[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

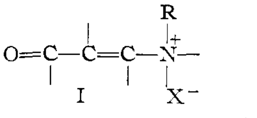
Unsaturated Amines. XIII. The Sites of Alkylation and Protonation in Certain Enaminoketones. Substituted Trimethinium Compounds from O-Alkylated Enaminoketones[1]

BY NELSON J. LEONARD AND JOE A. ADAMCIK[2,3]

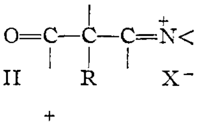
RECEIVED JULY 28, 1958

We have established that 5,5-dimethyl-3-N-pyrrolidylcyclohex-2-en-1-one (IV) forms O-alkylated products (XIII) on treatment with methyl and ethyl iodides. A study of the spectral and chemical properties of this representative O-alkylated enaminoketone (β-amino-α,β-unsaturated ketone) has now provided criteria which may be used to distinguish among O-, C- and N-alkylation of other enaminoketones. The site of protonation of an enaminoketone may also be determined to a limited extent in the solid salts (O- *vs.* C- or N-protonation) by comparison of the spectra of protonated with alkylated derivatives. The O-alkylated enaminoketones have provided a route to substituted trimethinium compounds (*e.g.*, XIV, XV, XVIII, XX), with the possibility of extensive variation in the structures produced.

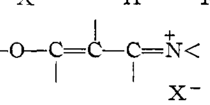
The problem of determining the site of alkylation would appear to increase progressively as one goes from an enamine $(>C{=}CN<)$[4] to a dienamine $(>C{=}CC{=}CN<)$[5] to an "enaminoketone"[6] or β-amino-α,β-unsaturated ketone[7] $(O{=}CC{=}CN<)$. Thus, treatment of a β-amino-α,β-unsaturated ketone, in which the nitrogen bears no hydrogen, with an alkyl halide (RX) may lead to N- (I), C- (II) and/or O-alkylation (III). Nevertheless, these possible structures should differ considerably in their spectral properties and in their susceptibility to hydrolysis and to attack by nucleophiles, and, if separable, should be distinguishable. Since undoubtedly the site of alkylation in an enaminoketone system will depend upon the steric requirement and the electronic character of both the alkyl halide and the substrate and upon the reaction conditions including solvent, temperature and time, we have concentrated our attention at the outset on the reaction of the methyl and ethyl halides with representative enaminoketones. Moreover, we have limited the conditions to prolonged heating of the substrate under reflux with an excess of the alkyl halide, reflecting the method usually employed to effect quaternization of a tertiary amine.


I

$$O{=}C{-}C{=}C{-}\overset{+}{N}(R){-}\quad X^-$$

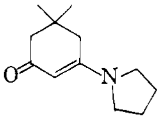

II

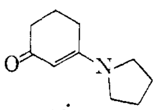
$$O{=}C{-}C(R){-}C{=}\overset{+}{N}<\quad X^-$$


III

$$R{-}O{-}C{=}C{-}C{=}\overset{+}{N}<\quad X^-$$

Prior to this investigation, we find examples of the C-alkylation of enaminoketones as employed in synthesis. Thus, A. and C. Combes[8] found that the action of methyl iodide on the product from acetylacetone and ammonia led to some C-methylation, since 3-methylpentane-2,4-dione was isolated from the reaction mixture.[9] The treatment of $CH_3COCH{=}CHNMe_2$ with methyl iodide in benzene led to a crystalline addition product from which Kochetkov[10] isolated $CH_3COC(CH_3){=}CHOH$ (17.5% yield) on treatment with hot water, indicating that C-methylation of the enaminoketone had occurred to at least this extent. More recently, this reaction has been extended to several other compounds without isolation of the intermediate salt. The alkylated ketoaldehydes (β-hydroxy-α,β-unsaturated ketones) were obtained in yields ranging from 22 to 52% after hydrolysis.[11] The preparation of N-alkylated salts of enaminoketones has been accomplished indirectly by the reaction of β-chlorovinylketones with tertiary amines.[12] It was felt that the methylation of 5,5-dimethyl-3-N-pyrrolidylcyclohex-2-en-1-one (IV)[13] and of 3-N-pyrrolidylcyclohex-2-en-1-one (V)[6] merited consideration since the evidence heretofore regarded as partially indicative of N-methylated structures in such cases has been their resistance to hydrolysis. There was no prior information in the literature pertaining to the stability of O-alkylated salts (III), and these might be less labile under hydrolysis conditions than previously expected or at least might not lead necessarily to diketone. The work presently described discloses the unusual properties of the O-alkylated salts of such enaminoketones as IV and V.


IV


V

---

[1] For preceding article in this series, see N. J. Leonard and D. F. Morrow, THIS JOURNAL, **80**, 371 (1958).

[2] Monsanto Chemical Co. Fellow, 1955–1956.

[3] National Science Foundation Fellow, 1956–1957.

[4] G. Stork, R. Terrell and J. Szmuszkovicz, THIS JOURNAL, **76**, 2029 (1954).

[5] J. L. Johnson, M. E. Herr, J. C. Babcock, R. P. Holysz, A. E. Fonken, J. E. Stafford and F. W. Heyl, *ibid.*, **78**, 430 (1956).

[6] J. J. Panouse and C. Sannié, *Bull. soc. chim. France*, 1374 (1956).

[7] N. H. Cromwell, *Chem. Revs.*, **38**, 83 (1946).

[8] A. and C. Combes, *Bull. soc. chim. France*, [3] **7**, 778 (1892).

[9] Related to the C-alkylation of β-amino-α,β-unsaturated ketones is the C-alkylation of β-amino-α,β-unsaturated esters, which has been examined sporadically over the course of many years; see (a) J. N. Collie, *Ann.*, **226**, 316 (1884); (b) R. Robinson, *J. Chem. Soc.*, **109**, 1038 (1916); (c) B. Mander-Jones and V. M. Trikojus, *J. Proc. Roy. Soc. N.S. Wales*, **66**, 300 (1932); (d) W. M. Lauer and G. W. Jones, THIS JOURNAL, **59**, 232 (1937); (e) G. Eglinton and M. C. Whiting, *J. Chem. Soc.*, 3052 (1953).

[10] N. K. Kochetkov, *Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk*, 47 (1954).

[11] N. K. Kochetkov, M. G. Ivanova and A. N. Nesmeyanov, *ibid.*, 676 (1956).

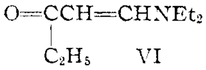
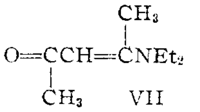
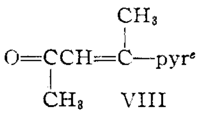
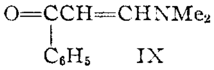
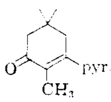
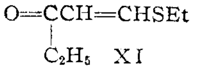
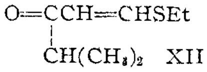
[12] V. T. Klimko, A. Ya. Khorlin, V. A. Mikhalev, A. P. Skoldinov and N. K. Kochetkov, *Zhur. Obshchei Khim.*, **27**, 62 (1957).

[13] R. C. Terrell, Ph.D. Dissertation, Columbia University, 1955; *Dissertation Abstr.*, **15**, 1176 (1955).

In addition to the known pyrrolidylcyclohexenones IV and V, we prepared 1-diethylamino-1-penten-3-one (VI- see Table I), by the addition of diethylamine to 1-pentyn-3-one[14]; 4-diethylamino-3-penten-2-one (VII), by the reaction of diethylamine with acetylacetone[8,15]; 4-N-pyrrolidyl-3-penten-2-one (VIII); β-dimethylaminoacrylophenone (IX)[16]; 2,5,5-trimethyl-3-N-pyrrolidylcyclohex-2-en-1-one (X), from 2,5,5-trimethylcyclohexane-1,3-dione and pyrrolidine; and the related β-alkylthio-α,β-unsaturated ketones, 1-ethylthio-1-penten-3-one (XI) and 1-ethylthio-4-methyl-1-penten-3-one (XII), by the addition of ethyl mercaptan to the corresponding acetylenic ketones.[17] The infrared absorption maxima of the aminoketones listed (Table I) follow the general pattern described earlier by Cromwell, Miller, Johnson, Frank and Wallace[18] for the double bond stretching region of β-amino-α,β-unsaturated ketones, the band at highest frequency representing C=O and the band between 1500 and 1600 cm.$^{-1}$ representing C=C (or possibly C–N) stretching. An additional band appears in examples VI and IX (*cf.* XI and XII), which bear hydrogen on the β-carbon.[19] It is considered that the series of carbonyl maxima (cm.$^{-1}$) for VI > VII > VIII > X > IV is consistent with the order of decreasing steric hindrance to electronic interaction between N and C=O acting through the carbon–carbon linkage. The higher carbonyl frequencies observed for the β-ethylthio-α,β-unsaturated ketones XI and XII are in the normal range (1685–1665 cm.$^{-1}$)[20] for α,β-unsaturated ketones and reflect the lower magnitude of interaction between sulfur and carbonyl through the α- and β-carbons. The order between nitrogen and sulfur is also maintained in comparing IV with a sulfur analog, 3-methylthiocyclohex-2-en-1-one, which has been reported by Bateman and Shipley[21] to have an infrared carbonyl maximum at 1655 cm.$^{-1}$.

