Graphite supported $BiCl_3$ as a new, efficient and heterogeneous catalyst for synthesis of β-enaminones compounds

Mistry Dipesh[1], Mahajan Dharmesh[2*], Chejara Dharmesh[1] and Desai Kishor[1]
1. Department of Chemistry, Uka Tarsadia University, Bardoli, Surat, Gujarat, INDIA
2. Government Science College, Vankal, Ta. Mangrol, Dist. Surat, Gujarat, INDIA
*mahajandh@gmail.com

Abstract

A novel graphite supported $BiCl_3$ as an efficient catalyst is developed and reported here in present study. Catalyst was used for the synthesis of β-enaminones compounds from condensation of various amines and dimedone at ambient temperature. Process exhibited high yields, shorter reaction time even at very lower amount of catalyst was seen.

Synthesized β-enaminones were characterized using FT-IR, ^1H NMR and ^{13}C NMR spectroscopy where the structure formation of the said compounds has been confirmed. The catalyst could also be recovered by simple filtration technique and can further be recycled in subsequent reactions.

Keywords: β-enaminones, amines, bismuth trichloride, graphite, heterogeneous catalyst.

Introduction

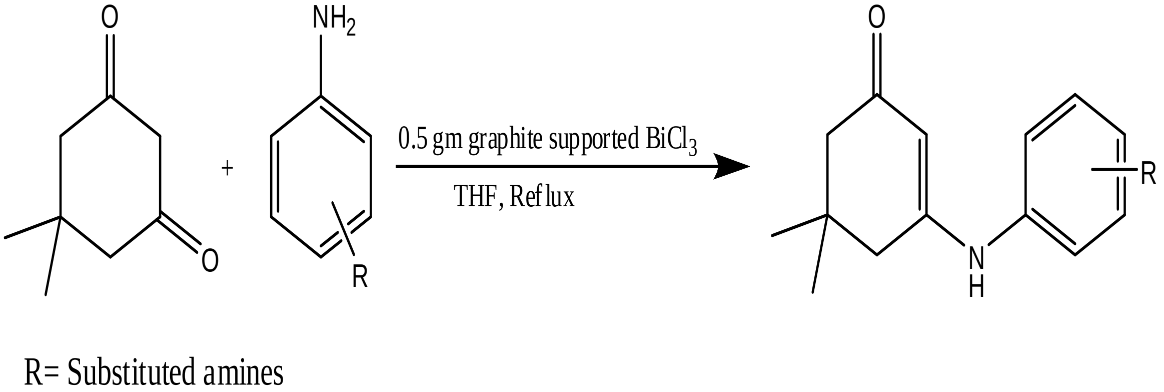
The enaminone derivatives are very important intermediates in pharmaceuticals and synthesis of a variety of heterocyclic compounds. In particular, pharmaceutical compounds are anti-inflammatory[1], antibacterial[2], antitumor[3], anticonvulsant[4], anti-epileptic[5] and other therapeutic agents[6]. Due to the importance of these compounds as intermediates in organic synthesis, a simple high yielding one-pot approach for this transformation is highly desirable.

The well known route for the synthesis is when β-enamino ketones and esters involve in the direct condensation of β-dicarbonyl compounds with amines at reflux in an aromatic solvent with azeotropic removal of water[7]. Several improved procedures including the reaction of amines and 1,3-dicarbonyl compounds such as silica supported H_2SO_4[8], silica supported $SbCl_3$[9], $Bi(OTf)_3$[10], $Sc(OTf)_3$[11], $Yb(OTf)_3$[12], $CeCl_3.7H_2O$[13], silica supported $NaHSO_4$[14], Cu nanoparticals[15], ionic liquid $[EtNH_3]NO_3$[16], $HClO_4.SiO_2$[17], MoO_3/CeO_2-ZrO_2[18] have been reported.

Nowadays, heterogeneous catalyst has gained much attention in recent years and they possess a number of advantages.[19,20] The solid supported catalysts provide ideal advantages of heterogeneous catalyst (easy separation of catalyst, long catalytic life, thermal stability, available active site, low hygroscopic properties, reusability of catalyst). Therefore, the uses of heterogeneous catalyst in organic transformation have been demonstrated for economical and environmental benefits.[21-26]

As far as green chemistry is concerned, heterogeneous catalysis has received a remarkable place in the field of chemistry because of stability, being economic, non-toxic nature, availability that leads them for the transformation of many organic compounds. Graphite supported bismuth trichloride is one of the green catalysts that is easily prepared and has been successfully applied in various organic transformation.

