[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, LOUISIANA STATE UNIVERSITY IN NEW ORLEANS]

An Infrared Examination of the C=N Link in Dihydro-1,3-oxazines and Dihydro-1,3-thiazines[1]

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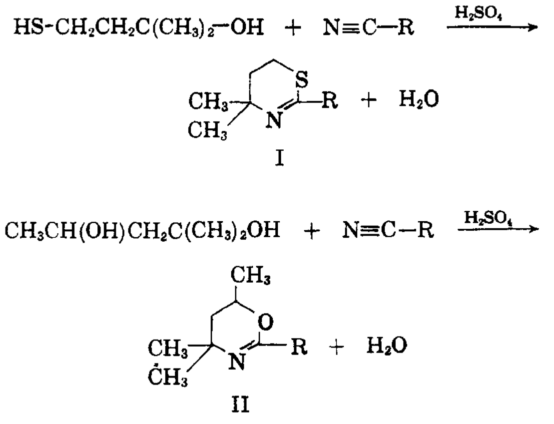
Received April 28, 1960

A series of dihydro-1,3-oxazines and dihydro-1,3-thiazines has been investigated with respect to the effects of various 2-substituents on the stretching frequency of the C=N link. It was observed that the C=N link in the thiazine derivatives exhibit a band at longer wavelengths than the C=N link in similarly substituted oxazines. This is attributed to the enhanced polarizability of the sulfur atom which effects a lower C=N bond order and results in a decrease in its stretching frequency.

As part of a continued study[2] on the spectral position of the C=N link in heterocyclic compounds, a series of previously unreported dihydro-1,3-thiazines (I) and dihydro-1,3-oxazines (II) was investigated. These heterocyclic bases were obtained *via* a new synthetic route[3] which involves the addition of various tertiary alcohol derivatives to a solution of nitriles in concentrated sulfuric acid.

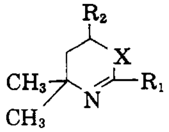


As a result of this ring closure reaction, the infrared spectra of sixteen heterocyclic compounds were examined and their absorption in the 6 μ region, which is the region containing the C=N stretching band, is given in Table I. Comparison of the oxazine and thiazine derivatives is made with respect to the influence exerted by the 2-substituent on their respective C=N linkages.

Table II contains the physical constants of several newly prepared oxazines to allow just comparison with all the correspondingly substituted thiazines. The physical constants for all other compounds used in this study have already been reported.[3,4]

TABLE I

INFRARED ABSORPTION OF THE C=N LINK IN DIHYDRO-1,3-THIAZINES AND DIHYDRO-1,3-OXAZINES



Compound	R_1	R_2	X	μC=N
III	CH_3	H	S	6.11
IV	C_2H_5	H	S	6.16
V	C_2H_5	CH_3	S	6.17
VI	$CH{=}CH_2$	H	S	6.32
VII	C_6H_5	H	S	6.22
VIII	2-$CH_3C_6H_4$	H	S	6.16
IX	4-$CH_3C_6H_4$	H	S	6.24
X	4-$H_2NC_6H_4$	H	S	6.25
XI	CH_3	CH_3	O	6.00
XII	C_2H_5	CH_3	O	6.01
XIII	CH_2CH_2CN	CH_3	O	6.00
XIV	$CH{=}CH_2$	CH_3	O	6.22
XV	C_6H_5	CH_3	O	6.10
XVI	2-$CH_3C_6H_4$	CH_3	O	6.04
XVII	4-$CH_3C_6H_4$	CH_3	O	6.09
XVIII	4-$H_2NC_6H_4$	CH_3	O	6.15

Examination of Table I reveals that the dihydro-1,3-thiazines (III–X) exhibit a single strong band in the 6 μ region. This region has been previously reported to contain the C=N stretching band in 1-pyrrolines,[2] 2-thiazolines,[5] dihydro-1,3-oxazines,[6] and other *N*-heterocyclic systems.[7] When the dihydro-1,3-thiazines containing 2-alkyl substituents (III–V) are considered, only one strong band in the 6.11–6.17 μ region appears. This is attributed to the stretching mode of the cyclic unconjugated C=N link. When the 2-substituent is the conjugated vinyl group (VI) a weak band at 6.14 μ and a strong band at 6.32 μ appears. These are

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(1) A portion of this work was presented at the 15th Southwest Regional Meeting of the American Chemical Society, Baton Rouge, La., Dec. 3–5, 1959.

