

*Supplements to the 2nd Edition (Editor S. Coffey) of*

# RODD'S CHEMISTRY OF CARBON COMPOUNDS

*A modern comprehensive treatise*

*Edited by*  
**MARTIN F. ANSELL**

*Supplement to*

**VOLUME IV HETEROCYCLIC COMPOUNDS**

**Part B:**

**Five-membered Heterocyclic Compounds with a  
Single Hetero-Atom in the Ring: Alkaloids, Dyes  
and Pigments**

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*Edited by*

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## PREFACE TO SUPPLEMENT IVB

The publication of this volume continues the supplementation of the second edition of Rodd's Chemistry of Carbon Compounds thus keeping this major work of reference up to date. This supplement covers the Chapters in volume IVB with the exception of Chapters 12 and 13 for which the manuscripts were not received in time. These chapters will appear in a subsequent supplement. Although each chapter in this book stands on its own, it is intended that it should be read in conjunction with the parent chapter in the second edition.

At a time when there are many specialist reviews, monographs and reports available, there is still in my view an important place for a book such as "Rodd", which gives a broader coverage of organic chemistry. One aspect of the value of this work is that it allows the expert in one field to quickly find out what is happening in other fields of chemistry. On the other hand a chemist looking for the way into a field of study will find in "Rodd" an outline of the important aspects of that area in chemistry together with leading references to other works to provide more detailed information.

As editor I have been fortunate in that each contributor to this supplement has produced a very readable critical assessment of their particular area of chemistry. As an organic chemist I have enjoyed reading the chapters and profited from learning of advances in areas of chemistry that are outside my own special interests.

This volume has been produced by direct reproduction of the manuscripts. I am most grateful to the contributors for all the care and effort both they and their secretaries have put into the production of the manuscripts, including the diagrams. I also wish to thank the staff at Elsevier for all the help they have given me and for seeing the transformation of authors' manuscripts to published work.

February 1985

Martin Ansell

## OFFICIAL PUBLICATIONS

B.P.	British (United Kingdom) Patent
F.P.	French Patent
G.P.	German Patent
Sw.P.	Swiss Patent
U.S.P.	United States Patent
U.S.S.R.P.	Russian Patent
B.I.O.S.	British Intelligence Objectives Sub-Committee Reports
F.I.A.T.	Field Information Agency, Technical Reports of U.S. Group Control Council for Germany
B.S.	British Standards Specification
A.S.T.M.	American Society for Testing and Materials
A.P.I.	American Petroleum Institute Projects
C.I.	Colour Index Number of Dyestuffs and Pigments

## SCIENTIFIC JOURNALS AND PERIODICALS

With few obvious and self-explanatory modifications the abbreviations used in references to journals and periodicals comprising the extensive literature on organic chemistry, are those used in the World List of Scientific Periodicals.

LIST OF COMMON ABBREVIATIONS AND  
SYMBOLS USED

A	acid
Å	Ångström units
Ac	acetyl
a	axial; antarafacial
as, <i>asymm.</i>	asymmetrical
at	atmosphere
B	base
Bu	butyl
b.p.	boiling point
C, mC and $\mu$ C	curie, millicurie and microcurie
c, C	concentration
C.D.	circular dichroism
conc.	concentrated
crit.	critical
D	Debye unit, $1 \times 10^{-18}$ e.s.u.
D	dissociation energy
D	dextro-rotatory; dextro configuration
DL	optically inactive (externally compensated)
d	density
dec. or decomp.	with decomposition
deriv.	derivative
E	energy; extinction; electromeric effect; Entgegen (opposite) configuration
E1, E2	uni- and bi-molecular elimination mechanisms
ElcB	unimolecular elimination in conjugate base
e.s.r.	electron spin resonance
Et	ethyl
e	nuclear charge; equatorial
f	oscillator strength
f.p.	freezing point
G	free energy
g.l.c.	gas liquid chromatography
g	spectroscopic splitting factor, 2.0023
H	applied magnetic field; heat content
h	Planck's constant
Hz	hertz
I	spin quantum number; intensity; inductive effect
i.r.	infrared
J	coupling constant in n.m.r. spectra; joule
K	dissociation constant
kJ	kilojoule

