N-Bridged Heterocycles. Part II.[1] Synthesis and Aromaticity of 1,3-Polymethylene-benzimidazolium Salts {[n](1,3)Benzimidazolophanium Salts}, -benzimidazolones, and -benzimidazolethiones

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[n](1.3)Benzimidazolophanium salts have been synthesised from NN'-polymethylene-o-phenylenediamines with 6—12 methylene groups in the bridge, by the action of dichloromethyl methyl ether. The aromaticity of this series of compounds is compared to that of the corresponding series of benzimidazol-ones and -thiones with 5—12 bridging methylene groups by a study of their u.v.. i.r.. and ^{1}H and ^{13}C n.m.r. spectra. It is concluded that aromaticity is significant in the salts with $n \geqslant 6$. in the bridged benzimidazolones with $n \geqslant 7$. and in the bridged benzimidazolethiones with $n \geqslant 7$ or 8.

NUMEROUS examples of para- and meta-cyclophanes have been elaborated,[2] the lower limit for the bridging chain being seven[3] † and six methylene groups[2] respectively. Also a variety of analogous 'meta-bridged' five-membered heterocycles (including thiophens,[4] pyrroles,[5] furans,[5a,6] isoxazoles,[6a] and pyrazoles[6a,7]) have

been reported, the lower limit for the polymethylene bridge being six members. However, no examples have yet been reported in which the bridging chain is attached to hetero-atoms, and no study of the degree of aromaticity of a bridged heterocycle with variation of the bridging chain length has been undertaken. We now report the synthesis of the 1,3-polymethylene-benzimidazolium salts (1) (benzimidazolophanium salts), -benzimidazolones (2), and -benzimidazolethiones (3).

† *Note added in proof:* A recent paper (V. V. Kane, A. D. Wolf, and M. Jones, jun., *J. Amer. Chem. Soc.*, 1974, **96**, 2643) reports the synthesis of [6]paracyclophane.

[1] Part I, R. J. Hayward and O. Meth-Cohn, preceding paper.
[2] B. H. Smith, 'Bridged Aromatic Compounds,' Academic Press, New York, 1964.
[3] N. L. Allinger and T. J. Walter, *J. Amer. Chem. Soc.*, 1972, **94**, 9267; A. D. Wolf, V. V. Kane, R. H. Levin, and M. Jones, jun., *ibid.*, 1973, **95**, 1680.
[4] *E.g.* see Ya. L. Gol'dforb, S. Z. Taits, and L. I. Belenkii, *Tetrahedron*, 1963, **19**, 1851 and references cited therein; O. Meth-Cohn, *Quart. Reports Sulphur Chem.*, 1970, **5**, 129 and references cited therein.

[5] (a) H. Nozaki, T. Koyama, and T. Mori, *Tetrahedron*, 1969, **25**, 5357; (b) H. H. Wasserman, T. C. Rodgers, and D. D. Keith, *J. Amer. Chem. Soc.*, 1969, **91**, 1263, 1264.
[6] (a) S. Bradamante, R. Fusco, A. Marchesini, and G. Pagani, *Tetrahedron Letters*, 1970, 11; (b) S. Fujita, T. Kawaguti, and H. Nozaki, *Bull. Chem. Soc. Japan*, 1970, **43**, 2596.
[7] (a) W. E. Parham and J. F. Dooley, *J. Org. Chem.*, 1968, **33**, 1476; (b) K. Schant, B. Eistert, and J. H. Felzmann, *Chem. Ber.*, 1966, **99**, 1414; (c) S. Fujita, Y. Hayashi, and H. Nozaki, *Tetrahedron Letters*, 1972, 1645.

In Part I [1] the synthesis of NN'-polymethylene-o-phenylenediamines (4) and their conversion into dihydrobenzimidazoles (5), benzimidazolones (2), and benzimidazolethiones (3) was reported.

