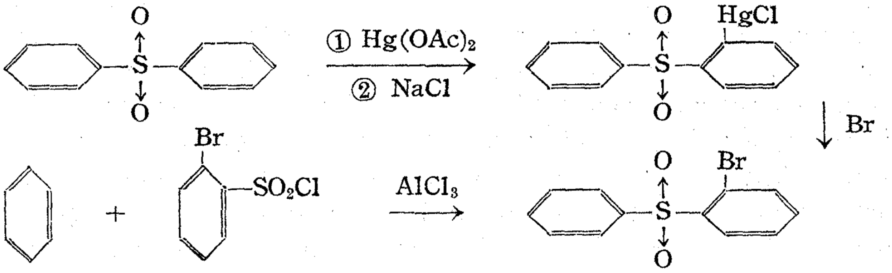
## 21. Teiji Ukai*, Yuzuru Yamamoto, Shozo Hirano, and Masaru Yotsuzuka : Studies on Organic Mercurials. XVI.[1] On the Mechanism of Aromatic Mercuration and the Mercuration of Diphenyl Sulfone.

(*Pharmaceutical Faculty, Uuiversity of Kanazawa***)

In previous papers of this series, the mercuration of several aromatic compounds has been reported. The present paper is on the mercuration of diphenyl sulfone together with the mechanism of aromatic mercuration as a general conclusion of our recent work.

The mercuration of benzophenone[2], one of the *meta*-directors, was reported to have occurred *ortho* to the keto group. Our attention was called to the mercuration of diphenyl sulfone which is ordinarily thought of as a *meta*-director to electrophilic agents.

The mercuration of diphenyl sulfone was worked up in the usual manner and the crude chloromercuridiphenyl sulfone obtained was purified from ethanol to fine plates, m.p. 247~248°(decomp.). This was subjected to bromination in glacial acetic acid to give a bromo derivative corresponding to formula, $C_{12}H_9O_2BrS$, m.p. 117~119°, undepressed on admixture with an authentic sample synthesized from benzene and *o*-bromobenzenesulfonyl chloride by the Friedel-Crafts reaction.[3] Hence the mercuration of diphenyl sulfone in the 2-position.



Although the history of the study of direct aromatic mercuration is long,[4] few studies have been made on its reaction mechanism.

Maschmann[5] and Albert[6] reported that the mercuration of aromatic amines goes through the initial formation of the mercuric salt of the bases, successive rearrangement of the mercuric acid group, and then the substitution. Klapproth[7] tried the mercuration of nitrobenzene and of toluene with mercuric perchlorate and acetate, and found that the position to be mercurated differs according to the mercurating agent employed, the cause of which was attributed to the difference in the degree of ionization between the two reagents.

Though aromatic mercuration has been thought of as an electrophilic substitution reaction, many anomalous cases have also been observed. The compounds possessing *ortho-para* directing group, such as phenols,[8] anilines,[9] and chlorobenzene,[10] are usually

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* Present address : Shizuoka College of Pharmacy, Oshika, Shizuoka (鵜飼貞二).

** Tsuchitoriba-naga-machi, Kanazawa (山本 譲, 平野昌三, 四塚 勝).

1) Part XV : J. Pharm. Soc. Japan, **75** (1955) (in press).

2) O. Dimroth : Ber., **35**, 2863(1902) ; V. Grignard, A. Abelmann : Bull. soc. chim., (4), **19**, 24(1916).

3) W. E. Truce, M. E. Amos : J. Am. Chem. Soc., **73**, 3013(1951).

4) L. Pesci : Gazz. chim. ital., **22**, I, 373(1892) ; O. Dimroth : Ber., **31**, 2154(1898).

5) L. Maschmann : Ann., **450**, 85(1926).

6) A. F. Albert, W. Schneider : *Ibid.*, **465**, 257(1928).

7) W. I. Klapproth : J. Am. Chem. Soc., **72**, 4461(1951).

