FULL PAPER

Synthesis of Fluorescent 2,6-Dicyano-3,5-Disubstituted Anilines Using Cellulose Sulfuric Acid in Aqueous Media

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The synthesis of some fluorescent 2,6-dicyano-3,5-disubstituted anilines using cellulose sulfuric acid (Cellulose-SA) as an environmentally benign catalyst in H_2O is described. The one-pot reaction of 1,3-diketone and three equiv. of malononitrile was carried out in the presence of one equiv. of a secondary amine, Cellulose-SA as catalyst, and H_2O as solvent. The photophysical properties ($\lambda_{Abs.}$, $\lambda_{Flu.}$) of the synthesized compounds in CH_2Cl_2, MeCN, and MeOH have been measured. The emission spectra of the new compounds in the solid state are also reported.

Keywords: Cellulose sulfuric acid, Fluorescence, 2,6-Dicyanoaniline, Photophysical properties, *Thorpe–Ziegler* reaction.

Introduction

One of the key areas of ‘green chemistry’ is the elimination of solvents or the replacement of hazardous solvents by relatively benign solvents in chemical processes, especially for industrial compounds. The best solvent for this purpose is H_2O [1][2]. In addition, cellulose sulfuric acid (Cellulose-SA) is one of the common organic polymers which can be used as an inexpensive and biodegradable heterogeneous catalyst in organic reactions. Recently, it has attracted attention from both environmental and economic points. Cellulose-SA can be easily separated from reaction mixtures, has a high turnover number, and since it can replace liquid homogenous acids, it is desirable in chemical industry. In recent years, Cellulose-SA as an environmentally benign catalyst has been used for the synthesis of some heterocyclic compounds [3 – 9].

Optoelectronic devices, such as fiber switches, tunable lasers and amplifiers, modulators with various applications, require compounds emitting in the blue spectral region [10][11]. Cyanobenzene derivatives are good candidates for producing nonlinear optical materials [12] and molecular switches [13]. It seems that designing a highly efficient environmentally benign procedure for the preparation of fluorescent-substituted cyanobenzene derivatives is of great interest. Following our interest in the synthesis of fluorescent compounds [14 – 17], here we wish to report the synthesis of fluorescent 2,6-dicyano-3,5-dialkyl anilines using environmentally benign cellulose sulfuric acid as the catalyst in aqueous media (*Scheme 1*).

Results and Discussion

In 2007, *Tu et al.* [18] used the condensation reaction of 1,3-diphenylprop-2-en-1-one, malononitrile, and primary amines in DMF under microwave irradiation for the synthesis of 2,6-dicyanoaniline derivatives [18]. They postulated that amines in non-acidic or basic media acted only as a base for deprotonation of reactants and intermediates. They also reported the synthesis of 2-aminopyridine derivatives using the same reactants in DMF and the presence of AcOH and microwave irradiation. They suggested that under acidic conditions, contrary to basic media, the primary amines which could not act as a base, reacted as a reactant and appeared in the structure of the products. In agreement to their suggestion, we have recently reported the synthesis of some new fluorescent 2-amino-3-cyanopyridines using pentane-1,4-dione, malono nitrile, and amines in the presence of organic acids (*N*-hydroxybenzamide or TsOH) [14]. When Cellulose-SA was used as the catalyst, the only products were 2,6-dicyanoaniline derivatives instead of 2-amino-3-cyano pyridines. We have already used some acidic catalysts in organic synthesis [14 – 17]. In this report, we used 1,3-

