lang geschüttelt, vom Raney-Nickel abfiltriert und EtOH abdestilliert. Der hierbei erhaltene Rückstand wurde im Vakuum destilliert, wobei IX bei 120～125°/2 mmHg gewonnen wurde. Die Ausbeute betrug 18.1 g (95% d. Th.). (X), (XI) sowle (XII) wurden analogerweise wie oben erhalten (Tabelle 2).

1-Benzyl-2-dimethylaminomethyl-1,2,3,4-tetrahydrochinolin (XIII)——3.9 g $NaNH_2$ wurden zu getrocknetem Toluol hinzugefügt, dazu 19 g IX in 20 ml Toluol unter Umrührung bei 60° zugetropft. Nachdem die Lösung bei 80° 1 Std. behalten wurde, wurde 12.7 g Benzylchlorid zugetropft, unter Rückfluß noch weitere 5 Stdn. erhitzt. Die Reaktionslösung wurde mit 10% iger Natronlauge alkalisch gemacht und mit Äther extrahiert. Das Äther-Extrakt wurde mit 10% iger Salzsäure ausgezogen, die erhaltene HCl-lösung mit 10% iger Natronlauge neutralisiert und mit Äther wieder ausgezogen. Der Äther-Auszug wurde mit Na_2SO_4 getrocknet, dazu getrockneter HCl eingeleitet, der hierbei abfallende Niederschlag abgesaugt und aus Isoamylalkohol umkristallisiert, wobei sich das Chlorhydrat vom XIII erhalten ließ. Farblose Prismen vom Zers. Pkt. 230°. Ausbeute: 26.3 g (83% d. Th.). XIV～XX wurden analogerweise wie oben erhalten (Tabelle III).

Zum Schluß sind wir Herrn Dr. T. Akiba, dem Direktor unseres Laboratoriums, für die Anregung zu dieser Arbeit und das entgegengebrachte Interesse zu großem Dank verpflichtet.

Zusammenfassung

Durch Einwirkung von sekundären Aminen auf 2-Chlormethylchinolin wurden 2-Aminomethylchinolin-derivate erhalten. Die letzteren wurden in Gegenwart von Raney-Nickel unter Druck katalytisch reduziert. Die so erhaltenen 2-Aminomethyl-1,2,3,4-tetrahydrochinoline lieferten durch Einwirkung von Benzylchlorid bzw. *p*-Chlorbenzylchlorid 1-Benzyl-2-aminomethyl-1,2,3,4-tetrahydrochinoline.

(Eingegangen am 22, Oktober 1964)

[Chem. Pharm. Bull.
13(4) 503～510 (1965)]

UDC 547.834.2.07

67. **Tetsuo Miyadera**: Studies on Quinolizinium Salts. III.[*1] Ring Opening Reactions of Monomethylquinolizinium Bromides by Phenylmagnesium Bromide.

(*Research Laboratories, Sankyo Co., Ltd.*[*2])

In an earlier paper[*1] dealing with the reactions of quinolizinium bromide (I) toward various Grignard reagents, it was shown that the C_4-N bond of I was readily cleaved by anionic moiety of Grignard reagents furnishing 1-*cis*-3-*trans* isomer (II) of 1-(2-pyridyl)-4-substituted-1,3-butadiene accompanied by a small amount of *trans*-*trans*-isomer (III).

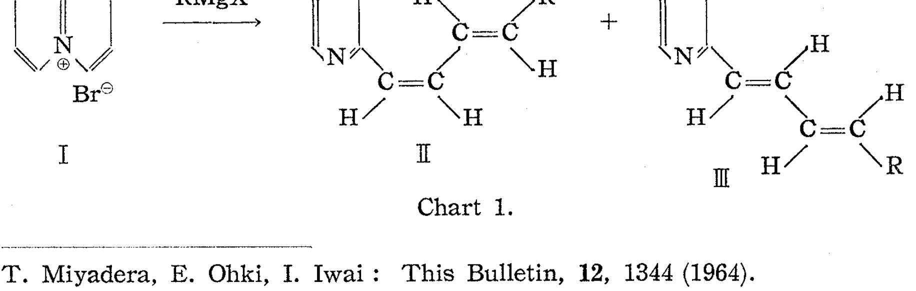

Chart 1.

[*1] Part II. T. Miyadera, E. Ohki, I. Iwai: This Bulletin, **12**, 1344 (1964).

[*2] 2-58, 1-Chome, Hiromachi, Shinagawa-ku, Tokyo (宮寺哲男).

The present paper describes the substituent-effects on the ring opening reactions of four monomethylquinolizinium bromides by a Grignard reagent.

