

## Ammonium Bromide as an Effective and Viable Catalyst in the Oxidation of Sulfides Using Nitro Urea and Silica Sulfuric Acid

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A new catalytic method for the chemoselective oxidation of sulfides to the sulfoxides has been studied. A variety of dialkyl, alkylaryl and diaryl sulfides were subjected to the oxidation reaction by a mixture of nitro urea, derived from urea nitrate, silica sulfuric acid ( $\text{SiO}_2\text{-OSO}_3\text{H}$ ) and catalytic amounts of ammonium bromide in  $\text{CH}_2\text{Cl}_2$  at room temperature.

**Keywords:** Sulfoxide, Nitro urea, Urea nitrate, Ammonium bromide, Silica sulfuric acid, ( $\text{SiO}_2\text{-OSO}_3\text{H}$ )

### INTRODUCTION

The selective oxidation of sulfides to sulfoxides is an important transformation because of the great significance sulfoxides have as intermediates in organic synthesis and the key role they play in the enzyme activation [1]. Sulfoxides are useful elements of stereocontrol in both asymmetric synthesis and important targets of pharmaceutical interest [2-5]. Sulfoxides are usually prepared *via* oxidation of the sulfides by different oxidizing systems [6-17]. Unfortunately, it is often very difficult to stop the oxidation at the sulfoxide stage. Moreover, there are several limitations on the application of the reported procedures for the oxidation of sulfides such as low selectivity, low yields of products, tedious work-up, toxicity, and expensive reagents or catalysts. As a matter of fact, the main drawback of the reported oxidizing systems is their unsuitability for medium to large-scale syntheses.

### EXPERIMENTAL

Chemicals were purchased from Fluka, Merck and Aldrich

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chemical companies. The oxidation products were characterized by comparison of their spectral (IR,  $^1\text{H}$  NMR, and  $^{13}\text{C}$  NMR) and physical data with those of authentic samples. Silica sulfuric acid was prepared employing a previously reported procedure [18].

#### Preparation of Nitro Urea ( $\text{NH}_2\text{CONHNO}_2 \cdot x\text{H}_2\text{O}$ )

In a 50-ml round-bottomed flask, 4 ml of  $\text{HNO}_3$  (65%) and 3.46 g of urea was stirred for 2 h, and a white crystalline solid ( $\text{NH}_2\text{CONHNO}_2 \cdot x\text{H}_2\text{O}$ ) was obtained quantitatively. M.p.: 156-158.4 °C (Ref. [19] 157-159 °C); MS (70 eV):  $m/z = 105$  ( $\text{M}^+$ ), 91, 69, 63, 60, 46 (base peak,  $\text{NO}_2^+$ ), 44.

#### Oxidation of Allyl Methyl Sulfide **1h** to Allyl Methyl Sulfoxide **2h** Using Nitro Urea and Silica Sulfuric Acid in the Presence of a Catalytic Amount of Ammonium Bromide

$\text{NH}_4\text{Br}$  (0.005 g, 0.05 mmol) and nitro urea (0.32 g) were added to a solution of allyl methyl sulfide **1h** (0.088 g, 1 mmol) in  $\text{CH}_2\text{Cl}_2$  (5 ml), followed by addition of silica sulfuric acid (0.4 g). The resulting mixture was stirred at room temperature for 38 min (the reaction progress was monitored by TLC) and then filtered. The residue was washed with

$\text{CH}_2\text{Cl}_2$  (20 ml). Anhydrous  $\text{Na}_2\text{SO}_4$  (1.5 g) was added to the filtrate and filtered off after 20 min. Finally  $\text{CH}_2\text{Cl}_2$  was evaporated and allyl methyl sulfoxide **2h** obtained as colorless oil (0.066 g, 64%).  $^1\text{H}$  NMR (200 MHz,  $\text{CD}_3\text{SOCD}_3$ ):  $\delta$  = 5.75-5.97 (m, 1H), 5.31-5.39 (m, 2H), 3.34-3.62 (m, 2H), 2.50 (s, 3H) ppm;  $^{13}\text{C}$  NMR (50 MHz,  $\text{CD}_3\text{SOCD}_3$ ):  $\delta$  = 127.5, 123.3, 56.5, 37.4 ppm; (Ref. [20]).

