

## Oxidation of Urazoles with 1,3-Dihalo-5,5-dimethylhydantoin, both in Solution and under Solvent-Free Conditions

Mohammad Ali Zolfigol,<sup>\*a</sup> Hossein Nasr-Isfahani,<sup>b</sup> Shadpour Mallakpour,<sup>c</sup> Maliheh Safaiee<sup>a</sup>

<sup>a</sup> Chemistry Department, College of Science, Bu-Ali Sina University, Hamadan, 65174, Iran  
E-mail: zolfi@basu.ac.ir

<sup>b</sup> College of Chemistry, Shahrood University of Technology, Shahrood, Iran

<sup>c</sup> Organic Polymer Chemistry Research Laboratory, College of Chemistry, Isfahan University of Technology, Isfahan, 84156, Iran

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**Abstract:** 1,3-dichloro-5,5-dimethylhydantoin (DCH) and 1,3-dibromo-5,5-dimethylhydantoin (DBH) were used as effective oxidizing agents for the oxidation of urazoles and bis-urazoles to their corresponding triazolinediones under mild conditions at room temperature with good to excellent yields.

**Key words:** 1,3-dichloro-5,5-dimethylhydantoin (DCH), 1,3-dibromo-5,5-dimethylhydantoin (DBH), urazoles, bis-urazoles, triazolinediones

Among five-membered heterocyclic compounds, 4-substituted-1,2,4-triazole-3,5-diones (**TADs**) are notable for their ability to participate in a wide range of reaction types, e.g. [4+2]<sup>1</sup> and [2+2] cycloadditions, ene reactions, electrophilic aromatic substitution, dehydrogenating processes and the oxidation of alcohols to aldehydes and ketones.<sup>2</sup> However, the unusual reactivity which makes 1,2,4-triazoline-3,5-diones (**2**, **4**) of interest to organic chemists also makes them difficult to prepare and purify.<sup>3</sup> For example: 4-phenyl-1,2,4-triazoline-3,5-dione (**2f**) is an extremely reactive dienophile and enophile which is at least 1000 times more reactive than tetracyanoethylene (**TCNE**) in the Diels–Alder reaction with 2-chlorobutadiene and 2000 times more reactive than maleic anhydride. All known methods of synthesis for these compounds require oxidation of the corresponding 1,2,4-triazolidine-3,5-diones (**1**, **3**), more commonly known as urazoles.<sup>4</sup>

Although a wide variety of reagents is capable of effecting the oxidation of urazoles<sup>1–15</sup> this transformation remains capricious because these compounds are very sensitive to the oxidizing agents and reaction conditions. Moreover, most of the reported reagents produce some by-products, which either destroy, or are difficult to remove from, the sensitive triazolinediones. Another major drawback to the older procedures is their use of reagents which are either highly toxic or produce serious disposal problems (or both).<sup>8</sup> Recently, we have demonstrated the remarkably practical use of in situ generated N<sub>2</sub>O<sub>4</sub> gas as a clean and efficient oxidant.<sup>1,4,5</sup> Since heterogeneous reagent systems<sup>9–15</sup> have advantages such as simple experimental procedures, mild reaction conditions and minimization of

chemical waste as compared to their solution phase counterparts, we were interested to find a heterogeneous system for urazole oxidation. In continuation of our studies in this regard,<sup>9–15</sup> we have found that 1,3-dihalo-5,5-dimethylhydantoin (**I** and **II**, Figure 1),<sup>16,17</sup> cheap commercially available chemicals, have found little application in organic chemistry.<sup>18–34</sup> 1,3-Dihalo-5,5-dimethylhydantoin (**I** and **II**) have been known for many years as efficient substitutes for classic halogenating agents such as: *N*-chlorosuccinimide (NCS),<sup>33</sup> *N*-bromosuccinimide (NBS) and *N*-bromoacetamide (NBA).<sup>34</sup> Herein, we wish to report a simple, cheap and convenient method for the effective conversion of urazoles as well as bis-urazoles to their corresponding triazolinediones (**2**, **4**) by using 1,3-dichloro-5,5-dimethylhydantoin (DCH: **I**) and 1,3-dibromo-5,5-dimethylhydantoin (DBH: **II**) under mild conditions (Table 1 and Table 2).