Since quinolizinium ion and naphthalene are isoelectronic[1] showing a close correspondence of ultraviolet absorption bands,[2] some correlation might be expected between their chemical behaviors. Quinolizinium ion with chemical behavior similar to quaternary pyridinium ion[*1] has not been investigated on an electrophilic reaction towards the parent ion. However, the chemical correlation between quinolizinium ion and naphthalene could be made by comparison with the substituent-effect on nucleophilic or electrophilic reaction towards both substituted aromatic compounds. Fozard and Jones[3,4] have obtained the 1- and 2-bromo derivative on bromination of 2- and 1-hydroxyquinolizinium bromide respectively. The preferential attack of bromine at C_1-position of 2-hydroxyquinolizinium bromide indicates that the position is more reactive than C_3-position corresponding to the bromination of 2-naphthol.[5,6] On the other hand, the electrophilic reaction of 1-hydroxyquinolizinium bromide does not correspond to the predominant production of the 4-bromo derivative on mild brominations[6,7] of 1-naphthol. In molecular orbital calculations of the parent ion, Acheson and Goodall[8] have suggested that the high positive charge at the nitrogen may repel an incoming cation at the C_4-position, although electrophilic localization energies are lowest at C_1- and C_4-positions.

Among Grignard and other nucleophilic reagents toward quinolizinium ion phenylmagnesium bromide was proved excellent as a nucleophile, because it afforded stable and easily crystallizable product in good yield.

When a suspension of 1-methylquinolizinium bromide (IV) was treated with excess phenylmagnesium bromide in tetrahydrofuran, an oily substance (V) was produced.

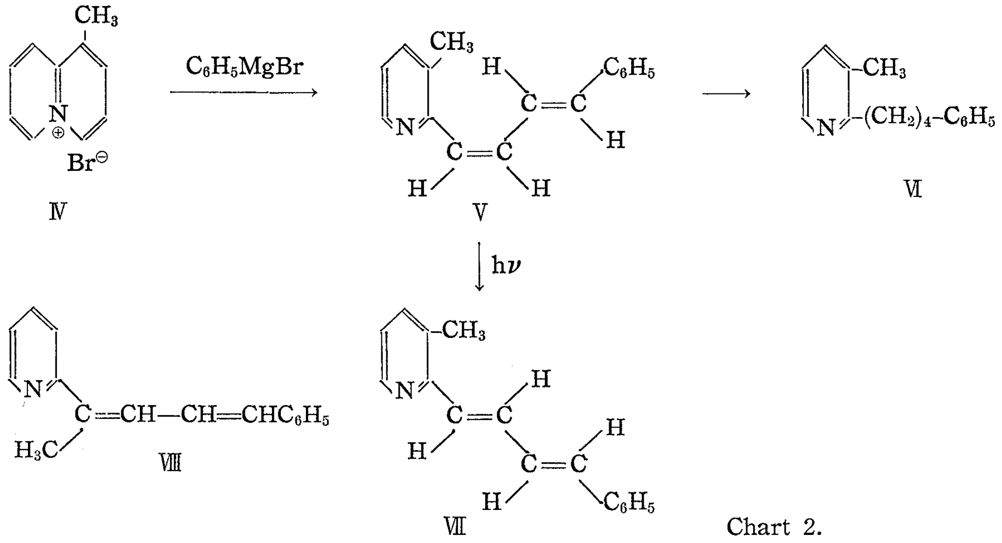

Chart 2.

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1) T.E. Peacock: J. Chem. Soc., **1959**, 3645.
2) H.H. Jaffé, M. Orchin: "Theory and Applications of Ultraviolet Spectroscopy," 374 (1962), John Wiley & Sons, Inc., New York.
3) A. Fozard, G. Jones: J. Chem. Soc., **1963**, 2203.
4) *Idem*: *Ibid*., **1964**, 2760.
5) P.S. Varma, D.N. Mozumdar, K.K. Rajah: J. Indian Chem. Soc., **10**, 595 (1933).
6) L.A. Yanovskaya, A.P. Terent'ev, L.I. Belen'kiĭ: Zhur. Obshcheĭ Khim., **22**, 1594 (1952).
7) W. Militzer: J. Amer. Chem. Soc., **60**, 256 (1938). The position of entry of bromine into substituted naphthalene ring depends upon brominating conditions: Bromination of 1-naphthol in dimethylsulfoxide yields 2-bromo derivative as the major product (T.L. Fletcher, M.J. Namkung, HsiLung Pan: Chem. & Ind., **1957**, 660); with pyridinium bromide perbromide 2-naphthol gives 6-bromo derivative (J.A. Vona, P.C. Merker: J. Org. Chem., **14**, 1048 (1949)).
8) R.M. Acheson, D.M. Goodall: J. Chem. Soc., **1964**, 3225.

The oil showed single spot on silica gel thin-layer chromatogram, and was chromatographed and purified as the picrate, m.p. 162.5~163°. On catalytic hydrogenation the free base gave a tetrahydro derivative (VI) and on irradiation in the absence of solvent (V) was isomerized to a *trans-trans*-isomer (VII), m.p. 68.5~69.5°, which formed the picrate of m.p. 242.5~243° and gave the same tetrahydro derivative (VI).

