#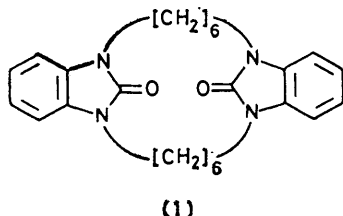 N-Bridged Heterocycles. Part 5.[1] α,ω-Bis-(2-oxobenzimidazolinyl)-alkanes and -ethers as Selective Ligands for Group-1 and -2 Metals

By Otto Meth-Cohn * and David I. Smith, The Ramage Laboratories, Department of Chemistry and Applied Chemistry, University of Salford, Salford M5 4WT
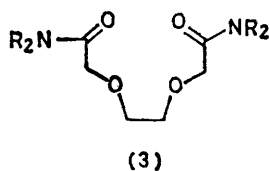
A series of the title compounds (10), (12), and (13) and several analogues were synthesised from the readily available 1-isopropenylbenzimidazolin-2-one. Various substituents were attached to the unsubstituted nitrogen atoms of the benzimidazolinone moieties and the series of products obtained were tested for their complexing ability with group-1 and -2 metal-salts. The isolation of crystalline complexes, the solubilisation of the salts in chloroform by the ligand, the i.r. carbonyl absorption shift, and the ion-transport ability of the ligand were examined as an index of complexation. Selective complexation, particularly for calcium, was noted in several cases.

In earlier papers [1,2] we showed that bridged benzimidazolinones such as compound (1) showed a remarkable selectivity in complexing calcium in preference to other group-1 and -2 metal-ions. This property could have significant biological implications, particularly in the light of recent developments in the isolation of a variety of naturally occurring ion-transporting (ionophoric) antibiotics, some of which show similar selectivity.[3] Thus, ionophoric oligo-amides, such as peptides and depsipeptides, are well documented,[4] as are numerous polyether antibiotics,[5] some of which incorporate nitrogen heterocyclic moieties and make use of carbonyl as well as ether groups in their ligand functionality [e.g. calcimycin (2),[6] also known as A23187; the starred groups are involved in bonding to the metal ion].

strated the efficient and selective role of acyclic diamides [e.g. compound (3)] as neutral ionophores, which are particularly suited as ion-selective electrode components.[7,8] We have thus extended our studies of bridged benzimidazolinones to the acyclic series.

Synthetic Methods.—To this end we required an efficient route to the N-monosubstituted benzimidazolinones. Attempts to mono-alkylate the benzimidazolinone (4) did not give the mono-compound (5), but only the disubstituted derivative (6) while other classical routes are tedious (Scheme 1). We have found that the interaction of ethyl acetoacetate with o-phenylenediamines,[9] is an ideal entry to the desired systems (Scheme 2).

The initially formed azepine (7) was efficiently transformed thermally into the isopropenylbenzimidazolinone

(1)

(2)

An important feature of the polyether antibiotics is the fact that they are acyclic, only taking on a ' cyclic ' conformation at the requirement of the metal ion, by hydrogen bonding of terminal acidic- and hydroxy-groups. This fact allows easier transport of the uncomplexed ionophore through membranes, lowers the kinetic barrier to complexation, and allows the ionophore to change from a hydrophilic (acyclic) to a lipophilic (cyclic) system. Furthermore, the best ionophores have high rates of formation and collapse of the complex, allied with only moderate stability constants, properties better suited to acyclic rather than cyclic ligands.[7]
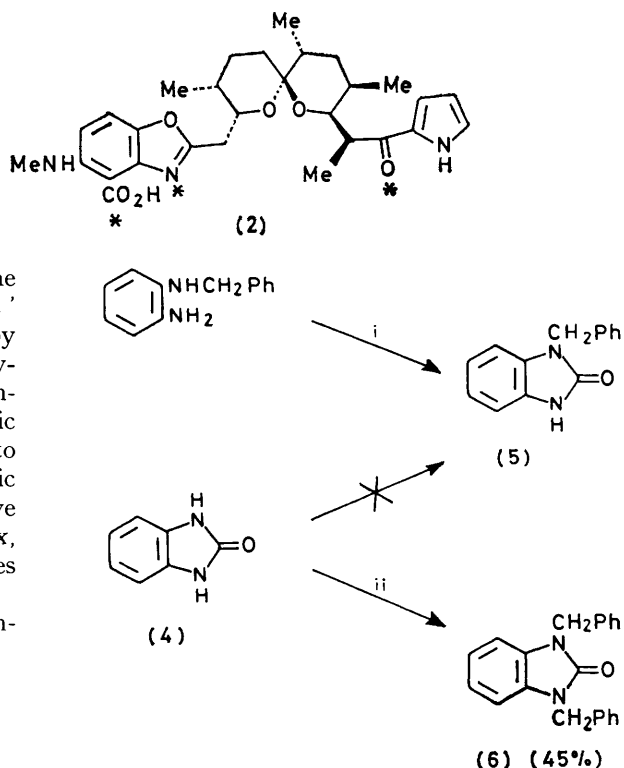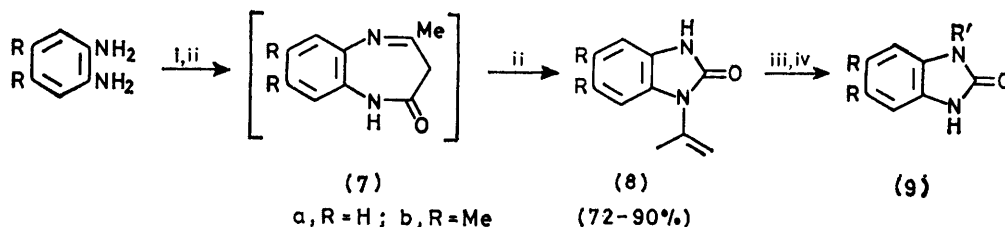
Simon and his co-workers, in particular, have demon-

(3)

Scheme 1 *Reagents:* i, NH_2CONH_2, heat; ii, NaH, dimethylformamide (DMF), $PhCH_2Cl$, 20 °C

(7)

a, R = H ; b, R = Me

(8)

(72—90%)

(9)

Scheme 2 Reagents: i, AcCH₂CO₂Et; ii, heat; iii, NaH, DMF, R' X, 20 °C; iv, cold aqueous H₂SO₄

(8) in a one-pot high-yield reaction, the product being readily isolated from the reaction mixture as its insoluble sodium salt. The reaction was equally efficient on a large scale [thus 510 g of o-phenylenediamine gave 602 g of compound (8a)] and, if desired, it can be conducted in steps. Thus, in refluxing xylene, 4,5-dimethyl-o-phenylenediamine gave the diazepine (7b) in 80% yield while in refluxing o-dichlorobenzene the benzimidazolinone (8b) was efficiently produced (90%). The isopropenyl group is stable to acetic acid, water, and basic solutions, but quantitatively cleaved with cold mineral acid, thus allowing the ready mono-alkylation and deprotection to give the desired products (9).

By this means we prepared several series of acyclic bridged benzimidazolinones, all in high yield (Table 1).

Table 1

Bridged benzimidazolinones (10) obtained from
compound 8a

Compound	n	Yield (%)	M.p. (°C) [b.p. (°C)/mmHg]
(10a)	3	89	246 ᵃ
(10a)	4	72	332 ᵇ
(10a)	5	80	220 ᶜ
(10a)	6	90	241—243
(10a)	7	73	139—140
(10a)	10	87	146—147
(10a)	12	81	148—149
(10a)	20	82	106—107
(10b)	3	61	155—157
(10b)	5	51	141—142
(10b)	6	81	129—130
(10b)	7	56	110—111
(10b)	10	72	75—76
(10b)	12	66	[245/0.05]
(10b)	20	53	77—77.5
(10c)	6	68	84—85
(10d)	6	70	[260/0.02]
(10e)	6	81	65—66
(10f)	6	76	[300/0.02]
(10g)	6	41	165—169
(10h)	6	59	148—150
(10i)	6	86	122—123
(10j)	6	72	113—115
(10k)	6	74	61—64
(10l)	6	57	[280/0.01]
(10m)	6	72	240—243
(10n)	6	62	188—189
(10o)	6	53	184—186

ᵃ Lit.,[10,11] m.p. 246—247 °C. ᵇ Lit.,[11] m.p. 331—332 °C.
ᶜ Lit.,[11] m.p. 218—219 °C.

