trans-β-Chlorovinyl Ketones and *trans*-(β-Acylvinyl)trimethylammonium Chlorides[1,2]

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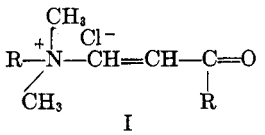
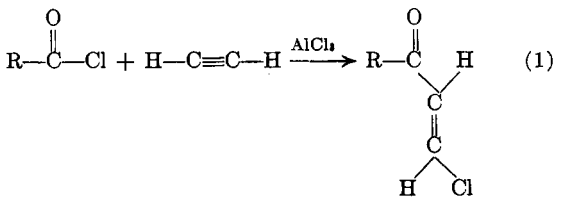
When acid chlorides were added to acetylene in the presence of aluminum chloride, *trans*-β-chlorovinyl ketones were formed as shown by n.m.r. spectra. When these ketones were treated with trimethylamine in an inert solvent, a series of β-acylvinyltrimethylammonium chlorides were formed which gave complete retention of the *trans* configuration. The ultraviolet and infrared spectra of these systems were examined and indicated the C=C–C=O system to be most likely in the transoid conformation.

In connection with the synthesis of compounds to be used as drugs,[5] it seemed of interest to investigate the synthesis of type I compounds.

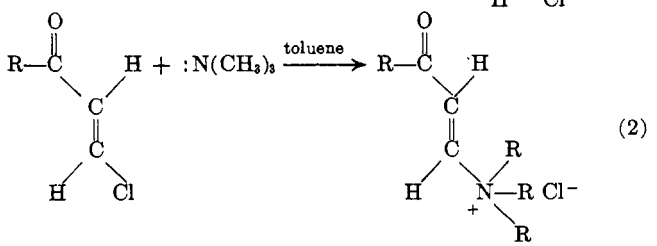


I

A possible preparative reaction scheme is outlined in eq. 1 and 2.



(1)



(2)

The acylation of unsaturated compounds is well-known, but no data have been reported on the geometry of the acyl and the chloro groups about the double bond where acetylene was used. Kroeger, Sowa, and Nieuwland[6] reported a number of condensations of acid chlorides with alkylacetylenes which led to two (probably *cis* and *trans*) isomers in most cases. Kochetkov and co-workers[7,8] have prepared many β-chlorovinyl ketones by adding acid chlorides to acetylene. To determine the *cis–trans* structure, Kochetkov reported[9] recently that methyl β-chlorovinyl ketone (I) was oxidized with sodium hypochlorite to the known *trans*-β-chloroacrylic acid. The 50% yield certainly gave an indication that one compound in the series was probably *trans*, but the method may have destroyed the *cis* isomer (if it was present) through isomerization, elimination, preferential oxidation, etc.

The addition of acid chlorides to vinyl chloride proceeds first by addition followed by elimination with the intermediate formation of β,β-dichloroethyl ketones.[10,11]

It was found that the β-chlorovinyl ketones prepared from vinyl chloride were very unstable, decomposing in short periods to hydrogen chloride and black tar. It has been shown that the instability could be avoided through the use of calcium carbonate or sodium bicarbonate.[10] However, when acetylene was used the products were much more stable and could be stored for several months at various temperatures with only a slight darkening in color. A list of the β-chlorovinyl ketones prepared is given in Table I.

In general it was found that the addition of acid chlorides to acetylene led to fairly good yields (60–70%) of stable β-chlorovinyl ketones. Benzoyl chloride, however, led to only 30.8% of VII while acetyl chloride gave a 92.7% yield of methyl β-chlorovinyl ketone (I). Pivaloyl chloride led to a mixture of at least six different products as indicated by gas-liquid chromatography (g.l.c.). Therefore, compound VI was prepared in a manner previously described by Kochetkov[12] and co-workers.

All of these colorless, vessicant, lachrymatory ketones exhibited the characteristic AB pattern in their n.m.r. spectra resulting from spin–spin interactions between the *trans* nonequivalent protons of the double bond. In the case of compound VII, the aromatic protons interfered with the protons on the double bond so that an interpretation of its spectrum was not possible. The J_{AB} values are given in Tables I and III. For absolute certainty, the constants of the *cis* compounds should be compared.[13]

Thus the addition of acid chlorides to acetylene in the presence of aluminum chloride after distillation resulted in pure *trans*-β-chlorovinyl ketones. When vinyl chloride was condensed with isobutyryl chloride, a product was formed with correct analysis, but its n.m.r. spectrum exhibited a pattern which could be considered a mixture of both the *cis* and the *trans* protons. This possibly could indicate that the second step, elimination, has led to both isomers. In all other

(1) Taken in part from the dissertation of A. E. Pohland which was submitted in partial fulfillment of the requirements of the doctorate degree, 1963.

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(4) Boettcher Foundation Fellow, 1962-1963.

(5) D. Nachmansohn and I. Wilson, "Molecular Biology," Academic Press, New York, N. Y. 1960, p. 168.

(6) J. W. Kroeger, F. J. Sowa, and J. A. Nieuwland, *J. Org. Chem.*, **1**, 163 (1936), and references therein.

(7) A. N. Nesmeyanov, N. K. Kochetkov, and M. I. Rubinskaya, *Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 350 (1950); *Chem. Abstr.*, **45**, 1585 (1951).

(8) N. K. Kochetkov, *Dokl. Akad. Nauk SSSR*, **84**, 289 (1952); *Chem. Abstr.*, **47**, 3309 (1953).

(9) N. K. Kochetkov, B. P. Gottikh, and M. Ya Karpeiskii, *Khim. Nauka i Promy.*, **3**, 834 (1958); *Chem. Abstr.*, **53**, 10021 (1959).

(10) J. R. Catch, *et al.*, *J. Chem. Soc.*, 278 (1948).

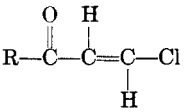
(11) V. J. Klimko, V. A. Mikhalev, and A. P. Sholdinov, *J. Gen. Chem. USSR*, **27** 415 (1957).