Although the Grignard reaction products could be the geometric isomers of either 1-(3-methyl-2-pyridyl)-4-phenyl- or 1-methyl-1-(2-pyridyl)-4-phenyl-1,3-butadiene (VIII), the elimination of the latter structure was made on the basis of the nuclear magnetic resonance spectrum of the isomerized diene (VII) in which the α' proton appeared as a quartet centered at $1.33\,\tau$ ($J_{\alpha'\beta'}=4.9$ c.p.s., $J_{\alpha'\gamma}=1.7$ c.p.s.) and the methyl protons, as a singlet at $7.63\,\tau$. This assignment was supported by the appearance of methyl protons of tetrahydro derivative (VI) as a singlet in the almost same region ($7.77\,\tau$). The structure of VII was identified by synthesis from the condensation of 2,3-lutidyllithium and cinnamaldehyde, followed by dehydration. Hence the original product (V) should be the 1-*cis*-3-*trans* isomer of VII.

The fact that the 1,4-disubstituted butadiene (V) was exclusively obtained in the reaction indicates that the C_4-position of IV is appreciably influenced by the C_1-methyl group, having a higher electron density or being more unreactive towards nucleophilic reactions as compared with the C_6-position. This is roughly comparable to the fact that electrophilic reaction of 1-methylnaphthalene (*i.e.*, bromination with bromine[9]) gives 1-methyl-4-substituted naphthalene as the major product.[10,11]

From the same considerations 3-methylquinolizinium bromide (IX) was reacted with phenylmagnesium bromide forming a mixture of two colorless crystalline compounds X, m.p. 99~100° and XI, m.p. 122°, and a small amount of inseparable product.

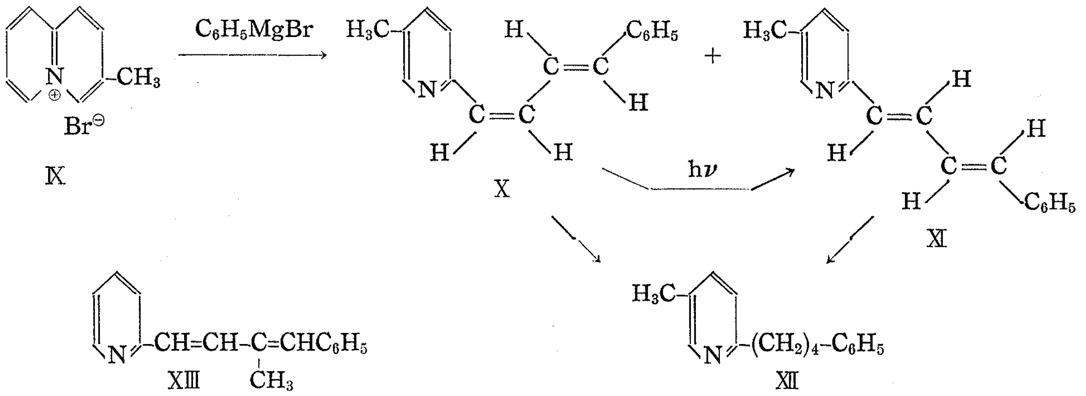

Chart 3.

The lower melting substance (X) exhibited ultraviolet absorption maxima at 330 (27000), 248.5 (13000), and 242 mμ (ε 14200) and infrared absorption bands due to a conjugated diene and a *trans* olefin $\left({}^{H}\rangle C=C\langle_{H}\right)$. The diene (X) was photochemically isomerized in benzene solution to the higher melting compound (XI) with more intense maximum at 333 mμ (ε 55000). The nuclear magnetic resonance spectrum of XI showed

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[9] F. Mayer, A. Siglitz: Ber., **55**, 1835 (1922).

[10] V. Veselý, M. Jakeš: Bull. soc. chim. France, **33**, 955 (1923).

[11] W. N. Ufimzew: Ber., **69**, 2188 (1936). In electrophilic reactions of monosubstituted naphthalene the position of entry of a second substituent is influenced by many factors showing very complicated behaviors. Naphthalene derivatives carrying an *o*- and *p*-directing group promote electrophilic substitution in the substituted ring (cf. E. H. Rodd, J. van Alphen: "Chemi stry of Carbon "Compounds, III B, Ed. by E. H. Rodd, p. 1275 (1956), Elsevier Publishing Company, New York.).

peaks due to methyl protons as a singlet at $7.67\,\tau$ and α' proton as a rather broad doublet ($J_{\alpha'\gamma}=1.7$ c.p.s.) at $1.43\,\tau$, indicative of the absence of a β' proton. On catalytic hydrogenation both dienes gave the same tetrahydro derivative (XII) whose nuclear magnetic resonance spectrum also confirmed the above assignment in which all proton peaks remains in the same region except for the eight aliphatic protons. These facts eliminate the possibility of the structure being 1-(2-pyridyl)-3-methyl-4-phenyl-1,3-butadiene (XIII). In addition, from the spectral and mechanistic considerations the geometries of X and XI were assumed to be the 1-*cis*-3-*trans*- and *trans*-*trans*-isomer of 1-(5-methyl-2-pyridyl)-4-phenyl-1,3-butadiene respectively.

The fact that the unsubstituted ring was more reactive toward the Grignard reagent suggests the C_4-position to be higher in electron density as compared with the C_6-position in accordance with a preferential attack at C_1 by a cationoid reagent in the case of 2-methylnaphthalene. However in the 3-methyl homolog (IX), the C_6-position would be more favored for nucleophilic attack owing to some steric hindrance at C_4-position.

