Synthesis of Novel Dinaphthosulfide, Aza, Oxa, Thia Lariats Containing Urea and Thiourea Groups in the Side Chain and Their Nanostructures

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Abstract: Dinaphthosulfide aza, oxa, thia crown was prepared; its urea and thiourea derivatives were synthesized by the reaction with ethyl and 4-chlorophenyl isocyanate, ethyl and phenylisothiocyanate. Self-assembled structures are as micro and nano fibers and discs.

Keywords: Aza oxa thia crown, Synthesis, receptor, Macrocycle, Lariat, Nano and Microstructures

Introduction

Crown ethers were reported in 1967 by Pedersen for the first time^{1,2}. The chemistry of crown ethers has been developed in four decades by a lot of research groups³⁻⁶. The first crown ethers are all oxa crowns but modification of their properties have been performed using other heteroatoms such as N and S in their rings and addition of groups on the rings⁷. Modified crown ethers and aza crowns are compounds bearing various kinds and number of oxa, aza and thia heteroatom in their structures⁸. The second strategy for the modification of crown ethers and their derivatives is the synthesis of crown compounds with different structures, such as cryptands, calixarenes, lariats and biscrowns⁹⁻¹².

Crown ethers and their derivatives are important role in host-guest chemistry and supramolecular chemistry¹³. The complexation properties of these compounds towards metal ions were reported by pedersen¹ and other researchers were investigated and explored the complexation and interaction of these compounds towards metal ions and neutral or ionic molecules and groups¹⁴. Noncovalent interactions and

bonds are the main interactions in host-guest and supramolecular chemistry¹⁵. These interactions led to the molecular aggregations and these studies are active route in chemical researches in recent years¹⁶. Nanotechnology is mainly based on the supramolecular chemistry and noncovalent interactions. A lot of natural or synthetic crown ether derivatives are an important role in nanosciences¹⁷.

In this research work, a new dinaphthosulfide oxa, aza, thia crown was prepared and its urea and thiourea derivatives were synthesized using a series of isocyanate and isothiocyanate derivatives. The aggregations of these macrocycles were studied by scanning electron microscopy using their SEM images. SEM images show the aggregations of molecules based on the noncovalent interactions as the micro and nano discs and fibres.

Experimental

The reactions were carried out in an efficient hood cupboard. All the materials were purchased from Merck, Fluka, Across Organics and Aldrich chemical companies. Methanol and CH_2Cl_2 were distilled and stored under Lind 4Å molecular sieve. The melting points (uncorrected) were measured with an Electrothermal engineering LTD 9100 apparatus. Elemental analyses were performed by a CHN-O- Rapid Heraeus elemental analyzer. IR spectra were measured on a Perkin-Elmer model 543, the ^1H NMR and ^{13}C NMR spectra were obtained using BRUKER AVANCE DPX 300 MHz and BRUKER AVANCE DRX 500 MHz apparatus. Mass spectra were obtained with Shimadzu GC-MS-QP 1100 EX model. Scanning electron micrograph (SEM) images were obtained using a XL30 (Philips) apparatus.

General procedure for the synthesis of lariats

To aza crown (**3**, 1 mmol) in CH_2Cl_2 (50 ml) was added triethylamine (1 mmol) and then isocyanates (isothiocyanates) (1 mmol). The resulting mixtures were stirred at room temperature for 24 hours. After completion of the reactions (monitored by TLC), water was added and the resulting reaction mixture was extracted with CH_2Cl_2 (3×30 mL). The combined organic layer were washed with dilute hydrochloric acid twice, dried (Na_2SO_4) and evaporated to afford crude products which was purified by recrystallization in chloroform.

Synthesis of 7,10,13-triaza-1-thia-4,16-dioxa-6,14-dioxo-10-(2-aza-1-thio-3-phenylethyl)-2,3; 17,18-dinaphtho-cyclooctadecane (8)

