Tetrahedron Vol. 49, No. 47, pp. 10945-10958, 1993
Printed in Great Britain

0040-4020/93 $6.00+.00

Synthetic Approaches to Chlorinated 5-Hydroxy-5-Methyl-2-Furanones

Robert Franzén and Leif Kronberg*

Department of Organic Chemistry, Åbo Akademi University, Akademigatan 1,

SF-20500, Turku/Åbo, Finland

(*Received in UK* 28 *June* 1993; *accepted* 24 *September* 1993)

Abstract : The syntheses of chlorinated 5 - hydroxy- furanones with a mono-, di-, and trichloromethyl group at C-5 are described. The 5-chloromethyl hydroxyfuranones were obtained by chlorination of levulinic acid followed by triethylamine promoted elimination of hydrogen chloride. Hydrolyses of chlorinated 4 - cyclopentene- 1,3 -diones yielded 5-dichloromethyl hydroxyfuranones. The trichloromethyl group was incorporated to maleic anhydride through thermal decomposition of sodium trichloroacetate.

INTRODUCTION

Chlorinated 5-hydroxy-2-furanones are formed during chlorine bleaching of pulp and during chlorine disinfection of drinking water.[1-4] The compounds are of interest since they generate mutagenicity in the Ames mutagenicity assay.[5-8] Much attention has been paid to the compound 3-chloro-4-(dichloromethyl)-5-hydroxy-2(5*H*)-furanone (MX) which is one of the most active compound ever tested in the Ames assay.[6,8,9] In previous work our interest has been focused on 4-methyl substituted chloro hydroxyfuranones.[4] In the present work we describe the synthesis of 5-methyl substituted chlorohydroxyfuranones. The pure compounds are needed

SO2Cl2, ca. 16h
50 - 70 %
A
B
Et3N / CH2Cl2
3h
flash chrom.
7 %
1a
SO2Cl2 + UV, 1h
96 %
C
Et3N / CH2Cl2
24 h
5 %
1b

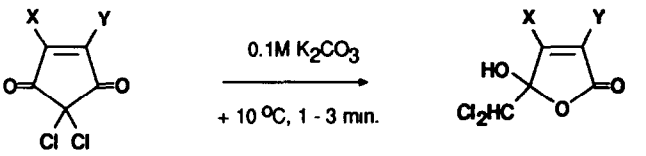
Scheme 1

as standards for their qualitative and quantitative determinations in chlorinated water and for the study of their mutagenic potency.

RESULTS and DISCUSSION

5-(Chloromethyl)-5-hydroxy-2-furanone **1a** and 4-chloro-5-(chloromethyl)-5-hydroxy-2-furanone **1b** were prepared from levulinic acid (Scheme 1). The acid was chlorinated with SO_2Cl_2 and 3,5-dichloro-4-oxo-pentanoic acid **A** and 5,5-dichloro-4-oxo pentanoic acid **B** were obtained as a 4:1 mixture (NMR data in Tables III and IV). Chlorination of levulinic acid with SO_2Cl_2 under UV light produced 2,3,5-trichloro-4-oxo-pentanoic acid **C**, in 96% yield. NMR and MS data showed that the open chain tautomer of chlorinated levulinic acids is greatly favoured over the lactone form (Tables III and IV). The desired 5-chloromethyl hydroxyfuranones were obtained in yields of 5-7% by triethylamine-promoted elimination of hydrogen chloride from the chlorinated levulinic acids **A** and **C**.

The preparation of hydroxyfuranones with a dichloromethyl group at C-5 was carried out by hydrolyses of various 2,2-dichlorocyclopentene-1,3-diones with 0.1M K_2CO_3 (Scheme 2).[10]

