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Synthesis and resolution of 1,11-diamino-dibenzo[d,f][1,3]dioxepine: A route to new asymmetric ligands and their complexes

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ABSTRACT

Reaction of 2-iodo-3-nitrophenol with methylene iodide and Ullmann intramolecular coupling of the produced 1,1'-[methylenebis(oxy)]bis[2-iodo-3-nitro]benzene afforded 1,11-dinitro-dibenzo[d,f] [1,3]-dioxepine, characterized by single crystal X-ray analysis. The title diamine was obtained by reduction of the nitroderivate with hydrazine hydrate. Resolution of the enantiomers of the novel C₂-symmetric ligand can be easily obtained by use of tartaric acid. A test on the coordinating ability of the diamine has produced a complex examined by X-ray diffraction analysis.

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The attainment of new asymmetric ligands is the subject of continuous research effort, because of the high specificity displayed by these molecules in inducing chiral discrimination in asymmetric syntheses. In this field atropoisomeric ligands attract quite a relevant interest [1].

This investigation deals with dibenzo[d,f][1,3]dioxepine derivatives (**doxp**-2D, Fig. 1) disubstituted in positions 1,11 with groups bearing D donor groups.

As for the choice of this subject we note: (i) it could be observed that the coordinative environment offered by the **doxp** ligands is substantially the same of that of the corresponding C₂-symmetric unbridged bi-arene derivatives. However, the differences in the residual part of analogous molecules are expected to be responsible of significant variations of stereoselective ability [2]. For instance, the more rigid **doxp** core appears more suited to prompt chelation than a simple diaryl central moiety in case the two donors are different [3]. (ii) Although the preparation of some **doxp** type ligands such as **doxp**-2PPh₂ [4], and their use in catalysis are known by far, the important [5] diaminic $(D = NH_2)$ environment largely useful for the attainment of catalytic complexes has not yet been described for doxp type compounds. (iii) doxp-2NH₂ is a most suitable starting material for the synthesis of the di-iodide (D = I), a choice key intermediate for a variety of conceivable doxp ligands.

The synthesis of the diamine is shown in Fig. 2 [6].

The starting 2-iodo-3-nitrophenol was previously obtained from commercial 2-amino-3-nitrophenol according to a known procedure [7]. Reaction with methylene iodide in presence of potassium carbonate afforded 1,1'-[methylenebis(oxy)]bis[2-iodo-3-nitro]benzene [8] that underwent intramolecular coupling prompted by activated copper bronze in dimethylformamide to give **doxp**-2NO₂ [9].

In addition to the analytical and spectroscopic characterization performed on all new compounds, in the case of **doxp**-2NO₂, taking also in count the paucity of structural characterization data for diazepines, the molecular structure was determined by single crystal X-ray diffraction. Single crystals, suitable for X-ray analysis, were obtained from a methyl cyanide solution by slow evaporation at room temperature [10]. The compound crystallizes in the monoclinic C2/c group with one half molecule in the independent unit. The molecule is C₂ symmetric, being located in the 4e Wyckoff position on the binary axis at (0, y, 1/4). The molecular structure is shown in Fig. 3. Bond distances and angles are in agreement with those displayed by the only X-ray previously characterized 1,11disubstituted diazepine [11]. The O-CH₂-O etheral bridge allows a moderate degree of flexibility to the molecule. The diphenyl group is not planar $(C6-C7-C7^{i}-C6^{i}=47.7(7)^{\circ}, i=-x, y, -z+1/2)$ and the deviation from coplanarity is in the range found in similar compounds [12]. The nitro group is in plane with the attached phenyl ring (distance N1···N1^{*i*} = 3.040(6) Å, *i* = -x, *y*, -z + 1/2) and is involved in weak intermolecular C-H···O interactions in the crystal packing.

According to a few non-optimized preliminary tests the reduction of **doxp**-2NO₂ to **doxp**-2NH₂ can be effected [13] with N₂H₄·H₂O in presence of FeCl₃ on carbon. The diamine can be easily recovered from the reaction mixture by removing solids on a filter and evaporating the solvent from the mother liquor. The residue is

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Fig. 1. General formulae of doxp-2D.

extracted with diethyl ether and addition of gaseous HCl affords precipitation of fairly pure diamine hydrochloride.

