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An Infrared Examination of the C=N Link in Some Hindered 1-Pyrrolines

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Received February 23, 1959

The spectra of a series of 1-pyrrolines containing a 3-isoalkylidene group have been investigated in the 6μ region to determine the effect of 2-substituents on the C=N band. It was observed that the C=N band did not shift in the expected manner when the 2-substituent was varied from hydrogen to alkyl to aryl. This is explained on the basis of out-of-plane twisting of the exocyclic alkylidene group and/or the 2-substituent.

A recent communication[1] described the synthesis of several new 1-pyrrolines containing an exocyclic double bond, from the sulfuric acid–catalyzed condensation of nitriles and di-tertiary glycols. The spectra of these compounds were discussed briefly with respect to the exact position of the C=N band. The spectral position of this link was determined by the stepwise reduction of the exocyclic double bond and the C=N link. Eight additional 1-pyrrolines of this type have since been prepared containing 2-substituents of various electronic and steric characteristics and these are considered (Table I) along with the original series. Comparison is also made with 1-pyrrolines prepared by other workers.

In simple 1-pyrrolines, containing only a 2-alkyl substituent, the C=N band lies in the 6.05–6.10μ region (compounds I–IV). 2,5,5-Trimethyl-2-thiazoline (V) is included in the table to show that its C=N link possesses similar absorption characteristics. When the 2-substituent is aromatic the C=N band is shifted, as expected, to longer wave lengths (VI–IX). Several 2-aryl-2-thiazolines (X–XII) are included and it can be seen that the presence of a cyclic sulfur linkage in place of the cyclic methylene linkage has little effect on the position of the C=N band.

Considering now the C=N absorption of the 2-substituted-3-isoalkylidene-5,5-dialkyl-1-pyrrolines (XIII–XXVIII) some interesting features regarding the structure of these compounds are brought into view. By comparing the C=N bands of the 2-H (XV), 2-CH_3 (XIII), 2-C_6H_5 (XVIII), and 2-CH=CH_2 (XXV) derivatives, it is seen that their respective values are 6.37 μ, 6.31 μ, 6.40 μ, and 6.41 μ. The relative constancy of the C=N band for the 2-H, 2-CH=CH_2, and 2-C_6H_5 groups may be interpreted to mean that the phenyl and vinyl groups are twisted away from coplanarity with the pyrroline ring thus minimizing their conjugative effects. The differences in the C=N absorption of the 2-H and 2-CH_3 compounds can also be considered due to the exocyclic double bond being forced out of the plane of the ring by the methyl group resulting in partial destruction of the conjugation effect. This argument is supported by employing molecular models which clearly show the interaction of the exocyclic double bond with all types of 2-substituents except hydrogen. Perhaps a more accurate explanation for the loss of the conjugation effect in these compounds lies in the possibility that both the 2-substituent and the exocyclic double bond are partially twisted away from coplanarity and the C=N band observed is the net result of this combined interaction.

Examination of Table I reveals that all the 2-aryl-5,5-dimethyl-1-pyrrolines (XVII–XXIV) exhibit the C=N band in the 6.36–6.40 μ region. In the case of the 2-vinyl-5,5-dimethyl-1-pyrrolines, those containing an exocyclic isopropylidene group (XXV–XXVI) also have a strong C=N absorption in the 6.41–6.43 μ region. However, when the exocyclic group is *sec*-butylidene (XXVII–XXVIII) the C=N band is shifted to considerably shorter wave lengths. This is explained on the basis of increased interaction of the 2-substituent with the exocyclic *sec*-butylidene group which can only arise if the exocyclic ethyl group is *cis* to the 2-substituent. This assumption is reasonable since if the ethyl group is *trans* to the 2-substituent, there should be little or no effect on the absorption of the C=N link. The effect of this type of interaction is seen to a lesser degree when the 2-substituent occupies a smaller radius as in the case of the 2-H and 2-CH_3 derivatives (XIII–XVI).[2]

If, as previously mentioned, the C=N band in 2-thiazolines can be considered to lie in the same position as correspondingly substituted 1-pyrrolines then it is noteworthy to mention that the C=N link in the, as yet unreported, 2-vinyl-1-pyrrolines should absorb in the 6.3-μ region as does the C=N link in 2-vinyl-5,5-dimethyl-2-thiazoline (XXIX). According to the data reported herein the vinyl group shifts the C=N absorption to longer wave lengths than a phenyl group. This indicates that an isolated double bond produces a larger conjugation effect on the C=N link than an aromatic system (compare compounds XI, VI, and XXIX).