This compound was prepared from the reaction of **3** and phenylisothiocyanate based on the general procedure, afforded **8** as a white powder in the yield of 94% and melting point of 201-202 °C. IR (KBr): 3396, 3387, 3299, 3052, 2936, 1688, 1679, 1623, 1558, 1543, 1446, 1323, 1265, 1226, 1153, 1077, 763 cm^{-1} ; ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ : 3.49 (broad, 4H), 3.62 (s, 4H), 4.46 (s, 4H), 7.24 - 7.46 (m, 11H), 7.86 - 7.95 (m, 4H), 8.09 (s, broad, 1H), 8.33 - 8.40 (m, broad, 2H), 8.77 (s, broad, 1H), 9.11 (s, broad, 1H) ppm.; ^{13}C NMR (75 MHz, $\text{DMSO}-d_6$) δ : 169.39, 163.10, 155.67, 143.36, 134.05, 129.99, 129.31, 128.62, 128.38, 127.32, 126.99, 126.09, 124.09, 124.05, 116.50, 114.41, 67.19, 64.92, 54.68, 53.47, 48.66, 33.90 ppm.; MS (EI) m/z : 501 (initial macrocycle (**3**), 2%), 500 (1%), 434 (4%), 376 (3%), 318 (1%), 300 (21%), 216 (26%), 202 (24%), 187 (42%), 144 (81%), 115 (100%), 93 (24%), 77 (12%), 63 (28%), 39 (27%); Anal. Calcd. for $\text{C}_{35}\text{H}_{32}\text{N}_4\text{O}_4\text{S}_2$: C, 66.02%; H, 5.07%; N, 8.80%; Found: C, 66.18%; H, 5.01%; N, 8.94%.

Synthesis of 7,10,13-triaza-1-thia-4,16-dioxo-6,14-dioxo-10-(2-aza-1-thio-buthyl)-2,3; 17,18-dinaphtho-cyclooctadecane (9)

This larite was prepared from the reaction of ethylisothiocyanate and **3** based on the general procedure and afforded **9** in 87% yield and melting point of 191-192 °C. IR (KBr): 3395, 3297, 3059, 2925, 1678, 1542, 1503, 1432, 1265, 1236, 1089, 1076, 814, cm^{-1} ; ^1H NMR (300 MHz, DMSO- d_6) δ : 3.37 – 3.39 (m, 4H), 3.76 (dd, 4H, $J = 3, 6$ Hz), 4.06 (dd, 2H, $J = 3, 6$ Hz), 4.50 (s, 4H), 4.94 (dd, 1H, $J = 2, 10$ Hz), 5.03 (dd, 1H, $J = 3, 16$ Hz), 5.70 – 5.81 (m, 1H), 7.32 – 7.42 (m, 6H), 7.61 (t, 1H, $J = 6$ Hz), 7.86 – 7.93 (m, 6H), 8.27 (dd, 2H, $J = 3, 7$ Hz) ppm; ^{13}C NMR (75 MHz, DMSO- d_6) δ : 169.90, 155.60, 130.85, 130.66, 129.94, 128.55, 128.48, 127.96, 125.38, 125.16, 124.99, 119.95, 113.74, 112.92, 68.60, 68.11, 53.00, 49.90, 48.49, 39.24, 37.55 ppm; MS (EI) m/z : 501 [initial macrocycle (**3**)]⁺ (4%), 500 (2%), 483 (2%), 300 (8%), 218 (6%), 187 (9%), 144 (100%), 115 (62%), 56(5%), 28 (16%); Anal. Cald. for $\text{C}_{31}\text{H}_{32}\text{N}_4\text{O}_4\text{S}_2$: C, 63.24%; H, 5.48%; N, 9.52%; Found : C, 63.18%; H, 5.53%; N, 9.65%.

Synthesis of 7,10,13-triaza-1-thia-4,16-dioxo-6,14-dioxo-10-(2-aza-1-oxo-3-(4-chlorophenyl)-ethyl)-2,3; 17,18-dinaphtho-cyclooctadecane (10)

This compound was prepared from the reaction of **3** and 4-chlorophenylisocyanate according to the general procedure and afforded **10** in 88% yield and melting point of 221-222 °C. IR (KBr): 3396, 3299, 3058, 2928, 1674, 1624, 1540, 1505, 1445, 1380, 1327, 1268, 1245, 1086, 1077, 813 cm^{-1} ; ^1H NMR (300 MHz, DMSO- d_6) δ : 3.37 – 3.39 (m, 4H), 3.76 (dd, 4H, $J = 3, 6$ Hz), 4.06 (dd, 2H, $J = 3, 6$ Hz), 4.50 (s, 4H), 4.94 (dd, 1H, $J = 2, 10$ Hz), 5.03 (dd, 1H, $J = 3, 16$ Hz), 5.70 – 5.81 (m, 1H), 7.32 – 7.42 (m, 6H), 7.61 (t, 1H, $J = 6$ Hz), 7.86 – 7.93 (m, 6H), 8.27 (dd, 2H, $J = 3, 7$ Hz) ppm; ^{13}C NMR (75 MHz, DMSO- d_6) δ : 169.90, 155.60, 130.85, 130.66, 129.94, 128.55, 128.48, 127.96, 125.38, 125.16, 124.99, 119.95, 113.74, 112.92, 68.60, 68.11, 53.00, 49.90, 48.49, 39.24, 37.55 ppm; MS (EI) m/z : 501 [initial macrocycle (**3**)]⁺ (3%), 500 (1%), 483 (2%), 300 (8%), 212 (6%), 187 (7%), 144 (100%), 115 (62%), 44 (16%); Anal. Cald. for $\text{C}_{35}\text{H}_{31}\text{ClN}_4\text{O}_5\text{S}$: C, 64.16%; H, 4.77%; N, 8.55%; Found : C, 64.07%; H, 4.83%; N, 8.63%.

