

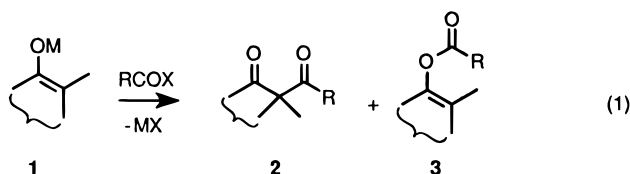
First Catalytic C-Acylation of Enoxysilanes: An Efficient Route to β -Diketones¹

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Acylation reactions are one of the most important group of reactions. The acylation of ketones is one of these. A variety of methods exist in the literature for the synthesis of β -diketones. For example, the reaction of ketone metal enolates with acyl chlorides² or acyl cyanides³ (eq 1, X = Cl, CN), the acylation of enamines,⁴ and the direct BF_3 acylation of ketones⁵ are some reactions which preferentially lead to C-acylated ketones (**2**) usually contaminated with variable amounts of O-acylated products (**3**).



Because of their ease of preparation and stability, silyl enol ethers (**1**, M = SiR₃) derived from ketones have been acylated without any catalyst or promoter. However, the methods reported are restricted to polyhalogenated acid chlorides with complete C-acylation⁶ or to oxalyl and malonyl dichlorides.⁷ Rathke et al. reported the acylation of silyl enol ethers by acetyl tetrafluoroborate⁸ or by acyl chlorides,⁹ the latter reaction being promoted by a stoichiometric amount of Lewis acid, among which zinc chloride and antimony trichloride are the most efficient.

The catalytic acylation of enoxysilanes has been observed in the presence of a heavy metal catalyst such as mercury(II) chloride¹⁰ or tris(dimethylamino)sulfonium difluorotrimethylsilicate ("TASF"),¹¹ but these two methods lead exclusively to O-acylation.

Recently, we reported the catalytic activity, in heterogeneous medium, of bismuth(III) chloride–metallic iodide

Table 1. Reaction of Cyclohexanone Trimethylsilyl Enol Ether with Acetyl Chloride Catalyzed by MCl_n – $n\text{NaI}$ Lewis Acid Systems^a (Eq 2)

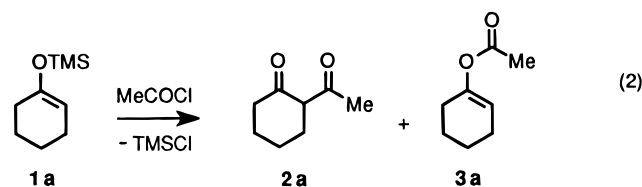
entry	MCl (mol %)	products and yield ^b	
		2a	3a
1	ZnCl ₂ (5)	32	8
2	SbCl ₃ (5)	0	0
3	SbCl ₅ (5)	0	0
4	SnCl ₄ (5)	26	8
5	BiCl ₃ (5)	65	5
6	BiCl ₃ ^c (5)	64	5

^a Solvent $\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}$ (9/1); rt, 1 h. ^b Yields determined by GC analysis. ^c BiCl_3 is added alone without sodium iodide.

systems toward condensation reactions involving enoxysilanes and various electrophiles such as aldehydes, ketones, and α,β -unsaturated ketones.^{12,13} In search of new applications for these heavy metal catalytic systems, we decided to attempt the acylation of enoxysilanes using acyl chlorides as electrophiles.

Results and Discussion

Our previous studies on the dramatic increase in the catalytic activity of bismuth(III) chloride by metallic iodides revealed that a *partial* Cl/I exchange reaction occurs with the concomitant formation of bismuth(III) iodide and the corresponding metallic chloride.¹² We were interested to know if such an activation could be extended to Lewis acids like those reported by Tirpak and Rathke.⁹ Thus, we examined the catalytic activities of some Lewis acid/sodium iodide systems for the acetylation of the enoxysilane derived from cyclohexanone (**1a**) (eq 2) (Table 1, entries 1–5). The study revealed that



activation by sodium iodide is stronger in the case of bismuth(III) chloride than in any other of the Lewis acids tested. However, we found later that the addition of sodium iodide to BiCl_3 was not necessary for the acetylation of the enoxysilane **1a** (see Table 1, entry 6). We also found that sodium chloride and bismuth iodide, formed by halogen exchange between BiCl_3 and NaI ,¹² are not the catalysts for the reaction 2.

In order to extend these results, we carried out other acylations using various enoxysilanes with acetyl chloride and 3-pentanone trimethylsilyl enol ether (**1c**) with various acyl chlorides. The overall yields and the selectivities in C-acylation, summarized in Tables 2 and 3, clearly confirmed the efficiency of these catalysts compared to any other metallic chloride. In particular, note that whereas benzoyl acetone was synthesized in 5% yield using 100 mol % of SbCl_3 ,⁹ only 5 mol % of BiCl_3 – 3NaI raised this yield to 61% (Table 2, entry 4).

