[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLLEGE OF PHARMACY, UNIVERSITY OF ILLINOIS]

Some Schiff Bases of *p*-Dimethylamino- and *p*-Diethylaminobenzaldehyde[1]

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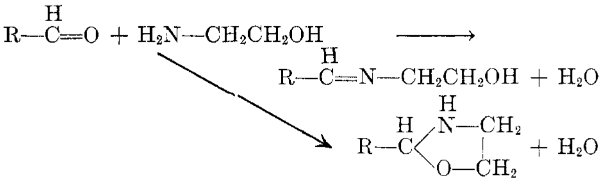
Fifteen new Schiff bases of *p*-dimethylamino- and *p*-diethylaminobenzaldehyde have been prepared. Infrared spectral studies were made on four Schiff bases of *p*-diethylaminobenzaldehyde.

Since the synthesis of Procaine in 1909,[3] its structure has been the prototype upon which the synthesis of hundreds of compounds has been based. In attempts to find an agent with a larger therapeutic index than Procaine, Adams and his group prepared aminophenyl-2-oxazoline,[4] aminophenyl-2-pentoxazoline,[5] and aminophenyl-2-oxazole.[6] The marked activity of these compounds as local anesthetics suggested that other closely related structures might exhibit similar physiological properties. The compounds resulted from the condensation of *p*-dimethylamino and *p*-diethylaminobenzaldehyde with various primary aminoalcohols and aminoethers could be visualized as the N-alkylated analogs of aminophenyl-2-oxazoline and aminophenyl-2-pentoxazoline.

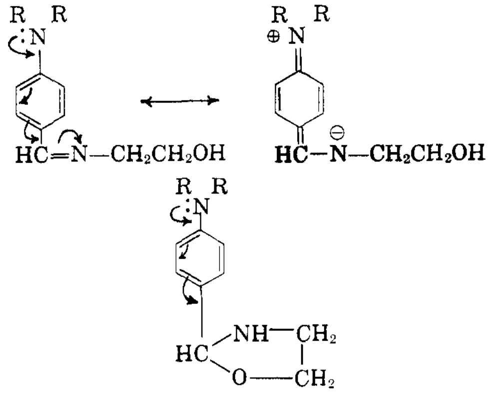
The condensation of an aromatic aldehyde with a primary aliphatic aminoalcohol can result in the formation of either the Schiff base or of the isomeric oxazolidine.[7]



It was necessary to determine whether our condensation products had the open Schiff base or the oxazolidine structure.

The chemical properties of the Schiff bases and of the oxazolidines are so similar that classical chemical methods of distinguishing between them are not successful. Physical methods such as infrared[8] and ultraviolet[9] spectroscopy, and molecular refraction[8,10] are used. Bergmann and his co-workers[7] have shown that aromatic aldehydes, like the *alpha, beta* unsaturated carbonyl compounds, tend to form Schiff bases rather than oxazolidines. They rationalized that *o*-methoxybenzaldehyde reacted with 2-aminoethanol to form the Schiff base, since the Schiff base can form an *ortho*-quinonoid resonance structure not possible in the case of the oxazolidine without cleavage of the hetero ring.

An analogous rationalization of the contribution of a *para*-quinonoid resonance structure might be applied to the condensation products of *p*-dimethylamino- and *p*-diethylaminobenzaldehyde with primary aminoalcohols and aminoethers. Here again, a quinonoid structure is not possible if the oxazolidine moiety is present.



Further evidence for the predominance of the Schiff base structure is demonstrated in the infrared spectra of the condensation products of *p*-diethylaminobenzaldehyde with 2-aminoethanol, 3-aminopropanol, 1-amino-2-propanol, and 2-amino-1-butanol. (The infrared spectral results for these compounds are listed in Table II.) The infrared spectra of oxazolidines may be expected to show the following:

1. The characteristic absorption due to the O—C—N system, a triplet of bands in the 1080–1200 cm.$^{-1}$ region (1149–1185, 1116–1139, 1080–1200 cm.$^{-1}$).[7]

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(1) Abstracted from a thesis submitted by Masumi Nakamichi to the Graduate College of the Chicago Professional Colleges of the University of Illinois in partial fulfillment of the requirements of the degree of Master of Science in Pharmaceutical Chemistry.

(2) Graduate Fellow in the Chicago Professional Colleges of the University of Illinois.

(3) A. Einhorn and E. Uhlfelder, *Ann.* **371**, 131 (1909).

(4) M. T. Leffler, and R. Adams, *J. Am. Chem. Soc.*, **59**, 2252 (1937).

(5) A. Novelli, and R. Adams, *J. Am. Chem. Soc.*, **59**, 2259 (1937).

(6) B. S. Friedman, M. Sparks, and R. Adams, *J. Am. Chem. Soc.*, **59**, 2262 (1937).

(7) E. D. Bergmann, *Chem. Revs.*, **53**, 309 (1953).

(8) E. D. Bergmann, E. Zimkin, and S. Pinchas, *Rec. trav. chim.*, **71**, 168 (1952).

