

Clean synthesis of azo compounds using MagtrieveTM in the ionic liquid [bmim][Br]

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Abstract A series of azo compounds, *N*-aryl-2-phenyl-diazene-carboxamides, and 4-substituted-1,2,4-triazoline-3,5-diones, were synthesized using MagtrieveTM, a magnetically retrievable and recyclable oxidant, in the ionic liquid [bmim][Br] under neutral condition. This procedure has several advantages, such as greenness, mild reactions, simple manipulation, and reusability of reagent and solvent.

Keywords Azo compounds; Oxidations; Magtrieve; Ionic liquids; Green chemistry.

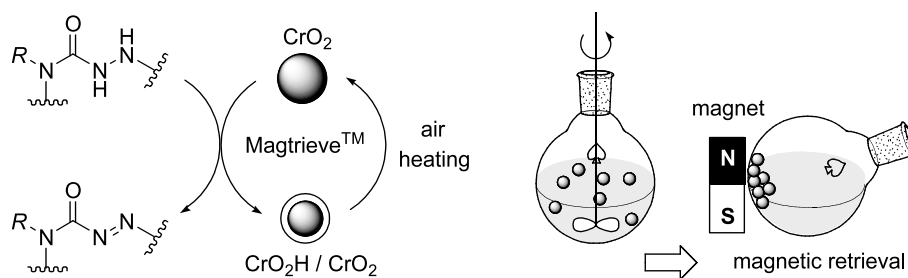
Introduction

Azo compounds have caused great interest in organic synthesis [1] and have been widely utilized as dyes, analytical reagents, and as materials to store optics information in laser disks [2]. Recently, many noteworthy studies have shown that azo compounds possess excellent photoelectric properties [3]. The research of synthesizing azo compounds has received much attention over the years. Fuming nitric acid can be employed as a relatively economical oxidant to convert substituted hydrazines to azo compounds, but the evolution of large amounts of

nitrogen oxides causes air pollution [4]. More recently, a variety of reagents, such as NO₂-DMF [5], FeCl₃ · 6H₂O [6], Fe(NO₃)₃ · 6H₂O [7], K₃Fe(CN)₆/KOH [8], NO₂-PEG [9], NaBrO₃/H₂SO₄ [10], active MnO₂ [11], and NaNO₂/Ac₂O [12], have been developed to convert hydrazine derivatives into the corresponding azo compounds. However, these methods are deficient in some aspects, such as: non-recoverable reagents, tedious work-up, acidic or basic media, complicated purification procedure, and so on. Hence, there is still a strong need for the development of new methods for azo compounds synthesis, which employ safer oxidants and produce little waste.

The development of environmentally friendly technologies is the most challenging goal of contemporary chemistry and chemical engineering. One of the aims of green chemistry is to replace the environmentally unacceptable solvents and/or reagents with environmentally benign ones. Among the alternative solvents, room-temperature ionic liquids [13] have shown great promise as environmentally benign reaction media because of their good solubility for a wide range of organic, organometallic, and inorganic compounds as well as their excellent chemical and thermal stabilities. Further, as salts, they exhibit no detectable vapor pressure under ambient conditions and are nonflammable. On the other hand, MagtrieveTM, a magnetically retrievable oxidant, has recently been employed in a series of organic transformations, *e.g.*,

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Scheme 1

oxidation of alcohols [14], benzophenone hydrazone [15], thiols [16], 1,4-dihydropyridines [17], deprotection/oxidation of protected alcohols [18] and acetals [19], side chain oxidation of arenes [20], and aromatization of imidazolines [21]. Here, we wish to report the use of MagtrieveTM – [bmim][Br] as a recoverable and regenerable system for the green synthesis of azo compounds from corresponding semicarbazides or carbazides (Scheme 1). To the best of our knowledge, this is the first example using such a reagent couple in organic synthesis.

Results and discussion

MagtrieveTM (trademark of E.I. Du Pont de Nemours & Co. Inc.) is a superior heterogeneous oxidizer of organic compounds which has been found more effective than activated MnO₂ in many reactions. It is tetravalent chromium dioxide (CrO₂) whose reduced form stays on the crystal surface. After reactions, used MagtrieveTM could be recovered readily by a magnet and regenerated by heating in air. In contrast to traditional chromium reagents, it is a good choice from the viewpoints of environmental protection and cost-effectiveness.

At the beginning, the reaction conditions were optimized using **1a** as a model substrate. In our procedure, two ionic liquids, [bmim][Br], and [bmim][BF₄], were chosen as alternatives to traditionally used chlorinated solvents or toluene. It was found that there are no considerable differences in reaction rates and yields either with [bmim][BF₄] or with [bmim][Br]. Hence, [bmim][Br] was chosen for further investigations due to its cheapness and simplicity of synthesis.