TABLE I

SELECTED INFRARED ABSORPTION MAXIMA OF β-AMINO- AND β-ETHYLTHIO-α,β-UNSATURATED KETONES

Compound	ν_{max} 1500–1800 cm.$^{-1}$ region,[a] cm.$^{-1}$
 $O{=}\underset{C_2H_5}{C}CH{=}CHNEt_2$ VI	1664, 1616, 1574
 $O{=}\underset{CH_3}{C}CH{=}\overset{CH_3}{C}NEt_2$ VII	1643, 1540
 $O{=}\underset{CH_3}{C}CH{=}\overset{CH_3}{C}\text{—pyr}^{e}$ VIII	1623, 1535[b]
 $O{=}\underset{C_6H_5}{C}CH{=}CHNMe_2$ IX	1653, 1604, 1591 (phenyl), 1568
IV[d]	1607, 1560[b,c]
 X	1619, 1573
 $O{=}\underset{C_2H_5}{C}CH{=}CHSEt$ XI	1682, 1669, 1558
 $O{=}\underset{CH(CH_3)_2}{C}CH{=}CHSEt$ XII	1680, 1666, 1553

[a] Solution in CCl_4 (2%) unless otherwise stated. [b] Nujol mull. [c] Reported for a chloroform solution: 1610, 1560 cm.$^{-1}$,[13] [d] See text for formula. [e] pyr = N-pyrrolidyl.

The structure of "5,5-dimethyl-3-N-pyrrolidylcyclohex-2-en-1-one methiodide," m.p. 146–149.5° dec., was chosen as the starting point for the investigation of the alkylation of the enaminoketones because it could be obtained cleanly and in high yield (86%). The formulation as the N-methiodide is not tenable since it was found that the infrared absorption (Nujol mull) in the double bond stretching region consisted of strong bands at 1610 and 1587 cm.$^{-1}$. The N-methiodide structure I would be expected to absorb strongly above 1650 cm.$^{-1}$.[22] If this product of the treatment of 5,5-dimethyl-3-N-pyrrolidylcyclohex-2-en-1-one (IV) with methyl iodide were C-alkylated, the infrared spectrum would be difficult to predict since it could conceivably have any of the three structures corresponding to C-, N- or O-protonation. However, this possibility was easily eliminated by synthesizing unequivocally the C-methylated base, 2,5,5-trimethyl-3-N-pyrrolidylcyclohex-2-en-1-one (X). The perchlorate of this base melted at 179.5–180.5°, whereas the methiodide of IV was convertible to a methoperchlorate of m.p. 132–133°, which had infrared absorption similar to that of the methiodide in the 6 μ region. In addition to this differentiation, compound X was readily recovered from its perchlorate salt by addition of sodium hydroxide and immediate extraction with chloroform, whereas similar treatment applied to IV-methiodide yielded an entirely different product, discussed in the sequel.

The evidence against the N- and C-alkylated structures led to the tentative conclusion that the methiodide of IV was O-methylated, that is, N-(3-methoxy-5,5-dimethylcyclohex-2-en-1-ylidene)-pyrrolidinium iodide (XIIIa, R = CH_3). The corresponding perchlorate salt (XIIIc, R = CH_3) exhibited an ultraviolet absorption maximum at 286 mμ (ε 24,300) in 95% ethanol, consistent with the structure assigned and representing a slight bathochromic shift from the range of the maxima reported[5] for conjugated ternary iminium salts of the type $>C{=}\underset{|}{\overset{|}{C}}C{=}\overset{+}{N}<$: 274–278 mμ (ε > 20,000) in methanol. Structure XIIIa, R = CH_3, was also supported by the susceptibility of the compound to prolonged hydrolysis with hydriodic acid and by the nature of the product ob-

---

(14) K. Bowden, E. A. Braude, E. R. H. Jones and B. C. L. Weedon, *J. Chem. Soc.*, 45 (1946).

(15) K. von Auwers and W. Susemihl, *Ber.*, **63B**, 1072 (1930).

(16) E. Benary, *ibid.*, **63B**, 1573 (1930).

(17) K. Bowden, E. A. Braude and E. R. H. Jones, *J. Chem. Soc.*, 945 (1946).

18) N. H. Cromwell, F. A. Miller, A. R. Johnson, R. L. Frank and D.(J. Wallace, THIS JOURNAL, **71**, 3337 (1949).

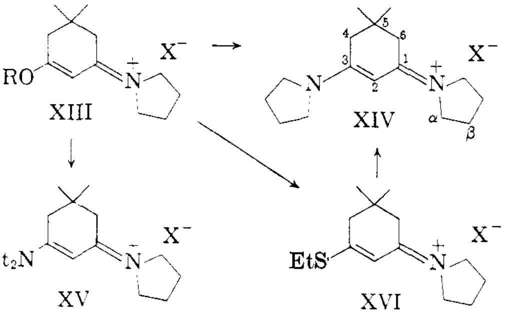
(19) No attempt was made to separate geometrical isomers in any case.

(20) L. J. Bellamy, "The Infra-red Spectra of Complex Molecules," Methuen and Co., Ltd., London, 1954, p. 114.

(21) L. Bateman and F. W. Shipley, *J. Chem. Soc.*, 1996 (1955).

(22) Conclusions based on mull spectra in this series appear to be safe and are supported by other physical and chemical properties.

tained from the treatment of IV-methiodide with aqueous sodium hydroxide and extraction with chloroform, namely, an iodide salt, $C_{16}H_{27}IN_2$, m.p. 203–205° dec., ν_{max}^{Nujol} 1545 cm.$^{-1}$ (broad, strong). The isolation of an iodide from chloroform in the presence of aqueous base was considered noteworthy. It was apparent that the ethiodide of 5,5-dimethyl-3-N-pyrrolidylcyclohex-2-en-1-one (IV), $C_{14}H_{24}INO$, m.p. 177–178.5° dec., ν_{max}^{Nujol} 1626, 1607 cm.$^{-1}$, had a structure (XIIIa, R = C_2H_5) similar to that of the methiodide. The ethoxyl determination (1 OC_2H_5) revealed this. In titration of the ethodide with standard alkali, the end-point drifted and the consumption of alkali was not complete. After standing at high *p*H the solution was back-titrated with standard acid, and a *p*K_a of 10.6 ± 0.1 (66% DMF) was observed for the conjugate acid of the basic (partial) hydrolysis product present (pyrrolidine). Treatment of the ethiodide of IV with aqueous sodium hydroxide and extraction of the solution with chloroform yielded some of the same $C_{16}H_{27}IN_2$ product obtainable from the methiodide. According to the elemental composition of the common product from the methiodide and ethiodide of IV, the compound was seen to be composed of one methone and two pyrrolidine residues. If postulated as N-(5,5-dimethyl-3-N′-pyrrolidylcyclohex-2-en-1-ylidene)-pyrrolidinium iodide[23] (XIVa), its formation may be rationalized logically on the basis of hydrolysis of a portion of the N-(3-methoxy(or ethoxy)-5,5-dimethylcyclohex-2-en-1-ylidene)-pyrrolidinium iodide (XIII) to alcohol, methone and pyrrolidine and nucleophilic attack by the pyrrolidine on unhydrolyzed alkiodide to form XIVa directly or after an intervening addition step. If this reaction course were correct, a facile reaction between XIII and pyrrolidine would be expected. It was found that combination of the two reactants in methanol caused the immediate evolution of heat, and both methiodide and ethiodide produced the substituted 1,3-bis-(N-pyrrolidyl)-trimethinium salt (XIV) in 92% yield. Compound XIII resembles the type of intermediate, an ethoxyvinylene quaternary salt, employed by Brooker and Sprague[24] for further condensation with substituted pyrrole to give a pyrrolocyanine dye.



a, X = I; b, X = Br; c, X = ClO_4

The following properties of the $C_{16}H_{27}IN_2$ compound, in addition to its mode of synthesis and the properties already given, confirm structure XIVa. The n.m.r. spectrum of the compound in a concentrated solution in chloroform[25] indicated the following chemical shifts, with respect to water, in parts per 10^8 (intensity ratios are also indicated): +336 (six CH_3 hydrogens), +246 (eight β-CH_2 hydrogens), +193 (four 4,6-CH_2 hydrogens), +91, +79 (eight α-CH_2 hydrogens), −53 (one =CH— hydrogen). Potentiometric titration with dilute sodium hydroxide failed to give evidence of any acid property. For the compound to behave as an acid, it would have to lose a proton from *carbon* (C-4 or the equivalent C-6) in the highly resonance-stabilized cation.[26] The ultraviolet spectrum (in 95% ethanol) of the perchlorate XIVc, formed from the iodide by treatment with aqueous perchloric acid, exhibited a maximum at 331 mμ (ϵ 47,000), with a shoulder at 325 mμ (ϵ 44,200), comparable—when one takes into account the bathochromic effect of the 1,3-alkylene chain—with the ultraviolet maximum of 1,3-bis-(dimethylamino)-trimethinium perchlorate, $(CH_3)_2NCH{=}CHCH{=}N^+(CH_3)_2ClO_4^-$, λ_{max}^{MeOH} 310 mμ (ϵ 49,200).[27–29] The infrared spectra (mull) of all the salts (XIVa, b, c) were transparent in the 3 μ region, and each exhibited a single strong broad band in the 5.5–6.5 μ region (1545, 1550 and 1561 cm.$^{-1}$, respectively).