The expected result was also obtained in the reaction of 2-methylquinolizinium bromide (XIV) with phenylmagnesium bromide which yielded a completely inseparable mixture of four isomers.

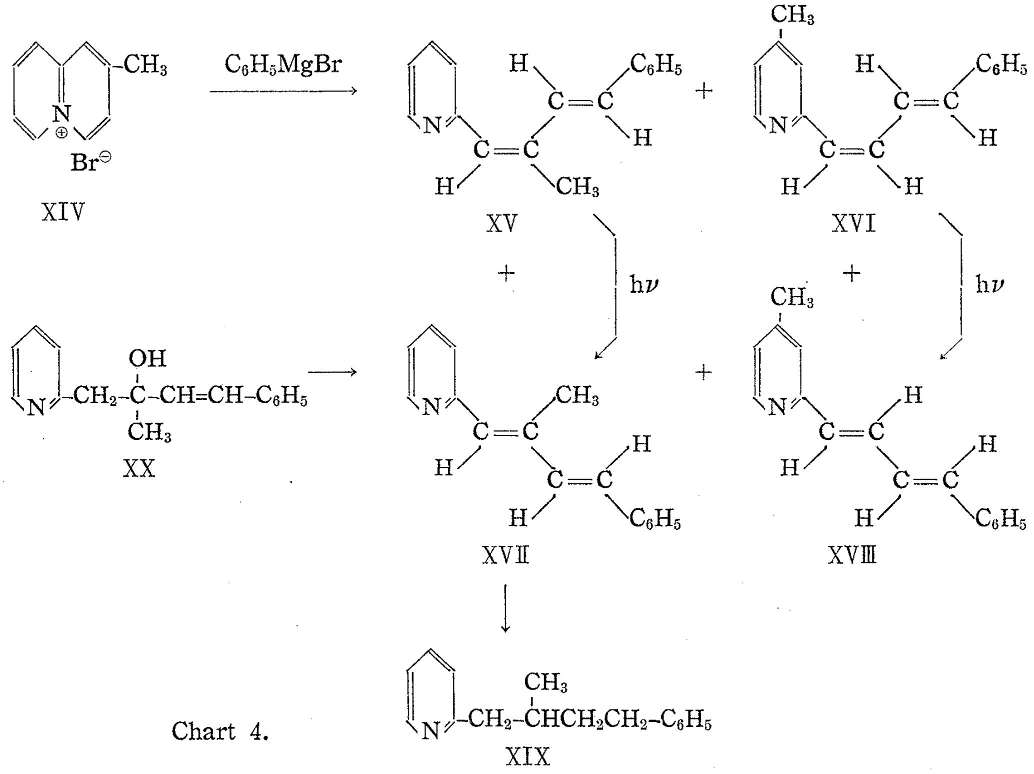

Chart 4.

The methyl protons of the freshly prepared reaction mixture appeared as a singlet at $7.69\,\tau$ and as two doublets at 7.55 and $7.78\,\tau$. The integrated area of the doublet at $7.55\,\tau$ had been very small in the beginning, but on standing in ordinary light with no solvent for a long period the area was increased in proportion to the decrease of the area at $7.78\,\tau$, however, the singlet peak was apparently unchanged. The column chromatography of the freshly prepared mixture provided XVII, m.p. 83~84°, responsible for the doublet peak at $7.55\,\tau$ and XVIII, m.p. 95.9~96.5°, for the singlet peak in poor yield. On the other hand, the chromatography of the photoisomerized mixture afforded XVII and XVIII in good yields, and the third product (XV), responsible for the doublet at $7.78\,\tau$, isolated as the picrate, m.p. 161~162°.

The observation mentioned above indicates that the mixture should contain four products, two components of which were readily isomerized by light (XV→XVII, XVI→XIII. The forth compound (XVI) was not isolated). Compound (XVIII) exhibited doublet peak ($J_{\alpha'\beta'}=5.2$ c.p.s.) at 1.53 τ indicating the presence of a substituent at γ-position, together with singlet methyl at 7.69 τ. Furthermore, the ultraviolet and infrared spectra enabled one to conclude that the structure of XVIII should be *trans-trans*-1-(4-methyl-2-pyridyl)-4-phenyl-1,3-butadiene.

On the other hand, the α' proton of XVII appeared characteristically as two quartets centered at 1.17 τ assignable to an α' proton of α-monosubstituted pyridine and the methyl protons, as a doublet at 7.55 τ indicative of being adjacent to an olefinic proton. The nuclear magnetic spectrum of a tetrahydro derivative (XIX) formed on catalytic hydrogenation of XVII further supports the previous assignment, exhibiting a doublet at 9.08 τ (J=6.4 c.p.s.) assignable to methyl protons adjacent to a tertiary proton. The diene (XVII) showed infrared absorption bands due to *trans* olefin $\left({}^{H}\!\!>C=C<_{H}\right)$ and a broader ultraviolet absorption maximum at 325 mμ (ε 44500) whose intensity is rather low for *trans-trans* diene, probably owing to some steric inhibition of planarity of the chromophoric system.[12] The above discussion suggested that the structure of XVII should be 1-(2-pyridyl)-2-methyl-4-phenyl-1,3-butadiene. Assignment was finally confirmed by the synthesis from condensation of picolyllithium and benzalacetone and subsequent dehydration without isolation of the alcohol (XX). The above Grignard reaction of XIV yielded 2,4-disubstituted-(XVI, XVIII) and 2-monosubstituted pyridine (XV, XVII) whose product ratio (52:48) was given by relative integrated area of the two types of methyl signals: singlet *vs.* doublets. This fact led to the conclusion that C_4- and C_6-positions of 2-methylquinolizinium ion should have almost the same reactivity toward the nucleophilic reagent which concurs with the prediction from the reactivities at C_4- and C_5-positions in naphthalene carrying *o*- and *p*-directing group at the 2-position.[11]

