ISOXAZOLES

Part Two

Edited by

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Part Two

This is the forty-ninth volume in the series

THE CHEMISTRY OF HETEROCYCLIC COMPOUNDS

THE CHEMISTRY OF HETEROCYCLIC COMPOUNDS

A SERIES OF MONOGRAPHS

EDWARD C. TAYLOR AND PETER WIPF, *Editors*

ARNOLD WEISSBERGER, *Founding Editor*

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The Chemistry of Heterocyclic Compounds
Introduction to the Series

The chemistry of heterocyclic compounds is one of the most complex and intriguing branches of organic chemistry, of equal interest for its theoretical implications, for the diversity of its synthetic procedures, and for the physiological and industrial significance of heterocycles.

The Chemistry of Heterocyclic Compounds, published since 1950 under the initial editorship of Arnold Weissberger, and later, until Dr. Weissberger's death in 1984, under our joint editorship, has attempted to make the extraordinarily complex and diverse field of heterocyclic chemistry as organized and readily accessible as possible. Each volume has traditionally dealt with syntheses, reactions, properties, structure, physical chemistry, and utility of compounds belonging to a specific ring system or class (e.g., pyridines, thiophenes, pyrimidines, three-membered ring systems). This series has become the basic reference collection for information on heterocyclic compounds.

Many broader aspects of heterocyclic chemistry are recognized as disciplines of general significance that impinge on almost all aspects of modern organic chemistry, medicinal chemistry, and biochemistry, and for this reason we initiated several years ago a parallel series entitled General Heterocyclic Chemistry, which treated such topics as nuclear magnetic resonance, mass spectra, and photochemistry of heterocyclic compounds, the utility of heterocycles in organic synthesis, and the synthesis of heterocycles by means of 1,3-dipolar cycloaddition reactions. These volumes were intended to be of interest to all organic, medicinal, and biochemically oriented chemists, as well as to those whose particular concern is heterocyclic chemistry. It has, however, become increasingly clear that the above distinction between the two series was unnecessary and somewhat confusing, and we have therefore elected to discontinue *General Heterocyclic Chemistry* and to publish all forthcoming volumes in this general area in *The Chemistry of Heterocyclic Compounds* series.

It is a major challenge to keep our coverage of this immense field up to date. One strategy is to publish Supplements or new Parts when merited by the amount of new material, as has been done, *inter alia*, with purines, pyrimidines, quinazolines and pyrimidines. This is also the case with *Condensed Isoxazoles*, which were last covered in Volume 17 published in 1962. Professors Grünanger and Vita Finzi have done a heroic job in covering almost 30 years of condensed isoxazole chemistry in the present volume, and efforts are currently underway to update further their coverage of both mononuclear and condensed isoxazoles.

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EDWARD C. TAYLOR

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Preface

Part 1 of the present work on isoxazole chemistry appeared within this series (Vol. 49) in 1991. It was a complete, new reelaboration of the previous monograph published in 1962 by A. Quilico and G. Speroni, *Isoxazoles and Related Compounds* (Vol. 17 of this series). Owing to the huge development in the field of isoxazole derivatives in the last decades, from both synthetic and theoretical points of view, Part 1 was restricted to mononuclear isoxazoles and their hydrogenated counterparts (isoxazolines and isoxazolidines), with the notable exception of isoxazolones.

This second part is devoted to the chemistry of condensed isoxazoles: 1,2- and 2,1-benzisoxazoles and related compounds such as isoxazoles fused with carbocyclic or heterocyclic rings. Contrary to the previous part, each of the above cited groups was entrusted to different eminent specialists in that field. Each chapter illustrates the syntheses and reactions of these classes of compounds; physical properties are also included whenever they differ notably from those of the corresponding mononuclear isoxazoles already reported in Part 1. In order to facilitate the text writing and to avoid possible draft complications, references are collected at the end of each chapter, although this might be somewhat uncomfortable to the reader. Notwithstanding the advantages offered by computerization to text composition, the literature survey was ended, except for some items in Chapter 2, with Volume 115 of *Chemical Abstracts* (1991). We apologize for the long gap between literature deadline and publication year, and hope to update both Part 1 and Part 2 in the planned Part 3, which will include a chapter on isoxazolones. As a rule, patent literature has been evaluated only in those cases when the factual material therein has not subsequently appeared in the regular literature. An effort has been made to bring the chemical nomenclature in line with more recent IUPAC recommendations; nevertheless, sometimes the *Chemical Abstracts* names (e.g., 1,2-benzisoxazole) as well as some more commonly used names (e.g., 2-isoxazolines instead of 4,5-dihydro-1,2-oxazoles) have been utilized for the sake of simplicity.

