

A Convenient and Mild Procedure for the Synthesis of Hydrazones and Semicarbazones from Aldehydes or Ketones under Solvent-free Conditions†

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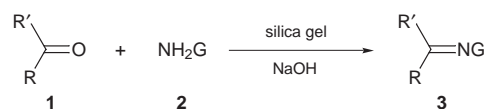
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Hydrazone and semicarbazone derivatives are readily prepared from the corresponding aldehydes or ketones, hydrazine derivatives and semicarbazides under solvent-free conditions.

Highly crystalline hydrazone and semicarbazone derivatives constitute a very efficient method for the isolation, purification and characterization of aldehydes and ketones. The most common method for the preparation of hydrazone and semicarbazone derivatives is the reaction of aldehydes or ketones with hydrazone derivatives and semicarbazides in the presence of base or acid as catalyst.^{1,2} Other methods for the preparation of hydrazone and semicarbazone derivatives are also known.^{3,4}

Heterogeneous reactions that are facilitated by supported reagents on various solid inorganic surfaces have received attention in recent years.^{5–7} The advantage of these methods over conventional homogeneous reactions is that they provide greater selectivity, enhanced reaction rates, cleaner products and manipulative simplicity. In continuation of our ongoing program to develop environmentally benign methods using solid supports,^{8–12} we now report an extremely convenient one-step synthesis of hydrazone and semicarbazone derivatives **3** from the corresponding aldehydes and ketones **1** under solid-phase conditions (Scheme 1). The process in its entirety involves a simple mixing of aldehydes and ketones **1** and supported hydrazine derivatives and semicarbazides **2** on silica gel in a mortar in the presence of sodium hydroxide. The mixture was then



- a R = R' = Ph, G = PhNH
 b R = Me, R' = Ph, G = PhNH
 c R = Me, R' = 3,4-(MeO)₂C₆H₃, G = PhNH
 d R = Me, R' = 4-PhC₆H₄, G = PhNH
 e R = Ph, R' = 2-pyridyl, G = PhNH
 f R = Me, R' = 4-pyridyl, G = PhNH
 g R = Me, R' = 4-MeOC₆H₄, G = PhNH
 h R = Me, R' = 2-MeOC₆H₄, G = PhNH
 i R = R' = Ph, G = *p*-NO₂C₆H₄NH
 j R = H, R' = 4-MeOC₆H₄, G = *p*-NO₂C₆H₄NH
 k R = Me, R' = 4-ClC₆H₄, G = *p*-NO₂C₆H₄NH
 l R = Me, R' = 4-PhC₆H₄, G = *p*-NO₂C₆H₄NH
 m R = R' = Ph, G = NMe₂
 n R = Me, R' = Ph, G = NMe₂
 o R = Me, R' = 3,4-(MeO)₂C₆H₃, G = NMe₂
 p R = Me, R' = 4-MeOC₆H₄, G = NMe₂
 q R = H, R' = Ph, G = NH₂CONH
 r R = Me, R' = Ph, G = NH₂CONH
 s R = Me, R' = 4-MeOC₆H₄, G = NH₂CONH
 t R = Me, R' = 3,4-(MeO)₂C₆H₃, G = NH₂CONH

Scheme 1

Table 1 Synthesis of hydrazones and semicarbazones **3** from aldehydes and ketones **1**

Starting material	Product ^a	Reaction time/min	Yield ^b (%)	Mp/°C or bp/°C/Torr (lit. ¹³)
1a	3a	10	92	134–136 (137)
1b	3b	1	95	104–106 (105)
1c	3c	10	95	138–140 (—)
1d	3d	3	94	161–163 (—)
1e	3e	10	94	131–133 (—)
1f	3f	10	93	135–137 (—)
1g	3g	7	95	143 (—)
1h	3h	8	94	135–137 (—)
1i	3i	8	92	154–156 (157)
1j	3j	10	90	160–162 (161)
1k	3k	10	95	237–239 (239)
1l	3l	10	94	203–205 (—)
1m	3m	8	96	110–112/0.7 (101–103/0.3)
1n	3n	8	98	72–75/0.6 (55–56/0.15)
1o	3o	10	100	121–124/0.8 (—)
1p	3p	5	95	40–42 (41–42)
1q	3q	10	97	197–199 (199)
1r	3r	10	92	165–167 (165)
1s	3s	5	95	199–201 (—)
1t	3t	10	80	210–213 (—)

^aIdentity confirmed by comparison with authentic samples (IR, TLC and NMR).^{13–15} ^bYield of isolated pure product.

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ground for the time specified in Table 1 at room temperature. The yields of the reactions are excellent (80–100%) and the reaction times are exceedingly short (1–10 min). To the best of our knowledge, this technique

is completely novel and has not been reported in the literature. Compounds **3** were characterized by ¹H NMR, IR spectra and their mps.

The importance of silica gel in the reaction was demonstrated by reacting benzaldehyde with phenylhydrazine in the presence of sodium hydroxide but in the absence of silica gel. Benzaldehyde was converted to the corresponding hydrazone to an extent of < 20% after > 1 h of reaction.

In conclusion, to the best of our knowledge, this is the first example for silica gel catalysis of this reaction. The reported method is an interesting, easy and novel method for the preparation of hydrazone and semicarbazone derivatives. These reactions are fast, the procedure is simple and of low cost, and it is possible to work under mild conditions.

Experimental

All yields refer to isolated products after purification. All the products were identified by spectroscopy data (IR, NMR) and mp.¹³⁻¹⁵ All mps were taken on a Gallenkamp melting apparatus and are uncorrected. ¹H NMR spectra were recorded on a Varian EM-390 NMR Spectrometer operating at 90 MHz. The spectra were measured in CDCl₃ unless otherwise stated, relative to TMS (δ 0.00).

General Procedure.—A mortar was charged with the aldehyde or ketone (1 mmol), hydrazine derivative or semicarbazide (1 mmol), sodium hydroxide (0.04 g, 1 mmol) and silica gel (0.1 g). The reaction mixture was ground with a pestle in the mortar for the time specified in Table I. When TLC showed no remaining aldehyde or ketone, the reaction mixture was poured into a mixture of dichloromethane (20 ml) and 5% HCl (10 ml). The ethereal layer was washed with saturated NaHCO₃, dried (MgSO₄), and evaporated by rotary evaporation to give the pure product.

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