neat exhibited a triplet centering around τ 8.97 representing the ethyl group, peaks at τ 2.57 and 1.82 owing to the chloromethylene hydrogen atom, and one at τ 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.

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

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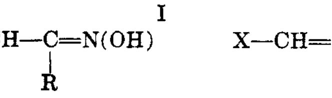
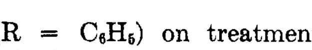
Although previous attempts by other investigators to form β-substituted (trimethylammonium, arylamino, and halogeno) vinyl ketoximes have been unsuccessful, the synthesis of several such substances has now been achieved. Conformational and steric factors apparently are important considerations in forestalling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



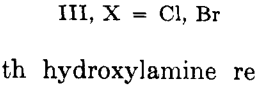
$$(CH_3)_3\overset{+}{N}{-}CH{=}CH{-}\underset{\displaystyle R}{\underset{|}{C}}{=}N(OH) \quad Cl^-$$

I



$$ArNH{-}CH{=}CH{-}\underset{\displaystyle R}{\underset{|}{C}}{=}N(OH)$$

II



$$X{-}CH{=}CH{-}\underset{\displaystyle R}{\underset{|}{C}}{=}NOH$$

III, X = Cl, Br

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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[1] (a) Taken in part from the dissertation of A. E. Pohland which was submitted in partial fulfillment of the requirements of the doctorate degree, 1963. (b) Supported in part by the Research Corporation, the Colorado State University Research Foundation, and the National Institute for Neurological Diseases and Blindness (Project NB 04088-01). (c) To whom correspondence should be addressed at the Food and Drug Administration, Division of Food Chemistry, Bureau of Scientific Research, Washington, D. C. 20204. (d) Boettcher Foundation Fellow, 1962–1963.

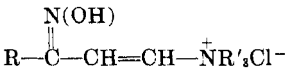
[2] I. B. Wilson, *Mol. Biol.*, 163 (1960) (Symposium, New York, N. Y., Sept. 1958).

[3] W. Madelung, *Ann.*, **405**, 86 (1914).

[4] N. Kochetkov, *et al.*, *J. Gen. Chem. USSR*, **27**, 511 (1957).

TABLE I

TYPE I COMPOUNDS



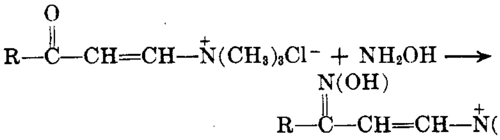
$$\mathrm{R-\overset{\overset{\displaystyle N(OH)}{\|}}{C}-CH{=}CH-\overset{+}{N}R'_3Cl^-}$$

R	R'	Compd.	M.p., °C.	Yield, %	Formula	% C		% H		% N	
						Calcd.	Found	Calcd.	Found	Calcd.	Found
CH_3	CH_3	Ia[a]	190–195 dec.	84.8	$C_7H_{15}ClN_2O$	47.05	47.21	8.46	8.55	15.68	15.41
C_2H_5	CH_3	Ib[b]	182–185 dec.	75.4	$C_8H_{17}ClN_2O$	49.86	49.84	8.89	8.95	14.54	14.54
i-C_3H_7	CH_3	Ic[c]	165–170 dec.	18.5	$C_9H_{19}ClN_2O$	52.29	52.07	9.26	9.25	13.55	13.74
t-C_4H_9	CH_3	Id[c]	218 dec.	47.5	$C_{10}H_{21}ClN_2O$	54.41	54.52	9.59	9.58	12.75	12.85
CH_3	$(C_5H_5)_{1/3}$	Ie[a]	171–173 dec.	93.6	$C_9H_{11}ClN_2O$	54.41	54.33	5.58	5.80	14.10	14.05

[a] Recrystallized from acetonitrile. [b] Not recrystallized but found to be insoluble in boiling absolute alcohol. [c] Recrystallized from absolute alcohol.

