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RING-CHAIN VALENCE TAUTOMERISM IN CHLORINATED 2H-PYRAN SYSTEMS

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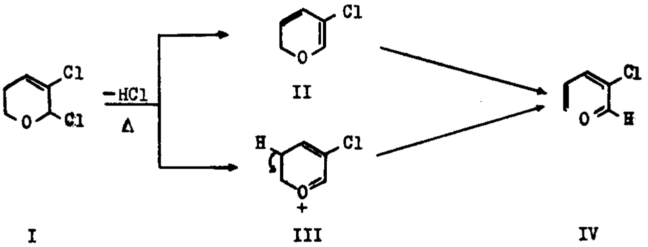
The quinoline-promoted dehydrochlorination of 2.3-dichloro-5.6-dihydro-2H-pyran (I) into 2-chloro-penta-2.4-dienal (IV) has previously been described as involving the formation of 5-chloro-2H-pyran (II) as a reaction intermediate[1]. The possibility of another path, proceeding *via* an oxonium ion, III, has been pointed out by Anderson, Lindsay, and Reese, in an independent study[2].



In order to ascertain whether the reaction follows the I → II → IV, or the I → III → IV path, a study of the vapor-phase chromatography of products, resulting from the thermal dehydrochlorination of I, was undertaken. It was thought, that in contrast to the ionic form (III), which could not give a signal in the vapor-phase chromatograph (v.p.c.), the neutral species, II, should do so, provided it could survive at the experimental temperature. Indeed, when samples of I, heated at 100-110° for the period of 5 to 75 min., were analysed by v.p.c.[3], the presence of a volatile thermolabile entity (presumably, II) could be detected along with I and IV (see, Fig.1).

Fig. 1

Vapor-Phase Chromatogram of Thermal Dehydrochlorination of I at 107°

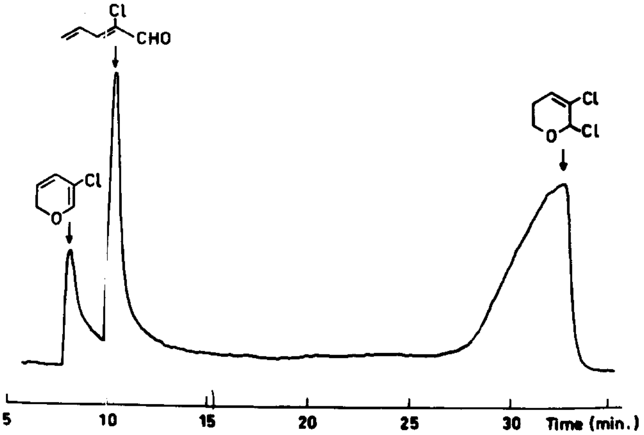


TABLE 1

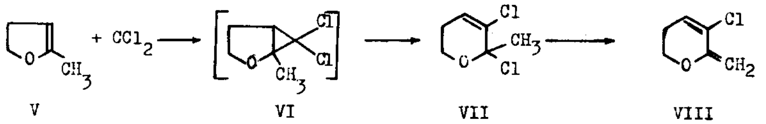
V.P.C. Determination of Time-Composition Variations in the Thermal Dehydrochlorination of I.

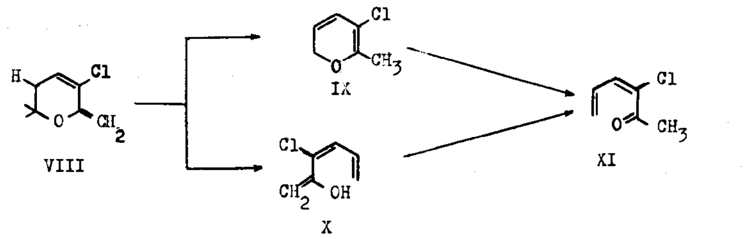
Reaction Temp. °C	Reaction Time min.	I %	II %	IV %
107	0	100	0	0
107	8	76	9	14
107	25	68	12	20
107	35	62	15	23
112	30	68	9	23
112	40	50	5	45
112	75	3	-	95