(2) A. I. Meyers, *J. Org. Chem.*, **24**, 1233 (1959).

(3) A. I. Meyers, *J. Org. Chem.*, **25**, 1147 (1960).

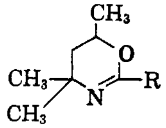
(4) J. J. Ritter and E. J. Tillmanns, *J. Org. Chem.*, **23**, 839 (1957); J. W. Lynn, *J. Org. Chem.*, **24**, 711 (1959).

(5) H. M. Randell, R. G. Fowler, N. Fuson, and J. R. Dangl, *Infrared Determination of Organic Compounds*, Van Nostrand, New York, 1949. p. 211; W. Otting and F. Drawert, *Ber.*, **88**, 1469 (1955). A. I. Meyers and J. J. Ritter, *J. Org. Chem.*, **23**, 1918 (1958).

(6) A. I. Meyers, *J. Org. Chem.*, **25**, 142 (1960).

(7) L. J. Bellamy, *The Infrared Spectra of Complex Molecules*, 2nd Ed., J. Wiley and Sons, Inc., New York, 1958, p. 268.

2-SUBSTITUTED 4,4,6-TRIMETHYL-5,6-DIHYDRO-1,3-OXAZINES



Compound	R_1	B.P.	mm.	n_D^{30}	Formula	Carbon, %		Hydrogen, %	
						Calcd.	Found	Calcd.	Found
XII	CH_2CH_3	67–68	20	1.4385	$C_9H_{17}NO$	69.67	10.96	69.62	10.91
XIII	CH_2CH_2CN	104–106	3.5	1.4544	$C_{10}H_{16}N_2O$	66.66	8.88	66.57	8.84
XVI	$2\text{-}CH_3C_6H_4$	118–119	1.3	1.5246	$C_{14}H_{19}NO$	77.41	8.75	77.32	8.68
XVII	$4\text{-}CH_3C_6H_4$	1.5	1.5	1.5403	$C_{14}H_{19}NO$	77.41	8.75	77.38	8.69
XVIII	$4\text{-}H_2NC_6H_4$	124–126[a]			$C_{13}H_{18}N_2O$	71.55	8.25	71.43	8.29

[a] Melting point. Recrystallized from 50% aqueous ethanol.

considered to represent the stretching frequency of the CH_2=CH and C=N linkages, respectively. As expected, the bond order and therefore the stretching frequency of the C=N link is lowered by virtue of its conjugation with the vinyl group.

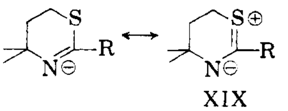
Substitution of an aromatic ring in the 2-position (VII–X) produces a shift of the C=N band to longer wave lengths than that observed for 2-alkylthiazines, but not as pronounced as the shift resulting from the introduction of the 2-vinyl group. The fact that the vinyl substituent produces a greater C=N bond shift than the aromatic substituent has been observed in several previous studies of this type.[2,5]

Another substituent effect which is plainly evident from the data in Table I is the fact that the C=N absorption for the 2-(*o*-tolyl)dihydrothiazine (VIII) appears at shorter wave lengths than it does for the 2-(*p*-tolyl) derivative (IX). This can be explained by considering the configuration of the molecule about the 2-position. For the *ortho* isomer there apparently exists considerable crowding between the methyl group and the thiazine ring and this would force the aromatic ring somewhat out of the plane of the thiazine ring. This results in partial destruction of the conjugative effect by making maximum *pi* electron overlap difficult. In the case of the *para* isomer, there exists no crowding between the phenyl substituents and the thiazine ring and this fact is obvious by comparing the C=N absorption of (VIII, II, and X).