(1)

(2) X = O
(3) X = S

(4)

(5)
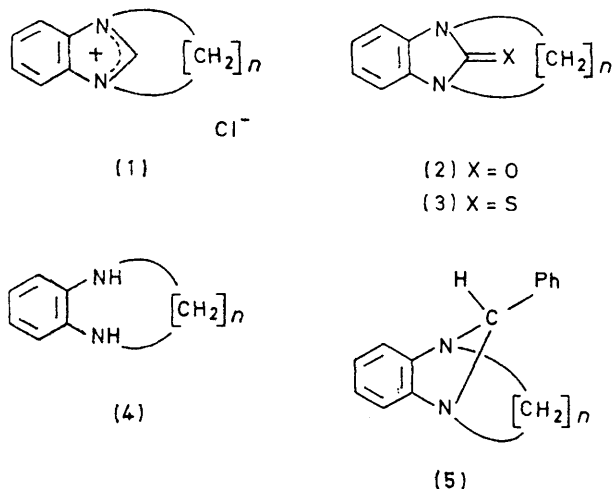
Synthesis of the Benzimidazolophanium Salts.—Our first attempts to produce [n](1,3)benzimidazolophanium salts (1) lay in the aromatisation of the bridged 2,3-dihydrobenzimidazoles [*e.g.* (5)], since the unbridged

the bridge proton which is most probably located between the polymethylene chain and the phenyl substituent (5).

A second potential method, the classical Phillips benzimidazole synthesis,[9] employing the action of a carboxylic acid on the diamines (4), was equally ineffective. However, the salts (1) were readily obtained in high yield (see Table 1) by use of dichloromethyl methyl ether in dry tetrahydrofuran.[10] The anhydrous salt was isolated by removal of the solvent, while the monohydrates crystallised out when the solution was left open to the atmosphere. The method proceeded well for the series (1; $n = 6$—12) (see Table 1) but not at all with the amines (4; $n = 5$ or 4). The hexa- and hepta-methylenebenzimidazolium salts (1; $n = 6$ or 7) formed rapidly and exothermically in the cold but higher members required heating. The hexamethylenebenzimidazolium salt was an unstable compound unlike the higher members, readily converting into 1-(6-chlorohexyl)benzimidazole (6; $n = 6$) on standing. Consequently it was not obtained in a pure form. The higher homologues only underwent this ring opening at *ca.* 240°, to give good yields of the appropriate benzimidazole (6). The salts were stable to water but ring-opened immediately with aqueous alkali to give the N-formyl derivative of the parent amine (4). Attempted

TABLE 1
Properties of the 1,3-polymethylenebenzimidazolium chlorides (1)

| | | | Analyses [c] | | | | | | | | ¹H N.m.r. spectra (τ values) [a] | | | |
| | | | Found (%) | | | | Required (%) | | | Aromatic | | Aliphatic | |
n	M.p.[a] (°C)	M^+ [a,b]	C	H	N	Formula	C	H	N	CH (s)	Others (m)	NCH₂	Other CH₂
6		201								−1·75	2·35	5·5-12, m; 5·58, m	7·8 (4H, m), 8·0—9·9 (8H, m)
7	262—263 (decomp.)	215	62·5	7·9	10·4	C₁₄H₁₉ClN₂,H₂O	62·6	7·9	10·4	−1·91	2·30	5·21, q	7·8—9·3 (9H, m), 12·4 (1H, m)
8	260—261	229	64·5	8·1	10·1	C₁₅H₂₁ClN₂,H₂O	63·7	8·2	9·9	−2·00	2·35	5·42, t	7·9—9·1, m
9	277—278	243	64·6	8·5	9·4	C₁₆H₂₃ClN₂,H₂O	64·7	8·5	9·4	−1·80	2·30	5·32, t	7·94 (4H, m), 8·76 (8H, m), 9·4 (4H, m)
10	224—225	257	65·7	8·7	9·3	C₁₇H₂₅ClN₂,H₂O	65·7	8·8	9·0	−2·12	2·30	5·32, t	7·92 (4H, m), 8·52 (4H, m), 8·92 (4H, m), 9·40 (4H, m)
12	255—256	285	67·2	9·2	8·5	C₁₉H₂₉ClN₂,H₂O	67·3	9·2	8·3	−1·58	2·36	5·35, t	8·02 (4H, m), 8·6—9·1 (20H, m)