### Selected Representative Spectral Data

**2-(Phenylsulfinyl)ethanol (2e).**  $^1\text{H}$  NMR (200 MHz,  $\text{CD}_3\text{SOCD}_3$ ):  $\delta$  = 7.51-7.94 (m, 5H), 5.89 (s, 1H), 3.63-3.88 (m, 2H), 2.83-3.01 (m, 2H) ppm;  $^{13}\text{C}$  NMR (50 MHz,  $\text{CD}_3\text{SOCD}_3$ ):  $\delta$  = 144.9, 132.1, 131.1, 123.6 ppm.

**4-Thianthrene mono sulfoxide (2g).**  $^1\text{H}$  NMR (400 MHz,  $\text{CD}_3\text{SOCD}_3$ ):  $\delta$  = 7.80-7.84 (m, 2H), 7.65-7.68 (m, 1H), 7.55-7.58 (m, 1H) ppm;  $^{13}\text{C}$  NMR (100 MHz,  $\text{CD}_3\text{SOCD}_3$ ):  $\delta$  = 141.2, 130.9, 129.8, 129.3, 128.2, 124.7 ppm.

**Benzyl methyl sulfoxide (2k).**  $^1\text{H}$  NMR (200 MHz,  $\text{CD}_3\text{SOCD}_3$ ):  $\delta$  = 7.34 (s, 5H), 5.07 (s, 2H), 3.91-4.16 (dd,  $J$  = 24.1, 12.7 Hz, 2H) ppm;  $^{13}\text{C}$  NMR (50 MHz,  $\text{CD}_3\text{SOCD}_3$ ):  $\delta$  = 131.7, 130.7, 128.9, 128.2, 59.0, 37.6 ppm.

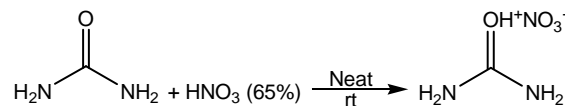
**4-Chlorophenyl methyl sulfoxide (2o).**  $^1\text{H}$  NMR (200 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.47-7.63 (dd,  $J$  = 14.0, 8.6 Hz, 4H) 2.75 (s, 3H), ppm;  $^{13}\text{C}$  NMR (50 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 143.8, 137.1, 129.5, 125.0, 43.7 ppm.

## RESULTS AND DISCUSSION

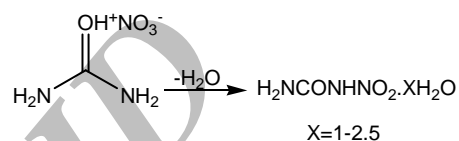
Recently, we have introduced different approaches for the chemoselective oxidation of sulfides to the sulfoxides *via in situ* generation of bromonium ion [21-28]. In continuation of this investigation, we decided to explore catalytic and metal-free media for the *in situ* generation of  $\text{Br}^+$ . To this end, we synthesized urea nitrate by reaction of urea with nitric acid (Scheme 1). Urea nitrate has been reported previously by Shead [29].

Urea nitrate can be readily dehydrated to nitro urea ( $\text{NH}_2\text{CONHNO}_2 \cdot x\text{H}_2\text{O}$ ) (Scheme 2). This structure might be easily approved by its mass spectrum (Fig. 1), whose molecular ion peak appears at  $m/e = 105$  and base peak ( $\text{NO}_2^+$ ) appears at  $m/e = 46$ .

In continuation of our studies on the properties of nitro urea ( $\text{NH}_2\text{CONHNO}_2 \cdot x\text{H}_2\text{O}$ ), we found that this reagent has



Scheme 1



Scheme 2

oxidizing property in the presence of an acid. Therefore, we decided to apply nitro urea in the presence of silica sulfuric acid ( $\text{SiO}_2\text{-OSO}_3\text{H}$ ) and catalytic amounts of ammonium bromide for the chemoselective oxidation of sulfides to the sulfoxides.

Initially, to find an appropriate solvent for this transformation, we screened different solvents for the oxidation of dibenzyl sulfide, as a standard model the results of which are summarized in Table 1. As is evident from Table 1, oxidation reaction proceeds more rapidly and selectively in dichloromethane and acetonitrile compared to other solvents. However, dichloromethane has been selected as the reaction solvent in all reactions because dichloromethane has lower toxicity than acetonitrile.

