lide was shown to be present by a comparative infrared spectrum with authentic formanilide in $CCl_4$. All the bands in the spectrum of formanilide were present in the spectrum of the residue, and they indicated formanilide to be the major component of the residue. There were also impurity bands probably due to decomposition products from aniline.

The presence of formanilide in the reaction mixture was further confirmed by vapor phase chromatography as follows. The last 5 ml. of residue was treated with ether to remove dissolved oxanilide, the ether was removed, and the remaining aniline solution was passed through 20% S.E. 30 silicone oil on firebrick at 220°. Although the base line became unsteady after peaks corresponding to aniline and formanilide were observed (probably owing to oxidation products of aniline), the presence of a peak due to formanilide was confirmed by its enhancement on adding formanilide to the solution.

# Aliphatic β-Chlorovinyl Aldoximes[1a]

WALTER R. BENSON[1b] AND ALBERT E. POHLAND[1c]

*Department of Chemistry, Colorado State University, Fort Collins, Colorado*

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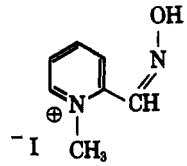
A number of aliphatic β-chlorovinyl aldehydes have been converted to their oximes. Infrared, ultraviolet, and n.m.r. spectral data verify the proposed structures. The β-chlorine atom of the conjugated aldehydes was found to be more stable toward replacement when a substituent other than hydrogen was also in the β-position. These compounds appear where possible to be mixtures of *cis* and *trans* isomers detectable by n.m.r.

There is a need for better antidotes against organophosphate poisoning. Compounds modeled after one of the present drugs, 2-PAM,[2] were sought because 2-PAM, although effective, is unstable over long periods in water.



2-PAM

$(CH_3)_3\overset{+}{N}-CR=CR'-CH=N(OH)$

1

The attempted synthesis of compounds of type 1, whose similarity to 2-PAM is readily apparent, is reported here. The following reaction paths were investigated.

$$R-\underset{Cl}{\underset{|}{C}}=CR'-CHO + (CH_3)_3N: \longrightarrow R-\underset{\overset{+}{N}(CH_3)_3\ Cl^-}{\underset{|}{C}}=CR'-CHO$$

2 3

$$2 + NH_2OH \longrightarrow RC(Cl)=CR'CH=N(OH)\ \text{and/or isoxazoles}$$

4

$$3 + NH_2OH \longrightarrow 1\ \text{and/or isoxazoles}$$

$$4 + :N(CH_3)_3 \longrightarrow 1\ \text{and/or isoxazoles}$$

Until very recently, β-chlorovinyl aldehydes were quite difficult to obtain but are now readily prepared through the formylation of ketones with the phosphorus oxychloride–dimethylformamide reagent.[3] In the course of our research, it was found that increasing the quantities of reactants gave yields comparable to, and in some cases better than, those reported. The products are unstable, but decomposition could be inhibited by dissolving the aldehyde in toluene containing a small amount of trimethylamine.

Treatment of these β-chlorovinyl aldehydes with trimethylamine in toluene under pressure at elevated temperatures failed to yield the expected quaternary salts. In most cases, small amounts of trimethylamine hydrochloride and varying amounts of intractable tars were formed, the unchanged β-chlorovinyl aldehydes being recovered in good yields (usually >65%). 2-Chlorocyclohexene carboxaldehyde was recovered nearly quantitatively. In a few cases dimethylamine was found to be equally unreactive.

The low reactivity of these aldehydes toward trimethylamine is in sharp contrast to the great reactivity of β-chlorovinyl ketones with trimethylamine,[4] where there apparently is less steric hindrance to attack by the trimethylamine molecule. The addition of various nucleophiles to β-chlorovinyl aldehydes has been investigated by other workers,[3e,5-7] who report the formation of both aldehyde derivatives and products arising through displacement of the β-chlorine atom.

When the chlorovinyl aldehydes prepared in this work were treated with hydroxylamine in aqueous alcohol, the corresponding oximes were usually formed (see Table I). The pure solid oxime of β-chlorocrotonaldehyde was not obtained. This is not surprising since crotonaldoxime does not easily form at room temperature.[8] 2-Chlorocycloheptene carboxaldehyde formed the oxime in a very low yield, the major product being 1-cyano-2-chlorocycloheptene.[9]

No analyses were found in the literature for the β-chlorovinyl aldehydes prepared, presumably because of their great instability. The analyses of the oxime derivatives and the gas chromatograms of the aldehydes therefore constitute a better measure of their purity than has yet been reported. The oximes were generally unstable even when purified.

