

SbCl₅-SiO₂: an efficient reagent system for regio- chemo- and stereoselective claisen-schmidt condensation

Bahareh Sadeghi* and Mohammad Baradaran

Department of Chemistry, Islamic Azad University, Yazd Branch, P.O.Box 89195-155, Yazd, Iran.

Abstract: Silica supported antimony pentachlorid (SbCl₅.SiO₂) as a mild solid acid catalyst is applied to regio-, chemo- and stereoselective Claisen Schmidt condensation under solvent free conditions in 40-50 °C. The procedure is very simple and the products are isolated with an easy workup in good-to-excellent yields.

Keywords: Claisen-Schmidt condensation; Silica supported antimony pentachlorid; Solvent free conditions; Aldehydes; Ketones.

Introduction

In the Claisen Schmidt condensation, as a kind of crossed aldol condensation, an aromatic aldehyde combines with alkyl ketones or aldehyde to form a β-hydroxyl ketone, which is easily dehydrated to form an α,β-unsaturated ketone. Note that dehydration is especially favorable because the resulting enone is also conjugated with the aromatic ring. The resulting α,β-unsaturated ketones are useful intermediates for a large variety of compounds. Mixed or crossed aldol condensation is an effective pathway for the preparation of α,α-bis(substituted benzylidene) cycloalkanones as precursors for the synthesis of bioactive pyrimidine derivatives or nikkomyicine.

Aldol condensation can be catalyzed by acids, bases, organometallic compounds or metal ions such as Mg(HSO₄)₂ [1], TiCl₃(SO₃CF₃) [2], silica sulfuric acid [3], CsOH/SiO₂ [4], V₂O₅-P₂O₅ [5], RuCl₃ [6], LiClO₄ [7], TiCl₄ [8], ZrO₂/SO₄²⁻ [9], Cu(OTf)₂ [10], Mg/Al mixed oxides [11], [Cp*Rh(η⁶-C₆H₆)](BF₄)₂ [12], proline-TEA [13], FeCl₃.6H₂O [14], ZrCl₄ [15], LiOH.H₂O [16], I₂ [17], acid-base functionalized catalyst [18] and acyclic acidic ionic liquids [19].

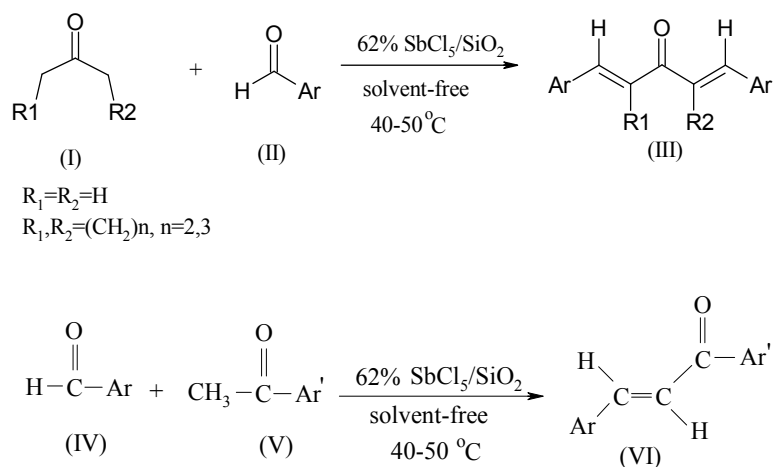
Antimony pentachlorid (SbCl₅), a thin, colored and fuming liquid, is used in industry and organic synthesis. Since, Antimony pentachloride is a liquid with a high specific gravity that fumes in air and reacts

with the moisture to form HCl, The handling and the usability of SbCl₅ as a liquid form is laborious and the supported form is indeed preferable. It has been claimed that the supported SbCl₅ is a solid superacid. SbCl₅ is used extensively in organic synthesis as a Lewis acid for enhancing a variety of organic reactions such as the Friedel-Craft alkylation [20], electrophilic additions to alkenes and 1,3-dienes [21] and aromatization of enamines [22]. In the present research, we wish to describe a mild and efficient approach for the Claisen Schmidt condensation using a catalytic amount of SbCl₅ as a Lewis acid catalyst (Scheme 1).

