troduced at the second mixing point, only *m* disappeared specifically. In the first place, this phenomenon may eliminate the possibility of the consecutive reaction, $m \rightarrow l$, because *l* should also disappear if the species were to be produced from *m*. Secondly, it indicates that even if both *l*- and *m*-species were generated during the oxidation with Fe^{2+}-H_2O_2, *m*-species could not necessarily be detectable because of its short lifetime caused by the rapid oxidation by the Fe^{3+} ion formed. In the case of the Ti^{3+}-H_2O_2 oxidation, *m* could be alive, because of the lower oxidation potential of Ti^{4+} ion (*ca.* 0.05 V[4]) as compared with Fe^{3+}(0.771 V[5]).

On the contrary, specific disappearance of *m*-species was not observable when a Ce^{4+} solution (0.001, 0.005 M) was introduced at the second mixing point into the admixed solution of Ti^{3+}, H_2O_2 and L-ascorbic acid; both *l*-and *m*-species remained to be unchanged. The oxidation potential of Ce^{4+} is known to be as high as 1.61 V[5] and so Ce^{4+} may well be expected to oxidize at leat *m*-species as Fe^{3+} has been presumed to do so. This was not actually the case. Therefore, the simple redox mechanism that Fe^{3+} oxidizes the *m*-species is still unsettled.

The *l*-species are quite stable and readily producible with a number of oxidizing agents while the *m*-species are not. The latter species may not be detected, even if produced, because of its short life-time or of absence.

Experimental

Acidified (0.1M H_2SO_4) solutions of 0.005M Ti^{3+} containing L-ascorbic acid (0.02 M) and of 0.1 M H_2O_2 were mixed at the first mixing point, and Fe^{3+} or Ce^{4+} solution, as the third reactant, was introduced at the second mixing point. Usual experimental conditions were as follows: The flow rates of Ti^{3+}, H_2O_2, and the third reactant solutions were 40, 40 and 30 ml/min, respectively, and the time interval between the first and second mixing was 6 msec, and between the second mixing and the ESR cavity was 9 msec.

Acknowledgement The authors wish to thank Takeda Chemical Industries, Inc. for generous supply of the pure sample of L-ascorbic acid.

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Synthesis of 1-Substituted-1,2,5,6-tetrahydro-4*H*-pyrrolo(3,2,1-*ij*) quinolin-2-one

TETSUZO KATO, TAKUITSU NIITSUMA and KAZUYO MAEDA

Pharmaceutical Institute, Tohoku University[1]

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There is considerable litrature dealing with the ring closure reaction *via* intramolecular nucleophilic addition to aryne intermediate. Pioneering work has been done by Huisgen[2] and by Bunnett.[3] Bunnett and his co-workers[4,5] reported the cyclization forming oxindole

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2) R. Huisgen and H. König, *Anegew. Chem.*, **69**, 268 (1957).
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derivatives from N-acyl-*o*-chloroanilines. As a principle of synthesis, this reaction has wide applicability and considerable practical value. As an application of this reaction, this work was undertaken in order to prepare tricyclic compounds from N-acyl-8-chlorotetrahydroquinolines.

Starting materials used in this reaction were as follows; *i.e.*, 1-acetyl (IIa), 1-propionoyl (IIb), 1-acetoacetyl (IIc), 1-phenylacetyl (IId), 1-phenylcarbamoyl (IIe), and 1-(α-naphthylcarbamoyl) (IIf) derivatives of 8-chloro-1,2,3,4-tetrahydroquinoline (I). All these compounds (II) were prepared from I and appropriate acylating reagents. Table I summarizes data of N-acyl-8-chlorotetrahydroquniolines.