Here in present work, we report an efficient protocol for the synthesis of β-enaminones using graphite supported bismuth trichloride (G-$BiCl_3$) as a heterogeneous and recyclable catalyst. The catalyst exhibited a remarkable activity and the system tolerates a wide variety of amines and dicarbonyl compounds with good to excellent yields of desired products. The catalyst was also found to be reusable up to consecutive cycles without any significant loss in activity.



Scheme 1: Synthesis of β-eneminones in presence of G-$BiCl_3$

Material and Methods

All chemicals were purchased from SD Fine Chemicals Ltd., Mumbai. ^{1}H-NMR (400 MHz) and ^{13}C-NMR (100 MHz) spectra were recorded on a Burcker Avance instrument as in $CDCl_3$. IR spectra were recorded in 740 FTIR spectrometer. TLC was performed on 0.25 mm E. Merck per coated silica gel plates.

Preparation of catalyst: Take $BiCl_3$ (10mmol, 3.15 gm) and graphite (1.57gm), mix well followed by addition of methanol drop by drop till a uniform slurry obtained. The catalyst was collected after evaporating the solvent and dried at 100 ˚C for 2-4 hours.

Typical Procedure for β-enaminones compounds: Substituted amines (10mmol) and dimedone (10mmol) in tetrahydrofuran (THF) (10 ml) were taken and mixed well in the RBF. Graphite supported bismuth trichloride (0.5gm) was added to the above reaction mixture under continuous stirring followed by applying a temperature (Reflux temperature) to the reaction mixture. The completion of the reaction was confirmed by thin layer chromatography. After completion of the reaction, tetrahydrofuran (5 ml) was added into the reaction mass and filtered through a Whatmann filter paper, catalyst was washed with additional tetrahydrofuran (5 ml). Further, the extra solvent from the filtrate was evaporated and the crude product was purified by recrystallization in methanol. The residues of the catalyst were further dried and reused in subsequent reactions.

Results and Discussion

Optimization of the procedure for the preparation of 5,5-Dimethyl-3-(phenylamino)cyclohex-2-enone was carried out using various amount of catalyst. Dimedone (10 mmol) was treated with aniline (10 mmol) in the presence of different amount of G-$BiCl_3$ in tetrahydrofuran(10 ml) as a solvent at reflux temperature. Significantresults were observed in the presence of 0.5 gm G-$BiCl_3$ at molar ratio of dimedone: aniline (1:1) (Table 1, entry 5). Higher amount of catalyst did not improve the yield. Results including some physicochemical data are displayed in table 1.

In another study, a mixture of dimedone (10 mmol), aniline (10 mmol) and G-$BiCl_3$ (0.5gm) was stirred in various polar and non-polar solvents at different temperature (Table 2). The optimized results was obtained in non-polar solvent i.e. tetrahydrofuran at reflux temperature (Table 2, entry 3). The study indicates that the performance of the reaction with respect to yield was better in the non-polar solvent compared to polar solvents.

Table 1
Optimization of catalyst concentration.

Entry	Amount of G-$BiCl_3$, gm	Molar ratio	Time (min)	Yield[a] %
1	0.1	1:1	35	47
2	0.2	1:1	20	62
3	0.3	1:1	12	77
4	0.4	1:1	9	85
5	**0.5**	**1:1**	**5**	**96**
6	0.6	1:1	12	80
7	0.7	1:1	17	74
8	0.8	1:1	23	70
9	0.9	1:1	25	67
10	1.0	1:1	30	59

Dimedone (10 mmol), aniline (10 mmol) and 0.5 gm graphite supported bismuth trichloride were used,THF, reflux
[a] Yield refers to the pure isolated products

