The Mechanism of the Reaction of Quinolines with Organolithium Compounds[1]

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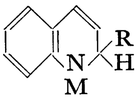
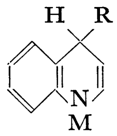
The treatment of lepidine (IV) with phenyllithium in ether afforded 2-phenyl-4-methylquinoline (V) along with small amounts of 2-phenylquinoline (VI) and 2-methyl-4-phenylquinoline (VII). The similar treatment of IV with phenyllithium and then with ethyl chloroformate gave 1-ethoxycarbonyl-4-methyl-4-phenyl-1,4-dihydroquinoline (VIIIa). The alkaline hydrolysis of VIIIa produced a mixture of V, VI, and VII. Similar experiments were carried out on the reactions between IV and *n*-butyllithium and between quinoline and phenyllithium. On the basis of these results and other observations, a new mechanism involving an addition-rearrangement-elimination was proposed for the reaction of quinolines with organolithium compounds.

Many investigations have already been made into the mechanism of the reactions of quinolines with organometallic compounds.[2] However, the mechanism still seems not to be well established. For example, quinoline reacts with phenyllithium,[3] butyllithium,[4] and phenylmagnesium bromide[5] to give mainly the 2-substituted products, *i.e.*, 2-phenyl- or 2-butylquinoline, along with only a small amount of the corresponding 4-substituted product. On the other hand, the treatment of quinoline with the methylsulfinyl carbanion in DMSO undergoes the substitution reaction exclusively at the 4-position of quinoline to produce lepidine in a quantitative yield.[6,7]

Throughout a whole series of these reactions between quinolines and organometallic reagents, it has always been assumed that the reactions proceed *via* the intermediate I or II. However, no conclusive evidence for the existence of these intermediates has yet been appeared in the literature.[8] Furthermore, the factors which cause the difference in the orientation of the reactions (1,2- or 1,4-additions) remain unexplained.



I

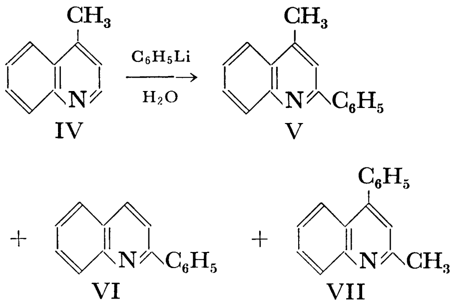


II

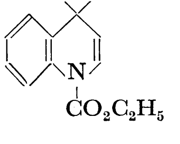
In this paper we wish to report our findings on the isolation and characterization of the intermediates in the reactions of quinolines with organolithium compounds. We will also propose a new mechanism of the reactions based on the chemical properties of these intermediates.

Results and Discussion

Products of the Reaction of Lepidine with Phenyllithium. The treatment of lepidine (IV) with phenyllithium in ether at −70°C for 30 min produced a yellow precipitate. After the hydrolysis of the precipitate with water, the mixture was analyzed by the vpc. The analysis revealed that the mixture contained 2-phenyl-4-methylquinoline (V), 2-phenylquinoline (VI) and 2-methyl-4-phenylquinoline (VII) in a ratio of 96.5 : 3.0 : 0.5 respectively.



Isolation and Characterization of the Intermediates in the Reactions of Quinolines with Organolithium Compounds. When an ethereal solution of ethyl chloroformate was added to the suspension of the yellow precipitate in ether which had been produced by the reaction of lepidine with phenyllithium, the precipitate disappeared and a homogeneous solution was obtained. From this solution, 1-ethoxycarbonyl-4-methyl-4-phenyl-1,4-dihydroquinoline (VIIIa) was isolated as white crystals in a 51% yield, along with small amounts of V and VII. The similar treatment of lepidine with *n*-butyllithium and then with ethyl chloroformate gave 1-ethoxycarbonyl-4-*n*-butyl-4-methyl-1,4-dihydroquinoline (VIIIb) as a pale yellow liquid in a 45% yield.



VIII a, $R_1=CH_3$ $R_2=C_6H_5$
b, $R_1=CH_3$ $R_2=n\text{-}C_4H_9$
c, $R_1=H$ $R_2=C_6H_5$

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[1] A part of this work was presented at the 2nd Symposium on the Chemistry of Heterocyclic Compounds, Nagasaki, November, 1969.

[2] K. Blaha and O. Cervinka, "Advances in Heterocyclic Chemistry," Vol. 6, ed. by A. R. Katritzky, Academic Press, New York, N. Y. (1966), p. 147; R. G. Shepherd and J. L. Fedrick, *ibid.*, Vol. 4 (1965), p. 145; *cf.* the references cited therein.

[3] K. Ziegler and G. Zeiser, *Ann. Chem.*, **485**, 174 (1931).