good yields.[5] Vinyl ketones of type III have been found to react readily with hydroxylamine to form mixtures of the corresponding 3- and 5-substituted isoxazoles resulting from initial attack by hydroxylamine at the carbonyl carbon and at the β-carbon atoms, respectively.[4-8]

Type of Compounds.—We report here the first synthesis of compounds of type I. Treatment of *trans*-β-acylvinyltrimethylammonium chlorides[9] with hydroxylamine led to the formation of the corresponding oximes (see eq. 1). These oximes and their analyses



$$\mathrm{R-\overset{\overset{\displaystyle O}{\|}}{C}-CH{=}CH-\overset{+}{N}(CH_3)_3Cl^- + NH_2OH \longrightarrow R-\overset{\overset{\displaystyle N(OH)}{\|}}{C}-CH{=}CH-\overset{+}{N}(CH_3)_3Cl^-} \quad (1)$$

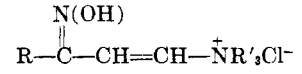
are listed in Table I. The reactions were carried out at 0° using sodium acetate as the base in absolute alcohol. No isoxazoles were isolated.

The infrared spectra of these oximes exhibited absorption bands in the 3100–3300- (OH), 1620–1660- (C=C), and 931–936-cm.$^{-1}$ (*trans* HC=CH) regions and showed, as expected, complete loss of carbonyl absorption. The n.m.r. spectra fully corroborated the proposed structures and also indicated a *trans* arrangement about the double bond. The splitting constants (J_{AB}) for the two adjacent protons on the double bond lie at 14–15 c.p.s. (see Table II). In the ultraviolet spectra, the oximes showed a bathochromic shift of the absorption bands when compared with the original quaternary salts. The decrease in absorption intensity as R becomes more bulky may be explained as being due to a loss of conjugation, a gradual nonplanar conformation resulting rather than a complete reversion of the cisoid conformation as the size of R increases.

Type II Compounds.—Since arylaminovinyl (cisoid *cis*) ketones had not been previously treated by various methods with hydroxylamine, four such compounds were prepared from acetylacetone and the appropriate aromatic amine. In aqueous solutions, these ketones failed to react under normal conditions.[10] Under anhydrous conditions, only anilines were recovered (see eq. 2).

TABLE II

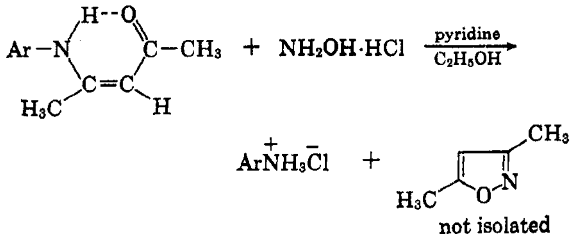
ULTRAVIOLET AND N.M.R. SPECTRA



$$\mathrm{R-\overset{\overset{\displaystyle N(OH)}{\|}}{C}-CH{=}CH-\overset{+}{N}R'_3Cl^-}$$

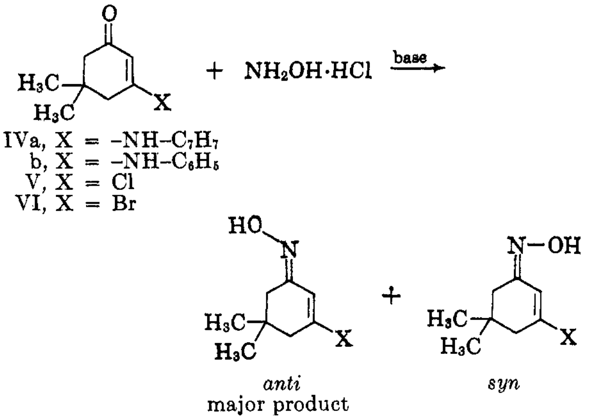
Compd.	λ_{max}, mμ[a]	$\epsilon \times 10^{-4}$[a]	J_{AB}, c.p.s.[b]
Ia	232.5	1.25	14
Ib	232	1.57	15
Ic	242	0.60	15
Id	242.5	0.35	15
Ie	226	1.00	Covered
	312	0.78	

[a] Determined in 95% ethanol. [b] Determined in D_2O at 60 Mc. using CH_3CN as the internal reference.



