

68

**Fortschritte der Chemie
organischer Naturstoffe**

**Progress in the
Chemistry of Organic
Natural Products**

**Founded by
L. Zechmeister**

**Edited by
W. Herz, G. W. Kirby,
R. E. Moore, W. Steglich,
and Ch. Tamm**

SpringerChemistry



SpringerWienNewYork

0054911

68

**Fortschritte der Chemie
organischer Naturstoffe**

**Progress in the
Chemistry of Organic
Natural Products**

**Founded by
L. Zechmeister**

**Edited by
W. Herz, G. W. Kirby,
R. E. Moore, W. Steglich,
and Ch. Tamm**

**Author:
G. W. Gribble**

SpringerWienNewYork

Prof. W. HERZ, Department of Chemistry,
The Florida State University, Tallahassee, Florida, U.S.A.

Prof. G. W. KIRBY, Chemistry Department,
The University, Glasgow, Scotland

Prof. R. E. MOORE, Department of Chemistry,
University of Hawaii at Manoa, Honolulu, Hawaii, U.S.A.

Prof. Dr. W. STEGLICH, Institut für Organische Chemie der Universität
München, München, Federal Republic of Germany

Prof. Dr. CH. TAMM, Institut für Organische Chemie der Universität Basel,
Basel, Switzerland

This work is subject to copyright.

All rights are reserved, whether the whole or part of the material is concerned, specifically those
of translation, reprinting, re-use of illustrations, broadcasting, reproduction by photocopying
machines or similar means, and storage in data banks.

© 1996 by Springer-Verlag/Wien
Printed in Austria

Library of Congress Catalog Card Number AC 39-1015

Typesetting: Macmillan India Ltd., Bangalore-25
Printing: Novographic, Ing. W. Schmid, A-1238 Wien
Cover design: Ecke Bonk
Printed on acid-free and chlorine-free bleached paper

ISSN 0071-7886

ISBN 3-211-82702-1 Springer-Verlag Wien New York

List of Contributors

GRIBBLE, Prof. Dr. G. W., Department of Chemistry, 6128 Burke Laboratory, Dartmouth College, Hanover, New Hampshire 03755-3564, USA.

Contents

List of Contributors	VIII
----------------------------	------

Naturally Occurring Organohalogen Compounds – A Comprehensive Survey.

By G. W. GRIBBLE	1
------------------------	---

1. Introduction	3
2. Origins	5
3. Occurrence	6
3.1. Simple Alkanes	6
3.1.1. Chloromethane	8
3.1.2. Dichloromethane	9
3.1.3. Chloroform	10
3.1.4. Carbon Tetrachloride.	10
3.1.5. Other Simple Haloalkanes.	10
3.2. Simple Functionalized Acyclic Organohalogens	12
3.3. Simple Functionalized Cyclic Organohalogens.	19
3.3.1. Cyclopentanes	19
3.3.2. Cyclitols and Benzoquinones	20
3.4. Terpenes	24
3.4.1. Monoterpenes	24
3.4.1.1. Acyclic Monoterpenes	24
3.4.1.2. Alicyclic Monoterpenes.	30
3.4.2. Sesquiterpenes	36
3.4.2.1. Terrestrial Sesquiterpene Lactones	36
3.4.2.2. Indanone Sesquiterpenes	42
3.4.2.3. Other Terrestrial Sesquiterpenes	42
3.4.2.4. Marine Sesquiterpenes	42
3.4.2.4.1. Monocyclic and Other Simple Sesquiterpenes .	43
3.4.2.4.2. Chamigrene and Related Types	50
3.4.2.4.3. Eudesmane and Other Types	57
3.4.2.4.4. Cuparene, Laurene, and Other Aromatic Types	61
3.4.3. Diterpenes	66
3.4.3.1. Terrestrial Diterpenes	66
3.4.3.2. Marine Diterpenes	68
3.4.3.2.1. Diterpenes of <i>Aplysia</i>	68
3.4.3.2.2. Diterpenes of <i>Laurencia</i>	70
3.4.3.2.3. <i>Sphaerococcus</i> and Other Red Algae Diterpenes	73

