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A Mild and Convenient Synthetic Method for Arylhydrazones of Methyl Benzoate

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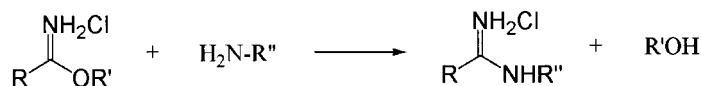
ABSTRACT

A series of ester arylhydrazones were prepared by treating methyl benzimidate hydrochloride with arylhydrazine hydrochlorides. Treatment of benzimidate hydrochloride with a mixture of arylhydrazine hydrochlorides and sodium methoxide in absolute methanol at room temperature produced the arylhydrazones of methyl benzoate with moderate yield.

Key Words: Arylhydrazine hydrochloride; Methyl benzimidate hydrochloride; Arylhydrazones of methyl benzoate.

Ester arylhydrazones can be used as intermediates in the syntheses of heterocyclic compounds. Two methods to synthesize ester arylhydrazones

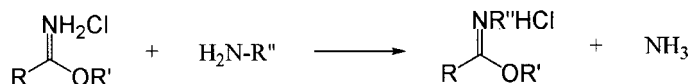
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Scheme 1.

have been explored in the literature: substitution reactions of orthoesters and arylhydrazines, and the reactions of imidates with arylhydrazines. The former method has been extensively investigated.^[1] The hydrochlorides of 2-nitro-, 4-nitro-, and 2,4-dinitrophenylhydrazine react with orthoesters to produce arylhydrazones of the ethyl esters of the corresponding carboxylic acids in yield of 31–86%.^[1] The latter method, however, has not been extensively investigated. Imidates are susceptible to nucleophilic attack by amino compounds. The usual pathway involves the loss of alcohol from an imidate and the formation of an amidine (Sch. 1). For example, it was reported previously that acyl hydrazines reacted with imidates to yield N¹-acylamidrazones.^[2,3] Alternatively, the loss of ammonia and its replacement by a nucleophile may also occur (Sch. 2). Ester formylhydrazones were obtained from the reaction of alkyl imidate hydrochlorides with formylhydrazines.^[4] As to ester arylhydrazones, only one compound of this type has been prepared by the reaction of phenylhydrazine and an imino ester.^[5] Generally, arylhydrazines react with imino esters to yield N-arylamidrazones due to the decreased activity of the aryl nitrogen of the hydrazine.^[6,7] In this paper, we systematically investigated the reactivity of several arylhydrazine hydrochlorides in their reaction with methyl benzimidate hydrochloride. 3-Nitro-, 4-nitro-, 2-chloro-, 3-chloro-, 4-chloro-, 3-bromo-, 4-bromo-, and 4-methoxyphenylhydrazine hydrochloride reacted with methyl benzimidate hydrochloride to produce arylhydrazones of methyl benzoate in moderate yield (Table 1). The reaction was performed by adding one equivalent of methyl benzimidate hydrochloride to the mixture of one equivalent of an arylhydrazine hydrochloride and one equivalent of sodium methoxide in absolute methanol with stirring at room temperature (Sch. 3). In addition, benzimidates can be obtained easily from their corresponding nitriles.^[8]

In conclusion, a convenient and easy method for the preparation of arylhydrazones of benzoates under mild conditions has been established.



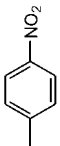
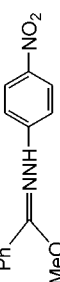
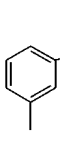
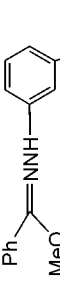
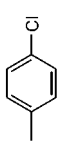

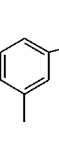
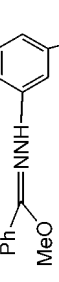
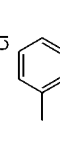
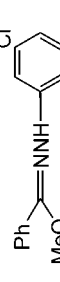
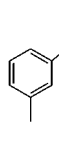

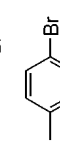
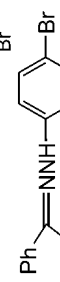
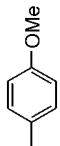
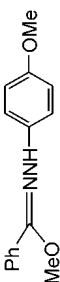
Scheme 2.