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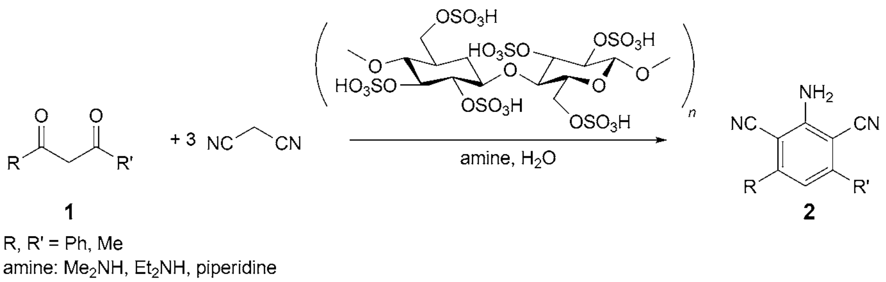
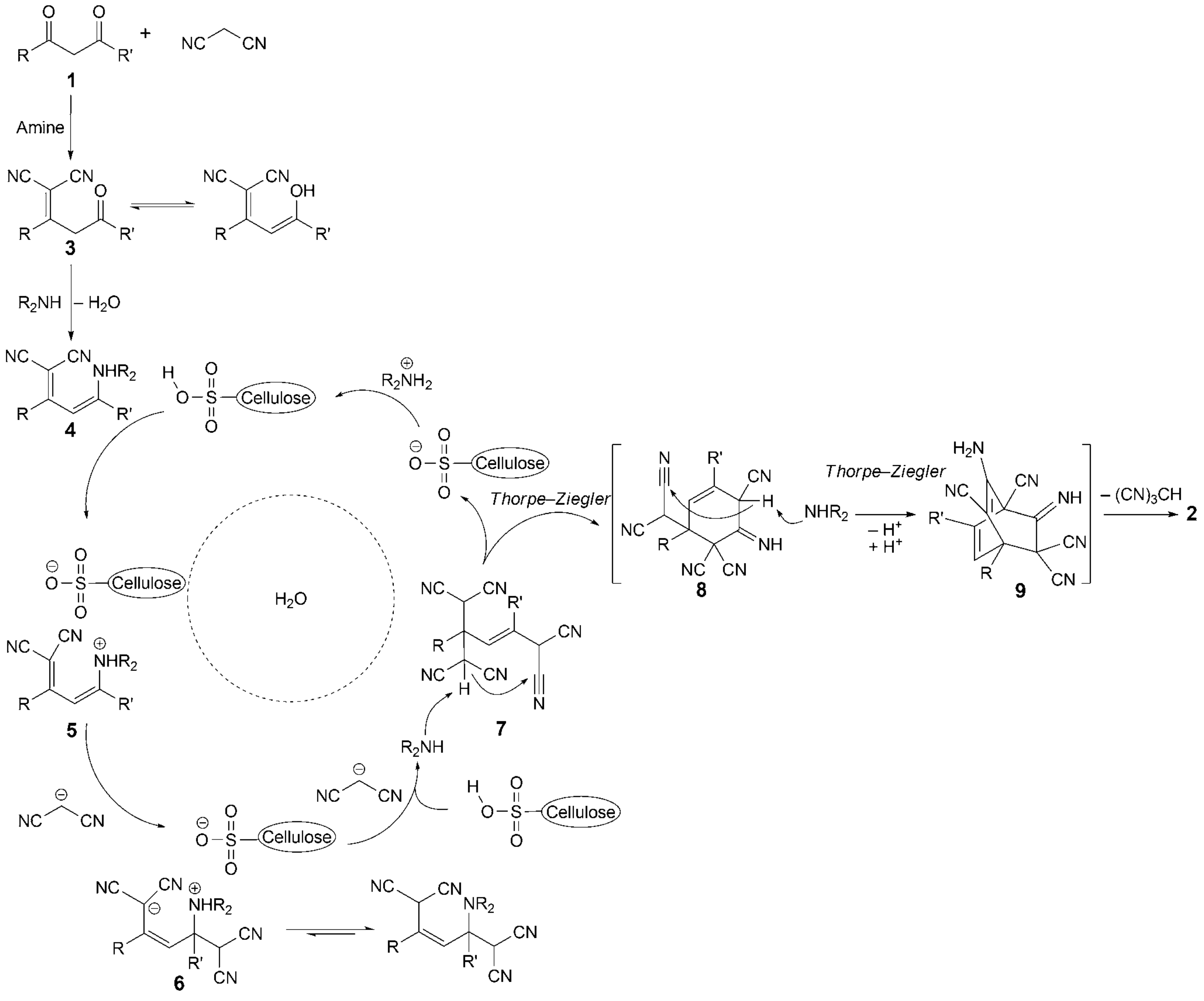
Scheme 1. Synthesis of 2,6-dicyano-3,5-disubstitued anilines **2a** – **c**



