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Amino-Claisen Rearrangement. III. The Effects of Alkyl Substituents on the Allyl Group upon the Rearrangement

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The effects of mono- and dimethylation of the allyl group upon tertiary and quaternary amino-Claisen rearrangements were investigated with 1,2,3,4-tetrahydroquinoline as the framework for the rearrangement. The introduction of γ-methyl onto the allyl group accelerated the rearrangement and increased the yield of *para* rearrangement product. The introduction of two γ-methyls on the allyl group resulted in complex reactions, of which the major ones were *para* rearrangement and deprenylation. Two reaction pathways, sigmatropic and dissociative, were observed. The reaction conditions used strongly influenced the products pattern. The presence of a 6-methoxy group retarded the reaction but did not have a major effect upon the reaction pattern. Tertiary and quaternary N-Claisen rearrangements are effective for the migration of allyl and crotyl groups but seem not to be very useful for the migration of the prenyl group.

Keywords——amino-Claisen rearrangement; effect of alkyl substituent; 1-crotyl-1,2,3,4-tetrahydroquinoline; 1-prenyl-1,2,3,4-tetrahydroquinoline; 1-crotyl-1-methyl-1,2,3,4-tetrahydroquinolinium halide; 1-methyl-1-prenyl-1,2,3,4-tetrahydroquinolinium halide; *ortho* rearrangement; *para* rearrangement; [3,3]tropic rearrangement; dissociation–recombination mechanism

We have been engaged in studies of the quaternary amino (N)-Claisen rearrangement.[1] In this paper we describe how the introduction of methyl substituents on the allyl group affects the course of tertiary and quaternary N-Claisen rearrangements. In order to achieve this goal we employed crotyl (2-butenyl) as the monomethylated ally moiety[2] and prenyl (3-methyl-2-butenyl) as the dimethylated allyl moiety. As the framework for the rearrangement, 1,2,3,4-tetrahydroquinoline was adopted since it allows N-Claisen rearrangement in high yields.[1b] 6-Methoxy-1,2,3,4-tetrahydroquinoline was also used to investigate the effect of a *para* substituent upon the course of rearrangement if the allyl moiety migrates to the *para* position.[1c]

Preparation of the Starting Material for Rearrangement

Compounds **2a**, **2b**, **4a** and **4b** were described in a previous report.[1b] Tertiary amines **2** were prepared from **1** and excess allyl halides in acetonitrile in the presence of sodium carbonate. Isomerically pure **2c** and **2d** were obtained by recrystallizations of their hydrohalides. Compound **5** was formed as a by-product in the prenylation of **1b** and was isolated as its tetrafluoroborate, **5** ($X=BF_4$).

Quaternary halides **4** were prepared by the treatment of 1-methyltetrahydroquinoline (kairoline) **3** with excess allyl halides in acetonitrile containing a few drops of dimethylformamide (DMF). The bromide **4d** (X=Br) was a highly hygroscopic amorphous solid. The bromide **4f** (X=Br) was obtained as a mixture with **3b**:HBr (*ca.* 1:1) and purified by repeating washings with hot acetone. Because of the poor yield and instability of **4f** (X=Br) during recrystallization, the bromide was transformed into the tetrafluoroborate **4f** (X=

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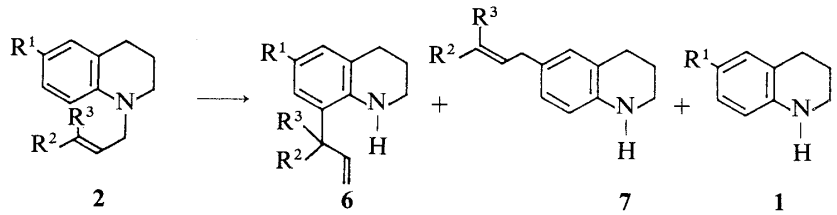
TABLE I.



2 6 7 1

Substrate	R.C.[a] (h)	C.Y.[b] (%)	Products (%)[b]				
			ortho	*para*	Deallyl.	S.M.	Miscellaneous
2a			**6a**	**7a**	**1a**	**2a**	
	C/2.5[c]	97	91.9	6.0		1.4	
	D/8	104	80.9	1.3	0.6	6.1	6.5[e]
2c			**6c**	**7c**	**1a**		
	C/2	97	72.0	25.0*	0.8		* $E:Z=97:3$
	D/4	100.4	88.6	1.8	0.7		4.4,[e] 4.5[e]
2e				**7e**	**1a**	**2e**	
	C/2	93.1		54.4	16.7		8.3,[f] 8.2,[g] 7.0, 4.6
	D/2	98.3		9.3	29.9	12.6	34.2,[e] 9.6
2b			**6b**			**2b**	
	C/2.5	70[d]	84.4			1.0	12.6[h]
	D/4	96.7	68.7			28.3	1.8
2d			**6d**		**1b**	**2d**	
	D/4	98.4	90.2		0.5	3.8	4.5[f]
2f					**1b**	**2f**	
	D/2	94			27.7	55.8	11.5,[e] 2.5, 1.2, 1.1

a) Reaction conditions.[1b] C, a mixture of amine (2 mmol) and boron trifluoride etherate (4.2 mmol) was heated at 140 °C with removal of ether; D, a solution of amine (2 mmol) in 2 N sulfuric acid in glycerol–water (2 : 1, 8 ml) was heated at 140 °C (bath temp.).
b) C.Y.: crude yield. Crude products were analyzed by GLC (10%SE-30, nitrogen 30 ml/min, 180—210 °C).
c) Reaction at 150 °C.
d) Phenolic product was produced in 22% yield.
e) Hydrated products.
f) Rearrangement products.
g) 8-Prenyl-1,2,3,4-tetrahydroquinoline **15**.
h) 8-Allyl-6-hydroxykairoline **18**.

BF_4). Tetrafluoroborate is preferable to hydrohalides in rearrangement reactions.[1a] The bromide **4e** (X=Br) was also converted into **4e** ($X=BF_4$).

Rearrangement and Identification of Reaction Products

Tertiary N-Claisen Rearrangement——For this rearrangement, two reaction conditions were employed.[1b] Tertiary allylamines were treated with borontrifluoride etherate at 140 °C (reaction condition C) or heated in 2 N sulfuric acid in glycerol–water (2 : 1) at 140 °C (bath temperature) (reaction condition D). Rearrangement is faster under condition C than condition D. Rearrangements of **2a** and **2b** were reported in a previous paper.[1b] The reaction of **2a** under condition D gave, in addition to **6a** and **7a**, a polar product (6.5% yield) having M^+ (*m/z* 191) and two exchangeable protons (NH+OH) in the nuclear magnetic resonance (NMR) spectrum. Its NMR spectrum was also indicative of the $Ar–CH_2–CH(OH)–CH_3$ group, *i.e.*, the hydrated allyl group. Since 8-allyltetrahydroquinoline **6a** is the predominant product, and the mass spectrum shows a distinct fragment at *m/z* 146 (P^+, M^+-45), the structure **10** is assigned for this hydrated product (Chart 3).

Rearrangement of **2c** under condition C gave *ortho* and *para* rearrangement products **6c**

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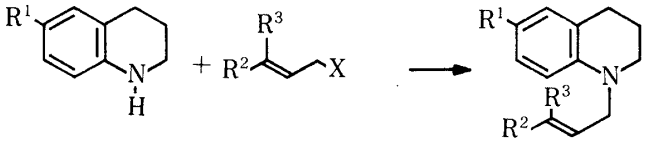

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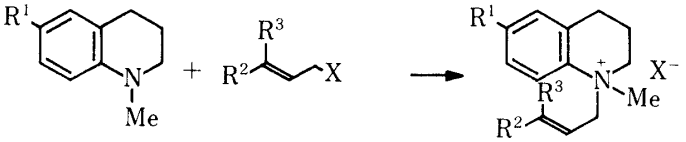

3 4

	R^1	R^2	R^3
a	H	H	H
b	MeO	H	H
c	H	Me	H
d	MeO	Me	H
e	H	Me	Me
f	MeO	Me	Me

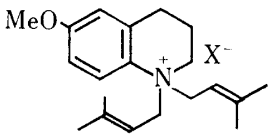

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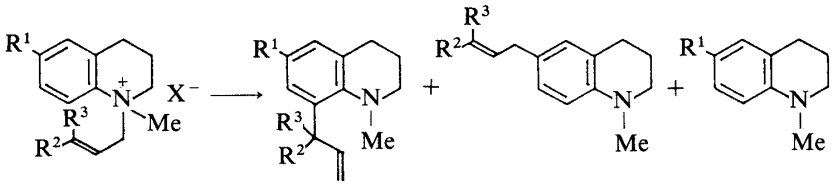
Chart 1

TABLE II.



4 8 9 3

Substrate X=	R.C.[a]	C.Y.[b] (%)	Products (%)[b]			
			ortho	*para*	Deallyl.	Miscellaneous
4a			**8a**	**9a**	**3a**	
Br	A	88.0	90.1	4.3	5.5	
Br	B	94.6	92.1	4.4	3.2	
4c			**8c**	**9c**	**3a**	
Br	A	78.8	45.5	52.5*	2.0	* $E:Z=95:5$
Br	B	74.4	87.5	4.3*	8.2	* $E:Z=91:9$
4e			**8e**	**9e**	**3a**	
Br	A	83.6	4.9	4.6	81.5	2.3,[c] 2.8,[d] 3.4[d]
Br	B	86.6	5.2	38.1	47.0	9.3[c]
BF_4	B	89.8	9.2	37.1	38.0	15.6[c]
4b			**8b**		**3b**	
Br	B	88	96.4		2.9	0.6
4d			**8d**		**3b**	
Br	B	86	95.0		4.7	
4f					**3b**	
BF_4	B	71			72.0	15.2,[e] 12.6[e]

a) Reaction conditions.[1b] A, a solution of the quaternary salt (2 mmol) in glycerol–water (2:1, 8 ml) was heated at 140 °C (bath temp.) for 2 h; B, similar reaction in the presence of sodium bicarbonate (2.1 mmol).
b) C.Y.: crude yield. Crude products were analyzed by GLC (see Table I).
c) 8-Prenylkairoline **16**.
d) Hydrated products.
e) Rearrangement products.

