Studies on Pyridotropolones. VI[1]. *Rearrangement Reactions of Brominated 8-Isopropyl-pyrido[3, 2-d]tropolones to 7-Isopropyl-6-quinolinols*

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Previously the author[2] reported that nitroso-, amino-, quinoxalo- and oxazolo-compounds were obtained from 2-methyl-8-isopropyl-pyrido [3, 2-*d*] tropolone. The present work was carried out for the purpose of elucidating the chemical reactivity of pyrido [3, 2-*d*] tropolone, and the rearrangement reactions of brominated 8-isopropyl-pyrido [3, 2-*d*] tropolones to 7-isopropyl-6-quinolinols were studied.

Bromination of 2-methyl-8-isopropyl-pyrido-[3, 2-*d*] tropolone (Ia) with 1 molar equivalent of NBS gave 5-bromo-compound IIa. IIa showed brownish yellow coloration in benzene layer with ferric chloride solution. Heating IIa in 2 N potassium hydroxide solution afforded pale yellow (nearly colorless) needles, m. p. 229.5∼230°C (IIIa), 2-methyl-8-isopropyl-pyrido-[3, 2-*d*] -tropolone (Ia) and a red oily matter. IIIa gave no Beilstein test, whose analytical values agreed with formula $C_{13}H_{15}ON$. Its ultraviolet absorption spectrum (Fig. 1) closely resembled that of 6-quinolinol[3]. The infrared spectrum of IIIa exhibited several absorption bands (2980 cm^{-1} for CH stretching vibrations, 1530, 1568, 1607 and 1630 cm^{-1} for C=C and C=N streching vibrations, and 1245 cm^{-1} for phenolic OH deformations). Furthermore, the compound IIIa readily underwent some typical electrophilic substitution reactions. Namely, IIIa was readily brominated in acetic acid solution to form a monobromo compound

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[1] This work was presented at the 13th Annual Meeting of the Chemical Society of Japan, Tokyo, April 1960.

[2] K. Yamane, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zasshi*), **80**, 1175 (1959).

[3] G. W. Ewing and E. A. Steck, *J. Am. Chem. Soc.*, **68**, 2181 (1946).

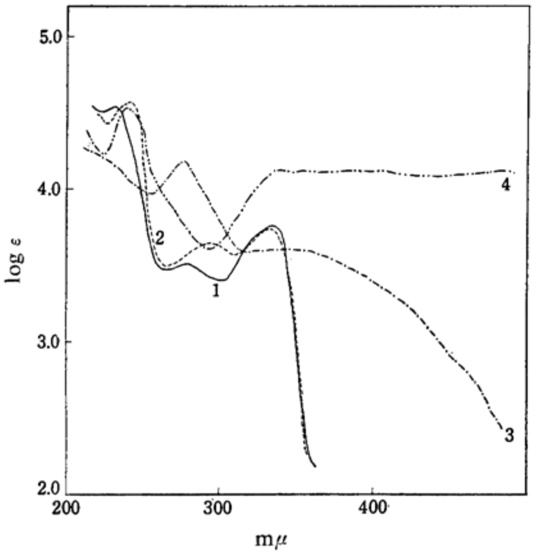


Fig. 1. Ultraviolet absorption spectra (in methanol).

1 : 2-Methyl-7-isopropyl-6-quinolinol (IIIa)
2 : 2-Methyl-5-bromo-7-isopropyl-6-quinolinol (IVa)
3 : 2-Methyl-5-nitroso-7-isopropyl-6-quinolinol (Va)
4 : 2-Methyl-5-(*p*-tolylazo)-7-isopropyl-6-quinolinol (VIa)

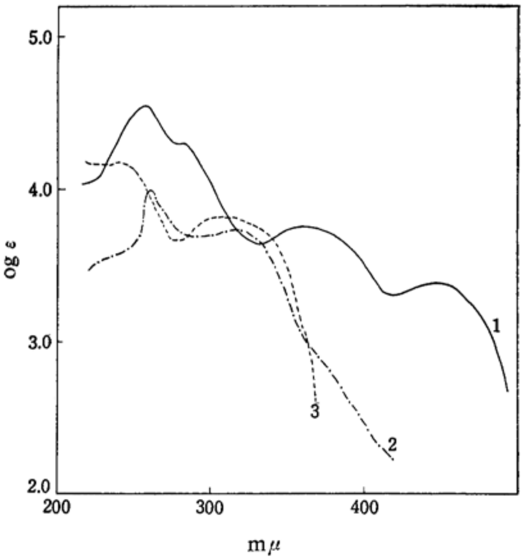


Fig. 2. Ultraviolet absorption spectra.