3.4.3.2.4. Sponge Diterpenes	74
3.4.3.2.5. Gorgonian Diterpenes	76
3.4.4. Higher Terpenes	81
3.5. Steroids	84
3.6. Marine Nonterpenes—C ₁₅ Acetogenins	87
3.7. Iridoids	100
3.8. Lipids and Fatty Acids	101
3.9. Fluorine-Containing Carboxylic Acids	108
3.10. Prostaglandins	110
3.11. Furanones	112
3.12. Amino Acids and Peptides	114
3.13. Alkaloids	126
3.14. Heterocycles	133
3.14.1. Pyrroles	133
3.14.2. Indoles	141
3.14.3. Carbazoles	160
3.14.4. Indolocarbazoles	161
3.14.5. Carbolines	161
3.14.6. Quinolines and Other Nitrogen Heterocycles	165
3.14.7. Benzofurans and Related Compounds	169
3.14.8. Pyrones	169
3.14.9. Coumarins and Isocoumarins	170
3.14.10. Flavones and Isoflavones	171
3.15. Polyacetylenes	173
3.15.1. Terrestrial Polyacetylenes and Derived Thiophenes	173
3.15.2. Marine Polyacetylenes	181
3.16. Eneidyne	184
3.17. Macrolides	186
3.18. Naphthoquinones and Higher Quinones	193
3.19. Tetracyclines	197
3.20. Aromatics	198
3.21. Simple Phenols	199
3.21.1. Terrestrial	200
3.21.2. Marine	202
3.22. Complex Phenols	209
3.22.1. Diphenylmethanes and Related Compounds	209
3.22.2. Diphenyl Ethers and Related Compounds	212
3.22.3. Tyrosines	214
3.22.3.1. Simple Tyrosines, Thyroxine, and Related Compounds	215
3.22.3.2. Transformed Single Tyrosines	216
3.22.3.3. Transformed Multiple Tyrosines	224
3.22.3.4. Bastadins	226
3.22.4. Depsides	232
3.22.5. Depsidones	234
3.22.6. Xanthones	238
3.22.7. Anthraquinones and Related Compounds	248
3.22.8. Griseofulvin and Related Compounds	251
3.22.9. Miscellaneous Fungal Metabolites and Other Complex Phenols	254
3.23. Glycopeptides	261
3.24. Orthosomycins	272

3.25. Dioxins	273
3.26. Humic Acids	276
4. Biohalogenation	278
4.1. Introduction and Early Examples	278
4.2. Chloroperoxidase	278
4.3. Bromoperoxidase	281
4.4. Other Peroxidases	283
5. Biodegradation	284
6. Natural Function	286
7. Significance	288
8. Future Outlook	290
Addendum	291
Acknowledgements	302
References	302
Author Index	425
Subject Index	467

Naturally Occurring Organohalogen Compounds – A Comprehensive Survey*

G. W. GRIBBLE, Department of Chemistry, Dartmouth College,
Hanover, New Hampshire 03755, USA

Contents

1. Introduction	3
2. Origins	5
3. Occurrence	6
3.1. Simple Alkanes	6
3.1.1. Chloromethane	8
3.1.2. Dichloromethane	9
3.1.3. Chloroform	10
3.1.4. Carbon Tetrachloride	10
3.1.5. Other Simple Haloalkanes	10
3.2. Simple Functionalized Acyclic Organohalogens	12
3.3. Simple Functionalized Cyclic Organohalogens	19
3.3.1. Cyclopentanes	19
3.3.2. Cyclitols and Benzoquinones	20
3.4. Terpenes	24
3.4.1. Monoterpenes	24
3.4.1.1. Acyclic Monoterpenes	24
3.4.1.2. Alicyclic Monoterpenes	30
3.4.2. Sesquiterpenes	36
3.4.2.1. Terrestrial Sesquiterpene Lactones	36
3.4.2.2. Indanone Sesquiterpenes	42
3.4.2.3. Other Terrestrial Sesquiterpenes	42
3.4.2.4. Marine Sesquiterpenes	42
3.4.2.4.1. Monocyclic and Other Simple Sesquiterpenes	43
3.4.2.4.2. Chamigrene and Related Types	50
3.4.2.4.3. Eudesmane and Other Types	57
3.4.2.4.4. Cuparene, Laurene, and Other Aromatic Types	61

* Dedicated to the memory of my father, Waldron Boger Gribble, 1907–1980.

