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Conjugated Addition of Amines to Electron Deficient Alkenes: A Green Approach

A very simple approach has been developed for conjugate addition of a variety of aliphatic and aromatic amines to electron deficient alkenes in presence tea extract at room temperature. General applicability, operational simplicity, aqueous media, mild reaction conditions, environment friendly, high yields and applications of inexpensive and easily available catalyst are the advantages of the present procedure.

Keywords: Michael addition; amines; α , β -ethylenic compounds; tea extract

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Introduction

The formation of carbon-nitrogen bond is very important task in organic synthesis and conjugate addition of amines to electron deficient alkenes is an efficient route to develop the carbon-nitrogen bond [1]. As a consequence, β -amino ketone, nitriles, amide and carboxylic ester functionalities occur in many natural products [2–4]. It provides an easy route to produce β -amino derivatives, which are attractive for their use as synthetic intermediates of anticancer agents, antibiotics and other drugs [5, 6]. It is noteworthy to mention that the classical method for the preparation of β -amino derivatives is *via* Mannich reaction [7]. The conjugate addition of amine

to electron deficient alkenes is an alternate route to synthesize β -amino derivatives. In comparison with Michael reaction the conjugate addition of amine to electron deficient alkenes is, in contrast, atom economical and easy to operate. But usually both these additions are carried out in presence of a strong base or acid [8, 9]. Several methods are available in the literature by using different catalysts such as Yb(OTf)₃ [10], CeCl₃·7H₂O-NaI [11], InCl₃ [12], Cu(OTf)₂ [13, 14], CAN [15], KF/alumina [16,17], LiClO₄ [18], Bi(OTf)₃ [19], Bi(NO)₃ [20], SmI₂ [21], Cu(acac)₂/ionic liquid [22], ionic liquid/quaternary ammonium salt [23, 24], boric acid [25], borax [26], ZrOCl₂·8H₂O [27],

β -cyclodextrin [28], bromodimethylsulfonium bromide [29], [HP(HNCH₂CH₂)₃N]NO₃ [30], MnCl₂ [31] etc. Although these methods have their own advantages and quite useful, but some of these methods used a large excess of reagents, hazardous solvents such as acetonitrile or 1,2-dichloroethane, require long time and harsh reaction. Ranu *et al.* reported these addition in the absence of catalysts or water as the reaction medium, but due to the solubility problem of organic compounds the scope of the method is limited [32, 33]. So far, the reported methodologies are effective for either aromatic amines or aliphatic amines. So, in a consequence, development of a general, simple and environmentally benign method is highly desirable. Considering the environmental consciousness in chemical research, reactions in water have attracted much attention in recent times [34, 35]. In 2008, Varma *et al.* reported that tea and coffee extract can be used as good stabilizer for green synthesis of silver and palladium na-

Results and discussion

First of all, we prepared the required tea extract. In a typical experimental procedure, 2 g of tea leaves were dissolved in 20 mL of water and boiled it for 10–15 min. After filtration we got the extract which was used for the said reactions. It was observed that 2 mL of tea extract is sufficient to get the best result. Several structurally varied amines were coupled with the wide range of α , β -ethylenic compounds and the results are summarized in Table 1. A variety of aliphatic amines was examined to prove the general applicability of this present procedure and the corresponding Michael adducts were isolated in excellent yields within a short reaction time. The aliphatic primary amines

nanoparticles [36]. The authors first synthesized nanoparticles in presence of tea and coffee extract. This observation promoted us to consider the tea extract for some organic reactions. Interestingly, from the recent research we observed according to normal expectation that the extraction of normal tea is acidic in nature [37]. This observation motivated us to investigate the catalytic role of tea extract for simple organic reaction. So, in continuation of our research to develop green methodology [38–41], we have observed that tea extract is very useful as solvent as well as catalyst for conjugate addition of a variety of amines to different Michael acceptors (Fig. 1).

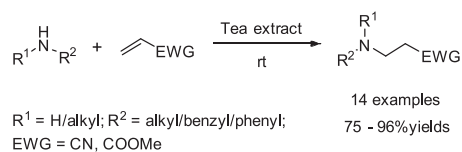




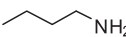

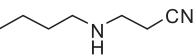


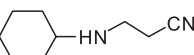


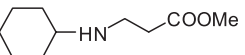
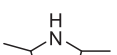

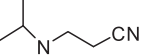
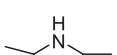

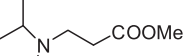


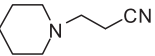


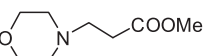




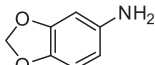

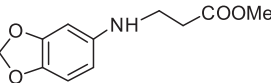
Fig. 1. Tea extract mediated conjugated addition of amines to electron deficient alkenes

such as benzylamine, butylamine and cyclohexylamine were treated with different Michael acceptors and corresponding monoadducts were isolated in good yields (Table 1, entries 1–5). The reaction of open chain bulky secondary amine like diisopropylamine proceeded very well (entries 6, 7). Cyclic secondary amines such as piperidine and morpholine underwent facile additions with acrylonitrile and acrylic esters respectively (Table 1, entries 6, 7). Aromatic amines are less reactive than aliphatic amines and took long reaction time. Both activated and weakly activated anilines were investigated. The reactions proceeded smoothly at room temperature and the products were

obtained in excellent yields. Several substituted anilines such as methyl and methoxy anilines underwent efficient additions with acrylonitrile and methyl acrylate giving only monoadduct in high

yields under present reaction conditions (Table 1, entries 10–14). Acid sensitive functional group in aniline such as 3,4-(methylenedioxy)aniline also reacted well to give the desired product in good