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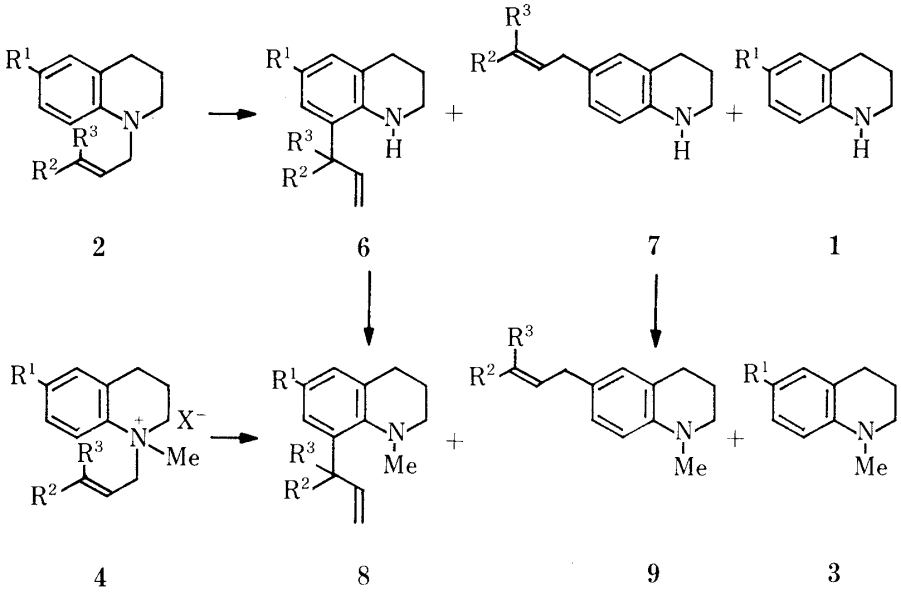

Chart 2

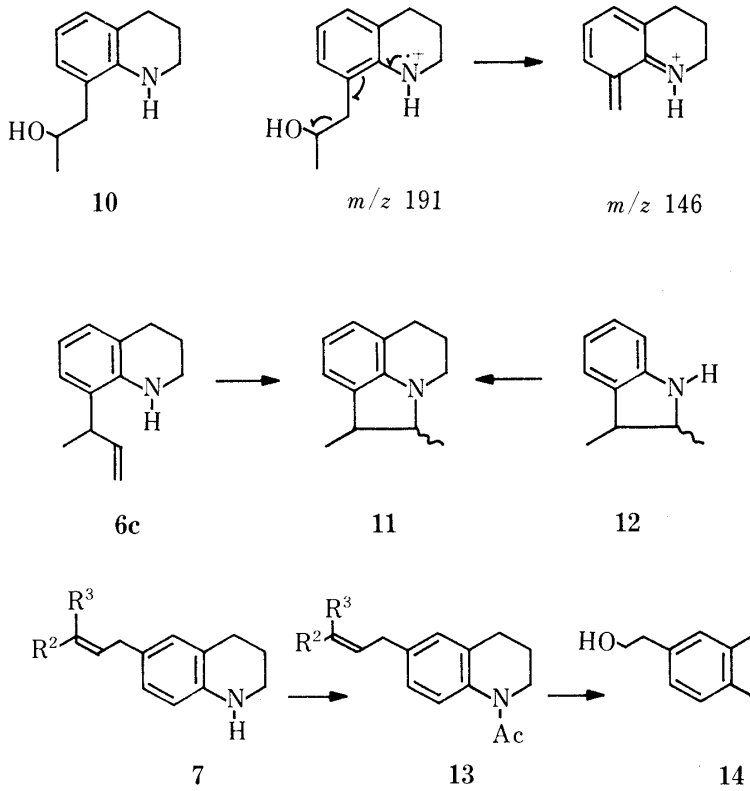

Chart 3

and **7c** in the ratio of 72:25. However, **2c** under condition D gave the *ortho* product **6c** exclusively (**6c**:**7c**=88.6:1.8). In this reaction the formation of **7c** was demonstrated by gas chromatography-mass spectrometric (GC-MS) analysis, and the polar product obtained was a mixture of three hydrated products according to GC-MS analyses. The *ortho* product **6c** was cyclized to 1,2-dimethyllilolidine **11**, a mixture of stereoisomers, which was shown to be identical with a specimen prepared from 2,3-dimethylindoline **12**[3] (Chart 3). Thus the site of the substituent was confirmed. The *E* configuration of the crotyl group of **7c** was deduced

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from the characteristic *trans* vinyl methyl signals in the NMR spectrum. The *E* isomer **7c** was 97% pure; the accompanying *Z* isomer was detectable by GC-MS. The product with *E* configuration is expected to be predominant from the mechanistic standpoint, *vide infra*. The position of the crotyl group was confirmed by the transformation of **7c** into the known compound **14**[1b] (Chart 3).

The reaction of **2e** under condition C gave six products. Column chromatography of the products separated three of them. The deprenylated product **1a** (6%) was the most polar of them. The least polar product (6.9%) has the same molecular weight (*m/z* 201) as **2e** and retains the prenyl (δ 1.67, 6H, s) and NH ν_{max} 3430 cm^{-1}) groups as judged from the NMR and infrared (IR) spectra. The structure **15** was assigned to this product (Chart 4) because the splitting patterns of the aromatic protons, including the signals at δ 6.50 (dd, J=6, 8 Hz) due

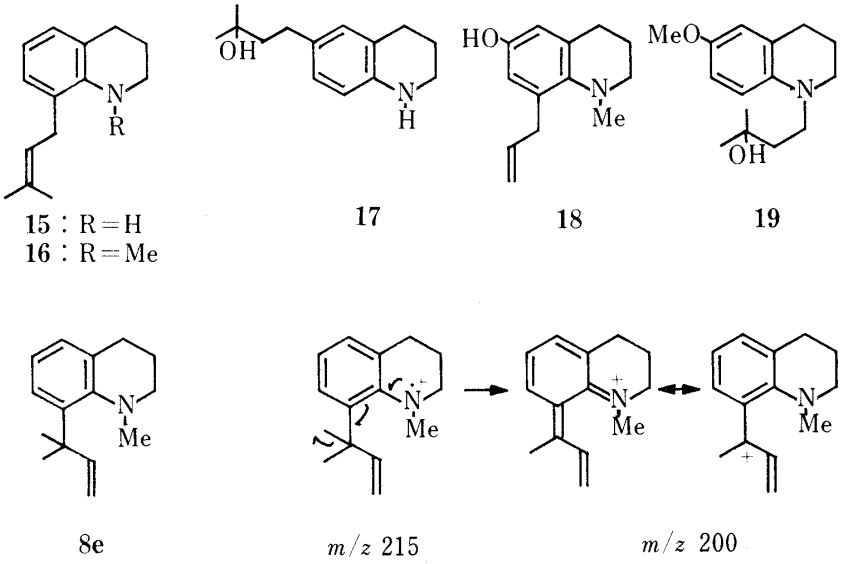

Chart 4

to the C-6 proton, were identical with those of **6a**.[1b] The third product was the major one (45% yield), and the structure **7e** was assigned to this product since the C-8 proton appears at δ 6.40 (d, J=8 Hz). The structure of **7e** was confirmed by the transformation of its acetamide **13e** into **14** (Chart 3). On the other hand the reaction of **2e** under condition C gave **7e** in 2% yield. The major products were **1a** (25.3% yield) and the hydrated product (30.5% yield). The structure **17** was assigned to this hydrated product on the basis of detailed analyses of the mass, IR and NMR spectra.

For the rearrangement of **2b**, reaction condition C was first applied. Besides the basic products (mainly **6b**), a phenolic product was obtained in 22% yield, from which **18** was isolated and methylated to provide **8b**. Thus, the reaction of **2b** under condition C involved ether cleavage and transfer of the methyl group. On the other hand, the reaction of **2b** under condition D was slow but gave **6b**[1b] in good yield without producing phenolic compounds. Henceforth we adopted condition D for tertiary amines with a 6-methoxy group.

The reaction of **2d** under condition D was smooth and gave **6d** in 84% yield; **6d** has two aromatic protons with *meta* coupling (J=3 Hz). The product **6d** (purity 90.9%) was contaminated with an isomeric product (9.1%) having the same M^+ (*m/z* 217) and the same fragmentation pattern as **6d**. The reaction of **2f** under condition D was slow and took a different course. Besides **1b** (23% yield) and **2f** (40% yield), a polar product was isolated in 17% yield. The structure **19** was assigned for this product since it has M^+ at *m/z* 249, OH at ν_{max} 3430 cm^{-1} and δ 2.53, and N–CH_2–CH_2–C(OH)Me_2 (δ 1.26, 6H, s; δ 1.73, 2H, t, J=7.5 Hz;

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δ 3.45, 2H, t, J=7.5 Hz), as well as three aromatic protons.