(1) (a) Financed in part by the Institute of Neurological Diseases and Blindness (under Grant NB 04088-01) and the Research Corporation; taken in part from the dissertation of A. E. Pohland. (b) Person to whom correspondence should be directed at the Division of Food Chemistry, Bureau of Scientific Research, Food and Drug Administration, U. S. Department of Health, Education and Welfare, Washington, D. C. 20204. (c) Boettcher Fellow, 1962–1963.

(2) P. Holton, and H. Ing, *Brit. J. Pharmacol.*, **4**, 190 (1949).

(3) (a) Z. Arnold and J. Zemlicka, *Chem. Listy*, **52**, 2013 (1958); (b) Z. Arnold and J. Zemlicka, *Proc. Chem. Soc.*, 227 (1958); (c) Z. Arnold, *Collection Czech. Chem. Commun.*, **24**, 4048 (1959); (d) Z. Arnold and A. Holy, *ibid.*, **26**, 3059 (1961); (e) Z. Arnold and J. Zemlicka, *ibid.*, **24**, 2378 (1959); (f) W. Ziegenbein and W. Lang, *Chem. Ber.*, **93**, 2743 (1960).

(4) W. R. Benson and A. E. Pohland, *J. Org. Chem.*, **29**, 385 (1964).

(5) L. Rylski, F. Sorm, and Z. Arnold, *Collection Czech. Chem. Commun.*, **24**, 1667 (1959); *Chem. Abstr.*, **53**, 20066 (1959).

(6) J. Zemlicka and Z. Arnold, *Collection Czech. Chem. Commun.*, **26**, 2852 (1961).

(7) W. Ziegenbein and W. Franke, *Angew. Chem.*, **71**, 628 (1959).

(8) M. Gouge, *Ann. chim.*, **6**, 648 (1951).

(9) W. R. Benson and A. E. Pohland, unpublished data. Under certain conditions isoxazole formation is the major product.

TABLE I

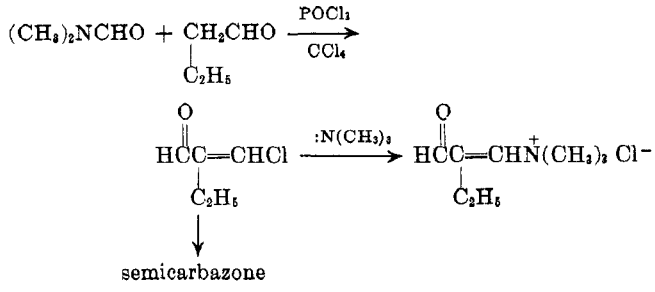
SUBSTITUTED β-CHLOROVINYL ALDOXIMES

$R_1C(Cl)=CR_2CH=NOH$

| Oxime | | Solvent for recrystn.[a] | M.p., °C. | Yield, % | Formula | Carbon | | Hydrogen | | Nitrogen | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| $R_1$ | $R_2$ | | | | | Calcd. | Found | Calcd. | Found | Calcd. | Found |
| $CH_3$ | $CH_3$ | A | 118–119 | 90 | $C_5H_8ClNO$ | 44.95 | 45.12 | 6.02 | 6.19 | 10.49 | 10.72 |
| $C_2H_5$ | $CH_3$ | B | 75.0–75.5 | 46.1 | $C_6H_{10}ClNO$ | 48.59 | 48.33 | 6.83 | 6.91 | 9.71 | 9.88 |
| $-(CH_2)_3-$ | | A | 117.5–118 | 98.4 | $C_6H_8ClNO$ | 49.50 | 49.44 | 5.54 | 5.53 | 9.62 | 9.69 |
| $-(CH_2)_4-$ | | A | 108.0–108.5 | 99.0 | $C_7H_{10}ClNO$ | 52.67 | 52.53 | 6.32 | 6.49 | 8.78 | 8.48 |
| $-(CH_2)_5-$ | | C | 37–40 | 3.22 | $C_8H_{12}ClNO$ | Not pure enough for elemental analysis | | | | | |
| $-(CH_2)_6-$ | | A | 83.5–84.5 | 97.2 | $C_9H_{14}ClNO$ | 57.60 | 57.83 | 7.52 | 7.30 | 7.47 | 7.66 |

[a] A = aqueous methanol, B = petroleum ether, C = not recrystallized.