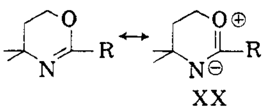
By examining the spectra of the dihydro-1,3-oxazines, only a single strong band is found for the 2-alkyl derivatives (XI–XIII) in the 6 μ region whereas several bands appear in this region for the aryl and vinyl derivatives (XIV–XVIII). However, for the latter compounds, only one strong band is observed which is much greater in intensity than any of its nearest neighbors. It is this strong band which is believed to arise from the stretching frequency of the C=N link. The other bands of intermediate intensity present for the aryl derivatives in the 6 μ region are undoubtedly due to the aromatic C=C vibrations.

Comparing the C=N absorption of the dihydro-1,3-oxazines the effects produced by their 2-substituents appear to closely parallel the effects produced by similar substituents in the thiazine series. Thus, a 2-vinyl group (XIV) causes the C=N band to shift to a greater extent than a 2-aryl group (XV–XVII) and an *ortho*-substituted aryl group (XVI) on the oxazine ring yields a C=N band at shorter wave lengths than that derived from a *para*-substituted (XVIII) or unsubstituted aryl group (XV).

The one major difference, seen in Table I, between the dihydro-1,3-oxazines and the dihydro-1,3-thiazines is clearly evident by the overall absorption at longer wavelengths by the latter group. If each dihydro-1,3-oxazine and dihydro-1,3-thiazine containing identical 2-substituents is compared, it is obvious that the C=N link in the latter compound has a lower stretching frequency. The differences in the spectral position of the C=N link for each pair of identically 2-substituted heterocycles is approximately 0.1 μ. This decrease in the bond order of the dihydro-1,3-thiazine C=N linkage is attributed to the enhanced polarizability of the divalent sulfur atom and therefore the significant contribution of the canonical structure, XIX, to the thiazine hybrid. This behavior has been previously observed in fluorine-containing thioesters in which the carbonyl stretching frequency is shifted towards longer wave lengths than the carbonyl frequency in oxygenated esters.[8]



XIX



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In the case of dihydro-1,3-oxazines, canonical forms such as XX must make little or no contribution to the hybrid and thus the bond character of the C=N link remains virtually unaltered. It is noteworthy to mention that the C=N link in unconjugated 1-pyrrolines containing a 2-alkyl group exhibits a single intense band[2,9] between 6.05–6.06 μ, whereas the dihydro-1,3-oxazines containing the same 2-alkyl group show a C=N band

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(8) M. Hauptschein, C. S. Stokes, and E. A. Nodiff, *J. Am. Chem. Soc.*, **74**, 4005 (1952).

(9) G. G. Evans, *J. Am. Chem. Soc.*, **73**, 5230 (1951).

at 6.00–6.01 μ (XI–XIII). If the Pauling electronegativities[10] of carbon (2.5) and oxygen (3.5) are considered, then it appears reasonable that the stronger electronegative element, oxygen, will "tighten" the C═N link by its inductive effect to a greater extent than the carbon atom. It has been found that for some cases group frequency shifts parallel electronegativities of the atoms concerned.[11] This fact is borne out herein when the 1-pyrrolines, dihydro-1,3-thiazines, and dihydro-1,3-oxazines are compared.[12]

In order to exclude the possibility that the comparison of the dihydro-1,3-thiazines and dihydro-1,3-oxazines reported herein is not valid because of the presence of a 6-methyl group in the oxazine system, a dihydro-1,3-thiazine containing a 6-methyl group (V) was compared with one not containing this substituent (IV). The C═N absorption of both these compounds revealed no significant differences.

EXPERIMENTAL[13,14]

All the infrared spectra were performed in a Perkin-Elmer 21 Recording Spectrophotometer using sodium chloride optics. All the samples were studied in a 5–7% solution in chloroform.

