

Basic Al_2O_3 as a Recyclable Reagent for the Protection of Carbonyl Groups with Phenylhydrazine Derivatives and Semicarbazides

Khodabakhsh NIKNAM^{1,*}, Ali Reza KIASAT², Bahador KARAMI³, Nima HEYDARI⁴

¹*Department of Chemistry, Faculty of Sciences, Persian Gulf University, Bushehr 75169-IRAN
e-mail: nikanam@pgu.ac.ir and kh_nikanam@yahoo.com*

²*Chemistry Department, College of Science, Shahid Chamran University, Ahvaz-IRAN*

³*Department of Chemistry, Yasouj University, Yasouj 75914-353-IRAN*

⁴*Islamic Azad University, Gachsaran Branch-IRAN*

Received 20.09.2006

Basic alumina is employed as an inorganic basic solid catalyst for the clean and less hazardous protection of carbonyl compounds, such as phenylhydrazones, 2,4-dinitrophenylhydrazones, semicarbazones, and thiosemicarbazones, under solvent-free conditions. The reactions proceed smoothly and require a short reaction time with good to excellent yields, and the alumina used can be recycled.

Key Words: Basic alumina, phenylhydrazine derivatives, semicarbazides, carbonyl compounds, protection, recyclable.

Introduction

Considerable attention has recently been paid to run reactions on the surface of solids.¹⁻⁴ These reactions are not only of interest from an environmental point of view, but in many cases also offer considerable synthetic advantages with the following features: (i) it is often easy to isolate the products and to separate the catalyst; (ii) comparing the reaction conditions with those of related homogeneous reactions, they are so mild that a high yield of specific products and suppression of by-product formation are expected; (iii) selectivity and activity of the catalysts are often comparable to those of enzymes.⁵ Several classes of solids have commonly been used for surface organic chemistry, including alumina, silica gel, and clays.⁶⁻¹⁰ Basic alumina, the material commonly used for column chromatography, certainly has one of the most interesting of these surface properties, which suggests that a very rich organic chemistry may occur there.

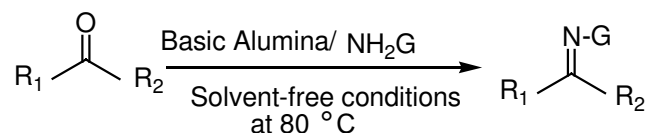
Protection of carbonyl groups is often a requirement in reactions involving substrates with multifunctional groups.^{11,12} Derivatives of carbonyl compounds, such as phenylhydrazone, 2,4-dinitrophenylhydrazones, semicarbazones, and thiosemicarbazones, are not only used for the characterization and purification of carbonyl compounds, but also play an important role in the protection of carbonyl compounds.¹³ The formation

*Corresponding author

of these derivatives involves Brønsted and Lewis acid catalysis.^{13,14} As the conventional acids used in the preparation of these derivatives are highly corrosive, they pose severe environmental hazards. Heterogeneous reactions that are facilitated by supported reagents on various solid inorganic surfaces have received attention in recent years; a protection system consisting of phenylhydrazine or 2,4-dinitrophenylhydrazine and acidic zeolite in hexane/methanol was recently reported.¹¹ In continuation of our recent report¹³ on the protection of carbonyl compounds using Dowex polymer as a heterogenic catalyst, herein we report a smooth and facile conversion of carbonyl compounds to phenylhydrazones, 2,4-dinitrophenyl-hydrazones, semicarbazones, and thiosemi-carbazones in the presence of basic alumina as a catalyst under solvent-free conditions.

Results and Discussion

In this simple and efficient method the starting carbonyl compounds were converted to the corresponding hydrazone derivatives and semicarbazones in the presence of basic alumina under solvent-free conditions at 80 °C (Scheme).



