

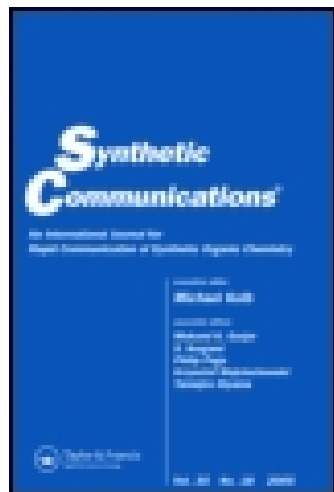
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### Selective Protection of Carbonyl Compounds as Azines and Their Facile Regeneration

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## Selective Protection of Carbonyl Compounds as Azines and Their Facile Regeneration

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**Abstract:** Carbonyl compounds with freshly prepared hydrazinium formate successfully yielded the corresponding azines in excellent yields. In turn, azines were deprotected to the corresponding carbonyls using triethylammonium chlorochromate chemoselectively.

**Keywords:** Carbonyl compounds, protection, hydrazinium formate, azines, deprotection

### INTRODUCTION

Carbonyl compounds occupy a central position in organic syntheses. The selective protection of the carbonyl group and its subsequent regeneration is an important transformation in synthetic organic chemistry. On the other hand, azines have generated attention because of their ability to be used in a variety of chemical reactions, such as 1,3-dipolar cycloadditions with dienophiles and 3 + 2 cycloadditions<sup>[1]</sup> in the construction of five-membered rings, which parallels the Diels–Alder reaction in construction of six-membered rings.

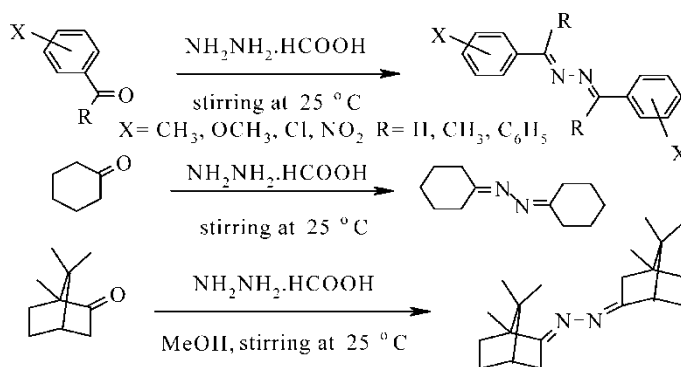
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Methods have been developed for the preparation of these compounds under various conditions,<sup>[2]</sup> but none of them are simple and most require elevated temperature, complex catalysts, and unstable starting materials. Hussein et al. have reported the synthesis of azines under microwave irradiation but the chemistry community fails to obtain gram-scale preparation.<sup>[3]</sup> In this communication, we show that hydrazinium formate is an efficient reagent for the generation of azines without any catalyst, without solvent if the substrate is liquid or with a minimum amount of methanol to dissolve the solid substrates as shown in Scheme 1. The results of the experiments are summarized in Table 1.

An effort was made to get unsymmetrical azines by performing the reaction with 1 equiv of hydrazinium formate in combination with different aldehydes and ketones, but recovered symmetrical aldazines left the ketones unaffected, which proves the selectivity and exclusive conversion of aldehydes despite the presence of ketones. The reaction has been found to be sensitive to the electronic and steric effects of the substituents. The electron-donating (inductive and mesomeric) groups seem to enhance the extent of reaction period whereas electron-withdrawing groups facilitate it in less than 50 s. Carbonyl compounds generally display strong absorption bands in the region between 1690 and 1750  $\text{cm}^{-1}$  of the IR spectra, due to  $\text{C}=\text{O}$ . This cannot be observed in the products that showed the strong absorption band between 1610 and 1650  $\text{cm}^{-1}$ , due to the  $\text{C}=\text{N}$  group, which clearly indicates the conversion of carbonyl compounds to azines. This trend is noticed in all the azines prepared by our procedure.

Although many methods have been developed for the oxidative cleavage of oximes, hydrazones, and semicarbazones to the corresponding carbonyl compounds, little attention has been paid to the cleavage of the carbon–nitrogen double bonds of azines. After successfully generating very stable azines, we have succeeded to develop a method for the facile regeneration



Scheme 1.