With the optimal conditions at hand, herein we report chemoselective oxidation of a wide range of aliphatic and aromatic sulfides **1** to the corresponding sulfoxides **2** *via* treatment of nitro urea ( $\text{NH}_2\text{CONHNO}_2 \cdot x\text{H}_2\text{O}$ ) **I**, silica sulfuric acid ( $\text{SiO}_2\text{-OSO}_3\text{H}$ ) **II** in the presence of catalytic amounts of  $\text{NH}_4\text{Br}$  **III** in dichloromethane at room temperature with good to excellent yields (Scheme 3 and Table 2).

As is evident from Table 2, a good range of turn over number (TON) and turn over frequency (TOF) of the catalyst is observed. To prove the catalytic role of  $\text{NH}_4\text{Br}$ , dibenzyl sulfide (as typical example) was selected for the oxidation reaction in the absence of this catalyst. Surprisingly, no sulfoxide was observed for 24 h (Table 2, entry 4). We found that the sulfoxidation reaction for dibenzyl sulfid did not

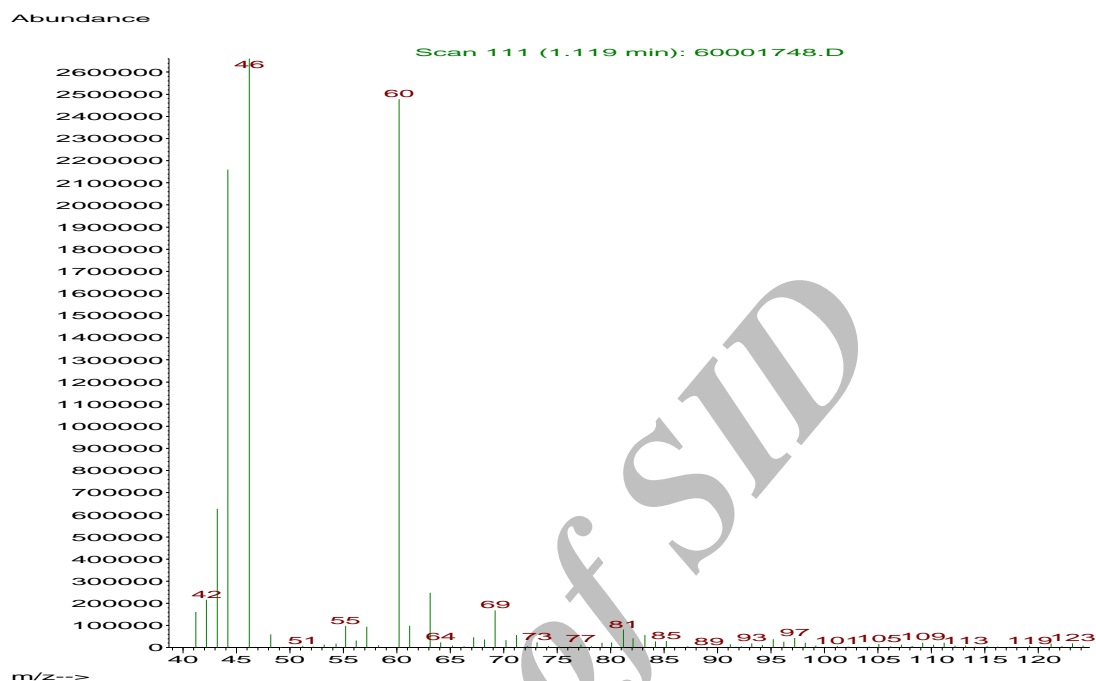


Fig. 1. Mass spectrum of nitro urea ( $\text{NH}_2\text{CONHNO}_2 \cdot x\text{H}_2\text{O}$ ).