## LIST OF COMMON ABBREVIATIONS

<i>k</i>	Boltzmann constant; velocity constant
kcal.	kilocalories
<i>L</i>	laevorotatory; laevo configuration
<i>M</i>	molecular weight; molar; mesomeric effect
<i>Me</i>	methyl
<i>m</i>	mass; mole; molecule; <i>meta</i> -
<i>ml</i>	millilitre
<i>m.p.</i>	melting point
<i>Ms</i>	mesyl (methanesulphonyl)
[ <i>M</i> ]	molecular rotation
<i>N</i>	Avogadro number; normal
<i>nm</i>	nanometre ( $10^{-9}$ metre)
<i>n.m.r.</i>	nuclear magnetic resonance
<i>n</i>	normal; refractive index; principal quantum number
<i>o</i>	<i>ortho</i> -
<i>o.r.d.</i>	optical rotatory dispersion
<i>P</i>	polarisation, probability; orbital state
<i>Pr</i>	propyl
<i>Ph</i>	phenyl
<i>p</i>	<i>para</i> -; orbital
<i>p.m.r.</i>	proton magnetic resonance
<i>R</i>	clockwise configuration
<i>S</i>	counterclockwise config.; entropy; net spin of incompleated electronic shells; orbital state
<i>S<sub>N</sub>1, S<sub>N</sub>2</i>	uni- and bi-molecular nucleophilic substitution mechanisms
<i>S<sub>N</sub>i</i>	internal nucleophilic substitution mechanisms
<i>s</i>	symmetrical; orbital; suprafacial
<i>sec</i>	secondary
<i>soln.</i>	solution
<i>symm.</i>	symmetrical
<i>T</i>	absolute temperature
<i>Tosyl</i>	<i>p</i> -toluenesulphonyl
<i>Trityl</i>	triphenylmethyl
<i>t</i>	time
<i>temp.</i>	temperature (in degrees centigrade)
<i>tert.</i>	tertiary
<i>U</i>	potential energy
<i>u.v.</i>	ultraviolet
<i>v</i>	velocity
<i>Z</i>	<i>zusammen</i> (together) configuration



## LIST OF COMMON ABBREVIATIONS

$\alpha$	optical rotation (in water unless otherwise stated)
$[\alpha]$	specific optical rotation
$\chi_A$	atomic susceptibility
$\chi_E$	electronic susceptibility
$\epsilon$	dielectric constant; extinction coefficient
$\mu$	microns ( $10^{-4}$ cm); dipole moment; magnetic moment
$\mu_B$	Bohr magneton
$\mu_g$	microgram ( $10^{-6}$ g)
$\lambda$	wavelength
$\nu$	frequency; wave number
$\chi, \chi_d, \chi_\mu$	magnetic, diamagnetic and paramagnetic susceptibilities
$\sim$	about
(+)	dextrorotatory
(-)	laevorotatory
( $\pm$ )	racemic
$\ominus$	negative charge
$\oplus$	positive charge

## CONTENTS

## VOLUME IV B

Five-membered Heterocyclic Compounds with a Single Hetero-Atom in the Ring: Alkaloids, Dyes and Pigments

Preface . . . . .	VII
Official publications: Scientific journals and periodicals . . . . .	XIII
List of common abbreviations and symbols used . . . . .	XIV

*Chapter 7. Five-membered Monoheterocyclic Compounds:  
Alkaloids (continued): Pyrrolidine Alkaloids*  
by J.D. ROBINS

