Pergamon

Tetrahedron Letters, Vol. 35, No. 36, pp. 6745-6748, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $7.00+0.00

0040-4039(94)01410-8

The Preparation of Space-Separated Chelating Agents Based on the 3,6-Dipyridyl Pyridazine Ligand

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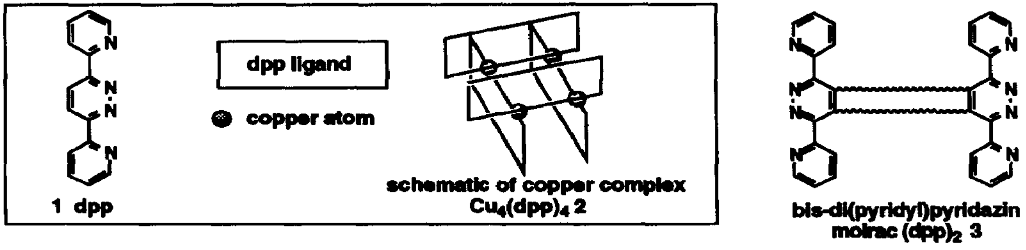
Abstract: Linear, bent, cavity and Z-shaped molracs of varying length are converted to end-functionalised bis-chelating agents 3 containing the 3,6-(di-2′-pyridyl)pyridazine ligand by reaction of their norbornenyl end-groups with 3,6-di-(2′-pyridyl)-*s*-tetrazine 4 followed by oxidation with DDQ, sometimes in a one pot reaction. New representative molracs as well as new chelating agents are described. Molecular mechanics (MM2) has been used to evaluate geometric parameters for these systems which display ligand separations from 6-21Å; however shorter or longer systems are possible.

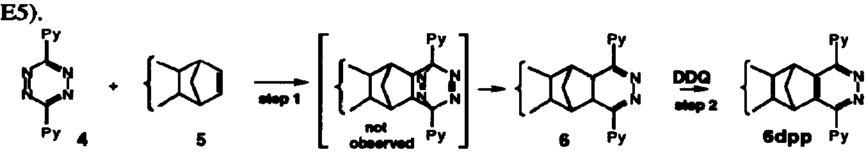
The 3,6-di-(2′-pyridyl)-pyridazine (dpp) **1**[1] is a recognised polydentate ligand which forms complexes with a range of metals.[2] Transition metals such as ruthenium form unsymmetrical 1:1-complexes with ligands containing the dpp chromophore. In these complexes dpp acts as a bidentate ligand where a pyridine nitrogen and one of the pyridazine ring-nitrogen atoms provide the donor sites. Steric crowding in these octahedral complexes stops the entry of the metal into the second available bidentate coordination site. In contrast, the tetrahedral geometry of copper is less sterically demanding and allows both coordination sites to be used. The copper complex **2** is particularly interesting as dpp can totally satisfy the coordination needs of the copper and so form the orthogonally stacked complex where four copper atoms are associated with four dpp ligands and each dpp ligand is itself linked to two copper atoms.[3] The high symmetry of **2** offered potential for aligning substituents attached to the dpp ligand; where bis-dpp molecules of type **3** as described herein are involved, this opens the way for producing new self-assembly systems with novel geometry.



Scheme 1

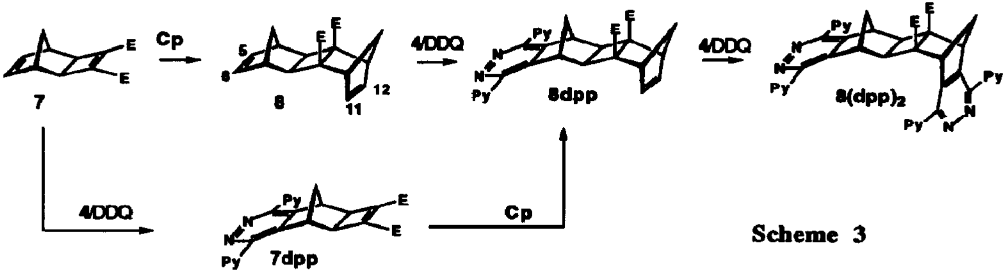
This communication describes the preparation of new rigid polydentate ligands where two dpp groups are space separated to form individual chelating centres within the same molecule of general structure **3**. By using molrac spacers[4] it has been possible to produce a new class of ligand, molrac(dpp)$_2$, where the two chelating groups can be space-separated (from 3-20Å in the present examples) and the interplanar angle between the pyridazine rings varied roughly from parallel, through orthogonal to fully opposed (see Table 1).

The basic reaction used for the synthesis of dpp ligands has been described[5] and here involves the reaction of the π-bond of the prototype end-terminal norbornene molrac **5** with 3,6-di-(2′-pyridyl)-s-tetrazine **4**[6] to form the dihydropyridazine **6** (Scheme 2) and its conversion to the molrac ligand **6dpp** by dehydrogenation with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ). This reaction was applied twice over to the molrac dienes **11**, **18-21** to produce the corresponding extended bis-ligands, molracs **11(dpp)$_2$**, **18(dpp)$_2$-29(dpp)$_2$** (see Table 1; E1-E5).