3.4.3. Diterpenes	66
3.4.3.1. Terrestrial Diterpenes	66
3.4.3.2. Marine Diterpenes	68
3.4.3.2.1. Diterpenes of <i>Aplysia</i>	68
3.4.3.2.2. Diterpenes of <i>Laurencia</i>	70
3.4.3.2.3. <i>Sphaerococcus</i> and Other Red Algae Diterpenes	73
3.4.3.2.4. Sponge Diterpenes	74
3.4.3.2.5. Gorgonian Diterpenes	76
3.4.4. Higher Terpenes	81
3.5. Steroids	84
3.6. Marine Nonterpenes—C ₁₅ Acetogenins	87
3.7. Iridoids	100
3.8. Lipids and Fatty Acids	101
3.9. Fluorine-Containing Carboxylic Acids	108
3.10. Prostaglandins	110
3.11. Furanones	112
3.12. Amino Acids and Peptides	114
3.13. Alkaloids	126
3.14. Heterocycles	133
3.14.1. Pyrroles	133
3.14.2. Indoles	141
3.14.3. Carbazoles	160
3.14.4. Indolocarbazoles	161
3.14.5. Carbolines	161
3.14.6. Quinolines and Other Nitrogen Heterocycles	165
3.14.7. Benzofurans and Related Compounds	169
3.14.8. Pyrones	169
3.14.9. Coumarins and Isocoumarins	170
3.14.10. Flavones and Isoflavones	171
3.15. Polyacetylenes	173
3.15.1. Terrestrial Polyacetylenes and Derived Thiophenes	173
3.15.2. Marine Polyacetylenes	181
3.16. Eneidyne	184
3.17. Macrolides	186
3.18. Naphthoquinones and Higher Quinones	193
3.19. Tetracyclines	197
3.20. Aromatics	198
3.21. Simple Phenols	199
3.21.1. Terrestrial	200
3.21.2. Marine	202
3.22. Complex Phenols	209
3.22.1. Diphenylmethanes and Related Compounds	209
3.22.2. Diphenyl Ethers and Related Compounds	212
3.22.3. Tyrosines	214
3.22.3.1. Simple Tyrosines, Thyroxine, and Related Compounds	215
3.22.3.2. Transformed Single Tyrosines	216
3.22.3.3. Transformed Multiple Tyrosines	224
3.22.3.4. Bastadins	226
3.22.4. Depsides	232
3.22.5. Depsidones	234

3.22.6. Xanthones	238
3.22.7. Anthraquinones and Related Compounds	248
3.22.8. Griseofulvin and Related Compounds	251
3.22.9. Miscellaneous Fungal Metabolites and other Complex Phenols	254
3.23. Glycopeptides	261
3.24. Orthosomycins	272
3.25. Dioxins	273
3.26. Humic Acids	276
4. Biohalogenation	278
4.1. Introduction and Early Examples	278
4.2. Chloroperoxidase	278
4.3. Bromoperoxidase	281
4.4. Other Peroxidases	283
5. Biodegradation	284
6. Natural Function	286
7. Significance	288
8. Future Outlook	290
Addendum	291
Acknowledgements	302
References	302

Author's Note

Only naturally occurring halogenated compounds are numbered. However, in a few cases, it was necessary to number a nonhalogenated compound to avoid a gap in the numbering sequence. These unavoidable exceptions are approximately balanced by a few late-addition halogenated compounds that have to share a number. Thus, the total number of compounds in this review is essentially equal to the number of known naturally occurring organohalogen compounds. This numbering scheme allows one readily to determine that there are, for example, 189 natural halogenated indoles and 208 halogenated marine sesquiterpenes.

1. Introduction

Natural chlorine-, bromine-, iodine-, and fluorine-containing organic chemical compounds are abundant on our planet. Occurring on land, in the oceans, and in the atmosphere, they pervade every form of life. They are produced by marine and terrestrial plants, bacteria, fungi, insects, marine animals, and even mammals. Natural combustion processes, such as volcanoes and other geothermal events, and forest and brush fires contribute large quantities of halogenated compounds to the environment. In 40 years, the number of known natural organohalogens has multiplied 200 times, from a dozen in 1954 to nearly 2400 today (Table 1) (1-12).

In addition to the reviews cited in Table 1, a number of other excellent reviews of portions of this field are available (13–40), especially of marine products. More specific reviews will be cited as appropriate. However, no single review to date covers natural organohalogen compounds of all types, from all sources, over the entire period of human discovery. An attempt was made to cover the literature through mid-1994, but the sheer enormity of this task almost guarantees omissions. Since the author felt that it was more important to document all known organohalogens, the discussion of most individual compounds is severely limited. Compound characterization and synthesis are omitted. Biosynthetic pathways and proposals are discussed only to a limited extent. Man-made organohalogens are presented only when they also have a natural origin. Organohalogen isolation artifacts and “forced” metabolites are generally not included.

