[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Quinoxaline Formation and the Ortho Effect

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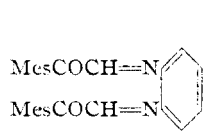
The observation that α-naphthylglyoxal and *m*-xylylglyoxal reacted with *o*-phenylenediamine to form quinoxalines, whereas mesitylglyoxal and 2,4,6-triisopropylphenylglyoxal yielded Schiff bases[4] suggested that this reaction might serve as a useful tool in distinguishing differences in the degree of steric hindrance.

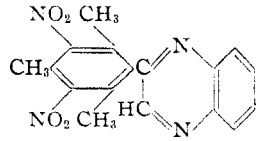
As a further test of this idea the action of *o*-phenylenediamine on 2,4-dimethyl-6-methoxyphenylglyoxal and 2,6-dimethoxyphenylglyoxal was studied. Each was found to yield a quinoxaline. It is clear, then, that two methoxyl groups or one methoxyl and one methyl group when in the *ortho* positions provide less hindrance to quinoxaline formation than do two methyl radicals.

A possible way of diminishing the hindrance of the mesityl radical is to introduce nitro groups. Thus, it has been reported that 3-nitromesitonitrile and 3,5-dinitromesitonitrile are hydrolyzed more readily than is mesitonitrile.[5] Similarly 3,5-dinitrobenzaldehyde undergoes the Perkin condensation[6] at a normal rate whereas mesitaldehyde itself reacts very slowly. The failure to bring about hydrolysis of 4-nitro-2,3,5,6-tetramethylbenzonitrile[7] suggested further that the effect of the nitro groups might be exerted only when they are in a position *meta* to the reacting group.

Experiments with mesitylglyoxal and 3,5-dinitromesitylglyoxal have yielded similar results. Mesitylglyoxal had been shown to react with *o*-phenylenediamine to yield only the Schiff base (I).[4] The dinitro derivative, however, was found to form a quinoxaline (II).



I



II

It seems probable that this effect of nitro groups on the steric hindrance offered by the mesityl radical is due to hydrogen bonding. Chelation involving a nitro group and an *ortho* methyl group would be expected to lessen the blocking effect exerted by the latter on a group in the adjoining position on the ring.[8]

Experimental

2,4-Dimethyl-6-methoxyacetophenone.—This compound was prepared from 3,5-dimethylanisole and acetic anhydride according to the general procedure of Adams and Noller.[9] A mixture of 300 g. of anhydrous aluminum chloride, 136 g. of 3,5-dimethylanisole and 400 cc. of carbon disulfide was heated to boiling, and 82 g. of acetic anhydride was added over a period of thirty minutes to the refluxing mixture. Refluxing was continued for one hour, and the mixture was allowed to stand two hours. Decomposition of the reaction mixture in the usual way yielded 76 g. of crude 2,4-dimethyl-6-hydroxyacetophenone and 61 g. of 2,4-dimethyl-6-methoxyacetophenone. The crude phenol, methylated with methyl sulfate, yielded an additional 54 g. of the ether; b. p. 140–144° (18 mm.).[10] The product solidified in the receiver.

2,4-Dimethyl-6-methoxyphenylglyoxal.—To a refluxing solution of 11.5 g. of selenium dioxide in 75 cc. of dioxane and 5 cc. of water was added 18 g. of 2,4-dimethyl-6-methoxyacetophenone. The reaction mixture was stirred and refluxed for five hours and was then allowed to stand overnight at room temperature. The precipitated selenium was removed by filtration and the filtrate was distilled under diminished pressure. After removal of the dioxane the crude 2,4-dimethyl-6-methoxyphenylglyoxal distilled at 90–120° (4 mm.). The glyoxal was allowed to stand under water for several months. There resulted a partial conversion to a white crystalline material.

A solution of 1.0 g. of 2,4-dimethyl-6-methoxyphenylglyoxal and 1.0 g. of *o*-phenylenediamine in 25 cc. of glacial acetic acid was refluxed for one hour. The warm solution was diluted with 100 cc. of water and the resulting turbid mixture was allowed to stand at room temperature for three days. The semi-solid precipitate was crystallized from aqueous ethyl alcohol. The light yellow 2-(2,4-dimethyl-6-methoxyphenyl)-quinoxaline melted at 83.5–84°.

Anal. Calcd. for $C_{17}H_{18}N_2O$: C, 77.24; H, 6.10. Found: C, 77.26; H, 6.07.

2-(2,6-Dimethoxyphenyl)-quinoxaline.—2,6-Dihydroxyacetophenone, prepared by the method of Russell and Frye,[11] was methylated with methyl sulfate according to

(1) Rohm and Haas Research Assistant, 1938–1940.
(2) Rohm and Haas Research Assistant, 1940–1942.
(3) Rohm and Haas Research Assistant, 1938–1939.
(4) Fuson, Emerson and Gray, THIS JOURNAL, **61**, 480 (1939).
(5) Küster and Stallberg, *Ann.*, **278**, 207 (1894).
(6) Lock and Bayer, *Ber.*, **72**, 1064 (1939).
(7) Cain, *ibid.*, **28**, 967 (1895).
(8) A similar explanation has been advanced to account for certain anomalous properties of o-nitrotoluene (Sidgwick and Callow, *J. Chem. Soc.* **125**, 538 (1924)) and of o-nitrophenylacetic acid (Dippy and Lewis, *ibid.*, **1426** (1937)).
(9) Adams and Noller, "Organic Syntheses," Coll. Vol. I, second edition, 1941, p. 109.
(10) von Auwers and Borsche, *Ber.*, **48**, 1698 (1915).
(11) Russell and Frye, "Organic Syntheses," Vol. 21, p. 22.

