Ein kristallinisches Alkylphenathren vom Schmp. 82~84° (Pikrat : Zers. Pkt. 142~144°; Trinitrobenzolat : Zers. Pkt. 156~158°) besitzt die Zusammensetzung $C_{19}H_{20}$. Das zweite kristallinische Alkylphenanthren vom Schmp. 145~147° (Trinitrobenzolat : Zers. Pkt. 160~162°; Pikrat : Zers. Pkt. 135~137°) entspricht der Formel $C_{19}H_{20}$ oder $C_{19}H_{18}$. Die beiden anderen flüssigen Alkylphenanthrene wurden als Trinitrobenzolat charakterisiert. Die Komponente mit dem Trinitrobenzolat vom Zers. Pkt. 173~175° bildet auch ein Pikrat vom Zers. Pkt. 155~157° und ihre Zusammensetzung als $C_{20}H_{22}$ vermutet. Die anderen Komponente mit dem Trinitrobenzolat vom Zers. Pkt. 175~177°, deren UV-Absorptionsspektrum mit demselben der ersteren fast ähnlich ist, wurde wegen Materialmangel nicht analysiert. Von dem basischen Dehydrierungsprodukt wurden zwei Komponente als ein Pikrat vom Zers. Pkt. 234~237° und als ein Perchlorat vom Zers. Pkt. 280~284° isoliert, die noch nicht näher untersucht wurden. Als flüchtiges Amin wurde Ammoniak nachgewiesen.

(Eingegangen am 10. September 1954)

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## 89. **Takuo Kosuge and Schuichi Miyashita** : Syntheses of Nitro Compounds by Oxidation of Acylamino Compounds. VIII. Oxidation of Quinoline and its Derivatives.

(*Pharmaceutical Faculty, University of Kanazawa**)

One of the authors (T. Kosuge) found that aromatic acylamino compounds were oxidized into nitro compounds with hydrogen peroxide.[1)]

It is also already well-known that quinoline is oxidized with hydrogen peroxide of a suitable concentration to its 1-oxide or carbostyril. As carbostyril is considered to be a kind of acylamino compound, it was expected that quinoline will be derived to a nitro compound via the carbostyril as an acylamino compound, when it is treated with hydrogen peroxide. As was expected, quinoline was found to be oxidized with hydrogen peroxide to form nitrobenzoic acid.

Generally speaking, when quinoline is treated with ordinary oxidizing agents such as potassium permanganate, it is transformed into quinolinic acid or nicotinic acid, that is, the benzene moiety of quinoline is cleaved but the pyridine moiety remains unattacked. Therefore, our novel reaction where the pyridine moiety of quinoline is preferentially attacked, is worth extensive study.

Oxidation procedure for quinoline was the same as one reported[2)] before, except that some modification was made in the separation of the product. That is, after the oxidation was completed, a large part of acetic acid was removed from the reaction mixture by means of steam distillation. The residue was concentrated under a reduced pressure in the hope of isolating the product. However, the product was contaminated with a resinous substance, showing that effective separation of the crystalline product by recrystallization would be a difficult task. Therefore, the residue contaminated with the resinous substance was subjected to further oxidation with potassium permanganate in order to decompose the resinous contaminants. This procedure effectively isolated the crystalline products in a pure state.

Beside the desirable reaction described above, an inevitable side-reaction, viz.,

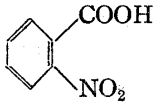
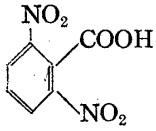
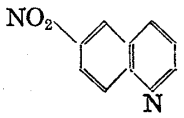
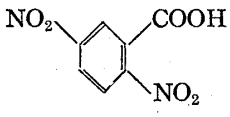
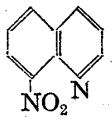
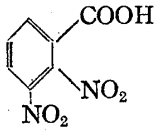
* Tsuchitoribanagamachi, Kanazawa (小菅卓夫, 宮下修一).