(2)

In a similar study of dimedone derivatives[11,12] where the molecule was held in a fixed *trans*-transoid conformation, it was found that 5,5-dimethyl-3-(*p*-toluidino)-2-cyclohexen-1-one (IVa) did not form an oxime and was cleaved by semicarbazide to form the disemicarbazone of dimedone. We now report the first example of an oxime of such a β-aminovinyl ketone. When IVa (yellow) was treated with hydroxylamine hydrochloride in anhydrous pyridine and absolute alcohol the oxime of IVa was formed (eq. 3) as a white



IVa, X = -NH-C_7H_7
b, X = -NH-C_6H_5
V, X = Cl
VI, X = Br

(3)

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(5) N. Kochetkov, *Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 47, (1954); *Chem. Abstr.*, **49**, 6090 (1955).

(6) N. Kochetkov, A. Nesmeyanov, N. Semenov, *Izvest. Akad. Nauk SSSR, Otdel. Khim. Nauk*, 87 (1952).

(7) N. Kochetkov and A. Khorlin, *Zh. Obshch. Khim.*, **28**, 1937 (1958).

(8) N. Kochetkov, *et al.*, *ibid.*, **27**, 452 (1957).

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

(10) R. Shriner, R. Fuson, and D. Curtin, "Systematic Identification of Organic Compounds," 4th Ed., John Wiley and Sons, Inc., New York, N. Y., 1956, p. 255.

(11) P. Haas, *J. Chem. Soc.*, **89**, 187 (1906).

(12) A. R. Crossley and H. R. LeSeuer, *ibid.*, **83**, 160 (1903).

compound showing absorption in the infrared at 1610 (C=N) and 1625 (C=C) cm.$^{-1}$ in addition to bands attributed to NH and OH stretching. In a similar way, the oxime of IVb was prepared.

The successful preparation of the oximes of IVa and IVb may indicate the necessity for having a fixed transoid conformation thus preventing isoxazole formation during oximation. However, steric hindrance toward displacement has not been completely eliminated.

Since aniline has been shown to catalyze the formation of oximes from ketones, presumably through intermediate Schiff base formation,[13] oximation of the anil of IVb was attempted. However, the Schiff base was quantitatively recovered after treatment with NH_2OH in absolute ethanol and pyridine.

Type III Compounds.—β-Chlorovinyl ketones (RCOCH=CHCl) form isoxazoles when treated with hydroxylamine (see above). However, compounds of type RCOCH=C(Ar)Cl are reported to form oximes.[14] In addition, compounds having the structure RC(Cl)=CR′CHO have been found to form either oximes or isoxazoles depending upon the experimental conditions.[15] The factors which contribute to successful oxime formation in the latter two cases may include (1) the presence of a ring in the conjugated system, (2) β-substitution, and (3) the reaction conditions.

We now report the successful preparation of the oximes of two β-halovinyl ketones. The oximes of 3-chloro- and 3-bromo-5,5-dimethyl-2-cyclohexen-1-ones (V and VI) were prepared in high yields. Both oximes existed in two forms. *syn* and *anti* compounds were suspected and the oximes of isophorone were prepared as model compounds.

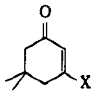
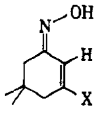
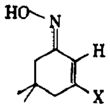
Isophorone forms a mixture of *syn* and *anti* oximes which may be separated through fractional crystallization from methanol. Mazur,[16] in a study of the Beckmann rearrangement in polyphosphoric acid showed that the lower melting isomer was *syn*, whereas the higher melting form was *anti*. These assignments subsequently were confirmed by n.m.r.[17]