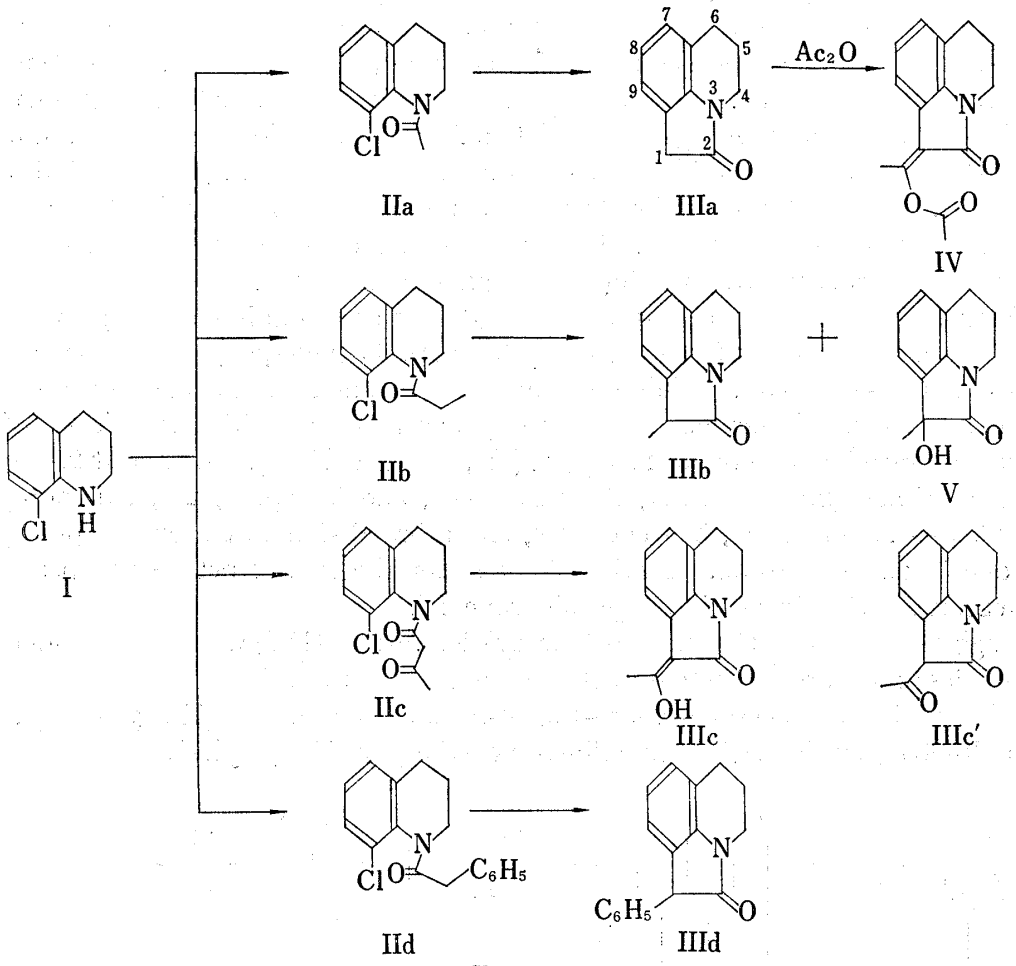

Chart 1

When 1-acetyl-8-chloro-1,2,3,4-tetrahydroquinoline (IIa) was allowed to react with potassium amide in liquid ammonia, chlorine free pale yellowish needles of mp 92—92.5°, $C_{11}H_{11}ON$ (IIIa), were obtained in 63% yield. In its infrared (IR) spectrum a strong absorption due to amide carbonyl was observed at 1695 cm^{-1} (CCl_4). The nuclear magnetic resonance (NMR) spectrum of IIIa (CCl_4) showed a singlet due to C-1 methylene protons (3.31 ppm, 2H), two sets of triplets due to C-6 (2.76 ppm, 2H) and C-4 methylene protons (3.65 ppm, 2H), and two multiplets centered at 1.97 ppm (2H, C-5 methylene protons) and at 6.85 ppm (3H, benzene ring protons). These spectral data are consistent with 1,2,5,6-tetrahydro-4*H*-pyrrolo-(3,2,1-*ij*)quinolin-2-one (IIIa).[6]

Heating of IIIa with acetic anhydride afforded yellow crystals of mp 125—126°, $C_{15}H_{15}O_3N$ (IV). The IR spectrum (CCl_4) showed the presence of enol acetate (-CO-O-C=C-) at

6) N. Sugimoto, *Yakugaku Zasshi*, **64** (B), 15 (1944) (lit. mp 91—92°).