1 : 2-Methyl-5-bromo-8-isopropyl-pyrido-[3,2-*d*]tropolone (IIa) (in methanol)
2 : Dibromo-compound VIIa (in carbon tetrachloride)
3 : Dibromo-compound VIIa (in methanol)

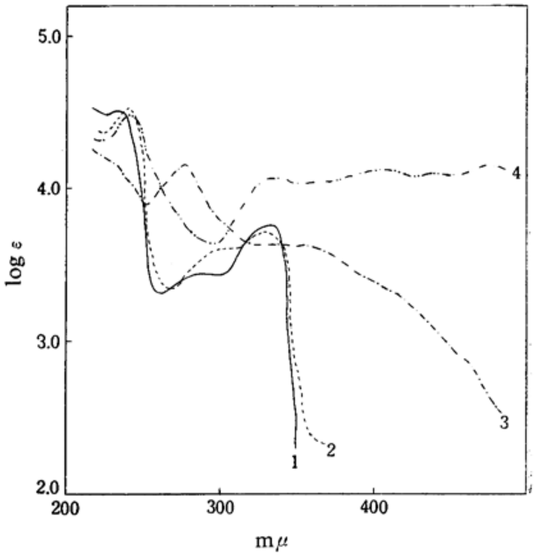


Fig. 3. Ultraviolet absorption spectra (in methanol).

1 : 7-Isopropyl-6-quinolinol (IIIb)
2 : 5-Bromo-7-isopropyl-6-quinolinol (IVb)
3 : 5-Nitroso-7-isopropyl-6-quinolinol **(Vb)**
4 : 5-(*p*-Tolylazo)-7-isopropyl-6-quinolinol (VIb)

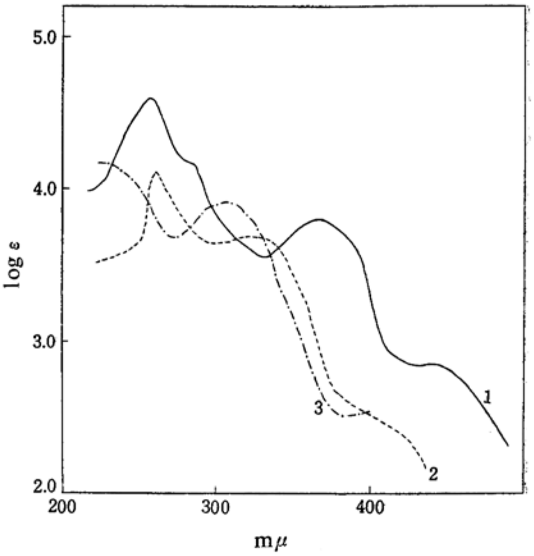
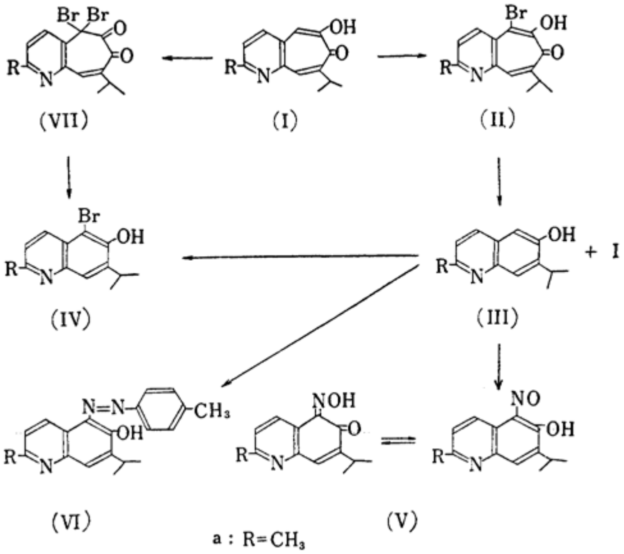


Fig. 4. Ultraviolet absorption spectra.