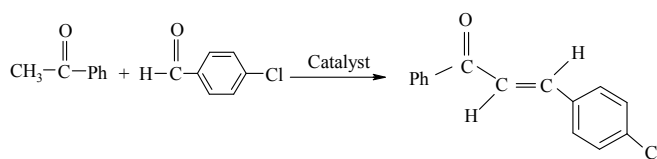
Results and Discussion

In continuation of our investigation about application of solid acids in organic synthesis [23, 24], we investigated the Claisen Schmidt condensation reaction in the presence of various available Lewis acids. The reaction has performed in organic solvents under thermal or reflux but solvent free condition was especially suitable for providing eco-friendly system. The results have shown that the 62% SbCl₅/SiO₂ (10 mol%) was the best catalyst for this reaction (Table 1).

*Corresponding author. Tel: +(98) 351 8211391-9; Fax: +(98) 351 8214810; E-Mail: bsadeghia@gmail.com



Scheme 1.

Table 1. Claisen Schmidt condensation of acetophenone and 4-chlorobenzaldehyde in different acidic media

Entry	catalyst	Condition/solvent	Yield(%) ^a
1	FeCl ₃ (10 mol%)	40-50 °C/-	34
2	AlCl ₃ (10 mol%)	40-50 °C/-	30
3	ZnCl ₂ (10 mol%)	40-50 °C/-	27
4	SnCl ₄ (10 mol%)	40-50 °C/-	35
5	SbCl ₅ (10 mol%)	40-50 °C/-	45
6	BF ₃ ·Et ₂ O (10 mol%)	40-50 °C/-	38
7	31% SbCl ₅ / SiO ₂ (5 mol%)	40-50 °C/-	52
8	31% SbCl ₅ / SiO ₂ (10 mol%)	40-50 °C/-	60
9	48% SbCl ₅ /SiO ₂ (8 mol%)	40-50 °C/-	72
10	48% SbCl ₅ /SiO ₂ (11 mol%)	40-50 °C/-	83
11	62% SbCl ₅ /SiO ₂ (10 mol%)	40-50 °C/-	91
12	62% SbCl ₅ /SiO ₂ (10 mol%)	Reflux/ <i>n</i> -Hexane	85
13	62% SbCl ₅ /SiO ₂ (10 mol%)	Reflux/HOAc	86
14	62% SbCl ₅ /SiO ₂ (10 mol%)	Reflux/EtOH	81
15	62% SbCl ₅ /TiO ₂ (10 mol%)	40-50 °C/-	57
16	62% SbCl ₅ /ZrO ₂ (10 mol%)	40-50 °C/-	44
17	62% SbCl ₅ /Al ₂ O ₃ (10 mol%)	40-50 °C/-	68

a) Isolated yield

The best condition for this reaction was solvent free in 40-50 °C and the best ratio of aldehyde (mmol): 62% SbCl₅/SiO₂ (g) was 1:0.05. Therefore, some aldehydes and ketones were subjected to Claisen Schmidt condensation (Scheme 1 and Table 2). The results have

shown that the reactions were completed within 25-60 min and α,β-unsaturated carbonyl compounds were obtained with good-to-excellent yields (72-90%) without any self-condensation products.

Table 2. Claisen Schmidt condensation promoted 62% SbCl₅/SiO₂ under solvent-free condition in 40-50 °C^a