When butyraldehyde was chloroformylated, a liquid was obtained which gave physical constants comparable with those reported.[5] However, it was prepared by a different method, and its g.l.c. showed two large peaks. The oxime could not be prepared but the semicarbazone was prepared and it analyzed correctly. The liquid was possibly a mixture of *cis* and *trans* isomers. When this chloroaldehyde mixture was treated with trimethylamine, a solid was slowly formed. This solid was extremely hygroscopic so that an elemental analysis was difficult to obtain, but an infrared spectrum showed a conjugated carbonyl and a double bond peak. All this evidence indicates that the following reaction sequence had probably taken place.




Treatment of the cyclic β-chlorovinyl aldoximes with trimethylamine gave no reaction even under pressure and 100° temperature. The starting oximes were recovered unchanged and in high yields. The aliphatic acyclic oximes decomposed to a greater extent under similar conditions.

The ultraviolet spectra of these β-chlorovinyl aldehydes and their oximes are compiled in Table II. All spectra were run in 95% ethanol. It is obvious from inspection of this table that each aldehyde and each oxime exhibits a well-defined K band in the 241–260-mμ range (ε 11,000–20,000). The presence of the chlorine substituent is reflected in a bathochromic shift of approximately 23 mμ accompanied by a marked increase in the intensity of the K band of these β-chlorovinyl derivatives over their nonhalogenated analogs. This may be ascribed to the extension of the conjugated system through resonance with the halogen atom. It is of interest to note that the cyclic structure is accompanied by a shift to a longer wave length when compared with the similarly disubstituted but noncyclic aldehydes. Finally, a slight hypsochromic shift is noted in all cases on conversion from the aldehyde to the oxime.

It is of interest to compare the effect of the various halogen atoms on the absorption maxima of α,β-unsaturated carbonyl compounds. In the case of

TABLE II

ULTRAVIOLET SPECTRA OF β-CHLOROVINYL ALDEHYDES AND THEIR OXIMES

| Compound | | $R_1C(Cl)=C(R_2)CHO$ | | $R_1C(Cl)=C(R_2)CH=NOH$ | |
|---|---|---|---|---|---|
| $R_1$ | $R_2$ | $\lambda_{max}$ | $\epsilon \times 10^{-4}$ | $\lambda_{max}$ | $\epsilon \times 10^{-4}$ |
| $-(CH_2)_3-$ | | 257.5 | 1.32 | 252 | 1.55 |
| $-(CH_2)_4-$ | | 255 | 1.82 | 247.5 | 1.42 |
| $-(CH_2)_5-$ | | 260 | 1.16 | 255 | 1.72 |
| $-(CH_2)_6-$ | | 258 | 1.13 | 252 | 1.72 |
| $CH_3$ | H | 241 | 1.36 | ... | ... |
| $CH_3$ | $CH_3$ | 248 | 1.39 | 245.5 | 1.93 |
| $C_2H_5$ | $CH_3$ | 247.5 | 1.34 | 245 | 1.95 |

β-chlorovinyl ketones, a shift of *ca.* 15 mμ has been noted in several instances.[4,10,11] Arnold and Holy[3d] found that β-bromo-α,β-unsaturated aldehydes absorb maximally at about 30 mμ longer wave length than their nonhalogenated analogs. Bowden and coworkers[12] also listed a value of 30 mμ as the shift to be expected on substitution of the β-hydrogen atom by bromine in a conjugated system.

Very few data are available on the effect produced through substitution of the β-carbon with iodine. Methyl β-iodovinyl ketone was found to absorb maximally at 259 mμ (ε 8100), a shift of 49 mμ based on methyl vinyl ketone, $\lambda_{max}$ 210 (ε 7000). Sanchez[10] found that methyl diiodovinyl ketone absorbed maximally at 274 mμ, indicating a further bathochromic shift of 15 mμ as a result of disubstitution.

