

Silica-Supported Antimony(III) Chloride as an Efficient Heterogeneous Catalyst for the Synthesis of Aminopropenones and 3-Aminopropenoates under Solvent-Free Conditions*

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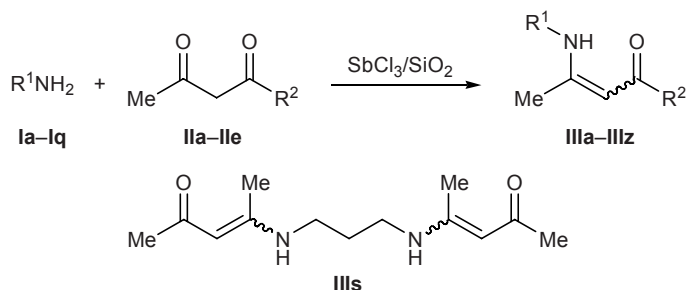
Abstract—A convenient and efficient procedure has been developed for the synthesis of 3-aminoprop-2-en-1-ones and 3-aminoprop-2-enoates catalyzed by silica-supported antimony(III) chloride at room temperature under solvent-free conditions. The reaction takes a short time and ensures good to excellent yields of the products. Both aromatic and aliphatic amines and various 1,3-dicarbonyl compounds, including β -ketoesters and β -diketones, can be involved.

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3-Aminoprop-2-en-1-one derivatives which are also known as β -enaminones are very useful components of natural products and versatile precursors for the preparation of pharmaceuticals [1–3]. Because of this significant position of these compounds, numerous methods have been reported for the preparation of β -enaminone derivatives [4–6]. Among these, the reaction of 1,3-dicarbonyl compounds with amines is one of the simplest and most straightforward approaches. This method usually requires removal of water as azeotrope with an aromatic solvent using a Dean–Stark trap [7]. Recently, some synthetic methods have been reported, including the use of Lewis acids such as $\text{Zn}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$ [8], $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}$ [9], NaAuCl_4

[10], $\text{Bi}(\text{OTf})_3$ [11], $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$ [12], CAN [13, 14], $\text{Yb}(\text{OTf})_3$ [15, 16], $\text{SnCl}_4 \cdot 5\text{H}_2\text{O}$ [17], ZrCl_4 [18], $\text{ZrOCl}_2 \cdot 8\text{H}_2\text{O}$ [19], CuBr_2 [20], $\text{Sc}(\text{OTf})_3$ [21], I_2 [22], and InBr_3 [23], solid acids such as montmorillonite K10 [24], silica chloride [25], silica gel [26], natural clays [27], $\text{HClO}_4/\text{SiO}_2$ [28], and sulfated zirconia [29], to improve and modify this reaction. Occasionally, the reaction can be performed in the absence of catalysts using ionic liquid [30] or water [31] as reaction medium or under ultrasound irradiation [32]. However, some of the reported methods are not free from such drawbacks as long reaction time, unsatisfactory yield, harsh reaction conditions, and the necessity of using excess reagents or catalyst. There-

Scheme 1.



* The text was submitted by the authors in English.

fore, it is important to develop more convenient methods for the synthesis of β -enaminone derivatives.

Antimony trichloride has recently attracted attention due to its accessibility as inexpensive commercial reagent and easier handling as compared to other metal halides, e.g., InCl_3 , GdCl_3 , and TiCl_4 [33]. It was reported to catalyze various organic transformations, including conversion of epoxides into β -hydroperoxy alcohols [34], selective cleavage of trityl [35] and silyl ethers [36], Knoevenagel condensation [37], synthesis of 9-aryl-3,4,5,6,7,9-hexahydroanthene-1,8-diones [38], pyrano- and furanoquinoline derivatives [33, 39], dihydropyrimidinones [40], and bis(indolyl)methanes [41], Michael addition of indoles to α,β -unsaturated ketones [42], ring opening of epoxides [43], and Biginelli reaction [44]. The use of silica-supported reagents as recoverable and reusable catalysts in organic synthesis has received considerable attention [45]. In continuation of our studies on the applications of Lewis acids as catalysts in the development of new synthetic methodologies [46, 47], in the present communication we report a novel and efficient solvent-free procedure for the preparation of 3-aminoprop-2-en-1-ones and 3-aminoprop-2-enoates using silica-supported SbCl_3 as heterogeneous catalyst (Scheme 1).