The synthesis of a platinum complex was attempted by reaction of the diamine with $(Me_2S)_2PtMeCI$ [14]. The X-ray analysis on a single crystal obtained from methanol solution by slow solvent evaporation displayed the molecular structure shown in Fig. 4.

According to the present X-ray analysis [15], the complex is formed by centrosymmetric dimers with two dimethylsulfide moieties as the Pt-bridging groups. Each diamine acts as bidentate ligand towards two Pt atoms. The two Pt atoms, whose square planar coordination environment is completed by a methyl and a dimethylsulfide group, are located up and down with respect to the mean plane of the ligand and are at 2.99 Å distance from each other, which is consistent with literature data for amido-bridged Pt complexes [16].

A rough resolution of the diamine was accomplished very simply by use of tartaric acid [17]. In fact, addition in methanol solution of $\frac{1}{2}$ equimolar amount of (+)-tartaric acid, slow removal of solvent and extraction of the microcrystalline residue with Et₂O afforded (-)-**doxp**-2NH₂ ([α]_D = -19.6, in diethyl ether at 27 °C). After 2 h at 27 °C the specific rotation had lowered to 20% of the initial value. No attempt was made to recrystallize the tartrate (a 1:1 acid/base associate, according to NMR) or to assess the optical purity of the diamine.

Further work is in progress, mainly on regard of applications of metal complexes of doxp-2NH₂ and of N-substituted derivatives of it.

Supplementary material

CCDC 749894 (**doxp**-2NO₂) and CCDC 752587 (complex) contain the supplementary crystallographic data for this paper. These



Fig. 2. Synthetic pathway for the attainment of doxp-2NH₂.



Fig. 3. ORTEP view of doxp-2NO₂ with ellipsoids drawn at 30% probability level (i = -x, y, -z + 1/2).



Fig. 4. Ortep diagram of the platinum complex. Thermal ellipsoids are drawn at 30 % probability level. H atoms are omitted for clarity.

data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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- [6] Unless otherwise specified, all experiments were performed under nitrogen using standard Schlenk techniques. All solvents were reagent grade, and, if necessary, were dried by standard methods. The synthesis of 2-iodo-3-nitrophenol from commercial 3-nitrophenol was made according to previous work [7]. The ¹H and ¹³C NMR spectra were recorded on Varian XL 200 MHz and Gemini 300 MHz instruments. ¹H [¹³C] chemical shifts are referenced using the residual solvent peak at δ 7.26 [77.0] for CDCl₃, 2.49 [39.4] for DMSO-d6 and 2.05 [20.8] for acetone-d6. Routine coupling constants are not listed. For describing multiciplities the following abbreviations were used: s, singlet; d, doublet, dd, double doublet; t, triplet; app, apparent; m, multiplet; br, broad. Mass spectrometry was performed using a Shimadzu GC-MS QP-5000 equipped with silicone column instrument.
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- [8] 1,1'-[Methylenebis(oxy)]bis[2-iodo-3-nitro]benzene. 2-lodo-3-nitrophenol (60 g, p.m. 265.01, 0.226 mol), potassium carbonate (125 g, p.m.138.21, 0.904 mol), methylene iodide (30.49 g, pm 269.85, 0.113 mol) were added to magnetically stirred cold dry DMF (300 mL). Stirring of the red mixture was continued at r.t. during 48 h. The most of DMF was removed in vacuo (bath temperature ca. 50 °C). Ice (200 g) and water (50 mL) were added with stirring. A yellow solid precipitated and was collected after 1 h on a Gooch filter, washed with water and dried in air. The crude product was recrystallized from methylene chloride/methanol: a crop of 37.5 g was recovered. (p.m. 542.03, 61.2% yield). ¹H NMR (CDCl₃) δ = 7.44–7.51 (m, 6H), 5.94 (s, 2H). ¹³C NMR (CDCl₃) δ = 157.1, 155.9, 130.6, 119.4, 117.9, 92.1, 81.5. Elemental analysis, calcd. (%) for C₁₃H₈l₂N₂O₆: C 28.81, H 1.49, N 5.17. Found: C 28.96, H 1.59, N 5.08.
- [9] 1,11-dinitro-dibenzo[d,f][1,3]dioxepine. In argon atmosphere to a solution of 1,1'-[methylenebis(oxy)]bis[2-iodo-3-nitro]benzene (21.68 g, 40 mmol) in dry DMF (120 mL), stirred at 155 °C, activated copper bronze (Vogel, Practical Organic Chemistry, p. 323) (28 g) was added. A second aliquot of copper bronze (28 g) was added after 3 h and heating and stirring were continued for 16 h. The cooled mixture was filtered and the solvent was removed in vacuo to give a yellow brown residue. This was added to the copper containing solid and the combined solids were washed with water (100 mL), dryed in vacuo, and extracted with methylene chloride in a Soxlet apparatus. The solvent was available and the solvent was washed

