Facile One-pot Transformation of Carboxylic Acid Chlorides into 2-Substituted Allyl Alcohols

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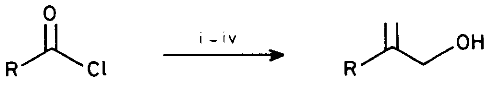
The reaction of carboxylic acid chlorides (**1**) with chloromethyl-lithium generated *in situ* (1 : 2 molar ratio) in the presence of lithium iodide leads, after hydrolysis, to the corresponding homologated 2-substituted allyl alcohols (**2**).

Recently we reported the use of *in situ*-generated chloromethyl-lithium[1] for the preparation of terminal and exocyclic olefins,[2] cyclopropanols,[3] and bifunctionalized organic compounds[4] by reaction with carbonyl compounds and further lithiation. We now report a new methodology for transforming carboxylic acid chlorides into 2-substituted allyl alcohols, using the same carbenoidic precursor.

The successive treatment of several carboxylic acid chlorides (**1**) with a mixture of chloroiodomethane–lithium bromide (1:2 molar ratio) and then with methyl-lithium containing lithium iodide (1:2 molar ratio, prepared from methyl iodide and lithium) at −78 °C leads, after warming, evaporation to dryness *in vacuo* (essential), and final hydrolysis, to the corresponding 2-substituted allyl alcohols (**2**) (Scheme 1, Table 1).



(**1**) (**2**)

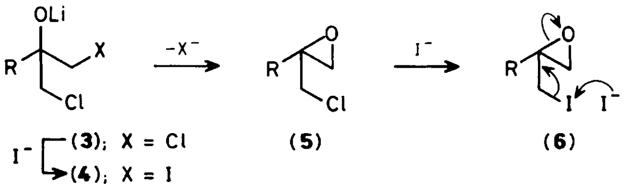
Scheme 1. *Reagents and conditions*: i, 2 $ClCH_2I$–LiBr; ii, 2 MeLi–LiI, −78 °C; iii, −78 to 25 °C, then evaporation; iv, NH_4Cl–H_2O.

Table 1. 2-Substituted allyl alcohols (**2**) from carboxylic acid chlorides (**1**).[a]

R	% Yield[b]	R	% Yield[b]
$CH_2{=}CMe$	57	Bu^t	45
$MeCH{=}CH$[c]	60	Bu^n	75
$\overline{\text{CH}_2\text{CH}_2\text{C}}\text{H}$	70	Ph	85
$\overline{\text{CH}_2[\text{CH}_2]_2\text{C}}\text{H}$	70	$\overline{\text{CH}_2[\text{CH}_2]_4\text{C}}\text{H}$	88

[a] All compounds (**2**) gave satisfactory spectral data (i.r., ^{1}H and ^{13}C n.m.r., and mass spectra). [b] Isolated yield based on the starting carboxylic acid chlorides (**1**). [c] *E* or *Z*.

In the reaction, a stoicheiometric amount of iodine is obtained, the suggested mechanism involving the intermediates (**3**)—(**6**). Thus, after the double addition of chloromethyl-lithium to the starting material (**1**) the intermediate (**3**) is formed,† which, either in this form or *via* the corresponding iodinated derivative (**4**),‡ yields the epichlorhydrin (**5**);§ in the final chlorine–iodine exchange with lithium iodide‡ intermediate (**6**)¶ is formed, which by reaction with iodide** suffers opening of the epoxide yielding after hydrolysis the allylic alcohol (**2**) (Scheme 2).



Scheme 2

In a typical reaction, to a stirred solution of chloroiodomethane (11 mmol), the starting carboxylic acid chloride (**1**) (5 mmol) and lithium bromide (11 mmol) in tetrahydrofuran (thf, 20 ml) was added a diethyl ether solution of methyl-lithium (1 M, 11 mmol, prepared from methyl iodide and lithium) over 15 min at −78 °C under argon. Stirring was continued for 1 h at the same temperature and then the solution was allowed to warm to room temperature. The reaction mixture was evaporated (0.1 mmHg) at 50 °C (bath temperature). The resulting residue was dissolved in hexane (10 ml) and hydrolysed with a saturated aqueous solution of NH_4Cl, extracted with diethyl ether, washed with a saturated aqueous solution of $Na_2S_2O_3$, the ethereal layer dried (Na_2SO_4), and evaporated (15 mmHg). The resulting residue was distilled *in vacuo* to afford the allylic alcohol (**2**).

In conclusion we believe that the methodology described in this communication represents a convenient, rapid, and versatile procedure for the synthesis of allylic alcohols of the type (**2**).

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† The hydrolysis of the reaction mixture after this step leads to the corresponding dichlorohydrin (see reference 3).

‡ Lithium iodide is formed either in the initial preparation of methyl-lithium or in the *in situ* formation of chloromethyl-lithium.

§ In the absence of lithium iodide and for R = Ph, the hydrolysis at this point afforded the compound (**5**) in 90% yield.

¶ The treatment of compound (**5**, R = H) with lithium iodide leads to a mixture of products, (**6**) and 1,3-di-iodopropan-2-ol (4 : 1) (by ^{1}H and ^{13}C n.m.r.).

** The iodide-induced β-elimination from 1,2-chloroiodo compounds has been already described (ref. 5).