The reaction of N-(3-methoxy-5,5-dimethylcyclohex-2-en-1-ylidene)-pyrrolidinium iodide (XIIIa, R = CH_3) with diethylamine furnished a $C_{16}H_{29}IN_2$ product which may be formulated with assurance as N-(3-diethylamino-5,5-dimethylcyclohex-2-en-1-ylidene)-pyrrolidinium iodide (XVa), closely analogous to XIVa. The broad infrared maximum at 1558 cm.$^{-1}$ for XVa and at 1556 cm.$^{-1}$ for the corresponding perchlorate XVc, coupled with the ultraviolet spectrum of the latter, λ_{max}^{EtOH} 332 mμ (ϵ 48,800), ~326 mμ (45,700), confirmed the assignment. Treatment of XIIIa, R = CH_3, with ethyl mercaptan (in the presence of a trace of sodium methoxide) yielded N-(3-ethylthio-5,5-dimethylcyclohex-2-en-1-ylidene)-pyrrolidinium iodide (XVIa), the assignment being based on the method of formation, analysis ($C_{14}H_{24}INS$), infrared (ν_{max}^{Nujol} 1619, 1568 cm.$^{-1}$) and ultraviolet spectra (λ_{max}^{EtOH} 333 mμ (ϵ 30,500), 228 mμ (ϵ 4560)) for XVIc, and titration with dilute alkali, with results similar to those observed for XIIIa

---

[23] We wish to express our appreciation to Dr. L. G. S. Brooker of the Eastman Kodak Co., Rochester, N. Y., for suggesting suitable names for some of the compounds which we have prepared.

[24] L. G. S. Brooker and R. H. Sprague, This Journal, **67**, 1869 (1945). It should be noted that S. Hünig, E. Benzing and E. Lücke, *Chem. Ber.*, **90**, 2833 (1957), have observed the *O-acylation* of enaminoketones.

[25] The instrument employed was a Varian Associates V-4300-B high resolution n.m.r. spectrometer with associated 12″ electromagnet system equipped with a VK-3506 flux stabilizer. A 40 mc. probe was employed. Audio-frequency side bands were generated with a Hewlett-Packard 200-CD audio oscillator.

[26] G. Schwarzenbach and K. Lutz, *Helv. Chim. Acta*, **23**, 1162 (1940), have reported *p*K 12.13 for the singly charged cation analogous to XIV but having the ethylamino moiety in place of the N-pyrrolidyl moiety on both sides of the ring. Their compound can lose a proton from *nitrogen*.

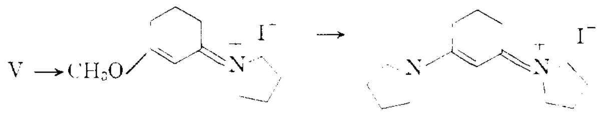
[27] G. Feniak, Ph.D. Thesis, University of Washington, 1955; *Dissertation Abstr.*, **15**, 974 (1955); also, Professor H. Dauben, University of Washington, private communication.

[28] For a theoretical treatment of the spectra of methinium salts in this series, see W. T. Simpson, *J. Chem. Phys.*, **16**, 1124 (1948); W. T. Simpson, This Journal, **71**, 754 (1949); S. P. McGlynn and W. T. Simpson, *J. Chem. Phys.*, **28**, 297 (1958).

[29] For recent reviews, see M. G. S. Dewar in Chem. Soc. Special Publ. No. 4, "Recent Advances in the Chemistry of Colouring Matters," 1956, p. 64; F. M. Hamer, *Quart. Revs.*, **4**, 327 (1950).

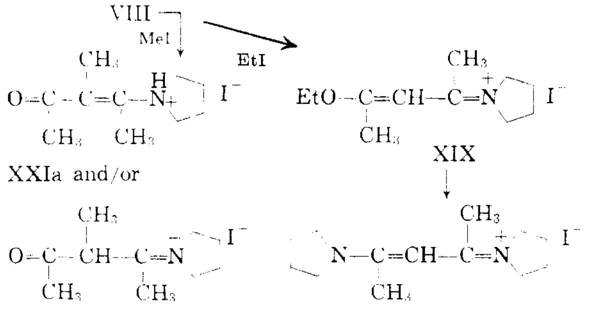
($R = C_2H_5$). Pyrrolidine reacted with the ethylthio compound XVIa in a manner similar to its replacement of the alkoxy group of XIII, with the formation of N-(5,5-dimethyl-3-N′-pyrrolidylcyclohex-2-en-1-ylidene)-pyrrolidinium iodide (XIVa) in excellent yield.

The methiodide of 3-N-pyrrolidylcyclohex-2-en-1-one (V) which had been made by Panouse and Sannié[6] was reinvestigated. The material could not be obtained pure, but treatment of the crude V-methiodide with pyrrolidine gave a $C_{14}H_{23}IN_2$ product in 64% yield, $\nu_{\max}^{\text{Nujol}}$ 1556 cm.$^{-1}$. The corresponding perchlorate had a comparable infrared maximum at 1556 cm.$^{-1}$ and an ultraviolet maximum at 328 mμ (ε 48,700), with an inflection at 320 mμ (ε 44,100), similar to XIVc. These data indicated that the $C_{14}H_{23}IN_2$ compound may be represented as N-(3-N′-pyrrolidylcyclohex-2-en-1-ylidene)-pyrrolidinium iodide (XVIII) and accordingly that the methiodide as prepared is O-methylated (therefore XVII, N-(3-methoxycyclohex-2-en-1-ylidene)-pyrrolidinium iodide) to the extent of at least 64%.



XVII XVIII

In the open-chain enaminoketone series, the reaction of 4-N-pyrrolidyl-3-penten-2-one (VIII) with ethyl iodide at the reflux temperature gave a viscous oil from which a $C_{11}H_{20}INO$ product, m.p. 113–114°, could be obtained in pure form (31% yield), $\nu_{\max}^{\text{Nujol}}$ 1587 cm.$^{-1}$. Treatment of this compound with pyrrolidine yielded $C_{13}H_{23}IN_2$ (70% yield), with spectra indicative of XX, N-(4-N′-pyrrolidyl-3-penten-2-ylidene)-pyrrolidinium iodide: $\nu_{\max}^{\text{Nujol}}$ 1553 cm.$^{-1}$ (transparent in the 3 μ region); $\lambda_{\max}^{\text{EtOH}}$ 342 mμ (ε 44,400), 218 mμ (18,100). The intermediate ethiodide (m.p. 113–114°) of 4-N-pyrrolidyl-3-penten-2-one is therefore N-(4-ethoxy-3-penten-2-ylidene)-pyrrolidinium iodide (XIX). By contrast, the major component of the product of treatment of VIII with methyl iodide at the reflux temperature was the C-methiodide. The crude product (97% yield) exhibited strong infrared bands at 3430 cm.$^{-1}$ (broad) and at 1728, 1662 and 1590 cm.$^{-1}$, the last of which corresponds to the maximum expected for the O-methiodide (XIX, Me in place of Et). This band disappeared and the other three remained after recrystallization from acetone, giving a $C_{10}H_{18}INO$ product, m.p. 116–119°. This purified material was shown to be at least partially the C-methiodide, that is the hydriodide of 3-methyl-4-N-pyrrolidyl-3-penten-2-one, by its hydrolysis to a product showing color tests for 3-methylpentane-2,4-dione as distinctive from acetylacetone. The infrared maxima, while suggestive of the form XXIb, do not rule out form XXIa as a constituent of the product studied. The differing results obtained with methyl iodide (< *ca.* 8% of O-methylated product) and ethyl iodide (31% of O-ethylated product) may have been due to steric considerations or may have reflected a temperature dependence since the reactions were carried out at the reflux temperature of each alkyl halide. This question has not been answered.



