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Silica-Supported ICl as a Novel Heterogeneous System for the Rapid Oxidation of Urazoles to Triazolinediones

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ABSTRACT: *ICl–SiO$_2$ as a new reactive system was prepared by the treatment of iodine monochloride with an activated silica gel in chloroform. ICl–SiO$_2$ in a heterogeneous system efficiently oxidized urazoles to the corresponding triazolinediones under mild conditions in high yields at room temperature.* © 2008 Wiley Periodicals, Inc. Heteroatom Chem 19:389–393, 2008; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.20444

INTRODUCTION

In recent years, iodine monochloride (**1**) has been widely used for various organic transformations, such as iodination of activated aromatic substrates [1], synthesis of 6-iodo quinazoline-4(3*H*)-one derivatives [2], iodination of nucleic acids in organic solvents [3], generation of electrophilic iodine from the reaction of ICl (**1**) with CF_3COOAg, CH_3COONa, or $(CH_3COO)_2Pb$ [4], stereoselective iododeboronations and chlorodeboronations of hindered alkenyl boronate esters using either ICl–NaOMe or ICl-pyridine [5], addition to branched *E*-alkenes [6], synthesis of α-iodo β-ketosulfones from corresponding β-ketosulfones [7], and application of it as a volumetric reagent [8]. Furthermore, ICl (**1**), in the absence of a catalyst, has also been used as an iodinating agent. Iodine monochloride (**1**) has two crystalline forms α and β, and in both structures there are nonplanar chains of ICl (**1**) molecules in a zig-zag formation [9]. This compound (**1**) has high vapor pressure, and similarly to I_2 evaporates easily. Although it has been used frequently, it is sometimes hazardous in the use of pure iodine monochloride (**1**).

Recently, silica-supported reagents have received considerable attention because of higher activity due to the larger surface area, high mechanical and thermal stabilities, easy handling, low toxicity, noncorrosiveity, easy separation, and work-up [10]. On the other hand, heterogeneous processes have been well studied recently for its prospective applications in organic synthesis. The high efficiency of these processes is traditionally thought to be due to the above-mentioned advantages. In continuation of our studies on heterogeneous systems and solid acids [11], we report here a novel heterogeneous reagent (**2**) using iodine monochloride (**1**) supported on silica gel, as an efficient and mild reagent for iodination and oxidation of urazoles (**3**) and bisurazoles (**4**) to the corresponding triazolinediones (**5** and **6**). We decided to use ICl (**1**) supported on the surface of activated silica gel to obviate practical difficulties and to have better handling of the reactions (Scheme 1).

4-Substituted-1,2,4-triazoline-3,5-diones have been used in a variety of reactions such as ene

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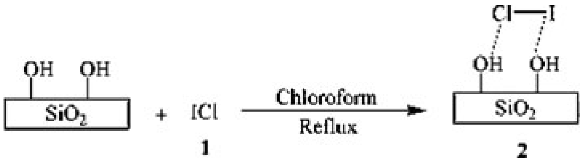


SCHEME 1

reactions, electrophilic aromatic substitution, dehydrogenating properties, and oxidation of alcohols [12–14]. From the biochemical point of view, some of them have been identified as protein cross-linkers and conformational probes for some enzymes [15]. Although several methods have been reported for the oxidation of urazoles to related triazolinediones [16], this transformation is not so easy because these compounds are very sensitive to oxidants and reaction conditions. Therefore, a mild system for the nondestructive oxidation and simple work-up is proposed and that will be useful for chemists.

