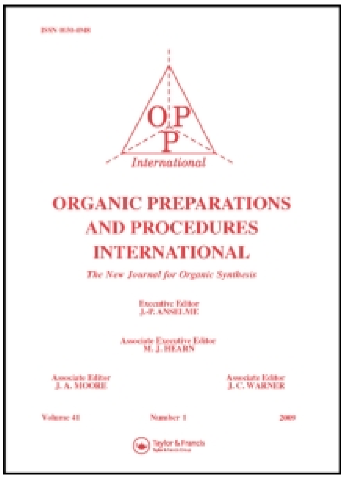

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1,3-DIBROMO-5,5-DIMETHYLHYDANTOIN AS AN EFFICIENT AND CHEMOSELECTIVE AGENT FOR THE REGENERATION OF CARBONYL COMPOUNDS FROM SEMICARBAZONES AND OXIMES

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1,3-DIBROMO-5,5-DIMETHYLHYDANTOIN AS AN EFFICIENT AND CHEMOSELECTIVE AGENT FOR THE REGENERATION OF CARBONYL COMPOUNDS FROM SEMICARBAZONES AND OXIMES

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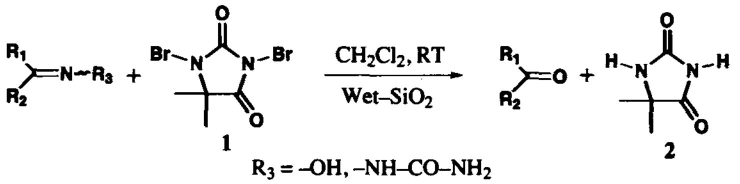
There has been considerable interest in the development of mild methods for the conversion of oximes and semicarbazones to the corresponding carbonyl compounds.[1] Such derivatives of carbonyl compounds are used not only for isolation, purification and characterization but also for the protection of carbonyl compounds.[2] Since oximes can be prepared from non-carbonyl compounds,[3-4] the regeneration of carbonyl compounds from oximes provides an alternative method for the preparation of aldehydes and ketones. A large number of methods based on hydrolytic (acid and basic hydrolysis, photo-hydrolysis),[5] reductive,[6] and oxidative,[7-19] reactions have been developed for deoximation. Oxidative methods have hitherto continued to be developed as they have advantages over the classical hydrolytic procedure. In spite of the many reagents available, there is still room for newer reagents as the existing methods suffer from one or more disadvantages such as long reaction times,[7] necessity for reflux temperature[8] and difficulties in isolation of products.[9] Other disadvantages of the reported reagents are over-oxidation of products, hazardous use, expense and instability; some of these reagents cannot oxidize both oximes and semicarbazones derivatives of carbonyl compounds.

Although a number of methods for the regeneration of carbonyl compounds from semicarbazones have been reported, *e. g. via* sodium nitrite/glacial acetic acid,[20] pyruvic acid,[21] mercury(II) acetate, thallium(III) acetate, lead(IV) acetate,[22] clayfen,[23] Dowex-50,[24] *tetrakis*(pyridine) silver dichromate/benzene,[25] copper chloride,[26] 3-carboxypyridinium chlorochromate/MeCN,[27] zirconium sulfophenylphosphonate,[28] and other reagents,[29-35] the discovery of new, efficient and rapid methods is a goal of the organic chemists.

During the course of our systematic study on oxidation and halogenation of organic compound with *N*-halo reagents,[37-43] we found that 1,3-dibromo-5,5- dimethylhydantoin (*DBDMH*) is a inexpensive, commercially available reagent (Aldrich, price: 49.00 € per 500 g). Therefore we now report a convenient method for the cleavage of the carbon-nitrogen double bonds of oximes and semicarbazones using DBDMH, as an oxidizing agent, that overcomes the disadvantages associated with oxidative methods developed so far. Various oximes and semicarbazones were converted to corresponding carbonyl compounds in the presence DBDMH and wet-SiO_2 (50% *w/w*) in dichloromethane at room temperature (*Scheme 1*).



