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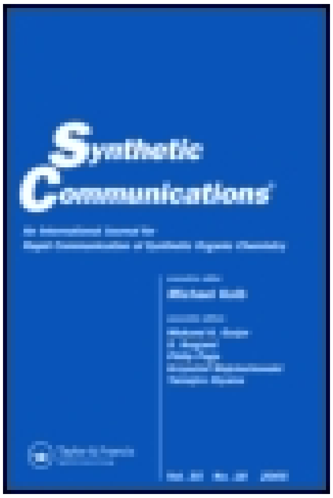

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Rapid, Chemoselective and Facile Synthesis of Azines by Hydrazine/I_2

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Rapid, Chemoselective and Facile Synthesis of Azines by Hydrazine/I_2

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Abstract: We report the reaction of hydrazine hydrate with carbonyl compounds in the presence of molecular iodine at 0–10°C, which affords symmetrical azines in excellent yields in 1 to 4 min without any adverse effect on other substituents. The reactions are rapid and chemoselective, afford excellent yields, and have high-purity products. The workup procedure is environmentally benign and does not require solvent extraction.

Keywords: azines, carbonyl compounds, hydrazine hydrate, iodine

INTRODUCTION

In continuation of our research program on effective utilization of hydrazine and its derivatives for organic transformations, recently we reported hydrazinium formate as an efficient reagent for the generation of azines,[1a] which are versatile intermediates in the construction of many heterocycles and in a variety of chemical reactions.[1b] We also have been engaged in the search for simple, nonhazardous methods for organic transformations using iodine and reported some important and efficient transformations.[2]

We found that hydrazine hydrate in the presence of iodine is an exceedingly efficient system for the rapid generation of azines at 0–10°C as shown in

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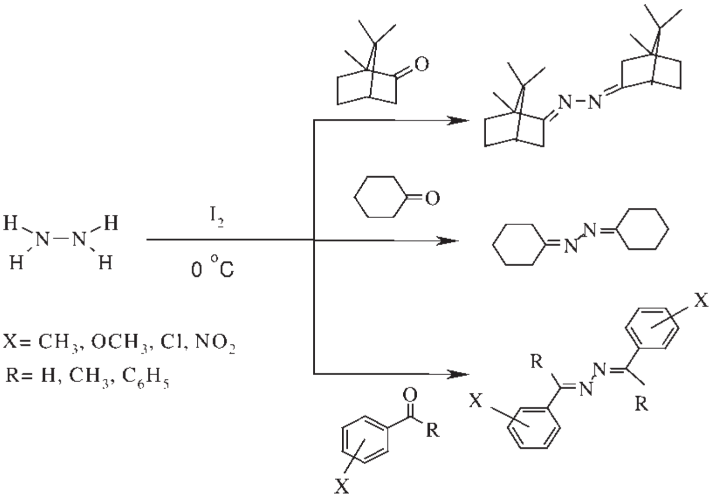

Scheme 1.

Table 1. Rapid generation of azines from carbonyl compounds by hydrazine hydrate/I_2

Entry	R	X	Time (min)	Yield[a] (%)	Mp (°C)	
					Found	Reported
1	H	H	1	98	92–93	93[3a]
2	H	3-NO_2	1	98	197–199	196–197[3b]
3	H	4-NO_2	1	98	299–302	297–298[3b]
4	H	4-Cl	1	97	207–209	207[3c]
5	H	4-CH_3	1.5	98	152–153	153[3a]
6	H	4-OMe	1.5	97	179–181	179–180[3b]
7	H	4-OH	1.5	96	265–268	268[3d]
8	H	3,4-OMe	1.5	96	192–193	193[3c]
9	CH_3	H	3.5	97	120–121	121–122[3a]
10	CH_3	4-OH	2	96	222–224	222–223[3d]
11	Ph	Ph	2	95	163–165	164[3a]
12	Cyclohexanone		0.5	97	36	36[3c]
13	Camphor		2	92	186–187	185–186[3e]
14	Cinnammaldehyde		1	96	161–162	162[3b]
15	Furfuraldehyde		1	93	111–112	110–111.5[3b]

Notes: Products were characterized by the comparison of TLC of melting point, IR, and NMR spectra with those of authentic samples.

[a] Isolated yields.

CAUTION: Hydrazine hydrate is toxic and corrosive in nature, and the reaction of hydrazine with iodine is very vigorous. Handle carefully.

Scheme 1, and the results of the experiments are summarized in Table 1. There was no adverse effect on many other substituents such as nitro, methyl, methoxy, hydroxy, halogens, which proves the selectivity and exclusive conversion of both aliphatic and aromatic carbonyls to the corresponding symmetrical azines. The reactions have been carried out without solvent in the case of liquid carbonyls; a solution of solid substrates dissolved in a minimum amount of either THF or methanol can be employed. The reaction has been found to be sensitive to the electronic and steric effects of the substituents. The electron-donating (inductive and mesomeric) groups enhance the extent of reaction period, whereas electron-withdrawing groups facilitate the reactions for the complete conversion in less than 2 min. Carbonyl compounds generally display strong absorption bands in the region between 1690 and 1750 cm^{-1} of the IR spectra due to C=O, which cannot be observed in the products that showed the strong absorption band between 1610 and 1650 cm^{-1} due to the C=N group. This clearly indicates the conversion of carbonyl compounds to azines. This trend is noticed in all the azines prepared by our procedure.

EXPERIMENTAL

Melting points were obtained with a Büchi B-540 apparatus. GC analyses were performed on a Shimadzu GC-MS QP 5050A instrument. IR and ^{1}H NMR spectra were recorded on Nicolet 400D FT-IR and Bruker 400-MHz spectrometers respectively.

CONCLUSION

In summary, we have developed a new methodology for the rapid generation of symmetrical azines, which are useful compounds in organic synthesis whose derivatives have been reported to possess a broad spectrum of biological activity in excellent yields from carbonyls by hydrazine/I_2. The workup procedure is environmentally benign, which does not involve solvent extraction, as the separated solid can be filtered and recrystallized to get the pure product.

Typical Procedure for the Rapid Generation of Benzalazine from Benzaldehyde

Iodine (equal moles) in small portions was added to hydrazine hydrate in a round-bottomed flask at 0°C carefully with constant stirring. Benzaldehyde (10.6 g, 0.1 mol) was added to this mixture (0.1 mol) in a 100-mL round-bottomed flask while stirring at 0–10°C. The yellow solid separated within a minute, was filtered, and was recrystallized from ethanol to give 10.3 g of benzalazine crystals (98%).

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