Quaternary N-Claisen Rearrangement——For this reaction, quaternary salts were heated in glycerol–water (2 : 1) at 140 °C (bath temperature) in the absence (reaction condition A) or in the presence (reaction condition B) of sodium bicarbonate. Rearrangements of **4a** and **4b** are described in a previous report.[1b] The product **9a** was prepared from **7a**[1b] and identified by detailed gas liquid chromatography (GLC) (hydrogen flame ionization detector (FID)) and GC-MS analyses. The reaction of **4c** (X=Br) under condition A gave a mixture of **8c** and **9c** (45.5 : 52.5). On the other hand, the reaction of **4c** (X=Br) under condition B yielded **8c** exclusively (**8c** : **9c**=87.5 : 4.3). These two products **8c** and **9c** were identical with the *N*-methylated products derived from **6c** and **7c**, respectively. The isomeric purity of **9c** was 91—95% on the basis of GLC. The configuration of **9c** is characterized by the methyl signal at δ 1.67 (3H, doublet with small couplings, J=4 Hz).

As in the case of tertiary N-Claisen rearrangement, the prenyl group behaved in a complicated manner in the quaternary N-Claisen rearrangement. The reaction of **4e** (X=BF_4) under condition B gave a mixture of four major products, from which kairoline **3a** and **9e** were isolated. The structure of **9e** was deduced from mass and NMR spectra and **9e** was identical with a specimen prepared by *N*-methylation of **7e** (Chart 2). The presence of **16** in the mixture was assumed from the NMR spectrum. The signals of the allylic methylene group of **16** (δ 3.40) are decisive as regards the site of the prenyl group, because allylic methylene at C-8 appears at lower than δ 3.40 and that at C-6 appears at δ 3.10—3.20. The fourth major product, **8e** has characteristic signals in the NMR spectrum and characteristic fragmentation due to loss of the methyl group (M^+-15, P^+) from the 1,1-dimethylpropenyl group. The rearrangement of **4e** was also conducted under condition A and gave a complicated mixture, from which two hydrated rearrangement products (M^+, m/z 213), in addition to **3a**, **8e**, **9e** and **16**, were detected by GC-MS analyses.

Since condition B is more suitable for quaternary N-Claisen rearrangement[1a] than condition A, condition B was used for the reaction of **4b** (X=Br) and **4d** (X=Br) and the products **8b** and **8d** were obtained in good yields. The splitting patterns (d, J=3 Hz) of aromatic protons indicated the position of the substituent in these products. Reaction of **4f** (X=BF_4) under condition B afforded mostly **3b** (72%). After the removal of **3b** by distillation the residue was separated by preparative thin layer chromatography (TLC). The purified specimen was homogeneous on TLC but was a mixture of two isomeric compounds on GLC (21.6 : 78.2). These isomers possess essentially identical fragmentation patterns in the mass spectrum (M^+ and P^+, m/z 245). The structure 6-methoxy-7-prenylkairoline was assumed to the major component of this mixture since it has two singlets at δ 6.47 and 6.50 due to aromatic protons in the NMR spectrum.

Discussion

On the basis of the amount of starting material remaining after the reaction, the rearrangement under condition C proceeds faster than that under condition D and gives better yields. However, condition C results in ether cleavage, so condition D is preferable for a substrate with a 6-methoxy group such as **2b**, **2d** or **2f**. Condition D gives a high yield of *ortho* product in the cases of **2a** and **2c**. The rearrangement mechanisms are summarized in Chart 5.

The introduction of γ-methyl onto the *N*-allyl moiety resulted in acceleration of the reaction.[4] The reaction times for **2c** and **2d** were shorter than those for **2a** and **2b**. As exemplified by **2a** and **2c**, the introduction of the γ-methyl group did not affect the ratio of *ortho* and *para* products under condition D, but under condition C the ratio of *para* product increased from **6a** : **7a**=91.9 : 6.0 to **6c** : **7c**=72.0 : 25.0. On the basis of the [3,3]sigmatropic path-

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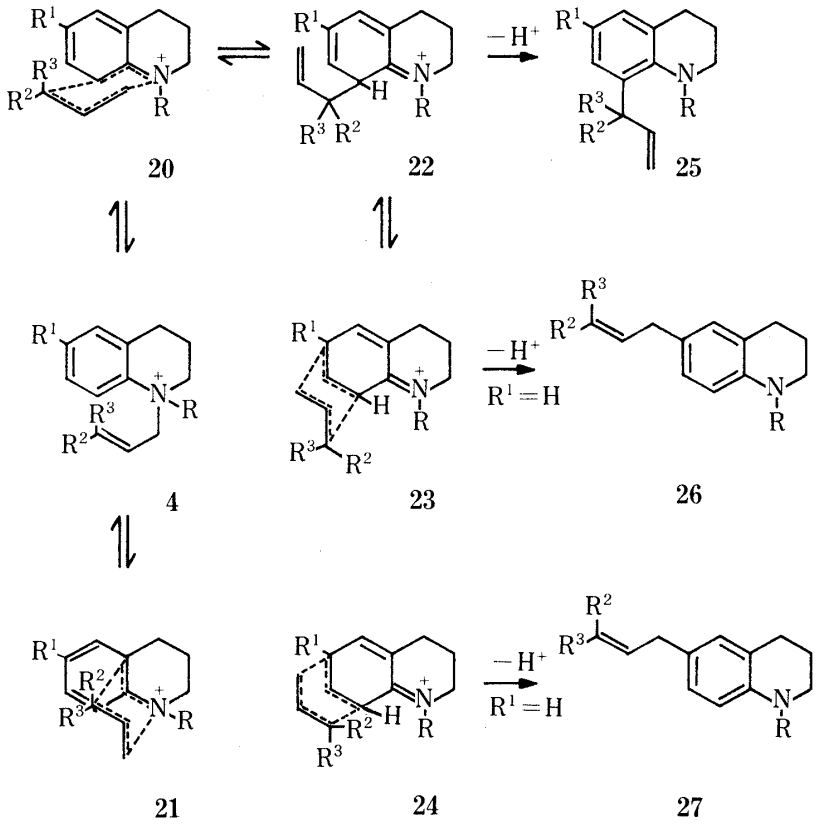

Chart 5

way (Chart 5) the increase of *para* product can be attributed to the difference of steric effects between **22a** and **22c**. The *sec*-butenyl group in **22c** can migrate more readily than the allyl group.[5a] Further, the allyl group can migrate to the *para* position *via* **21**, but the contribution of **21** should be small since the conformation **21** has severe steric interaction between the C-3 methylene proton and the vinylic proton on the allyl group. In the reaction of **2c**, condition C gave greater *para* production than condition D. Since the abstraction of proton from **22c** is slower under condition C than under condition D, this difference is responsible for the greater *para* rearrangement under condition C. The product **7c** was isomerically 97% pure was slightly contaminated with *Z* isomer (*E*:*Z*=97:3) according to GC-MS analyses. Since the *E*-crotyl moiety of **2c** was isomerically pure, the retention of *E*-configuration in **7c** means that the crotyl migration proceeded mostly *via* chair conformations.[5b] Contaminating *Z* isomer should be derived from the boat conformation, such as **24c**.

The introduction of two γ-methyls onto the *N*-allyl moiety completely changed the course of the reaction. Under both conditions **2e** did not produce **6e** but gave a considerable amount of **1a**. Under condition C the major product was **7e** together with two other products, one of which was **15**. Under condition D the yield of **7e** was poor and the major product was **17**, a product of the hydration of **7e**. No **15** was detected.

On the other hand the reaction of **2f** under condition D was slow and did not give any rearrangement product. Deprenylation and hydration to **19** were the major reactions. The production of **7e** and **17** from **2e** can be explained by the mechanism in Chart 5, but the formation of **15** requires a dissociation–recombination mechanism (Chart 6). Thus, the prenyl group migrates *via* two different pathways. The absence of *ortho* product formed *via* [3,3]sigmatropic rearrangement suggests that the deprotonation of **22e** is slow and the transformation of **22e** into **27** is quite fast. The observation of large amounts of **1a** and **1b**

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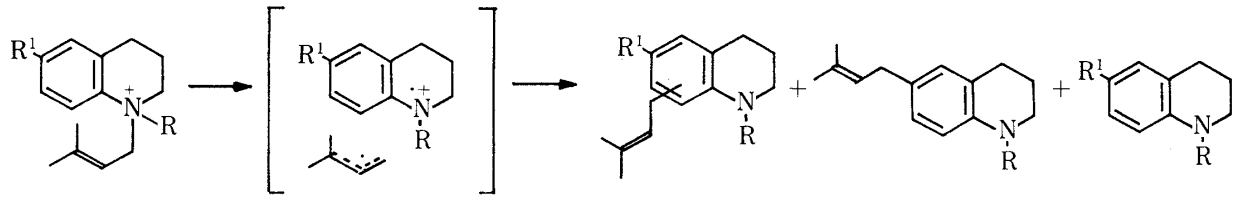

2e: R=H, R^1=H
4e: R=Me, R^1=H

28

7e: R=H
9e: R=Me

1: R=H
3: R=Me

Chart 6

shows that the deprenylation is competitive with deprotonation. Since the presence of a 6-methoxy group blocks the formation of *para* product, an increase of the *ortho* isomer **6d** was observed in the reaction of **2d**. However, the purified **6d** was contaminated with an isomer which has essentially the same fragmentation pattern as **6d** on GC-MS. This isomeric contaminant may be the derivative formed *via* the dissociation–recombination mechanism.

