

Facile and Mild Deprotection of Semicarbazones Under Solvent-Free Conditions with *N,N,N',N'*-Tetrabromo-benzene-1,3-disulfonylamide

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N,N,N',N'-tetrabromobenzeno-1,3-disulfonylamida [TBBDA] reagiu com semicarbazonas e estas foram convertidas aos seus correspondentes compostos carbonilicos, com excelente rendimento, na ausência de solvente.

N,N,N',N'-tetrabromo-benzene-1,3-disulfonylamide [TBBDA] was reacted with semicarbazones and converts them to their corresponding carbonyl compounds in excellent yields under solvent-free conditions.

Keywords: deprotection, semicarbazones, solvent-free, TBBDA

Introduction

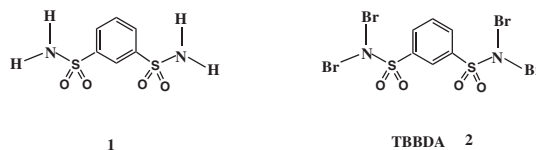
Regeneration of carbonyl compounds from semicarbazones is an important reaction and has assumed added importance not least because such derivatives of carbonyl compounds can serve as protecting groups for aldehydes and ketones in organic synthesis.¹⁻¹³ Extensive studies on the deprotection of these derivatives have been carried out using various catalysts.^{1,2,6,7,14-17} Most of the reported procedures used for this purpose involve hydrolysis under acidic and frequently stringent conditions^{5,18} or oxidation.^{3,6} These methods invariably require reflux conditions,^{1,5,6,8} longer reaction times,^{7,8} toxic metal ions¹⁷ as catalysts which are detrimental to the environment. There has therefore been considerable interest in the development of novel techniques for the conversion of semicarbazones back into carbonyl compounds, which work under mild conditions.

In recent years, the organic reactions on solid supports¹⁹⁻²⁷ and under solventless conditions,²⁸⁻³³ have attracted attention because of their enhanced selectivity, milder reaction conditions and associated ease of manipulation.

Results and Discussion

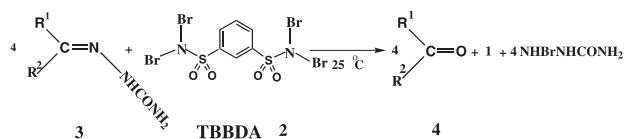
Herein, we now report a convenient method for rapid regeneration of carbonyl compounds from their

semicarbazones using a new reagent [TBBDA] (**2**)³⁴ in high yields under mild and solvent-free conditions (Scheme 1).



Scheme 1.

The reaction of semicarbazones **3** with TBBDA under solvent-free conditions afforded carbonyl compounds **4** without the formation of side products (Scheme 2).



Scheme 2.

The results of the conversion of various semicarbazones are presented in Table 1.

The products of the reaction with TBBDA were isolated simply by filtering off and evaporating the solvent from the filtrate. This solvent-free deprotection methodology of semicarbazones is superior to conventional deprotection methodology using a solvent. The most remarkable advantage to this methodology is that no trace of acid was formed owing to over oxidation of regenerated aldehyde. The recovered starting material **1** was brominated and used many times without any reduction in this efficiency.

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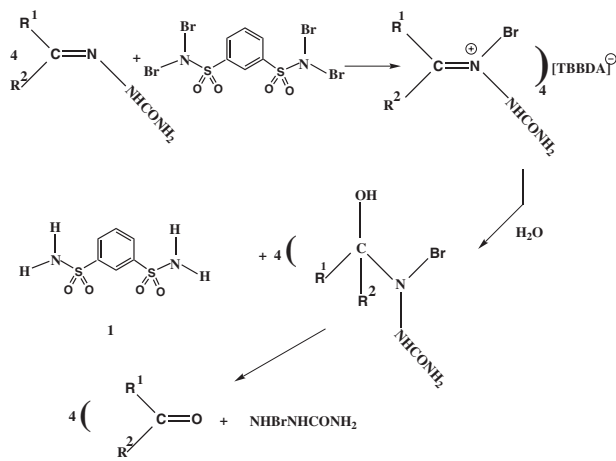
Table 1. Regeneration of carbonyl compounds from semicarbazones with TBBDA

Entry	Semicarbazone	time (min)	^a Yield (%)
1	Acetophenone	3	90
2	4-Chloroacetophenone	3	85
3	4-Bromoacetophenone	3	88
4	4- (Dimethylamino)benzaldehyde	4	98
5	2-Acethylnaphthalene	5	92
6	Crotonaldehyde	3	94
7	Benzaldehyde	3	87
8	4-Methoxybenzophenone	4	98
9	Benzophenone	3	97
10	4-Methoxybenzaldehyde	3	96

^aProducts were characterized by their physical properties, comparison with authentic samples and by spectroscopic methods.