8) "Org. Syntheses", Coll. Vol., **1**, 161.

9) O. Dimroth : Ber., **35**, 2039(1902).

10) M. E. Hancke : J. Am. Chem. Soc., **45**, 322(1923) ; B. Kalinowsky : Chem. Zentr., **1922**, I, 2301.

mercurated in the *ortho*- and *para*-positions as expected. Pyridine[11] is mercurated in the 3-position, and pyridine 1-oxide[12] in the 4-position. However, when mercurating compounds having *meta*-directing group, such as nitrobenzene,[13] benzoic acid,[14] or benzophenone,[2] the substitution does not proceed normally, as it gives the *ortho*-mercurated compound as the main product. Moreover, the prediction that the compounds of quinoline 1-oxide series would be mercurated in the 4-position, was borne out by experimental results, since the substitution in the 8-position took place.[12,15] In other cases, azoxybenzene (m.p. 36°)[16] undergoes mercuration in both the *ortho*- and *para*-positions in the ratio of about 4 : 1 (no other electrophilic reactions of azoxybenzene itself yields 2-substituted derivative). Further, 4-bromoazoxybenzene[15] is easily mercurated in the 2-position, but 2-bromoazoxybenzene[15] is mercurated with great difficulty in the 4-position, most of the starting material being recovered even under drastic conditions. The mercuration of benzyl alcohol[17] proceeds smoothly, yielding the *ortho*- and *para*-isomers and polymercurated derivatives with *ortho*-isomer predominating. Thus, orientation anomaly in aromatic mercuration, which the mere electrophilic view fails to account for, is observed not only with *meta*-directors, but, in some cases, with *ortho-para* directors and with the compounds of other types, e.g. quinoline 1-oxides.

Attempts to explain these irregular experimental results led to the following conclusions, that, (1) aromatic mercuration, as a rule, is an electrophilic reaction, but (2) when mercurating compounds possessing the substituents that has lone-pair electrons, the mercuric salt employed functions, at first, as a coördinating agent with the substituent already present, forming a transient ring complex by the approach of the coördinated mercury to an appropriate carbon atom, if any, in the ring. It is then that the substitution takes place, from which it can be taken for granted that the spatial condition is the determining factor as to where mercuration occurs.

The great coördinating tendency of mercuric salts is shown by the fact that they give a coördination complex even with anisole,[18] to say nothing of those they give with organic bases and heterocyclic N-oxides.[12] When no coördination is possible, the reaction proceeds just as in other electrophilic substitution reactions.

As to the spatial factors in quinoline 1-oxide series, it is possible for the mercury atom attached to the lone pair of the oxygen atom to be in the vicinity of the carbon atom at the 8-position; but in the case of pyridine 1-oxide no such mutual approach between the mercury and the carbon atoms is possible. Therefore, the former is mercurated in the 8-position, but the latter in the 4-position where the highest electron density is expected.[19] The predominant or exclusive *ortho* mercuration of azoxybenzenes, benzyl alcohol, diphenyl sulfone, or other *meta*-directors, is well accounted for by these hypotheses.

Similarly, the well-known facts that the sulfonation of anthraquinone in the presence of a mercury catalyst gives $\alpha$-sulfonic acid[20], and that without the catalyst, it gives

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[11] G. Sachs, R. Eberhartinger: Ber., **56**, 2223 (1923); D. A. Reynolds, G. W. Birge: Ind. Eng. Chem., **32**, 363 (1940).

[12] T. Ukai, Y. Yamamoto, S. Hirano: J. Pharm. Soc. Japan, **73**, 823 (1953).

[13] O. Dimroth: Ber., **35**, 2036 (1902); Ann., **446**, 148 (1925); J. Jürgens: Rec. trav. chim., **45**, 61 (1928).

[14] O. Dimroth: Ber., **32**, 765 (1899); *ibid.*, **35**, 2872 (1902).

[15] Part XIV: J. Pharm. Soc. Japan, **75** (1955) (in press).