XXIa and/or XIX XXIb XX

Returning to the problem encountered in attempting to assign the structure of the salt XXI, it would appear that spectral information relating to the structure of the alkylated products of enaminoketones could also be applied to the problem of determining the structure of the protonated forms (I, II, III, R = H). Thus, the O-protonated salts (III, R = H) would be expected to show the same general band pattern in the 6 μ region as do the O-alkylated salts, *i.e.*, either two strong maxima near 1600 cm.$^{-1}$ or one strong maximum in this region, with no strong band in the region 1650–1800 cm.$^{-1}$. Although no accurate models are available, the C-protonated salt (II, R = H) would be expected to show a "normal" ketone and a "normal" ternary iminium salt band, both above 1650 cm.$^{-1}$ in wave number. N-Protonated salts (I, R = H) would be expected to show at least one and possibly two bands above 1650 cm.$^{-1}$. Differentiation between O-protonation on one hand and either C-protonation or N-protonation on the other hand should therefore be possible by an infrared examination of the solids. Significant infrared absorption bands of the protonic salts studied are given in Table II.

Examination of these data indicates that with the exception of 4-diethylamino-3-penten-2-one (VII) perchlorate (the corresponding pyrrolidine derivative formed a C-methiodide) these salts have no strong bands above 1650 cm.$^{-1}$ (for the 6–5.5 μ region) but show either one strong band near 1600 cm.$^{-1}$ or two strong bands, one above 1600 cm.$^{-1}$ and the other below. The hydriodide and perchlorate of 5,5-dimethyl-3-N-pyrrolidylcyclohex-2-en-1-one (IV), with their strong maxima at 1600 and 1957 cm.$^{-1}$, respectively (*cf.* XIIIa, c, $R = CH_3$), appear to exist mainly in the O-protonated form (XIIIa, c, R = H) in the solid state (in solution, pK_a' 3.15 (water), 3.6 (66% DMF)). The other bands cited are probably due to –O–H, their position depending upon the anion and any hydrogen bonding to the anion, as observed[30,31] for certain amine hydrohalides. In the case of the perchlorate of 1-diethylamino-1-penten-3-one (VI), which also appears to be essentially O-protonated (liquid film), the shoulder at 3400 cm.$^{-1}$ in the infrared spectrum may be an artifact since the salt could not be obtained in pure crystalline form and since no other salt absorbed in this region. The 2,5,5-trimethyl-3-N-pyrrolidylcyclohex-2-en-1-one

---

[30] B. Witkop, THIS JOURNAL, **76**, 5597 (1954).

[31] R. C. Lord and R. E. Merrifield, *J. Chem. Phys.*, **21**, 166 (1953).

TABLE II

SELECTED INFRARED ABSORPTION MAXIMA OF β-AMINO-α,β-UNSATURATED KETONE PROTONIC SALTS

Compound	$\nu_{\max}$, cm.$^{-1a}$
1-Diethylamino-1-penten-3-one perchlorate (VI-$HClO_4$)[b]	1635, 1590[c] 3400(sh, broad), 3130(broad)
4-Diethylamino-3-penten-2-one perchlorate (VII-$HClO_4$)	1713, 1672 no significant bands >3000
β-Dimethylaminoacrylophenone perchlorate (IX-$HClO_4$)	1644, 1578 3260, 1611(arom.?)
5,5-Dimethyl-3-N-pyrrolidylcyclohex-2-en-1-one hydriodide (IV-HI)	1597 3330(w, broad), 2610(w), 2550(w)
5,5-Dimethyl-3-N-pyrrolidylcyclohex-2-en-1-one perchlorate (IV-$HClO_4$)	1600 3140(mod. broad)
2,5,5-Trimethyl-3-N-pyrrolidylcyclohex-2-en-1-one perchlorate (X-$HClO_4$)	1619, 1573 3155(mod. broad)

[a] Nujol mull unless otherwise stated. [b] Liquid film. [c] Strong unless otherwise indicated (w = weak, sh = shoulder).

(X) perchlorate is like IV-perchlorate and thus assumed to be O-protonated. The spectrum of β-dimethylaminoacrylophenone (IX) perchlorate is complicated by the presence of the phenyl group and thus does not point clearly to the correct structure. By contrast, the perchlorate of 4-diethylamino-3-penten-2-one (VII) is shown by the spectrum clearly *not* to be O-protonated. Whether it is N-protonated and/or C-protonated remains open to question, since an $-\overset{|}{\underset{|}{N}}{}^{+}-H$ stretching vibration (3050 cm.$^{-1}$ for quinolizidine perchlorate) could be slightly shifted to lower frequency and hence be obscured by the C–H stretching bands. These examples may serve to illustrate some of the possibilities of ascertaining the site of protonation of an enaminoketone and some of the attendant difficulties.

Experimental[32]

1-Pentyn-3-ol.—The preparation from sodium acetylide and propionaldehyde followed the directions used for 1-hexyn-3-ol,[33] b.p. 121–124°, $n^{20}D$ 1.4330 (reported[34] b.p. 126–129°, $n^{18}D$ 1.4344).

4-Methyl-1-pentyn-3-ol was prepared similarly, substituting isobutyraldehyde for propionaldehyde, b.p. 131–133°, $n^{20}D$ 1.4365 (reported[35] b.p. 131–133°, $n^{20}D$ 1.4357). **The *p*-nitrobenzoate** was formed by the general procedure of Brewster and Ciotti[36]; colorless plates from aqueous ethanol, m.p. 57.5–58.5°.

Anal. Calcd. for $C_{13}H_{13}NO_4$: C, 63.15; H, 5.30; N, 5.67. Found: C, 63.21; H, 5.40; N, 5.53.

The 3,5-dinitrobenzoate was formed in the same manner as pale yellow plates from aqueous ethanol, m.p. 83–84°.

Anal. Calcd. for $C_{13}H_{13}N_2O_6$: C, 53.43; H, 4.14; N, 9.59. Found: C, 53.53; H, 3.84; N, 9.82.

1-Pentyne-3-one.—Oxidation of 1-pentyn-3-ol was effected by chromium trioxide and sulfuric acid,[33] b.p. 104–107°, $n^{20}D$ 1.4177 (reported[34] b.p. 105–107°, $n^{20}D$ 1.4188).

4-Methyl-1-pentyn-3-one was obtained similarly from 4-methyl-1-pentyn-3-ol, b.p. 117–118°, $n^{25}D$ 1.4170.

Anal. Calcd. for C_6H_8O: C, 74.97; H, 8.38. Found: C, 75.23; H, 8.55.

The 2,4-dinitrophenylhydrazone recrystallized from aqueous methanol as yellow needles, m.p. 138.5–139.5°.

Anal. Calcd. for $C_{12}H_{12}N_4O_4$: C, 52.17; H, 4.38; N, 20.28. Found: C, 52.18; H, 4.36; N, 20.02.

1-Ethylthio-1-penten-3-one (XI).—The method of synthesis employed was based on the general procedure of Bowden, Braude and Jones.[17] To 8.2 g. (0.10 mole) of 1-pentyn-3-one contained in a flask fitted with a condenser was added dropwise 6.2 g. (0.10 mole) of ethyl mercaptan in which a small piece of sodium had been dissolved. The reaction mixture was allowed to stand 72 hours and was filtered through glass wool. The filtrate was twice distilled at reduced pressure through a Holzman column; yellowish liquid, b.p. 117–118° (13 mm.), $n^{20}D$ 1.5352, yield 7.45 g. (52%).

Anal. Calcd. for $C_7H_{12}OS$: C, 58.29; H, 8.39. Found: C, 58.07; H, 8.45.

1-Ethylthio-4-methyl-1-penten-3-one (XII) was obtained similarly from 4-methyl-1-pentyn-3-one as a yellowish liquid, b.p. 120–121° (13 mm.), $n^{20}D$ 1.5259.

Anal. Calcd. for $C_8H_{14}OS$: C, 60.71; H, 8.92; S, 20.26. Found: C, 60.74; H, 9.15; S, 19.77.

1-Diethylamino-1-penten-3-one (VI) was prepared by the addition of diethylamine to 1-pentyn-3-one, similar to the synthesis of its homolog[14]; yellowish liquid, b.p. 121° (4 mm.), $n^{20}D$ 1.5282, yield 72%.

Anal. Calcd. for $C_9H_{17}NO$: C, 69.63; H, 11.04; N, 9.02. Found: C, 69.74; H, 11.16; N, 8.87.