The reaction of 4-methylquinolizinium bromide (XXI) with phenylmagnesium bromide occurred smoothly forming an oily substance (XXII), but this substance could not be completely purified because of the facile isomerization into a crystalline compound (XXIII), m.p. 107~108°, just on standing in ordinary light.

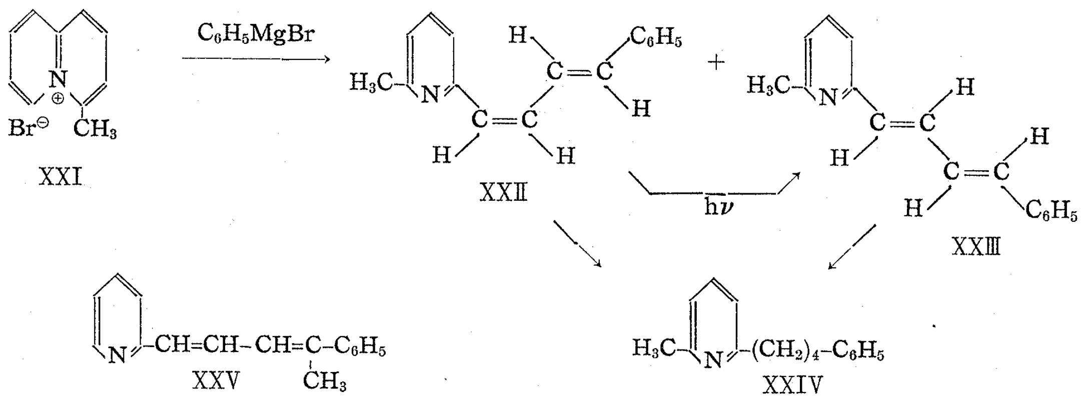

Chart 5.

Although both isomers gave the same tetrahydro derivative (XXIV) on catalytic hydrogenation, that one was different from another was evidenced by their different infrared, ultraviolet spectra and melting points of the picrates. The oily substance

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12) E. A. Braude, E. S. Waight: "Progress in Stereochemistry," Vol. I, Ed. by W. Klyne, p. 139 (1954), Butterworths Scientific Publications, New York.

(XXII) was assigned *cis-trans* isomer and the isomerized crystalline compound (XXIII), *trans-trans* isomer of either 1-(6-methyl-2-pyridyl)- or 1-(2-pyridyl)-4-methyl-4-phenyl-1,3-butadiene (XXV) on the basis of the ultraviolet absorption.*[1] The choice of the former structure for XXII and XXIII was readily made on the basis of nuclear magnetic resonance spectrum where methyl protons appeared as a singlet at 7.44 τ, but no α' proton, in the corresponding region. The assignment was confirmed by synthesis of XXIII according to the method reported by Späth, *et al.*[13] The formation of an 2,6-disubstituted pyridine (XXII) in the reaction does not necessarily suggest that the electron density at C_6-position should be less than at another site carrying methyl group, because of the presence of a steric hindrance at C_4-position.

Since 4-methylquinolizinium bromide is interestingly most reactive toward an anion (*i.e.*, potassium hydroxide) as compared with the parent compound and the other methyl derivatives, the bromide will be further investigated in nucleophilic reactions.

Experimental

Reaction of 1-methylquinolizinium Bromide (IV) with Phenylmagnesium Bromide——To a solution of C_6H_5MgBr prepared from C_6H_5Br (2.22 g.) and Mg (0.344 g.) in 70 ml. of absolute tetrahydrofuran was added IV hemihydrate (1.1 g.) and the mixture was stirred for 6 hr. at room temperature. After the resulting solution was treated with aq. NH_4Cl solution and washed with H_2O, the organic layer was extracted with dil. HCl solution. The acidic extract was washed with ether, made alkaline with Na_2CO_3 and a deposited oil extracted with ether. The ether extract was washed with H_2O and dried over Na_2SO_4. Removal of the solvent gave the oily substance which was chromatographed in benzene on silica gel and then distilled to afford 0.54 g. of 1-*cis*-3-*trans*-1-(3-methyl-2-pyridyl)-4-phenyl-1,3-butadiene (V) as an oil. Although this oil was not completely purified, the thin-layer chromatogram showed a single spot. IR $\nu_{\text{max}}^{\text{liq.}}$ cm^{-1}: 1615, 1595 (conj. diene), 952, 991 $\left({}^{H}\!\!>C=C<_{H}\right)$.

