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TRIS - TRIMETHYLSILYLOXYETHYLENE: THE CONVERSION OF CARBOXYLIC ACID CHLORIDES TO HYDROXYMETHYLKETONES

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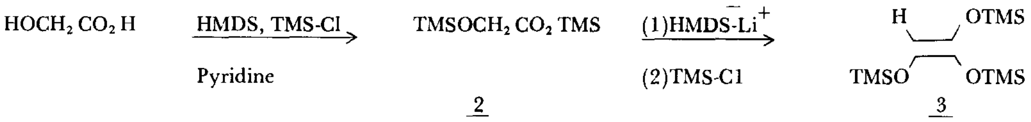
We wish to report a new method to convert carboxylic acid chlorides to terminal hydroxyketones 1 (equation 1). The method involving the reaction of a carboxylic acid chloride with an excess of diazomethane and subsequent

$$\mathrm{RCOCl} \longrightarrow \underset{\underline{1}}{\mathrm{RCOCH_2OH}} \qquad (1)$$

hydrolysis of the resulting diazoketone[1], although satisfactory for the preparation of relatively small quantities of 1, is not amendable to large scale preparations due to the potential hazards associated with the use of large quantities of diazomethane. Consequently, we have developed a new reagent which accomplishes this transformation in good yield under mild conditions.

A report describing the use of ketene dimethyl acetal in the preparation of methylketones[2] and the reported nucleophilicity of silylated ketene acetals[3] suggested that an appropriately functionalized silylated ketene acetal might provide a facile conversion of a carboxylic acid chloride to a hydroxymethylketone. Accordingly, treatment of glycolic acid with 1,1,1,3,3,3 - hexamethyldisilazane (HMDS) followed by the addition of chlorotrimethylsilane (TMS-Cl) gives the bis-silylated derivative 2[4]. Treatment of 2 with lithium 1,1,1,3,3,3-hexamethyldisilazane amide[5] in the THF at -78° and trapping of the resulting enolate with chlorotrimethylsilane gives tris-trimethylsilyloxyethylene(3).



Heating octanoyl chloride and two equivalents of 3 at 90° for 4 hours gives 5 in 75% yield (CMR: $\delta^{\mathrm{CDCl_3}}_{\mathrm{TMS}}$, 166.36(C1), 154.99 (C3), 128.89 (C2), 33.17 (C4), 31.93 (C8), 29.41 (C6) 29.24 (C7), 27.93 (C5), 22.70 (C9), 14.11 (C10), 1.03, 0.69, - 0.01 (TMS's), 2, and chlorotrimethylsilane. This transformation likely involves nucleophilic attach of 3 on the acid chloride to furnish intermediate 4. Silyl transfer and loss HCl (not necessarily concerted) than gives 5. The HCl liberated in the reaction consumes a second equivalent of 3 to give 2 and chlorotrimethylsilane. Treatment of 5 with dilute HCl in THF or dioxane results in an immediate exothermic hydrolysis and decarboxylation to furnish the desired hydroxymethylketone 6 in 89% yield.[6] In practice, 5 need not be isolated; direct hydrolysis-decarboxylation of the reaction mixture gives 6 in 84% yield. It was subsequently observed that this reaction can be efficiently catalyzed by Lewis acids; the reaction of octanoyl chloride and 3 in the presence of a catalytic amount of stannic chloride (exothermic !) followed by direct hydrolysis-decarboxylation of the reaction mixture gives 6 in 90% yield.

Table 1 below illustrates the reaction of 3 with a number of carboxylic acid chlorides under both thermal and catalytic conditions. Of particular significance is the sensitivity of this reaction to steric effects as exemplified by the fact that no reaction occured between 3 and 1-adamantanecarbonyl chloride on heating at 95° for 4.5 hours. Furthermore, on a qualitative basis it appears that less reactive acid chlorides such as aromatic acid chlorides and those which have a secondary β carbon require somewhat longer reaction times.

Tris-Trimethylsilyloxyethylene (3):

To a solution of 118 g (1.55 mol) of glycolic acid in 400 ml of pyridine was added under nitrogen 260g (1.60 mol) of HMDS over 30 min during which time the reaction temperature reached 75° and a slurry formed. To the stirred mixture was added dropwise 88 g (0.80 mol) of TMS-C1. After 1 hour, the mixture was filtered, dissolved in petroleum ether and filtered again. The filtrate was concentrated and distilled (78-80°, 12 mm) giving 275g of 2.