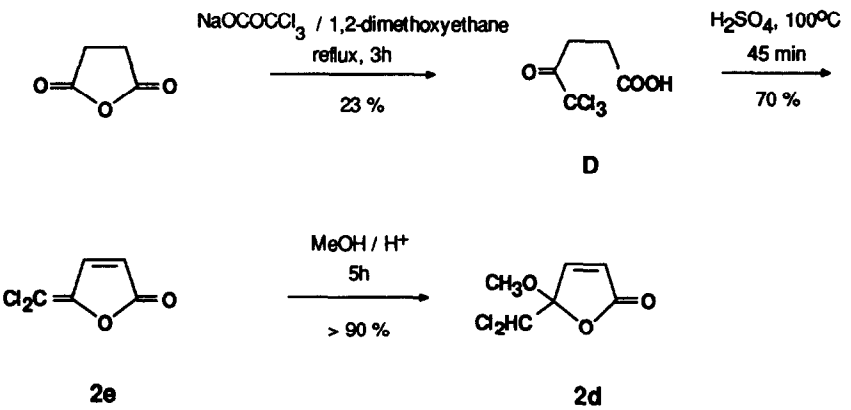


2a X = Y = H
2b X = H, Y = Cl
2c X = Cl, Y = Cl

Scheme 2

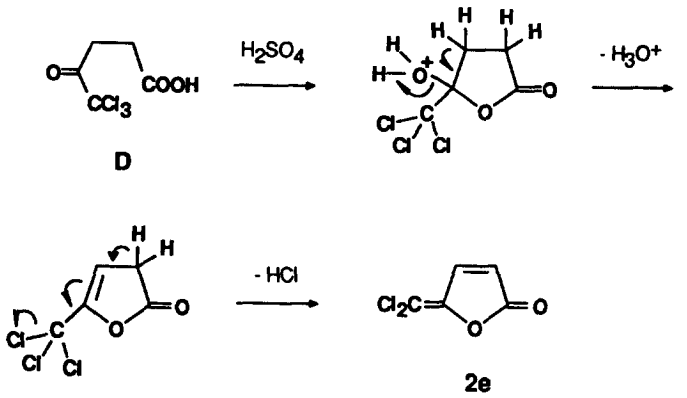
The hydroxyfuranone **2b** was prepared by hydrolysis of 2,2,4-trichlorocyclopentene-1,3-dione which in turn was produced by chlorination of cyclopentene-1,3-dione with Cl_2. The compound 2,2,4,5-tetrachlorocyclopentene-1,3-dione, needed for the preparation of **2c**, was obtained by reacting Cl_2 under UV-light with cyclopentene-1,3-dione. The compound 2,2-dichlorocyclopentene-1,3-dione, used in the synthesis of **2a** was obtained by UV-promoted dechlorination[11,12] of one of the chlorine atoms at the double bond in

2,2,4-trichlorocyclopentene-1,3-dione. The hydroxyfuranone **2a** was found to be highly unstable at the hydrolysis conditions of the cyclopentenedione and **2a** could be obtained in yields of only ca.1%. However, prior to qualitative and quantitative determination of the hydroxyfuranones in extracts of water the compounds were converted to methyl ethers by derivatization with acidic methanol. Therefore, the methyl ether **2d** serves as a standard as well as **2a**. The preparation of **2d** started from succinic anhydride which was treated with sodium trichloroacetate according to the method of Winston et al..[13] The product 5,5,5-trichloro-4-oxo pentanoic acid **D** was dissolved in sulphuric acid at 100°C and the dichloromethylene 2-furanone **2e** was obtained in 70% yield (Scheme 3).



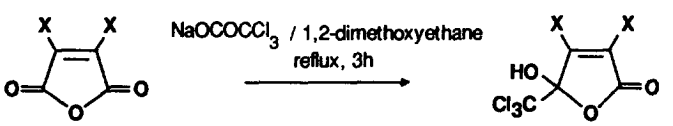
Scheme 3

Carbonyl absorption at 1800 cm^{-1} was present in the infrared spectra of **2e**, and the ^{13}C NMR showed that the compound contained only one carbonyl group (δ = 167.5). Upon treatment of **2e** with acidic methanol the 5-methoxy derivative **2d** of **2a** was obtained. A plausible mechanism for the formation of **2e** by sulphuric acid treatment of the chlorinated keto acid is outlined in Scheme 4.



Scheme 4

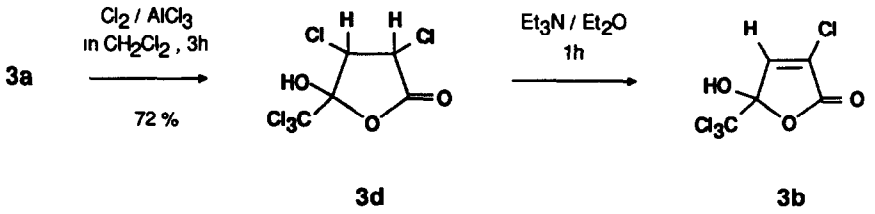
The incorporation of a trichloromethyl group to C-5 was performed according to methods developed by Winston et al..[13] Treatment of maleic anhydride and dichloromaleic anhydride with sodium trichloroacetate resulted in the formation of **3a** (5%) and **3c** (16%) (Scheme 5).



