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Synthesis of 1-Methylthio-2-nitrovinyl Arylamine Derivatives

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ABSTRACT

The reaction of 1,1-*bis*(methylthio)-2-nitroethylene with various aromatic amines produces 1-methylthio-2-nitrovinyl arylamines derivatives in excellent yields. The reactions occur in ethanol as solvent and avoiding the addition of any catalyst. The workup procedure is very simple and the products do not require further purification.

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KEYWORDS

1,1-*Bis*(methylthio)-2-nitroethylene, Aromatic amines, 1-Methylthio-2-nitrovinyl arylamine, Nitroethylene derivatives.

INTRODUCTION

Nitroethylene derivatives especially conjugated nitroethylene are fundamental intermediate in chemical synthesis [1-3]. These compounds are widely used in synthesis pharmaceuticals such as anticancer, antitumor, antiepileptic, antiulcer and antibiotic, particularly blockbuster drugs [4,5]. Several compounds having a nitroethene unit in their structures claimed to have insecticidal, pesticide and antifungal properties [6-8].

Nitroethylene derivatives keen to undergo various condensation reactions intramolecular-cyclizations involving nitrile oxides (INOC reactions), radical additions and nucleophilic additions especially Michael reaction [9-14].

A potential synthon for the preparation of nitroethylene derivatives is 1,1-*bis*(methylthio)-2-nitroethene [15]. Reaction of this compound with primary amine, diamine, benzylamine and *para*-substituted benzylamine are already reported [16-18]. In present paper we investigate reaction of 1,1-*bis*(methylthio)-2-nitroethene with aromatic amines to synthesize derivatives of 1-methylthio-2-nitrovinyl arylamine.

EXPERIMENTAL

All starting materials were commercially available and used without further purification. Electrothermal 9100 was used to take melting points of the products. The progress of the reactions was monitored by thin layer chromatography (TLC).

General procedure: 1,1-*Bis* (methylthio)-2-nitroethene (1 mmol) and the aromatic amine (1 mmol) were heated together

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in refluxing absolute ethanol (10 mL) and the reaction followed by thin-layer chromatography. The reaction was completed after 6 h. The solid product was isolated by simple filtration and dried.

Detection method: The solid products **3a-3g** were fully characterized by ^{1}H NMR and ^{13}C NMR spectra using Avance 300 MHz in $CDCl_3$ as a solvent and chemical shift values are recorded in units δ (ppm) relative to tetramethylsilane (Me4Si) as an internal standard.

Selective data for the compounds are given below:

Compound 3a: ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.378 (s, 3H, SCH_3), 6.698 (s, 1H, CH), 7.308-7.434 (m, 5H, Ar), 7.283-7.434 (s, 1H, NH). ^{13}C NMR ($CDCl_3$, δ ppm): 14.72 (SCH_3), 107.83 (CH), 126.05, 128.23, 129.47, 136.22 (aromatic carbons), 163.56 (-NH-C=).

Compound 3b: ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.359 (s, 3H, SCH_3), 3.836 (s, 3H, OCH_3), 6.676 (s, 1H, CH), 6.915-6.945 (d, 2H, 2CH), 7.188-7.217 (d, 2H, 2CH), 7.259 (s, 1H, NH). ^{13}C NMR ($CDCl_3$, δ ppm): 14.64 (SCH_3), 55.53 (OCH_3), 107.41(CH), 114.57, 127.74, 128.84,159.45 (aromatic carbons), 164.52 (-NH-C=).

Compound 3c: ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.365 (s, 3H, SCH_3), 2.384 (s, 3H, CH_3), 6.685 (s, 1H, CH), 7.153-1.181 (d, 2H, 2CH), 7.213-7.214 (d, 2H, 2CH), 7.258 (s, 1H, NH). ^{13}C NMR ($CDCl_3$, δ ppm): 14.69 (SCH_3), 21.16 (CH_3), 107.61 (CH), 125. 97, 130.05, 133.58, 138.46 (aromatic carbons), 163.87 (-NH-C=).

Compound 3d: ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.389 (s, 3H, SCH_3), 6.681 (s, 1H, CH), 7.170-7.198 (d, 2H, 2CH), 7.539-7.567 (d, 2H, 2CH), 7.258 (s, 1H, NH). ^{13}C NMR ($CDCl_3$, δ ppm):14.74 (SCH_3), 107.23 (CH), 126.40, 129.96, 133.69, 134.74 (aromatic carbons), 162.13 (-NH-C=).

Compound 3e: ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.386 (s, 3H, SCH_3), 6.680 (s, 1H, CH); 7.229-7.257 (d, 2H, 2CH), 7.384-7.414 (d, 2H, 2CH), 7.257 (s, 1H, NH). ^{13}C NMR ($CDCl_3$, δ ppm): 14.72 (SCH_3), 108.23 (CH), 127.40, 129.66, 133.99, 134.76 (aromatic carbons), 163.14 (-NH-C=).