Table 1

Tea extract-mediated Michael addition of amines to conjugated alkenes ^a					
Entry	Amine	Alkene	Product	Time [min (h)]	Yield (%) ^b
1	PhCH ₂ NH ₂		PhCH ₂ NHCH ₂ CH ₂ CN	20	92
2	PhCH ₂ NH ₂		PhCH ₂ NHCH ₂ CH ₂ CO ₂ Me	40	90
3				20	96
4				20	96
5				50	90
6				15	95
7				20	94
8				10	96
9				20	90
10	PhNH ₂		PhNHCH ₂ CH ₂ CN	(18)	75
11	PhNH ₂		PhNHCH ₂ CH ₂ CO ₂ Me	(20)	85
12	4-(OMe)-C ₆ H ₄ NH ₂		4-(OMe)-C ₆ H ₄ NHCH ₂ CH ₂ CN	(24)	75
13	4-Me-C ₆ H ₄ NH ₂		4-Me-C ₆ H ₄ NHCH ₂ CH ₂ CN	(24)	80
14				(12)	88

^aReaction conditions: 2 mmol of amine and 2 mmol of alkene were stirred in 2 mL of tea extract at room temperature; ^bIsolated yields.

yields keeping methylenedioxy group unaffected (Table 1, entry 14). With regard to Michael acceptors, a wide range of structurally diverse electron deficient alkenes was used such as α , β -unsaturated nitrile and carboxylic ester. In general, the reactions are very clean. Both aliphatic and aromatic amines give the products in equally fair yields. In particular, in the case of primary amines the method pro-

Conclusions

In conclusion, we have developed a tea extract-mediated a highly efficient methodology for the synthesis of β -amino derivatives under milder reaction conditions at room temperature. General applicability, operational simplicity, aqueous media, mild reaction conditions, environment friendly, high yields, and applica-

Experimental

General: ^1H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were run in CDCl_3 solutions. IR spectra were taken as KBr plates. Elemental analyses were done by Perkin-Elmer autoanalyzer. Column chromatography was performed on silica gel (60–120 mesh, SRL, India). $\text{MnCl}_2 \cdot 4\text{H}_2\text{O}$ was purchased from NICE Chemicals, India. Tea leaves were purchased from market. Amines and alkenes are all commercial materials. All liquid reagents were distilled before use.

Preparation of tea extract: 2 g of tea leaves (any marketed) were dissolved in 20 mL of water and boiled it for 10–15 min. After filtration we got the extract which was used for the reactions.

General procedure for the synthesis of β -amino derivatives: A mixture of amine (2 mmol) and alkene (2 mmol) was stirred in 2 mL of tea extract at room temperature as required for completion

duces the corresponding β -amino derivatives without the problem of double-conjugate addition. We have not observed any by-products for all reaction combinations which are supported by high yields of the protocol. All of the known synthesized compounds have been characterized by spectral data and the new compounds by spectral and analytical data.

tions of inexpensive and easily available catalyst are the advantages of the present procedure. We believe this aza-Michael reactions are of significant importance in both synthetic chemistry and industrial processes for the synthesis of β -amino derivatives.

(TLC). After completion of the reaction the reaction mixture was extracted with ethyl acetate (40 mL). The extract was washed with water (2×10 mL) and brine solution (1×10 mL) and dried over anhydrous sodium sulphate. Evaporation of solvent followed by short column chromatography of the crude product over silica gel (hexane/ ethyl acetate) furnished the analytically pure product. The known compounds have been identified by comparison of spectra data (IR and NMR). The spectral and analytical data of the compounds which are not readily found provided below.

3-(Cyclohexylamino)propanenitrile (Table 1, entry 4): Colorless oil; IR 2928, 2246, 1722, 1666, 1558, 1455 cm^{-1} ; ^1H NMR δ 2.85 (t, $J = 5.1$ Hz, 2H), 2.45 (t, $J = 5.1$ Hz, 2H), 2.43 (m, 1H) 1.80–1.63 (m, 5H), 1.25–1.16 (m, 6H). Calculated for

C₉H₁₆N₂: C, 71.01; H, 10.59; N, 18.40 %. Found: C, 60.82; H, 10.35; N, 18.13 %.

3-(4-Methoxy-phenylamino)-propanenitrile (Table 1, entry 12): Colorless liquid; IR3377, 2244, 1842, 1617, 1514, 1289 cm⁻¹; ¹H NMR δ 6.80 (d, J = 5.1 Hz, 2H), 6.61 (d, J = 5.1 Hz, 2H), 3.75 (s, 3H), 3.47 (t, J = 4.8 Hz, 2H), 2.61 (t, J = 4.8 Hz, 2H), (N-H) not identified; ¹³C NMR δ 152.9, 140.3, 118.5, 115.1 (2C), 114.8 (2C), 55.8, 40.8, 18.2. Calculated for C₁₀H₁₂N₂O: C, 68.16; H, 6.86; N, 15.90 %. Found: C, 67.98; H, 6.53; N, 15.62 %.

3-(4-Methyl-phenylamino)-propanenitrile (Table 1, entry 13): Colorless liquid; IR3559, 2253, 1615, 1522, 1404 cm⁻¹; ¹H NMR δ 7.00 (d, J = 6.0 Hz, 2H), 6.53 (d, J = 6.0 Hz, 2H), 3.47 (d, J = 5.1 Hz, 2H), 2.60 (d, J = 5.1 Hz, 2H), 2.24 (s, 3H) (N-H) not identified; ¹³C NMR δ 143.9, 130.2 (2C), 127.7, 118.5, 113.2 (2C), 40.0, 20.4, 18.0. Calculated for C₁₀H₁₂N₂: C, 74.97; H, 7.55; N, 17.48 %. Found: C, 74.63; H, 7.38; N, 17.16 %.

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