

Chemo- and diastereoselective Bi(OTf)₃-catalyzed benzylation of silyl nucleophiles

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Abstract

The direct alkylation of silyl enol ethers with *para*-methoxybenzyl alcohols or their corresponding acetates was efficiently catalyzed by Bi(OTf)₃ in CH₃NO₂ as the solvent. The reaction provided the α -benzylated carbonyl compounds in high yields after short reaction times using 1–2.5 mol % of the catalyst. Benzyl acetates other than *para*-methoxybenzyl acetates also underwent the reaction. High facial diastereoselectivities were observed with acetates derived from chiral α -branched *para*-methoxybenzyl alcohols. In addition, a catalytic reduction with Et₃SiH as the reducing agent is reported.

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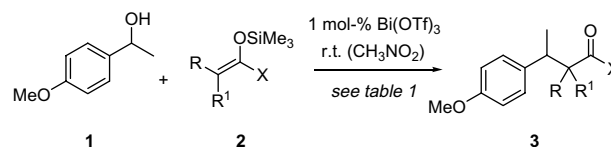
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The counterpart of the conventional enolate alkylation under basic conditions is the acid-promoted alkylation of silyl enol ethers.^{1,2} The latter reaction is most frequently applied to substrates which allow for a facile S_N1-type substitution. Important examples include *tert*-alkylation³ and benzylation⁴ reactions, which have been extensively studied in recent years.² Our interest in the benzylation and more specifically in the methoxybenzylation of silyl enol ethers stems from previous work, in which we studied the Friedel–Crafts alkylation of various arenes with chiral α -branched *para*-methoxybenzyl alcohols.⁵ We envisioned that silyl enol ethers could serve as possible nucleophiles for related reactions under catalytic reaction conditions. It turned out that bismuth tris(trifluoromethanesulfonate) (Bi(OTf)₃) is a very efficient catalyst⁶ for these reactions and we report in this Letter on our preliminary results in this area.

The suitability of Bi(OTf)₃ to activate benzylated alcohols for nucleophilic attack has been demonstrated earlier

by Rueping et al.^{7,8} Given the high temperatures (55–100 °C) required in these benzylation reactions, it was a pleasant surprise to note that the methoxybenzylation of silyl enol ethers can be achieved at ambient temperature in nitromethane as the solvent (Scheme 1, Table 1).

Sterically more congested *para*-methoxyphenyl-1-ethanol (**1**) was used in a first set of experiments as the alkylating agent (instead of the parent methoxybenzylalcohol) to mimic the situation in α -branched *para*-methoxybenzyl alcohols (vide infra). Silyl enol ethers **2** were prepared according to known procedures.⁹ Reactions proceeded smoothly and provided the desired products¹⁰ in high yields (73–96%, entries 1–8). The only exception was observed with the α,α' -disubstituted silyl ketene acetal **2i** (entry 9), which gave only a mediocre result. All reactions

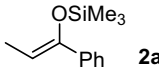
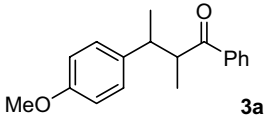
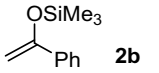
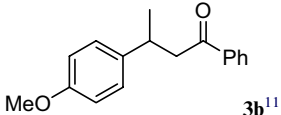
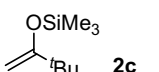
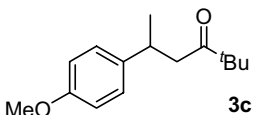
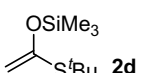
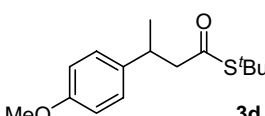
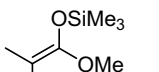
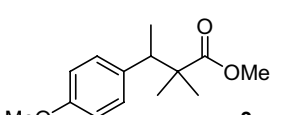
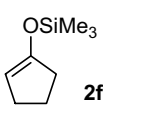
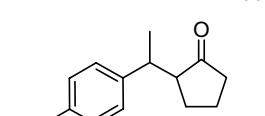
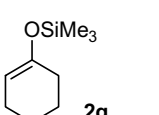
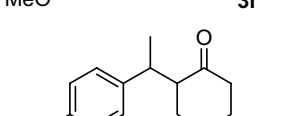
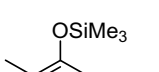
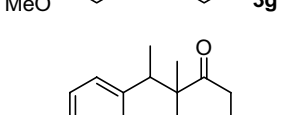
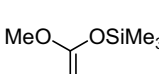
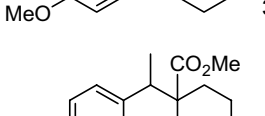


Scheme 1.

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Table 1
Reaction of alcohol **1** with different silyl enol ethers **2** (cf. Scheme 1)

Entry	Enol ether	Product	Time (h)	Yield ^a (%)
1	 2a	 3a	4	89 ^b
2	 2b	 3b ¹¹	3	76
3	 2c	 3c	5	79
4	 2d	 3d	4	77
5	 2e	 3e	4	73
6	 2f	 3f	2	91 ^c
7	 2g	 3g	1	96 ^c
8	 2h	 3h	1	96 ^c
9	 2i	 3i	0.5	48

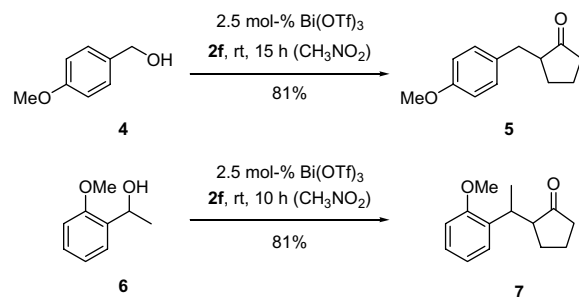
^a Yield of isolated product after column chromatography.

^b Diastomeric ratio (¹H NMR) dr = 69:31.

^c Diastomeric ratio (¹H NMR) dr = 50:50.

were run at room temperature with the initially clear solution becoming slightly turbid after ca. 15 min.

It was shown in a second set of experiments (Scheme 2) with silyl enol ether **2f** as the nucleophile that other methoxybenzylic alcohols can be equally well employed as electrophile precursors. The parent alcohol **4** yielded the substitution product ketone **5**¹² and *ortho*-methoxyphenyl-1-ethanol (**6**) gave with the same silyl nucleophile product **7** (Scheme 2). Yields were high but a larger amount of Bi(OTf)₃ had to be employed for full conversion and reaction times were required to be longer.



Scheme 2.

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