

PII: S0040-4020(97)00434-1

N,N'-Linked 1,2-Ethanediyl-Poly(Benzimidazolin-2-ones) and the X-Ray Crystal Structure of a Benzimidazolin-2-one Trimer

Enrique Díez-Barra,^a Julio Dotor^{*,a} Antonio de la Hoz,^a Concepción Foces-Foces^{*,b} Christine Enjalbal,^c Jean Louis Aubagnac^c Rosa María Claramunt^d and José Elguero^d

^aDepartamento de Química Inorgánica, Orgánica y Bioquímica, Universidad de Castilla-La Mancha, 13071 Ciudad Real, Spain

> ^bDepartamento de Cristalografía, Instituto de Química-Física "Rocasolano", C.S.I.C., Serrano, 119, 28006 Madrid, Spain

CESA 5075, LAPP, Université de Montpellier II, 34095 Montpellier Cédex 5, France

^dDepartamento de Química Orgánica y Biología, UNED, Senda del Rey s/n, E-28040 Madrid, Spain

^eInstituto de Química Médica, C.S.I.C., Juan de la Cierva, 3. 28006 Madrid, Spain

Abstract.— A series of N,N'-linked 1,2-ethanediyl-poly(benzimidazolin-2-ones) that can be classified as podands, are described. Seven dimers (21-27), three trimers (28-30), a cyclic tetramer (31) and an open-chain benzimidazolin-2-one heptamer (32) have been prepared and characterized by 1 H, 13 C NMR and by MS. The crystal and molecular structure of the trimer, 1,3-bis-2-(2-oxobenzimidazol-1-yl)ethyl-2-oxobenzimidazole monohydrate (30) has been solved by X-Ray analysis. The benzi-midazolin-2-one fragments display a pattern of bond distances and angles similar to that of analogue derivatives retrieved form the CSD. The molecules are hydrogen bonded to four others in a continuous two-dimensional network by N-H···O=C and C-H···O=C interactions in which all N-H donors and O=C acceptors are involved. © 1997 Elsevier Science Ltd.

INTRODUCTION

In order to correctly situate this paper's contribution to the topic, let us briefly summarize the knowledge about neutral N,N'-poly(benzimidazolin-2-ones) (benzimidazolin-2-ones are often improperly called benzimidazolones) 1 and the related N,N'-polybenzimidazolium salts 2 both linear and cyclic will allow to better situate our own contribution.



Pozharski described the reaction of bis(1-benzimidazolyl)alkanes with potassium hydroxide which affords bis(1-benzimidazolin-2-ones) **3** when n = 3-5 (for n = 1 or 2 the alkanes decompose).¹ Compound **3**, n = 3 [1,1'-(1,3-propandiyl)bis(benzimidazolin-2-one] was also prepared by Weber by treating 1-isopropenyl-benzimidazolin-2-one with 1,3-dibromopropane.² More recently, Thummel prepared compounds **4** (n = 4) by deprotonation and oxidation by air of the corresponding benzimidazolium salt (see later on).³



The main contribution to polybenzimidazolinone chemistry was due to Meth-Cohn.⁴⁻⁸ This author prepared derivatives of compounds 3 and 4 with n = 3, 4, 5, 6, 7, 10, 12 and 20. He also prepared an open-chain trimer 5.8



The first macrocycles formed by benzimidazolin-2-one units 1 were prepared by Meth-Cohn, for instance 6 (n = 5, 6, 7, 8 and 10) and 7 (n = 4 and 6).⁶ Afterwards, Weber prepared the trimer 8 (7, n = 3) and determined its complexation constants towards several cations.²



Thummel has also prepared the ureaphanes 6 (n = 3, 4) by oxidation of the corresponding 2,2'dibenzimidazolidinylidene (see later on)⁹ as well as the tetramer (n = 3) corresponding to 8 by deprotonation /oxidation of the corresponding benzimidazolium salts (see later on).³ Very recently, Weber reported the synthesis and X-ray structural studies of solvent inclusions of a series of heterocalixarenes featuring the benzimidazolin-2-one subunit 9a and 9b.¹⁰



Concerning N,N'-disubstituted polybenzimidazolium salts 2 and the corresponding benzimidazolinylidenes we have already reported that Thummel^{3,9} used these compounds as precursors of compounds 4 and 6. Recently, he described a related pair of derivatives (10 and 11).¹¹



In summary, the results so far obtained correspond: i) to polymethylene chains $n \ge 3$; ii) to p = 2-4benzimidazolinone units; iii) to p = 2 (open) or p = 4 (ring) benzimidazolium units. The purpose of this paper is to explore the case n = 2 (ethanediyl). This case is the most complex [the simpler case of n = 1, methanediyl, has been reported for bis(benzimidazolium) derivatives]¹² since both benzimidazolinones and especially benzimidazolium salts are good leaving groups which make the formation of N-vinyl compounds a competitive reaction.¹³ To the best of our knowledge, so far the only known compound is the double quaternary salt 12.¹⁴



RESULTS AND DISCUSSION

Chemistry

Due to the complexity of the reactions, we have preferred to summarize in Schemes 1 to 5 the different molecules involved in this work.







Benzimidazoles and benzimidazolium salts. Starting from benzimidazole 13 the reaction with 1,2dibromoethane in different PTC conditions led to bis(benzimidazol-1-yl)ethane 19, a compound already described.¹³ The treatment of 19 with 2 equivalents of 1,2-dibromoethane yields the double quaternary salt 20; no macrocyclic structures were detected. This rather unstable compound, is oxidized by air in basic medium, depending on the base, to 23 and 24 (Et₃N) or to 25 (NaH like Thummel).¹¹ The strongest base produces the total elimination of HBr.