diketones **1** and malononitrile in the aqueous media and presence of secondary amines (Me_2NH, Et_2NH, and piperidine) for the synthesis of some fluorescent 2,6-dicyanoanilines **2**. We used Cellulose-SA as the catalyst in this procedure. Cellulose-SA changed the reaction path completely. It performed its role as an acidic catalyst which can be considered as a catalytic cycle (*Scheme 2*). On the other hand, Cellulose-SA allows the use of H_2O as the solvent instead of organic solvents without the need of microwave irradiation used in the previous report by *Tu et al.* [18]. The more effective role of H_2O on the

Scheme 2. The proposed mechanism for the synthesis of compounds **2**



synthesis of **2a** is compared with MeCN, EtOH, MeOH, and DMF (*Table 1*).

The reaction did not proceed in the absence of amines. For exploring the role of the amine in the above reaction, we replaced the secondary amine with Et_3N and other tertiary amines, but no products were observed. Therefore, we guessed that the amine not only acts as a base in the first stage of the reaction, but also can assist Cellulose-SA to proceed the reaction. Replacing one of the Me groups or both of them in pentane-2,4-dione by Ph moieties produced **2b** – **c** in high yields by the present procedure. Compound **2b** has attracted a lot of interest. It has been the subject of many studies in recent years, and some approaches have been reported for its synthesis [19 – 21]. Here, we report the Cellulose-SA catalyzed synthesis of **2b** using 1-phenylbutane-1,3-dione as reactant in H_2O as solvent. The present procedure meets the 'green chemistry' using Cellulose-SA as a biodegradable catalyst and H_2O as the best environmentally benign solvent.

Compound **2c**, which also had been the subject of some previous reports [22 – 24], is also synthesized by this new procedure. The Ph groups do not seem to affect the role of catalytic activity of Cellulose-SA in this synthetic procedure (85% yield). Optimal times, yields, and melting points of the synthesized compounds **2a** – **c** using this procedure are compared in *Table 2*.

Structures of compounds **2a** – **c** were assigned on the basis of their elemental analysis, IR, ^1H- and ^{13}C-NMR, and MS data. Single crystals of **2a** were obtained from a mixture of AcOEt and hexane, and its X-ray crystal structure confirms unambiguously the proposed structure (*Fig. 1*).

A plausible reaction mechanism which can explain the catalytic role of Cellulose-SA is shown in *Scheme 2* and the final step is very similar to the *Thorpe–Ziegler* reaction [19]. Primary condensation of 1,3-diketone **1** and malononitrile produced adduct **3**, which exist in equilibrium with its enolic form, and in the presence of the secondary amine afforded the conjugated enamine **4**. Cellulose-SA was added in this stage of the reaction. Thus, enamine **4** was protonated to produce **5**. *Michael* addition of malononitrile anion to **5** produced adduct **6**, which is stabilized by the anion of Cellulose-SA. Addition of a third anion of malononitrile and elimination of the secondary amine yields **7**. The acidic proton of **7** can be removed and intermediate **8** was produced by an intramolecular cyclization (*Thorpe–Ziegler* reaction). Intermediate **8** was converted to **9** by the aid of the amine and finally product **2** was obtained by a second *Thorpe–Ziegler* reaction. This part of mechanism is closely related to the one reported by *Yi et al.* [19]. In contrast to our previous report, the amine did not act as the reactant; it played its interesting role twice, first, by producing enamine **4** as precursor of the more effective *Michael* acceptor **5** in the presence of Cellulose-SA, and second, by deprotonation of intermediates **7** and **8**. Comparing our previous report on 2-aminopyridines using the same reactants [14], in the present reaction, Cellulose-SA prevents nucleophilic addition to the nitrile group and controls the reaction path.

