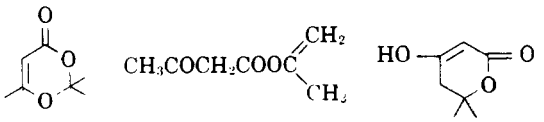

I II III

clusively that the structure is I, the 2,2-dimethyl-4-methyl-6-keto-1,3-dioxene.

The proton spectrum of the liquid adduct at room temperature under conditions of moderate resolution is given in Fig. 1A. Three absorption lines are present, with relative intensities of approximately 6:3:1 suggesting immediately that they arise respectively from the $C(CH_3)_2$, CH_3—C=C and C=CH—C groups of structure I. Structure II would be expected to have four lines with relative intensities of 3:3:2:2 and structure

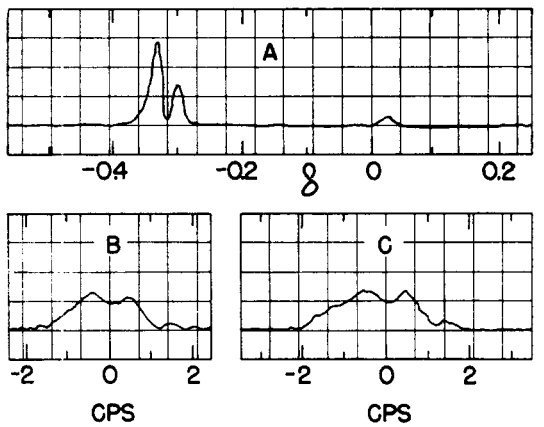

FIG. 1. THE PROTON MAGNETIC RESONANCE ABSORPTION spectrum of the liquid diketene-acetone adduct at room temperature, using a spinning sample with an effective volume of 0.02 ml. A. The entire spectrum under conditions of moderate resolution; the total sweep in magnetic field is 34 milligauss; sweep time, 10 sec. B and C. The line at a δ of -0.305 and the line at a δ of $+0.025$, respectively, under higher resolution. The intensity scale for C is one-fourth that for B.

III, which has also been considered,[2] four lines, 6:2:1:1. The δ-values, referred to H_2O, of the three lines observed are -0.335, -0.305, and $+0.025$, which agree very well with the characteristic absorption regions of CH_3—C, CH_3—C=C, and C=CH—C groups in compounds of known structure.[5] The enolic form of II is eliminated by similar arguments.

Conclusive support of structure I is afforded by the multiplet structure,[6] shown in Fig. 1B and 1C, exhibited under higher resolution by the lines assigned to the CH_3—C=CH—C protons. The CH_3 group resonance is a doublet while that of the C=CH—C group is a 1:3:3:1 quartet, as expected for a 3-proton system coupled to a single proton with a chemically shifted resonance.[6] Structure I is the only one in which such an interaction can occur. Moreover, the protons in the CH_3—C=CH=C group are "insulated" by six chemical bonds from the $C(CH_3)_2$ protons so there should be no splitting of the latter, again agreeing with experiment.

(6) H. S. Gutowsky, D. W. McCall, and C. P. Slichter, *J. Chem. Phys.*, **21**, 279 (1953).

EXPERIMENTAL

Sample. The commercially available diketone acetone adduct (Aldrich Chemical Company, Inc.) was carefully redistilled (b.p. 66.0–66.5°/2 mm.; n_D^{20} 1.464) a few days before the spectrum was observed. The spectra of samples several months old exhibited absorption in addition to that shown in Fig. 1, indicating a small amount of decomposition. There was no evidence in the spectrum of the newly distilled sample of other than the one component.

Procedure. The apparatus and experimental procedure were similar to those used earlier,[5] with some modifications described elsewhere.[7] The spectra were recorded at a fixed frequency of 17.735 Mc using the permanent magnet with a field of about 4165 gauss. The standard deviations of the measured δ-values are no more than ± 0.01.

Acknowledgment. We are indebted to G. A. Williams for his interest in this problem and for some preliminary experiments.

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(7) H. S. Gutowsky and C. H. Holm, *J. Chem. Phys.*, **24**, in press (1956).

