

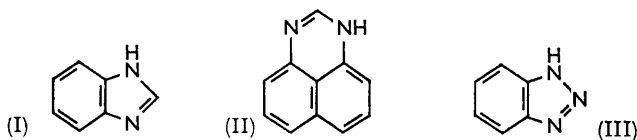
455. *The Infrared Spectra of Some Simple Benzimidazoles.*

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Infrared spectra of some simple alkyl-, perfluoroalkyl-, and carboxyl-substituted benzimidazoles and of some of their simple derivatives and analogues are reported and discussed.

WHILE the infrared spectrum of imidazole¹ and of some of its simple derivatives and salts² have been discussed, the spectra of few benzimidazoles have been recorded in the literature.³ As the benzimidazole ring system (I) is of considerable chemical and biological interest it seemed desirable that fuller information of its spectroscopic characteristics should be available. The preparation (for other purposes) of a number of benzimidazoles has enabled us to investigate their spectra; the results are reported in this paper.

The spectra of solid specimens of the simple alkyl- and perfluoroalkyl-benzimidazoles are characterised by a series of strong, broad bands in the region 2400—3200 cm.⁻¹; they show no band in the region normally associated with the simple N-H stretching frequency (Fig. 1). In solution (concentration <0.01 mole/l.) this region of the spectrum is completely changed: the broad-banded absorption is replaced by a single sharp band near 3400 cm.⁻¹ which must be ascribed to the N-H stretching vibration. It has been shown that in relatively concentrated solutions (0.02—0.6 mole/l.) benzimidazoles are strongly associated⁴ and indeed the spectra of more concentrated solutions (0.01—0.03 mole/l.) possess a broad band near 3200 cm.⁻¹ indicating the presence of polymeric association.



It seems beyond doubt that the strong bands near 2400—3200 cm. in the spectra of the solid benzimidazoles are best ascribed to a strong hydrogen bond of the type N-H...N showing proton transfer.⁵ This receives confirmation from examination of the spectra of a number of 1-deuterated benzimidazoles. The strong, banded absorption is displaced to a *ca.* 2200 cm.⁻¹ and it is simultaneously rendered less diffuse (Fig. 1). Equally significantly,⁶ the ratio $\nu(\text{N-H}) : \nu(\text{N-D})$ [the value of $\nu(\text{N-H})$ being taken for the centre of the strong bands] is approximately 1.30. Together, these facts indicate that the association is weaker for the deuterated compounds and in accordance with the representation of the hydrogen bond as a proton-transfer system.

The position of the N-H bands in the spectra of solutions of benzimidazoles (Table I) is similar to that found for pyrroles⁷ and indoles;⁸ the bands show typical displacements (of +10—20 cm.⁻¹) when tetrachloroethylene replaces methylene chloride as solvent. The effect of substituents is in accord with expectation: the small increases in frequency of the alkyl derivatives and the larger decreases in frequency of the perfluoroalkyl compounds diminish as the orientation of substitution varies: 2- > 4- ≥ 5-. It seems probable that these shifts are due mainly to induction and that there is little hydrogen bonding to adjacent fluorine atoms (this would have necessitated a larger shift for 4-perfluoroalkyl compounds), but re-examination of these bands under conditions of greater

¹ Garfinkel and Edsall, *J. Amer. Chem. Soc.*, 1958, **80**, 3807.

² Otting, *Chem. Ber.*, 1956, **89**, 1940, 2887.

³ Randall, Fowler, Fuson, and Dangel, "Infrared Determination of Organic Structures," Van Nostrand, New York, 1949, p. 216; Baganz and Pflug, *Chem. Ber.*, 1956, **89**, 691; O'Sullivan, *J.*, 1960, 3278.

⁴ Hunter and Marriot, *J.*, 1941, 777.

⁵ Cannon, *Spectrochim. Acta*, 1958, **10**, 341.

⁶ Bellamy and Rogasch, *Proc. Roy. Soc.*, 1960, *A*, **257**, 98.