We are greatly indebted to Dr. L. Toma and Dr. E. Magistrali for outstanding help in data collection and references control, to Mr. J. Dowling for critical supervision and language improvement of the whole text, and to the series editor Professor E. C. Taylor for constant advice.

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Part Two

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THE CHEMISTRY OF HETEROCYCLIC COMPOUNDS

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CHAPTER 1

1,2-Benzisoxazoles

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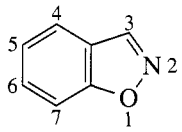
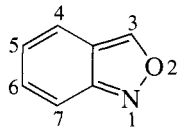
1.1. INTRODUCTION

The annulation of an isoxazole nucleus with a benzene ring gives rise to two bicyclic ring systems, **A** and **B**; only one of them, **A**, can properly be called a *benzisoxazole*, in that it has a formal benzenoid ring.



A



B

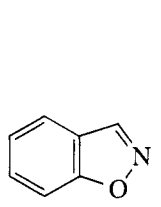
Each of these two compounds is known in the literature under several names.

Ring system **A** has been described as indoxazene, 1,2-benzisoxazole, 4,5-benzisoxazole, α,β-benzisoxazole, benzo[*d*]isoxazole (IUPAC nomenclature), and benzisoxazole. It is indexed in *Chemical Abstracts* as 1,2-benzisoxazole and numbered as shown in the figure; its ring index is 1123.

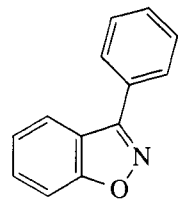
Ring system **B** has been described as anthranil, anthroxan, 2,1-benzisoxazole, 3,4-benzisoxazole, β,γ–benzisoxazole, benzo[*c*]isoxazole (IUPAC nomenclature), and benzpseudoxazole. It is indexed in *Chemical Abstracts* as anthranil and numbered as shown in the figure; its ring index is 1124.

This chapter deals only with ring system **A**, which henceforth will be named and numbered in accordance with the *Chemical Abstracts* system.

The first member of the family, 3-phenyl-1,2-benzisoxazole (**2**), was synthesized by Cathcart and Meyer a century ago,[1/892] and the parent compound, 1,2-benzisoxazole (**1**), was obtained by Conduché in 1908.[1/08]



1



2

This ring system was first reviewed by Quilico,[1/62] while a systematic coverage of the subject was made by Wünsch and Boulton[1/67] and updated 15 years later by Smalley.[1/81]

1.2. PHYSICOCHEMICAL PROPERTIES

The physicochemical behavior of 1,2-benzisoxazole and its derivatives was investigated early, especially with regard to establishing its correct structure However, extensive examination and recording of physicochemical properties have occurred only in more recent years. The subject has been briefly reviewed by Speroni.[2/62]

1.2.1. Infrared and Raman Spectra

A complete analysis and the attribution of the fundamental vibrations and of some overtones and combination vibrations of 1,2-benzisoxazole (**1**) have been performed in liquid and in solution.[1/80] Vapor spectra could not be recorded for **1** because of its decomposition at high temperature (see § 1.4.4).

If the molecule is considered to have a planar structure, it can be attributed to the C_s group of symmetry. In this case there are 36 fundamental vibrations, all of which are IR- and Raman-active, and which can be classified as 10 in-plane bending (γ) and stretching (δ) CH vibrations and 15 ring vibrations (ν_i) with A' symmetry; 5 deformation vibrations (γ CH) and 6 out-of-plane bending vibrations (Γ_i) with a A'' symmetry. The frequencies of the fundamental vibrations are

reported in Tables 1.1 and 1.2, while the original IR and Raman spectra are illustrated in the reference above cited.

