

NOTE

Synthesis of Semicarbazones from Carbonyl Compounds under Solvent Free Conditions

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A convenient and mild procedure for the synthesis of semicarbazone derivatives from the corresponding aldehydes or ketones under solvent-free conditions has been reported. The reaction is clean and work-up is very simple.

Key Words: Synthesis, Semicarbazones, Solvent free conditions.

The protection of carbonyl groups plays an important role in organic, medicinal, carbohydrate and drug design chemistry. Tremendous effort has been made to search for a suitable protective group for carbonyl compounds¹. Highly crystalline 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 semicarbazone derivatives is the reaction of aldehydes or ketones with semicarbazide hydrochloride in the presence of base or acid as catalyst²⁻⁵.

Heterogeneous reactions that are facilitated by supported reagents on various solid inorganic surfaces have received attention in recent years⁶. As the surfaces have properties that are not duplicated in the solution or gas phase, a surface reaction may be more desirable than a solution counterpart, because the reaction is more convenient to run, or a high yield of product is attained, and these reactions provide greater selectivity, enhanced reaction rates, cleaner products, and manipulative simplicity. In the case of semicarbazone's preparation, there is an interesting report using silica gel/NaOH system⁷. In continuation of our ongoing program to develop environmentally benign methods using solid supports⁸⁻¹⁰, we report an extremely convenient synthesis of semicarbazone derivatives **3** from the corresponding aldehydes and ketones under solvent-free conditions (**Scheme-1**) has been reported.

All products are known compounds and are identified by comparison of their physical and spectral data with those of authentic samples¹¹. The purity determination of the products and reaction monitoring were accomplished by TLC on silica gel polygram SILG/UV 254 plates.

General procedure for the preparation of semicarbazones

A mortar was charged with the aldehyde or ketone (1 mmol), semicarbazide hydrochloride (1.5 mmol), sodium acetate (1.5 mmol) and silica gel (0.5 g). The reaction mixture was ground with a pestle in a mortar for the time specified in Table-1. When TLC showed no remaining aldehyde or ketone, the reaction mixture was poured into CH₃OH (20 mL). The solid was filtered off and the solvent

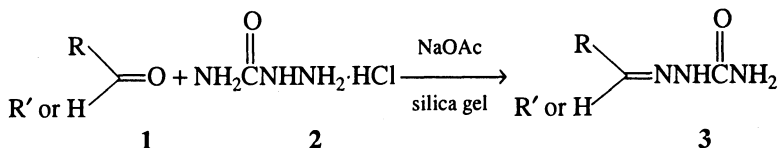
evaporated under reduced pressure to give the product which was recrystallized from a suitable solvent and afford the TLC and ^1H NMR pure products in 66–95% isolated yields.

TABLE-I
PROTECTION OF CARBONYL COMPOUNDS AS SEMICARBAZONES^{a, b}

Compd. No.	Substrate	Product	Time (min)	Yield (%)
1			2	77
2			2	88
3			2	70
4			2	72
5			3	95
6			3	68
7			3	75
8			3	74
9			3	74
10			2	66

(a) Yields refer to pure isolated products. (b) Products were characterized by comparison of their physical data, IR, NMR spectra with known samples.

This process involves a simple mixing of aldehydes and ketones **1** and supported semicarbazide hydrochloride **2** on silica gel in a mortar in the presence of sodium acetate.



Scheme 1

The mixture was then ground for the time specified in Table-1 at room temperature. The yields of the reactions are very good (66–95%) and the reaction times are exceedingly short (2–3 min). It should be noted that for rapid and clean conversion of carbonyl compound to semicarbazone derivatives, addition of a few drops of water and *t*-BuOH in the reaction media is essential. The optimum molar ratio of the substrate to the reagent is found to be 1 : 1.5. The reaction remains incomplete when lower amounts of the reagent are used or if the reaction was performed in the absence of silica gel.

In conclusion, an efficient, mild and novel protection methodology of carbonyl groups using semicarbazide hydrochloride in the presence of silica gel under solvent free conditions has been reported. Reaction of benzaldehyde with semicarbazide hydrochloride in the presence of sodium acetate without silica gel showed a low yield of product and long reaction time. Also, the necessity of sodium acetate as a base was examined and emphasized.

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