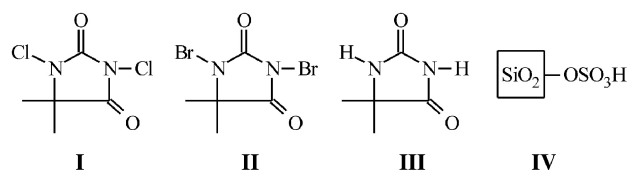
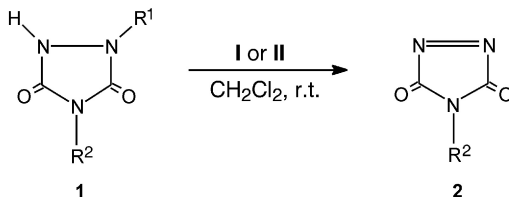


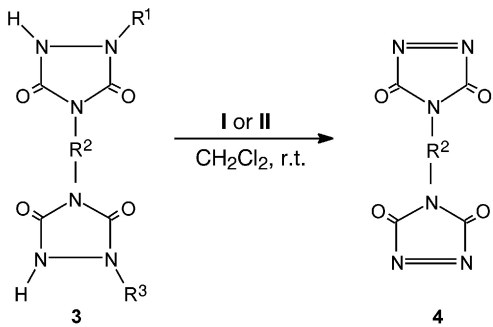
Figure 1

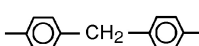
A wide range of urazoles and bis-urazoles was subjected to oxidation in the presence of DCH or DBH in dichloromethane or under solvent-free conditions (Table 1 and Table 2) at room temperature and all reactions proceeded with good to excellent yields. After completion of the reaction, silica sulfuric acid (**IV**)<sup>35</sup> was added to the reaction mixture to remove the excess of the reagent and 5,5-dimethylhydantoin (**III**) which was formed during the course of this reaction. The resultant triazolinedione (**2**) or bis-triazolinedione (**4**) was obtained by simple filtration and evaporation of the solvent.<sup>36,37</sup> The results and reaction conditions are given in Table 3 and Table 4. The oxidations of urazole sodium salts **1c** and **3a** with DBH were very fast and violently exothermic (Table 4). Therefore, DCH, which is milder than DBH, is recommended for oxidation of the urazole salts under solvent-free condition. As these reagents are effective substrates for the in situ generation of halonium species, the following mechanism may be proposed for the reaction (Scheme 1).

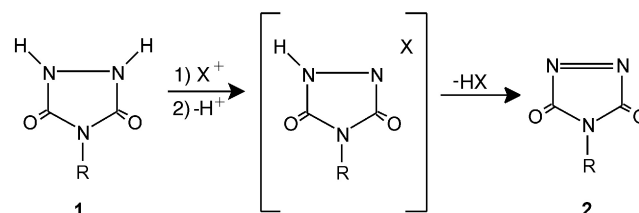
**Table 1** Conversion of Urazoles **1** to their Corresponding Triazolinediones **2**


<b>1</b>	R <sup>1</sup>	R <sup>2</sup>
<b>a</b>	H	Me
<b>b</b>	H	Et
<b>c</b>	Na	<i>n</i> -Pr
<b>d</b>	H	<i>n</i> -Bu
<b>e</b>	H	Cyclohexyl
<b>f</b>	H	Ph
<b>g</b>	H	4-Cl-C <sub>6</sub> H <sub>4</sub>
<b>h</b>	H	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>
<b>i</b>	H	3,4-Cl <sub>2</sub> -C <sub>6</sub> H <sub>3</sub>

In conclusion, a practical and efficient oxidation of urazoles and bis-urazoles has been achieved. We suggest that the reagents DCH and DBH could be used for the oxidation of a wide variety of urazole derivatives under mild conditions.