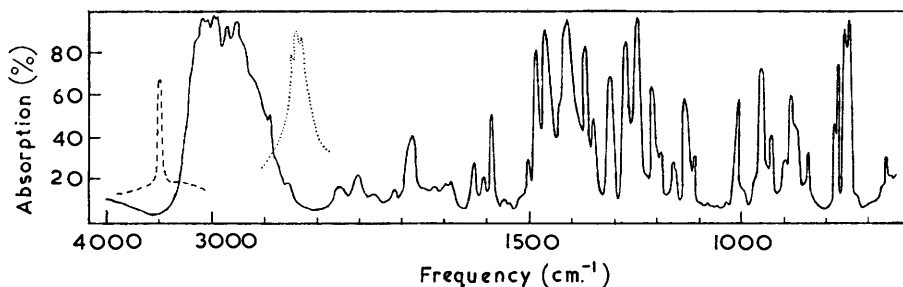
⁷ Eisner and Erskine, *J.*, 1958, 971.

⁸ Millich and Becker, *J. Org. Chem.*, 1958, **23**, 1096.

dispersion would be of interest. The intensities of the N-H bands show analogous variations. In general, those compounds with perfluoroalkyl substituents show more intense absorption, giving both higher values of extinction coefficients and broader bands, but no simple correlation between orientation of substitution and intensity is apparent.

Bands derived primarily from aromatic C-C and C-N stretching modes are found in the region 1620—1500 cm^{-1} . In the spectrum of benzimidazole itself (Fig. 1) and of

FIG. 1. Infrared spectrum of benzimidazole. — Mull with Nujol or Fluorolub; — — — solution in methylene chloride; 1-deuterobenzimidazole, mull with Nujol or Fluorolub.



those derivatives which carry no substituent in the heterocyclic ring a consistent pattern of three weak bands is found in this region, near 1620, 1600, and 1500 cm^{-1} (Tables 1, 2). When the heterocyclic ring is substituted, a fourth band of variable intensity appears near 1550 cm^{-1} . (The band near 1500 cm^{-1} is frequently partly masked in solution by a strong band in the spectrum of the solvent.) Other bands probably derived from C-C stretching modes appear near 1420 and 1460 cm^{-1} .

TABLE I. Some characteristic bands in the spectra of solutions^a of benzimidazoles and some related compounds.

Benzimidazole	N-H bands				Other bands							
	ν ^b	ϵ ^c	t ^d	ν	ϵ	ν	ϵ	ν	ϵ	ν	ϵ	
Unsubst.	3460	130	4.5	1620	25	1603, 1592	40	—	—	—	—	
2-Me	3460	125	4.9	1622	30	1599	—	1542	105	—	—	
2-Et	3470	135	6.0	1620	35	1599	—	1540	160	—	—	
2-Pr ⁿ	3460	120	5.4	1622	30	1591	—	1535	115	—	—	
2-Pr ⁱ	3470	135	6.0	1622	25	1594	—	—	—	—	—	
4-Me	3460	135	5.3	1616	20	1599	15	—	—	—	—	
5-Me	3460	95	3.3	1618	—	1596	—	1543	80	—	—	
2,5-Me ₂	3460	130	5.0	1620	40	1601	15	1548	95	—	—	
2-CF ₃	3430	150	8.2	1625	10	1597	50	1538	40	—	—	
2-C ₂ F ₅	3420	165	9.9	1618	—	1593	25	1538	45	—	—	
2-C ₃ F ₇	3430	170	10.1	1618	10	1591	20	—	—	—	—	
4-CF ₃	3430	140	7.1	1625	20	1610	10	—	—	—	—	
5-CF ₃	3440	—	—	1632	—	1598	—	—	—	—	—	
2-Me-4-CF ₃	3450	145	7.3	1627	50	1610	35	1545	105	—	—	
4-Me-2-CF ₃	3440	200	10.9	1619	25	1601	40	1545	105	—	—	
4-Me-2-C ₃ H ₇	3440	165	10.0	1620	20	1604	20	1532	50	—	—	
2,4-(CF ₃) ₂	3430	150	11.4	1628	—	1610	50	1554	85	—	—	
2,5-(CF ₃) ₂	3420	150	9.0	1632	—	—	—	1550	70	—	—	
2-Me-4,5-(CF ₃) ₂ ...	3450	175	7.9	1642	35	1599	10	1545	115	—	—	
2,4,5-(CF ₃) ₃	3400	145	10.1	1626	—	—	—	1553	40	—	—	
5-MeO-2-CF ₃	3440	165	9.0	1630	125	1619	90	1574	200	—	—	
4,5,6,7-F ₄ -2-CF ₃ ...	3390	85	5.2	—	—	1604	80	1566	410	1548	295	
Other compounds												
Benzotriazole	3450	150	7.6	1618	30	1596	15	—	—	1510	10	
Perimidine	3420	105	3.6	1632	185	1615	220	1596	200	—	—	
2-Methylperimidine	3430	135	5.1	1635	260	1620	745	1595	405	1524	55	
2-Ethylperimidine	3420	135	5.4	1635	260	1614	600	1596	410	1525	55	
2-Propylperimidine	3420	130	5.2	1633	305	1615	685	1597	405	1524	55	