Thus, N-isopropenylbenzimidazolinone (8a) was alkylated by treatment with sodium hydride in DMF followed by an α,ω-dibromoalkane. The isopropenyl group was then cleaved with cold acid to give a series of α,ω-bis-(2-oxobenzimidazolinyl)alkanes (10a). These com-

pounds were further alkylated as shown in Table 1 using the same type of procedure. The three acids in Table 1 were obtained by acid hydrolysis of the corresponding esters.

Another series of N-hydroxyalkylbenzimidazolones

(10)

(11)
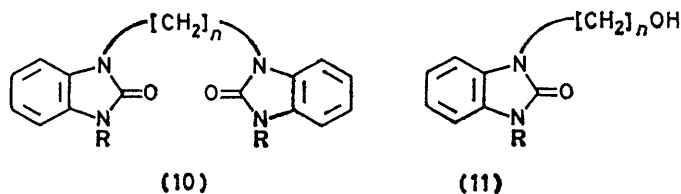
a; R = H
b; R = Me
c; R = Et
d; R = Pr
e; R = Bu
f; R = [CH₂]₇Me
g; R = COEt
h; R = CH₂CO·CH₂CO₂Et
i; R = CH₂CO₂Et
j; R = [CH₂]₂CO₂Et
k; R = [CH₂]₃CO₂Et
l; R = CH(Et)CO₂Et
m; R = CH₂CO₂H
n; R = [CH₂]₂CO₂H
o; R = [CH₂]₃CO₂H

a; R = H
b; R = MeC=CH₂
c; R = [CH₂]₂OH

(11) was next synthesised (Table 2). Several methods were employed. The N-hydroxyethyl- [(11a) or (11b); n = 2] and NN'-bis-(hydroxyethyl- (11c; n = 2) benzimidazolones were prepared by the action of ethylene oxide on the isopropenylbenzimidazolinone (8a) and

Table 2

Oxobenzimidazolinyl alcohols (11) from compound (8a)

Compound	n	Yield (%)	M.p. (°C) [b.p. (°C)/mmHg]
(11b)	2	91	[160/0.04]
(11b)	3	41	[160/0.04]
(11b)	4	68	[180/0.04]
(11b)	6	90	[195/0.04]
(11a)	2	60	142 ᵃ
(11a)	3	20	118—119
(11a)	4	35	106—107
(11a)	6	47	115—116
(11c)	2	72	163 ᵇ

ᵃ Lit.,[10] m.p. 140—141 °C. ᵇ Lit.,[12] m.p. 165—166 °C.

on benzimidazolinone, respectively, in the presence of base. 3-Hydroxypropyl- and 4-hydroxybutyl-groups were introduced indirectly by alkylating the isopropenyl-benzimidazolinone (8a) with α,ω-bromochloroalkanes and then hydrolysing the terminal chloro-groups. However, this hydrolysis step again required an indirect approach.
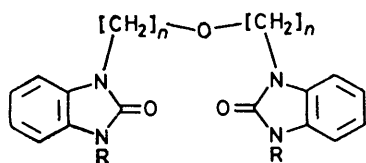
(12)

a; R = C(Me)=CH$_2$
b; R = H
c; R = Me
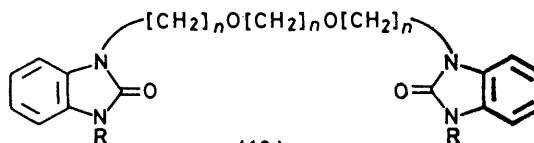
(13)

a; R = C(Me)=CH$_2$
b; R = H
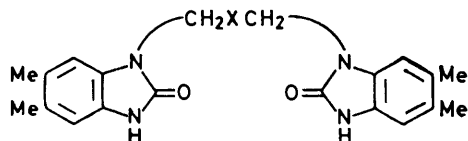c; R = Me
d; R = CH$_2$CO$_2$Et
e; R = CH$_2$CO$_2$H

The chloroalkylbenzimidazolinone was treated with sodium acetate followed by alkaline hydrolysis of the resulting acetate ester to give the products listed in Table 2. Direct hydrolysis of the chloroalkyl-compounds with aqueous alkali, toluene, and a quaternary ammonium phase-transfer catalyst efficiently yielded the ethers (12a; $n = 3$ or 4, respectively) rather than the alcohols. These useful bridged benzimidazolinones were supplemented by other analogues, prepared conventionally by the action of suitable α,ω-dichloroethers on the isopropenylbenzimidazolinone (8a) (Table 3).

toluene-p-sulphonyl derivative of 1-(6-hydroxyhexyl)-3-isopropenylbenzimidazolin-2-one (Scheme 3).
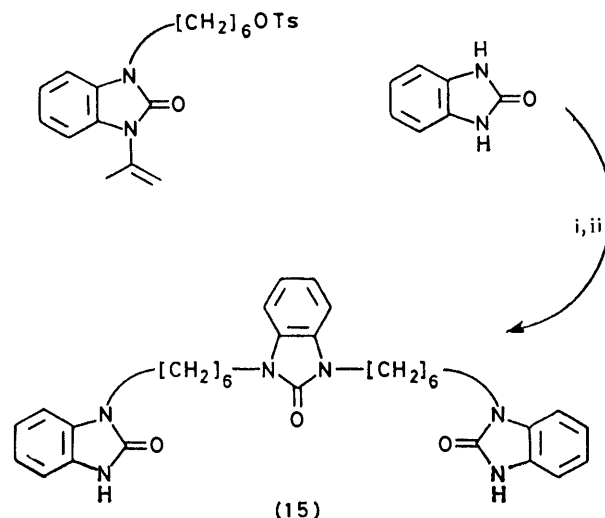
Scheme 3   Reagents: i, K$_2$CO$_3$, DMF, 100 °C; ii, aqueous H$_2$SO$_4$

Also the bisbenzimidazolyl derivatives (16) were made conventionally by alkylation of benzimidazole. Other model systems included the ester (17a), the amide (17b), and the bisureidoalkane (17c).

TABLE 3

Ether-bridged benzimidazolones (12) and (13) obtained from compound (8a)

Compound	n	Yield (%)	M.p. (°C) [b.p. (°C)/mmHg]
(12b)	2	76	217—218
(12b)	3	86	184—185
(12b)	4	54	170—171
(12c)	2	61	151—152
(12a)	3	90	[270/0.04]
(12c)	3	69	117—118
(12a)	4	54	[280/0.04]
(12c)	4	39	[260/0.04]
(13b)	2	65	132—134
(13a)	2	66	116—117
(13c)	2	28	109—110
(13d)	2	56	122—123
(13e)	2	49	194—195

Finally, several miscellaneous benzimidazolinones were synthesised as well as a variety of model compounds, designed to test the complexing and ion-transporting properties of the benzimidazolinones. In an endeavour to improve the lipophilicity of the mono-substituted bridged benzimidazolinones, a series of methyl sub-


(16)

a; X = [CH$_2$]$_2$
b; X = OCH$_2$CH$_2$O

(17)

a; X = OBz
b; X = NHBz
c; X = NEtCONHPh

X[CH$_2$]$_6$X

(14)

a; X = CH$_2$
b; X = [CH$_2$]$_3$
c; X = CH$_2$OCH$_2$

stituted analogues (14a)—(14c) were produced in the above manner from the precursor (8b). A higher analogue, the trimeric benzimidazolone (15), was synthesised by treatment of benzimidazolinone with the

Complexation Studies.—We have previously noted some quick qualitative tests for complexation based on solubilisation and a colour test. A more reliable and semi-quantitative method, ideally suited to our ligands, involves the i.r. shift to lower wavenumber, on complexation, of the carbonyl group stretching frequency. This test is often further corroborated by isolation of stable complexes (and occasionally rendered ineffective by the rapid precipitation of the complex from the spectral solution!). Also, with appropriate counter-ions (*e.g.* SCN$^-$), the dissolution of a metal salt is further indicated

by the appearance of the ion's characteristic absorption (ν 2 070 cm^{-1} for SCN$^-$). Only slight hypsochromic shifts of u.v. absorptions were noted on complexation and unreliably small changes were noted in ^{1}H and ^{13}C n.m.r. spectra obtained in a pilot study.