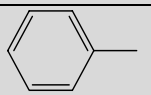
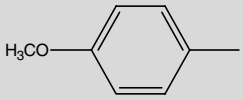
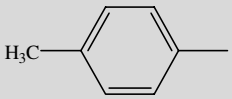
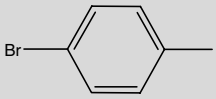
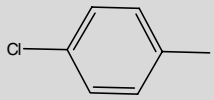
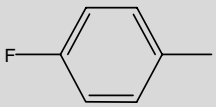
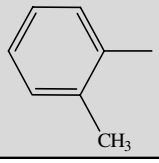
Compound 3f: ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.387 (s, 3H, SCH_3), 6.681 (s, 1H, CH), 7.229-7.258 (d, 2H, 2CH), 7.385-7.414 (d, 2H, 2CH), 7.257 (s, 1H, NH). ^{13}C NMR ($CDCl_3$, δ ppm): 14.74 (SCH_3), 108.24 (CH), 127.42, 129.64, 133.97, 134.78 (aromatic carbons), 163.13 (-NH-C=).

Compound 3g: ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.291 (s, 3H, SCH_3), 2.348 (s, 3H, CH_3), 6.700 (s, 1H, CH), 7.239-7.293 (m, 4H, 4CH), 7.239-7.293 (m, 1H, NH). ^{13}C NMR ($CDCl_3$, δ ppm): 15.13 (SCH_3), 17.58 (CH_3), 107.40 (CH), 125.11, 126.83, 128.99, 131.23, 135.18 (aromatic carbons), 164.63 (-NH-C=).

RESULTS AND DISCUSSION

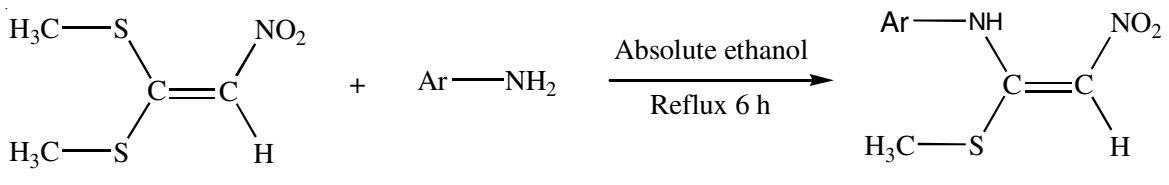
The reactions of 1,1-*bis*(methylthio)-2-nitroethene with various aromatic amines in refluxing absolute ethanol afforded the corresponding 1-methylthio-2-nitrovinyl arylamine **3a-g** (**Scheme-I**) in excellent yields. The results are given in Table-1.

TABLE-1
YIELDS AND MELTING POINTS OF PRODUCTS **3a-3g**

Products	Ar	Yield (%)	m.p. (°C)
3a		96	160-155
3b		98	165-160
3c		97	150-145
3d		98	130-125
3e		96	175-170
3f		96	155-150
3g		95	135-130

Nitroethylene moiety in 1,1-*bis* (methylthio)-2-nitroethene is an electron deficient center. Presence of electron withdrawing nitro group in adjacent of the C=C bond has an activating effect on double bond [19]. As a result, 1,1-*bis*(methylthio)-2-nitroethylene acts as the electrophile in this nucleophilic addition reaction. So in this Michael addition reaction, 1,1-*bis*(methylthio)-2-nitroethene served as a good Michael acceptor and in the reaction with arylamine as a nucleophilic Michael products was obtained.

We found that conjugated addition of 1,1-*bis*(methylthio)-2-nitroethene and arylamines gave only E-isomer of corresponding 1-methylthio-2-nitrovinyl arylamine while two isomers of these products are possible to produce. We explain this result that (E)-isomer configuration allows the formation of an intramolecular hydrogen bonding between the N–H and one



1 **2** **3**

Scheme-I: Reactions of 1,1-*bis* (methylthio)-2-nitroethene with various aromatic amines absolute ethanol

of the oxygen atoms of the planar $–NO_2$ groups. In compare with previous reported nitroethylene derivatives, synthesized products in present work assist conjugated system in their structure.

We observed that the electron and the nature and position of substituents on the aromatic ring did not show strongly effects in terms of yields under the reaction condition. Various arylamines containing electron-donating groups groups (such as methoxy and methyl group) or electronwithdrawing groups (halide) were employed and reacted well to give corresponding 1-methylthio-2-nitrovinyl arylamine derivatives in good to excellent yields.

Conclusion

In summary, in order to develop 1,1-*bis* (methylthio)-2-nitroethene reactions, we investigated the reaction of this more applied compound with aromatic amines. The reaction and workup procedure is very simple and the products do not require further purification.

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