[a] Determined for anhydrous material. [b] In each case the observed M^+ value is that required. [c] Determined for the hydrate.

analogues (*e.g.* 1,3-dimethyl-2,3-dihydrobenzimidazole) are noted for their hydride lability,[8] so that very mild electrophiles (even carbon tetrachloride) cause aromatisation. However, these bridged systems (5) resisted aromatisation by the action of carbon tetrachloride, mineral acid [resulting in reversion to the amine (4) and benzaldehyde], iodine, and silver nitrate. Even with such powerful hydride abstracting reagents as triphenylmethylium tetrafluoroborate, aromatisation of the dihydrobenzimidazole (5; $n = 10$) was not observed. It is evident that the potential hydride lability of this system is completely masked by the inaccessibility of

reduction of the salts with sodium borohydride again gave only the N-formyl derivative, probably owing to the basic conditions.

The benzimidazolophanium salts (1) and bridged benzimidazol-ones (2) and -thiones (3) are the first extensive series of heterocyclic cyclophanes available and a study of their changes in properties with change in bridge size is clearly of interest. These compounds are isosteres of the benzotropylium (7) and benzotropone (8) cyclophanes. A full study of the u.v. and i.r. spectra of the latter compounds has been made by Kloster-Jensen and her co-workers [11] and inferences
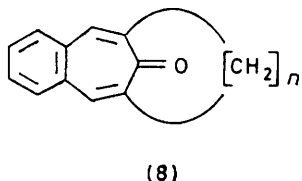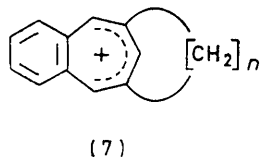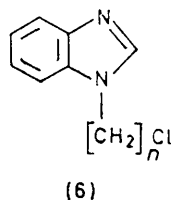
[8] A. V. El'tsov and Kh. L. Muravitch-Aleksandr, *J. Org. Chem. U.S.S.R.*, 1965, 1695.
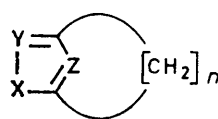[9] M. A. Phillips, *J. Chem. Soc.*, 1928, 172, 2393.

[10] *Cf.* K. Poduska and H. Gross, *Chem. Ber.*, 1961, **94**, 527.
[11] E. Kloster-Jensen, N. Tarkoy, A. Eschenmoser, and E. Heilbronner, *Helv. Chim. Acta*, 1956, **39**, 786.

concerning their aromaticity noted. These compare favourably with our results.

(6)

(7)

(8)

U.v. Spectroscopy of the Heterophanes (1)—(3).—The u.v. spectra of cyclophanes generally show loss of fine structure (due to loss of vibrational freedom) and shifts to longer wavelengths and lower intensities (associated
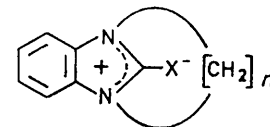
highest two absorptions (278 and 271 nm) remained virtually unchanged throughout the series ($n = 12$—7) while the intensities decreased almost linearly (Table 2 and Figure 1) with decrease in the size of the bridge. Thus while some deformation is evident, the whole

(9) X = NH, Y = N, Z = CH   (11)
(10) X = Y = CH, Z = S

series ($n = 12$—7) shows little steric inhibition of resonance and is clearly aromatic. This is in contrast to the large shift noticed in the only reported benzo-tropylium salts [13] (7; $n = 12$) [450 nm (ε 1800)] and (7; $n = 10$) [440 nm (ε 2000)].

The benzimidazol-ones (2) and -thiones (3) are also potentially aromatic, and thus planar systems, since mesomeric structures such as (11) may be envisaged.