RESULTS AND DISCUSSION

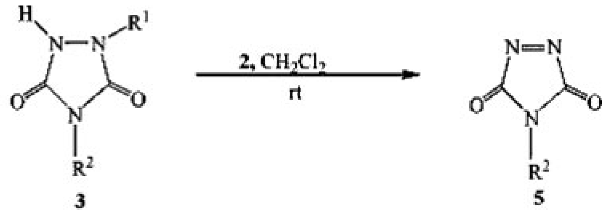
Silica gel supported iodine monochloride (**2**) is a stable (even after 5 months) light pink solid. It can be prepared from the reaction of ICl (**1**) with the activated silica gel in refluxing chloroform for 12 h (Scheme 1). There are reports about intermolecular charge-transfer complexes between a wide range of carbonyl compounds and ICl (**1**) [17] and also about a π-type complex formed by acetylene and ICl (**1**) [18]. It has been reported that in these charge-transfer complexes, I_2 or ICl (**1**) molecules use an antibonding σ^*-orbital to accept π-electrons from an aromatic molecule or a lone-pair of electrons from an n-donor molecule according to Mulliken's theory [19]. On the basis of these results, we believe that iodine monochloride (**1**) binds to the surface of silica gel via an interaction between the hydroxyl group of silica gel and positively charged iodine in ICl (**1**) (Scheme 1). Unreacted ICl (**1**) in the reaction with water produces HCl and HOI. These two acids were measured via titration by sodium hydroxide (Scheme 2) [1c,20]. By this way, the amount of ICl (**1**) supported on silica gel was determined.

Oxidation of the urazoles (**3** and **4**) is a common way for the preparation of triazolinediones (**5** and **6**), and a wide variety of methods and reagents have been reported in the literature [16]. However in some of these methods, byproducts were produced or the products decomposed under the reaction conditions and/or the work-up was difficult. So, after preparation of ICl–SiO_2 (**2**), we were interested to use it in an organic solvent for the in situ generation of ICl (**1**) to oxidize urazoles (**3**) and bisurazoles (**4**) under mild and heterogeneous conditions (Schemes 3 and 4). At first, different types of urazoles (**3**) and bisurazoles (**4**) were subjected to the oxidation reaction in the presence of ICl–SiO_2 (**2**) in dichloromethane. The oxidation reaction was performed under mild and heterogeneous conditions at room temperature, and this gave good to excellent yields of the products at relatively short time (Table 1).

$$ICl + H_2O \longrightarrow HCl + HOI$$

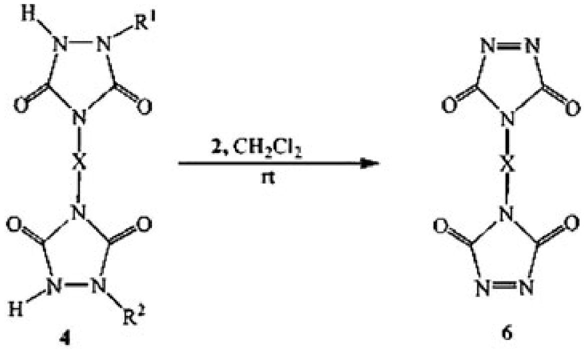
$$HCl + HOI + 2NaOH \longrightarrow NaOI + NaCl + 2H_2O$$

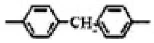
SCHEME 2



3	R^1	R^2
a	H	Ph
b	H	4-Cl-C_6H_4
c	H	4-NO_2-C_6H_4
d	H	Me
e	H	*n*-Bu
f	Na	*n*-Pr
g	H	Cyclohexyl

SCHEME 3



4	R^1	X	R^2
a	Na	$-(CH_2)_6-$	Na
b	H		H

SCHEME 4

TABLE 1 Oxidation of Urazoles (**3**) and Bisurazoles (**4**) to Their Corresponding Triazolinediones (**5** and **6**) with ICl–SiO$_2$ (**2**) in Dichloromethane at Room Temperature

Urazoles or Bisurazoles	*Product*[a]	*Time (min)*	*Yield*[b] *(%)*	*Melting Point (°C) Found (Reported) [16]*
3a	**5a**	10	98	165–169 (168–175)
3b	**5b**	10	97	132–135 (134–135)
3c	**5c**	10	95	126–127 (125–126)
3d	**5d**	10	96	99–100 (97–99)
3e	**5e**	12	80	44–46 (43–45)
3f	**5f**	20	81	43–46 (42–45)
3g	**5g**	10	84	97–99 (97–98)
4a	**6a**	120	80	147–151 (145–150)
4b	**6b**	90	80	184 (dec.) [182–185 (dec.)]