The picrate of V was prepared and recrystallized from EtOH yielding yellow needles, m.p. 162.5~163°. *Anal.* Calcd. for $C_{22}H_{18}O_7N_4$: C, 58.66; H, 4.03; N, 12.44. Found: C, 58.49; H, 4.16; N, 12.38.

Photoisomerization of V——The oil (V) was allowed to stand for a week under ordinary light and chromatographed in benzene on silica gel giving the *trans-trans*-isomer (VII) from the last part of fraction. It was recrystallized from petr. ether, m.p. 68.5~69.5°. *Anal.* Calcd. for $C_{16}H_{15}N$: C, 86.84; H, 6.83; N, 6.33. Found: C, 86.76; H, 6.84; N, 6.35. IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1}: 1616 (sh.), 1608 (conj. diene), 967, 1001 $\left({}^{H}\!\!>C=C<_{H}\right)$. UV $\lambda_{\text{max}}^{\text{EtOH}}$ mμ (ε): 340 (47300), 288.5 (19500), 234 (10700).

The picrate of VII was prepared and recrystallized from EtOH, m.p. 242.5~243.0°. *Anal.* Calcd. for $C_{22}H_{18}O_7N_4$: C, 58.66; H, 4.03; N, 12.44. Found: C, 58.52; H, 3.94; N, 12.37.

***Trans-trans*-4-Phenyl-1-(3-methyl-2-pyridyl)-1,3-butadiene (VII)**——To a solution of 3-methylpicolyllithium prepared from 2,3-lutidine (27.0 g.), C_6H_5Br (39.6 g.) and Li (3.5 g.) in 300 ml. of dry ether cinnamaldehyde (33.3 g.) was added dropwise with stirring and cooling in ice-bath. Then, the mixture was stirred for several hr. at room temperature and treated with H_2O. The solution was extracted with ether, the ether extract washed with H_2O and dried over Na_2SO_4. Evaporation of the solvent gave crude 4-phenyl-1-(3-methyl-2-pyridyl)-3-buten-2-ol which was refluxed in 500 ml. of Ac_2O for 3 hr. A basic portion was extracted with dil. HCl, the extract washed with ether, made alkaline with Na_2CO_3 and extracted with ether. The ether extract was dried over Na_2SO_4 and distilled, after removal of the solvent, to afford an oil, b.p. 130~150°/3 × 10^{-5}mm., which was chromatographed in benzene on silica gel and recrystallized from petr. ether giving colorless crystals (VII), m.p. 68.5~69.5°. This melted undepressed on admixture with the sample obtained in the above Grignard reaction and gave the same picrate.

Hydrogenation of V and VII——A solution of V (251 mg.) in 20 ml. of AcOH was hydrogenated with 5% Pd-C (50 mg.) absorbing 2 equivalents of H_2. The usual treatment of the reduction mixture yielded 4-phenyl-1-(3-methyl-2-pyridyl)butane (VI) as a colorless oil, b.p. 115~120°/3 × 10^{-5} mm. (bath temp.). *Anal.* Calcd. for $C_{16}H_{19}N$: C, 85.28; H, 8.50; N, 6.22. Found: C, 84.99; H, 8.50; N, 6.26.

The picrate of VI was prepared and recrystallized from EtOH as fine yellow needles, m.p. 125~126°. *Anal.* Calcd. for $C_{22}H_{22}O_7N_4$: C, 58.14; H, 4.88; N, 12.33. Found: C, 58.00; H, 4.90; N, 12.67.

Hydrogenation of VII gave the same tetrahydro derivative (VI) which was identified by IR and mixed melting point of the picrate.

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13) E. Späth, G. Kubiczek, E. Dubensky: Ber., **74**, 873 (1941).

Reaction of 3-Methylquinolizinium Bromide (IX)——A suspension of IX (1.2 g.) was reacted with C_6H_5MgBr prepared from C_6H_5Br (3.14 g.) and Mg (0.486 g.) in 100 ml. of absolute tetrahydrofuran for 6 hr. at room temperature. Treatment of the reaction mixture in the similar manner gave a crystalline product which was chromatographed in benzene on silica gel. The first fraction gave 107 mg. of 1-*cis*-3-*trans*-1-(5-methyl-2-pyridyl)-1,3-butadiene (X) which was recrystallized from hexane as colorless prisms, m.p. 99~100°. *Anal.* Calcd. for $C_{16}H_{15}N$: C, 86.84; H, 6.83; N, 6.33. Found : C, 86.67; H, 6.83; N, 6.45. IR ν_{max}^{Nujol} cm^{-1} : 1620, 1610 (sh.) (conj. diene), 961, 1000 $\left({}^{H}\!>C=C<_{H}\right)$. UV λ_{max}^{EtOH} mμ (ε) : 330 (27000), 248.5 (13000), 242 (14200).