1. Pyrrolidine Bases . . . . .	1
2. Pyrrolidones . . . . .	7
3. <i>N</i> -Acylpyrrolidines . . . . .	9
4. <i>N</i> -Acylpyrrolidones . . . . .	13

*Chapter 8. Five-membered Monoheterocyclic Compounds:  
Alkaloids (continued): Pyrrolizidine Alkaloids*  
by D.J. ROBINS

Introduction . . . . .	15
1. Necines . . . . .	17
(a) Unhydroxylated derivatives . . . . .	17
(b) Monohydroxylated derivatives . . . . .	18
(c) Dihydroxylated derivatives . . . . .	22
(d) Trihydroxylated derivatives . . . . .	24
2. Necic acids . . . . .	26
(a) $C_6$ -Acids . . . . .	26
(b) $C_7$ -Acids . . . . .	26
(c) $C_8$ -Acids . . . . .	26
(d) $C_9$ -Acids . . . . .	28
(e) $C_{10}$ -Acids . . . . .	29
3. Alkaloids . . . . .	32
4. Miscellaneous types of pyrrolizidine alkaloids . . . . .	67
5. Pharmacology of the pyrrolizidine alkaloids . . . . .	68

*Chapter 9. The Indole Alkaloids*  
by K.S.J. STAPLEFORD

Introduction . . . . .	71
1. Alkaloids lacking a tryptamine unit . . . . .	72
(a) Simple indoles . . . . .	72
(b) Carbazole derivatives . . . . .	76

2. Alkaloids containing a tryptamine unit . . . . .	79
(a) Compounds without an isoprene moiety . . . . .	79
(i) Simple tryptamine and tryptophan derivatives, 79 — (ii) Eserine types, 84 —	
(b) Compounds containing isoprene (but not terpene derived moiety) . . . . .	85
(i) The ergot alkaloids, 85 — (ii) Mould metabolites, 87 —	
(c) Compounds containing a terpene derived moiety . . . . .	97
(i) Alkaloids with the Corynanthe-Strychnos unit 97 — (ii) Alkaloids with a seco-type unit, 120 — (iii) Alkaloids with the Aspidosperma unit, 121 — (iv) Alkaloids containing the Iboga unit, 127 — (v) Novel types, 132 —	
3. Bis-indole alkaloids . . . . .	135
(a) Compounds containing two identical "halves" linked symmetrically . . . . .	135
(b) Compounds not composed of identical halves nor linked symmetrically . . . . .	138
(i) Sesquimeric compounds, 138 — (ii) The secamines and presecamines, 141 — (iii) Bis-indoles from <i>Vinca rosea</i> , 141 — (iv) Other representative bis-indole alkaloids, 145 —	

*Chapter 10. Five-membered Monoheterocyclic Compounds:*

*Amaryllidaceae Alkaloids*

by M. SAINSBURY

1. Introduction . . . . .	151
2. Biosynthesis . . . . .	151
3. New alkaloids and plant sources . . . . .	154
(a) Lycorine and pretazettine . . . . .	154
(b) 4,5-Etheno-8,9-methylenedioxy-6-phenanthridone . . . . .	157
(c) Carinatine and goleptine . . . . .	158
(d) Alkaloids from plants of the genus <i>Crinum</i> . . . . .	159
(e) Havanine, varadine, zaidine and caribine . . . . .	160
(f) Ungvedine and ungspiroline . . . . .	162
(g) Hippadine, hippafine and hippagine . . . . .	163
(h) Galanthamine and its <i>N</i> - and <i>O</i> -demethyl derivatives . . . . .	163
(i) Clivatine and clivacetine . . . . .	164
4. Crystal structure determinations . . . . .	166
(a) Maritidine . . . . .	166
(b) Norgalanthamine . . . . .	166
(c) Cocculine and cocculidine . . . . .	166
(d) Lycorine chlorohydrin . . . . .	166
(e) Lycorine (9). . . . .	167
5. Spectroscopy . . . . .	167
6. Photochemical reactions . . . . .	168
7. Synthesis . . . . .	168
(a) The synthesis of lycorine and related structures . . . . .	168
(b) Clividine and clivonine . . . . .	177
(c) Clivimine . . . . .	178
(d) Maritidine, (+)- and (-)-galanthamine . . . . .	179
(e) (+)-Lycoramine (dihydrogalanthamine). . . . .	182
(f) Apogalanthamine analogues . . . . .	184
(g) Tetrahydrometinoxocrinine and crinine . . . . .	184

