

Electronic Supplementary Information (ESI) for:

**Green synthesis of the 1-substituted 1*H*-1,2,3,4-tetrazoles by application of the Natrolite zeolite as a new and reusable heterogeneous catalyst**

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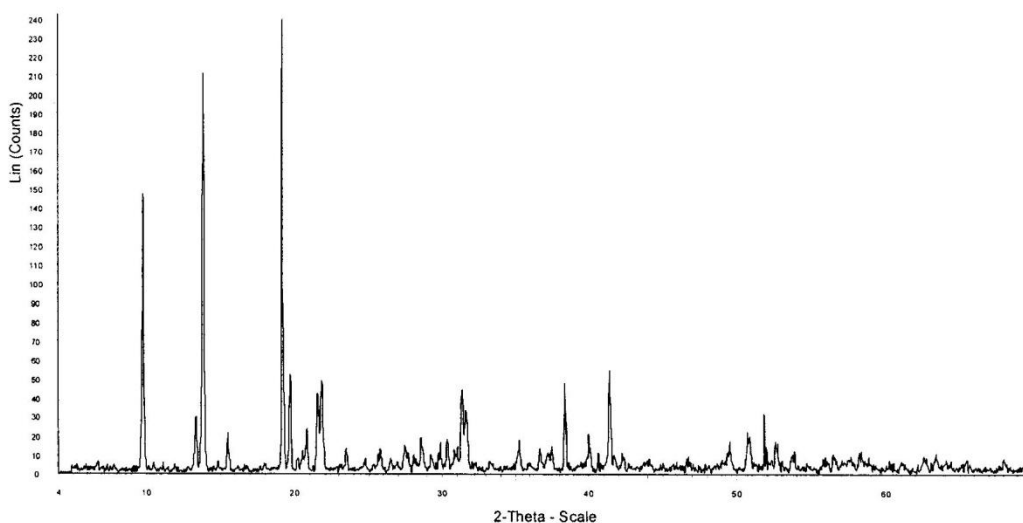
## Instrumentation, Analysis and Starting Materials:

### Experimental:

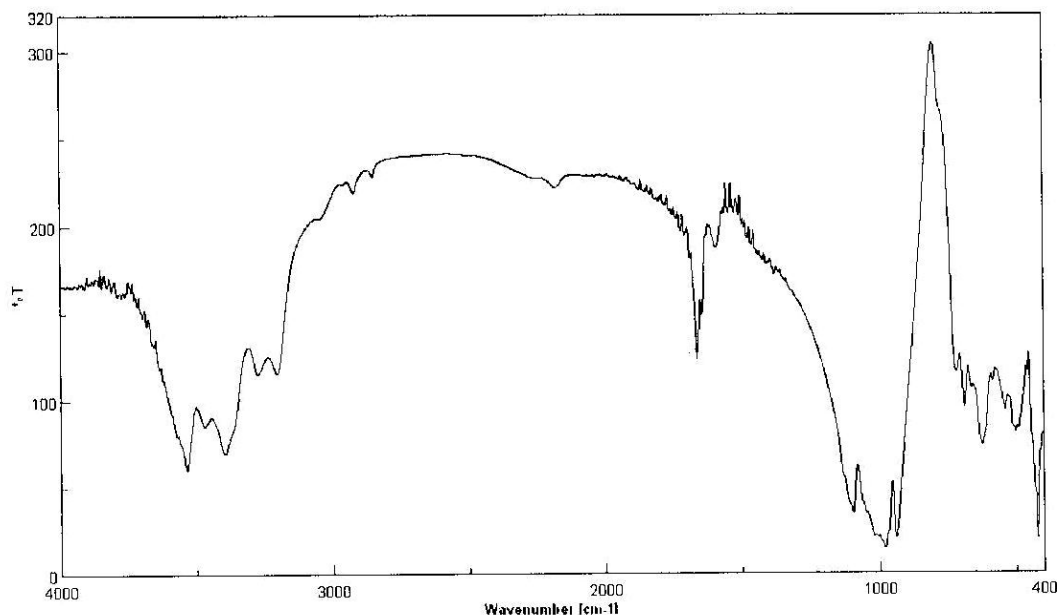
**General:** All reagents were purchased from the Merck and Aldrich chemical companies and used without further purification. The Natural Iranian Natrolite zeolite was obtained from the Hormak area (Zahedan city, Sistan & Baluchestan province, Iran), and used in this work.<sup>1</sup> The Natural Natrolite zeolite was characterized by using the powder XRD, XRF, TGA, SEM and FT-IR spectroscopy.