For quaternary N-Claisen rearrangement we have employed two reaction conditions, A and B. Under condition A the reaction solution becomes acidic after the reaction, whereas under condition B the reaction mixture remains weakly basic. In general, condition B gives a better result than condition A.[2b] The introduction of γ-methyl onto the allyl group affected the reaction pattern only under condition A. The reaction of **4c** under condition A gave **9c** as a major product (52.5%). Under condition B, the yield of **9c** decreased and the yield of **8c** increased. The change of the major product with shift of the reaction conditions can be explained by assuming that the deprotonation of **22c** is fast under condition B but slow under condition A. Considering the rapid deprotonation of **22** and the constant low yields of *para* products **9a** and **9c** under condition B despite the difference of migration group it can be concluded that **9a** and **9c** are probably derived from **21** but not from **20** (Chart 5). The isomeric composition of **9c** can be explained by considering the conformations of reaction intermediates as in the case of tertiary N-Claisen rearrangement, *vide supra*. For 6-methoxylated quaternary salts, condition B was applied. The salts **4b** and **4d** gave **8b** and **8d** in good yields without other contaminating products.

As in the case of tertiary N-Claisen rearrangement, the rearrangement of the prenyl group was complicated in quaternary N-Claisen rearrangement. The reaction of **4e** gave the products **8e**, **9e** and a large amount of **3a**. The *ortho* product **8e** should be formed by the [3,3]sigmatropic mechanism (Chart 5). This type of product was not detected in tertiary N-Claisen rearrangement. This difference presumably arises because removal of a proton from **22e** is easier when R is methyl than when R is a proton, since **22e** (R=H) can be in equilibrium with the free imine. Further, deprotonation is accelerated under condition B. In addition to **8e** and **9e** the other rearrangement product **16** was detected in the reaction of **4e**. The formation of **16** suggests that the dissociation–recombination mechanism (Chart 6) is also involved in the reaction of **4e**. In the case of **4f** the *ortho* product **8f** was not observed but two other rearrangement products were detected by GC-MS, one of which was identified as 6-methoxy-7-prenylkairoline. This product is derivable *via* a dissociation–recombination mechanism but may also arise *via* a two [3,3]- and one [1,2]sigmatropic rearrangement mechanism[1c] as in the quaternary N-Claisen rearrangement of the 9-substituted julolidinium halides,[1c] in which all *ortho* and *para* positions are occupied and the *meta* rearrangement product was formed.

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Experimental[6]

Typical Procedure for the Preparation of *N*-Allyltetrahydroquinolines 2——A solution of 1,2,3,4-tetrahydroquinoline (25 mmol), allyl halide (43 mmol) and sodium carbonate (22 mmol) in acetonitrile (25 ml) was stirred at room temperature for the period required for completion of the reaction. Heating was applied when necessary. The progress of reaction was followed by TLC (silica gel, chloroform). The reaction mixture was evaporated to dryness *in vacuo*. The residue was diluted with water (50 ml) and extracted three times with ether (3 × 20 ml). The organic extracts were washed twice with saturated brine (2 × 20 ml) and dried over anhydrous sodium sulfate. The ether was removed to give the crude product, which was purified by either distillation or column chromatography.

1-*E*-Crotyl-1,2,3,4-tetrahydroquinoline 2c——Distillation of the crude product gave **2c** in 45% yield. The distillate consisted of the *E* isomer (97%) with some *Z* isomer (3%). The isomeric contaminant was removed by recrystallization of the hydrochloride from acetone. **2c**: bp 84—85 °C/0.1 mmHg. IR ν_{max}^{film} cm^{-1}: 1670, 965, 745. NMR δ 1.70 (3H, m, =CH–Me. Singlet when irradiated at δ 5.60), 1.93 (2H, quintet, J = 5.5 Hz, C-3-H), 2.77 (2H, t, J = 6 Hz, C-4-H), 3.23 (2H, t, J = 5.5 Hz, C-2-H), 3.80 (2H, m, N–CH$_2$–CH=), 5.60 (2H, m, N–CH$_2$–CH=CH–Me), 6.43—7.17 (4H, m, Ar–H). Hydrochloride **2c**·HCl: colorless needles, mp 126—136 °C (acetone). IR ν_{max}^{KBr} cm^{-1}: 2100—2500, 1677, 982. NMR δ: 1.80 (3H, d, J = 4 Hz, =CH–Me. Singlet by irradiation at δ 4.93), 2.17 (2H, quintet, J = 6 Hz, C-3-H), 2.97 (2H, t, J = 6.5 Hz, C-4-H), 3.57 (2H, distorted t, J = 6 Hz, C-2-H), 3.97 (2H, m, N–CH$_2$–CH=), 4.93 (2H, m, N–CH$_2$–CH=CH–Me), 7.37 (3H, m, Ar–H), 7.70 (1H, m, Ar–H). *Anal.* Calcd for $C_{13}H_{18}ClN$: C, 69.79; H, 8.11; N, 6.26%. Found: C, 69.14; H, 8.12; N, 6.51%.

1-*E*-Crotyl-6-methoxy-1,2,3,4-tetrahydroquinoline 2d——Reaction of 6-methoxy-1,2,3,4-tetrahydroquinoline **1b** (5.5 g, 33.7 mmol) and crotyl bromide (8.1 g, 60 mmol) in acetonitrile (30 ml) at room temperature for 3 months gave 2.90 g of hydrobromide after concentration of the reaction mixture and suspension of the residue in acetone. Recrystallization of the hydrobromide from acetone–ethyl acetate three times gave pure 1-*E*-crotyl-6-methoxy-1,2,3,4-tetrahydroquinoline hydrobromide **2d**·HBr. The treatment of this hydrobromide with sodium carbonate gave the free amine **2d**. **2d**: colorless liquid. IR ν_{max}^{film} cm^{-1}: 1050, 965, 800. NMR δ: 1.70 (3H, d, J = 4 Hz, =CH–Me), 1.93 (2H, m, C-3-H), 2.76 (2H, t, J = 6 Hz, C-4-H), 2.17 (2H, t, J = 5.5 Hz, C-2-H), 3.73 (3H, s, OMe), 3.77 (2H, overlapping with the signals at δ 3.73, N–CH$_2$–CH=), 5.60 (2H, m, N–CH$_2$–CH=CH–Me), 6.63 (3H, s, Ar–H). Hydrobromide **2d**·HBr: colorless fine crystals, mp 151 °C (dec.) (acetone–ethyl acetate). IR ν_{max}^{KBr} cm^{-1}: 1670, 1610, 1028, 840. NMR δ: 1.80 (3H, d, J = 4.5 Hz, =CH–Me. Singlet on irradiation at δ 5.97), 2.17 (2H, m, C-3-H), 2.93 (3H, t, J = 6.5 Hz, C-4-H), 3.57 (2H, t, J = 5.5 Hz, C-2-H), 3.80 (3H, s, OMe), 3.97 (2H, d, J = 5 Hz, N–CH$_2$–CH=), 5.97 (2H, m, N–CH$_2$–CH=CH–Me), 6.80 (1H, br s, C-5-H), 6.90 (1H, dd, J = 3, 8.5 Hz, C-7-H), 7.70 (1H, d, J = 8.5 Hz, C-8-H). *Anal.* Calcd for $C_{14}H_{20}BrNO$: C, 56.38; H, 6.76; Br, 26.80; N, 4.70%. Found: C, 56.16; H, 6.92; Br, 26.57; N, 4.77%.

1-Prenyl-1,2,3,4-tetrahydroquinoline 2e——The crude product was purified by distillation at 115—117 °C/4 mmHg then by Kugelrohr distillation at 149 °C/10 mmHg. **2e**: colorless liquid. IR ν_{max}^{film} cm^{-1}: 1675, 1452, 745. NMR δ: 1.73 (6H, s, =CMe$_2$), 1.93 (2H, m, C-3-H), 2.73 (2H, t, J = 6 Hz, C-4-H), 3.23 (2H, t, J = 5.5 Hz, C-2-H), 3.83 (2H, d, J = 6 Hz, N–CH$_2$–CH=), 5.23 (1H, br t, J = 6 Hz, N–CH$_2$–CH=CMe$_2$), 6.4—7.2 (4H, m, Ar–H). *Anal.* Calcd for $C_{14}H_{19}N$: C, 83.53; H, 9.51; N, 6.96%. Found: C, 83.75; H, 9.53; N, 6.75%.

1-Prenyl-6-methoxy-1,2,3,4-tetrahydroquinoline 2f——The crude product was purified by flash column chromatography[7] on silica gel (100 g) with petroleum ether–ethyl acetate (95 : 5 and 94 : 6). Further purification was effected by Kugelrohr distillation at 147 °C/3 mmHg. **2f**: colorless liquid. MS *m/z*: 231 (M^+, 11%), 163 (62), 159 (base). IR ν_{max}^{film} cm^{-1}: 1673, 1505, 1060, 800. NMR δ: 1.70 (6H, br s, =CMe$_2$), 1.93 (2H, quintet, J = 6 Hz, C-3-H), 2.73 (2H, d, J = 6 Hz, C-4-H), 3.13 (2H, distorted t, J = 5.5 Hz, C-2-H), 3.70 (3H, s, OMe), 3.75 (2H, d, J = 6 Hz, N–CH$_2$–CH=. Singlet when irradiated at δ 5.23), 5.23 (1H, m, N–CH$_2$–CH=CMe$_2$. Triplet, J = 7 Hz on irradiation at δ 1.70), 6.57 (3H, s, Ar–H).

