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Synthesis and characterization of new 5-substituted 1H-tetrazoles in water: a greener approach

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Abstract: In energetic materials research, much effort has been devoted to the development of environmentally benign, "green" energetic materials. Tetrazoles are readily accessible nitrogen-rich energetic compounds. Herein, we would like to report a novel, facile, eco-friendly and one-pot process for synthesis of 5-substituted 1H-tetrazoles via a domino Knoevenagel condensation and 1, 3 dipolar cycloaddition reactions. This general protocol provides 5-substituted 1H-tetrazoles in good yields under mild reaction conditions. These tetrazoles were characterized by FT-IR and ^{1}H-NMR, ^{13}C-NMR spectroscopy and thermogravimetric analysis.

Keywords: Green chemistry, Tetrazoles, Knoevenagel Condensation, 1,3 Dipolar cycloaddition.

Introduction

Nowadays, the main goals of 'green chemistry' are to increase process selectivity, maximize the use of starting materials, and to replace hazardous reagents with eco-friendly materials. Organic reactions in water without using harmful organic solvents have attracted a great deal of interest in both academic and industrial research because, in addition to environmental concerns, there are beneficial effects of aqueous solvents on rates and selectivities of important organic transformations [1-5]. Tetrazoles are a class of heterocycles that have received attention due to their wide range of applications [6]. In general, this nitrogen-rich ring system is used in propellants [7], explosives [8], and in pharmaceuticals [9]. In addition, tetrazoles are important synthons in synthetic organic chemistry [10], and also used as precursors of carbenes in flash vacuum pyrolysis [11]. Various tetrazole-based compounds have also shown good coordination properties and are able to form stable complexes with several metal ions [12]. Furthermore, the tetrazole ring has strong electronwithdrawing property and tetrazolyl halides have been successfully used in organic synthesis as derivatising agents for the chemical modification of alcohols [13]. Therefore, a number of methods have been reported for the preparation of tetrazoles [14, 15]. One of the major synthetic routes to tetrazole formation is the [2+3] cycloaddition of an organonitrile and an azide salt [16- 18]. However, many of these protocols have some disadvantages, such as the use of toxic metals, strong Lewis acid, expensive reagents, low yield, drastic reaction conditions, water sensitivity and the presence of hydrazoic acid, which is toxic and explosive. In addition, all of the known methods use organic solvents, in particular, dipolar aprotic solvents, such as DMF [19, 20]. Thus, the development of a convenient and safe process for the preparation of new tetrazole derivatives is an interesting target for investigation. In the present work, an efficient method for the preparation of 5-substituted 1H-tetrazole derivatives via multi-component domino Knoevenagel condensation/1, 3 dipolar cycloaddition reaction of carbonyl compounds, malononitrile and sodium azide in water without assistance of any catalyst is reported. This method has

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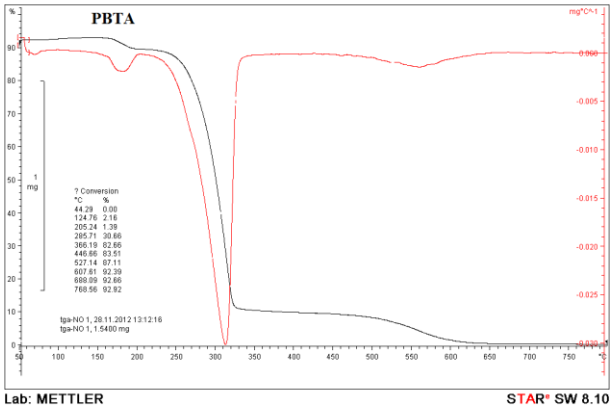
the advantages of high yields, simple methodology and easy work-up.

Results and discussion

This general protocol provides derivatives of 5-substituted 1H-tetrazoles in good yields (near 80%), under mild reaction conditions and in the absence of any catalyst. The catalyst-free reactions carried out in water are safe, nontoxic, environmentally friendly and inexpensive. The absence of catalyst for the reaction avoids the use of moisture-sensitive heavy metals, such as Lewis acids. Mechanistically, the formation of tetrazoles can be rationalized by initial formation of arylidenemalononitrile through a Knoevenagel condensation reaction, which this intermediate undergoes [2+3] cycloaddition reaction with the sodium azide to afford product. In FT-IR spectra of the products, an absorption band appears around 2230 cm^{-1}, which are assigned to the stretching vibrations of the nitrile groups.

