that they also obtained III in one experiment, which they could not repeat in subsequent attempts.

We now wish to report that heating I with strong acids as catalysts to 185° gives only the carbanilate (II) and no cyclized product (III or IV). The addition of excess base readily converts II to III with no appearance of IV. Now, however, on adding acid, III is quantitatively converted to IV. In all cases, III must be formed prior to the isomerization to IV.

We assigned the structure[1] of III by n.m.r. spectrum which showed a singlet at τ 2.75, a triplet at 5.05, and a quartet at 5.85 with an intensity ratio of 5:2:2 (m.p. 97.1–97.8°). After treatment with acid, the n.m.r. spectrum showed a singlet at τ 2.75, a quartet at 3.40, and a doublet at 8.15 with an intensity ratio of 5:1:3 (m.p. 56.5–57.2°). This product (IV) has the same melting point and the same n.m.r. spectrum of that reported by Shachat, *et al.*,[6] as a minor product in the preparation of III.

We note that Sisido, *et al.*,[5] neutralized with excess acid during the work-up of their product which accounts for the isolation of IV in all cases but one. Shachat, *et al.*,[6] used "just sufficient acid to neutralize the base,[1]" but even so this would probably account for a minor amount of IV found. A similar acid-catalyzed isomerization has been reported in the related triazole series.[9,10]

Experimental

4-Methylene-3-phenyl-2-oxazolidinone (III).—A solution of phenyl isocyanate (11.9 g., 0.1 mole), propargyl alcohol (5.6 g., 0.1 mole), and sodium acetate (0.1 g.) was stirred until a strongly exothermic reaction had subsided. Two recrystallizations from methanol gave small white granules, m.p. 97.2–97.5°; the yield was 82.5%.

Anal. Calcd. for $C_{10}H_9NO_2$: C, 68.6; H, 5.18; N, 8.00. Found: C, 68.4; H, 5.22; N, 8.11.

The same compound was obtained using pyridine, potassium hydroxide, or by heating to 160° without catalyst.

4-Methyl-3-phenyl-4-oxazolin-2-one (IV).—One-gram samples of III were dissolved in sulfuric, *p*-toluenesulfonic, and trifluoroacetic acids. Dilution with water or evaporation on a Rinco evaporator gave the isomerized product. Recrystallization from hexane gave soft white plates, m.p. 56.5–57.2°.

Anal. Calcd. for $C_{10}H_9NO_2$: C, 68.6; H, 5.18; N, 8.00. Found: C, 68.5; H, 5.21; N, 8.06.

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[9] Y. Yura, *Chem. Pharm. Bull.* (Tokyo), **10**, 1087 (1962).

[10] W. Batty and B. Weedon, *J. Chem. Soc.*, 786 (1949).

The Effect of Ionic Structure on the Hydrogenation of 1-Methyl-4-(2,2-diphenyl-2-hydroxyethyl)piperazine

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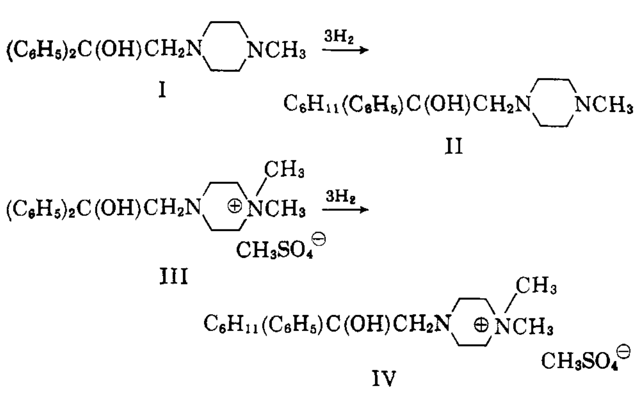
Maxted has discussed the poisoning effect of nitrogen bases on catalytic hydrogenation and the means of overcoming it by converting the offending atom to an ionic or shielded form.[1] It, therefore, appeared of interest to study the reduction of 1-methyl-4-(2,2-diphenyl-2-hydroxyethyl)piperazine (I) as acid salt or quaternary salt to determine whether there is any difference in the protective effect of the two ionic forms.



Results of the hydrogenation studies are summarized in Table I. It is evident that, despite the large group at N⁴ which may prevent poisoning to some extent, more rapid and more complete reaction takes place when sufficient acid is present to neutralize that nitrogen atom. A comparison of reduction B, where the dihydrochloride salt is partially neutralized to the monohydrochloride salt, and reduction D seems to give an indication that quaternization gives better protection against poisoning. This is more clearly indicated in the attempts to reduce both rings with platinum oxide. No success was achieved with the dihydrochloride salt of I. In contrast when III is hydrogenated in the presence of acid to neutralize the N⁴ atom, 1,1-dimethyl-4-(2,2-dicyclohexyl-2-hydroxyethyl)piperazinium methosulfate V is obtained in good yield. This shows that the difficulty in converting both rings is due to partial poisoning, not geometry. Hydrogenation results also indicate that rhodium catalysts are less sensitive to base effect than platinum.