^a In methylene chloride. ^b Band frequency (in cm^{-1}). ^c Extinction coefficient = $(1/d)(\log T_0/T)$. ^d $t = 10^{-3}\epsilon \cdot \Delta\nu$.

Bands which appear regularly in the spectra of the simple benzimidazoles near 1000 and 960 cm^{-1} may be associated with benzenoid ring breathing modes and bands near 760 and 880 cm^{-1} with heterocyclic ring breathing modes. Elsewhere the spectra of the

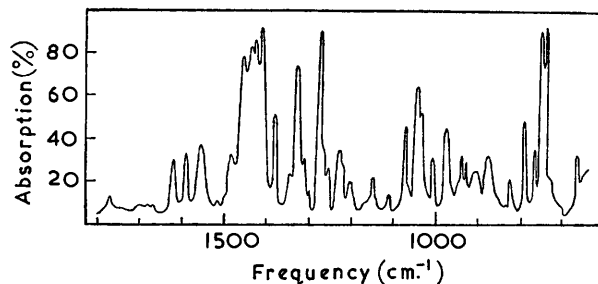


FIG. 2. Infrared spectrum of 2-ethylbenzimidazole (mull with Nujol or Fluorolub).

alkyl-substituted compounds show absorption corresponding to the pattern of substitution.⁹ Compounds containing trifluoromethyl groups show additional strong bands characteristic of aromatic trifluoromethyl compounds¹⁰ (Table 2). The symmetrical C-F stretching

TABLE 2. Some characteristic bands (cm^{-1}) in the spectra^a of alkyl- and perfluoroalkylbenzimidazoles.