(h) ( $\pm$ )-Crimamine, ( $\pm$ )-6-hydroxycrimamine, ( $\pm$ )-criwelline and ( $\pm$ )-macronine . . . . .	186
(i) Lycoricidine and related compounds . . . . .	188
(j) Elswesine . . . . .	191
(k) ( $\pm$ )-Tazettine . . . . .	192

*Chapter 11. Five-membered Monoheterocyclic Compounds:*  
*Alkaloids (continued): Tropane Alkaloids*  
 by J.G. WOOLLEY

Introduction . . . . .	199
1. Synthesis . . . . .	206
2. New alkaloids . . . . .	219
(a) Proteaceae . . . . .	219
(b) 2,3-Disubstituted tropanes . . . . .	223
(c) 2,3,6-Trisubstituted tropanes . . . . .	225
(d) 2,3,7-Trisubstituted tropanes . . . . .	226
(e) 3,6-Disubstituted tropanes . . . . .	227
(f) Pyranotropanes . . . . .	227
(g) Erythroxylaceae . . . . .	228
(h) Solanaceae . . . . .	234
(i) Littorine and related topics . . . . .	234
(j) Heterodiesters and related topics . . . . .	239
(k) <i>N</i> -oxides . . . . .	241
(l) Secotropanes . . . . .	246
3. Spectroscopy . . . . .	246

*Chapter 12. Five-membered Monoheterocyclic Compounds*  
*(continued) – The Pyrrole Pigments*

Key references . . . . .	251
--------------------------	-----

*Chapter 13. Five-membered Monoheterocyclic Compounds*  
*(continued): Azaporphyrins; Benzoporphyrins;*  
*Benzoazaporphyrins; Phthalocyanines and Related*  
*Structures*

Key reviews . . . . .	252
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*Chapter 14. Five-membered Monoheterocyclic Compounds:*  
*The Indigo Group*  
 by M. SAINSBURY

Introduction . . . . .	253
1. Indigo and its derivatives . . . . .	253
(a) Methods of synthesis . . . . .	253
(b) Spectroscopy and <i>E</i> – <i>Z</i> isomerism of indigo and thioindigo derivatives . . . . .	260
(c) Tyrianpurple and its biological precursors . . . . .	262
(d) Deoxyindigo (structural reassignment) . . . . .	264
(e) Reaction between indigo and hydrazine . . . . .	266
(f) Indigo diimine . . . . .	266

*Chapter 15. Cyanine Dyes and related Compounds*  
by D.J. FRY

Introduction .....	267
1. Cyanines .....	269
1.1 Fluoro-substituted dyes .....	269
1.2 Long-chain dyes .....	270
1.3 Physical properties .....	272
1.4 Reaction of cyanines .....	278
1.5 Miscellaneous syntheses and uses .....	282
2. Acetylenic dyes .....	283
3. Aza-, phospho- and arsa-cyanines .....	288
3.1 Azacyanines .....	288
3.2 Phospho- and arsa-cyanines .....	290
4. Merocyanines .....	290
5. Oxonols .....	291
6. Styryl dyes .....	292
7. Pyrilium dyes .....	293
8. Reaction mechanisms .....	294
Index .....	297

## Chapter 7

### FIVE-MEMBERED MONOHETEROCYCLIC COMPOUNDS: ALKALOIDS (CONTINUED):

#### PYRROLIDINE ALKALOIDS

DAVID J. ROBINS

Annual reviews in this area are available in "The Alkaloids", Vols 1-10, The Chemical Society, London, 1971-1980. Pyrrolidine alkaloids are included in a review of nitrogen-containing compounds in tobacco (I. Schmeltz and D. Hoffmann, Chem. Rev., 1977, 77, 295).

