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ORIGINAL PAPER

Multicomponent synthesis of 3,5-diaryl-2,6-dicyanoanilines under thermal solvent-free conditions

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Abstract A facile parallel synthesis of 3,5-diaryl-2,6-dicyanoanilines via three-component reaction of aryl aldehydes, acetophenone derivatives, and malononitrile under thermal green solvent-free conditions in the presence of potassium carbonate and also potassium bicarbonate without using any hazardous materials is described.

Keywords Multicomponent · Aryl aldehydes · Acetophenones · Malononitrile · Carbonate salts

Introduction

Combinatorial chemistry techniques have evolved very rapidly and are playing significant roles in the development of modern synthetic organic chemistry [1–3]. This methodology allows molecular complexity and diversity to be created by the facile formation of several new covalent bonds in a one-pot transformation quite closely approaching the concept of an ideal synthesis and is particularly well adapted for combinatorial synthesis [4, 5]. Combinatorial chemistry has been successfully applied to development and improvement of novel pharmaceutics [6], materials, and catalysts by using rapid parallel syntheses in solvent-free systems [7] and also on polymer supports [8]. Combinatorial synthesis on the solid phase can generate very large numbers of products, using a method described as mix and split synthesis [9].

3,5-Diaryl-2,6-dicyanoanilines are useful intermediates and act as building blocks for cyclophanes [10] to create a large molecular cavity [11] and host–guest complexes [12]. Some of these molecular systems are the basis for artificial photosynthetic systems [13, 14], materials presenting semiconducting or nonlinear optical properties [15–18], and molecular electronic devices [19]. These compounds have been prepared from arylidenemalonodinitriles and 1-arylethylidenemalonodinitriles in the presence of piperidine [20]. The reaction between malononitrile and α,β-unsaturated ketones can also give 3,5-diaryl-2,6-dicyanoanilines, but the yields were very poor (5–20%) [21, 22]. A literature survey showed that several methods have been reported for the synthesis of 3,5-diaryl-2,6-dicyanoanilines [23–27], but they suffer from several drawbacks, such as multistep reactions, long reaction times, an excess of volatile organic solvents, harsh refluxing conditions, and especially lower product yields. To improve the synthesis of 3,5-diaryl-2,6-dicyanoanilines, we developed a practical three-component reaction that significantly reduces the reaction time and increases the yields. In addition, according to the reported literature, some of these products show fluorescent properties [25]. The α,β-unsaturated ketones are generated in situ from the corresponding aryl aldehydes and aromatic enolizable acetophenone derivatives in the presence of potassium carbonate and also potassium bicarbonate, the desired products are captured one-pot by two equivalents (eq) of malononitrile under the same experimental conditions, forming the corresponding 3,5-diaryl-2,6-dicyanoaniline derivatives under thermal green solvent-free conditions (Scheme 1).

Results and discussion

First, a mixture of 1 eq benzaldehyde, 1 eq acetophenone, and 2.5 eq malononitrile was reacted in the presence of

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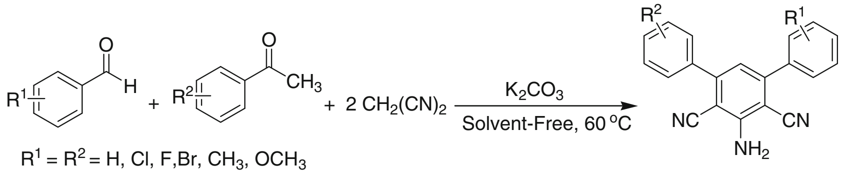


Scheme 1

0.5 g potassium carbonate under thermal solvent-free conditions in an oil bath (60 °C) and also at room temperature. The reaction proceeded at 60 °C, whereas the starting materials remained unchanged at room temperature. Next, we synthesized some 3,5-diaryl-2,6-dicyanoaniline derivatives via three-component reaction of aryl aldehydes, acetophenone derivatives, and malononitrile under thermal solvent-free conditions in the presence of K_2CO_3 at 60 °C (Table 1). As shown in Table 1, the reaction completed within only a few minutes and the yields were extensively increased as compared with the published methods. When potassium bicarbonate was used instead of potassium carbonate, the yields decreased dramatically despite much longer reaction times.

A mechanistic rationale for the three-component reaction is shown in Scheme 2.

We studied the products of the reactions and found 3,5-diaryl-2,6-dicyanoaniline derivatives, accompanied by a small quantity of the α,β-unsaturated ketones **I** and nitriles **II** as by-products. In this methodology, the products were purified by recrystallization in ethanol.

In conclusion, we have demonstrated a facile method for the preparation of 3,5-diaryl-2,6-dicyanoanilines via a three-component reaction of aryl aldehydes, acetophenone, and malononitrile under thermal green solvent-free conditions at short reaction times without using any hazardous materials. Use of potassium carbonate as catalyst has inherent advantages including operational simplicity, low cost, and suitability in industrial applications.

Experimental

All reagents were purchased from Merck and Aldrich and used without further purification. All yields refer to isolated products after purification. Products were characterized by comparison with authentic samples and by spectroscopic data (IR, ^{1}H NMR spectra). The NMR spectra were recorded on a Bruker Avance 400-MHz instrument. The spectra were measured in DMSO-d_6 and $CDCl_3$ relative to TMS (0.00 ppm). IR spectra were recorded on a JASCO 460 Plus spectrophotometer. Melting points were determined in open capillaries with a BUCHI 510 melting point apparatus. TLC was performed on silica gel polygram SIL G/UV 254 plates.