Benzimidazoles						<i>b</i>	<i>b</i>	<i>b</i>	<i>b</i>
Unsubst.	1621w	1605w	—	1500w	1351w	—	—	—	—
		1591m							
2-Me	1628m	1592w	1562m	1512w	—	—	—	—	—
2-Et	1626m	1595m	1547m	1510m	1330m	—	—	—	—
2-Pr ⁿ	1625w	1592w	1540m	1508w	1320w	—	—	—	—
2-Pr ⁱ	1620w	1590w	1540m	—	1324m	—	—	—	—
4-Me	1613w	1595mw	—	—	—	—	—	—	—
5-Me	1628w	1590w	—	—	1345w	—	—	—	—
2,4-Me ₂	1622m	1604w	1553ms	1505w	—	—	—	—	—
2-CF ₃	1625w	1597mw	1555m	1501mw	1329ms	1192s	1172s	1143ms	—
								1132ms	
2-C ₂ F ₅	1625w	1596mw	1538mw	1500m	1345ms	—	1154s	—	—
2-C ₃ F ₇	—	1595w	1536w	1499mw	1346s	—	1179ms	—	—
4-CF ₃	1634mw	1611w	1540w	1492m	1338s	1188s	1178s	1122s	1110s
5-CF ₃	1633mw	1604w	—	1510w	1335s	—	1175s	1125m	1100s
2-Me-4-CF ₃	1624w	1608mw	1550m	1510m	1340ms	1195s	1165s	1127s	1119s
2-Me-5-CF ₃	1634mw	1607w	1540m	—	1337s	—	1170s	1130s	1110s
4-Me-2-CF ₃	1625mw	1610mw	1551m	1514mw	1325s	1182s	1170s	1142s	—
4-Me-2-C ₃ F ₇	1625w	1610w	1540mw	1515mw	1325ms	1195s	1153s	1150s	1126s
					1353s				
5-Me-2-CF ₃	1627mw	1612mw	1552ms	1515m	1325s	1188s	1175s	1144s	—
2,4-(CF ₃) ₂	1636w	1615w	1562w	1526m	1330s	—	1168s	1137s	—
2,5-(CF ₃) ₂	1630mw	1604w	1560m	1510mw	1329ms	1199s	1166s	1136s	1120s
4,5-(CF ₃) ₂	1645mw	1600w	—	1510w	1336s	1190s	—	1150s	—
5,6-(CF ₃) ₂	1660m	1610m	—	1525mw	1350s	1193s	1170s	1144s	1120s
2-Me-4,5-(CF ₃) ₂	1630mw	1601w	1555m	1492w	1333s	—	1176s	1148s	1135s
4,5-Me ₂ -2-CF ₃	1632mw	1610mw	1545ms	1513w	1328s	1188s	1170s	1146s	—
5,6-Me ₂ -2-CF ₃	—	1596w	1555ms	—	1332ms	1191s	1172s	1138s	1107s
2,4,5-(CF ₃) ₃	1653w	1606w	1570m	1500w	1345s	1190s	1162s	1148s	—
2-HO-CH ₂	1622w	1594w	1547w	1533w	1349m	—	—	—	—
4-CF ₃ -2-CH ₂ -OH ...	1635m	1610m	1538m	1505w	1334s	1198s	1170s	—	1122s
5-CF ₃ -2-CH ₂ -OH ...	1635m	—	1545m	1502w	1332s	—	1168s	—	1125s
2-CH ₂ -CN	1622mw	1605w	1547m	1490mw	1325m	—	—	—	—
		1593w							
5-MeO-2-CF ₃	1642m	1593w	1550ms	1504w	1344m	1175s	1163s	1130s	1118s
5-Cl-2-CF ₃	—	1605mw	1558m	1500w	1325s	1195s	1170s	—	—
5-NO ₂	1625w	1590mw	1560w	1518s	1344s	—	—	—	—
				1491mw	1320s				
5-NO ₂ -2-CF ₃	1648w	1598w	1558m	1533s	1348s	1192s	1163s	—	—
	1638w			1492s	1322s				

^a As mulls with Nujol and Fluorolub. ^b Only strong bands in this region are listed.

⁹ Randle and Whiffen, "Molecular Spectroscopy," Institute of Petroleum, London, 1954.

¹⁰ Randle and Whiffen, *J.*, 1955, 1311.

band occurs close to 1330 cm.^{-1} in both solid and solution spectra. The antisymmetrical CF_3 stretching frequency gives rise to two bands between 1100 and 1200 cm.^{-1} , but coupling of these vibrations with the out-of-plane C-H deformation modes produces several strong bands of mixed character. The spectra usually contain four strong bands in this region: *viz.*, near 1190 , 1170 , 1140 , and 1120 cm.^{-1} ; as a tentative correlation it was noted that those compounds with 2-trifluoromethyl groups absorb regularly at 1140 cm.^{-1} , and those with 4- or 5-trifluoromethyl groups at 1120 cm.^{-1} .