1 : 5-Bromo-7-isopropyl-pyrido[3,2-*d*]-tropolone (IIb) (in methanol)
2 : Dibromo-compound VIIb (in carbon tetrachloride).
3 : Dibromo-compound VIIb (in methanol)

(IVa). Nitrosation of IIIa in acetic acid solution gave nitroso compound Va. The compound IIIa coupled with diazotized *p*-toluidine in alkaline solution to yield an azo compound VIa. From these facts shown above, IIIa was assumed to be 2-methyl-7-isopropyl-6-quinolinol.

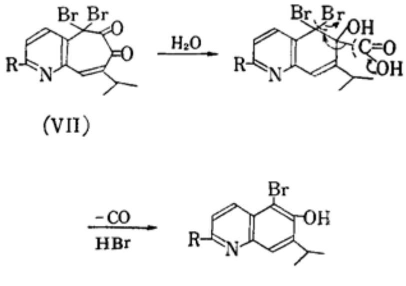
Bromination of 2-methyl-8-isopropyl-pyrido[3, 2-*d*] tropolone gave dibromo compound as yellow rhombic prisms, m. p. 129∼130°C (VIIa). The analytical values of this compound agreed with formula $C_{14}H_{13}O_2NBr_2$, and its ultraviolet absorption spectrum (Fig. 2) differed from that of 2-methyl-5-bromo-8-isopropyl-pyrido [3, 2-*d*] tropolone (IIa). Moreover, the infrared spectrum of VIIa exhibited two bands at 1742 and 1684 cm^{-1} due to the carbonyl group, and no bands in the hydroxyl region. The compound VIIa was unstable against water, acid, alkali and alcohols. In fact when heated with water, it dissolved gradually under foaming and gave 2-methyl-5-bromo-7-isopropyl-6-quinolinol (IVa) which was obtained by bromination of IIIa described above. Heating VIIa with 1 N hydrochloric acid also gave IVa in good yield. VIIa, however, gave 2-methyl-5-bromo-8-isopropyl-pyrido [3, 2-*d*] tropolone (IIa) when it was heated with 2 N potassium hydroxide solution. These facts indicated that the dibromo compound VIIa possessed the structure shown as *o*-diketone formula (VIIa).



a : R=CH_3
b : R=H

8-Isopropyl-pyrido [3, 2-*d*] tropolone (Ib)[4] showed almost the similar reactions as in the case of Ia. Namely, Ib was readily brominated with NBS to form 5-bromo-compound (IIb) and dibromo compound (VIIb). Heating IIb in 2 N potassium hydroxide solution afforded 7-isopropyl-6-quinolinol (IIIb). IIIb afforded bromo compound (IVb), nitroso compound (Vb) and *p*-tolylazo-compound (VIb). Furthermore VIIb was rearranged to 5-bromo-7-isopropyl-6-quinolinol (IVb) when treated with water or 1 N hydrochloric acid, and or 2 N potassium hydroxide solution.

It is thought that the mechanism of this interesting rearrangement of VII to 5-bromo-7-isopropyl-6-quinolinols (IV) goes on first through benzilic acid rearrangement, followed by decarboxylation and dehydrobromination as follows:



In the case of the rearrangement reaction of 5-bromo-8-isopropyl-pyrido [3, 2-*d*] tropolones (II) to 7-isopropyl-6-quinolinols (III) with potassium hydroxide solution, it is thought

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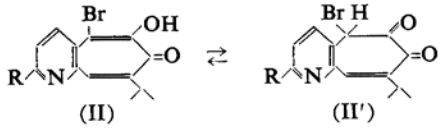
[4] K. Yamane, *J. Chem. Soc. Japan, Pure Chem. Sec. (Nippon Kagaku Zasshi)*, **81**, 509 (1960).

that II undergoes rearrangement in like manner as VII via its tautomeric structure II′.



(II) (II′)

Experimental

2-Methyl-5-bromo-8-isopropyl-pyrido[3,2-*d*]tropolone (IIa).—A mixture of 0.2 g. of 2-methyl-8-isopropyl-pyrido[3,2-*d*]-tropolone (Ia) and 0.18 g. of NBS in 4 cc. of carbon tetrachloride was refluxed for 2 hr. After cooling, succinimide and the solvent were removed and the residue was recrystallized from ethanol to give 0.25 g. of yellow needles, m. p. 145∼145.5°C.