Scheme 5

3a X = H
3c X = Cl

Chlorination of the carbon-carbon double bond in **3a** with Cl_2 in the presence of aluminium chloride produced the pentachloro compound **3d** (Scheme 6).



Scheme 6

However, in the ^{13}C NMR spectra two carbonyl signals at 168.3 and 182.2 ppm in addition to a carboxyl signal at 164.2 ppm indicated that a mixture of the ring form and the open form of **3d** was obtained. Following triethylamine-promoted elimination of hydrogen chloride from **3d** the desired compound 3-chloro-5-hydroxy-5-(trichloromethyl)-2-furanone **3b** was obtained. Although the overall yield of the compounds cannot be regarded as outstanding, the target compounds are obtained pure and in quantities high enough to make possible the use of them as analytical standards and in assays for mutagenicity.

Discussion of the Spectroscopic data.

The location of the chlorine at C-4 in **1b** was evident from the ^1H NMR spectrum of the compound. The signal of the β-proton was absent while a signal corresponding to the α - proton was observed at 6.27 ppm. This signal was weakly splitted because of long-range coupling to one of the two diastereotopic protons in the chloromethyl group (J = 0.31 Hz, Table II).

It is known that nearly in all α,β-unsaturated carbonyl compounds the β-carbon has a higher δ_C value than the α-carbon.[14,15] LaLonde et al.[16] observed this same chemical shift pattern when they studied hydroxyfuranones with chlorine at the α - carbon and chlorine at both the α - and β - carbons. In accordance with this the signals at δ 120.5 - 131.5 and at δ 140.6 - 157.3 were assigned to the α - and β - carbons, respectively (Table I). The effect on the carbon chemical shift of hydrogen substitution by a chlorine atom at

α - and β carbons is mainly inductive at the C-Cl carbon while a resonance effect affects the shifts of the vicinal carbons.[17,18] These substitutions resulted in a small upfield shift for the C-5 and C-6 carbons. In the 3,4-dichloro substituted compounds a mutual compensation of inductive effects and resonance effects takes place and the shifts of C-3 and C-4 in **2c** and **3c** are moved towards the shifts observed for **2a** and **3a**, respectively.

The lactone structure rather than the keto acid tautomer was assigned for all studied hydroxyfuranones on the basis of the strong hydroxyl and lactone carbonyl absorption in the infrared spectra. In the case of 5,5,5-trichloro-4-oxo-pentanoic acid the two carbonyl peaks in the IR spectra, one for the carbonyl group and the other for the carboxyl group showed that the open keto acid is the favoured tautomer.

Table I ^{13}C Chemical Shifts δ_{C_i} (ppm[a]) for 5-Methyl Chlorohydroxyfuranones

Cmpd[b]	$\delta_{C\,2}$	$\delta_{C\,3}$	$\delta_{C\,4}$	$\delta_{C\,5}$	$\delta_{C\,6}$
1a	170 0	125 1	152 1	105 4	46 6
1b	167 2	120 5	157 3	104 8	44 1
2a	168 5	126 4	149 9	105 2	72 9
2b	163 8	130 8	141 4	103 5	72 7
2c	161 8	125 4	147 1	102 5	71 1
3a	169 2	126 1	151 7	108 1	99.8
3b	163 6	131 5	140 6	105 7	99 4
3c	160 5	128 0	145 3	103 3	96 9

[a]Relative to TMS at δ=0 00 ppm [c] Dissolved in $CDCl_3$

Table II ^{1}H Chemical Shifts (ppm[a]) and Couplings (Hz) for 5-Methyl Chlorohydroxyfuranones

Cmpd[b]	$\delta_{H\text{-}3}$	^5J	^3J	$\delta_{H\text{-}4}$	^3J	$\delta_{H\,6}$	^5J	^2J	other
1a	6 26(d,1H)		5 6	7 32(d,1H)	5 6	3 84(d,1H_B) 3 80(d,1H_A)		11 83 11 83	4.8(br s,OH)
1b	6 27(d,1H)	0.31				3.93(dd,1H_B) 3 82(d,1H_A)	0.31	12 06 12 06	5 1(br.s,OH)
2a	6 37(d,1H)		5.6	7 40(d,1H)	5 6	5 82(s,1H)			4 5(br s,OH)
2b				7.27(s,1H)		5 84(s,1H)			4.1(br s,OH)
2c						6 00(s,1H)			4.1(br.s,OH)
3a	6.40(d,1H)		5 8	7.52(d,1H)	5 8				6 3(br.s,OH)
3b				7.37(s,1H)					4 1(br.s,OH)
3c									2 2(br.s,OH)

