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Synthesis and characterization of some derivatives of 1,3-Diisopropyl-4,5-dimethylimidazol-2-ylidene

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A B S T R A C T

N-Heterocyclic carbenes are widely used in organic reactions and coordination chemistry. In the present study, 2,3-dihydro-1,3-diisopropyl-4,5-dimethylimidazol-2-ylidene **(1)** is reacted with diphenyl disulfide, methyl phenyl disulfide, and bis(methylsulfonyl)methane to yield target compounds **5**, **6**, and **7** respectively. Structures of these compounds are well established using nuclear magnetic resonance, mass spectrometry and elemental analysis. Possible reaction mechanisms are proposed.

1. Introduction

N-Heterocyclic carbenes (NHCs) have played an important role in various fields of chemistry, including medicinal chemistry, transition metal catalysis, and material chemistry.[1-3] More specifically, NHCs have recently received significant attention for the development of materials and novel drugs.[1,3] Further, NHCs are proven major ligand class.[2] On the other hand, a 2,3-dihydro-1,3-diisopropyl-4,5-dimethylimidazol-2-ylidene (**1**) has a strong basic character and consequently can form various imidazolium salts (**2**) [4-6], and in parallel it poses a good nucleophilic property to form new derivatives (**3**-**4**).[7-8] There is a much interest in imidazolium salts based on their uses as ionic liquids.[9-10]

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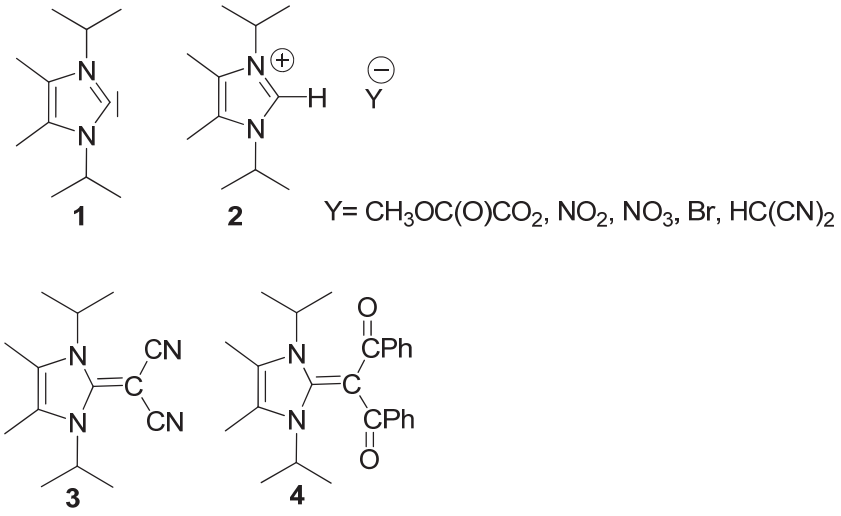
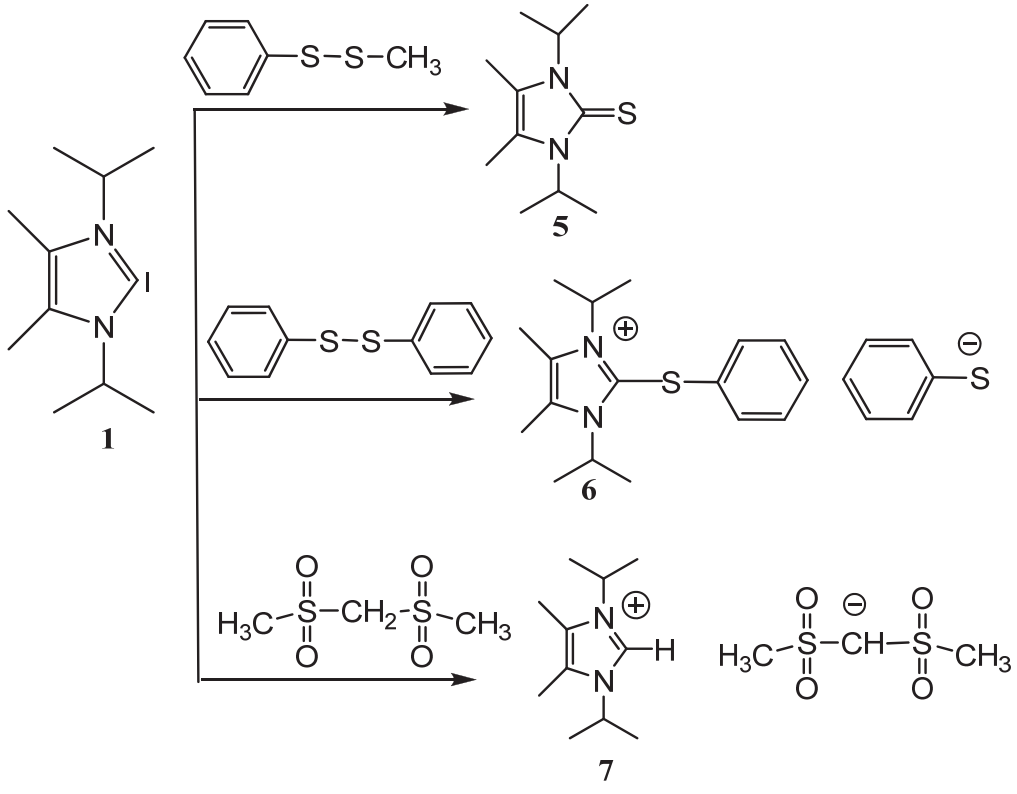


