Tetrahedron Letters 51 (2010) 5454–5458

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Benzylation of β-dicarbonyl compounds and 4-hydroxycoumarin using TMSOTf catalyst: a simple, mild, and efficient method

Palani Theerthagiri, Appaswami Lalitha *

Department of Chemistry, Periyar University, Salem 636 011, India

ARTICLE INFO

Article history:
Received 25 April 2010
Revised 3 August 2010
Accepted 8 August 2010
Available online 11 August 2010

Keywords:
TMSOTf-catalyzed
Benzylation
Benzylic alcohols
β-Dicarbonyl compounds
4-Hydroxycoumarin

ABSTRACT

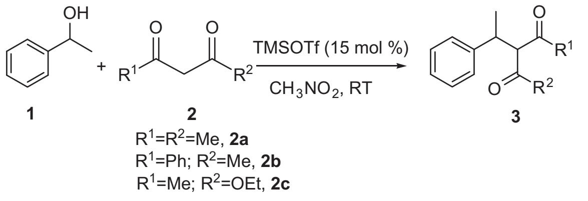
The direct benzylation of 1,3-dicarbonyl compounds and 4-hydroxycoumarin with a wide variety of benzylic alcohols was achieved using trimethylsilyl trifluoromethanesulfonate as an efficient catalyst. The reaction proceeded under very mild conditions at room temperature providing the desired products in good to excellent yields.

The construction of carbon-carbon bonds is one of the fundamental tasks in synthetic organic chemistry.[1] Among the several methods employed to achieve this goal, the alkylation of 1,3-dicarbonyl compounds[2] is found to be one of the best opted. In view of the demand for ecologically valuable processes to avoid large quantities of waste production,[3] the catalytic direct alkylation with unmodified electrophiles such as alcohols, which provides water as the only by-product, would be a suitable alternative. However, the main limitation of this strategy is due to the poor leaving ability of the hydroxyl group. Direct alkylations of 1,3-dicarbonyl compounds with alcohols catalyzed by Pd,[4] Co,[5] Cu,[6] $BF_3 \cdot OEt_2$,[7] $InCl_3$,[8] InBr,[9] $FeCl_3$,[10] $Bi(OTf)$,[11] $Ln(OTf)_3$ [Ln = La, Yb, Sc, Hf],[12] *p*-toluenesulfonic acid,[13] dodecyl benzene sulfonic acid,[14] molecular iodine,[15] PMA/SiO_2,[16] and $B(C_6F_3)_3$[17] have been reported. Alkylation reactions using metal-triflates as heterogeneous catalysts have also been studied.[11] Inspired by this, we developed a new, mild alkylation of 1,3-dicarbonyl compounds with alcohols, where an organic-triflate could be used as a homogeneous catalyst that leads to reduction of the reaction time and practical difficulties of using the heterogeneous catalyst in large-scale experiments. Trimethylsilyl trifluoromethane sulfonate (TMSOTf) has recently been shown to be a versatile reagent in mediating a wide variety of organic transformations such as aldol and Sakurai allylation,[18] bis-silylation,[19] deprotection,[20] and Baylis–Hillman reaction.[21a] As part of our ongoing research program in the development of new synthetic methods of important organic products,[21b] herein we wish to report the use of TMSOTf as a powerful catalyst for the alkylation of β-dicarbonyl compounds with secondary benzylic alcohols that proceeded in good to excellent yields (Scheme 1).

Initially, the reaction of 1-phenylethanol (**1**) with acetyl acetone (**2a**) in the presence of TMSOTf was selected as a model reaction to develop the optimum reaction conditions. The effect of solvents was investigated and it was observed that the rate of the reaction and the yield were highly influenced by the solvent used which may be attributed to the stability of benzylic carbocation and also the stability of the catalyst in the particular solvent.

The reaction of 1-phenylethanol with acetyl acetone in acetonitrile and dichloroethane afforded the product in only moderate yields. However, the corresponding product was obtained in low yields even after 6 h when toluene or tetrahydrofuran was used as the solvent. The best result was achieved in nitromethane, affording the desired product in 92% yield within 30 min at room temperature.

We then turned our attention to optimize the amount of catalyst. The conversion was very slow at room temperature when



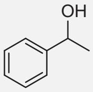
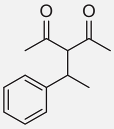
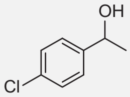
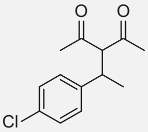
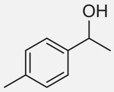
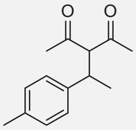
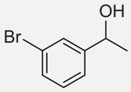
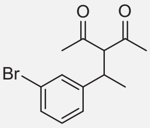
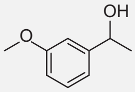
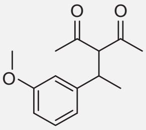
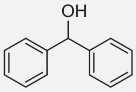
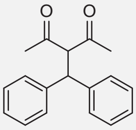
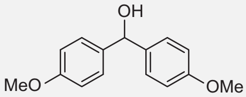
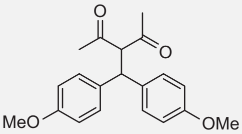
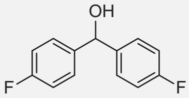
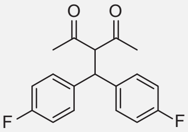
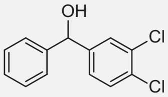
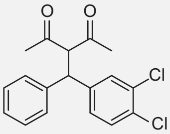
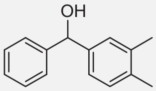
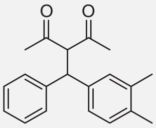
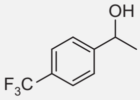
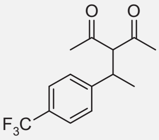
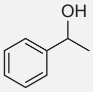
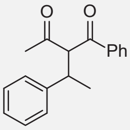
Scheme 1. Benzylation of β-dicarbonyl compound.

---

* Corresponding author. Tel.: +91 427 2345271; fax: +91 427 2345124.
E-mail address: lalitha2531@yahoo.co.in (A. Lalitha).

0040-4039/$ - see front matter © 2010 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2010.08.019

Table 1
TMSOTf-catalyzed alkylation of 1,3-dicarbonyl compounds under the optimum conditions

Entry[a]	Alcohol	Nu-H	Product	Time[b] (h)	Yield[c] (%)
1		**2a**		0.5	85
2		**2a**		0.5	78
3		**2a**		0.5	91
4		**2a**		1.0	67
5		**2a**		0.75	73
6		**2a**		0.5	94
7		**2a**		0.5	96
8		**2a**		0.5	90
9		**2a**		0.75	86
10		**2a**		0.5	88
11		**2a**		1.0	65
12[d]		**2b**		0.5	82

(*continued on next page*)