The picrate was formed in ether and was recrystallized from ethyl acetate as short yellow needles, m.p. 75.5–76°.

Anal. Calcd. for $C_{15}H_{20}N_4O_8$: C, 46.87; H, 5.25; N, 14.58. Found: C, 47.19; H, 5.37; N, 14.53.

The perchlorate was formed in ether and proved to be an oil which was unstable. It deposited long needles of diethylamine perchlorate when allowed to stand. As the melting point of the **diethylamine perchlorate** was different from that previously reported (107°)[37] it was purified by recrystallization from ethyl acetate as colorless needles, m.p. 156.5–157.5°, and analyzed.

Anal. Calcd. for $C_4H_{12}ClNO_4$: C, 27.67; H, 6.97; N, 8.07. Found: C, 27.89; H, 6.90; N, 8.24.

Formation of diethylamine perchlorate from perchloric acid and diethylamine in ether gave material melting at 155.5–158°, undepressed upon admixture with the sample described above.

A sample of the oily **perchlorate of 1-diethylamino-1-penten-3-one** was prepared, rapidly washed with several portions of cold (*ca.* 0°) dry ether, dried 14 hours at 0° *in vacuo*, and analyzed.

Anal. Calcd. for $C_9H_{18}ClNO_5$: C, 42.27; H, 7.09; N, 5.48. Found: C, 43.10; H, 6.98; N, 4.78.

4-Diethylamino-3-penten-2-one (VII) was prepared from diethylamine and acetylacetone,[8,15] b.p. 116–117° (4 mm.), $n^{20}D$ 1.5429.

Anal. Calcd. for $C_9H_{17}NO$: C, 69.63; H, 11.04; N, 9.02. Found: C, 69.67; H, 11.00; N, 8.96.

The picrate was formed in ether and was recrystallized from ethyl acetate as yellow prisms, m.p. 94.5–96°.

Anal. Calcd. for $C_{15}H_{20}N_4O_8$: C, 46.87; H, 5.25; N, 14.58. Found: C, 47.35; H, 5.16; N, 14.90.

The perchlorate was formed in ether and was recrystallized from acetone as large, colorless prisms, m.p. 106–107°.

Anal. Calcd. for $C_9H_{18}ClNO_5$: C, 42.27; H, 7.09; N, 5.48. Found: C, 42.47; H, 6.92; N, 5.64.

The perchlorate was stable to recrystallization from hot water and also could be formed in water.

4-N-Pyrrolidyl-3-penten-2-one (VIII).—To a solution of 50 g. (0.50 mole) of acetylacetone in 100 ml. of ethyl ace-

---

[32] All melting points are corrected; boiling points are uncorrected. Microanalyses (C, H, N) were performed by Mr. Josef Nemeth and his associates of the University of Illinois. Sulfur analyses were performed by the Clark Microanalytical Laboratory, Urbana, Ill. The infrared spectra were determined by Mr. James Brader and Mr. Brian Clooney of the University of Illinois using a Perkin–Elmer model 21 double beam recording instrument, and the ultraviolet spectra by Miss Gerardine Meerman and Mr. Mou-shu Chao using a Cary recording spectrometer, model 11.

[33] K. Bowden, I. M. Heilbron, E. R. H. Jones and B. C. L. Weedon, *J. Chem. Soc.*, 39 (1946).

[34] F. D. Gunstone and R. M. Heggie, *ibid.*, 1437 (1952).

[35] V. Krestinskiĭ and V. Martin, *Ber.*, **60B**, 1866 (1927).

[36] J. H. Brewster and C. J. Ciotti, Jr., THIS JOURNAL, **77**, 6214 (1955).

[37] R. L. Datta and N. R. Chatterjee, *J. Chem. Soc.*, **115**, 1006 (1919).

tate was added in small portions 35.6 g. (0.50 mole) of pyrrolidine. The mixture was allowed to stand for 3 hours at room temperature, scratched to induce crystallization, and cooled in an ice-bath. The crude product which was collected weighed 58.9 g. (77% yield), m.p. 106–114°. A recrystallization from ethyl acetate gave pale yellow needles, and a further recrystallization from hexane yielded product of m.p. 115–116°.

Anal. Calcd. for $C_9H_{15}NO$: C, 70.54; H, 9.87; N, 9.14. Found: C, 70.87; H, 10.25; N, 9.22.

β-Dimethylaminoacrylophenone (IX) had been prepared previously by Benary,[16] m.p. 90–91.5°. **The perchlorate** was formed in ether and was recrystallized from ethyl acetate–acetone as pale yellow needles, m.p. 155.5–156°.

Anal. Calcd. for $C_{11}H_{14}ClNO_5$: C, 47.92; H, 5.12; N, 5.08. Found: C, 47.88; H, 5.14; N, 5.23.

5,5-Dimethyl-3-N-pyrrolidylcyclohex-2-en-1-one (IV).—The procedure used was based on that of Terrell,[13] involving the removal of water from a mixture of methone and pyrrolidine in refluxing benzene, using a Dean–Stark trap. Three recrystallizations from benzene–petroleum ether yielded pale yellow prisms, m.p. 131–133°. **The perchlorate** was formed in ether containing 5% ethanol and was recrystallized from ethanol–ethyl acetate as colorless needles, m.p. 179–180.5°; pK_a' 3.15 (water), 3.6 (66% DMF).

Anal. Calcd. for $C_{12}H_{20}ClNO_5$: C, 49.06; H, 6.86; N, 4.77; mol. wt., 293.75. Found: C, 48.97; H, 6.63; N, 4.89; mol. wt. (by titration), 293, 310.

The hydroiodide was formed in ether containing 7.5% ethanol and was recrystallized from methanol–ethyl acetate as colorless prisms, m.p. 201.5–205.5° dec.

Anal. Calcd. for $C_{12}H_{20}INO$: C, 44.87; H, 6.28; N, 4.36. Found: C, 45.40; H, 6.04; N, 4.13.

Recovery of 5,5-Dimethyl-3-N-pyrrolidylcyclohex-2-en-1-one from the Hydroiodide.—To a solution of 0.64 g. (0.0020 mole) of the hydroiodide (above) in 20 ml. of water was added 3.0 ml. of 10% aqueous sodium hydroxide. The mixture was extracted with four 4-ml. portions of chloroform, the chloroform solution was partially dried with Drierite, and the chloroform was removed on the steam-bath. The residue was recrystallized from ethyl acetate to yield 0.24 g. (62%) of 5,5-dimethyl-3-N-pyrrolidylcyclohex-2-en-1-one, m.p. 131–133°. Evaporation of the mother liquor yielded an additional 0.13 g. (34%).

2,5,5-Trimethyl-3-N-pyrrolidylcyclohex-2-en-1-one (X).—A mixture of 12.68 g. (0.082 mole) of 2,5,5-trimethylcyclohexane-1,3-dione[38] and 6.39 g. (0.090 mole) of pyrrolidine in 300 ml. of benzene was refluxed under a Dean–Stark trap for 6 hours. The benzene was removed at reduced pressure. The viscous residue was dissolved in 1.25 l. of ether, and 7.8 ml. of 70% perchloric acid (containing 0.090 mole) was added. The mixture deposited light brown crystals of impure perchlorate, m.p. 120–149.5°, yield 17.59 g. (70%). Recrystallization from methanol–ethyl acetate gave 9.53 g. (38%) of colorless crystals, m.p. 179–180°. A second crop (2.83 g., 11%) of less pure material, which had a light brown tint and melted at 178.5–180°, was obtained from the mother liquor. A second recrystallization yielded **perchlorate,** m.p. 179.5–180.5°.

Anal. Calcd. for $C_{13}H_{22}ClNO_5$: C, 50.73; H, 7.21; N, 4.55. Found: C, 50.67; H, 7.23; N, 4.48.

To a solution of 3.08 g. (0.01 mole) of the perchlorate in 200 ml. of water was added 15 ml. of 10% aqueous sodium hydroxide solution. The solution was then extracted repeatedly with chloroform, and the chloroform solution was partially dried over sodium sulfate. As much chloroform as possible was removed on the steam-bath, 20 ml. of hexane was added to the residual oil, and the hexane was removed on the steam-bath. The residual crystalline material weighed 1.78 g. (86% from the perchlorate) and melted at 78–79.5°. The 2,5,5-trimethyl-3-N-pyrrolidyl-cyclohex-2-en-1-one was recrystallized from hexane with decolorization, very pale yellow plates, m.p. 78–79.5°.

Anal. Calcd. for $C_{13}H_{21}NO$: C, 75.32; H, 10.21; N, 6.76. Found: C, 75.44; H, 10.16; N, 6.87.