[16] T. Ukai, Y. Ito: *Ibid.*, **73**, 821 (1953).

[17] Part XV: *Ibid.*, **75** (1955) (in press).

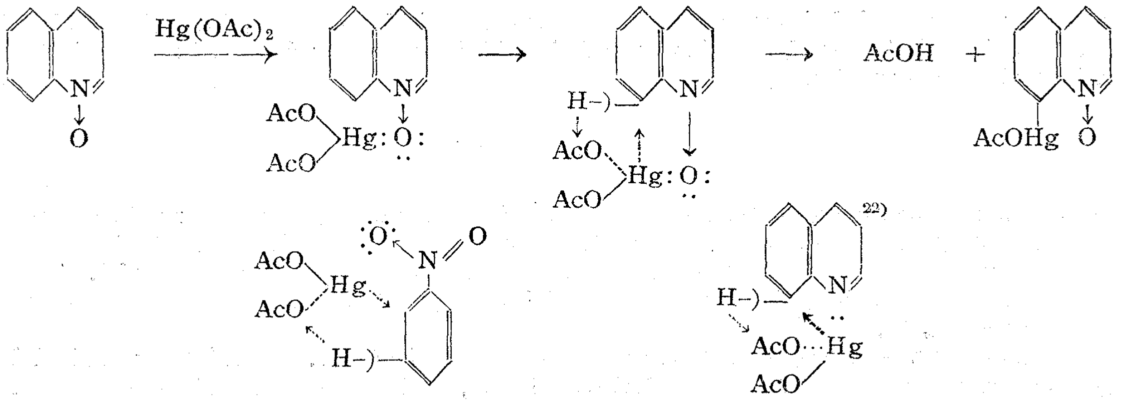
[18] W. Manchot: Ann., **421**, 334 (1920).

[19] E. Ochiai: J. Org. Chem., **18**, 534 (1953), *et seq.*

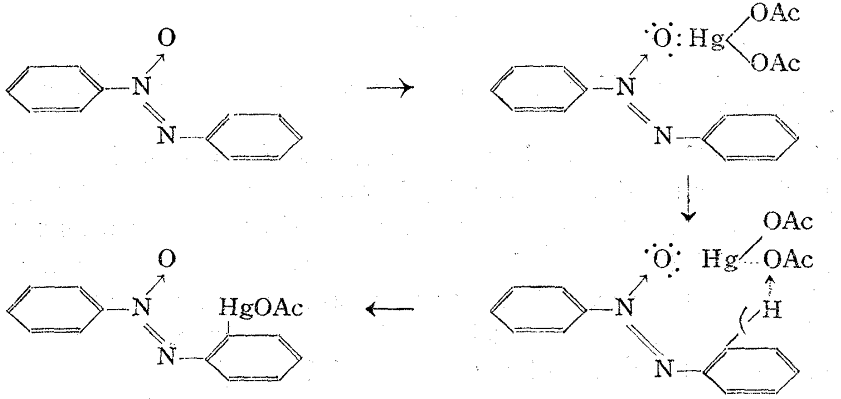
[20] K. Lauer: J. prakt. Chem., **130**, 180 (1931); P. Karrer: "Lehrbuch der organischen Chemie" Elfte Auflage, Georg Thieme Verlag, Stuttgart, 648 (1950).

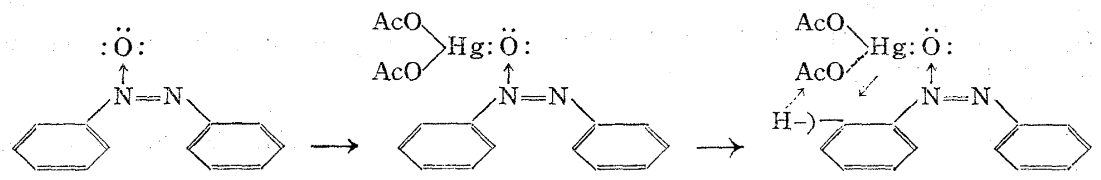
$\beta$-sulfonic acid,[20] are also understandable, for the $\alpha$-mercurated anthraquinone gives the corresponding sulfonic acid in high yields when treated with oleum.[21]

