

Efficient Synthesis and Deprotection of Semicarbazones under Solvent-Free Conditions

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ABSTRACT: *Effective methodologies for efficient preparation of semicarbazones from aldehydes or ketones via milling and the subsequent regeneration of the parent carbonyls by gaseous nitrogen dioxide are described under solid-solid and gas-solid reaction conditions, respectively. These methods are fast, simple and environmentally benign which do not require the use of any auxiliaries such as catalysts or solid supports in their procedures.*

KEY WORDS: *Carbonyl compounds, Semicarbazones, Ball-milling, Deprotection, Nitrogen dioxide, Waste-free.*

INTRODUCTION

Protection-deprotection of the functional groups in organic chemistry is often an essential step in the manipulation of carbonyl functional groups playing a special role in the organic synthesis, because of their widespread presence in the structure of drugs, carbohydrates, etc. Different methodologies have been offered so far to develop suitable protective groups for carbonyl compounds. Semicarbazone derivatives are especially interesting, as they are highly crystalline and stable. Therefore, these compounds are extensively used for the isolation, purification and characterization of aldehydes and ketones [1-3]. Usually, semicarbazone derivatives are prepared *via* the reaction of aldehydes or ketones with semicarbazide in the presence of an acid or a base as catalyst [1-5]. Many efforts to develop more

environmentally friendly methods for the preparation of semicarbazones have been recently described. For example, a lot of studies have been performed in the recent years to use the advantages of solvent-free routes to establish greener methods for preparation of carbonyl derivatives [6, 7]. Among them, grinding of carbonyl compounds and semicarbazide with NaOH [8], sodium acetate [9], silica gel or basic alumina [10], and activation by microwave irradiation [11-13] are noteworthy. However, most of these methods suffer from disadvantages such as the use of solid supports or other auxiliaries, solvents for the extraction from solid supports, excess of reagents, low yields of the desired products, and laborious and time consuming recycling of the solid supports [6, 8-13]. Therefore, development of simple, efficient and fast

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procedures, which operate under solvent-free and mild conditions, and avoids the use of any solid supports or other auxiliaries is a very engaging research effort.

Moreover, the application of ball-milling technique in various important organic transformations has been developed in the recent years [14-20]. On the basis of our previous results [14-18] and to overcome the aforementioned problems and facilitate product formation, we decided to examine the feasibility of the application of ball-milling technique in the waste-free quantitative synthesis of semicarbazones. Herein, we wish to report a superior green, facile, and clean synthesis of diverse semicarbazones from aldehydes or ketones using a quantitative, wasteless and stoichiometric solid-solid or solid-liquid reactions through ball-milling technique.

On the other hand, the regeneration of carbonyl compounds from their nitrogen derivatives is an important step in many organic transformations. Therefore, deprotection of some of these nitrogen derivatives such as oximes has received considerable attention in the recent years [17, 21-22]. In contrast to the oximes, little attention has been paid to the conversion of semicarbazones to their parent carbonyl compounds and the number of effective methods for this reaction remains quite limited. However, most of the reported procedures used for this purpose require the use of solid supports or other auxiliaries, solvents for the extraction from solid supports, high temperature, long reaction time, expensive and not readily available reagents, and tedious work-up procedures [21-33].

Consequently, there is a demand for the development of protocols using readily available reagents which operate under extremely mild reaction conditions. In continuation of our studies on the development of solvent-free quantitative deprotection methods [17, 34], we also wish to report a simple, rapid and efficient method for recovery of carbonyl compounds from their corresponding semicarbazones.