**Table 2** Conversion of Bis-urazoles **3** to their Corresponding Bis-triazolinediones **4**


<b>3</b>	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>
<b>a</b>	Na	-(CH <sub>2</sub> ) <sub>6</sub> -	Na
<b>b</b>	H		H

**Scheme 1****Table 3** Oxidation of Urazoles **1** and Bis-urazoles **3** to their Corresponding Triazolinediones **2** and **4** with 1,3-Dibromo-5,5-dimethylhydantoin (**I**) and 1,3-Dichloro-5,5-dimethylhydantoin (**II**) in Dichloromethane at Room Temperature

Urazole/bis-urazole	Product <sup>a</sup>	Reagent/substrate (mmol)		Time (h)	Yield (%) <sup>b</sup>	Mp (°C)	
		<b>I</b>	<b>II</b>			<b>I (II)</b>	Found
<b>1a</b>	<b>2a</b> <sup>8</sup>	1	1	2 (2)	100 <sup>c</sup> (100) <sup>c</sup>	97–98	98–98.5 <sup>3</sup>
<b>1b</b>	<b>2b</b> <sup>13</sup>	1	1	2 (2)	100 <sup>c</sup> (100) <sup>c</sup>	54–55	53 <sup>7</sup>
<b>1c</b>	<b>2c</b> <sup>11,13</sup>	1	1	2 (2)	99 (96) <sup>c</sup>	40–42	44 <sup>5</sup>
<b>1d</b>	<b>2d</b> <sup>8</sup>	1	1	2 (2)	96 (93) <sup>c</sup>	42–43	44–44.5 <sup>3</sup>
<b>1e</b>	<b>2e</b> <sup>8</sup>	1	1	2 (2)	99 (98) <sup>c</sup>	95–97	95–96 <sup>3</sup>
<b>1f</b>	<b>2f</b> <sup>8,10</sup>	1	1	2 (2)	97 (80) <sup>c</sup>	171–175	170–178 <sup>4</sup>
<b>1g</b>	<b>2g</b> <sup>8</sup>	1	1	2 (2)	98 (98) <sup>c</sup>	132–135	130–132 <sup>3</sup>
<b>1h</b>	<b>2h</b> <sup>8,17</sup>	1	1	2 (2)	95 (98) <sup>c</sup>	125–126	128–129 <sup>8</sup>
<b>1i</b>	<b>2i</b> <sup>14</sup>	1	1	2 (2)	98 (89) <sup>c</sup>	111–113	113–115 <sup>6</sup>
<b>3a</b>	<b>4a</b> <sup>17</sup>	2	2	4 (4)	99 (97) <sup>c</sup>	145–150	146–149 <sup>8</sup>
<b>3b</b>	<b>4b</b> <sup>17</sup>	2	2	4 (4)	100 (99) <sup>c</sup>	180–185 (dec.)	185 (dec.) <sup>8</sup>

<sup>a</sup> All of the isolated products are known compounds and their spectra and physical data have been reported in the literature.

<sup>b</sup> Isolated yields.

<sup>c</sup> Conversion.

**Table 4** Oxidation of Urazoles **1** and Bis-urazoles **3** to their Corresponding Triazolinediones **2** and **4** with 1,3-Dibromo-5,5-dimethylhydantoin (**I**) and 1,3-Dichloro-5,5-dimethylhydantoin (**II**) under Solvent-Free Conditions at Room Temperature