1,1-Diprenyl-6-methoxy-1,2,3,4-tetrahydroquinolinium Tetrafluoroborate 5——When the aqueous layer of the extract obtained from the reaction mixture of 6-methoxytetrahydroquinoline **1b** (4.17 g, 25.5 mmol), prenyl bromide (6.37 g, 43 mmol) and sodium carbonate (2.34 g, 22 mmol) in acetonitrile (25 ml) was left at room temperature for 2 d, tarry material collected around the bottom of the flask. Excess sodium tetrafluoroborate and dichloromethane were added and the mixture was stirred overnight. The organic layer was collected and worked up as usual to give an amorphous product, which was recrystallized from acetone–ethyl acetate. The yields of **2f** and **5** in this reaction were 41.5 and 22.5%, respectively. **5**: mp 142—143 °C (dec.) (acetone–ethyl acetate). IR ν_{max}^{KBr} cm^{-1}: 1673, 1503, 1290, 1070, 1038, 857. NMR δ: 1.70 (12H, m, =CMe$_2$ × 2. Singlet at δ 1.68 and 1.72 when irradiated at δ 5.06), 2.20 (2H, m, C-3-H), 2.87 (2H, t, J = 6 Hz, C-4-H), 3.70 (2H, t, J = 6 Hz, C-2-H), 3.77 (3H, s, OMe), 4.33 (4H, d, J = 7 Hz, N–CH$_2$–CH= × 2), 5.06 (2H, m, N–CH$_2$–CH=CMe$_2$ × 2. Triplet, J = 7 Hz on irradiation at δ 1.70), 6.67 (1H, d, J = 3 Hz, C-5-H), 6.83 (1H, dd, J = 3, 9 Hz, C-7-H), 7.47 (1H, d, J = 9 Hz, C-8-H). *Anal.* Calcd for $C_{20}H_{30}NOBF_4$: C, 62.03; H, 7.81; N, 3.62%. Found: C, 62.02; H, 8.02; N, 3.61%.

Typical Procedure for the Preparation of *N*-Allylkairolinium Halides 4——A solution of kairoline **3** (30 mmol) and an allyl halide (44 mmol) in acetonitrile (40 ml) containing three drops of DMF was left at room temperature for a prolonged period. Crystals usually appeared and were collected by suction filtration. If no crystals appeared, the

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reaction mixture was concentrated *in vacuo* and the residue was purified by either crystallization or column chromatography.

1-*E*-Crotyl-1-methyl-1,2,3,4-tetrahydroquinolinium Bromide 4c (X=Br)——Crude crystals (obtained in 52% yield) were purified by recrystallization from dichloromethane–acetone. **4c** (X=Br): mp 141—143 °C (dec.) (dichloromethane–acetone). IR ν_{max}^{KBr} cm^{-1}: 1667, 970, 789. NMR δ: 1.73 (3H, d, J=7 Hz, =CH–Me. Singlet when irradiated at δ 6.43), 2.33 (2H, m, C-3-H), 3.03 (2H, t, J=6 Hz, C-4-H), 3.92 (3H, s, NMe), 4.17 (2H, m, C-2-H), 4.9—5.6 (3H, m, N–C$\underline{H}_2$–C$\underline{H}$=CHMe), 6.43 (1H, qd, J=7, 14 Hz, N–CH$_2$–CH=C$\underline{H}$–Me. Doublet, J=14 Hz on irradiation at δ 1.73), 7.40 (3H, m, Ar–H), 8.33 (1H, m, C-8-H). *Anal.* Calcd for $C_{14}H_{20}BrN$: C, 59.58; H, 7.14; Br, 28.31, N, 4.96%. Found: C, 59.56; H, 7.25; Br, 28.54, N, 4.73%.

1-*E*-Crotyl-1-methyl-6-methoxy-1,2,3,4-tetrahydroquinolinium Bromide 4d (X=Br)——After 14 months of reaction, the reaction mixture was evaporated to dryness. The crystals that appeared were suspended in acetone, collected and recrystallized from methanol, giving 6-methoxykairoline hydrobromide **3b**·HBr: colorless needles, mp 192—193 °C, in 14.7% yield. This product was identical with an authentic specimen (IR and NMR spectra). The filtrates were concentrated and the residue was chromatographed on silica gel (105 g) with dichloromethane–methanol (85:15) to give **4d** in 64.4% yield. **4d**: highly hygroscopic amorphous solid. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1662, 1604, 1037, 970, 842. NMR δ: 1.77 (3H, d, J=6.5 Hz, =CH–M$\underline{e}$), 2.33 (2H, m, C-3-H), 3.03 (2H, t, J=6 Hz, C-4-H), 3.82 and 3.83 (3H, each s, N–Me), 3.87 (3H, s, OMe), 4.10 (2H, m, C-2-H). Singlet when irradiated at δ 2.33), 4.92 (2H, d, J=7 Hz, N–C$\underline{H}_2$–CH=), 5.33 (1H, br td, J=7, 14 Hz, N–CH$_2$–C$\underline{H}$=CH–Me), 6.35 (1H, qd, J=6.5, 14 Hz, N–CH$_2$–CH=C$\underline{H}$–Me. Doublet J=14 Hz when irradiated at δ 1.77), 6.77 (1H, d, J=3 Hz, C-5-H), 7.02 (1H, dd, J=3, 9 Hz, C-7-H), 8.26 (1H, d, J=9 Hz, C-8-H).

1-Methyl-1-propenyl-1,2,3,4-tetrahydroquinolinium Bromide 4e (X=Br)——The reaction mixture generated heat just after mixing, so the solution was briefly cooled with water. After 7 h the crystals (71.6% yield) were collected. (Crystals were not obtained if the mixture had been warmed.) The crude crystals were quickly recrystallized from dichloromethane–acetone in 55.7% yield. Partial decomposition was observed (odor of prenyl bromide). **4e** (X=Br): mp 140—142 °C (dec.) (methanol–acetone). IR ν_{max}^{KBr} cm^{-1}: 1665, 785. NMR δ(CD$_3$OD): 1.83 (6H, s, =CMe$_2$), 2.33 (2H, m, C-3-H), 3.06 (2H, t, J=6.5 Hz, C-4-H), 3.60 (3H, s, NMe), 3.87 (2H, m, C-2-H. Singlet on irradiation at δ 2.33), 4.53 (2H, d, J=8 Hz, N–C$\underline{H}_2$–CH=), 5.23 (1H, m, N–CH$_2$–C$\underline{H}$=CMe$_2$. Double d, J=6, 8 Hz, when irradiated at δ 1.83), 7.47 (3H, m, Ar–H), 7.86 (1H, m, C-8-H). *Anal.* Calcd for $C_{15}H_{22}BrN$: C, 60.81; H, 7.49; N, 4.73%. Found: C, 60.73; H, 7.61; N, 4.47%.

Tetrafluoroborate **4e** (X=BF$_4$): Prepared from the bromide **4e** (X=Br) (1.137 g, 3.8 mmol) by treatment with sodium tetrafluoroborate (0.756 g, 6.9 mmol) in water (12 ml) in 86% yield. **4e** (X=BF$_4$): colorless plates, mp 143—144 °C (ethanol). IR ν_{max}^{KBr} cm^{-1}: 1670, 1450, 1060. *Anal.* Calcd for $C_{15}H_{22}NBF_4$: C, 59.43; H, 7.32; N, 4.62%. Found: C, 59.52; H, 7.50; N, 4.69%.

1-Methyl-1-prenyl-6-methoxy-1,2,3,4-tetrahydroquinolinium Bromide 4f (X=Br)——The crude product obtained after 14 d of reaction was recrystallized from methanol–acetone, but the crystals obtained were a mixture of the desired bromide **4f** (X=Br) and the hydrobromide **3b**·HBr in the ratio of 43:57 according to NMR analysis as well as titration with 0.1 N sodium hydroxide. This mixture (2.2 g) was boiled in acetone (40 ml) and filtered while hot. This procedure was repeated with acetone (30 ml), giving the quaternary bromide **4f** (X=Br) as insoluble crystals (0.691 g). **4f** (X=Br): colorless plates, mp 126—128.5 °C (dec.) (dichloromethane–acetone). IR ν_{max}^{KBr} cm^{-1}: 1675, 1030, 840. NMR δ: 1.75 (3H, s, =CMeM$\underline{e}$), 1.88 (3H, s, =CM$\underline{e}$Me), 2.27 (2H, m, C-3-H), 2.96 (2H, m, C-4-H), 3.83 (3H, s, OMe), 3.90 (3H, s, N–Me), 3.7—4.2 (2H, m, C-2-H), 4.97 (3H, br s, N–C$\underline{H}_2$–C$\underline{H}$=), 6.73 (1H, d, J=3 Hz, C-5-H), 6.97 (1H, dd, J=3, 9 Hz, C-7-H), 8.27 (1H, d, J=9 Hz, C-8-H). *Anal.* Calcd for $C_{16}H_{24}BrNO$: C, 58.90; H, 7.41; Br, 24.49, N, 4.29%. Found: C, 59.09; H, 7.52; Br, 24.74; N, 4.16%.

1-Methyl-1-prenyl-6-methoxy-1,2,3,4-tetrahydroquinolinium Tetrafluoroborate, 4f (X=BF$_4$)——A mixture of quaternary bromide **4f** (X=Br) and hydrobromide **3b**·HBr (73.5:26.5, 2.0 g) in water (16 ml) was treated with sodium tetrafluoroborate (1.5 g) for 3 h under stirring to give 1.2 g (73.5% yield) of the tetrafluoroborate. **4f** (X=BF$_4$): colorless plates mp 70—90 °C (dec.) (benzene–acetone). IR ν_{max}^{KBr} cm^{-1}: 1674, 1060, 840. NMR δ: 1.76 (6H, s, =CMe$_2$), 2.27 (2H, m, C-3-H), 2.93 (2H, t, J=6.5 Hz, C-4-H), 3.50 (3H, s, N–Me), 3.73 (2H, t, J=5.5 Hz, C-2-H), 3.83 (3H, s, OMe), 4.43 (2H, d, J=7 Hz, N–C$\underline{H}_2$–CH=), 5.03 (1H, m, N–CH$_2$–C$\underline{H}$=CMe$_2$. Double d, J=7, 9 Hz, on irradiation at δ 1.76), 6.73 (1H, d, J=3 Hz, C-5-H), 6.94 (1H, dd, J=3, 9.5 Hz, C-7-H), 7.66 (1H, d, J=9.5 Hz, C-8-H). *Anal.* Calcd for $C_{16}H_{24}NOBF_4$: C, 57.68; H, 7.26; N, 4.20%. Found: C, 58.25; H, 7.25; N, 4.05%.

