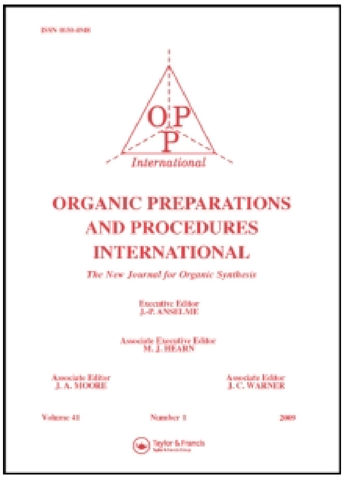

Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

ALTERNATIVE SYNTHESIS OF *N,N'*-DJPHENYLTHIOUREA AND ITS ANALYSIS BY LC-MS

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To cite this Article Xiong, Yu-Chun , Zong, Zhi-Min , Jiang, Fa-Qin , Yuan, Xin-Hua , Wang, Xiao-Hua , Ji, Ya-Fei , Xu, Li , Xiao, Hong-Zhan , He, Lin-Tao , Li, Chun-Qi and Wei, Xian-Yong(2003) 'ALTERNATIVE SYNTHESIS OF *N,N'*-DJPHENYLTHIOUREA AND ITS ANALYSIS BY LC-MS', Organic Preparations and Procedures International, 35: 4, 409 — 411

To link to this Article: DOI: 10.1080/00304940309355849

URL: http://dx.doi.org/10.1080/00304940309355849

ALTERNATIVE SYNTHESIS OF *N,N'*-DIPHENYLTHIOUREA AND ITS ANALYSIS BY LC-MS

Submitted by
(11/15/02)

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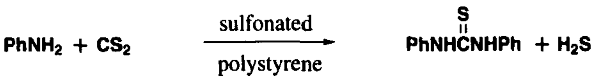
N,N'-Diphenylthiourea (DPTU) has been widely used during the past decades as medicine for leprosy, as a flotation agent to separate ferric sulfide from other metal sulfides, as a ligand to form *N,N'*-diphenylthioureido complexes with some metals such as ruthenium, osmium and iridium,[1] as a curing accelerator for caoutchouc and synthetic rubber (especially for natural latex and neoprene),[2,3] as an extractant for isolating precious metals[4] and as a thermal stabilizer for PVC. It also serves as an intermediate and a starting material for the preparation of diphenylguanidine, dyestuffs, curing bladder, rubber bag, tire cement, wires, cables, as a detergent for cleaning airport runways and many other commercial products. Therefore, extensive investigations have been carried out to devise an effective synthesis of DPTU and other *N,N'*-disubstituted thioureas.[5,6] However, there still exist many practical limitations in current DPTU syntheses and some problems in DPTU analysis.

Ramadas *et al.*[7] investigated the direct preparation of a series of *N,N'*-disubstituted thioureas from amines and carbon disulfide. Although DPTU was obtained in very high yields (98%), the need to add triethanolamine, Lac sulfur powder and a large amount of water makes the method inconvenient and less economically feasible. Ballabeni *et al.*[8] studied the reaction of aniline with carbon disulfide at 100°C both in the presence and in the absence of catalyst. The maximum yield of DPTU was 83% with a basic catalyst, 43% with an acidic clay and 17% without any catalyst. They considered that the basic catalyst favored the elimination of H_2S and thereby significantly promoted the reaction. However, as they noted, since the catalyst activity is diminished by the H_2S generated during the reaction, higher yields of DPTU could not be achieved. Moreover, the necessity of using an autoclave makes their process inconvenient. Mohanta *et al.*[9] recently reported an investigation of the synthesis of substituted thioureas using 1-(methyldithiocarbonyl)imidazole as a thiocarbonyl transfer reagent and obtained a high yield of DPTU, albeit of low purity (mp. 150-152°C). In addition, their method is limited by the use of expensive 1-(methyldithiocarbonyl)imidazole or of *N*-methyl-*N*'-(methyldithiocarbonyl)imidazolium iodide as a reactant. We report herein our study on the reaction of aniline with carbon disulfide over sulfonated polystyrene.



$$PhNH_2 + CS_2 \xrightarrow[\text{polystyrene}]{\text{sulfonated}} PhNH\overset{S}{\overset{\|}{C}}NHPh + H_2S$$

