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Antimony Trichloride: An Efficient and Mild Catalyst for Cyclization of 2-Aminochalcones to the Corresponding 2-Aryl-2,3-Dihydroquinolin-4(1H)-ones

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ANTIMONY TRICHLORIDE: AN EFFICIENT AND MILD CATALYST FOR CYCLIZATION OF 2-AMINOCHALCONES TO THE CORRESPONDING 2-ARYL-2,3-DIHYDROQUINOLIN-4(1*H*)-ONES

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Antimony trichloride is an efficient catalyst for the cyclization of 2-amino chalcones to the corresponding 2-aryl-2,3-dihydroquinolin-4(IH)-ones under mild reaction conditions and in almost quantitative yields.

Keywords: 2-Aminochalcones; 2-aryl-2,3-dihydroquinolin-4(1*H*)-ones; antimony trichloride; intramol-ecular aza-Michael

INTRODUCTION

2-Aryl-2,3-dihydroquinolin-4-(1*H*)-ones bearing substituents on the aromatic rings exhibit various pharmacological activities.^[1] They are also valuable precursors^[2] for the synthesis of medicinally important compounds^[3] that are eventually not readily accessible.^[3,4] These compounds reportedly had been prepared from the corresponding 2-aminochalcones bearing substituents in the aromatic rings by an intramolecular aza-Michael reaction catalyzed by either an acid or base^[5] and also by microwave-assisted reaction on solid support such as clay, silica gel, or neutral alumina. Most of the existing procedures involve the use of corrosive reagents such as orthophosphoric acid, acetic acid, or strong alkalis. Moreover, many of them are of limited synthetic scope because of their poor yields, long reaction times, and need for large amount of catalyst, specialized solvents,^[6] or either microwave irradiation with solid support^[7] or high temperature on solid support.^[8] Therefore, the development of new methods that lead to a convenient procedure and better yield are still desirable.

In continuation of our effort in exploring antimony trichloride $(SbCl_3)^{[9]}$ as a mild and efficient catalyst, we report herein an efficient method for the synthesis of 2-aryl-2,3-dihydroquinolin-4(1*H*)-ones through the cyclization of 2-aminochalcones using SbCl₃ in acetonitrile at 55°C. The salient features of this methodology include quantitative conversion, operational simplicity, inexpensive catalyst, ease of isolation of product, clean reaction, and mild conditions. To our knowledge, there is no report of this catalyst for such type of intramolecular aza-Michael reactions.

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RESULTS AND DISCUSSION

By using very simple experimental procedures, a wide range of substituted and structurally diverse 2-aminochalcones were subjected to cyclization reaction. We carried out the aza-Michael reaction of 2-aminochalcones in the presence of SbCl₃ (10–30 mol%) at 55°C in dry acetonitrile to furnish the corresponding 2,3-dihydroquinolin-4(1H)-ones in a quantitative yield (Scheme 1). Thus, a series of 2-aminochalcones bearing substituents with various stereoelectronic effects were subjected to SbCl₃-catalyzed cyclization reaction, and the results are summarized in Table 1. The structures of the products were established from their spectral analysis [infrared (IR), ¹H, ¹³C NMR, and high-resoultion mass spectrometry (HRMS)] and also by comparison with the literature values.^[7b] A few other solvents such as dichloromethane (DCM), ethanol, and tetrahydrofuran (THF) were also tested but they required longer reaction times and gave poorer yields compared to acetonitrile. The reaction was also carried out at room temperature, which required a longer reaction time (48 h) but resulted in almost quantitative cyclization without formation of any side product (Table 1, entry 3). Increasing the temperature from 55°C to refluxing condition has a negligible effect on the reaction rate. An electron-donating group in the aromatic ring increases the rate, whereas an electron-withdrawing group decreases the rate of the reaction. Moreover, in the case of synthesis of 2-(4'-nitrophenyl)-2,3-dihydroquinolin-4(1H)-one derivative, the corresponding2-(4'-nitrophenyl) aminochalcone did not undergo cyclization to a considerable extent after heating at 55°C for 24 h with 30 mol% catalyst loading, but 50% conversion was noted after it was left for 7 days at room temperature. It is known that silica gel or neutral alumina coated with *p*-toluenesulphonic acid catalyzes the reaction with relatively poor yield, whereas basic alumina spoils the substrate. Microwave irradiation of montmorillonite K-10 as solid support^[7a] and InCl₃ on silica gel^[7b] gave good yields of the products, but the catalyst systems are reported to be less efficient under conventional thermal conditions. Although SiO₂-TaBr₅ at high temperature (140°C)^[8a] gave good yields of products, TaBr₅ alone in solution gave the product in poor yield (30-40%), even after a prolonged reaction time. Very recently, $CeCl_3 \cdot 7H_2O \cdot NaI$ on either silica gel or alumina support^[8b] has been reported to afford good yield of products, whereas CeCl₃ · 7H₂O · NaI in refluxing DCM gave only 20–25% of desired products after 3 days. Hence, the present study unequivocally has proved that antimony trichloride acts as a better catalyst in the solution phase for the intramolecular aza-Michael reaction.

With these encouraging results in hand, we also performed the aza-Michael reaction with 10 mol% SbCl₃ on silica gel support (60–120 mesh) under solvent-free



Scheme 1.

