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Synthesis and Characterization of *N,N',N'*-Trichloro-6,7-epoxy-*o*-MeO-cinnamaldehyde Semicarbazone: A Potent Decontaminating Agent for Toxic Compounds

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A series of novel substituted cinnamaldehyde derivatives were designed and successively synthesized in three steps starting from *o*-methoxy-cinnamaldehyde semicarbazone to epoxy and finally to the *N*-chloro derivatives respectively, on the basis of semicarbazone based chemical decontaminants model to meet the structural requirements necessary for decontamination activity. Epoxidation with *t*-BuOOH in alkaline condition and chlorination using calcium hypochlorite were carried out. The structures of the synthesized compounds were confirmed on the basis of IR, Mass, ¹H NMR spectral analysis. The presence of *o*-methoxy moiety in the system might play a significant role in the reactivity of the compound as a whole. It is well known that chloramines possess strong decontamination properties against toxic compounds and warfare agents. A more in-depth biological and chemical evaluation of the synthesized chloramine derivative(s) on toxic compounds of phosphorus and chemical warfare agents under suitable conditions requires a highly sophisticated laboratory.

Keywords: Semicarbazone, Epoxidation, Chloramines, Decontamination, Organophosphates.

INTRODUCTION

Contamination of environment by chemical warfare agents (CWA) can cause serious health hazards. In general, decontamination of toxic chemicals¹ is an important task required to eliminate the hazard of toxic chemicals both in laboratories and field conditions. Decontamination may be performed by mechanical, physical and chemical methods. The chemical decontamination involved either hydrolysis or elimination or oxidation reactions converting toxic substances into non-toxic² products.

Bleaching powder, *i.e.*, calcium hypochlorite or sodium hypochlorite were the first decontaminants employed against chemical warfare agents. The other category of decontaminants is *N*-chloro compounds. They are quite promising but lack stability which hindered their widespread application². Recently, zirconium hydroxide³ has been found to be potential and versatile detoxifying substance against chemical warfare agents GD, HD, VX. In addition, titania materials⁴ such as anatase (TiO₂), nanotubular titania (NTT) and nanocrystalline titania (nTiO₂) were also found to be having promising chemical warfare agents decontamination properties.

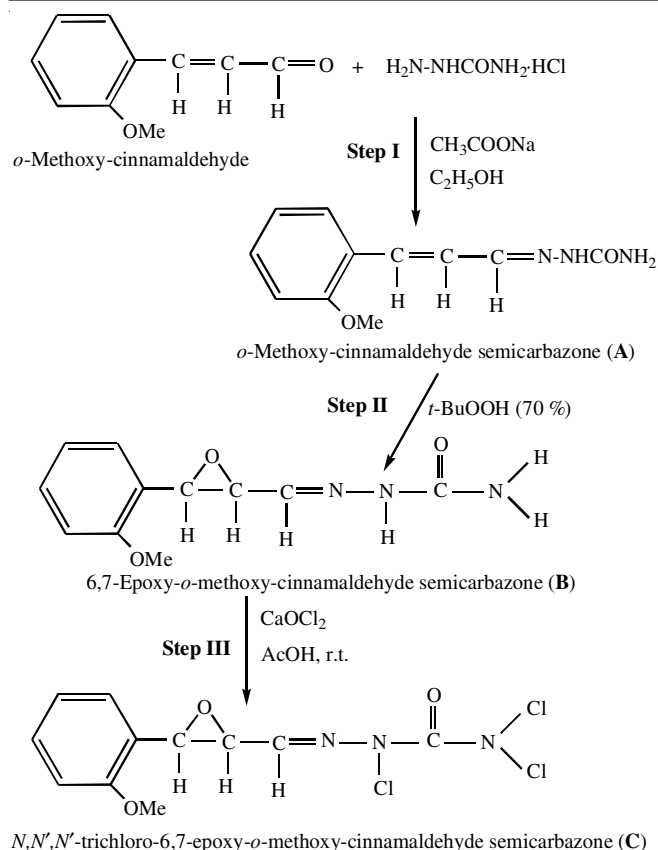
Semicarbazones⁵⁻⁷ act as important synthetic intermediates and have been preferably used for the isolation, purification, characterization⁵ and even protection of both aldehydes and ketones. Epoxidations under acidic conditions were a matter of

discussion for quite sometime because it was assumed that the end products were either α -glycols or their monoacetates when peracetic acid was employed for olefins. *tert*-Butyl hydroperoxide⁸ (TBHP) is considered to be superior to hydrogen peroxide for epoxidations, as it is soluble in hydrocarbon solvents. Calcium hypochlorite is one of the commonly used chlorinating agents⁹ for various chemical compounds. Various organic compounds containing either *N*-chloro groups or epoxide moiety are reported as efficient decontamination agents^{10,11} for chemical warfare agents¹² and various other chemical compounds.