Initially, a systematic study was carried out to evaluate the efficiency of this catalyst in a model reaction of ethyl acetoacetate (10 mmol) with aniline (10 mmol). The reaction was complete within 1 h in the presence of 0.5 mmol (5 mol %) of $\text{SbCl}_3/\text{SiO}_2$ under solvent-free condition at room temperature. Increase in the amount of the catalyst did not enhance the yield, but the use of smaller amount of the catalyst led to lower yield and longer reaction time. Only 30% of the product was obtained even after stirring for 24 h in the absence of catalyst. The solvent-free procedure is more advantageous than the use of solvents such as acetonitrile, ethanol, methylene chloride, ethyl acetate, or dimethylformamide in terms of the reaction time and yield. We also found that silica-supported SbCl_3 ensured higher yield than did SbCl_3 alone.

Following the developed procedure, a number of 3-aminoprop-2-en-1-ones and 3-aminoprop-2-enoates were prepared in good to excellent yields (see table). The results indicated general character of the proposed method which was efficient for the synthesis of not only β -diketones but also β -ketoesters. As a rule, primary aliphatic amines and benzylamines reacted with a broad range of structurally diverse 1,3-dicarbonyl compounds to afford the corresponding 3-amino-

Synthesis of 3-aminoprop-2-en-1-ones and 3-aminoprop-2-enoates **IIIa–IIIz** in the presence of $\text{SbCl}_3/\text{SiO}_2$

Comp. no.	R ¹	R ²	Time, min	Yield, %
IIIa	Bu	OEt	20	93
IIIb	Bu	OBzl	22	92
IIIc	Ph	OEt	20	94
IIId	$\text{H}_2\text{C}=\text{CHCH}_2$	OEt	18	93
IIIe	(<i>R</i>)-PhCH(Me)	OEt	20	90
IIIf	PhCH ₂	OEt	22	95
IIIg	PhCH ₂	OBzl	25	92
IIIh	Ph	OEt	60	95
IIIi	Ph	OBzl	60	92
IIIj	4-MeC ₆ H ₄	OMe	50	95
IIIk	4-EtOC ₆ H ₄	OEt	50	93
IIIl	4-(<i>i</i> -Pr)C ₆ H ₄	OEt	55	92
IIIm	2,4-F ₂ C ₆ H ₃	OEt	120	85
IIIo	2,6-(<i>i</i> -Pr) ₂ C ₆ H ₃	OEt	360	72
IIIp	4-Br-C ₆ H ₄	OEt	360	73
IIIq	2-Furyl	OEt	60	90
IIIr	Bu	Me	15	93
IIIr	$\text{H}_2\text{C}=\text{CHCH}_2$	Me	15	95
IIIs	$\text{H}_2\text{NCH}_2\text{CH}_2\text{CH}_2$	Me	15	93
IIIt	PhCH ₂ CH ₂	Me	15	91
IIIu	PhCH(Me)	Me	18	80
IIIv	Ph	Me	20	92
IIIw	4-MeC ₆ H ₄	Me	20	93
IIIx	2-EtOC ₆ H ₄	Me	50	81
IIIy	Ph	Ph	120	75
IIIz	4-EtOC ₆ H ₄	Ph	120	80

prop-2-en-1-ones and 3-aminoprop-2-enoates in high yields and in short time. Furthermore, the reaction was highly regioselective, and no by-products were detected. The reactions with 4-bromoaniline (**Io**) having an electron-withdrawing group was slower, and the yield was lower. Prolonged reaction time was necessary to obtain the corresponding product from sterically hindered 2,6-diisopropylphenylamine (**In**) in 72% yield. Optically active (*R*)-(+)- α -methylbenzylamine (**Ie**) was converted into the corresponding β -enaminoester (**IIIe**) without racemization or inversion, which was confirmed by measuring the optical rotation. Two equivalents of acetylacetone were used in the reaction with propane-1,3-diamine (**Is**), and the product was bis-enaminone (**IIIIs**). It should be emphasized that unsymmetrical 1,3-diketones, such as 1-phenylbutane-

1,3-dione, reacted with amines to give exclusively the product in which the double bond was adjacent to the methyl group (**IIIy** and **IIIz**).

We also examined the possibility for recycling the catalyst in the above model reaction. When the reaction was complete, ethyl acetate was added to the reaction mixture, the mixture was stirred, and the catalyst was filtered off, washed with ethyl acetate, and activated by heating for 2 h at 110°C. The recovered catalyst was used in another reaction with the same substrates without significant loss of activity after two cycles.

We can conclude that the proposed procedure for the synthesis of 3-aminoprop-2-en-1-ones and 3-aminoprop-2-enoates by condensation of 1,3-dicarbonyl compounds with amines in the presence of silica-supported antimony(III) chloride under solvent-free conditions is very promising due to its general character, experimental simplicity, clean reaction, convenient workup, and the possibility for reusing the catalyst.

EXPERIMENTAL

The IR spectra were recorded on a Bio-Rad FTS 135 spectrometer. The ¹H NMR spectra were recorded on a Bruker AV 300 spectrometer from solutions in CDCl₃ using TMS as internal standard. The elemental compositions were determined on a Vario EL III CHNOS Analyzer.