We discovered that for less reactive acyl chlorides the addition of zinc iodide (instead of sodium iodide) to

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





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Table 2. Reactions of Trimethylsilyl Enol Ethers with Acetyl Chloride Catalyzed by BiCl₃-3NaI (5 mol %)^a (Eq 1, R = Me, X = Cl)

entry	silyl enol ether	reaction time, min	products and % yield ^b	
			2	3
1	 (1a)	20	2a, 65	3a, 5
2	 (1b)	20	2b, 84	3b, 2
3	 (1c)	40	2c, 88	3c, 3
4	 (1d)	40	2d, 61	3d, 4
5	 (1e)	40	2e, 93	3e, 0
6	 (1f)	60	2f, 92	3f, 2

^a Solvent CH₂Cl₂/Et₂O (9/1). ^b Yields determined by GC analysis.

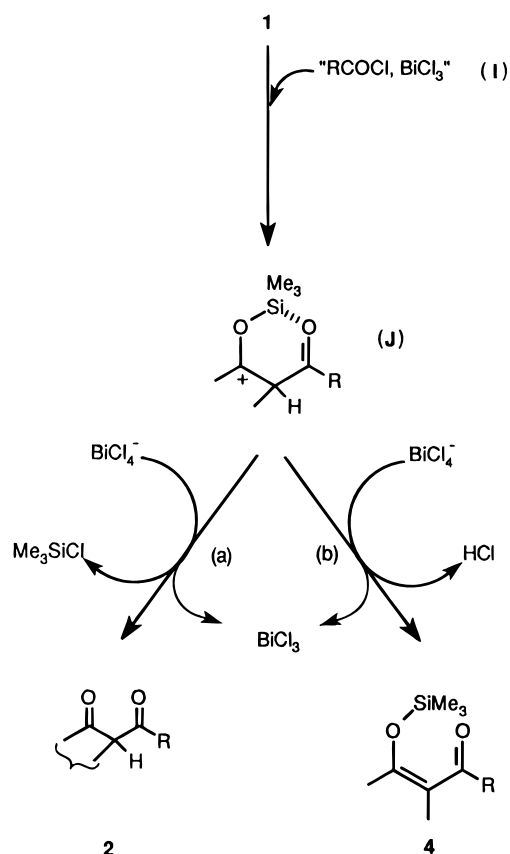
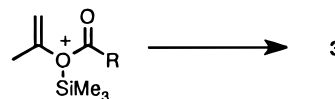
Table 3. Reaction of Acid Chlorides with 3-Pentanone Trimethylsilyl Enol Ether (1c) (Eq 1)^a

entry	R	catalyst ^b	reaction time	product and yield ^c (%)	
				2	3
1	Me	A	20 min	2c, 66	3c, 10
2	Me	B	10 min	2c, 88	3c, 3
3	Et	A	30 min	2g, 65	3g, 3
4	Et	B	20 min	2g, 79	3g, 1
5	<i>i</i> -Pr	A	1 h	2h, 54	3h, 5
6	<i>i</i> -Pr	B	30 min	2h, 84	3h, 2
7	<i>t</i> -Bu	A	10 h	2i, 50	3i, 3
8	<i>t</i> -Bu	B	1 h	2i, 81	3i, 1
9	Ph	A	6 h	2j, 58	3j, 17
10	Ph	B	2 h	2j, 87	3j, 0

^a Solvent CH₂Cl₂/Et₂O (9/1); rt. ^b Catalyst A; BiCl₃ (5 mol %). Catalyst B; BiCl₃-1.5ZnI₂ (5 mol %). ^c Yields determined by GC analysis.

bismuth(III) chloride gave shorter reaction times and higher yields (Table 3; results for BiCl₃-3NaI not reported). Our previous studies on these catalysts have also shown that BiCl₃-1.5ZnI₂ was a more powerful catalyst than BiCl₃-3NaI.^{12,13} This enhancement is directly related to the specific surface of the catalyst,¹² but with the Bi/Zn system, owing to the formation of ZnCl₂, one cannot preclude that the latter plays a minor part in the reaction.

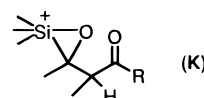
As we do not know the nature of the interaction between BiCl₃ and the acyl chloride, this latter will be represented by "RCOCl-BiCl₃" in our discussion. Our mechanistic proposal (Scheme 1) involves the initial formation of a cationic intermediate **J** resulting from the attack of the complex **I** on the enoxysilane **1**. The intermediate could decompose in a second step through two plausible pathways. In the first route (path a) the β-diketone **2** and the chlorotrimethylsilane are formed after desilylation. The second path (path b) leads to, after deprotonation, the enoxysilane **4**. Our observations before aqueous workup have shown that the β-diketone **2** and chlorotrimethylsilane are formed directly and no enoxysilane **4** is detected by ¹H NMR, and also the acetylation of the enoxysilane derived from isobutyropnone proceeds easily although no proton is available for deprotonation (Table 2, entry 6). This set of observations seems to preclude path b. However, for ketones other

Scheme 1**Scheme 2**

than isobutyropnone, deprotonation may partially contribute to the overall process and this could explain the presence of variable amounts of the starting ketone in the final mixture (before workup) resulting from the protidesilylation of the ketone enol silane by HCl. One cannot also preclude that such a protidesilylation might lead to the diketone from the enoxysilane **4**. Another plausible mechanism involves a concerted electronic process (not shown).