For practical purposes the stretching frequency of the nuclear C=N bond is characteristic of the cyclic system, and it is mostly reported in the literature as the IR signature of 1,2-benzisoxazole derivatives. It has a medium to strong absorption that shows some variation according to the structure of the compounds. Some representative examples of this band are reported in Table 1.3. The C=N absorption band is lost in 2,3-dihydro-1,2-benzisoxazole derivatives as shown by the spectrum of 2-*t*-butyl-2,3-dihydro-1,2-benzisoxazole.[1/84]

In most cases reported IR spectra deal primarily with the assignment of significant side-chain functions, and are therefore not worth taking into account in this review. In other cases the reported absorptions have not been assigned, or the proposed designation is questionable. In Table 1.4 a few complete IR spectra of selected 1,2-benzisoxazole derivatives are reported; the assignments in brackets are those proposed by the authors.

The absorption frequency of the C=N bond does not seem to change after quaternization of the nitrogen, as shown by the $\nu_{C=N}$ of *N*-ethyl-1,2-benzisoxazolium fluoborate (ν = 1620 cm^{-1}).[1/65]

The C=N absorption frequency of polynuclear 1,2-benzisoxazole derivatives also seems to remain fairly constant.[2/80,4/87] However, in derivatives such as **3** the $\nu_{C=N}$ is reported to be as low as 1530 cm^{-1}.[2/77]

TABLE 1.1. ASSIGNMENTS OF FUNDAMENTAL C–H VIBRATIONS OF 1,2-BENZISOXAZOLE[a]

	Raman			IR Neutral solvents		DMSO	Acetone
Assignment[1/80]	ν (cm^{-1})	I	ρ	ν (cm^{-1})	ε	ν (cm^{-1})	(cm^{-1})
A′ symmetry							
ν CH isoxazole	3102	23	0.17	3096	9	—	—
ν_1 CH	3079	14	0.19	3078	13	—	—
ν_2 CH	—	—	—	3063	25	—	—
ν_3 CH	—	—	—	3055	19	—	—
ν_4 CH	—	—	—	3045	10	—	—
δ_1 CH	1259	46	0.18	1257	46	1258	—
δ CH isoxazole	1177	9	0.14	1173	90	1175	1175
δ_2 CH	—	—	—	1154	15	~1157	1157
δ_3 CH	1145	5	0.19	1141	46	1145	1145
δ_4 CH	1119	7	0.69	1116	50	1116	1116
A″ symmetry							
γ_1 CH	—	—	—	980 w (°)	—	—	—
γ_2 CH	—	—	—	~936s	—	—	945
γ_3 CH	888	3	0.75	886	101	886	886
γ CH isoxazole	—	—	—	873	100	—	—
γ_4 CH	—	—	—	752	422	763(°)	—

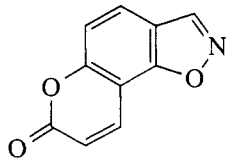
[a] Key: I = Intensity; ρ = depolarization factor; ε = apparent molar extinction coefficient; w = weak; s = shoulder; (°) = observed only in liquid sample.

TABLE 1.2. FUNDAMENTAL SKELETON VIBRATION OF 1,2-BENZISOXAZOLE[a]

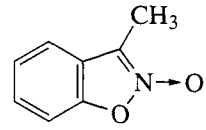
	Raman			IR Neutral solvents	
Assignment[1/80]	ν (cm^{-1})	I	ρ	ν (cm^{-1})	ε
A' symmetry					
ν_1	1613	13	0.45	1610	100
ν_2	1582	2	—	1585	14
ν_3	1514	36	0.25	1511	100
ν_4	1473	6	0.18	1470	71
ν_5	1432	45	0.19	1427	175
ν_6	1344	26	0.16	1341	55
ν_7	1306	7	0.26	1303	24
ν_8	1227	24	0.10	1227	105
ν_9	1003	38	0.05	1003	24
ν_{10}	934	22	0.06	933	101
ν_{11}	843	17	0.16	846	100
ν_{12}	763	100	0.05	764	94
ν_{13}	620	18	0.75	618	34
ν_{14}	534	28	0.20	532	11
ν_{15}	—	—	—	421	45
A″ symmetry					
Γ_1	—	—	—	744	362
Γ_2	—	—	—	667 (w)[a]	—
Γ_3	607	2	dp	604	141
Γ_4	562	3	0.75	556	6
Γ_5	—	—	—	394	41
Γ_6	260	4	0.75	256	29
	218	6	0.73	—	—

