was washed with more solvent. The combined filtrates were treated with a mixture of methanol, 9.20 g. (0.29 mole), and triethylamine, 25.2 g. (0.25 mole). The addition required 10 min. and the temperature rose to a maximum of 69°. The mixture was stirred for 2 hr. and filtered, and the solids were washed with more solvent. Evaporation of the carbon tetrachloride left a dark oil which was distilled three times at about 0.2 μ to obtain a pale yellow oil, 20.2 g. (26.2% theory). This was 99% pure by vapor phase chromatography. Its physical constants and analyses are given in Table IV.

Acknowledgment.—The author wishes to express his appreciation to Professors J. C. Martin and J. W. Crump for helpful discussions and to Dr. J. P. Heeschen for the side-band n.m.r. chemical shift data.

Some Reactions and Properties of 2-Phenyl-3,3-dimethyl-3,4,5,6-tetrahydropyrazine

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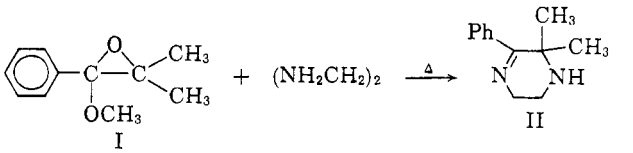
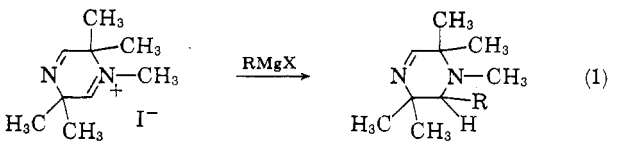
The reaction of epoxy ether I with ethylenediamine produced the 3,4,5,6-tetrahydropyrazine II in high yield. The reduction and hydrolysis reactions of II were studied. Also, the use of the >C=N function of II as a blocking group in the synthesis of unsymmetrically N-substituted piperazines was briefly investigated.

When epoxy ether I was refluxed with ethylenediamine in toluene, 2-phenyl-3,3-dimethyl-3,4,5,6-tetrahydropyrazine (II) was isolated in 91% yield. Relatively little is reported concerning the chemistry of this type of tetrahydropyrazine with only two authors reporting chemical characterization in the literature. Aston[2] and co-workers prepared three tetrahydropyrazines *via* the Grignard reaction on 1,2,2,5,5-pentamethyldihydropyrazinium iodide (1). More recently Plante[3] and co-workers isolated tetrahydropyrazine III

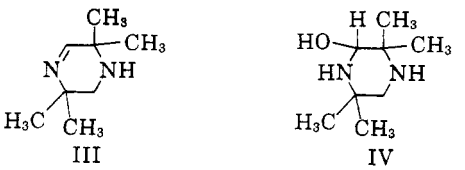


I II



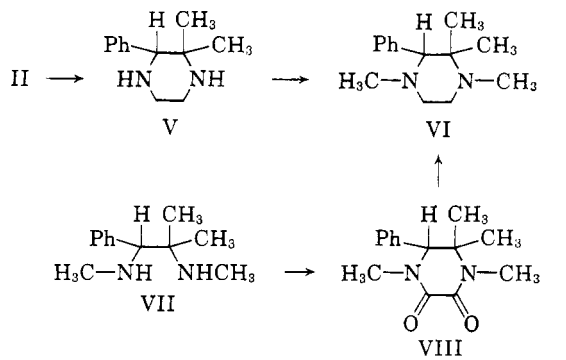
(1)

from the Raney nickel dehydrogenation of 5-amino-2,2,5-trimethyl-3-azahexan-1-ol and characterized it as the monohydrate dihydrochloride salt, formulated as IV.