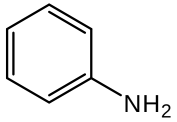
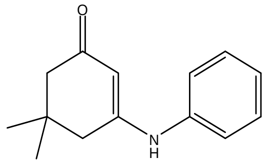
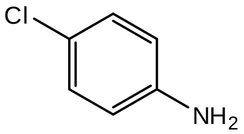
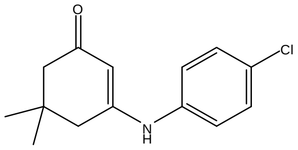
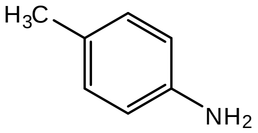
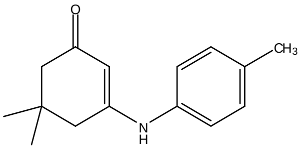
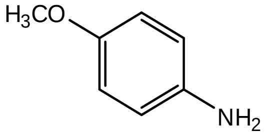
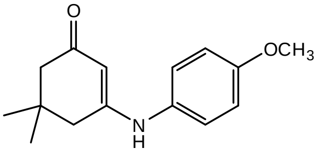
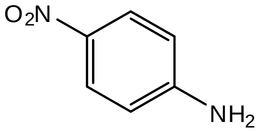
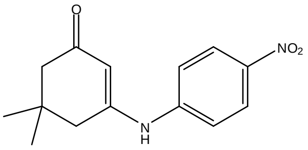
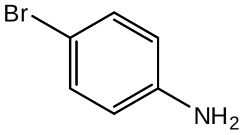
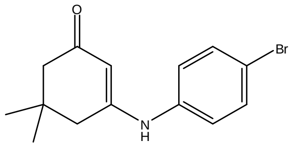
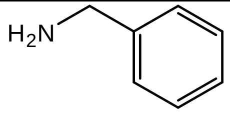
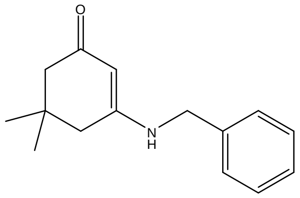
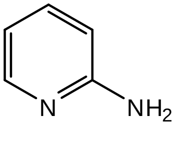
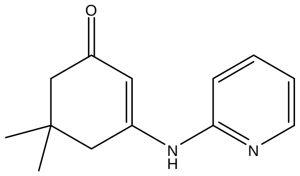
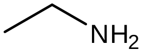
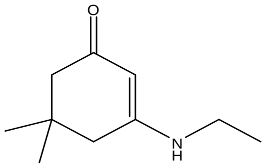
Table 2
Effect of different solvent

Entry	Solvent	Temperature, ˚C	Time, min	Yield[a]%
1	Dichloromethane	R.T	8	85
2	Toluene	80	30	52
3	**Tetrahydrofuran**	**Reflux**	**5**	**96**
4	Acetonitrile	Reflux	17	65
5	Methanol	Reflux	15	70
6	Solvent free	80	20	63

Dimedone (10 mmol), aniline (10 mmol) and 0.5 gm graphite supported bismuth trichloride
[a] Yield refers to the pure isolated products

Furthermore, in the formation of β-enaminones, aniline possessing electron-donating functional groups react with dimedone to give excellent yield (Table 3, entry 2-6) but electron withdrawing substitution at the aniline leads to slightly decreasing yield of β-enaminones (Table 3, entry 2,5,6). In addition to that, the reaction of dimedone and aliphatic amines under optimal reaction condition yielded β-enaminones in good to excellent formation. (Table 3, entry 9).

Table 3
Synthesis of enaminones by using 0.5 gm graphite supported $BiCl_3$ catalyst.

Entry	Amines	Product	Time	Yield[a] %	M.P ˚C
1			5 min	96	178-180
2			15 min	90	188-190
3			35 min	93	196-198
4			5min	97	192-193
5			1 hr 30 min	86	216-218
6			60 min	90	196-198
7			2.0 hr	87	120-121
8			2.5 hr	88	Oily
9			30 min	80	Oily

Dimedone (10 mmol), aniline (10 mmol) and 0.5 gm graphite supported bismuth trichloride were used, THF, reflux;
[a] Yield refers to the pure isolated products

Table 4
The condensation of dimedone and aniline in presence of recycled Graphite supported-BiCl$_3$ catalyst