[a] See legend in Table 1.1 Footnote; dp = depolarized.

In a series of substituted 1,2-benzisoxazole-2-oxides, of which **4** is an example, the $\nu_{C=N}$ absorption occurred in the range 1570–1620 cm^{-1}, which is quite similar to that for 3,4-diphenylfuroxan (1575–1570 cm^{-1}), and the most characteristic absorptions were those in the ranges 1200–1240 and 1520–1590 cm^{-1}.[1/86,1/87]



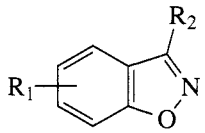
3

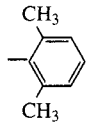
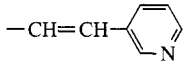


4

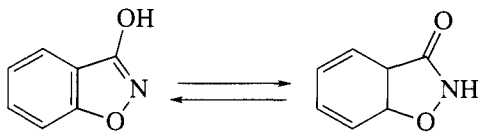
IR spectroscopy has been very useful in establishing the position of the tautomeric equilibrium in 1,2-benzisoxazolin-3-one. The enol form **5a** is preferred in the solid state as shown by the strong absorption at 3000–2500 cm^{-1}, the lack of carbonyl absorption and the C=N absorption at 1620 cm^{-1}. Both forms are

TABLE 1.3. IR DATA FOR THE C=N STRETCHING ABSORPTION OF SELECTED 1,2-BENZISOXAZOLE DERIVATIVES



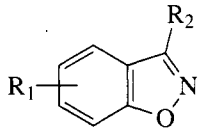
R_1	R_2	ν_{CN} (cm^{-1})	Phase	References
H	H	1607	CCl_4	1/65
4-OH	$-CH_3$	1613	Nujol	1/73
6-OCH_3,7-$COCH_3$	$-CH_3$	1595	CCl_4	2/80
6-OCH_2CHCH_2 (O)	$-CH_3$	1630	Nujol	2/87
H	$-C_6H_5$	1610	$CHCl_3$	3/84
H		1600	$CHCl_3$	3/84
6-OH,7-$COCH_3$	$-C_6H_5$	1630	$CHCl_3$	3/87
5-CH_3		1550	Nujol	4/84
6-OCH_3, 7-Cl		1620	Nujol	1/77
H	$-CHO$	1609	Nujol	1/82
6-OMe		1540	Nujol	1/74
H	$-CHBrCOOEt$	1600	Nujol	2/83
H	$-CHOHCOOEt$	1610	Nujol	2/83
H	$-OCH_2CH_2NMe_2$	1534	KBr	1/68
H	$-Cl$	1613	KBr	3/67

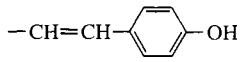
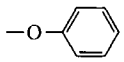
present in chloroform solution (OH absorption as above and carbonyl absorption at 1670 cm^{-1}).[2/67,1/69,1/71] Methylation with diazomethane gives both 3-methoxy-1,2-benzisoxazole ($\nu_{C=N}$ 1615 cm^{-1}) and 2-methyl-1,2-benzisoxazolin-3-one (ν_{CO} 1675 cm^{-1}).[1/71]