A 275 g (1.25 mol) portion of 2 was added dropwise under nitrogen at -78° to a solution of 1.52 mol of lithium 1,1,1,3,3,3-hexamethyldisilazane amide[5] in 1.21 of THF. After 30 minutes, 205 g (1.9 mol) of TMS-C1 was added dropwise. The solution was allowed to warm to room temperature over 30 minutes, diluted with petroleum ether, and filtered through diatomaceous earth. The solvent was removed in vacuo and the residue was again dissolved in petroleum ether and filtered. The solvent was concentrated and the residue upon distillation (54-56°, 0.1 mm) gave 366 g of 3; PMR: $\delta^{CDCl_3}_{TMS}$, 5.44(s, IH, CH), 0.26, 0.22, 0.18 (ss, 27H, $Si(CH_3)_3$).

1-Hydroxy-2-nonanone(6):

To a stirred mixture of 4.0 g (24.6 mmol) of octanoyl chloride and 15.47 g (53.0 mmol) of 3 was added three drops of $SnCl_4$ (exotherm !). After 1 hour, the mixture was slowly poured into a stirring mixture of 10 ml of 0.6N HCl and 25 ml of dioxane. After gas evolution ceased, the mixture was maintained at 90° for 10 minutes, cooled, saturated with NaCl, and extracted with ether. The solution was washed with saturated $NaHCO_3$

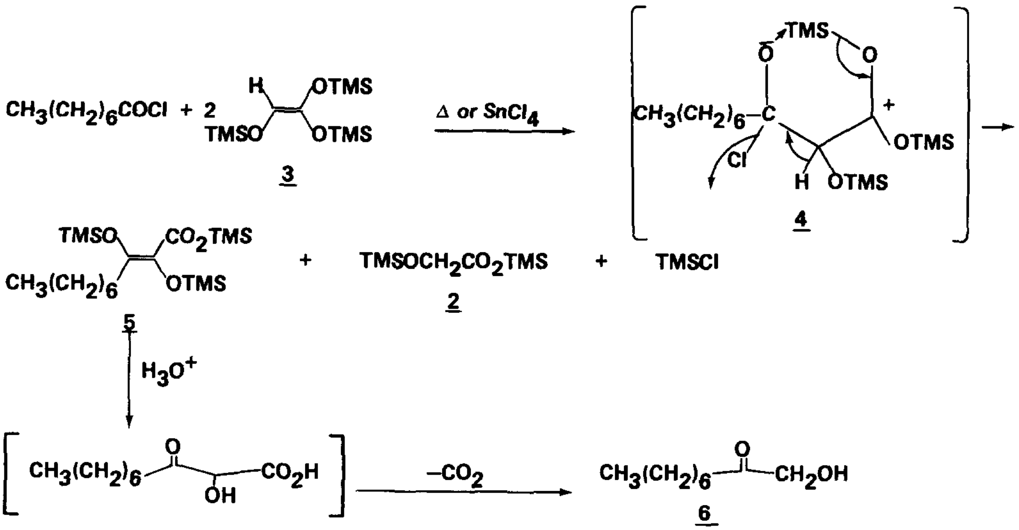
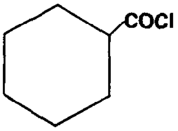
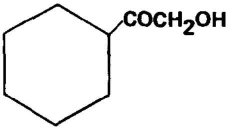
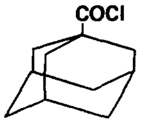
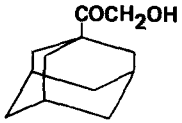


TABLE I. HYDROXYMETHYLKETONES PREPARED.

CARBOXYLIC ACID CHLORIDE	HYDROXYMETHYLKETONE	% YIELD^a
$PhCH_2COCl$	$PhCH_2COCH_2OH$	81(76)
$CH_3(CH_2)_6COCl$	$CH_3(CH_2)_6COCH_2OH$	84(90)
$PhCOCl$	$PhCOCH_2OH$	62
$Br(CH_2)_4COCl$	$Br(CH_2)_4COCH_2OH$	(79)
		71(48)
		b

a. Yields are for purified products; yields in parentheses refer to $SnCl_4$ catalyzed reactions. No attempt was made to optimize individual reaction parameters.

b. No product formation after 4.5 hr at 95°.

and dried ($MgSO_4$). The solvent was removed and the residue was distilled (83-85°, 0.3 mm) giving 3.51 g (90%) of 6.

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6. The absence of any α-hydroxyaldehyde product can presumably be accounted for by an acid catalyzed tautomerzation of the α-hydroxyaldehyde to the hydroxymethyl ketone under the equilibrating conditions of the reaction; see: K. Ogura and G. Tsuschihashi, *Tetrahedron Lett.*, 2681 (1972).