The organization follows an earlier, limited review (11), and is by structural type. Classification is sometimes arbitrary, especially for those substances that do not fall into a well-defined biogenetic or structural group. For example, 2-bromoindole-containing cyclic peptides are “Cyclic Peptides” rather than “Indoles”. References are generally in chronological sequence within each section.

Table 1. *Discovery of Naturally Occurring Organohalogen Compounds*

Year	Reviewer(s)	Summary	Reference
1954	Bracken	12 organochlorine natural products	(1)
1961	Petty	29 organochlorines	(2)
1968	Fowden	30 organochlorines and a few containing bromine, iodine, and fluorine	(3)
1971	Turner	70 chlorinated fungal metabolites	(4)
1973	Siuda and DeBernardis	200 organohalogens from all sources (150 organochlorines, 50 organobromines)	(5)
1976	Minale	100 organobromines (all but one from marine sources)	(6)
1978	Thomson	150 organohalogens from marine sources	(7)
1981	Fenical	400 organohalogens from marine sources	(8)
1983	Turner and Aldridge	80 new chlorinated fungal metabolites	(9)
1986	Engvild	130 organochlorines from higher plants	(10)
1992	Gribble	611 new organohalogens from all sources isolated between 1980–1991	(11)
1993	Naumann	500 organochlorines from all sources are discussed	(12)
1994	Gribble	2,450 organohalogens from all sources	(this work)

Due to the intense scrutiny under which organohalogens—particularly those containing chlorine—have come in recent years, it seemed urgent to review comprehensively the entire field of naturally occurring organohalogen compounds. It is hoped that this review will provide important background material for regulatory and government agencies worldwide to facilitate informed decisions regarding the use of halogenated chemicals in our society.

2. Origins

The halide salts of the four common halogens are abundant to various degrees on earth (Table 2). As discussed in Biohalogenation (Sect. 4), enzymatic oxidation of chloride, bromide, and iodide is the initial biochemical event leading to the production of natural organohalogens. Whereas halide in the oceans (Cl^- , Br^- , I^-) serves as the origin of the vast number of marine organohalogens to be discussed, it is believed that chloride ion as sea salt spray can also be oxidized to free chlorine by ozone and thence to chlorine atoms and HCl (44, 45). The concentration of sea level gaseous chlorine (Cl_2) is 1 ppb (45), which may explain the low concentration of ozone near the surface of the ocean. The major source of natural HCl and HF in the atmosphere is volcanoes (43, 46–56), and several recent eruptions have been studied with regard to their gas emissions. For example, the Mt. Pinatubo eruption in 1991 released 4.5×10^6 tons of total chlorine (HCl and Cl^-) into the atmosphere (48), and the 1976 Mt. Augustine eruption in Alaska emitted 0.6×10^6 tons of chlorine, of which up to 0.2×10^6 tons was HCl (49–51). Likewise, Hekla in 1970 (52), El Chichón in 1982 (53, 54), Guatemala volcanoes in 1978 (55), and the ten-year Kilauea eruptions all produced large quantities of HCl , HF and perhaps HBr (56). For example, the El

Table 2. *Distribution of Halides in the Environment*

Halide	Oceans (41, 2245) mg/l	Sedimentary Rocks (39, 2245) mg/kg	Fungi (42) mg/kg	Wood Pulp (43) mg/kg	Plants (70, 2245) mg/kg
Cl^-	19,000	10–320		70–2100	200–10,000
Br^-	65	1.6–3	100		
I^-	0.05	0.3			
F^-	1.4	270–740			

Chichón eruptions produced 9% of the global HCl (0.04×10^6 tons); over a large part of the globe there was a 40% increase in the amount of gaseous HCl (54). Hydrogen chloride has also been detected outside of our solar system (57, 58).