Expanding our systematic study on heterocyclic carbenes and continuing our investigations on the chemistry of imidazol-2-ylidene, we report herein its reactions with diphenyl disulfide, methyl phenyl disulfide and bis(methylsulfonyl)methane. To the best of our knowledge, none of these reactions have been reported previously.

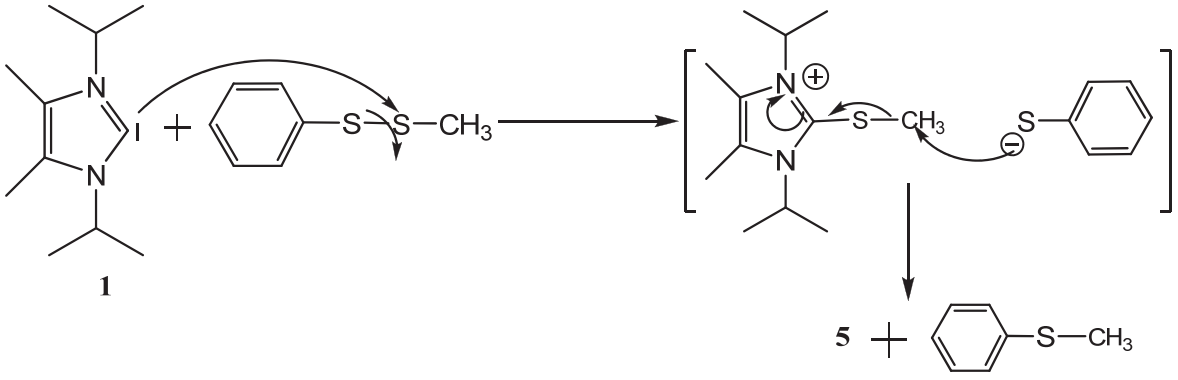
2. Results and Discussion

Compounds **5** and **6** were prepared in good yields from reactions of **1** with methyl phenyl disulfide and diphenylsulfide respectively (**Scheme 1**). These reactions were performed based on the strong nucleophilicity of 2,3-dihydro-1,3-diisopropyl-4,5-dimethylimidazol-2-ylidene (**1**).



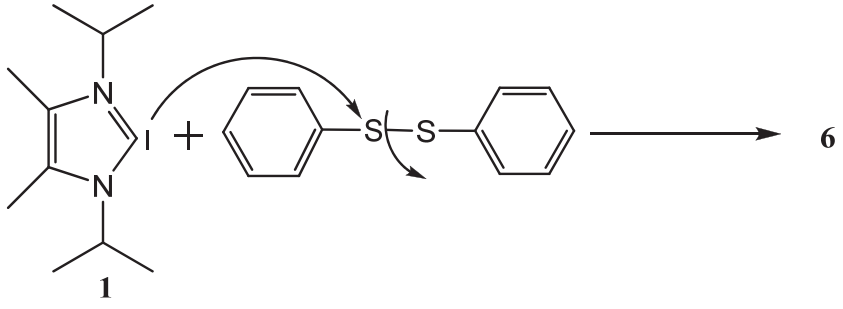
Scheme 1. Synthesis of the target products **5**, **6**, and **7**.

