

[a018]

A Simple and Efficient Method for Quantitative Solvent-Free Synthesis of Phenylhydrazones and 2,4-Dinitrophenylhydrazones

J. Mokhtari,^a M. R. Naimi-Jamal^{*a}, H. Hamzehali^b, Mohammad G. Dekamin^a

^a Organic Chemistry Research Laboratory, College of Chemistry, Iran University of Science and Technology, Tehran 16846, Iran

^b Member of young research club, Islamic Azad University of Saveh, Saveh, Iran

Email address: naimi@iust.ac.ir

Abstract

An effective methodology for the quantitative preparation of phenylhydrazones and 2,4-dinitrophenylhydrazones from aldehydes and ketones is described. The method is environmentally friendly and easy to handle, while requires short reaction times and solventless conditions.

Introduction

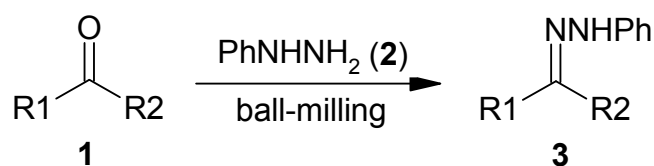
Derivatization of carbonyl compounds as phenylhydrazones, 2, 4-dinitrophenylhydrazones, etc. is of great interest to organic chemists. This is not only because the products are readily prepared and highly stable, but also they serve for protection, purification, and characterization of carbonyls, as well as for functional group transformations. The most common method for the preparation of hydrazone derivatives is the reaction of aldehydes or ketones with hydrazone derivatives in the presence of a basic or an acidic catalyst.^{1,2} Some modification of these methods are also known.^{3,4}

Ball milling is a mechanochemical technique, which is widely applied to the grinding of minerals into fine particles and the preparation and modification of inorganic solids.⁵ Its use in synthetic organic chemistry is relatively scarce, but attains more importance during the past decade. Kaupp et al. have discovered the usefulness of Ball-milling in synthetical organic chemistry, which have been the subject of some papers and reviews.⁶ Some recent examples include solvent-free Knoevenagel condensation,^{7a} protection of diols and diamines,^{7b} functionalization of fullerenes,^{7c} reductive benzylation of malononitrile,^{7d} preparation of phosphorus ylides,^{7e} and Heck-type cross-coupling reactions^{7f}.

In continuation of our earlier works on the application of ball-milling in organic synthesis, we now wish to report a facile, environmentally friendly and clean synthesis of phenylhydrazones, and 2,4-dinitrophenylhydrazones from carbonyl compounds in a ball-mill.

Results and Discussion

Solvent-free reaction of 1 eq of an aldehyde or a ketone (**1**) and 1 eq of phenylhydrazine in a ball-mill proceeds just as a one-step condensation to afford the corresponding phenylhydrazone (**3**) in 100% yield (Scheme 1).



Scheme 1 Ball-milling solvent-free preparation of phenylhydrazones

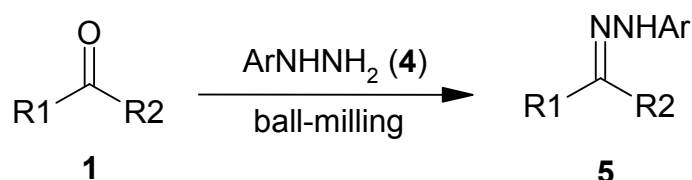
Various phenylhydrazones have been prepared by milling of the corresponding carbonyls (**1a-q**) with phenylhydrazine (**2**) at the suitable temperature for the given time (Table 1). Not only no acidic or basic catalyst, but also no excess phenylhydrazine is required. The method is superior, as it produces in most cases 100% yield products with no waste, or any need of further purification. Mps and spectral data of the crude reaction products correlate well with the literature values.

As it is shown in Table 1, Ketones (**1m-1q**) generally require higher temperatures than aldehydes. For example, acetophenone (**1n**) and benzil (**1q**) reacts quantitatively to their corresponding phenylhydrazone at 65-70 °C and 85-90 °C, respectively. Some ketones like anthraquinone (**1r**), benzophenone (**1s**) or 4-fluorobenzophenone (**1t**) remain unreacted, even at elevated temperatures. This is probably due to steric hindrance in these ketones

Table 1 Condensation of aldehydes and ketones with phenylhydrazine (**2**) giving phenylhydrazones (**3**) under solvent-free conditions