Since TBBDA contain four bromine atoms which are attached to nitrogen atoms it is very possible that this reagent releases Br⁺ in situ which can act as an electrophilic species. An evidence for this claim has been reported in our previous work³⁵ in which Br⁺ was generated in situ from

N,N'-dibromo-*N,N'*-1,2-ethanediylobis(*p*-toluenesulphonamide). Therefore, the following mechanism can be suggested for the conversion semicarbazones to their corresponding carbonyl compounds (Scheme 3).

**Scheme 3.**

In conclusion, the method has advantage in terms of yield, simplicity of reaction conditions, short reaction times, solvent-free conditions and no side products.

IR and NMR spectra were recorded using a Shimadzu 435-U-04 spectrophotometer (KBr pellets) and a 90 MHz Jeol FT-NMR spectrometer, respectively.

Experimental

Procedure for preparation of benzene-1,3-disulfonylamide

To benzene-1,3-disulfonyl acid sodium salt (0.016

mol) was added PCl_5 (0.0165 mol), as chlorination agent. For starting reaction, the vessel should be heated (40-50 °C), then reaction complete spontaneously. After complete conversion (2 h), ice-crushed (100 g) was added, the product was separated from inorganic materials by chloroform. Then to the solution was added NH_3 (l) (400 mL), the reaction mixture was stirred with mechanical stirrer. After complete addition, removal solvent under reduced pressure gave the crude product. The pure product (90%, mp 228-230 °C) was obtained by crystallization with ethanol. IR spectrum (KBr pellets) $\nu_{\text{max}}/\text{cm}^{-1}$: 3320, 3090, 1600, 1320, 1130. ¹H NMR (acetone-*d*⁶): δ 6.7 (s, 4H), 7.7 (t, 1H), 8.1 (d, 2H), 8.3 (s, 1H). ¹³C NMR: 124.2, 130.6, 129.8, 124.2.

Procedure for preparation of *N,N,N',N'*-tetrabromo-benzene-1,3-disulfonylamide [TBBDA]

Benzene-1,3-disulfonylamide (0.003 mol) was dissolved in a slight molar excess of chilled sodium hydroxide solution (3 mol L⁻¹) at room temperature and transferred the solution to a beaker. Then bromine (0.0584 mol) was added to the solution with vigorous stirring (at -10 °C) and immediately precipitate was formed. The product was collected on a buchner funnel and it was washed with 30 mL distilled cold water and then dried in a vacuum desicator at room temperature for 6 h. The yield of pure TBBDA, mp 267-270d °C, was 90%. The reagent was identified by NMR, IR spectroscopies. IR spectrum (KBr pellets) $\nu_{\text{max}}/\text{cm}^{-1}$: 3070, 1620, 1310, 1130. ¹H NMR (acetone-*d*⁶): δ 7.9 (t, 1H), 8 (d, 2H), 8.3 (s, 1H). ¹³C NMR spectrum (acetone): δ 123.4, 128.7, 127.9, 122.3.

Typical procedure for deprotection of semicarbazones

Benzophenone semicarbazone (0.5 g, 0.56 mmol), *N,N,N',N'*-tetrabromo-benzene-1,3-disulfonylamide (0.5 g, 1.3 mmol) and a few drops of water were added to mortar and the mixture was pulverized vigorously with a pestle. A spontaneous reaction took place [3-5 min., Table 1, monitored by TLC (9:1, carbon tetrachloride/acetone)]. After completion of the reaction, CH_2Cl_2 (15 mL) was added, and the insoluble sulfonamide **1** was removed by filtration. The organic phase was washed with Na_2CO_3 solution (10 mL, 5%), H_2O (10 mL) and dried (MgSO_4). After removal of the solvent under vacuum gave product in excellent yield (97%).

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