Benzimidazolin-2-ones. The reaction of benzimidazolinone 14 with 1,2-dichloroethane in PTC affords different products depending on the small experimental differences (see experimental part). Monomers 16 and 17, dimers 21 and 22, and the trimer 28 were isolated and fully characterized while tetramer 31 was formed in very low amount and its structure was established by mass spectrometry (see below). However, the construction

of N,N'-linked 1,2-ethanediyl-poly(benzimidazolin-2-ones) can be achieved by a synthetic scheme of protection of compound 14, alkylation with 1,2-dichloroethane, and deprotection. As protecting group we have used the 2propenyl group since it has been employed with success in benzimidazole chemistry.^{2,15-17}

1-Isopropenylbenzimidazolin-2-one 15 and 1,3-di(2-chloroethyl)-benzimidazolin-2-one 17 obtained previously, were allowed to react in different conditions: i) in PTC conditions (toluene, KOH, tetrabutylammonium bromide [TBAB]) the reaction affords a mixture of 26, 27 and 29 all of them in very low yields (the most abundant, 29, was formed in 8.5% yield). ii) in another PTC conditions (acetonitrile, K₂CO₃, tetrabutylammonium bisulfate) a mixture of 18, 27 and 29 was obtained, but the yield of 29 was 78%. iii) in a microwave oven in the presence of KOH the same mixture was obtained but the yield of trimer 29 was only 49%. Since this was the desired product, conditions ii) were selected to prepare a larger quantity of the trimer which was subsequently deprotected cleaving off the two isopropenyl groups by treatment with HCl in hydroalcoholic solution: trimer 30 was obtained in 89% yield.

The reaction between trimer 30 and 1,3-di(2-chloroethyl)-benzimidazolin-2-one 17 was expected to offer a way of preparing tetramer 31 but, although a 1:1 molar ratio and high dilution techniques were used, the only compound isolated in reasonable yield was heptamer 32.

¹H and ¹³C NMR spectroscopy

Assignment of the NMR resonances of dimers 21-27, trimers 28-30 and heptamer 32 was done by comparison with the monomer 15 and the symmetrically substituted compounds 17, 18 and 19, because in these compounds only one chain NCH₂CH₂N, NCH₂CH₂Cl, NCH=CH₂ or NC(CH₃)CH₂ is present. Cyclic tetramer 31 was isolated in too small amount to be characterized by NMR.

In ¹H-NMR, the NCH₂CH₂N groups appear as broad singlets even if they are substituted by two different benzimidazolin-2-one derivatives. The NCH₂CH₂Cl(Br) group shows two triplets, being the NCH₂ group the less shielded. The NCH=CH₂ group was assigned considering the coupling constants in the vinyl group.¹³ Finally, the geminal protons of the NC(CH₃)CH₂ group were assigned by NOE difference spectroscopy and considering that in these compounds ${}^{4}J_{cis}$ is larger than ${}^{4}J_{trans}$. In most cases, signals derived from the aromatic protons are not differentiated.



	Table 1. ¹ H NMR of benzimidazolinones (chemical shifts in ppm, coupling constants in Hz)										
Comp	Solv ^a	H4-H7	CH ₂ N	CH ₂ Cl(B	Br) CH ₂ d	H _{cis}	H _{trans}	Hgem	CH ₃		
14 ^e	ь	6.90 (bs)							*****		
15 ^e	b	7.06-7.17				5.41(q)	5.25(q) J = 1.2,	J = 0.6	2.25(dd)		
16 ^e	с	7.09-6.85	4.11(t) J =	3.68(t) 6.6			•••••				

17	c	7.08-7.15	4.22(t) J = 6.	3.82(t) .7					
18	c	7.18-7.35				5.67(dd) $J_{ct} = 1.0, J$	5.50(dd) tg = 9.5, J _{cg}	7.01(dd) =16.1	
21 ^e	с	6.80-7.20	4.10(t) J = 6.	3.67(t) .4	4.25(s)				
22	c	6.83-7.04	4.10(t) J = 6.	3.67(t) .5	4.24(s)				
23	с	6.82-7.02	4.19(t) = 6	3.52(t) .8	4.24(s)				
24	с	6.82-7.19	4.17(t) J = 6	3.49(t) .8	4.24(s) $J_{ct} = 1.0$,	5.55(dd) J _{tg} = 9.3, J _c	5.00(dd) g =16.4	(under H ₄ -I	H7)
25	с	6.97-7.21			4.24(s) $J_{ct} = 1.0$,	5.55(dd) J _{tg} = 9.5, J _c	5.00(dd) g =16.1	6.97(dd)	
26	c	6.83-6.96	4.10(t) J = 6.	3.68(t) .6	4.22(s)	5.28(q) J = 1.2	5.04(s)		2.10 J = 1.2
27	с	6.86-7.20			$4.23(s)^{f}$ J _{ct} = 1.0,	$5.55(dd)^{f}$ J _{tg} = 9.3, J _c	$4.95(dd)^{f}$ g =16.4	(under H4-I	H7)
						5.29(q) ^g	$5.06(q)^{g}$ J = 1.4, J	= 0.8	2.13(dd)
28	c	6.70-7.15	3.30-3	3.40					
29	c	6.78-6.98	4.20			5.27	5.05		2.10
30 ^e	b	6.75-6.92	3.89-3.99		10.8				
32 ^e	с	6.83-7.00	3.98-4.14		10.6				

^a: b = DMSO-d₆, c = CDCl₃; ^d central CH₂CH₂ in dimers, trimers and heptamer; ^e δ NH \approx 10.4-10.8 ppm (broad); ^f vinyl: ^g isopropenyl.

In the ¹³C-NMR spectra, signals from the aromatic carbons are different even if the heterocyclic rings are very similar. They have been assigned by comparison with the symmetrically substituted monomers and dimers but some of them can be interchanged. Compound **28** decomposes in solution and its ¹³C NMR spectrum cannot be properly recorded. Compounds **16** and **21** were obtained in too low quantities for ¹³C NMR spectroscopy.