Rearrangement of 2a under Reaction Condition D——The crude product (363 mg) was chromatographed on silica gel (15 g). Elution with benzene gave **2a** (10 mg, 2.9%) and **6a** (189 mg, 54.3%). Elution with methanol yielded a polar product (136 mg) which was rechromatographed on silica gel (5.0 g) with dichloromethane–methanol (97:3) to give the hydrated product **10** (41 mg). **10**: MS m/z: 191 (M$^+$), 146 (P$^+$). IR ν_{max}^{film} cm^{-1}: 3400, 1310, 1265, 1110, 740. NMR δ: 1.25 (3H, d, J=6 Hz, CH–M$\underline{e}$. Singlet when irradiated at δ 3.96), 1.90 (2H, quintet, J=6 Hz, C-3-H), 2.60 (2H, d, J=6 Hz, Ar–C$\underline{H}_2$–CH=), 2.77 (2H, t, J=7 Hz, C-4-H), 3.03 (2H, br s, NH+OH. Exchangeable with deuterium oxide), 3.30 (2H, t, J=5.5 Hz, C-2-H), 3.96 (1H, quintet, J=6 Hz, CH$_2$–C$\underline{H}$(OH)–Me. Triplet, J=6 Hz on irradiation at δ 1.25), 6.43—6.93 (3H, Ar–H).

Rearrangement of 2c——a) Reaction conditon C: Flash column chromatography of the crude product on silica

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gel (50 g) with petroleum ether–ethyl acetate (95 : 5) gave **6c** and **7c** in 54 and 24.4% yields, respectively. **6c**: colorless liquid. MS *m/z*: 187 (M^+, base), 172 (75%), 168 (68), 144 (66). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3440, 1630, 918; ν_{max}^{film} cm^{-1}: 3430, 1630, 912, 745. NMR δ: 1.37 (3H, d, J=7 Hz, CH–Me. Singlet on irradiation at δ 3.40), 1.90 (2H, m, C-3-H), 2.80 (2H, t, J=6 Hz, C-4-H), 3.33 (2H, t, J=5.5 Hz, C-2-H), 3.40 (1H, m, =CH–CH–Me. Overlapping with the signals at δ 3.33), 3.90 (1H, br, NH. Exchangeable with deuterium oxide), 4.96 and 5.20 (2H, each m, CH=CH_2), 6.00 (1H, ddd, J=6, 9, 18 Hz, CH–CH=CH_2. Double d, J=9, 18 Hz, when irradiated at δ 3.40), 6.5—7.1 (3H, m, Ar–H). **7c**: colorless liquid. MS *m/z*: 187 (M^+, 16%), 166 (base), IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3450, 1613, 965. NMR δ: 1.70 (3H, dm, J=4 Hz, CH_2–CH=CH–Me. Singlet on irradiation at δ 5.56). 1.90 (2H, m, C-3-H), 2.76 (2H, t, J=6 Hz, C-4-H), 3.20 (2H, m, Ar–CH_2–CH=CH–Me. Singlet when irradiated at δ 5.56), 3.26 (2H, t, J=5.5 Hz, C-2-H), 3.63 (1H, br s, NH. Exchangeable with deuterium oxide), 5.56 (2H, m, CH_2–CH=CH–Me), 6.40 (1H, d, J=9 Hz, C-8-H), 6.77 (2H, m, Ar–H). b) Reaction condition D: Flash column chromatography of the crude product (376 mg) on silica gel (47 g) with petroleum ether–ethyl acetate (96 : 4 and 95 : 5) gave **2c** (2.7% yield) and **6c** (59.7% yield). The column was further eluted with methanol to give a polar product (105 mg), which was a mixture of **7c** (23%) and three hydrated products (68%, M^+; *m/z* 205) according to GC-MS.

1,2-Dimethylliloidine 11——a) From **6c**: Amine **6c** (187 mg, 1 mmol) was treated with mercuric acetate (367 mg, 1.2 mmol) in anhydrous methanol (5 ml) at room temperature for 1 h.[8] The reaction mixture was concentrated and the residue was dissolved in chloroform to separate organomercuric acetate, which was then dissolved in dry methanol (5 ml) and reduced with 0.5 M sodium borohydride in 2 N sodium hydroxide (5 ml) for 43 h. After refluxing for 1 h, the reaction mixture was evaporated to dryness *in vacuo*. The residue was diluted with water then extracted with ether three times. The crude product (109 mg, 58%) was purified by silica gel column (5 g) chromatography with dichloromethane, giving 25.2 mg (14% yield) of **11**: colorless liquid, a mixture of two stereoisomers (55 : 45) on GLC. MS *m/z*: 187 (M^+), 172 (base). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1480, 1450, 1330, 1278, 1042. NMR: 1.07—1.37 (6H, m, 2×CH–Me), 6.63—7:03 (3H, m, Ar–H). b) From 1,2-dimethylindoline **12**. A solution of **12**[3] (*trans* : *cis* = 79 : 21. 1.0 g, 6.9 mmol) in 1,3-bromochloropropane (15 g) was refluxed for 20 h. After the addition of 3 N hydrochloric acid (25 ml), the solution was steam-distilled. The residue was basified with sodium hydroxide and extracted with ether (2×30 ml). The crude product (1.13 g) was chromatographed on silica gel (50 g) with dichloromethane to give 673 mg (53% yield) of **11**. NMR δ: 1.10—1.47 (6H, m, CH–Me×2), 1.9—3.6 (8H, m), 6.5—7.0 (3H, m, Ar–H). The composition of stereoisomers was different from that obtained in a). Both products were identified by IR, GLC and GC-MS comparisons.

1-Acetyl-6-*E*-crotyl-1,2,3,4-tetrahydroquinoline 13c——Acetylation of **7c** (70 mg) with pyridine–acetic anhydride (1 : 1) gave **13c**: oil. MS *m/z*: 229 (M^+, base). 187, 172. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1630, 1382, 965. NMR δ: 1.73 (3H, m, =CH–Me), 1.93 (2H, quintet, J=6.5 Hz, C-3-H), 2.23 (3H, s, Ac), 2.70 (2H, t, J=6.5 Hz, C-4-H), 3.30 (2H, m, Ar–CH_2–CH=), 3.80 (2H, t, J=6.5 Hz, C-2-H), 5.57 (2H, m, CH_2–CH=CH–Me), 7.06 (3H, m, Ar–H).

1-Acetyl-6-(2-hydroxyethyl)-1,2,3,4-tetrahydroquinoline 14——a) From **13c**: A solution of the acetamide **13** (55 mg, 0.24 mmol) in methanol (20 ml) was cooled to −55 °C and oxidized with ozonized air (0.33 mmol). After warming to 0 °C the reaction mixture was reduced with sodium borohydride (50 mg, 1.32 mmol) for 0.5 h, then concentrated *in vacuo*. The residue was diluted with water and extracted with ether three times to give 42 mg (79.3% yield) of **14**, which was identical with the specimen prepared from **13a** (NMR spectra). b) From **13a**: A solution of the acetamide **13a** (114 mg, 0.53 mmol) in methanol (20 ml) was oxidized with ozonized air (1.2 mol eq) at −40 °C. The reaction mixture was reduced with sodium borohydride (0.1 g) at 0 °C then at room temperature for 0.5 h. The crude product (57 mg) was purified by column chromatography (silica gel 1.2 g, dichloromethane with 2% methanol) to give 45 mg (39% yield) of **14**: oil. MS *m/z*: 219 (M^+, 9%), 188 (3), 146 (base). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3640, 3350, 1640, 1050, 882. NMR δ: 1.93 (2H, quintet, J=6.5 Hz, C-3-H), 2.22 (3H, s, NAc), 2.50 (1H, br s, OH. Exchangeable with deuterium oxide), 2.72 (2H, t, J=6.5 Hz, C-4-H), 2.83 (2H, t, J=6.5 Hz, Ar–CH_2–CH_2–OH), 3.77 (2H, t, J=6 Hz, C-2-H), 3.83 (2H, t, J=6.5 Hz, Ar–CH_2–CH_2–OH. Singlet on irradiation at δ 2.83), 7.07 (3H, m, Ar–H). c) From **13e**: A solution of the acetamide **13e** (258 mg) in methanol (20 ml) was oxidized with ozonized air (1.2 mol eq) at −40 °C. The crude product (214 mg) was chromatographed on silica gel (4.0 g) with dichloromethane containing increasing amounts of methanol (1, 2 and 3%), giving 1-acetyltetrahydroquinoline (19 mg; contaminant) and 165 mg (83% yield) of **14**, which was identical with the above specimen (TLC and NMR spectrum).