It was found that the lower melting isomer of each *syn–anti* pair (eq. 3) was in all cases the most soluble in methanol. Repeated fractional crystallization failed to yield the pure *syn* (low melting) oxime, although the *anti* (higher melting) form was easily obtained pure in both cases as was shown through proton magnetic resonance spectroscopy (see later). The ultraviolet spectra of these oximes were consistent in that in every pair the *syn* (lower melting) isomer absorbed maximally at a longer wave length and with slightly less intensity than the *anti* (higher melting) isomer. It was on this basis, by analogy with the isophorone oximes, that the structures were initially assigned. Inspection of Table III also revealed that in all cases the β-halogeno substituent had caused a bathochromic shift and, as expected, this shift to longer wave lengths was greater for bromine than for chlorine.

The n.m.r. spectra of these oximes were investigated. There have been relatively few recorded cases in which the separation of both members of an isomeric pair of oximes has been reported.[18–20] In a classic paper, Phillips was able to demonstrate through the use of proton magnetic resonance, the presence of both *syn* and *anti* forms in a series of aldoximes, RCH=NOH. By assigning the R*H*C=NOH resonance at lower field to the *syn* form, he noticed that, as the R group became more bulky, the proportion of *syn*-aldoxime increased, as would be expected from steric considerations. The other =C—*H* peak was therefore assigned to the *anti* isomer. These assignments were confirmed (1) through the n.m.r. examination of the two aldoxime isomers of *p*-chlorobenzaldehyde,[21] whose structures were known from X-ray diffraction, and (2) through further studies on aliphatic ketoximes.[22] In 1962, Slomp and Wechter[17] published the n.m.r. spectrum of the mixture of isomers obtained on oximation of isophorone and accounted for the various lines on the basis that both *syn* and *anti* oximes were present. Their spectra were run in deuterated dimethyl sulfoxide.

TABLE III

DATA ON SUBSTITUTED DIMEDONES AND THEIR OXIMES

Compd.		X	λ_{max}, mμ	ε	τ, =C<^{H}
	V	Cl	238	13,500	
	VI	Br	246	13,400	
		CH_3	226	13,900	
		Cl	242^{a}	11,600	3.10
syn		Br	244^{a}	10,400	2.80
		CH_3	239	13,000	3.40
		Cl	241	12,800	3.78
anti		Br	242.5	15,000	3.48
		CH_3	238.5	14,000	4.11

[a] *syn* and *anti* mixture.

The results reported here are in general agreement with the isophorone oximes. The spectra (see Table III) for the six oximes were obtained in dioxane solvent and fully corroborated the proposed structures. These n.m.r. spectra showed that the *anti* form in each case could be obtained *pure*, whereas the *syn* form was only obtained as approximately a 1:1 mixture of *syn* to *anti* forms.

Neither pure *anti* oxime reacted with trimethylamine even under pressure. Ketone V, however, gave a 91% yield of tetramethylammonium chloride.

The ketones IV, V, and VI thus readily form oximes, probably owing to a combination of factors. The cyclohexyl ring may protect the β-carbon somewhat from nucleophilic attack by hydroxylamine and, in addition, holds the molecule in a fixed transoid conformation preventing cyclization to an isoxazole. It is possible that the transoid conformation alone is the determining factor in oxime rather than isoxazole formation in

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[13] E. H. Cordes and W. P. Jencks, *J. Am. Chem. Soc.*, **82**, 826 (1962).

[14] V. Belov and G. Shekhtman, *J. Gen. Chem. USSR*, **23**, 1501 (1953); *Chem. Abstr.*, **48**, 12025 (1954).

[15] W. Benson and A. Pohland, unpublished data.

[16] R. Mazur, *J. Org. Chem.*, **26**, 1289 (1961).

[17] G. Slomp and W. Wechter, *Chem. Ind.* (London), **1**, 42 (1962).

[18] W. D. Phillips, *Ann. N. Y. Acad. Sci.*, **70**, 769 (1959).

[19] J. Meisenheimer and W. Theilacker, "Stereochemie des Stickstoffs," in "Stereochemie," K. Freudenberg, Ed., Leipzig, Franz Deuticke, 1932, p. 693.