[4] H. Gilman and G. C. Gainer, *J. Amer. Chem. Soc.*, **69**, 877 (1947).

[5] F. W. Bergstrom and S. H. McAllister, *ibid.*, **52**, 2845 (1930).

[6] H. Nozaki, Y. Yamamoto, and R. Noyori, *Tetrahedron Lett.*, **1966**, 1123.

[7] G. A. Russell and S. A. Weiner, *J. Org. Chem.*, **31**, 248 (1966).

[8] Recently, G. Fraenkel and J. C. Cooper (*Tetrahedron Lett.*, **1968**, 1825), in studying the reaction of pyridine with butyllithium, and C. S. Gian and J. L. Stout (*Chem. Commun.*, **1969**, 142), in studying the reaction of pyridine with phenyllithium, have characterized the intermediate of the type III on the basis of the NMR data.

III

The structures of VIIIa and VIIIb were established by a study of the results of their elemental analyses and spectral data, which are summarized in Table 1. The absorptions due to the C=C double bond in the IR spectra partly support the assigned structures; the comparison of the IR spectra of 1,4-dihydroquinolines and those of 1,2-dihydroquinolines suggests that the C=C double bond of the former absorbs at higher wave numbers than that of the latter compounds, which appears at$<$1630 cm^{-1}, probably because the C=C bond in the latter is in conjugation with the benzene ring.[9] However, the final confirmation of the structures was attained from the NMR spectra, shown in Figs. 1 and 2. The spectra for the protons of the hetero-ring were readily analyzed as of the AB and AX types.

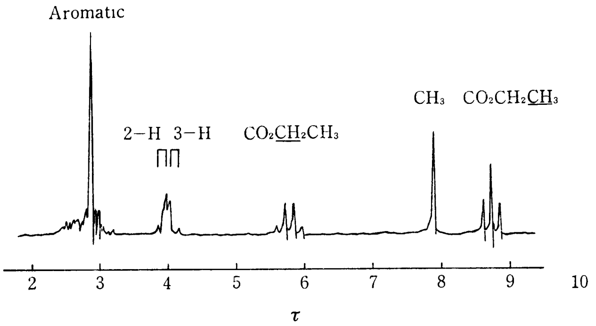

Fig. 1. NMR spectrum of 1-ethoxycarbonyl-4-methyl-4-phenyl-1,4-dihydroquinoline (VIIIa) in CCl_4.

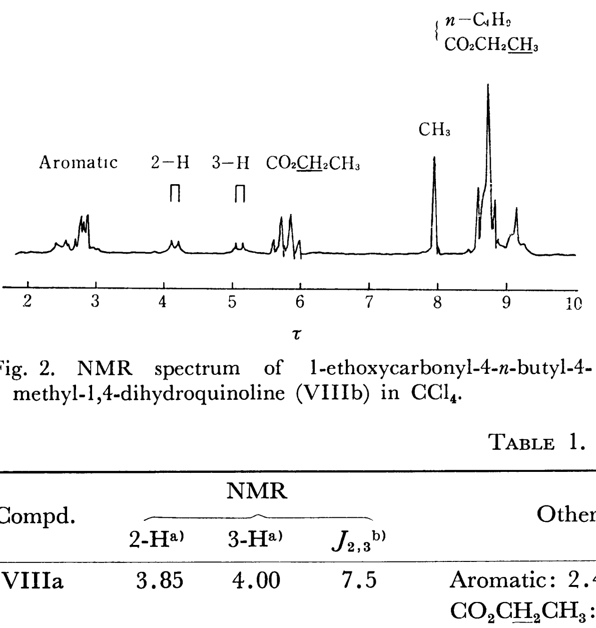

Fig. 2. NMR spectrum of 1-ethoxycarbonyl-4-n-butyl-4-methyl-1,4-dihydroquinoline (VIIIb) in CCl_4.

The chemical shifts for 2-H and 3-H, and the coupling constants, $J_{2,3}$ listed in Table 1, clearly indicate that they are of the olefinic protons in the hetero-ring; therefore, the structures identified as VIIIa and VIIIb are correct. It is now worthwhile to point out that the $J_{2,3}$ values obtained in this investigation are very close to those found by Bramley and Johnson[10] for the majority of 1,4-dihydroquinolines.