Thermal analysis:

An explosion occurs when a great deal of energy is released in a very short period of time. To study the explosive properties of the compounds we studied thermal properties of these compounds. TGA is generally combined with DTA, and a plot of the loss in weight together with the DTA thermogram is recorded. These plots give information on the physical and chemical processes which are taking place. The results presented in Figure **1** show the exothermic effect of the thermal decomposition peaks of the samples based on tetrazoles of (E)-3-(3-Nitrophenyl)-2-(1H-tetrazole-5-yl) acrylonitrile (NPTA) and (E)-3, 3′-(phenyl)-bis (1, 4 (2-(1H-tetrazole-5-yl)) acrylonitrile) (PBTA). Compound PBTA with two tetrazole rings in its structure shows more explosive properties than NPTA with one tetrazole ring.



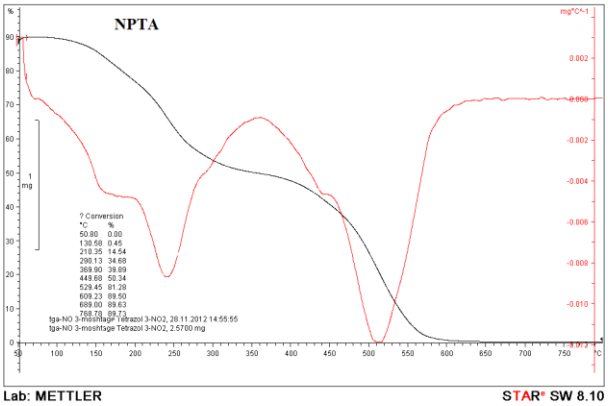


Figure 1: TGA of NPTA and PBTA.

Conclusion

In conclusion, an efficient, green and convenient method for the preparation of new 5-substituted-tetrazoles in water is reported. This new process provides an opportunity to use water and avoid environmentally harmful conventional organic solvents, easy work-up and reduced waste production by the lack of catalyst or additive agent.

Experimental

Materials:

The chemicals used in this work were obtained from Fluka and Merck companies and were used without purification.

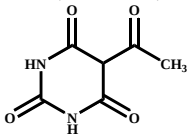
Measurements:

^{1}H-NMR and ^{13}C-NMR spectra were recorded on a Brucker 400 AC spectrometer in DMSO-d_6. The IR spectra were recorded on a Shimadzu FT IR-408 spectrophotometer. The DSC curves were obtained on a TGA/SDTA 851 calorimeter at heating and cooling rates of 10 ˚C/min in air.

*Preparation of 5- acetyl pyrimidine- 2, 4, 6(1H, 3H, 5H) – trione (Scheme **1**):*

The reaction was carried out in various conditions. In the best condition, while stirring, 25 mL of water was added to a mixture of 10 mmol of barbituric acid and 10 mmol sodium bicarbonate for 30 min under dry argon. Then, the mixture was filtered and 20 mmol acetic anhydride was added to the colorless solution under stirring. The reaction was carried out for 12 h. After completion of reaction, the reaction mixture was filtered and the white filtrate washed with water and then was dissolved in ammonium hydroxide (10%). For removing of remaining ammonium hydroxide on

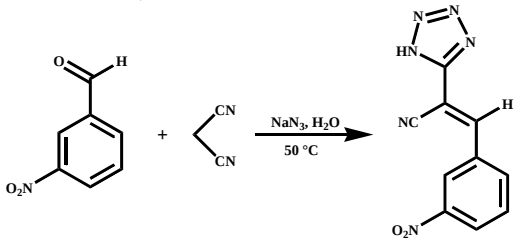
solution, the 10% HCl solution was used. Then the mixture was filtered and the product was dried in the air. The yield of final product was above 95%. White powder. M.p.: 398-400 ˚C; FT-IR (KBr, cm^{-1}): $\overline{\nu}$ = 3210 and 3276 (stretching N-H), 2996 (stretching C-H), 1737 (stretching C=O), 1250 (bending C=O).