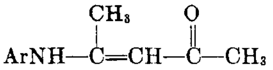
[20] B. Loev and M. F. Kormendy, *J. Org. Chem.*, **28**, 3421 (1963).

[21] E. Lustig, *J. Phys. Chem.*, **65**, 491 (1961).

[22] E. Lustig, private communication.

TABLE IV

CLEAVAGE OF II WITH HYDROXYLAMINE HYDROCHLORIDE



$ArNH-C(CH_3)=CH-C(=O)-CH_3$

Compd.	Ar	Mol. wt., g.	II used, g. (mole)	$NH_2OH \cdot HCl$ used, g.	% $ArNH_2 \cdot HCl$ recovered	Identified as
IIa	Ph	175.23	3.5 (0.02)	2	82	$ArNHCOCH_3$ (m.p. 114°)
IIb	p-CH_3-Ph	189	3.8 (0.02)	2	70	$ArNH_2$ (m.p. 41–42°)
IIc	p-Cl-Ph	209.68	4.2 (0.02)	2	80	$ArNH_2$ (m.p. 68–69°)
IId	m-NO_2-Ph	220.2	4.4 (0.02)	2	75	$ArNH_2$ (m.p. 112°)

other noncyclic systems, although no definite experimental evidence for this has been found.

In compounds having the general structure YCH=CH-CO-R where Y = R-CO-, R-CONH, or RO-CO-, oxime formation is usually observed.[23] Thus substitution of an electron-withdrawing group in the β-position does not prevent oxime formation, and therefore it was not unexpected that the β quaternary ammoniumvinyl ketones were easily oximated.

Experimental

Elemental analyses were performed by Drs. Weiler and Strauss, Microanalytical Laboratory, Oxford, England, and Huffman Microanalytical Laboratories, Wheatridge, Colo. 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 A. 110 C was used for all g.l.c. analyses utilizing a silicone Dow II column. The n.m.r. spectra were measured on a Varian A-60 spectrometer. Infrared spectra were measured on a Beckman IR-5 spectrophotometer.

General Oxime Formation. Treatment of 2-Acetylvinyltrimethylammonium Chloride with Hydroxylamine.—A mixture of 27.60 g. (0.17 mole) of the ketone, 11.72 g. (0.17 mole) of hydroxylamine hydrochloride, 14.50 g. (0.18 mole) of sodium acetate, and 200 ml. of absolute ethanol was stirred 12 hr. at room temperature and then filtered to yield 10.42 g. of white solid, m.p. 300°. After the ethanol had been evaporated, a brown semisolid was obtained which on trituration with acetonitrile yielded 25.42 g. (84.8%) of oxime Ia, m.p. 185–195° dec.; the odor of amine during decomposition was noticeable at *ca.* 177°. Recrystallization from methanol yielded a white solid, m.p. 189–193° dec.; however, an analytical sample was prepared by continuous extraction of the product with acetonitrile, m.p. 190–195° dec.

Anal. Calcd. for $C_7H_{15}ClN_2O$: C, 47.05; H, 8.46; N, 15.68. Found: C, 47.21; H, 8.55; N, 15.41.

The other oximes were treated similarly and are listed in Table I. Their spectral data are given in Table II.

Preparation of 2-Acetylvinylpyridinium Chloride.—To 10.45 g. (0.10 mole) of methyl 2-chlorovinyl ketone in 50 ml. of dry ether was added dropwise with stirring 7.91 g. (0.10 mole) of pyridine in 50 ml. of anhydrous ether. A white precipitate slowly formed. The mixture was allowed to stand at room temperature 12 hr. and then was filtered to yield 18.33 g. (100%), m.p. 191–193° dec. Recrystallization from methanol–ether yielded a white, crystalline solid, m.p. 192–193° dec. (lit.[3] m.p. 163–165° dec.). This compound exhibited a strong O–H absorption band at 3333 cm.$^{-1}$ even after vacuum drying over phosphorus pentoxide; its analysis corresponded to a hemihydrate.