The results of the i.r. test and metal-salt solubilisation studies are summarised in Table 4. The method involved dissolving the ligand in chloroform to make a 37mM solution and adding this solution (1 ml) to an excess of the metal salt (as a thiocyanate or iodide).

of extra ligand sites (ether function in the bridge, ester groups in pendant chains, or NH groups in the benzimidazolinone).

(d) Apart from complexation with the lithium ion (which may be viewed as a higher analogue of proton) the benzimidazolinones are virtually specific for divalent cations and particularly effective for calcium. Calcium specificity is particularly significant for the bisbenzimidazolin-2-ones (10) with at least six bridging methylene groups.

TABLE 4

Dissolution and i.r. shifts of metal salts with benzimidazolinone [a]

Compound	n	NH$_4$SCN	LiSCN	NaSCN [b]	KSCN	MgI$_2$ [c]	Ca(SCN)$_2$	SrI$_2$ [d]	Ba(SCN)$_2$ [e]
(10a)	7		A	A		A	A	A	A
(10a)	10		A			A	A	A	A
(10a)	12		A			A	A	A	
(10a)	20		A			A	A	A	A
(10b)	3		A			A	B	A	
(10b)	5		A			A	A		
(10b)	6		A				A		
(10b)	7		A				A		
(10b)	10		A				B		
(10b)	12		A				A		
(10b)	20		A				A		
(10c)	6		A				A		
(10d)	6		A				A		
(10e)	6		A				A		
(10f)	6		A				A		
(10g)	6		A				B		
(10h)	6		A			A	A		
(10i)	6		A				A		
(10j)	6		A			A	A	A	A
(10k)	6		A			A	A	A	A
(11b)	2		A			A	A	A	A
(11b)	3		A			A	A	A	A
(11b)	4		A			A	A	A	
(11b)	6		A				A		
(11a)	3		A			A	A	A	A
(11a)	4		A			A	A	A	A
(11a)	6		A			A	A	A	A
(12c)	2		A				A	A	
(12c)	3		A				A	A	
(12c)	4		A				A		
(13b)	2	A	A	A	A	A	A	A	A
(13c)	2		A	A	A	A	A	A	A

[a] A indicates dissolution and/or carbonyl shift; B indicates extensive precipitation. [b] 2H$_2$O. [c] 8H$_2$O. [d] 6H$_2$O [e] 3H$_2$O.

After 30 min of equilibration, the i.r. spectrum was measured in the ν 2 200—2 000 cm^{-1} (SCN$^-$ stretching frequency) and 1 800—1 600 cm^{-1} (CO stretching frequency) regions. Solubilisation of the metal salt, with or without a carbonyl shift, was also noted. Large shifts (20—30 cm^{-1}) were observed with calcium, but smaller shifts (5—10 cm^{-1}) are characteristic of the other ions.

A number of interesting points emerge. (a) Certain potential ligands were too insoluble to be tested, including the α,ω-bis-2-oxobenzimidazolinylpropane (10a; $n = 3$), the corresponding acids (10m), (10a), and (10o) (all $n = 6$), the bis-2-oxobenzimidazolinyl ethers (12b), and the systems (14) and (15).

(b) Rubidium and caesium iodide did not complex with any of the ligands, probably because of high crystal-lattice energies.

(c) Selectivity for a specific metal ion is reduced by either shortening of the bridging group or introduction

(e) Complexation of the ligand-bearing pendant acetic ester groups (10i; $n = 6$) showed an i.r. shift for the ring carbonyl group only, while the corresponding propionic ester (10j; $n = 6$) and butyric ester (10k; $n = 6$) underwent carbonyl shifts for both ring and ester groups, the latter from ν 1 725 to 1 710 cm^{-1}. This change mirrored the increased ligand range of the latter two esters with divalent metal ions other than calcium. Similarly, the acetoacetate (10h; $n = 6$) only showed a shift for its ring carbonyl group on complexation. We thus conclude that complexation is only sterically feasible in the compounds with δ-dicarbonyl groups.

(f) The N-hydroxyalkyl group also appears to facilitate complexation, showing similar specificity effects to those noted for the bis-2-oxobenzimidazolinyl alkanes.

Similar tests were conducted with the model compounds. Significantly, the diester (17a) was totally ineffective while the bis-ureide (17c) dissolved lithium thiocyanate and caused a carbonyl shift (and a pre-

cipitation) with calcium thiocyanate. The corresponding amide (17b) was too insoluble for testing purposes. The two benzimidazoles (16) also showed some interaction with lithium and calcium, possibly in a manner related to the known co-ordination of 1,10-phenanthroline with the same ions.[13] Finally, 1,3-dimethylbenzimidazolin-2-one also underwent complexation with magnesium iodide (precipitation), lithium thiocyanate (solubilisation), and calcium thiocyanate (carbonyl shift and precipitation).

A number of the complexes were isolated and proved sufficiently stable to be recrystallised and analysed (see Experimental section). While magnesium complexes were heavily hydrated, non-stoicheiometric, and not very stable, the calcium complexes were generally stable with a 2 : 1 ligand–calcium stoicheiometry [in contrast with the 1 : 1 complex derived from compound (1)]. The only lithium complex isolated was reasonably stable and showed a 1 : 1 stoicheiometry.

Ion-transport Studies.—In order to quantify the above

qualitative tests for complexation, we next made an extensive study of the ionophoric efficiency of the above ligands. A convenient and simple method of determining ion transport utilises a cylinder in which a lower chloroform layer containing the proposed ligand is gently stirred below two separated aqueous phases, one containing the metal ion (the 'donor' phase). The separation is achieved by a fixed glass plate, and an appropriate counter ion (picrate or tetraphenylborate) and buffers render an easy assay of transport. This system (referred to as a Schulman Bridge[14] or a Pressman cell[15]) was utilised with metal chlorides (sodium, calcium, strontium, and barium) or sulphates (magnesium and lithium), which are known not to be transported in the absence of a lipophilic counter-ion.[16] The extent of transport was monitored at various times by either u.v. absorption measurement of the picrate- or calcium-ion concentration (as a blue lake with Methyl Thymol Blue indicator) in the 'acceptor' aqueous phase.[17] In a series of 20 non-thermostatted determinations at ambient