The second fraction yielded 585 mg. of the *trans-trans* isomer (XI) which was recrystallized from hexane as colorless leaflets, m.p. 122°. *Anal.* Calcd. for $C_{16}H_{15}N$: C, 86.84; H, 6.83; N, 6.33. Found : C, 86.87; H, 6.87; N, 6.48. IR ν_{max}^{Nujol} cm^{-1} : 1620, 1610 (conj. diene), 1000, 991 (sh.) $\left({}^{H}\!>C=C<_{H}\right)$. UV λ_{max}^{EtOH} mμ (ε) : 333 (55000), 229 (8700).

The mother liquors must contain a small amount of an inseparable substance on the basis of thin-layer chromatogram.

Photoisomerization of X to XI——A solution of X (39 mg.) in 25 ml. of benzene was irradiated for 10 hr. using UV lamp with stirring and cooling. The solution was concentrated and chromatographed in benzene on silica gel yielding 9 mg. of *trans-trans* isomer (XI) and 22 mg. of the recovered starting material (X).

Hydrogenation of X and XI——A solution of X in AcOH was hydrogenated using 5% Pd-C in the similar manner to yield 1-(5-methyl-2-pyridyl)-4-phenylbutane (XII) as a colorless oil, b.p. 120°/3 × 10^{-5} mm. (bath temp.). *Anal.* Calcd. for $C_{16}H_{19}N$: C, 85.28; H, 8.50; N, 6.22. Found : C, 85.18; H, 8.40; N, 6.50.

The picrate of XII was prepared and recrystallized from EtOH as yellow prisms, m.p. 122~123°. *Anal.* Calcd. for $C_{22}H_{22}O_7N_4$: C, 58.14; H, 4.88; N, 12.33. Found : C, 58.02; H, 4.96; N, 12.46.

The catalytic hydrogenation of XI also the same tetrahydro derivative (XII).

Reaction of 2-Methylquinolizinium Bromide (XIV) with Phenylmagnesium bromide——To a solution of C_6H_5MgBr prepared from C_6H_5Br (2.1 g.) and Mg (0.325 g.) in 100 ml. of absolute tetrahydrofuran was added XIV (1.0 g.) and the mixture was treated in the same manner at the reaction of IX. The usual work up gave 0.85 g. of a reaction mixture which could not be separated on chromatography in benzene on silica gel giving only two crystalline compounds (XVII) and (XVIII) in very small quantities respectively. On the other hand, the mixture was chromatographed after standing for 3 weeks under ordinary light to give the following three dienes. The first fraction gave an inseparable oil (0.5 m.) which contained *cis-trans*-1-(2-pyridyl)-2-methyl-4-phenyl-1,3-butadiene (XV) as the major component. This was purified by formation of the picrate as yellow prisms, m.p. 161~162°. *Anal.* Calcd. for $C_{22}H_{18}O_7N_4$: C, 58.66; H, H, 4.03; N, 12.44. Found : C, 58.79; H, 4.10; N, 12.43.

The second fraction yielded *trans-trans*-1-(2-pyridyl)-2-methyl-4-phenyl-1,3-butadiene (XVII, 95 mg.) which was recrystallized from hexane as colorless leaflets, m.p. 73~74°. *Anal.* Calcd. for $C_{16}H_{15}N$: C, 86.84; H, 6.83; N, 6.33. Found : C, 86.75; H, 6.81; N, 6.21. IR ν_{max}^{Nujol} cm^{-1} : 1615, 1604 (conj. diene), 958, 991 $\left({}^{H}\!>C=C<_{H}\right)$. UV λ_{max}^{EtOH} mμ (ε) : 325 (44500). The picrate of XVII was prepared and recrystallized from EtOH as yellow needles, m.p. 214°. *Anal.* Calcd. for $C_{22}H_{18}O_7N_4$: C, 58.66; H, 4.03; N, 12.44. Found : C, 58.50; H, 3.99; N, 12.16.

The third fraction gave *trans-trans*-1-(4-methyl-2-pyridyl)-4-phenyl-1,3-butadiene (XVIII, 173 mg.) which was recrystallized from hexane as colorless prisms, m.p. 95.5~96.5°. IR ν_{max}^{Nujol} cm^{-1} : 1623, 1613 (conj. diene). UV λ_{max}^{EtOH} mμ (ε) : 332 (52000), 231.5 (10000). The picrate of XVIII was prepared from EtOH, m.p. 246° (decomp.). *Anal.* Calcd. for $C_{22}H_{18}O_7N_4$: C, 58.66; H, 4.03; N, 12.44. Found : C, 58.35; H, 3.91; N, 12.38.

Synthesis of XVII——To a solution of 2-picolyllithium prepared in the usual manner from C_6H_5Br (47.1 g.), Li (4.2 g.) and 2-picoline (27.9 g.) in 500 ml. of dry ether was added a solution of benzalacetone (36.2 g.) in 100 ml. of dry ether with stirring and cooling. Then the mixture was stirred for several hr. The usual work up of the reaction mixture gave a crude 1-(2-pyridyl)-2-methyl-4-phenyl-3-buten-2-ol which was, without isolation, dehydrated by refluxing in Ac_2O to yield XVII, as an oil, b.p. 124~128°/4 × 10^{-5}mm. This crystallized readily and was recrystallized from hexane as colorless leaflets, m.p. 83~84°, which melted undepressed with the sample obtained in the above Grignard reaction and the both IR spectra were completely identical.