A number of compounds with structures closely related to the benzimidazoles were also examined. The spectra of perimidines (II) and benzotriazole (III) (Table I) conform closely to the pattern established for benzimidazoles. Spectra of the solids show broad-banded absorption from 2400 to 3200 cm.^{-1} which on deuteration is displaced to 2200 cm.^{-1} . In solution spectra these bonded N-H bands are replaced by sharp bands near 3400 cm.^{-1} . Bands near 1600 cm.^{-1} also follow a pattern similar to that of the bands in the spectra of benzimidazoles. Perimidines show three strong bands, at 1595 , 1615 , and 1635 cm.^{-1} ; an additional band at 1540 cm.^{-1} (1520 cm.^{-1} in solution) is shown by 2-alkyl-substituted compounds.

TABLE 3. Bands (cm.^{-1}) in the spectra of some benzimidazolecarboxylic acids.^a

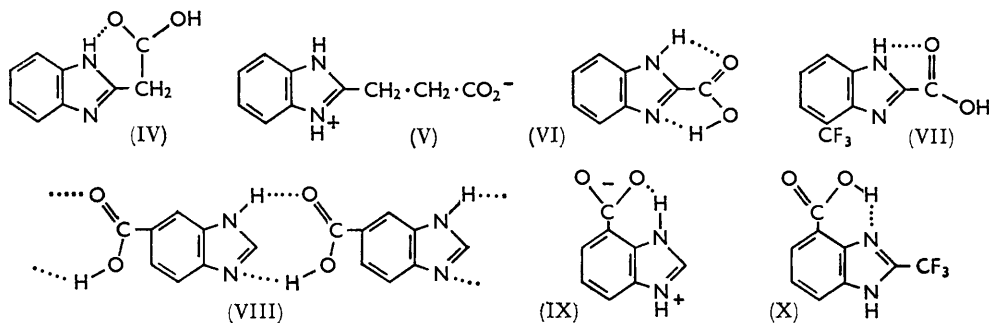
Acid	N-H and O-H		C=O	Other bands	
2-Benzimidazolylacetic	3400m	2200—2800w	1645s	1612s	1565m
	3160m				
2-Benzimidazolyl difluoroacetic	3380mw	2400—3100m	1690s	1625m	1535w
β -2-Benzimidazolylpropionic	—	2200—3200m	—	1635m	1550ms
				1600m	
β -2-Benzimidazolyltetrafluoropropionic	3400mw	2200—3000mw	1676s	1630mw	1540w
Benzimidazole-5-carboxylic	3200m	2200—2600w	1670s	1625m	—
Benzimidazole-5,6-dicarboxylic (mono-	3400w	2300—3200m	1686s	[1620]	—
hydrate)	3140m				
Benzimidazole-4-carboxylic	3400m	2200—2800m	1670w	1625s	1540m
	3200m			1600s	
2-Trifluoromethylbenzimidazole-4-carb-	3430m	2400—3200w	1700s	1630w	1543m
oxylic				1607w	
Benzimidazole-2-carboxylic	—	2200—3200s	1650s	[1620]	1520m
4-Trifluoromethylbenzimidazole-2-carb-					
oxylic	3500m	2200—3100ms	[1660]	1623s	—
5-Trifluoromethylbenzimidazole-2-carb-					
oxylic	—	2300—3200ms	1648s	—	1520m

^a As mulls in Nujol and Fluorolub. [] denotes inflexion.