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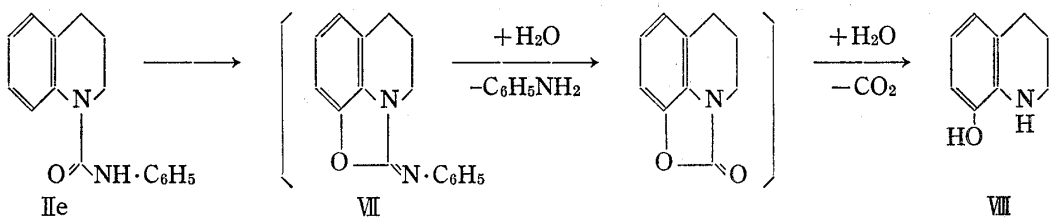
1760, 1640 cm^{-1} and amide carbonyl at 1700 cm^{-1}. The NMR spectrum in chloroform-*d* had two singlets due to methyl protons (2.39 ppm, 3H and 2.70 ppm, 3H), a multiplet centered at 2.00 ppm (2H, C-5 methylene), two triplets C-4 and C-6 methylene (3.75 ppm, 2H and 2.80 ppm, 2H), and a multiplet owing to benzene ring protons (6.80—7.40 ppm, 3H). These spectral data are consistent with 1-(1'-acetoxyethylidene)-1,2,5,6-tetrahydro-4*H*-pyrrolo(3,2,1-*ij*) quinolin-2-one (IV).

Treatment of 1-propionoyl-8-chloro-1,2,3,4-tetrahydroquinoline (IIb) with potassium amide in liquid ammonia gave colorless crystals of mp 76.5—77.5°, $C_{12}H_{13}ON$ (IIIb), and of mp 174—175°, $C_{12}H_{13}O_2N$ (V). The former product was characterized as 1-methyl-1,2,5,6-tetrahydro-4*H*-pyrrolo(3,2,1-*ij*)quinolin-2-one (IIIb) after comparison of its IR and NMR spectral data with those of IIIa. The second product was obtained in 10% yield, and its IR spectrum ($CHCl_3$) showed OH streching at 3530 cm^{-1} and amide carbonyl at 1708 cm^{-1}. The NMR spectrum in chloroform-*d* showed a singlet at 1.61 ppm(3H, C-1 methyl), multiplet centered at 1.98 ppm (2H, C-5 methylene), two triplets (2.78 ppm, 2H, C-6 methylene, and 3.68 ppm, 2H, C-4 methylene), and a signal due to OH proton at near 3.70 ppm (1H), which disappeared by adding D_2O. Although the details of the mechanism of the formation is obscure at present, these spectral data are consistent with the structure of the second product (V) as 1-hydroxy-1-methyl-1,2,5,6-tetrahydro-4*H*-pyrrolo(3,2,1-*ij*)quinolin-2-one (V).

Similar reaction of 1-acetoacetyl-8-chloro-1,2,3,4-tetrahydroquinoline (IIc) with potassium amide in liquid ammonia afforded 1-(1'-hydroxyethylidene)-1,2,5,6-tetrahydro-4*H*-pyrrolo (3,2,1-*ij*) quinolin-2-one (IIIc). This structure was assigned on the basis of the following facts. The IR spectrum indicated amide carbonyl absorption at 1655 cm^{-1}. The NMR spectrum showed a multiplet centered at 2.05 ppm (2H, C-5 methylene), a singlet at 2.40 ppm (3H, methyl), two triplets (2.82 ppm, 2H, C-6 methylene, and 3.80 ppm, 2H, C-4 methylene), a multiplet (6.90—7.25 ppm, 3H, benzene ring), and a broad signal at near 11.0 ppm (1H) presumably due to an OH proton. Ferric color test for the enol structure was positive (deep blue). Heating of IIIc in acetic anhydride gave IV.

Although the isomer of IIIc such as 1-acetyl derivative (IIIc') would be considerable, the data above described are consistent with the enol structure (IIIc).

Reaction of 1-phenylacetyl-8-chloro-1,2,3,4-tetrahydroquinoline (IId) gave 1-phenyl-1,2,5,6-tetrahydro-4*H*-pyrrolo(3,2,1-*ij*)quinolin-2-one (IIId) in 57.6% yield.



IIe VII VIII

Chart 2

In order to obtein 1-substituted-tetrahydro-4*H*-imidazoquinolin-2-one such as VI, reaction of 1-phenylcarbamoyl-1,2,3,4-tetrahydro-8-chloroquinoline (IIe) with potassium amide in liquid ammonia was investigated. However, the reaction did not give the expexted tricyclic product (VI), but afforded colorless prisms of mp 120—120.5°, $C_9H_{11}ON$ (VIII), which was identified with 8-hydroxy-1,2,3,4-tetrahydroquinoline (VIII)[7] by the comparison of IR spectrum and admixture with an authentic sample prepared by the catalytic reduction of 8-hydroxyquinoline with rhodium catalyst.