TABLE 5

Rate of transport of metal ions with various ligands

Ligand	n	H A	H B	Li A	Li B	Na A	Na B	Mg A	Mg B	Ca A	Ca B	Sr A	Sr B	Bu A	Bu B
(1)			1.4				2.7				7.5				
(10a)	3	0.2				0.4		0.1		1.4		0.5		1.0	
(10a)	5	0.3		3.9		1.0		0.2		8.0		4.9			d
(10a)	6									2.4					
(10a)	7	0.2	1.7		17	0.3	3.1	0.1	1.0	2.4	110	1.2		0.7	
(10a)	10									0.5	21				
(10a)	12		0.5				0.2				3.6				
(10a)	20										0.2				
(10b)	3										3.6				
(10b)	5										1.2				
(10b)	6										1.4	0.6			0.7
(10b)	12										0.3				
(10d)	6										1.4				
(10g)	6										0.7				
(10h)	6										17.5				
(10i)	6										4.6				
(10j)	6	0.4		0.3		0.3		0.5		8.7	125 b	6.8		8.0	
(10k)	6										7.1				
(10m)	6									ca. 0 c					
(10n)	6										c,d				
(10o)	6									60 c					
(11a)	3										1.4				
(11a)	4										1.0				
(11a)	6										2.5				
(12b)	2									11.6					
(12b)	3		1.7				6.5			4.8	233				
(12b)	4									2.2					
(13b)	2									5.6					
(13d)	2										4.1				
(14a)								0.1		6.1		2.7		6.0	
(14b)								0.2		11.0		8.7		10	
(14c)								0.4		26.5		22		26	
(15)										31.0					
(16a)			3.7								3.7				
(17a)											0.3				
(17b)											0.5				
(17c)											0.2				
18-C-6 e		1				65				25		120			d
X537A f										140 c					

Rate of ion transport a (μM/h)

a The rate of transport through the chloroform solutions were recorded at two ligand concentrations: A, 0.15mM and B, 3mM. The rates were measured after 3 h and after 20 h in each case. b All the rates were the same after 3 h or 20 h except for this one; 125μM/h at 3 h and 66μM/h at 20 h. c Measured for a 0.4mM solution of ligand. d Precipitation occurred. e Dibenzo-18-crown-6. f Also called lasalocid acid.

temperature a maximum deviation of 16% was observed, comparable with a literature value of 10% for related thermostatted results.[16] The results of our transport tests are recorded in Table 5, the results being taken at two different ligand concentrations. Some interesting features emerge. (*a*) The transport of proton (*i.e.* picric acid) is, in effect, a blank experiment. The only case which showed significant transport [the 1,6-bisbenzimidazol-1-ylhexane (16a)] was also the only significantly basic compound used; the rate of transport in this case was unchanged on addition of calcium.

(*b*) Several model compounds were also studied. Thus the bisbenzimidazolylhexane (16a), the bis-ester (17a), the bis-amide (17b), and the bis-ureide (17c) all showed negligible transport of calcium, underlining the importance of the benzimidazolinone unit. Also, transport using dibenzo-18-crown-6 has been measured for comparison with the neutral ionophores, and the commercially available antibiotic ionophore, lasalocid acid (X 537A), was used for comparison with the acidic benzimidazolones.

(*c*) The *N*-alkyl- or *N*-acyl-substituted bisbenzimidazolinones (10b), (10d), and (10g) were generally poor ionophores, despite the earlier qualitative indications. The cyclic bisbenzimidazolinone (1) was significantly better.

(*d*) However, the corresponding unsubstituted bisbenzimidazolinones (10a) were dramatically more efficient, the most effective being that with a pentamethylene link. Calcium selectivity, but not specificity, was evident. This efficiency was even more marked by (*i*) the introduction of an ether oxygen into the bridge as in compound (12b; *n* = 2); (*ii*) the addition of lipophilic methyl groups to the benzimidazolinone ring as in compound (14b); (*iii*) the addition of both ether and methyl groups, which more than doubled the transport efficiency, as in compound (14c); and (*iv*) the addition of an extra benzimidazolinone ligand as in compound (15), probably the most effective of the ligands yet measured.

(*e*) Pendant hydroxy-groups [compound (11)] were not particularly effective ligands.

(*f*) Pendant ester groups have some value, especially a propionic ester unit as in compound (10j; *n* = 6) which dramatically improves the transport of calcium, strontium, and barium over the other metals. The corresponding acids were of interest, but precipitation occurred with the propionic acid while the butyric acid was highly efficient for calcium transport.

In summary, it would appear that the ideal ligand in this series needs: (*i*) proper separation of ligand groups (5-methylene groups or equivalent); (*ii*) suitable lipophilicity, most effectively introduced by addition of alkyl groups distant from the complexing site; and (*iii*) more than two donor groups.

EXPERIMENTAL

Light petroleum refers to the fraction of b.p. 40—60 °C while petroleum refers to that of b.p. 60—80 °C. Dimethyl-

formamide (DMF) was distilled from phosphorus pentoxide (b.p. 153—155 °C). All of the halogenoalkanes were obtained commercially and distilled before use. Benzimidazol-in-2-one (4) was prepared by heating *o*-phenylenediamine with urea in ethylene glycol solution.[18] Sodium hydride in mineral oil (50%) was washed with light petroleum immediately before use. U.v. spectra were recorded on a Unicam SP 800 spectrophotometer, i.r. spectra on a Perkin-Elmer 257 or 297 instrument, and [1]H n.m.r. spectra on a Varian EM360A (60 MHz) or Perkin-Elmer R32 (90 MHz) using CDCl$_3$ as solvent and tetramethylsilane as an internal standard, unless otherwise indicated. [13]C N.m.r. spectra were obtained on a Varian CFT20 instrument (20 MHz) while mass spectra were recorded on an AEI MS12 or MS902S instrument.

Benzylation of Benzimidazolinone (4).—Benzimidazolinone (4) (3.30 g, 25 mmol) was added to a stirred suspension of sodium hydride (0.60 g, 25 mmol) in dry DMF (25 ml). After the effervescence had ceased, benzyl chloride (3.0 ml, 25 mmol) was added and the mixture was stirred overnight (16 h), poured into water, and the product filtered off and washed. The residue was recrystallised from ethanol to give 1,3-dibenzylbenzimidazolin-2-one (6) (3.3 g, 45%), m.p. 109 °C (lit.,[19] m.p. 107—108 °C).

1-*Isopropenylbenzimidazolin-2-one* (8a).—A mixture of *o*-phenylenediamine (510 g, 4.72 mmol) and xylene (2 l) was heated under reflux in a flow of nitrogen. A mixture of ethyl acetoacetate (690 g, 5.30 mol) and xylene (300 ml) was added over 1.5 h, during which time aqueous ethanol was recovered (260 ml). The mixture was heated for a further 3 h under reflux. The cooled solution was filtered to give a white, crystalline precipitate of the benzimidazolinone (8a) (372 g, 45%). The filtrate was treated with aqueous sodium hydroxide solution (800 g in 4 l of water) and the precipitated sodium salt of the benzimidazolinone (8a) was filtered off. This salt was treated with acetic acid (to pH 6) and the iso-propenylbenzimidazolinone filtered off, washed successively with acetic acid and water, and dried to give the product (8a) (230 g, 27%, combined yield 602 g, 72%), m.p. 121 °C (lit.,[9] m.p. 121 °C), which was pure enough for further use.

1-*Isopropenyl-5,6-dimethylbenzimidazolin-2-one* (8b).—(*a*) 4,5-Dimethyl-*o*-phenylenediamine (20.6 g, 150 mmol) in boiling xylene (400 ml) was treated with ethyl acetoacetate (19.5 g, 150 mmol) in xylene (60 ml), added over 30 min as above, and the mixture was refluxed for a further 4 h. On cooling the solution a yellow, crystalline mass was filtered off to give 2,3-dihydro-4,7,8-trimethyl-1H-1,5-benzodiazepin-2-one (7b) (18.0 g, 59%). Evaporation of the solvent and purification of the dark residue by medium-pressure chromatography on silica gel (Kieselgel 60 H, Merck) gave, on elution with ethyl acetate and chloroform (1 : 4), the *benzimidazolinone* (8b) (2.8 g, 9%) followed by more of the diazepinone (7b) (6.2 g, combined yield 24.2 g, 80%). The *diazepinone* (7b) 182—184 °C, was recrystallised from toluene, (Found: C, 71.6; H, 6.9; N, 13.5. C$_{12}$H$_{14}$N$_2$O requires C, 71.3; H, 6.9; N, 13.9%); ν (Nujol) 3 200 (NH), 1 670 (CO), and 1 640 cm^{-1} (C=N); δ 2.28 (s, 2 × Me) 2.40 (s, Me), 3.10 (s, CH$_2$), 6.90 (s, Ar-H), 7.10 (s, Ar-H), and 9.11 (NH). The *benzimidazolinone* (8b), m.p. 174—176 °C, was recrystallised from toluene and petroleum (b.p. 100—120 °C) (Found: C, 71.6; H, 6.9; N, 13.9. C$_{12}$H$_{14}$N$_2$O requires C, 71.3; H, 6.9; N, 13.9%); ν (Nujol) 3 150 (NH), 1 680 (CO), and 1 650 1 650 cm^{-1}; δ 2.28 (s, 3 × Me), 5 23 and 5 40 (both s, C=CH$_2$), 6.90 and 6.95 (both s, Ar-H), and 10.6 (NH).