Anal. Calcd. for $C_9H_{10}ClNO \cdot 0.5H_2O$: C, 56.11; H, 5.76; N, 7.27. Found: C, 56.16; H, 6.11; N, 6.77.

This compound formed a picrate which after recrystallization from 95% ethanol had m.p. 141–142°. The infrared spectrum of the picrate exhibited a carbonyl band at 1706 cm.$^{-1}$.

5,5-Dimethyl-3-(*p*-toluidino)-2-cyclohexen-1-one (IVa).—This compound was synthesized by the method of Haas,[11] m.p. 183–185° (lit.[11] m.p. 180°).

The Oxime of IVa.—A mixture of 4.60 g. (0.02 mole) of IVa in 15 ml. of anhydrous pyridine and 2.30 g. (0.03 mole) of hydroxylamine hydrochloride in 15 ml. of absolute ethanol was refluxed for 1.5 hr. The solvent was removed in a stream of air. Trituration of the residue with ethyl acetate gave a crystalline product, m.p. 234–245° dec. This crude product did not react with 5% aqueous sodium carbonate and was therefore not the hydrochloride. Recrystallization from ethyl acetate–acetone–ethanol yielded 2.50 g. (57.3%) of white solid, m.p. 252° dec.

Anal. Calcd. for $C_{15}H_{20}N_2O$: C, 73.78; H, 8.21; N, 11.47. Found: C, 73.63; H, 7.96; N, 11.72.

5,5-Dimethyl-3-anilino-2-cyclohexen-1-one (IVb) was prepared, m.p. 183–185° (lit.[11] m.p. 183–185°), and was treated similarly to yield an oxime, m.p. 237–242° dec.

Anilides of Acetylacetone.—In the preparation of anilides of acetylacetone, known methods[24] were modified. The rate of reaction under reflux was crudely followed by measuring the temperature of the condensate with a thermometer lowered into the condenser and quantitatively by measuring the amount of water which collected in a water separator. These four anilides were prepared: 4-(*p*-toluidino)-3-penten-2-one, m.p. 67–68° (lit. m.p. 68°), 91.3% yield; 4-(*p*-chloroanilino)-3-penten-2-one, m.p. 59–60° (lit. m.p. 61°), 88% yield; 4-anilino-3-penten-2-one, m.p. 48–49° (lit. m.p. 48°), 81.2% yield; and 4-(*m*-nitroanilino)-3-penten-2-one, m.p. 79–81° (lit. m.p. 81°), 43% yield.

Cleavage of 4-(Substituted anilino)-3-penten-2-one with Hydroxylamine Hydrochloride. Nonaqueous Method.—Following the anhydrous pyridine method,[10] various aniline products were recovered and identified as shown in Table IV. All reactions were carried out under reflux for about 2 hr. The hydrochlorides were washed with ethyl acetate and were treated usually with a 5% solution of Na_2CO_3 to liberate the aromatic amine. High yields of these amines were obtained indicating the magnitude of the cleavage.

Aqueous Method.—After dissolving 1.0 g. of IIb (toluidide) in a minimum of dilute hydrochloric acid, the clear solution was treated with a solution of 1 g. of $NH_2OH \cdot HCl$ and 1 g. of sodium acetate in 10 ml. of water. After 20 min. dilute NaOH was added. The oil which separated smelled like toluidine and solidified on chilling. About 70% of the theoretical amount of toluidine, m.p. 40–41°, was recovered.

Preparation of 5,5-Dimethyl-3-chlorocyclohex-2-en-1-one (V).—The method of Crossley and LeSeuer[12] was used in the preparation of this compound. From 60.0 g. (0.43 mole) of dimedone, 120 g. of chloroform, and 20.0 g. (0.145 mole) of phosphorus trichloride was obtained 42.3 g. (62.4%) of colorless product, b.p. 99–101° (14 mm.), $n^{25}D$ 1.4935, lit.[12] b.p. 109–111 (14 mm.). This product was shown to be pure by gas chromatography. The average yield in three runs was 61.5%. The yield was 75.6% if a ratio of 1 mole of dimedone to 1 mole of phosphorus trichloride was used. An acetone solution of V and sodium iodide did not precipitate sodium chloride even after standing at room temperature for 3 *months!* The infrared of V showed bands at 1681 (C=O) and 1616 (C=C) cm.$^{-1}$.

