Communications to the Editor

[Chem. Pharm. Bull. 23(9)2179—2181(1975)]

UDC 546.13.04 : 547.562.1.04

Interaction of Chlorine and Selected Plant Phenols in Water

Reaction of *p*-hydroxycinnamic acid (I) with chloride water afforded a mixture of chlorinated styrene derivatives, whose structure were proved to be III, IV, and V. Similarly, *p*-methoxycinnamic acid (II) afforded VIII, IX, and X as degradation products. Tyrosine (XI), epigenin (XIV), I and II were ultimately converted to chlorinated quinones.

Recent controversy on the potential hazards of compounds resulting from chlorination of organic molecules in drinking or waste water[1] prompted us to report here some of our related experimental results.

Phenylpropanoids are the most abundant plant constituents which are likely to be eluated into the water system. In particular, the presence of *p*-hydroxycinnamic acid and its derivatives in polluted waters, especially in a part of the metropolitan Tokyo water system, was a subject of dispute for their alleged connection with a chronic bone disease (Kaschin-Beck disease).[2] To deny this assertion, Sawamura, *et al.* reported that *p*-hydroxycinnamic acid and 4-hydroxy-3-methoxycinnamic acid are rapidly decomposed by chlorine.[3] However, the nature of the degradation products was not clarified.

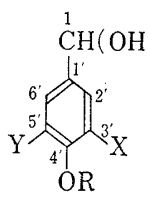
We observed by EC gas chromatography the formation of a number of chlorine containing compounds following the treatment of *p*-hydroxycinnamic acid (*p*-coumaric acid) (I) and *p*-methoxycinnamic acid (II) with a dilute chlorine water (*e.g.* 10 ppm). In order to identify these chlorinated products, I was reacted with 3 moles of chlorine water on a large scale. Three compounds were isolated in pure form, and their structures were established as 1-(4′-hydroxyphenyl)-2,2-dichloroethanol (III), $C_8H_8O_2Cl_2$, mp 92—94°, UV λ_{max}^{EtOH} nm (ε) 228 (19370), 276 (2557), IR ν_{max}^{KBr} cm^{-1}: 3400 (OH), 1604 (aromatic); 1-(3′-chloro-4′-hydroxyphenyl)-2,2-dichloroethanol (IV), mp 86—88°, UV λ_{max}^{EtOH} nm (ε) 230 (20098) 280 (3389), IR ν_{max}^{KBr} cm^{-1}: 3480 (OH), 1560 (aromatic); and 1-(3′,5′-dichloro-4′-hydroxyphenyl)-2,2-dichloroethanol (V), mp 114—116°, UV λ_{max}^{EtOH} nm (ε) 225 (31486), 274 (4908), 282 (4844), IR ν_{max}^{KBr} cm^{-1}: 3370 (OH), 1580 (aromatic). The nuclear magnetic resonance (NMR) spectra of the compounds are in full agreement with the structures, and the mass spectra shows a characteristic cleavage of the 2,2-dichloroethanol moieties (Table I). When the amount of chlorine was increased to 5 moles, 1,3-dichloro-2,5-dihydroxybenzene (VI), mp 161—162°, and 2,6-dichloro-1,4-benzoquinone (VII), mp 120—122° were isolated and identified with the authentic specimens.

Similarly, when *p*-methoxycinnamic acid (II) was treated with 3 moles of chlorine water at ambient temperature, 1-(4′-methoxyphenyl)-2,2-dichloroethanol (VIII), oil, $C_9H_{10}OCl_2$, UV λ_{max}^{EtOH} nm (ε) 234 (13264), 278 (3038), IR ν_{max}^{liquid} cm^{-1}: 3460 (OH), 1609 (aromatic), 1-(3′-chloro-4′-methoxyphenyl)-2,2-dichloroethanol (IX), oil, $C_9H_9OCl_3$, UV λ_{max}^{EtOH} nm (ε) 338 (27084), 276 (4514), IR ν_{max}^{KBr} cm^{-1}: 3450 (OH), 1610 (aromatic), 1-(3′,5′-dichloro-4′-methoxyphenyl)-2,2-dichloroethanol (X), mp 91—93°, $C_9H_8O_2Cl_4$, UV λ_{max}^{EtOH} nm (ε) 225 (39362), 274 (4003), 281 (3593), IR ν_{max}^{KBr} cm^{-1}: 3480 (OH), 1560 (aromatic), and 2,6-dichlorobenzoquinone (VII) were isolated in pure form. The NMR and mass spectra of these compounds are in support of the structures (Table I).

The proposed reaction mechanisms for the formation of the products are shown in Chart 1. Initial addition of chlorine to the double bond is followed by concerted decarboxylation and

1) J.L. Marx, *Science*, **186**, 809 (1974); Anonymous, *Chem. Eng. News*, **52** (45), 5 (1974).
2) E. Takizawa, "Study on Kaschin-Beck Disease in Japan" (in Japanese), Ogata-Shoten, Tokyo, 1970.
3) R. Sawamura, T. Koyama, Y. Kimura, T. Imamura, T. Tonomura, Y. Sayato, and K. Nakamuro, *Eisei Kagaku*, **18**, 96 (1972).

