Summary

2,6-Bis-methylthio- and 2,6-bis-benzylthio-9-(2′,3′,5′-tri-O-benzoyl)-β-D-ribofuranosylpurines were synthesized by the condensation of chloromercury salt of 2,6-bis-alkylthiopurines with 2,3,5-tri-O-benzoyl-D-ribofuranosyl chloride. The transformation to 6-dimethylamino- and 6-methylamino-9-β-D-ribofuranosylpurine by the successive amination and desulfurization was achieved.

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107. Shozo Kamiya : Azidoquinoline and Azidopyridine Derivatives. IV.*1 Reactions of Azido Group in the Quaternary Salts of 4-Azidoquinoline, 4-Azidopyridine, and their 1-Oxides.

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In general, quaternary salts of pyridine and quinoline derivatives have increased polar effect in their nitrogen and the reactivity of 2- and 4-positions to nucleophilic reagents is further potentiated. This reactivity is further increased in the quaternary salts of their N-oxide derivatives.

Ochiai and his co-workers[1] obtained 4-substituted pyridines and quinolines by alkaline decomposition of the methiodide of 4-substituted pyridine and quinoline 1-oxides. Okamoto,[2] Tani,[3] and Feely[4] obtained numerous cyanopyridine derivatives by the reaction of potassium cyanide with the quaternary salt of various pyridine 1-oxide derivatives, thereby developing a new field in the chemistry of quaternary salts.

Previously, the present author synthesized 4-azidoquinoline 1-oxide and 4-azidopyridine 1-oxide, and reaction of the azido group in these compounds was examined.[5] In the present paper, reaction of the quaternary salts of 4-azido-quinoline and -pyridine, and their 1-oxides will be described.

4-Azidoquinoline (I) reacts with methyl iodide or dimethyl sulfate in chloroform, at room temperature, and quantitatively forms the quaternary salts (IIa and IIb).

On the other hand, if 4-azidoquinoline 1-oxide (III) is refluxed with methyl iodide in chloroform, only a small amount of 4-azidoquinoline and 4,4′-azidoquinoline are formed and the majority of the starting material is recovered unchanged. Reaction of (III) with dimethyl sulfate in chloroform, at room temperature, affords 1-methoxy-4-azidoquinolinium methosulfate (IVa). The use of diethyl sulfate gives 1-ethoxy-4-azidoquinolinium methosulfate (IVb).

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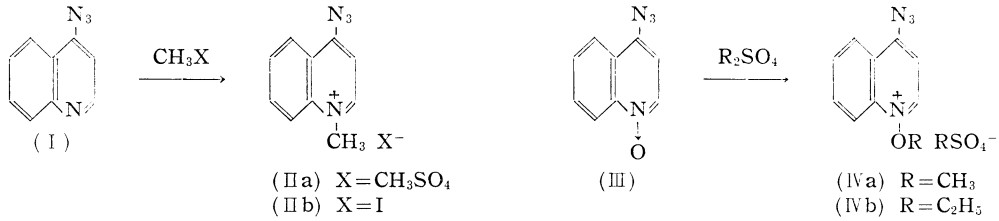
1) E. Ochiai, M. Katada, T. Naito : Yakugaku Zasshi, **64**, 210 (1944).
2) T. Okamato, H. Tani : This Bulletin, **7**, 925, 930 (1959).
3) H. Tani : Yakugaku Zasshi, **80**, 1418 (1960).
4) W. E. Feely, E. M. Beavers : J. Am. Chem. Soc., **81**, 4003 (1959).
5) T. Itai, S. Kamiya : This Bulletin, **9**, 87 (1961); S. Kamiya : *Ibid.*, **10**, 471 (1962).



(I) (IIa) X=CH_3SO_4 (IIb) X=I (III) (IVa) R=CH_3 (IVb) R=C_2H_5

Unexpectedly, (II) and (IV) formed hygroscopic crystals stable to light and the crystals exploded on being heated. Both were recrystallized from dehyd. acetone and their picrates also formed crystals.