(12) N. K. Kochetkov, *et al.*, *ibid.*, **28**, 3053 (1958).

(13) W. E. Truce and B. Groten, *J. Org. Chem.*, **27**, 128 (1962).

TABLE I

β-CHLOROVINYL KETONES



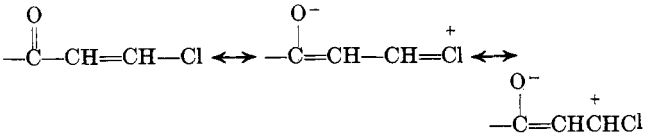
R	Compound	B.p. (mm.), °C.	Yield, %	Found n^tD (temp., °C.)	Reported at 20°	J_{AB}, c.p.s.
CH_3	I	76 (98)	92.7	1.4678 (20)	1.4675[a]	13.0
C_2H_5	II	56 (22)	69.0	1.4628 (26.5)	1.4596[a]	14.0
n-C_3H_7	III	61–64 (18)	83.2	1.4641 (20)	1.4640[a]	14.0
i-C_3H_7	IV	69–69.5 (34)	67.6	1.4610 (20)	1.4585[a]	13.1
i-C_4H_9	V	84–80 (25)	78.4	1.4579 (28)	1.4590[a]	14.0
t-C_4H_9[d]	VI	72 (25)	71.1	1.4573 (24)	1.4593[b]	13.0
C_6H_5	VII	97–102 (7)	30.8	1.5836 (25)	1.5860[c]	

[a] See ref. 8. [b] See ref. 12. [c] See ref. 28. [d] Prepared by different method.

cases where acetylene was used, the *cis* isomer was not detectable to the limit of the n.m.r. instrument (less than 5%) and was not separable by g.l.c.

The conformation of the β-chlorovinyl ketone system was examined through the ultraviolet and infrared spectra of these compounds and spectra of similar systems.

Julia[14] found that methyl vinyl ketone itself absorbed at 210 mμ (ε 7000), whereas methyl β-chlorovinyl ketone absorbed at 228 mμ (ε 10,000). Thus substitution of a chlorine atom had resulted in a bathochromic shift of 18 mμ and a slight hyperchromic effect. Sanchez[15] found through the substitution of a second chlorine atom in the β-position that a further bathochromic shift of 13 mμ resulted. In the present study, it was found that the β-chlorovinyl ketones absorbed consistently at longer wave lengths (*ca.* 16 mμ) than their nonhalogenated analogs. A marked hyperchromic effect also was noted. These effects were undoubtedly due to an extension of the conjugated system by the chlorine atom through such dipolar structures as the following.



Although no data were found regarding the difference in energy of the cisoid and transoid forms, it might be suggested that the energy difference would be about the same as the difference in energy between cisoid and transoid butadiene, *ca.* 2.5 kcal./mole or somewhat higher for the unsubstituted α,β-unsaturated ketone. However, in the β-chlorovinyl ketones this energy difference may be much larger due to resonance structures. In such systems the transoid conformation generally has been considered to be the most stable.[16]

An examination of Dreiding models revealed that in all cases, except the *t*-butyl and phenyl β-chlorovinyl ketone, the transoid conformation was planar and free of steric strain. However, in the *t*-butyl and phenyl analogs there appeared to be some steric interference. The latter two compounds, therefore, conceivably could lie in the cisoid or some nonplanar conformation.

Turner and Voitle[17] assumed and Mecke and Noack[1] postulated that α,β-unsaturated carbonyl systems must lie either in the transoid or cisoid conformation since only in these instances is there maximum conjugation or resonance energy. However, Braude and Timmons[18] have pointed out that this need not be the case and that, indeed, when the transoid conformation is sterically unfavored, nonplanar conformations may result rather than a complete inversion to the cisoid conformation. These authors developed the equation $\epsilon/\epsilon_0 = \cos^2(\theta_1 - \theta_2)$ to obtain the value of the interplanar angle from spectral data in sterically hindered compounds, and this equation was revised recently by Forbes and Mueller[19] to account more rigorously for the spectra of unsymmetrical molecules. In these equations ϵ_0 is the molar absorption coefficient of the planar model, while ϵ is that of the nonplanar molecule. θ_1 represents the interplanar angle in the ground state between the plane of the carbonyl group and that of the double bond, whereas θ_2 represents the interplanar angle in the excited state (usually considered to be zero).

On examination of the ultraviolet data of the alkyl β-chlorovinyl ketones (see Table II), it was apparent that all of the these open-chained ketones absorbed maximally in the same wave-length range (229–232.5 mμ) and with approximately the same intensity (ε 14,600–11,200). This could indicate that all are of the same conformation.[14] Since, in methyl β-chlorovinyl ketone, both the cisoid and transoid forms are assumed to be unstrained and planar, one would predict that in this compound the transoid conformation predominates to the virtual exclusion of the cisoid form. If this is so, then the remainder of this series are probably transoid. However, as was noted before, in *t*-butyl β-chlorovinyl ketone the planar transoid conformation is sterically unfavored. Thus, one would expect this compound to be slightly nonplanar or cisoid. This may be the reason that a decrease in the intensity of the K-band of this compound, when compared with the intensity of the K-band of I, gave no accompanying hypsochromic effect. This phenomenon previously had been ascribed to electronic transitions between nonplanar ground states and near-planar excited states. However, even with the *t*-butyl derivative the effect was quite small and, if one uses Braude's equation for

(14) M. Julia, *Ann. chim.* (Paris), [12] **5**, 595 (1950).

(15) R. Sanchez, Ph.D. dissertation, Kansas State University, 1962, and references therein.

(16) R. Mecke and K. Noack, *Ber.*, **93**, 210 (1960); see also ref. 22.

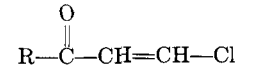
(17) R. B. Turner and D. M. Voitle, *J. Am. Chem. Soc.*, **73**, 1403 (1951).