"4-N-Pyrrolidyl-3-penten-2-one (VIII) Ethiodide."—A mixture of 15.3 g. (0.10 mole) of 4-N-pyrrolidyl-3-penten-2-one and 30 ml. of ethyl iodide was heated under reflux on the steam-bath. After about 15 minutes a second liquid phase began to separate. Heating was continued 4 hours, and most of the excess ethyl iodide was removed on the steam-bath. The residual viscous oil was washed with four 50-ml. portions of anhydrous ether, dissolved in 40 ml. of hot acetone, and ethyl acetate was added until the solution became slightly cloudy. The cloudiness was cleared by addition of a few drops of acetone, and the solution was allowed to cool. The crude material which crystallized weighed 23.5 g., m.p. 105–145°. It was stirred with 150 ml. of hot acetone, and the mixture was filtered. The undissolved material weighed 4.07 g., m.p. 233–249°, and recrystallization from methanol–ethyl acetate yielded colorless needles, m.p. 247–251° dec., with the composition $C_7H_{14}IN$ (see below). The acetone–ethyl acetate filtrate yielded a lower melting solid on addition of further ethyl acetate and cooling in the refrigerator for 3 hours; weight 13.0 g., m.p. 102.5–111°. Recrystallization from the same mixed solvent produced nearly colorless prisms having the elemental composition of an **ethiodide** (the O-ethiodide; see Discussion), m.p. 113–114°. When the melt was heated to about 140°, gas evolution was observed.

Anal. Calcd. for $C_{11}H_{20}INO$: C, 42.73; H, 6.52; N, 4.53. Found: C, 42.58; H, 6.54; N, 4.26.

The less soluble material described above was not fully characterized but the following infrared maxima may be cited (Nujol): 3450(s, broad), 2715(w), 2315(w), and 1687 (s) cm.$^{-1}$.

Anal. Calcd. for $C_7H_{14}IN$: C, 35.16; H, 5.90; N, 5.86. Found: C, 34.96; H, 5.96; N, 5.93.

"4-N-Pyrrolidyl-3-penten-2-one (VIII) Methiodide."—A mixture of 15.3 g. (0.10 mole) of 4-N-pyrrolidyl-3-penten-2-one and 30 ml. of methyl iodide was heated at reflux for 24 hours. The excess methyl iodide was removed at reduced pressure. The viscous oil that remained was induced to crystallize by cooling and scratching, and the solid was washed with dry ether and dried to yield 28.7 g. (97%) of very deliquescent material, m.p. 94.5–107°; $\nu_{\max}^{\text{Nujol}}$ 1728(s), 1662(s), 1590, 3430(s, broad) cm.$^{-1}$. Three recrystallizations from acetone yielded short thick colorless needles of the **methiodide,** m.p. 116–119° (deliquescent); $\nu_{\max}^{\text{Nujol}}$ 1727 (s), 1662(s), 3410(m, broad) cm.$^{-1}$. No maximum was observed at 1590 cm.$^{-1}$.

Anal. Calcd. for $C_{10}H_{18}INO$: C, 40.69; H, 6.15; N, 4.75. Found: C, 40.98; H, 6.42; N, 4.73.

This compound was shown to be the C-methiodide, that is, N-(3-methyl-2-oxopent-4-ylidene)-pyrrolidinium iodide and/or N-(3-methyl-2-oxopent-3-en-4-yl)-pyrrolidinium iodide, by hydrolysis. A solution in water was heated on the steam-bath for 10 minutes. Ether extraction followed by evaporation yielded an oil which gave a deep purple ferric-chloride test and a gray copper salt. The results of these tests agree with those reported[39] for 3-methylpentane-2,4-dione. They are typical for diketones, of the type RCO-CHR″COR′, whereas diketones of the type $RCOCH_2$-COR′ give a red ferric chloride test and a blue or green copper salt.[40] The 1590 cm.$^{-1}$ band in the crude methiodide as first formed, m.p. 94.5–107°, corresponds closely to the expected absorption of an O-methiodide (O-ethiodide, $\nu_{\max}$ 1587 cm.$^{-1}$), but this compound was not isolated in pure form.

"5,5-Dimethyl-3-N-pyrrolidylcyclohex-2-en-1-one Methiodide" (XIIIa, R = CH_3).—The procedure of Terrell[13] was employed, namely heating 10 g. (0.052 mole) of 5,5-dimethyl-3-N-pyrrolidylcyclohex-2-en-1-one under reflux for 16 hours with 50 ml. of methyl iodide. The reaction mixture was cooled in an ice-bath, filtered, and the pale yellow prisms were washed with ether; m.p. 146–148° dec., yield 15.0 g. (86%). Recrystallization from methanol–ethyl acetate gave material of m.p. 146–149.5° (dec., gas evolution) (reported[13] 144–150° dec.), $\nu_{\max}^{\text{Nujol}}$ 1610, 1587 cm.$^{-1}$.

"5,5-Dimethyl-3-N-pyrrolidylcyclohex-2-en-1-one Methoperchlorate" (XIIIc, R = CH_3).—To a solution of 1.0 g. (0.003 mole) of the methiodide in 20 ml. of water was added 3.3 ml. of 1 *N* perchloric acid. Recrystallization of the solid which separated gave 0.44 g. (48%) of long colorless needles, m.p. 132–133°; $\nu_{\max}^{\text{Nujol}}$ 1613, 1593 cm.$^{-1}$.

Anal. Calcd. for $C_{13}H_{22}ClNO_6$: C, 50.73; H, 7.21; N, 4.55. Found: C, 51.01; H, 7.13; N, 4.53.

---

[38] R. D. Desai, *J. Chem. Soc.*, 1079 (1932).

[39] C. R. Hauser and J. T. Adams, THIS JOURNAL, **66**, 345 (1944).

[40] G. T. Morgan, H. D. K. Drew and C. R. Porter, *Ber.*, **58B**, 333 (1925).

"5,5-Dimethyl-3-N-pyrrolidylcyclohex-2-en-1-one Ethiodide" (XIIIa, R = C_2H_5).—A mixture of 1.93 g. (0.01 mole of 5,5-dimethyl-3-N-pyrrolidylcyclohex-2-en-1-one and 20 ml. of ethyl iodide was heated under reflux for 2 hours. The reaction mixture was cooled in an ice-bath, filtered and the crystals were washed with ether; pale yellow needles, m.p. 176–177.5° (dec., gas evolution), yield 3.18 g. (91%). The material was recrystallized from methanol–ethyl acetate to yield nearly colorless needles, m.p. 177–178.5° (dec., gas evolution); $\nu_{\max}^{\text{Nujol}}$ 1626, 1607 cm.$^{-1}$.

Anal. Calcd. for $C_{14}H_{24}INO$: C, 48.14; H, 6.93; N, 4.01; OEt, 12.87. Found: C, 48.18; H, 7.21; N, 3.95; OEt, 13.25.

In electrometric titration with standard alkali, the end-point drifted, and the consumption of alkali was not complete. Back-titration after standing at high *p*H gave a *pK* value of 10.6 ± 0.1 (66% DMF).[41] The conjugate acid of pyrrolidine has pK_a' 10.6 in 66% DMF.

"5,5-Dimethyl-3-N-pyrrolidylcyclohex-2-en-1-one Ethobromide" (XIIIb, R = C_2H_5).—A solution of 9.66 g. (0.05 mole) of 5,5-dimethyl-3-N-pyrrolidylcyclohex-2-en-1-one in 150 ml. of ethyl bromide was heated under reflux for 48 hours. The solid which separated on cooling, m.p. 140.5–142.5° dec., yield 10.44 g. (69%), was recrystallized from methanol–ethyl acetate as short, colorless, deliquescent needles, m.p. 138.5–139.5° (dec., gas evolution); $\nu_{\max}^{\text{Nujol}}$ 1605, 1590 cm.$^{-1}$.

Anal. Calcd. for $C_{14}H_{24}BrNO$: C, 55.63; H, 8.00; N, 4.63. Found: C, 55.68; H, 8.04; N, 4.65.

N-(5,5-Dimethyl-3-N'-pyrrolidylcyclohex-2-en-1-ylidene)-pyrrolidinium Iodide (XIVa) from 5,5-Dimethyl-3-N-pyrrolidylcyclohex-2-en-1-one Methiodide and Pyrrolidine.—To a solution of 6.7 g. (0.020 mole) of methiodide in 10 ml. of methanol was added 1.7 g. (0.024 mole) of pyrrolidine, with the evolution of heat. Then 100 ml. of ethyl acetate was added and the solution was evaporated on the steam-bath to incipient cloudiness, cooled and filtered to yield 6.89 g. (92%) of nearly colorless needles, m.p. 203–205° dec., $\nu_{\max}^{\text{Nujol}}$ 1545 cm.$^{-1}$.