When quinoline was treated in ether with phenyllithium and then with ethyl chloroformate in a manner similar to that described above, a pale yellow liquid was obtained in a 59% yield. The structure of this liquid was supposed to be 1-ethoxycarbonyl-4-phenyl-1,4-dihydroquinoline (VIIIc). Though the IR spectrum supported the assigned structure, showing absorptions at 1695 and 1650 cm^{-1} (shoulder) due, respectively, to the C=O and C=C double bonds, the NMR spectra in CCl_4 exhibited a complex pattern which could not be readily analyzed; τ 2.5—3.2 (9H, multiplet, aromatic), 3.25—3.98 (3H, multiplet, 2-H, 3-H, 4-H), 5.78 (2H, quartet, J=7.0 Hz, $CO_2\mathbf{CH_2}CH_3$), 8.72 (3H, triplet, J=7.0 Hz, $CO_2CH_2\mathbf{CH_3}$). However, further suport for the structure was secured by the experiments to be described below.

Hydrolysis of 1-Ethoxycarbonyl-1,4-dihydroquinolines. Surprisingly, VIIIa, VIIIb, and VIIIc were all unable to hydrolyze with hydrochloric acid or sodium hydroxide in an aqueous ethanol even when the mixtures were refluxed for 2 hr; all were recovered in quantitative yields. The hydrolysis of these compounds was satisfactorily performed with sodium hydroxide in DMSO-water (5 : 1) by heating on a water bath. The vpc analysis of the reaction mixtures after almost complete hydrolysis gave the following products in the molar ratios shown in the parentheses:

VIIIa → V(87.5%) + VI(7.5%) + VII(5%)
VIIIb → 2-n-butyl-4-methylquinoline(IX)(100%)
VIIIc → VI(74.5%) + VII(25.5%)

The hydrolysis of VIIIc yielded an unexpected product, VII. The reason for this result was, however, soon clarified. The treatment of VIIIc with the dimethylsulfinyl carbanion in DMSO, followed

TABLE 1. SPECTRAL DATA

Compd.	NMR			Others$^{a,b)}$	IR, cm^{-1}		UV, mμ
	2-H$^{a)}$	3-H$^{a)}$	$J_{2,3}$$^{b)}$		C=O	C=C	$\lambda_{\max}^{n\text{-hexane}}$
VIIIa	3.85	4.00	7.5	Aromatic: 2.41—2.98(m) $CO_2\underline{CH_2}CH_3$: 5.76 (q, J=7.5) $CO_2CH_2\underline{CH_3}$: 8.72 (t, J=7.5) CH_3: 7.85(s)	1686$^{c)}$	1660$^{c)}$	267 ($\varepsilon=5\times10^3$) 307 ($\varepsilon=2\times10^3$)
VIIIb	4.14	5.12	6.5	Aromatic: 2.41—3.10(m) $CO_2\underline{CH_2}CH_3$: 5.78 (q, J=7.5) $\{CO_2CH_2\underline{CH_3}$, n-$C_4H_9\}$: 8.62—9.17(m) CH_3: 7.95(s)	1695$^{d)}$	1660$^{d)}$	270 ($\varepsilon=2\times10^3$) 305 ($\varepsilon=2\times10^3$)

a) Chemical shifts are represented as τ-values. b) Coupling constants are represented in the Hz unit. c) in KBr. d) in liquid film. The absorption at 1660 cm^{-1} appeared as a shoulder.

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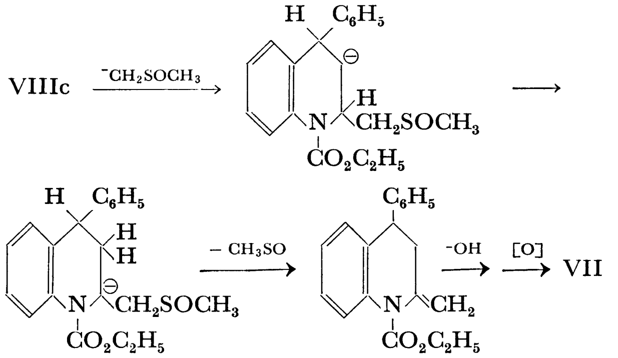
[9] H. Ahlbrecht and F. Kröhnke, *Ann. Chem.*, **717**, 96 (1968).

[10] R. Bramley and M. D. Johnson, *J. Chem. Soc.*, **1965**, 1372.

by the hydrolysis, resulted in an increase in the yield of VII to 38.4%. A plausible explanation of these results is that VII is produced by the attack of the carbanion on the 2-position of VIIIc. Thus, the above results support the structure VIIIc.



Rate of the Hydrolysis of 1-Ethoxycarbonyl-4-methyl-4-phenyl-1,4-dihydroquinoline (VIIIa). The hydrolysis of VIIIa was carried out with sodium hydroxide in DMSO-ethanol-water (60 : 15 : 15) at 72°C. The rate of the reaction was followed by analyzing the amounts of the products by means of vapor-phase chromatography. The results are depicted in Fig. 3. The amount of V produced reached a maximum after about 3 hr and then gradually decreased. On the other hand, the amount of VI increased with the decrease in the amount of V.