Found: C, 54.37; H, 4.65; N, 4.84. Calcd. for $C_{14}H_{14}O_2NBr$: C, 54.54; H, 4.58; N, 4.55%.

5-Bromo-8-isopropyl-pyrido[3,2-*d*]tropolone (IIb).—A mixture of 0.7 g. of 8-isopropyl-pyrido-[3,2-*d*]tropolone (Ib) and 0.64 g. of NBS in 40 cc. of carbon tetrachloride was refluxed for 2 hr. After cooling, succinimide and the solvent were removed and the residue was recrystallized from ethanol to give 0.72 g. of yellow needles, m. p. 155.5∼156°C.

Found: C, 53.22; H, 4.02; N, 4.92. Calcd. for $C_{13}H_{12}O_2NBr$: C, 53.07; H, 4.11; N, 4.76%.

2-Methyl-7-isopropyl-6-quinolinol (IIIa).—**a**) A solution of 1 g. of IIa in 3 cc. of 2 N potassium hydroxide solution was heated for 2 hr. on a water bath. After cooling, 10 cc. of water was added and acidified with 1 N hydrochloric acid to deposite dark brown precipitates. The precipitates were collected and sublimated, yielding yellow sublimates, which were recrystallized from ethanol in pale yellow needles, m. p. 127∼128°C, about 0.1 g. These did not depress by admixture with 2 methyl-8-isopropyl-pyrido[3,2-*d*]tropolone (Ia). The mother liquor of the dark brown precipitates was evaporated on a water bath to dryness and the residue was extracted with acetone. Acetone extracts were purified by passing through an alumina column to give about 30 mg. of crystals. Recrystallization from alcohol gave pale yellow (nearly colorless) needles, m. p. 229.5∼230°C.

Found: C, 77.32; H, 7.19; N, 6.84. Calcd. for $C_{13}H_{15}ON$: C, 77.58; H, 7.51; N, 6.96%.

b) A solution of 0.4 g. of IIa in 3 cc. of 2 N potassium hydroxide solution was heated on a water bath for 2 hr. After cooling, the solution was slightly acidified with acetic acid to deposit brown precipitates (20 mg., m. p. 240°C). The filtrate of the precipitates was evaporated on a water bath to dryness and the residue was sublimated to give 130 mg. of pink prisms. Recrystallization from alcohol gave red needles, m. p. 228∼229°C, undepressed by admixture with IIIa. Furthermore, the red needles were dissolved in acetone and purified by passing through an alumina column to give pale yellow (nearly colorless) needles, m. p. 229∼230°C.

7-Isopropyl-6-quinolinol (IIIb).—A solution of 0.4 g. of IIb in 2.3 cc. of 2 N potassium hydroxide solution was heated on a water bath and acidified with 2 N hydrochloric acid to deposite pale brown precipitates. The precipitates were recrystallized from methanol to give yellow needles, m. p. 160∼161°C, undepressed by admixture with Ib. Mother liquor of the pale brown precipitates was evaporated on a water bath to dryness and the residue was extracted with acetone. Acetone extracts were purified by passing through an alumina column to give colorless plates, m. p. 193°C. Yield 90 mg.

Found: C, 76.67; H, 6.85; N, 7.46. Calcd. for $C_{12}H_{13}ON$: C, 76.97; H, 7.00; N, 7.48%.

Picrate, yellow plates, m. p. 229∼230°C (decomp.) from methanol.

Found: N, 13.43. Calcd. for $C_{18}H_{16}O_8N_4$: N, 13.46%.

2-Methyl-5-bromo-7-isopropyl-6-quinolinol (IVa).—To a solution of 0.13 g. of IIIa in 2 cc. of acetic acid, a solution of 0.1 g. of bromine in 0.5 cc. of the same solvent was added dropwise with stirring. When the addition had been nearly completed some yellow crystals were deposited. After removal of the crystals, water was added and neutralized with ammonia to give precipitates, which were recrystallized from dilute alcohol in pale yellow (nearly colorless) needles, m. p. 129∼130°C.

Found: C, 55.84; H, 4.79; N, 4.92. Calcd. for $C_{13}H_{14}ONBr$: C, 55.72 H, 5.04; N, 5.00%.