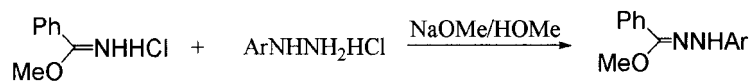
Synthetic Method for Arylhydrazones

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Table 1. Reaction of methyl benzimidate hydrochloride with arylhydrazine hydrochloride.

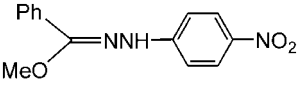
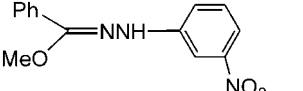
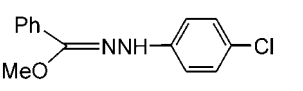
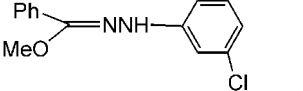
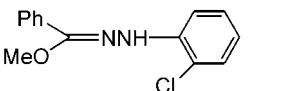
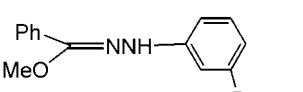
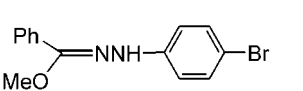
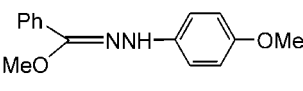
Entry	Ar	Product	Yield (%)	M.p. (°C)	R_f^a	Elemental analysis (%) ^b		
						C	H	N
1			87	174–176	0.25	61.68 (61.98)	4.46 (4.83)	15.15 (15.49)
2			84	132–134	0.44	61.69 (61.98)	4.60 (4.83)	15.11 (15.49)
3			65	semisolid	0.53	64.12 (64.45)	4.60 (4.99)	10.35 (10.74)
4			58	78–80	0.58	64.31 (64.45)	4.65 (4.99)	10.42 (10.74)
5			64	Oil	0.86	64.38 (64.45)	4.67 (4.99)	10.46 (10.74)
6			62	84–86	0.58	55.14 (55.10)	4.15 (4.29)	8.95 (9.18)
7			60	58–59	0.71	55.04 (55.10)	4.21 (4.29)	8.85 (9.18)
8			55	62–65	0.33	69.99 (70.29)	5.99 (6.29)	10.73 (10.93)

^aThe R_f values were obtained using a mixture of petroleum ether and dichloromethane with a volume ratio of 2 : 1.^bData in the brackets were calculated results.



Scheme 3.

Table 2. IR and NMR data for the products listed in Table 1.

Product	IR (cm ⁻¹)		H ¹ -NMR	
	NH	C=N	Ar-H	CH ₃
	3310	1600	7.13–8.19 (m,9H)	3.90 (s,3H)
	3344	1621	7.39–8.08 (m,9H)	3.87 (s,3H)
	3300	1610	7.05–7.70 (m,9H)	3.92 (s,3H)
	3320	1590	6.90–7.80 (m,9H)	3.80 (s,3H)
	3368	1595	6.80–7.70 (m,9H)	3.90 (s,3H)
	3270	1605	6.95–7.58 (m,9H)	3.80 (s,3H)
	3290	1605	7.00–7.58 (m,9H)	3.82 (s,3H)
	3200	1620	6.83–8.07 (m,9H)	3.94,3.83 (2s,6H)



REACTION PROCEDURE

Equimolar amounts of arylhydrazine hydrochloride and sodium methoxide in absolute methanol were first mixed in a round bottom flask. Then, an equimolar amount of methyl benzimidate was added. The resulting mixture was stirred at room temperature. The reaction was monitored by TLC. After the reaction reached completion, the solvent was removed under diminished pressure. The residue was dissolved in dichloromethane, washed with water several times, and dried over anhydrous Na_2SO_4 . Dichloromethane was then evaporated under reduced pressure. The crude products were further purified by column chromatography on silica gel ($-239 + 400$ mesh, S.A. $500-600 \text{ m}^2/\text{g}$) with varying proportions of petroleum ether and dichloromethane (15:1 to 5:1). The purified products were analyzed by CHN elemental analysis (Table 1), NMR (Table 2), and IR (Table 2). The R_f values and melting points of these products were determined (Table 1). In addition, the purified products derived from Entry 6 and Entry 8 were analyzed by MS analysis, giving the m/z : 305 ($\text{M}^+ + \text{H}$) and 257 ($\text{M}^+ + \text{H}$), respectively.

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