EXPERIMENTAL SECTION

All chemicals were purchased from Merck, Aldrich or Fluka and used as received except for benzaldehyde, which a fresh distilled sample was used. The ball-mill was a Retsch MM 200 swing mill with a 10 mL stainless steel double-walled beaker with fittings for circulating liquids for heating or cooling. Two stainless steel balls with 12 mm diameter were used. Ball-milling

was performed at 20-25 Hz frequency usually at room temperature (without circulating liquid the temperature did not rise above 30 °C). Melting points were measured by using the capillary tube method with an electro thermal 9200 apparatus and are uncorrected. Analytical TLC was carried out using Merck 0.2 mm silica gel 60 F-254 Al-plates. Infrared (IR) spectra were recorded on a Perkin-Elmer 1720-X FT-IR spectrometer using KBr pellets. ¹H NMR (500 MHz) and ¹³C NMR (125 MHz) spectra were obtained using a Bruker DRX-500 AVANCE spectrometer. All NMR spectra were determined in CDCl₃ at ambient temperature. GC chromatograms were recorded on a Perkin-Elmer 8420 gas chromatograph using a capillary column. All of the products were well characterized by comparison of their physical constants, IR or NMR spectral data with those reported in literature.

General Procedure for the Preparation of Semicarbazones (3)

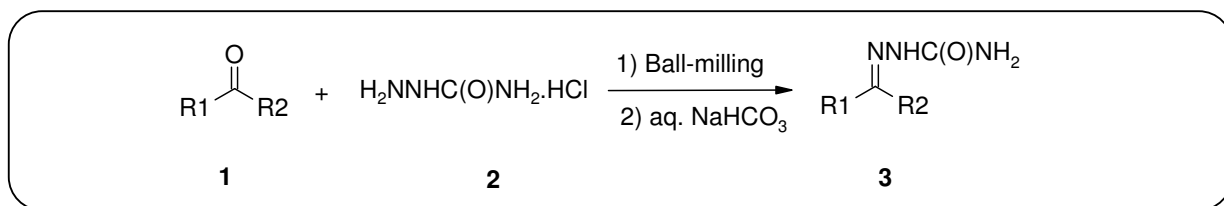
A clean and dry 10-mL stainless steel ball-milling vessel equipped with 2 stainless steel balls was charged with 1.0 mmol of an aldehyde or a ketone and 1.0 mmol of semicarbazide.HCl. The vessel was closed and the milling started at the given temperature in Table 1. After each 10 min, the progress of the reaction was monitored by TLC. The milling cycle was repeated, if necessary, until the reaction was completed. The obtained solid was treated with 2.0 mL of 5% aq. NaHCO₃, filtered, and dried to afford the desired products, which in most cases were essentially pure semicarbazones. Further purification was achieved by recrystallization from 96% ethanol, if necessary.

General Procedure for the Regeneration of Carbonyl Compounds (1) from Semicarbazones (3)

In a typical experiment, semicarbazone (1.0 mmol) was placed in a 100 mL round-bottom flask. The flask was evacuated and filled with 2.2 mmol of 0.6 bar NO₂/N₂O₄ (g). After the required time, hexane (3-10 mL) was added and the organic layer was washed with 0.01 M aq. HCl (3-10 mL) and dried over anhydrous Na₂SO₄. Evaporation of the solvent under reduced pressure gave the carbonyl compound which was pure in most cases.

RESULTS AND DISCUSSION

At first place, It was found that the solvent-free reaction of 1.0 mmol of *p*-chlorobenzaldehyde (**1a**) with



Scheme 1: Solvent-free ball-milling preparation of semicarbazones.

1.0 mmol of semicarbazide.HCl (**2**) proceeds as a model reaction simply by ball-milling the reaction mixture for 45 min at room temperature. The Condensation reaction afforded the corresponding semicarbazone (**3a**) in quantitative yield (Table 1). Other milling times (5, 10, 30, and 60 min) were also investigated and the reaction was monitored by TLC. It was found that some unreacted *p*-chlorobenzaldehyde remains in the reaction mixture by milling times less than 45 min. The *p*-chlorobenzaldehyde semicarbazone was obtained in solid form after treating the obtained reaction mass with an aqueous solution of NaHCO₃ in all cases studied. (Scheme 1).