Table 2. ¹³ C NMR of benzimidazolinones (chemical shifts in ppm)									
Comp	Solv ^a C2	C3a, C7a	C4, C7	C5, C6	C2'	C3a', C7a'	C4', C7'	C5',	C6'
14 b	155 3 12	9.7 129.7 10	08 5 108 5	120.4 120.4					
15 c	154.5 12	8.3. 130.0 10	09.1. 109.8	121.3, 121.9					
16 c	153.8 12	9.0, 129.1 10	07.1, 107.7	121.4, 121.5					
17 c	153.7 129	9.3, 129.3 10	08.0, 108.0	121.7, 121.7					
18 c	152.7 12	7.7, 127.7 10	09.6, 109.6	122.6, 122.6					
22 c	153.7 12	8.9, 129.0 10	07.0, 107.7	121.4, 121.5					

23 c 24 c 25 c 26 c 27 c 29 c 30 t 32 c	<pre>c 153.7 c 153.7 c 152.8 c 152.5 c 152.7 c 153.9 c 153.5 c 154.0</pre>	128.8, 129.1 128.8, 129.1 127.3, 129.1 128.9, 129.1 128.6, 129.2 128.8, 128.8 128.9, 128.9 129.1, 129.1	107.1, 107.1, 107.4, 107.1, 107.1, 107.0, 107.1, 106.9, 107.2,	107.7121.4,107.1121.5,109.5121.8,107.6121.3,108.9121.3,107.1121.5,106.9120.9,107.2121.5,	121.6 121.7 122.4 121.5 121.7 121.5 120.9 121.5	128.6, 127.2, 152.5 127.2, 154.1 128.3, 155.8 127.9,	107.3, 129.2 106.9, 129.2 107.3, 128.6 107.0, 130.1 107.2, 130.4 107.2,	109.5 108.8 109.4 107.3 108.7 109.4	121.7, 122.3 121.3, 121.5 121.6, 122.3 121.3, 121.6 120.4, 121.0 121.5, 121.5
Com	p Solv ^a	CH ₂ CH ₂	CH ₂ N	CH ₂ Cl(Br)	=CH ₂	=CH	CH3	=CH	2 =C
15	с						20.2	113.8	137.8
16	с		42.8	41.1					
17	с		43.0	41.2					
18	с				102.4	126.7			
22	с	39.0	42.8	41.0					
23	с	39.1	42.7	28.0					
24	с	38.9, 39.0	42.7	29.7	101.5	127.0			
25	с	38.8			101.5	127.0			
26	с	38.8, 38.9	42.8	41.0			20.0	113.2	137.7
27	с	38.7, 38.8	42.8	41.0			20.0	113.2	137.7
29	с	38.7, 38.8					20.0	113.2	137.4
30	b	38.1, 38.3							
32	с	38.8							

a: $b = DMSO-d_6$, $c = CDCl_3$

Mass spectrometry

FAB MS has been used to characterize several of the above structures, especially, the cyclic nature of tetramer 31 was only established by MS. Instead of discussing one by one the different compounds we have preferred to summarize the information in Table 3 adding, when necessary, some comments (G = glycerol, NBA = m-nitrobenzylic alcohol).

Table 3. Mass spectra of some representative compounds

Comp.	Mol. formula	MW (Da)a	Matrix	MH+	Other fragments
20 23 24 25 31 32	[C ₂₀ H ₂₂ N ₄ Br ₂] ⁺⁺ C ₂₀ H ₂₀ N ₄ O ₂ Br ₂ C ₂₀ H ₁₉ N ₄ O ₂ Br C ₂₀ H ₁₈ N ₄ O ₂ C ₃₆ H ₃₂ N ₈ O ₄ C ₆₁ H ₅₄ N ₁₄ O ₇	476 506 426 346 640 1094	G G, NBA G, NBA G, NBA NBA NBA	475-477-479 (1:2:1) 507-509-511 (1:2:1) 427-429 (1:1) 347 641 1095 (100), 1096 (75)	555-557-559-561 (1:3:3:1) [CBr]+ 186 [18], 187 481 (M-160) 1117 [MNa]+, 1133 [MK]+

^aFor ⁷⁹Br.

X-ray crystallographic study of trimer 30.

The most relevant intra and intermolecular parameters are given in Table 4 according to the numbering system displayed in Fig. 1a.¹⁸ There are no significant differences between the three benzimidazolinone moieties as tested by half normal probability plots ¹⁹ except for the internal angle at the nitrogen atoms. Replacement of one hydrogen atom of five-membered rings with the ethylene chains results in a narrowing of the endocyclic angles at that N atom. A search of the Cambridge Structural Database (CSD hereinafter)²⁰ revealed only four structures

a) Benzoimidazolir	one moiety	Prese		C	CSD		
N(1)-C(2) C(9)-N(1) C(2)-N(3) N(3)-C(4) C(4)-C(9) C(2)-O(10)	1.379(3) N(13 1.392(3) C(21 1.366(4) C(14 1.400(3) N(15 1.392(4) C(16 1.232(3) C(14	i)-C(14))-N(13))-N(15) i)-C(16) i)-C(21) -)-O(22)	1.379(3) 1.392(3) 1.363(4) 1.384(3) 1.397(3) 1.223(4)	N(25)-C C(33)-N C(26)-N N(27)-C C(28)-C C(26)-O	(26) (25) (27) (28) (33) (34)	1.390(3) 1.389(4) 1.359(3) 1.391(4) 1.397(3) 1.226(4)	1.393(21) 1.402(14) 1.362(10) 1.383(17) 1.396(8) 1.227(13)
C(9)-N(1)-C(2) N(1)-C(2)-N(3) C(2)-N(3)-C(4) N(1)-C(2)-O(10) N(3)-C(2)-O(10)	109.3(2) C(21 107.0(2) N(13 109.8(2) C(14 126.2(2) N(13 126.8(2) N(15)-N(13)-C(14))-C(14)-N(15))-N(15)-C(16))-C(14)-O(22))-C(14)-O(22)	109.6(2) 106.4(2) 110.5(2) 125.6(2) 127.9(3)	C(33)-N(N(25)-C(C(26)-N(N(25)-C(N(27)-C((25)-C(26) (26)-N(27) (27)-C(28) (26)-O(34) (26)-O(34)	109.4(2) 106.4(2) 110.7(2) 126.3(2) 127.3(2)	109.9(7) 105.9(12) 110.7(5) 126.2(6) 127.8(10)
b) Substituents							
N(1)-C(11) N(3)-C(23)	1.449(5) N(13 1.454(4) C(11)-C(12))-C(12)	1.455(3) 1.520(5)	N(25)-C(C(23)-C((24) (24)	1.451(3) 1.506(5)	
C(9)-N(1)-C(11) C(2)-N(1)-C(11) C(4)-N(3)-C(23) C(2)-N(3)-C(23)	126.0(2) C(21) 123.6(2) C(14) 126.3(2) N(1)- 123.5(2) N(13))-N(13)-C(12))-N(13)-C(12) ·C(11)-C(12))-C(12)-C(11)	126.1(2) 122.7(2) 111.8(3) 111.0(3)	C(33)-N(C(26)-N(N(3)-C(2 C(23)-C((25)-C(24) (25)-C(24) (23)-C(24) (24)-N(25)	126.1(2) 124.5(2) 112.9(2) 113.0(2)	
N15-C(14)-N(13)- N(13)-C(12)-C(11) C(11)-N(1)-C(2)-N C(2)-N(3)-C(23)-C C(23)-C(24)-N(25)	C(12) -168.1(2 -N(1) 57.6(3 (3) 169.9(2 (24) -95.1(3 -C(26) 105.4(3)) C(14)) C(12)) N(1)-0) N(3)-0) C(24)	-N(13)-C(12 -C(11)-N(1) C(2)-N(3)-C C(23)-C(24) -N(25)-C(26	2)-C(11) -C(2) 2(23) -N(25) 5)-N(27)	78.1(3 -90.8(3 -173.9(2 -62.9(3 178.3(2	s) 1) 2) 3) 2)	
c) Hydrogen intera	ctions						
D-HA		D-H	DA		HA	D-H	.A
N(15)-H(15)O(10 N(27)-H(27)O(22 C(32)-H(32)O(34))(-x,-y,-z) 2)(x, ¹ / ₂ -y, ¹ / ₂ +z) 4)(-x,- ¹ / ₂ +y, ¹ / ₂ -z)	0.93(3) 0.89(4) 0.98(3)	2.833(3) 2.799(3) 3.314(3)		1.95(4) 1.91(4) 2.34(3)	156(4 176(4 177(3)))
C-H…Centroid		С-Н	C…Centr	•	H…Centr.	C-H	Centr.
C(11)-H(112)C(A C(18)-H(18)C(B) C(18)-H(18)C(C)		0.98(4) 1.02(4) 1.02(4)	3.565(3) 3.814(3) 3.527(4)		2.91(4) 2.94(4) 2.75(4)	125(3 144(2 133(3))