Phenazine Syntheses. VI.[1] N-Methylphenazinium Methyl Sulfates

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In the course of investigating the activity of different classes of phenazines against Sarcoma 37, a number of water-soluble quaternaries were prepared by the action of dimethyl sulfate on various phenazines in nitrobenzene, following Kehrmann and Havas.[2]

In general, the base was dissolved in dry nitrobenzene in the proportion of 5 cc. of the solvent per gram of phenazine. Freshly-distilled dimethyl sulfate (1.5 cc. per gram of phenazine) was added to the solution when it had been heated slightly above 110° by means of an oil-bath at about 120°. The mixture was maintained at 105–110° for 5 minutes with stirring, then removed from the bath. The spontaneous precipitate was filtered off when the solution had cooled to room temperature, and was

(1) Paper V, *J. Org. Chem.*, **21**, 565 (1956).

(2) Kehrmann and Havas, *Ber.*, **46**, 343 (1913); *Cf.* Hillemann, *Ber.*, **71**, 37 (1938).

N-METHYLPHENAZINIUM METHYL SULFATES

From action of dimethyl sulfate on:	M.p.,[a] °C.	Crystalline form and color	Yield, %	Empirical Formula	Analyses[b] Carbon Calc'd	Carbon Found	Hydrogen Calc'd	Hydrogen Found
Benzo[*a*]phenazine (3)	167–170 (d)	Orange prisms	44	$C_{18}H_{16}N_2O_4S$	60.6	60.2	4.55	4.83
2-Bromophenazine (4)	147–150 (d)	Brown microcrystals[c]	22	$C_{14}H_{13}BrN_2O_4S$	43.7	43.5	3.42	3.57
2-Bromo-8-methoxyphenazine (5)	Not completely melted by 300°, though black	Brown microcrystals	40	$C_{15}H_{15}BrN_2O_5S$	43.4	43.4	3.64	4.01
2-Chlorophenazine (6)	144–148 (d)	Dark brown plates[d]	52	$C_{14}H_{13}ClN_2O_4S$	49.4	49.5	3.85	3.97
2-Chloro-7-ethoxyphenazine (7)	166–185 (d)	Short orange needles	30	$C_{16}H_{17}ClN_2O_5S$	50.0	50.5	4.45	4.74
2-Chloro-7-methoxyphenazine (7)	205–207 (d)	Dark orange rhomboids	50	$C_{15}H_{15}ClN_2O_5S$	48.6	48.7	4.08	4.16
2-Chloro-8-methoxyphenazine (7)	171–186 (d)	Short brown needles	45	$C_{15}H_{15}ClN_2O_5S$	48.6	48.3	4.08	4.30
2-Chloro-8-phenylphenazine (8)	145–150 (d)	Small orange prisms	29	$C_{20}H_{17}ClN_2O_4S$	57.6	57.8	4.11	4.26
2-Ethoxyphenazine (5)	164–166 (d)	Small orange plates	41	$C_{16}H_{18}N_2O_5S$	54.9	54.8	5.18	5.34
2-Fluorophenazine (4)	124–126 (d)	Brown microcrystals	35	$C_{14}H_{13}FN_2O_4S$	51.8	51.8	4.05	4.25
2-Iodophenazine (4)	140–153 (d)	Brown microcrystals	40	$C_{14}H_{13}IN_2O_4S$	38.9	38.8	3.03	3.41
1-Methylphenazine (8)	140–143 (d)	Brown plates[d]	39	$C_{15}H_{16}N_2O_4S$	56.2	55.9	5.04	5.13
2-Methoxyphenazine (6)	186–187 (d)	Yellowish-brown plates	47	$C_{15}H_{16}N_2O_5S$	53.6	53.8	4.79	4.89

[a] All melting points are corrected. [b] Analyses by the Microanalytical Laboratory of the National Institutes of Health, under the direction of Dr. W. C. Alford. [c] Precipitated by chilling. [d] Precipitated by ether.

freed from nitrobenzene by washing with anhydrous ether. Recrystallization was in all instances from absolute ethanol. The yields given in the table are of the spontaneous precipitates before recrystallization.