The process in its entirety involves a simple charging of the appropriate aldehyde or ketone (**1**) and semicarbazide.HCl (**2**) into a 10 mL stainless steel chamber and subsequent ball-milling at specified temperature and time given in Table 1. None acidic or basic catalyst and excess of semicarbazide is required. Compatible with the fact that the solid-solid reactions in a simple commercial ball-mill proceeds more effective than in a mortar using a pestle [14-17], we also found that the alternative grinding of the 1.0 mmol of 4-chlorobenzaldehyde (**1a**) and 1.0 mmol of semicarbazide.HCl (**2**) in a mortar was not complete even after 1 h.

By adopting the above method, various semicarbazones were prepared in quantitative yields by milling of stoichiometric amounts of an appropriate aldehyde with semicarbazide.HCl at room temperature for the given time (Table 1, **1a-1s**). As it is shown in Table 1, ketones (Entries **1t-1z'**) generally require higher temperatures than aldehydes for complete conversion. For example, acetophenone (**1t**), benzil (**1x**), cyclohexanone (**1y**) and (+)-carvone (**1z'**) react quantitatively to their corresponding semicarbazones at 65-90 °C after 30-45 min of milling.

The method is superior to other introduced methods [7-13] as it produces in most cases quantitative yields of

the desired products with no waste, or any need of tedious purification procedures. The sustainability of this environmentally friendly technique is compared to some previous techniques in Table 2 for some semicarbazones.

Difference in the required conditions for transformation of aldehydes and ketones to their semicarbazones can serve as a platform for protecting aldehydes in the presence of a ketone functional group. In order to show this chemoselectivity, we performed two competitive reactions. As shown in the Scheme 2, when a 1:1 mixture of *p*-hydroxy- or *p*-nitrobenzaldehyde and *p*-hydroxy- or *p*-nitroacetophenone was allowed to react with 1.0 eq semicarbazide.HCl at room temperature for 45 min, the aldehydes in turn were transformed quantitatively to their corresponding semicarbazones, whereas the ketones remain 100% unreacted.

In continuation of our previous studies on the usefulness of gaseous NO₂/N₂O₄ on oxidation and oxidative deprotection reactions [17, 35], we observed that on exposing the semicarbazone products with NO₂/N₂O₄ gas (**4**) at room temperature, a very rapid exothermic reaction takes place. Subsequent hydrolysis (treatment of the reaction mixture with water) afforded the desired carbonyl compounds in almost quantitative yields (Scheme 3). To find the optimal reaction conditions, *p*-chlorobenzaldehyde semicarbazone (**3a**) was used as a model substrate and effect of different amounts of NO₂/N₂O₄ gas and temperature on its oxidative cleavage to *p*-chlorobenzaldehyde was studied. By introducing NO₂/N₂O₄ gas to an evacuated flask including solid *p*-chlorobenzaldehyde semicarbazone, the solid became liquid immediately and its colour turned to brown. Further investigations revealed that just a minute is enough for the complete conversion of the model compound at room temperature when at least two equivalent of gaseous NO₂/N₂O₄ was used. No further oxidation of *p*-chlorobenzaldehyde to the corresponding carboxylic acid was observed.

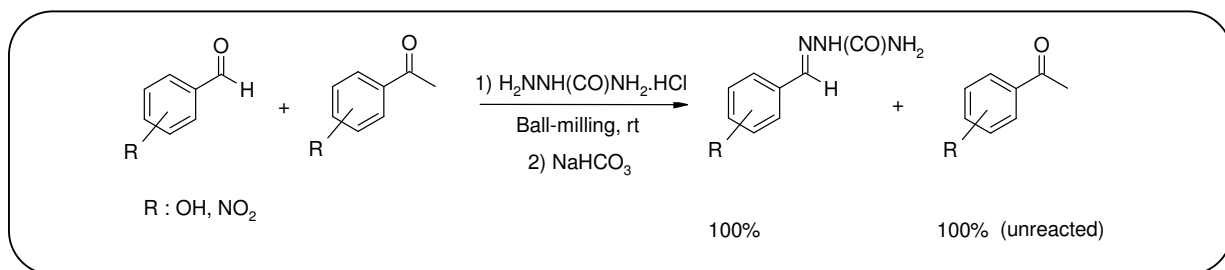
Table 1: Condensation of aldehydes and ketones with semicarbazide.HCl under solvent-free conditions.