The formation of VIII suggests that the reaction also proceeded *via* aryne intermediate. Namely, the first stage of this reaction should be the formation of the benzyne intermediate,

7) K. Bedall and O. Fischer, *Chem. Ber.*, **14**, 1368 (1881).

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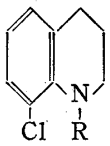
which cyclized not to VI but to VII, because a strong nucleophile suitably located in oxygen than in nitrogen added intramolecularly to the aryne structure resulting in the formation of VII, which was readily hydrolyzed to VIII.

Similarly, reaction of IIf did not give the VI nor the VII type product, but gave VIII.

Table I. 

	R	mp (bp) (°C)	Yield (%)	Formula	Analysis (%) Calcd. C	H	N	Found C	H	N	IR $\nu_{max}^{CHCl_3}$ cm^{-1} >C=O
IIa	CH_3CO acetyl	56— 58.5 (133(3 mmHg))	95.2	$C_{11}H_{12}ONCl$	63.01	5.77	6.68	62.85	5.61	6.58	1645
IIb	CH_3CH_2CO propionyl	(132(3 mmHg))	96.4	$C_{12}H_{14}ONCl$	64.43	6.31	6.26	64.50	6.17	6.47	1645
IIc	CH_3COCH_2CO acetoacetyl	60— 62.0	39.7	$C_{13}H_{14}O_2NCl$	62.03	5.61	5.56	62.35	5.40	5.44	1645 1725
IId	$C_6H_5CH_2CO$ phenylacetyl	74— 75.5	92.0	$C_{17}H_{16}ONCl$	71.45	5.60	4.90	71.47	5.40	4.46	1650
IIe	C_6H_5NHCO phenylcarbamoyl	127—128.0	86.6	$C_{16}H_{15}ON_2Cl$	67.02	5.24	9.77	66.77	5.13	9.84	1670
IIf	α-$C_{10}H_7NHCO$ α-naphthyl carbamoyl	137—138.5	95.0	$C_{20}H_{17}ON_2Cl$	71.32	5.05	8.32	71.44	4.90	8.25	1665

Experimental

8-Chloro-1,2,3,4-tetrahydroquinoline (I)[8]——A mixture of 8-chloroquinoline (3.3 g, 0.02 mole) and 5% Rh-Al_2O_3 (0.5 g) in abs. EtOH (25 ml) was shaken in H_2 until 2 mole equivalent (975 ml at 24°) had been absorbed. The time required was *ca.* 2 hr. The catalyst was filtered off and the solvent was removed from the filtrate by evaporation under reduced pressure. The residue was purified by vacuum distillation, bp 100—102° (4 mmHg). Yield, 2.5 g (75%).

1-Acetyl-8-chloro-1,2,3,4-tetrahydroquinoline (IIa)——A solution of I (8.4 g) and sodium acetate (0.5 g) in Ac_2O (45 ml) was heated at reflux for 4 hr. Removal of Ac_2O by vacuum distillation yielded an oily residue, which was made alkaline with K_2CO_3, and the mixture was extracted with benzene. The benzene solution was dried over K_2CO_3, filtered, and the solvent was removed from the filtrate by distillation. The residue was purified by redistillation under reduced pressure, bp 133° (3 mmHg), mp 56—58.5°. Yield, 10.0 g (95.2%).

1-Propionoyl-8-chloro-1,2,3,4-tetrahydroquinoline (IIb)——A solution of I (4.19 g) and propionoyl chloride (4.62 g) in $CHCl_3$ (25 ml) was stirred at 40° for 1 hr. Anhydrous K_2CO_3 (10 g) was added, and the stirring was continued for additional 4 hr. To the mixture was added H_2O, and the $CHCl_3$ layer was removed. The aqueous layer was extracted with $CHCl_3$, and the combined $CHCl_3$ solution was condensed. The resulting oily residue was dissolved in ether, and the ether solution was washed with 10% NaOH, and dried over Na_2SO_4. The ether extract was purified by vacuum distillation, bp 132° (3 mmHg). Yield, 5.4 g (96.4%).