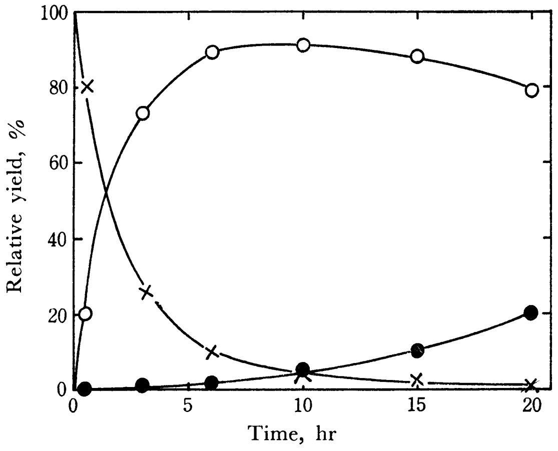
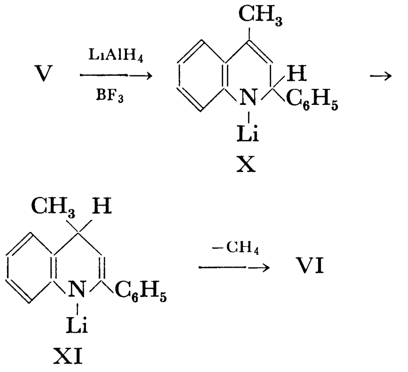


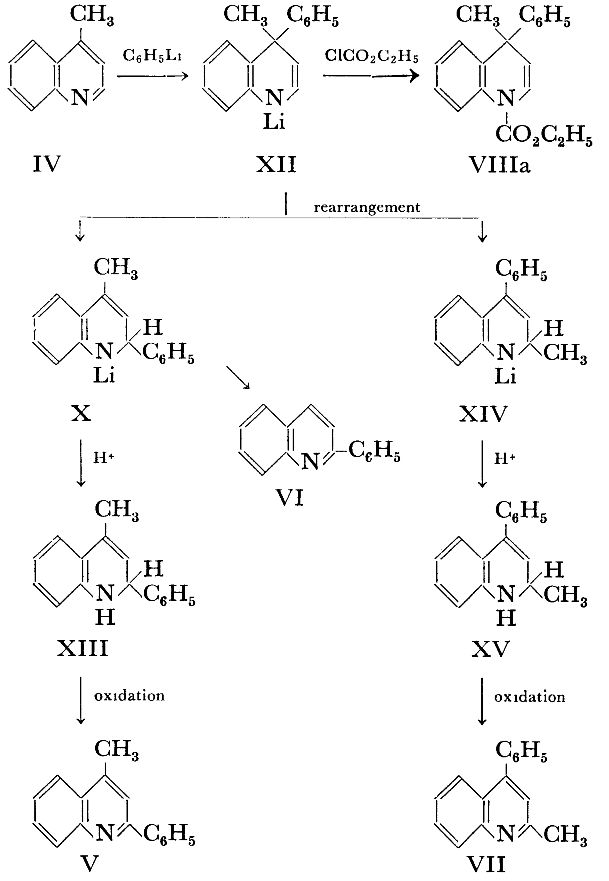
Fig. 3. Rate of the hydrolysis of 1-ethoxycarbonyl-4-methyl-4-phenyl-1,4-dihydroquinoline (VIIIa) in DMSO-H_2O-C_2H_5OH (60 : 15 : 15) at 72±1°C.
—×—, VIIIa; —○—, 2-phenyl-4-methylquinoline (V); —●—, 2-Phenylquinoline (VI)

Reaction of 2-Phenyl-4-methyl-1,2-dihydroquinoline (X). Since the rate profile of the hydrolysis of VIIIa described in the preceding paragraph suggested that VI is produced from X which is a precursor of V, the chemistry of X was studied; V itself was stable under the reaction conditions used for the hydrolysis of VIIIa.

It is well known that quinolines can be reduced to 1,2-dihydroquinolines by the action of $LiAlH_4$, though with some difficulty.[11] Hence, V was treated with $LiAlH_4$ in boiling ether. However, no reaction took place, and the starting material was recovered unchanged. This is probably because of a steric hindrance due to the phenyl group at the 2-position. The methiodides of quinolines are, however, readily reduced to the corresponding 1,2-dihydro derivatives with $LiAlH_4$.[12] In view of these facts, V was treated in ether with BF_3-etherate and then with $LiAlH_4$. After hydrolysis, the vpc analysis of the reaction mixture revealed that the mixture consisted of 31% of V and 69% of VI. This result suggests that VI is produced from X. A probable mechanism of this reaction is as follows:



Mechanism. On the basis of the observations presented earlier, we propose a new mechanism, involving addition-rearrangement-elimination(or-oxidation), for the reaction of quinolines with organolithium



Scheme 1

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[11] K. W. Rosenmund, *Chem. Ber.*, **87**, 1229 (1954).