Rearrangement of 2e——a) Reaction condition C: The crude product was a mixture of **1a** (16.7%), unidentified products (7.0% and 4.6%), **15** (8.2%), rearrangement product (8.3%) and **7e** (54.4%). Flash column chromatography of the crude product (188 mg) on silica gel (37 g) with petroleum ether–ethyl acetate (95 : 5, 93 : 7 then 90 : 10) gave 8-prenyl-1,2,3,4-tetrahydroquinoline **15** (14 mg, 6.9% yield) of 81% purity, 6-prenyl-1,2,3,4-tetrahydroquinoline **7e** (97 mg, 48% yield) of 75% purity and tetrahydroquinoline **1a** (8 mg, 6.0% yield). **15**: 81% pure oil. MS *m/z*: 201 (M^+), 146 (base). IR ν_{max}^{film} cm^{-1}: 3430, 1498, 1320, 745. NMR δ: 1.67 (6H, s, $=CMe_2$), 1.85 (2H, quintet, J=6 Hz, C-3-H), 2.72 (2H, t, J=6 Hz, C-4-H), 3.03 (2H, d, J=6 Hz, Ar–CH_2–CH=), 3.63 (1H, br, NH. Exchangeable with deuterium oxide), 5.20 (1H, br t, J=7 Hz, CH_2–CH=CMe_2. Triplet, J=7 Hz on irradiation at δ 1.67), 6.50 (1H, dd, J=6, 8 Hz, C-6-H), 6.80 (1H, d, J=6 Hz, C-5-H), 6.80 (1H, d, J=8 Hz, C-7-H). **7e**: 81% pure oil. MS *m/z*: 201 (M^+), 186 (P^+). Calcd for $C_{14}H_{19}N$: 201.1517. Found: 201.1544. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3450, 1620. ν_{max}^{film} cm^{-1}: 3420, 1615, 1513, 1315, 810. NMR δ: 1.72 (6H, s, $=CMe_2$), 1.90 (2H, m, C-3-H), 2.72 (2H, t, J=6 Hz, C-4-H), 3.20 (2H, d, J=7.5 Hz, CH_2–

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CH=), 3.23 (2H, t, J=6 Hz, C-2-H), 3.77 (1H, s, NH. Exchangeable with deuterium oxide), 5.30 (1H, br t, J=7.5 Hz, CH_2–C<u>H</u>=CMe_2. Triplet, J=7.5 Hz on irradiation at δ 1.72), 6.40 (1H, d, J=8 Hz, C-8-H), 6.6—6.9 (2H, m, Ar–H). Contaminants according to GC-MS are **1a** and an unidentified product (m/z 197, M^+: m/z 146, base). b) Reaction condition D: The crude product (199 mg) was chromatographed on silica gel (7 g). Elution with benzene gave the starting material **2e** (12 mg, 5.9% yield), tetrahydroquinoline **1a** (34 mg, 25.3% yield) and 6-prenyl-1,2,3,4-tetrahydroquinoline **7e** (4 mg, 2.0% yield). Elution with methanol afforded a polar product (134 mg, 30.5% yield) which was purified by column chromatography (silica gel 5 g, dichloromethane–methanol=97:3), giving 55 mg (24.9% yield) of 6-(3-hydroxy-3-methylbutyl)-1,2,3,4-tetrahydroquinoline **17**: MS m/z: 219 (M^+), 146 (base). IR ν_{max}^{film} cm^{-1}: 3480, 1617, 1312, 935, 910, 818. NMR δ: 1.23 (6H, s, HO–CMe_2), 1.73 (2H, m, Ar–CH_2–C<u>H</u>$_2$–C(OH)Me_2), 1.90 (2H, m, C-3-H), 2.50 (2H, s, NH+OH. Disappeared on addition of deuterium oxide), 2.53 (2H, m, Ar–C<u>H</u>$_2$–CH_2. Singlet on irradiation at δ 1.73), 2.73 (2H, t, J=6 Hz, C-4-H), 3.25 (2H, t, J=5.5 Hz, C-2-H), 6.40 (1H, d, J=8 Hz, C-8-H), 6.80 (2H, m, Ar–H).

1-Acetyl-6-prenyl-1,2,3,4-tetrahydroquinoline 13e——Impure **7e** was acetylated with a mixture of pyridine and acetic anhydride (1:1) at room temperature for 4.5 h. The crude acetamide (1.30 g) was purified by chromatography on silica gel (15 g) with dichloromethane–acetone (95:5) then by Kugelrohr distillation at 152 °C/3 mmHg, giving **13e** of 82% purity. **13e**: oil. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1660, 1618, 1380. NMR δ: 1.73 (6H, br s, =CMe_2), 1.93 (2H, quintet, J=6.5 Hz, C-3-H), 2.23 (3H, s, Ac), 2.73 (2H, t, J=6.5 Hz, C-4-H), 3.33 (2H, d, J=7 Hz, C<u>H</u>$_2$–CH=), 3.80 (2H, t, J=6.5 Hz, C-2-H), 5.33 (1H, m, CH_2–C<u>H</u>=CMe_2. Triplet, J=7 Hz when irradiated at δ 1.73), 6.9—7.4 (3H, m, Ar–H).

Rearrangement of 2b——a) Reaction condition C:[1b] The reaction product derived from **2b** (410 mg, 2.0 mmol) was separated into basic (288 mg) and phenolic (84 mg) products. The basic product was a mixture of **6b** (84.4%), **18** (12.6%) and **2b** (1.0%) and gave **6b** in 57% yield after column chromatography.[1b] The phenolic product, containing **6b** (7.8%) and **18** (91.0%), was chromatographed on silica gel (2.7 g) with dichloromethane–methanol (98:2). The purified specimen (58 mg) was mainly **18**, but was contaminated with 8-allyl-6-hydroxytetrahydroquinoline. **18**: liquid. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3625, 3350, 1639, 910. NMR δ: 1.87 (m, C-3-H), 2.63 (s, NMe), 2.72 (t, J=6.5 Hz, C-4-H), 3.10 (m, C-2-H), 3.38 (d, J=6 Hz, Ar–C<u>H</u>$_2$–CH=), 4.50 (br, NH. Disappeared on addition of deuterium oxide), 4.93 and 5.16 (each m, CH_2–CH=C<u>H</u>$_2$), 5.90 (m, CH_2–C<u>H</u>=CH_2. Double d, J=9, 18 Hz on irradiation at δ 3.38), 6.40 (m, Ar–H). Treatment of **18** with diazomethane in ethanol and purification of the product (33 mg) by column chromatography (silica gel 0.8 g, dichloromethane) gave 15 mg of **6b**, which was identical with an authentic specimen of **6b** (NMR spectrum). b) Reaction condition D: Column chromatography of the crude product (395 mg) on silica gel (18 g) with benzene–ethyl acetate (98:2) gave the starting material **2b** (98 mg, 24.0% yield) and **6b**[1b] (261 mg, 63.8% yield). Elution with methanol afforded 15 mg of a polar mixture.

Rearrangement of 2d under Reaction Condition D——The crude product (429 mg) was subjected to flash column chromatography on silica gel (43 g) with petroleum ether–ethyl acetate (95:5, 94:6, 91:9). The starting amine **2d** (17 mg, 3.9% recovery) was recovered in the first eluate, then 8-*sec*-butenyl-6-methoxy-1,2,3,4-tetrahydroquinoline **6d** emerged. **6d**: colorless liquid. MS: m/z: 217 (M^+), 202 (base). IR ν_{max}^{film} cm^{-1}: 3400, 1630, 914. NMR δ: 1.35 (3H, d, J=7 Hz, CH–<u>Me</u>. Singlet on irradiation at δ 3.43), 1.90 (2H, quintet, J=6 Hz, C-3-H), 2.80 (2H, t, J=6 Hz, C-4-H), 3.30 (2H, t, J=5.5 Hz, C-2-H), 3.33 (NH. Overlapping with the signals at δ 3.30. Exchangeable with deuterium oxide), 3.43 (1H, m, Ar–C<u>H</u>MeCH=CH_2), 3.73 (3H, s, OMe), 5.00 and 5.23 (2H, each m, CH–CH=C<u>H</u>$_2$), 5.93 (1H, ddd, J=6, 9, 17.5 Hz, CH–C<u>H</u>=CH_2. Double d, J=9, 17.5 Hz by irradiation at δ 3.43), 6.45 (1H, d, J=3 Hz, Ar–H), 6.57 (1H, d, J=3 Hz, Ar–H). This liquid was 90.9% pure. The contaminant (9.1%) had essentially the same fragmentation pattern (M^+ and base at m/z 217) as **6d** according to GC-MS. Further elution with ethyl acetate–acetone gave 45 mg of an intractable mixture.

Rearrangement of 2f under Reaction Condition D——The crude product (436 mg) was chromatographed on silica gel (13 g) with dichloromethane–acetone (1, 2.5%), giving the starting amine **2f** (184 mg, 39.7% recovery) and **1b** (76 mg, 23.2% yield). Elution with methanol gave a polar product (142 mg, 28.4%), which was purified by column chromatography on silica gel (4 g) with dichloromethane–methanol (96:4), affording 87 mg (17.4% yield) of 1-(3-hydroxy-3-methylbutyl)-6-methoxy-1,2,3,4-tetrahydroquinoline **19**: oil. MS m/z: 249 (M^+), 176 (base). IR ν_{max}^{film} cm^{-1}: 3430, 1265, 1240, 1203, 1023, 800. NMR δ: 1.26 (6H, s, CMe_2), 1.73 (1H, t, J=7.5 Hz, N–CH_2–C<u>H</u>CMe_2OH. Singlet on irradiation at δ 3.45), 1.92 (2H, m, C-3-H), 2.53 (1H, OH. Disappeared on addition of deuterium oxide), 2.83 (2H, t, J=6 Hz, C-4-H), 3.26 (2H, t, J=5.5 Hz, C-2-H. Singlet on irradiation at δ 1.92), 3.45 (2H, t, J=7.5 Hz, N–C<u>H</u>$_2$–CH_2–. Singlet when irradiated at δ 1.73), 3.80 (3H, s, OMe), 6.70 (1H, br s, Ar–H), 6.77 (2H, s, Ar–H).