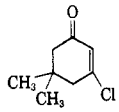
(18) E. A. Braude and C. J. Timmons, *J. Chem. Soc.*, 3766 (1955).

(19) W. F. Forbes and W. A. Mueller, *Can. J. Chem.*, **33**, 1340 (1956).

TABLE II

SPECTRAL DATA ON β-CHLOROVINYL KETONES



R	Compound	Infrared spectra bands, cm.$^{-1}$ $\nu_{C=O}$	$\nu_{C=C}$	ν_{C-H}	ν_{C-Cl}	$\Delta_{C=O-C=C}$	Ultraviolet spectral data: λ_{max}, mμ ($\epsilon \times 10^4$)	Lit. λ_{max}, mμ ($\epsilon \times 10^4$)
CH_3–	I	1678	1587	946.1	841.9	91	229 (1.46)	228 (1.00)
C_2H_5–	II	1686	1587	941.6	845.3	99	229 (1.32)	229 (1.26)
n-C_3H_7–	III	1678	1582	941.6	827	96	230 (1.24)	230
i-C_3H_7–	IV	1698	1592	940.7	846	106	232 (1.12)	
i-C_4H_9–	V	1689	1582	940.7	854.7	107	231.5 (1.16)	
t-C_4H_9–	VI	1686	1582	939.8	831.9	104	232.5 (1.22)	
C_6H_5–	VII	1664	1582	935.5		82	203 (1.04) 260 (1.65)	
	VIII (fixed transoid)	1681	1616		843.2	65	238 (1.35)	

calculation of the interplanar angle between the plane of the carbonyl group and the plane of the double bond, one arrives at an angle of 23° 55′. In view of the high intensity of the absorption maximum, one would not expect these compounds to be very highly nonplanar. We are still working on the *cis* compounds.

The infrared spectral data for the β-chlorovinyl ketones were collected in Table II and were in complete agreement with the proposed structures.

Examination of the infrared data indicated also a high degree of planarity, the carbonyl and double bond absorptions being significantly displaced to longer wave lengths. A split carbonyl peak has been found in the infrared spectrum of methyl vinyl ketone itself at 1701 and 1683 cm.$^{-1}$ corresponding possibly to the cisoid and transoid conformations, respectively.[20] All the β-chlorovinyl ketones exhibited only one carbonyl absorption band. In all cases, both the carbonyl and the double bond absorption were of about the same intensity, the double bond absorption band being slightly more intense than the carbonyl band. In addition, the carbonyl and double bond absorption bands were separated by *ca.* 99 cm.$^{-1}$. These data according to some hypotheses[22] would indicate that the compounds were in the cisoid form, since in the cisoid form the intensities of $\nu_{C=O}$ and $\nu_{C=C}$ are normally comparable and the difference between $\nu_{C=O}$ and $\nu_{C=C}$ is usually[21] greater than 75 cm.$^{-1}$. Erskine and Waight[22] concluded that the ratio of the integrated band intensities of the carbonyl and double bond stretching vibrations lies between 0.6 and 3.5 for cisoid and is greater than 6 for transoid ketones, but these authors also indicated that strongly electronegative substituents on the double bond may alter these values considerably.

This appeared to be the case in the β-chlorovinyl ketones. The above rules did not seem to apply because of the β-chlorine substituent whose effect appeared to be one of increasing the intensity of the double bond absorption band and displacement of this band to longer wave lengths without greatly affecting the carbonyl absorption band (normally[21] found at 1675 cm.$^{-1}$). The double bond absorption band of α,β-unsaturated ketones usually has been found in the 1650–1600-cm.$^{-1}$ region. In all the β-chlorovinyl ketones, this band was shifted to considerably longer wave lengths. Thus infrared data support transoid conformations.

Quaternary Salts.—Several reviews have been written on the replacement reaction of β-chlorovinyl ketones[23-25] and there are also reviews on their use as intermediates in the synthesis of a large variety of heterocyclic compounds.[26,27] However, no work has been reported on the stereochemistry of this replacement reaction.

β-Chlorovinyl ketones have been treated with tertiary amines,[28,29] but, with the exception of (β-acetyl- and β-benzoylvinyl)trimethylammonium chloride,[28] no β-acylvinyltrimethylammonium salts have been found in the literature.

When the β-chlorovinyl ketones were treated with trimethylamine in toluene, an immediate, exothermic reaction followed in all cases giving nearly a quantitative yield of the quaternary salt (eq. 2). These salts were white, water-soluble solids with variable melting point ranges, dependent presumably on the rate of heating; the solids appeared to decompose before the melting point was reached. On standing, unless carefully purified, they slowly turned light brown. The quaternary salts had correct analyses (see Table III).

The picrate of each salt was prepared because of the wide melting point ranges displayed by these quaternary salts. These light yellow picrates, after recrystallization from 95% ethanol, exhibited very sharp melting points (Table III).

Bromine was added to these quaternary salts in chloroform. In every case the bromine color rapidly disappeared, and the quaternary salt, originally only slightly soluble in chloroform, completely dissolved. In the case of the isopropyl derivative, a white solid

(20) K. Noack and R. N. Jones, *Can. J. Chem.*, **39**, 2225 (1961).

(21) K. Nakanishi, "Infrared Absorption Spectroscopy," Holden-Day, Inc., San Francisco, Calif., 1962.

(22) R. L. Erskine and E. S. Waight, *J. Chem. Soc.*, 3425 (1960).

(23) N. K. Kochetkov, *Prakt. Chem.*, **12**, 336 (1961).

(24) N. K. Kochetkov, L. I. Kudryaskov, and B. P. Gottikh, *Tetrahedron*, **12**, 63 (1961).

(25) N. Sugiyama and G. Inoui, *Yuki Gosei Kagaku Kyokai Shi*, **19**, 373 (1961); *Chem. Abstr.*, **55**, 17,484 (1961).

(26) A. N. Nesmeyanov and N. K. Kochetkov, *Uch. Zap. Mosk. Gos. Univ.*, **No. 175**, 85-95 (1956); *Chem. Abstr.* **51**, 10,470 (1957).

