SYNTHESIS OF SYDNOQUINOXALINES AND BIS(SYDNONYLPHENYL)UREA

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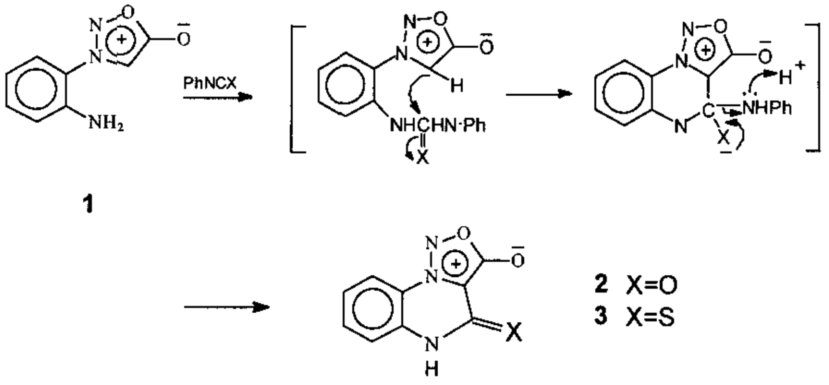
Abstract- Sydno[3,4-*a*]quinoxalin-4-one (**2**) and -4-thione (**3**) were prepared directly from 3-(o-aminophenyl)sydnone (**1**) with phenyl isocyanate, 1,1'-carbonyl diimidiazol ($CoIm_2$) and phenyl isothiocyanate respectively in good yield. *N,N'*-Bis[o-(3-sydnonyl)phenyl]urea (**4**) was also obtained under slightly different conditions between **1** and $CoIm_2$.

INTRODUCTION

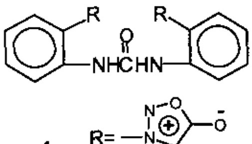
Sydnones have been the most extensively studied heterocyclic mesoionic system. However, prior to the review by Ohta and Kata in 1969,[1] no fused sydnones have been reported. Fused sydnones have been synthesized from the o-aminophenylsydnone (**1**) by treatment with some appropriate reagents. These can be seen in the synthesis of sydno[3,4-*a*]quinoxalin-4-one,[2,3] sydno[3,4-*a*]quinaxaline,[2,4] and [1,2,3]oxadiazolo[3,4-*a*][1,2,4]-benzotriazinium-3-olate.[2]

RESULTS AND DISCUSSION

The synthesis of fused sydnones in this report was based upon the addition of an electrophilic centre to the amino nitrogen atom of o-aminophenylsydnone (**1**). The adduct may then react with the C_4 atom of the sydnone ring to give the desired product. In this regard, phenyl isocyanate, $CoIm_2$ and phenyl isothiocynate were chosen in consideration of the reactivity with amino group and the commercial availability of these reagents, since resulting intermediates formed were anticipated to be converted into **2** or **3** by the subsequent cyclization.



Reaction of **1** with phenyl isocyanate yielded **2** *via* an intermediate, *N*-[o-(3-sydnonyl)phenyl]-*N'*-phenylurea (**5**). In the analogous reaction with phenyl isothiocyanate, attempts were failed to isolate the thio-intermediate. The product (**2**) obtained, was identified by comparing with an authentic sample prepared by the method of Coburn and O'Donnell.[2] The reactions of **1** with $CoIm_2$ yielded **2** and *N,N'*-bis[o-(3-sydnonyl)phenyl]urea (**4**). An isocyanate intermediate (**6**) would react with **1** to afford **4** and intramolecular cyclization of **6** gave **2**.



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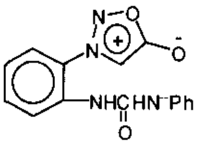

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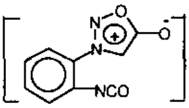

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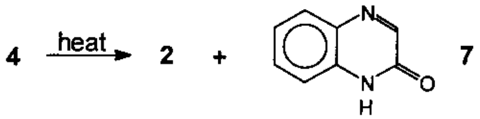
The consistency of the main product (**4**) and by-product (**2**) in different runs of the reaction of **1** with various excess amount of $CoIm_2$ heating in toluene has suggested that the formation of **2** was much less in favor than the reaction of **1** with **6**. However, over 90% yield of **2** has been achieved by adding the solution of **1** dropwise into a hot solution of $CoIm_2$. Decomposition of **4** occurred at 210 °C to give **2** and 2-quinoxalinone (**7**). The latter was also found to be the main product in pyrolysis of **1**. The structure of **7** was confirmed by its melting point (mp 271 °C; lit., 271 °C) and uv spectrum reported[5] as well as the spectral data.



