Carbonyl Regeneration from Semicarbazones, Tosylhydrazones, Phenylhydrazones, and 2,4-Dinitrophenylhydrazones by Clay-Supported Ferric Nitrate

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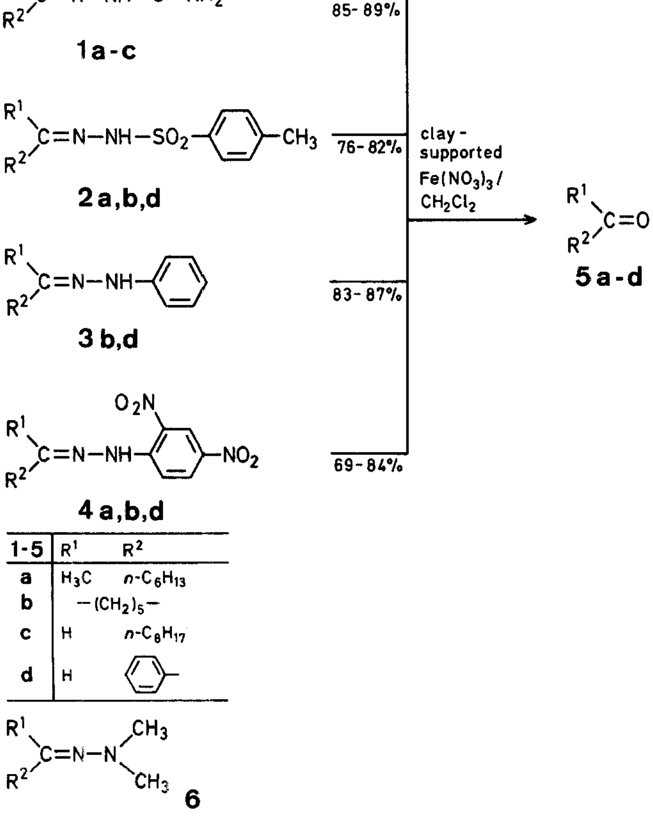
Semicarbazones **1**, tosylhydrazones **2**, phenylhydrazones **3**, and 2,4-dinitrophenylhydrazones **4** serve as important synthetic intermediates[1] and are also extensively used for purification and characterization of carbonyl-containing molecules and to protect the ketone and the aldehyde functions[2]. Most of the published methods for regeneration of carbonyl functions from such nitrogen derivatives[3-6] require strongly oxidative or reducing conditions, basic or acidic media, and involve tedious procedures or expensive reagents.



We recently reported[7] that the extremely inexpensive clay-supported ferric nitrate ("clayfen")[8] cleanly cleaves *N,N*-dimethylhydrazones **6** under extremely mild conditions, with good yields. We are now able to report that this method has been extended to semicarbazones **1**, tosylhydrazones **2**, phenylhydrazones **3**, and to 2,4-dinitrophenylhydrazones **4** (Table 1).

In contrast, treatment of the title derivatives of α,β-unsaturated ketones does not result in satisfactory regeneration of the parent carbonyl compounds **5**, but leads to a mixture of products. Similar problems with other reagents such as sodium nitrite in glacial acetic acid[3], *N*-bromosuccinimide in methanol[4], and thallium(III) nitrate[5]

Table 1. Regeneration of Carbonyl Compounds **5** from Semicarbazones **1**, Tosylhydrazones **2**, Phenylhydrazones **3**, and 2,4-Dinitrophenylhydrazones **4**

Nitrogen No.	Derivative n.p. [°C] (Lit., m.p. [°C])	Carbonyl Compound[a,b]	Yield [%]
1a	122–122.6° (123°)[9]	**5a**	87
1b	166.5–167° (167°)[9]	**5b**	85
1c	99–100° (100°)[9]	**5c**[c]	89
2a	96–97.5° (98°)[4]	**5a**	82
2b	148–150° (152–153°)[10]	**5b**	76
2d	126–127° (127°)[10]	**5d**	79
3b	74–75° (77°)[9]	**5b**	87
3d	156–158° (158°)[9]	**5d**	83
4a	55–57.5° (58°)[9]	**5a**	84
4b	160–161° (162°)[9]	**5b**	78
4d	233–235° (236°)[9]	**5d**	69

[a] Purity: ≧ 98% by G.L.C.

[b] The melting points of the 2,4-dinitrophenylhydrazones of the products **5** were in agreement with those of substrates **4**.

[c] m.p. of 2,4-dinitrophenylhydrazone: 100 °C (Ref.[9], m.p. 100 °C).