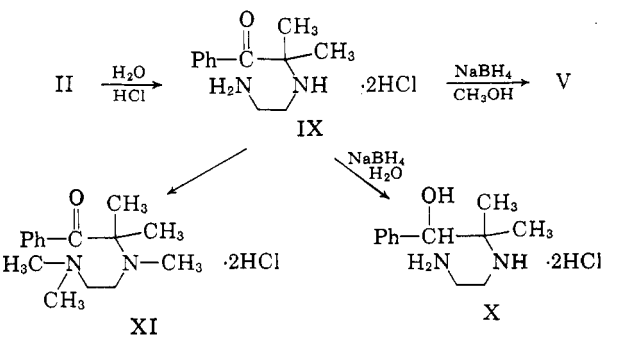
III IV

The structural assignment of II was supported by its infrared spectrum which indicated NH absorption at 3.08 and a strong C=N band at 6.13 μ and confirmed by the following sequence of reactions. Sodium borohydride reduction of II afforded piperazine V in high yield. The tetramethylpiperazine VI was then prepared from V by the Clarke–Eschweiler procedure.[4] Piperazine VI was then synthesized by an alternate route. Diamine VII[5] was converted with oxalyl chloride[6] to oxamide VIII which in turn was reduced with lithium aluminum hydride to VI, identical with that prepared *via* tetrahydropyrazine II.



V VI VII VIII

The cyclic imine II provided an interesting example for a hydrolysis study. An ultraviolet spectrum of II in ethanol showed only end absorption; however, in 5 *N* hydrochloric acid a maximum developed at 254 mμ (ϵ 6500). These values were close to those reported for α-amino ketones[7] and suggested the existence in solution of 2-(2-aminoethylamino)-2-methylpropiophenone dihydrochloride (IX). Indeed, when an aqueous hydrochloric acid solution of II was evaporated to dryness, the amino ketone dihydrochloride IX was isolated in high yield. That the structure of IX was as shown and



IX XI X

(1) Abstracted from a portion of the Ph.D. Thesis of K. G. Taylor, Wayne State University, 1963.

(2) J. G. Aston, D. Ailman, C. Scheuermann, and J. Koch, *J. Am. Chem. Soc.*, **56**, 1163 (1934).

(3) L. T. Plante, W. Lloyd, C. Shilling, and L. Clapp, *J. Org. Chem.* **21**, 82 (1956).

(4) Piperazines V and VI were conveniently isolated as their hydrochloride salts.

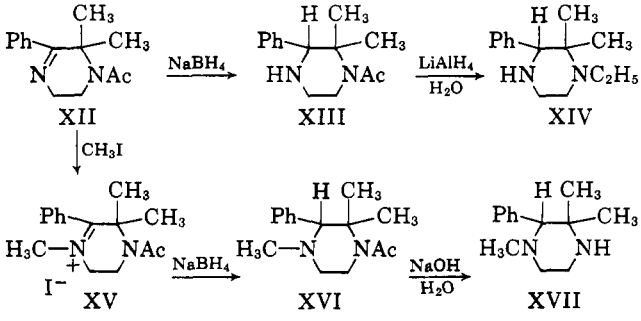
(5) Prepared by reduction of the corresponding α-aminoimine, made in turn from the epoxy ether I *via* the α-amino ketone: *cf.* ref. 7.

(6) The procedure of B. Ambrecht, L. Rice, C. Grogan, and E. Reid, [*J. Am. Chem. Soc.*, **75**, 4829 (1953)] was used.

(7) C. L. Stevens and C. H. Chang, *J. Org. Chem.*, **27**, 4392 (1962).

not a closed form analogous to the formula IV reported by Plante was supported by the infrared spectrum of a mull which exhibited a conjugated carbonyl band at 5.95 μ. In solution the properties of the dihydrochloride IX varied. When dissolved in alcohol, the ultraviolet spectrum resembled that of II, showing mainly end absorption. Sodium borohydride reductions of IX were in accord with this ultraviolet spectrum since in alcohol the piperazine V was formed in quantitative yield. In water, the reduction followed a different course. The product was the amino alcohol X isolated in 86% yield as its dihydrochloride salt. Thus, in alcohol the dihydrochloride was reduced in the closed form and in water the same dihydrochloride was reduced in the open form. Another reaction in aqueous media yielded a product resulting from reaction of IX in the open form. Thus, Clarke–Eschweiler methylation of IX afforded amino ketone XI in 72% yield.

Tetrahydropyrazine II offered some interesting possibilities for the synthesis of unsymmetrically N-substituted piperazines. Since the amine nitrogen is protected from reaction with acylating agents, the other nitrogen atom may be preferentially acylated. Once acylated, the amino nitrogen would be inert toward alkylation with alkyl halides while the imino nitrogen would be free to react. By appropriate acylations, alkylations and reductions various N-substituted piperazines could be synthesized. Some of these possibilities were briefly investigated and are summarized below. Acetylation of II produced N-acetate XII,



which could be reduced with sodium borohydride to the monoacylated piperazine XIII. Lithium aluminum hydride reduction of XIII afforded the mono-N-ethyl piperazine XIV. Also, N-acetate XII could be converted to a methiodide salt, XV, on mild treatment with methyl iodide. Methiodide XV was readily reduced with sodium borohydride to XVI. Basic hydrolysis of XVI hydrolyzed the acetyl protection yielding the trimethyl piperazine XVII. The reactions mentioned above proceeded in 78–90% yields and the products, with the exception of XV, were isolated as their hydrochloride salts.