(27) M. Julia, *Compt. rend.* **228**, 1807 (1949).

(28) V. T. Klimko, *et al.*, *J. Gen. Chem. USSR*, **27**, 69 (1957).

(29) R. P. Hills and F. J. McQuillin, *J. Chem. Soc.*, 4060 (1953).

TABLE III

DATA FOR R—C(=O)—C(H)=C(H)—X

R	X	Compound	Found m.p. or b.p. (mm.), °C.	Reported m.p. or b.p. (mm.), °C.	Yield, %	Recrystallizing medium	Analyses or n_D (temp., °C.) Lit. or calcd.	Found	M.p., °C. (picrate $\nu_{C=O}$ infrared band, cm.$^{-1}$)	Splitting constants c.p.s. J_{AB}
CH_3	$N(CH_3)_3\ Cl^-$	X	154–158 dec.	150 dec. 135–136 dec.	90.5	1-Butanol acetonitrile			124.5–125.0 (1709)	14.2
C_2H_5	$N(CH_3)_3\ Cl^-$	XI	171–172 dec.		88.4	1-Butanol acetonitrile	$C_8H_{16}ClNO$ C, 54.10 H, 9.10 N, 7.80	 C, 54.00 H, 9.00 N, 7.96	114.0 (1715)	14.2
n-C_3H_5	$N(CH_3)_3\ Cl^-$	XII	142–150 dec.		89.0	Acetonitrile	$C_9H_{18}ClNO$ C, 56.39 H, 9.46 N, 7.31	 C, 56.18 H, 9.63 N, 7.09	104.0–104.5 (1712)	14.0
i-C_3H_7	$N(CH_3)_3\ Cl^-$	XIII	153–155 dec.		82.6	1-Butanol acetonitrile	$C_9H_{18}ClNO$ C, 56.39 H, 9.46 N, 7.31	 C, 56.39 H, 9.74 N, 7.28	141.5 (1712)	14.1
i-C_4H_9	$N(CH_3)_3\ Cl^-$	XIV	108–110 dec. (impure)		85.8	Acetonitrile (difficult)	$C_{10}H_{20}ClNO$ C, 58.38 H, 9.80 N, 6.81	 C, 56.78 H, 9.75 N, 6.58	...	14.0
t-C_4H_9	$N(CH_3)_3\ Cl^-$	XV	152–154 dec.		91.5	1-Butanol	$C_{10}H_{20}ClNO$ C, 58.38 H, 9.80 N, 6.81	 C, 58.31 H, 9.95 N, 6.87	148.0–148.5 (1706)	0
C_6H_5	$N(CH_3)_3\ Cl^-$	XVI	160–161 dec.	159 dec.	86.4	95% ethanol			185.5–186.5	
CH_3	-I	XVII	56.0–56.5	55–56	96.4	Petroleum ether (30–60)				15.0
CH_3	-SCN	XVIII	39–40	39–40	96.0	Petroleum ether				8.5
CH_3	$-N(CH_3)_2$	XIX	132–133 (20)	131–133 (20)	72.0	G.l.c. pure	1.5560 (20)	1.5562 (20)		13.0
CH_3	-CN	XX	71 (11)	73 (11)	54.9	G.l.c. pure	1.4622 (20)	1.4590 (27)		16.0
t-C_4H_9	-OH	XXI	53–56 (25)	53–56 (25)	47.9	G.l.c. pure	1.4503 (25)	1.4523 (20.5)		4.5

then precipitated quantitatively and it had the correct analysis for the desired dibromide. In all cases where a solid was recovered the strong double bond absorption band of the salts disappeared in the infrared spectrum leaving a low intensity band in its place. The carbonyl band remained unchanged. These results may be taken as evidence for unsaturation.

The substitution of vinylic halides is normally not a facile process.[30] However, if the vinylic halide is activated by an electron-withdrawing group or a group which may stabilize a negative charge in the α-position (to the stabilizing group), then replacement of the halide is known to occur quite easily.[15,31–33]

No work had been reported,[23] however, on the mechanism by which the β-chlorine atom of β-chlorovinyl ketones is replaced by the various nucleophiles.

As was discussed previously, the β-chlorovinyl ketones were found to be at least 95% *trans* through n.m.r. spectroscopy. The n.m.r. spectra of the β-acylvinyltrimethylammonium chlorides were then obtained. Inspection of these spectra revealed that the two hydrogens of the double bond were *trans* to one another, the splitting constants being *ca.* 14 c.p.s. as shown in Table III. It is safe to say from examination of these spectra that *at least* 95% of the *trans* product was obtained in these reactions.[34] The spectrum of the *t*-butyl derivative, however, was anomalous in that, instead of the characteristic quartet of lines of the AB pattern, a single broad band appeared. In some manner the electronic effect of the trimethylammonium moiety and the pivaloyl moiety has caused the protons of the double bond to experience identical magnetic fields. The protons thus have become equivalent under the resolution used. A satisfactory explanation of this must await further experimentation on similar structures.

Thus retention of configuration was observed in the reaction of β-chlorovinyl ketones with trimethylamine leading to *trans* products. The fact that these reactions were kinetically very fast and exothermic would appear to rule out the formation of acetylenic intermediates, as these could only be formed through *cis* elimination of hydrogen chloride which is usually a slower, more difficult process. However, it should be noted that there is a second route to these compounds which involves the addition of trimethylamine to acetylenic ketones in the presence of trimethylamine hydrochloride, but the stereochemistry and generality of this reaction has not been established.[35]

The addition–elimination reaction was unlikely in the present instance, because there were no hydrogen

(30) E. L. Eliel, "Stereochemistry of Organic Compounds," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, pp. 368–70 and references therein.

(31) W. Autenreith, *Ann.*, **254**, 222 (1889); **259**, 332 (1890); F. Montanari, *Gazz. chim. ital.*, **86**, 747 (1956); G. Modena and P. E. Todesco, *ibid.*, **89**, 854 (1959).