Table 2. Control Experiments[a] with Nitrogen Derivatives of 2-Octanone **(5a)**

Nitrogen Derivative	Oxidizing Agent (amount)	Conversion to Ketone **5a** [%]
1a	K-10 clay-supported $Fe(NO_3)_3$ (6.0 g)	100
	K-10 clay alone (3.5 g)	20
	K-10 clay/$FeCl_3 \cdot 6H_2O$ (3.5 g/1.8 g)[b]	20
	$FeCl_3 \cdot 6H_2O$ (1.8 g)	0
	K-10-$Fe^{3\oplus}$ (3.5 g)[c]	25
2a	K-10 clay-supported $Fe(NO_3)_3$ (6.0 g)	100
	K-10 clay alone (3.5 g)	15
4a	K-10 clay-supported $(Fe(NO_3)_3$ (6.0 g)	100
	K-10 clay alone (3.5 g)	5

[a] Under the same conditions as decribed in the experimental section.

[b] Prepared by grinding $FeCl_3 \cdot 6H_2O$ (1.8 g) and K-10 montmorillonite clay (3.5 g) together; the yellow powder thus obtained is used immediately.

[c] The K-10 montmorillonite is exchanged with $Fe^{3\oplus}$ ions according to published procedures; see, e.g., Ref.[13].

have been reported. Our control experiments, summarized in Table 2, clearly demonstrate the crucial role of the association between the K 10 clay and ferric nitrate. For carbonyl-containing compounds of the types **5a–d**, "clayfen" effects easy and clean deprotection and will serve as an inexpensive alternative to the existing methods.

Warning: *Whereas these procedures worked out very safely in our hands, nitrates are dangerous compounds, and appropriate caution is to be applied in each step. In particular, we urge to avoid confinement conditions, and to proceed to significant scaling-up only after appropriate safety tests.*

The starting semicarbazones **1**, tosylhydrazones **2**, phenylhydrazones [3], and 2,4-dinitrophenylhydrazones **4** are prepared from the corresponding carbonyl compounds by the usual methods[4,9]. Melting points are uncorrected and are determined with a Mel-Temp apparatus. I.R. spectra are recorded with a Perkin-Elmer spectrophotometer Model 1320 and ^{1}H-N.M.R. spectra with a Varian 60 MHz spectrometer. T.L.C. analysis is performed on Polygram SilG/UV$_{254}$ plates eluted with dichloromethane or hexane/ethyl acetate solution (6 : 4 or 8 : 2) and visualized with U.V. light or phosphomolybdic acid reagent. G.L.C. analysis is performed on an Intersmat Chromatograph IGC 121 with on OV 1701 capillary column. Carbonyl compounds **5** were generally characterized as their 2,4-dinitrophenylhydrazones[9]. The purity of the isolated compounds were checked by comparison of I.R. and ^{1}H-N.M.R. spectra, T.L.C. and G.L.C. analyses with those of authentic samples.

Regeneration of Carbonyl Compounds 5 from Semicarbazones 1; General Procedure:

To an efficiently stirred solution of the semicarbazone **1** (5 mmol) in dichloromethane (50–100 ml) at room temperature is added freshly prepared "clayfen" reagent[8] (3 g, 3.3 mmol of ferric nitrate). The solution quickly turns red and after 20–30 min the colour of the solution fades. Stirring is continued, if necessary (T.L.C. monitoring), until the disappearance of the semicarbazone **1** (approximately 30–40 min). The mixture is filtered on sintered glass, and the solid residue is washed with dichloromethane (3 × 25 ml). To the colorless filtrate, 10 % sodium hydroxide solution (50 ml) is added[11], the mixture is shaken for a few minutes, and the two layers are separated. The organic phase is washed with water (2 × 50 ml) and dried with magnesium sulfate. Evaporation of the solvent yields the colorless, pure carbonyl compound **5**. Sometimes, if the obtained product is colored, it is purified by filtration through a column of neutral alumina using dichloromethane as eluent.

Regeneration of Carbonyl Compounds 5 from Tosylhydrazones 2, Phenylhydrazones 3, or 2,4-Dinitrophenylhydrazones 4; General Procedure:

The tosylhydrazone **2** (10 mmol), phenylhydrazone **3**, or 2,4-dinitrophenylhydrazone **4** (5 mmol) is dissolved in dichloromethane (50 ml) and freshly prepared "clayfen" reagent[8] (6 g, 6.6 mmol of ferric nitrate or 3 g, 3.3 mmol of ferric nitrate, respectively) is added portionwise. The mixture is stirred at reflux temperature until the reaction is complete (for tosylhydrazones 2–3 h, for phenylhydrazones 3–5 h, and for 2,4-dinitrophenylhydrazones 15–20 h) as monitored by T.L.C. After cooling, the solution is filtered on sintered glass and the solid residue is washed with dichloromethane (3 × 25 ml). The organic phase is washed with water, dried with magnesium sulfate, and evaporated under reduced pressure. The residue is chromatographed[4,6] on a column of silica gel using dichloromethane or hexane/ethyl acetate mixture (6 : 4 or 8 : 2) as eluent yielding the pure[12] carbonyl compound **5**. The isolated products were identified by comparison with authentic samples and with the respective 2,4-dinitrophenylhydrazone derivatives **4** prepared by standard methods[9].

This work was made possible by generous support from Programmation de la Politique Scientifique, Brussels (Action Concertée 82–87/34).

Received: October 15, 1984

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