$R_3 = -OH, -NH-CO-NH_2$

The results of the conversion of aliphatic (cyclic and acyclic), aromatic (with electron-withdrawing and electron-releasing groups), heterocyclic oximes, and semicarbazones to the corresponding carbonyl compounds in the presence of DBDMH in CH_2Cl_2 are presented in *Table 1*. The reaction proceeds in good yields within a short time and the optimum molar ratios

Table 1. *Regeneration of Carbonyl Compounds from Oximes and Semicarbazones*

Entry	Substrate	Yield[a,b] (%)	mp (°C)	*lit.* (°C)	Time (hrs)	Oxidant/ Substrate
1	Diisopropyl ketone oxime	80	85-87	88[44]	1	2
2	Isobutyraldehyde oxime	83	185	187[44]	1.2	2
3	Cyclohexanone oxime	80	159-161	162[44]	1	2
4	Camphor oxime	90	174-176	177[45]	4	2
5	Acetophenone oxime	91	245-248	248-249[44]	2	2
6	4-Methylacetophenone oxime	90	257-259	260[44]	2.5	2
7	Benzophenone oxime	93	235-237	238[44]	1	2
8	Benzaldehyde oxime	89	234-237	237[44]	1.3	2
9	3-Nitrobenzaldehyde oxime	91	290-292	292[44]	2	2
10	4-Chlorobenzaldehyde oxime	90	250-254	254[44]	2	2
11	Pyridine 4-carboxaldehyde oxime	90[d]	175-177	178 -179[45]	2.5	2
12	Cyclohexanone semicarbazone	80	160	162[44]	0.9	2.5
13	3-Nitrobenzaldehyde semicarbazone	90	290-292	292[44]	3	2.5
14	3-Bromobenzaldehyde semicarbazone	92	202- 204	205[45]	3.5	2.5
15	Pyridine 3-carboxaldehyde semicarbazone	91[c]	214	216[45]	1.8	2.5
16	Pyridine 4-carboxaldehyde semicarbazone	89	177-179	178-179[45]	2.2	2.5
17	Benzoin semicarbazone		187	189[45]		
18	Benzophenone semicarbazone	94	234-237	238[44]	2.5	2.5
19	4-Methylacetophenone semicarbazone	92	258-260	260[44]	2	2.5
20	4-Nitrobenzaldehyde semicarbazone	92	316-319	320[44]	2	2.5
21	Camphor semicarbazone	90	174-176	177[45]	3.5	2.5

a) Products were characterized by melting points the corresponding of 2,4-dinitrophenylhydrazone derivatives and their IR and ^1H NMR spectra. b) Isolated yields as their 2,4-dinitrophenylhydrazone derivatives. c) Melting point of semicarbazone derivatives. d) Melting point of phenylhydrazone derivatives of substrate to reagent was found to be 1:2 for oximes and 1:2.5 for semicarbazones. When lower amounts of the reagent were used, the reaction was incomplete.

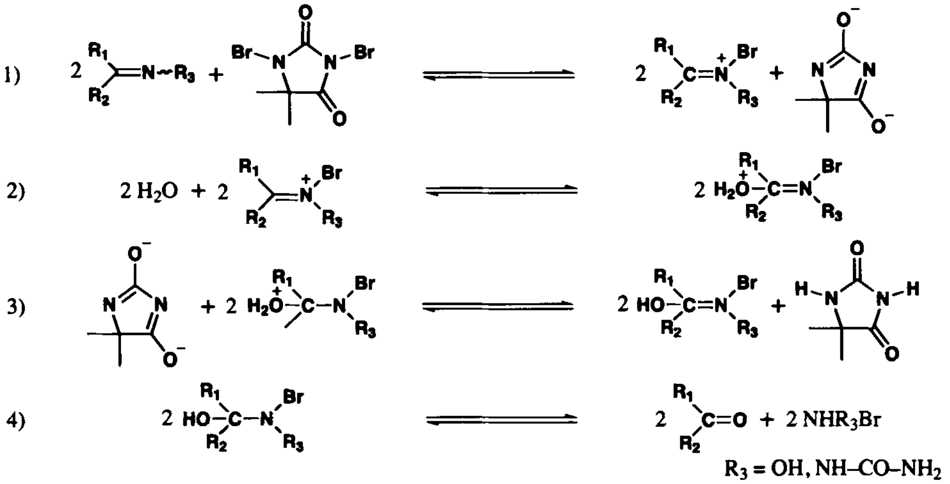
The conversion of these derivatives to the corresponding carbonyl compounds with DBDMH under solvent-free conditions at room temperature is very rapid, strongly exothermic and explosive with the rapid evolution of gas.[43] Recently we reported a few *N*-halo reagents[36-38] for the oxidation oximes to the corresponding carbonyl compounds. However, we found that these reagents were not suitable for oxidation of derivatives semicarbazone and heterocyclic oximes.[36-38] Also in most cases, reaction with sterically hindered oximes such as camphor oxime does not occur,[37] or required forcing conditions and prolonged reaction times.[38] This observation encouraged us to investigate the ability of the protocol for the efficient conversion of highly crowded, heterocyclic oximes and derivatives semicarbazone to the corresponding carbonyl compound. A comparison of this method with other selected *N*-halo reagents previously reported is shown in *Table 2*.