The infrared spectra of the β-chlorovinyl aldehydes are in full agreement with the proposed structures. The carbonyl absorption band is found (consistently) in the 1679 ± 7 cm.$^{-1}$ region. Thus the β-chlorine substituent has little effect on the wave length of the carbonyl band since the carbonyl group of α,β-unsaturated aldehydes normally is found to absorb near 1685 cm.$^{-1}$.

The double-bond frequency of the β-chloro-α,β-unsaturated aldehydes is found consistently at 1619 ± 12 cm.$^{-1}$. Although in every case the double-bond absorption maximum is quite strong, it is only about two-thirds as intense as the carbonyl band. In addition the difference between $\nu_{C=O}$ and $\nu_{C=C}$ is always less than 75 cm.$^{-1}$. On this basis and on the basis of steric considerations, these compounds might be written in the transoid form.[13,4]

The infrared spectra of the β-chlorovinyl aldoximes indicate that, as expected, the carbonyl band has disappeared. In addition, a strong band between 1608

(10) R. Sanchez, Ph.D. Thesis, Kansas State University, 1962.
(11) K. Bowden, *et al.*, *J. Chem. Soc.*, 45 (1946).
(12) K. Bowden, E. A. Braude, and E. R. H. Jones, *ibid.*, 945 (1946).
(13) K. Nakanishi, "Infrared Absorption Spectroscopy," Holden-Day Inc., San Francisco, Calif., 1962, p. 165.

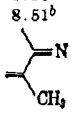
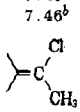
and 1639 cm.$^{-1}$ appears which has been ascribed previously to the C=C—C=N moiety.[3d] Finally, these spectra show free -OH bands in the 3546–3610-cm.$^{-1}$ region and hydrogen-bonded -OH bands in the 3226–3322-cm.$^{-1}$ region.

The nuclear magnetic resonance spectra of the β-chlorovinyl aldoximes were obtained and fully substantiate the proposed structures (see Table III). Dioxane ($\tau$ 6.43) was used as the internal standard. 3-Chloro-2-methyl-2-butenal itself exhibits absorption at $\tau$ 8.17 corresponding to the 2-methyl group, at $\tau$ 7.58 and 7.33 due to the 3-methyl group shifted downfield by the deshielding effect of the chlorine atom, and at $\tau$ −0.88 and −0.17 due to -C*H*O protons. This spectrum indicates the presence of a mixture of *cis* and *trans* isomers.

TABLE III

N.M.R. SPECTRA[a] OF β-CHLOROVINYL ALDOXIMES

RC(Cl)=CR′CH=NOH

| Compound R | R′ | $\tau$ values -CH$_2$- | -CH$_2$C= | HC=N- | -OH |
|---|---|---|---|---|---|
| -(CH$_2$)$_3$- | | 8.10[b] | 7.43[b] | 1.98 | 0.29 |
| -(CH$_2$)$_4$- | | 8.35[b] | 7.58[c] | 1.75 | 0.35 |
| -(CH$_2$)$_5$- | | 8.36[b] | 7.40[b] | 2.06 | 0.53 |
| -(CH$_2$)$_6$- | | 8.51[b] | 7.46[b] | 1.88 | 0.51 |
| | |  |  | H>C=N | -OH |
| CH$_3$ | CH$_3$ | 8.09[c] 8.17 | 7.83[d] | 1.81 | 0.40 |
| | | —CH$_2$—*CH*$_3$ |  | —CH$_2$— | H>C=N | -OH |
| C$_2$H$_5$ | CH$_3$ | 8.93[e] | 8.10 | 7.47[d] | 1.90 | -0.84 |

[a] All spectra were determined in dioxane at 60 Mc. [b] Center of complex multiplet. [c] Centers of two quartets. [d] Center of quartet. [e] Center of triplet.

In 3-chloro-2-methyl-2-butenaldoxime again two different -C*H*=NOH protons are found at $\tau$ 1.62 and 1.81 in the ratio of 1:5.5. There was no indication of *syn* and *anti* isomerism.[14] A new peak (OH) at $\tau$ 0.40 was also found. The high-field methyl absorption (Table III) consists of two quartets of intensities in the ratio of 5.5:1.