1-Acetoacetyl-8-chloro-1,2,3,4-tetrahydroquinoline (IIc)——To a solution of I (4.18 g) in $CHCl_3$ (4 ml) were added diketene (2.52 g) and a few drops of triethylamine with ice-cooling. After allowing to stand for 3 days in a refrigirator, the mixture was condensed *in vacuo* at room temperature. The residue was extracted with ether, and from the ether extract colorless plates of mp 60—62° were obtained. Yield, 2.5 g (39.7%).

1-Phenylacetyl-8-chloro-1,2,3,4-tetrahydroquinoline (IId)——To a solution of I (5 g) and phenylacetyl chloride (10 g) in $CHCl_3$ (25 ml) was added a solution of K_2CO_3 (15 g) in H_2O (22 ml). The mixture was stirred for 3 hr, and allowed to stand overnight at room temperature. The $CHCl_3$ layer was separated, and the aqueous layer was extracted with $CHCl_3$. The combined organic layer was dried, evaporated, and the residue was washed with petroleum ether (bp 45—65°) to give a crystalline solid. Recrystallization from ether–petroleum ether gave colorless needles of mp 74—75.5°. Yield, 7.9 g (92%).

8) A. Claus and M. Scholler, *J. Prakt. Chem.*, (2) **48**, 140 (1893).

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1-Phenylcarbamoyl-8-chloro-1,2,3,4-tetrahydroquinoline (IIe)——A solution of I (4.2 g) and phenyl isocyanate (3 g) in benzene (7 ml) was refluxed for 2 hr. Removal of the solvent by distillation *in vacuo* gave a crystalline residue, which was purified by recrystallization from benzene to give colorless needles, mp 127—128°. Yield, 6.2 g (86.6%).

1-(α-Naphthylcarbamoyl)-8-chloro-1,2,3,4-tetrahydroquinoline (IIf)——Following the procedure given for the above run, I (5 g) was treated with α-naphthyl isocyanate (5.4 g) to give 4.5 g (95%) of IIf, mp 137—138.5°, colorless needles from AcOEt.

1,2,5,6-Tetrahydro-4*H*-pyrrolo (3,2,1-*ij*) quinolin-2-one (IIIa)——According to the procedure reported by Bunnett and Skorcz,[9] 200 ml of liq. NH_3 was placed in a 500 ml three-necked flask equipped with a mechanical stirrer and a dry ice-aceton condenser. NH_3 was dried with a small piece of sodium metal, and a trace of ferric chloride was added, followed by the calculated amount of potassium metal (3.15 g, 0.08 gram atom). After the metal had been dissolved completely, as indicated by a color change from blue to deep gray, 4.19 g of IIa was added. After stirring for 30 min, the reaction mixture was quenched with NH_4Cl (5.4 g), and NH_3 was evaporated.

The residue was extracted with ether. The ether solution was dried over Na_2SO_4, filtered, and condensed to dryness *in vacuo*. The crystalline residue was recrystallized from ether to give pale yellow needles, mp 92—92.5° (*lit.* mp 91—92°).[6] Yield, 2.19 g (63%). *Anal.* Calcd. for $C_{11}H_{11}ON$ (IIIa): C, 76.27; H, 6.40; N, 8.09. Found: C, 76.16; H, 6.31; N, 8.08.

1-Methyl-1,2,5,6-tetrahydro-4*H*-pyrrolo (3,2,1-*ij*) quinolin-2-one (IIIb) and 1-Hydroxy-1-methyl-1,2,5,6-tetrahydro-4*H*-pyrrolo (3,2,1-*ij*) quinolin-2-one (V)——Employing the similar procedure given for the above run, IIb (3.35 g) was treated with potassium amide (prepared from 2.35 g of potassium metal in 200 ml of liq. NH_3). After being quenched with 4 g of NH_4Cl, NH_3 was evaporated from the reaction mixture. The resulting residue was extracted with hot ether. The ether solution was condensed to dryness, and the residual solid was washed with cold ether. The residue, which was sparingly soluble in cold ether, was recrystallized from AcOEt to give colorless prisms, mp 174—175°. Yield, 0.33 g (10.8%). *Anal.* Calcd. for $C_{12}H_{13}O_2N$ (V): C, 70.91; H, 6.45; N, 6.89. Found: C, 70.99; H, 6.41; N, 6.58.