Table 1. Oxidation of Dibenzyl Sulfide Using Nitro Urea, Silica Sulfuric Acid and Catalytic Amounts of  $\text{NH}_4\text{Br}$  in Different Solvents at Room Temperature<sup>a</sup>

Entry	Solvent	Time (min)	Yield (%) <sup>b</sup>
1	Acetonitrile	28	98
2	Acetone	48 h	- <sup>c</sup>
3	Chloroform	127	98
4	Dichloromethane	30	94
5	<i>n</i> -Hexane	48 h	- <sup>d</sup>
6	Ethanol	48 h	- <sup>c</sup>
7	Ethyl acetate	50	98

<sup>a</sup>Substrate: Nitro urea:  $\text{NH}_4\text{Br}$ : Silica sulfuric acid = 1 mmol: 0.32 g: 0.05 mmol: 0.4 g. <sup>b</sup>Isolated yield. <sup>c</sup>No reaction. <sup>d</sup>Reaction was not complete and impurity of sulfone was observed.

complete without silica sulfuric acid ( $\text{SiO}_2\text{-OSO}_3\text{H}$ ) within 24 h (Table 2, entry 5), which means that the presence of the acid is necessary for the sulfoxidation to realize.

In this investigation, we observed that thianthrene, which

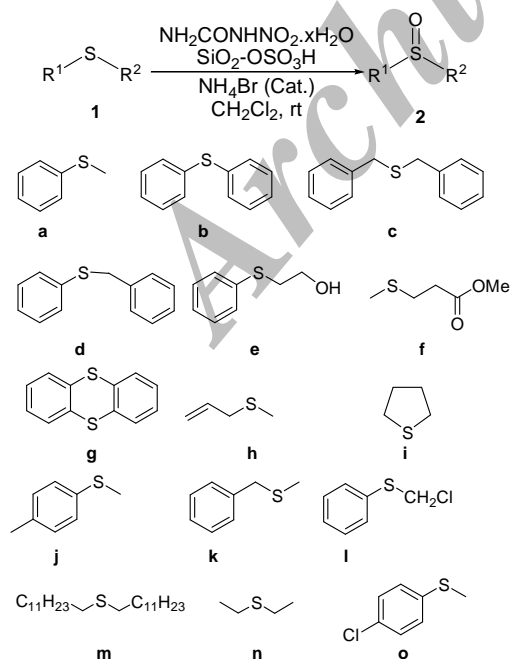
has two similar sulfide moieties, undergoes homoselective oxidation. Such a finding is in close agreement with our previously reported works on the oxidation of sulfides to the sulfoxides [17-22]. This can be clearly demonstrated by <sup>13</sup>C

**Table 2.** Oxidation of Sulfides **1** to the Corresponding Sulfoxides **2** Using Nitro Urea ( $\text{NH}_2\text{CONHNO}_2 \cdot x\text{H}_2\text{O}$ ) **I**,  $\text{SiO}_2\text{-OSO}_3\text{H}$  **II** and Catalytic Amounts of  $\text{NH}_4\text{Br}$  **III** in Dichloromethane at Room Temperature

Entry	Substrate	Product	Substrate/Reagents/Catalyst <sup>a</sup>			Time (min)	Yield (%) <sup>b</sup>	TON	TOF ( $\text{min}^{-1}$ )
			I	II	III				
1	<b>1a</b>	<b>2a</b>	0.32	0.4	0.05	31	95	19.0	0.61
2	<b>1b</b>	<b>2b</b>	0.48	0.6	0.1	180	99	9.9	0.05
3	<b>1c</b>	<b>2c</b>	0.32	0.4	0.05	30	94	18.8	0.63
4	<b>1c</b>	<b>2c</b>	0.32	0.4	-	24 h	- <sup>c,d</sup>	-	-
5	<b>1c</b>	<b>2c</b>	0.32	-	0.05	24 h	- <sup>e,f</sup>	-	-
6	<b>1d</b>	<b>2d</b>	0.32	0.4	0.05	45	99	19.8	0.44
7	<b>1e</b>	<b>2e</b>	0.32	0.4	0.05	270	89	17.8	0.07
8	<b>1f</b>	<b>2f</b>	0.32	0.4	0.05	24	91	18.2	0.76
9	<b>1g</b>	<b>2g</b>	0.32	0.4	0.05	28	95	19.0	0.68
10	<b>1h</b>	<b>2h</b>	0.32	0.4	0.05	38	64	12.8	0.34
11	<b>1i</b>	<b>2i</b>	0.32	0.4	0.05	23	99	19.0	0.83
12	<b>1j</b>	<b>2j</b>	0.32	0.4	0.05	22	99	19.0	0.86
13	<b>1k</b>	<b>2k</b>	0.32	0.4	0.05	51	99	19.0	0.37
14	<b>1l</b>	<b>2l</b>	0.32	0.4	0.1	160	84	8.4	0.05
15	<b>1m</b>	<b>2m</b>	0.32	0.4	0.05	5	99	19.0	0.38
16	<b>1n</b>	<b>2n</b>	0.32	0.4	0.05	53	97	19.4	0.37
17	<b>1o</b>	<b>2o</b>	0.32	0.4	0.05	50	80	16.0	0.32