Substrate	R1	R2	Temp. (°C)	Time (min)	Conversion ^a (%)	3 Mp (°C) (refs) [3, 36-39]
1a	p-ClC ₆ H ₄	H	25	45	100	228-230 (231)
1b	C ₆ H ₅	H	25	30	100	222-224 (224)
1c	p-NO ₂ C ₆ H ₄	H	25	45	100	218-220 (221)
1d	o-NO ₂ C ₆ H ₄	H	25	45	100	252-254 (256)
1e	m-NO ₂ C ₆ H ₄	H	25	45	100	241-244 (246)
1f	p-BrC ₆ H ₄	H	25	45	100	226-228 (228)
1g	Furyl	H	25	15	100	200-202 (203)
1h	2-thienyl	H	25	20	100	218-220 (223-224)
1i	p-MeC ₆ H ₄	H	25	30	100	231 (234)
1j	p-OHC ₆ H ₄	H	25	45	100	220-221 (223)
1k	o-OHC ₆ H ₄	H	25	45	100	228-230 (226-230)
1l	p-MeOC ₆ H ₄	H	25	45	100	206-208 (209)
1m	o-MeOC ₆ H ₄	H	25	45	100	211-214 (215)
1n	p-N(Me) ₂ C ₆ H ₄	H	25	30	100	218-220 (221)
1o	Vanillin		25	75	100	236-238 (238)
1p	PhCH=CH	H	25	30	100	210-213 (215)
1q	CH ₃ CH=CH	H	25	45	100	196-199 (199)
1r	CH(Me) ₂	H	25	45	100	122-124 (126)
1s	CH ₃ (CH ₂) ₆	H	25	45	100	98-100 (101)
1t	C ₆ H ₅	Me	75-80	30	100	195-198 (199)
1u	p-NO ₂ C ₆ H ₄	Me	65-70	40	100	226-227 (222-224)
1v	p-OHC ₆ H ₄	Me	80-90	50	100	196-198 (198)
1w	m-OHC ₆ H ₄	Me	80-90	45	100	192-194 (195)
1x	C ₆ H ₅	OCC ₆ H ₅	80-90	30	100	242-244 (244)
1y	Cyclohexanone		65-70	45	100	163-165 (167)
1z	CH ₃ (CH ₂) ₄	Me	65-70	35	100	124-126 (127)
1z'	(+)-Carvone		80-90	30	100	159-162 (163)

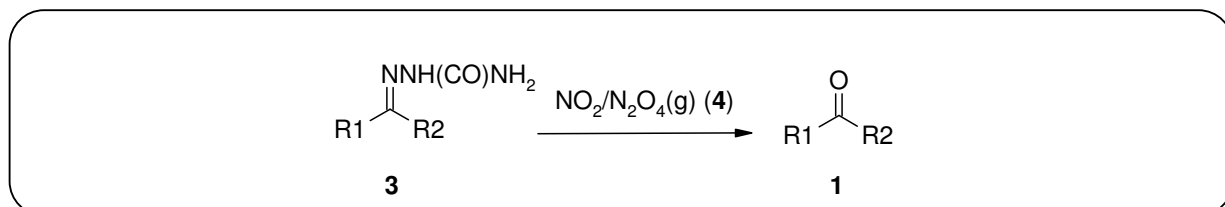
^a Isolated yields were generally 2-3 % less than the reported conversion. All of the products are well known materials and characterized by comparison of their IR, NMR spectral data or physical constants with those reported in the literature.

Table 2: Comparison of the present method with some others previously reported.