Experimental

2-Phenyl-3,3-dimethyl-3,4,5,6-tetrahydropyrazine (II).—A solution of 17.8 g. (0.1 mole) of epoxy ether I[8] and 12.0 g. (0.2 mole) of anhydrous ethylenediamine in 25 ml. of toluene was refluxed in a Stark water separator for 2 days, methanol, water, and some ethylenediamine being azeotroped off. Toluene and excess ethylenediamine were evaporated *in vacuo* and the remaining yellow liquid was distilled under reduced pressure. The fraction boiling at 85° (0.05 mm.) was collected: 17.1 g. (91%); $n^{25}D$ 1.5590; infrared spectrum, 3.08 (NH) and 6.13 μ (C=N—); ultraviolet spectrum in ethanol, end absorption, and, in 5 *N* HCl, λ_{max} 254 mμ (ϵ 6510).

Anal. Calcd. for $C_{12}H_{16}N_2$: C, 76.55; H, 8.57; N, 14.88. Found: C, 76.43; H, 8.71; N, 15.08.

An N-benzoyl derivative was prepared and purified by recrystallization from ether to give white needles, m.p. 155–156°.

Anal. Calcd. for $C_{19}H_{20}N_2O$: C, 78.04; H, 6.89. Found: C, 77.93; H, 6.76.

2-Phenyl-3,3-dimethylpiperazine Dihydrochloride (V).—To a solution of 6.0 g. (0.032 mole) of II in 25 ml. of absolute ethanol was added 1.3 g. (0.034 mole) of sodium borohydride. A vigorous exothermic reaction ensued and the solution was left at room temperature overnight. Excess borohydride was decomposed by the addition of dilute (6 *N*) hydrochloric acid, and, after basification with solid potassium hydroxide, the solution was washed seven times with ether. The combined ether extracts were dried (potassium carbonate) and the product was precipitated as the dihydrochloride salt by the addition of isopropyl alcohol saturated with hydrogen chloride. Recrystallization from methanol–ether yielded 8.1 g. of white crystals: 96%; m.p. 298–299° dec; pK_a 3.7 and 8.6 (50% methanol); infrared spectrum, 2.81, 2.96 (NH), and 6.32 μ (NH_2^+) (mineral oil mull).

Anal. Calcd. for $C_{12}H_{20}Cl_2N_2$: C, 54.75; H, 7.66; N, 10.65. Found: C, 54.80; H, 7.46; N, 10.43.

Preparation of 2-Phenyl-3,3-dimethylpiperazine.—The dihydrochloride salt (450 mg.) was dissolved in water and the corresponding free base was isolated after basification and thorough extraction with ether. Sublimation of the resulting oily solid at 50° *in vacuo* yielded 200 mg. (62%) of white crystals: m.p. 64–65°; infrared spectrum ($CHCl_3$), 3.1 (broad, NH), 6.25 (C_6H_5), 7.22 and 7.32 μ (*gem*-dimethyl).

Anal. Calcd. for $C_{12}H_{18}N_2$: C, 75.76; H, 9.53; N, 14.73. Found: C, 75.82; H, 9.27; N, 14.84.

1,2,2,4-Tetramethyl-3-phenylpiperazine Dihydrochloride (VI).—A water solution containing 0.5 g. (0.00019 mole) of dihydrochloride (V) was made strongly alkaline with solid potassium hydroxide and the corresponding free base was isolated by thorough extraction with ether. The ether was removed *in vacuo* and the resulting oily residue was dissolved in 10 ml. of water. Formic acid (10 ml., 98%) and 10 ml. of 34% formalin were then added and the solution was heated at reflux for 15 hr. After cooling, 15 ml. of 12 *N* hydrochloric acid was added and the volume was reduced to 3 ml. by warming *in vacuo*. After dilution with 15 ml. of water and an ether wash, the solution was made strongly alkaline and washed with ether. The ether extracts were dried (potassium carbonate) and the product was precipitated as the dihydrochloride salt by the addition of isopropyl alcohol–hydrogen chloride. Recrystallization from methanol–ether yielded 0.41 g. (74%) of white needles: m.p. 260–261° dec.; pK'_a 2.7 and 8.2 (50% methanol); infrared spectrum, 2.9 (NH), 6.25 (C_6H_3), 7.25, and 7.35 μ (s) (*gem*-dimethyl).