Table 4. Selected geometrical parameters (Å, °). C(A), C(B), C(C) stand for the centroids of the centroid of the C(4)...C(9), C(28)...C(33) and N(25)..C(33) rings.





Fig. 1c

Fig. 1. (a) Molecular structure showing the atomic numbering and 30% probability ellipsoids. (b) Projection along the line joining the C(26) and C(14) atoms. (c) Hydrogen bonding scheme displaying the donor and acceptor groups (i=-x,-y,-z; ii=x,1/2-y,-1/2+z; iii=-x,-1/2+y,1/2-z).

with neither substituents in the benzene ring nor disorder and R < 0.010 (DRPRDL,²¹ KAMCIK,²² VUCFOO²³ and YILFUU²⁴) apart from that of the 2,3-dihydrobenzimidazolin-2-one (ZEFXIR²⁵ and ZEFXIR01²⁶). The average geometry is also gathered in Table 4 and it is in good agreement with that of the present work. The benzimidazolinone rings are significantly not planar ($\chi^2 = 247.01$, 131.25 and 287.17 vs. the tabulated value of 12.60) and the angles that the central ring [N(1),...,C(9)] forms with the other two [N(13),..., C(21) and N(25),..., C(33)] are 25.6(1) and 54.4(1)° respectively giving rise to an almost helical conformation (Fig. 1b). Although pairs of benzene rings related by center of inversion (Fig. 1c) are parallel with an interplanar separation of 2.966(1) Å they are completely offset from each other, the distance between their centroids being 6.812(2) Å preventing any stack.

The inclusion of the ethylene chains which join two benzimidazolinone molecules drastically modify the crystal packing of the *N*,*N'*-unsubstituted molecules.²⁵⁻²⁷ In compound **30**, the molecules are linked by one N(15)-H(15)···O(10) hydrogen bond into dimer units (Fig 1c and Table 4) through a symmetry center at (0,0,0) and the equivalent ones. Pairs of these dimers related by twofold screw axis and glide planes (ii and iii in Fig. 1c) are joined through the other N(27)-H(27)···O(22) bond and reinforced by C-H···O interactions to form a 2D network. Since four molecules per unit cell form this net, the I-body centring generates a second motif in which the dimers lie across the symmetry center at (1/4, 1/4, 1/4) and their symmetry related ones. Only weak C-H··· π electronic cloud interactions are between both nets (Table 4). This crystal packing leads to a structure with no-accessible voids²⁸ and the total packing coefficient of 0.66 is rather low. There are no hydrogen interactions involving the disordered water molecule, the shortest distance being O(35)···H(6) = 3.39(5) Å.

CONCLUSIONS

Although cyclic tetramer **31** cannot be obtained in preparative yields by the methodologies we have used, we succeed in preparing trimer **30** and heptamer **32** which can be classified as *podands* (acyclic hosts).²⁹ Our methodology can be used for the controlled construction of *N*,*N'*-linked α,ω -alkanediyl-poly(benzimidazolin-2-ones), with the general structure:



where *m*, number of benzimidazolin-2-one units and *n*, alkyl chain length, can be varied as desired. In the present paper, we have reported the case n = 2, where elimination side-reactions are present in all steps.

EXPERIMENTAL SECTION

Synthesis.- IR spectra were recorded with a Perkin-Elmer PE-883 spectrometer. Mass spectra of the intermediate compounds were recorded on a SX102 type mass spectrometer (Jeol Ltd, Tokyo, Japan). Elemental analyses were determined with a Perkin-Elmer microanalyzer. Column chromatography was performed using silica gel Merck 60 (230-400 mesh) or neutral aluminium oxide (Merck 100-125 mesh). Benzimidazole 13, benzimidazolin-2-one 14 and TBAB are commercial compounds; compound 15 was prepared according to ref. 2. NMR Spectroscopy.- Most spectra were recorded on a Varian Unity 300 spectrometer.