TABLE 2

I.r. and u.v. spectra of the benzimidazolium salts (1) and benzimidazol-ones (2) and -thiones (3)

Compound No.	n	$\nu_{max}.(C{=}X)/$ cm^{-1} [a]	$\lambda_{max}./$nm (ε) [b]				
(1)	7		211 (10,025)	259 (5010)	264·5 (5355)	271 (6150)	278·5 (5125)
(1)	8		210 (10,990)	257 (5290)	264 (5565)	271 (6240)	278 (5430)
(1)	9		210 (11,960)	257 (5125)	264 (5390)	271 (6310)	278 (5520)
(1)	10		210 (10,270)	257 (5090)	263·5 (5470)	271 (6425)	278 (5640)
(1)	12		210·5 (11,210)	257·5 (5380)	263·5 (5720)	271 (6720)	278 (61610)
(2)	5	1750	217 (14,220)		281·5 (3130)	287 (2360)	
(2)	6	1724	216 (22,050)	232 (7050)	284 (4615)	289 (4030)	
(2)	7	1715	217 (17,850)	233 (6460)	284 (6130)	289 (5480)	
(2)	9	1710	216 (14,650)	234 (5950)	284 (6470)	289 (5860)	
(2)	10	1710	216·5 (15,120)	234 (5630)	284 (6520)	289 (5870)	
(2)	12	1710	215 (17,070)	234 (6120)	284 (6880)	289 (6130)	
(3)	5	1370	217 (15,700)	227 (600)	274 (2380)	336 (17,620)	
(3)	6	1390	209 (16,450)	231 (11,610)	266 (2530)	326 (20,650)	
(3)	7	1403	207 (10,540)	232 (10,950)	260 (4600)	322 (21,350)	
(3)	8	1405	206 (9540)	231 (11,100)	257 (6500)	318 (21,400)	
(3)	9	1410		229 (15,380)	252 (10,700)	314 (25,800)	
(3)	10	1412		229 (18,200)	249 (15,200)	313 (31,200)	
(3)	12	1412		228 (20,090)	249 (17,200)	312 (32,400)	

[a] For 2% solution in CCl$_4$.   [b] For solution in MeOH.

with decrease in the π–π* transition energy) as the bridging group shortens.[2] Allinger [12] has calculated the shift of absorption wavelength as a function of the angular deformation of the benzene ring in the para-cyclophane series. His predictions concerning the then unknown [7]paracyclophane [3] proved remarkably accurate. By analogy one would expect less deformation in a five-membered aromatic system and consequently smaller shifts. In the (3,5)pyrazolophane series (9) [7c] a small bathochromic shift and reduction in intensities accompanies the change of n from 10 to 7. In the only other such series, the (2,5)thiophenophanes [4] (10; $n = 10$, 11, and 12), the intensity was again reduced but a slight hypsochromic shift was observed. In the case of our benzimidazolophanium salts (1) the

As the polymethylene chain length decreases, a change from the planar, aromatic structure (11) to the non-planar, non-aromatic system (2) or (3) can be expected. This should be accompanied by a loss of conjugation and thus a large change in the u.v. spectra. This is clearly seen in the case of the benzimidazolones (2) (Table 2 and Figure 1). With $n = 12$—7, the two highest absorptions (which again vary only slightly in their wavelengths throughout the series) show a decrease in intensity almost parallel to that of the benzimidazolium salts (1). However, below $n = 7$, a sharp downward change in the slope of the curve is seen which we attribute to loss of conjugation and hence loss of aromaticity. A similar dramatic change in the spectra of the benzotropones (8; $n = 4$—13) was observed with

[12] N. L. Allinger, L. A. Freiberg, R. B. Hermann, and M. A. Miller, *J. Amer. Chem. Soc.*, 1963, **85**, 1171.