Compound **5** was characterized by NMR and IR spectroscopy, mass spectrometer and elemental analysis. NMR and mass data are in good agreement with those published in the literature.[11,12] Mechanism of synthesis is proposed in **Scheme 2**. It seems that C2 of compound **1** attacks a sulfur atom in methyl phenyl disulfide that is less-hindered followed by attacking the sulfur atom of thiophenolate to the methyl group under S_N2 mechanism to produce the target product **5**. This sulfur-sulfur bond cleavage mechanism was observed in selective desulfurization of trisulfides.[13]



Scheme 2. Proposed mechanism for synthesis of **5**

The structure of compound **6** was assigned obviously from data of NMR and IR spectroscopy, mass spectrometry and elemental analysis. Diphenyl disulfide shows only four signals in the ^{13}C NMR spectra due to the presence of symmetry between phenyl groups, while in **6** the symmetry between the two phenyl rings have been disappeared due to the cleavage of S-S bond and formation of the salt. In addition, all the imidazolium ion signals are existing in the expected range. ^{1}H and ^{13}C NMR data of **6** imply the presence of separated ions. A proposed mechanism for synthesis of compound **6** is shown in **Scheme 3**; carbon atom (S-C) of the phenyl group in imidazolium cation cannot be attacked by sulfur atom of thiophenolate anion due to the electronic and steric effects.



Scheme 3. Proposed mechanism for synthesis of **6**

2,3-Dihydro-1,3-diisopropyl-4,5-dimethylimidazol-2-ylidene is considered a strong organic base, and consequently can be employed as a deprotonation reagent[14] to form imidazolium compounds which have an important role in developing ionic liquids. These liquids were applied as pharmaceutical solvents.[15] In the present study, the reaction of compound **1** with bis(methylsulfonyl)methane (Broenstedt acid) represents an acid-base reaction.

^{1}H and ^{13}C NMR spectra also exhibit all signals of the imidazolium ion. The structure of **7** can be assigned obviously from the NMR spectroscopy. Concerning the ^{13}C spectrum, the chemical shift of methyl group for the anion is downfield (46.5 ppm), while the signal of methine group is upfield (63.0 ppm), with respect to those found in bis(methylsulfonyl)methane, 41.4 ppm and 70.3 ppm, respectively. A similar chemical shift for methine group of the anion in **7** has been observed after deprotonation of bis (phenylsulfonyl)methane with methyl lithium.[16] On the other hand, the corresponding

imidazoliumacetylacetonate (acac) salt showed a significant downfield chemical shift in ^{13}C spectrum for the CH_{acac} (δ = 101.7 ppm).[17] Comparing with the present value (63.01 ppm), this difference might be attributed to the electronegativity difference of sulfur and oxygen atoms. All attempts to get single crystals from **7** were failed due to the very low stability of the salt and high sensitivity towards the moisture.

3. Conclusion

Target compounds **5**, **6**, and **7** were prepared successfully in a reasonable yield from the reaction of 2,3-dihydro-1,3-diisopropyl-4,5-dimethylimidazol-2-ylidene **(1)** with diphenyl disulfide, methyl phenyl disulfide and bis(methylsulfonyl)methane respectively. Structures of these compounds were fully characterized using various spectroscopic techniques. Compound **1** may act as good nucleophile and strong base in various organic reactions under dry conditions.

Conflicts of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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4. Experimental

All experiments have been performed in purified solvents under argon. The following chemicals were purchased and used without further purification: methyl phenyl disulfide, diphenyldisulfide and bis(methylsulfonyl)methane from Sigma Aldrich. 1,3-Diisopropyl-4,5-dimethyl-4,5-dimethylimidazol-2-ylidene was prepared according to the published work[11]. NMR analysis was done using Bruker-Avance III 500 MHz spectrometers with TMS as the internal standard. Coupling constant (*J*) values are given in Hertz (Hz). Thin Layer Chromatography (TLC) was performed using Merck aluminum plates pre-coated with silica gel PF254; (20 x 20) cm x 0.25 mm, and detected by visualization of the plate under UV lamp (λ = 254 nm). Elemental analysis was obtained using Euro Vector Elemental analyzer model EUROEA3000 A, (Redavalle), Italy. Mass spectra were recorded on a Finnigan Triple-Stage-Quadrupol spectrometer (TSQ-70) from Finnigan-Mat and the ionization methods were electron-impact (EI) by 70 eV at 200°C or Fast-atom bombardment (FAB) by 70 eV in Nitrobenzylalcohol-Matrix at 60°C.

Synthesis of 1,3-diisopropyl-4,5-dimethyl-1,3-dihydro-imidazole-2-thione (5). To a solution containing 1,3-diisopropyl-4,5-dimethyl-4,5-dimethylimidazol-2-ylidene (**1**) (0.400 g, 2.22 mmol) in 30 mL Et_2O, methyl phenyl disulphide (0.302 ml, 2.23 mmol) was added at room temperature. After stirring overnight, the solution was kept to stand at -35 ºC for 24 h, a white crystals was formed, filtered off and dried in *vacuo*. Yield: 0.250 g (53%).