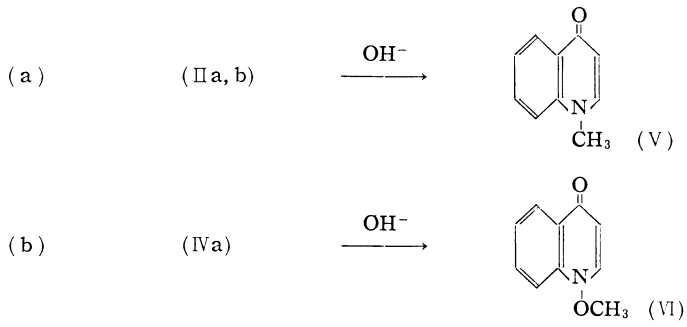
Reaction of 4-azidopyridine and 4-azidopyridine 1-oxide with dimethyl sulfate gives a methosulfate from each, forming highly hygroscopic crystals. Their picrates are hardly crystallizable but their reineckates formed crystals whose analytical values agreed well with calculated values.

The infrared spectra (KBr disc) of these quaternary salts exhibited strong absorptions due to the asymmetric stretching vibration of the azido group at 2128 and 2150 cm^{-1} in (IIa), at 2115 and 2140 cm^{-1} in (IVa), at 2120 cm^{-1} in 1-methyl-4-azidopyridinium methosulfate, and at 2238 and 2125 cm^{-1} in 1-methoxy-4-azidopyridinium methosulfate.

Alkaline Decomposition

Treatment of (IIa) or (IIb) with 5% sodium hydroxide solution, either by heating on a water bath or standing over night, results in the formation of needle crystals of m.p. 149°. The analytical values of this product and its picrate agree with those for 1-methyl-4-quinolone, and the infrared spectrum of this product agreed with that of 1-methyl-4(1*H*)-quinolone[6] (V) synthesized by another route. The yield was quantitative (Reaction route (a)).

In the case of corresponding pyridine derivatives, 1-methyl-4(1*H*)-pyridone was similarly obtained, though in a low yield.



Similar alkaline decomposition of (IVa) quantitatively forms 1-methoxy-4-quinolone (VI), which had been synthesized by Ochiai and others[7] from 4-hydroxyquinoline 1-oxide and methyl iodide.

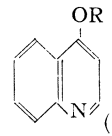
Alkaline decomposition of 1-methoxy-4-azidopyridinium methosulfate affords, besides 8% of 1-methoxy-4(1*H*)-pyridone,[7] a yellow powder which easily explodes. The infrared spectrum of this yellow product indicates the presence of an azido group, but its structure has not been determined as yet.

6) E. Späth, A. Kobe: Monatsh., **43**, 469 (1922).
7) E. Ochiai, E. Hayashi: Yakugaku Zasshi, **67**, 151, 154 (1947).

Reaction with Sodium Alkoxide

Treatment of (IIa) and (IIb) with sodium methoxide (or ethoxide) gives (V). (IVa) forms 4-alkoxyquinoline (VII) on merely being left to stand with sodium alkoxides at room temperature. Under the same condition, 4-azidoquinoline 1-oxide forms 4-alkoxyquinoline 1-oxide.

(c) (IIa, b) + RONa ⟶ (V) + NaN_3

(d) (IVa) + RONa ⟶  (VII) + NaN_3

(VIIa) R = CH_3
(VIIb) R = C_2H_5
(VIIc) R = $C_6H_5CH_2$
(VIId) R = $(CH_3)_2NCH_2CH_2$
(VIIe) R = C_6H_5

In the case of 1-methoxy-4-azidopyridinium methosulfate, this reaction requires heating but 4-alkoxypyridine is formed similarly. Yield from the reaction route (d) is listed in Table I.

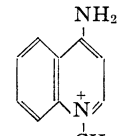
Table I. Yield (%) of 4-Alkoxyquinoline or -pyridine

R	VIIa	VIIb	VIIc	VIId	VIIe
4-Alkoxyquinoline	87	92	89	95	86
4-Alkoxypyridine	83	80	65	—	13

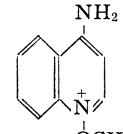
Reaction with Compounds possessing Active Methylene

The azido group in 4-azidoquinoline 1-oxide undergoes enol-type addition with acetoacetate and diethyl malonate to form a triazole ring,[5] but (IIa) and (IVa) do not form a triazole ring. In the latter case, the compound having an active methylene group acts as a hydrogen donor and (IIa) forms 1-methyl-4-aminoquinolinium methosulfate (VIII) and (IVa) forms 1-methoxy-4-aminoquinolinium methosulfate (IX), both in quantitative yield.