In addition to the presence of I^- and Br^- in the oceans, free iodine was identified in marine organisms long before organoiodides were characterized. The algae *Asparagopsis armata*, *Falkenbergia doubleti*, and *Bonnemaisonia asparagoides* contain iodine (59). Fifty species of Cyanophyceae, Chlorophyceae, Phaeophyceae, and Rhodophyceae contain iodide (or organic iodides) (60), and, of 46 species of sponges examined, all contained iodine and all but one contained bromine (61) (probably organic halides). The total halogen content (dry weight) of the common algae *Laurencia pacifica* and *Plocamium pacificum* is 0.29% and 0.64%, respectively. These algae are found in all of the oceans (tropical, temperate, and polar), and *Plocamium* occurs from the intertidal regions to depths of greater than 35 meters (62).

Although the concentration of fluoride in seawater is only 1.3 mg/l (41), the sponge *Halichondria moorei* contains potassium fluorosilicate (K_2SiF_6) to the extent of 10% (dry weight) (64). Whereas this animal is able to sequester and concentrate fluoride, another sponge species from the same taxonomic order and in a nearby location contains no fluoride.

It is clear that ample halide and/or halogen is available for incorporation by marine and terrestrial organisms into specific organohalogens by enzymatic processes and for conversion into organohalogens by geothermal processes. To what extent these natural sources of halogen affect the ozone layer is still a matter of debate (45, 47, 49, 65, 66), but unfortunately, this area is outside the scope of the present review.

3. Occurrence

3.1. Simple Alkanes

Large numbers of simple chloro-, bromo-, and iodoalkanes, and their mixed derivatives, are found in nature, being produced by both plants and animals and formed during natural combustion processes. Many of these same compounds are also anthropogenic and are used industrially (67, 68). Table 3 lists the known natural simple halogenated alkanes.

Table 3. *Simple Halogenated Alkanes and Alkenes that Occur Naturally*

Compound	Source (Ref)
CH ₃ Cl (1)	see text
CH ₂ Cl ₂ (2)	see text
CHCl ₃ (3)	see text
CCl ₄ (4)	see text
CH ₃ Br (5)	giant kelp (79, 119), volcanoes (94–96), biomass combustion (151), Arctic atmosphere (116, 117), other atmospheres (Point Barrow, Mauna Loa, Samoa, New Zealand) (118) (Japan) (120), Antarctic ice algae (121), oceans (126)
CH ₃ I (6)	giant kelp (79, 119, 123), volcanoes (94–95), marine algae (77, 102, 122, 123, 2210), oceans (125, 126, 147), Antarctic atmosphere and seawater (124)
CH ₂ Br ₂ (7)	marine algae (122, 123, 132, 133, 137, 2210), Arctic atmosphere (116, 117, 135), Atlantic ocean (122, 134, 147), Japan atmosphere (120), Arctic seawater (135), phytoplankton (136), Antarctic air and seawater (138)
CHBr ₃ (8)	marine algae (77, 102, 122, 123, 132, 133, 137, 141–143, 2210), Arctic atmosphere (116, 135), Arctic seawater (112, 135, 140, 141), Atlantic air and seawater (122, 134), atmosphere over Pt. Barrow, Mauna Loa, Samoa, and New Zealand (118), atmosphere over Japan (120), open ocean (144, 147), Arctic and Antarctic microalgae (121, 136, 150), Antarctic air and seawater (138)
CBr ₄ (9)	marine algae (102, 132, 133, 145)
CH ₂ ClBr (10)	marine algae (121, 122), Arctic air and water (117, 135), Atlantic air and water (134), Japan air (120)
CH ₂ ClI (11)	marine algae (102, 137, 2210), phytoplankton (136), Antarctic air and water (124), Atlantic air and water (134, 146), open ocean (144), Arctic water and air (135)
CH ₂ BrI (12)	marine algae (132, 133)
CH ₂ I ₂ (13)	marine algae (77, 122, 132, 133, 137, 2210), Atlantic air and water (122, 134), open ocean (137, 144), Arctic air and water (135)
CHI ₃ (14)	marine algae (132, 133, 145)
CHCl ₂ Br (15)	marine algae (77, 102, 121, 122, 134, 2210), oceans (77, 122, 134, 138, 147)
CHClBr ₂ (16)	marine algae (77, 102, 121, 122, 132, 133, 134, 137, 145, 2210), oceans (77, 122, 134, 137, 138, 147), phytoplankton (136)
CHBr ₂ I (17)	marine algae (102, 132, 133, 145)
CHBrI ₂ (18)	marine algae (132, 133, 145)
CHClBrI (19)	marine algae (132, 133, 145)
CH ₃ CH ₂ Br (20)	marine algae (122, 134), mine air (103)
CH ₃ CH ₂ I (21)	marine algae (77, 122, 134, 137), oceans (77, 137)
BrCH ₂ CH ₂ I (22)	marine algae (132, 133)
CH ₃ CH ₂ CH ₂ Br (23)	marine algae (77), oceans (77)
CH ₃ CH ₂ CH ₂ I (24)	marine algae (77, 137), oceans (77, 135, 137, 144)