G: C₆H₅-NH-, 2,4-(NO₂)C₆H₃-NH-, NH₂CONH-, NH₂CSNH-

R₁, R₂: aryl, alkyl, H

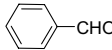
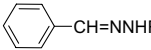
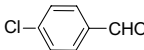
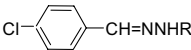
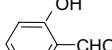
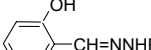

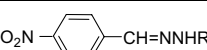
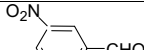
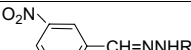
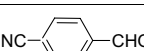
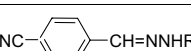
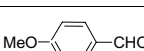
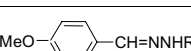
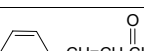
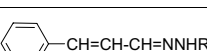

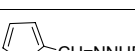

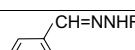
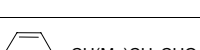
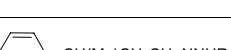
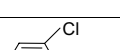
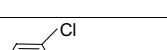

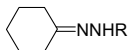
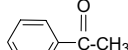
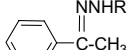
Scheme



The feasibility of the present protection of carbonyl compounds was first examined using benzaldehyde as a model substrate. Thus, benzaldehyde, protecting agent (phenylhydrazine), and 2 g of basic alumina were well mixed in a mortar. Then, they were poured into a round-bottomed glass equipped with a condenser and heated with stirring in an oil bath at 80 °C for 10 min under solvent-free conditions (Table 1, Entry 1). We examined the catalytic ability of basic alumina for the protection of such carbonyl compounds as phenylhydrazones and 2,4-dinitrophenylhydrazones. The catalyst acted very efficiently and it was observed that 2 g of basic alumina was sufficient to convert carbonyl compounds to their corresponding arylhydrazones in excellent yield within 10-15 min. It is worthy to mention that lower quantities of alumina (i.e. 0.5 g) also gave satisfactory results, although with much longer reaction times.

With the first successful result in hand, protection of other aldehydes and ketones with phenyl or aryl hydrazine, and semicarbazide and thiosemicarbazide as protecting agents were carried out under similar reaction conditions. Satisfactory results were obtained in the reaction of a variety of aromatic and aliphatic aldehydes, and ketones with hydrazine derivatives and semicarbazides under solvent-free conditions in the presence of basic alumina as a catalyst (Table 1). However, the results of the hindered aliphatic ketones, like diisopropyl ketone, were unsatisfactory.¹³

Table 2 describes the times and yields of 4 consecutive protections leading to hydrazone derivatives and semicarbazone derivatives. In these experiments the product was isolated by soxhlet extraction of the crude using CH₂Cl₂ as the solvent. Then, the remaining catalyst was reloaded with fresh reactants for

Table 1. Basic alumina catalyzed conversion of carbonyl compounds to corresponding phenylhydrazone derivatives and semicarbazones at 80 °C.^{i,ii,iii}

Entry	Substrate	Product	Time (min.)				Yield (%)			
			a	b	c	d	a	b	c	d
1			5	15	10	10	85	87	77	73
2			10	15	7	8	87	82	70	77
3			10	15	-	-	77	86	-	-
4			6	13	4	5	78	72	84	70
5			-	13	-	-	-	71	-	-
6			7	13	5	5	85	78	70	87
7			10	15	10	10	94	88	78	74
8			8	15	8	7	97	90	81	70
9			5	14	5	5	90	88	75	69
10			-	15	-	-	-	77	-	-
11			-	15	-	-	-	89	-	-
12			-	15	-	-	-	87	-	-
13	CH ₃ CHO	CH ₃ CH=NNHR	-	15	-	-	-	77	-	-
14	CH ₃ (CH ₂) ₂ CHO	CH ₃ (CH ₂) ₂ CH=NNHR	10	15	-	-	65	78	-	-
15			25	25	15	15	54	52	68	58
16			20	30	20	15	52	51	66	54

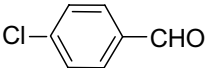
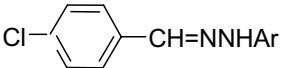
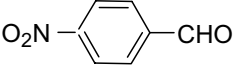
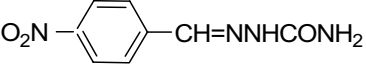
i) a; R =  , b; R =  , c; R = -CONH₂ , d; R = -CSNH₂

ii) Yields refer to isolated products after 24, 36, 12, and 12 h soxhlet extraction with CH₂Cl₂ in the case of a, b, c, and d respectively.

iii) Products were characterized by comparison of their physical data, IR, NMR spectra with known samples.

further runs. No decrease in the yield was observed, demonstrating that basic alumina can be recycled as a catalyst in the protection of carbonyl compounds.