[13] R. E. Harmon, R. Suder, and S. K. Gupta, *Canad. J. Chem.*, 1970, **48**, 195; *J.C.S. Perkin I*, 1972, 1746.

less than seven methylene groups in the bridge.[11] With $n \geqslant 7$ the spectra varied only slightly. The u.v. spectra of the benzimidazolethiones (3) show more complex changes involving wavelength, intensity, and appearance of new peaks with decrease in bridge size
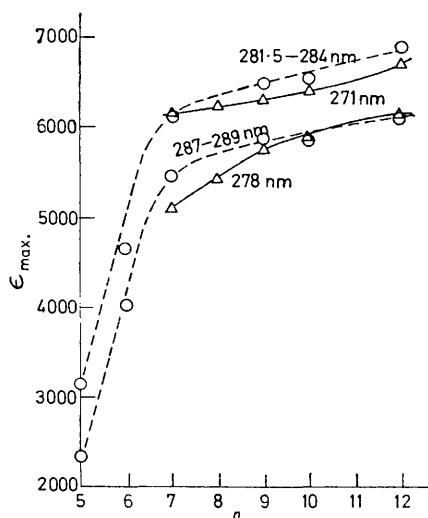

FIGURE 1 Variation of intensity of the u.v. absorption maxima with bridge size for the benzimidazolium salts (1) (solid lines) and benzimidazolones (2) (dashed lines) in chloroform solution

(Table 2). We attribute this to the fact that the unconjugated C=S group is a chromophore in its own right.

I.r. Spectra of the Heterophanes (1)—(3).—Kloster-Jensen and her co-workers [11] also showed that while the i.r. carbonyl stretching frequency of the benzotropones (8; $n = 4$—13) varied only slightly with $n \geqslant 7$, a large increase was observed with $n = 4$—6 (Figure 2). A
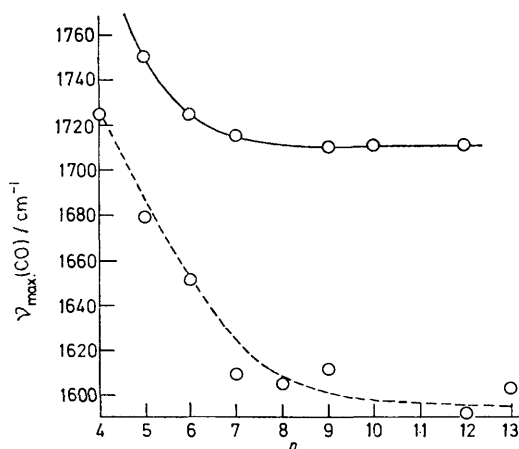

FIGURE 2 Variation of the i.r. carbonyl stretching frequencies with bridge size for the benzimidazolones (2) (solid line) in 2% carbon tetrachloride and the benzotropones (8) as Nujol mulls[11] (dashed line)

similar trend is observed with the benzimidazolones (2) (Table 2 and Figure 2) which again supports the change from a planar, urea-like carbonyl group to a non-

planar, non-conjugated carbonyl group involving considerable strain. The stretching frequency of the thiocarbonyl group is, however, much less clearly defined. Thus thioketones absorb [14a] in the region 1200—1050 cm^{-1} while thioureas appear [14b] as high as 1400 cm^{-1}. Thus, the benzimidazolethione (3) absorptions might be expected to decrease in frequency with decrease in the bridge size. This is seen with variations from 1412 to 1370 cm^{-1} for values of n from 12 to 5. Again a transition in the magnitude of this change is seen below $n = 7$ but this effect is not as marked as with the benzimidazolones (Table 2).