^1H NMR ($CDCl_3$): δ = 1.37 (d, 12H, 1,3-$CHMe_2$, ^3J = 6.65 Hz), 2.11 (s, 6H, 4,5-Me), 5.60 (sept, 2H, 1,3-$CHMe_2$), 7.24 (m, 3 H, Ph), 8.16 (d, 2 H, Ph), 10.13 (s, 1 H, CIm2).

^{13}C NMR ($CDCl_3$): δ = 10.3 (4,5-Me), 20.7 (1,3-$CHMe_2$), 49.3 (1,3-$CHMe_2$), 159.8 (CS), 121.4 ($C_{Im}^{4,5}$).

Anal. Calcd. for $C_{11}H_{20}N_2S$ (212.20 g/mol): (C, 62.22; H, 9.49; N, 13.19; S, 15.10)%. Found for $C_{11}H_{20}N_2S$: (C, 62.56; H, 9.39; N, 12.99; S, 15.11) %.

MS (EI): m/z (%) = 212.2 [40].

Synthesis of 1,3-diisopropyl-4,5-dimethyl-2-phenylsulfanylimidazoium benzenethiol (6). To a solution containing 1,3-diisopropyl-4,5-dimethyl-4,5-dimethylimidazol-2-ylidene (**1**) (0.240 g, 1.33 mmol) in 30 mL Et_2O, diphenyldisulfide (0.290 g, 1.33 mmol) was added at -50 °C. After stirring overnight at room temperature, the precipitate was filtered off, washed with Et_2O and dried in *vacuo*. Yield: 0.350 g (66%).

^{1}H NMR ($CDCl_3$): δ = 1.58 (d, 12H, 1,3-CH*Me*$_2$, ^3J = 6.80 Hz), 2.19 (s, 6H, 4,5-Me), 4.44 (sept, 2H, 1,3-C*H*Me$_2$), 7.39 (m, 3 H, Ph), 7.70 (d, 2 H, Ph).

^{13}C NMR ($CDCl_3$): δ = 8.8 (4,5-Me), 22.8 (1,3-CH*Me*$_2$), 51.1 (1,3-CHMe$_2$), 125.5 (C_{Ph}^4), 127.1 ($C_{Im\text{-}Ph}^{2,6}$), 127.4 ($C_{Ph}^{3,5}$), 128.4 ($CS_{Im\text{-}Ph}$), 129.0 ($C_{Ph}^{2,6}$), 129.2 ($C_{Im\text{-}Ph}^{3,5}$), 137.3 (CS_{Ph}), 132.8 (C_{Im}^2),131.70 ($C_{Im}^{4,5}$).

Anal. Calcd. for $C_{23}H_{30}N_2S_2$ (398.63 g/mol): (C, 68.35; H, 7.82; N, 7.25; S, 16.59)%. Found for $C_{23}H_{30}N_2S_2$: (C, 68.56; H, 7.42; N, 6.91; S, 16.54) %.

MS (FAB pos.): m/z (%) = 289.1 [100].

MS (FAB neg.): m/z (%) = 108.8 [60].

Synthesis of 1,3-diisopropyl-4,5-dimethylimidazolium bis-methanesulfonyl-methane (7). To a solution containing 1,3-diisopropyl-4,5-dimethyl-4,5-dimethylimidazol-2-ylidene (**1**) (0.320 g, 1.77 mmol) in 30 mL Et_2O, bis(methylsulfonyl)methane (0.307 g, 1.78 mmol) was added at room temperature. After stirring for about 48 h, the resulting precipitate was isolated, washed with Et_2O and dried in *vacuo*. Yield: 0.520 g (83%).

^{1}H NMR (CD_3CN): δ = 1.41 (d, 12H, 1,3-CH*Me*$_2$, ^3J = 6.72 Hz), 2.15 (s, 6H, 4,5-Me), 4.41 (sept, 2H, 1,3-C*H*Me$_2$), 2.73 ($CH_{3\ sulfone}$), 3.41 ($CH_{sulfone}$), 8.36 (s, 1 H, C_{Im}^2).

^{13}C NMR (CD_3CN): δ = 7.3 (4,5-Me), 21.4 (1,3-CH*Me*$_2$), 49.9 (1,3-CHMe$_2$), 46.5 ($CH_{3\ sulfone}$), 63.0 ($CH_{sulfone}$), 126.3 (C_{Im}^2), 129.1 ($C_{Im}^{4,5}$).

Anal. Calcd. for $C_{14}H_{28}N_2O_4S_2$ (352.51 g/mol): (C, 47.70; H, 8.01; N, 7.95; S, 18.19) %. Found: (C, 47.41; H, 7.88; N, 7.11; S, 17.81) %.

MS (FAB neg.): m/z (%) = 170.8 [100].

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