Crystal data			
Chemical formula	C ₂₅ H ₂₂ N ₂ O ₂ .H ₂ O	Crystal system	Monoclinic
Mr	472.50	Space group	12/a
a (Å)	19.7316(25)	α(°)	90
$b(\mathbf{A})$	11.8232(9)	β(°)	114.303(10)
$c(\mathbf{A})$	22.5666(37)	γ(°)	90
Z	8	$Dx (gr/cm^3)$	1.31
V (Å ³)	4798.0(11)	Radiation	CuKα
Wavelength (Å)	1.5418	No. of reflections for	
θ range for lattice parameters (°)	2-45	lattice parameters:	53
Absorption coefficient (cm ⁻¹)	7.53	Crystal colour	Colorless
Crystal description	Prism	Crystal size (mm)	0.46 x 0.20 x 0.20
Data collection			
Diffractometer type	Seifert XRD3000-S four c	ircle diffractometer. Graphite oriented n	ionocromator.
Measurement time	1 min./reflection	Detector apertures (°)	1 x 1
Collection method	ω/2θ scans	θmax (°)	65
No. of standard reflections (interval)	2 (90 min.). 4.8%decay	Scan width (°)	1.5
No. of independent reflections	3737	No. of observed reflections, $I>2\sigma(I)$	2516
Refinement			
Treatment of hydrogen atoms Secondary extinction correction (10 ⁴	See experimental part 0.23(3)	Refinement: Least-Squares on Fo. Fo.	ıll matrix
R	0.045	No. of parameters refined	404
wR	0.048	Degrees of freedom	2112
(Δρ)max (e/Å ³)	0.55	Ratio of freedom	6.2
<shift error=""></shift>	0.02	Max. thermal value (Å ²)	U[O(351)]=0.24(1)
Weighting scheme: Empirical as to gi	ve no trends in $\langle \omega \Delta^2 F \rangle$ vs. $\langle $	Fobsl> and $<\sin\theta/\lambda>$.	

Table 5. Crystal analysis parameters at room temperature.

Table 6. Final atomic coordinates and Ueq= $(1/3)\Sigma[Uij \cdot a_i^* \cdot a_i \cdot a_j \cdot a_j \cdot \cos(a_i, a_j)]$.

Atom	x	у	Z	Ueq	Atom	x	У	z	Ueq
N(1)	0.6869(1)	0.6370(2)	0.6740(1)	0.043(1)	C(20)	0.6969(2)	0.3588(2)	0.6543(1)	0.047(1)
C(2)	0.6128(1)	0.6113(2)	0.6555(1)	0.040(1)	C(21)	0.6625(1)	0.4110(2)	0.5949(1)	0.040(1)
N(3)	0.6070(1)	0.5588(2)	0.7071(1)	0.040(1)	O(22)	0.6307(1)	0.5965(2)	0.4685(1)	0.066(1)
C(4)	0.6775(1)	0.5488(2)	0.7583(1)	0.042(1)	C(23)	0.5384(1)	0.5089(2)	0.7044(1)	0.045(1)
C(5)	0.7005(2)	0.5001(2)	0.8186(1)	0.050(1)	C(24)	0.4951(2)	0.5876(3)	0.7283(1)	0.048(1)
C(6)	0.7763(2)	0.5021(3)	0.8578(1)	0.058(1)	N(25)	0.5349(1)	0.6180(2)	0.7962(1)	0.043(1)
C(7)	0.8263(2)	0.5500(3)	0.8368(2)	0.058(1)	C(26)	0.5680(1)	0.7224(2)	0.8181(1)	0.047(1)
C(8)	0.8032(2)	0.5996(2)	0.7760(1)	0.051(1)	N(27)	0.5973(1)	0.7181(2)	0.8841(1)	0.050(1)
C(9)	0.7276(1)	0.5978(2)	0.7369(1)	0.040(1)	C(28)	0.5817(1)	0.6148(2)	0.9052(1)	0.042(1)
O(10)	0.5618(1)	0.6318(2)	0.60229(8)	0.050(1)	C(29)	0.5963(2)	0.5733(3)	0.9658(1)	0.056(1)
C(11)	0.7173(2)	0.6771(2)	0.6293(1)	0.050(1)	C(30)	0.5712(2)	0.4647(3)	0.9699(2)	0.059(1)
C(12)	0.7439(2)	0.5802(2)	0.6001(1)	0.049(1)	C(31)	0.5339(2)	0.4009(3)	0.9146(2)	0.057(1)
N(13)	0.6839(1)	0.5009(2)	0.56657(9)	0.042(1)	C(32)	0.5187(2)	0.4422(2)	0.8533(1)	0.048(1)
C(14)	0.6292(1)	0.5217(2)	0.5055(1)	0.045(1)	C(33)	0.5430(1)	0.5508(2)	0.8493(1)	0.040(1)
N(15)	0.5753(1)	0.4425(2)	0.4951(1)	0.048(1)	O(34)	0.5706(1)	0.8018(2)	0.7841(1)	0.060(1)
C(16)	0.5933(1)	0.3743(2)	0.5493(1)	0.042(1)	O(35)	0.731(1)	0.264(2)	0.9728(8)	0 239(10)
C(17)	0.5562(2)	0.2864(2)	0.5629(1)	0.052(1)	O(35')	0.679(1)	0.213(2)	0.924(1)	0.226(15)
C(18)	0.5905(2)	0.2353(3)	0.6228(2)	0.060(1)	pp[O(35)]	=0.60(3), pp[C	(35') = 0.400	3)	0.220(15)
C(19)	0.6593(2)	0.2700(2)	0.6677(2)	0.059(1)	pp= popul	lation paramete	er	-,	

Mass Spectrometry.- Mass spectra were recorded on a SX102 type spectrometer (Jeol Ltd, Tokyo, Japan). Xenon was used in the FAB experiments. The energy of the neutral atom beam was 3 keV (emission current: 20 mA). Calibration was accomplished using Ultramark 1621 (Heraeus, Karlsruhe, Germany) as a reference. Samples were placed on a target after dissolving them directly in the matrix. Glycerol and *m*-nitrobenzyl alcohol were obtained from Aldrich.

X-ray Analysis.- The details of the X-ray data collection, structure solution and refinement are provided in Table 5. The structure was solved by direct methods $(SIR92)^{30}$ and refined by least-squares procedures on F_{obs.} The water molecule, located close a binary axis, appears to be disordered over two positions O(35) and O(35') with site occupation factors of 0.60(3) and 0.40(3) respectively. All hydrogen atoms except those of the water molecule were obtained from difference Fourier synthesis and included and refined isotropically in the last cycles. The scattering factors were taken from the *International Tables for X-Ray Crystallography.*³¹ Table 6 list the final atomic coordinates and equivalent thermal factors for non-hydrogen atoms. The calculations were carried out with the XTAL3.4 System,¹⁸ PESOS³² and PARST³³ set of programs running on a DEC3000-300X workstation.

1,2-Bis(benzimidazol-1-yl)ethane (19).