Catalytic reduction of (IIa) and (IVa) over palladium-carbon in methanol results in the formation of (VIII) and (IX), respectively.

(e) (IIa) $\xrightarrow[C_2H_5ONa]{\text{H-donor}}$  $\xleftarrow[\text{Pd-C}]{H_2}$ (IIa)

(VIII) CH_3 $CH_3SO_4^-$

(f) (IVa) $\xrightarrow[C_2H_5ONa]{\text{H-donor}}$  $\xleftarrow[\text{Pd-C}]{H_2}$ (IVa)

(IX) OCH_3 $CH_3SO_4^-$

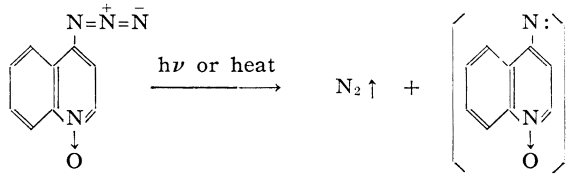
Thermal decomposition of (IVa) in toluene also gives (IX) in 69% yield.

In general, an azido group may be indicated by the following resonance formulae (Xa and Xb).

(Xa) (Xb)

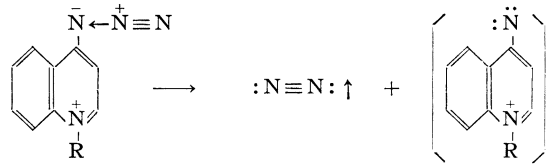
In 4-azidoquinoline 1-oxide (XI), the azido group activated by the polar effect of the N-oxide group undergoes homolysis at its N-N (1-2) bond by heat or light and forms an imino diradical (XII) with liberation of nitrogen gas. (XII) then undergoes dimerization to

form 4,4′-azodiquinoline 1,1′-dioxide[5] (XIII). In the case of the N-oxide compound, therefore, the resonance structure (Xa) is assumed to be more predominant in the azido group at 4-position.



(XI) (XII)

In order to explain the fact that neither dimerization reaction nor addition reaction of active methylene occurs in the quaternary salts (II and IV), formation of an electron-deficient species (XIV) resembling the so-called "nitrene" is assumed.



(II) R=CH_3
(IV) R=OCH_3 (XIV)

In the quaternary salt, the structure (Xb) is predominant for the azido group and its N-N (1-2) bond is thought to be in an easily heterolysable state.

Antibacterial, antitumor, and other pharmacological activities of these quaternary salts are now being examined.

Experimental*3

1-Methyl-4-azidoquinolinium Methosulfate (IIa)——To a solution of 4.3 g. of 4-azidoquinoline dissolved in 20 cc. of benzene, 5.0 g. of Me_2SO_4 was added, by which exothermic reaction occurred and the whole underwent solidification. After allowing the mixture to stand over night, the solid was collected by suctional filtration, washed with benzene, and recrystallized from dehyd. Me_2CO to pale brownish leaflets, m.p. 150~152° (decomp.). Yield, quantitative. *Anal.* Calcd. for $C_{11}H_{12}O_4N_4S$: C, 44.59; H, 4.08; N, 18.91. Found : C, 43.12; H, 3.43; N, 19.05.

Picrate : Yellow needles, m.p. 165~167° (decomp., with explosion). *Anal.* Calcd. for $C_{10}H_9N_4 \cdot C_6H_2O_7N_3$: C, 46.50; H, 2.68; N, 23.24. Found : C, 46.57; H, 2.68; N, 23.01.

Methiodide (IIb) : Reddish brown needles, m.p. 127° (decomp., with explosion).

1-Methoxy-4-azidoquinolinium Methosulfate (IVa)——To a solution of 1.0 g. of 4-azidoquinoline 1-oxide dissolved in 10 cc. of $CHCl_3$, 0.8 g. of Me_2SO_4 was added and the mixture was allowed to stand at room temperature for 3 days. The solvent was evaporated to dryness in a reduced pressure and the residue was allowed to stand in a desiccator by which it solidified. Recrystallization from dehyd. Me_2CO gave pale yellow pillars, m.p. 159~160° (decomp.). *Anal.* Calcd. for $C_{11}H_{12}O_5N_4S$: N, 17.79. Found : N, 18.51.