(32) S. I. Miller and P. K. Yonan, *J. Am. Chem. Soc.*, **79**, 5931 (1957).

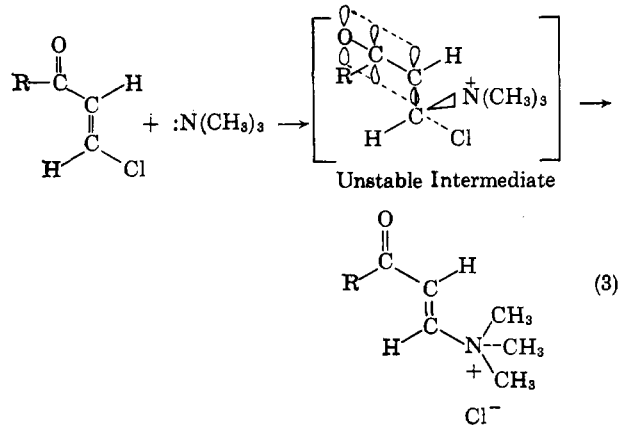
(33) D. E. Jones, *et al.*, *J. Chem. Soc.*, 2349 (1960).

(34) M. Hanna, private communication, University of Colorado.

(35) C. J. Cavallito, *J. Am. Chem. Soc.*, **77**, 4159 (1955).

atoms readily available for formation of the intermediate proposed for this path.

Thus the most likely path for the reaction of β-chlorovinyl ketones with trimethylamine probably involved conjugate addition elimination (eq. 3).



(3)

Essentially the same mechanism was proposed by Miller and Yonan,[32] Jones and co-workers,[33] and Sanchez[15] for other systems.

The stereochemistry might be explained well by using bimolecular nucleophilic displacements on aromatic rings as a model. We have not been able as yet to prepare the pure acyclic *cis* β-chlorovinyl carbonyl compounds to see if this reaction is stereospecific. β-Chlorovinyl aldehydes which are *cis* due to a fixed ring system even at higher temperatures gave no reaction with trimethylamine.[36] *trans* compounds may be preferred, however, as indicated in the conversion of *cis* XXI to *trans* V.

The infrared and ultraviolet spectral data seen in Table IV indicate that there is less interaction of the C=O with the C=C in these β-acylvinyltrimethylammonium chlorides than normally found.

TABLE IV

SPECTRAL DATA FOR (β-ACYLVINYL)TRIMETHYLAMMONIUM CHLORIDES

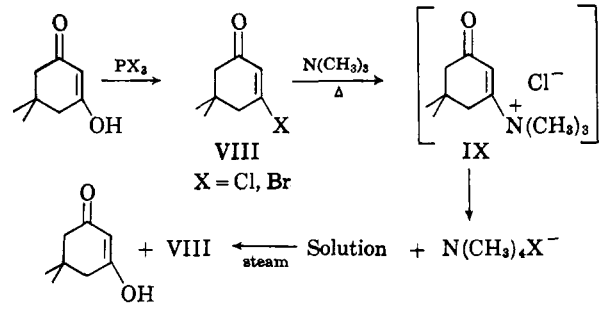
$$RCOCH{=}CH{-}\overset{+}{N}Me_3\ Cl^-$$

R	Compound	Infrared data, cm.$^{-1}$ $\nu_{C=O}$	$\nu_{C=C}$	$\nu_{HC=CH}$	Ultraviolet data λ_{max} mμ, (ε × 10⁴)
$-CH_3$	X	1686	1645	937.2	206.5 (7.30)
$-C_2H_5$	XI	1686	1645	938.1	207.5 (6.95)
n-C_3H_7	XII	1684	1661	934.6	208 (7.20)
$-i$-C_3H_7	XIII	1712	1637	944.3	208 (7.41)
$-i$-C_4H_9	XIV	1712	1645	945.2	208 (7.80)
$-t$-C_4H_9	XV	1704	1642	944.3	207.5 (8.44)
$-C_6H_5$	XVI	1681	1639	943.4	206.5 (8.98) 216 sh (7.19) 267 (7.82)
$CH_3C(=O)-CH=CH_2$					212.5 (7.00)

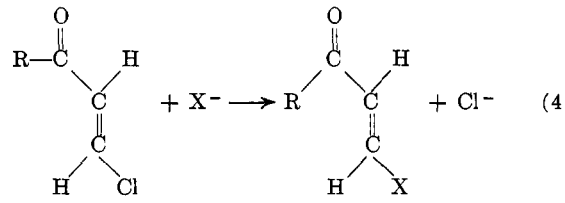
When compared with the β-chlorovinyl ketones, it was observed that the double bond absorption bands lay at shorter wave lengths in the quaternary salts. It also was observed that in the quaternary salts the double bond absorption band was only about two-thirds as intense as the carbonyl absorption band, and the two bands lay well within the range of 75 cm.$^{-1}$ of one another. On this basis one might qualitatively conclude that these compounds were also transoid. Finally, the bands in the 937–945-cm.$^{-1}$ range appearing in each spectrum indicated a *trans* arrangement about the double bond.

The ultraviolet spectra were obtained in 95% ethanol. Each spectrum exhibited a medium intensity band in the 206.5–208-mμ range. A large hypsochromic shift was observed when the spectra of the β-chlorovinyl ketones (Table II) were compared with the spectra of the β-acylvinyltrimethylammonium salts. In fact, the quaternary salts were found to absorb in the same wave-length range and with approximately the same intensities as do the unsubstituted vinyl ketones. A similar result has been observed in the case of aniline when compared with the anilinium cation.[37]

A fixed transoid β-chlorovinyl ketone, VIII, was prepared[38] for comparison with the labile systems and VIII gave an ultraviolet spectrum [λ_{max} 238 mμ (ε 13,500)] which compared favorably with I–VII. When VIII was treated with trimethylamine, a high conversion to tetramethylammonium chloride was found. Incidentally, VIII was inferred to be water sensitive.[38] However, it steam distilled in part along with toluene and was later recovered as unchanged VIII. The over-all reaction is given as the following.