[a] All of the isolated products are known compounds and their spectra and physical data have been reported in the literature [16].
[b] Isolated yields.

As shown in Table 1, **3a–3g** were converted to **5a–5g** with similar yields and reaction times, whereas **4a–4b** were oxidized slowly than those of **3a–3g**.

The oxidation reactions are heterogeneous because urazoles (**3**) and bisurazoles (**5**) (white solids) are insoluble in dichloromethane, whereas all of the triazolinediones (**5** and **6** are red and pink, respectively) are very soluble in dichloromethane. Hence, the oxidation reaction presumably occurs at the surface of the heterogeneous reagent (**2**) via a slow in situ release of ICl in small amounts. Next, the oxidation products (**5** and **6**) migrate to the liquid phase (CH_2Cl_2) very fast.

ICl (**1**) in many of organic transformations acts as an iodinating reagent, and the iodinating species is an electrophilic (I^+) that is produced by the ionization of ICl (**1**). Examples are iodination of toluene [1b], α-iodination of β-ketosulfones [7], iodination of nitroarenes [1f], and other similar reports [1–9]. On the other hand, there are some reports on oxidation of the urazoles using the precursor of halonium species (with the suggested mechanism therein) such as 1,3-dihalo-5,5-dimethylhydantoin [14], silica sulfuric acid/$KClO_3$ or silica chloride/oxone® systems [16b], and periodic acid or oxone®/KBr system [16a]. Therefore, we propose a mechanism based on these previously reported results on the application of ICl (**1**) and oxidation of urazoles (see Scheme 5).

EXPERIMENTAL

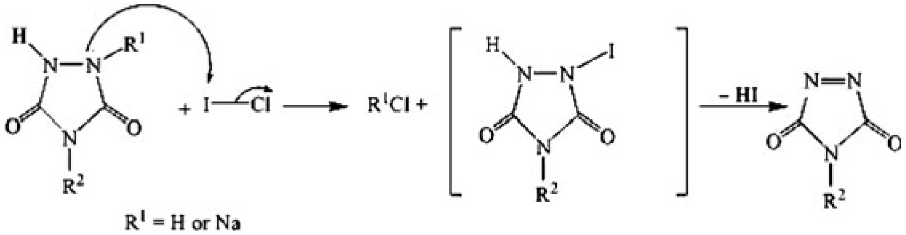
Chemicals were purchased from Aldrich (DM/Germany), Fluka (Buchs/Switzerland), and Merck (Darmstadt/Germany) chemical companies and were freshly used after purification following standard procedures. Urazoles (**3** and **4**) were prepared using the method described in the literature [16]. The products were isolated and identified by comparing their physical and spectral data with those described in the literature [16]. IR spectra were recorded on FT-IR JASCO-680 using KBr disks, and the ^{1}H-NMR spectra were obtained on a Brucker instrument 300 MHz model as $CDCl_3$ solution, and the chemical shifts are expressed in δ units with Me_4Si (TMS) as an internal standard.

Activation of Silica Gel

Chromatography-grade silica gel (10 g, 70–230 mesh) was heated in an electric furnace at 400°C for 4 h. Then it was cooled to room temperature to obtain activated silica gel (9.12 g).

Preparation of Silica-Supported ICl (2)

To a stirred solution of iodine monochloride (**1**) (0.487 g, 3 mmol) in 10 mL of chloroform, activated silica gel (9.12 g) was added and the mixture was refluxed for 12 h. Then it was cooled



SCHEME 5

to room temperature, and the mixture was filtered and washed three times with 10 mL chloroform to remove unreacted ICl (**1**). Then solid was dried to yield silica-supported ICl (**2**) (9.485 g), which contained 0.365 g (2.247 mmol) of supported ICl (**1**). This amount was in agreement with titration of unreacted ICl (**1**) with 0.1 M NaOH solution [1c,20].

