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TAMARIND WATER-PROMOTED SYNTHESIS OF AMINO-SCHIFF'S BASES AND 1-ARYLMETHYL-2-ARYLBENZIMIDAZOLES UNDER GRINDING METHOD: A GREEN ALTERNATIVE APPROACH

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ABSTRACT

An efficient and eco-friendly procedure was developed for the green synthesis of various amino-Schiff's bases and 1-arylmethyl-2-arylbenzimidazoles in high yields by tamarind water-promoted condensation of *o*-phenylenediamine with aromatic aldehydes under grinding protocol. This method is experimentally simple, clean, high yielding, and with reduced reaction times. The product is purified by simple filtration followed by crystallisation with ethanol and drying processes.

KEYWORDS: Green synthesis, amino-Schiff's bases, 1-arylmethyl-2-arylbenzimidazoles, grinding, tamarind water

1. INTRODUCTION

Development of non-hazardous synthetic methodologies for organic synthesis is one of the latest challenges to organic chemists.[1] The growing concern for the environmental demands the development of eco-friendly and economic processes wherein even less hazardous by-products are not desirable. Organic reactions under grinding have gained in popularity in recent years. These grinding methods usually need shorted reaction times, simpler reactors, resulting simpler and more efficient work up procedures, easier separations and purifications than conventional solvents.

Schiff's bases have been playing vital roles in pharmaceuticals, rubber additives[2], as amino protecting groups in the synthetic organic chemistry and several biological active organic compounds. It possesses a lot of biological activities such as anticancer[3], antidepressant[4],

anticonvulsant[5], antibacterial[6], antimicrobial[7], insecticidal[8] and anti-inflammatory[9] activity. The benzimidazole nucleus represents a class of medicinally important nitrogen heterocycles which exhibit significant activities such as analgesic[10], antiamoebic[11], antihypertensive[12], antiparasitic[13] and antitumor.[14] Benzimidazole derivatives also show significant activity against several viruses such as HIV[15], human cytomegalovirus (HCMV)[16], influenza[17] etc. Considering the numerous applications of such compounds in various fields of chemistry there has been tremendous interest in developing efficient method for their preparation. A good number of methods have been reported in the literature for the synthesis of Schiff bases and benzimidazoles using different precursors but all these methodologies have some drawbacks like long reaction time, use of expensive catalyst and toxic organic solvents.[18-19] Therefore, introduction of clean procedures and eco-friendly catalysts have attracted attention of workers for synthesis of such compounds. Recently, a good number of organic reactions using fruit juice were reported in the literature.[20] Due to acidic nature, aqueous extract of that fruits has been found to be a suitable replacement for various homogeneous acid catalysis reactions.

Tamarind (*Tamarindus indica*) has long been one of the most popular of the non-citrus tropical and subtropical fruits, largely because of its attractive flavour and refreshing sugar-acid balance. The composition of the tamarind water varies with geographical, cultural and seasonal harvesting and processing. It contains plant acid (16-18%) composed mainly of tartaric acid (up to ca. 18%) with minor amount of ascorbic acid. Other constituents include sugar (20-40%), flavonoids, polyphenolics, fat, vitamin, minerals (Ca, K, P etc.) and tartarates.[21-22] We have used “tamarind water” (aqueous extract of tamarind) as natural acid catalyst for the synthesis of amino-Schiff’s bases and benzimidazoles. As tamarind water is acidic in nature and contains tartaric acid mainly along with ascorbic acid, so it works as an acid catalyst for amino-Schiff’s base and benzimidazole formation.

It is evident from the literature that the reaction of *o*-phenylenediamine with aromatic aldehydes using tamarind water under grinding protocol has not been studied so far, although there are reports of condensation of varieties of amines with aldehydes.[23-24] In this paper, we report a facile synthesis of amino-Schiff’s bases and 1-arylmethyl-2-arylbenzimidazoles by tamarind water-promoted condensation of *o*-phenylenediamine with aromatic aldehydes under grinding protocol.