On these grounds, the high-field methyl band may be assigned to the 2-methyl group. Moreover, the low-field methyl band is then assigned to the 3-methyl group. Its chemical shift depends mainly on the deshielding effect of the chlorine atom on the same carbon atom rather than on the more remote oximino group. Since both isomers have the chlorine atom in the same position relative to this methyl group, only a slight chemical shift is expected and, indeed, only one quartet is observed. The intensity of this low-field quartet is equal to the sum of the intensities of the two high-field quartets. Therefore an assignment of *cis* and *trans* structures may be attempted on chemical shift arguments. In both mixtures of compounds the (weaker) low-field -C*H*= peak should belong to the *cis*-chloro aldehyde and oxime. This seems to be consistent with the purely chemical considerations that the *cis* isomer (chloro aldehyde) is expected to be the less abundant one.

(14) E. Lustig, *J. Phys. Chem.*, **65**, 494 (1961).

Thus it appears feasible to prepare compounds of type 1 when R in the β-position is H. Alkyl substitution in the β-position of β-chlorovinyl aldehydes essentially prevents displacement of the β-chlorine atom by the trimethylamine molecule. Substitution of ethyl, however, in the α-position qualitatively does not prevent this β-chlorine displacement by trimethylamine. More evidence for this is becoming available in the continuation of this work.

## Experimental

Elemental analyses were performed by Drs. G. Weiler and F. B. Strauss, Microanalytical Laboratory, Oxford, England. Melting points were taken on a Fisher-Johns melting point apparatus and were corrected. The Aerograph A 110-C was used for all vapor phase chromatographic analyses; unless otherwise specified a silicone DC 11 column was used. The nuclear magnetic resonance spectra were measured on a Varian A-60 spectrometer. Infrared spectra were measured on a Beckman IR-5 spectrophotometer.

**Preparation of 2-Chlorocyclopentene Carboxaldehyde.**—The general procedure used here for cyclic aldehydes was a modification of that reported by Arnold and Zemlicka.[3] This modified process is illustrated in this preparation and has the advantage of allowing the preparation of much larger quantities than those reported. To a 500-ml., three-necked flask fitted with a dropping funnel, Trubore stirrer, and drying tube was added 73.10 g. (1.00 mole) of dimethylformamide (DMF). After cooling in an ice bath, 123 g. (0.8 mole) of phosphorus oxychloride was added, forming a yellow solution. The mixture was allowed to warm to room temperature and stirred an additional 30 min. After cooling again in the ice bath, 42.04 g. (0.5 mole) of cyclopentanone was added over a period of 30 min. The mixture was allowed to warm to room temperature and then stirred 1 hr. It was then poured over ice and solid sodium bicarbonate was added until no further rapid release of carbon dioxide was observed. The resulting mixture was steam distilled by dripping it into boiling water. The product was separated from the water layer in the distillate. The water layer was extracted with ether. The organic layer and ether extracts were combined, washed with 50 ml. of 10% sodium bicarbonate, washed once with 50 ml. of water, and dried over anhydrous magnesium sulphate. The ether was stripped off, and the residue was distilled to yield 35.17 g. of product, b.p. 67–69° at 12 mm. (53.9%). A center cut had $n^{18.5}$D 1.5163 (lit.[3e] b.p. 58° at 12 mm., $n^{20}$D 1.5162; lit.[3] b.p. 42–44° at 1 mm., $n^{20}$D 1.5145). The product was gas chromatographically pure, but slowly turned brown on standing. The other cyclic chlorovinyl aldehydes were prepared similarly. Steam distillation was not always used.

**2-Chlorocyclohexene carboxaldehyde** was prepared as described in the literature: b.p. 86–88° at 13 mm.; $n^{20}$D 1.5221; 68.2%; lit.[3e] b.p. 87° at 10 mm.; $n^{20}$D 1.5225; semicarbazone m.p. 230–231° dec.; 2,4-DNP m.p. 178°; anil m.p. 180–182°. These derivatives are reported here for the first time for all of the aldehydes.

**2-Chlorocycloheptene carboxaldehyde** was prepared as described in the literature: b.p. 103° at 13 mm.; $n^{20}$D 1.5218; 71.4%; lit.[3e] b.p. 95–98° at 13 mm.; $n^{20}$D 1.5227; semicarbazone m.p. 226–226.5° dec.; 2,4-DNP m.p. 156–156.5°.