[a] Relative to TMS at δ = 0.00 ppm. [b] Dissolved in $CDCl_3$

Table III ^{1}H Chemical Shifts (ppm[a]) for 4-oxo-pentanoic acids

Cmpd[b]	$\delta_{H\,2}$	^3J	^2J	$\delta_{H\text{-}3}$	^3J	$\delta_{H\text{-}5}$	^2J	other
A	3 05(dd,1H_B) 3 26(dd,1H_A)	5 7 7 6	17.6 17.6	4 85(dd,1H)	5 7 7.6	4 53(d,1H_B) 4 48(d,1H_A)	16 04 16 04	9 5(br s,COOH)
B	3 17(t,2H,CH_2)	6 5		2,75(t,2H,CH_2)	6 5	5 92(s,1H,$CHCl_2$)		9 5(br s,COOH)
C	4 85(m,CHCl)[c]			4 85(m,CHCl)[c]		4 04(d,1H_B) 4 19(d,1H_A)	12 05 12 05	9 2(br s,COOH)
D	3 38(t,2H,CH_2)	6.6		2 81(t,2H,CH_2)	6 6			10 1(br s,COOH)

[a] Relative to TMS at δ = 0.00 ppm [b] Dissolved in $CDCl_3$. [c] The signals were not unambiguously assigned due to interference from background

Table IV ^{13}C Chemical Shifts $\delta_{C,i}$ (ppm[a]) for 4-oxo-pentanoic acids

Cmpd[b]	$\delta_{C\,2}$	$\delta_{C\,3}$	$\delta_{C\,4}$	$\delta_{C\,5}$	δ_{COOH}
A	38 1	53 3	195 8	45 8	174 8
B	27 8[c]	29 9[c]	190 3	69 8	177 8
C	47 8	51 3	190.3	44 6	172 3
D	28 4[c]	29 0[c]	189 7	95 9	176 7

[a] Relative to TMS at δ=0 00 ppm [b] Dissolved in $CDCl_3$ [c] An unambiguous assignment could not be made

EXPERIMENTAL

General. All compounds were characterized by their spectral properties. IR spectra were recorded by a Perkin-Elmer 297 Infrared Spectrophotometer. Designations s, m, w and br refer to strong, medium, weak and broad bands. The NMR spectra were recorded with a Jeol GX 400 Fourier transform NMR Spectrometer, with TMS added as internal standard. Full scan mass spectra were recorded using a Hewlett-Packard 5971A Mass Selective Detector (MSD) coupled to a Hewlett-Packard 5890 Gas Chromatograph. The GC was equipped with a HP-1 fused silica capillary column (25m x 0.20 mm i.d.,film thikness 0.33μm). HRMS analyses were performed on a Dani 3800 capillary gas chromatograph interfaced to a VG7070E mass spectrometer. The ionization mode was electron impact (70 eV), and the resolving power was 1000. Low resolution accurate mass determination was based on reference ions 126.9045 (I), 140.9201 (CH_2I), 253.8089 (I_2), and 267.8246 (CH_2I_2) from diiodomethane. EIMS were also recorded for the methyl ether derivates of the hydroxyfuranones and Isotope Cluster Abundance Calculations were used to analyze chlorine patterns. Column chromatography utilized Merck (Kieselgel 60) silica gel (40 - 63 μm particle size, 230 - 400 mesh ASTM). Thin layer chromatography utilized Merck art. 5719 silica gel 60 F_{254} pre-coated plates. Spots were visualized by UV radiation. Melting points were determined in capillary tubes with a Gallenkamp melting point apparatus and are uncorrected.

5-(Chloromethyl)-5-hydroxy-2-furanone 1a Levulinic acid (5.0 g, 43.1 mmole) and SO_2Cl_2 (15 mL) was stirred overnight to yield a yellow oil which upon distillation at 170°C / 9mm Hg gave 1.5g of a mixture of

3,5-dichloro-4-oxo-pentanoic acid and 5,5-dichloro-4-oxo-pentanoic acid (4:1). The chlorinated 4-oxo-pentanoic acids (1g) were dissolved in CH_2Cl_2 (10 mL) and NEt_3 (550 mg) in CH_2Cl_2 (5 mL) was added at 0°C over a period of 3 hours. After 24 h the solvent was evaporated to yield a brown oil which upon purification on SiO_2 with CH_2Cl_2 - n-hexane (3:1) + 0.1% acetic acid as eluent yielded 57.4 mg (7%) of pure **1a**.; IR(KBr) : ν = 1770 (C=O) cm^{-1}.; MS (EI), m/z (%) = 149 (3), 133 (10), 131 (5), 113 (1), 100 (5), 99 (100), 87 (5), 71 (9).; HRMS : m/z , calc. for $C_5H_6O_3Cl$ (M^++H) 149.0005; found 149.0002.
5-(chloromethyl)-5-methoxy-2-furanone : MS(EI) m/z (%) = 113 (100), 131 (18), 133 (6).