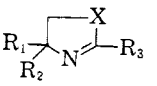
Further work on heterocyclic syntheses from nitriles is currently in progress and a wide variety of 2-thiazolines, 2-thiazines, and other *N*-heterocyclics are being prepared. This will also allow a

(1) A. I. Meyers and J. J. Ritter, *J. Org. Chem.*, **23**, 1918 (1958).

(2) See footnote *h*, Table I.

TABLE I

C=N AND C=C INFRARED BANDS



Compound	R_1	R_2	R_3	X	$\mu_{C=N}$	$\mu_{C=C}$
I	H	H	CH_3	$-CH_2-$	6.05[a]	
II	H	H	$CH_2C_6H_5$	$-CH_2-$	6.10[b]	
III	H	CH_3	CH_3	$-CH_2-$	6.05[a]	
IV	CH_3	CH_3	CH_3	$-CH-C(CH_3)_2$	6.06[c]	
V	CH_3	CH_3	CH_3	—S—	6.09[c]	
VI	H	H	C_6H_5	$-CH_2-$	6.18[d]	
VII	H	H	$4-CH_3OC_6H_4$	$-CH_2-$	6.20[b]	
VIII	H	H	$2-C_4H_3S$	$-CH_2-$	6.20[b]	
IX	H	H	$3-C_5H_5N$	$-CH_2-$	6.15[e]	
X	H	H	C_6H_5	—S—	6.19[f]	
XI	CH_3	CH_3	C_6H_5	—S—	6.19	
XII	H	H	$3-C_5H_5N$	—S—	6.20[g]	
XIII	CH_3	CH_3	CH_3	$C=C(CH_3)_2$	6.31	6.09
XIV	CH_3	C_2H_5	CH_3	$C=C(CH_3)(C_2H_5)$	6.28[h]	6.06
XV	CH_3	CH_3	H	$C=C(CH_3)_2$	6.37	5.98
XVI	CH_3	C_2H_5	H	$C=C(CH_3)(C_2H_5)$	6.35[h]	6.01
XVII	CH_3	CH_3	C_6H_5	$C=C(CH_3)_2$	6.40	6.07
XVIII	CH_3	CH_3	$4-CH_3C_6H_4$	$C=C(CH_3)_2$	6.40	6.04
XIX	CH_3	CH_3	$3-CH_3C_6H_4$	$C=C(CH_3)_2$	6.39	6.04
XX	CH_3	CH_3	$2-CH_3C_6H_4$	$C=C(CH_3)_2$	6.37	6.05
XXI	CH_3	CH_3	$4-O_2NC_6H_4$	$C=C(CH_3)_2$	6.37	6.04
XXII	CH_3	CH_3	$4-CH_3OC_6H_4$	$C=C(CH_3)_2$	6.38	6.08
XXIII	CH_3	CH_3	$3-C_5H_5N$	$C=C(CH_3)_2$	6.36	6.09
XXIV	CH_3	CH_3	$4-C_5H_5N$	$C=C(CH_3)_2$	6.36	6.06
XXV	CH_3	CH_3	$CH=CH_2$	$C=C(CH_3)_2$	6.41	6.09
XXVI	CH_3	CH_3	$(CH_3)C=CH_2$	$C=C(CH_3)_2$	6.39	6.07
XXVII	CH_3	C_2H_5	$CH=CH_2$	$C=C(CH_3)(C_2H_5)$[h]	6.29	6.08
XXVIII	CH_3	C_2H_5	$(CH_3)C=CH_2$	$C=C(CH_3)(C_2H_5)$[h]	6.28	6.11
XXIX	CH_3	CH_3	$CH=CH_2$	—S—	6.30	6.10

