to give olefins)[5] or rearrange (to give *S*-alkyl dithiocarbonates)[6] quite readily. Nonetheless, there are few examples of tertiary xanthates reported in the literature.[5,7] However, these derivatives are stable either because they are derived from a bridgehead tertiary hydroxyl group, where the elimination to the corresponding olefin is forbidden, or due to the presence of a stabilizing functional group like an alkoxycarbonyl moiety or high ring strain.

Here, we report the first isolated and stable 'true' tertiary xanthates 1-3 which have been properly characterized. We employed dehydro-*iso*-androsterone 4 to prepare the 17-α-methyl-17-β-hydroxy drivative 5 by first protecting the 3-hydroxyl group using ${}^{t}BuMe_2SiCl$/imidazole to give the silyl ether 6, followed by reaction with $MeCeCl_2$ to give the desired tertiary alcohol 5 in 95% yield. The stereochemistry at 17-C was confirmed to be the β-methyl by comparison of the physical data of 7 with those recorded in the literature.[8]



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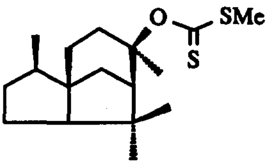

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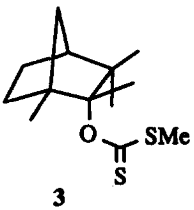

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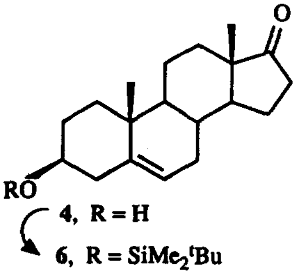
In a typical procedure, the tertiary alcohol was deprotonated using potassium hydride in refluxing THF, followed by the addition of CS_2 at room temp., and methylation with excess iodomethane to give the desired tertiary xanthate. Deprotonation using alkyl lithium or NaH did not give satisfactory yields. The xanthate **1** was obtained in 78% isolated yield from the alcohol **4**, and no olefin (**8** or **9**) formation was observed. When cedrol **10** was subjected to the same conditions, it gave **2** in 84% yield with 7% of olefin formation (**11** and **12**). Similarly, homofenchyl alcohol **13** (readily available from fenchone **14**) gave the corresponding xanthate **3** in 80% yield with 3% of the corresponding olefin (**15**). All these xanthates gave satisfactory spectroscopic data, and **1** also gave a correct elemental analysis.[9]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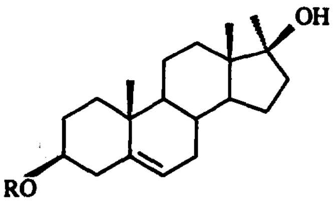
6, R = SiMe$_2{}^t$Bu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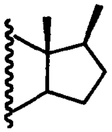
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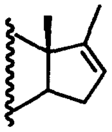
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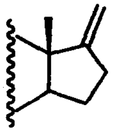
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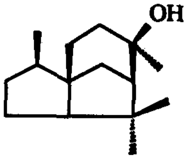
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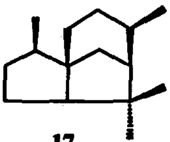
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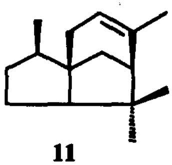
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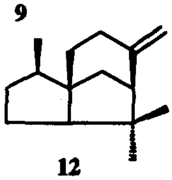
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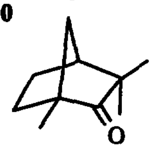
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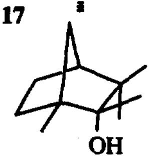
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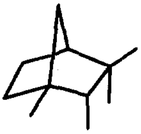
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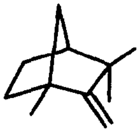
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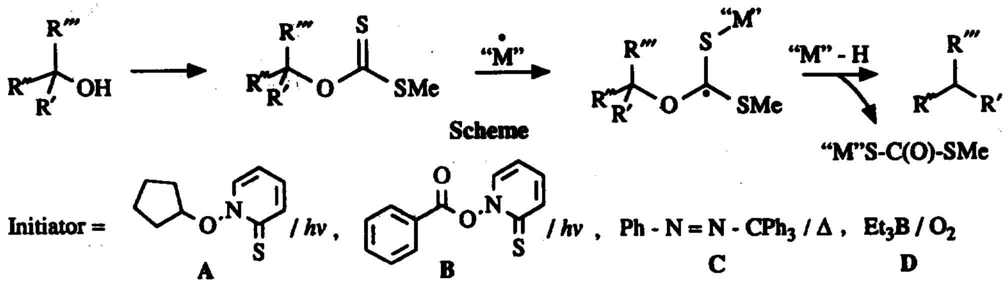
Upon successful isolation and proper characterization of these xanthates, they were subjected to radical deoxygenations using various initiation conditions (**A**-**D**, Scheme) and with different hydrogen atom transfer agents, as depicted in the Scheme. The results of these deoxygenation reactions are reported in the Table.