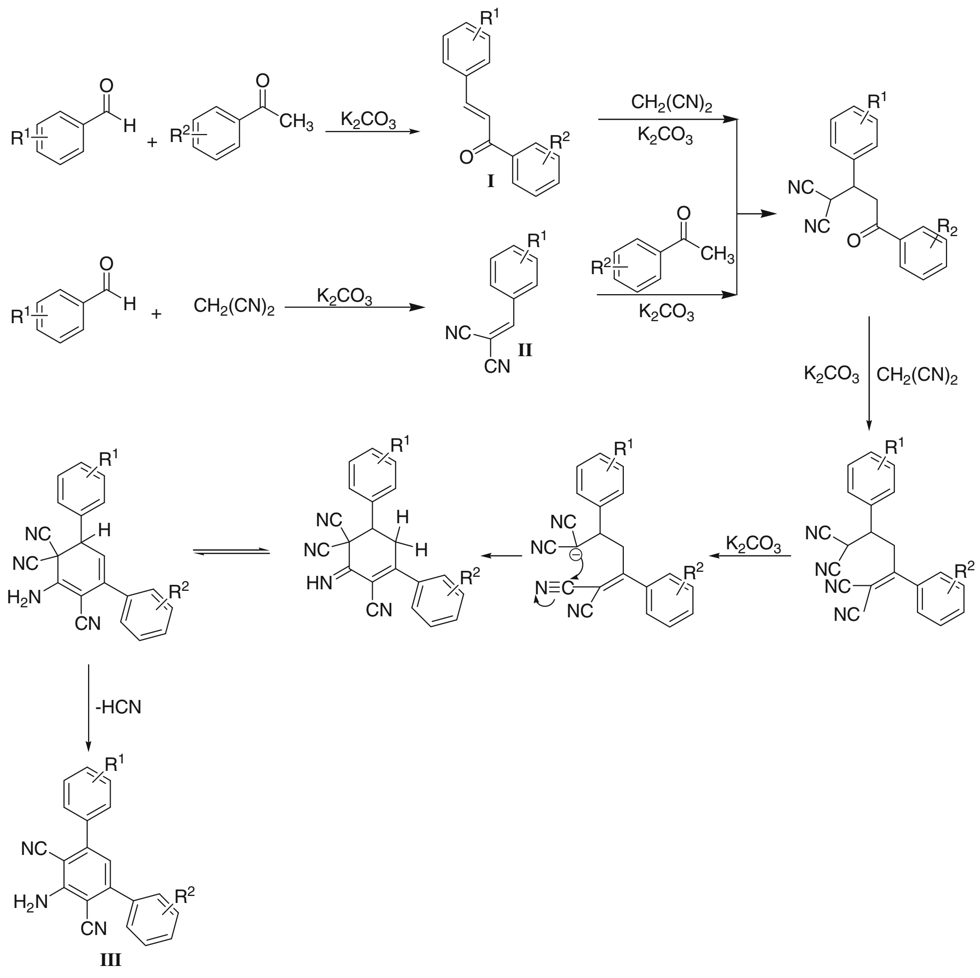
General procedure for preparation of 3,5-diaryl-2,6-dicyanoanilines

To a mixture of 1 mmol aryl aldehyde, 1 mmol acetophenone, and 2.5 mmol malononitrile, 0.5 g K_2CO_3 (3.5 mmol) was added. The mixture was stirred at 60 °C in an oil bath.

Table 1 Synthesis of 3,5-diaryl-2,6-dicyanoaniline derivatives using K_2CO_3 as base

Entry	Aldehyde	Ketone	Time (min)/yield (%)[a]	M.p. (°C)	
				Found	Literature [Ref.]
1	4-CH_3–C_6H_4	C_6H_5	2/72	200–202	201–202 [26]
2	4-CH_3–C_6H_4	4-Cl–C_6H_4	15/75	191–193	191–192 [27]
3	4-F–C_6H_4	C_6H_5	6/68	222–224	221–223 [27]
4	4-Cl–C_6H_4	C_6H_5	15/70	246–247	244–246 [27]
5	2-Cl–C_6H_4	C_6H_5	8/67	209–211	208–210 [27]
6	3-Cl–C_6H_4	C_6H_5	8/69	220–221	221–223 [27]
7	4-Br–C_6H_4	C_6H_5	10/74	253–254	251–254 [27]
8	4-Cl–C_6H_4	4-Br–C_6H_4	3/65	278–279	278–280 [27]
9	4-Cl–C_6H_4	4-CH_3O–C_6H_4	4/70	185–187	188–191 [27]
10	4-Cl–C_6H_4	4-Cl–C_6H_4	4/72	271–273	271–273 [27]

[a] Yields refer to pure isolated products. All known products have been reported previously in the literature and were characterized by comparison of melting points, IR, and NMR spectra with authentic samples



Scheme 2

The completion of the reaction was monitored by TLC (Table 1). For work-up the mixture was cooled to 25 °C, ethyl acetate added, and the mixture stirred for 5 min. Then water was added to the solutions, and the organic phase was extracted twice with 10 cm^3 of ethyl acetate. The organic solution was separated and concentrated; the solid so obtained was filtered and recrystallized from ethanol. The desired pure products were characterized by comparison of their physical data with those of known compounds [26, 27].

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