SYNTHESIS OF BISSYDNO[3,4-*a*:4',3'-*c*]QUINOXALINE: A HETEROAROMATIC FUSED-RING BISMESOIONIC SYSTEM

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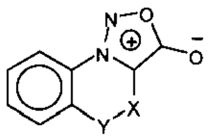
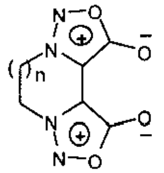
Abstract -The synthesis of 1,2-di(sydnonyl)benzene (**7a**) and its conversion to the heteroaromatic fused-ring bismesoionic system, bissydno[3,4-*a*:4',3'-*c*]-quinoxaline (**3**) have been reported.

INTRODUCTION

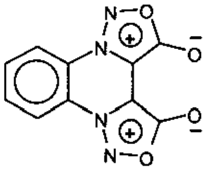
Although a large number of monocyclic sydnones are known,[1] derivatives containing fused-rings, especially those with the fused-ring aromatic or heteroaromatic are much less common, being mainly sydnoquinoxaline (**1a**)[2-4] or sydnobenzotriazine (**1b**)[3] systems Whilst the literature contains a variety of bissydnones in which the individual mesoionic rings are joined through a series of intermediate groups, the only fused-ring examples are those recently reported by Tien and Lee[5] in which the intermediate ring (**2**) is fully saturated. We now report here the synthesis of the novel compound (**3**), which we believe to be the first heteroaromatic fused-ring bismesoionic system.



1a (X-Y)=(-NH-CO-)
b (X-Y)=(-N=N-)



2a n=1
b n=2



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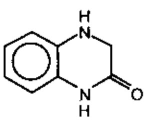
RESULTS AND DISCUSSION

The potential of compounds with two adjacent mesoionic rings as precursors to the required polycyclic systems prompted us to undertake the synthesis of the hitherto unknown 1,2-di(3-sydnonyl)benzene (**7a**). In the 1,4-di(3-sydnonyl)benzene[6] and the 1,3,5-tri(3-sydnonyl)benzene[7], the functional groups are sufficiently far apart to allow the simultaneous formation of the sydnone rings from 1,4-diaminobenzene and 1,3,5-triaminobenzene respectively. When this approach was attempted with 1,2-diaminobenzene, reaction with bromoacetic acid, produced only 3,4-dihydro-2(1*H*)-quinoxalone (**4**), none of the required 1,2-diglycylbenzene (**5**; R=CH_2CO_2H) being obtained, whilst the attempted synthesis of 1,2-dicyanomethylaminobenzene (**5**; R=CH_2CN) using formaldehyde bisulphite according to the procedure of Yashunskii *et al.*[6] failed to give any recognisable product. In spite of the apparent simplicity of this route, the proximity of the functional groups prevented the simultaneous formation of the mesioionic rings and led to the lengthier alternative of constructing the second mesoionic ring on to a pre-formed sydnone derivative, an approach successfully applied to the synthesis of the heteroaromatic **1a** and **1b** systems.[2-4]

Refluxing 3-(2-aminophenyl)sydnone (**6a**) with an equimolar quantity of sodium bromoacetate in aqueous solution produced the *N*-[2-(3-sydnonyl)phenyl]glycine (**6b**). Nitrosation of **6b** to the *N*-nitrosoglycine (**6c**), followed by cyclodehydration with trifluoroacetic anhydride yielded the required 1,2-di(3-sydnonyl)benzene (**7a**) in an overall yield of 15%. In addition to satisfactory elemental and spectral data for **7a**, the identity was further confirmed by the participation of both mesoionic rings in 1,3-dipolar cycloaddition with dimethylacetylene dicarboxylate to produce the bispyrazole derivative (**8**).

Attempted synthesises of mercuric chloride derivative of **7a** were failed. This inablity to prepare the required precursor for coupling and cyclization of the two sydnone nuclei with $LiPdCl_3$-$CuCl_2$, according to Tien and Lee in the synthesis of **2**,[5] forced an alternative approach in which the dibromo compound (**7b**) was used.

Bromination of **7a** by reaction with bromine in glacial acetic acid in the presence of sodium acetate at 15 °C gave the dibromo derivative (**7b**), which on heating with copper powder in DMF at 120 °C for 6 h gave a modest yield of the required bissydno[3,4-*a*:4',3'-*c*]quinoxaline (**3**).



