too high temperature. This conclusion was verified by experimental elimination of hydrogen bromide from several substances brominated at low temperature and then warmed to 75°.

The practical application of the findings by the aeration procedure requires the use of bromination temperatures low enough to prevent excessive consumption of bromine by reactions other than addition, and thereby to prevent or minimize spontaneous cleavage of hydrogen bromide in excess of that actually due to substitution. Some substances brominate normally at 75°, others at room temperature, while others yield entirely meaningless results unless brominated near 0°, which for some substances is perhaps still too high a temperature. The new procedure permits the necessary temperature regulation, and appears to be unique in that it permits bromination at elevated temperature and avoids complications due to contact of water, iodide and iodate with the brominated sample. There is now under investigation a new aeration apparatus designed to effect bromination with a minimal excess of bromine, thus decreasing the quantity of bromine to be transferred by aeration and shortening the analysis, especially when low temperatures are used.

Philadelphia, Pennsylvania

[Contribution from the Chemical Laboratories of the College of Liberal Arts of Northwestern University and of the School of Chemistry and Physics of the Pennsylvania State College]

PSEUDO BASES. I. CERTAIN N-METHYLPYRAZINIUM SALTS AND THEIR CORRESPONDING BASES

By John G. Aston

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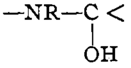
The work of Hantzsch and of Decker[1] has demonstrated that a quaternary base of the type $[-N^+ R{=}C<]\ OH^-$ in which the N=C grouping is part of a closed ring (*e. g.*, N-methylpyridinium hydroxide) may exist in two tautomeric modifications. One of these with the formula written above is a quaternary ammonium compound and therefore in aqueous solution necessarily a strong electrolyte.[2] The other weakly basic modification has the formula  $-\mathrm{NR}-\underset{\mathrm{OH}}{\underset{|}{\mathrm{C}}}<$ and has been called by Hantzsch a "pseudo base;" it is a tertiary amine and has, to a certain extent, the properties of a carbinol. We shall speak of the equilibrium mixture between these two forms as a "pseudo basic system."

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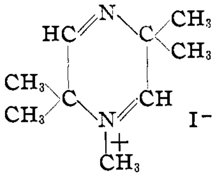
[1] Hantzsch and Kalb, *Ber.*, **32**, 3109 (1899); Decker, *J. prakt. Chem.*, **192**, 425 (1911).

[2] Lewis, "Valence and the Structure of Atoms and Molecules," The Chemical Catalog Company, New York, 1923, p. 111.

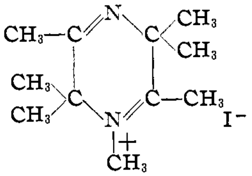
Although certain evidence regarding the properties of and the equilibrium between the two forms has been obtained in the case of some N-methylated pyridines, quinolines and acridines and of cotarnine and berberine,[1] wider information upon a variety of simpler compounds is necessary in order to make any generalizations regarding the effect of structure on the properties of a pseudo basic system.

In order to study the effect of ring conjugation in such a system it was decided to prepare and investigate certain pyrazine derivatives in which a pseudo basic system formed part of the pyrazine nucleus and to study the effect of reduced conjugation caused by partial hydrogenation of the nucleus.

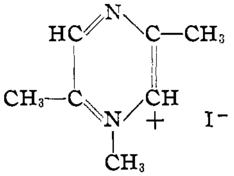
Two salts, 1,2,2,5,5-pentamethyldihydropyrazinium iodide (Formula I) and 1,2,2,3,5,5,6-heptamethyldihydropyrazinium iodide (Formula II) were prepared by the action of methyl iodide on the corresponding dihydropyrazines.



I



II



III

In addition, 1,2,5-trimethylpyrazinium iodide (Formula III), already described by Stoehr,[3] was prepared and studied. Bases were prepared from these salts by the action of potassium hydroxide.

A quarternary salt of the general type $\left[R{-}N{=}C{-}CH_2R\right]^+ X^-$ in which the dotted line represents the rest of a cyclic system, might yield the true base, A, $\left[R{-}N{=}C{-}CH_2R\right]^+ OH^-$ or the pseudo base, B, $R{-}N{-}C(OH)CH_2R$. The pseudo base might lose water to form C, $R{-}N{-}C{=}CH{-}R$, or D, $\left[R{-}N{-}C(CH_2R){-}\right]_2O$. In addition the pseudo base may split at the N—C linkage to form E, $RNH\ \ COCH_2R$. The form C can also be formed directly from the true base A by a type of change discussed later. A base of the general formula D was obtained by Hantzsch and Kalb[1] as an anhydride of N-methylquinolinium hydroxide. Anhydro bases of the form C are discussed by Decker.[4] The salt I cannot yield a base of the type C. With this exception all five types of base might be yielded by any of the salts.