Picrate : Golden yellow needles, m.p. 151° (decomp.). *Anal.* Calcd. for $C_{10}H_9ON_4 \cdot C_6H_2O_7N_3$: C, 44.76; H, 2.59; N, 22.84. Found : C, 44.84; H, 2.67; N, 22.74. Yield, quantitative.

1-Ethoxy-4-azidoquinolinium Methosulfate (IVb)——To a solution of 0.5 g. of 4-azidoquinoline 1-oxide dissolved in 10 cc. of $CHCl_3$, 0.6 g. of Et_2SO_4 was added and the mixture was allowed to stand at room temperature for 2 days. $CHCl_3$ was evaporated and the residue was allowed to stand in a desiccator. The reddish brown needle crystals thereby formed were highly hygroscopic and the melting point measurement was impossible.

Picrate : Yellow needles, m.p. 150~151° (decomp.). *Anal.* Calcd. for $C_{11}H_{11}ON_4 \cdot C_6H_2O_7N_3$: C, 46.05; H, 2.95; N, 22.12. Found : C, 46.30; H, 3.00; N, 21.70. Yield, quantitative.

*3 All m.p.s are uncorrected.

1-Methoxy-4-azidopyridinium Methosulfate——A mixture of 0.50 g. of 4-azidopyridine 1-oxide dissolved in 10 cc. of $CHCl_3$ and added with 0.50 g. of Me_2SO_4 was allowed to stand at room temperature for 3 days, by which the quaternary salt precipitated in oily state. $CHCl_3$ was evaporated in a reduced pressure, the residue was washed with Et_2O, and allowed to stand in a desiccator but did not crystallize.

Reineckate : Reddish purple leaflets (from Me_2CO), m.p. 164～167°(decomp.). *Anal.* Calcd. for $C_6H_7ON_4 \cdot C_4H_6N_6CrS_4$: N, 29.77. Found : N, 29.83.

Platinate : Orange-red prisms, m.p. 188～189°(decomp.). *Anal.* Calcd. for $2C_6H_7ON_4 \cdot H_2PtCl_6$: N, 14.75. Found : N, 14.97.

Alkaline Decomposition of 1-Methyl-4-azidoquinolinium Methosulfate (IIa)——To a solution of 0.50 g. of (IIa) dissolved in 3 cc. of H_2O, 10 cc. of 5% NaOH was added and the mixture was allowed to stand for 5 hr. The mixture was warmed on a water bath for 30 min., cooled, and extracted with $CHCl_3$. The extract was dried over Na_2SO_4 and $CHCl_3$ was evaporated. The residue of pale brownish needles, m.p. 84～87°, was recrystallized from benzene and dried over P_2O_5 to white needles, m.p. 152～153°. Yield, 0.33 g. quantitative. This product was identified with 1-methyl-4(1*H*)-quinolone. The aqueous solution of this substance colors blood red with 10% $FeCl_3$ solution. *Anal.* Calcd. for $C_{10}H_9ON$: C, 75.47; H, 5.65; N, 8.80. Found : C, 75.26; H, 5.59; N, 8.47.

Picrate : Yellow plates, m.p. 226°. *Anal.* Calcd. for $C_{10}H_9ON \cdot C_6H_3O_7N_3$: N, 14.43. Found : N, 14.47.

Alkaline Decomposition of 1-Methoxy-4-azidoquinolinium Methosulfate (IVa)——A mixture of 0.2 g. of (IVa) and 5 cc. of 5% NaOH was allowed to stand at room temperature for 2 days. The reaction mixture was extracted with $CHCl_3$, the extract was dried over Na_2SO_4, and $CHCl_3$ was evaporated. The residue was allowed to stand in a desiccator by which it gradually crystallized, but m.p. measurement was impossible. Its infrared spectrum agreed with that of 1-methoxy-4(1*H*)-quinolone.

Picrate : Orange needles, m.p. 193～194°. *Anal.* Calcd. for $C_{10}H_9O_2N \cdot C_6H_3O_7N_3$: C, 47.53; H, 2.99; N, 13.86. Found : C, 47.93; H, 2.75; N, 14.16.