EXPERIMENTAL

N-[o-(3-Sydnonyl)phenyl]-*N'*-phenylurea (5)

A mixture of 3-(o-aminophenyl)sydnone (**1**) (0.5 g, 0.0028 mol) and phenyl isocyanate (0.35 ml, 0.0032 mol) in dry benzene (10 ml) was refluxed for 2 h and then cooled to precipitate colourless amorphous solid, which was washed with ether (10 ml). Recrystallization from ethanol yielded colourless powders of **5** (0.65 g, 74%), mp 178-179 °C; ir 3640m, 3140w, 1745s, 1705s, 1600m, 1540m, 1530m, 1520m, 1500w, 1445m, 1350w, 1320w, 1305m, 1265w, 1245m, 1205m, 1165m, 940w, 860w, 755m, 730w, 720w cm^{-1}; ^{1}H nmr (DMSO-d_6, 60 MHz) δ 9.40(s, 1H), 7.00-8.43(m, 11H); Anal. Calcd for $C_{15}H_{12}N_4O_3$: C, 53.08; H, 2.41; N, 20.53; ms (m/z 296). Found: C, 52.89; H, 2.27; N, 20.51; ms (m/z 296).

Sydno[3,4-*a*]quinoxalin-4-one (2)

(a). Compound (**5**) (0.5 g, 0.00246 mol) was refluxed in toluene (10 ml) for 4 h in the presence of pyridine (1 ml). After cooling, the contents were filtered and the residue was washed with ether (10 ml) to yield a colourless amorphous powders (0.2 g). Colourless white solid of **2** was obtained in 0.17 g (50%), after recrystallization from ethanol, mp 305 °C (decomp.)(lit.,[2] mp 306 °C decomp.); which was also confirmed by comparing the ir with that of an authentic sample.[2]

(b). A solution of 3-(o-aminophenyl)sydnone (**1**) (0.5 g, 0.0028 mol) in dry toluene (25 ml) was added dropwise, over a period of 1 h, into a hot solution of 1,1'-carbonyldiimidiazol (0.6 g, 0.0037 mol) in dry toluene (10 ml) at 100 °C. After cooling and filtering, a colourless solid was obtained, which was recrystallized from ethanol to give **2** (0.52 g) in 91.5% yield.

Sydno[3,4-*a*]quinoxalin-4-thione (3)

A mixture of 3-(o-aminophenyl)sydnone (**1**) (1.0 g, 0.0057 mol), phenyl isothiocyanate (1.5 ml, 0.0113 mol) and pyridine (0.5 ml) in dry benzene (10 ml) was refluxed for 4 h with stirring and then cooled. The resulting solid was collected and washed with ether (10 ml) to yield a yellow amorphous solid (0.6 g). The crude product was recrystallised from ethanol to give light orange needles of **3** (0.56 g, 47%), mp 254 ^{o}C (decomp.); ir (nujol) 3210w, 3180w, 3120w, 1750s, 1600m, 1530m, 1430m, 1360m, 1280m, 1250w, 1180w, 1140w, 1120m, 1020m, 890w, 845w, 740w, 720w cm^{-1}; ^{1}H nmr (DMSO-d$_6$, 60 MHz) δ 7.1-8.2(m); Anal. Calcd for $C_9H_5N_3O_2S$: C, 49.31; H, 2.28; N, 19.18; ms(m/z 219). Found: C, 49.45; H, 2.21; N, 19.46; ms(m/z 219).

N,N'-Bis[o-(3-sydnonyl)phenyl]urea (4)

A mixture of 3-(o-aminophenyl)sydnone (**1**) (0.5 g, 0.0028 mol) and 1,1'-carbonyldiimidiazol (0.5 g, 0.008 mol) in dry toluene (15 ml) was heated for 1 h at 100 ^{o}C. The content was cooled and filtered. Colourless precipitate obtained was crystallized from DMSO/EtOH mixture to give colourless powders of **4** (0.43 g, 80%), mp 210 ^{o}C (decomp.); ir (nujol) 3345w, 3140w, 1756s, 1731m, 1710s, 1607s, 1550m, 1362m, 1302s, 1257w, 1216w, 1161w, 1079w, 939m, 845w, 752m, 732m cm^{-1}; ^{1}H nmr (DMSO-d$_6$, 90 MHz) δ 8.82(b)(disappeared after D_2O exchange), 8.07-7.36(m); ^{13}C nmr (DMSO-d$_6$) 172.89(s), 165.48(s), 136.97(s), 136.81(d), 130.52(d), 128.95(d), 128.84(d), 102.62(d); Anal. Calcd for $C_{17}H_{12}N_6O_5$: C, 53.68; H, 3.18; N, 22.09; ms (FAB) (m/z+1 381). Found: C, 53.53; H, 3.04; N, 22.35; ms (m/z+1 381).

Pyrolysis of *N,N'*-bis[o-(3-sydnonyl)phenyl]urea (4)

N,N'-Bis[o-(3-sydnonyl)phenyl]urea (0.1 g, 0.00026 mol) was placed in a test tube fitted with a cold finger. The content was heated to 210 ^{o}C for 20 min, greenish crystals collected from the the wall of the test tube and the cold finger were identified as 2-quinoxalinone (**7**) (0.009 g, 24%) (all spectral data matched with those reported; mp 271^{o}C; lit., mp 271^{o}C).[5] The residue was triturated in small amount of ether and the solid obtained was then crystallized from ethanol to give colourless solid of sydno[3,4-*a*]quinoxalin-4-one (**2**) (0.023 g, 42%).

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