TABLE I

HYDROGENATION CONDITIONS[a]

Experiment	Substrate	Catalyst	Ratio, %	Time, hr.	Product	Yield, %
A	I[b]	[f]	3		II	85
B	I[b,c]	[f]	3	[i]	II	84
C	I[b,d]	[g]	7	7	II	80
D	III	[f]	5	20	IV	78
E	III[e]	[f]	2.5	20	IV	80
F	III	[h]	35	14[j]	IV	84
G	III[e]	[h]	35	6	IV	85

[a] Except where noted, hydrogenations were carried out at 55–60° and 2-atm. pressure with 0.03 mole of substrate in 3.0 ml. of water. [b] Dihydrochloride salt used, pH of solution 1.5. [c] Solution adjusted to pH 3.0 by the addition of sodium hydroxide solution. [d] pH of solution changed to 4.0–5.0. [e] Three cubic centimeters of acetic acid added. [f] Platinum oxide. [g] 5% rhodium on alumina. [h] 5% rhodium on carbon. Reduction carried out at room temperature. [i] Uptake of hydrogen only 30% in 20 hr. When the pH of the solution was lowered to 1.5 by the addition of hydrochloric acid the rate of uptake increased markedly. Reduction was complete in 6 hr. more. [j] Uptake was 70% in 5–6 hr.

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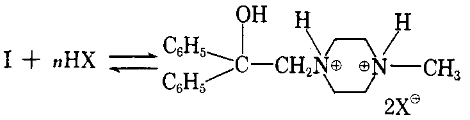
[1] E. B. Maxted, "Advances in Catalysis," Vol. III, Academic Press, Inc., New York, N. Y., 1951.

[2] Examination of molecular models of I and II shows that one of the benzene rings is generally out of plane, but they can be rotated so that both rings will make contact with the catalyst surface.

It appears from this study that ionic structure does exert a strong and helpful influence on the hydrogenation of the title compound. Furthermore, we would like to suggest that the difficulty in reducing both rings when starting with the dihydrochloride salt of I can be due to the fact that the conversion of I to Ia is reversible. Therefore, complete or sufficient conversion of the poisoning nitrogen atom, particularly at N^1, to a nonpoisoning form cannot be achieved.



Ia

n = 2 or more; X = Cl, CH_3COO

In the case of the quaternary salt III, a single species, incapable of reversibility, exists at N^1, and only a small amount of acid is necessary to counteract the effect of the other nitrogen atom.

Experimental

Compound II was prepared from I by the method described in the literature[3,4] (experiment I in the Table). Compound IV was prepared from III and identified by melting point and mixture melting point with a known standard.[3,4]

Attempts to Reduce Both Rings.—Experiment I was followed using a 5% weight ratio of platinum oxide. After 48 hr., uptake of hydrogen, which had stopped, amounted to about 4 molar equivalents (3 equivalents were absorbed in 7 hr.). About 70% of impure II dihydrochloride hemihydrate was recovered, plus 25% of a product, which from analysis could be a mixture of the hemihydrate and the anhydrous salt of II, melting up to 255°.[3]

Other attempts with more catalyst or with the base I in glacial acetic acid also failed to go to completion.

1,1-Dimethyl-4-(2,2-dicyclohexyl-2-hydroxyethyl)piperazinium Methosulfate (V).—A solution of 12.67 g. (0.03 mole) of III in 30 ml. of water and 3 ml. (0.05 mole) of glacial acetic acid was hydrogenated under 2-atm. pressure at 55–60° in the presence of 0.63 g. of platinum oxide. Uptake for 0.18 mole (6 H_2) was complete in 20 hr. The solution was filtered from the catalyst and concentrated to dryness under reduced pressure. The residue was treated with anhydrous alcohol and benzene and reconcentrated to ensure complete removal of water and acetic acid. The residue was recrystallized from hot isopropyl alcohol and dried to constant weight before analysis; yield 78%.

Anal. Calcd. for $C_{21}H_{42}N_2O_5S$: C, 58.03; H, 9.74; N, 6.45; O, 18.41; S, 7.38. Found: C, 58.30; H, 9.75; N, 6.58; O, 18.38; S, 7.45.

The melting point of the product varied because of the difficulty of removing water or solvent. After recrystallization, it melted at 175–178°. After thorough drying for 3 days at 100°, the melting point rose to 182–185°.

In a similar reduction 8 g. of 5% rhodium on carbon[5] was used. In another reduction in the absence of acid, 10 g. of the same catalyst brought about uptake of 0.18 moles of hydrogen in 36 hr. (3 equivalents were absorbed in 3 hr.). In each case, V was obtained in 75–80% yield.