Compound	Conditions	Yield (%)	Ref.
3b	pestle and mortar, silica gel, 10 min	97	8
3b	pestle and mortar, basic alumina, 80 °C, 5 min	85	10
3b	microwave irradiation, 1.5 min	85	11
3b	NaOAc, MeOH	78	41
3b	ball-milling, 25 °C, 30 min	100	present work
3t	pestle and mortar, silica gel, 10 min	92	8
3t	pestle and mortar, Basic alumina, 80 °C, 20 min	52	10
3t	ball-milling, 75 °C, 30 min	100	present work



Scheme 2: Chemoselective protection of aldehydes in the presence of ketones.



Scheme 3: Deprotection of semicarbazones by gaseous nitrogen dioxide.

To obtain the parent carbonyl compounds, different semicarbazones were reacted with NO₂/N₂O₄ gas at room temperature. For some aldehydes, e.g. benzaldehyde, some overoxidation to the corresponding carboxylic acid was observed at room temperature, but this can be avoided if the reaction is carried out at lower temperature. The reactivity of various aldehyde semicarbazones were investigated in different temperatures and the optimized results have been summarized in Table 3.

The effectiveness of this environmentally friendly technique is compared to some previous techniques for the examples of **3p**, **3t**, and **3y** in Table 4. While **1p** was regenerated from its semicarbazone in quantitative yield using gaseous NO₂ at 0 °C in just 1 min, other methods are much more complicated, less atom-economic, and afford lower yields under severe conditions and longer reaction times.

As evident from Table 3, the reaction is completely general. Semicarbazones of aromatic aldehydes and ketones as well as aliphatic and α,β -unsaturated aldehydes reacted smoothly to regenerate the corresponding carbonyl compounds in quantitative yields within very short reaction time. Interestingly, the α,β -unsaturated compounds such as cinnamaldehyde semicarbazone (**3p**) and crotonaldehyde semicarbazone (**3q**) underwent chemoselective oxidation in quantitative yields without affecting the C=C bond. However, the reaction conditions utilized in this study are not suitable

for deprotection of semicarbazones **3j-3l** bearing hydroxy or methoxy group on their aromatic ring. These semicarbazones produced a mixture of the corresponding aldehyde, carboxylic acid, and some unidentified compounds (presumably nitrated products). All attempts to improve selectivity and yield of these aldehydes failed.

CONCLUSIONS

In conclusion, alternative methodologies for both quantitative protection of carbonyl compounds as semicarbazone derivatives and their regeneration have been established. Attractive features of these methods include the general application, avoiding the need for any solid support, auxiliaries, and solvent, high efficiency, and simple work up, together with mildness of the reactions and chemoselectivity. In addition, by development of large scale ball mills, the protection of carbonyl compounds may gain industrial application, where the absence of solvents and the low costs of the method may lead to substantial environmental and financial advantages. On the other hand, the suggested deprotection method is of special interest as it is very simple, very fast, and does not need any solid support or catalyst and regenerates carbonyls mostly in quantitative yields in a short time. The regenerated aldehydes mostly were not overoxidized to the carboxylic acids under reaction conditions.

Table 3: Deprotection of semicarbazones under solvent-free conditions.

Substrate	R1	R2	Temp. (°C)	Time (min.)	Conversion ^a (%)
3a	p-ClC ₆ H ₄	H	25	1	100
3b	C ₆ H ₅	H	0	1	100
3c	p-NO ₂ C ₆ H ₄	H	0	3	100
3d	o-NO ₂ C ₆ H ₄	H	0	1	100
3e	m-NO ₂ C ₆ H ₄	H	-5	1	100
3i	p-MeC ₆ H ₄	H	0	1	100
3j	p-OHC ₆ H ₄	H	-10	1.5	78
3k	o-OHC ₆ H ₄	H	-10	1.5	60
3l	p-MeOC ₆ H ₄	H	-10	1.5	50
3n	p-Me ₂ NC ₆ H ₄	H	0	1	100
3p	PhCH=CH	H	0	1	100
3q	CH ₃ CH=CH	H	0	1	100
3r	CH(Me) ₂	H	0	2	100
3s	CH ₃ (CH ₂) ₆	H	25	2	100
3t	Ph	Me	0	1	100
3u	p-NO ₂ C ₆ H ₄	Me	25	5	100
3y	Cyclohexanone		0	1	100
3z	(+)-Carvone		25	2	100

^a Isolated yields were generally 2-3 % less than the reported conversion. All of the products are well known materials and characterized by comparison of their IR, NMR spectral data or physical constants with those reported in the literature.