1, 2) Ann. Repts. Faculty Pharmacy, Kanazawa Univ., **2**, 3~29.

formation of ammonia, was observed in this case, too.[3)]

Other than quinoline itself, several nitroquinolines were also oxidized with hydrogen peroxide, in a similar manner, and the corresponding dinitrobenzoic acids were found to be formed as expected. The results along with the yields are shown in Table I.

Table I.

| Substance | (g.) | $H_2O_2$ (cc.) | AcOH (cc.) | Time (hrs.) | Reaction Product | (g.) [%] | $NH_3$ (%) | Total (%) |
|---|---|---|---|---|---|---|---|---|
|  | 3.6 | 60 | 40 | 20 |  | 0.51 [10.9] | 48.5 | 59.4 |
|  | 4.8 | 〃 | 〃 | 〃 |  | 1.36 [23.2] | 31.5 | 55.3 |
|  | 4.8 | 〃 | 〃 | 〃 |  | 1.4 [23.9] | 33.3 | 56.4 |
|  | 4.8 | 〃 | 〃 | 〃 |  | 0.51 [8.9] | 62.5 | 71.4 |

As given in Table I, better yields than that of quinoline were obtained in cases where the nitro group was introduced into the benzene moiety of quinoline.

Here, the authors would like to call attention to the fact that a similar observation has been made by them in the case of acylamino compounds.

The yield of oxidation product was bettered by the introduction of electron attracting groups probably because the benzene moiety of quinoline was stabilized and its decomposition with hydrogen peroxide was depressed by the introduction of the nitro group.

In the case of 8-nitroquinoline the yield was found to be exceptionally poor, when compared with other nitroquinolines. This shows that the formation of 1-oxide was hindered by the steric factor of nitro group introduced in 8-position of quinoline.

Lastly, studies on the mechanism of this reaction was made.

When considering the mechanism, attention should be called to the formation of ammonia and to the improved effect of nitro group on the yield of the product. These facts will show that this reaction proceeded by the same mechanism as in the case of the oxidation of acylamino compounds reported before.[4)]

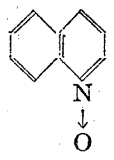
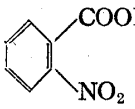
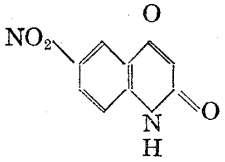
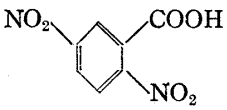
In order to substantiate this view, it is necessary to show explicitly that quinolines are oxidized to carbostyrils, considered as a kind of acylamino compounds, via their 1-oxides and further oxidation of the carbostyrils to nitrobenzoic acids takes place. Thus, oxidation of quinoline 1-oxide and 6-nitrocarbostyril was examined. Results are given in Table II.

As given in Table II, *o*-nitro- and 2,5-dinitro-benzoic acids were obtained from quinoline 1-oxide and 6-nitrocarbostyril, and the yields were almost the same as that of the corresponding quinoline and 6-nitroquinoline, respectively, showing that our view on the oxidation mechanism was valid.

However, there also was found to be some difference between oxidation of acylamino compounds and the present compounds. That is, in the former, the total yield, nitro compound plus ammonia, reached 80~90%, but in the latter, the yield ranged from 50

3, 4) J. Pharm. Soc. Japan, **74** (In Press).

Table II.

| Substance | (g.) | Reaction Product | (g.) [%] | $NH_3$(%) | Total(%) |
|---|---|---|---|---|---|
|  | 4.0 |  | 0.48 [10.4] | 48.2 | 58.6 |
|  | 5.3 |  | 1.2 [20.3] | 19.1 | 39.4 |

to 60%, showing that reaction other than formation of nitrobenzoic acid and ammonia took place. This point will be reserved for further examination.

In summarizing the results of the present study, it may be expected that the present novel reaction may help in the examination of the structure of a reaction product, e.g. determination of the position in which a nitro group has been introduced by the nitration of a nitrogenous heterocyclic compounds.