[12] R. C. Elderfield and B. H. Wark, *J. Org. Chem.*, **27**, 543 (1962).

compounds. The mechanism is represented Scheme 1, taking as an example the reaction of lepidine with phenyllithium. A similar mechanism would operate for the other reactions.

The possibility of the rearrangement of XII to X and XIV can be explained by the Woodward-Hoffmann rule for the sigmatropic reactions.[13] In this rearrangement, the transition state could be envisaged as being made up by the combination of the orbital of the phenyl or methyl radical with those of the quinoline radical anion, which contains eleven π electrons. The highest occupied orbital of the radical anion possesses the symmetry shown in Fig. 4.[14] Since the migrating group, the phenyl or methyl radical, can possess an accessible π orbital, the appreciable positive overlap between the framework orbital and that of the migrating group can be maintained in the transition state (Fig. 5). Hence, the rearrangement is possible. Furthermore, the overlap of the above sort would be larger between C_4 and C_2 than between C_4 and C_3, since the coefficients of the component π AO's on the highest occupied MO are larger at C_2 than at C_3. The migration can, therefore, be expected to take place from C_4 to C_2 rather than from C_4 to C_3. The migratory aptitudes of the migrating groups would be proportional to the availability of the π orbital on the groups in the transition state of the rearrangement. Thus, the phenyl migration is favored over the methyl migration in the rearrangement of XII to X and XIV.

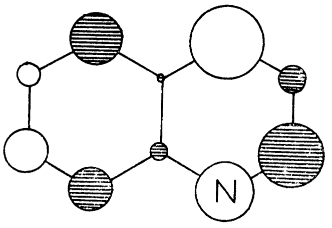

Fig. 4. HO MO of the quinoline radical anion. The phase of π AO's on the one side of the molecular plane are depicted: the shaded circle represents the positive phase and the unshaded one the negative phase.

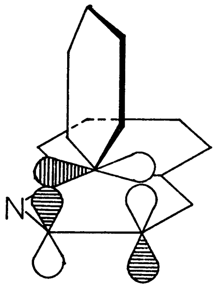

Fig. 5. Transition state of the phenyl migration.

The existence of the dihydro species, XIII and XV, although their structures were not unambiguously confirmed, was inferred from the facts that the NH absorption appeared in the IR spectra of the initially-isolated products and that this absorption disappeared upon the oxidation of the products with air or nitrobenzene.

Experimental

The melting points are uncorrected. The IR spectra were recorded on a Hitachi EPI-S_2 infrared spectrophotometer. The UV spectra were determined on a Hitachi EPU-2U recording spectrophotometer. The NMR spectra were obtained on a Hitachi H-60 high-resolution NMR spectrometer, with TMS as the internal standard. The elemental analyses were performed with a Yanagimoto MT-1 CHN Corder. The vpc analyses were carried out with a Yanagimoto GCG 5DH chromatograph, employing a stainless steel column (2 m×6 mm o.d.) packed with 25% PEG-20 M or 25% Apiezon N on chromosorb (80 mesh). The column temperature was generally maintained at 300°C with a helium flow rate of 30 m*l*/min. For quantitative analyses, the respective authentic samples were used as the internal standards.

Materials. Lepidine (IV) was prepared from methyl vinyl ketone and aniline hydrochloride by the method of Campbell and Schaffner,[15] bp 86—88°C/1 mmHg. 2-Phenyl-4-methylquinoline (V) was prepared from benzylideneacetone and aniline hydrochloride by the method of John and Noziczka,[16] mp 58—59°C. 2-Phenylquinoline (VI) was prepared from quinoline and phenyllithium by the method of Ziegler,[17] mp 81—82°C. 2-Methyl-4-phenylquinoline was prepared, starting with paraldehyde, acetophenone, and aniline, by the method of Knövenagel and Goos,[18] mp 98—99°C. The other chemicals were of commercial origin and were used after purification by distillation or recrystallization.

Reaction of Lepidine and Phenyllithium. A solution of 5.3 g (0.034 mol) of bromobenzene in 25 m*l* of ether was stirred, drop by drop and over a period of 30 min, into a suspension of 0.47 g (0.067 mol) of small pieces of lithium foil in 100 m*l* of ether under nitrogen and at room temperature. Stirring was continued for 30 min to complete the reaction, during which time the reaction mixture was refluxed. During this period the lithium dissolved completely and lithium bromide was precipitated. The mixture was cooled in a dryice - acetone bath, and a solution of 4.0 g (0.0167 mol) of lepidine in 25 m*l* of ether was stirred, drop by drop, into this mixture under a nitrogen atmosphere. A yellow solid soon started to precipitate. After stirring for 30 min, the reaction mixture was hydrolyzed by adding 25 m*l* of water under cooling in a dry ice - acetone bath. The yellow precipitate disappeared, and a homogeneous mixture was obtained. The ether layer was separated, and the aqueous layer was extracted with ether. The combined ether solution was washed with water, dried over sodium sulfate, and then evaporated to produce 6.1 g (almost quantitative) of a yellow oil. The oil was directly subjected to the vpc analysis, which revealed that the oil consisted of a mixture of V, VI, and VII.