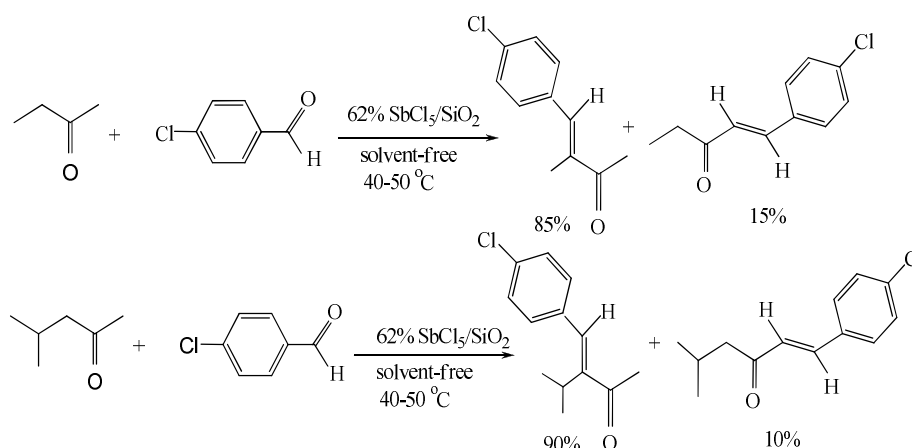
Entry	Product	Time(min)/Yield (%) ^b	Ref. ^c	M.P. °C
1	III: R ₁ ,R ₂ =(CH ₂) ₃ , Ar=4-CH ₃ -C ₆ H ₄	83/60	14	165-166
2	III: R ₁ ,R ₂ =(CH ₂) ₃ , Ar= -C ₆ H ₅	79/25	7	116-117
3	III: R ₁ ,R ₂ =(CH ₂) ₃ , Ar=3-OCH ₃ , 4-OH-C ₆ H ₃	72/50	17	168-170
4	III: R ₁ ,R ₂ =(CH ₂) ₃ , Ar=2-Cl-C ₆ H ₄	87/30	16	88-89
5	III: R ₁ ,R ₂ =(CH ₂) ₃ , Ar=4-OCH ₃ -C ₆ H ₄	60/73	7	202-204
6	III: R ₁ ,R ₂ =(CH ₂) ₂ , Ar=4-OCH ₃ -C ₆ H ₄	60/75	17	215-216
7	III: R ₁ ,R ₂ =(CH ₂) ₂ , Ar=4-CH ₃ -C ₆ H ₄	45/73	7	245-246
8	III: R ₁ ,R ₂ =(CH ₂) ₂ , Ar=4-NO ₂ -C ₆ H ₄	35/88	1	230-231
9	III: R ₁ ,R ₂ =(CH ₂) ₂ , Ar=-C ₆ H ₄	45/88	14	189-190
10	III: R ₁ ,R ₂ =(CH ₂) ₂ , Ar=4-Cl-C ₆ H ₄	73/25	3	225-226
11	VI: Ar'=Ph, Ar=4-NO ₂ -C ₆ H ₄	77/70	15	159-160
12	VI: Ar'=Ph, Ar=3-NO ₂ -C ₆ H ₄	75/20	15	144-145
13	VI: Ar'=Ph, Ar=4-Cl-C ₆ H ₄	90/45	3	108-109
14	VI: Ar'=Ph, Ar=4-OMe-C ₆ H ₄	80/45	3	75-76
15	VI: Ar'=Ph, Ar=4-CH ₃ -C ₆ H ₄	77/40	3	97-98
16	VI: Ar'=4-Cl-C ₆ H ₄ -C≡C-, Ar=4-Cl-C ₆ H ₄	45/86	18	192-194

^a ratio of aldehyde(mmol):catalyst(g) is 1:0.05^b Isolated yield^c All products are known and were identified by their melting points, IR and ¹H NMR spectra.

The stereoselectivity of this method was confirmed by the formation of a trans double bond in the Claisen-Schmidt condensation of methyl ketones (Table 2, entries 13-16).

The regioselectivity of this method was examined by the crossed aldol condensation of 2-butanone and 4-methyl-2-pentanone with 4-chlorobenzaldehyde

(Scheme 2). Because of the preference for acid catalyzed enolization to give more substituted enol, under SbCl₅/SiO₂ catalyzed condensation, the branched-chain ketol was formed with the most rapidity, (Scheme 2).

**Scheme 2.**

Additionally, the chemoselectivity of the reaction was evaluated via a competitive SbCl₅/SiO₂ catalyzed Claisen Schmidt reaction of 4-chlorobenzaldehyde (2 mmol) with a mixture of cyclohexanone (1 mmol) and acetone (1 mmol). It was found that cyclohexanone

reacted with benzaldehyde in a high yield. No chemoselectivity was observed for cyclohexanone versus acetophenone or 4-nitrobenzaldehyde versus 4-methylbenzaldehyde.