Table 1. Solvent effect on the Cellulose-SA catalyzed synthesis of 2,6-dicyano-3,5-dimethylaniline (**2a**[a]))

Entry	Solvent	Time [h]	Yield [%]
1	MeCN	16	55
2	EtOH	12	75
3	MeOH	12	70
4	DMF	14	66
5	H_2O	8	92

[a]) 0.05 g of cellulose-SA has been used.

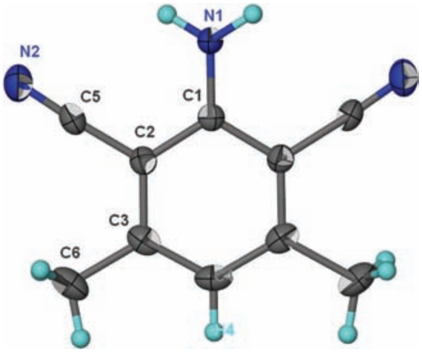


Fig. 1. X-Ray crystal structure of **2a**.

Cellulose-SA has already been used as a catalyst for the reaction between amines and other reactants [9][25][26].

The reusability of cellulose sulfuric acid was checked by recovering the Cellulose-SA from the reaction mixture of the synthesis of **2a**. Simple filtration and washing the recovered Cellulose-SA with 5 ml of 10% H_2SO_4, then with 5 ml of CH_2Cl_2 for 2 – 3 times, and drying in a

Table 2. Reaction times and yields of the synthesis and melting points of 2,6-dicyano-3,5-disubstitued anilines **2a** – **c**

Entry	Compound	R	R′	Time [h]	Yield [%][a])	M.p. [°]
1	**2a**	Me	Me	8	92	211 – 212 ([29]: 211 – 213)
2	**2b**	Me	Ph	11	72	179 – 180 ([20]: 191; [21],188 – 190)
3	**2c**	Ph	Ph	10	85	224 – 225 ([23]: 216 – 218)

[a]) Yield of isolated product.

vacuum oven at about 60 °C for 6 h were enough. The recovered Cellulose-SA was used for at least four additional times for the proposed reaction without any significant loss in the product yield (*Fig. 2*).

The products **2a** – **c** have shown fluorescent properties in the solid state and in solution. In the literature, 3,5-disubstituted-2,6-dicyano anilines have been the subject of many fluorescent studies [27]. The synthesis of **2a** has been reported by *Hull et al.*, using 1-acetyl-2-aminopropen and malononitrile [28]. Also photophysical properties of compound **2a** were previously reported *via* quantum mechanical calculations by *Kolek et al.* [29].

Fluorescence properties of **2a** – **c** including $\lambda_{\text{Abs.}}$ (nm), $\lambda_{\text{Flu.}}$ (nm) have been measured in CH_2Cl_2, MeCN, and MeOH (2×10^{-5} M conc.). The results in *Table 3* show that the fluorescence maxima ($\lambda_{\text{Flu.}}$) of **2a** and **2b** are shifted to longer wavelength by increasing the solvent polarity. On the other hand, $\lambda_{\text{Flu.}}$ of **2c** in MeOH is at lowest wavelength than in MeCN, probably as a result of the presence of two Ph groups in its structure lowering the stability in MeOH as a protic solvent.

We were delighted to find that the synthesized compounds not only showed strong fluorescence in different solvents, but also two of them are highly fluorescent even in the solid state that is necessary for the development of electronic devices, such as solid-state organic lasers. Fluorescence molecular spectroscopy of the new compounds has been studied. Each sample (0.5 ml) in $CHCl_3$ (10^{-10} M) was first coated on a glass sheet and dried at room temperature, then placed in a 1 cm length quartz cell. The excited and emission slits were adjusted to 5 nm. The fluorescence emission intensity of compounds after excitation at 290 nm is shown in *Fig. 3*.