Anal. Calcd. for $C_{14}H_{24}Cl_2N_2$: C, 57.73; H, 8.30; N, 9.62. Found: C, 57.81; H, 8.40; N, 9.32.

Preparation of 1,4,6,6-Tetramethyl-5-phenyl-2,3-diketopiperazine (VIII).—To a solution of 0.60 g. (0.0031 mole) of N,N′-2-trimethyl-1-phenyl-1,2-propanediamine VII [b.p. 47–48° (0.05 mm.), $n^{25}D$ 1.5160, d^{25}_4 0.959] and 0.8 g. (0.008 mole) of triethylamine in 20 ml. of benzene was added 0.4 g. (0.0035 mole) of oxalyl chloride in benzene. An exothermic reaction took place during the dropwise addition and cooling with a water bath was necessary. The mixture was warmed to 80° for 0.5 hr. and stirred for an additional 10 hr. at room temperature. The reaction mixture was then poured into dilute acid and washed with chloroform. The chloroform extracts were then washed with dilute base and water and then dried over potassium carbonate. A solid remained after removal of solvents which was crystallized from acetone–ether–pentane: 0.53 g. (72%); m.p. 205–207°; infrared spectrum (mull), 6.0 (broad, C=O), 7.25 and 7.35 μ (s), (*gem*-dimethyl). An analytical sample was prepared by recrystallization from benzene–ether; m.p. 207–208°.

Anal. Calcd. for $C_{14}H_{18}N_2O_2$: C, 68.27; H, 7.36; N, 11.38. Found: C, 68.33; H, 7.35; N, 11.27.

1,2,2,4-Tetramethyl-3-phenylpiperazine Dihydrochloride (VI) *via* Reduction of 1,4,6,6′-Tetramethyl-5-phenyl-2,3-diketopiperazine.—A solution of 0.17 g. (0.7 mmole) of the diketopiperazine VIII in dry dioxane was added dropwise to a stirred slurry of 0.19 g. (0.005 mole) of lithium aluminum hydride in 25 ml. of dioxane. After addition, the reaction was refluxed for 8 hr. A small amount of water was then added and the inorganic salts

(8) C. L. Stevens and T. Coffield, *J. Am. Chem. Soc.*, **80**, 1919 (1958).

were removed by filtration over Celite. The dioxane was removed *in vacuo* and the residue was dissolved in ether. The product was precipitated as the dihydrochloride salt in the usual manner. Recrystallization from methanol–ether yielded white needles, 0.15 g. (75%), m.p. 259–260°. A mixture melting point with product from the methylation of 1-phenyl-2,2-dimethylpiperazine was undepressed. Also, the infrared spectra of the two samples were identical.

2-(2-Aminoethylamino)-2-methylpropiophenone Dihydrochloride (IX).—Dissolution of 0.94 g. (0.005 mole) of pyrazine II in 4 ml. of 6 *N* hydrochloric acid followed by evaporation *in vacuo* yielded a glassy solid. Crystallization from methanol–ether afforded 1.23 g. (88%) of fluffy white needles, m.p. 200° dec. An analytical sample was prepared by recrystallization from methanol–ether and decomposed over a wide range, 205–220°.

Anal. Calcd. for $C_{12}H_{20}Cl_2N_2O$: C, 51.62; H, 7.22; N, 10.04. Found: C, 51.42; H, 7.44; N, 10.04.

Ultraviolet spectrum showed $\lambda_{max}^{H_2O}$ 224 mμ (ε 3430); $\lambda_{max}^{C_2H_5OH}$ 267 mμ (ε 274), 263 (385), 260 (410), 256 (500), and 254 (503) (all as shoulders on end absorption). Infrared spectrum (mull) showed 2.9 (doublet, NH), 5.95 (C=O), 6.30 (NH_2^+), 7.23, and 7.33 μ (*gem*-dimethyl).