Urazole/bis-urazole	Product <sup>a</sup>	Reagent/substrate (mmol)		Time (h)	Yield (%) <sup>b</sup>	Mp (°C)	
		<b>I</b>	<b>II</b>			<b>I (II)</b>	Found
<b>1a</b>	<b>2a</b> <sup>8</sup>	1	1	2 (2)	100 <sup>c</sup> (100) <sup>c</sup>	97–98	98–98.5 <sup>3</sup>
<b>1b</b>	<b>2b</b> <sup>15</sup>	1	1	2 (2)	100 <sup>c</sup> (100) <sup>c</sup>	54–55	53 <sup>7</sup>
<b>1c</b>	<b>2c</b> <sup>11,15</sup>	1	1	– <sup>d</sup> (2)	– <sup>d</sup> (80) <sup>c</sup>	40–42	44 <sup>5</sup>
<b>1d</b>	<b>2d</b> <sup>8</sup>	1	1	2 (2)	91 (80) <sup>c</sup>	42–43	44–44.5 <sup>3</sup>
<b>1e</b>	<b>2e</b> <sup>8</sup>	1	1	2 (6)	86 (94) <sup>c</sup>	95–97	95–96 <sup>3</sup>
<b>1f</b>	<b>2f</b> <sup>8,10</sup>	1	1	2 (6)	80 (96) <sup>c</sup>	171–175	170–178 <sup>4</sup>
<b>1g</b>	<b>2g</b> <sup>8</sup>	1	1	2 (6)	77 (69) <sup>c</sup>	132–135	130–132 <sup>3</sup>
<b>1h</b>	<b>2h</b> <sup>8,15</sup>	1	1	2 (6)	38 (65) <sup>c</sup>	125–126	128–129 <sup>8</sup>
<b>1i</b>	<b>2i</b> <sup>12</sup>	1	1	2 (6)	71 (86) <sup>c</sup>	111–113	113–115 <sup>6</sup>
<b>3a</b>	<b>4a</b> <sup>15</sup>	2	2	– <sup>d</sup> (6)	– <sup>d</sup> (56) <sup>c</sup>	145–150	146–149 <sup>8</sup>
<b>3b</b>	<b>4b</b> <sup>15</sup>	2	2	4 (6)	33 (33) <sup>c</sup>	180–185 (dec.)	185 (dec.) <sup>8</sup>

<sup>a</sup> All of the isolated products are known compounds and their spectra and physical data have been reported in the literature.

<sup>b</sup> Isolated yields.

<sup>c</sup> Conversion.

<sup>d</sup> Reaction is very fast and explosive.

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- (36) Chemicals were purchased from Fluka, Merck, Riedel-De Haen AG and Aldrich chemical companies. Yields refer to isolated pure products. The oxidation products were characterized by comparison of their spectral (IR, UV,  $^1\text{H}$  NMR, and  $^{13}\text{C}$  NMR) and physical data with authentic samples. Silica sulfuric acid (**III**) was prepared according to our previously reported procedure.<sup>35</sup> All urazoles and bis-urazoles were also synthesized according to our previously reported procedures.<sup>1,4,5</sup>
- (37) **Oxidation of 4-Chlorophenyl Urazole (1g) to 4-Chlorophenyl-1,2,4-triazoline-3,5-dione (2g) with DBH.**  
**A Typical Procedure.**  
A mixture of compound **1g** (0.212 g, 1 mmol) and DBH (0.286 g, 1 mmol) in  $\text{CH}_2\text{Cl}_2$  (15 mL) was stirred at r.t. for 2 h. Silica sulfuric acid (0.5 g) was added to the reaction mixture and stirred for 15 min. Then the reaction mixture was filtered and the  $\text{CH}_2\text{Cl}_2$  removed to give a red crystalline solid **2g** (0.205 g, 92% yield), mp 132–135 °C [lit.<sup>3</sup> mp 130–132 °C]. These compounds are sensitive to the light, heat, alcohols, ethers, transition metals and some nucleophiles. Also they are very volatile so that, if the temperature rises over 50 °C in the course of removing  $\text{CH}_2\text{Cl}_2$ , some of TADs are lost with solvent.