4-Chloro-5-(chloromethyl)-5-hydroxy-2-furanone 1b A solution of (5.0 g, 27.2 mmole) 4- oxo-pentanoic acid and SO_2Cl_2 (10 mL) was UV-irradiated for 1h to produce (5.7 g, 26.1 mmole) 2,3,5-trichloro-4-oxo-pentanoic acid (96%). The chlorinated 4-oxo-pentanoic acid (5.0 g, 22.9 mmole) and NEt_3 (4.6 g, 45.8mmole) were dissolved in CH_2Cl_2. Stirring was continued for 24 h and after removal of the solvent the crude product was obtained as a brown oil. Purification on SiO_2 with CH_2Cl_2 - diethyl ether (3:1) and 0.1% acetic acid gave the 157 mg of **1b** as a yellow oil (5% from the chlorinated 4-oxo-pentanoic acid.).; IR (KBr) : ν = 3350 (br), 1770 (br), 1630 (s), 1420 (br), 940 (m) cm^{-1}.; MS (EI) : m/z (%) = 183 (M^+ + 1) (1), 165 (2), 164 (1), 146 (1), 133 (100), 99 (13), 88 (12), 69 (9).; HRMS : m/z , calc. for $C_5H_3O_2Cl_2$ (M^+-OH) 164.9510; found 164.9487.
4-chloro-5-(chloromethyl)-5-methoxy-2-furanone : MS (EI) m/z (%) = 147 (100), 149 (31), 165 (11), 167 (7), 169 (2).

5-(Dichloromethyl)-5-hydroxy-2-furanone 2a 2,2-dichloro-4-cyclopentene-1,3-dione was obtained by UV-irradiation of 2,2,4-trichloro-4-cyclopentene-1,3-dione in ethylacetate/CCl_4. After evaporation of the solvent the residue was redissolved in diethyl ether (20 mL). The hydroxyfuranone **2a** was prepared by shaking the diethyl ether solution with 0.1M K_2CO_3 (20 mL) for 1 minute. Purification on a TLC-plate with dichloromethane - diethyl ether - acetic acid (50:50:0.1) as eluent gave pure **2a** in low yield (<1%) as a semicrystalline oil.; MS (EI) : m/z (%) = 183 (1), 167 (10), 165 (8), 133 (12), 99 (100), 71 (8), 54 (8), 43 (30).; HRMS : m/z, calc. for $C_5H_3O_2Cl_2$ (M^+-OH) 164.9510; found 164.9515.
5-(dichloromethyl)-5-methoxy-2-furanone **2d** : MS (EI) m/z (%) = 113 (100), 165 (6), 167 (4), 169 (2).

3-Chloro-5-(dichloromethyl)-5-hydroxy-2-furanone 2b (876 mg, 4.4mmole) 2,2,4-trichloro-4-cyclopentene-1,3-dione (85%) was obtained by chlorination of 4-cyclopentene-1,3-dione (500 mg, 5 mmole) in CH_2Cl_2 (20 mL) for 5 h. After evaporation of the solvent the chlorinated 4-cyclopentene-1,3-dione in diethyl ether (20 ml) was vigorously shaken with 0.1M K_2CO_3 solution (100mL) at +10°C for 1 minute. Following acidification and

extraction with diethyl ether the solvent was evaporated to yield the crude product which was fractionated on SiO_2 eluting with CH_2Cl_2-diethyl ether (1:1) and 0.1% acetic acid. Evaporation of the solvent yielded 185 mg (20%) of white crystals, **2b**: mp 95 - 97°C ; IR (KBr) : ν = 3350 (br), 2990 (w), 1780 (s), 1630 (m), 1390 (m), 1160 (m), 1075 (m), 970 (m) cm^{-1}.; MS (EI) : m/z (%) = 217 (1), 199 (1), 167 (11), 133 (100), 87 (6).; HRMS : m/z , calc. for $C_5H_2O_2Cl_3$ (M^+-OH) 198.9120; found 198.9114.
3-chloro-5-(dichloromethyl)-5-methoxy-2-furanone : MS (EI) m/z (%) = 147 (100), 149 (31), 199 (3.2), 201 (3.0), 203 (1), 205 (0.3).