2-Substituted 4,4,6-trimethyldihydro-1,3-oxazines. The method of preparation of these compounds was taken from the procedure described by Ritter and Tillmanns.[4]

2-Ethyl-4,4,6-trimethyldihydro-1,3-thiazine (V). This compound was prepared by treating the corresponding dihydro-1,3-oxazine with phosphorus pentasulfide and the details are described in a previous communication;[3] b.p. 66–67° (1.5 mm.), n_D^{30} 1.4842, picrate, m.p. 113–114°.

2-Substituted 4,4-dimethyldihydro-1,3-thiazines. The experimental details describing the preparation of these compounds have recently been reported.[3]

Acknowledgment. The author wishes to express his gratitude to the National Institutes of Health (RG-6248) for funds granted to support a study of which the present work is a part.

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(10) L. Pauling, *The Nature of the Chemical Bond*, Cornell Univ. Press, Ithaca, New York, 1948, p. 60.

(11) See ref. 7, p. 394.

(12) It is considered reasonable here to compare a five-membered ring (1-pyrrolines) containing the C═N link with the two six-membered ring systems (oxazines and thiazines) since it has been found that 2-thiazolines containing the same 2-substituents as the dihydro-1,3-thiazines exhibited C═N absorptions in exactly the same spectral region. Compare data of thiazines given in Table I with data of thiazolines reported in ref. 2.

(13) All melting points and boiling points are uncorrected.

(14) Microanalyses performed by Alfred Bernhardt, Mulheim (Ruhr), West Germany.

[CONTRIBUTION FROM THE ORGANIC CHEMISTRY DIVISION, U. S. NAVAL ORDNANCE LABORATORY]

Absorption Spectra and Positions of Protonation of 2-Arylindoles

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Received April 14, 1960

Structure-spectra correlations are drawn for the 2-arylindoles. It is shown that substitution at the 3-position causes a "type 1" steric effect, substitution on the nitrogen a "type 2" steric effect. At the 4(6)- and 5-positions substituents exert electromeric effects and shift maxima accordingly. In acid media the spectra are consistent with the indoleninium salt structure (XXIV).

In order to lay the groundwork for a proposed study of the more complex spectral behavior of indole alkaloids related to alstoniline and sempervirine, it was deemed desirable to determine the ultraviolet spectra in neutral and acidic media of a number of 2-arylindoles and related compounds. These spectra were of interest *per se*, as they illustrated electronic and steric effects in this series and offered evidence regarding the position of protonation. In Table I are listed the positions and extinction coefficients of maxima and minima determined in the course of the present investigation.[1]

EXPERIMENTAL

Materials. 3-Phenylindole (II), 1-methyl-2-phenylindole (III) and 2-(*p*-biphenylyl)indole (XII) were kindly supplied to us by Dr. B. Witkop, National Institutes of Health. They had been prepared by the Fisher indole synthesis using polyphosphoric acid.[2] Dr. K. Schofield, Washington Singer Laboratories, Exeter, was good enough to furnish us a sample of 6-nitro-2,3-diphenlyindole (XI), prepared by the cyclization of desoxybenzoin *m*-nitrophenylhydrazone.[3] The compound had decomposed slightly on arrival, but a single recrystallization from ethanol gave a pure sample as orange crystals, m.p. 227° (lit.,[3] m.p. 225–227°). 2-Phenylindole (I) was commercially available from K. and K. Laboratories, Long Island City, N. Y. The material melted at 187.5–188° (lit.,[2] m.p. 187–188°) after one recrystallization from ethanol.

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(1) The method used to describe spectra conforms with the recommendations of the Editorial Board of Organic Electronic Spectral Data, Inc., J. D. Cawley and H. E. Ungnade, *Anal. Chem.*, 31, No. 2, 42A (1959).

(2) H. M. Kissman, D. W. Farnsworth, and B. Witkop, *J. Am. Chem. Soc.*, 74, 3948 (1952).

(3) D. W. Ockenden and K. Schofield, *J. Chem. Soc.*, 3175 (1957).