The compound was prepared by liquid PTC following the procedure reported in ref. 13. Purification was performed by column chromatography on silica gel (50 g). Elution with dichloromethane/ethanol 9:1 afforded 70% of compound **19**, mp 225-226 °C, lit. mp 216-220 °C.¹³

Bis(2-bromoethyl)-1,2-bis(benzimidazol-1-ium)ethane dibromide (20).

A suspension of **19** (520 mg, 2.24 mmol) in 5 mL of 1,2-dibromoethane was refluxed for 72 h resulting in a black precipitate. The solid was filtered off, dissolved in water, treated by charcoal, filtered and the clear solution evaporated affording 0.37 g (26 %) of **20** as a white solid mp > 300 °C (from methanol). ¹H NMR (DMSO-d₆) δ 5.18 (4H, s, A₄ system), 4.93 and 3.95 (8H, t, AA'BB' system, $J_{AB} = 5.7$ Hz), 7.66 (4H, m, H5 and H6), 8.14 (t, 2H, H4) and 7.95 (t, 2H, H7) and 9.8 (2H, s, H2). ¹³C NMR (DMSO-d₆) δ 30.79 (CH₂Br), 45.79 (CH₂CH₂Br), 48.14 (CH₂CH₂), 129.00 and 130.76 (C5 and C6), 112.95 and 113.56 (C4 and C7), 143.22 (C2). Anal. calcd for C₂₀H₂₂N₄Br₄: C, 37.65%; H, 3.48%, N, 8.78%. Found: C, 37.38%; H, 3.54%, N, 9.08%.

Reaction of 20 with triethylamine and air.

Compound 20 (0.35 g, 0.55 mmol) was dissolved in freshly distilled acetonitrile (70 mL). Triethylamine (2.1 mL, 14 mmol) was added and the resulting solution was stirred for 7 days at r.t. Afterwards, water (175 mL) and 35% hydrochloric acid (17.5 mL) were added and the acid solution was extracted with CHCl₃ (3 x 50 mL) and the solution was boiled with charcoal and filtered. By evaporation, 80 mg of a solid was obtained. Column chromatography (CHCl₃/ethanol 8:2) yields a mixture of compounds 23 (34 %) and 24 (28 %). *Reaction of 20 with sodium hydride and air*.

Compound 20 (0.1 g, 0.16 mmol) was mixed with NaH (0.1 g, 4 mmol) in anhydrous acetonitrile (20 mL). After 5 min of stirring the white solution turns yellow; the stirring was maintained for 2 h at r.t. in the open. Then, the solvent was removed and the residue was extracted with chloroform. The dark solution was refluxed 10 min with charcoal. The solution was filtered, the solvent evaporated off and the residue washed with hexane to afford 40 mg of 1,2-[bis(2-oxo-3-vinylbenzimidazolin-1-yl]ethane 25 were obtained (90 %), mp 165-167 °C (from dichloromethane-hexane).

Reaction of benzimidazolin-2-one (14) with 1,2-dichloroethane.

E. DÍEZ-BARRA et al.

1.- Benzimidazolin-2-one (3.35 g, 25 mmol), finely ground potassium hydroxide (4.2 g, 75 mmol) and water (1 mL) were stirred at room temperature for 1 h. 1,2-Dichloroethane (50 mL) and TBAB (240 mg, 0.75 mmol) were added and the mixture heated slowly to the final temperature to minimize the elimination reaction (4h to 50 °C, 2.5 h to 80 °C and 2h to 100 °C). The mixture was filtered off and the residue was washed with dichloromethane. The residue was dissolved in 1,2-dichloroethane (50 mL) and the stirring continued at 100 °C for 4 h. The mixture was filtered off and the combined organic solutions were dried over anhydrous magnesium sulfate. The crude product was purified by column chromatography on silica gel (50 g). Elution with dichloromethane afforded successively 3.75 g of 1,3-bis(2-chloroethyl)benzimidazolin-2-one 17 (58 %), mp 130-132 °C, 1,2-bis[3-(2-chloroethyl)benzimidazolin-2-one] 22 (60 mg, 1.1 %) mp > 300 °C and 1-[3-(2-chloroethyl)-2-oxobenzimidazol-1-yl]-2-(2-oxobenzimidazol-1-yl)ethane 21 (100 mg, 2.2 %). Anal. calcd. for 17 (C₁₁H₁₂N₂Cl₂O): C, 50.97 %; H, 4.67 %; N, 10.80 %. Found: C, 51.26 %; H, 4.87 %; N, 10.78 %. Anal. calcd. for 22 (C₂₀H₂₀N₄Cl₂O₂): C, 57.29 %; H, 4.81 %; N, 16.91 %. Found: C, 57.19 %; H, 4.95 %; N, 17.00 %.

2.- Similarly, but extending the reaction time to 48 h at room temperature after the first addition of 1,2-dichloroethane and to 4 h at 100 °C after the second addition of 1,2-dichloroethane. The mixture was filtered off and the combined organic solutions were dried over anhydrous magnesium sulfate. The crude product was purified by column chromatography on silica gel (50 g). Elution with ethyl acetate afforded 2.1 g of 17 (32.4 %) and 1-(2-chloroethyl)benzimidazolin-2-one 16 (100 mg, 2 %), mp > 300 °C. Compound 16 is unstable and do not give good analytical results, it was characterized by 1 H and 13 C NMR.

3.- Similarly, but extending the reaction time to 15 h at room temperature after the first addition of 1,2-dichloroethane and to 2h at 100 °C after the second addition of 1,2-dichloroethane. The mixture was filtered off and the combined organic solutions were dried over anhydrous magnesium sulfate. The crude product was purified by column chromatography on silica gel (50 g). Elution with dichloromethane afforded 2.35 g of 17 (36.3 %), 22 (560 mg, 10.7 %) and 1,3-bis-{2-[3-(2-chloroethyl)-2-oxobenzimidazol-1-yl]ethyl}-2-oxobenzimidazole 28 (340 mg, 7.1 %). Cyclic tetramer 31 was isolated in very small amounts, about 1% and characterized only by MS. Anal. calcd. for 28 ($C_{29}H_{28}N_6Cl_2O_3$): C, 60.11 %; H, 4.87 %; N, 14.50 %. Found: C, 59.23 %; H, 4.99 %; N, 14.62 %.