with water (50 mL) and cold acetone (3 \times 15 mL) and dried. Yield 79% (9.8 g). Further purification of this fairly pure product can be accomplished by recrystallization from acetone. ¹H NMR (CDCl₃) δ = 8.15 (dd, 2H), 7.60 (m, 4H), 5.51 (m, 2H). ¹³C NMR (d6-DMSO) δ = 157.62, 152.16, 136.48, 133.20, 128.94, 127.36, 108.08. Elemental analysis, calcd. (%) for C₁₃H₈N₂O₆: C 54.18, H 2.80, N 9.72. Found: C 54.11, H 2.91, N 9.60.

- [10] Crystal data for **doxp**-2NO₂: C₁3H₈N₂O₆, M_r = 288.21, monoclinic, C2/c, Z = 4, plate shaped orange crystal (0.30 × 0.25 × 0.01 mm), a = 13.257(6) Å, b =9.366(3) Å, c = 10.198(4) Å, $\beta = 91.54(3)^\circ$, V = 1265.8(9) Å³, T = 173 K, $\rho_{calcd.} =$ 1.512 g/cm³, $\mu = 0.123$ mm⁻¹. Data were collected in flowing N₂ at 173 K on a Bruker–Nonius KappaCCD diffractometer (Mo Kα radiation, $\lambda = 0.71073$ Å, CCD rotation images, thick slices, φ scans + ω scans to fill asymmeryc unit). Semiempirical absorbtion correction (multi-scan SADABS) was applied. The structure was solved by direct methods (SIR 97 program [A. Altomare, M.C. Burla, M. Camalli, G.L. Cascarano, C. Giacovazzo, A. Guagliardi, A.G.G. Moliterni, G. Polidori, R. Spagna, J. Appl. Cryst. 32 (1999) 115]) and refined by the full matrix least-squares method (SHELX-97 package [G.M. Sheldrick, Acta Cryst. A 64 (2008) 112]) on F² against all independent measured reflections. Anisotropic thermal parameters were used for all non-hydrogen atoms. H atoms placed in calculated positions and refined by the riding method. Refinement converged to $R_1 = 0.0710$, $wR_2 = 0.1300$ [$I > 2\sigma(I)$]. 5722 reflections collected, 1452 unique [$R_{int} = 0.1071$], 96 parameters. Largest difference peak and hole: 0.253 and -0.238 eÅ³.
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- [12] From search of Cambridge Structural Database, CSD version 5.30 November 2008 F.H. Allen, Acta Cryst. B 58 (2002) 380.
- [13] 1,1'-Dibenzo[d,f][1,3]dioxepin-1,11-diyl-diamine. A mixture of FeCl₃·6H₂O (0.100 g, 0.37 mmol), active charcoal (1 g) and **doxp**-2NO₂ (2.88 g, 10 mmol) in methanol (50 mL) was refluxed for 10 min in argon atmosphere. To the refluxing mixture hydrazine hydrate (6.1 mL, 126 mmol) was added dropwise. Solids were separated by filtration on a small bed of Celite and washed with methanol. Washing was added to the mother liquor and the solvent was evaporated in vacuo to give a whitish residue. This crude diamine was extracted with diethyl ether (2 × 25 mL) and gaseous HCl was bubbled through the solution to precipitate faitly pure diamine hydrochloride. **dopx**-2NH₂ was obtained in 23% yield by dissolving the hydrochloride in methanol containing a slight excess of KOH, removing of solvent in vacuo and recovering the product with diethyl ether. Analytically pure product could be obtained by recrystallization from methanol. ¹H NMR: ($\Delta = 7.18$ (t, 2H), 6.63 (app. d, 4H), 5.47 (s, 2H). ¹³C NMR: $\delta = 154.2$, 144.19, 129.36, 113.44, 110.89, 102.40. *M*⁺ = 228. Elemental analysis, calcd. (%) for C₁₃H₁₂N₂O₂: C 68.41, H 5.30, N 12.27. Found: C 68.19, H 5.35, N 12.20.