Our results also indicate that C-acylation is preferred over O-acylation. This high regioselectivity can be rationalized by examining the stabilities of the two possible intermediates: the carbocation intermediate **J**, which is the result of C-acylation, and the oxonium intermediate (Scheme 2) resulting from O-acylation. We propose that an anchimeric assistance between silicon and the oxygen of the carbonyl group might be responsible for an additional stability of the intermediate **J** by leading to a six-membered ring carbocation.¹⁴ A similar assistance has previously been postulated for the halogenation of β-silyloxy carbonyl compounds.¹⁵

(14) As suggested by a referee the assistance of the silicon to stabilize the cationic intermediate would be also described in **K**, although silicon is known to stabilize positive charges at the beta position through hyperconjugation. However, the intermediate **K** would explain the selective desilylation in our mechanism.



Concerning the activation of bismuth(III) chloride by metallic iodides, this activation might be due to the formation of the very reactive mixed bismuth(III) halides, BiCl_2I or BiClI_2 , resulting from the disintegration of the crystal lattice of BiCl_3 by NaI or ZnI_2 . Other mechanisms are also plausible, as for example the "in situ" formation of an acyl iodide in the catalytic cycle. In effect, an acyl chloride can be converted to an acyl iodide by a metallic iodide,¹⁶ and such a conversion might be realized by one of the mixed bismuth(III) halide mentioned above and/or by NaI or ZnI_2 .

Conclusion

Bismuth(III) chloride–metallic iodide systems are the first catalysts for the C-acylation of enoxysilanes. In almost all cases studied, reactions proceed rapidly at room temperature with excellent regioselectivity and yields. These catalysts are inexpensive and have low toxicity.¹⁷ Moreover, it seems that the metallic iodide activation observed might be extended to other metallic chlorides leading to the possible modulation of Lewis acid strength. An understanding of the mechanism of this reaction and a search for the active species are currently underway. Attempts to apply these catalysts to the acylation of other organosilanes are now in progress.

Experimental Section

General. Dichloromethane and ether were purified using known procedures.¹⁸ Bismuth(III) chloride, metallic iodides, and acyl chlorides were purchased and used without further purification. All transfer of bismuth(III) chloride and metallic iodides were done in a glovebag under argon. Ketone silyl enol

ethers and acyl chlorides were added by syringe. Silyl enol ethers were prepared from the corresponding ketone by reaction with trimethylchlorosilane, triethylamine, and sodium iodide in acetonitrile according to the procedure described by Dunoguès and co-workers.¹⁹

All product yields were determined by GC analysis with *n*-alkanes as internal standards.

Typical Procedure. 1-Phenyl-2-methyl-1,3-butanedione²⁰ (**2e**, Table 2, entry 5). Bismuth(III) chloride (158 mg, 0.5 mmol) and sodium iodide (225 mg, 1.5 mmol) were transferred under argon to a flame-dried 50 mL flask equipped with a septum inlet and magnetic stir bar. The flask was removed from the glovebag and connected to an argon line, and 10 mL of a mixture of dichloromethane/ether (9/1) was added by a syringe. This was followed by the addition of acetyl chloride (860 mg, 11 mmol), and the suspension was stirred for 5 min at room temperature. Then, propiophenone silyl enol ether (2 g, 10 mmol) in 2 mL of the same solvent mixture was added all at once under rapid stirring. The reaction was monitored by following the formation of chlorotrimethylsilane (¹H NMR). After 40 min at ambient temperature, the reaction mixture was quenched with 40 mL of a saturated sodium hydrogen carbonate solution. The layers were separated, and the aqueous layer was washed three times with 10 mL of dichloromethane. The organic layers were combined, dried over sodium sulfate, and analyzed by GC. The organic layer was concentrated under reduced pressure and analyzed by ¹H NMR and IR. Spectral analyses clearly indicated the presence of 1-phenyl-2-methyl-1,3-butanedione as the major component of the crude mixture: ¹H NMR (CDCl_3) δ 1.32 (d, 3H, $J = 7$ Hz), 2.05 (s, 3H), 4.43 (q, 1H, $J = 7$ Hz), 7.3–7.5 (m, 3H), 7.8–8 (m, 2H); IR (neat) 1720 and 1678 (C=O), 1596 cm^{-1} (C=C, enol form).

All other compounds synthesized had spectra identical to those previously reported.⁹

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