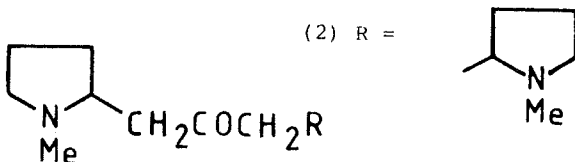
#### 1. Pyrrolidine Bases

Hygrine (1) and cuscohygrine (2) are present in roots of Salpichroa origanifolia (W.C. Evans, A. Ghani, and V.A. Woolley, Phytochem., 1972, 11, 469). Cuscohygrine has also been obtained from roots of Solanum carolinense (Evans and A. Somanabandhu, *ibid.*, 1977, 16, 1859); Convolvulus erinacius (S.F. Aripova, V.M. Malikov, and S. Yu. Yunusov, Chem. Abs., 1972, 77, 162 010); Scopolia tangutica (S.A. Minina and I. Barene, *ibid.*, 1972, 77, 111 461); and Cyphomandra betacea (Evans, Ghani, and Woolley, J. Chem. Soc. Perkin 1, 1972, 2017). The roots of nine Datura species (*idem*, Phytochem., 1972, 11, 2527) and five of the twelve known species of Solandra contain cuscohygrine (*idem*, *ibid.*, 1972, 11, 470). The pharmacological activity of cuscohygrine has been studied (Minina and Barene, *loc. cit.*).

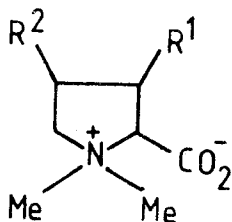
Stachydrine (3) occurs in Asphodelus microcarpus (F.M. Hammouda, A.M. Rizk, and M.M. Abdel-Gawad, Curr. Sci., 1971, 40, 631); Capparis spinosa (S. Mukhamedova, S.T. Akramov, and Yunusov, Khim. Priir. Soedin., 1965, 67); Courbonia glauca (D.A. Taylor and A.J. Henry, Phytochem., 1973, 12, 1178); Desmodium triflorum (S. Ghosal *et al*; Planta Med., 1973, 23,

(1) R = H

(2) R =

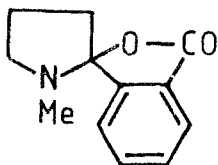


321) and (named cadabine) in Cadaba fruticosa (V.U. Ahaman, A. Basha, and A. Rahman, Phytochem., 1975, 14, 292). The alkaloid content of 36 species of the Cappariidaceae family has been studied. Stachydrine (3) is present in 27 species, and 3-hydroxystachydrine (4) has been found in 18 species (P. Dealaveau, B. Koudogbo, and J.L. Pousset, ibid., 1973, 12, 2893).

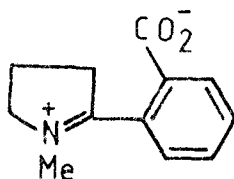
(3)  $\text{R}^1 = \text{R}^2 = \text{H}$ (4)  $\text{R}^1 = \text{OH}$ ,  $\text{R}^2 = \text{H}$ (5)  $\text{R}^1 = \text{H}$ ,  $\text{R}^2 = \text{OH}$ 

Combretine,  $\text{C}_7\text{H}_{13}\text{NO}_3$ , discovered in Combretum micranthum, appears to be a stereoisomer of betonicine (5) (A.U. Ogan, Planta Med., 1972, 21, 210).