Table 4: Comparison of the present method with some others previously reported.

Compound	Conditions	Yield (%)	Ref.
3p	H ₆ PMo ₉ V ₃ O ₄₀ in refluxing acetic acid, 5 min.	93	21
3p	(CTA) ₂ S ₂ O ₈ in acetonitrile at reflux	88	22
3p	hexamethylenetetramine-bromine (HMTAB) and N-bromosuccinimide (NBS), 25 °C,	80	23
3p	NO ₂ gas, 0 °C, 1 min.	100	present work
3t	MoO ₃ or KBrO ₃ , in refluxing CH ₃ CN-H ₂ O	90	40
3t	NO ₂ gas, 0 °C, 1 min.	100	Present work
3y	H ₆ PMo ₉ V ₃ O ₄₀ in refluxing acetic acid, 35 min.	97	21
3y	NO ₂ gas, 0 °C, 1 min.	100	present work

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REFERENCES

- [1] Greene T.W., Wust P.G., "Protective Groups in Organic Synthesis", 3rd ed; John Wiley & Sons: New York, (1999).
- [2] Hanson J.R., "Protective Group in Organic Synthesis", 1st ed; BlackWell Science, Malden: MA, (1999).
- [3] Shriner R.L., Fuson R.C., The Systematic Identification of Organic Compounds, 3rd ed., John Wiley & Sons. Inc., (1980).
- [4] Yoa H.C., Resnick P.J., Azo-Hydrazone Conversion. III. The Autoxidation of Benzaldehyde Phenylhydrazones, *J. Org. Chem.*, **30**, p. 2832 (1965).
- [5] Fusco R., Sannicola F., New Rearrangement of Arylhydrazones in Polyphosphoric Acid: Formation of Diaryl Ethers, *J. Org. Chem.*, **46**, p. 90 (1981).
- [6] Sartori G., Ballini R., Bigi F., Bosica G., Maggi R., Righi P., Protection (and Deprotection) of Functional Groups in Organic Synthesis by Heterogeneous Catalysis, *Chem. Rev.*, **104**, p. 199 (2004).
- [7] Niknam K., Kiasat A.R., Karimi S., Dowex Polymer-Mediated Protection of Carbonyl Groups, *Synth. Commun.*, **35**, p. 2231 (2005).
- [8] Hajipour A.R., Mohammadpoor-Baltork I., Bigdeli M., A Convenient and Mild Procedure for the Synthesis of Hydrazones and Semicarbazones from Aldehydes or Ketones under Solvent-Free Conditions, *J. Chem. Research (S)*, p. 570 (1999).
- [9] Kiasat A.R., Kazemi F., Fallah Mehrjardi M., Synthesis of Semicarbazones from Carbonyl Compounds under Solvent Free Conditions, *Asian J. Chem.*, **17**, p. 2830 (2005).
- [10] Niknam K., Kiasat A.R., Karami B., Heydari N., Basic Al₂O₃ as a Recyclable Reagent for the Protection of Carbonyl Groups with Phenylhydrazine Derivatives and Semicarbazides, *Turk. J. Chem.*, **31**, p. 135 (2007).