The ether easily soluble fraction was condensed, and the residue was purified by recrystallization from ether to give colorless plates, mp 76.5—77.5°. Yield, 0.7 g (24%). *Anal.* Calcd. for $C_{12}H_{13}ON$ (IIIb): C, 76.97; H, 7.00; N, 7.48. Found: C, 76.97; H, 6.92; N, 7.56. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1693 (CO). NMR (CCl_4, ppm): 1.40 (3H, doublet, C-1 methyl), 2.00 (2H, quartet, C-5 methylene), 2.75 (2H, triplet, C-6 methylene), 3.25 (1H, quartet, C-1 proton), 3.65 (2H, triplet, C-4 methylene), 6.74—7.06 (3H, multiplet, benzene ring protons).

1-(1′-Hydroxyethylidene)-1,2,5,6-tetrahydro-4*H*-pyrrolo (3,2,1-*ij*) quinolin-2-one (IIIc)——Following the procedure given for IIIa, IIc (2.52 g) was treated with potassium amide (prepared from 1.56 g of potassium metal) in 200 ml of liq. NH_3. After removal of NH_3, the residue was extracted with petroleum ether, ether and then with $CHCl_3$. From the petroleum ether soluble fraction 0.1 g of IIc was recovered. The ether and $CHCl_3$ soluble fraction was condensed, and combined residue was purified by recrystallization from benzene to give colorless needles, mp 154—155°. Yield, 1 g (45%). *Anal.* Calcd. for $C_{13}H_{13}O_2N$ (IIIc): C, 72.54; H, 6.09, N, 6.51. Found: C, 72.40; H, 5.85; N, 6.61.

1-Phenyl-1,2,5,6-tetrahydro-4*H*-pyrrolo (3,2,1-*ij*) quinolin-2-one (IIId)——Following to the procedure given for IIIa, the reaction of IId (4.25 g) with potassium amide prepared from 2.35 g of potassium metal in 200 ml of liq. NH_3 afforded 2.15 g (57.6%) of IIId as colorless prisms (from ether), mp 122.5—123.5°. *Anal.* Calcd. for $C_{17}H_{15}ON$ (IIId): C, 81.90; H, 6.06; N, 5.62. Found: C, 81.63; H, 6.00; N, 5.90. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1700 (CO). NMR ($CDCl_3$, ppm): 2.05 (2H, quartet, C-5 methylene), 2.80 (2H, triplet, C-6 methylene), 3.70 (2H, triplet, C-4 methylene), 4.58 (1H, singlet, C-1 proton).

1-(1′-Acetoxyethylidene)-1,2,5,6-tetrahydro-4*H*-pyrrolo (3,2,1-*ij*) quinolin-2-one (IV)——1) A solution of IIIa (1 g) and sodium acetate (0.1 g) in Ac_2O (10 ml) was heated under reflux for 2 hr. The reaction mixture was condensed *in vacuo*, and the residue was made alkaline with 10% Na_2CO_3. The mixture was extracted with benzene, and the benzene solution was condensed to give a crystalline solid. Recrystallization from ether gave yellow plates, mp 125—126°. Yield, 0.49 g (33%). *Anal.* Calcd. for $C_{15}H_{15}O_3N$ (IV): C, 70.02: H, 5.88; N, 5.44. Found: C, 69.72; H, 5.98; N, 5.40.

2) A solution of IIIc (0.5 g) in Ac_2O (25 ml) was refluxed for 2 hr. Similar treatment as above gave 0.33 g (58%) of IV, undepressed on admixture with a sample obtained in the above run.

8-Hydroxy-1,2,3,4-tetrahydroquinoline (VIII)[7]——1) Following the procedure given for IIIa, treatment of IIe (4.3 g) with potassium amide prepared from potassium metal (2.35 g) in liq. NH_3 (200 ml) gave colorless needles (ether), mp 120—120.5°. Yield, 0.34 g (15%). *Anal.* Calcd. for $C_9H_{11}ON$ (VIII): C, 72.45; H, 7.43; N, 9.39. Found: C, 72.14; H, 7.10; N, 9.31.

2) Similar treatment of IIf (6 g) and potassium metal (3 g) in liq. NH_3 (200 ml) afforded 0.2 g of VIII.

Acknowledgement The authors are indebted to Mrs. Ayako Satō, Miss Chieko Yokoyama for the elementalanalysis, and to Miss Yuko Tadano for the NMR measurement.

9) J.F. Bunnett and J.A. Skorcz, *J. Org. Chem.*, **27**, 3836 (1962).

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