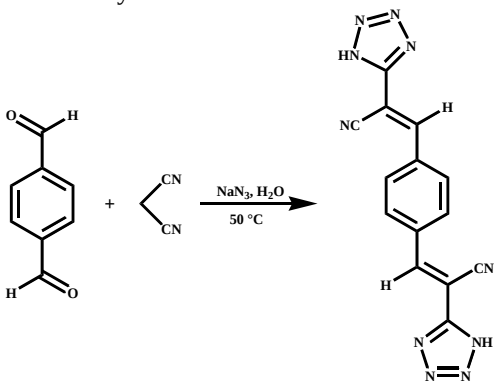
Scheme 1: Structure of 5- acetyl pyrimidine- 2, 4, 6(1H, 3H, 5H) – trione.

General procedure for the synthesis of tetrazoles:

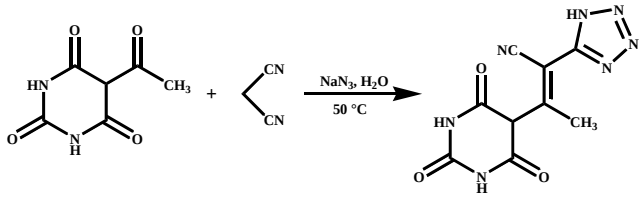
A mixture of carbonyl compound (1 mmol), malononitrile (1 mmol) and sodium azide (2 mmol) in H_2O (5 mL) was stirred at 50 °C for appropriate time, after completion of the reaction, as indicated by TLC, the reaction mixture was filtered. To the filtrate was added 30 mL of 2 N HCl with vigorous stirring causing the tetrazole to precipitate. The precipitate was filtered and dried in a drying oven to furnish the tetrazole (Schemes **2**-**4**).



Scheme 2: Synthesis of NPTA.



Scheme 3: Synthesis of PBTA.



Scheme 4: Synthesis of BTBN.

(Z)-3-(hexahydro- 2, 4, 6- trioxopyrimidine- 5-yl) - 2-(1H-tetrazole-5-yl)-2- butane nitrile: BTBN:

Cream powder. M.p.: 287-289 ˚C; FT-IR (KBr, cm^{-1}): $\overline{\nu}$ = 3421, 1653, 2051 and 2155; ^{1}H NMR (400MHz, DMSO-d_6): δ (ppm) = 3.35 (1H, s, NH, overlap with NMR analysis solvent), 3.4 (1H, s, H-sextet ring, overlap with NMR analysis solvent), 9.57 (2H, s, NH), 2.28 (3H, s, CH_3); ^{13}C NMR (300MHz, DMSO-d_6): δ (ppm) = 32, 88, 95, 150, 151, 156, 165.3, 165.8, 194.

(E)-3-(3-Nitrophenyl)-2-(1H-tetrazole-5-yl) acrylonitrile: NPTA:

Brown powder. M.p.: 218-220 °C; FT-IR (KBr, cm^{-1}): $\overline{\nu}$ = 2226, 3440, 1353, 1529, 1613; ^{1}H NMR (400MHz, DMSO-d_6): δ (ppm) = 3.40 (1H, s, NH, overlap with NMR analysis solvent),7.91 (1H, t, $^3J_{HH}$=2 Hz, H-Ar), 8.32 (1H, d, $^3J_{HH}$=2 Hz, H-Ar), 8.48 (1H, d, $^3J_{HH}$=2 Hz, H-Ar), 8.71 (1H, s, CH), 8.76 (1H, s, H-Ar); ^{13}C NMR (400MHz, DMSO-d_6): δ (ppm) = 84, 112, 113, 124, 127, 131, 132, 135, 148, 159.

(E)-3, 3′-(phenyl)-bis (1, 4 (2-(1H-tetrazole-5-yl)) acrylonitrile): PBTA:

Cream powder. M.p.: 249-252 ˚C; FT-IR (KBr, cm^{-1}): $\overline{\nu}$ = 2232, 3448 and 1585; ^{1}H NMR (400MHz, DMSO-d_6): δ (ppm) = 3.39 (1H, s, NH, overlap with NMR analysis solvent), 8.09 (4H, s, H-Ar), 8.63 (2H, s, H-olefines); ^{13}C NMR (400MHz, DMSO-d_6): δ (ppm) = 84, 112, 113, 130, 135, 159.

Acknowledgments

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