The spectra of the carboxylic acids derived from benzimidazole present some unexpected features. Hunter and Marriot⁴ noted that when a carbonyl group is so located as to permit chelation with the benzimidazole N-H grouping, the compound is no longer strongly associated. 2-Benzimidazolyl-acetic acid and -difluoroacetic acid have spectra (Table 3) indicating a strongly bonded carbonyl group and discrete (though bonded) OH and NH groups; these compounds are undoubtedly correctly represented as the chelate compounds (IV) although some non-bonded material may be present in the fluoro-acid. β -2-Benzimidazolylpropionic acid shows marked differences. The carbonyl band is replaced by a broad band at 1550 cm.^{-1} and the C-O stretching frequency is displaced to 1410 cm.^{-1} . These shifts and the absence of a discrete hydroxyl band indicate that this acid is best regarded as a zwitterionic compound (V). The high melting point (225°) of this acid may be compared with that of the acetic acid (123°). Conversely, the spectrum of β -2-benzimidazolyltetrafluoropropionic acid is closely similar to that of the difluoroacetic acid: it seems probable that the inductive effect of the adjacent fluorine grouping so reduces the basicity of the ring that salt formation is destabilized relative to the cyclic, hydrogen-bonded system. The formation of a 7-membered hydrogen-bonded ring is of interest; Hunter and Marriot⁴ found no indication of chelation in solution when this would have led to a 7-membered ring.

Benzimidazole-2-carboxylic acid has a bonded carbonyl group but shows no discrete

hydroxyl or amino-bands and is consequently best described by the unsymmetrical structure (VI) which is one of two equivalent tautomers. 5-Trifluoromethylbenzimidazole-2-carboxylic acid has a similar structure, but a band at 3500 cm^{-1} and a low carbonyl frequency suggest that the 4-trifluoromethyl analogue is best written as the



monobonded compound (VII). Proximity of the trifluoromethyl group to the heterocyclic ring will reduce the basic strength the ring (and increase the acidity of the N-H grouping)¹¹ and so stabilise the N-H \cdots O bond at the expense of the O-H \cdots N bond.

Benzimidazole-5-carboxylic and -5,6-dicarboxylic acid cannot show intramolecular bonding to the heterocyclic ring. The latter (as monohydrate) appears to be a simple carboxylic acid; the former shows a band at 3200 cm^{-1} which may well be derived from polymeric association of the carboxyl group with the heterocyclic ring (VIII). The spectrum of benzimidazole-4-carboxylic acid differs considerably from this and appears to be consistent with a hydrogen-bonded zwitterionic structure (IX); introduction of a 2-trifluoromethyl group profoundly modifies the spectrum. The carbonyl group is now largely non-bonded and the structure must be written with a bonded hydroxyl group and a free imino-group (X). Comparison of this structure with that of the unsubstituted acid shows that the presence of a 2-trifluoromethyl group reduces the basicity of the ring, so that the adjacent oxygen atom becomes a stronger basic centre than the ring nitrogen atom.

The acids proved insufficiently soluble in the usual solvents to permit the measurement of solution spectra.

Experimental.—Benzimidazoles were prepared and purified by conventional routes. Some of the fluorine-containing compounds have been described;^{11,12} details of the properties of the others will be published elsewhere. 1-Deutero-, 1-deutero-2-ethyl-, and 1-deutero-2-trifluoromethyl-benzimidazole, 1-deutero-2-ethylperimidine, and 1-deuterobenzotriazole were prepared by crystallisation of the protium compound twice from deuterium oxide.

Spectra of the solids were determined for mulls with Nujol and Fluorolub; a few specimens were also examined as discs with potassium bromide: no significant differences could be detected. Spectra of solutions in methylene chloride were determined in matched cells; a few samples were also examined in tetrachloroethylene but the majority of the compounds were insufficiently soluble in this medium to yield useful spectra. Spectra were measured with a Perkin-Elmer model 21 spectrophotometer with sodium chloride optics.

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¹¹ Belcher, Sykes, and Tatlow, *J.*, 1954, 4159; Lane, *J.*, 1955, 534.

¹² Sykes and Tatlow, *J.*, 1952, 4078; Smith and Steinle, *J. Amer. Chem. Soc.*, 1953, **75**, 1292; Fernandez-Bolaños, Overend, Sykes, Tatlow, and Wiseman, *J.*, 1960, 4003.