(*b*) The diazepinone (7b) (3.04 g, 15 mmol) in *o*-dichloro-

benzene (50 ml) was heated under reflux for 12 h under nitrogen, and the solvent evaporated off. The solid residue was purified by chromatography as above to give the benzimidazolinone (8b) (2.80 g, 90%) followed by a little of the starting material (0.27 g, 9%).

Preparation of the Bridged Benzimidazolinones (10), (12), (13), *and* (14).—(a) A typical procedure is as follows. The benzimidazolinone (8a) (8.7 g, 50 mmol) was added to a stirred suspension of sodium hydride (1.20 g, 50 mmol) in DMF (50 ml). 1,3-Dibromopropane (5.05 g, 25 mmol) was added and the mixture was stirred overnight. A solution of sulphuric acid (20 g) in water (10 ml) was then added and again stirred overnight, after which the mixture was poured into water, filtered, and the solid washed with water and recrystallised from ethanol to give 1,3-(2-oxo-benzimid-azolin-1-yl)propane (10a; $n = 3$) (6.39 g, 89%).

Other products prepared in this way are recorded in Tables 1 and 3. In order to isolate the isopropenyl derivatives sulphuric acid treatment was not applied. α, ω-Dibromoalkanes were used for the polymethylene-bridged compounds, while bis-(2-chloroethyl) ether and 1,8-dichloro-3,6-dioxaoctane were employed for the ether-bridged systems. Further details of these products are recorded in Table 6.

(b) N-*Alkylation of the bridged benzimidazolinones.* A typical procedure is as follows. The above bis-(2-oxo-benzi-midazolinyl)propane (10a; $n = 3$) (4.0 g, 13 mmol) was added to a stirred suspension of sodium hydride (0.7 g, 30 mmol) in dry DMF (30 ml). Methyl iodide (3.69 g, 26 mmol) was added and the mixture was stirred overnight and then poured into water. The mixture was extracted with diethyl ether ($\times$ 3) and the extract was dried (MgSO$_4$) and evapor-ated to give bis-(3-methyl-2-oxobenzimidazolinyl)propane (10b; $n = 3$) as an oil (3.0 g, 68%) which slowly solidified and was recrystallised from acetone. Similar alkylations were conducted with ethyl iodide, 1-bromopropane, 1-bromo-butane, 1-bromo-octane, ethyl 4-chloroacetoacetate, ethyl bromoacetate, ethyl 3-bromopropanoate, ethyl 4-bromo-butanoate, and ethyl 2-bromobutanoate, to give the products recorded in Tables 1, 3, and 6. With ethyl 4-chloroaceto-acetate, 2 mol equiv. of sodium hydride were employed. The dipropanoyl derivative (10g; $n = 6$) was prepared by treatment of the bisbenzimidazolinone (10a; $n = 6$) with refluxing propanoic anhydride for 5 min, after which the mixture was cooled and the product filtered off and crystal-lised from butanol. The carboxylic acids (10; $n = 6$, R $= [\text{CH}_2]_n\text{CO}_2\text{H}$) were prepared by hydrolysis of the corres-ponding ethyl esters with boiling concentrated hydrochloric acid (8 h). The products were filtered off, washed with water, and recrystallised from aqueous acetic acid.

Preparation of the 2-Oxobenzimidazolinyl Alcohols (11) *and Ethers* (12; $n = 3$ *and* 4).—(a) 1-(2-Hydroxyethyl)benzi-midazolin-2-one (11a; $n = 2$)[10] and 1,3-bis-(2-hydroxyethyl)-benzimidazolin-2-one (11c; $n = 2$)[12] were prepared accord-ing to the literature methods.

(b) 1-(3-*Hydroxypropyl*)*benzimidazolin*-2-*one* (11a; $n = 3$) *and* 1,7-*Bis*-(2-*oxobenzimidazolinyl*)-4-*oxaheptane* (12b; $n = 3$).—The benzimidazolinone (8a) (5.22 g, 30 mmol) was added to a stirred suspension of petroleum-washed sodium hydride (0.72 g, 30 mmol in dry DMF (30 ml). 1-Bromo-3-chloro-propane (5.20 g, was added and the mixture was stirred overnight. The solution was poured into water and extract-ed with diethyl ether. The extracts were then washed with water, dried (MgSO$_4$), and evaporated to give 1-(3-chloropro-pyl)-3-isopropenylbenzimidazolin-2-one as an oil which was

distilled (in kugelrohr; 7.10 g, 95%), b.p. 160 °C/0.04 mmHg. This oil (5.0 g, 20 mmol) was dissolved in toluene (50 ml) and sodium acetate (4.1 g, 50 mmol) in water (5 ml), and aqueous tetrabutylammonium hydroxide (4 ml, 40%) was added. The mixture was refluxed overnight. On cool-ing, potassium hydroxide (5.6 g, 100 mmol) was added and the mixture was again refluxed overnight. To the solution was added diethyl ether and water and the organic layer was washed well with water, dried (MgSO$_4$), and evaporated to give 1-(3-hydroxypropyl)-3-isopropenylbenzimidazolin-2-one as an oil which was distilled (2.00 g, 43%), b.p. 160 °C 0.04 mmHg; $\nu_{\text{max.}}$ (liquid film) 3 400 (OH), 1 700 (CO), 1 660 (C=C), and 900 cm^{-1} (=CH$_2$); δ [(CO$_3$)$_2$SO] 1.95 (q, CH$_2$CH$_2$-CH$_2$), 2.20 (s, Me), 3.60 (t, CH$_2$O), 3.80br (OH), 4.05 (t, NCH$_2$), 5.20 and 5.35 (both s, =CH$_2$), and 7.05 (s, Ar-H). This oil (1.16 g, 5 mmol) was dissolved in ethanol (20 ml), concentrated hydrochloric acid (5 ml) was added, and the solution was allowed to stand overnight. It was poured into water (100 ml) and extracted with diethyl ether. The extract was dried and evaporated to give the benzimidazolin-2-one (11a; $n = 3$) as white crystals (from ethyl acetate) (0.47 g, 49%), m.p. 118—119 °C (Found: C, 62.8; H, 6.4; N, 14.5. C$_{10}$H$_{12}$N$_2$O$_2$ requires C, 62.5; H, 6.3; N, 14.6%); $\nu_{\text{max.}}$ (Nujol) 3 300 (OH), 3 150 (NH), and 1 670 cm^{-1} (C=O); δ [CDCl$_3$–(CO$_3$)$_2$SO] 1.95 (q, CH$_2$CH$_2$CH$_2$), 3.61 (t, CH$_2$O), 4.02 (t, NCH$_2$), 4.3br (OH), 7.05 (s, Ar-H), and 10.7br (NH).