Table 3 (continued)

Compound	Source (Ref)
$(\text{CH}_3)_2\text{CHI}$ (25)	marine algae (77, 137), oceans (77, 135, 137, 144)
$\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{I}$ (26)	marine algae (77, 137, 2210), oceans (77, 137, 144)
$\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{Br}$ (27)	marine algae (77), oceans (77)
$\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{I}$ (28)	marine algae (77), oceans (77)
$\text{CH}_3\text{CH}_2\text{CH}(\text{CH}_3)\text{I}$ (29)	oceans (144)
$\text{Cl}_2\text{C}=\text{CHCl}$ (30)	volcanoes (93), marine algae (1653, 2210)
$\text{Cl}_2\text{C}=\text{CCl}_2$ (31)	volcanoes (86, 1183), marine algae (1653)
CH_3CCl_3 (32)	oceans (112)
CHFCl_2 (33)	volcanoes (86, 93, 1183)
CHF_2Cl (34)	volcanoes (93)
CFCl_3 (35)	volcanoes (86, 93, 1183), drill wells (106), mine air (103)
CF_2Cl_2 (36)	volcanoes (86, 1183), drill wells (106), mine air (103)
$\text{F}_2\text{C}=\text{CF}_2$ (37)	volcanoes (93)
$\text{FClC}=\text{CF}_2$ (38)	volcanoes (93)
$\text{CCl}_2\text{FCClF}_2$ (39)	volcanoes (93)
$\text{CF}_3\text{CF}=\text{CF}_2$ (40)	volcanoes (93)
$(\text{CH}_3)_2\text{SiF}_2$ (41)	volcanoes (86, 1183)
CF_4 (42)	unknown (148, 149)
$\text{Br}_2\text{C}=\text{CHCHCl}_2$ (43)	marine algae (132, 133, 145)
$\text{Br}_2\text{C}=\text{CHCHClBr}$ (44)	marine algae (132, 133, 145)
$\text{Br}_2\text{C}=\text{CHCHBr}_2$ (45)	marine algae (132, 133, 145)
$\text{BrIC}=\text{CHCHBr}_2$ (46)	marine algae (132, 133, 145)

3.1.1. Chloromethane

Chloromethane (1) is probably the most abundant natural organohalogen and accounts for 25% of the chlorine in the atmosphere (63). It is estimated that the natural production of global CH_3Cl is 5 million tons per year (69, 70), whereas the level of anthropogenic CH_3Cl is only 26,000 tons per year (70). A number of biogenic and combustion sources contribute to the former total (71). Chloromethane is produced by several species of wood-rotting fungi which occur worldwide, including *Fomes* (*F. conchatus*, *F. occidentalis*, *F. pomaceus*, *F. ribis*, *F. rimosus*, *F. vinosus*) (72), *Phellinus* (*P. pomaceus*, *P. ribis*, *P. occidentalis*, *P. robiniae*, *P. ignarius*, *P. lundelli*, *P. pachyphloes*, *P. pini*, *P. populicola*, *P. trivialis*) (70, 73–75), and *Inonotus* (*I. andersonii*, *I. hispidus*) (74) in 75–90% yield based on chloride. It is also found in cultivated mushrooms (*Agaricus bisporus*) (76), potato tubers (*Solanum tuberosum*) (100), phytoplankton (77), marine algae (*Endocladia muricata*) (78), giant kelp (*Macrocystis pyrifera*) (79), a bryozoan (*Biflustra per-*

fragilis) from Tasmania (80), the ice plant (*Mesembryanthemum crystallinum*) (78), the pencil cedar (81), the northern white cedar (81), and the evergreen cypress (81).