- [11] Varma R.S., Dahiya R., Microwave-Assisted Facile Synthesis of Imines and Enamines Using Envirocat Epzgf as a Catalyst, *Synlett.*, p. 1245 (1997).
- [12] Kamakshi R., Boreddy S., Reddy R., Solvent Less Rapid Synthesis of Oxime, Semicarbazone and Phenyl Hydrazone Derivatives from Carbonyl Compound Under Microwave Conditions, *Aus. J. Chem.*, **58**, p. 603 (2005).
- [13] Bandger B.P., Sadavarte V.S., Uppalla L.S., Govande R., Chemoselective Preparation of Oximes, Semicarbazones, and Tosylhydrazones Without Catalyst and Solvent, *Monatsh. Chem.*, **132**, p. 403 (2001).
- [14] Kaupp G., Naimi-Jamal M.R., Schmeyers J., Solvent-Free Knoevenagel Condensations and Michael Additions in the Solid State and in the Melt with Quantitative Yield, *Tetrahedron*, **59**, p. 3753 (2003).
- [15] Kaupp G., Naimi-Jamal M.R., Stepanenko V., Waste-Free Solid-State Protection of Diols, Diamines, Amino Acids and Polyols with Phenylboronic Acid, *Chem. Eur. J.*, **9**, p. 4156 (2003).
- [16] Naimi-Jamal M.R., Mokhtari J., Dekamin M.G., Kaupp G., Sodium Tetraalkoxyborates: Intermediates for the Quantitative Reduction of Aldehydes and Ketones to Alcohols Through Ball Milling with NaBH₄, *Eur. J. Org. Chem.*, **21**, p. 3567 (2009).
- [17] Mokhtari J., Naimi-Jamal M.R., Hamzeali H., Dekamin M.G., Kaupp G., Kneading Ball-Milling and Stoichiometric Melts for the Quantitative Derivatization of Carbonyl Compounds with Gas-Solid Recovery, *ChemSusChem.*, **2**, p. 83 (2009).
- [18] Mashkouri S., Naimi-Jamal M.R., Mechanochemical Solvent-Free and Catalyst-Free One-Pot Synthesis of Pyrano[2,3-d]Pyrimidine-2,4(1H,3H)-Diones with Quantitative Yields, *Molecules*, **14**, p. 474 (2009).
- [19] Kaupp G., Mechanochemistry: the Varied Applications of Mechanical Bond-Breaking, *CrystEngComm.*, **11**, p. 388 (2009).
- [20] Tullberg E., Schacher F., Peters D., Frejd T., Solvent-Free Heck-Jeffery Reactions Under Ball-Milling Conditions Applied to the Synthesis of Unnatural Amino Acids Precursors and Indoles, *Synthesis*, p. 1183 (2006).
- [21] Heravi M.M., Ranjbar L., Derikvand F., Oskooie H.A., Bamoharram F.F., Catalytic Oxidative Cleavage of C N Bond in the Presence of Mixed-Addenda Vanadomolybdophosphate, H₆PMo₉V₃O₄₀ as a Green and Reusable Catalyst, *J. Mol. Catal. A: Chem.*, **265**, p. 186 (2007).