5-Bromo-7-isopropyl-6-quinolinol (IVb).—To a solution of 20 mg. of IIIb in 0.5 cc. of acetic acid, 20 mg. of bromine dissolved in 0.5 cc. of the same solvent was added dropwise with stirring. After standing for 2 hr., water was added and neutralized with ammonia to give colorless precipitates, which were recrystallized from acetone in pale yellow needles, m. p. 128∼129°C. Yield about 25 mg.

Found: C, 54.04; H, 4.26; N, 5.24. Calcd. for $C_{12}H_{12}ONBr$: C, 54.15; H, 4.55; N, 5.26%.

2-Methyl-5-nitroso-7-isopropyl-6-quinolinol (Va).—To a solution of 0.15 g. of IIIa in 1 cc. of acetic acid, a solution of 0.08 g. of sodium nitrite in a small amount of water was added dropwise. The yellow crystals that separated out were collected by filtration and washed with water. Yield 0.15 g. Recrystallization from methanol yielded yellow prisms, m. p. 181°C (decomp.).

Found: C, 67.76; H, 5.72; N, 11.59. Calcd. for $C_{13}H_{14}O_2N_2$: C, 67.81; H, 6.13; N, 12.17%.

5-Nitroso-7-isopropyl-6-quinolinol (Vb).—To a solution of 41 mg. of IIIb in 1 cc. of acetic acid, 23 mg. of sodium nitrite in a small amount of water was added dropwise. The yellow crystals that separated out were collected by filtration and washed with water. Recrystallization from methanol yielded bright yellow scales, m. p. 156°C (decomp.). Yield about 45 mg.

Found: C, 66.66; H, 5.76; N, 13.02. Calcd. for $C_{12}H_{12}O_2N_2$: C, 66.65; H, 5.59; N, 12.96%.

2-Methyl-5-(*p*-tolylazo)-7-isopropyl-6-quinolinol (VIa).—To a cold solution of 45 mg. of *p*-toluidine in 2 cc. of 3 N hydrochloric acid, a solution of 42 mg. of sodium nitrite in 0.5 cc. of water was dropped, and the resultant cold diazonium solution was added dropwise to the cold solution of 80 mg. of IIIa in 10 cc. of 2 N-potassium hydroxide solution. The red precipitates thereby formed were collected by filtration. These were recrystallized from methanol in orange red needles, m. p. 109.5∼110°C. Yield 90 mg.

Found: C, 75.46; H, 6.35; N, 13.57. Calcd. for $C_{20}H_{21}ON_3$: C, 75.21; H, 6.63; N, 13.16%.

5-(*p*-Tolyl-azo)-7-isopropyl-6-quinolinol (VIb).—A cold solution of diazonium salt prepared from 35 mg. of *p*-toluidine, 1 cc. of 3 N hydrochloric acid and 55 mg. of sodium nitrite was added dropwise to a solution of 60 mg. of IIIb in 2 cc. of 2 N sodium hydroxide solution. The reddish brown precipitates which formed were recrystallized from methanol in red needles, m. p. 122∼123°C. Yield 50 mg.

Found: C, 74.62; H, 6.02; N, 13.92. Calcd. for $C_{19}H_{19}ON_3$: C, 74.73; H, 6.27; N, 13.76%.

Bromination of 2-Methyl-8-isopropyl-pyrido[3, 2-*d*]tropolone (Ia) with 2 Molar Equivalents of NBS. (Dibromo-Compound VIIa).—A mixture of 1.43 g. of Ia and 2.21 g. of NBS in 30 cc. of carbon tetrachloride was refluxed on a water bath for 2 hr. After cooling, succinimide and the solvent were removed, the residue was recrystallized from carbon tetrachloride to give 1.16 g. of yellow rhombic prisms, m. p. 129∼130°C.

Found: C, 43.37; H, 3.56; N, 3.56. Calcd. for $C_{14}H_{13}O_2NBr_2$: C, 43.44; H, 3.39; N, 3.62%.

Bromination of 8-Isopropyl-pyrido[3, 2-*d*]tropolone (Ib) with 2 Molar Equivalents of NBS. (Dibromo-Compound VIIb).—A mixture of 1.72 g. of Ib and 2.85 g. of NBS in 100 cc. of carbon tetrachloride was refluxed on a water bath for 2 hr. After cooling, succinimide and the solvent were removed, and the residue was recrystallized from chloroform or carbon tetrachloride to give 2.21 g. of dibromo compound VIIb in yellow polyhedrones, m. p. 142∼143°C.