Treatment of V with Trimethylamine.—In a 200-ml. pressure bottle was placed 15.86 g. (0.10 mole) of V and 75 ml. (0.15 mole) of a 2 *M* solution of trimethylamine in toluene. The

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(23) C. Koelsch and H. Walker, *J. Am. Chem. Soc.*, **72**, 346 (1950), for example.

(24) D. F. Martin, *et al.*, *ibid.*, **83**, 73 (1961), and references therein.

bottle was sealed and heated in the steam bath 36 hr. During this time a light yellow solid precipitated. This solid was filtered, washed with toluene, and dried to yield 6.51 g. (0.059 mole) of a light yellow solid, m.p. 300°. This solid was recrystallized from acetonitrile; it showed no carbonyl band in the infrared, the spectrum indicating the presence of a quaternary salt. The analysis indicated that it was tetramethylammonium chloride.

Anal. Calcd. for $C_4H_{12}ClN$: C, 43.83; H, 11.05; Cl, 32.35. Found: C, 43.55; H, 10.94; Cl, 31.20.

The infrared spectrum of this product and an authentic sample of tetramethylammonium chloride (Eastman Kodak) were identical. The picrates were prepared (m.p. 314–315°) and were identical.[25]

The filtrate was subsequently steam distilled. The toluene and water phases were separated; the toluene layer was dried over anhydrous sodium sulfate and finally fractionated to yield 5.48 g. (0.035 mole) of the starting ketone V, b.p. 208° (635 mm.). It was identified through its infrared spectrum and through its vapor phase chromatogram.

The steam distillation pot was acidified to yield 2.59 g. of a yellow-brown solid, m.p. 148–149°, which was shown by infrared to be dimedone. On evaporation of the filtrate, 4.43 g. of additional solid was obtained. Recrystallization of these solids from acetone using decolorizing carbon yielded a white solid whose mixture melting point with authentic dimedone was undepressed.

Thus from 0.10 mole of V there was obtained 0.035 mole of unreacted V, 0.05 mole of dimedone, and 0.059 mole of tetramethylammonium chloride (91% yield). The yield was based on 0.065 mole of the starting chloro ketone (V). Very similar results were obtained from VI and trimethylamine. The analysis checked for $N(CH_3)_4Br$.

Treatment of V with Aniline.—To 7.93 g. (0.05 mole) of V in 50 ml. of benzene was added 10.0 g. (0.11 mole) of aniline. The mixture was refluxed 3 hr. On cooling to room temperature, the yellow hydrochloride was filtered off, 6.21 (38%). The hydrochloride was dissolved in 1 l. of boiling water and filtered into 300 ml. of 5% potassium hydroxide, whereupon a light yellow precipitate of the desired Schiff base of IVb was formed, 4.70 g., m.p. 180–185°. Recrystallization from 95% ethanol gave a product, m.p. 193–194° (lit.[11] m.p. 193–195°).

Treatment of the Schiff Base of IVb with Hydroxylamine.—A mixture of 1.45 g. (0.005 mole) of the Schiff base of IVb, 1.0 g. (0.015 mole) of hydroxylamine hydrochloride, 10 ml. of absolute ethanol, and 10 ml. of pyridine was refluxed 3 hr. and then cooled to room temperature. Evaporation of the solvent yielded a yellow-brown solid which was triturated with water, filtered, and recrystallized from aqueous ethanol to yield 1.45 g. of product, m.p. 190–192°. A mixture melting point with the starting anil showed no depression, and the infrared spectra were superimposable.

