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N-Bromo Reagent Mediated Oxidation of Urazoles to Their Corresponding Triazolinediones under Mild and Heterogeneous Conditions

Mohammad Ali Zolfigol[1,*], Gholamabbas Chehardoli[1,*], Ezat Ghaemi[1], Elaheh Madrakian[1], Reza Zare[1], Tahereh Azadbakht[1], Khodabakhsh Niknam[2], and **Shadpour Mallakpour[3]**

[1] Faculty of Chemistry, Bu-Ali Sina University, Hamedan, Iran
[2] Department of Chemistry, Faculty of Sciences, Persian Gulf University, Bushehr, Iran
[3] Organic Polymer Chemistry Research Laboratory, College of Chemistry, Isfahan University of Technology, Isfahan, Iran

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Summary. Various *N*-bromo reagents [*HMTAB*, *DABCO*-bromine, *DPTBE*, and *TBCA*] were used as effective oxidizing agents for the oxidation of urazoles and bisurazoles to their corresponding triazolinediones under mild and heterogeneous conditions at room temperature with good to excellent yields. Also the oxidation of some new 4-phenylurazole derivatives with these reagents is discussed.

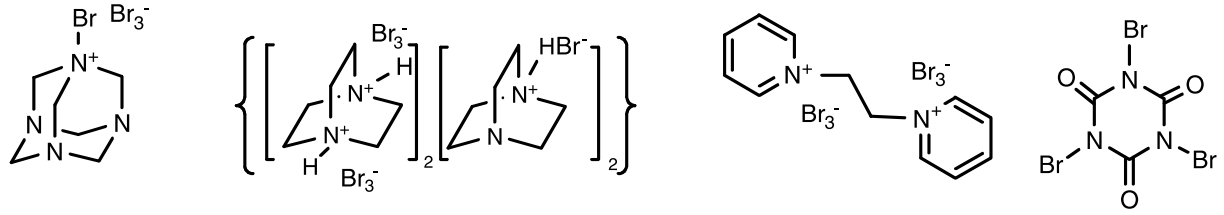
Keywords. Urazoles; Bisurazoles; Triazolinediones; *N*-Bromo reagents; Heterogeneous conditions.

Introduction

4-Substituted-1,2,4-triazole-3,5-diones (*TAD*s), have been used both as substrates and reagents in various organic reactions, such as *Diels-Alder* reaction, ene reactions, [2 + 2] cycloadditions, dehydrogenation reactions, electrophilic aromatic substitution, condensation of dicarbonyl compounds, oxidation of alcohols to aldehydes and ketones [1]. Very recently aromatization of 1,4-dihydropyridines and pyrazolines as well as oxidation of thiols with *TAD*s have been reported [2]. The unusual reactivity of *TAD*s (**2**, **4**) makes them interesting compounds, but also hard to prepare and purify [3]. It is interesting to note, that 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 in the *Diels-Alder* reaction with 2-chlorobutadiene and 2000 times more reactive than maleic anhydride [1]. All known methods for the preparation of these compounds (1,2,4-triazolidine-3,5-diones) require oxidation of the corresponding urazoles (**1**, **3**). Although a variety of reagents are capable of efficient oxidations of urazoles (**1**, **3**) to *TAD*s, this transformation is not easy as these compounds are very sensitive to the oxidizing agents and reaction conditions. In addition, most of the reported reagents produce by-products which either destroy the sensitive triazolinediones, or are difficult to remove from the reaction product. Another major drawback of the older procedures is their use of reagents which are either highly toxic or impose serious disposal problems (or both) [4–8]. Recently, we among many others have demonstrated that the application of heterogeneous systems for the above reported oxidations has many advantages over their liquid phase counterparts such as simple experimental procedures, mild reaction conditions, and minimization of chemical waste materials [9].

Hexamethylenetetramine-bromine (*HMTAB*) (**I**) [10a], *DABCO*-bromine [$(H_2DABCO)_2(HDABCO)_2(Br)_2(Br_3)_4$] (**II**) [10b], and 1,2-(dipyridiniumditribromide)ethane (*DPTBE*) (**III**) [10c] are three stable

* Corresponding authors. E-mails: zolfi@basu.ac.ir, mzolfigol@yahoo.com and cheh1002@gmail.com.