Since trimethylamine gave complete retention of configuration when it replaced the chloride, it was desirable to determine whether this process was general for other nucleophiles (eq. 4).



(4)

The R group was held constant (as a methyl) and the X^- was represented by I^-, CN^-, ^-SCN, and $H\ddot{N}(CH_3)_2$. The results of this work also are given in Table III and show complete retention. The XVII is somewhat lower in its J_{AB} value than the other substituents (except for the XXI group, which is considered to lie in the *cis* configuration due to the added stability acquired through internal chelation). Although 8 c.p.s. is somewhat lower than the range expected for *trans* hydrogens (10–20 c.p.s.), only one isomer appeared to form and this compound is probably *trans*. This work is continuing.

(36) Unpublished results of W. R. Benson and A. E. Pohland.

(37) A. E. Gillam and E. S. Stern, "Electronic Absorption Spectroscopy," Ed. Arnold, Ltd., London, 1954.

(38) A. W. Crossley and H. R. LeSeuer, *J. Chem. Soc.*, **83**, 110 (1903).

Experimental

Elemental analyses were performed by Dr. G. Weiler and Dr. F. B. Strauss, Microanalytical Laboratory, 164 Banbury Road, Oxford, England. Melting points were taken on a Fisher-Johns melting point apparatus and were corrected. The refractive indices were obtained through use of a Bausch and Lomb refractometer. The Aerograph A110-C was used for all g.l.c. analyses; unless otherwise specified a silicone Dow II column was used. The n.m.r. spectra were measured on a Varian A-60 megacycle spectrometer. Infrared spectra were measured on a Beckman IR-5 spectrophotometer. The reported wave lengths were estimated to be within ± 1 cm.$^{-1}$ in the 1250–650-cm.$^{-1}$ range, ± 2 cm.$^{-1}$ in the 1250–1400-cm.$^{-1}$ region, ± 3 cm.$^{-1}$ in the 1400–1500-cm.$^{-1}$ range, ± 4 cm.$^{-1}$ in the 1600–1500-cm.$^{-1}$ region, ± 5 cm.$^{-1}$ in the 1600–3000-cm.$^{-1}$ region, and ± 10 in the 3500–3000-cm.$^{-1}$ region. All ultraviolet spectra were obtained using a Bausch and Lomb Spectronic 505 recording spectrophotometer.

Preparation of β-Chlorovinyl Ketones.—The preparation of β-chlorovinyl ketones generally involved the Friedel–Crafts addition of acid chlorides to acetylene. The acid chlorides were redistilled before use and were shown to be pure by gas chromatography. All the alkyl β-chlorovinyl ketones were unstable and decomposed slowly to brown liquids even when kept at low temperatures, except for the *t*-butyl derivative, which was quite stable. However, these brown liquids could still be redistilled before use. All were vesicants, the lower members being strongly lachrymatory. The phenyl β-chlorovinyl ketone was quite stable at room temperature.

Preparation of 1-Chlorobuten-3-one (I).—The method generally used here was that of Catch and co-workers.[39] In a 2-l. three-necked flask fitted with a gas inlet tube, Trubore stirrer, and condenser protected by a calcium chloride drying tube was placed 1.5 l. of carbon tetrachloride. The mixture was cooled to 0° in an ice–salt bath while acetylene was introduced over a period of *ca.* 15 min. The acetylene was dried and purified by passing it through a trap of concentrated sulfuric acid, protected on each side by an empty trap and by a mercury pressure release valve. The gas inlet tube was replaced by a dropping funnel and 333 g. (4.24 moles) of acetyl chloride was added dropwise over 15 min. The gas inlet tube was replaced and 650 g. (4.87 moles) of aluminum chloride was added in 50-g. lots each half hour through the neck containing the gas inlet tube. On completion of addition of the aluminum chloride, the mixture was stirred at room temperature an additional 6 hr. At the end of this time, the black viscous complex which had formed was hydrolyzed by pouring over chopped ice, the carbon tetrachloride layer separated, and the aqueous layer extracted with chloroform. The combined carbon tetrachloride–chloroform extracts were distilled at reduced pressure to yield 314.74 g. (71.8%) of crude product, b.p. 72–74° (95–100 mm.), which was shown to be slightly impure by gas chromatography. The mixture was refractionated to yield pure I, b.p. 76° (98 mm.), n^{20}D 1.4678 [lit.[42] b.p. 74° (100 mm.), n^{18}D 1.4649]. To the forerun of the initial distillation was added a 2 *M* solution of trimethylamine in toluene; 142.3 g. of β-acetylvinyltrimethylammonium chloride (X) was obtained, m.p. 142–146° dec. This corresponded to an additional 91.30 g. of I; thus the total yield was 406.04 g. or 92.7%. The other ketones were prepared similarly except for VI.

Preparation of 1-Chloro-4,4-dimethyl-1-penten-3-one (VI).—The procedure followed here was that of Kochetkov and co-workers.[11] The yield was 47.9% of hydroxymethylene pinacolone, b.p. 53–56° (25 mm.), n^{25}D 1.4503 [lit.[11] b.p. 53–56° (25 mm.), $n^{20.5}$D 1.4523]. This product was shown to be pure XXI by g.l.c.

In a 200-ml., single-necked flask fitted with a 60-ml. addition funnel protected by a calcium chloride drying tube, was placed 80 ml. of dry benzene and 16.4 g. (0.13 mole) of hydroxymethylenepinacolone. To this mixture was added dropwise with ice cooling 16.2 g. (0.14 mole) of thionyl chloride in 40 ml. of benzene. The mixture was allowed to warm to room temperature, after which it was refluxed for 8 hr. The solution was then fractionated to yield 5.42 g. of forerun, b.p. 68–72° (25 mm.), and 13.31 g. (71.1%) of VI, b.p. 72° (25 mm.), n^{24}D 1.4573 [lit.[11] b.p. 66–67.5° (27 mm.), n^{20}D 1.4593]. This product was shown to be pure by g.l.c.