The schematic formulae that illustrate how aromatic mercuration might take place can be drawn as follows :

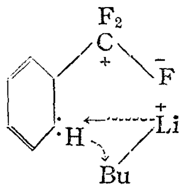


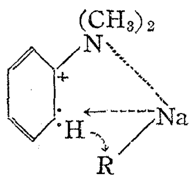
With respect to the mercuration of azoxybenzenes, according to our hypotheses, the orientation can be explained only by their *trans*-configuration, for by their *cis*-configuration the mercuration should occur, just as in nitrobenzene, in the *ortho*-position of the benzene ring united to the nitrogen atom carrying oxygen, which fact is contradictory to the experimental data, as shown below :





The metalation of diphenyl sulfone[3] and of N,N-dimethylaniline[23] is reported to occur *ortho* to the substituents, and that of benzotrifluoride[24] takes place in both *ortho*- and *para*-positions at the ratio of about 5 : 1. This *ortho*-predomination in metalation has some similarity to that in mercuration. Concerning the reaction mechanism, Morton[25] postulated the initial coördination of the metal atom with the substituent





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[21] V. V. Kozulov : Zhur. Obshcheĭ Khim., **18**, 2094 (1948) (C.A., **43**, 3815 (1949)).
[22] T. Ukai : J. Pharm. Soc. Japan, **51**, 543 (1931).
[23] H. Gilman, R. L. Bebb : J. Am. Chem. Soc., **61**, 109 (1938).
[24] J. D. Roberts, D. Y. Cutin : *Ibid.*, **68**, 1658 (1946).
[25] A. A. Morton : *Ibid.*, **69**, 969 (1947).

and proposed the schema shown.

It is of much interest that the present authors reached essentially the same conclusion in another field of metalation, though their work has been done almost independently from his.

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## Experimental

**Mercuration of Diphenyl Sulfone**—A mixture of diphenyl sulfone(2.5 g.), mercuric acetate(3.7 g.), and few drops of glacial AcOH was heated at 170~180° under reflux until solid. This was put into brine, boiled for a few mins., and filtered hot to remove the unreacted starting material. The residue (4.2 g.) was repeatedly recrystallized from EtOH. Colorless fine plates, m.p. 247~248°(decomp.), giving positive tests for Hg, Cl, and S.

**Bromination of the Mercurial**—A mixture of the mercurial (1 g.), $Br_2$(0.4 g.), and glacial AcOH (15 cc.) was heated at 80~90° until in colorless solution, cooled, and neutralized with conc. KOH solution under ice cooling. The extraction and the recrystallization of the resinous residue from EtOH yielded colorless crystals, m.p. 117~119°, unchanged by an authentic sample prepared from benzene and *o*-bromobenzenesulfonyl chloride by the Friedel-Crafts reaction. *Anal.* Calcd. for $C_{12}H_9O_2BrS$: C, 48.48; H, 3.03. Found: C, 48.70; H, 3.32.

## Summary

1) The mercuration of diphenylsulfone with mercuric acetate was found to occur in the 2-position.

2) Following reaction mechanism was proposed for aromatic mercuration.

i) Aromatic mercuration, as a rule, is an electrophilic reaction.

ii) When mercurating the compound possessing a substituent which has lone-pair electrons, the initial coördination of the mercury atom with the substituent, and the transient ring complex formation by the approach of the mercury atom to an appropriate carbon atom, if any, in the nucleus might take place. It is then that the substitution occurs. It is therefore clear that spatial condition is the determining factor as to where it is mercurated.

When the coördination is impossible or has no effect, the reaction proceeds just as in other electrophilic substitution reaction.

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