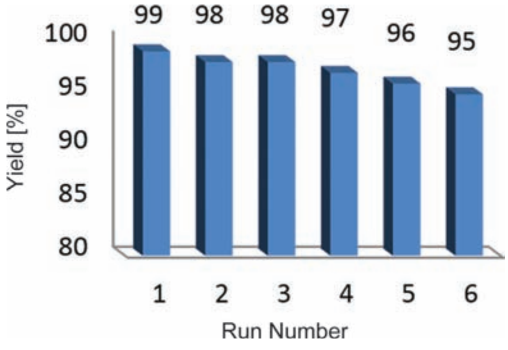


Fig. 2. Reusability of Cellulose-SA as catalyst in the preparation of 2,6-dicyano-3,5-dimethyl aniline **2a**.

Conclusions

Biodegradable cellulose sulfuric acid catalyzed the formation of some 2,6-disubstituted dicyanoaniline derivatives in aqueous media in excellent yields. The reaction workup is very simple because of the aqueous media. The catalyst can be easily separated from the reaction mixture and reused several times in subsequent reactions without significant loss in the yields of products. The present procedure meets the 'green chemistry' using Cellulose-SA as a reusable biodegradable catalyst and H_2O as the best environmentally benign solvent. Further investigation of this method is currently in progress to establish its scope and utility. The products showed fluorescence properties in solution and in the solid state. Photophysical properties of the synthesized compounds ($\lambda_{\text{Abs.}}$, $\lambda_{\text{Flu.}}$) in CH_2Cl_2, MeCN, and MeOH are measured. The fluorescence emission intensity of compounds after excitation at 290 nm is reported too. We are hopeful that the synthesized fluorescent compounds can play a significant role in biochemical research and technology upgrading, probably useful for electronic devices, such as organic lasers.

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Experimental Part

General

Chemicals and solvents were obtained from *Merck* (Germany) and *Fluka* (Switzerland). M.p. was measured on a *Barnstead Electrothermal* melting point apparatus and was not corrected. IR Spectra were measured on a *Bruker EQUINOX 55* spectrophotometer using the ATR method. ^{1}H- and ^{13}C-NMR spectra were determined on a *Bruker* spectrometer at 500 MHz and 128 MHz, respectively. Mass spectra were recorded on a *Finnigan-MAT 8430* spectrometer at an ionization potential of 70 ev. All fluorescence intensity measurements and fluorescence emissions were obtained by a luminescence *PERKIN ELMER LS 50B* spectrometer. The photo is taken under a lamp at λ = 366 nm (*TL8W/08F8T5/BLC Philips* made

Table 3. The photophysical data, electronic absorption (*Abs.*) and fluorescence (*Flu.*) of **2a** – **c** in solution

Entry	Compound	$\lambda_{\text{Abs.}}$ (CH_2Cl_2)	$\lambda_{\text{Flu.}}$ (CH_2Cl_2)	$\lambda_{\text{Abs.}}$ (MeCN)	$\lambda_{\text{Flu.}}$ (MeCN)	$\lambda_{\text{Abs.}}$ (MeOH)	$\lambda_{\text{Flu.}}$ (MeOH)
1	**2a**	340	366	335	375	341	386
2	**2b**	340	396	342	416	360	431
3	**2c**	345	396	344	409	333	391

$\lambda_{\text{Abs.}}$ [nm], $\lambda_{\text{Flu.}}$ [nm] have been measured for 2×10^{-5} M in CH_2Cl_2, MeOH, MeCN.