- [14] A solution of **doxp**-2NH₂ (0.0228 g, 0.1 mmol) in diethyl ether (3 mL) was added with stirring to solid (Me₂S)₂PtMeCl (0.0369 g, 0.1 mmol). Stirring was continued for 20 h and the precipitate was collected by filtration, washed with 1 mL ether and dried. Recrystallization was attained by slow partial evaporation of solvent from a methanol solution and the precipitate resulted to be a mixture of different crystals. Manual separation of morphologically similar single crystals gave a small amount of homogeneous material, used for X-ray and ¹H NMR investigations. ¹H NMR (CDCl₃ cont. 10% CD₃OD.) δ = 6.4–6.7 (m, 12H), 5.48 (br s, 2H), 5.38 (br s, 2H), 2.05 (s, 6H, ³J_{Pt-H} = 20 Hz), 1.98 (s, 6H, ³J_{Pt-H} = 20 Hz), 0.18 (s, 12H, ³J_{Pt-H} = 8 Hz).
- [15] Many attempts to obtain single crystals of the complex resulted only in very small irregular shaped crystals. One of these, thought poor quality and weakly diffracting, allowed to solve the structure. Crystal data: $C_{34}H_{44}N_4O_4S_2Pt_4$, $M_r = 1417.19$, monoclinic, $P2_1/c$, T = 173 K, a = 18.826(4) Å, b = 9.512(3) Å,

c = 22.969(8) Å, *β* = 111.24(5)°, *V* = 3834(2) Å³, *Z* = 4, *ρ*_{calcd} = 2.455 g/cm³, *μ* = 14.699 mm⁻¹. Data were collected in flowing N₂ at 173 K on a Bruker-Nonius KappaCCD diffractometer (Mo Kα radiation, *λ* = 0.71073 Å, CCD rotation images, thick slices, *φ* scans + *ω* scans to fill asymmetryc unit). Semiempirical absorbtion correction (multi-scan SADABS) was applied. The structure was solved by direct methods (SIR 97 program [A. Altomare, M.C. Burla, M. Camalli, G.L. Cascarano, C. Giacovazzo, A. Guagliardi, A.G.G. Moliterni, G. Polidori, R. Spagna, J. Appl. Cryst. 32 (1999) 115]) and refined by the full matrix least-squares method (SHELX-97 package [G.M. Sheldrick, Acta Cryst. A 64 (2008) 112]) on F² against all independent measured reflections. Anisotropic thermal parameters were used for all non-hydrogen atoms. H atoms placed in calculated positions and refined by the riding method. Refinement converged to *R*₁ = 0.0785, *wR*₂ = 0.1265 [*I* > 2*σ*(*I*)]. 20,734

Pt1). The assignment of phases in the structure is largely dominated by the heavy atoms, so that light atoms were located with some difficulties in the difference Fourier maps. Constrains were introduced in the last stage of refinement to regularize the diphenyl group. ISOR instruction of SHELXL was also introduced for light atoms (C, O, N) to prevent negative *B* values in the anisotropic refinement.

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