3,4-Dichloro-5-(dichloromethyl)-5-hydroxy-2-furanone 2c Dry chlorine was bubbled through a mixture of 4-cyclo-penten-1,3-dione (200 mg, 2 mmole) in CCl_4 (10 mL) until saturation. The reaction flask was then irradiated with UV-light for approximately 6 hours to yield (310 mg, 1.3 mmole) 2,2,4,5-tetrachloro-4-cyclopentene-1,3-dione (75%). 3,4-dichloro-5-(dichloromethyl)-5-hydroxy-2-furanone **2c** was prepared according to the same sequence that yielded compound **2a** from the chlorinated 4-cyclopentene-1,3-dione. Purification on SiO_2 with CH_2Cl_2-diethyl ether (1:1) and 0.1% acetic acid gave 60mg (18%) of the hydroxyfuranone **2c**.;IR (KBr) : ν = 3360 (br), 1780 (br), 1630 (s), 1380 (m), 930 (m) cm^{-1}.; MS (EI) : m/z (%) = 251 (1), 227 (1), 179 (1), 167 (100), 122 (6), 95 (11), 87 (28).; HRMS : m/z , calc. for $C_5HO_3Cl_3$ (M^+-HCl) 213.8991; found 213.8995.
3,4-dichloro-5-(dichloromethyl)-5-methoxy-2-furanone : MS (EI) m/z (%) = 181 (100), 183 (64), 185 (12), 233 (1.3), 235 (1.6), 237 (0.7), 239 (0.2).

5-(Dichloromethyl)-5-methoxy-2-furanone 2d (1.0 g, 4 mmole) 5,5,5-trichloro-4-oxo-pentanoic acid in H_2SO_4 (10 mL) was heated at 100°C for 45 minutes. The reaction mixture was cooled, diluted with ice-water and extracted with three portions of ethyl acetate. The combined extract was evaporated to dryness to yield a brown oil. Purification on SiO_2 with CH_2Cl_2-ether (1:1) as eluent gave 520 mg (70%) of white crystals of **2e**: mp 92 - 94°C.;IR (KBr) : ν = 1800 (C=O) cm^{-1}.; ^1H NMR($CDCl_3$) δ 6.34 (1H,d,^3J = 5.49 Hz,H), 7.72 (1H,d,^3J = 5.49 Hz,1H).; ^{13}C NMR($CDCl_3$) δ 147.5 (C6), 111.4 (C5), 121.5 (C3), 139.9 (C4), 167.5 (C2).; MS (EI, 70eV) : m/z (%) = 164 (100), 136 (63), 117 (16), 110 (42), 99 (63), 82 (35), 73 (42), 54 (49).; HRMS : m/z , calc. for $C_5H_2O_2Cl_2$ (M^+) 163.9432; found 163.9424. **2e** was methylated by 2% (v/v) H_2SO_4 in methanol for 5h at 70°C. The mixture was neutralized by addition of aqueous $NaHCO_3$ and extracted three times with n-hexane to yield **2d**.

5-Hydroxy-5-(trichloromethyl)-2-furanone 3a A mixture of maleic anhydride (10.3 g, 0.11 mole) and solid sodium trichloroacetate (19.5 g, 0.11 mole) in 1,2-dimethoxyethane (65 mL) was heated under reflux for 3

hours after which the solvent was removed. The solid was then extracted several times with ether and washed with aqueous sodium bicarbonate and water. Evaporation of the ether left a black solid which upon recrystallisation from toluene and cyclohexane gave 1.4g (5%) of **3a**: mp 128 - 129°C (lit.[13] mp. 137 - 138°C).; IR (KBr): ν = 3250 (br), 2860 (w), 1770 (s), 1450 (m), 1250 (m), 1210 (m), 1075 (m), 950 (m) cm^{-1}.; MS (EI) : m/z = 217 (1), 199 (2), 117 (3), 110 (2), 99 (100), 89 (8), 82 (4), 71 (6).; HRMS : m/z , calc. for $C_5H_2O_2Cl_3$ (M^+-OH) 198.9120; found 198.9065.