When the phenazines were negatively substituted, as by halogen, it was found advisable in a few instances to increase the temperature slightly, or to prolong the heating for 2 or 3 minutes in order to complete the reaction. In none of these longer and higher temperature runs with negatively substituted phenazines has there been observed any formation of the green complexes which result when unsubstituted phenazine is heated too high or too long with dimethyl sulfate.[2]

In most instances, the volume of nitrobenzene used has been such as to allow spontaneous precipitation of the quaternaries without the necessity for cooling the solutions below room temperature or diluting with anhydrous ether, although these measures have been used in a few instances, as shown in the table. It has not proved profitable to isolate additional amounts of the products by cooling or by dilution with ether, for the crude compounds so obtained generally require an inordinate amount of recrystallization before they are completely water-soluble.

No attempt has been made to determine which of the two nitrogens in the pyrazine ring bears the methyl group and the positive charge. In the instances of those phenazines with a substituent in the 1-position, spatial considerations more or less require the nitrogen atom which is farthest from the 1-substituent to be the quaternized one. It is not out of the question for the quaternaries in some instances to be mixtures of both types of compounds, *i.e.*, compounds in which either the 5- or the 10-nitrogen is quaternized.

In the table which follows, it should be emphasized that the "melting-points" given are really decomposition temperatures, since all of the quaternaries decompose on melting and undergo shrinking and darkening long before they melt. Hence too

(3) Witt, *Ber.*, **20**, 575 (1877).
(4) Vivian and Hartwell, *J. Org. Chem.*, **18**, 1065 (1953).
(5) Vivian, Hartwell, and Waterman, *J. Org. Chem.*, **19**, 1136 (1954).
(6) Waterman and Vivian, *J. Org. Chem.*, **14**, 289 (1949).
(7) Vivian, Greenberg, and Hartwell, *J. Org. Chem.*, **16**, 1 (1951).
(8) Vivian, Hartwell, and Waterman, *J. Org. Chem.*, **19**, 1641 (1954).

much significance should not be attributed to the temperatures of melting given, since these, as well as their limits, can be made to vary considerably by changes in the rate of heating.

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Phenazine Syntheses. VII.[1] Certain Disubstituted Phenazines

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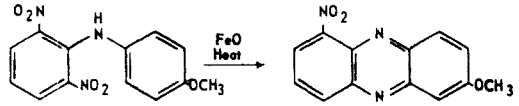
The compounds given in this paper continue the illustration of the applicability of ring closure through the nitro group to the synthesis of several types of phenazines. These compounds were prepared during the course of work directed toward the chemistry of vital stains.

One of the compounds described, 7-methoxy-1-nitrophenazine, is of special interest because its formation, although in lower than average yield, furnishes the first reported example of a ring closure by this method in which one nitro group remains unchanged:[2]



Another of the compounds reported, 2-chloro-8-N,N-dimethylaminophenazine, is an alternative intermediate for the preparation of 2-amino-8-N,N-dimethylaminophenazine, which can be modified to form a vital stain.[3] referred to in German usage as "Neutral Violet."

Slack and Slack[4] have reported the formation of 2,3-dimethoxyphenazine by the same method given herein, but do not give the melting point and analysis.

Another of the compounds included in this paper, 2,7-dibromophenazine, is also a known compound,[5] but has not been reported before as having been made by nitro-group ring closure.

EXPERIMENTAL[6]

7-METHOXY-1-NITROPHENAZINE

(*a*). *2,6-Dinitro-4'-methoxydiphenylamine.* A mixture of 25 g. of 1-chloro-2,6-dinitrobenzene,[7] 24 g. of *p*-anisidine, 37.5 g. of sodium acetate trihydrate, and 375 cc. of 95% ethanol was refluxed for 16 hours. The precipitate formed on cooling to room temperature was washed once with 125 cc. of ethanol, then with water, and air-dried. The dull, brick-red crude so obtained weighed 32.6 g. (91%), and on recrystallization from absolute alcohol formed small, yellowish-red needles, m.p. 171–173°.

Anal.[8] Calc'd for $C_{13}H_{11}N_3O_5$: C, 54.0; H, 3.81. Found: C, 53.9; H, 3.80.