[a] G. G. Evans, *J. Am. Chem. Soc.*, **73**, 5230 (1951). [b] J. H. Burckhalter and J. H. Short, *J. Org. Chem.*, **23**, 1278 (1958). [c] A. I. Meyers and J. J. Ritter, *J. Org. Chem.*, **23**, 1918 (1958). [d] M. C. Kloetzel, J. L. Pinkus, and R. M. Washburn, *J. Am. Chem. Soc.*, **79**, 4222 (1957). [e] B. Witkop, *J. Am. Chem. Soc.*, **76**, 5597 (1954). [f] H. M. Randall, R. G. Fowler, N. Fuson, and J. R. Dangl, *Infrared Determination of Organic Compounds*, Van Nostrand, New York, 1949, p. 211. [g] W. Otting and F. Drawert, *Ber.*, **88**, 1469 (1955). [h] It can be seen that these compounds are capable of geometric isomerism. However, repeated distillation and several attempts at adsorption chromatography failed to produce more than one isomer. For compound XVI, only one sharp melting picrate salt was obtained (Table II) although several attempts were made to isolate its geometric isomer. It is therefore assumed that these compounds are free of geometric isomer or at best contain only a trace of this impurity.

continued study on the spectral position of the C=N link.

EXPERIMENTAL[3,4]

Infrared determinations. The method of purification of the heterocyclic compounds reported herein consisted of distillation through a 40-cm. Vigreux column packed with glass helices. All the spectra, except for the compounds listed in Table II, were obtained using a Baird Associates infrared recording spectrophotometer containing sodium chloride optics. The spectra of the compounds listed in Table II were obtained using a Perkin-Elmer, Model 21, infrared spectrophotometer equipped with a sodium chloride prism. Each compound was studied by using a 5–7% solution in carbon tetrachloride, except in the case of compounds XXI and XXIV whose spectra were determined in 5–7% chloroform solution.[5]

2-Substituted-3-isoalkylidene-5,5-dialkyl-1-pyrrolines. The compounds containing the isopropylidene group and those containing the *sec*-butylidene group were prepared from 2,5-dimethyl-2,5-hexanediol and 2,6-dimethyl-2,6-octanediol, respectively. Both glycols were obtained from the Air Reduction Chemical Co., Murray Hill, N. J., and used without further purification.

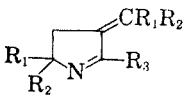
The preparation of a typical 1-pyrroline by this method is described as follows: 200 g. of concentrated sulfuric acid in a 500-ml. 3-necked round bottomed flask equipped with a dropping funnel, thermometer, and an efficient stirrer was cooled to 3° by means of an ice bath. The nitrile (0.25 mole) was added dropwise over a 0.5-hr. period. The temperature of the resulting clear colorless solution was kept at 8–10° while the glycol was added portionwise through a powder funnel. The addition of the glycol usually required 1.5–2 hr. The solution was stirred at 10–15° for an

(3) Microanalyses were performed by Dr. Alfred Bernhardt, Max-Planck Institüt für Kohlenforschung, Mulheim (Ruhr), Germany.

(4) Melting points and boiling points are uncorrected.

(5) In order to eliminate the possibility that the observed differences in absorption peaks are due only to differences in solvent and not to differences in structure, a representative group of heterocyclic bases (compounds XIV, XIX, XX, XXVI, and XXVIII) whose C=N bands were determined in carbon tetrachloride were also determined in chloroform. No significant shifts in the C=N band were observed.

TABLE II



R_1	R_2	R_3	Formula	B.P., °C.	mm. Hg	$n_D^{t°}$	Picrate	Calculated, % C	Calculated, % H	Found, % C	Found, % H
CH_3	CH_3	2—$CH_3C_6H_4$	$C_{16}H_{21}N$	108–110	3	1.5370^{23}	146–148[a]	84.5	9.2	84.3	8.5
CH_3	CH_3	3—$CH_3C_6H_4$	$C_{16}H_{21}N$	120–121	1	1.4805^{20}	124–125[b]	84.5	9.2	84.2	8.8
CH_3	CH_3	4—$CH_3C_6H_4$	$C_{16}H_{21}N$	121–122	0.7	1.5399^{20}	136–138	84.5	9.2	83.2[c]	8.7
CH_3	CH_3	H	$C_9H_{15}N$	90–91	30	1.4835^{17}	148–150[d]	78.8	10.9	78.8	10.5
CH_3	CH_3	—$C(CH_3)$=CH_2	$C_{12}H_{19}N$	86–88	5	1.4905^{20}	149–150	81.4	10.7	80.9	10.2
CH_3	C_2H_5	H	$C_{11}H_{19}N$	74–75	3	1.4940^{20}	117–118[e]	80.0	11.5	79.8	11.0
CH_3	C_2H_5	CH_3	$C_{12}H_{21}N$	62–64	2	1.4780^{17}	[f]	80.4	11.7	80.1	11.5
CH_3	C_2H_5	—CH=CH_2	$C_{13}H_{21}N$	88–90	10	1.4857^{21}	[f]	81.5	10.9	81.1	10.6
CH_3	C_2H_5	—$C(CH_3)$=CH_2	$C_{14}H_{23}N$	107–108	18	1.4868^{17}	[f]	81.9	11.1	81.8	10.8