The reaction was conducted at reflux temperature (*ca.* 60°C) under ambient pressure to afford DPTU selectively. After being cooled to room temperature, the reaction mixture deposited a large amount of crystals. To separate DPTU from the sulfonated polystyrene and to recover the catalyst, the solids, including the sulfonated polystyrene and DPTU, were extracted into carbon disulfide. DPTU can be readily separated from the extraction solution by crystallization and purified by recrystallization from carbon disulfide and the sulfonated polystyrene can be easily recovered. Carbon disulfide was used both as a reactant and as a solvent during the reaction and the extraction. Under the reaction conditions, the resulting H_2S is rapidly released from the reaction solution and easily collected as a pure gas or absorbed in NaOH aqueous solution.

Because of its thermal lability and low volatility, DPTU cannot be analyzed by GC/MS. Only Mohanta *et al.*[9] reported mass spectral data of DPTU, but the data are not reliable since GC/MS was used for the analysis. We analyzed DPTU using GC and GC/MS. The results show that DPTU decomposed completely to aniline and phenyl isothiocyanate (PITC). We performed LC/MS analysis of DPTU using 85% methanol-H_2O as mobile phase and obtained data (m/z: 251, 229, 136 and 94) which suggest that DPTU was only partly decomposed to aniline and PITC by the "soft ionization" of LC/MS, and thus LC/MS provides an effective approach to a less destructive analysis of DPTU.

EXPERIMENTAL SECTION

Aniline, carbon disulfide and sulfonated polystyrene (D001-FC, macroporous type, total exchange capacity 4.35 ≥ mmol/g, purchased from Shandong Dongda Chemical Industry Company) are commercially available and were used without further purification and any treatment. Mp was determined in capillaries on a domestic WRC-1B melting point apparatus and is uncorrected. ^{1}H NMR spectrum was recorded on a JEOL Lambda 400 spectrometer (400 MHz) with TMS as the internal standard in C_4D_8O. Chemical shifts are expressed in parts per million (δ, ppm). FTIR spectrum was obtained on a Nicolet Magna IR-560 spectrometer. LC/MS analysis was performed on a Bruker Esquire system (C18 column, 4.6 mm x 250 mm x 5 μm; ESI source, positive ion detection, 113.4 V). Elemental analyses for C, H, N and S were carried out on a Leco CHN-2000 Elemental analyzer and a Leco SC-32 Sulfur Determinator, respectively.

Typical Procedure.- A mixture of aniline (10 mL, 0.11 mol), carbon disulfide (13 mL, 0.22 mol) and sulfonated polystyrene (1 g) in a 150 mL, round bottom flask was stirred under reflux for 2 h. After being cooled to room temperature, the reaction mixture was transferred with the help of *ca.* 100 mL carbon disulfide into a Soxhlet extractor to separate catalyst from the resulting DPTU. After being allowed to cool to room temperature, the extract deposited a large amount of crystals, which were recrystallized from carbon disulfide to afford 22.5 g (90%) of DPTU (99.9% pure by LC) as white, flaky crystals, mp. 153.5-154°C, *lit.*[4] 152-153°C. IR (KBr): 3211, 1596, 1551, 1494, 1450, 1342, 1241, 761, 757, 698, 486 cm^{-1}. ^{1}H NMR: δ 9.00 (s, 2H, S=C-N**H**), 7.44 (d, *J* = 8.3 Hz, 4H, Ar**H** on 2-position), 7.27 (t, *J* = 7.7 Hz, 4H, Ar**H** on 3-position), 7.07 (t, *J* = 7.9 Hz, 2H, Ar**H** on 4-position). MS (*m/z*, %): 251.1 [(M+Na)$^+$, 17.5], 229.1 [(M+H)$^+$, 95.2], 136.1 [(M-PhNH$_2$+H)$^+$, 100], 94.2 [(M-PhN=C=S+H)$^+$, 68.0].

Anal. Calcd for $C_{13}H_{12}N_2S$: C, 68.39; H, 5.30; N, 12.27; S, 14.04
Found: C, 68.42; H, 5.32; N, 12.25; S, 14.01

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