When the 1-(3-chloropropyl)-3-isopropenylbenzimidazol-inone (7.5 g, 30 mmol) in toluene was hydrolysed as above with potassium hydroxide (5 g) in water (20 ml) and aqueous tetrabutylammonium hydroxide (4 ml, 40%) by heating under reflux for 2 d, work-up as above gave 1,7-bis-(3-iso-propenyl-2-oxobenzimidazolinyl)-4-oxaheptane (12a; $n = 3$) which was distilled (kugelrohr 6.40 g, 95%), b.p. 270 °C/ 0.04 mmHg. This ether (2.23 g, 5 mmol) was further hydrolysed with acid as above to give the title *ether* (12b; $n = 3$), the properties of which are recorded in Tables 3 and 6.

(c) 1-(4-*Hydroxybutyl*)*benzimidazolin*-2-*one* (11a; $n = 4$) *and* 1,9-*Bis*-(2-*oxobenzimidazolinyl*)-5-*oxanonane* (12b; $n = 4$). In a similar manner to that described in (b) the benzimidazolinone (8a) and 1-bromo-4-chlorobutane gave 1-(4-*chlorobutyl*)-3-*isopropenylbenzimidazolin*-2-*one* (90%), b.p. 160 °C/0.04 mmHg, which was similarly converted into the *benzimidazolinone* (11a; $n = 4$), some properties of which are recorded in Table 2 (Found: C, 64.4; H, 7.0; N, 13.5. C$_{11}$H$_{14}$N$_2$O$_2$ requires C, 64.1; H, 6.8; N, 13.6%); $\nu_{\text{max.}}$ (Nujol) 3 500 (OH), 3 150 (NH), and 1 690 cm^{-1} (C=O); δ 1.75 (m, CH$_2$CH$_2$CH$_2$), 3.35br (OH), 3.65 (t, CH$_2$O), 3.85 (t, NCH$_2$), 7.0 (m, Ar-H), and 10.6br (NH).

Also, by the method described in (b), hydrolysis of 1-(4-chlorobutyl)-3-isopropenylbenzimidazolin-2-one with aque-ous potassium hydroxide and aqueous tetrabutylammonium hydroxide in toluene gave, after further acidic hydrolysis, the title *ether* (12b; $n = 4$), the properties of which are recorded in Tables 3 and 6.

(d) 1-(6-*Hydroxyhexyl*)*benzimidazolin*-2-*one* (11a; $n = 6$). The benzimidazolinone (8a) (1.74 g, 10 mmol), powdered potassium carbonate (2.8 g, 20 mmol), and 6-chlorohexanol (1.50 g, 11 mmol) were stirred in dry DMF (50 ml) at 100 °C for 8 h and then poured into water. The solution was ex-tracted with diethyl ether, the extract was dried (MgSO$_4$) and evaporated, and the residual oil was distilled to give 1-(6-hydroxyhexyl)-3-isopropenylbenzimidazolin-2-one (11b; $n = 6$) (2.51 g, 90%), b.p. 195 °C/0.04 mmHg. This oil (2.74 g, 10 mmol) in ethanol (50 ml) was treated with

TABLE 6

Properties of the bridged benzimidazolinones (10), (12), (13), and (14)

Compd.	n	Found (%) C	H	N	Formula	Required (%) C	H	N	¹H N.m.r. (δ) NCH₂	Other CH₂	Ar-H	NH	Pendant group
(10a)	3				$C_{17}H_{16}N_4O_2$								
(10a)	4				$C_{18}H_{18}N_4O_2$								
(10a)	5				$C_{19}H_{20}N_4O_2$								
(10a)	6	68.2	6.4	15.8	$C_{20}H_{22}N_4O_2$	68.5	6.3	16.0	3.80 (t)	1.1—1.9	7.0 (m)	10.6br	
(10a)	7	69.4	6.8	15.3	$C_{21}H_{24}N_4O_2$	69.2	6.6	15.4					
(10a)	10	70.5	7.5	13.6	$C_{24}H_{30}N_4O_2$	70.9	7.4	13.8					
(10a)	12	71.7	8.1	12.7	$C_{26}H_{34}N_4O_2$	71.8	7.9	12.9					
(10a)	20	74.6	9.4	9.8	$C_{34}H_{50}N_4O_2$	74.7	9.2	10.2					
(10b)	3	67.7	6.0	16.7	$C_{19}H_{20}N_4O_2$	67.8	6.0	16.65					
(10b)	5	69.4	6.8	15.3	$C_{21}H_{24}N_4O_2$	69.2	6.6	15.4					
(10b)	6	69.6	7.0	14.5	$C_{22}H_{26}N_4O_2$	69.8	6.9	14.8					
(10b)	7	70.5	7.3	14.2	$C_{23}H_{28}N_4O_2$	70.4	7.2	14.3	3.80 (t)	1.1—1.9	7.0 (m)		3.35 (s, Me)
(10b)	10	72.0	8.0	12.7	$C_{26}H_{34}N_4O_2$	71.8	7.9	12.9					
(10b) [a]	12	71.7	8.4	12.1	$C_{28}H_{38}N_4O_2$	72.7	8.3	12.1					
(10b)	20	75.4	9.7	9.5	$C_{36}H_{54}N_4O_2$	75.2	9.5	9.75					
(10c)	6	71.1	7.3	13.9	$C_{24}H_{30}N_4O_2$	70.9	7.4	13.8					
(10d) [b]	6	70.6	7.8	12.2	$C_{26}H_{34}N_4O_2$	71.8	7.9	12.9	3.80 (t)	1.2—2.0	7.0 (m)		0.90 (t, Me)
(10e)	6	72.9	8.0	12.1	$C_{28}H_{38}N_4O_2$	72.7	8.3	12.1					
(10f) [c]	6	74.5	9.7	9.6	$C_{36}H_{54}N_4O_2$	75.2	9.5	9.75					
(10g)	6	67.7	6.5	11.8	$C_{26}H_{30}N_4O_4$	67.5	6.5	12.1	3.82 (t)	1.2—1.9	7.05 (6 H, m) 8.20 (2 H, m)		1.25 (t, Me), 3.14 (q, COCH₂)
(10h)	6	63.1	6.3	8.9	$C_{32}H_{38}N_4O_8$	63.3	6.3	9.2	3.85 (t)	1.2—1.9	7.0 (m)		1.20 (t, Me), 3.50 (s, COCH₂CO), 4.13 (s, OCH₂), 4.77 (NCH₂CO)
(10i) [d]	6	65.4	6.8	9.5	$C_{28}H_{34}N_4O_6$	64.35	6.6	10.7					1.20 (t, Me), 4.15 (q, OCH₂), 4.60 (s, NCH₂CO)
(10j)	6	65.2	7.1	10.1	$C_{30}H_{38}N_4O_6$	65.4	7.0	10.2	3.85 (t)	1.2—1.9	7.05 (m)		1.20 (t, Me), 2.75 (t, CH₂CO₂), 4.15 (NCH₂ and OCH₂)
(10k)	6	66.3	7.4	9.5	$C_{32}H_{42}N_4O_6$	66.4	7.3	9.7					1.20 (t, Me), 2.10 (q, mid-CH₂), 2.35 (t, CH₂CO₂), 3.95 (NCH₂), 4.15 (q, CH₂O)
(10t) [e]	6				$C_{32}H_{42}N_4O_6$								0.85 (t, Me), 1.20 (t, Me), 2.20 (m, CH₂), 4.15 (q, OCH₂), 4.97 and 5.10 (m, CH)
(10m) [f]	6	61.1	5.5	11.6	$C_{24}H_{26}N_4O_6 \cdot \frac{1}{4}H_2O$	61.2	5.6	11.9	3.85 (t)	1.2—1.9	7.05 (m)		4.60 (s, CH₂), 12.30 (s, CO₂H)
(10n) [g]	6	62.6	6.1	11.1	$C_{26}H_{30}N_4O_6 \cdot \frac{1}{4}H_2O$	62.6	6.2	11.2	3.85 (t)	1.2—1.9	7.05 (m)		2.65 (t, CH₂CO), 4.05 (t, NCH₂), 12.30 (s, CO₂H)
(10o) [h]	6	63.5	6.5	10.4	$C_{28}H_{34}N_4O_6 \cdot \frac{1}{4}H_2O$	63.5	6.5	10.4	3.85 (t)	1.2—1.9	7.05 (m)		1.95 (q, CH₂CH₂CH₂), 2.30 (t, CH₂CO), 3.85 (t, NCH₂), 12.30 (s, CO₂H)
(12b)	2	64.0	5.5	16.6	$C_{18}H_{18}N_4O_3$	63.9	5.4	16.6	3.90 (t)	3.65 (t)	7.00 (m)	10.8br	
(12b)	3	65.7	6.2	15.2	$C_{20}H_{22}N_4O_3$	65.6	6.1	15.3	3.85 (t)	3.35 (t), 1.85 (q)	7.00 (m)	10.8br	
(12b)	4	67.0	6.5	13.8	$C_{22}H_{26}N_4O_3$	67.0	6.6	14.2	3.80 (t)	3.35 (t), 1.3—1.8 (m)	7.00 (m)	10.8br	
(12c)	2	65.5	6.1	15.2	$C_{20}H_{22}N_4O_3$	65.6	6.1	15.3	3.85 (t)	3.70 (t)	7.00 (m)		3.35 (s, Me)
(12c)	3	66.7	6.4	14.2	$C_{22}H_{26}N_4O_3$	67.0	6.6	14.2	3.95 (t)	3.40 (t), 2.00 (q)	7.00 (m)		3.35 (s, Me)
(12c)	4				$C_{24}H_{30}N_4O_3$				3.85 (t)	3.35 (t), 1.4—1.9 (m)	7.00 (m)		3.35 (s, Me)
(13b)	2	62.8	5.6	14.5	$C_{20}H_{22}N_4O_4$	62.8	5.8	14.5	4.00 (t)	3.50 (s), 3.65 (t)	7.05 (m)	10.8br	
(13c)	2	64.3	6.3	13.2	$C_{22}H_{26}N_4O_4$	64.4	6.4	13.6	3.98 (t)	3.50 (s), 3.68 (t)	7.05 (m)		3.35 (s, Me)
(13d)	2	60.9	6.2	10.3	$C_{26}H_{34}N_4O_8$	60.7	6.1	10.1	4.00 (t)	3.50 (s), 3.65 (t)	7.05 (m)		1.25 (t, Me), 4.20 (q, CH₂O), 4.60 (s, CH₂CO)