From Table 1 it can be seen that while the amounts of II and IV were increased initially, at the expense of I, the II/IV ratio decreases with the elapse of time, at the end of which IV become predominant. In an experiment aimed at isolating II, by way of triethylamine-promoted dehydrochlorination of I, at 60°, followed by fractional distillation at reduced pressure, the desired product (colorless liquid) was obtained in an impure state, showing characteristic bands at 240mμ in the ultraviolet spectrum.

Next, we studied the preparation and dehydrochlorination of 2-methyl-2.3-dichloro-5.6-dihydropyran (VII), because it was assumed, that the resulting product, 6-methyl-5-chloro-2H-pyran (IX), would be more stable than II, requiring lower temperatures for its formation.

When dichlorocarbene, formed by the interaction of sodium methoxide with ethyl trichloroacetate, was allowed to react with 5-methyl-2.3-dihydro-furan (V) in hexane at 0°, a 66% yield of VII (b.p. 35-40°/0.05 mm, analysed as $C_6H_8Cl_2O$, λ_{max}^{KBr} 1667 cm^{-1}) was obtained. The initial adduct, VI, could not be isolated, since it underwent isomerization into VII, as soon as formed. The dehydrochlorination of VII was effected by means of quinoline at room temperature, providing a 54% yield of a C_6H_7ClO product (b.p. 17° (0.1 mm), n_D^{20} 1.5315) isomeric with the expected 2H-pyran derivative, IX. This is shown to be 2-methylene-3-chloro-5.6-dihydropyran (VIII). The structure of the product follows from (i) the absence of nmr signals at 1.6 ppm, typical

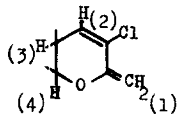


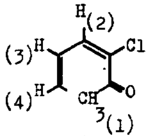


for protons of a methyl group, ii) its absorption at 231mμ (log ε 3.86), 251mμ (log ε 3.73)[4] (ethanol), iii) its typical bands at 3060(m) and 900(m)($CH_2 = C\langle$), 1650(s), 1618(vs) (double-bond), 1100(vs) cm^{-1} (enol-ether) (KBr) in the infrared spectrum[5].

TABLE 2

NMR Signals of VIII and XI





	Chemical Shifts (p.p.m.)	Relative intensities	Splitting	Chemical Shifts (p.p.m.)	Relative intensities	Splitting
$H_{(1)}$	4.62 4.81	2	multiplets	2.48	3	singlet
$H_{(2)}$	6.17	1	multiplet	7.1	(1	multiplet
$H_{(3)}$	2.40	2	multiplet	7.1	1	"
$H_{(4)}$	4.00	2	triplet	5.8	2	multiplet

An examination of the nmr spectrum of VIII (see, Table 2), reveals that the two terminal vinylic protons, $H_{(1)}$, give separate absorptions, at 4.62 and 4.81 ppm[6], probably due to deshielding arising from the neighboring oxygen and chlorine atoms. The numerical values of chemical shifts and splitting of the hydrogens, H_2, H_3 and H_4, are essentially the same in VIII as in I and its derivatives.

Heating of VIII in vacuum at 120° afforded a 90% yield of a C_6H_7ClO product (b.p.15°/0.1 mm, n_D^{20}1.5336, m.p.2-4°), isomeric with the expected 5-methyl-3-chloro-2H-pyran, IX, shown to be 3-chloro-hexa-3.5-diene 2-one, XI. The structural assignment follows from i) the infrared spectrum (KBr) showing bands (cm^{-1}) at 1698 (conjugated carbonyl), 1639 and 1600 (double-bond), 1379 (methyl) ii) the ultra-violet spectrum displaying bands at 226mμ, 230mμ and 274mμ, iii) the appearance of an absorption at 2.48 ppm (singlet) in the nmr spectrum, typical for hydrogens in a methyl ketone group, iv) the formation of a 2.4-dinitrophenylhydrazone, m.p.181-182°, λmax 242mμ (log ε 4.17), 270mμ (log ε 4.14), 298mμ (log ε 4.05), analysed as $C_{12}H_{11}N_4ClO_4$.