N.m.r. Spectra of the Heterophanes.—The effect of stretching a polymethylene chain across an aromatic ring forces methylene protons into the π-cloud of the ring causing anomalous, high-field shifts. Thus [9](3,5)-pyrazolophane (9; $n = 9$) shows the central methylene group at τ 9·22 instead of the usual position (τ *ca.* 8·6), while [7](3,5)pyrazolophane (9; $n = 7$) displays only one proton at τ 11·96, with four others in the region τ 9·0—9·5.[7c] Other cyclophanes reveal similar anisotropic effects, in accord with their unusual structures.[2,3,6a] The salts (1; $n = 6$—12) all showed the characteristic low-field singlet absorption (τ —1·0 to —2·2) associated with the aromatic 2-H of the benzimidazole ring (Table 1). Also the aromatic protons appeared as a symmetrical multiplet (AA'BB') associated with an *o*-disubstituted benzene ring (τ 2—2·5). However, the NCH_2 protons (τ 5·0—5·5) appeared as a triplet for $n = 12$—8, but were non-equivalent for $n = 6$ and 7, indicating the restricted ' swinging ' of the polymethylene chain. In all the analogues with 6—10 methylene groups (but not 12) the diamagnetic shielding of the mid-chain methylene groups is evident (τ 9·1—10·0). Thus the decamethylene derivative (1; $n = 10$) exhibits distinct multiplets for the β- (τ 7·92), γ- (8·52), δ- (8·92), and ε- (9·40) protons each showing a higher shielding effect, as indicated by decoupling experiments. This effect is most dramatic with the heptamethylene case (1; $n = 7$) where a one-proton multiplet appears at τ 12·4 due to one mid-chain (δ) proton, as indicated by molecular models (*cf.* the [7]pyrazolophane mentioned above), being thrust into the π-cloud of the aromatic ring. Double irradiation at τ 8·00 simplifies this signal to a doublet (*J* 12 Hz) indicating the chemical shift of the γ-protons (τ 8·00) while triple resonance at τ 8·00 and 8·87 simplifies the multiplet to a singlet indicating that the δ'-proton absorbs at τ 8·87. Similar decoupling experiments allowed the verification of the chemical shifts of the other analogues (see Table 1). The [1]H n.m.r. spectra of the bridged benzimidazol-ones (2) and -thiones (3) show similar features to the salts (1).[1] Thus the shielding of the mid-chain methylene protons (which is generally greater in the thione series) is at a maximum for one δ-proton of the heptamethylene derivatives [(2; $n = 7$) τ 10·8; (3; $n = 7$) τ 11·2]. The increasing size of the 2-substituent of the benzimidazole ring is reflected in the non-equivalence of the NCH_2 protons of the benzimidazol-ones (2; $n = 5$—10 but *not* 12) and

-thiones (3; $n = 5$—12). Even at 150° the dodeca-methylenebenzimidazolethione (3; $n = 12$) shows this non-equivalence, while the analogous benzimidazolone (2; $n = 12$) shows equivalent protons even at —60°.

Because of the uncertainty of other spectral methods in confirming the aromaticity of the bridged benz-imidazolethiones, we have also studied their ^{13}C n.m.r. spectra and, for comparison, those of some benz-imidazolones (Table 3). It is well known that the effect of strain generally is to cause an upfield shift of ^{13}C resonances.[15] In the molecules in question this should show itself at the C=X, NCH$_2$, and C–N carbon atoms in particular. This effect in our series might be

EXPERIMENTAL

Preparation of the Benzimidazolophanium Salts (1).—To the NN'-polymethylene-o-phenylenediamine (4) [1] (0·01 mol) in dry tetrahydrofuran (15 ml) was added dichloromethyl methyl ether [16] (0·04 mol) and the mixture was refluxed for 3 h. The condenser was then removed and the mixture left open to the atmosphere overnight. The salts precipitated as white crystalline hydrates in virtually quantitative yield. The salts could be further purified by dehydration (at 180—200° *in vacuo*) and immediately dissolving the anhydrous material in dry tetrahydrofuran, followed by precipitation of the hydrate as above. The properties of the products are recorded in Tables 1 and 2.

TABLE 3

^{13}C N.m.r. spectra of benzimidazol-ones (2) and -thiones (3)