Anal. Calcd. for $C_{16}H_{27}IN_2$: C, 51.33; H, 7.27; N, 7.48. Found: C, 51.48; H, 7.14; N, 7.37.

A solution of 0.1445 g. of this compound in 25 ml. of water was titrated potentiometrically with 0.1031 *N* sodium hydroxide. No inflection was observed near the equivalence point, indicating the pK_a of this compound (mono-cation) is too high for determination by this method.

N-(5,5-Dimethyl-3-N'-pyrrolidylcyclohex-2-en-1-ylidene)-pyrrolidinium Iodide (XIVa) from 5,5-Dimethyl-3-N-pyrrolidylcyclohex-2-en-1-one Methiodide and Sodium Hydroxide.—To a solution of 0.67 g. (0.0020 mole) of the methiodide in 10 ml. of water was added 3.0 ml. of 10% aqueous sodium hydroxide. The mixture was extracted with four 4-ml. portions of chloroform, and the chloroform was removed on the steam-bath. To the residue was added 0.5 ml. of methanol and 5 ml. of ethyl acetate. The solution was evaporated to incipient cloudiness on the steam-bath, cooled and filtered to yield 0.26 g. (70% based on available pyrrolidine) of N-(5,5-dimethyl-3-N'-pyrrolidylcyclohex-2-en-1-ylidene)-pyrrolidinium iodide, identical with that prepared from pyrrolidine.

N-(5,5-Dimethyl-3-N'-pyrrolidylcyclohex-2-en-1-ylidene)-pyrrolidinium Iodide (XIVa) from 5,5-Dimethyl-3-N-pyrrolidylcyclohex-2-en-1-one Ethiodide.—The reaction of the ethiodide with pyrrolidine in the manner described for the reaction of the methiodide gave a 92% yield of N-(5,5-dimethyl-3-N'-pyrrolidylcyclohex-2-en-1-ylidene)-pyrrolidinium iodide. The reaction of the ethiodide with aqueous sodium hydroxide produced the same compound in 67% yield (based on pyrrolidine available).

N-(5,5-Dimethyl-3-N'-pyrrolidylcyclohex-2-en-1-ylidene)-pyrrolidinium Bromide (XIVb).—To a solution of 3.78 g. (0.0125 mole) of 5,5-dimethyl-3-N-pyrrolidylcyclohex-2-en-1-one ethobromide in 4 ml. of methanol was added 1.07 g. (0.0150 mole) of pyrrolidine. Heat was evolved. Ethyl acetate (40 ml.) was added to the solution, and it was evaporated on the steam-bath to incipient cloudiness, allowed to cool and filtered. The product was dried *in vacuo* for 6 hours at 56° as it held solvent (and water) tenaciously, m.p. 186–187.5°, yield 3.78 g. (92%). Five recrystallizations from methanol–ethyl acetate and drying for 24 hours at 56° *in vacuo* yielded colorless plates, m.p. 185.5–188°, $\nu_{\max}^{\text{Nujol}}$ 1550 cm.$^{-1}$, which was found to be slightly impure on the basis of the analysis.

Anal. Calcd. for $C_{16}H_{27}BrN_2$: C, 58.71; H, 8.32; N, 8.56. Found: C, 58.11; H, 8.20; N, 8.67.

N-(5,5-Dimethyl-3-N'-pyrrolidylcyclohex-2-en-1-ylidene)-pyrrolidinium Perchlorate (XIVc).—To a solution of 0.75 g. (0.0020 mole) of N-(5,5-dimethyl-3-N'-pyrrolidylcyclohex-2-en-1-ylidene)-pyrrolidinium iodide in 15 ml. of water was added 2.20 ml. of 1.0 *N* perchloric acid. The precipitate was isolated by filtration and was recrystallized from 50 ml. of water to yield 0.42 g. (61%) of colorless needles, m.p. 194.5–195.5°, $\nu_{\max}^{\text{Nujol}}$ 1561 cm.$^{-1}$.

Anal. Calcd. for $C_{16}H_{27}ClN_2O_4$: C, 55.40; H, 7.85; N, 8.08. Found: C, 55.39; H, 7.78; N, 7.87.

N-(3-Diethylamino-5,5-dimethylcyclohex-2-en-1-ylidene)-pyrrolidinium Iodide (XVa).—To a solution of 3.23 g. (0.0096 mole) of 5,5-dimethyl-3-N-pyrrolidylcyclohex-2-en-1-one methiodide in 5 ml. of methanol was added 0.85 g. (0.0117 mole) of diethylamine. The mixture was allowed to stand in a stoppered flask at room temperature for two days, 80 ml. of ethyl acetate was added, and the solution was evaporated to incipient cloudiness of the steam-bath and cooled. There was obtained 2.81 g. (78%) of product, m.p. 166–168.5° dec. An additional 9% of less pure material was obtained from the mother liquor. The product was recrystallized from methanol–ethyl acetate as colorless needles, m.p. 167–169° dec., $\nu_{\max}^{\text{Nujol}}$ 1558 cm.$^{-1}$.

Anal. Calcd. for $C_{16}H_{29}IN_2$: C, 51.07; H, 7.77; N, 7.44. Found: C, 51.47; H, 7.54; N, 7.60.

N-(3-Diethylamino-5,5-dimethylcyclohex-2-en-1-ylidene)-pyrrolidinium Perchlorate (XVc) was prepared by adding 0.30 ml. of 70% perchloric acid (containing 0.0035 mole) to a solution of 1.13 g. (0.0030 mole) of the iodide just described in 20 ml. of water. The solid was recrystallized from 45 ml. of water as colorless needles, m.p. 131.5–132.5°, yield 0.75 g. (72%), $\nu_{\max}^{\text{Nujol}}$ 1556 cm.$^{-1}$.

Anal. Calcd. for $C_{16}H_{29}ClN_2O_4$: C, 55.08; H, 8.38; N, 8.03. Found: C, 55.39; H, 8.31; N, 8.22.

N-(3-Ethylthio-5,5-dimethylcyclohex-2-en-1-ylidene)-pyrrolidinium Iodide (XVIa).—To a solution of 5.03 g. (0.015 mole) of 5,5-dimethyl-3-N-pyrrolidylcyclohex-2-en-1-one methiodide in 5 ml. of methanol was added 12.6 g. (0.20 mole) of ethyl mercaptan and 0.25 ml. of a solution of sodium methoxide (prepared by dissolving about 5 g. of sodium in 50 ml. of methanol). The flask containing the mixture was tightly stoppered and allowed to stand at room temperature for 4 days. Then 150 ml. of ethyl acetate and 4 ml. of methanol were added to the reaction mixture, and it was evaporated to incipient cloudiness on the steam-bath and allowed to cool. The product separated as pale yellow needles, m.p. 166.5–167.5° dec. The yield was 3.64 g. (66%). An additional 0.79 g. (14%) of material melting at 165–167° dec. could be obtained by evaporation of the filtrate. This compound was not allowed to remain in contact with its mother liquor for any longer time than necessary either after initial separation or upon recrystallization, as it developed an orange color when this precaution was not taken. The analytical sample was recrystallized from methanol–ethyl acetate as pale yellow needles, m.p. 160.5–166.0° dec; $\nu_{\max}^{\text{Nujol}}$ 1619, 1568 cm.$^{-1}$.

Anal. Calcd. for $C_{14}H_{24}INS$: C, 46.03; H, 6.62; N, 3.83; S, 8.78. Found: C, 46.46; H, 6.49; N, 3.93; S, 8.63.

N-(3-Ethylthio-5,5-dimethylcyclohex-2-en-1-ylidene)-pyrrolidinium Perchlorate (XVIc).—To a solution of 4.38 g. (0.012 mole) of the iodide described above in 60 ml. of water was added 15 ml. of 1.0 *N* perchloric acid. The precipitate was separated and recrystallized from 130 ml. of water to yield 3.05 g. (75%) of colorless needles, m.p. 177.5–178.5°; $\nu_{\max}^{\text{Nujol}}$ 1619, 1570 cm.$^{-1}$.

In electrometric titration with standard alkali, the end-point drifted, and the consumption of alkali was not complete. Back-titration after standing at high *p*H gave a *pK* value of 10.6 ± 0.1 (66% DMF).[40]

Anal. Calcd. for $C_{14}H_{24}ClNO_4S$: C, 49.77; H, 7.16; N, 4.15; S, 9.49. Found: C, 49.94; H, 7.11; N, 4.17; S, 9.89.

---

(41) We are indebted to Dr. Harold Boaz and Mr. Donald O. Wolff, Jr., of Eli Lilly and Co., Indianapolis, Ind., for making these data available to us.