Alkaline Decomposition of 1-Methoxy-4-azidopyridinium Methosulfate——A solution of 0.30 g. of the methosulfate dissolved in 2 cc. of water and 5 cc. of 5% NaOH were mixed and allowed to stand at room temperature for 3 days. The greyish brown precipitate that formed was collected by suctional filtration, washed with H_2O, and dried to slightly brownish powder (highly explosive!) Analysis impossible and structure still undetermined. The filtrate from the above precipitate was extracted with $CHCl_3$, the extract was dried over Na_2SO_4, and $CHCl_3$ was evaporated, leaving a syrupy residue.

Picrate : Yellow needles, m.p. 198～200°. These data agreed with those given in the literature[7] for 1-methoxy-4-(1*H*)-pyridone picrate. Yield, 12 mg. (8%). *Anal.* Calcd. for $C_6H_7O_2N \cdot C_6H_3O_7N_3$: C, 40.68; H, 2.85; N, 15.82. Found : C, 41.05; H, 2.67; N, 15.70.

Reaction of 1-Methoxy-4-azidoquinolinium Methosulfate (IVa) and Sodium Alkoxide——i) MeONa: To a solution of 50 mg. of metallic Na dissolved in 20 cc. of dehyd. MeOH, 0.31 g. of (IVa) was added and the mixture was allowed to stand over night at room temperature. MeOH was evaporated and the residue was extracted with benzene. Evaporation of benzene from the extract left a brown oil. Yield, 0.14 g.

Picrate : Orange leaves (from EtOH), m.p. 198～199°. *Anal.* Calcd. for $C_{10}H_9ON \cdot C_6H_3O_7N_3$: N, 14.43. Found : N, 14.34.

Platinate : Pale yellow needles, m.p. 228～229°(decomp.).

These data were in good agreement with those given for 4-methoxyquinoline.

ii) EtONa : A mixture of 0.30 g. of (IVa) added to a solution of 50 mg. of metallic Na in 20 cc. of dehyd. EtOH was allowed to stand over night at room temperature. NaN_3 that precipitated out was filtered off and EtOH was evaporated from the filtrate. The residue was 0.17 g. (92%) of brown oil.

Picrate : Yellow needles, m.p. 206～207°. *Anal.* Calcd. for $C_{11}H_{11}ON \cdot C_6H_3O_7N_3$: N, 13.93. Found: N, 13.99.

Platinate : m.p. 216°(decomp.).

These data were in good agreement with those for 4-ethoxyquinoline.

iii) $Me_2NCH_2CH_2ONa$: A mixture of 0.30 g. of (IVa) in a solution of 50 mg. of metallic Na dissolved in 5 cc. of dimethylaminoethanol was allowed to stand over night at room temperature. The solution was evaporated to dryness in a reduced pressure and the residue was extracted with $CHCl_3$. The extract solution was dried and evaporated, leaving 0.20 g. of an oil.

Picrate : Brownish needles (from MeOH), m.p. 207～208°. *Anal.* Calcd. for $C_{13}H_{16}ON_2 \cdot 2C_6H_3O_7N_3$: C, 44.52; H, 3.29; N, 16.61. Found : C, 44.05; H, 3.13; N, 16.75.

iv) PhONa : A mixture of 0.30 g. of (IVa) in a solution of 50 mg. of metallic Na dissolved in 5 cc. of PhOH with warming was allowed to stand over night at room temperature. The reaction mixture was dissolved in 5% NaOH and extracted with benzene. The extract was dried over Na_2SO_4 and benzene was distilled off, leaving 0.18 g. of a brown oil.

Picrate : Yellow needles, m.p. 176～177°(reported) m.p. 174～176° for 4-phenoxyquinoline picrate). *Anal.* Calcd. for $C_{15}H_{11}ON \cdot C_6H_3O_7N_3$: N, 12.44. Found : N, 12.31.

The aqueous solution left after extraction with benzene was extracted with $CHCl_3$, the extract was dried over Na_2SO_4, and $CHCl_3$ was evaporated, leaving 19 mg. of a syrupy residue.
Picrate : m.p. 193°, undepressed on admixture with 1-methoxy-4-quinolone picrate. Yield, 11%.