HMTAB (**I**) [10a] *DABCO*-bromine (**II**) [10b] *DPTBE* (**III**) [10c] *TBCA* (**IV**) [11]

Scheme 1

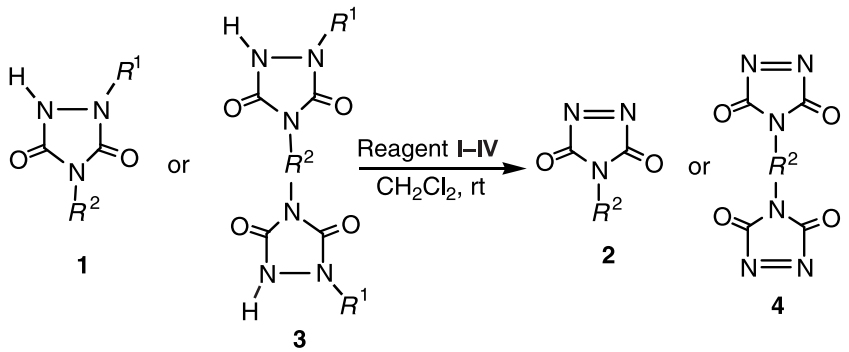
and suitable oxidants that can be prepared easily. Simple work-up and the stability of these reagents make them a safe and convenient source of active bromine in comparison to molecular bromine which is a highly toxic oxidizing agent. These reagents are transformed during reaction into easily removable products [10j]. There are several reports that demonstrate the use of these reagents for various organic transformations under mild conditions [10]. Recently, it has been reported that tribromoisocyanuric acid (*TBCA*) (**IV**) was used for the regioselective bromination of activated aromatic rings, and regioselective cobromination of alkenes [11]. These reagents are shown in Scheme 1.

Therefore, in continuation of our studies on the use of *N*-halo reagents in organic transformations [12], we found that *N*-bromo reagents such as [*HMTAB* (**I**), *DABCO*-bromine (**II**), *DPTBE* (**III**), and *TBCA* (**IV**)] could be used as oxidizing agents for the oxidation of urazoles and bisurazoles under mild and heterogeneous conditions (Scheme 2).

Herein, we wish to report a simple, inexpensive, and convenient method for the effective oxidation of urazoles **1** and bisurazoles **3** to their corresponding triazolinediones **2** and **4** by using the described reagents **I**–**IV**.

A range of urazoles **1** and bisurazoles **3** were subjected to the oxidation reaction in the presence of the oxidizing agents **I**–**IV** in dichloromethane. All oxidation reactions were performed under mild and completely heterogeneous conditions, at room temperature with good to excellent yields (Table 1).

The present oxidation reaction can be readily carried out by adding one of the oxidation reagents



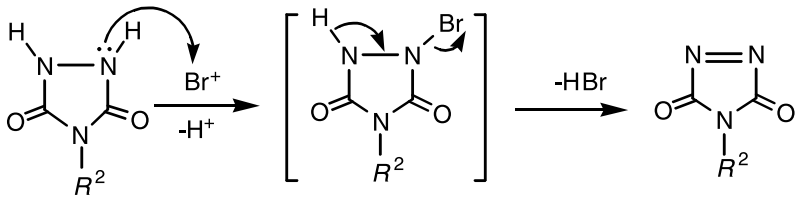
	R^1	R^2		R^1	R^2
1a	H	*Me*	**1h**	H	3,4-Cl_2-*Ph*
1b	H	*Et*	**1i**	H	4-NO_2-*Ph*
1c	Na	*n*-Pr	**1j**	H	4-O*Me*-*Ph*
1d	H	*n*-Bu	**1k**	H	4-*t*-Bu-*Ph*
1e	H	Cyclohexyl	**1l**	H	4-Napht-l-yl
1f	H	*Ph*	**3a**	Na	-$(CH_2)_6$-
1g	H	4-Cl-*Ph*	**3b**	H	-*Ph*-CH_2-*Ph*-

Scheme 2

Table 1. Oxidation of urazoles **1** and bisurazoles **3** to their corresponding triazolinediones **2** and **4** with either one of the oxidation reagents *HMTAB* (**I**), *DABCO*-bromine (**II**), *DPTBE* (**III**), or *TBCA* (**IV**) in dichloromethane at room temperature