the directions of Limaye and Gangal.[12] The product, 2,6-dimethoxyacetophenone, was oxidized with selenium dioxide by the procedure described for the production of 2,4-dimethyl-6-methoxyphenylglyoxal. The 2,6-dimethoxyphenylglyoxal, boiling at 115–117° (5 mm.), was converted to the corresponding quinoxaline by the usual procedure. The product separated from aqueous ethanol as yellow needles; m. p. 95.5–96.5°.

Anal. Calcd. for $C_{16}H_{14}N_2O_2$: C, 72.16; H, 5.30. Found: C, 72.03; H, 5.46.

2,6-Dimethoxymandelic Acid.—Confirmation of the structure of the 2,6-dimethoxyphenylglyoxal was obtained by conversion to the corresponding mandelic acid. A mixture of 0.8 g. of 2,6-dimethoxyphenylglyoxal and 12 cc. of 30% sodium hydroxide solution was shaken for thirty minutes at room temperature. It was allowed to stand in the icebox for one hour and acidified with dilute hydrochloric acid. The 2,6-dimethoxymandelic acid was extracted with ether and recrystallized from chloroform; m. p. 146–147°.

Anal. Calcd. for $C_{10}H_{12}O_5$: C, 56.61; H, 5.66; neut. equiv., 212. Found: C, 56.59; H, 5.84; neut. equiv., 206.

2-(3,5-Dinitromesityl)-quinoxaline.—To a solution of 70 cc. of dioxane, 4 cc. of water and 7.8 g. of selenium dioxide was added, with stirring, 17.6 g. of dinitroacetomesitylene. The mixture was heated under reflux for four hours, cooled and filtered. Benzene (50 cc.) was added to the filtrate and the benzene, dioxane and water were distilled under diminished pressure. To the residual dark oil was added a small amount of methanol. The product crystallized when allowed to stand. It was recrystallized from a mixture of benzene and low-boiling petroleum ether and finally twice from methanol; m. p. 122–125°, with softening at 116°.

A solution of 1 g. of the glyoxal and 1 g. of *o*-phenylenediamine in 25 cc. of glacial acetic acid turned red immediately. It was heated under reflux for thirty-five minutes, allowed to stand for three and one-half hours and poured on ice. The quinoxaline separated as a yellow semi-solid mass. It was decolorized by treatment with Norite in ethanol. It crystallized from methanol in almost white needles; m. p. 197.5–198°; yield, 0.7 g.

Anal. Calcd. for $C_{17}H_{14}N_4O_4$: C, 60.35; H, 4.17; N, 16.56. Found: C, 60.68, 60.65; H, 4.15, 4.19; N, 16.73.

(12) Limaye and Gangal, *Rasāyanam*, **1**, 64 (1936); (*Chem. Abstr.*, **31**, 2182 (1937)).

Summary

Quinoxaline formation, which is inhibited by the mesityl radical in mesitylglyoxal, has been found to take place with 2,4-dimethyl-6-methoxyphenylglyoxal, 2,6-dimethoxyphenylglyoxal and 3,5-dinitromesitylglyoxal.

The effect of the nitro groups in diminishing the steric hindrance provided by the mesityl group has been ascribed to chelation.

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The Catalytic Hydrogenation of Benzene over Metal Catalysts

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Introduction

As part of his multiplet theory of catalysis, Balandin[2] in 1929 postulated that a metallic catalyst in order to be active at low reaction temperatures in the hydrogenation of benzene to cyclohexane must possess developed crystal faces with a triangular configuration and with lattice dimensions standing in a definite relation to the dimensions of the benzene ring. By plotting on rectangular coördinates atomic radii *vs.* metal to carbon distances Balandin showed that only the (111) planes of face-centered cubic metallic lattices with atomic radii between about 1.2 and 1.4 Å., and a few hexagonal lattices, fulfill the requirements. As two corollaries of his hypothesis he predicted that five- and seven-membered hydrocarbon rings should not be acted upon in the same manner as the benzene compounds, and that simultaneous addition of all six hydrogen atoms should take place with no formation of the intermediates in the hydrogenation of benzene.

The first of Balandin's corollaries is proved untrue by experiments of Kistiakowsky and his collaborators,[3] who in their determinations of the heats of hydrogenation of all the unsaturated intermediates in the five-, six- and seven-membered series used nickel–cobalt catalysts at temperatures below 150°. Apparently, for these hydrogenations any flat symmetrical adsorption of five- and seven-membered rings cannot be imagined.

Balandin's second corollary has been shown recently by Taylor[4] to be explainable on thermodynamic grounds, the intermediates cyclohexene

(1) From the thesis of Nis Skau presented to the faculty of The Johns Hopkins University in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(2) Balandin, *Z. physik. Chem.*, **B2**, 289 (1929).

(3) Kistiakowsky, THIS JOURNAL, **58**, 137, 146 (1936).

(4) Taylor, *ibid.*, **60**, 627 (1938).