EXPERIMENTAL

During the present study, *o*-methoxy-cinnamaldehyde, one of the important members of α , β -unsaturated aldehyde was chosen as the starting compound and converted into the corresponding *N*-chloro compound *via* the epoxide route, which is expected to be formed as an active decontaminating agent in the following crucial three-step synthesis^{13,14} (**Scheme-I**).

Starting materials, reagents and solvents were of analytical reagent grade or of the highest quality commercially available and were purchased from Sigma-Aldrich and Merck Chemicals and were dried where necessary. The progress of the reaction was monitored by thin layer chromatography with silica gel precoated sheet (Merck) using suitable solvent mixture and



Scheme-I: Stepwise synthesis of *N,N',N''*-trichloro-6,7-epoxy-*o*-methoxy-cinnamaldehyde semicarbazone

iodine vapour were used for detection. IR spectra were recorded, as KBr pallets on a Shimadzu PRESTIGE 21 FT-IR Spectrometer. ^1H NMR spectra, in CDCl_3 solution were recorded on a Bruker Instrument at 298 K. Chemical shifts are reported as ppm relative to TMS as internal standard. Melting points ($^\circ\text{C}$) were determined with an open glass capillary tube and uncorrected.

Stepwise synthetic procedure

Synthesis of *o*-methoxy-cinnamaldehyde semicarbazone (A): *o*-Methoxy-cinnamaldehyde, an α,β -unsaturated aldehyde, was converted¹⁵ into the corresponding semicarbazone derivative using semicarbazide hydrochloride in the presence of sodium acetate in an aqueous-alcoholic medium. The reaction was carried out with uninterrupted stirring for 1.5 h and obtained as the light yellow solid semicarbazone derivative. The same product was also obtained by refluxing method with much lesser time period of about 35 min. In both, the final product was recrystallised with alcohol and recorded a m.p. of 198-199 $^\circ\text{C}$.

Synthesis of 6,7-epoxy-*o*-methoxy-cinnamaldehyde semicarbazone (B): The next step was the epoxidation¹⁶ of the above semicarbazone derivative under neutral condition using TBHP (*tert*-butyl hydroperoxide, 70 %). *o*-Methoxy-cinnamaldehyde semicarbazone was dissolved in methanol and was epoxidized by gradual addition of TBHP maintaining the pH of the solution at pH 6, 7 by the addition of sodium hydroxide solution carefully¹⁷. The reaction mixture was stirred on a magnetic stirrer for 5 h with pH kept constant as above. The

reaction mixture was diluted with excess of distilled water and extracted with ether. Then, the ethereal extract on evaporation gave a yellow solid, the epoxy derivative which has a m.p. of 170-174 $^\circ\text{C}$.

Synthesis of *N,N',N''*-trichloro-6,7-epoxy-*o*-methoxy-cinnamaldehyde semicarbazone (C): 6,7-Epoxy-*o*-methoxy-cinnamaldehyde semicarbazone was dissolved in acetic acid followed by the addition of calcium hypochlorite^{18,19} (maintaining the ratio 1:2) in instalments for 2.5 h. with continuous stirring on a magnetic stirrer. During the process, there was addition of acetic acid in excess so as to maintain the pH of the reaction mixture at 2 throughout the stirring. Later, the reaction mixture was neutralized with sodium hydroxide solution until the pH reached nearly 7. The brown precipitate thus separated out was collected, properly washed with excess water and kept for drying. The final product trichloro-derivative is found to have a m.p. of 158-162 $^\circ\text{C}$.

RESULTS AND DISCUSSION

Identification of compound (A): The mass spectral^{20,21} data of (A) require mention of the following important fragments: m/z 219 (76 %), 188 (100 %), 175 (53 %), 159 (90 %), 145 (40 %), 131 (60 %), 115 (26 %), 108 (32 %), 91 (20 %), 89 (21 %), 77 (29 %), 69 (43 %), 51 (11 %), *etc.* The base peak at 188 (100 %) is formed due to the loss of HNC=O.

The following absorption bands are observed in the IR spectrum²² of *o*-methoxy-cinnamaldehyde semicarbazone: 3307.8 cm^{-1} (N-H), 3069.4 cm^{-1} (Ar-H), 1667.7 cm^{-1} (C=O), 1591.0 cm^{-1} (C=N), 1246.9 cm^{-1} (C-N) and 1024.6 cm^{-1} (C-O).

