Tetrahedron Letters 56 (2015) 4207–4210

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Straightforward syntheses of nitriles, acrylates, and acrylamides in aqueous propan-1,2-diol: a catalyst free and waste free methodology

Lakshmi Narayanan Jayalakshmi, Ayyanar Karuppasamy, Kesavan Stalindurai, Ramar Sivaramakarthikeyan, Vellasamy Devadoss, Chennan Ramalingan *

Centre for Nanotechnology/Department of Chemistry, Kalasalingam University, Krishnankoil 626 126, Tamilnadu, India

ARTICLE INFO

Article history:
Received 10 February 2015
Revised 15 May 2015
Accepted 17 May 2015
Available online 21 May 2015

Keywords:
Olefin
Malononitrile
Acrylamide
Propan-1,2-diol
Reusability

ABSTRACT

A mild, elegant, catalyst free, and waste free methodology has been developed for the clear-cut synthesis of a diverse range of nitriles, acrylates, and acrylamides in good to excellent yields using aqueous propan-1,2-diol, a green reaction medium, at ambient temperature. Operational simplicity and recyclability of the reaction medium are added advantages of the methodology.

Condensation between aldehydes and compounds possessing an active methylene moiety, known as the Knoevenagel reaction, is one of the efficient techniques for the construction of olefins. Numerous methodologies have been developed for this reaction in the recent past including employment of inorganic/organic bases,[1] metal based/encapsulated nanoparticles,[2] zeolites,[3] metal organic frameworks,[4] ionic liquids,[2a,5] mesoporous materials,[6] ammonium salts/phase-transfer catalysts,[7] and other metal based reagents[8] as catalysts. Further, a few other methods such as microwave assisted as well as Baker's yeast and fiber catalyzed reactions have also been developed.[9] In most of the cases, however, catalysts and/or external energy (elevated temperature), long reaction period or more toxic solvents have been used and, in many cases, wastage is inevitable as well. Considering the energy, environmental and expenditure concern, various research groups around the globe have developed new methods for this reaction utilizing water as a reaction medium. However, catalysts are vital in those cases to afford the products in good yields. For example, Fujita and co-workers[10] reported a cage-catalyzed method in water at ambient temperature, but it was not proficient in the absence of catalyst even after 2 h. Akin to the same, Zhang and Xia,[2a] Ren and Cai,[4a] Phadtare and Shankarling,[11] Zhang *et al.*[9c] and Xie and co-workers[8] also developed similar methods in water. Still, utilization of a catalyst is crucial in all the cases. Processes with the use of simple polar protic solvents such as ethanol and methanol along with catalysts have also been reported.[2c,7b,9b,12] Further, various catalyst-free methods have been developed in elegant ways, however, the requirement of elevated temperatures, unusual conditions, or toxic solvents is vital and substrate scope is limited in many cases. For instance, Tewari and co-workers[13] reported the condensation in water, nevertheless, the method needs elevated temperature and is also limited to substituted benzaldehydes and cyanoacetamide. While the method of Xue et al.[14] requires DMSO as solvent and is also restricted to selected substrates, the method of Feroci et al.[15] necessitates an electrochemical setup and is also limited to malononitrile. Ondruschka and co-workers[16] developed a mechanochemical method, again limited to only malononitrile and selected aldehydes, also requiring long reaction periods. We herein disclose an elegant and waste free method for the construction of olefins without employing external energy or catalyst, by means of aqueous propan-1,2-diol, an environmentally benign solvent, at room temperature.

In a search of bio-significant heterocyclic chemical entities, we firstly synthesized 2-[(3-(4-chlorophenyl)-1-phenyl-1*H*-pyrazol-4-yl)methylene]malononitrile **(3)** (Fig. 1) from 3-(4-chlorophenyl)-1-phenyl-1*H*-pyrazole-4-carbaldehyde **(1)** and malononitrile **(2)** in the presence of piperidine in ethanol. This compound exhibits good antioxidant property as evidenced from its preliminary antioxidant evaluation. It is certain that synthesis of this class of chemical entities, through a simple and green methodology would be beneficial.