By the addition of potassium hydroxide to 1,2,2,5,5-pentamethyldihydropyrazinium iodide a base, 1,2,2,5,5-pentamethyl-6-hydroxypyrazine,

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[3] Stoehr, *J. prakt. Chem.*, 47, 463, 470 (1893).

[4] Decker, *Ber.*, 38, 2493 (1905).

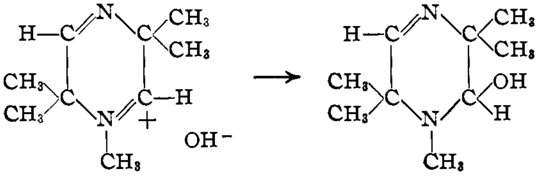
m. p. 110° (Formula V), was isolated. The base is of type B. It is associated in benzene but shows normal molecular weights in water. The normal molecular weight in water shows that the ring system is in all probability stable to water over at least short periods.

By the method of Kohler, Stone and Fuson[5] it was shown that the base reacted with slightly more than two molecules of methylmagnesium iodide per molecule and liberated one molecule of methane, which further points to the presence of the hydroxyl group.

It does not seem likely, in view of these results, that the base to which Formula V has been assigned has undergone ring fission to yield a base of type E, especially as in the open chain the remaining —C=N— would probably be hydrolyzed. Further, no carbonyl derivatives could be obtained from solutions of the base.

Measurement of the conductivity of a dilute solution of equimolar quantities of the iodide and sodium hydroxide by the method of Stewart and Maeser[6] for detecting association of hydroxyl ion showed that there was no strong base present even at 0° immediately after mixing, the base formed having $K_b < 3 \times 10^{-5}$.

In the pseudo basic system from salt I the equilibrium between IV and V is evidently established quite rapidly and is in the direction of the pseudo base, V.


IV V

When the base, V, was titrated in water solution with hydrochloric acid, using methyl orange as indicator, at first the neutralization was instantaneous and the indicator stayed yellow until one equivalent of acid per mole had been added. More acid then caused the indicator to turn red but upon standing the yellow color slowly returned. Further increments of acid caused the same effect and finally when two equivalents of acid had been added per mole the red color became permanent.

An explanation of this effect is that the base strength of the pseudo basic system involved in the equilibrium between IV and V is much less than that of the unmethylated nitrogen which is consequently titrated first. Upon adding a fraction of the second equivalent of acid the methylated nitrogen in the strongly basic form (IV) reacts, the methylated nitrogen in the pseudo basic form (V) being so weak that it reacts but slightly

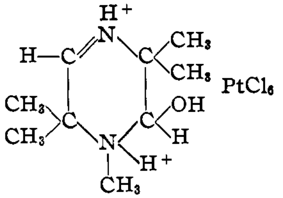
[5] Kohler, Stone and Fuson, THIS JOURNAL, 49, 3181 (1927).

[6] Stewart and Maeser, *ibid.*, 46, 2583 (1924).

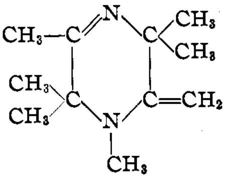
before the methyl orange changes to red. The system being now no longer in equilibrium, more pseudo base changes into the strong base, which reacts with the added acid and the system becomes basic, causing the reappearance of the yellow color.

As would be expected, the original iodide from which the base was prepared, when dissolved in water, produces a system in all ways similar to that produced by adding one equivalent of acid to the base. Addition of hydrochloric acid to the former produced the same changes as those produced by further increments of hydrochloric acid to the latter.

If the iodide of Formula I is changed into the chloride and treated with chloroplatinic acid, a chloroplatinate is obtained whose analysis corresponds to the Formula VI. The same platinum double salt is obtained from the base itself. The possibility that this salt is a hydrated form of the salt of the base IV is unlikely since it is obtained in better yields from solutions of the base in which V predominates.



