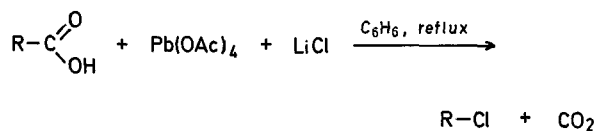


Improved Preparation of Tertiary Chlorides by Halodecarboxylation

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The preparation of chlorides by decarboxylation of carboxylic acids with lead tetraacetate and lithium chloride in refluxing benzene has been described by Kochi¹.



The reaction has been applied especially to the preparation of secondary and tertiary chlorides² in cases where the classical Hunsdiecker reaction³ and its modification by Cristol and Firth⁴ give low yields.

In the preparation of tertiary chlorides by Kochi's procedure two major drawbacks came to light.

- Although good yields may be obtained on a micro or semimicro scale, yields are lowered substantially in large scale work. This is probably due to the low solubility of lithium chloride in benzene.
- Heat sensitive chlorides obtained by Kochi's procedure are contaminated with appreciable amounts of acetates and olefins⁵. These side products are formed either by ionic pathways when the initially formed alkyl radical is not trapped efficiently by chlorine radicals or by decomposition of the chloride when the latter is unstable under the reaction conditions.

Experiments designed to overcome these drawbacks showed that yields can be improved if a 5:1 mixture of dimethylformamide and glacial acetic acid is used as solvent and N-chlorosuccinimide as chlorine donor. Under these conditions, the reaction can be carried out at temperatures as low as 40–55° and is completed in 5–15 min on a 20 mmol scale. Tertiary chlorides are formed in good yields and only

minor impurities are present. Secondary chlorides are also obtained in good yields from secondary carboxylic acids. Primary acids give low yields of primary chlorides, and benzoic acid does not react at all.

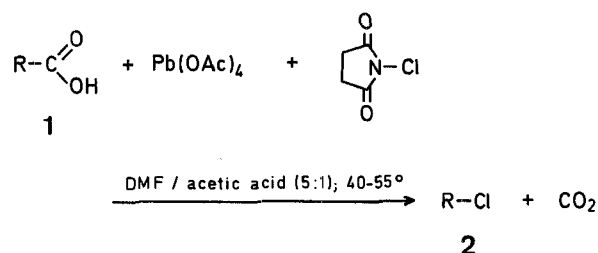


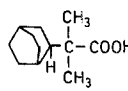
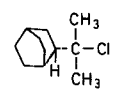






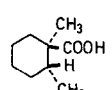
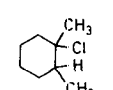
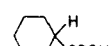

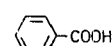



Table. Chlorides from Carboxylic Acids by Reaction with Lead Tetraacetate and N-Chlorosuccinimide in Dimethylformamide/Acetic Acid (5:1)

Acid (1)	Chloride (2)	Yield (%)
		95
		65 ^{a, b}
		85 ^a
	25% <i>cis</i> 75% <i>trans</i>	
		85 ^a
	18% <i>cis</i> 82% <i>trans</i>	
		54 ^c
	95% <i>cis</i> 5% <i>trans</i> ^c	
		81
	46% <i>cis</i> ^d 54% <i>trans</i>	
		83 ^a
$\text{H}_3\text{C}-\text{CH}_2-\underset{\text{COOH}}{\text{CH}}-\text{CH}_2-\text{CH}_3$	$\text{H}_3\text{C}-\text{CH}_2-\underset{\text{Cl}}{\text{CH}}-\text{CH}_2-\text{CH}_3$	61 ^a
$\text{H}_3\text{C}-(\text{CH}_2)_6-\text{CH}_2-\text{COOH}$	$\text{H}_3\text{C}-(\text{CH}_2)_6-\text{CH}_2-\text{Cl}$	30 ^e
$\text{H}_3\text{C}-\underset{\text{CH}_3}{\overset{\text{CH}_3}{\text{C}}}-\text{CH}_2-\text{COOH}$	$\text{H}_3\text{C}-\underset{\text{CH}_3}{\overset{\text{CH}_3}{\text{C}}}-\text{CH}_2-\text{Cl}$	12 ^a
		0

^a Yield after distillation.

^b Contains traces of acetates.

^c Yield after chromatography on aluminium oxide at -10° , contains ~15% olefins. *Trans*-8-chlorohydrindane is partially decomposed to olefins and acetates under the reaction conditions.

^d Methyl group *cis*.

^e Yield after chromatography on silica gel. Extraction with potassium carbonate to remove unreacted acid was omitted.

The Kochi reaction proceeds by a radical pathway^{1,2}. This is especially useful in cases where an ionic pathway would give rise to rearrangement as in the case of 2-(1'-chloro-1'-methylethyl)bicyclo[2.2.2]octane (**2b**), which under ionic conditions forms 2-chloro-2-isopropylbicyclo[2.2.2]octane by a hydride shift⁶. In the decarboxylation of *cis*- and *trans*-9-decalincarboxylic acids (**1c**) and (**1d**), *trans*-9-chlorodecalin is formed preferentially. However, *cis*-1,2-dimethylcyclohexanecarboxylic acid (**1f**) gives *cis*- and *trans*-chlorides (**2f**) in almost equal amounts.

1-Chlorobicyclo[2.2.2]octane:

N-Chlorosuccinimide (18 g, 134 mmol) and bicyclo[2.2.2]octanecarboxylic acid (3.60 g, 23.3 mmol) were dissolved in dimethylformamide and glacial acetic acid (10 ml). The solution was freed of oxygen by repeated evacuation and addition of nitrogen. Lead tetraacetate (10.0 g, 22.5 mmol, stabilized with ca. 15% acetic acid) was added and the reaction mixture again degassed. Warming at 40–50° initiated the exothermic evolution of carbon dioxide which was completed after 5–15 min. The solution was cooled and extracted with several portions of pentane. The pentane extractions were washed with 20% perchloric acid, 10% aqueous potassium carbonate and water, dried over sodium sulfate and distilled. The remaining solid was chromatographically pure 1-chlorobicyclo[2.2.2]octane; yield: 3.20 g (95%); m.p. after sublimation at 70°/12 torr): 103–104° (Lit.⁷ m.p. 103.5–104.5°).

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² For examples see R. D. Stolow, T. W. Giants, *J. Amer. Chem. Soc.* **93**, 3536 (1971); *Tetrahedron Lett.* **1971**, 695; and references therein.

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⁴ S. J. Cristol, W. C. Firth, *J. Org. Chem.* **26**, 280 (1961).

⁵ Compare also E. Ritchie, R. G. Senior, W. C. Taylor, *Austral. J. Chem.* **22**, 2371 (1969).

⁶ H. G. Enderle, Doctoral thesis, Basel 1967.

⁷ F. W. Baker, H. D. Holtz, L. M. Stork, *J. Org. Chem.* **28**, 514 (1963).