Reduction of 2-(2-Aminoethylamino)-2-methylpropiophenone Dihydrochloride (IX) with Sodium Borohydride in Methanol.—To a solution of 0.28 g. (0.001 mole) of the dihydrochloride in 20 ml. of methanol, 1 g. of sodium borohydride was added in small portions. The reaction then was left to stand at room temperature for 8 hr. The solution was then made acidic with dilute hydrochloric acid and washed with ether. After basification (solid potassium hydroxide), the aqueous solution was extracted three times with chloroform. After drying, the chloroform was removed *in vacuo* and replaced with ether. The product was then precipitated as the hydrochloride salt in the usual manner. Recrystallization from methanol–ether afforded white crystals, 0.25 g. (96%) of 2-phenyl-3,3-dimethylpiperazine dihydrochloride (V), m.p. 300° dec. An infrared spectrum was identical with that of an authentic sample.

Reduction of 2-(2-Aminoethylamino)-2-methylpropiophenone Dihydrochloride (IX) with Sodium Borohydride in Water (Synthesis of X).—A solution of 0.43 g. (0.00154 mole) of the dihydrochloride in 5 ml. of distilled water was added to a solution of 0.76 g. (0.02 mole) of sodium borohydride in 15 ml. of water. Immediate reaction took place which quickly subsided and the solution was left at room temperature for 24 hr. The excess borohydride was decomposed by the addition of 6 *N* hydrochloric acid and the aqueous solution was washed once with ether. After basification with solid potassium hydroxide, the aqueous solution was washed three times with chloroform; the combined chloroform extracts were dried and evaporated to dryness *in vacuo*. The residue (oily) was dissolved in ether and the product was precipitated as the dihydrochloride by the usual procedure. Recrystallization from methanol–ether gave white crystals: 0.37 g. (86%); m.p. 250–251° (after melting, the compound would resolidify at 265–270° and then decompose in the neighborhood of 300°); pK'_a 6.5 and 9.3 (50% methanol); ultraviolet spectrum, λ_{max}^{EtOH} 267 mμ (ε 96), 263 (165), 257 (204), and 251 (153); infrared spectrum (mull), 3.09 (NH or OH), 6.25 (C_6H_5), 6.29 (NH_2^+), 7.25(s), and 7.33 μ (*gem*-dimethyl).

Anal. Calcd. for $C_{12}H_{22}Cl_2N_2O$: C, 51.25; H, 7.89; N, 9.96. Found: C, 51.45; H, 7.92; N, 9.85.

2-[2-(N^1,N^2,N^2-Trimethyl)aminoethylamino]-2-methylpropiophenone Dihydrochloride (XI).—A solution of 0.14 g. (0.0005 mole) of dihydrochloride IX in 10 ml. of 37% formalin and 10 ml. of 97% formic acid was refluxed for 48 hr. The solution was then made strongly acidic with 5 ml. of 12 *N* hydrochloric acid and evaporated to half its volume *in vacuo*. After basification with solid potassium hydroxide, the solution was washed with three portions of ether. The combined ether extracts were dried (potassium carbonate), the drying agent was removed by filtration, and the product was precipitated as the dihydrochloride salt by the usual procedure. Recrystallization from methanol–ether afforded 0.11 g. of long, white needles, m.p. 231–232°. A second crop, 20 mg., had m.p. 227–229°. The total yield was 0.13 g. (72%). An analytical sample, prepared by recrystallization from methanol–ether, melted at 231–232°: pK'_a 3.5 and 8.6 (50% methanol); ultraviolet spectrum, λ_{max}^{EtOH} 243 mμ (ε 9620). A portion of the dihydrochloride was converted to the free base for an infrared spectrum ($CHCl_3$) of 5.95 (C=O), 6.23 (C_6H_5), 7.25, and 7.35 μ (s) (*gem*-dimethyl).

Anal. Calcd. for $C_{15}H_{26}Cl_2N_2O$: C, 56.08; H, 8.16. Found: C, 56.29; H, 8.24.

