Tetrahedron Vol. 48, No. 37, pp. 7863-7868, 1992
Printed in Great Britain

0040-4020/92 $5.00+.00

The Synthesis and Ligand Properties of N,N'-Polymethylene-Bridged Imidazole-2-thiones and Benzimidazole-2-thiones[1]

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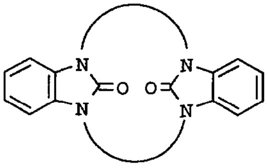
Dedicated to the finest heterocyclist and gentleman, Charles W Rees FRS, on his 65th birthday

(*Received in USA* 5 *August* 1992)

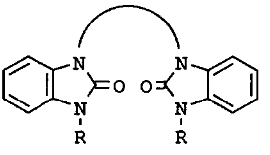
Abstract: A series of N,N'-polymethylene-bridged imidazole- and benzimidazole- 2-thiones have been made with the bridge containing 1 to 6 methylenes, the former by alkylation of N-methylimidazole by α,ω-dibromoalkanes followed by thiation with sulphur and the latter from the previously described bridged benzimidazolones by treatment firstly with phosphoryl chloride followed by thiourea. The bridged benzimidazolethiones formed complexes with mercury, palladium and copper salts but not with iron, cobalt, nickel, zinc, platinum, cadmium, silver or thallium. The imidazolethiones complexed with iron, cobalt, nickel, copper, zinc, tin, cadmium, palladium, platinum and silver salts.

Introduction

We have demonstrated previously the synthesis and value of 'crown benzimidazolones' such as (1)[2] and their acyclic analogues (2)[1] where the bridging chain was either a polymethylene or a polyether unit. This work was elegantly developed by Cram and his co-workers who engineered a range of cyclic ureide ligands with



(1)



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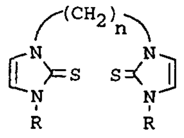
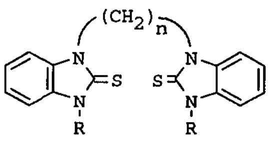


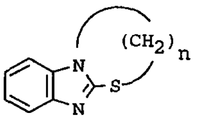
(3)

n = 1-10



(4)

n = 3-6



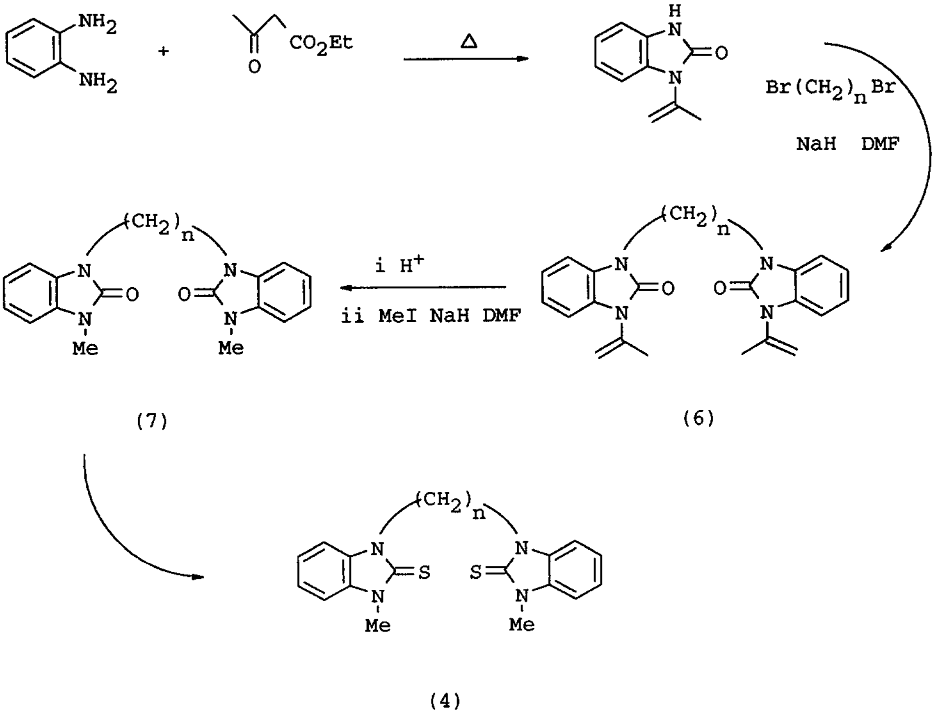
(5)

defined shapes and complexing properties[3]. We now describe the synthesis of α,ω-bis-(3-methylimidazole-2-thione-1-yl)alkanes (3) and their benzimidazole analogues (4) and a study of their ligand properties towards transition metals. Some of the acyclic series (2) showed remarkable specificity in their metal transport properties[1] (e.g. with n = 5 towards calcium ions). It was hoped that similar selectivity for transition metal ions would be shown with the thiones.