### Typical procedure for preparation of the 1-substituted 1*H*-1,2,3,4-tetrazoles:

The Natrolite zeolite (0.02 g) was added to a mixture of amine (2.0 mmol),  $\text{NaN}_3$  (2.0 mmol), triethyl orthoformate (2.4 mmol) and stirred at 120 °C for 4 h. After completion (as monitored by TLC), the reaction mixture was diluted with cold water (5 mL) and extracted with ethyl acetate ( $3 \times 10$  mL). The catalyst was separated by filtration and the combined organic layers were washed with brine and dried over the anhydrous  $\text{Na}_2\text{SO}_4$ . After concentration, a crystallization step was performed using EtOAc-hexane to afford the pure product.



**Figure S1.** XRD diffraction pattern of the Natrolite zeolite



**Figure S2.** FT-IR spectrum of the Natrolite zeolite

### Information on sodium azide: An effective reagent in organic synthesis

**Sodium azide** is the inorganic compound with the formula  $\text{NaN}_3$  which is commercially available and widely used in industry, agriculture, medical, and organic transformations. This colorless azide salt is the gas-forming component in many car airbag systems. It is an ionic substance and is highly soluble in water. Sodium azide is a very powerful reagent that gives access to a broad variety of structures avoiding costly and long alternative routes. It has been used for the synthesis of azidoarylketones,<sup>2</sup> dialkylcarbonyl azides,<sup>3</sup> diphenylphosphoryl azides,<sup>4</sup> acyl azides,<sup>5</sup> aryl azides,<sup>6</sup> allyl azides,<sup>7</sup> aminotetrazoles,<sup>8</sup> 5-substituted 1*H*-tetrazoles,<sup>9</sup> 1,2,3-triazoles,<sup>10</sup> 1-aryl-1,2,3-triazoles,<sup>11</sup> 1,4-disubstituted 1,2,3-triazoles,<sup>12</sup> and 1-*N*-glycosylthiomethyl-1,2,3-triazoles.<sup>13</sup> In addition, sodium azide has been widely employed for preparation of  $\alpha$ -azidoketones,<sup>14</sup> 1-aryl-1*H*-benzotriazoles,<sup>15</sup> 3-cyanoindoles,<sup>16</sup> and Fmoc-protected amino alcohols,<sup>17</sup> as a suitable nucleophile for the Michael-induced ring closure of 2-bromoalkylidenemalonates to 3,3-dialkyl-2-azidocyclopropane-1,1-dicarboxylates.<sup>18</sup>

The conventional methods of synthesizing tetrazoles have drawbacks including the use of strong Lewis acids or expensive and toxic metals,<sup>19a</sup> the use of tin azides,<sup>19b,c</sup> and employment of acidic media.<sup>19d</sup>

Recently, Sharpless and co-workers reported a safe and convenient route for the synthesis of 5-substituted 1*H*-tetrazoles via [2+3] cycloaddition of sodium azide to the corresponding nitriles using stoichiometric amounts Zn(II) salts in water.<sup>26</sup> After that, various homogeneous catalysts have been reported such as iron salts<sup>27</sup> and copper complex<sup>28</sup> in organic solvents. However, natural catalyst in preparation of tetrazoles has never been reported. Most of the catalysts in previous works still have drawbacks such as separation of the reaction mixture, complicated synthesis methods, or containing polluted metals as the catalytically active site. As a result, it is a challenging subject to find the natural separable heterogeneous catalyst which is easy prepared, environmentally benign and of low cost for the synthesis of 1-substituted 1*H*-1,2,3,4-tetrazoles. Due to the safety considerations, we must avoid methods which use hydrazoic acid or azide sources which produce hydrazoic acid in situ. If hydrazoic acid is used, care must be taken by monitoring the concentration of hydrazoic acid in the reaction mixture to avoid an explosion.<sup>9a,19a,19h,22a,29</sup> Replacement of hydrazoic acid by inorganic azides, which are poorly soluble in organic solvents with low dielectric constants, increase the reaction times and decrease the tetrazole yields.<sup>9a,19h,19n,22a</sup> A substitute for hydrazoic acid is a mixture of sodium azide and ammonium chloride, with dimethylformamide as the solvent.<sup>29,19k</sup> Combining azides and acids may yield gaseous HN<sub>3</sub>, which is toxic and flammable. In dimethylformamide, the reaction mixture must be heated to 150 °C for several hours to several days. An additional disadvantage of dimethylformamide is its solubility in both organic solvents and water, thus removing DMF from tetrazole is difficult. Therefore, it is desirable to develop a more efficient and convenient method for the synthesis of tetrazoles.