Reaction of N-(3-Ethylthio-5,5-dimethylcyclohex-2-en-1-ylidene)-pyrrolidinium Iodide with Pyrrolidine.—To a solution of 0.91 g. (0.0025 mole) of N-(3-ethylthio-5,5-dimethylcyclohex-2-en-1-ylidene)-pyrrolidinium iodide in 1 ml. of methanol was added 0.21 g. (0.0030 mole) of pyrrolidine. A strong odor of ethyl mercaptan was noted. Ethyl acetate (10 ml.) was added, and the solution was evaporated to incipient cloudiness on the steam-bath and allowed to cool. The product was recrystallized from methanol–ethyl acetate, m.p. 201–204° dec., yield 0.89 g. (95%). The iodide salt was discovered (yellow) and was therefore converted to the perchlorate, colorless needles, m.p. 193.5–195.5°, identical with the authentic N-(5,5-dimethyl-3-N′-pyrrolidylcyclohex-3-en-1-ylidene)-pyrrolidinium perchlorate (XIVc).

Reaction of 5,5-Dimethyl-3-N-pyrrolidylcyclohex-2-en-1-one Methiodide with Dilute Hydroiodic Acid.—When a solution of 5,5-dimethyl-3-N-pyrrolidylcyclohex-2-en-1-one methiodide was heated under reflux for 30 minutes with 10% hydriodic acid, an 88% recovery of impure methiodide was realized. In a similar experiment in which the reaction time was increased to 24 hours the crude product, m.p. 110–148° dec., was recrystallized from methanol–ethyl acetate to yield 32% of material, m.p. 195–197° dec., which was shown to be somewhat impure 5,5-dimethyl-3-N-pyrrolidylcyclohex-2-en-1-one hydriodide by recovery of the base in 79% yield and its identity with the 5,5-dimethyl-3-N-pyrrolidylcyclohex-2-en-1-one described earlier.

N-(3-N′-Pyrrolidylcyclohex-2-en-1-ylidene)-pyrrolidinium Iodide (XVIII).—A solution of 6.61 g. (0.040 mole) of 3-N-pyrrolidylcyclohex-2-en-1-one,[6] m.p. 81–82°, in 40 ml. of methyl iodide was heated under reflux for 18 hours. A second liquid phase separated. The excess methyl iodide was removed on the steam-bath. The viscous oil could not be induced to crystallize either alone or from methanol–ethyl acetate solvent. The crude methiodide XVII was dissolved in 15 ml. of methanol, and 2.98 g. (0.042 mole) of pyrrolidine was added. Evolution of heat was observed. The solution was heated, and sufficient ethyl acetate (20 ml.) was added to produce cloudiness. A few milliliters of methanol cleared the solution. The solution was then evaporated on the steam-bath until separation of solid began. The product was separated by cooling and filtration, m.p. 251–252.5° dec., yield 7.54 g. (54%). An additional 1.36 g. (10%) of less pure material could be obtained from the mother liquor. This compound was recrystallized from methanol–ethyl acetate as pale yellow needles, m.p. 251–252° dec., $\nu_{\max}^{\text{Nujol}}$ 1556 cm.$^{-1}$.

Anal. Calcd. for $C_{14}H_{23}IN_2$: C, 48.56; H, 6.69; N, 8.09. Found: C, 48.69; H, 6.78; N, 7.96.

N-(3-N′-Pyrrolidylcyclohex-2-en-1-ylidene)-pyrrolidinium perchlorate was prepared by adding 0.30 ml. of 70% perchloric acid (containing 0.0035 mole) to a solution of 1.04 g. (0.0030 mole) of the iodide XVIII described in the preceding paragraph in 30 ml. of water. The precipitate was recrystallized from water as colorless needles, m.p. 231.5–233° dec., yield 0.71 g. (74%), $\nu_{\max}^{\text{Nujol}}$ 1556 cm.$^{-1}$.

Anal. Calcd. for $C_{14}H_{23}ClN_2O_4$: C, 52.74; H, 7.27; N, 8.79. Found: C, 52.93; H, 7.16; N, 8.89.

N-(4-N′-Pyrrolidyl-3-penten-2-ylidene)-pyrrolidinium Iodide (XX).—To a solution of 6.18 g. (0.020 mole) of 4-N-pyrrolidyl-3-penten-2-one ethiodide (XIX) in 50 ml. of acetone was added 1.70 g. (0.024 mole) of pyrrolidine. Evolution of heat was noted. The solution was warmed on the steam-bath, and 100 ml. of ethyl acetate was added. The product which separated was recrystallized from acetone–ethyl acetate as pale yellow needles, m.p. 144.5–146.0°, yield 4.70 g. (70%), $\nu_{\max}^{\text{Nujol}}$ 1553 cm.$^{-1}$.

Anal. Calcd. for $C_{13}H_{23}IN_2$: C, 46.71; H, 6.93; N, 8.38. Found: C, 46.91; H, 7.04; N, 8.26.

1,1′-*m*-Phenylenedipyrrolidine.—To a stirred mixture of 55.3 g. (0.40 mole) of anhydrous potassium carbonate and 10.81 g. (0.10 mole) of *m*-phenylenediamine in 200 ml. of absolute ethanol was added over a period of about 10 minutes 43.2 g. (0.20 mole) of 1,4-dibromobutane. The reaction mixture was stirred at the reflux temperature for 12 hours, cooled and filtered, and the salts were washed with ethanol. The filtrate was evaporated to a volume of about 60 ml., cooled and filtered. The crystals which were obtained were washed with ethanol and air-dried to yield 5.82 g. (27%) of colorless prisms of 1,1′-*m*-phenylene-dipyrrolidine, m.p. 92–93°. The salts were extracted repeatedly with boiling alcohol and the extracts were combined with the mother liquor. The alcohol was removed, and the residue (which solidified on cooling) was distilled through a Holzman column. The fraction boiling at 170–178° (1.6–2.0 mm.) constituted most of the distillate. It solidified on cooling and melted at 78–86°, yield 5.15 g. (24% additional). Recrystallization from ethanol gave colorless prisms, m.p. 92–93°. The infrared spectrum exhibited no N–H stretching absorption and was consistent with the structure assigned.

Anal. Calcd. for $C_{14}H_{20}N_2$: C, 77.73; H, 9.32; N, 12.95. Found: C, 77.98; H, 9.10; N, 12.95.

The physical properties observed did not agree with those previously reported by Yuryev *et al.*[42] These authors reported: b.p. 137–139° (8 mm.), $d^{20}{}_4$ 1.071, $n^{25}{}_D$ 1.5910. The only proof of structure was the molar refraction, nitrogen analysis, and method of synthesis. As the latter involved reaction of *m*-phenylenediamine with tetrahydrofuran over alumina at 400°, a procedure which might lead to complications, it was concluded that these authors did not have pure 1,1′-*m*-phenylenedipyrrolidine.

Infrared—$\overset{|}{\underset{|}{N}}{}^+$—H Stretching Frequency for a Tertiary Amine Perchlorate.—Quinolizidine perchlorate (Nujol) was found to exhibit a strong sharp band at 3050 cm.$^{-1}$.

---

[42] Y. K. Yuryev, L. E. Alexandrov, A. V. Arbatsky, V. M. Karatayev, I. K. Korobschyna and M. A. Pryanishnikova, *Zhur. Obshcheĭ Khim.*, **19**, 1730 (1949).

URBANA, ILL.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUKE UNIVERSITY]

Rates of Condensation of Sodio Ketones with Esters to Form Sodio β-Diketones in Ether Solution

BY DOUGLAS G. HILL, JOHN BURKUS[1] AND CHARLES R. HAUSER

RECEIVED JANUARY 13, 1958

Bimolecular rate constants were obtained for a number of acylations of sodio ketones with esters in dilute ether solution at 0 and 30°. The sodio ketones were prepared by means of sodium triphenylmethide. In general the rates of acylation of sodio methyl isobutyl ketone with various esters parallel qualitatively those reported for the alkaline hydrolysis of the esters. Evidence is presented for the intermediate formation of an addition product from the sodio ketone and ester. The formation of this intermediate is considered to involve the nucleophilic attack of the ketone anion on the carbonyl group of the ester within a coördination complex. A lithio ketone underwent acetylation more slowly than the corresponding sodio ketone.

The acylation of a methyl ketone with a methyl or ethyl ester to produce a β-diketone may be effected by means of a strong base such as sodium ethoxide, sodium amide or sodium triphenylmethide.[2] The reaction is called a Claisen condensation. The initial function of the base is to

---

[1] Du Pont Fellow, 1952–1953.

[2] See C. R. Hauser, F. W. Swamer and J. T. Adams, "Organic Reactions," Vol. VIII, John Wiley and Sons, Inc., New York, N. Y., 1954, Chapter 3.