Reaction of 1-Methoxy-4-azidopyridinium Methosulfate and Sodium Alkoxide——i) MeONa : To a solution of 50 mg. of metallic Na dissolved in 20 cc. of dehyd. MeOH, 0.27 g. of the methosulfate was added and the mixture was warmed on a water bath for 3 hr. MeOH was evaporated from the mixture, the residue was extracted with benzene, and evaporation of benzene from the extract solution left an oil with a pyridine odor.
$HgCl_2$ salt : m.p. 190°.
Picrate : Yellow needles, m.p. 176°. *Anal.* Calcd. for $C_6H_7ON \cdot C_6H_3O_7N_3$: C, 42.61; H, 2.98; N, 16.57. Found : C, 42.82; H, 3.19; N, 16.61. Yield, 0.10 g. (83%).
ii) EtONa : To a solution of 80 mg. of metallic Na dissolved in 10 cc. of dehyd. EtOH, 0.39 g. of the methosulfate was added and the mixture was heated on a water bath for 5 hr. EtOH was evaporated, the residue was extracted with $CHCl_3$, and the extract was passed through a column of alumina. The column was developed with $CHCl_3$ and the effluent was evaporated to dryness, leaving 0.16 g. of an oil with a pyridine odor.
Picrate : Yellow leaves m.p. 126～127°. *Anal.* Calcd. for $C_7H_9ON \cdot C_6H_3O_7N_3$: C, 44.32; H, 3.43; N, 15.91. Found : C, 44.91; H, 3.30; N, 15.45.
iii) $C_6H_5CH_2ONa$: A mixture of 0.30 g. of the methosulfate in a solution of 60 mg. of Na dissolved in 10 cc. of benzyl alcohol was heated at 150～160° for 3 hr. Benzyl alcohol was evaporated in a reduced pressure, the residue was extracted with $CHCl_3$, and evaporation of $CHCl_3$ from the extract left a brown oil.
Picrate : Yellow needles, m. p. 147—149°. Yield, 0.15 g. *Anal.* Calcd. for $C_{12}H_{11}ON \cdot C_6H_3O_7N_3$: C, 52.18; H, 3.41; N, 13.52. Found: C, 51.20; H, 3.14; N, 13.83.
iv) PhONa : A mixture of 0.30 g. of the methosulfate in a solution of 60 mg. of metallic Na dissolved in 3 cc. of warm PhOH was heated at 150～160° for 3 hr. The reaction mixture was dissolved in 5% NaOH and extracted with benzene. The extract was washed with 5% NaOH and H_2O, dried over Na_2SO_4, and benzene was evaporated. The residue was a brown oil.
Picrate : Yellow needles, m.p. 152～157°. Yield, 28 mg. (13%). *Anal.* Calcd. for $C_{11}H_9ON \cdot C_6H_3O_7N_3$: N, 14.00. Found : N, 13.87.

Reaction of 1-Methyl-4-azidoquinolinium Methosulfate (IIa) and Ethyl Acetoacetate——To a solution of 50 mg. of metallic Na dissolved in 30 cc. of dehyd. EtOH, 2.5 g. of ethyl acetoacetate was added, followed by 0.30 g. of (IIa), and the mixture was allowed to stand over night at room temperature. The mixture was concentrated in a reduced pressure and the needle crystals that separated out were collected by suctional filtration. The crystals were washed with Et_2O and recrystallized from Et_2O-EtOH to white needles, m.p. 148～150°. Yield, quantitative. *Anal.* Calcd. for $C_{11}H_{14}O_4N_2S$: C, 48.87; H, 5.22; N, 10.36. Found : C, 50.42; H, 5.54; N, 10.57.
Picrate : Yellow needles, m.p. 214～215°. *Anal.* Calcd. for $C_{10}H_{11}N_2 \cdot C_6H_2O_7N_3$: C, 49.62; H, 3.38; N, 18.08. Found : C, 49.10; H, 3.02; N, 18.38.

Catalytic Hydrogenation of (IIa)——A solution of 0.30 g. of (IIa) dissolved in 20 cc. of MeOH, added with a catalyst prepared from 8.4 cc. of 1% $PdCl_2$ solution and 0.2 g. of charcoal, was shaken in H_2 stream for 30 min. The catalyst was filtered off and washed with EtOH. Evaporation of EtOH and addition of a few drops of Et_2O to the residue afforded white needle crystals which were collected by suctional filtration and recrystallized from Et_2O-EtOH, m.p. 145°. Yield, 0.15 g. (55%).
Picrate : Yellow fine needles, 214～215°, undepressed on admixture with 1-methyl-4-aminoquinolinium picrate.