Entry	Substrate	Product ^b	Catalyst (mol %)	Time	Yield
1	NH ₂		30	3.0	99
2	la O NH ₂ Ib	2a O N H 2b Me	10	3.0	99
3	NH ₂ 1c OMe		10	1.0	99
4	NH ₂ Id	O N 2d OMe	10	0.75	90
5	NH ₂ 1e OMe	De OMe 2e OMe	10	1.0	91
6	NH ₂ If NMe ₂		10	1.25	97
7	NH ₂ 1g		10	1.25	98
8	NH ₂ Ih		30	5.0	97
9	Br NH ₂ 1i		30	3.5	98

 Table 1. Antimony trichloride-catalyzed efficient synthesis of 2,3-dihydroquinolin-4(1H)-ones^a

(Continued)

Entry	Substrate	Product ^b	Catalyst (mol %)	Time	Vield
Litti y	Substrate	Tioduct	Catalyst (1101 70)	Time	1 iciu
10			30	10.0	97
11			30	3.0	96

Table 1. Continued

^{*a*}All reactions were carried out using SbCl₃ in acetonitrile at 55°C (method A).

^bAll products were characterized by mp, IR, NMR, and HRMS data and are agreement with the literature values.

^cYield refers to pure isolated products.

conditions (method B) in four cases [Table 1, entries 1 (97%), 3 (96%), 10 (98%), and 11 (96%)], and it was found that the reaction was completed within 10 min on conventional heating at 100°C in almost quantitative yield. In the case of 2-(4'-nitrophenyl) aminochalcone, the reaction was completed within 2.5 h at 100°C in 95% yield. It can be interpreted that the rate of the reaction is very much dependent on the electronic nature of the aromatic ring substituents.

In conclusion, we have developed a mild and efficient methodology for the synthesis of 2-aryl-2,3-dihydroquinolin-4(1H)-ones both in solution phase and under solventless conventional heating condition on solid silica-gel support. Antimony trichloride was found to be the better catalyst in terms of cost, handling, remarkable operational simplicity, and ease of product isolation.

EXPERIMENTAL

Representative Procedure (Method A)

Solid antimony trichloride (68 mg, 0.3 mmol) was added to a stirred solution of 2-amino chalcone, **1i** (303 mg, 1.0 mmol), in acetonitrile (1.0 mL). The reaction mixture was heated at 50–55°C for 3.5 h (completion was monitored by thin-layer chromatography (TLC). The reaction mixture was decomposed with 5 mL water and extracted with DCM (2×15 mL), washed with brine solution (5 mL), and dried over anhydrous Na₂SO₄. Volatiles were removed, and the crude residue was purified by short-column chromatography using 10% ethyl acetate–petroleum ether as eluent to afford **2i** solid (297 mg, 98%).

Spectral data of 2i. Mp 126°C; ¹H NMR (300 MHz, CDCl₃) δ 2.74 (dd, J = 12.6, 16.3 Hz, 1H), 2.95 (dd, J = 3.9, 16.3 Hz, 1H), 4.58 (s, 1H), 5.20 (dd, J = 3.9, 12.5 Hz, 1H), 6.74 (d, J = 8.2 Hz, 1H), 6.80 (t, J = 7.7 Hz, 1H), 7.19 (dt, J = 1.5, 7.7 Hz, 1H), 7.32–7.39 (m, 2H), 7.58 (d, J = 8.0 Hz, 1H), 7.68 (dd, J = 1.3, 7.8 Hz,

1H), 7.88 (d, J = 7.9 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 44.2, 56.8, 116.1, 118.7, 119.1, 122.9, 127.6, 127.7, 128.2, 129.7, 133.3, 135.5, 139.9, 151.5, 192.8. HRMS calcd. for [C₁₅H₁₂NBrO + Na⁺] 323.9999; found 324.0032.

Spectral data of 2k. Mp 92°C, ¹H NMR (300 MHz, CDCl₃) δ 2.92 (dd, J = 5.4, 16.1 Hz, 1H), 3.00 (dd, J = 9.8, 16.3 Hz, 1H), 4.79–4.84 (m, 2H), 6.25 (d, J = 3.2 Hz, 1H), 6.32 (m, 1H), 6.70 (d, J = 8.3 Hz, 1H), 6.76 (t, J = 5.9 Hz, 1H), 7.31 (dt, J = 1.5, 7.3 Hz, 1H), 7.37 (s, 1H), 7.84 (dd, J = 1.2, 7.9 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 441.9, 50.7, 106.8, 110.3, 116.0, 118.5, 119.1, 127.3, 135.4, 142.4, 150.4, 153.3, 192.6. HRMS calcd. for [C₁₃H₁₁NO₂ + Na⁺] 236.0687; found 236.0685.

Representative Procedure (Method B)

A solution of 2-aminochalcone (1j) (121 mg, 0.5 mmol) in 0.5 mL of acetonitrile was added to silica gel impregnated with SbCl₃ (12 mg, 0.05 mmol) [prepared by adding a solution of SbCl₃ in acetonitrile (1 mL) to silica gel (200 mg, 60–120 mesh)], followed by evaporation of the solvent in vacuum. The dry reaction mixture was heated at 100°C for 10 min, and on completion, the reaction mixture was directly charged onto a small silica-gel column (10% ethyl acetate–petroleum ether) to afford the pure product **2j** (118 mg, 98%).

Spectral data of 2j. Mp 134°C; ¹H NMR (300 MHz, CDCl₃): δ 2.67–2.85 (m, 2H), 4.64 (s, 1H), 4.70 (dd, J=4.3, 13.2 Hz, 1H), 6.74 (d, J=8.5 Hz, 1H), 6.79 (d, J=8.5 Hz, 1H), 7.06 (t, J=8.6 Hz, 2H), 7.34 (dt, J=1.4, 7.7 Hz, 1H), 7.41 (dd, J=5.4, 8.6 Hz, 2H), 7.84 (d, J=7.9 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃): δ 46.5, 57.8, 115.9 (d, J=22 Hz), 116.0, 118.6, 119.0, 127.6, 128.3 (d, J=8 Hz), 135.5, 136.8 (d, J=3 Hz), 151.5, 162.8 (d, J=262 Hz), 193.1.

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