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THALLIUM IN ORGANIC SYNTHESIS. XXIV. A ONE-STEP SYNTHESIS OF ALIPHATIC α-ACYLOXY CARBOXYLIC ACIDS[1]

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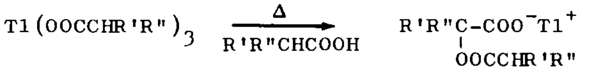
We wish to report that the reaction of thallium(III) acetate with an excess of various aliphatic carboxylic acids results in the direct formation of the corresponding α-acyloxy carboxylic acids, which can be readily hydrolysed to α-hydroxy acids.[2a-e]

It has been noted previously that thallium(III) acetate "decomposes" in boiling acetic acid, but the products have never been identified.[3-6] We have found that the product of this simple reaction is thallium(I) acetoxyacetate, which is formed in 97% yield.[7-9] Furthermore, the reaction of thallium(III) acetate with other aliphatic carboxylic acids proceeds similarly; initial metathesis with an excess of a given carboxylic acid gives the corresponding thallium(III) carboxylate[10-12] and acetic acid (eq. 1), which is readily removed from the reaction mixture by distillation. Then, refluxing (under N_2) the thallium(III) carboxylate in the carboxylic acid as solvent results in conversion to the α-acyloxycarboxylic acid, with concomitant reduction of Tl(III) to Tl(I) (eq. 2).[13] The products were isolated from the reaction mixture by passing in gaseous HCl to precipitate the thallium(I) as TlCl,

$$\mathrm{Tl(OOCCH_3)_3} + 3\ \mathrm{R'R''CHCOOH} \longrightarrow \mathrm{Tl(OOCCHR'R'')_3} + 3\ \mathrm{CH_3COOH} \qquad (1)$$



$$\mathrm{Tl(OOCCHR'R'')_3} \xrightarrow[\mathrm{R'R''CHCOOH}]{\Delta} \mathrm{R'R''}\underset{\mathrm{OOCCHR'R''}}{\underset{|}{\mathrm{C}}}\mathrm{-COO^-Tl^+} \qquad (2)$$

filtering through Celite, and removal of the excess starting carboxylic acid by vacuum distillation. Typical conversions [14,15] are summarised in Table 1.

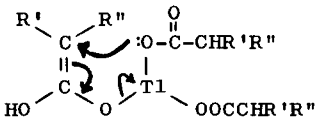
Table 1

Representative Conversions of Carboxylic Acids to α-Acyloxy Carboxylic Acids with $Tl(OOCCH_3)_3$

Starting material[a]	Product	Yield,%[b]
Acetic acid	Acetoxyacetic acid	96[c]
Propionic acid	α-Propionyloxypropionic acid	88
n-Butyric acid	α-*n*-Butyroxy-*n*-butyric acid	81
iso-Butyric acid	α-*iso*-Butyroxy-*iso*-butyric acid	68
n-Valeric acid	α-*n*-Valeroxy-*n*-valeric acid	71
n-Hexanoic acid	α-*n*-Hexanoyloxy-*n*-hexanoic acid	65
Cyclopentane carboxylic acid	α-Cyclopentanoyloxycyclopentane carboxylic acid	27

[a] All acids were redistilled prior to use. [b] Yields were determined by conversion to methyl esters with diazomethane followed by vpc analysis. [c] Compares well with that (97%) determined by isolation of the thallium(I) salt.

We suggest that the conversion of thallium(III) carboxylates to α-acyloxy carboxylic acids on heating may be an intramolecular process involving the enolised carboxylate intermediate 1.[16] Consonant with this suggestion



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is the observation that steric crowding at the α-carbon atom results in lower yields (cf α-*iso*-butyroxy-*iso*-butyric acid (68%) vs. α-*n*-butyroxy-*n*-butyric acid (81%); α-cyclopentanoyloxycyclopentane carboxylic acid (27%)). Further experiments in progress should clarify this point.

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11. Dissolving thallium(III) acetate in an excess of iso-butyric acid, removal of the liberated acetic acid by vacuum distillation, and crystallisation of the thallium(III) *iso*-butyrate from the residual iso-butyric acid gave thallium(III) iso-butyrate identical with an authentic sample.[12]
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13. Completion of the reaction could be judged by observation of a negative starch-iodide test.

14. α-Acyloxy acids may be alternatively prepared, albeit in somewhat lower yields, by heating thallium(III) oxide in the appropriate carboxylic acid (cf acetoxyacetic acid, 83%; α-propionyloxypropionic acid, 63%).
15. Hydrolysis of these α-acyloxy derivatives to the corresponding α-hydroxy derivatives may be conveniently effected via the methyl esters by stirring in methanol containing conc. sulphuric acid; thus, stirring 1.00 g of methyl α-n-butyroxy-n-butyrate in 10 ml of methanol containing 2ml of conc. sulphuric acid yields methyl α-hydroxy-n-butyrate in 78% yield.
16. A cyclic enolic intermediate has been proposed for the alkaline permanganate hydroxylation of alicyclic carboxylic acids (ref. 2c).