Scheme 2

The formation of bent bis-ligands can be illustrated by the preparation of molrac **8(dpp)$_2$** (Scheme 3) which takes advantage of the reverse electron-demand requirement of *s*-tetrazine **4**. Thus reaction of Smith's diester **7** with *s*-tetrazine gives a product where the norbornene π-bond alone is attacked; in the presence of DDQ the fused mono-ligand **7dpp**, m.p. 182 °C, can be formed in 90% yield and its structure has been confirmed by X-ray analysis (see Fig 1, below). Treatment of Smith's diester **7** with cyclopentadiene, on the other hand, has already been reported[4b] to occur specifically at the electron-deficient π-centre to form predominantly the bent adduct **8**. This adduct contains two norbornene π-bonds and shows site specificity in its reaction with *s*-tetrazine **4**; the $\Delta^{5,6}$ π-bond is preferentially attacked to form **8dpp** (also available from **7dpp** and cyclopentadiene). Reaction does occur at the $\Delta^{11,12}$ π-centre of **8dpp** under more forcing conditions and the bent bis-ligand **8(dpp)$_2$** can be isolated in good yield.



Scheme 3

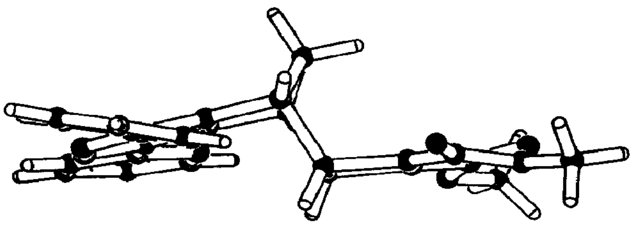
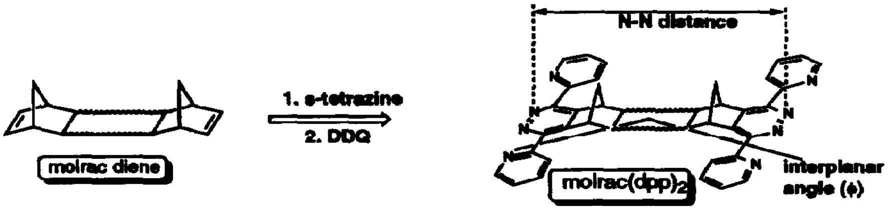
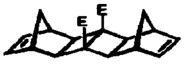
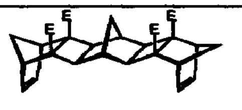
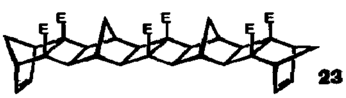
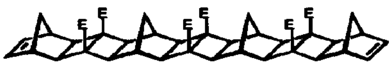
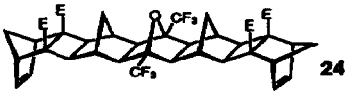
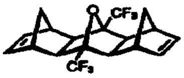
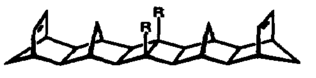
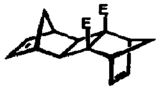


Fig 1. Pluton diagram of the fused molrac ligand 7dpp based on X-ray crystallographic data.

Table 1: New bis-ligands based on the dpp ligand

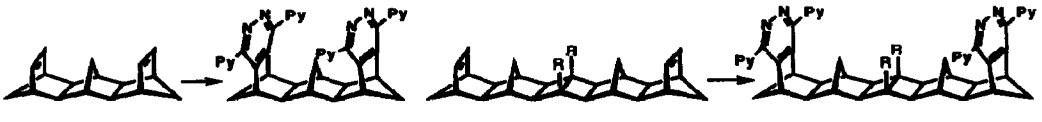


Exp no	starting molrac diene	distances/ angles* in molrac(dpp)$_2$	Exp no	starting molrac diene	distances/ angles* in molrac(dpp)$_2$
E1	 11^{4b}	11.04 +102.8	E7	 22^{4b}	6.58 -17.8
E2	 18^{4b}	15.86 +93.8	E8	 23	11.01 -27.4
E3	 19^{4b}	20.60 +84.4	E9	 24	9.78 -40.0
E4	 20^{11a}	10.20 +81.8	E10	 9^{7}	6.93 +25.0
E5	 21	13.62 +53.0	E11	 10 R=CH$_2$OAc	12.51 +32.0
E6	 8^{4b}	6.84 +72.6			

NOTE
The numbers in this table refer to the molrac diene. The related bis-ligands are given the diene number suffixed by (dpp)$_2$.
Physical properties given in ref 9 are related to this system of numbering.