(39) J. R. Catch, *et al.*, *J. Chem. Soc.*, 278 (1948).

Preparation of β-Acylvinyltrimethylammonium Chlorides.—Generally this involved the addition of a 2 *M* solution of trimethylamine (Rohm and Haas) in toluene to a solution of the chlorovinyl ketone in toluene. The solution immediately began to precipitate a white-tan solid and the solution warmed from the exothermic reaction. This solid was filtered and washed with toluene followed by absolutely dry ether. The melting point of this solid was usually 5 to 10° below the final melting point. In all cases the melting points varied depending upon how slowly the block was heated. The difficulty of identification by melting point in this case was overcome by the formation of the picrate derivative which easily gave a very pure, characteristic, reproducible melting point range without apparent decomposition. The substituted ammonium chloride salts were recrystallized from 1-butanol, acetonitrile, and/or 95% ethanol. The infrared spectrum of each picrate was taken and the new C=O and C=C bands were recorded in Table III. The yields were based on the crude products. A slight excess of the amine was used.

Preparation of β-Acetylvinyltrimethylammonium Chloride (X).—The method generally used here was that of Kochetkov and co-workers[28] and a typical experiment is given here in the preparation of compound X.

In a 500-ml. erlenmeyer flask was placed 36.36 g. (0.35 mole) of I and 200 ml. (0.40 mole) of a cold 2 *M* solution of trimethylamine in toluene. The reaction began immediately on mixing and was exothermic, yielding a light tan solid, 51.93 g. (90.5%), m.p. 143–145°. Recrystallization from 1-butanol yielded a product, m.p. 151–153° (dec.); recrystallization from acetonitrile yielded a product, m.p. 154–158° dec. (lit.[28] m.p. 150° dec., lit.[40] m.p. 135–136°). The picrate was prepared by dissolving 3.10 g. (0.014 mole) of X and 2.20 g. (0.014 mole) of picric acid in 75 ml. of 95% ethanol, heating to boiling, and then cooling to 0°. The product was filtered and recrystallized from 95% ethanol, m.p. 124.5–125°. The infrared spectrum of the picrate exhibited a carbonyl band at 1709 cm.$^{-1}$ and a double bond absorption band at 1689 cm.$^{-1}$. The other products and their physical properties are given in Table III.

Treatment of β-Isobutyrylvinyltrimethylammonium Chloride (XIII) with Bromine.—In a 125-ml. erlenmeyer flask were placed 3.84 g. (0.02 mole) of XIII and 50 ml. of chloroform. To this solution was added with stirring 3.20 g. (0.02 mole) of bromine in 10 ml. of chloroform. After *ca.* 15 min. all of the solid had disappeared; the mixture was stirred 24 hr. during which time a white solid slowly precipitated. Filtration yielded 3.18 g. of white solid, m.p. 131° dec. Evaporation of the filtrate yielded 3.80 g. of a second crop, m.p. 110–130° dec. Thus the total yield was 6.98 g. (99.3%). Recrystallization from methanol yielded a product, m.p. 133–134° dec. The dibromide of XIII is being studied further.

Anal. Calcd. for $C_{10}H_{29}Br_2ClNO$: C, 32.85; H, 5.51; N, 3.84. Found: C, 33.17; H, 5.43; N, 3.88.

Preparation of Methyl 2-Iodovinyl Ketone (XVII).—In a 250-ml., single-necked flask fitted with a condenser protected by a calcium chloride drying tube was placed 10.45 g. (0.10 mole) of I, 14.99 g. (0.10 mole) of sodium iodide, and 100 ml. of dry acetone. The mixture was refluxed 4 hr. and then cooled to room temperature. The white solid which had precipitated was filtered and washed with acetone to yield 5.43 g. (92.7%) of sodium chloride, m.p. >300°. The filtrate was flash evaporated to yield 19.72 g. of light yellow solid; recrystallization from petroleum ether (b.p. 30–60°) yielded 18.90 g. (96.4%) of XVII, m.p. 56–56.5° (lit.[41] m.p. 55–56°). This compound was highly vesicant and lachrymatory; it decomposed to a brown solid within an hour after drying and was, therefore, kept under petroleum ether until used. The infrared spectrum in Nujol exhibited strong carbonyl absorption at 1721 cm.$^{-1}$ and double bond absorption at 1629 cm.$^{-1}$. The ultraviolet spectrum in 95% ethanol exhibited maximal absorption at 203.5 mμ (ϵ 3960) and 259 (9860).

Preparation of Methyl 2-Thiocyanovinyl Ketone (XVIII).—In a 200-ml., single-necked flask fitted with a condenser was placed 8.00 g. (0.077 mole) of I in 140 ml. of acetone and 10.00 g. (0.103 mole) of potassium thiocyanate in 10 ml. of water. The mixture was refluxed 3 hr., whereupon 5.21 g. (77%) of potassium chloride was filtered off, washed with acetone, and dried, m.p. >300°.

(40) A. N. Nesmeyanov and M. T. Rubinskaya, *Dokl. Akad. Nauk SSSR*, **115**, 315 (1957).

(41) N. K. Kochetkov, *ibid.*, **82**, 593 (1952); *Chem. Abstr.*, **47**, 2691 (1953).

The filtrate was flash evaporated to yield 8.22 g. (96.0%) of a yellow-orange solid, which was recrystallized from petroleum ether (b.p. 30–60°) to yield 8.15 g. of XVIII, m.p. 39–40° (lit.[41] m.p. 39–40°). This product also was a strong vesicant and lachrymator. Its infrared spectrum in Nujol exhibited absorption bands at 2410 (—SCN), 1672 (C=O), and 1550 (C=C) cm.$^{-1}$. The ultraviolet spectrum in 95% ethanol exhibited maximal absorption at 205 mμ (ε 1154) and 276.5 (9234).