Oximation of V.—To 15.86 g. (0.10 mole) of V in 25 ml. of 95% ethanol was added a solution of 10.00 g. (0.145 mole) of hydroxylamine hydrochloride, and 12.00 g. (0.146 mole) of sodium acetate in 25 ml. of water. The solution was heated to boiling, enough 95% ethanol was added to produce miscibility, and then the solution was cooled to 0°. A white solid precipitated and was filtered, 9.46 g., m.p. 80–88°. On partial evaporation of the filtrate, a second crop of white solid was obtained, 1.46 g., m.p. 123–124°. On addition of water to the filtrate, 5.53 g. of a third crop of white crystals was obtained, m.p. 80–90°. Thus the total yield of oxime was 16.55 g. (95.2%). Fractional recrystallization of the first filtered product (m.p. 80–88°) from aqueous methanol yielded a product, m.p. 124–125°, and a more soluble isomer, m.p. 77.5–78.0°. The infrared spectrum of the higher melting isomer shows bands at 3367 (OH), 1639 (C═N), and 1631 (C═C) cm.$^{-1}$. The lower melting isomer exhibits bands at 3175 (OH), 1637 (C═N), and 1616 (C═C) cm.$^{-1}$.

Anal. Calcd. for $C_8H_{12}ClNO$: C, 55.33; H, 6.97; N, 8.07. Found (for *anti* isomer, m.p. 124–125°): C, 55.52; H, 7.01; N, 8.12. Found (for *syn-anti* mixture, m.p. 77.5–78.0°): C, 54.65; H, 7.18; N, 7.97.

Attempted Addition of Trimethylamine to V (*anti*) Oxime.—In a pressure bottle was placed 4.34 g. (0.025 mole) of V (*anti*) oxime, m.p. 123–124°, and 50 ml. (0.10 mole) of a 2 *M* solution of trimethylamine in toluene. The bottle was sealed and heated in the steam bath 24 hr. At the end of this time, the mixture was cooled to room temperature and flash evaporated to yield 4.21 g. of white solid, m.p. 121–122° (97.1% recovery). Recrystallization from aqueous methanol yielded a product, m.p. 123–124°. A mixture melting point with the starting oxime showed no depression.

Preparation of 5,5-Dimethyl-3-bromocyclohex-2-en-1-one (VI).—The method of Crossley and LeSeuer[12] was followed in this preparation. From 30 g. (0.214 mole) of dimedone and 20 g. (0.074 mole) of phosphorus tribromide was obtained 18.59 g. (42.85%) of colorless product, b.p. 115–118° (25 mm.), $n^{24.2}{}_D$ 1.5202 [lit.[12] b.p. 129° (25 mm.)]. The semicarbazone was prepared, m.p. 190° (lit.[12] m.p. 190°). The infrared spectrum exbits bands at 1695 (C═O) and 1616 (C═C) cm.$^{-1}$.

Oximation of VI.—To 10.15 g. (0.05 mole) of VI in 25 ml. of 95% ethanol was added a solution of 4.12 g. (0.06 mole) of hydroxylamine hydrochloride and 5.33 g. (0.065 mole) of sodium acetate in 25 ml. of water. The solution was cooled to 0°, whereupon two layers formed; on further cooling, crystallization occurred. The mixture was filtered, and the filtrate was evaporated to yield a total of 10.62 g. (97.5%) of product, m.p. 73–120°. Careful fractional recrystallization from methanol yielded the two isomeric oximes, one melting at 73–74°, the other at 123–124°. The infrared spectrum of the higher melting oxime (*anti*) exhibited bands at 3135 (OH) and 1621 (C═C) cm.$^{-1}$.

Anal. Calcd. for $C_8H_{12}BrNO$: C, 44.05; H, 5.55. Found (for *anti* oxime, m.p. 123–124°): C, 44.45; H, 5.54.

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(25) C. R. Hauser and D. N. Van Eenam, *J. Am. Chem. Soc.*, **79**, 6274 (1957).