*Synthesis of 4-n-Propylurazole Sodium Salt (**3f**)*

Typical Procedure. In a 1000-mL three-necked round-bottle flask, which was equipped with a water-cooled condenser, a constant pressure-dropping funnel, and a mechanical stirrer, 0.1690 mol of sodium metal (3.88 g) was placed. To this metal, absolute ethanol (300 mL) was added dropwise over a period of 60 min. Although being stirred magnetically, at the end of addition a clear solution was obtained (to obtain EtONa/EtOH, and for H-urazole, use 4 M KOH/H_2O as a base). 1-Ethoxycarbonyl-4-*n*-propyl semicarbazide 0.1690 mol (32.00 g) was added to the resulting clear solution under reflux conditions. Upon addition, an orange and then a red solution were obtained. After 2 h, slurry was formed that was refluxed for 54 h. The hot reaction mixture was filtered, and the desired solid compound was isolated as a white solid (17.82 g). Concentration of the filtered to about 30 mL afforded more material 6.12 g; yield: 23.94 g, 85.5%, mp 230°C. IR (KBr, cm^{-1}): 3480 (m, sh), 3400 (s), 3200 (s), 2990 (m), 2920 (m), 2880 (m), 1690 (s), 1620 (s, sh), 1590 (s), 1460 (s), 1420 (m), 1370 (m), 1260 (m), 1050 (m), 910 (w), 807 (s), 770 (w), 720 (w), 640 (m, br); ^1H NMR (D_2O, DSS): δ 0.85 (t, 3H, $J = 9.0$ Hz), 1.63 (sextet, 2H, $J = 7.5$ Hz), 3.46 (t, 2H, $J = 7.5$ Hz) [16a].

*Oxidation of Urazoles (**3a–3g**) and Bisurazoles (**4a–4b**) to Corresponding 1,2,4-Triazoline-3,5-diones (**5** and **6**)*

General Procedure. To a solution of 0.5 mmol of urazoles (**3a–3g**) or 0.25 mmol of bisurazoles (**4a–4b**) in 10 mL of CH_2Cl_2, 2 g of silica-supported ICl (**2**) (equivalent to 0.5 mmol ICl) was added at room temperature, and the reaction mixture was stirred for 10–120 min. After completion of the reaction, the reaction mixture was filtered and then residue was washed with dichloromethane (10 mL). Dichloromethane was removed under water bath (50°C) and simple distillation. Red crystalline solid (**5** and **6**) was obtained as listed in Table 1.

*Oxidation of 4-Phenyl Urazole (**3a**) to 4-Phenyl-1,2,4-triazoline-3,5-dione (**5a**)*

Typical Procedure. To a solution of 0.5 mmol (0.0885 g) of urazole (**3a**) in 10 mL of CH_2Cl_2, 2 g of silica-supported ICl (**2**) (equivalent to 0.5 mmol ICl) was added at room temperature, and the reaction mixture was stirred for 10 min. After completion of the reaction, the reaction mixture was filtered and then the solid was washed with dichloromethane (10 mL). Dichloromethane was removed under water bath (50°C) and simple distillation. Red crystalline solid (**5a**) was obtained as 0.171 g (98%), mp 165–169°C (reported [16] mp 168–175°C).

CONCLUSIONS

In conclusion, in this work we have prepared an efficient reagent for the heterogeneous oxidation of urazoles and bisurazoles. This new system is equivalent to iodine monochloride but more stable, easy to work with, and to handle it. In addition, we suggest that this reagent could be used for the iodination of a wide variety of organic compounds. Therefore, other applications of the reagent are under progress in our laboratory.

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