TABLE 6 (continued)

Compd.	n	Found (%) C	H	N	Formula	Required (%) C	H	N	¹H N.m.r. (δ) NCH₂	Other CH	Ar-H	NH	Pendant group
(13e)	2	57.9	5.9	11.2	C₂₄H₂₆N₄O₈	57.8	5.3	11.2	4.15 (t)	3.70 (s), 3.90 (t)	7.25 (m)		4.85 (s, CH₂)
(14a)		69.3	6.7	15.1	C₂₁H₂₄N₄O₂	69.2	6.6	15.4	4.20 (t)	2.60 (q)	7.25 (s), 7.00 (s)	10.8br	2.35 (s, Me)
(14b)		70.2	7.5	13.8	C₂₃H₂₈N₄O₂	70.0	7.2	14.2	4.00 (t)	1.4—2.1 (m)	7.20 (s), 7.05 (s)	10.8br	2.35 (s, Me)
(14c) [k]		66.8	6.4	13.9	C₂₂H₂₆N₄O₃	67.0	6.6	14.2	4.15 (m)	4.15 (m)	7.05 (s), 7.15 (s)		2.35 (s) 2.40 (s, Me) 5g

[a] Hygroscopic oil; M^+, 462.2993 (Calc. M, 462.2993). [b] Hygroscopic oil; M^+, 434.2679. Calc. M, 434.2680. [c] Hygroscopic oil; M^+, 574.4240. Calc. M, 574.4244. [d] Probably contains toluene of crystallisation (i.e. ⅓ mol of toluene of crystallisation required C, 65.8; H, 6.7; N, 10.1%); M^+, 522.2477. Calc. M, 522.2476. [e] Hygroscopic oil; M^+, 578.3098. Calc. M, 578.3102. [f] M^+, 466.1851. Calc. M, 466.1851. [g] M^+, 494.2612. Calc. M, 494.2613. [h] M^+, 522.2492. Calc. M, 522.2476. [j] Hygroscopic oil; M^+, 422.2318. Calc. M, 422.2316. [k] N.m.r. solvent CF_3CO_2D.

sulphuric acid (8 g) in water (4 ml) overnight and the solution was then poured into water. The solution was extracted with diethyl ether, the extract dried (MgSO₄) and evaporated, and the solid residue recrystallised from acetonitrile to give the title alcohol (11a; $n = 6$), some of the properties of which are recorded in Table 2 (Found: C, 66.5; H, 7.9; N, 12.1. C₁₃H₁₈N₂O₂ requires C, 66.6; H, 7.7; N, 12.0%); $\nu_{max.}$ (Nujol) 3 300 (OH), 3 150 (NH), and 1 680 cm⁻¹ (C=O); δ 1.2—1.9 (m, [CH₂]₄), 3.52 (t, CH₂O), 3.85 (t, NCH₂), 3.90br (OH), 7.05 (m, Ar-H), and 10.60br (NH).

Preparation of 1,3-Bis-[6-(2-oxobenzimidazolin-1-yl)-hexyl]benzimidazolin-2-one (15).—The benzimidazolinone (11b; $n = 6$) (27.4 g, 100 mmol) in dry pyridine (100 ml) was treated with drops of toluene-p-sulphonyl chloride (28.6 g, 150 mmol) in pyridine (50 ml) over a period of 2 h at 0—5 °C. The solution was allowed to stand for a further 5 h at ambient temperature and then poured into water and extracted with diethyl ether. The diethyl ether extract was washed well with aqueous hydrochloric acid (2M), dried, and evaporated to give 1-isopropenyl-3-(6-toluene-p-sulphonyloxyhexyl)benzimidazolin-2-one as an oil (30.8 g, 72%) which was used directly as follows. (a) The above toluene-p-sulphonate (1.64 g, 5 mmol) and potassium carbonate (1 g) in dry DMF (10 ml) was heated, with stirring, at 100 °C for 6 h, after which a solution of sulphuric acid (6 g) in water (4 g) was added and the mixture left overnight. The precipitate obtained on pouring the mixture into water was filtered off and recrystallised from aqueous acetic acid to give the hexane (10a; $n = 6$) (1.5 g, 86%), m.p. 243 °C, identical with that reported earlier.

(b) The above toluene-p-sulphonate (21.4 g, 50 mmol), the benzimidazolinone (4) (3.35 g, 25 mmol), and potassium carbonate (13.8 g) were added to dry DMF (100 ml) and heated, with stirring, at 100 °C for 1.5 h. A solution of sulphuric acid (20 g) in water (10 ml) was then cautiously added and the mixture was left overnight. The precipitate which was obtained on pouring the mixture into water was filtered off and recrystallised from aqueous DMF to give the title product (15) (7.07 g, 50%), m.p. 240—242 °C). (It is probable that this compound contained some benzimidazolin-2-one.) (Found: C, 68.5; H, 6.7; N, 15.7%; M^+, 566.300 2. C₃₃H₃₈N₆O₃ requires C, 69.9; H, 6.8; N, 14.9%; M, 566.300 3); $\nu_{max.}$ (Nujol) 3 150 (NH) and 1 690 (C=O); δ [(CD)₃SO] 1.2—1.9br ([CH₂]₄), 3.82 (t, NCH₂), 7.05 (s, Ar-H), and 10.8br (NH).