The authors gratefully acknowledge their indebtedness to Prof. Dr. Eiji Ochiai and Prof. Dr. Y. Mizuno for their interest and advice, and to Mr. Y. Itatani for the elementary analyses.

## Experimental

(1) **Oxidation of Quinoline**—A mixture of 3.6 g. of quinoline, 60 cc. of 30% $H_2O_2$, and 40 cc. glacial AcOH was heated on a water bath for 20 hrs. From the reaction mixture a greater part of AcOH was removed by steam distillation. The residue was concentrated under a diminished pressure and oxidized with potassium permanganate. $MnO_2$ formed was removed by filtration. The concentration of the filtrate produced yellow crystals. Recrystallization of the crystals from water produced *o*-nitrobenzoic acid, m.p. 146°, in the yield as shown in Table I. This did not lower the melting point of an authentic *o*-nitrobenzoic acid.

The solution from which acetic acid was removed by steam distillation was neutralized with NaOH and the quantity of ammonia evolved was measured by titration in a similar way used in the Kjeldahl measurement of nitrogen. *Anal.* Calcd. for $C_7H_7O_5N$: C, 45.40; H, 3.78; N, 7.57. Found: C, 45.47; H, 4.11; N, 7.63.

(2) **Oxidation of 5-Nitroquinoline**—4.8 g. of 5-nitroquinoline was oxidized by the same procedures as in (1). 2,6-Dinitrobenzoic acid, m.p. 202°; yield, 1.36 g. *Anal.* Calcd. for $C_7H_4O_6N_2$: C, 39.62; H, 1.89; N, 7.57. Found: C, 45.47; H, 4.11; N, 7.63.

(3) **Oxidation of 6-Nitroquinoline**—4.8 g. of 6-nitroquinoline was oxidized by the same procedures as in (1). 2,5-Dinitrobenzoic acid, m.p. 177°; yield, 1.4 g. *Anal.* Calcd. for $C_7H_4O_6N_2$: C, 39.62; H, 1.89; N, 13.21. Found: C, 39.38; H, 1.66; N, 13.13.

(4) **Oxidation of 8-Nitroquinoline**—4.8 g. of 8-nitroquinoline was oxidized by the same procedures as in (1). 2,3-Dinitrobenzoic acid, m.p. 201.5°; yield, 0.51 g. *Anal.* Calcd. for $C_7H_4O_6N_2$: C, 39.62; H, 1.89; N, 13.21. Found: C, 39.36; H, 2.02; N, 12.99.

(5) **Oxidation of quinoline 1-oxide**—4 g. of quinoline 1-oxide was oxidized by the same procedures as in (1). *o*-Nitrobenzoic acid, m.p. 146°; yield, 0.48 g. This did not lower the melting point of the authentic *o*-nitrobenzoic acid.

(6) **Oxidation of 6-Nitrocarbostyril**—5.3 g. of 6-nitrocarbostyril was oxidized by the same procedures as in (1). 2,5-Dinitrobenzoic acid, m.p. 177°; yield, 1.2 g. This did not lower the melting point of 2,5-dinitrobenzoic acid obtained in (1). *Anal.* Calcd. for $C_7H_4O_6N_2$: C, 39.62; H, 1.89; N, 13.21. Found: C, 39.80; H, 1.85; N, 13.45.

## Summary

1) Quinoline was found to be oxidized with hydrogen peroxide to form *o*-nitrobenzoic acid, and several nitroquinolines were also oxidized to corresponding dinitrobenzoic acids.

2) Formation of ammonia was observed as a side-reaction.

3) Quinoline 1-oxide and 6-nitrocarbostyril were oxidized to *o*-nitrobenzoic acid and

2,5-dinitrobenzoic acid, respectively, showing that quinolines were oxidized to carbostyrils, considered as a kind of acylamino compounds, via their 1-oxide and further oxidation of the carbostyrils to nitrobenzoic acids takes place.