VI

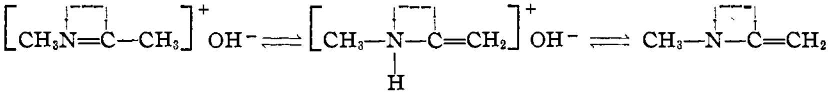


VII

By the addition of concentrated potassium hydroxide to a solution of heptamethyldihydropyrazinium iodide a liquid anhydro base of the type C (Formula VII) was obtained. It showed a normal molecular weight in benzene. This base dissolved slowly in water, yielding a strongly basic solution whose electrolytic conductivity corresponded to a base with a basic dissociation constant of $K_B = 4 \times 10^{-3}$, and was the same as that obtained for an equivalent mixture of original salt and sodium hydroxide after subtracting the conductivity due to the sodium iodide.

The second basic nitrogen in heptamethyldihydropyrazinium iodide was too weak to be titrated using methyl orange as indicator. When the base was titrated rapidly with 0.1 *N* hydrochloric acid using methyl orange as indicator, only one equivalent of acid reacted per mole, the second equivalent of base being too weak to react under these circumstances. Upon allowing a solution of the base, which had a slight excess of acid over one equivalent, to stand, none of the excess acid was used up even on standing. Solutions of the base in water to which no acid had been added underwent slow decomposition and upon titration, after standing, part of the second equivalent of basic nitrogen could be titrated to methyl orange. This pointed to cleavage of the ring in alkaline solution.

It seems necessary in this case to attribute the strong basicity to the methylated nitrogen, which can exist in the quaternary form because the unmethylated nitrogen is formally tertiary and has no possibility of becoming a quaternary base (except by the addition of hydrogen ion). A simple tertiary amine has not been found with $K_B > 10^{-3}$. It is reasonable to assume that the base (Formula VII) is formed from the quaternary base by the following mechanism



$$[CH_3N{=}C{-}CH_3]^+OH^- \rightleftharpoons [CH_3{-}\underset{H}{N}{-}C{=}CH_2]^+OH^- \rightleftharpoons CH_3{-}N{-}C{=}CH_2$$

If the pseudo base $\left((CH_3{-}N{-}COHCH_3)\right)$ were an intermediate in the production of VII, this would mean that the system is in equilibrium with the pseudo base. Equilibrium with the pseudo base was attained in the basic system from 1,2,2,5,5-pentamethyldihydropyrazinium iodide and an extremely feeble basicity of the methylated nitrogen resulted. If the pseudo bases were in equilibrium with the system under discussion, a weak basicity would also be expected. However, the basic properties of the methylated nitrogen are, in this case, far from weak and therefore equilibrium with the pseudo base or any reaction involving it is thought unlikely. Equilibrium with the quaternary base is probably responsible for the strongly basic properties of VII.

Addition of chloroplatinic acid to concentrated aqueous solutions of the base yielded a chloroplatinate whose analysis corresponded to the chloroplatinate of a base of type B. This same platinum double salt was obtained when a concentrated heptamethyldihydropyrazinium chloride solution which had stood for several days was treated with chloroplatinic acid. It is probable, however, that these chloroplatinates are hydrated forms of salts of bases of type A, especially in view of the large yields (66%) in which it is obtained from the salt.

The above results show that when ring conjugation is absent the mere substitution of a simple methyl group on the carbon atom attached to nitrogen in the system $[CH_3N{=}C{-}]^+OH^-$ can give rise to a relatively stable anhydro base of type C.

Attempts to obtain a solid or liquid base from 1,2,5-trimethylpyrazinium iodide (Formula III) in a pure state have failed. However, certain evidence has been obtained that in water solution the base, immediately after liberation from the salt, is of the type A in rapid equilibrium with a very small amount of the pseudo base (type B), which slowly changes into an anhydro base of type D. This evidence will be presented in the second paper of this series, where a more detailed study of the equilibrium in and the mechanism of some of the above reactions, which further substantiates the conclusions reached in this paper, is presented.

Experimental

1,2,2,5,5-Pentamethyldihydropyrazinium Iodide.—Thirty-four and a half grams (0.25 mole) of 1,2,2,5,5-tetramethyldihydropyrazine and 34.0 g. (0.24 mole) of methyl iodide dissolved in 123 cc. of sodium-dried ether were allowed to react for thirteen days at room temperature. At the end of this time about 100 cc. of dry ether was added and the mixture stirred. The crystalline salt was washed with dry ether; yield, 54.0 g. (0.193 mole) (80.4% of the theoretical); m. p., with decomp., 204°. The material was recrystallized by dissolving in methyl alcohol (1.7 cc. per g.) heating to boiling to dissolve and while hot adding twice the volume of *n*-butyl alcohol. The salt crystallized on cooling, leaving a red solution. The red color is not due to iodine. The crystals were washed with ether; m. p., with decomp., 194°. The lowered melting point on crystallization is peculiar.