(*b*). *7-Methoxy-1-nitrophenazine.* When a mixture of 1.0 g. of crude 2,6-dinitro-4'-methoxydiphenylamine, 1.3 g. of ferrous oxalate dihydrate, and 10 g. of granulated lead was heated in an open flask in an oil-bath at 250–262° for 20 minutes, no internal temperature rise above that of the bath occurred. Vacuum sublimation from the entire reaction mixture gave 0.15 g. of greenish-yellow needles, m.p. 235–236°.

Anal. Calc'd for $C_{13}H_9N_3O_3$: C, 61.2; H, 3.55. Found: C, 61.3; H, 3.61.

2-CHLORO-8-N,N-DIMETHYLAMINOPHENAZINE

(*a*). *4-Chloro-4'-N,N-dimethylamino-2-nitrodiphenylamine.* A mixture of 76.5 g. of N,N-dimethyl-*p*-phenylenediamine, 96.0 g. of 2,5-dichloronitrobenzene, and 90 g. of anhydrous sodium acetate was heated for 40 hours in an oil-bath at 195–210°. Steam-distillation to remove unchanged dichloronitrobenzene was followed by the addition of 100 cc. of HCl, and further steam-distillation until all acid was removed. Extraction of the residue with ether after air-drying gave about 60 g. of very crude, semi-soft product, which was nevertheless satisfactory for ring closure. Recrystallization from alcohol (Norit) gave brick-red microcrystals, m.p. 144–146°.

Anal. Calc'd for $C_{14}H_{14}ClN_3O_2$: C, 57.7; H, 4.84. Found: C, 57.6; H, 5.08.

(*b*). *2-Chloro-8-N,N-dimethylaminophenazine.* When 1.0 g. of the preceding crude compound was heated for 10–15 minutes with 1.3 g. of ferrous oxalate dihydrate and 10 g. of granulated lead, in an open flask immersed in an oil-bath at 250–260°, vacuum sublimation of the whole reaction mixture yielded 0.4 g. of crude product. Recrystallization from ethanol gave brownish-red needles of the 2-chloro-8-N,N-dimethylaminophenazine, m.p. 194–195°.

Anal. Calc'd for $C_{14}H_{12}ClN_3$: C, 65.3; H, 4.70. Found: C, 65.5; H, 4.92.

2,3-DIMETHOXYPHENAZINE[4]

(*a*). *4,5-Dimethoxy-2-nitrodiphenylamine.* A mixture of 20 g. of 4,5-dinitroveratrole,[9] 24.5 g. of aniline, and 40 cc. of absolute alcohol was refluxed for three weeks, and the unreacted material was removed by steam-distillation. Chromatography on alumina from a benzene solution gave 17.4 g. of dull red-orange crude product melting at 111–117°. Three recrystallizations from 95% alcohol gave orange needles, m.p. 120.5–121.5°, Lit.,[10] 91°.

Anal. Calc'd for $C_{14}H_{14}N_2O_4$: C, 61.3; H, 5.14; N, 10.2. Found: C, 61.5; H, 4.83; N, 10.2.

(*b*). *2,3-Dimethoxyphenazine.* A mixture of 2.0 g. of 4,5-dimethoxy-2-nitrodiphenylamine, 2.6 g. of ferrous oxalate dihydrate, and 20 g. of granulated lead gave 0.43 g. of crude 2,3-dimethoxyphenazine on vacuum sublimation after 15 minutes' heating in an oil-bath at 255–260°. During the reaction the internal temperature rose to a maximum of 320°.

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(1) Paper VI: Vivian, *J. Org. Chem.*, **21**, 822 (1956).

(2) Efforts to prepare 1-nitrophenazine by nitro group ring closure with 2,6-dinitrodiphenylamine have so far yielded no definite product.

(3) Vivian and Belkin, *Nature*, in press.

(4) Slack and Slack, *Nature*, **160**, 437 (1947).

(5) Bamburger and Ham, *Ann.*, **382**, 106 (1911).

(6) All melting points reported by the author are corrected.

(7) *Org. Syntheses*, **32**, 23 (1952).

(8) Microanalyses by the Microanalytical Laboratory of the National Institutes of Health, under the supervision of Dr. W. C. Alford.

(9) Erlich and Bogert, *J. Org. Chem.*, **8**, 331 (1943).

(10) Hughes, Lions, Maunsell, and Wright, *J. Proc. Roy. Soc. N. S. Wales*, **71**, 428 (1938).