<sup>a</sup>**I** and **II** refer to grams of nitro urea and silica sulfuric acid, respectively; **III** refers to mmol of ammonium bromide.

<sup>b</sup>Isolated yield. <sup>c</sup>In the absence of  $\text{NH}_4\text{Br}$ . <sup>d</sup>No reaction. <sup>e</sup>In the absence of silica sulfuric acid. <sup>f</sup>Reaction not complete.



Scheme 3

NMR of the oxidation product (thianthrene mono sulfoxide), (Fig. 2). It is interesting to note that the described system allowed the chemoselective oxidation of 2-(phenylthio)ethanol to 2-(phenylsulfinyl)ethanol and that hydroxyl group was intact in the course of the reaction (Scheme 4, entry 7).

The suggested mechanism of this transformation is outlined in Scheme 5 based on our previously reported works [21-28]. Initially, nitro urea ( $\text{NH}_2\text{CONHNO}_2 \cdot x\text{H}_2\text{O}$ ) directly generates nitronium ion *via* protonation by silica sulfuric acid. Then, nitronium ion converts bromide ion ( $\text{Br}^-$ ) to bromonium ion ( $\text{Br}^+$ ). Finally, the reaction of bromonium ion with sulfide in the presence of water generates the corresponding sulfoxide.

In summary, we reported above a novel catalytic protocol for the chemo- and homoselective oxidation of sulfides to the sulfoxides under metal-free, mild and heterogeneous conditions. This method offers the advantage of shorter reaction times, high selectivity, non-toxic conditions, cost-effective reagents and catalyst and easy workup.

