

Synthesis of Macrobicyclic Ligands containing Pyrazole Subunits: the *N,N'*-Bipyrazolyl Cryptand

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The pyrazolyl cryptands [bpz.bpz.bpz] (**1**) and [2.2.bpz] (**2**) have been obtained in a one-step, non high-dilution macrobicyclization reaction, from a 1,1'-bipyrazole derivative; similarly, tripodal ligands (**7**)—(**9**) with pyrazole structures are described.

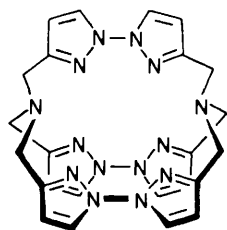
Macropolycyclic ligands incorporating heterocyclic subunits are of particular interest in co-ordination chemistry, since macrocycles having heteroatoms situated inside the rigid cavity display enhanced metal ion binding properties. In the 2,2'-bipyridine (bpy) and 1,10-phenanthroline (phen) series, macrobicyclic cryptands containing one ([2.2.bpy],¹ [2.1.phen],² [2.2.phen]²) or three ([bpy.bpy.bpy],² [bpy.bpy.phen],² [phen.phen.phen]^{2,3}) heterocyclic chains have been reported. These compounds can combine the 'cation inclusion' nature of cryptands with the photoactivity of metal complexes of polypyridine or phenanthroline ligands in electron- and energy-transfer processes.⁴

No similar examples of macrobicyclic cryptand structures have yet been described in the pyrazole series, despite the known ability of this heterocycle to bind diverse metal ions.⁵ We report herein the first examples of 1,1'-bipyrazolyl (bpz) cryptands, namely [bpz.bpz.bpz] (**1**) and [2.2.bpz] (**2**). Molecular models (Corey–Pauling–Koltun) revealed that these molecules are endowed with cavities somewhat smaller than their bipyridine analogues, but better adapted to form either

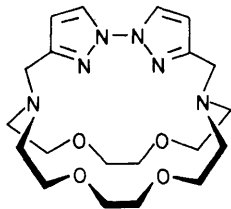
hexa- or octa-co-ordinate complexes, due mainly to the ease of twisting around the N–N bond in *N,N'*-linked biazoles.⁶

For the synthesis of (**1**), 3,3'-dimethoxycarbonyl-1,1'-bipyrazole (**3a**)⁷ was reduced to the corresponding bis-alcohol (**3b**) (LiAlH₄, tetrahydrofuran, 89%),[†] which was, in turn, transformed into the bis-bromomethyl derivative (**3c**) (PBr₃, diethyl ether, 76%). Reaction of (**3c**) with anhydrous NH₃ (Na₂CO₃, dry MeCN, 100 °C) afforded (**1**) in 19% yield. On the other hand, the reaction of (**3c**) with 1,7,10,16-tetraoxa-4,13-diazacyclo-octadecane (Merck's Kryptofix 22) under analogous conditions, gave [2.2.bpz] cryptand (**2**) in 56% yield. It is noteworthy that no high-dilution conditions were needed for the last, direct one-step macrobicyclization reaction yielding (**1**) from (**3c**), nor for the synthesis of (**2**). As for bpy and phen analogues,² this may result from both a templating effect of the sodium cation and from the rigidity of

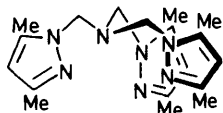
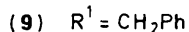
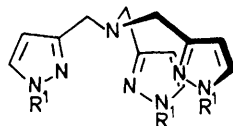
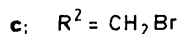
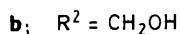
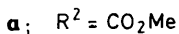
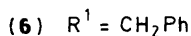
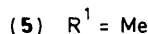
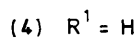
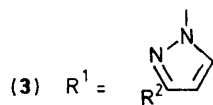
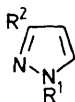
[†] Satisfactory elemental analyses, as well as n.m.r. (¹H and ¹³C) and mass spectra were obtained for all new compounds. (**1**) M.p. >250; (**2**) 225–227; (**7**) and (**8**) oils; (**9**) 93–95 °C.



[bpz . bpz . bpz]
(1)



[2 . 2 . bpz]
(2)



(10)

the bridges introduced. Nevertheless, no sodium cation was detected in a purified sample of (1), contrary to the result observed in the bpy and phen families.

In addition to the synthesis of macrobicycles (1) and (2), we have also prepared, by analogous routes, the tripodal pyr-

azolyl ligands (7)—(9) from the corresponding 1-substituted 3-pyrazolyl esters (4a)—(6a), in 35, 41, and 39% overall yields, respectively. A related pyrazolyl tripod (10) has been prepared by Bertini *et al.* from $N(CH_2Cl)_3$ and 3,5-dimethylpyrazole, and its Co^{2+} complex has been tested as a model for carbonic anhydrase.⁸ The synthesis of compounds like (7)—(9) is not limited to symmetrical pyrazoles, and allows for further structural variation, *i.e.*, the separation of two tripodal units by appropriate chains, joined together to form a large enough cryptand to accommodate two metal ions. These possibilities, and the complexation studies of (1) and (2), are being investigated, and will be published elsewhere.

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