Found: C, 42.09; H, 2.90; N, 3.69. Calcd. for $C_{13}H_{11}O_2NBr_2$: C, 41.85; H, 2.97; N, 3.76%.

Rearrangement Reaction of Dibromo Compound VIIa to 2-Methyl-5-bromo-7-isopropyl-6-quinolinol (IVa).—a) **By Water.**—When a mixture of 0.39 g. of dibromo compound VIIa and 3 cc. of water was heated on a water bath, VIIa slowly dissolved under foaming. The mixture was further heated for 2 hr. After removal of a small amount of brownish yellow resinous matter which appeared during the heating, the solution gradually deposited orange needles (hydrochloride of IVa) on standing. The needles were dissolved in 6 cc. of hot water and neutralized with 2 N potassium hydroxide solution to give precipitates, which were recrystallized from dilute alcohol in pale yellow (nearly colorless) needles, m. p. 129∼130°C. Yield, 0.1 g. No depression in m. p. was observed on admixture of 2-methyl-5-bromo-7-isopropyl-6-quinolinol (IVa) which was obtained by bromination of IIIa described above.

b) **By 1 N Hydrochloric Acid.**—A mixture of 0.39 g. of VIIa and 3 cc. of 1 N hydrochloric acid solution was heated on a water bath for 30 min. On cooling, 0.31 g. of yellow crystals, m. p. 223∼224°C (decomp.) were obtained. The crystals were dissolved in 5 cc. of hot water and neutralized with a 2 N potassium hydroxide solution to give colorless precipitates, which were recrystallized from dilute methanol in pale yellow (nearly colorless) needles, m. p. 129∼130°C. Yield, 0.13 g. The needles were undepressed on admixture with IVa.

Reaction of Dibromo Compound VIIa with 2 N Potassium Hydroxide Solution.—When 0.16 g. of VIIa was mixed with 0.68 cc. of 2 N potassium hydroxide solution, an exothermic reaction began immediately to give a dark greenish yellow solution. After being heated for 20 min., the solution was slightly acidified with acetic acid to give yellow precipitates, which were recrystallized from alcohol in yellow prisms, m. p. 145∼146°C, undepressed by admixture with 2-methyl-5-bromo-8-isopropyl-pyrido-[3,2-*d*]tropolone (IIa). Yield, about 0.04 g.

Rearrangement Reaction of Dibromo Compound VIIb to 5-Bromo-7-isopropyl-6-quinolinol (IVb).—a) **By Water.**—A mixture of 0.37 g. of VIIb and 1 cc. of water was heated on a water bath for 2 hr. After cooling, a small amount of water was added and neutralized with 2 N potassium hydroxide solution to deposit brown precipitates. Recrystallization from acetone yielded 0.17 g. of colorless needles, m. p. 128.5∼129°C. No depression in m. p. was observed on admixture with the authentic sample of IVb which was obtained by bromination of IIIb described above.

b) **By 1 N Hydrochloric Acid.**—A mixture of 0.37 g. of VIIb and 3 cc. of 1 N hydrochloric acid solution was heated on a water bath for 1 hr. After cooling, the resultant red solution was neutralized with a 2N potassium hydroxide solution to give precipitates, which were recrystallized from acetone in colorless needles, m. p. 127∼128°C. Yield 0.2 g. The needles also were undepressed on admixture with the authentic sample of IVb.

c) **By 1 N Potassium Hydroxide Solution.**—A mixture of 0.3 g. of VIIb and 3 cc. of 1 N potassium hydroxide solution was heated on a water bath for 10 min. After cooling, the mixture was neutralized with acetic acid to give brown precipitates, which were recrystallized from acetone in pale yellow needles, m. p. 129°C. The mother liquor was evaporated on a water bath to dryness and the residue was extracted repeatedly with acetone. The extracts were purified by passing through an alumina column. After removal of the solvent, the residue was crystallized from a dilute acetone to yield another crop of yellow needles, m. p. 129°C. Total yield 43 mg. These were found to be identical with IVb by mixed fusion.

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