**2-Chlorocyclooctene carboxaldehyde** was prepared as described in the literature: b.p. 104° at 5 mm.; $n^{20}$D 1.5250; 47.9%; lit.[3e] b.p. 135–140° at 13 mm.; $n^{20}$D 1.5247; semicarbazone m.p. 224–224.5° dec.; 2,4-DNP m.p. 162.5–163.5°; anil m.p. 173–174°.

**3-Chloro-2-butenal** was prepared as described in the literature: b.p. 46–48° at 24 mm.; $n^{20}$D 1.4788; 34.1%; lit.[3e] b.p. 60–65° at 26 mm.; $n^{20}$D 1.4790.

**3-Chloro-2-methyl-2-butenal** was prepared as described in the literature: b.p. 54–56° at 23 mm.; $n^{20}$D 1.4922; 43.3%; lit.[3e] b.p. 53–55° at 23 mm.; $n^{20}$D 1.4915.

**3-Chloro-2-methyl-2-pentenal** was prepared as described in the literature: b.p. 62.0–62.2° at 16 mm.; $n^{20}$D 1.4840; 49.6%; lit.[3e] b.p. 57° at 12 mm.; $n^{20}$D 1.4871.

**2-Chloromethylenebutanal** was prepared as described in the method above: b.p. 52–53° at 30 mm.; $n^{20}$D 1.4743; 24.8%; lit.[3b] b.p. 52–58° at 30 mm.; $n^{20}$D 1.4745. The n.m.r. spectrum run

neat exhibited a triplet centering around $\tau$ 8.97 representing the ethyl group, peaks at $\tau$ 2.57 and 1.82 owing to the chloromethylene hydrogen atom, and one at $\tau$ 0.45 owing to the aldehydic hydrogen. The semicarbazone was prepared, m.p. 195–195.5°.

*Anal.* Calcd. for $C_6H_{10}ClN_3O$: C, 41.03; H, 5.74; N, 23.94. Found: C, 41.24; H, 5.76; N, 24.19.

Treatment of the starting aldehyde with trimethylamine in toluene led to the slow formation of a white solid, m.p. 83–86°, which was hygroscopic and water soluble.

The general oxime preparation is illustrated by the following procedures.

**Preparation of 2-Chlorocyclopentene Carboxaldoxime.**—To 22.93 g. (0.18 mole) of 2-chlorocyclopentene carboxaldehyde in 50 ml. of 95% ethanol was added a solution of 18.05 g. (0.22 mole) of sodium acetate and 13.80 g. (0.20 mole) of hydroxylamine hydrochloride in 50 ml. of water. The reaction was instantaneous, yielding a white solid with evolution of heat. This solid was filtered, yielding 22.31 g. of white solid, m.p. 120–122°. An additional 2.85 g., m.p. 115–118°, was obtained by adding water to the filtrate: total yield 25.16 g., 98.4%. This product was recrystallized from petroleum ether three times, m.p. 116.5–117°. Recrystallization from methanol yielded a product, m.p. 117.5–118°. The other oximes were prepared in a similar manner and their analyses and melting points are listed in Table I.

**Treatment of 2-Chlorocyclopentene Carboxaldoxime with Trimethylamine.**—To 7.86 g. (0.054 mole) of 2-chlorocyclopentene carboxaldoxime in 25 ml. of toluene was added 50 ml. of 2 *M* trimethylamine in toluene (0.10 mole). This mixture was sealed in a pressure bottle and heated on the steam bath for 33 hr. At the end of this time the pressure bottle was cooled and opened; the odor of trimethylamine was still prevalent. Flash evaporation yielded 6.26 g. of a tan solid which, on recrystallization from aqueous methanol using decolorizing carbon, gave a pure white solid, m.p. 116.5–117°. A mixture melting point with the original oxime showed no depression. This was the typical experiment for all of the oximes.