Synthesis of 7,10,13-triaza-1-thia-4,16-dioxo-6,14-dioxo-10-(2-aza-1-oxo-buthyl)-2,3; 17,18-dinaphtho-cyclooctadecane (11)

This larite was prepared from the reaction of **3** and ethylisocyanate according to the general procedure afforded **11** in 91% yield and melting point of 184-185 °C. IR (KBr): 3391, 3294, 3055, 2925, 1678, 1542, 1503, 1432, 1265, 1236, 1089, 1076, 814 cm^{-1} ; ^1H NMR (300 MHz, DMSO- d_6) δ : 3.37 – 3.39 (m, 4H), 3.76 (dd, 4H, $J = 3, 6$ Hz), 4.06 (dd, 2H, $J = 3, 6$ Hz), 4.50 (s, 4H), 4.94 (dd, 1H, $J = 2, 10$ Hz), 5.03 (dd, 1H, $J = 3, 16$ Hz), 5.70 – 5.81 (m, 1H), 7.32 – 7.42 (m, 6H), 7.61 (t, 1H, $J = 6$ Hz), 7.86 – 7.93 (m, 6H), 8.27 (dd, 2H, $J = 3, 7$ Hz) ppm; ^{13}C NMR (75 MHz, DMSO- d_6) δ : 169.90, 155.60, 130.85, 130.66, 129.94, 128.55, 128.48, 127.96, 125.38, 125.16, 124.99, 119.95, 113.74, 112.92, 68.60, 68.11, 53.00, 49.90, 48.49, 39.24, 37.55 ppm; MS (EI) m/z : 501 [initial macrocycle (**3**)]⁺ (4%), 500 (2%), 483 (2%), 300 (8%), 218 (6%), 187 (9%), 144 (100%), 115 (62%), 56(5%), 28 (16%); Anal. Cald. for $\text{C}_{31}\text{H}_{32}\text{N}_4\text{O}_5\text{S}$: C, 65.02%; H, 5.63%; N, 9.78%; Found : C, 65.05%; H, 5.57%; N, 9.84%.

Results and Discussion

Dihydroxy naphthosulfide (**1**) was prepared based on the reported procedure.¹⁸ Corresponding diester (**2**)^{19,20} and aza crown (**3**) were synthesized, according to the Figure 1, based on the published procedure²⁰. Lariats were prepared from the reaction of **3** and isocyanates (isothiocyanates) in CH_2Cl_2 in the presence of Et_3N in room temperature for 24 hours. All of the products recrystallized in chloroform and their IR, ^1H NMR, ^{13}C NMR and Mass spectra were obtained and showed correct structures. Their elemental analyses showed desired proportions of elements.

Figure 1. SEM images of **3**

Scanning electron microscopy (SEM) images of macrocycles (**3** and **8**) were obtained and showed their structures in micro and nano scales as disc and fibrous structures (Schemes 1 and 2). Urea and thiourea functional groups in molecules spread the hydrogen bondings in the crystal structure and create flatten and rigid structures, these phenomena led to self-assemble and high organized structures^{21,22}. Urea and thiourea groups interact with other molecules and in this conditions intramolecular hydrogen bonding is weaker than intermolecular hydrogen bondings^{21,22}. According to the Schemes (1 and 2) phenyl as a side arm led to a flate and rigid structures and show the disc like structure of aggregated molecules. In all, the resonance between phenyl and thiourea led to a flatten structure in that region of molecule and in comparison between **3** and **8** because of the presence of this group, **8** is more flattened and rigid than **3** and intermolecular hydrogen bonding is stronger than **3**. The more aggregated structures resulted from the stronger intermolecular hydrogen bonding and weaker intramolecular hydrogen bonding²³. On the other hand, the phenyl group may lead to the π - π interactions and more aggregations²³.

Scheme 1. Synthesis of macrocycle (**3**)

Scheme 2. Synthesis of lariats (8-11)

Figure 2. SEM images of 8

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