5a **5b**

TABLE 1.4. IR DATA OF SELECTED 1,2-BENZISOXAZOLE DERIVATIVES



R_1	R_2	ν (cm^{-1})	Phase	References
6-CH_3	$-CH_3$	2920 (CH), 1625 (C=N), 1604, 1575 (aromatic), 1346, 1391, 1256, 1152, 860, 800, 761, 638	Neat	1/79
H		1630 (CN), 1595, 1550 (C=C), 1510, 1475, 1440 (−O−C=N), 1385, 1335, 1280, 1230, 1105, 1015 (aromatic and isoxazole), 965 (HC=CH *trans*), 940, 830, 750 (aromatic)	KBr	2/79
H		2900(w), 1608(s), 1510(s), 1482(w), 1440(s), 1393(s), 1333(w), 1247(w), 1224(w), 911(m), 870(m), 747(s)	Neat	1/72
5-Cl	$-N_3$	2137(s), 1499(s), 1460(s), 1361(s), 1310(s), 1093(m), 930(m), 820(s), 752 (s), 717(m)	KBr	3/67
5-Cl		1527(s), 1460(s), 1366(s), 1316(m), 1193(m), 926(m), 820(m), 810(m), 763(s), 749(m), 690(m)	KBr	3/67

On this basis two kinds of derivatives obtained after alkylation or arylation can be recognized.[1/83,2/84] Accordingly, 3-chloro-1,2-benzisoxazole showed a sharp absorption at 1613 cm^{-1} ($\nu_{C=N}$),[3/67] while in a series of *N*-aryl derivatives of substituted 1,2-benzisoxazolin-3-one the absorption of the carbonyl function ranged from 1728 to 1753 cm^{-1}.[2/69]

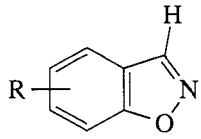
IR spectroscopy in solution at different dilutions has been used to support the attribution of the *E* or *Z* configurations of the isomeric α-oxyimino-1,2-benzisoxazole-3-acetic acid ethyl esters on the basis of the absorption frequency of the OH groups, which for the *Z* series indicates a bonded OH group as opposed to the free OH group of the *E* series.[2/83]

1.2.2. Ultraviolet Spectra

1,2-Benzisoxazole and its derivatives show only $\pi \rightarrow \pi^*$ transitions in the UV region in accordance with other heterocycles of this kind.

The UV spectrum of the parent compound has been reported by several authors.[1/41,1/65,1/79] In cyclohexane the band at 280 nm is clearly resolved into a fine structure.[1/41] Compared to the spectrum of the corresponding open com-

TABLE 1.5. UV DATA OF SELECTED 1,2-BENZISOXAZOLE DERIVATIVES



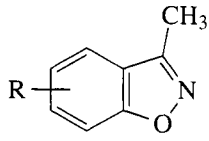
R	λ_{max}(nm)	log ε	Solvent	References
H	229	3.88	EtOH	1/79
	234	3.98		
	240	3.91		
	280	3.44		
H	235	4.00	EtOH	1/65
	243	3.91		
	280	3.46		
6-OCH_3	219	3.97	H_2O	2/73
	251	3.88		
	283	3.76		
	291	3.73		
5-OCH_3	236	3.92	H_2O	2/73
	306	3.54		
6-Cl	244	4.00	H_2O	2/73
	284	3.47		
5-Cl	236	3.95	H_2O	2/73
	293	3.50		
6-NO_2	275	4.18	H_2O	2/73
5,7-$(NO_2)_2$	255	4.15	H_2O (pH 3)	2/73
	305	3.61		

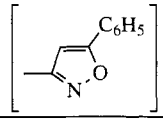
pound, salicylaldoxime, there is a hypsochromic shift of about 20 nm, which is indicative of the reduced electronic availability and the increased rigidity of the chromophore.

Calculations of $\pi \rightarrow \pi^*$ transitions with a variety of theoretical methods [including Pariser–Parr–Pople self-consistent field (PPP SCF) and modified CNDO-CI (complete neglect of differential overlap–configuration interaction)] are in good agreement with experimental data (see § 1.2.8).[3/69,1/70,2/71,2/72,1/78] The UV spectra of some 1,2-benzisoxazole compounds are reported in Table 1.5. From a comparison of 1,2-benzisoxazole and isoxazole spectral data, von Auwers first proposed the actual structure of this heterocycle.[1/24] The decomposition kinetics of 1,2-benzisoxazole and several substituted derivatives to the corresponding salicylonitriles have been followed using UV spectra that are fairly different for the two species, especially at pH 10.[2/73] On the basis of UV studies it has been found that 1,2-benzisoxazole derivatives are very weak bases, weaker than the corresponding isoxazoles (see § 1.2.9).[1/66]

