A Novel Lead Tetra-acetate Reaction

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WHILE attempting to functionalise[1] the acetyl moiety of acid[2] (Ia) we had occasion to try the improved method for the α-acetoxylation of ketones described by Cocker *et al.*[3] The methyl ester (Ib) with the $Pb(OAc)_4$–BF_3·Et_2O–MeOH reagent gave the α-acetoxyketo-ester[1] (Ic), as expected. However, when the same reaction conditions were applied to acid (Ia), the expected α-acetoxyketo-acid (Id) was not formed. Instead the α-methoxyketo-acid (Ie) resulted. The structure of (Ie) was

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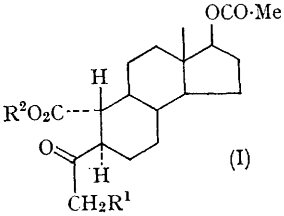
deduced from its analysis and an n.m.r. spectrum of its methyl ester (If). The spectrum exhibited, among other, singlets at 204·5 c./sec. for the ether methyl and at 243·5 c./sec. for the two C-3 protons.

Further exploration of the oxidation by substituting higher alcohols reavealed that the reaction is not confined to methanol. With ethanol the ethoxyketo-acid (Ig) was obtained. Again, the structure was definitely established by a n.m.r. spectrum of the corresponding ester (Ih). Similarly, n-butyl alcohol gave the n-butyl ether (IIa) in a low yield. The butyl product (IIa) was isolated by extensive thin-layer chromatography of the methyl esters and subsequent hydrolysis. When propan-2-ol is used, only a small amount of ether (Ii) is formed. The presence of isopropyl ether (Ii) was indicated by a n.m.r. spectrum which revealed secondary methyl signals and a signal at 247 c./sec. for the C-3 methylene protons.

Though not all the requirements of the ether formation are known, certain aspects have been elucidated. In the absence of either lead tetraacetate or boron trifluoride etherate, no reaction took place. When the 5-ethyl acid (IIb) was treated under the same conditions used for the formation of (Ie), only starting material was recovered. It appears, therefore, that both the carboxylic acid moiety and the ketone group participate in the reaction, as evidenced by the fact that esterification of the acid or removal of the ketone prevents ether formation. It has been also noted that the yield of ether decreases as the alcohol chain becomes larger. The drop in yield seems to parallel the decrease in acidity of boron trifluoride–alcohol complexes.[4,5]

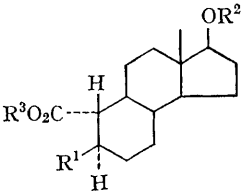
TABLE

Compound	m.p.	Yield, %
(Ia)	230—238°	—
(Ic)	142—146°	68
(Ie)	186—192°	80
(If)	107—108°	—
(Ig)	167—171°	60
(Ih)	101—104°	—
(IIa)	153—156°	*ca.* 25
(IIb)	200—204° (sint.)	—



(I)

a; $R^1 = R^2 = H$
b; $R^1 = H$, $R^2 = Me$
c; $R^1 = OCO{\cdot}Me$, $R^2 = Me$
d; $R^1 = OCO{\cdot}Me$, $R^2 = H$
e; $R^1 = OMe$, $R^2 = H$
f; $R^1 = OMe$, $R^2 = Me$
g; $R^1 = OEt$, $R^2 = H$
h; $R^1 = OEt$, $R^2 = Me$
i; $R^1 = OCHMe_2$, $R^2 = H$



(II)

a; $R^1 = Me[CH_2]_3{\cdot}OCH_2{\cdot}CO{\cdot}$, $R^2 = R^3 = H$
b; $R^1 = Et$, $R^2 = CO{\cdot}Me$, $R^3 = H$

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