2-Phenyl-3,3-dimethyl-4-acetyl-3,4,5,6-tetrahydropyrazine (XII).—A solution of 3.8 g. (0.02 mole) of pyrazine IIa in 5.5 g. (0.05 mole) of acetic anhydride and 4.0 g. (0.05 mole) of pyridine was allowed to stand at room temperature for 24 hr. Excess acetic anhydride and pyridine were removed *in vacuo* and the oily residue was dissolved in ether. The ether solution was washed with dilute sodium bicarbonate solution and water and then dried over sodium sulfate. Removal of solvents *in vacuo* left an oil. The oil was distilled in a microdistillation apparatus at a temperature of 140° (0.06 mm.) and yielded 2 g. (43%) of a very viscous, pale yellow liquid: $n^{25}D$ 1.5536; infrared spectrum ($CHCl_3$), 6.1 (broad C=O, C=N), 7.1, 7.25 (s) (*gem*-dimethyl), and 7.40 μ (acetyl—C—CH_3). An ultraviolet spectrum showed only end absorption.

Anal. Calcd. for $C_{14}H_{18}N_2O$: C, 73.01; H, 7.86. Found: C, 73.13; H, 7.99.

A stable hydrochloride salt could be prepared in 90% yield by the usual procedure. Recrystallization from methanol–ether afforded shiny plates: m.p. 226–228° dec.; pK'_a 4.05 (50% methanol); infrared spectrum (KBr), 5.93 (short), 6.10 (s) (C=O, C=N), 7.10, 7.25 (sh) (*gem*-dimethyl), and 7.38 μ (acetyl–C–CH_3).

Anal. Calcd. for $C_{14}H_{19}ClN_2O$: C, 63.03; H, 7.18; N, 10.23. Found: C, 62.72; H, 7.23; N, 10.23.

1-Acetyl-2,2-dimethyl-3-phenylpiperazine Hydrochloride (XIII).—A solution of 0.94 g. (0.005 mole) of piperazine II in 1.1 g. (0.01 mole) of acetic anhydride and 1.6 g. (0.02 mole) of pyridine was allowed to stand at room temperature for 15 hr. Excess acetic anhydride and pyridine were removed *in vacuo* and the oily residue was dissolved in ethanol. Excess sodium borohydride, about 0.5 g., was added in small portions to the ethanol solution and, after a vigorous reaction subsided, was left at room temperature for 2 hr. The solution was made strongly acidic with 6 *N* hydrochloric acid and washed with ether. The aqueous portion was then made basic by slowly pouring it into 50 ml. of 10% sodium hydroxide. The basic solution was washed three times with ether, the combined ether extracts were dried, and the solvents were removed *in vacuo* leaving an oily residue. This residue was left under high vacuum for 4 hr. to remove traces of pyridine and then dissolved in dry ether. The product was isolated as the hydrochloride salt prepared in the usual manner. Recrystallization from methanol–ether afforded white crystals: 1.2 g. (90%); m.p. 237–238°; pK'_a 6.71 (50% methanol); ultraviolet spectrum, $\lambda_{max}^{C_2H_5OH}$ 268 mμ (ε 181), 262 (258), 257 (282), and 251 (260); infrared spectrum (mull), 6.05 (C=O), 6.25 (sh) (NH_2^+), 7.23, 7.30 (*gem*-dimethyl) and 7.35 μ (shoulder) (acetyl–C–CH_3).

Anal. Calcd. for $C_{14}H_{21}ClNO$: C, 62.56; H, 7.88: N, 10.43. Found: C, 62.62; H, 7.88; N, 10.29.

1-Ethyl-2,2-dimethyl-3-phenylpiperazine Dihydrochloride (XIV).—N-Acetate hydrochloride XIII (1 g.) was neutralized with aqueous potassium hydroxide and the corresponding free base was isolated as an oil by extraction with ether. An ethereal solution containing 0.12 g. (0.5 mmole) of the free base was added dropwise to a stirred slurry of 0.19 g. (0.005 mole) of lithium aluminum hydride in ether. After addition, the mixture was heated at gentle reflux for 12 hr. The excess lithium aluminum hydride was then decomposed by the careful addition of water, and the inorganic salts were removed by filtration over Celite. The filtrate was then washed with three portions of 1 *N* hydrochloric acid; the aqueous acid was neutralized with solid potassium hydroxide and then washed with three portions of ether. The combined ether extracts were dried and the product was isolated as the dihydrochloride salt prepared in the usual manner. Recrystallization from methanol–ether afforded 0.11 g. (79%) of white crystals which slowly decomposed over 265°; pK'_a 3.7 and 8.8 (50% methanol); ultraviolet spectrum, $\lambda_{max}^{C_2H_5OH}$ 267μ (ε 202), 262 (268), 257 (259), and 251 (187). A second recrystallization gave an analytical sample of the same decomposition point.