Entry	Carbonyl	Mp (Lit.) (°C)	Temp. (°C)	Time (min.)	Yield (%)
1	R1=H, R2= <i>p</i> -OHPH (1a)	174-176 (178)	r.t	10	100
2	R1=H, R2= <i>p</i> -ClPh (1b)	124-126 (127)	r.t	10	100
3	R1=H, R2= <i>p</i> -BrPh (1c)	112-114 (113)	r.t	10	100
4	R1=H, R2= <i>p</i> -CNPh (1d)	149-150	r.t	10	100
5	R1=H, R2= <i>o</i> -NO ₂ Ph (1e)	154-156 (156)	r.t	10	100
6	R1=H, R2= <i>m</i> -NO ₂ Ph (1f)	120-122 (121)	r.t	10	100
7	R1=H, R2= <i>p</i> -NO ₂ Ph (1g)	156-158 (159)	r.t	10	100
8	R1=H, R2= <i>p</i> -MePh (1h)	90-92	r.t	10	100
9	R1=H, R2= <i>p</i> -N(Me) ₂ Ph (1i)	142-144 (148)	r.t	10	100
10	R1=H, R2= <i>o</i> -OMePh (1j)	86-88 (88-90)	r.t	10	100
11	R1=H, R2= <i>p</i> -OMePh (1k)	128-130 (132)	45-50	10	100
12	R1=H, R2=(Me) ₂ CH (1l)	oil	r.t	10	100
13	R1=Me, R2= <i>o</i> -NO ₂ Ph (1m)	oil	90-95	60	72
14	R1=Me, R2= Ph (1n)	100-102 (105)	65-70	15	100
15	R1=Me, R2= <i>p</i> -NO ₂ Ph (1o)	132-134 (132)	65-70	30	100
16	R1=Me, R2= CH ₃ (CH ₂) ₄ (1p)	204-206 (207)	65-70	15	100
17	benzil(1q)	234-236 (235)	85-90	30	100
18	Anthraquinone (1r)	-	50-96	60	N.R
19	Benzophenone (1s)	-	45-96	60	N.R
20	4-Fluorobenzophenone (1t)	-	45-96	60	N.R

Not only phenylhydrazones, but also 2,4-dinitrophenylhydrazones were prepared in a similar procedure using the ball-mill (Scheme 2). For example, *p*-chlorobenzaldehyd-2,4-dinitrophenylhydrazone (**5b**) was prepared by 10 min ball-milling of a mixture of 1 eq of *p*-chlorobenzaldehyd (**1b**) and 1 eq of 2,4-dinitrophenylhydrazine (**4**) at 60-70 °C.



Ar: 2,4-dinitrophenyl

Scheme 2 Ball-milling solvent-free preparation of 2,4-dinitrophenylhydrazones

Table 2 Condensation of aldehydes and ketones with 2,4-dinitrophenylhydrazine (**4**) giving 2,4-dinitrophenylhydrazones(**5**) under solvent free conditions

Entry	Carbonyl	Mp (Lit.) (°C)	Temp. (°C)	Time (min.)	Yield (%)
1	1a	278-280 (280)	60-70	10	100
2	1b	260-262 (265)	60-70	10	100
3	1c	242-244	60-70	10	100
4	1d	280	60-70	10	100
5	1e	260-262 (265)	60-70	20	100
6	1f	289-290 (292)	60-70	20	100
7	1g	316-318 (320)	60-70	20	100
8	1h	198-200	60-70	10	100
9	1i	320-322 (325)	60-70	10	100
10	1j	248-250 (253)	60-70	10	100
11	1k	250-252 (254)	60-70	10	100
12	1l	182-184 (187)	60-70	10	100
13	1m	-	85-90	60	81
14	1n	246-248 (250)	80-85	40	100
15	1o	-	85	60	58
16	1p	90-92 (89)	75-80	15	100
17	1q	-	96	60	68
18	1r	-	45-96	60	79
19	1s	-	45-96	60	-
20	1t	-	45-96	60	-

Generally, the reaction of carbonyls (**1a-t**) with **4** at room temperature does not yield the corresponding 2,4-dinitrophenylhydrazones quantitatively, but raising the reaction temperature completed the reaction, often in few minutes (Table 2).

Experimental

All the products were identified by comparison of their spectral data and/or melting point with those reported in literatures.⁸⁻¹¹

General procedure for the preparation of phenylhydrazones and 2,4-dinitrophenylhydrazones

A clean and dry ball-milling vessel equipped with 2 stainless steel balls was filled with 1 mmol of an aldehyde or a ketone and 1 mmol of phenyl- or 2,4-dinitrophenylhydrazine. The vessel was closed and the milling started at the given temperature in Table 1 or 2, at a speed of 40 Hz. After 10 min, the

progress of the reaction was tested by TLC. This milling cycle was repeated, if necessary, until the reaction was complete. Further purification was recrystallization from 96% ethanol, if necessary.

