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Deacetylation of α–Bromo-α-substituted-acetoacetates

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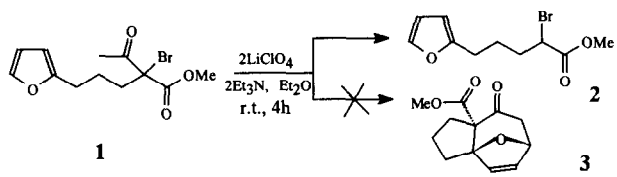
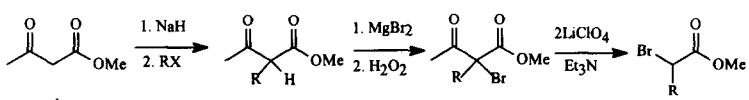
Abstract: A new and efficient method for the deacetylation of α–bromo-α-substituted-acetoacetates to obtain α–bromoesters has been achieved by treatment with $LiClO_4/Et_3N$ in ether at room temperature.

During the course of the study of [4+3] intramolecular cycloaddition, we used α-bromo-α-3-(2-furyl)propylacetoacetate(**1**) as one of the precursors. Under the conditions for the formation of allylic cation (**Scheme 1**), only deacetylated product **2** was obtained instead of the desired [4+3] cycloadduct **3**. It is well-known that the hydrolysis of acetoacetates is readily accompanied with decarboxylation,[1] but the efficient removal of the acetyl group from acetoacetates is rare.[2] α-Bromoesters are versatile intermediates in organic synthesis for the preparation of phosphoranes and phosphonates in Wittig reaction or of α-amino acids and esters. This communication describes a facile method for the preparation of α–bromoesters by means of deacetylation of α–bromo-α-substituted-acetoacetates (**Scheme 2**).



1 **2** **3**

Scheme 1



4 **5** **6** **7**

Scheme 2

Methyl acetoacetate was converted to **5** in high yields by alkylation. The α-methine in **5** was brominated

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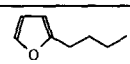
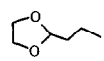
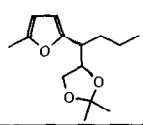
by using $MgBr_2$ in the presence of H_2O_2, affording α-bromides **6** [3] in 72-82% yields. Deacetylation of **6** was achieved by treatment with $LiClO_4/Et_3N$ in ether at room temperature for 4h to obtain α-bromoesters. The reaction sequence in **Scheme 2** offers the possibility for preparation of α-bromoesters containing sensitive functionality in the substituent R to bromine and $Ba(OH)_2$.[2a]

A typical procedure is as follows: Methyl α-bromo-α-3-(2-furyl)propylacetoacetate(**1**) (303mg, 1mmol) was dissolved in freshly distilled ether (20mL), $LiClO_4$ (203mg, 2mmol)and freshly distilled (from CaH_2) triethylamine (0.28mL, 2mmol) were added. The mixture was stirred at room temperature for 4h. The reaction was quenched with H_2O (5mL), and the mixture was extracted with Et_2O (15mL×3). The combined organic layer was washed with H_2O (10mL), brine (10mL), and dried over anhydrous Na_2SO_4. The solvent of the organic layer was removed in vacuum. The residual oil was purified by column chromatography on silica gel(petroleum ether : EtOAc = 20 : 1) to give compound **2** as a colorless oil (215mg) in 83% yield. In order to verify the generality of this reaction, the other five α-bromo-α-substituted-acetoacetates were tested and the yields of the deacetylated products **7** is in a range of 70 ~ 82% (**Table 1**). All the compounds obtained were characterized by ^1H NMR and IR spectra and new compounds were also characterized by MS, HRMS or elemental analysis.

Table 1. Deacetylation of α-bromo-α-substituted-acetoacetate **6**

R		Reaction Time	Product	Yield%
	**1**	4h	**2***	83
	**6a**	6h	**7a**	76
$CH_3(CH_2)_2CH_2$-	**6b**	5h	**7b**	72
	**6c**	4h	**7c***	82
	**6d**	2d	**7d***	70

* New compound

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