[a] From aqueous picric acid and the pyrroline hydrochloride. [b] Mixture with picric acid melted at 85–112°. [c] Performed in duplicate; second result C, 82.9; H, 8.8. [d] With decomposition. [e] Mixture with picric acid melted at 82–108°. [f] Does not form a picrate.

additional hour at which time it was poured over 300–400 g. of chipped ice. The aqueous solution was extracted several times with chloroform and then neutralized with 30% sodium hydroxide solution. The alkaline solution was extracted several times with ether and the ethereal layer was dried overnight with anhydrous potassium carbonate. The ether was removed by a steam bath and the residue containing the heterocyclic base was distilled *in vacuo*.

Acknowledgment. This investigation was supported in part by a grant from Research Corporation. The author is indebted to R. T. O'Connor of the U. S. Department of Agriculture, Southern Regional Laboratories, for the infrared spectra.

NEW ORLEANS 22, LA.

[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY, PRINCETON UNIVERSITY]

Preparation and Solvolysis of Epi-ψ-cholesterol

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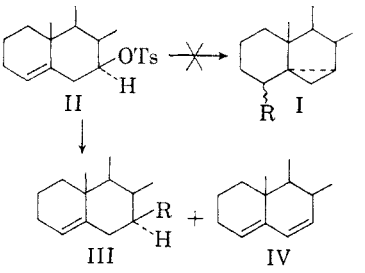
Received March 25, 1959

The preparation of cholest-4-en-7-one, epi-ψ-cholesterol, and epi-ψ-cholesteryl tosylate is discussed. Solvolysis of epi-ψ-cholesteryl tosylate under three different *i*-steroid-forming conditions afforded predominantly cholesta-4,6-diene with no evidence of a 5,7-cyclosteroid.

Recently Shoppee and co-workers[3,4] attempted to prepare a 5,7-cyclosteroid (I) by solvolyzing ψ-cholesteryl tosylate (cholest-4-en-7β-*p*-toluenesulfonate) (II), under a variety of *i*-steroid-forming conditions. In the reactions studied the major products were a 4,5 unsaturated, 7β-substituted steroid (III) (the 7 substituent depends upon the solvent used) and the conjugated diene, cholesta-4,6-diene (IV), with no observed ring B *i*-steroid formation. Also, an attempt by Shoppee[3] to prepare epi-ψ-cholesterol (cholest-4-en-7α-ol)



(XI), through the unknown cholest-4-en-7-one (X), proved to be unsuccessful.

In the present paper we would like to report the synthesis of cholest-4-en-7-one (X), epi-ψ-cholesterol (XI), epi-ψ-cholesteryl tosylate (XII), and the solvolysis of the latter under conditions in which *i*-steroids are known to be formed. The route used for the preparation of cholest-4-en-7-one (X) and epi-ψ-cholesterol (XI) may be seen below. Cholesteryl acetate (VI), by allylic oxidation with

(1) This article is based upon a dissertation by Gerald J. Kent in partial fulfillment of the requirements for the degree of Doctor of Philosophy at Princeton University.

(2) General Electric Fellow 1957–58.

(3) R. J. W. Cremlyn, R. W. Rees, and C. W. Shoppee, *J. Chem. Soc.*, 3790 (1954).

(4) C. W. Shoppee, G. H. R. Summers, and R. J. W. Williams, *J. Chem. Soc.*, 1893 (1956).