Entry	Urazole	Product	Reagent/substrate/mmol				Time/h				Yields[a]/%				Mp/°C
			I	**II**	**III**[b]	**IV**	**I**	**II**	**III**	**IV**	**I**	**II**	**III**	**IV**	Ref. [12]
1	**1a**	**2a**	2	0.2	0.75	1	1	2	0.08	0.83	100[c]	100[c]	100[c]	100[c]	97–98
2	**1b**	**2b**	2	0.2	0.75	1	1	2	0.08	0.83	100[c]	100[c]	100[c]	100[c]	52–55
3	**1c**	**2c**	2	0.2	0.75	1	1	2	0.08	0.83	90	72	91	83	42–44
4	**1d**	**2d**	2	0.2	0.75	1	1	2	0.08	0.58	99	99	90	85	42–45
5	**1e**	**2**[e]	2	0.2	0.75	1	1	2	0.5	0.83	90	85	90	97	94–97
6	**1f**	**2f**	2	0.2	1	1	1	2	0.5	0.83	91	80	95	93	173–175
7	**1g**	**2g**	2	0.2	1	1	1	2	0.5	1	94	83	89	94	132–133
8	**1h**	**2h**	2	0.2	1.25	1	1	2	0.5	1	90	92	80	90	112–114
9	**1i**	**2i**	2	0.2	1	1	1	2	0.5	1	89	81	100[c,d]	86	126–128
10	**1j**	**2j**	2	0.2	1	1	1	2	0.5	1.25	93	75	70	85	89–93
11	**1k**	**2k**	2	0.2	1	1	1	2.5	0.5	0.5	98	94	96	97	122–126
12	**1l**	**2l**	2	0.2	1.25	1	1	2.5	0.5	0.83	87	80	84	80	109–111
13	**3a**	**4a**	4	0.4	2	2	2	4	0.5	2.5	85	82	94	trace	146–148
14	**3b**	**4b**	4	0.4	2	2	2.5	5	0.5	1.5	90	99	93	70	184–186

[a] Isolated yields. [b] In the presence of a few drops of water. [c] Conversion. [d] (4-Nitrophenyl)triazolinedione is very labile. Therefore, it decomposed in the course of passing through a pad of silica gel

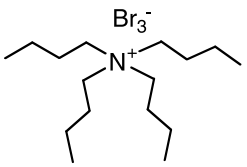


Scheme 3

HMTAB (**I**), *DABCO*-bromine (**II**), *DPTBE* (**III**) (and few drops of H_2O), or *TBCA* (**IV**) to a suspension of urazoles **1** or bisurazoles **3** in CH_2Cl_2 and efficiently stirring the resulting heterogeneous mixture at room temperature. The triazolinediones **2** and bistriazolinediones **4** are obtained by simple filtration and evaporation of the solvent. As reported above the oxidation reactions are heterogeneous because urazoles and bisurazoles [(**1**, **3**) as white solids] are insoluble in dichloromethane whereas all of the triazolinediones and bistriazolinediones [(**2**, **4**), red, pink, or brown solids] are very well soluble in dichloromethane. According to our previously reported results with other reagents [12], the following mechanism for the oxidation reaction *via in situ* generation of Br^+ may be suggested (Scheme 3).

We also applied our new reaction protocols for the oxidation of three new urazoles (Table 1, entries 10–12). Spectral and physical data for the obtained products are in close agreement with their structures.

Unfortunately, several attempts for the oxidation of urazoles by another *N*-bromo reagent namely ''tetra-*n*-butylammonium tribromide (*TBATB*) [13] have failed. Although conversion of urazoles to their corresponding triazolinediones was completed, we were not able to isolate the products from residue of reagent. Therefore, this reagent is not practical and suitable for this purpose.



TBATB

In conclusion, we described a practical, efficient, and convenient method for the oxidation of urazoles and bisurazoles. We suggest that these systems could be used for the oxidation of a wide variety of urazole derivatives under mild and safe conditions.

Experimental

General Procedure

Chemicals were purchased from Fluka, Merck, and Aldrich chemical companies. Yields refer to isolated pure products. The oxidation products were characterized by comparison of their spectral (IR and ^{1}H NMR) and physical data with authentic samples which were produced by other reported procedures [12a]. Tribromoisocyanuric acid (*TBCA*) was prepared according to a recently reported procedure by *De Mattos et al.* [11b]. Urazoles and bisurazoles [7, 8], hexamethylenetetramine-bromine (*HMTAB*) (**I**) [10a], *DABCO*-bromine (**II**) [10b], and 1,2-(dipyridiniumditribromide)ethane (*DPTBE*) (**III**) [10c] were synthesized according to previously reported procedures.