Anal. Calcd. for $C_{14}H_{24}Cl_2N_2$: C, 57.73; H, 8.30; N, 9.62. Found: C, 57.50; H, 8.30; N, 9.68.

1,3,3-Trimethyl-2-phenyl-4-acetyl-tetrahydropyrazinium Iodide (XV).—A solution of 0.090 g. (0.39 mmole) of acetate XII in 20 ml. of dried acetone and 1 g. of methyl iodide was heated at gentle reflux for 1 hr., and then cooled. During the heating, a white crystalline solid precipitated out. This was collected by filtration and weighed 0.10 g. The filtrate was concentrated to

yield an additional 0.025 g. Both crops, 0.125 g. (86%), had the same m.p. 261–262° dec.; infrared spectrum (KBr), 6.00 (broad C=N + C=O), 7.10 (broad, *gem*-dimethyl), and 7.38 μ (acetyl-C-methyl).

Anal. Calcd. for $C_{15}H_{21}IN_2O$: C, 48.42; H, 5.69; N, 7.53. Found: C, 48.42; H, 5.83; N, 7.58.

1,3,3-Trimethyl-2-phenyl-4-acetylpiperazine Hydrochloride (XVI).—A solution of 0.16 g. (0.43 mmole) of methiodide XV in 25 ml. of 50:50 methanol–ethanol was swirled with 0.19 g. (0.005 mole) of sodium borohydride. An immediate exothermic reaction ensued which slowly subsided. After standing at room temperature for 4 hr., the solution was poured into 50 ml. of 3 *N* hydrochloric acid and washed with ether. After basification with solid potassium hydroxide, the aqueous solution was washed four times with ether. The combined ethereal extracts were dried, and the product was precipitated as the hydrochloride salt. Recrystallization from methanol–ether yielded 0.10 g. (80%) of white needles, m.p. 244–245° dec. A portion was recrystallized again from the same solvents for an analytical sample: m.p. 245–246° dec.; pK'_a 5.60 (50% methanol); infrared spectrum (KBr), 5.95 (C=O), 7.10 (*gem*-dimethyl), and 7.38 (acetyl-CH_3).

Anal. Calcd. for $C_{15}H_{23}ClN_2O$: C, 63.73; H, 8.20; N, 9.91. Found: C, 63.47; H, 8.47; N, 9.90.

1,3,3-Trimethyl-2-phenylpiperazine Dihydrochloride (XVII).—A solution of 0.065 g. (0.34 mmole) of piperazine acetate XVI in 10 ml. of ethanol and 10 ml. of 10% sodium hydroxide solution was refluxed for 48 hr. The reaction was cooled, poured into 30 ml. of concentrated sodium chloride solution, and washed with five 30-ml. portions of ether. After drying (sodium sulfate–potassium carbonate), the ethereal solution was reduced (*in vacuo*) to about 25 ml. in volume. The hydrochloride salt was precipitated in the usual fashion, and recrystallized from methanol–acetone. The first crop weighed 0.035 g., decomposed over 250°. A second crop (same decomposition point) brought the total yield to 0.050 g. (78%). A portion of the first crop served as an analytical sample: pK'_a 3.10, 8.30 (50% methanol); infrared spectrum (KBr), 6.35 (NH_2^+), 7.11, and 7.23 μ (*gem*-dimethyl).

Anal. Calcd. for $C_{13}H_{22}Cl_2N_2$: C, 56.32; H, 8.00; N, 10.11. Found: C, 56.48; H, 8.09; N, 9.88.

Pyrolysis and Photolysis of 1-Methyl-3-diazooxindole. Base Decomposition of Isatin 2-Tosylhydrazone[1,2]