1,6-Bis(benzimidazol-1-yl)hexane (16a).—Benzimidazole (3.54 g, 30 mmol) was treated in dry DMF (20 ml) successively with sodium hydride (0.84 g, 35 mmol) and 1,6-dibromohexane (3.66 g, 15 mmol), with stirring, and the mixture was stirred overnight and then poured into water. The precipitate was filtered off, washed with water, dried, and recrystallised from ethyl acetate to give the title product (16a) (3.76 g, 79%), m.p. 140—142 °C (Found: C, 75.4; H, 7.0; N, 17.6. C₂₀H₂₂N₄ requires C, 75.4; H, 7.0; N, 17.6%); $\nu_{max.}$ (Nujol) 1 610 cm⁻¹; δ 1.25 (m, NCH₂CH₂-CH), 1.75 (m, NCH₂CH₂), 4.05 (t, NCH₂), 7.24 (m, Ar-H), and 7.79 (m, 2- and 4-H).

1,8-Bis(benzimidazol-1-yl)-3,6-dioxaoctane (16b).—Benzimidazole (3.54 g, 30 mmol) was treated as above with 1,8-dichloro-3,6-dioxaoctane (2.80 g, 15 mmol) at 100 °C for 5 h and then poured into water and extracted with diethyl ether. The dried extract was evaporated and distilled to give the title product (16b) (3.90 g, 74%), b.p. 240 °C/0.01 mmHg; δ 3.35 (s, OCH₂CH₂O), 3.55 (t, OCH₂), 4.10 (t, NCH₂), 7.25 (m, 5-, 6-, and 7-Ar-H), 7.80 (m, 4-H), and 7.90 (s, 2-H) (Found: m/e 350.174 5 (M^+). Calc. for C₂₀H₂₂N₄O₂: M, 350.174 4).

Other 1,6-Disubstituted Hexanes.—(a) 1,6-Bis(benzoyloxy)hexane (17a) and 1,6-bis(benzoylamino)hexane (17b) were prepared by conventional benzoylation of the corresponding alcohol and amine according to the literature method.

(b) 1,6-Bis(ethylamino)hexane (0.69 g, 4 mmol) in chloroform (10 ml) was treated with phenyl isocyanate (1.05 g, 8.8 mmol) acid, after 1 h, the solvent was removed and the residual solid was recrystallised from ethyl acetate and light petroleum to give 1,6-bis-(1-ethyl-3-phenylureido-1-yl)-hexane (17c) (1.50 g, 91%), m.p. 115—117 °C (Found: C, 70.4; H, 8.1; N, 13.7. C₂₄H₃₄N₄O₂ requires C, 70.2; H, 8.3; N, 13.7%); $\nu_{max.}$ (Nujol) 3 350 (NH) and 1 650 cm⁻¹ (C=O) δ 1.20 (t, Me), 1.39 (m, [CH₂]₄), 3.31 (m, CH₂N), 7.32 (Ar-H), and 6.83br (NH).

Complexation Studies.—(a) *Solubilisation and i.r. tests.* The appropriate potential ligand was dissolved in chloroform to give a 37mM solution. An aliquot of this solution (1 ml) was added to the metal salt (2 × 10⁻⁴M), which had been stored over phosphorus pentoxide, and the mixture was equilibrated for 30 min. The i.r. spectrum in the regions ν 2 000—2 200 and 1 600—1 800 cm⁻¹ was then recorded; the results are collected in Table 4.

(b) *Isolation of metal complexes.* The following complexes were prepared by interaction of the ligand and metal salt as above or in methanol or ethyl acetate solution. (i) 1,3-Dimethylbenzimidazolin-2-one and magnesium iodide (from chloroform solution) gave a *complex* which was recrystallised from acetonitrile and dried under reduced pressure for 12 h at 110 °C [Found: C, 36.4; H, 4.3; I, 36.0;

N, 9.4. $(C_9H_{10}N_2O)_7 \cdot (MgI_2)_3 \cdot 7H_2O$ requires C, **36.1**; H, 4.0; I, 36.3; N, 9.4%].

(ii) 1,3-Bis-(2-hydroxyethyl)benzimidazolin-2-one and calcium thiocyanate (from methanol) gave a complex precipitated by addition of diethyl ether. The *complex* was dried as above, m.p. 223—225 °C [Found: C, 45.0; H, 5.1; Ca, 6.8; N, 12.6. $C_{11}H_{14}N_2O_3 \cdot Ca(SCN)_2 \cdot 2H_2O$ requires C, 45.3; H, 5.1; Ca, 6.3; N, 13.2%].

(iii) 1,3-Bis-(3-methyl-2-oxobenzimidazolin-1-yl)propane with lithium thiocyanate, (from chloroform solution) gave a complex which was recrystallised from ethyl acetate and dried, as above, to give white *needles*, m.p. 266—268 °C (Found: C, 59.8; H, 5.0; N, 17.3. $C_{19}H_{20}N_4O_2 \cdot LiSCN$ requires C, 59.8; H, 5.0; N, 17.4%).

(iv) 1,3-Bis-(3-methyl-2-oxobenzimidazolin-1-yl)propane with magnesium iodide (from ethyl acetate solution) gave, when dried, a yellow *precipitate*, m.p. 297—298 °C. [Found: C, 36.3; H, 4.4; I, 30.9; N, 8.4. $(C_{19}H_{20}N_4O_2)_4 \cdot (MgI_2)_3 \cdot$ $19H_2O$ requires C, 36.6; H, 4.8; I, 30.6; N, 9.0%].

(v) 1,5-Bis-(3-methyl-2-oxobenzimidazolin-1-yl)pentane with calcium thiocyanate (from chloroform solution) gave a *complex*, recrystallised from methanol, m.p. 299—301 °C [Found: C, 59.4; H, 5.5; N, 15.7. $(C_{21}H_{24}N_4O_2)_2 \cdot Ca-$ $(SCN)_2$ requires C, 59.7; H, 5.5; N, 15.8%].

(vi) 1,6-Bis(2-oxo-3-propylbenzimidazolin-1-yl)hexane with calcium thiocyanate (from chloroform solution) gave a *complex*, recrystallised from methanol, m.p. 248—249 °C [Found: C, 63.3; H, 6.7; N, 13.6. $(C_{26}H_{34}N_4O_2)_2 \cdot Ca-$ $(SCN)_2$ requires C, 63.2; H, 6.7; N, 13.6%].

(vii) 1,10-Bis-(3-methyl-2-oxobenzimidazolin-1-yl)decane with calcium thiocyanate (from chloroform) gave a *complex*, recrystallised from methanol, m.p. 307—315 °C [Found: C, 63.0; H, 6.7; N, 13.5. $(C_{26}H_{34}N_4O_2)_2 \cdot Ca(SCN)_2$ requires C, 63.2; H, 6.7; N, 13.6%].

Ion Transport Studies.—A Schulman Bridge [14] (or Pressman Cell [15]) was used. A chloroform solution of the ligand (25 ml) was added to the cell followed by the acceptor phase on one side of the partition and the donor phase (3 ml) on the other side. The cylinder was sealed with a paraffin wax film (Parafilm), covered, and stirred throughout the experiment. The concentrations of the ligands are recorded in Table 5. The donor and acceptor phases were prepared as follows:

(a) *For acidic ionophores.* *Donor phase*: The metal salt (200 mmol), tris(hydroxymethyl)methylamine (a buffer) (51.6mM), and hydrochloric acid (48mM) in de-ionised water *Acceptor phase*: The same buffer (51.6mM) and hydrochloric acid (48mM) in de-ionised water. These quantities gave pH 7.

(b) *For neutral ionophores.* *Donor phase*: The metal salt (200 mmol), picric acid (22mM), and the above buffer (50mM). *Acceptor phase*: De-ionised water.

The ion transport was measured either by measurement of the picrate concentration with time in the acceptor phase (by monitoring the absorption of the solution at 356 nm) or by

determining the calcium-ion concentration in the acceptor phase (by the Methyl Thymol Blue-lake method, monitored at 612 nm). The results are recorded in Table 5.

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