The nmr spectrum of XI (see, Table 2) contains also double triplet at 5.8 ppm (terminal vinylic protons, H_4) and a multiplet at 7.1 ppm, assigned to H_2 and H_3, almost identical with the signals of the dienic portion in IV[7].

Unlike I, which on exposure to atmospheric moisture yields bis [3-chloro-2(5.6-dihydro-2$\underline{H}$-pyranyl)] ether, no corresponding ether could be obtained from VII on comparable conditions, due to steric effects.

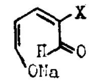
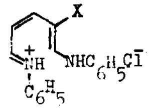
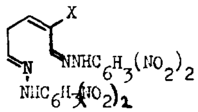
On the basis of the evidence now at hand it is not known whether the formation of XI originates from the 2H-pyran form (IX), involving 1.5-proton shift, or arises from an enol form, X, resulting from a 1.3-proton shift. The desired intermediate, IX, could not be isolated from the reaction mixture, presumably because it is much less stable than the open-chain valence-tautomer, XI. However, the opposite was observed in case of 4.6-dimethyl-hepta-3.5-dien-2-one, which spontaneously isomerizes into the ring valence-tautomer, 2.2.4.6-tetramethyl-2$\underline{H}$-pyran[4]. In view of this, it is possible that the electron density at oxygen-carbon-2 bond in α-pyrans, determines the stability of the cyclic structure. Methyl substituents at C-2 seem to stabilize the oxygen-carbon-2 bond through inductive effects. This implies that the electron density on the oxygen in II and in IX is more electron deficient than the oxygen in the 2.2-dimethyl-2H-pyran, causing the bond energies of the cyclic systems in II and IX to be higher than in the open-chain valence-tautomer.

In view of the foregoing, furan XII itself seemed to be an appropriate model for the direct production of the 2H-pyran system by way of carbene addition, following the route XII → XIII → XIV. The reaction product, resulting from the addition of dichlorocarbene to XII in hexane, at 0°, could not be isolated in a pure form, due to its tendency to decompose on distillation in high vacuum. Its structure was inferred from the presence of a peak at 285mμ (in hexane), but none in the 240-280mμ region of the ultraviolet spectrum[8], and from product studies, indicating the open-chain valence-tautomer structure, 4.5-dichloropent-2.4-dienal, XV, isomeric with the expected 2H-pyran structure, XIV. The structural assignment follows from i) the isolation of a brown 2.4-dinitro-phenylhydrazone XVII, m.p.140° (dec.) analysed as a $C_{11}H_8Cl_2N_4O_4$ product, obtained by way of direct addition of the DNPH reagent, at room temperature, to a purified sample of the reaction product. It had absorption bands at 239mμ, 366mμ, and 380mμ in the ultraviolet spectrum. ii) the presence of a reactive chlorine atom, positioned at the terminal dienic carbon (C-5 in XV), displaying enhanced reactivity in nucleophilic displacements[9]. Its hydrolysis could smoothly be effected by means of cold dilute aqueous sodium hydroxide to yield a stable sodium salt of 5-hydroxy-2-chloropent-2.4-dienal, XVI, obtained as a yellow powder, showing the expected absorption bands in the ultraviolet spectrum (see, Table 3).

It was further identified by its violet-red dianilide hydrochloride (XVIII), m.p.124° (reported[10] m.p.119°) and characterized by its deep-red bis-dinitrophenylhydrazone XIX, m.p.210°, analysed as a $C_{17}H_{13}ClN_8O_8$ compound, the ultraviolet absorption spectrum of which showed similarity with that of the parent compound, glutacone dialdehyde bis-dinitrophenylhydrazone (see, Table 3).