Synthesis of the Imidazole- and Benzimidazole-thiones (3 and 4)

The benzimidazoles (2) were prepared by treatment of readily available N-isopropenylbenzimidazolone (made from o-phenylenediamine and ethyl acetoacetate) with an α,ω-dibromoalkane, sodium hydride and dimethylformamide[1]. The isopropenyl group was easily cleaved with cold mineral acid. This approach is not feasible for the thione series due to the greater nucleophilicity of the sulphur atom, since the S,N-alkylated product (5) ensues[2a]. However the thiation of the bridged benzimidazolones made by the above method appeared a profitable approach (Scheme 1).

Preliminary experiments utilising phosphorus pentasulphide in pyridine proved totally ineffective and Lawesson's reagent gave incomplete thiation. However conversion of the benzimidazolones firstly into the benzimidazolium chlorides with phosphoryl chloride and then into the thiones using thiourea in ethanol proved effective. By this means the thiones (4) with n = 3-6 were obtained from the benzimidazolones (7) in yields of



Scheme 1

71-88%. The bridged benzimidazolone (7, n = 2) was incompletely transformed into the thione (4, n = 2) but the desired product was easily separated from the mixture.

N,N'-Dimethylimidazolethione has been synthesised by the alkylation of N-methylimidazole with methyl bromide in ethyl acetate followed directly by the action of sulphur and potassium carbonate in methanol[4]. Similar treatment of N-methylimidazole with α,ω-dibromoalkanes followed by the same thiating conditions gave the series of imidazole thiones (3). The overall conversions with n = 2-6 ranged from 61-85%. The monomethylene derivative gave a low yield (17%) of the corresponding thione. The application of this method to N-methylbenzimidazole using 1,5-dibromopentane gave the bridged benzimidazolethione (4, n = 5) in 20% yield.

Complex formation between the benzimidazolethiones (4) and transition metal salts

A preliminary study has shown that these thiones are effective ligands for a variety of transition metals. Thus mercury (II)salts, which are known to complex strongly with benzimidazolethione itself[5,6], form complexes with the whole range of thiones (4) . UV evidence indicates complex formation with salt : ligand ratios of both 1:1 and 1:2. Similar results were noted for palladium(II) and copper (II) salts a 1:1 ratio being preferred. No complex formation was observed with iron(III), cobalt(II), nickel(II), zinc(II), cadmium(II) or silver(I) salts.

Complex formation between the imidazolethiones (3) and transition metal salts

1,3-Dimethylimidazole is known to complex with cobalt, nickel and zinc salts[7]. The bridged thiones (3) gave precipitated complexes with distinct melting points with salts of these elements as well as with salts of iron(III), copper(II), cadmium(II), tin(II), palladium(II), platinum(IV) and silver(I). A 1:1 ratio was generally preferred

Full details of the complexation work will appear elsewhere including comments on the structure of the complexes and their uses in selective complexation.

Experimental

The general methods and equipment are as described in Part 5 of this series[1] in which also the synthesis of the benzimidazolones used in this work are described.

Preparation of benzimidazole-2-thiones (4).- The α,ω-(1-methyl-2-oxobenzimidazolin-3-yl) alkanes (7) were prepared as described previously[1]. **1,4-Bis (1-methyl-2-oxobenzimidazolin-3 -yl) butane** (83%) was obtained as colourless crystals from aqueous ethanol, m.p. 207°C. (Found: C,68.5; H,6.2; N,16.2%. $C_{20}H_{22}N_4O_2$ requires C,68.5; H,6.3; N,16.0%)

The benzimidazolone (7) (0.02mol) in phosphoryl chloride (10ml) was heated under reflux for 3h. The solvent was removed under reduced pressure and thiourea (5.0g) in ethanol (20mL) was added to the residue and the solution again refluxed for 1h. The reaction mixture was poured into water (100mL) and the crystalline precipitate was washed with water, air dried and recrystallised from methanol to give the thiones (4) the properties of which are recorded in Tables 1 and 2.

Table 1

Properties of the benzimidazolethiones (4)

Thione(4)	Yield	M.p.	Found(%)			Formula	Required(%)		
(n)	(%)	(°C)	C	H	N		C	H	N
3	86	167	62.0	5.6	15.3	$C_{19}H_{20}N_4S_2$	62.0	5.5	15.2
4	83	181	62.8	5.8	14.7	$C_{20}H_{22}N_4S_2$	62.9	5.8	14.7
5	88	150	63.6	6.2	14.3	$C_{21}H_{24}N_4S_2$	63.7	6.1	14.2
6	71	146	64.3	6.4	13.7	$C_{22}H_{26}N_4S_2$	64.4	6.4	13.7

The preparation of imidazole-2-thiones (3).- N-Methylimidazole (8.20g, 0.1mol) in ethyl acetate (10mL) was treated with the α,ω-dihaloalkane (0.05mol) and the mixture heated on a water bath for 1h. The crystalline mass was cooled, residual solvent decanted and sulphur (3.20g, 0.01mol), potassium carbonate (6.90g, 0.05mol) and methanol (100mL) added. This mixture was heated under reflux overnight and then poured into water (300mL) and the precipitate filtered. The product was recrystallised from either water (n = 2, 3 and 5), aqueous ethanol (n = 4 and 10), ethanol (n = 6) or methanol (n = 1) to give the products the properties of which are indicated in Tables 3 and 4.