Methyl substitution gives the expected slight bathochromic effect that seems higher when the methyl group is in position 6.[1/79] UV spectra allow better differ-

TABLE 1.6. UV DATA OF SELECTED 3-METHYL-1,2-BENZISOXAZOLE DERIVATIVES (EtOH)

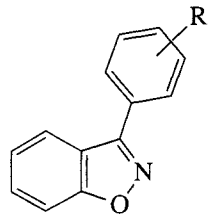


R	λ_{max}(nm)	log ε	References
H	231	3.85	1/79
	236	3.91	
	243	3.80	
	280	3.46	
	297(sh)	3.31	
H	236.5	3.92	4/69
	243.0	3.86	
	282.0	3.49	
	292.0(sh)	—	
H	235	3.89	3/71
	243	3.83	
	285	3.42	
	330	2.85	
5-CH_3	232	3.87	1/79
	237	3.92	
	243	3.83	
	289	3.51	
	297(sh)	3.36	
6-CH_3	240	3.98	1/79
	246(sh)	3.89	
	280	3.55	
	289(sh)	3.96	
4-OH	213	4.42	1/73
	242	3.39	
	292	3.36	
6-OH, 7-NH_2	228–232	4.03	4/87
	276–278	3.68	
6-OH, 7-$COCH_2COC_6H_5$	238	4.5	3/73
	285	4.5	
	370	4.6	
6-OH, 7-$N{=}CHC_6H_5$	225	4.41	4/87
	275	4.12	
	345	4.21	
6-OH, 7- 	230	4.13	3/87
	280	4.01	

entiation of 3-methyl-1,2-benzisoxazole and 1,2-benzisoxazole-3-acetic acid from the corresponding benzoxazole derivatives than do ^{1}H-NMR spectra.[4/69]

The spectral data of some 3-methyl-1,2-benzisoxazole derivatives are reported in Table 1.6.

TABLE 1.7. UV DATA OF SELECTED 3-PHENYL-1,2-BENZISOXAZOLE DERIVATIVES (EtOH)



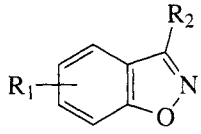
R	λ_{max} (nm)	log ε	References
3-NO_2	285	3.81	5/69
	224	4.29	
2-NHCHO	237(sh)	4.37	2/74
	246(sh)	4.29	
	291	3.90	
2-$NHCOCH_3$	235	4.32	2/74
	290	3.89	
2-NH_2, 5-Cl	225	4.33	2/74
	234	4.34	
	278	3.73	
	287(sh)	3.66	
	297	3.56	
	353	3.72	
2-NH_2	234	4.29	2/74
	277	3.63	
	284	3.63	
	295	3.65	
	332	3.66	

Even if a sound comparison is made difficult by the lack of sufficient data, substitution with a phenyl ring in position 3 seems to bring about the expected bathochromic and hyperchromic effect. Some UV spectral data of 3-phenyl-1,2-benzisoxazole derivatives are reported in Table 1.7.

The effect of other substituents on the various positions of the 1,2-benzisoxazole ring is reported in Table 1.8. In a series of 2-(1,2-benzisoxazolyl-3) acrylonitriles, UV spectra have been used to establish the *E* and *Z* configurations of the products obtained.[3/83] UV spectra have been used at different pH to evaluate the pK_a values of 4- and 6-hydroxy-1,2-benzisoxazole-3-carboxylic acid (see § 1.2.9).[1/75]

The spectral data of selected *O* and *N* derivatives of 1,2-benzisoxazolin-3-ones are reported in Table 1.9. Usually the *N*-alkyl and *N*-aryl derivatives show a bathochromic shift with respect to the corresponding *O*-alkyl and *O*-aryl derivatives. The *N* derivatives also show a higher ε. The spectra of some of these derivatives are reproduced in Böshagen and Geiger's work.[2/69]