Hydrogenation of XVII——A solution of XVII in AcOH was hydrogenated using 5% Pd-C to give 1-(2-pyridyl)-2-methyl-4-phenylbutane (XIX) as a colorless oil, b.p. 115~120°/5 × 10^{-5} mm. (bath temp.). *Anal.* Calcd. for $C_{16}H_{19}N$: C, 85.28; H, 8.50; N, 6.22. Found : C, 85.01; H, 8.35; N, 6.29.

The picrate of XIX was prepared from ether and recrystallized from EtOH as yellow prisms, m.p. 73~75°. *Anal.* Calcd. for $C_{22}H_{22}O_7N_4$: C, 58.14; H, 4.88; N, 12.33. Found : C, 58.08; H, 4.90; N, 12.36.

Reaction of 4-Methylquinolizinium Bromide (XXI) with Phenylmagnesium Bromide——To a solution of C_6H_5MgBr prepared from C_6H_5Br (3.14 g.) and Mg (0.486 g.) in 100 ml. of absolute tetrahydrofuran was added XXI hydrate (1.2 g.) and the mixture was stirred for 4 hr. at room temperature. The reaction mixture was treated in a similar manner to afford an oily substance which was distilled, after purification by silica gel chromatography, giving 1-*cis*-3-*trans*-1-(6-methyl-2-pyridyl)-4-phenyl-1,3-butadiene (XXII), b.p. 135~140°/3×10^{-5} mm. (bath temp.). IR $\nu_{max}^{liq.}$ cm^{-1}: 1628, 1610 (conj. diene), 957, 992, 1001 $\left({}^{H}\!\!>C=C<\!{}_{H}\right)$.

The *cis-trans* isomer (XXII) was photochemically too labile in the absence of solvent to be purified completely.

The picrate of XXII was prepared and recrystallized from EtOH as fine yellow needles, m.p. 171~173°. *Anal.* Calcd. for $C_{22}H_{18}O_7N_4$: C, 58.66; H, 4.03; N, 12.44. Found: C, 58.76; H, 3.94; N, 12.65.

The *cis-trans* isomer (XXII) was readily converted into the *trans-trans* isomer (XXIII) quantitatively just on standing under ordinary light. Recrystallization from petr. benzin gave colorless prisms, m.p. 107~108°. *Anal.* Calcd. for $C_{16}H_{15}N$: C, 86.84; H, 6.83; N, 6.33. Found: C, 86.92; H, 6.86; N, 6.31. IR ν_{max}^{Nujol} cm^{-1}: 1624, 1613 (conj. diene), 990, 1001 $\left({}^{H}\!\!>C=C<\!{}_{H}\right)$. UV λ_{max}^{EtOH} mμ (ε): 235 (54000), 231 (10200).

The *trans-trans* isomer (XXIII) was identified by the synthesis according to the method reported by Späth, *et al.*[13]

The picrate of XXIII was prepared and recrystallized from EtOH as yellow plates, m.p. 225°. *Anal.* Calcd. for $C_{22}H_{18}O_7N_4$: C, 58.66; H, 4.03; N, 12.44. Found: C, 58.39; H, 4.31; N, 12.38.

Hydrogenation of XXII and XXIII——A solution of XXII was hydrogenated in a similar manner to yield 1-(6-methyl-2-pyridyl)-4-phenylbutane (XXIV) as a colorless oil, b.p. 115~120°/3×10^{-5} mm. (bath temp.). *Anal.* Calcd. for $C_{16}H_{19}N$: C, 85.28; H, 8.50; N, 6.22. Found: C, 85.01; H, 8.63; N, 6.21.

The picrate of XXIV was prepared and recrystallized from EtOH as yellow plates, m.p. 113~114°. *Anal.* Calcd. for $C_{22}H_{22}O_7N_4$: C, 58.14; H, 4.88; N, 12.33. Found: C, 58.23; H, 4.96; N, 12.55.

The free base and the picrate was also obtained from a similar hydrogenation of XXIII.

Low pressure mercury lamp was used in the above photoisomerisations of *cis* olefin compounds to *trans* isomers.

All NMR spectra were taken with Varian Associates A-60, 60 Mc. high resolution spectrometer. Samples (40~50 mg.) were dissolved in 0.4~0.5 ml. of $CDCl_3$ or CCl_4. The positions of the signals were measured from tetramethylsilane as the internal standard.

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Summary

All four monomethylquinolizinium bromides were submitted to Grignard reactions using phenylmagnesium bromide in order to examine the substituent-effects on the ring opening reactions. The reaction of 1- and 3-methyl derivatives (IV, IX) gave exclusively disubstituted pyridines (V and X, XI) respectively and the 2-methyl derivative (XIV), 2-mono- (XV, XVII) and 2,4-disubstituted pyridines (XVI, XVIII) in almost equal ratio. These results were comparable to the substituent-effects of methylnaphthalenes. In the case of 4-methyl derivative (XXI) 2,6-disubstituted pyridine (XXII) was exclusively obtained probably owing to the steric hindrance at C_4-position of XXI.

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