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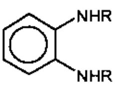

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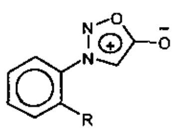
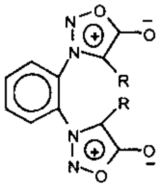
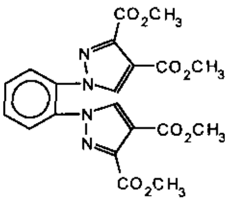


6a $R=NH_2$
b $R=NHCH_2CO_2H$
c $R=\underset{NO}{N}CH_2CO_2H$



7a R=H
b R=Br



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The prominent parent molecular ion of 3 exhibited facile loss of two NO fragments followed by the consecutive loss of two CO fragments, a clear indication of the disintegration of two sydnone rings.[8] Further structural confirmation was provided by elemental and spectral data, all were in good accordance to the structure (3).

EXPERIMENTAL

N-[2-(3-Sydnonyl)phenyl]glycine (6b)

3-(2-Aminophenyl)sydnone (5.0 g, 0.028 mol) was mixed with a solution of sodium bromaoacetate (4.6 g, 0.032 mol) in water (50 ml) and the mixture was refluxed for 3 h. The contents of the flask were cooled, filtered and the residue was treated with 5% ammonia solution, with cooling in ice and stirring, to about pH 10. Stirring was continued for 15 min, then the residue was filtered to give the unreacted sydnone (1.5 g, 30%). The combined filtrates were acidified with dilute hydrochloric acid, with cooling in an ice bath, to about pH 2. The precipitate formed was collected, washed with water and dried to give **6b** (4.0 g, 60%). Brown crystals were obtained after crystallisation from ethanol, mp 192 °C; ir (nujol) 3350w, 3100w, 1730s, 1700s, 1600s, 1560m, 1500m, 1390m, 1270s, 1220s, 1070w, 1010w, 960m, 940m, 890m, 760s, 730s cm^{-1}; ^{1}H nmr (DMSO-d$_6$, 60 MHz) δ 7.25-7.55 (m, 3H), 6.6-6.9 (m, 2H), 6.1-6.35 (t, 1H, J=6.0 Hz), 3.9-4.0 (d, 2H, J=6.0 Hz); Anal. Calcd for $C_{10}H_9N_3O_4$: C, 51.07; H, 3.85; N, 17.86; ms (m/z 236). Found: C, 50.59; H, 3.87; N, 17.85; ms (m/z 236).

N-Nitroso-*N*-[2-(3-sydnonyl)phenyl]glycine (6c)

A solution of *N*-[2-(3-sydnonyl)phenyl]glycine (4.0 g, 0.017 mol) in 36 N sulphuric acid (20 ml) was cooled in an ice-bath. Finely powdered sodium nitrite (2.0 g, 0.029 mol) was added with stirring over 15 min and the stirring continued at 0 °C for a further hour, then the mixture was poured on to crushed ice (100 g) with vigorous stirring. The sticky brown substance was separated and triturated under ice to give a brown amorphous solid which was separated, and dried to afford the crude nitrosoglycine (2.0 g, 44.5%), mp 120 °C (decomp.). Light brown crystals were obtained after crystallisation from aqueous ethanol, mp 140-141 °C (decomp.); ir (nujol) 3140w, 1740s, 1690s, 1500w, 1290w, 1250w, 1210m, 1190m, 1110m, 1080m, 1010w, 950s, 880m, 760s, 730m cm^{-1}; Anal. Calcd for $C_{10}H_8N_4O_5$: C, 45.46; H, 3.05; N, 21.21. Found: C, 45.40; H, 2.93; N, 21.33.