Anal. Calcd. for $C_9H_{17}N_2I$: I, 45.3. Found: I, (Volhard), 44.69. Recrystallization did not alter this analysis.

1,2,2,3,5,5,6-Heptamethyldihydropyrazinium Iodide.—A solution of 12.2 g. (0.073 mole) of anhydrous hexamethyldihydropyrazine and 12.2 g. (0.069 mole) of methyl iodide in 40 cc. of sodium-dried ether was sealed up in a bomb tube and heated to 85–110° for three days. At the end of this time 100 cc. of dry ether was added to the contents of the bomb tube. The crystalline salt was filtered off and washed with dry ether; yield, 16.6 g. (0.054 mole) (78% of the theoretical); m. p. 249.5° with decomposition. The salt was recrystallized in substantially the same manner described for pentamethyldihydropyrazinium iodide using the same solvents. The mother liquor from the crystallization was also dark red; m. p. of recrystallized product, 249° with decomp.

Anal. Calcd. for $C_{11}H_{21}N_2I$: I, 41.1. Found: I (Volhard), 40.4.

Recrystallization did not change this analysis. Rate of heating did not affect the melting point.

When the preparation of this compound was carried out by allowing the same quantities to stand at room temperature for eighteen days the yield was only 26% of the theoretical. Evidently the two extra methyl groups have a marked effect in slowing down the rate of addition of methyl iodide.

1,2,2,5,5-Pentamethyl-6-hydroxytetrahydropyrazine.—Fifteen grams (0.054 mole) of 1,2,2,5,5-pentamethyldihydropyrazinium iodide was dissolved in 30 cc. of water and 100 cc. of 33% potash was added with vigorous stirring. The oil which first separated crystallized to a crust which was filtered off by suction through a Witt plate without filter paper. The excess potassium hydroxide was removed by pressing on a porous plate. The material was dried over calcium chloride and dissolved in 17 cc. of hot benzene. To the hot filtered solution 5 cc. of ligroin (b. p. 40–60°) was added and the mixture shaken. Upon cooling crystallization took place. Finally, after cooling in the ice box, the crystals were filtered off and washed with petroleum ether; yield, 7.6 g. (0.045 mole) (83% of the theoretical); m. p. 108–110°. Further recrystallization in the same way did not alter this melting point.

Anal. Calcd. for $C_9H_{18}N_2O$: C, 63.50; H, 10.65; N, 16.48. Found: C, 63.78; 63.85; H, 10.75, 10.79; N (Dumas), 16.80. Molecular weight in water (freezing point): H_2O, 20.2 g.; sample, 0.3637, 0.3007; ΔT_F, 0.206, 0.160°. Calcd. for $C_9H_{18}N_2O$: mol. wt., 170.2. Found: mol. wt., 163, 170.

In Table I are given the results of molecular weight determinations on this compound in benzene. ΔT_F is the lowering of the pure solvent caused by the given total weight of added compound.

Behavior of 1,2,2,5,5-Tetramethyl-6-hydroxytetrahydropyrazine on Titration with Acid.—Sample: 0.0993 g. of $C_9H_{18}N_2O$ in 50 cc. of water; indicator, methyl orange.

TABLE I

MOLECULAR WEIGHT DETERMINATIONS

Wt. of benzene, 17.4 g.	I	II	III	IV
Total wt. of added compound, g.	0.0698	0.1563	0.1996	0.3354
ΔT_F, °C.	.123	.221	.272	.334
Molecular weight	167	208	216	286.5

These results show that the compound is quite highly associated in benzene.

The solution was titrated dropwise with vigorous shaking, using 0.1339 *N* hydrochloric acid solution. After 6.3 cc. of acid had been added the indicator turned definitely orange but changed back to yellow in forty-five seconds. Further increments of acid changed the indicator to red but the yellow color returned after about five-minute intervals. After 8.65 cc. of acid had been added the indicator became permanently red. Calcd.: cc. of 0.1339 *N* HCl required for 1st equivalent, 4.35; 2d equivalent, 8.70.

Addition of excess acid and back titration with alkali to the orange-yellow end-point after allowing to stand for two hours showed that the total acid required by the compound was 8.72 cc. Equivalent weight, calcd., 85.1. Found: 85.0.