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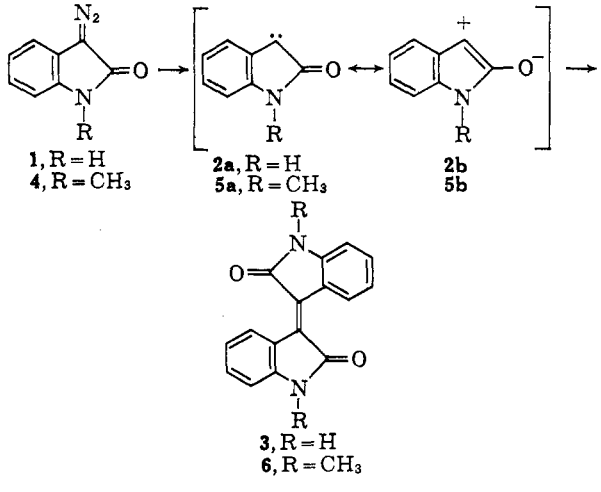
Pyrolysis of 1-methyl-3-diazooxindole (**4**) in refluxing ethanol led to 1,1′-dimethylisoindigo (**6**) and 1,1′-dimethylisatinazine (**16**), and in the presence of pyridine N-oxide produced **6**, **16**, and 1-methylisatin (**12**). Photolysis of **4** in ethanol gave 3-ethoxy-1-methyloxindole (**23**); photolysis in cyclohexene led to two geometric cyclopropane isomers (**24** and **25**) resulting from *cis* addition to the cycloolefin, and in hexane solution containing 1,1-diphenylethylene produced the spirooxindole (**26**). Compounds **6**, **12**, **16**, and **23**–**26** were probably formed by appropriate reaction with the pyrolytically and photolytically generated oxindolylene acting as a singlet (**5a**). This same oxindolylene also displayed triplet character (**5c**) in the e.s.r. spectrum at 4°K., in reaction with oxygen to form **12**, and with photolytically generated Cl· atoms and Cl_3C· free radicals (from CCl_4) to yield 3-chloro-3-trichloromethyl-1-methyloxindole (**28**). At room temperature, **4** reacted with bromine and triphenylphosphine to form 3,3-dibromo-1-methyloxindole (**17**) and the phosphazine adduct (**18**), respectively. Pyrolysis of **18** led to the triphenylphosphine, **6** and **16**, but no ylide. The mechanisms of these reactions are discussed. Base decomposition of isatin 2-tosylhydrazone (**9**) led to indigo blue (**38**), presumably *via* the unisolable 2-diazoindoxyl (**36**) and reactive indoxylene (**37**).

In 1916, Staudinger and Goldstein reported that a sealed-tube pyrolysis of 3-diazooxindole (**1**) at 200° in benzene afforded isoindigo (**3**).[3] In 1955, Huisgen proposed that this reaction proceeded *via* the intermediacy of a resonance-stabilized, "reaktionsträgen," carbene (**2**).[4]



1, R = H
4, R = CH_3

2a, R = H
5a, R = CH_3

2b
5b

3, R = H
6, R = CH_3

Our study of this system arose from our interest in the nature of **1**[5] and **2**[6] and the mode of formation of **3**. Since the isatin lactam–lactim controversy is as yet unresolved,[9] this variable could be eliminated by a study of the N-alkyl derivative. In this paper we report on the preparation of 1-methyl-3-diazooxindole (**4**), and its pyrolytic and photolytic decomposition in the presence of reagents which would react with carbene **5** in the sin-

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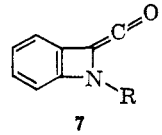
(2) Presented in part at the Organic Division of the 148th National Meeting of the American Chemical Society, Chicago, Ill., Sept., 1964, Abstracts of Papers, p. 55S.

(3) H. Staudinger and J. Goldstein, *Ber.*, **49**, 1923 (1916).

(4) R. Huisgen, *Angew. Chem.*, **67**, 457 (1955).

(5) Possibility of diazooxide character: (a) L. Horner, E. Spietschka, and A. Gross, *Ann.*, **573**, 17 (1951); (b) P. Yates and E. Robb, *J. Am. Chem. Soc.*, **79**, 5760 (1957).

(6) Possible reaction paths as a singlet electrophile include stereospecific insertions, 1,3-dipolar additions *via* **2b**,[7] and rearrangement *via* ketene **7** to ring contraction products.[8] As a triplet, **2** should undergo free-radical reactions.



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(7) R. Huisgen, H. König, G. Binsch, and H. J. Sturm, *Angew. Chem.*, **73**, 368 (1961).

(8) As in the thermolysis of naphthalene 1,2-diazooxide.[5]

(9) Summarized by P. L. Julian, E. W. Meyer, and H. C. Printy in "Heterocyclic Compounds," Vol. 3, R. C. Elderfield, Ed., John Wiley and Sons, Inc., New York, N. Y., 1952, p. 202; and W. C. Sumpter, *Chem. Rev.*, **34**, 398 (1944).