TABLE 1.8. UV DATA OF SUBSTITUTED 1,2-BENZISOXAZOLES



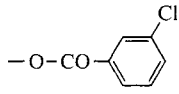
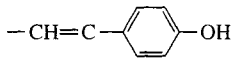
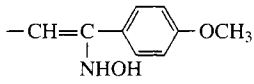
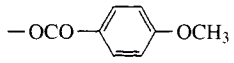
R_1	R_2	λ_{max} (nm)	log ε	Solvent	References
H	$-OH$	278	3.51	CH_3OH	2/69
		282	3.51		
		289	3.54		
H	$-OH$	236	3.70	CH_3OH	2/67
		274(sh)	3.39		
		278	3.50		
		282	3.50		
		288.5	3.53		
H	$-OCH_3$	236	3.76	CH_3OH	1/71
		273(sh)	3.45		
		278	3.57		
		282	3.57		
		288	3.58		
H	$-OCOC_6H_5$	279	3.70	CH_3OH	2/69
		289(sh)	3.51		
H		281	3.71	CH_3OH	2/69
		289(sh)	3.65		
H	$-OCOOCH_3$	279	3.50	CH_3OH	2/69
		289	3.45		
H	$-CH_2COOH$	237.5	3.78	EtOH	4/69
		244.0	3.67		
		283.0	3.40		
		293(sh)	—		
H		230	4.18	EtOH	2/79
		255	4.05		
		285	4.12		
		3.22	4.47		
5-CH_3		220	—		2/86, 5/87
		269	—		
		313	—		
5-Cl	$-OH$	291	3.47	$CHCl_3$	2/69
		295	3.47		
		302	3.46		
5-Cl	$-OCO-C_6H_5$	287	3.65	CH_3OH	2/69
		301(sh)	3.48		
5-Cl		268	4.35	CH_3OH	2/69
		302(sh)	3.72		
5-Cl	$-OCOOCH_3$	291	3.37	CH_3OH	2/69
		301	3.31		

TABLE 1.8 (*continued*)

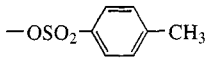
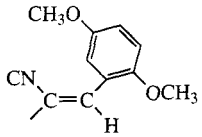
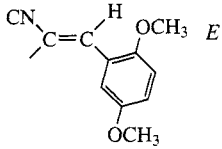
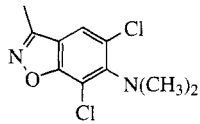
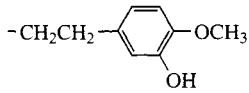
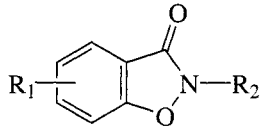
R_1	R_2	λ_{max} (nm)	log ε	Solvent	References
5-Cl		293 301(sh)	3.61 3.54	CH_3OH	2/69
5-Cl	 *E*	315 390	4.15 3.96	EtOH	3/83
5-Cl	 *E*	288 380	4.03 3.83	EtOH	3/83
5,7-Cl_2,6-$N(CH_3)_2$		218 323	3.75 3.13	EtOH	5/71
4-OH, 6-OCH_2COONa		259	4.01	H_2O	3/81
4-OH	−COOH	306 325	3.41 3,72	H_2O (pH 2) H_2O (pH 13)	1/75
6-OH	−COOH	289 312	3.93 4.07	H_2O (pH 3) H_2O (pH 10)	1/75

TABLE 1.9. UV DATA OF SELECTED 1,2-BENZISOXAZOLIN-3-ONE DERIVATIVES (CH_3OH)



R_1	R_2	λ_{max} (nm)	log ε	References
H	$-CH_3$	242(sh) 254(sh) 287 294	3.73 3.45 3.73 3.73	1/71
H	$-CH_2-CH=CH_2$	244(sh) 255(sh) 289 295	3.76 3.50 3.72 3.73	1/71

TABLE 1.9 (*continued*)