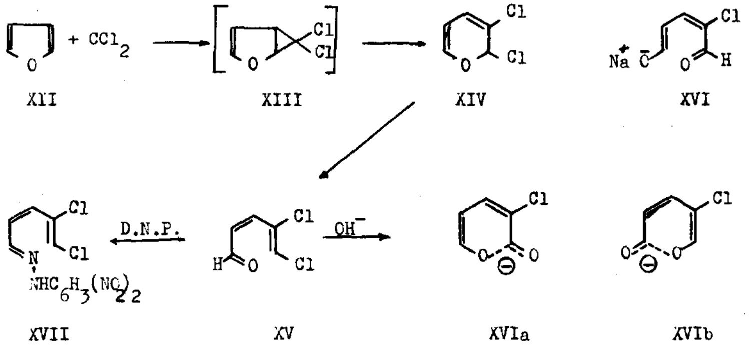
Table 3

Ultraviolet Absorption Spectra of XVI, XVIII and XIX and of their Parent Compounds

Compound	X = H		X = Cl		
	λmax mμ	log ε	λmax	log ε	
	362.5	$(4.7)^a$	368	(4.5)	
	409	4.53^b	405	4.35^b	XVIII
	244 363	4.33^c 4.43	268 366–372	- -	XIX

[a] Determined in ethanol. The compound was prepared according to P.Baumgarten, Ber., 66, 1805 (1933). [b] Determined in ethanol (C.0.00014 molar). [c] In chloroform.

In contrast to the benz-analogue[11], XIV appears to be much less stable relative to the open-chain valence-tautomer, XV, and this explains why it was not possible to obtain the bis [3-chloro-2(2*H*-pyranyl] ether on exposure to atmospheric moisture[12].



The stability of the anion $\overline{XVI}$, may be derived from structures, such as XVIa and XVIb, with 6π electrons, in which the trigonal hybridization of the carbonyl carbon is retained, thus conferring aromatic stabilization on the system.

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1) S.Sarel and J.Rivlin, Israel J. Chem., 1, 221 (1963)

2) J.C.Anderson, D.G.Lindsay and C.B.Reese, Tetrahedron, 20, 2091 (1964).

3) The vapor-phase chromatography was carried on a F and M model 500 instrument with a 3m long and 4.5 mm in diameter column, filled with chromorb W coated with 15% silicon rubber, using helium as eluent gas.

4) A.Hinnen and J.Dreux, Bull.Soc.Chim.France, 1492 (1964) record for 2.2.6-trimethyl-4-methylene-2.3-dihydropyran λmax 253 mμ (log ε 4.18) in methanol.

5) Ref.4 gives for exocyclic methylene in 2.2.6-trimethyl-4-methylene-2.3-dihydropyran λmax 3070 and 890 cm^{-1}, and 1644 cm^{-1} for C=C.

6) Ref.4 record chemical shifts of 4.34 and 4.54 p.p.m. for the exocyclic methylene protons at 4.

7) The central vinylic protons in IV give absorption at 7.1 p.p.m. and terminal vinylic protons appear at 5.96, J.Rivlin, Dissertation, 1964. See also ref. 2.

8) Although the absorption region in the uv-spectrum for XIV is not known, its absorption band is not expected to appear at higher wavelengths than the open-chain dienal system.

9) See, A.Roedig and G.Märkl, Ann., 659, 1 (1962). A.Roedig, G.Märkl, and V.Schall, Chem.Ber., 95, 2844 (1962). Z.Arnold, Coll.Czechosl.Chem.Comm., 2378 (1959).

10) P.Baumgarten, Ber., 58, 2018 (1925)

11) W.E.Parham, J.Org.Chem., 28, 577 (1963)

12) Compare, ref.2, and J.Rivlin, Dissertation, 1964.