* Corresponding author. Tel.: +91 4563 289042; fax: +91 4563 289322.
E-mail address: ramalinganc@gmail.com (C. Ramalingan).

http://dx.doi.org/10.1016/j.tetlet.2015.05.052
0040-4039/

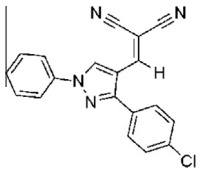
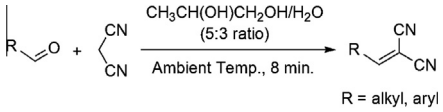


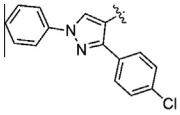
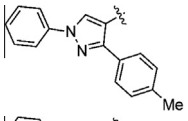
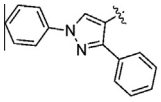
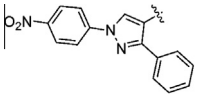
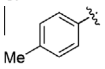
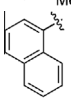
Figure 1.

Consequently, we developed a green and proficient method for olefin bond formation, the eventual step of the aforementioned target.

At the outset, compounds **1** and **2** were chosen as model reactants. When equimolar quantities of **1** and **2** were stirred in water at ambient temperature, the reaction did not proceed even after 1 h. Elevating the reaction temperature to reflux also culminated with similar results (the product was formed in trace amounts). The inefficiency of the reaction may be due to the insoluble nature of the aldehyde in water. On the other hand, it is known that propan-1,2-diol is a clear, stable, nonvolatile, and nonhazardous (Regulation (EC) No. 1272/2008) liquid and is classified as nondangerous (According to Directive 67/548/EEC). Also, it has been extensively utilized in pharmaceutical manufacturing, as a solvent and vehicle chiefly for drugs which are insoluble or unstable in water. It is used as a plasticizer, preservative, and stabilizing agent as well. Thus, we hypothesized that propan-1,2-diol would probably be a better alternative solvent. To our delight, when the model reaction was performed in aqueous propan-1,2-diol ($CH_3CH(OH)CH_2OH/H_2O$ – 5:3 ratio), the corresponding olefin **3** was obtained exclusively (97% yield) in 8 min. The reaction also proceeded in propan-1,2-diol alone, however, the yield of the product was diminished to 79%. Use of propan-1,2-diol and water with 1:2 and 1:4 ratios also ended up in lower yields. The typical experimental procedure is as follows: When compounds **1** (1.0 mmol) and **2** (1.0 mmol) were stirred in a mixture of propan-1,2-diol (4 mL) and water (2.5 mL) for 8 min at ambient temperature, a light yellow solid was obtained and then filtered. The filtrate was then taken out separately and the solid thus obtained was washed with water and dried. Recrystallization from ethanol-DMF mixture afforded analytically pure **3**. The general schematic representation is provided in Table 1.

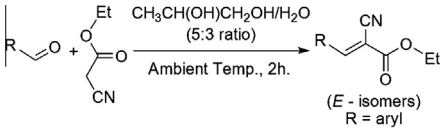
Table 1
Condensation of aldehydes with malononitrile

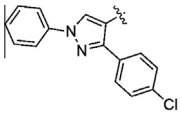
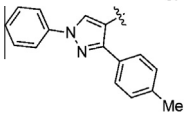
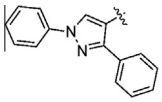
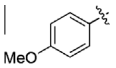
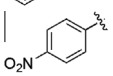
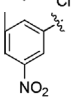
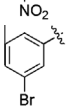
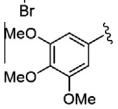


Entry	Product (R=)[a]	Yield[b] (%)	Mp[Ref] (°C)
1		97	217–218
2		90	185–186
3		91	214–215
4		94	249–250
5		95	167–168[17]
6		89	130–131[18]
7		92	86–87[18]
8		93	93–94[4a]
9		86	97–98[2c]
10		90	175–176[8]
11		66	—[6a]

[a] Heterocyclic aldehydes (entries 1–4) were synthesized from respective aryl hydrazines and aralkyl ketones by adopting condensation followed by Vilsmeier–Haack reactions.
[b] Reactions were performed for 8 min.

Table 2
Condensation of aldehydes with ethyl 2-cyanoacetate



Entry	Product (R=)[a]	Yield[b] (%)	Mp[Ref] (°C)
1		95	106–107[1c]
2		88	138–139[1c]
3		90	133–135[1c]
4		87	81–82[1e]
5		94	84–85[19]
6		90	51–52[20]
7		92	166–167[19]
8		93	54–55[21]
9		89	128–129[22]
10		95	80–81[23]
11		79	47–48[24]

[a] Heterocyclic aldehydes (entries 1–3) were synthesized from respective aryl hydrazines and aralkyl ketones by adopting condensation followed by Vilsmeier–Haack reactions.
[b] Reactions were performed for 2 h.