^1H NMR data^{22,23} of A showed a singlet at δ 3.3 which is due to the presence of -NH proton and also a singlet for -NH₂ protons at δ 7.17. Moreover, two doublets are observed at δ 7.50 and δ 7.65 which may be due to the 6-H and 7-H protons, respectively. Aromatic protons (1, 3, 4, 5-H) appear at δ 6.95 as expected. A triplet is observed at δ 7.27 which may be due to the 8-H proton due to coupling with the neighbouring protons. Also, the signal for the solvent methanol is observed at δ 4.84 as a singlet.

The above spectral studies establish the formation of *o*-methoxy-cinnamaldehyde semicarbazone.

Identification of compound B) Mass spectral^{20,21} data of 6,7-epoxy-*o*-methoxy-cinnamaldehyde semicarbazone shows the following well defined ion peaks, m/z 186 (17 %), 178 (100 %), 174 (20 %), 161 (14 %), 147 (98 %), 131 (38 %), 118 (46 %), 103 (20 %), 91 (68 %), 89 (26 %), 77 (22 %), 63 (21 %) and 51 (16 %) *etc.* The important fragment *i.e.* at 178 (100 %) is probably due to the loss of CO and N₂.

IR spectral²² details of compound B show the following characteristic absorption bands: 3070.0 cm^{-1} (Ar-H), 1074.5 cm^{-1} (R-C-O), 1666.6 cm^{-1} (C=O), 1589.6 cm^{-1} (C=N), 978.3 cm^{-1} (C-N), 3404.6 cm^{-1} (N-H) and 1246.4 cm^{-1} (C-O-C).

All the signals in the NMR region shift upfield *i.e.* appear as shielded protons. The introduction of an oxygen atom at the C=C bond resulting in an epoxy derivative of *o*-methoxy-compound. The aromatic protons (δ 5.4) are now observed at a lower δ value than in case of the semicarbazone form. Similarly, the protons at 6 and 7 carbon atoms have moved to 5.9 and 6.1 ppm values. The typical triplet (8-H *etc.*) has now

appeared at 5.70 ppm rather than 7.27 ppm in the former compound (semicarbazone). N-H proton has been noticed at a lower value of δ 3.025 again.

Identification of compound (C): The IR spectrum²² of *N,N',N'*-trichloro-6,7-epoxy-*o*-methoxy-cinnamaldehyde semicarbazone (C) shows the following characteristic absorption bands as: 3064.5 cm⁻¹ (Ar-H), 3293.2 cm⁻¹ (N-H), 1664.5 cm⁻¹ (C=O), 1594 cm⁻¹ (C=N), 1107.2 cm⁻¹ (C-N), 744.4 cm⁻¹ (N-Cl) and 1243.6 cm⁻¹ (C-O-C).

In the ¹H NMR spectrum²³, the introduction of the halogen atoms at -NH and -NH₂ positions brings about a reversal in the placement of signals at somewhat higher (*i.e.* downfield) ppm than the simple epoxy-carrying product (step II). The most important feature here is that no sign is seen for -NH proton which was earlier, present at 4.56 ppm and 3.025 ppm *i.e.* Steps I and II, respectively. Aromatic protons are observed between 6.94-7.04 ppm. The triplet (8-H) also appears at δ 7.332. This allotment for the triplet needs to be examined in detail by considering other related members of the series. Another observation in this case is that the doublets (6-H and 7-H) coalesce to give rise to a singlet (δ 7.623) and a doublet (δ 7.544-7.568). No clear cut assignment of this nature is found in literature, so that the changes in the trichloro derivative can be attributed to any characteristic proton presence in the above molecule.

The above spectral studies are able to identify and confirm the formation of *N,N',N'*-trichloro -6,7-epoxy-*o*-methoxy-cinnamaldehyde semicarbazone.

Conclusion

In summary, we have developed a series of compounds derived from *o*-methoxy-cinnamaldehyde which may possess significant and selective activity against toxic chemicals. The epoxy derivative²⁴ has been reported as having detoxifying character in special class of organophosphorus compounds.

The synthesized epoxy compound was finally converted into the trichloro-(*N,N',N'*-) compound having chloro-substituents at the -NH and -NH₂ hydrogens. This promising compound (chloramine) is expected to bring about chlorination²⁵ of toxic organic phosphorus compounds leading to the formation of their chloro-derivatives, which may possess a non-toxic character, justifying the role as chemical decontaminant. Such molecules bring about excessive chlorination with limited oxidation due to the presence of epoxy ethereal linkage. The decontaminating properties of the synthesized

compounds need to be investigated experimentally in a well-equipped laboratory so as to prove the above facts.

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