Table 2

Spectral properties of the benzimidazolethiones (4)

Thione (4)	Ultraviolet		Infrared	^{1}H NMR (δ) [b]	^{13}C NMR (δ) [b]
(n)	λ_{max} (nm)	ε x 10^4 (mol^{-1}cm^{-2})	C=S[a] (cm^{-1})	($CDCl_3$)	($CDCl_3$)
3	232	4.1	745(sh)	2.40m, 4.49tr	169.3s, 132.1d, 131.2d,
	252	3.3	735(s)	3.80s, 7.20m	122.5d, 108.5d, 41.9tr,
	315	5.1	660(m)		30.8q, 25.9tr
4	232	4.4	745(sh)	2.00m, 4.38tr	
	252	3.6	735(s)	3.80s, 7.21m	
	315	5.3	660(m)		
			620(m)		
5	232	4.2	740(sh)	1.4-2.1m, 4.28tr,	
	252	3.5	735(s)	3.80s, 7.20m	
	315	5.3	668(m)		
			658(m)		
6	232	4.5	760(s)	1.3-2.1m, 4.31tr	
	252	3.9	740(sh)	3.80s, 7.20m	
	315	5.9	735(s)		
			655(m)		

[a] Infrared spectra were recorded as a caesium iodide disc. sh = shoulder, s = strong, m = medium

[b] m = multiplet, tr = triplet, s = singlet, d = doublet

Table 3

Properties of the imidazole-2-thiones (3)

α,ω-dihaloalkane $X(CH_2)_nX$		Yield	M.p.	Found (%)				Required (%)		
X	n	(%)	(°C)	C	H	N	Formula	C	H	N
Br	1	17	195	44.7	5.0	23.4	$C_9H_{12}N_4S_2$	45.0	5.0	23.3
Cl	2	85	195	47.1	5.6	22.0	$C_{10}H_{14}N_4S_2$	47.2	5.6	22.0
Cl	3	71	157	49.1	6.1	20.9	$C_{11}H_{16}N_4S_2$	49.2	6.0	20.9
Br	4	61	195	51.0	6.4	19.9	$C_{12}H_{18}N_4S_2$	51.0	6.4	19.8
Br	5	80	105	52.7	6.9	19.0	$C_{13}H_{20}N_4S_2$	52.7	6.8	18.9
Br	6	72	126	54.1	7.2	18.1	$C_{14}H_{22}N_4S_2$	54.1	7.1	18.1
Br	10	10	68	59.0	8.2	15.3	$C_{18}H_{30}N_4S_2$	59.0	8.2	15.3

Table 4

Spectral properties of the imidazole-2-thiones (3)

Thiones (3)	Infrared (C=S) (cm^{-1})	^1H NMR spectra (δ) ($CDCl_3$)
1	795m 790sh 770m 712sh 708s 680s 672m	6.38s[2-H] 3.60s[6-H] 6.71d and 7.73d[J=8Hz,4-H]
2	780w 745s 703s 675s 520s	4.49s[4-H] 3.61s[6=H] 6.70m[4-H]
3	755w 735s 725s 665s	2.3m[4-H] 4.10t[J=8Hz, 4-H] 3.62s[6-H] 6.70d and 6.88d[J=8Hz, 4-H]
4	800s 735m 718s 670s	1.8m[4-H] 4.10t[J=8Hz, 4-H] 3.62s[6-H] 6.68d and 6.82d[J=8Hz, 4-H]
5	770m 740s 700s 690m 675m 665s	1.2 - 2.0m[6-H] 4.08t[J=8Hz, 4-H] 3.61s[6-H] 6.71s[4-H]
6	785m 765m 730s 720s 665s 655m	1.5 - 2.1m[8-H] 4.05t[J=8Hz, 4-H] 3.61s[6-H] 6.71s[4-H]
10	770m 720s 700s 672s	1.30br s[12-H] 1.5 - 2.0m[4-H] 4.03t [J=8Hz, 4-H] 3.61s[6-H] 6.71s[4-H]

References and footnotes

1 This is Part 6 in the Series 'N-Bridged Heterocycles'. Part 5: O Meth-Cohn and D I Smith, *J Chem Soc Perkin Trans 1* , 1982 , 261

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