Behavior of 1,2,2,5,5-Pentamethyldihydropyrazinium Iodide on Titration with Acid.—A solution of 0.1970 g. of the salt in 50 cc. of water was titrated with 0.1339 *N* hydrochloric acid as in the above experiment. After 2.80 cc. of acid had been added the methyl orange changed from yellow to red and then, over a distinct time interval, back to yellow. After 3.53 cc. had been added, a 0.74-cc. increment of acid produced a red color which changed back to orange-yellow in about five minutes. This effect continued throughout the titration. After 5.60 cc. had been added the solution became permanently red. Back titration with alkali showed 5.42 cc. of acid to have been used (calculated, 5.25 cc.). Alkali equivalent to all the acid which had been added was introduced and the titration repeated after allowing to stand for seven minutes. After 3.15 cc. of acid had been added, a red color changing back to yellow appeared. The effect continued until all the added alkali had been used up. Unquestionably, the effect is reversible.

The Reaction of 1,2,2,5,5-Tetramethyl-6-hydroxytetrahydropyrazine with Methyl magnesium Iodide.—The apparatus and method used was as described by Kohler, Stone and Fuson[6] with slight modifications.[7] To 0.0995 g. of compound was added 4.31 cc. of a 0.573 *M* solution of methylmagnesium iodide in isoamyl ether; 14.6 cc. of methane (corrected to S. T. P.) was liberated. The excess Grignard reagent upon treatment with water (4.05 cc.) yielded 25.1 cc. of methane (corrected to S. T. P.). Methane per mole of compound, 1.11 moles. Total CH_3MgI used per mole of compound, 2.31.

1,2,2,5,5-Pentamethyl-6-hydroxytetrahydropyrazine Chloroplatinate.—Thirty-four hundredths g. (0.002 mole) of pentamethyl-6-hydroxytetrahydropyrazine was dissolved in 5 cc. of water. Excess of 1 *N* chloroplatinic acid was added. The precipitated chloroplatinate was insoluble in hot alcohol and in hot water and could not be crystallized; yield, 0.74 g. (0.00127 mole) (63% of the theoretical); m. p. (with decomp.) 282°. The temperature of the bath in which this salt decomposed in ten seconds was 320°.

Anal. Calcd. for $C_9H_{20}N_2O\cdot PtCl_6$: Pt, 33.66. Found: Pt, 33.88.

By allowing the base to stand with hydrochloric acid for twenty minutes before adding the chloroplatinic acid, the above yield was reduced to 30%.

The same platinum double salt could be obtained from 1,2,2,5,5-tetramethyldi-

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[7] We wish to thank Mr. J. D. Pickens, Research Fellow in Chemistry at The Pennsylvania State College for these results.

hydropyrazinium iodide. A solution of 1.4 g. (0.005 mole) of the salt in 10 cc. of distilled water was stirred with 0.01 mole of silver chloride for sixteen hours. The chloroplatinate was precipitated with excess *M* chloroplatinic acid from the filtered solution of the chloride; yield, 0.3 g. (0.00052 mole) (10% of the theoretical); m. p. with decomp. 284–285° (started with bath at 130°). In the bath at 320° it decomposed in ten seconds.

Anal. Calcd. for $C_9H_{20}N_2O \cdot PtCl_6$: Pt, 33.66. Found: Pt, 33.65.

The two salts were unquestionably identical.

1,2,2,3,5,5-Hexamethyl-6-methylenetetrahydropyrazine.—Fourteen grams of heptamethyldihydropyrazinium iodide was dissolved in 35 cc. of water and 62 cc. of 40% potassium hydroxide was added. The non-aqueous layer was separated and dried for two hours over potassium hydroxide sticks and for one hour over anhydrous potassium carbonate. The filtered liquid was distilled *in vacuo* under 6.5 mm. pressure and the distillate collected in two portions: (1) 70 (about)–78.°, 1.1 g.; (2) 78.0–78.2°, 5.4 g. Both fractions were colorless; total yield of both fractions, 6.5 g. (79% of the theoretical). The fraction of b. p. 78.0–78.2° was used for analysis, molecular weight determinations, etc.

Anal. Calcd. for $C_{11}H_{20}N_2$: C, 73.28; H, 11.18. Found: C, 72.75, 73.08; H, 10.76, 10.83. *Molecular weight* by freezing point lowering in benzene: C_6H_6, 17.4 g.; sample, 0.1580, 0.1986 g.; ΔT_F, 0.261, 0.325°. Mol. wt. calcd. for $C_{11}H_{20}N_2$: 180.2. Found: 178.2, 179.9.