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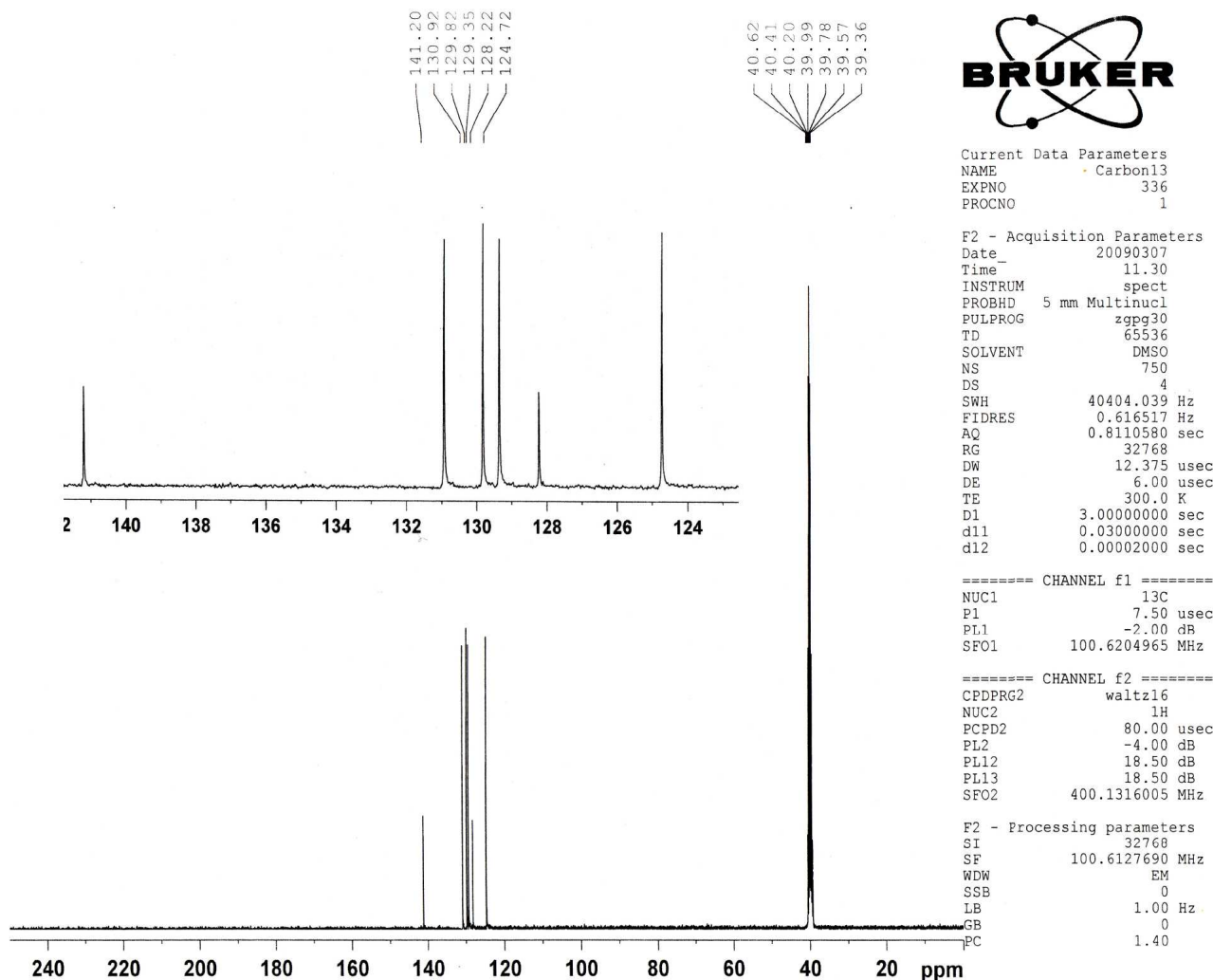
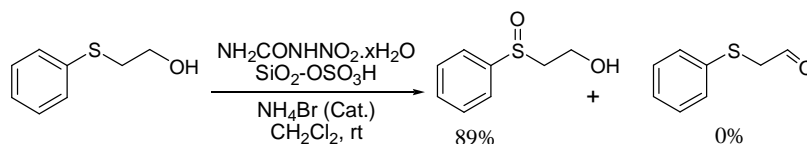
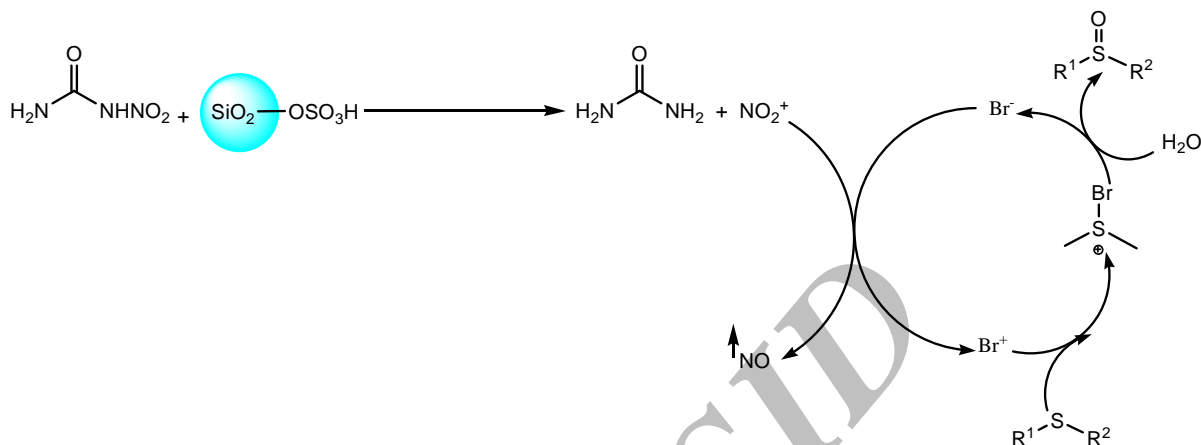


Fig. 2. <sup>13</sup>C NMR of thianthrene mono sulfoxide in CD<sub>3</sub>SOCD<sub>3</sub>.



Scheme 4



Scheme 5

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