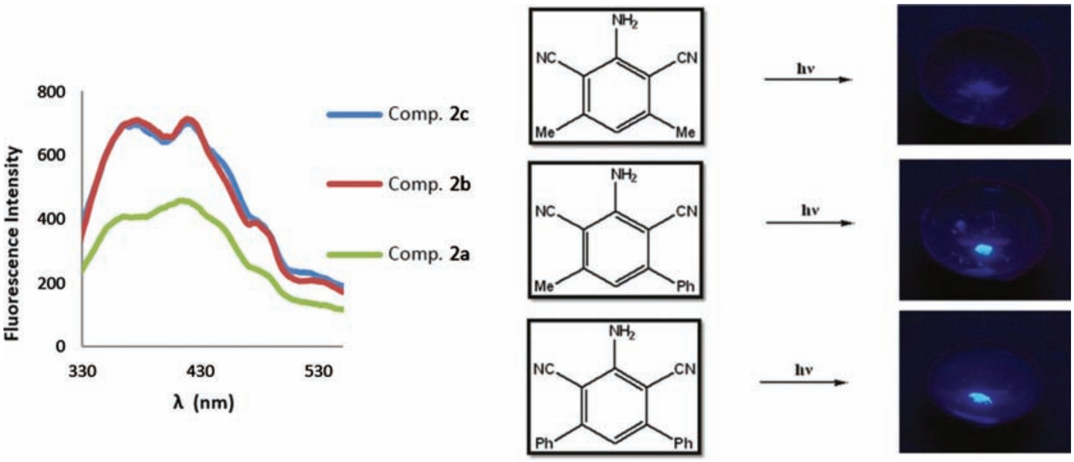

Fig. 3. Left: The fluorescence emission spectra of the synthesized compounds in the solid state after excitation at 290 nm. Right: Photos of compounds **2a** – **c** in the solid phase under the same fluorescence lamp λ = 366 nm.

in Holland, the Netherlands). Elemental analysis for C, H, and N were performed using a *Thermo Finnigan Flash EA1112* instrument. Crystallographic data for the structure of compound **2a** have been deposited with the *Cambridge Crystallographie Data Center* as CCDC-941206, which contains the supplementary crystallographic data for this work. These data can be obtained free of charge *via* http://www.ccdc.com.ac.uk/data_request/cif.

Preparation of Cellulose Sulfuric Acid

Cellulose-SA was prepared by the method described in [9]. To a magnetically stirred mixture of 5.0 g of cellulose in 20 ml of hexane, 1.0 g of chlorosulfonic acid (10 mmol) was added dropwise at 0 °C during a 3 h period. HCl gas was removed from the reaction vessel immediately. The mixture was stirred for 3 h at room temperature until HCl gas was removed completely. Then the mixture was stirred for 3 h, filtered, and washed with 30 ml of MeCN and dried at room temperature; 5.25 g of Cellulose-SA was obtained as a white powder. The sulfur content of the synthesized samples of Cellulose-SA was 0.55 mmol/g determined by conventional elemental analysis. The number of H^+ sites on the cellulose-SO_3H was determined by acid–base titration and was found to be 0.50 meq/g. This value corresponds to about 90% of the sulfur content indicating that most of the sulfur species are in the form of sulfonic acid [9].

General Procedure for the Synthesis of Compounds **2a** – **c**

To a mixture of 1,3-diketone **1** (1 mmol) and malononitrile (3 mmol) in H_2O (3 ml) was added a secondary amine **3** (1 mmol). The mixture was stirred for 5 min. When the synthesis of the conjugated enamine **4** was completed, cellulose sulfuric acid (0.05 g) was added to the above mixture. The mixture was stirred at room temperature for 8 – 11 h (*Table 1*). The progress of the reaction was monitored by TLC. When the enamine spot was disappeared and the spot of the product was reached to its maximum ($R_f \approx 0.6$ on silica gel, hexane/AcOEt 2:1), the product was extracted with AcOEt. Colorless crystals of the products were obtained by recrystallization in AcOEt/hexane 1:3.

Recovering the Catalyst (Cellulose-SA)

To recover the catalyst, the solid residue was washed using 5 ml of 10% H_2SO_4 and then 5 ml of CH_2Cl_2 for three times. The separated cellulose sulfuric acid was dried in the vacuum oven and it can be used at least another four times without significant loss of activity.

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