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[13] R. B. Woodward and R. Hoffmann, "The Conservation of Orbital Symmetry," Verlag Chemie, GmbH, Weinheim/Bergstr. (1970), Chapter 7.

[14] The highest occupied MO of the quinoline radical anion was calculated by the Hückel method, using as parameters $\alpha_N=\alpha+\beta$ and $\beta_{CN}=\beta$. The coeffcients of the component π AO's were: $N=-0.39354$, $C_2=0.42401$, $C_3=0.20559$, $C_4=-0.51515$, $C_5=0.36108$, $C_6=-0.18282$, $C_7=-0.28004$, $C_8=0.30696$, $C_9=0.14397$, and $C_{10}=0.02276$. The size of each π AO in Fig. 4 is so dipicted as to reflect the above coefficients.

[15] K. N. Campbell and I. J. Schaffner, *J. Amer. Chem. Soc.*, **67**, 86 (1945).

[16] H. John and F. Noziczka, *J. Prakt. Chem.*, [2], **111**, 68, 73 (1897).

[17] K. Ziegler, *Ann. Chem.*, **479**, 147 (1930); *ibid.*, **483**, 185 (1931).

[18] E. Knövenagel and O. Goos, *Ber.*, **55**, 1934 (1922).

The oil was distilled under reduced pressure to give again a pale yellow oil; bp 175—179°C/2 mmHg. The IR spectrum (liquid film) of this oil showed absorptions at 3400 and 1650 cm^{-1} due, respectively, to the NH and C=C bonds. These results indicate that the species initially produced by the reaction are the dihydro derivatives of V, VI, and VII (see Mechanism) and that they are oxidized to V, VI, and VII themselves in a column during the vapor-phase chromatography.

To isolate 2-phenyl-4-methylquinoline (V), 10.0 g (0.07 mol) of lepidine were treated with phenyllithium in ether, which had been prepared from 1.4 g (0.2 mol) of lithium and 15.7 g (0.1 mol) of bromobenzene, in a manner similar to that described above. The yellow oil obtained after the evaporation of the ether was refluxed in 60 m*l* of nitrobenzene for 3 hr. A 6 N sulfuric acid was added to the reaction mixture to yield a solid (sulfate of the bases), which was then filtered and washed with three 10-m*l* portions of ether. The filtrate was extracted with ether, and the organic layer was separated. The aqueous layer and the solid were combined, made alkaline with aqueous sodium hydroxide and sodium carbonate solutions, and then extracted with ether. The ether solution was washed with water, dried over sodium sulfate, and evaporated to yield 14 g (82%) of a crude V. Recrystallization from water-ethanol gave pure V as white needles; mp 58—59°C.

The IR spectrum (KBr) of the V thus obtained showed an absorption at 1600 cm^{-1} and was identical with that of the authentic sample, lacking absorptions due to the NH and C=C bonds.

The hydrochloride, mp 212—213°C, and the picrate, mp 208—209°C, were all identical with those of the authentic sample in every respect and gave satisfactory elemental analyses.

Isolation of 1-Ethoxycarbonyl-4-methyl-4-phenyl-1,4-dihydroquinoline (VIIIa). A suspension of phenyllithium in 170 m*l* of ether was prepared from 1.4 g (0.02 mol) of lithium and 15.7 g (0.1 mol) of bromobenzene as described above. Into this suspension we stirred, drop by drop, a solution of 14.3 g (0.1 mol) of lepidine in 20 m*l* of ether at room temperature under nitrogen. The mixture soon turned green and then started to precipitate a yellow solid. After stirring for 1 hr, a solution of 10.9 g (0.1 mol) of ethyl chloroformate in 50 m*l* of ether was added, drop by drop, to the above mixture. The yellow solid gradually dissolved with the evolution of heat. When stirring was continued for 1 hr, the yellow solid disappeared completely. The mixture was cooled in an ice bath, and then 50 m*l* of water was added. The ether layer was separated, and the aqueous layer was extracted with ether. The combined ether solution was washed with water, dried over sodium sulfate, and evaporated to yield 26.3 g of a yellow oil. The recrystalliation of the oil from water-ethanol gave 14.9 g (51%) of VIIIa as white needles; mp 74—75°C. No picrate was formed.