2. MATERIALS AND METHODS

2.1 Experimental

All reactions were run in dried glassware. Reagents were purchased from Spectrochem or SRL or Sigma-Aldrich and were used without further purification. Melting points were determined on a Kofler block and uncorrected. Reactions were performed in a mortar and pestle made of ceramic. ^{1}H NMR spectrum was recorded in $CDCl_3$/DMSO-d_6 on Bruker AV-300 (300 MHz) spectrometers using TMS as an internal standard. Infrared spectra were recorded on a Bruker Tensor 27 IR spectrometer (KBr pellets). Analytical samples were dried in *vacuo* at room temperature. The carbon, hydrogen and nitrogen percentages in synthesized products were analyzed by Perkin-Elmer 2400 series II C, H, N analyzers. Thin layer chromatography was carried out on silica gel G for TLC made of SRL Pvt. Ltd.

2.2 Preparation of tamarind water

The green tamarind fruit were purchased from the local market. The upper shell of the green tamarind and its inner grain were removed. The hard green material (50 g) was boiled with water (100 ml), cooled and it was centrifuged using micro centrifuge (REMI RM-12C). The clear portion of the aqueous extract of the tamarind generally called “tamarind water” (pH=3) was used as catalyst for the reactions.

2.3 General method for synthesis of Schiff bases and benzimidazoles

An intimate mixture of *o*-phenylenediamine (**1**, 1 mmol), an aromatic aldehydes (**2a-g**, 1 mmol) and tamarind water (2 ml) was taken in a mortar and it was ground by pestle in open air at room temperature for the time period mentioned in the **Table 1**. The progress of the reaction was monitored by TLC over silica gel. When the reaction was found to be complete, 10 ml of water was added to it. The resulting precipitate was filtered, washed with hot water. The products **3a-g** was pure enough but further purification can be obtained by crystallization from ethanol. In similar way, products **3h-j** was obtained when 2 molar proportions of the aldehydes were used. The structural elucidations of the products were based on their physical and spectral (IR, ^{1}H and ^{13}C) data as given below.

***Compound (3a)*:** Yellow crystal, m.p. 284-286 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) ppm: 8.51 (s, 1H, N=CH), 7.85 (d, J= 8.1 Hz, 2H), 7.44 (d, J= 8.1 Hz, 2H), 7.06 (d, J= 8.4 Hz, 2H), 6.77 (t, 2H), 4.25 (br. s, 2H, NH_2); IR (KBr) cm^{-1}: 3478 & 3376 (NH_2), 1599 (C=N); Anal. calcd for $C_{13}H_{11}N_2Cl$: C 67.68, H 4.81, N 12.14. Found: C 68.08, H 4.67, N 11.94.

***Compound (3b)*:** Yellow crystal, m.p. 242-244 ºC; ^{1}H NMR (300 MHz, DMSO-d_6) ppm: 8.56 (s, 1H, N=CH), 7.94 (d, J= 7.8 Hz, 2H), 7.70 (d, J= 7.8 Hz, 2H), 7.14 (d, J= 7.5 Hz, 1H), 6.97 (t, 1H), 6.71 (d, J= 7.8 Hz, 1H), 6.55 (t, 1H), 5.24 (br. s, 2H, NH_2); IR (KBr) cm^{-1}: 3475 & 3372 (NH_2), 1598 (C=N),; Anal. calcd for $C_{13}H_{11}N_2Br$: C 56.75, H 4.03, N 10.18. Found: C 56.98, H 4.16, N 10.35.

***Compound (3c)*:** Brown crystal, m.p. 298-300 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) ppm: 8.64 (s, 1H, N=CH), 8.32 (d, J= 8.7 Hz, 2H), 8.06 (d, J= 8.7 Hz, 2H), 7.15-7.11 (m, 2H), 6.82-6.74 (m, 2H), 4.34 (br. s, 2H, NH_2); IR (KBr) cm^{-1}: 3463 & 3370 (NH_2), 1598 (C=N); Anal. calcd for $C_{13}H_{11}N_3O_2$: C 64.72, H 4.60, N 17.42. Found: C 64.68, H 4.67, N 17.36.