1,2-Di(3-sydnonyl)benzene (7a)

Finely powdered nitroso compound **(6c)**, (2.0 g, 0.0075 mol) was suspended in dry ether (20 ml). The mixture was cooled in an ice bath with stirring and to which trifluoroacetic anhydride (2 ml, 14 mmol) in dry ether (5 ml) was added dropwise. After addition was completed, stirring was continued for 1 h at 0 °C and a further 4 h at room temperature. The precipitate was collected and washed with saturated sodium bicarbonate solution (20 ml). Light yellow crystals of **7a** (1.0 g, 53.5%) were obtained after recrystallisation from DMSO/EtOH mixture, mp 229-232 °C (decomp.); ir (nujol) 3130m, 1750s, 1360m, 1250w, 1230m, 1170m, 1080m, 1050m, 970w, 950s, 860s, 780s, 730s, 715m cm^{-1}; ^1H nmr (DMSO-d_6, 60 MHz) δ 8.1 (s, 4H), 7.6 (s, 2H); Anal. Calcd for $C_{10}H_6N_4O_4$: C, 48.79; H, 2.45; N, 22.76; ms (m/z 246.). Found: C, 48.49; H, 2.25; N, 22.54; ms (m/z 246).

1,2-Di[3-(4-bromosydnonyl)]benzene (7b)

The bissydone (7a)(1.0 g, 0.0043 mol) was mixed with fused sodium acetate (2.0 g, 23.5 mmol) in glacial acetic acid (40 ml). The contents of the flask were kept at 15 °C, and stirred whilst a solution of bromine (2.0 g, 12.5 mmol) in glacial acetic acid (10 ml) was added dropwise. Stirring was continued for a further 2 h at same temperature and then poured into cold water (500 ml). The precipitate was filtered off at the pump and washed with distilled water (20 ml). Crystallisation from methanol afforded brown crystals of **7b** (0.7 g, 46%), mp 162-163 °C (decomp.); ir (nujol) 1750s, 1200m, 1010s, 975w, 780s, 720w, 710w cm^{-1}; ^1H nmr (DMSO-d_6, 60 MHz) δ 8.3 (s); Anal. Calcd for $C_{10}H_4N_4O_4Br_2$: C, 29.72; H, 1.00; N, 13.86; ms (m/z 406, 404, 402). Found: C, 30.03; H, 1.16; N, 13.86; ms (m/z 406, 404, 402).

Bissydno[3,4-a:4',3'-c]quinoxaline (3)

1,2-Di[3-(4-bromosydnonyl)]benzene (0.3 g, 0.00074 mol) was mixed with cupper powder (0.36 g) in DMF (10 ml). The mixture was heated at 110 °C with stirring for 3 h, then another portion of cupper powder (0.63 g) was added and kept at the same temperature for a further 3 h. The contents of the flask were filtered and the residue was extracted twice with hot acetone (15 ml). The combined extracts and filtrate were kept in the refrigerator for 48 h to give pale orange crystals of **3** (0.0175 g, 10%). A further portion of brown powder (0.01 g, 6%) was obtained after evaporation of the solvent to one third of its original volume. Pale orange crystals were obtained after crystallization from a DMF/acetone mixture, mp 284 ^{o}C (decomp.); ir (nujol) 1775s, 1500w, 1400w, 1280m, 1170w, 980m, 965m, 795m, 710w cm^{-1}; ^{1}H nmr (DMSO-d_6, 60 MHz) δ 8.05-8.3 (m, 2H), 8.4-8.65 (m, 2H); Anal. Calcd for $C_{10}H_4N_4O_4$: C, 49.19; H, 1.65; N, 22.95; ms (m/z 244.). Found: C, 49.00; H, 1.59; N, 22.93; ms (m/z 244).

1,2-Di[1-(3,4-dimethoxycarbonyl)pyrazol]benzene (8)

1,2-Di(3-sydnonyl)benzene (0.35 g, 0.0014 mol) was added to a solution of dimethyl acetylene dicarboxylate (0.404 g, 0.00284 mol) in xylene (10 ml). The mixture was heated for 6 h at 120 ^{o}C, filtered whilst hot and the filtrate was chilled to give a pale yellow solid which was collected and dried to give the crude product of **8** (0.3 g, 50%). Light yellow crystals were obtained after recrystallisation from EtOH, mp 173-174 ^{o}C; ir (nujol) 3120w, 1730s, 1530m, 1480m, 1290s, 1240s, 1160w, 1080s, 965m, 830w, 790w, 770s, 765w cm^{-1}; ^{1}H nmr (DMSO-d_6, 60 MHz) δ 8.5 (s, 1H), 7.8 (s, 2H), 3.75 (s, 6H); Anal. Calcd for $C_{20}H_{18}N_4O_8$: C, 54.30; H, 4.10; N, 12.66; ms (m/z 442.). Found: C, 54.00; H, 3.94; N, 12.36; ms (m/z 442).

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