(Received September 15, 1954)

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## 90. Nobuo Ikekawa and Yoshihiro Sato : Studies on the Coal Tar Bases. IX.[1] Methylpyridine 1-Oxides and their Ultraviolet Absorption Spectra.

(*Pharmaceutical Institute, Medical Faculty, University of Kyushu**)

Some years ago, one of the authors (Ikekawa) took part in a study on the separation of pyridine bases in coal tar by fractional distillation of their 1-oxides.[2] It was found from the study that in methylpyridine 1-oxides the methyl groups exhibit more different character by their position than in the original methylpyridines. The present study was undertaken to investigate the structures of methylpyridine 1-oxides and the spectral properties of the methyl groups in pyridine 1-oxide ring.

Pyridine 1-oxide and nine kinds of methylpyridine 1-oxides were compared in regard to their physical constants and ultraviolet absorption spectra. As reported in the previous paper[1] of this series, the methyl group in the $\gamma$-position of methylpyridine series exhibited a hypsochromic effect and that in $\alpha$- or $\beta$-position, a bathochromic in the ultraviolet absorption spectra. In this study it was found that in their 1-oxides only the methyl group in $\alpha$-position exhibited a hypsochromic effect and that in $\beta$- or $\gamma$-position a bathochromic effect.

**Methylpyridine 1-oxide** There are some literatures[2~5] on six kinds of methylpyridine 1-oxide shown in Table I. In addition, 1-oxides of 2,3-lutidine, 2,4,5- and 2,3,4-collidine were newly synthesized. Although most methylpyridine 1-oxides were hygroscopic crystals, it was noticed that the 1-oxide possessing two methyl groups in $\alpha$- and

Table I. Physical Constants of Methylpyridine 1-Oxides

| 1-Oxide of | b.p$_4$ °C | m.p., °C | Picrate | | Analyses found | | |
|---|---|---|---|---|---|---|---|
| | | | m.p., °C | Crystal form | C% | H% | N% |
| Pyridine[5] | 113~114 | hygro. cryst. | 179~181 | yellow needles | | | |
| 2-Picoline[3] | 110 | — | 125 | yellow needles | | | |
| 3-Picoline[2] | 111~112 | 41~42 | 134.5~135.5 | yellow needles | | | |
| 4-Picoline[2,4] | 125 | 181~182 | 155 | yellow plates | | | |
| 2,6-Lutidine[2,3] | 93~94 | — | 123.5~124.5 | yellow plates | | | |
| 2,3-Lutidine | 95~98 | 82~85 | 114~115 | yellow needles | 44.50 | 3.48 | 15.95[a] |
| 2,4-Lutidine[2,3] | 115~117 | — | 141 | yellow plates | | | |
| 2,4,6-Collidine[3] | 105 | — | 168~169 | yellow needles | | | |
| 2,3,4-Collidine | 127~130 | hygro. cryst. | 122~123 | orange plates or yellow needles | 46.08 | 3.71 | 15.25[b] |
| 2,4,5-Collidine | 132 | 65~66 | 123~124 | orange plates | 45.52 | 3.81 | 15.10[b] |

*a*) Calcd. for $C_7H_9ON \cdot C_6H_3O_7N_3$ (lutidine 1-oxide picrate) : C, 44.31; H, 3.41; N, 15.99.
*b*) Calcd. for $C_8H_{11}ON \cdot C_6H_3O_7N_3$ (collidine 1-oxide picrate) : C, 45.90; H, 3.82; N, 15.30.

* Hakata, Fukuoka (池川信夫, 佐藤良博).

1) Part Ⅷ : This Bulletin, **2**, 209(1954).
2) E. Ochiai, M. Ikehara, T. Kato, N. Ikekawa : J. Pharm. Soc. Japan, **71**, 1385(1951).
3) M. Ishikawa, Z. Sai : *Ibid.*, **63**, 78(1943).
4) E. Ochiai, M. Ishikawa, Z. Sai : *Ibid.*, **65**, 72(1945).
5) E. Ochiai, Z. Sai : *Ibid.*, **65**, 73(1945).