5-methoxy-5-(trichloromethyl)-2-furanone : MS (EI) m/z = 113 (100), 199 (4.1), 201 (4.0), 203 (1.6), 205 (0.4)

3-Chloro-5-hydroxy-5-(trichloromethyl)-2-furanone 3b To a solution of **3a** (200 mg, 0.9 mmole) in CH_2Cl_2 (10 mL) was added $AlCl_3$ (20 mg). Chlorine was bubbled through the resulting mixture. After approximately 3 hours the reaction mixture was evaporated to yield 195mg (72%) of yellow oil **3d**.; MS (EI) : m/z (%) = 269 (1), 233 (2), 169 (3), 149 (2), 133 (100), 105 (16).; HRMS : m/z , calc. for $C_5HO_2Cl_4$ (M^+-(H_2O+Cl)) 232.8731; found 232.8742.

To the chlorination product **3d** dissolved in diethyl ether (15 mL) was added droppwise over a period of 2 hours triethylamine (70 mg, 0.7 mmole) dissolved in diethylether (10 mL). After 1 hour the solution was washed with 0.5M HCl, dried, filtered and evaporated. Purification on SiO_2 with CH_2Cl_2-diethyl ether (1:1) and 0.1% acetic acid as eluent gave 104mg (43% total yield) of **3b**.; IR (KBr) : ν = 3300 (br), 1790 (br), 1635 (s), 1380 (m), 1260 (w), 1170 (m), 1000 (s), 900 (w) cm^{-1}.; MS (EI) : m/z (%) = 251 (3), 233 (2), 217 (1), 199 (1), 151 (4), 133 (100), 117 (4), 105 (4).; HRMS : m/z , calc. for $C_5HO_2Cl_4$ (M^+-OH) 232.8731; found 232.8768.

3-chloro-5-methoxy-5-(trichloromethyl)-2-furanone : MS (EI) m/z (%) = 147 (100), 149 (27), 229 (3.7), 231 (3.6), 233 (1.1), 235 (1.0), 237 (0.5), 239 (0.2).

3,4-Dichloro-5-hydroxy-5-(trichloromethyl)-2-furanone 3c (Z)-2,3-dichlorobutene-dioic acid (**ox-MCA**) was obtained by oxidation of commercially available mucochloric acid (**MCA**) with fuming nitric acid at 70°C. After 24h. the mixture was cooled, diluted with ice-water and extracted with diethyl ether. The combined extract was washed with 0.01M HCl and evaporated to dryness. Recrystallisation from CH_2Cl_2 gave **ox-MCA** (50%): mp 115- 116°C.; IR (KBr) : ν = 3150 (br)(COOH), 1710 (br)(C=O) cm^{-1}.; ^1H NMR ($CDCl_3$ + acetone-d_6) δ 8.3 (1H,br.s,2xCOOH).; ^{13}C NMR ($CDCl_3$ + acetone- d_6) δ 162.1 (C5 and C2), 130.6 (C4 and C3).; MS (EI) : m/z (%) = 184 (1), 166 (10), 140 (13), 122 (12), 105 (31), 87 (56), 60 (59), 44 (100).; HRMS : m/z , calc. for $C_4O_3Cl_2$ (M^+-H_2O) 165.9225; found 165.9240.

2,3-Dichloromaleic anhydride was prepared from **ox-MCA** by refluxing with an excess of acetic anhydride

for 3 hours. After evaporation the crystals were washed with diethyl ether to yield pure 2,3-dichlormaleic anhydride (66% total yield from MCA). Preparing of **3c** was achieved using the same procedure as that employed to produce 5-hydroxy-5-(trichloromethyl)-2-furanone **3a** except that 2,3-dichloromaleic anhydride was used instead of maleic anhydride. Purification on SiO_2 with CH_2Cl_2-diethyl ether (1:1) and 0.1% acetic acid as eluent gave the compound **3c** as a yellow oil. (16% total yield from MCA after purification).; IR (KBr) : ν = 3420 (m), 2970 (w), 1810 (s), 1640 (s), 1380 (m), 1200 (s), 1120 (s), 1010 (s), 970 (s), 930 (s) cm^{-1}.; MS (EI) : m/z (%) = 267 (1), 234 (14), 232 (8), 213 (16), 167 (100), 142 (23), 122 (15), 87 (73).; HRMS : m/z , calc. for $C_5O_2Cl_4$ (M^+-(OH+Cl)) 231.8652; found 231.8649.

3,4-dichloromethyl-5-methoxy-5-(trichloromethyl)-2-furanone : MS (EI) m/z (%) = 181 (100), 183 (66), 185 (12), 263 (0.3), 265 (0.4), 267 (1), 269 (1.6), 271 (1), 273 (0.4).