TABLE I. NMR Chemical Shift and Principal Peaks in the Mass Spectra of the Chlorinated Styrene Derivatives



	R	X	Y
III	H	H	H
IV	H	Cl	H
V	H	Cl	Cl
VIII	CH_3	H	H
IX	CH_3	Cl	H
X	CH_3	Cl	Cl

Compounds	Chemical shift (δ)[a]						m/e (relative abundance %)[b]			
	3′H	5′H	6′H	2′H	1H	2H	M^++2	M^+	M^++2−($CHCl_2$)	M^+−($CHCl_2$)
III	6.85, d		7.34, d		4.95, d	5.84, d	208	206		123
	$J_{5'6'}=J_{2'3'}=9$				$J_{12}=5$		(7.2)	(11.1)		(100)
IV	7.17, d	7.41, q	7.60, d		5.02, d	5.89, d	242	240	159	157
	$J_{5'6'}=8$	$J_{5'6'}=8$	$J_{2'6'}=2$		$J_{12}=5$		(9.0)	(9.2)	(33.3)	(100)
		$J_{2'6'}=2$								
V			7.38, s		4.90, d	5.75, d	276	274	193	191
					$J_{12}=5$		(9.6)	(7.1)	(62.1)	(100)
VIII	6.57, d		7.03, d		4.71, d	5.78, d	222	220		137
	$J_{5'6'}=J_{2'3'}=9$				$J_{12}=5$		(8.6)	(12.5)		(100)
IX	6.58, d	6.93, q	7.07, d		4.90, d	5.78, d	256	254	173	171
	$J_{5'6'}=8$	$J_{5'6'}=8$	$J_{2'6'}=2$		$J_{12}=5$		(5.9)	(6.1)	(31.2)	(100)
		$J_{2'6'}=2$								
X			7.13, s		4.73, q	5.57, d	290	288	207	205
					$J_{12}=5$		(4.9)	(3.5)	(62.0)	(100)
					$J_{11}=4$[c]	$J_{12}=5$				