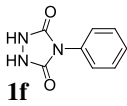
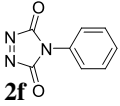
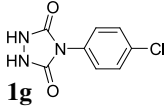
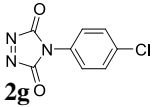
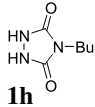
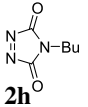
Having established the practicability of this procedure, attention was next focused on the regeneration and reuse of MagtrieveTM and [bmim][Br] in above-mentioned model reaction. The separation

procedure is very simple. MagtrieveTM oxidant was retrieved by magnetic separation, while the product was easily separated from ionic liquid by simple extraction with a mixture of ethyl acetate and diethyl ether. The remaining viscous ionic liquid was thoroughly washed with diethyl ether and reused in subsequent reactions. It is worthy to note that after several runs the recovered ionic liquid turned brown even after repeating solvent washing. It could be decolorized by the fluxing of its alcoholic solution with activated charcoal, affording regenerated [bmim][Br] as a pale yellow liquid after filtration and concentration. The reduced trivalent chromium oxyhydroxide coating can be reconverted to CrO₂ by heating in air. Thus, the regeneration could be performed by heating used MagtrieveTM in an oven at 350°C for 2 h. The same batch of ionic liquid and regenerated MagtrieveTM could be reused in successive four runs, affording similar isolated yields of **2a** (first run: 93%, second run: 91%, third run: 89%, fourth run: 90%, and fifth run: 92%).

The scope and generality of this process were further examined with respect to a range of substrates under optimized conditions (Table 1). The reactions proceeded smoothly at ambient temperature with high selectivity, affording corresponding *N*-aryl-2-phenyldiazene-carboxamides (**2a–2e**) and 4-substituted-1,2,4-triazoline-3,5-diones (**2f–2h**) in excellent yields. The presence of electron-donating and electron-withdrawing groups on the aromatic ring of starting materials does not make a difference in the oxidation. By all appearances, this synthesis approach is operationally simple and safe to scale up due to the unique properties of presented oxidant-solvent couple.

In conclusion, we found that MagtrieveTM/[bmim]Br can serve as an efficient system for the transformation of substituted semicarbazides or carbazides into corresponding azo compounds. The experimental procedure is quite simple, convenient,

Table 1 Clean synthesis of azo compounds with Magtrieve™ in [bmim][Br]

Entry	Substrate	Product	Time/ min	Yield/ %	mp/°C (lit.) [Ref.]
1	<i>Ph</i> -NHCONHNH- <i>Ph</i> 1a	<i>Ph</i> -NHCON=N- <i>Ph</i> 2a	50	93	114–116 (112–114) [7]
2	4- <i>Me</i> - <i>Ph</i> -NHCONHNH- <i>Ph</i> 1b	4- <i>Me</i> - <i>Ph</i> -NHCON=N- <i>Ph</i> 2b	40	94	105–107 (105–107) [7]
3	3- <i>Me</i> - <i>Ph</i> -NHCONHNH- <i>Ph</i> 1c	3- <i>Me</i> - <i>Ph</i> -NHCON=N- <i>Ph</i> 2c	40	96	71–73 (67–69) [7]
4	4- <i>Cl</i> - <i>Ph</i> -NHCONHNH- <i>Ph</i> 1d	4- <i>Cl</i> - <i>Ph</i> -NHCON=N- <i>Ph</i> 2d	50	95	142–143 (140–142) [11]
5	α - <i>Naph</i> -NHCONHNH- <i>Ph</i> 1e	α - <i>Naph</i> -NHCON=N- <i>Ph</i> 2e	55	92	136–138 (132–134) [12]
6	 1f	 2f	90	94	175–178 (171–175) [24]
7	 1g	 2g	80	91	132–134 (132–135) [24]
8	 1h	 2h	90	96	45–46 (42–43) [24]

and avoids tedious work-up procedures. The combination of regenerable oxidant with recoverable ionic liquids makes this procedure environmentally benign, economic and user-friendly.

Experimental

Magtrieve™ (98% as CrO₂, specific surface area ~30 m²/g) was purchased from Aldrich. The starting materials, substituted semicarbazides and urazoles, were prepared according to standard method [22]. Ionic liquids were prepared by following literature procedures [23]. All products are known compounds; their physical and spectroscopic data were compared with those reported in literatures and found to be identical. Melting points were determined on a XR-6 microscopical apparatus (made in Shanghai). IR spectra were recorded as KBr pellets with a Perkin-Elmer 1600 spectrophotometer. ¹H NMR spectra were recorded on Bruker AC 80 spectrometer in CDCl₃ with TMS as an internal standard.

General procedure for the synthesis of azo compounds

A mixture of 5 mmol substrate and 5 g Magtrieve™ in 30 cm³ of [bmim][Br] was mechanically stirred at room temperature and a colored heterogeneous suspension was obtained rapidly. On completion of the reaction (monitored by TLC), a magnet was held to the bottom of the reaction flask, and the supernatant liquid was then decanted into a separatory funnel. The desired product was extracted from the ionic liquid media by 3 × 10 cm³ EtOAc:Et₂O (1:1 v/v). The extracts were combined with the alcoholic solution from Magtrieve™ washing

(see regeneration procedure described below). Removal of solvents affords essentially pure product in good yields. If necessary, the product could be further purified by recrystallization from ethanol using water as an anti-solvent at room temperature.

Regeneration of Magtrieve™

The recovered Magtrieve™ was washed thoroughly with 2 × 20 cm³ ethanol in order to remove organic compounds adsorbed on the particles. Regeneration work-up was then performed by heating the used oxidant in an oven at 350°C for 2 h.

Acknowledgements

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