**Treatment of 2-Chlorocyclopentene Carboxaldehyde with Trimethylamine.**—In a pressure bottle was placed 13.10 g. (0.10 mole) of the named aldehyde and 75 ml. of 2 *M* trimethylamine in toluene (0.15 mole). The bottle was sealed and heated in a steam bath for 24 hr. On opening the bottle, the odor of trimethylamine was still evident, and a brown solution was obtained. No solid was observed. Flash evaporation of this mixture and vacuum distillation gave 7.9 g. of the starting aldehyde, b.p. 67–70° (12 mm.), $n^{20}D$ 1.5165, as the only product. The infrared spectrum of this material was identical with that of the starting aldehyde. Almost all of the aldehydes similarly gave no reaction.

**Preparation of 2-Chlorocycloheptene Carboxaldoxime.**—To 20 g. (0.126 mole) of 2-chlorocycloheptene carboxaldehyde in 50 ml. of 95% ethanol was added 8.97 g. (0.13 mole) of hydroxylamine hydrochloride and 11.46 g. (0.14 mole) of sodium acetate in 25 ml. of water. The mixture was then cooled to 0°; after 24 hr. only a small amount of white solid had precipitated which melted at 37–40° (0.68 g., 3.22%), and which was shown to be the desired oxime through n.m.r., ultraviolet, and infrared spectroscopy. Attempted recrystallization from hexane, petroleum ether, or alcohol led to oils.

Partial evaporation of the filtrate gave a solution of two immiscible liquids. This mixture was separated, the aqueous layer was extracted with ether, and the combined organic layers were dried over magnesium sulfate and distilled to yield 13.65 g. of a colorless liquid, b.p. 85° (2.4 mm.). The infrared spectrum of this liquid exhibited absorption bands at 2227 (C≡N) and 1635 (C=C) cm.$^{-1}$, indicating the presence of impure 1-cyano-2-chlorocycloheptene. However, gas chromatography showed that at least two components were present in about equal amounts.

**Treatment of 3-Chloro-2-methyl-2-butenal Oxime with Acetic Anhydride.**—The oxime was placed in acetic anhydride at room temperature with stirring and 1 drop of concentrated $H_2SO_4$ was added. The solution was stirred for several hours and then poured into an ice–water mixture. The solid obtained was recrystallized from aqueous alcohol, m.p. 48.5–49°. In contrast to the oxime itself, this compound was stable at room temperature. The infrared spectrum of the compund exhibited a band at 1783 cm.$^{-1}$ (acetate) and one at 1626 cm.$^{-1}$ (C=C—C=N).

**Acknowledgment.**—The authors wish to thank the Research Corporation and the National Institute of Neurological Diseases and Blindness for their generous support of this work. W. Butin is thanked for his technical assistance. Arapahoe Chemicals, Inc., is thanked for their generous samples of cyclopentanone and cyclooctanone. E. Lustig is thanked for his help in the interpretation of some of the n.m.r. data.

# *trans* Transoid β-Substituted Vinyl Ketoximes[1a,b]

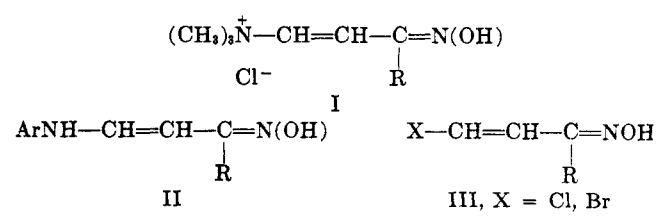
WALTER. R. BENSON[1c] AND ALBERT E. POHLAND[1d]

*Department of Chemistry, Colorado State University, Fort Collins, Colorado*

*Received September 25, 1964*

Although previous attempts by other investigators to form β-substituted (trimethylammonium, arylamino, and halogeno) vinyl ketoximes have been unsuccessful, the synthesis of several such substances has now been achieved. Conformational and steric factors apparently are important considerations in forestalling isoxazole formation.

In connection with acetylcholinesterase inhibition,[2] it was of interest to synthesize some α,β-unsaturated ketoximes of the types depicted (I–III). With the exception of the mono- and dioximes of indigo,[3] such substances are unknown, although several unsuccessful attempts to prepare them have been reported. Thus it has been reported that the ketone precursor of I




(R = $C_6H_5$) on treatment with hydroxylamine resulted in formation of phenylisoxazole as the only isolable product.[4] The ketone precursors of type II compounds have not been treated with hydroxylamine; however, β,β-dialkylaminovinyl ketones on treatment with hydroxylamine form 5-substituted isoxazoles in

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