Table 2. Comparison of Various Protocols (*N*-Halo Reagents) for Conversion of Oximes and Semicarbazones

Entry	Substrate	Reagent	Condition	Time	Yield (hrs)	Ref (%)
1	Camphor oxime	a) DBDMH	CH_2Cl_2, Wet-SiO_2, rt	3.5	90	This work
		b) Poly [4-vinyl-*N*,*N*-dichlorobenzensulfonamide]	CCl_4, 40°C	----	----	37
		c) *N*-Bromophthalimide	Acetone, H_2o, reflux	4	85	38[a]
		d) BNBTS (*N*,*N*'-Dibromo-*N*,*N*'-1,2-ethanediylbis (*p*-toluenesulfonamide)	CCl_4, rt	----	----	36
2	Pyridine 4-carboxaldehyde oxime	a) DBDMH	CH_2Cl_2, Wet-SiO_2, rt	2.5	90	This work
		b) Poly [4-vinyl-*N*,*N*-dichlorobenzensulfonamide]	CCl_4, 40°C	----	----	37
		c) N-Bromophthalimide	Acetone, H_2o, reflux	----	----	38[a]
		d) BNBTS (*N*,*N*'-Dibromo-*N*,*N*'-1,2-ethanediylbis (*p*-toluenesulfonamide)	CCl_4, rt	----	----	36
3	Cyclohexanone semicarbazone	a) DBDMH	CH_2Cl_2, Wet-SiO_2, rt	2.5	87	This work
		b) Poly [4-vinyl-*N*,*N*-dichlorobenzensulfonamide]	CCl_4, 40°C	----	----	37
		c) *N*-Bromophthalimide	Acetone, H_2o, reflux	----	----	38[a]
		d) BNBTS (*N*,*N*'-Dibromo-*N*,*N*'-1,2-ethanediylbis (*p*-toluenesulfonamide)	CCl_4, rt	----	----	36

Our observations for chemoselectivity are as follows: Oximes and semicarbazones of aldehydes are converted without over-oxidation; the oxidation of C=N bond of oximes and semicarbazones may be performed in the presence of hydroxy groups and N atoms and aromatic oximes and semicarbazones are oxidized without bromination of aromatic rings.

Although the role of DBDMH is not clear, as mentioned in our previous reports,[38,40] we suggest the following mechanism for these transformations.



The reaction occurs rapidly at room temperature and the reagent was converted to 5,5-dimethylhydantoin **2**, which can be isolated, brominated, and re-used.[45] Other advantages of this method are the facile work-up procedure, good yields of the products, chemoselectivity and mild nature of DMDBH.

EXPERIMENTAL SECTION

The oximes and semicarbazones were prepared by standard procedures. All of products were characterized by comparison of their spectral data (^{1}H-NMR and IR spectra) and melting points of 2,4-dinitrophenylhydrazone derivatives with those of authentic samples.

General Procedure for the Regeneration of Aldehydes and Ketones.- The oxidizing agent (2 mmol or 2.5 mmol) was added to a mixture of the substrate (1 mmol) and wet-SiO_2 [(SiO_2/H_2O: 50% w/w), 0.1 g] in dichloromethane (10 mL) at room temperature in a flask equipped with a stir bar (*CAUTION! Vigorous, possibly explosive, evolution of gas*). After 30 seconds, the mixture turned red and it was stirred vigorously at room temperature for the time indicated in *Table 1*. The progress of the reaction was monitored by TLC. After completion of the reaction, 0.5 g sulfuric acid (98%) supported on silica gel (w/w 50%) was added to the mixture which was stirred vigorously for 15 min, filtered and the filtrate was dried over anhydrous $CaCl_2$ (1 g). Evaporation of the filtrate gave the corresponding carbonyl compounds in 80-94% yields, isolated as their 2,4- dinitrophenylhydrazones which were recrystallized from ethanol.

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CONVENIENT AND RAPID PREPARATION OF INDENE DIMERS FROM INDENES OR INDANOLS

Submitted by (05/19/06)

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Functionalized indenes and indans have been the subject of attention from medicinal and industrial chemists. 1-Aminoindanes are effective dopamine re-uptake blockers,[1] active against neurological disorders and neurotrauma[2] and, as their sulfonylated derivatives, are potential potassium channel blockers.[3] 3-(ω-Phthalimidoalkyl)indenes undergo intramolecular cyclization to form 13-membered spirocyclic nitrogen heterocycles upon irradiation and are useful intermediates in the synthesis of biologically active polycyclic compounds.[4] Naphthylidene-substituted aminoalkylindenes have high affinity toward and average pharmacological potency values at the cannabinoid receptor CB1.[5] Since indenes bearing an aromatic ring as substituted group display broad bioactivities, it was thought that indene dimers might desire further research for their bioactivities.