Though the deoxygenation of **1** to **16**, using thiohydroxamic acid derivatives[3,10] **A** and **B**, worked well (entries 1, 2 and 5; Table); it required large amounts of initiators to complete the reaction. Phenylazotriphenylmethane (PAT) **C**, also gave excellent yields of deoxygenation but, isolation of **16** from the crude reaction mixture proved to be difficult. Triethylborane and molecular oxygen (**D**, Scheme) have been successfully employed as radical initiator both in polymerization reactions[11] and in radical deoxygenations of xanthates.[12] They gave the best results for the radical deoxygenation of tertiary xanthates **1**, **2**, and **3** to the alkanes **16**, **17**, and **18** respectively. Diphenylsilane[13] and diethylphosphite[14] worked well as H-atom transfer agents, however, tributylstannane worked slightly better under these conditions.



Scheme

Table

Entry	Xanthate	Initiator (Scheme) (amt. used)	H-atom transfer agent (amt. used)	Temperature	Yield of deoxygenation (%)
1	1	A (1.5 eq. 3 times)^a	Bu_3SnH (1.5 eq.)	0 °C	83
2	1	B (2 eq. 4 times)^a	Bu_3SnH (1.5 eq.)	0 °C	75
3	1	C (1 eq.)	Bu_3SnH (1.5 eq.)	40 °C	>99 ^{b}
4	1	D (1.5 eq.)	Bu_3SnH (1.5 eq.)	room temp.	91
5	1	A (1 eq. 4 times)^a	Ph_2SiH_2 (3 eq.)	0 °C	64 ^{c}
6	1	D (1.5 eq.)	Ph_2SiH_2 (5 eq.)	room temp.	70 ^{d}
7	1	D (1.1 eq.)	$(EtO)_2P(O)H$ (1.1 eq.)	room temp.	87
8	2	D (1.1 eq.)	Bu_3SnH (1.5 eq.)	room temp.	>99
9	3	D (1.1 eq.)	Bu_3SnH (1.5 eq.)	room temp.	74

[a] Photolysis was carried out using 500 W tungsten Lamp. [b] Yield was calculated on the basis of ^1H NMR. [c] Olefins **8** and **9** were obtained in 24% yields. [d] Olefins **8** and **9** were obtained in 30% yields.

Conclusion

These studies showed that given the use of the proper reaction conditions, xanthates of (nonbridgehead) tertiary alcohols are isolable. Based on these findings and those reported in the literature, it seems that the stability of these tertiary xanthates is substrate dependent. Upon isolation, tertiary xanthates give excellent yields of deoxygenated products without elimination with Et_3B/O_2 and Bu_3SnH.

Acknowledgements: We thank Quest International for financial support.

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9. Xanthate **1** was isolated in 78% overall yield from the alcohol; m.p. 134-136 ^{0}C (dec.); $[\alpha]_D$ = -17.83. Elemental analysis calcd. for $C_{28}H_{48}O_2SiS_2$; C, 66.09, H 9.51; Found, C, 65.88, H 9.57. IR (nujol) ν (cm^{-1}) 2927, 2852, 1459, 1375, 1306, 1247, 1232, 1221, 1142, 1095, 1030. ^{1}H NMR δ: 5.30 (m, 1H), 3.45 (m, 1H), 2.50 (s, 3H), 1.9-1.0 (m, 19H) 1.70 (s, 3H), 1.05 (s, 3H), 0.95 (s, 3H), 0.90 (m, 9H), 0.05 (s, 6H). ^{13}C NMR δ: 213.3, 141.6, 120.7, 100.9, 72.5, 50.1, 48.8, 47.7, 42.7, 37.4, 36.6, 35.6, 32.5, 32.0, 31.8, 31.7, 25.9, 24.2, 20.8, 20.6, 19.4, 19.2, 18.2, 14.7, -4.6. Xanthate **2** was obtained 84% yield. IR (film) ν (cm^{-1}) 2958, 2870, 1273, 1239, 1096, 1081. ^{1}H NMR, δ: 3.1 (d, J = 5.4 Hz, 1H), 2.5 (s, 3H), 2.0-0.95 (m, 12H), 1.8 (s, 3H), 1.1 (s, 3H), 0.98 (s, 3H), 0.85 (s, 3H). ^{13}C NMR δ: 212.5, 97.4, 56.9, 56.4, 53.8, 43.3, 41.1, 36.9, 33.9, 31.4, 28.0, 26.7, 25.3, 25.2, 19.1, 15.5. Xanthate **3** was obtained in 80 % yield. IR (film) ν (cm^{-1}) 2970, 2873, 1455, 1372, 1313, 1238, 1150, 1127, 1070, 1046, 1021. ^{1}H NMR δ: 2.48 (s, 3H), 1.9-1.0 (m, 7H), 1.76 (s, 3H), 1.16 (s, 3H), 1.12 (s, 3H), 1.05 (s, 3H). ^{13}C δ: 214.2, 101.2, 54.5, 50.0, 44.8, 40.4, 28.9, 26.9, 26.1, 23.9, 20.4, 19.6, 17.3.
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