Found: C, 77.67; H, 6.34; N, 4.87%. Calcd for $C_{19}H_{19}O_2N$: C, 77.79; H, 6.53; N, 4.77%.

Isolation of 1-Ethoxycarbonyl-4-methyl-4-butyl-1,4-dihydroquinoline (VIIIb). A suspension of 0.1 mol of *n*-butyllithium in 170 m*l* of ether was prepared by the reaction between a suspension of 1.4 g (0.2 mol) of lithium in 150 m*l* of ether and a solution of 13.8 g (0.1 mol) of *n*-butyl bromide in 20 m*l* of ether in a manner similar to that described for the preparation of phenyllithium. Into this suspension we then stirred a solution of 14.3 g (0.1 mol) of lepidine in 40 m*l* of ether at room temperature. A yellow solid soon started to precipitate. Stirring was continued for 30 min at room temperature, and then a solution of 10.9 g (0.1 mol) of ethyl chloroformate in 50 m*l* of ether was added to the reaction mixture. By the time the mixture has been stirred for 1 hr, the yellow solid had completely disappeared. The mixture was cooled in an ice bath, and then a 50-m*l* portion of water was added. The ether layer was separated, dried over sodium sulfate, and evaporated to yield 23.8 g of a pale yellow oil. Two distillations gave 12.3 g (45%) of VIIIb; bp 125—128°C/0.2 mmHg. No picrate was formed.

Found: C, 74.34; H, 8.59; N, 4.96%. Calcd for $C_{17}H_{23}O_2N$: C, 74.69; H, 8.47; N, 5.12%.

Isolation of 1-Ethoxycarbonyl-4-phenyl-1,4-dihydroquinoline (VIIIc). A suspension of 0.1 mol of phenyllithium in 170 m*l* of ether was prepared as has been described above. Into this suspension we then stirred a solution of 13 g (0.1 mol) of quinoline in 25 m*l* of ether at room temperature. A yellow solid precipitated. Stirring was continued for 1 hr at room temperature, and then a solution of 10.9 g of ethyl chloroformate in 50 m*l* of ether was added. The yellow solid disappeared, and the reaction mixture was worked up in a manner similar to that described above. The evaporation of the ether yielded 23.4 g of an oil. The distillation of this oil gave 12.6 g (59%) of VIIIc; bp 172—174°C/1 mmHg. No picrate was formed.

Found: C, 77.57; H, 5.87; N, 5.19%. Calcd for $C_{18}H_{17}O_2N$: C, 77.39; H, 6.13; N, 5.01%.

Hydrolysis of VIIIa. *A. Acid hydrolysis*: A mixture of 4.40 g (0.015 mol) of VIIIa in 20 m*l* of 95% ethanol and 30 m*l* of 2 N hydrochloric acid was heated on a boiling-water bath for 5 hr. The mixture was made alkaline with an aqueous sodium carbonate solution and then extracted with ether. The ether solution was washed with water, dried over sodium sulfate, and then evaporated to give 4.3 g of the starting material.

The heating of VIIIa in a mixture of acetic acid and concentrated hydrochloric acid(1 : 1) on a boiling-water bath for 5 hr resulted in the recovery of the starting material in a quantitative yield.

B. Alkaline Hydrolysis in an Aqueous Ethanol: A mixture of 1.7 g (0.0058 mol) of VIIIa in 30 m*l* of ethanol and 1.0 g (0.018 mol) of sodium hydroxide in 5 m*l* of water was refluxed for 2 hr. The work-up of the mixture resulted in the recovery of the starting material in an almost quantitative yield.

C. Alkaline Hydrolysis in an Aqueous DMSO: A mixture of 2.5 g (0.0085 mol) of VIIIa in 25 m*l* of DMSO and 1.5 g (0.027 mol) of sodium hydroxide in 5 m*l* of water was warmed at 72°C for 27 hr and then extracted with ether. The ether layer was washed thoroughly with water, dried over sodium sulfate, and evaporated to yield 2.0 g of an oil. When the oil thus obtained was subjected to the vpc analysis, the oil was found to be a mixture of V, VI, and VII.

The picrate formed from this oil was recrystallized from methanol; it melted at 208—209°C and was identical in every respect with that of the authentic sample of V.

Hydrolysis of VIIIb. *A*: The acid hydrolysis of VIIIb with a mixture of acetic acid and concentrated hydrochloric acid, and alkaline hydrolysis with an aqueous sodium hydroxide solution, were carried out under conditions similar to those described for VIIIa. In each case, the starting material was recovered in an almost quantitative yield.