***Compound (3d)*:** Brownish crystal, m.p. 150-152 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) ppm: 8.70 (s, 1H, N=CH), 8.55 (s, 1H), 8.32 (d, J= 8.1 Hz, 1H), 8.25 (d, J= 7.8 Hz, 1H), 7.65 (t, 2H), 7.35-7.32 (m, 2H), 7.24-7.20 (m, 1H), 4.61 (br. s, 2H, NH_2); IR (KBr) cm^{-1}: 3365 & 3273 (NH_2), 1606 (C=N); Anal. calcd for $C_{13}H_{11}N_3O_2$: C 64.72, H 4.60, N 17.42. Found: C 64.66, H 4.68, N 17.46.

***Compound (3e)*:** Yellow crystal, 132-134 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) ppm: 8.40 (s, 1H, N=CH), 7.78 (d, J= 8.7 Hz, 2H), 7.03-6.99 (m, 2H), 6.76 (d, J= 7.2 Hz, 2H), 6.73 (d, J= 7.8 Hz, 2H), 4.20 (br. s, 2H, NH_2), 3.05 (s, 6H, CH_3); IR (KBr) cm^{-1}: 3465 & 3365 (NH_2), 1594 (C=N); Anal. calcd for $C_{15}H_{17}N_3$: C 75.28, H 7.16, N 17.56. Found: C 75.61, H 7.29, N 17.51.

***Compound (3f)*:** Yellowish crystal, 270-272 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) ppm: 8.45 (s, 1H, N=CH), 7.82 (d, J= 8.4 Hz, 2H), 7.07-7.01 (m, 2H), 6.91 (d, J= 8.4 Hz, 2H), 6.79-6.73 (m, 2H), 4.22 (br. s, 3H, NH_2& OH); IR (KBr) cm^{-1}: 3486 (OH), 3394 & 3317 (NH_2), 1595 (C=N); Anal. calcd for $C_{13}H_{12}N_2O$: C 73.56, H 5.70, N 13.20. Found: C 73.61, H 5.78, N 12.09.

***Compound (3g)*:** Yellow crystal, 118-120 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) ppm: 8.56 (s, 1H, N=CH), 8.23 (d, J= 7.5 Hz, 2H), 8.00 (d, J= 7.8 Hz, 2H), 7.66 (t, 1H), 7.53 (t, 2H), 7.34 (d, J= 8.1 Hz, 2H), 7.06-7.11 (m, 2H), 6.73-6.80 (m, 2H), 4.25 (br. s, 2H, NH_2); ^{13}C NMR (75 MHz, $CDCl_3$): 115.5, 117.1, 118.4, 122.1 (2C), 127.8, 128.6 (2C), 129.2, 129.8 (2C),130.2 (2C), 133.8, 134.3, 136.9, 142.2, 153.0, 156.2, 164.9 (C=O); IR (KBr) cm^{-1}: 3348 & 3353

(NH_2), 1719 (C=O), 1600 (C=N); Anal. calcd for $C_{20}H_{16}N_2O_2$: C 75.93, H 5.10, N 8.86. Found: C 76.05, H 5.23, N 9.05.