Of 63 species of wood-rotting *Phellinus*, *Hymenochaete*, *Fomitoporia*, *Inonotus*, *Omnia*, and *Phaeolus* fungi, 34 were found to produce CH_3Cl (74) (Hymenochaetaceae). However, of 27 species of the Ganodermataceae and Polyporaceae only one, *Fomitopsis cytisina*, was capable of CH_3Cl biosynthesis (74). These results suggest that CH_3Cl production by wood-rotting fungi is massive, especially since *Phellinus* and *Inonotus*, for example, are widely distributed in both tropical and temperate regions (70, 74, 75). Biosynthetic studies reveal that *Phellinus pomaceus* utilizes methionine (probably *S*-adenosylmethionine) as the methyl donor to synthesize CH_3Cl (73, 82), and that CH_3Cl serves as a methyl donor for the biosynthesis of esters and anisoles (e.g., veratryl alcohol) in this fungus (83) and others (*Phanerochaete chrysosporium*, *Phlebia radiata*, *Coriolus versicolor*) (84, 85). Since veratryl alcohol plays a key role in the degradation of wood lignin, its biosynthesis involving CH_3Cl is of vital importance to these wood-rotting fungi (84, 85).

Chloride ion is normally present in plants, wood, and soil, as well as minerals (70, 86, 103), in levels ranging from 200–10,000 ppm (70), and the combustion of plant material leads to the formation of organochlorines such as CH_3Cl . Forest fires (71, 87, 88), brush fires (71, 89–91), tobacco smoke (71, 92), and volcanoes (43, 93–97) produce CH_3Cl . Chloromethane in volcanic gases can have two origins: hot lava flowing over chloride-rich vegetation as in Kilauea lava flows (96), and the combustion of vegetation, peat, or minerals during explosive eruptions such as those of Mt. St. Helens (97) and Santiaguito (93). More recently, CH_3Cl has been detected in mines and mineral processing plants and is present in several ores and minerals (103).

Since natural fires have occurred on earth since land plants evolved 350–400 million years ago (88), it is clear that CH_3Cl has been a natural component of our atmosphere and stratosphere for eons. A recent study of Australian brush fires reveals that the earlier estimates of the global release of CH_3Cl from vegetation combustion may be underestimated (91). This particular source of CH_3Cl is viewed skeptically by some (98, 99).

3.1.2. Dichloromethane

Dichloromethane (CH_2Cl_2) (2), which is a widely used industrial solvent and is classified as a Priority Pollutant (67, 68), is found in the

atmosphere in low concentrations (101) and has been identified in volcanic gases (86), barley (86), a bryozoan (*Biflustra perfragilis*) (80), several species of brown (*Ascophyllum nodosum*, *Fucus vesiculosus*), green (*Enteromorpha linza*, *Ulva lacta*) and a red alga (*Gigartina stellata*) (77). It is also present in mine air, minerals, and the gas emissions of mining industry plants (103).

3.1.3. Chloroform

Not only is chloroform (CHCl_3) (3) a widely-used industrial chemical (38, 67, 68), it is also dispersed in the environment (36, 101, 104) and appears to have several natural sources. Chloroform has been detected in deciduous moss (81), the northern white cedar (81), volcanoes (86, 1183), drill wells (86, 106), mine gas and minerals (103), lemon (86), orange (86), barley (86), mushroom (*Cantharellus cibarius*) (107), marine algae (*Asparagopsis taxiformis*, *A. armata*) (102), (*Meristiella gelidium*) (2210), terrestrial plants (*Farsetia aegyptia*, *F. ramosissima*) (108), sapodilla fruit (*Achras sapota*) (109), shrimp paste (*Sergia lucens*) (110), Malabar Nightshade (*Basella rubra*) (111). As will be seen later, the haloform reaction *in vivo* probably accounts for a huge percentage of CHCl_3 in the oceans, as well as in ground and surface water from the natural decomposition of humic substances.

3.1.4. Carbon Tetrachloride

Carbon tetrachloride (CCl_4) (4) which is more toxic than the other chloromethanes is also an important industrial chemical (67, 68) and is found in the oceans (36) and the atmosphere (101, 114). Natural sources of CCl_4 include volcanoes (86, 1183), drill wells (86, 106), mine gas and minerals (103), marine algae (102), terrestrial plants (108), arctic ocean (112), including the bottom (113), and perhaps the atmospheric chlorination of CH_4 (105, 114).

3.1.5. Other Simple Haloalkanes

Table 3 summarizes the other simple haloalkanes that are known to have one or more natural sources, and Table 4 lists the marine algal sources of simple haloalkanes. Methyl bromide (5) has a large number of sources, both marine and combustion, and is a widely used soil fumigant