Infrared examination of the products of the three experiments showed no evidence of benzenoid structure.

Acknowledgment.—The author is indebted to Mr. E. F. Shelberg (now retired) and Mr. O. Kolsto of this laboratory for the microanalyses and to Mr. W. Washburn also of this laboratory for infrared spectroscopy.

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[3] H. E. Zaugg, R. J. Michaels, H. J. Glenn, L. R. Swett, M. Freifelder, G. R. Stone, and A. W. Weston, *J. Am. Chem. Soc.*, **80**, 2763 (1958).

[4] H. E. Zaugg, M. Freifelder, R. J. Michaels, and A. W. Weston, U. S. Patent 2,980,683 (April 18, 1961).

[5] The rhodium catalysts are available from Engelhard Industries, Newark, N. J.

Condensation of Formaldehyde with Reissert Compounds

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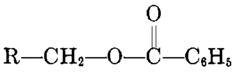
Formaldehyde has been condensed with Reissert compounds, 2-benzoyl-1,2-dihydroisoquinaldonitrile and 1-benzoyl-1,2-dihydroquinaldonitrile, in a reaction analogous to that previously described for other aldehydes[2–5] to yield 1-isoquinolylcarbinyl benzoate (I) and 2-quinolylcarbinyl benzoate (II), respectively.



$$R{-}CH_2{-}O{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}C_6H_5$$

I, R = 1-isoquinolyl
II, R = 2-quinolyl

$R{-}CH_2OH$

III, R = 1-isoquinolyl
IV, R = 2-quinolyl

Saponification of the hydrochlorides of esters I and II gave the expected 1-isoquinolylcarbinol (III) and 2-quinolylcarbinol (IV), respectively. The 1-isoquinolylcarbinol obtained had a melting point of 77–79° as compared with a reported value of 65°.[6] That this was actually 1-isoquinolylcarbinol (III) was confirmed by elementary analysis and by reduction by the method of Buck, *et al.*,[7] to the known 1-methylisoquinoline. This appears to be a more advantageous method for preparing III than that previously described.[6]

Experimental[8]

Hydrochloride of 1-Isoquinolylcarbinyl Benzoate (I).—To a solution of 10.4 g. (0.04 mole) of 2-benzoyl-1,2-dihydroisoquinaldonitrile[9] in 150 ml. of dry ether and 75 ml. of dry dioxane maintained at 0° in an atmosphere of pure nitrogen was added 0.04 mole of freshly prepared phenyllithium. Gaseous formaldehyde, formed by the depolymerization of paraformaldehyde, was introduced into the resultant red solution by means of a slow stream of nitrogen. The addition was continued until the red color was discharged and a white suspension formed. The mixture was stirred for 1 hr. at 0°, then for an additional hour at room temperature. Sufficient ether was added to increase the total volume to 500 ml., and the mixture was extracted with 12 ml. of water and then two 50-ml. portions of 10% hydrochloric acid. Cooling of the hydrochloric acid solution in an ice bath gave a white solid which was removed by filtration. This afforded 7.24 g. (61.4%) of the hydrochloride of I. After several recrystallizations from ethanol, the melting point was 177–180° dec.

Anal. Calcd. for $C_{17}H_{14}ClNO_2$: C, 68.15; H, 4.79; N, 4.67; Cl, 11.83. Found: C, 68.13; H, 4.64; N, 4.82; Cl, 12.07.

1-Isoquinolylcarbinol (III).—This compound was obtained by refluxing a solution of 8.6 g. (0.028 mole) of the hydrochloride of I and 10.0 g. of potassium hydroxide in a mixture of 60 ml. of ethanol and 25 ml. of water for 8 hr. The majority of the ethanol

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[1] Undergraduate Petroleum Research Fund Scholars for academic years, 1961–1962 and 1962–1963, respectively.

[2] L. R. Walters, N. T. Iyer, and W. E. McEwen, *J. Am. Chem. Soc.*, **80**, 1177 (1958).

[3] F. D. Popp and W. E. McEwen, *ibid.*, **79**, 3773 (1957).

[4] F. D. Popp and W. E. McEwen, *ibid.*, **80**, 1181 (1958).

[5] E. G. Podrebarac and W. E. McEwen, *J. Org. Chem.*, **26**, 1165 (1961).

[6] B. R. Brown, D. Ll. Hammick, and B. H. Thewlis, *J. Chem. Soc.*, 1145 (1951).

[7] J. S. Buck, W. H. Perkin, Jr., and T. S. Stevens, *ibid.*, 1471 (1925).

[8] All melting points are corrected. Microanalyses by Schwarzkopf Microanalytical Laboratory, Woodside, N. Y.

[9] J. J. Padbury and H. G. Lindwall, *J. Am. Chem. Soc.*, **67**, 1268 (1945).