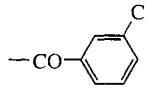
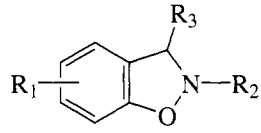
R_1	R_2	λ_{max} (nm)	log ε	References
H	$-COCH_3$	299	3.71	2/69
		309	3.69	
H		307	3.60	2/69
		315(sh)	3.59	
H	$-COOCH_3$	296	3.72	2/69
		306	3.70	
5-Cl	$-COCH_3$	312	3.65	2/69
		322	3.62	
5-Cl	$-COOCH_3$	309	3.64	2/69
		319	3.61	

TABLE 1.10. UV DATA OF 2,3-DIHYDRO-1,2-BENZISOXAZOLE DERIVATIVES



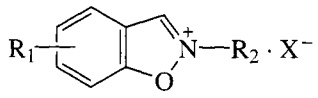
R_1	R_2	R_3	λ_{max} (nm)	log ε	Solvent	References
H	$-C_2H_5$	H	280	3.34	H_2O (pH 5–12)	4/67
			276	3.21	H_2O(pH1)	
			269	3.24		
5-NO_2	H	$-CH_2COOH$	232	4.06	EtOH	4/71
			309	3.87		
5-NO_2	H, HCl	$-CH_2COOH$	230	3.93	EtOH	4/71
			318	3.93		
5-NO_2	H	$-CH_2COOCH_3$	231	3.93	EtOH	4/71
			320	3.99		
5-NO_2	$-COCH_3$	$-CH_2COOH$	233.5	418	EtOH	4/71
			302	3.92		

The UV spectra of a few 2,3-dihydro-derivatives are known; they are reported in Table 1.10. There are no reported UV spectral data for 1,2-benzisoxazole-2-oxides.

UV spectra have been reported for only two 1,2-benzisoxazolium salts, and the data are shown in Table 1.11. Even if comparison is difficult because of the limited amount of data available, quaternization of nitrogen seems to induce a strong bathochromic shift in the spectra.

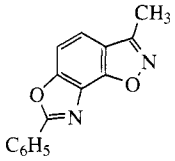
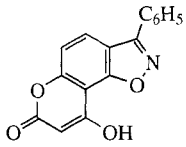
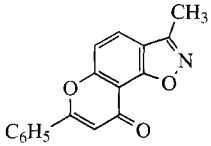
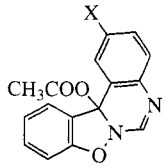
Finally, the data for a few polynuclear condensed 1,2-benzisoxazole derivatives are reported in Table 1.12. In a series of 9(*H*)-oxopyrano[2,3-*g*]1,2-benzisoxazoles, three maxima have been observed in all cases around 220, 265, and 320 nm. The former has been attributed to the isoxazole moiety acting as an independent chromophore.[3/73]

TABLE 1.11. UV DATA OF 1,2-BENZISOXAZOLIUM SALTS (H_2O)



R_1	R_2/X	λ_{max} (nm)	log ε	References
H	$-C_2H_5/BF_4^-$	258	4.12	1/65
		297	3.46	
7-OH	$-C_2H_5/BF_4^-$	307	3.42	3/74
		248	3.94	
		214	3.30	

TABLE 1.12. UV DATA OF SELECTED POLYCYCLIC 1,2-BENZISOXAZOLES

Compound	λ_{max} (nm)	log ε	Solvent	References
	220	4.19	EtOH	4/87
	250	4.30		
	280	4.43		
	240	4.10	EtOH	3/87
	280	3.86		
	305	3.91		
	220	4.10	EtOH	3/73, 3/87
	264(265)	4.39		
	294(303–306)	4.25		
	X=H; 230(sh)	3.97	*i*.PrOH	2/74
	286	3.56		
	X=Cl; 286	3.80	*i*.PrOH	2/74

1.2.3. Nuclear Magnetic Resonance Spectra

In the presence of condensed benzene and isoxazole rings, 1,2-benzisoxazole derivatives give NMR spectra that have the characteristics of both nuclei and generally lack original features. Perhaps for this reason NMR studies on this heterocyclic system are much less numerous than those concerning parent benzene and isoxazole rings.