1,3-Bis-{2-(3-isopropenyl-2-oxobenzimidazol-1-yl)ethyl}-2-oxobenzimidazole (29).

1.- In a two necked flask a mixture of 1-isopropenylbenzimidazolin-2-one **15** (350 mg, 2 mmol), potassium hydroxide (123 mg, 2.2 mmol) and TBAB (10 mg, 0.03 mmol) in toluene (10 mL) was heated to 100 °C for 30 min. At this temperature, a suspension of **17** (260 mg, 1 mmol) in toluene (5 mL) was added and the reaction was heated to reflux for 48 h. The reaction was filtered off and the residue washed with toluene (10 mL). Drying over anhydrous magnesium sulfate and removal of the solvent afforded the crude product which was purified by column chromatography on silica gel (40 g). Elution with dichloromethane afforded 50 mg of starting material **17**. Elution with dichloromethane:ethyl acetate 8:2 afforded 1-(3-isopropenyl-2-oxobenzimidazol-1-yl)-2-(3-vinyl-2-oxobenzimidazol-1-yl)ethane **27** (30 mg, 8%) mp 101-103 °C (from etharhexane) and 1-[3-(2-chloroethyl)2-oxobenzimidazol-1-yl)-2-(3-isopropenyl-2-oxobenzimidazol-1-yl)-2-(3-isopropenyl-2-oxobenzimidazol-1-yl)-2-(3-isopropenyl-2-oxobenzimidazol-1-yl)-2-(3-isopropenyl-2-oxobenzimidazol-1-yl)-2-(3-isopropenyl-2-oxobenzimidazol-1-yl)-2-(3-isopropenyl-2-oxobenzimidazol-1-yl)-2-(3-isopropenyl-2-oxobenzimidazol-1-yl)-2-(3-isopropenyl-2-oxobenzimidazol-1-yl)-2-(3-isopropenyl-2-oxobenzimidazol-1-yl)-2-(3-isopropenyl-2-oxobenzimidazol-1-yl)-2-(3-isopropenyl-2-oxobenzimidazol-1-yl)-2-(3-isopropenyl-2-oxobenzimidazol-1-yl)-2-(3-isopropenyl-2-oxobenzimidazol-1-yl)-2-(3-isopropenyl-2-oxobenzimidazol-1-yl)-2-(3-isopropenyl-2-oxobenzimidazol-1-yl)-2-(3-isopropenyl-2-oxobenzimidazol-1-yl)-2-(3-isopropenyl-2-oxobenzimidazol-1-yl)-2-(3-isopropenyl-2-oxobenzimidazol-1-yl)-2-(3-isopropenyl-2-oxobenzimidazol-1-yl)ethal **26** (10 mg, 2.5 %) mp 95-97 °C. Finally, elution with ethyl acetate afforded the trimer 1,3-bis-{2-(3-isopropenyl-2-oxobenzimidazole **29** (30 mg, 8.4 %) mp 122-124 °C. Anal. calcd. for **26** (C₂₁H₂₁N₄ClO₂): C, 63.55 %; H, 5.33 %; N, 14.12 %. Found: C, 63.31 %; H, 5.42 %; N, 14.11 %.

2.- A mixture of 1-isopropenylbenzimidazolin-2-one **15** (700 mg, 4 mmol), 1,3-bis(2-chloroethyl)benzimidazolin-2-one **17** (520 mg, 2 mmol) and potassium hydroxide (240 mg, 4.4 mmol) was irradiated in a microwave oven at 780 W for 22 min. (final temperature 167 °C). The crude product was washed with dichloromethane (20 mL) and the organic solution was dried over anhydrous magnesium sulfate. Removal of the solvent and column chromatography on silica gel (50 g), using chloroform:ethyl acetate 8:2 as eluent afforded 1,3-divinylbenzimidazolin-2-one **18** as an oil (20 mg, 2.7 %). Elution with chloroform:ethyl acetate 1:1 afforded **27** (310 mg, 43 %) and finally, elution with ethyl acetate afforded **29** (350 mg, 49.1 %), mp 122-124 °C. Anal. calcd. for **18** (C₁₁H₁₀N₂O): C, 70.95 %; H, 5.41 %; N, 15.04 %. Found: C, 71.13 %; H, 5.77 %; N, 14.93 %. Anal. calcd. for **27** (C₂₁H₂₀N₄O₂): C, 69.98 %; H, 5.59 %; N, 15.55 %. Found: C, 70.33 %; H, 5.78 %; N, 15.35 %.

3.- In a round bottom flask provided with a reflux condenser, potassium carbonate (8.28 g, 60 mmol) and tetrabutylammonium bisulfate (210 mg, 0.6 mmol) were added to a solution of 1-isopropenylbenzimidazolin-2-one **15** (1.05 g, 6 mmol) and 1,3-bis(2-chloroethyl)benzimidazolin-2-one **17** (780 mg, 3 mmol) and the solution was heated to reflux for 15 h. Inorganic salts were removed by filtration and washed with boiling acetonitrile. The combined organic solutions were evaporated to dryness, dissolved in dichloromethane and washed with water. The organic layer was dried over anhydrous magnesium sulfate and the solvent removed in vacuum. The crude product was purified as indicated before in 2, affording **18** (10 mg, 0.9 %), **27** (230 mg, 21.3 %) and the trimer **29** (830 mg, 77.6 %). Anal. calcd. for **29** (C₃₁H₃₀N₆O₃): C, 69.65 %; H, 5.66 %; N, 15.72 %. Found: C, 69.53 %; H, 5.67 %; N, 15.99 %.

1,3-Bis-{2-(2-oxobenzimidazol-1-yl)ethyl}-2-oxobenzimidazole (30).

35 % Hydrochloric acid (3.4 mL) was added to a solution of **29** (670 mg, 1.25 mmol) in methanol:water 1:1 (10 mL) and the mixture was heated to reflux for 1 h. A white solid that precipitates was identified as the trimer **30** (510 mg, 89.5 %) mp 294-296 °C (methanol). Anal. calcd. for $C_{25}H_{28}N_6O_3$: C, 66.07 %; H, 4.88 %; N, 18.49 %. Found: C, 65.85 %; H, 4.94 %; N, 18.05 %.