For identification of the structure of $\text{SbCl}_5/\text{SiO}_2$, we studied IR spectra of SbCl_5 , $\text{SbCl}_5/\text{SiO}_2$ and SiO_2 (Fig. 1). In all of the spectrums, OH stretching band is observed and strong intermolecular hydrogen bonding occurs in the hydroxyl groups. Therefore, the resulting O-H absorption is broad. The moisture in SbCl_5 causes presence of OH stretching band in its infrared spectra. Infrared spectra of $\text{SbCl}_5/\text{SiO}_2$ and SbCl_5 are similar. In

both of them, the absorption Si-OH and Si-O-Si bands appeared in $\sim 800\text{ cm}^{-1}$ and $\sim 1115\text{ cm}^{-1}$, respectively. In SbCl_5 spectrum, the absorption of Sb-Cl is observed in 1567 cm^{-1} . In IR spectrum of $\text{SbCl}_5/\text{SiO}_2$, the Sb-Cl, Sb-O, Si-OH and Si-O-Si are observed in 1567, 560, 3340 and 1115 cm^{-1} , respectively [16,17]. Based on these results, we suggest the following structure for $\text{SbCl}_5/\text{SiO}_2$ (Scheme 3).

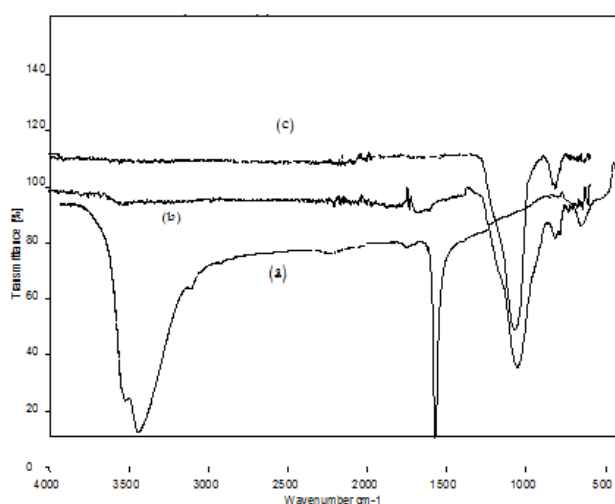
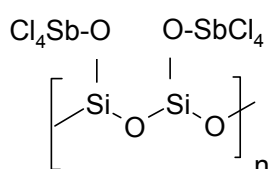


Fig 1: FT-IR (ATR) spectrum of (a) SbCl_5 , (b) $\text{SbCl}_5/\text{SiO}_2$ and (c) SiO_2



Scheme 3. Structure for $\text{SbCl}_5/\text{SiO}_2$

Conclusion

In Sum, silica supported SbCl_5 as a solid acid has a high efficiency and catalyses the Claisen Schmidt condensation reaction in solvent free conditions. This plain procedure offers several advantages including a simple work up, scale up, improved yields, regio-, stereo- and chemoselectivity and a clean reaction.

Experimental

SbCl_5 , aldehydes and ketones and other necessary chemical compounds were purchased from Fluka and Merck companies. The products were known and were characterized by IR and $^1\text{H-NMR}$ and by comparing their physical properties with those reported in the literature. IR spectras were run on a Shimadzu IR-470 spectrometer. $^1\text{H-NMR}$ was obtained using a Bruker Avans 300 MHz spectrometer. Melting points were determined with a Barnstead Electrothermal melting point apparatus.

General procedure for Claisen Schmidt condensation of aldehydes with ketones using SbCl₅-SiO₂ (62%w/w) under solvent-free conditions

Ketone (1 or 2 mmol), aldehyde (1 mmol) and SbCl₅-SiO₂ (62%w/w) (0.05 g) were placed in a round bottom flask. The materials were mixed and heated in 40-50 °C for 25-70 min (Table 2). The progress of the reaction was followed by TLC (3:1:*n*-hexane:ethylacetate). After the completion of the reaction, the mixture was cooled to room temperature. Chloroform was added to the mixture and filtered to remove the catalyst. By evaporation of the solvent, an oily residue or an impure solid was obtained. By adding ethanol and water to the residue, a yellow to orange solid was obtained. The solid was then crystallized with ethanol. All products are known and were identified by comparison of their physical or spectral data with those of authentic samples.

Preparation of silica-supported SbCl₅

The reagent was prepared by stirring a mixture of SbCl₅ (0.7 ml) and 1 g of silica gel in 5 ml of chloroform for 1 h at room temperature. The slurry was filtered and washed with chloroform. The obtained solid (62% SbCl₅.SiO₂) was dried at an ambient temperature for 2 h and then stored in a dry container.

Acknowledgments

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