Preparation of 1-(N,N-Dimethylamino)-1-buten-3-one (XIX).—In a 250-ml. erlenmeyer flask was placed 70 ml. (0.621 mole) of a 40% aqueous solution of dimethylamine. To this solution was added dropwise, with stirring and ice cooling, 16 g. (0.15 mole) of I. After 0.5 hr. at room temperature the mixture was saturated with solid potassium carbonate and continuously extracted with ether for 12 hr.; the ether extracts were dried over anhydrous magnesium sulfate and distilled to yield 8.17 g. (72%) of XIX, b.p. 132–133° (20 mm.), n^{20}D 1.5560 [lit.[42] b.p. 131–133° (20 mm.), n^{20}D 1.5562]. The infrared spectrum exhibited a strong carbonyl band at 1664 cm.$^{-1}$. A band at 960 cm.$^{-1}$ indicated a *trans* arrangement with the double bond. The ultraviolet spectrum 95% ethanol exhibited maximal absorption at 302 mμ (ε 24,900).

(42) N. K. Kochetkov, *Izvest. Akad. Nauk. SSSR Otdel. Khim. Nauk* 991 (1953); *Chem. Abstr.*, **49**, 2308 (1955).

Preparation of Methyl β-Cyanovinyl Ketone (XX).—In a 250-ml. erlenmeyer flask was placed 16.37 g. (0.10 mole) of X, 150 ml. of benzene, and 6.51 g. (0.10 mole) of potassium cyanide. To this solution was added 5.0 g. (0.052 mole) of trimethylamine hydrochloride in 5 ml. of water. The reaction mixture was heated to 50°, whereupon a solution of 3.25 g. (0.05 mole) of potassium cyanide in 15.0 ml. of water was added dropwise with stirring. Evolution of trimethylamine was observed. On cessation of trimethylamine evolution, the benzene layer was decanted and a new portion of benzene (100 ml.) added. The mixture was heated at 50° for 1 hr. with stirring, whereupon the benzene layer was decanted and a fresh portion of benzene added. The entire process was repeated twice more. The benzene extracts were combined, dried over anhydrous sodium sulfate, and distilled to yield 5.21 g. (54.9%) of XX, b.p. 71° (11 mm.), n^{20}D 1.4622 [lit.[40] b.p. 73° (11 mm.), n^{27}D 1.4590]. The infrared spectrum (neat) exhibited absorption bands at 2232 (C≡N), 1706 (C=O), and 1618 cm.$^{-1}$ (C=C). A strong band at 965 cm.$^{-1}$ indicated a *trans* arrangement about the double bond. The ultraviolet spectrum exhibited maximal absorption at 226 mμ (ε 8384).

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The Autoxidation of 4-Vinylcyclohexene[1a]

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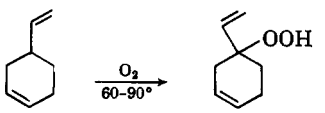
4-Vinylcyclohexene has been found to be autoxidized predominantly at the secondary allylic positions. All of the possible allylic hydroperoxides are formed to some extent. A similar product distribution is obtained from the attack on the olefin of *t*-butoxy radicals generated from *t*-butyl hydroperoxide–cobalt naphthenate and *t*-butyl peroxybenzoate–cuprous bromide.

The Diels–Alder dimer of butadiene, 4-vinylcyclohexene (**1**), has been reported[2] to be autoxidized in the liquid phase to yield the tertiary hydroperoxide **3b** exclusively. This result requires that the propagative species in the autoxidation chain, presumably a peroxy



1 **3b**

radical, removes a tertiary allylic hydrogen to the exclusion of the more abundant secondary. By contrast, our preliminary experiments with this system indicated that the oxidation produced a mixture of predominantly secondary hydroperoxides. Thus, the hydroperoxides could be catalytically hydrogenated and the resulting alcohols oxidized to a mixture of ketones in which the most abundant component would be 3-ethylcyclohexanone. A quantitative determination of the hydroperoxides produced in this autoxidation could provide valuable information regarding the selectivity of peroxy radicals toward attack on allylic carbon–hydrogen bonds of several types. Hence, our efforts were directed toward examining the isomer distribution obtained under differing conditions of temperature, solvent and initiation.

The autoxidation of **1** was effected by passing oxygen through the pure olefin or concentrated solutions of the olefin in *n*-decane, benzene, or *t*-butylbenzene at 60–80°. Most of the runs were terminated after sufficient oxygen was absorbed to oxidize 10–12% of **1**, but some cases were examined at conversion levels of 6 and 23%. Conversion level appeared to have no effect on isomer distribution. In a few instances, azobisisobutyronitrile (AIBN) initiation was employed. At low concentrations, AIBN had little effect, but at higher concentrations it eliminated a short induction period and increased the rate of oxygen absorption.

For low conversion runs, hydroperoxide of acceptable purity could be obtained by evaporation of the unoxidized olefin and evaporative distillation of the residue. The runs at higher conversions required extraction of the hydroperoxide with cold, dilute base and distillation to obtain hydroperoxide of satisfactory purity. Hydroperoxide with *ca.* 86% of the theoretical active oxygen could be obtained. It was feared that selective loss of secondary hydroperoxide by base-catalyzed decomposition[3] might occur during the extraction step, but a comparison of runs worked up by the two methods showed that these losses, if any, were not serious. That the distillation step (and the subsequent manipulations involved in analysis) did not change the isomer distribution was shown by analysis of the crude hydroperoxide by n.m.r. The secondary hydroperoxide fraction was estimated from a comparison of the area for the >CH-OO- hydrogen

(1) (a) Presented at the 18th Southwest Regional Meeting, American Chemical Society, Dallas, Tex., December 6, 1962; (b) The Carwin Company, Stiles Lane, North Haven, Conn.

(2) W. F. Brill, *J. Org. Chem.*, **24**, 257 (1959).

(3) N. Kornblum and H. E. De La Mare, *J. Am. Chem. Soc.*, **73**, 880 (1951).