(9) E. D. Bergmann, Y. Hirschberg, S. Pinchas, and E. Zimkin, *Rec. trav. chim.*, **71**, 192 (1952).

(10) E. D. Bergmann, E. Gil-Av, and S. Pinchas, *J.* **75**, *Am. Chem. Soc.*, 358 (1953).

TABLE I

SCHIFF BASES

Comp. No.	Primary Amine Used	Method Used	Yield, %	M.P. or B.P.	n_D^{20}	d^{27a}	Molecular Formula	N Analysis[b] Calcd.	N Analysis[b] Found
	N-(*p*-dimethylaminobenzylidene) derivatives of:								
I	2-aminoethanol[c]	A	57	103–104°			$C_{11}H_{16}N_2O$	14.57	14.33
II	3-aminopropanol	B	62	72–74°			$C_{12}H_{16}N_2O$	13.58	13.55
III	1-amino-2-propanol	A	67	98–99°			$C_{12}H_{16}N_2O$	13.58	13.55
IV	2-amino-1-butanol	A	25	70–71°			$C_{13}H_{20}N_2O$	12.72	12.72
V	2-methoxyethylamine	B	63	132–140° at 0.3 mm.	1.6052	1.049	$C_{12}H_{18}N_2O$	13.58	13.47
VI	3-methoxypropylamine	B	33	147–150° at 0.4 mm.	1.5892	1.016	$C_{13}H_{20}N_2O$	12.72	12.42
VII	3-isopropoxypropylamine	B	48	142–144° at 0.4 mm.	1.5680	1.076	$C_{15}H_{24}N_2O$	11.28	11.04
VIII	3-dimethylaminopropylamine	B	65	134–140° at 0.2 mm.	1.5870	1.073	$C_{14}H_{23}N_3$	18.01	17.62
	N-(*p*-diethylaminobenzylidene) derivatives of:								
IX	2-aminoethanol[d]	B	58	137–142° at 0.4 mm.	1.6253		$C_{13}H_{20}N_2O$	12.72	12.51
X	3-aminopropanol[d]	B	47	156–160° at 0.4 mm.	1.6120		$C_{14}H_{22}N_2O$	11.96	11.71
XI	1-amino-2-propanol[d]	B	39	56–57°			$C_{14}H_{22}N_2O$	11.96	12.06
XII	2-amino-1-butanol[d]	B	30	67–68°			$C_{16}H_{24}N_2O$	11.28	11.33
XIII	2-methoxyethylamine	B	70	132–138° at 0.3 mm.	1.5910	1.049	$C_{14}H_{22}N_2O$	11.96	11.75
XIV	3-methoxypropylamine	B	36	142–146° at 0.5 mm.	1.5818	1.036	$C_{16}H_{24}N_2O$	11.28	11.09
XV	3-isopropoxypropylamine	B	67	152–156° at 0.6 mm.	1.5600	0.975	$C_{17}H_{26}N_2O$	10.14	10.31
XVI	3-dimethylaminopropylamine	B	56	140–144° at 0.2 mm.	1.5755	0.976	$C_{16}H_{27}N_3$	16.08	15.94

[a] Density determination on a Fisher-Davidson Gravitometer. [b] Nitrogen analysis by a semi-micro Kjeldahl method. [c] This compound was listed in a table in reference (7) as an unpublished result of the work of E. D. Bergmann, E. Gil-Av, and S. Pinchas. [d] IR studies made.

TABLE II

INFRARED SPECTRAL RESULTS

Comp. No.	O—C—N System	Aromatic C=N System	Alcoholic System
IX	Absent No. 1116–1139 cm.$^{-1}$ band	C=N (STR)[a] 1641 cm.$^{-1}$	Primary alcohol OH (STR) 3240 and 3350 cm.$^{-1}$ Two maxima due to high intermolecular bonding with C=N C—O (STR) 1080 cm.$^{-1}$ region
X	Absent No. 1116–1139 cm.$^{-1}$ band	C=N (STR) 1639 cm.$^{-1}$	Primary alcohol OH (STR) 3300 cm.$^{-1}$ region C—O (STR) 1075 cm.$^{-1}$ region
XI	Absent No. 1116–1139 cm.$^{-1}$ band	C=N (STR) 1643 cm.$^{-1}$	Secondary alcohol OH (STR) 3540 cm.$^{-1}$ (unbonded) and 3230 cm.$^{-1}$ region (bonded) C—O (STR) 1080 cm.$^{-1}$ region
XII	Absent No. 1116–1139 cm.$^{-1}$ band	C=N (STR) 1639 cm.$^{-1}$	Primary alcohol OH (STR) 3590 cm.$^{-1}$ (unbonded) and 3220 cm.$^{-1}$ region (bonded) C—O (STR) 1080 cm.$^{-1}$ region

[a] STR = Stretching frequency.