- [22] Norouzi M., Tajbakhsh M., Alinezhad H., Geran Urimi G.A., Deprotection of Oximes, Phenylhydrazones, Semicarbazones and Thio-Semicarbazones to the Corresponding Carbonyl Compounds Using Cetyltrimethylammonium Peroxodisulfate as a New and Selective Oxidizing Agent, *J. Chin. Chem. Soc.*, **55**, p. 508 (2008).
- [23] Bandgar B.P., Makone S.S., Remarkably Fast Deprotection of Semicarbazones and Tosylhydrazones Under Mild, Neutral and Solvent-Free Conditions, *J. Chin. Chem. Soc.* **47**, p. 575 (2000).
- [24] Shirini M A., Zolfigol A., Safari I., Mohammadpoor B., Mirjalili B.F., Regeneration of Carbonyl Compounds by Cleavage of C-N Bonds Under Mild and Completely Heterogeneous Conditions *Tetrahedron Lett.*, **44**, p. 7463 (2003).
- [25] Hajipour A.R., Adibi H., Ruoho A.E., Wet Silica-Supported Permanganate for the Cleavage of Semicarbazones and Phenylhydrazones Under Solvent-Free Conditions, *J. Org. Chem.*, **68**, p. 4553 (2003).
- [26] Heravi M.M., Sabaghian A.J., Bakhtiari Kh., Ghassemzadeh M., Ammonium Chlorochromate adsorbed on Alumina for Cleavage of Semicarbazones and Phenylhydrazones Under Classical Heating and Microwave Irradiation in Solvent-Free System, *J. Braz. Chem. Soc.* **17**, p. 614 (2006).
- [27] Aghapoor K., Heravi M.M., Nooshabadi M.A., Ghassemzadeh M., Solid State Cleavage of Semicarbazones with Cerium Ammonium Nitrate Supported by Wet Alumina, *Monatsh. Chem.*, **133**, p. 107 (2002).
- [28] Mohammadpoor-Baltork I., Sadeghi M.M., Adibi A., Efficient Solvent-Free Oxidation of Organic Compounds with Potassium Dichromate in the Presence of Lewis Acids, *Molecules*, **6**, p. 900 (2001).
- [29] Bose D.S., Narraiah A.V., A Facile Method for the Conversion of Oximes and Tosylhydrazones to Carbonyl Compounds with Dess-Martin Periodinane, *Synth. Commun.* **29**, p. 937 (1999).
- [30] Zhang G.S., Yang D.H., Chen M.F., Cai K., Methylammonium Chlorochromate Adsorbed on Alumina: A Convenient and Efficient Reagent for Cleavage of Carbon-Nitrogen Double Bonds Under Non-Aqueous Condition, *Synth. Commun.*, **28**, p. 607 (1998).
- [31] Curini M., Rusati O., Pisani E., Costantino U.U., Heterogeneous Catalysis in Carbonyl Regeneration from Oximes, Semicarbazones, and Tosylhydrazones by Zirconium Sulfohenyl Phosphonate, *Synlett*, p. 333 (1996).
- [32] Ram R.N., Varsha K., Regeneration of Carbonyl Compounds from Semicarbazones by Copper (II) Chloride Dihydrate, *Tetrahedron Lett.*, **32**, p. 5829 (1991).
- [33] Narayanan S., Srinivasan V.S., Stereochemistry of Piperazine-2,5-Dione Formation by Self-Condensation of DL-Amino Acid Esters, *J. Chem. Soc. Perkin. Trans.*, **2**, p. 1557 (1986).
- [34] Naimi-Jamal M.R., Seyedalikhani M., Mokhtari J., Simple, Efficient and Solvent-Free Method for Quantitative Regeneration of Carbonyl Compounds From Oximes by Gaseous Bromine, *Asian J. Chem.*, **21**, p. 3253 (2009).
- [35] Mokhtari J., Naimi-Jamal M.R., Hamzeali H., Dekamin M.G., Kaupp G., Kneading Ball-Milling and Stoichiometric Melts for the Quantitative Derivatization of Carbonyl Compounds with Gas-Solid Recovery, *ChemSusChem*, **2**, p. 248, (2009).
- [36] Vogel A., "Textbook of Practical Organic Chemistry", (Eds.: Furniss, B.S ; Hannaford, A. J; Rogers, V; Smith, P. W. G; Tatchell, A. R.), Longman, London, (1986).
- [37] Hartough H.D., "Thiophene and Its Derivatives", Interscience, New York, (1952).
- [38] Sabnis R.W., "Handbook of Acid-Base Indicator", CRC press, New York, (2008).
- [39] Hanla M.M., Synthesis and Antibacterial Activity of Some Transition Metal Complexes of Oxime, Semicarbazone and Phenylhydrazone, *E-Journal of Chemistry*, **6**, p. 508 (2009).
- [40] Shirini F., Neyestani Z., Abedini, M., $\text{KBrO}_3/\text{MoO}_3$: An Efficient Reagent System for the Oxidative Deprotection of Semicarbazones, 1,1-Diacetates and Acetals, *Chinese Chemical Letters*, **20**, p. 514 (2009).
- [41] Shriner, Ralph L., Hermann, Christine K. F., Morrill, Terence C., Curtin, David Y., Fuson, Reynold C., "The Systematic Identification of Organic Compounds", 8th Edition, John Wiley & Sons, NewYork, (2004).