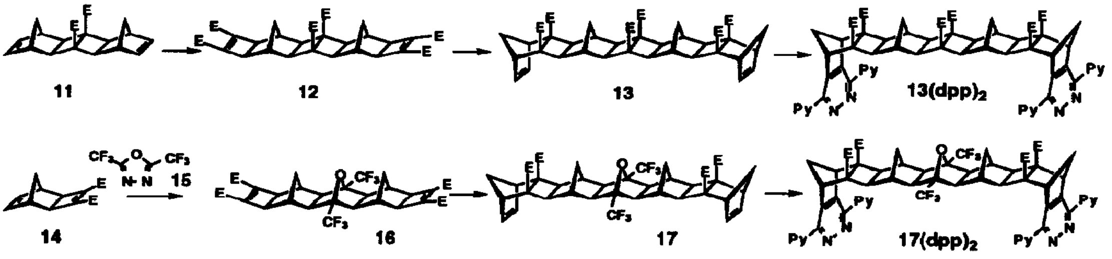
*N-N distances are given in Å and the interplanar angle in degrees. These were obtained using MM2 calculations (spartan √. 3 program). A positive angle implies divergence of the nitrogen-end of the pyridazine rings; a negative angle implies convergence.

The preparation of cavity bis-ligands has been approached using two protocols (Schemes 4 and 5), each of which starts from a bis-norbornene-ended molrac. In this way it is possible to develop the cavity arms so that they screen the upper or lower face of the molrac. Reaction of the known upward-facing molrac diene 9[7] as well as the stretched diene **10** made analogously to **9**, with the *s*-tetrazine **4** / DDQ reagents provided the corresponding bis-ligands **9(dpp)$_2$** and **10(dpp)$_2$** respectively (Table 1, E10, E11).



9 **9(dpp)$_2$** **10** R=CH$_2$OAc **10(dpp)$_2$** R=CH$_2$OAc

Scheme 4



Scheme 5

Preparation of downward-facing molrac bis-ligands is typified by the preparation of the bis-ligand **13(dpp)$_2$**. This involves conversion of the end-terminal norbornene π-bonds of molrac diene **11** to the bis-cyclobutene diester **12** by Ru-catalysed [2+2] cycloaddition of dimethyl acetylene dicarboxylate.[8] Subsequent [4+2] cycloaddition of cyclopentadiene onto **12** produces the doubly bent-adduct **13** as the major stereoisomer. Application of the *s*-tetrazine / DDQ sequence to **13** yields the molrac bis-ligand **13(dpp)$_2$** (see Table 1; E8).

The use of 1,3,4-oxadiazole **15** as a stereospecific coupling agent for linking norbornenes[9] opens an alternative avenue to molrac bis-ligands. Reaction of Smith's diester **7** with the 2,5-bistrifluoromethyl-1,3,4-oxadiazole **15**, another reverse electron-demand diene, forms the *exo,exo*-coupled product **16** where reaction has again occurred selectively at the norbornene π-bond. Reaction of **16** with cyclopentadiene produces the doubly bent-2:1-adduct **17** as the preferred product. Treatment of **17** with *s*-tetrazine **4** / DDQ yields the bis-ligand **17(dpp)$_2$**. The angle between the two ligand centres depends on the nature and the length of the spacer unit: the more norbornane compared to cyclobutane sub-units in the molrac, the greater the curvature of the spacer.[10] Thus the toe-in angle for bis-ligand **17(dpp)$_2$** at 40 deg is greater than that for bis-ligand **13(dpp)$_2$** at 27 deg, although each has a formal separation of 10σ-bonds. Calculated geometry for other bis-ligands is provided in Table 1.

Acknowledgements

We thank Dr. I.G. Pitt for conducting some of the initial experiments, Central Queensland University for research funding and the ARC for the award of a Senior Research Fellowship to RNW (1992-1996).

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8. All new compounds were characterised by elemental analysis (C,H,N)(often solvated) or high resolution mass spectrometry and exhibited ^1H and ^{13}C nmr spectra consistent with structure. **Compound number**, m.p. °C (yield %): **8dpp** 208-210 (95); **8(dpp)$_2$** 277-278 (53); **10(dpp)$_2$** 311-312 (25); **13(dpp)$_2$** >360 (44); **17(dpp)$_2$** >360 (40); **11(dpp)$_2$** 311-312 (60); **18(dpp)$_2$** 319-320 (34);**19((dpp)$_2$** 317-318 (60); **20(dpp)$_2$** 250-252 (80); **21(dpp)$_2$** >360 (76); **22(dpp)$_2$** 310-311 (60). Molrac dienes **13**, 252-254 (82); **16**, 303-304 (66); **17**, 243-245 (87).
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(*Received in UK* 8 *April* 1994; *revised* 20 *July* 1994; *accepted* 22 *July* 1994)