Shift relative to (2 or 3; $n = 10$) *

Compound	n	Ar-3	Ar-2	Ar-1	C=X	NCH$_2$	Other CH$_2$ (p.p.m.)
(2)	5	—6·18	—2·92	—8·58	—20·53	—14·75	23·53, 31·13
(2)	6	—2·93	—1·17	—6·13	—8·97	—4·94	24·18, 28·79
(2)	7	—1·76	—1·65	—2·08	—5·13	—2·53	24·83, 26·91, 27·30
(2)	10	0	0	0	0	0	25·35, 26·19, 26·52
(3)	5	—4·35	—1·76	—8·18	—33·53	—17·22	24·31, 33·08
(3)	6	—1·82	—0·52	—5·41	—11·77	—4·16	23·59, 28·27
(3)	7	—1·17	—0·39	—2·01	—5·98	—2·21	24·11, 26·19, 28·99
(3)	8	—0·71	—0·26	—0·91	—3·44	—0·52	22·42, 27·30, 28·14
(3)	9	—0·13	0	—0·84	—0·52	+0·59	22·88, 23·92, 25·54
(3)	10	0	0	0	0	0	24·50, 25·67, 26·06, 27·04
(3)	12	+0·07	+0·19	—0·19	+0·65	+0·65	24·24, 25·61, 26·65, 27·23

* Shift in p.p.m., negative indicates downfield: (3; $n = 10$) Ar-3, 109·38; Ar-2, 122·70; Ar-1, 132·13; CS, 170·86; NCH$_2$, 45·04; (2; $n = 10$) Ar-3, 108·01; Ar-2, 120·95; Ar-1, 129·33; CO, 154·94; NCH$_2$, 41·27.

expected to be modulated by any anisotropy associated with the aromaticity of the system or with the carbonyl or thiocarbonyl bond. However, exactly the reverse effect is observed. While only small shifts are seen in the aromatic CH carbon resonances, large downfield shifts of up to 34 p.p.m. accompany decrease in the bridge size. We attribute this effect primarily to the change in geometry of the system. Unlike the u.v. and i.r. data for the benzimidazolones a sharp transition is not observed in the chemical shifts of the thiones, supporting the indication from the i.r. spectra that the change from a planar, aromatic to the non-planar system is less distinct in the thiones. The change is most evident with 7—8 methylene groups in the bridge.

In conclusion, the benzimidazolophanium salts (1) show aromatic character in the series $n = 6$—12, the 2-oxo-analogues (2) with $n = 7$—12, and the 2-thioxo-analogues (3) with $n = 7$ or 8—12.

Thermolysis of the Benzimidazolium Salts.—The salt (1) (0·5 g) was distilled in a Kugelrohr apparatus at 240—250° and 0·5 mmHg. By this method was obtained 1-(9-*chlorononyl*)*benzimidazole* (6; $n = 9$) (0·4 g, 80%) as an oil [Found: C, 68·8; H, 8·1; N, 9·9%; M^+, 278. $C_{16}H_{23}ClN_2$ requires C, 69·1; H, 8·3; N, 10·1%; M (for ^{35}Cl), 278], τ (CDCl$_3$) 1·12br (1H, s), 2·50 (4H, m), 5·65 (2H, t, CH$_2$Cl), 6·50 (2H, t, NCH$_2$), and 7·8—8·9 (14H, m).

Reaction of the Salts (1) *with Alkali.*—The salt (1; $n = 10$) (0·5 g) in aqueous sodium hydroxide (20 ml; 4M) was kept for 30 min and then extracted with chloroform to give, on drying and evaporation of the solvent, 2,13-*diazabicyclo*-[12.4.0]*octadeca*-14,16,18-*triene*-2-*carbaldehyde* as an oil (0·3 g), ν_{max} (Nujol) 3360 (NH) and 1680 cm^{-1} (CO) (Found: C, 74·2; H, 9·3; N, 10·1%; M^+, 274. $C_{17}H_{26}N_2O$ requires C, 74·5; H, 9·6; N, 10·2%; M, 274).

[14] (*a*) K. Nakanishi, ' Infrared Absorption Spectroscopy—Practical,' Holden-Day, San Francisco, 1962, p. 54; (*b*) L. J. Bellamy, ' The Infrared Spectra of Complex Molecules,' Methuen, London, 2nd edn., 1962, p. 356.

[15] G. C. Levy and G. L. Nelson, ' Carbon-13 Nuclear Magnetic Resonance for Organic Chemists,' Wiley, New York, 1972, p. 24.
[16] H. Gross, A. Rieche, E. Hoft, and E. Beyer, *Org. Synth.*, 1967, **47**, 47.