Conclusion

Phenylhydrazone and 2,4-dinitrophenylhydrazone derivatives of aldehydes and ketones were prepared in a solventless method using a ball-mill. The procedure is very simple, efficient and environmentally friendly as it does not use any auxiliary or solvent.

Acknowledgements

We acknowledge Iran University of Science and Technology (IUST) for partial financial support of this work.

References

1. H. C. Yoa and P. Resnick, *J. Org. Chem.* **1965**, *30*, 2832.
2. R. Fusco and F. Sannicolo, *J. Org. Chem.* **1981**, *46*, 90.
3. T. Iida and F. C. Chang, *J. Org. Chem.* **1981**, *46*, 2786.
4. R. O. Hutchins, C. A. Milewski and B. E. Maryanoj, *J. Am. Chem. Soc.* **1949**, *71*, 2804.
5. (a) G. Kaupp, M. R. Naimi-Jamal, H. Ren and H. Zoz in *Advanced Technologies Based on Self-Propogating and Mechanochemical Reactions for Environmental Protection* (Eds.: G. Cao, F. Delogu, R. OrrJ), Research Signpost, Kerala, **2003**, pp. 83 – 100; (b) H. Ren, H. Zoz, G. Kaupp and M. R Naimi-Jamal, *Advances in Powder Metallurgy & Particulate Materials* **2003**, 216-222; (c) H. Zoz; G. Kaupp; H. Ren; K. Goepel; M. R. Naimi-Jamal, *Metall* **2000**, *59*, 293-296; (d) A. Bakhshai, R. Pragani And L. Takacs, *Metallurgical and materials transactions A*, **2002**, *33A*, 3521.
6. (a) G. Kaupp, *CrystEngComm*, **2003**, *5(23)*, 117–133; (b) M. R. Naimi-Jamal and G. Kaupp, *Mansura journal of Chemistry*, **2005**, *32(1)*, 83-106; (c) G. Kaupp, J. Schmeyers, M. R. Naimi-Jamal, H. Zoz and H. Ren, *Chem. Engin. Sci.* **2002**, *57*, 763-765; (d) G. Kaupp, M. R. Naimi-Jamal, H. Ren and H. Zoz, *Chemie Techni.* **2002**, *31(6)*, 58-60; (e) G. Kaupp; M. R. Naimi-Jamal; H. Ren and H. Zoz, *Process Worldwide* **2003**, *6(4)*, 24-27; (f) H. Zoz, G. Kaupp, H. Ren, K. Goepel, M.R. Naimi-Jamal, *Metall.* **2005**, *59 (5)*, 293-296; (g) E. Abdel-Latif, G. Kaupp, M.A. Metwally, *J. Chem. Res. (s)* **2005**, *3*, 187-189.
7. (a) G. Kaupp, M. R. Naimi-Jamal and J. Schmeyers, *Tetrahedron.* **2003**, *59*, 3753-3760; (b) G. Kaupp, M. R. Naimi-Jamal and V. Stepanenko, *Chem. Eur. J.* **2003**, *9*, 4156 – 4160; (c) K. Komatsu, *Top. Curr. Chem.* **2005**, *254*, 185 – 206; (d) Zhang, J. Gao, J.-J. Xia and G.-W. Wang, *Org. Biomol. Chem.* **2005**, *3*, 1617 – 1619; (e) V. P. Balema, J. W. Wiench, M. Pruski and V. K. Pecharsky, *J. Am. Chem. Soc.* **2002**, *124*, 6244 – 6245; (f) E. Tullberg, F. Schacher, D. Peters and T. Frejd, *Synthesis.* **2006**, 1183 – 1189
8. (a) R. Shriner, R. C. Fuson, D. Y. Curtin and T. C. Morrill, *The Identification of Organic Compounds*, John Wiley and Sons, New York, **1980**, pp. 558-560; (b) G. R. Newkome and D. L. Fishel, *J. Org. Chem.* **1966**, *31*, 677.
9. A. R. Hajipour and N. Mahboubghah, *Synth. Commun.* **1998**, *28*, 3143.
10. A. R. Hajipour and N. Mahboubghah, *Org. Prep. Proc. Int.* **1999**, *31*, 112.
11. Arthur Vogel in *Textbook of Practical Organic Chemistry*, (Eds.: B. S. Furniss, A. J. Hannaford, V. Rogers, P. W. G. Smith, A. R. Tatchell), Longman, London, **1986**.