Reaction of 1-Methoxy-4-azidoquinolinium Methosulfate (IVa) and Ethyl Acetoacetate——A mixture of 0.30 g. of (IVa) in a solution of 54 mg. metallic Na dissolved in 20 cc. of dehyd. EtOH and 2.5 g. of ethyl acetoacetate was allowed to stand over night at room temperature and EtOH was evaporated in a reduced pressure. The fine crystals that precipitated out were collected by suctional filtration and washed with Me_2CO. This product was highly hygroscopic and melted at ca. 90°.
Picrate : m.p. 197°. *Anal.* Calcd. for $C_{10}H_{11}ON_2 \cdot C_6H_2O_7N_3$: N, 17.37. Found : N, 17.97· These data were in good agreement with those of 1-methoxy-4-aminoquinolinium picrate. Yield, 0.24 g. (88%).

Catalytic Hydrogenation of (IVa)——A solution of 0.70 g. of (IVa) dissolved in 20 cc. of MeOH, added with a catalyst prepared from 5 cc. of 1% $PdCl_2$ solution and 0.20 g. of charcoal, was shaken in H_2 stream for 30 min. The catalyst was filtered off, MeOH was evaporated from the filtrate, and the residue solidified on being left in a desiccator. The solid was recrystallized from Et_2O-EtOH to crystals of m.p. 88～97°.
Picrate : Yellow needles, m.p. 200～201°, undepressed on admixture with 1-methoxy-4-aminoquinolinium picrate,[1] m.p. 199～200°. Yield, 0.54 g. (84%).

Thermal Decomposition of (IVa) in Solution——A suspension of 0.30 g. of (IVa) in 20 cc. of toluene was refluxed in an oil bath for 5 hr. Toluene was evaporated to dryness in a reduced pressure and the resinous residue was digested with H_2O. The aqueous solution was evaporated to dryness in a reduced pressure and the residue was allowed to stand in a desiccator but it did not crystallize. Picrate : m.p. 198°, undepressed on admixture with 1-methoxy-4-aminoquinolinium picrate. Yield, 0.18 g. (69%).

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Summary

Quaternary salts of 4-azidoquinoline and 4-azidoquinoline 1-oxide were synthesized and their reaction was examined. Their decomposition with alkali afforded 1-methyl-(or methoxy)-4(1*H*)-quinolone. Treatment of 1-methoxy-4-azidoquinolinium methosulfate with sodium alkoxides resulted in a reaction at room temperature to form 4-alkoxyquinolines. These compounds reacted with compounds possessing an active methylene to form 1-methyl (or methoxy)-4-aminoquinolinium methosulfate, instead of undergoing triazole cyclization. Thermal decomposition in toluene or catalytic hydrogenation also furnished the same amino compound.

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108. Yoshio Arata, Toshiko Nakanishi, and Yoko Asaoka : Constituents of Rhizoma Nupharis. XVIII.*1 Synthesis of Alkaloids from *Nuphar japonicum* DC. I. Synthesis of *rac*-Deoxynupharidine.

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The formula (XVII)[1~3] was proposed for deoxynupharidine isolated from the rhizome of *Nuphar japonicum* DC. (Japanese name "Kôhone") and this structure was proved to be correct by synthesis, as was briefly reported.[4] The route of this synthesis will be described in detail in the present paper.

In order to examine the reaction conditions necessary for the synthesis of deoxynupharidine, 4-(3-furyl)octahydroquinolizine (V) was synthesized by the route shown in Chart 2.

Reaction of octahydro-4-quinolizinone (I) and ethyl 3-furoate, in the presence of sodium hydride, afforded a condensate (II) of m.p. 86~88°, which colored reddish purple

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*1 Part XVII : Yakugaku Zasshi, **82**, 326 (1962).
*2 Tsuchitoriba-naga-machi, Kanazawa (荒田義雄, 中西外志子, 浅岡陽子).
1) Y. Arata : Yakugaku Zasshi, **76**, 1447 (1956).
2) Y. Arata, *et al.* : *Ibid.*, **77**, 236 (1957).
3) M. Kotake, *et al.* : Ann., **606**, 148 (1957).
4) Y. Arata, *et al.* : Yakugaku Zasshi, **80**, 856 (1960).