**Table 1.** Rapid generation of azines from carbonyl compounds with stirring at 25°C

Entry	R	X	Time (S)	Yield <sup>a</sup> (%)	Mp °C	
					Found	Reported
1	H	H	30	98	93	93 <sup>[4]</sup>
2	H	3-NO <sub>2</sub>	30	98	196–198	196–197 <sup>[5]</sup>
3	H	4-NO <sub>2</sub>	30	98	300–303	297–298 <sup>[5]</sup>
4	H	4-Cl	30	98	208–210	207 <sup>[2b]</sup>
5	H	4-CH <sub>3</sub>	50	98	154–155	153 <sup>[4]</sup>
6	H	4-OMe	50	98	177–179	179–180 <sup>[5]</sup>
7	H	4-OH	50	98	266–269	268 <sup>[5]</sup>
8	H	3,4-OMe	50	97	192–193	193 <sup>[2b]</sup>
9	CH <sub>3</sub>	H	180	97	121–122	121–122 <sup>[4]</sup>
10	CH <sub>3</sub>	4-OH	240	97	222–224	222–223 <sup>[6]</sup>
11	Ph	Ph	300	97	161–162	164 <sup>[4]</sup>
12	Cyclohexanone		40	98	35	36 <sup>[2b]</sup>
13	Camphor		300	97	185–186	185–186 <sup>[3]</sup>
14	Cinnamaldehyde		50	98	161–162	162 <sup>[5]</sup>
15	Furfuraldehyde		50	97	110–112	110–111.5 <sup>[5]</sup>

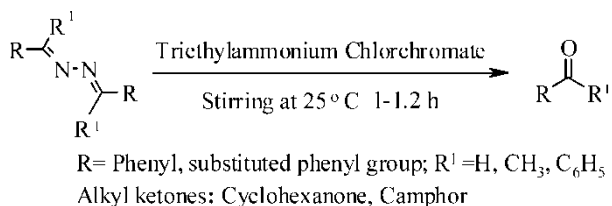
*Notes:* CAUTION: Hydrazine hydrate is toxic and corrosive in nature handle carefully. Products were characterized by the comparison with TLC, melting point, IR, and NMR spectra of authentic samples.

<sup>a</sup>Isolated yields.

of carbonyls using triethylammonium chlorochromate as shown in Scheme 2, and the results are summarized in Table 2.

## EXPERIMENTAL

Melting points were obtained with Büchi B-540 apparatus. Gas chromatography (GC) analyses were performed on a Shimadzu GC-MS QP 5050A instrument. IR and <sup>1</sup>H NMR spectra were recorded on Nicolet 400D FT-IR and Bruker 400-MHz spectrometer respectively. Elemental analysis was performed on Thermo Finnigan Flash EA 1112 CHNS analyzer.



**Scheme 2.**

**Table 2.** Regeneration of carbonyl compounds from azines by triethylammonium chlorochromate with stirring at 25°C

Entry	Substrate	Product <sup>a</sup>	Time (h)	Yield (%)
1	Benzalazine	Benzaldehyde	1	88
2	3,3'-Dinitrobenzalazine	3-Nitrobenzaldehyde	1	82
3	4,4'-Dinitrobenzalazine	4-Nitrobenzaldehyde	1	86
4	4,4'-Dichlorobenzalazine	4-Chlorobenzaldehyde	1	84
5	4,4'-Dimethylbenzalazine	4-Methylbenzaldehyde	1	85
6	4,4'-Dimethoxybenzalazine	4-Methoxybenzaldehyde	1	86
7	4,4'-Dihydrobenzalazine	4-Hydroxybenzaldehyde	1	82
8	3,3', 4,4'-Methoxybenzalazine	3,4-Dimethoxybenzaldehyde	1	83
9	Acetophenone azine	Acetophenone	1.2	89
10	4,4'-Dihydroxyacetophenone azine	4-Hydroxyacetophenone	1.2	79
11	Benzophenone azine	Benzophenone	1.2	86
12	Cyclohexanone azine	Cyclohexanone	1	88
13	Camphor azine	Camphor	1.2	78
14	Cinnammaldazine	Cinnamaldehyde	1	85
15	Furfuraldazine	Furfuraldehyde	1	82

<sup>a</sup>Products were characterized by their physical constants, comparison with authentic samples, and IR and NMR spectroscopy.

### Typical Procedure for the Rapid Preparation of Benzalazine

Hydrazinium monoformate was prepared by carefully neutralizing equal quantities of hydrazine hydrate (99–100%) and formic acid (85%) below 0°C, with constant stirring. To this neutral solution (15 mL) in a 500-mL round-bottomed flask, 0.1 mol of benzaldehyde (10.6 g) was added while stirring at 25°C. An exothermic reaction affords the yellow solid in 30 s, which was filtered and recrystallized from ethanol to get 10.2 g of benzalazine crystals (~98%).

### Typical Experimental Procedure for the Regeneration of 3-Nitrobenzaldehyde from 3,3'-Dinitrobenzalazine

3,3'-Dinitrobenzalazine (1.49 g, 5 mmol) is added to a rapidly stirred solution of triethylammonium chlorochromate (4 g) in dichloroethane (20 mL). The resultant dark mixture is stirred for 1 h, and the reaction mixture quenched by ether (25 mL) and filtered through a bed of celite. Removal of solvent and silica-gel chromatography gave 3-nitrobenzaldehyde (1.23 g, 82%), mp: 42–43°C. IR (KBr): 3050 (m), 2950 (m), 2760 (m), 1685 (s), 1610 (m), 1570 (m), 1360 (m), 828 (m), 760 (m)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\delta$ ): 9.7 (s, 2H), 8.0–8.4 (m, 8H). MS ( $m/z$ ): 151 ( $\text{M}^+$ ).

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