Silica-supported antimony(III) chloride. Antimony(III) chloride, 2.28 g (10 mmol), was dissolved in 100 ml of distilled ethanol, 60 g of silica (300–400 mesh) was added, and the mixture was stirred for 1 h at room temperature. The solvent was removed on a rotary evaporator, and the residue was heated for 5 h at 110°C under reduced pressure to obtain SbCl₃/SiO₂ as a free-flowing powder.

Typical procedure for the synthesis of 3-aminoprop-2-en-1-ones and 3-aminoprop-2-enoates. A mixture of 1.30 g (10 mmol) of ethyl acetoacetate, 0.93 g (10 mmol) of aniline, and 3.1 g (0.5 mmol) of SbCl₃/SiO₂ was stirred at room temperature, the progress of the reaction being monitored by TLC. When the reaction was complete, the mixture was treated with three 10-ml portions of ethyl acetate and stirred, and the catalyst was filtered off. The combined organic extracts were washed twice with water, dried over anhydrous Na₂SO₄, and concentrated under reduced pressure, and the residue was purified by column chromatography on silica gel using a 20% solution of ethyl acetate in *n*-hexane as eluent to isolate 1.95 g (95%) of

pure ethyl 3-phenylaminobut-2-enoate. The catalyst was repeatedly washed with diethyl ether and reused.

Compounds **IIIa** [29], **IIIc–IIIf** [23], **IIIh** [23], **IIIi** [20], **IIIj–IIIl** [23], **IIIo** [23], **IIIp** [13], and **IIIq–IIIz** [23] were reported previously; they were identified by comparing their spectral data with those reported in the literature. The spectral and analytical data for the newly synthesized compounds are given below.

Benzyl 3-butylaminobut-2-enoate (IIIb). IR spectrum, ν , cm⁻¹: 3238, 3056, 1618, 1581, 1509, 1323, 1265, 1135, 1082, 965. ¹H NMR spectrum, δ , ppm: 0.96 t (3H, *J* = 7.2 Hz), 1.36–1.46 m (2H), 1.50–1.62 m (2H), 1.90 s (3H), 3.18 q (2H, *J* = 7.2 Hz), 3.40 s (1H), 5.03 s (2H), 7.23–7.32 m (5H), 8.55 br.s (1H, NH). Found, %: C 72.62; H 8.75; N 5.88. C₁₅H₂₁NO₂. Calculated, %: C 72.84; H 8.56; N 5.66.

Benzyl 3-benzylaminobut-2-enoate (IIIg). IR spectrum, ν , cm⁻¹: 3275, 3066, 1635, 1608, 1506, 1380, 1250, 1170, 1055, 968. ¹H NMR spectrum, δ , ppm: 1.92 s (3H), 4.40 d (2H, *J* = 5.2 Hz), 5.06 s (1H), 5.18 s (2H), 7.22–7.42 m (10H), 8.95 br.s (1H). Found, %: C 76.60; H 7.02; N 5.18. C₁₈H₁₉NO₂. Calculated, %: C 76.84; H 6.81; N 4.98.

Ethyl 3-(2,4-difluorophenylamino)but-2-enoate (IIIh). IR spectrum, ν , cm⁻¹: 3258, 3084, 1658, 1622, 1516, 1481, 1261, 1142, 1097, 1058, 1020, 939. ¹H NMR spectrum, δ , ppm: 1.28 t (3H, *J* = 7.2 Hz), 1.88 s (3H), 4.16 q (2H, *J* = 7.2 Hz), 4.77 s (1H), 6.68–6.92 m (2H), 7.10–7.18 m (1H), 10.01 br.s (1H, NH). Found, %: C 56.95; H 5.72; N 6.06. C₁₂H₁₃F₂NO₂. Calculated, %: C 59.75; H 5.43; N 5.81.

Ethyl 3-(furan-2-ylamino)but-2-enoate (IIIi). IR spectrum, ν , cm⁻¹: 3382, 2931, 1651, 1614, 1514, 1485, 1384, 1263, 1163, 1024, 948. ¹H NMR spectrum, δ , ppm: 1.23 t (3H, *J* = 7.2 Hz), 1.99 s (3H), 4.08 q (2H, *J* = 7.2 Hz), 4.52 s (1H), 6.19 d.d (1H, *J* = 3.3, 0.6 Hz), 6.31 d.d (1H, *J* = 3.3, 1.8 Hz), 7.35 d.d (1H, *J* = 1.8, 0.6 Hz), 8.80 br.s (1H, NH). Found, %: C 61.35; H 6.98; N 6.95. C₁₀H₁₃NO₃. Calculated, %: C 61.53; H 6.71; N 7.18.

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