Shihunine,  $\text{C}_{12}\text{H}_{13}\text{NO}_2$ , has been isolated from Dendrobium lohohense (Y. Inubishi et al., Chem. pharm. Bull. Japan, 1964, 12, 749) and D. pierardii (M. Elander, L. Gawell, and K. Lander, Acta Chem. Scand., 1971, 25, 721). The  $^1\text{H}$ -nmr spectrum of shihunine in non-polar solvents suggests a phthalide structure (6), while the spectrum taken in methanol or water indicates a betaine structure (7), which is presumably the form present in the plant. The synthesis of shihunine has been achieved utilising the rearrangement of a cyclopropyl-imine to generate the pyrrolidine ring in the key step (E. Breuer and S. Zbaida, Tetrahedron, 1975, 31, 499). Shihunine has m.p. 78-79°, and the picrate m.p. 154-155.5°.

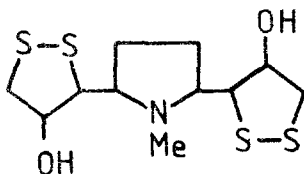


(6)



(7)

Gerrardine,  $C_{11}H_{13}NO_2S_4$ , is present in Cassipourea gerrardii (Rhizophoraceae) (W.G. Wright and F.L. Warren, J. Chem. Soc. (C), 1967, 283; 284). Its structure (8) has been established by X-ray crystallography (G. Gafner and L.J. Admiraal, Acta Crystallogr., Sect. B, 1971, 27, 565). Gerrardine has m.p. 180°. The hydrochloride,  $[\alpha]_D^{25} -172^\circ$  ( $H_2O$ ), has m.p. 207°.

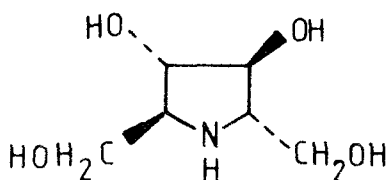


(8)

A tetraol,  $C_6H_{13}NO_4$ , isolated from the leaves of Derris elliptica (Leguminosae) has been shown to be 3,4-dihydroxy-2,5-dihydroxymethylpyrrolidine (9) by nmr and mass spectrometry (A. Welter et al., Phytochem., 1976, 15, 747). The relative configuration of the tetraol,  $[\alpha]_D^{20} +56.4^\circ$  ( $H_2O$ ), follows from the  $^1H$ -nmr spectral coupling constants, and a half-chair conformation for the molecule has been suggested.

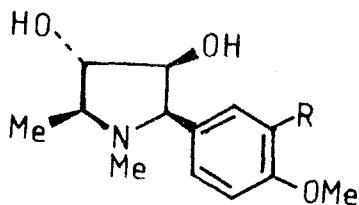
Codonopsine,  $C_{14}H_{21}NO_4$ , and codonopsinine,  $C_{13}H_{19}NO_3$ , are present in Codonopsis clematidea. The structures (10) and (11), respectively, are assigned to these two compounds on the basis of spectroscopic studies, Hofmann degradations, and permanganate oxidations (S.F. Matkhalikova et al., Chem. Abs.,





(9)

1970, 73, 15 050; 1971, 75, 36 409). The relative stereochemistry for each base has been deduced from double-resonance  $^1\text{H}$ -nmr studies, and again a half-chair conformation is indicated for each compound (M.R. Yagudaev *et al.*, *ibid.*, 1972, 77, 164 902). The pharmacology of codonopsine has been investigated (M.T. Khanov, M.B. Sultanov, and T.A. Egorova, *ibid.*, 1972, 77, 135 091).



(10) R = OMe

(11) R = H

Eight related alkaloids have been isolated from the stems and leaves of *Darlingia darlingiana*. The structure of darlingianine (12) has been established by X-ray diffraction analysis of the base, and by synthesis of the racemate from ( $\pm$ )-hygrine (1) and cinnamaldehyde (B.F. Anderson *et al.*, *Chem. Ind. (London)*, 1977, 764). The structures of the