Sodium azide is not explosive except when heated near its decomposition temperature (300 °C) or reacted with metals. Sodium azide (solid or concentrated solution) should never be flushed down the drain since this practice can cause serious incidents when the azide reacts with lead or copper in the drain lines and explodes.

The methods reported for the synthesis of 1-substituted tetrazoles so far, either in acidic conditions using acids such as hydrochloric, acetic, trifluoroacetic, and sulfuric or in high polar solvents such as 2-methoxyethanol, DMF, or methanol require very harsh reaction conditions such as refluxing for 6-24 h followed by very tedious work-up procedures involving distillation of high boiling solvents or neutralization followed by distillation under the reduced pressure. So, we needed to develop an efficient and convenient method for the synthesis of 1-substituted

tetrazoles without the application of organic solvent, water, strong acids and homogeneous system as well as the in situ generation of hydrazoic acid. Because of this, it was of interest to investigate the formation of 1-substituted tetrazoles from primary amines under the solvent-free conditions using natural Natrolite zeolite. Also, the first principle of green chemistry states that it is better to prevent waste production than to treat waste or clean it up after it has been created.<sup>30</sup> In our methods, 1-substituted tetrazoles were prepared using stoichiometric amounts of sodium azide (2.0 mmol) and amine (2.0 mmol) under the solvent-free conditions. So, after completion of the reaction, there is no sodium azide residue in the reaction mixture which can form the heavy-metal azide or potentially explosive hydrazoic acid and its toxic vapors. Compared to the reported methods, our method is convenient, fast, safe, and is easy to work-up.

Caution, however, should be exercised when using azides. Both organic and inorganic azides can be heat and shock sensitive and can explosively decompose with little input of external energy. Some organic and other covalent azides are classified as toxic and highly explosive, and appropriate safety measures must be taken at all times. However, in spite of azides explosive properties, sodium azide is valuable substance in organic synthesis and requires very careful treatment.<sup>31-33</sup> Because of the associated hazards, the following actions must be considered:<sup>34</sup>

- Azide ion has a similar toxicity as that of cyanide ion ( $LD_{50} = 27$  mg/kg for rats) and can be absorbed through the skin. It decomposes explosively upon heating to above 275 °C. Be sure to use appropriate gloves when weighing azido salts.
- Sodium azide reacts violently with several common laboratory organics such as:  $CS_2$ , bromine, Bronsted acids, dimethyl sulfate, and heavy metals. In reaction with water or Bronsted acids the highly toxic and explosive hydrogen azide is released. When attempting a new reaction, be relentless in your background research to determine the reactivity of sodium azide to all reaction components. Store sodium azide away from carbon disulfide, bromine, dimethyl sulfate and nitric acid. Avoid water and strong acids which can lead to the formation of potentially explosive hydrazoic acid and its toxic vapors.
- Never use chlorinated solvents as reaction media! Utilizing dichloromethane or chloroform will result in the formation of explosively unstable di- and triazidomethane, respectively.

- Heavy-metal azides that are highly explosive under pressure or shock are formed when solutions of  $\text{NaN}_3$  or  $\text{HN}_3$  vapors come into contact with heavy metals (e.g., Cu, Pb, Ba) or their salts. Heavy-metal azides can accumulate under certain circumstances, for example, in metal pipelines and on the metal components of diverse equipment (rotary evaporators, freeze-drying equipment, cooling traps, water baths, waste pipes), and thus lead to violent explosions. Store sodium azide away from heavy metals and their salts. Sodium azide solutions must not be stored in cabinets or refrigerators with exposed copper or lead parts. Do not use metal spatulas for weighing and transferring azides.
- Store azide waste in a container designated only for azide waste.
- Use the smallest amount of sodium azide possible for your experiment.
- Conduct dry runs to eliminate safety problems that may arise before azides are actually used.
- Store azides below room temperature and away from sources of heat, light, pressure, and shock. When sodium azide heated from 275 to 330 °C in dry air, the solid crystals decompose with the evolution of nitrogen gas, leaving a residue of sodium oxide.

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