B: A mixture of 1.0 g (0.0037 mol) of VIIIb in 25 m*l* of DMSO and 0.6 g (0.01 mol) of sodium hydroxide in 5 m*l* of water was heated on a boiling-water bath for 3 hr and then extracted with ether. The ether layer was washed thoroughly with water, dried over sodium sulfate, and evaporated to give an oil. The vpc analysis of the oil revealed that the oil consisted of only one compound. The distillation of the oil gave 0.5 g (68%) of 2-*n*-butyl-4-methylquinoline (IX); bp 115—117°C/mmHg.

Found: C, 84.01; H, 8.72; N, 7.25%. Calcd for $C_{14}H_{17}$-N: C, 84.37; H, 8.60; N, 7.03%.

IR($CHCl_3$): 1605, 1563, 1510, 1452 cm^{-1}. NMR(CCl_4): τ 1.98—3.00 (5H, *m*, aromatic), 7.12(2H, *t*, J=7.0 Hz, $\mathbf{CH_2}CH_2CH_2CH_3$), 7.39(3H, s, CH_3), 7.95—9.04(7H, *m*, $CH_2\mathbf{CH_2CH_2CH_3}$).

This compound did not form the picrate, probably due to bulky butyl substituent at the 2-position. The spectral data and the above result support the structure IX.

Hydrolysis of VIIIc. A mixture of 4.4 g (0.016 mol) of VIIIc in 30 m*l* of DMSO and 2.5 g (0.045 mol) of sodium hydroxide in 6 m*l* of water was heated on a boiling-water bath for 3 hr, and then the reaction mixture was worked up as has been described above. The evaporation of the ether extract produced 3.0 g of a yellow oil which was then analyzed by vapor-phase chromatography. The oil contained 2-phenylquinoline (VI) as the main product, along with a small amount of VII. The oil formed a pictrate which melted at 187—188°C after recrystallization from methanol and which was identical in every respect with that of the authentic sample of VI.

Reaction of VIIIc with the Dimethylsulfinyl Carbanion. The dimethylsulfinyl carbanion in DMSO was prepared from 0.02 mol of sodium hydride and 80 m*l* of DMSO by the method of Corey and Chaykovsky.[19] Into this solution we stirred, drop by drop, a solution of 2.7 g (0.01 mol) of VIIIc in 50 m*l* of DMSO over a period of 30 min at room temperature under nitrogen. The mixture, which soon turned red and then deep blue, was stirred for a further 3 hr at 50°C under nitrogen. A 20-m*l* portion of water was added, after which the reaction mixture was heated on a boiling-water bath for 2 hr while a white solid precipitated. The mixture was poured onto 200 m*l* of water and extracted with ether. The ether layer was washed thoroughly with water, dried over sodium sulfate, and then evaporated to give 2.2 g of an oil. The vpc analysis of this oil revealed that the oil consisted of 61.6% of VI and 38.4% of VII.

Rate of Hydrolysis of VIIIa. A homogeneous mixture was prepared by mixing a solution of 1.0 g (0.0034 mol) of VIIIa, 0.80 g (0.014 mol) of sodium hydroxide in 15 m*l* of water, and 15 m*l* of 95% ethanol (the ethanol was necessary to obtain a homogeneous mixture). Fourteen-m*l* portions of the mixture were pipetted into six 30-m*l* test tubes. The test tubes were then sealed and immersed into a constant-temperature bath at 72±1°C. The six tubes was withdrawn after 0.5-, 3-, 6-, 10-, 15-, and 20-hr intervals, respectively, and the contents were extracted with 50 m*l* of ether. The ether solution was washed twice with 20-m*l* portions of water, dried over sodium sulfate, and then concentrated. The residue was directly subjected to the vpc analysis. The proportion of the components in the mixture was calculated from the corresponding peak areas on the chromatogram; the peak areas for the components had been calibrated with the corresponding authentic samples.

Reaction of 2-Phenyl-4-methylquinoline (V) with $LiAlH_4$-BF_3. Into a solution of 1.0 g (0.0056 mol) of V in 50 m of ether we stirred 6.5 g of BF_3-etherate (47%) at room temperature under nitrogen. A pale yellow solid soon precipitated, after which the mixture was stirred for an additional 30 min. To this mixture 1.0 g (0.026 mol) of powdered $LiAlH_4$ was added in portions. Stirring was continued for 24 hr at room temperature, and then 10 m*l* of ice water were added, drop by drop, to the reaction mixture, which had been cooled in an ice bath. The mixture was filtered, and the filtrate was extracted with ether (when the filtrate was diluted with ethanol, the BF_3-salt of V precipitated as white needles). The evaporation of the ether yielded 0.5 g of an oil. The vpc analysis of the oil revealed that the oil was 69% 2-phenylquinoline (VI) and 31% V.

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[19] E. J. Corey and M. Chaykovsky, *J. Amer. Chem. Soc.*, **87**, 1345 (1965).