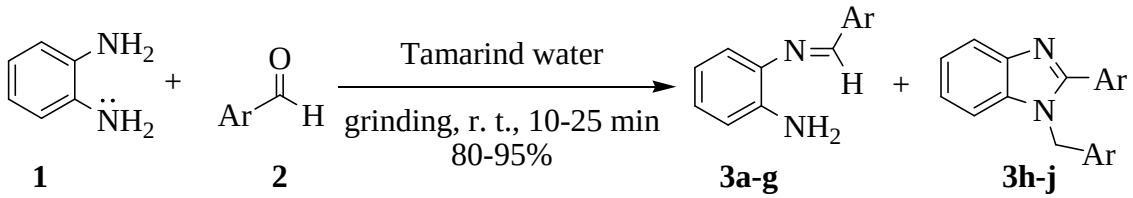
***Compound (3h)*:** White solid, 128-130 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) ppm: 7.83 (d, J= 8.1 Hz, 1H), 7.63 (d, J= 8.7 Hz, 2H), 7.30-7.20 (m, 3H), 7.03 (d, J= 8.4 Hz, 2H), 6.97 (d, J= 8.7 Hz, 2H), 6.85 (d, J= 8.4 Hz, 2H), 5.38 (s, 2H, -CH_2-), 3.85 (s, 3H, OMe), 3.78 (s, 3H, OMe); IR (KBr) cm^{-1}: 3055 (ArC-H), 1607 (ArC=C); Anal. calcd for $C_{22}H_{20}N_2O_2$: C 76.72, H 5.85, N 8.13. Found: C 76.34, H 5.46, N 8.57.

***Compound (3i)*:** White crystal, 218-220 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) ppm: 7.84 (d, J= 7.8 Hz, 1H), 7.40-7.28 (m, 3H), 7.15 (d, J= 8.1 Hz, 1H), 6.96 (d, J= 8.1 Hz, 1H), 6.87 (d, J= 8.1 Hz, 1H), 6.63(d, J= 8.1 Hz, 1H), 6.59(s, 2H), 6.02 (br. s, 1H,OH), 5.70 (br. s, 1H, OH), 5.38 (s, 2H, -CH_2-), 3.81 (s, 3H, OMe), 3.75(s, 3H, OMe); IR (KBr) cm^{-1}: 3387 (OH), 3000 (ArC-H), 1597 (ArC=C); Anal. calcd for $C_{22}H_{20}N_2O_4$: C 70.20, H 5.36, N 7.44. Found: C 70.28, H 5.42, N 7.49.

***Compound (3j)*:** Off-white solid, 96-98 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) ppm: 7.80-7.71 (m, 1H), 7.65-7.64 (m, 1H), 7.51-7.48 (m, 1H), 7.33-7.28 (m, 3H), 7.22-7.21 (m, 1H), 6.62-6.60 (m, 1H), 6.29-6.27 (m, 1H), 6.24-6.23 (m,1H), 5.64 (s, 2H, -CH_2-); IR (KBr) cm^{-1}: 3075 (ArC-H), 1616 (ArC=C); Anal. calcd for $C_{16}H_{12}N_2O_2$: C 72.72, H 4.58, N 10.60. Found: C 72.79, H 4.51, N 10.70.

4. RESULTS AND DISCUSSION

In continuation of our previously reported research on the use of edible fruit juice in various transformations[25-29] herein, a very simple and selective synthesis of various amino-Schiff's bases **3a-g** and 1-arylmethyl-2-arylbenzimidazoles **3h-j** by tamarind water-promoted condensation of *o*-phenylenediamine (**1**) and aromatic aldehydes (**2**) under grinding process was reported (**Scheme 1**).