2. Absence of the absorption due to the alcoholic hydroxyl group.

In contrast to this, the Schiff base would be expected to show:

1. Absorption due to the C=N system (1650 cm.$^{-1}$).[7,11]

2. Absorption due to the alcoholic hydroxyl group (3300 cm.$^{-1}$).[7,11]

The infrared spectra of our compounds showed excellent correlation with the spectra of Schiff bases and they differed markedly from those of oxazolidines. These Schiff bases might be considered to be the N-alkylated analogs of an open chain model of aminophenyl-2-oxazoline and aminophenyl-2-pentoxazoline.

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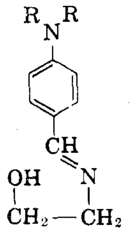
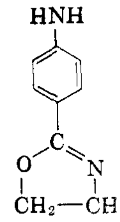
(11) G. E. McCasland, and E. C. Horswill, *J. Am. Chem. Soc.*, **73**, 3923 (1951).





Aminophenyl-2-oxazoline

EXPERIMENTAL[12]

Materials. *p*-Dimethylaminobenzaldehyde (m.p. 72–73°) and *p*-diethylaminobenzaldehyde (m.p. 38–39°) were prepared by the method of Duff.[13] All of the following reagents were used without further purification: 2-Aminoethanol was Eastman Reagent Grade. 1-Amino-2-propanol and 2-methoxyethylamine were Eastman Practical Grade. 3-Aminopropanol, 3-methoxypropylamine, 3-isopropoxypropylamine, and 3-dimethylaminopropylamine were furnished to us by the American Cyanamid Co. 2-Amino-1-butanol was furnished by the Commercial Solvents Corp.

Preparation of the Schiff base. A mixture of 0.1 mole of the *p*-dialkylaminobenzaldehyde, 0.12 mole of the primary amino compound, and 50 ml. of dry benzene contained in a Dean-Stark moisture determination apparatus was heated under reflux in an oil bath until the volume of water collected in the trap remained constant (2–3 hr.). The benzene was removed by distillation under reduced pressure, and the residual oil was poured onto an ice water mixture. If the organic layer solidified, Process A was used; if it did not, Process B was used.

Process A. The solid crystalline mass was triturated with cold water, collected on a suction filter, and washed on the filter with several portions of cold water. After drying the crystals on the filter by use of a rubber dam followed by air drying, the crude material was dissolved in boiling petroleum ether (b.p. 30–60°), treated with Norite A for 15 min., filtered, and the filtrate was cooled in an ice-water bath to induce crystallization. The crystals were collected on a suction filter and washed with several small portions of cold petroleum ether.

Process B. The organic layer was extracted with ether, and the ethereal solution was washed several times with cold water, the washings being discarded. After drying over anhydrous magnesium sulfate and filtering, the ether was removed on a steam bath. In some instances, the residual liquid solidified after standing at room temperature for several days, and the solid product was recrystallized from boiling petroleum ether as in Process A. If the liquid did not solidify, it was purified by distillation under reduced pressure.

Infrared spectra were recorded on a Perkin-Elmer Infrared Spectrophotometer Model 21, using a NaCl prism. A smear was used for the liquids and a 5% solution in CCl_4 was used for the solids.

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Chicago 12, Ill.

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[12] All melting points and boiling points are uncorrected.

[13] J. C. Duff, *J. Chem. Soc.*, **1945**, 276 (1945).

[Contribution from the Department of Chemistry of the University of Oregon]

Syntheses and Ultraviolet Spectra of 1-(5- and 8-Methyl-1-naphthyl)-1-cyclopentenes and 1-Cyclohexenes[1-3]

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Syntheses of the four 1-(5- and 8-methyl-1-naphthyl)cyclopentenes and cyclohexenes from 1-nitronaphthalene are described. The ultraviolet absorption spectral characteristics of these alkenes and of several 1,5- and 1,8-disubstituted naphthalene intermediates are presented and discussed.

In previous papers[4-6] we reported syntheses and ultraviolet absorption spectra of I, II, and their 2-naphthyl isomers as well as five derivatives (bearing methyl groups on the cycloalkenyl moiety) of these four parent naphthylcycloalkenes. The present paper extends these studies to four additional derivatives III–VI (bearing methyl groups on the naphthyl moiety).

The synthetic scheme for the 1,8-disubstituted naphthalenes III and IV is outlined herewith.

1-Nitronaphthalene was first nitrated *via* mixed acid to a mixture of 1,5- and 1,8-dinitronaphthalenes, resolved into its components by fractional crystallization. The latter isomer was reduced read-

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[3] Abstracted largely from the M.A. and Ph.D. dissertations of J. W. Sprague, University of Oregon, 1954 and 1955, respectively.

[4] L. H. Klemm and W. Hodes, *J. Am. Chem. Soc.*, **73**, 5181 (1951).

[5] L. H. Klemm and H. Ziffer, *J. Org. Chem.*, **20**, 182 (1955).

[6] L. H. Klemm, H. Ziffer, J. W. Sprague, and H. Hodes, *J. Org. Chem.*, **20**, 190 (1955).