1,3-Bis-{2-(3-(2-{3-[2-(2-oxobenzimidazol-1-yl)ethyl)}-2-oxobenzimidazol-1-yl]ethyl}-2-oxobenzimidazol-1-yl)ethyl-2-oxobenzimidazole (32).

A solution of **30** (300 mg, 0.66 mmol), sodium hydride (70 mg, 1.76 mmol) in DMF (50 mL) was heated to 90 °C for 2 h. Lithium bromide (120 mg, 1.38 mmol) was added and the stirring was continued for 15 min. At this time a solution of 1,3-bis(2-chloroethyl)benzimidazolin-2-one (165 mg, 0.66 mmol) in DMF (10 mL) was added during 20 min and the reaction was continued at 90 °C for 24 h. The reaction was poured into ice and the solid was filtered. The solid was chromatographed on silica gel using dichloromethane:methanol:acetone 5:1:1 as eluent. Compound **32** was purified by preparative TLC using dichloromethane:methanol:acetone 10:1:1 (83 mg, 23 %), mp 175-180 °C (dec.).

ACKNOWLEDGMENTS

Thanks are given to the DGICYT of Spain for financial support, project numbers PB93-0125, PB93-0197-CO2 and PB94-0742. This research was carried out within the framework of an INTAS project (94-972) whose coordinator is Prof. Edwin Weber (Freiberg University, Germany).

REFERENCES

 Medvedeva, M. M.; Pozhrskii, A. F.; Simonov, A. M. Chem. Heterocycl. Compd. (Engl. Transl.) 1972, 8, 1280.

- 2. Weber, E.; Piel, M.; Buschmann, H.-J.; Cleve, E. Chem. Ber. 1992, 125, 2483.
- 3. Shi, Z.; Thummel, R. P. Tetrahedron Lett. 1995, 36, 2741.
- 4. Hayward, R. J.; Meth-Cohn, O. J. Chem. Soc. Perkin Trans. 1 1975, 212.
- 5. Hayward, R. J.; Meth-Cohn, O. J. Chem. Soc. Perkin Trans. 1 1975, 219.
- 6. Htay, M. M.; Meth-Cohn, O. Tetrahedron Lett. 1976, 79.
- 7. Htay, M. M.; Meth-Cohn, O. Tetrahedron Lett. 1976, 469.
- 8. Meth-Cohn, O. Smith, D. I. J. Chem. Soc. Perkin Trans. 1 1982, 261.
- 9. Shi, Z.; Thummel, R. P. J. Org. Chem. 1995, 60, 5935.
- Weber, E.; Trepte, J.; Gloe, K.; Piel, M.; Czugler, M.; Kravtsov, V. Ch.; Simonov, Y. A.; Lipkowski, J.; Ganin, E. V. J. Chem. Soc. Perkin Trans. 2 1996, 2359.
- 11. Shi, Z.; Goulle, V.; Thummel, R. P. Tetrahedron Lett. 1996, 37, 2357.
- 12. Claramunt, R. M.; Elguero, J.; Meco, T. J. Heterocycl. Chem. 1983, 20, 1245.
- 13. Torres, J.; Lavandera, J.-L.; Cabildo, P.; Claramunt, R. M.; Elguero, J. J. Heterocycl. Chem. 1988, 25, 771.
- 14. Torres, J.; Lavandera, J.-L.; Cabildo, P.; Claramunt, R. M.; Elguero, J. Bull. Soc. Chim. Belg. 1992, 101, 29.
- 15. Davoll, J.; Laney, D. H. J. Chem. Soc. 1960, 314.
- 16. Vernin, G.; Domolog, H.; Siv, C.; Metzger, J.; El-Shafei, A. K. J. Heterocycl. Chem. 1981, 18, 85.
- 17. Meanwell, N. A.; Si, S. Y.; Gao, J.; Wong, H. S.; Gao, Q.; St. Laurent, D. R.; Balasubramanian, N. J. Org. Chem. 1995, 60, 1565 and references therein.
- 18. Hall, S. R.; Flack, H. D.; Stewart, J. M. 'Xtal3.2', Ed. Univ. of Western Autralia, Perth, 1994.
- 19. Abrahams, G.A.; Keve, E. T. Acta Crystallogr. Sect. A 1971, 27, 157.
- Allen, F. H.; Davies, J. E.; Galloy, J. J.; Johnson, O.; Kennard, O.; Macrae, C. F.; Mitchell, E. M.; Mitchell, J. F.; Smith, J. M.; Watson. D.G.; J. Chem. Info. Comput. Sci. 1991, 31, 187
- 21. Blaton, N. M.; Peeters, O. M.; de Ranter, C. J. Acta Crystallogr. Sect. B 1980, 36, 2828.
- 22. Klein, C. L.; Walch, J. L.; Southall, C. Acta Crystallogr. Sect. C 1989, 45, 650.
- 23. Raves, M. L.; Kanters, J. A.; Tollenaere, J. P. Acta Crystallogr. Sect. C 1992, 48, 1712.
- 24. Collin, S.; Moureau, F.; Quintero, M. G.; Vercauteren, D. P.; Evrard, G.; Durant, F. J. Chem. Soc. Perkin Trans. 2 1995, 77.
- 25. Murty, V. V. S.; Murthy, B. V. R. Z. Kristallogr. 1981, 157, 191.
- 26. Herbstein, F. H.; Kapon, M. Z. Kristallogr. 1985, 173, 249.
- 27. Schwiebert, K. E.; Chin, D. N.; MacDonald, J. C.; Whitesides, G. M. J. Am. Chem. Soc. 1996, 118, 4018.
- 28. Cano, F. H.; Martínez-Ripoll, M. J. Mol. Struc. (Theochem), 1992, 258, 139.
- 29. Cram, D. J. Angew. Chem. Int. Ed. Engl. 1988, 27, 1009.
- Altomare, A.; Burla, M.C.; Camalli, M.; Cascarano, G.; Giacovazzo, C.; Guagliardi, A.; Polidori, G. SIR92, J. Appl. Cryst. 1994, 27, 435.
- 31. International Tables for X-Ray Crystallography, Kynoch Press, Birmingham, England, 1974.
- 32. Martínez-Ripoll, M.; Cano, F.H. 'PESOS', unpublished program.
- 33. Nardelli, M. Comput. Chem. 1983, 7, 95.

(Received in UK 27 February 1997; revised 14 April 1997; accepted 17 April 1997)