Table 2. The recyclability of basic alumina in the conversion of carbonyl compounds into corresponding 2,4-dinitrophenylhydrazones and semicarbazone at 80 °C.ⁱ

Entry	Substrate	Product	Time (min) [Yield %]
1			15 (82), 18 (79), 20 (75), 25 (70) ⁱⁱ
2			4 (84), 6 (75), 7 (75), 10 (73) ⁱⁱ

i) Aryl is 2,4-dinitrophenyl. ii) The same recycled catalyst was used for each of the four runs.

Acid-sensitive substrates, like furfural and cinnamaldehyde, are also protected as hydrazone derivatives and semicarbazones, and are produced in very good yields (Table 1, entries 8 and 9), without the formation of any side products. It can be emphasized that the reaction is clean, the alumina is recycled without a decrease in efficiency, and that from the economic and environmental points of view the use of alumina is an improvement.

In summary, we have demonstrated an efficient, mild, and easy protection methodology for carbonyl groups using phenylhydrazine, 2,4-dinitrophenyl-hydrazine, semicarbazide, and thiosemicarbazide in the presence of basic alumina as a catalyst under solvent-free conditions. Basic alumina as a catalyst has inherent advantages, including operational simplicity and recyclability.

Experimental

General

Aluminum oxide 90 (active basic for column chromatography, mesh 70-230), aldehydes, and ketones were purchased from Fluka, Aldrich, and Merck, respectively. All products are known compounds and are identified by comparison of their physical and spectral data with those of authentic samples.¹⁴⁻¹⁵ The determination of the purity of the products and reaction monitoring were accomplished by TLC on silica gel polygram SILG/UV 254 plates.

General Procedure for the Preparation of Phenylhydrazones, 2,4-Dinitrophenyl-Hydrazones, Semicarbazones, and Thiosemicarbazones

A mixture of carbonyl compound (1 mmol) with reagent (hydrazine derivatives or semicarbazide derivatives) (1.1 mmol) and basic alumina (2 g) was ground in a mortar. The reaction mixture was then poured into a round-bottomed glass equipped with a condenser and heated with stirring in an oil bath at 80 °C for a specified time (Table 1). The progress of the reaction was monitored by TLC using n-hexane-ethyl acetate. The products were obtained after soxhlet extraction of the crude for 12-36 h using CH₂Cl₂ as the solvent. If

further purification was needed the product was recrystallized from a suitable solvent and afforded the TLC and ¹H-NMR pure products in 51%-89% isolated yields.

References

1. J.D. Metzger, **Angew. Chem., Int. Ed. Engl.** **37**, 2975 (1998).
2. K. Tanaka and F. Tada, **Chem. Rev.** **100**, 1025 (2000).
3. H. Sharghi and M. Hosseini Sarvari, **Tetrahedron** **58**, 10323 (2002).
4. H. Sharghi and M. Hosseini Sarvari, **Synthesis** 1057 (2002).
5. R.M. Pagni, G.W. Kobalka, R. Boothe, K. Gaetano, L.J. Stewart and R. Conaway, **J. Org. Chem.** **53**, 4477 (1998).
6. G.H. Posner, **Angew. Chem., Int. Ed. Engl.** **17**, 487 (1978).
7. A. McKillop and D.W. Young, **Synthesis** 401 (1979).
8. A. Cornelis and P. Laszlo, **Synthesis** 909 (1985).
9. P. Laszlo, **Acc. Chem. Res.** **19**, 121 (1986).
10. A. Cornelis and P. Laszlo, "Chemical Reactions in Organic and Inorganic Constrained Systems", ed. R. Setton, Reider: Dordrecht, p 212, 1986.
11. A. Lalitha, K. Pitchumani and C. Srinivasan, **Green Chemistry** 173 (1999).
12. S.D. Lepore and M.R. Wiley, **Org. Lett.** **5**, 7-10 (2003).
13. K. Niknam, A.R. Kiasat and S. Karimi, **Synth. Commun.** **35**, 2231 (2005).
14. R.L. Shriner and R.C. Fuson, "The Systematic Identification of Organic Compounds", John Wiley & Sons. Inc. 3rd Ed.; p 162-165, 1980.
15. A.R. Hajipour, I. Mohammahpoor-Baltork and M. Bigdeli, **J. Chem. Research (s)** 570-571 (1999).