The base undergoes decomposition slowly at room temperature to yield a red viscous oil.

Titration of 1,2,2,3,5,5-Hexamethyl-6-methylenepyrazine with Hydrochloric Acid.—The base was dissolved in 50 cc. of water and titrated immediately and rapidly to the yellow-orange end-point of methyl orange. Sample: 0.1754 g. required 7.45 cc. of 0.1339 *N* HCl. Eq. wt.: calcd. for $C_{11}H_{20}N_2$ (as a mono-acid base), 180.2. Found: 175.8. This equivalent weight was checked by adding excess acid and back titrating with alkali. Excess alkali equivalent to 5 cc. of the acid was then added and solution allowed to stand for three and one-half hours at room temperature. Upon back titrating to the yellow-orange end-point, the total acid used up by the base was found to have increased by 2.89 cc., corresponding to about 50% decomposition. In another experiment the base was allowed to stand in 50 cc. of water for about five minutes and then titrated to the orange end-point of methyl orange. Sample: 0.2243 g. required 10.80 cc. of 0.1339 *N* HCl. Eq. wt., found: 155.1, *i. e.*, 1 mole of base yielded 1.161 eqts. of titratable base, corresponding to 16.1% decomposition in five minutes at room temperature. Excess acid was added and the solution after standing for four hours was back titrated. The net amount of acid required by the base was unchanged. This points to the stability of the base in acid.

Upon titration 0.5674 g. of the heptamethyldihydropyrazinium iodide was found to require 0.09 cc. of 0.1339 *N* hydrochloric acid to reach the orange end-point of methyl orange.

The chloroplatinates from 1,2,2,3,5,5,6-heptamethyldihydropyrazinium iodide and from 1,2,2,3,5,5-hexamethyl-6-methylenetetrahydropyrazine were prepared by methods already described. The salt from the two sources was apparently the same; chloroplatinate from iodide, m. p. about 285° with decomp.; yield, 66%.

Anal. Calcd. for $C_{11}H_{24}N_2O \cdot PtCl_6$: Pt, 32.10. Found: Pt, 31.99.

These chloroplatinates underwent decomposition when crystallization was attempted. The large yield from the salt seems to indicate that the chloroplatinate is a hydrated form of the salt of the quaternary base.

Attempted Isolation of a Base Corresponding to 1,2,5-Trimethylpyrazinium Iodide.—

1,2,5-Trimethylpyrazinium iodide was prepared by the methylation of 2,5-dimethylpyrazine and recrystallized as described by Stoehr.[8] The product melted at 238° with decomposition whereas Stoehr records 230°.

Two grams of the iodide was dissolved in 5 cc. of water and 15 cc. of water and 15 cc. of 33% potassium hydroxide was added. The gum which separated was pressed out on a porous plate and dissolved in pure pyridine. After drying with solid potassium hydroxide for one hour the solution was treated with three times its volume of dry ether. A yellow crystalline material separated. This was filtered off by suction and washed several times with ether. The substance became dark red on standing. Its analysis varied from C, 53.2; H, 6.94, to C, 49.5; H, 6.63 on standing in a dry atmosphere for a day. This analysis does not correspond to that of any of the expected bases. Upon melting it gave a curious behavior. Heated slowly, it blackened at about 88° and melted at 179–190°, but, placed in a bath at 146°, it melted immediately. Evidently decomposition took place on slow heating. This compound will be investigated further. Various other attempts to obtain a pure base failed.

The experimental data upon the base strength of the above bases are recorded in the second paper of this series.

Summary

1. 1,2,2,5,5-Pentamethyldihydropyrazinium iodide and 1,2,2,3,5,5,6-heptamethyldihydropyrazinium iodide have been prepared.

2. 1,2,2,5,5-Pentamethyldihydropyrazinium iodide yields the base 1,2,2,5,5-pentamethyl-6-hydroxytetrahydropyrazine, whereas 1,2,2,3,5,5,6-heptamethyldihydropyrazinium iodide yields 1,2,2,3,5,5-hexamethyl-6-methylenetetrahydropyrazine. The ease of formation of the latter compound is attributed to lack of conjugation.

3. Possible tautomeric systems arising from these bases are discussed and related to their behavior on titration and salt-forming properties.

4. No base corresponding to 1,2,5-trimethylpyrazinium iodide could be isolated.

STATE COLLEGE, PENNSYLVANIA

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[8] Stoehr, *J. prakt. Chem.*, **47**, 463, 470 (1893).