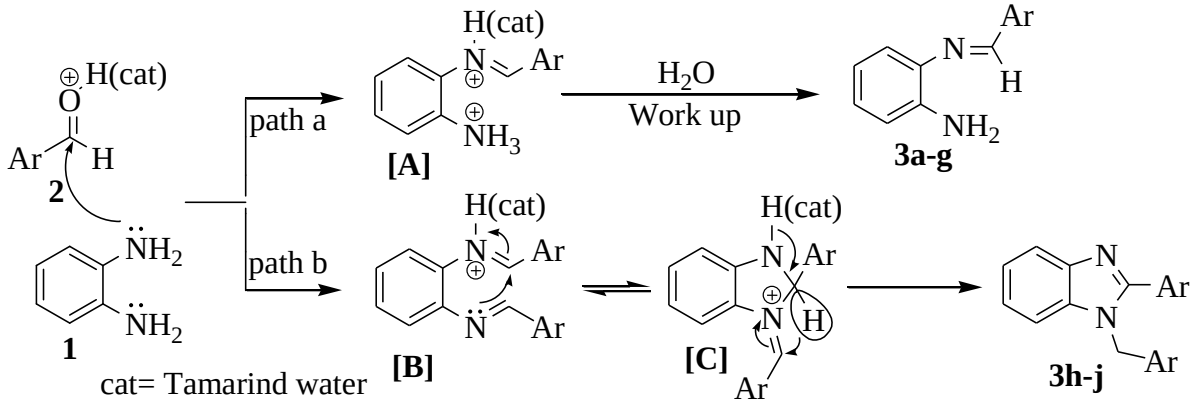
1 **2** **3a-g** **3h-j**

Scheme 1:Tamarind water-promoted synthesis of the title compounds

It was observed that amino-Schiff's bases **3a-g** was obtained as coloured compounds, its IR spectrum showed the characteristics peak of imine (C=N) linkage at the region of 1594-1606 cm^{-1} and a distinct doublet peak of amino group at the region of 3478-3273 (NH_2) cm^{-1}. ^{1}H-NMR spectrum also justify its structure by showing the signal of imine (HC=N) proton at the region of δ 8.40-8.70 (s, 1H, HC=N). The another product 1-arylmethyl-2-arylbenzimidazoles **3h-j** was obtained as colourless/off-white compounds, its IR spectrum showed there was no characteristics peak of imine (C=N) linkage, the lack of the doublet peak of amino group and ^{1}H-NMR spectrum also showing the lack of the signal of imine (HC=N) proton but appears a singlet peak of $–CH_2$- group at the region of δ 5.38-5.64 (2H, s, $-CH_2$-) which confirmed the formation of the products **3h-j**. During the experiment it was found that no product was obtained in the absence of tamarind water, therefore the role of tamarind water in catalyzing the condensation is very important for the formation of **3**.

Table 1: Synthesis of amino-Schiff's basses (3a-j) and 1-arylmethyl-2-arylbenzimidazoles (3h-j) using tamarind water.

Entry	Ar- in Ar-CHO (2)	Product (3)	Time (min)	Yield (%)	M.P. (ºC)
a	4-ClC_6H_4-	3a	20	85	284-286
b	4-BrC_6H_4-	3b	15	87	242-244
c	4-$O_2NC_6H_4$-	3c	10	95	298-300
d	3-$O_2NC_6H_4$-	3d	20	85	150-152
e	4-$Me_2NC_6H_4$-	3e	25	90	132-134
f	4-HOC_6H_4-	3f	25	85	270-272
g	4-$PhCOOC_6H_4$-	3g	20	93	118-120
h	4-$MeOC_6H_4$-	3h	25	90	128-130
i	3-MeO-4-HOC_6H_4-	3i	25	84	218-220
j	2-furayl-	3j	25	80	96-98



Scheme 2: The suggested mechanism for the formation of the title compounds

A possible mechanism proposed for these reactions is depicted in **Scheme 2**. This mechanism probably involves an initial tamarind water-promoted condensation of *o*-phenylenediamine with aromatic aldehydes **2a-g** (in 1:1 ratio) to yield a mono-imine intermediate **A** (path a) and with aromatic aldehydes **2h-j** (in 1:2 ratio) to yield a di-imine intermediate **B** (path b). The formation of **3a-g** in case of aldehydes **2a-g** (**Table 1**) can be explained possibly through deprotanation of **A** in the work up step. However, the formation of 1-arylmethyl-2-arylbenzimidazoles **3h-j** in case of aldehydes **2h-j** (**Table 1**) can be explained possibly through cyclization of **B**, followed by 1,3-hydride shift of **C**, according to previous suggested mechanism.[30]

5. CONCLUSION

We report here a very simple, efficient, eco-friendly and economic process for synthesis of various amino-Schiff's bases (**3a-g**) and 1-arylmethyl-2-arylbenzimidazoles (**3h-g**) avoiding the use of any hazardous organic solvent and catalyst. The sets yielding **3** as the only product did not require any chromatographic purification.

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