a) relative to TMS in $CDCl_3$
b) 70 ev, 180°
c) coupling with OH

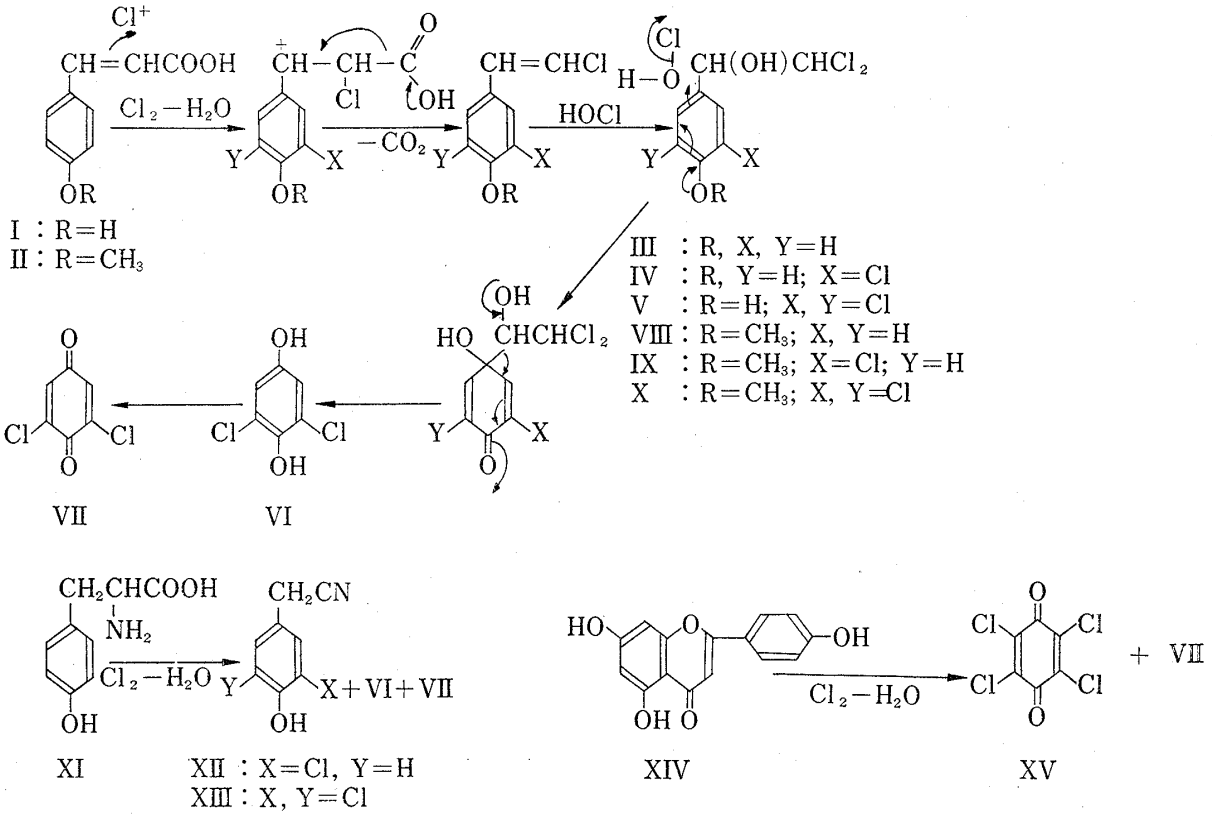


Chart 1

abstraction of the benzylic chlorine. Subsequent addition of chlorine followed by hydrolysis of the benzylic chlorine or addition of hypochlorous acid to the chlorostyrene gives the 2,2-dichloroethanol sidechain compounds. Analogy is found in the chlorination or hypochlorite treatment of cinnamic acid itself, where compounds such as chlorostyrene, 1,2,3-trichlorobenzene, and 1-hydroxy-2,2-dichloroethylbenzene have been reported besides the normal addition products.[4] Further oxidation results in the cleavage of the side-chain to form chlorobenzoquinone derivatives.

Upon treatment with 4 moles of chlorine water, tyrosine (XI), an α-amino acid closely related to the cinnamic acid derivatives afforded 3-chloro-4-hydroxybenzyl cyanide (XII),[5] mp 102—103°, C_8H_6ONCl, mass spectrum *m/e*: 167 (M^+), 132 (M^+–Cl, 100%), UV λ_{max}^{EtOH} nm (ε) 227 (40511), 275 (6445), 282 (6393), IR ν_{max}^{KBr} cm^{-1}: 3333 (OH), 2262 (CN), NMR ($CDCl_3$) δ 3.67 (2H, s, –CH–), 7.05 (1H, d, J=5 Hz), 7.12 (1H, q, J=3 and 5 Hz), 7.46 (1H, d, J=3 Hz), and 3,5-dichloro-4-hydroxybenzyl cyanide (XIII),[5] mp 162—164°, mass spectrum *m/e*: 201 (M^+), 166 (M^+–Cl, 100%), UV λ_{max}^{EtOH} nm (ε) 225 (71205), 275 (9090), 282 (8888), IR ν_{max}^{KBr} cm^{-1}: 3333 (OH), 2266 (CN), NMR ($CDCl_3$) δ 3.60 (2H, s, $-CH_2-$), 6.96 (2H, s, aromatic), both of which were identical with samples prepared by the chlorination of 4-hydroxybenzyl cyanide. When XI was treated with increased amounts of chlorine, XIII and VI were the predominant reaction products.

Chlorination of epigenin (XIV), a plant flavonoid, gave VII and 2,3,5,6-tetrachloro-1,4-benzoquinone (chloranil) (XV). The possible mechanism for the formation of these products from XI and XIV is comparable to that of the hydroxycinnamic acid derivatives. Chloranil (XV) seems to be the final product in the chlorination of those hydroxyphenol derivatives. In fact, when a large excess amount of chlorine was used, XV was also identified in the reaction mixture of I, II, and XI.

Gas chromatographic analysis showed that all these reaction products are formed even in very dilute solutions, and the corresponding peaks were detected the gas chromatographs although they are not necessarily the major peaks.

Correlation of these results to the problems in the chlorination of water or wastes must await future study, although we have compiled some of the biological test results.[7,8]

Acknowledgment This work was supported by the OWRR grant A-041-RI and B-057-RI, which is gratefully acknowledged.

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Received March 10, 1975

4) E. Erlenmeyer and A. Lipp, *Justus Liebigs Ann. Chem.* **219**, 179 (1883); J. Read and A.C.P. Andrews, *J. Chem. Soc.*, **119**, 1774 (1921); M.D. Forster and W.B. Saville, *ibid.*, **121**, 2595 (1922); E.H. Farmer and and C.G.B. Hose, *ibid.*, 962 (1933); M.C. Cabaleiro, M.D. Johnson, B.E. Swedlund, and J.G. Williams, *J. Chem. Soc.* (*B*), **1968**, 1022; P.B.O. de la Mare and M.A. Wilson, *J. Chem. Soc. Perkin Trans. II*, **1973**, 653; L.A. Cohen and W.M. Jones, *J. Am. Chem. Soc.*, **82**, 1907 (1960).

5) Pereira, *et al.*[6] reported the gas chromatography-mass spectrometry identification of these nitriles in the reaction products of tyrosine with hypochlorite; however, the physical and spectroscopic properties of the compounds were not recorded. Prior to their publication, we also reported the characterization of XII and XIII, and the nitrile formation in general from α-amino acids,[7] and compiled it along with their biological activities.[8]

6) W.E. Pereira, Y. Hoyano, R.E. Summons, V.A. Bacon, and A.M. Duffield, *Biochim. Biophys. Acta*, **313**, 170 (1973).

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8) Y. Shimizu, 8th Annual Report, The Rhode Island Water Resources Research Program, 1972, p. 36; Y. Shimizu, 9th Annual Report, The Rhode Island Water Resources Research Program, 1973, p. 15.