*Oxidation of 4,4′-(4,4′-Diphenylmethylene)bisurazole (**3b**) to Bis(p-(3,5-dioxo-1,2,4-triazoline-4-yl)phenyl)methane (**4b**): A General Procedure [for Applying HMTAB (**I**), DABCO-bromine (**II**) and TBCA (**IV**)]*

A mixture of 0.366 g **3b** (1 mmol), and reagent in CH_2Cl_2 (10 cm^3) was stirred for the specified time (molar ratio of reagents have been indicated in Table 1). Then the reaction mixture was filtered and the residue was washed with CH_2Cl_2 (2×10 cm^3). Dichloromethane was removed by using a distillation apparatus and a water-bath (40–50°C). A crystalline pink solid (**4b**) is obtained in good to excellent yields. Mp 182–185°C (Ref. [7] 185°C).

See these compounds are sensitive to light, heat, alcohols, ethers, transition metals, and any other nucleophiles. Also, they are very volatile so that, if the temperature rises over 50°C in the course of removing of CH_2Cl_2, some *TAD*s are removed with the solvent simultaneously (dichloromethane was evaporated with simple distillation). Therefore, the temperature must be controlled. Dichloromethane is the best solvent for the synthesis of this class of compounds.

*Oxidation of 4-Phenylurazole (**1f**) to 4-Phenyl-1,2,4-triazoline-3,5-dione (**2f**): A Typical Procedure [for DPTBE (**III**)]*

A suspension of 0.177 g **1f** (1 mmol), *DPTBE* (**III**) (0.664 g, 1 mmol), and 5 drops of water were added in dichloromethane (10 cm^3) and the suspension was vigorously stirred for 0.5 h (Table 1, entry 6). The residue was washed with CH_2Cl_2 (2×10 cm^3) and filtered. The filtrate was dried over 3 g anhydrous Na_2SO_4, which was filtered off after the appropriate time. Then the filtrate was passed through a short pad of silica gel for removing any remaining of reagent residue. Dichloromethane was removed by using a distillation apparatus and a water-bath (40–50°C). The yield was 0.1681 g (95%) of a crystalline red solid (**2f**), mp 171–175°C (Ref. [7] 170–178°C).

Melting Points and Spectral Data for the New Triazolinediones

4-(4-Methoxyphenyl)-4H-1,2,4-triazole-3,5-dione (**2j**, $C_9H_7N_3O_3$): dark red crystalline solid, mp 89–93°C; IR (KBr): $\bar{\nu} = 2968$, 1773, 1515, 1258, 1173 cm^{-1}; ^{1}H NMR (90 MHz, $CDCl_3$): $\delta = 3.85$ (s, 3H), 6.97–7.38 (m, 4H) ppm; ^{13}C NMR (22.5 MHz, $CDCl_3$): $\delta = 55.6$, 115.2, 125.6, 198.8 ppm.

4-(4-tert-Butylphenyl)-4H-1,2,4-triazole-3,5-dione (**2k**, $C_{12}H_{13}N_3O_2$): red crystalline solid, mp 122–126°C; IR (KBr): $\bar{\nu} = 2962$, 1788, 1714, 1518, 1407, 1185 cm^{-1}; ^{1}H NMR (90 MHz, $CDCl_3$): $\delta = 1.28$ (s, 9H), 7.33 (m, 4H) ppm; ^{13}C NMR (22.5 MHz, $CDCl_3$): $\delta = 31.2$, 34.9, 123.7, 126.9, 152.9, 157.9 ppm.

4-(Naphth-1-yl)-4H-1,2,4-triazole-3,5-dione (**2l**, $C_{12}H_7N_3O_2$): brown crystalline solid, mp 109–111°C; IR (KBr): $\bar{\nu} = 2923$, 1715, 1417, 770 cm^{-1}; ^{1}H NMR (90 MHz, $CDCl_3$): $\delta = 6.94$–7.83 (m) ppm; ^{13}C NMR (22.5 MHz, $CDCl_3$): $\delta = 119.3$, 125.7, 126.4, 127.6, 128.6, 129.6, 130.2, 138.5, 139.7, 148.5, 149.2 ppm.

Note: Spectral data of previously reported triazolinediones see Ref. [12a].

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