5,5,5-Trichloro-4-oxo-pentanoic acid **D** Succinic anhydride 0.10mole (9.0g) and solid sodium trichloroacetate 0.10mole (18.0g) in 50mL of 1,2-dimethoxyethane was heated under reflux over a period of 3 hours. The mixture was poured into 100mL of water after which the aqueous solution was extracted three times with diethyl ether. The combined extracts were dried and evaporated to yield a brown solid. Recrystallisation from ligroin gave 5g (23%) of white crystals of **A** : mp 73 - 75°C (lit.[13] 78 - 79.5°C).; NMR data in Tables III and IV.; IR (KBr) : ν = 3050 (br), 2950 (br), 1770 (m), 1720 (s) cm^{-1}.; MS (EI) : m/z (%) = 201 (2), 166 (2), 119 (8), 110 (6), 101 (100), 82 (6), 73 (25), 55 (40).; HRMS : m/z , calc. for $C_5H_4O_2Cl_3$ (M^+-OH) 200.9277; found 200.9266.

ACKNOWLEDGEMENTS

This work was supported by a research grant from the Maj and Tor Nessling Foundation. We are obliged to Mrs Päivi Pennanen for the ^1H NMR and ^{13}C NMR spectra. We also like to thank Mr. Markku Reunanen for performing the GC/MS analyses and Dr. Rainer Sjöholm and Dr. Osmo Hormi for valuable discussion.

LITERATURE CITED

1. Holmbom, B. R.; Voss, R. H.; Mortimer, R. D.; Wong A. *Tappi* **1981**, *64*, 172.
2. Hemming, J.; Holmbom, B.; Reunanen, M.; Kronberg, L. *Chemosphere* **1986**, *15*, 549.
3. Ishiguro, Y.; Santodonato, J.; Neal, M. W. *Environ.Mol.Mutagen* **1988**, *11*, 225.
4. Kronberg, L.; Franzén, R. *Accepted for publication in Environ.Sci.Technol.*
5. Maron, D. M.; Ames, B. N. *Mutat.Res.* **1983**, *113*, 173.
6. Kronberg, L.; Vartiainen, T. *Mutat.Res.* **1988**, *206*, 177.
7. Meier, J. R. *Mutat.Res.* **1988**, *196*, 211.
8. Horth, H.; Fielding, M.; Gibson, T.; James, H. A.; Ross, H. (**1989**) *Identification of Mutagens in Drinking Water* (EC 9105 SLD). PRD 2038-M. Water Research Centre, Medmenham, Bucks, SL7 2HD, Great Britain.
9. Meier, J. R.; DeAngelo, A. B.; Daniel, F. B.; Schenck, K. M.; Doerger, J. U.; Chang, L. W.; Kopfler, F. C.; Robinson, M.; Ringhand, H. (**1990**) Genotoxic and carcinogenic properties of chlorinated furanones - important by-products of water chlorination. In *Genetic Toxicology of Complex Mixtures* (Waters, M. D.; Lewtas, J.; Moore, M. M.; Newnow, S. J., Eds.) p185, Plenum Publishing Corp., New York.
10. Strömberg, L. M.; de Sousa, F.; Ljungquist, P.; McKague, B.; Kringstad, K. P. *Environ.Sci.Technol.* **1987**, *21*, 754.
11. Durand, A-P. Y.; Brattan, D.; Brown, R. G. *Chemosphere* **1992**, *25*, 783.
12. Zepp, R. G.; Lee Wolfe, N.; Gordon, J. A.; Fincher, R. C. *J. Agric Food Chem.* **1976**, *24*, 727.
13. Winston, A.; Bederka, J. P. M.; Isner, W. G.; Juliano, P. C.; Sharp, J. C. *J.Org.Chem.* **1965**, *30*, 2784.
14. Loots, M. J.; Weingarten, L. R.; Levin, R. H. *J.Am.Chem.Soc.* **1976**, *98*, 4571.
15. Tori, K.; Ishii, H.; Wolkowski, Z. W.; Chachaty, C.; Sangare, M.; Piriou, F.; Lukacs, G. *Tetrahedron Lett.* **1973**, 1077.
16. LaLonde, R. T.; Peräkylä, H.; Hayes, M. P. *J.Org.Chem.* **1990**, *55*, 2847.
17. Savitsky, G. B.; Ellis, P. D.; Namikawa, K.; Maciel, G. E. *J Chem.Phys* **1968**, *49*, 2395.
18. Savitsky, G. B.; Namikawa, K. *J.Phys.Chem.* **1963**, *67*, 2754.