Entry	Cycle	Time, min	Yield^a%
1	1st use	5	96
2	2nd use	9	84
3	3rd use	17	70
4	4th use	24	51

Dimedone (10 mmol), aniline (10 mmol), 0.5 gm graphite supported bismuth trichloride were used, THF, reflux
[a] Yield refers to the pure isolated products

Spectral analysis

5,5-Dimethyl-3-(phenylamino)cyclohex-2-enone, Table 1, Entry-1: IR, /cm^{-1}: 3234, 2953, 1716, 1273. ^{1}H NMR (CDCl$_3$, 300 MHz), δ: 7.36–7.15 (m, 5 × ArH), 6.54 (s, 1H, NH), 5.59 (s, 1H, 2-CH), 2.54–2.23 (m, 4H, 2-CH$_2$), 1.11 (s, 6H, 2CH$_3$). ^{13}C NMR (CDCl$_3$, 75 MHZ), δ: 29.25 3(2-CH$_3$), 32.75 (C-5), 50.28 (C-6), 97.66 (C-2), 122.26 (C-2', C-6'), 125.25 (C-4'), 129.19 (C-3', C-5'), 138.74 (C-1'), 162.74 (C-3), 198.17 (C-1).

3-(4-Toluidino)-5,5-dimethylcyclohex-2-enone, Table 1, Entry-3: IR, /cm^{-1}: 3242, 2955, 1707, 1570, 1274. ^{1}H NMR (CDCl$_3$, 300 MHz), δ: 7.28–7.05 (m, 4 × ArH), 6.78 (s, 1H, NH), 5.56 (s, 1H, 2-CH$_2$), 2.39 (s, 2H, 6-CH$_2$), 2.33 (s, 3H, 7-CH$_3$), 2.12 (s, 2H, 4-CH2), 1.05 (s, 6H). ^{13}C NMR (CDCl$_3$, 75 MHZ), δ: 21.44 (C-7), 28.67 (2-CH$_3$), 33.27 (C-5), 43.82 (C-4), 50.76 (C-6), 98.41 (C-2), 124.49 (C-2', C-6'), 130.18 (C-4'), 135.77 (C-3', C-5'), 136.03 (C-1'), 162.90 (C-3), 196.99 (C-1).

3-(Benzylamino)-5,5-dimethylcyclohex-2-enone, Table 1, Entry-7: IR, /cm^{-1}: 3225, 3028, 2953, 1716, 1369, 1276. ^{1}H NMR (CDCl$_3$, 300 MHz), δ: 7.37–7.27 (m, 5H, 5 × ArH), 5.74 (s, 1H, NH), 4.29 (s, 1H, 2-CH), 4.28 (m, 2H, 5-CH$_2$), 2.25 (s, 2H, 6-CH$_2$), 2.19 (s, 2H, 4-CH$_2$), 1.02 (s, 6H, 2-CH$_3$). ^{13}C NMR (CDCl$_3$, 75 MHZ), δ: 28.15 (5-CH$_3$), 32.80 (C-5), 42.14 (C-4), 47.02 (C-7), 49.35 (C-6), 95.16 (C-2), 127.46 (C-2', C-6'), 127.70 (C-4'), 128.77 (C-3', C5'), 136.68 (C-1'), 163.24 (C-3), 196.06 (C-1).

In order to evaluate the catalytic activity, we have investigated the reusability and recycling of G-BiCl$_3$ catalyst, the catalyst was recovered by simple filtration from the reaction mixture and washed with tetrahydrofuran. The catalyst was dried under 100°C for 1-2 hrs and reused for next reaction. The catalyst was used in model reaction up to three cycles (Table 4).

Conclusion

A new efficient heterogeneous catalyst based on graphite supported BiCl$_3$ was developed. The catalyst was studied for the synthesis of β-enaminones from amines and diketo compounds. The developed catalyst exhibited great efficiency and produced higher yield in shorter reaction time.

Moreover, the catalyst is economic in cost and can be easily isolated from the finished product. Further the catalyst was also studied for its recyclability where it was reused in the next consecutive batches and found to have a great potential even up to 3-4 cycles. Development of such graphite supported heterogeneous catalyst directs researchers towards the domain of catalysis and encourages them to get more and more catalyst that may have agreement with the green chemistry protocols.

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