6-Allylkairoline 9a——Acetic acid (0.2+0.15 ml) was added in two portions with an interval of 30 min into a solution of **7a** (245 mg, 1.4 mmol), 37% formalin (1.2 ml) and sodium cyanoborohydride (328 mg, 5.2 mmol) in acetonitrile (8 ml).[9] The reaction mixture was stirred overnight. The crude product (284 mg) obtained by dilution of the mixture with 1 N sodium hydroxide and extractions with ether was purified by column chromatography on silica gel (8 g) with benzene. **9a**: colorless liquid. MS m/z: 187 (M^+, base). IR ν_{max}^{film} cm^{-1}: 3080, 1640, 912, 807. NMR δ: 1.83 (2H, quintet, J=6 Hz, C-3-H), 2.63 (2H, t, J=6 Hz, C-4-H), 2.73 (3H, s, N–Me), 3.07 (2H, t, J=6 Hz, C-2-H), 3.13 (2H, d, J=6 Hz, Ar–CH_2–CH=CH_2. Singlet on irradiation at δ 5.87), 4.76—5.10 (2H, m, Ar–CH_2–CH=C<u>H</u>$_2$), 5.87 (1H, tdd, J=6, 9, 17 Hz, Ar–CH_2–C<u>H</u>=CH_2), 6.43 (1H, d, J=7.5 Hz, C-8-H), 6.70 (1H, br s, C-5-H), 6.77 (1H, dd, J=1.5, 7.5 Hz, C-7-H). Picrate: yellow crystals, mp 107—108 °C (ethanol). *Anal.* Calcd for $C_{19}H_{20}N_4O_7$: C,

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54.81; H, 4.84; N, 13.46%. Found: C, 54.76: H, 4.92; N, 13.43%.

Rearrangement of 4c——a) Reaction condition A: The crude product (303 mg) was chromatographed on silica gel (16 g) with dichloromethane. The *ortho* rearrangement product **8c** (14 mg) was collected in 3.5% yield. The other fractions were combined and chromatographed on silica gel (50 g) with dichloromethane to give the *para* rearrangement product **9c**. Both products were also obtained by *N*-methylation of **6c** and **7c**, respectively. The reaction of **6c** (70 mg, 0.33 mmol) with 35% formalin (0.3 ml), sodium cyanoborohydride (80 mg) and acetic acid (0.1+0.1 ml) in acetonitrile (5 ml) afforded **8c** in 65% yield (49 mg). Similarly, **9c** was prepared from **7c** (70 mg) in 68.5% yield (52 mg). 8-*sec*-Butenylkairoline **8c**: colorless liquid. MS *m/z*: 201 (M^+), 186 (base). IR ν_{max}^{film} cm^{-1}: 1632, 915. NMR δ: 1.30 (3H, d, J=7 Hz, CH–Me), 1.87 (2H, m, C-3-H), 2.73 (3H, s, N–Me), 2.53 (2H, t J=6 Hz, C-4-H), 3.10 (2H, t, J=5.5 Hz, C-2-H), 4.07 (1H, m, Me–CH–CH=CH_2), 4.93 and 5.17 (2H, each m, CH–CH=CH_2), 6.13 (1H, ddd, J=6, 9, 18 Hz, CH–CH=CH_2), 7.00 (3H, m, Ar–H). Picrate: mp 166—167 °C (ethanol). *Anal.* Calcd for $C_{20}H_{22}N_4O_7$: C, 55.81; H, 5.15; N, 13.12%. Found: C, 56.07; H, 5.04; N, 12.89%. 6-Crotylkairoline **9c** (*E* : *Z*= 95 : 5): colorless liquid. MS *m/z*: 201 (M^+, base). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1610, 965. NMR δ: 1.67 (3H, br d, J=4 Hz, CH=CH–Me), 1.93 (2H, m, C-3-H), 2.73 (2H, t, J=6 Hz, C-4-H), 2.83 (3H, s, N–Me), 3.17 (4H, m, C-2-H+Ar–CH_2–CH=), 5.50 (2H, m, Ar–CH_2–CH=CH–Me), 6.50 (1H, d, J=8 Hz, C-8-H), 6.80 (1H, br s, C-5-H), 6.83 (1H, br d, J=8 Hz, C-7-H). b) Reaction condition B: Column chromatography of the crude product (301 mg) on silica gel (50 g, dichloromethane) gave the *ortho* product **8c** (42 mg, 10.9% yield). The *para* product **9c** could not be isolated in a pure state, but its presence was confirmed by comparisons of the impure specimen with an authentic sample (GLC, TLC and NMR spectrum).

Rearrangement of 4e——a) Reaction condition B: The crude product (405 mg) obtained from the reaction of **4e** (X=Br) gave essentially a single spot on TLC (silica gel, petroleum ether–ethyl acetate=96 : 4). Kugelrohr distillation at 132 °C/23 mmHg gave 220 mg (74.7% yield) of kairoline **3a**. After further removal of distillate (39 mg) at 146 °C, the residue (72 mg) was purified by chromatography on silica gel (21 g) with benzene. The *para* rearrangement product **9e** (60 mg) was obtained in 13.9% yield with 82% purity . b) **4e** ($X=BF_4$) under reaction condition B: The crude product (389 mg) was subjected to flash column chromatography on silica gel (80 g) with petroleum ether–ethyl acetate (95 : 5) and separated into three major fractions I (113 mg), II (207 mg) and III (46 mg), which were analyzed by GLC.

	Products (%)			
	8e	**9e**	**3a**	**16**
I	10.8	10.9	45.6	32.7
II	9.7	61.3	18.9	10.1
III	4.1	86.3	5.5	4.1

Fraction III was identical with **9e** obtained by the above reaction a). 6-Prenylkairoline **9e** (86.3% purity): MS *m/z*: 215 (M^+, base). IR ν_{max}^{film} cm^{-1}: 1615, 1512, 1325, 1210, 1197; $\nu_{max}^{CCl_4}$ cm^{-1}: 1618, 1512, 1320, 1205, 1093. NMR δ: 1.74 (6H, s, $=CMe_2$), 2.03 (2H, quintet, J=6 Hz, C-3-H), 2.77 (2H, t, J=6 Hz, C-4-H), 2.84 (3H, s, N–Me), 3.17 (2H, t, J=5.5 Hz, C-2-H), 3.20 (2H, d, J=7 Hz, Ar–CH_2–CH=), 5.34 (1H, mt, J=7 Hz, Ar–CH_2–CH=CMe_2. Triplet, J=7 Hz on irradiation at δ 1.74), 6.54 (1H, d, J=8 Hz, C-8-H), 6.80 (1H, br s, C-5-H), 6.89 (1H, dd, J=1.5, 8 Hz, C-7-H). The product **9e** was also obtained from **7e**. Methylation of **7e** (195 mg in 68.5% purity) with 37% formalin (0.8 ml), sodium cyanoborohydride (201 mg) and acetic acid (0.15+0.1 ml) in acetonitrile (5 ml) for 2 h followed by column chromatography of the crude product (210 mg) on silica gel (5.0 g) with dichloromethane gave **9e** in 84% purity. This product was identical with the above specimen **9e**. The structures of other products in the three fractions were deduced from detailed GLC and NMR spectral analyses. In fraction I, signals assignable to **8e** were seen at δ 1.37 (s, CMe_2), 4.90 and 5.08 (each m, CH=CH_2) and 6.07 (dd, J=10, 17 Hz, CH=CH_2). Signals due to **16** were seen at δ 1.73 (br s, $=CMe_2$), 2.70 (s, N–Me), 3.40 (d, J=7 Hz, Ar–CH_2–CH=CMe_2) and 5.37 (br t, J=7 Hz, Ar–CH_2–CH=CMe_2. Triplet, J=7 Hz when irradiated at δ 1.73). A major component (45.6%) of fraction I was kairoline **3a** which shows a distinct singlet at δ 2.87 due to N–Me. The dimethyl group on the prenyl moiety of **9e** and **16** appears at δ 1.37 (s) and the dimethyl group of **8e** appears at δ 1.73 (s). The ratio of integrated intensities of these two signals is 4 : 1, which corresponds to the ratio of the amount of **9e**+**16** to **8e**. GLC gave (**9e**+**16**) : **8e**=43.6 : 10.3, which is in good agreement with the above NMR results. A similar ratio was obtained from the integrals of the signals at δ 4.90 and 5.08 (CH=CH_2) for **8e** and δ 5.37 (Ar–CH_2–CH=CMe_2) for **9e** and **16**. GC-MS of fraction I—**3a**: *m/z* 147 (M^+), 146 (base). Identical with the authentic spectrum; **16**: *m/z* 215 (M^+, base), 200, 160. Fragmentation pattern quite similar to that of **9e**; **8e**: *m/z* 215 (M^+), 200 (base), 172. c) Reaction condition A: The crude product (362 mg) obtained from **4e** (X=Br) was analyzed in detail by GC-MS and compared with the above products. Two hydrated products (M^+ *m/z*: 233) were detected in 2.8 and 3.4% yields in addition to **8e**, **9e**, **3a** and **16**.

Rearrangement of 4d under Reaction Condition B——The bromide **4d** (X=Br) (716 mg, 2.3 mmol) gave 456 mg of crude product. Flash column chromatography (silica gel 47 g) with petroleum ether–ethyl acetate (95 : 5, 94 : 6, 93 : 7)

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afforded **8d** (413 mg, 77.9% yield) and **3b** (17 mg, 4.2% yield). 8-*sec*-Butenyl-6-methoxy-1-methyl-1,2,3,4-tetrahydroquinoline **8d**: colorless oil. MS *m/z*: 231 (M^+), 216 (base). IR ν_{max}^{film} cm^{-1}: 1630, 1300, 1198, 1182, 1055, 908. NMR δ: 1.33 (3H, d, $J=7$ Hz, CH–Me), 1.90 (2H, m, C-3-H), 2.67 (3H, s, N–Me), 2.83 (2H, t, $J=6$ Hz, C-4-H), 3.05 (2H, t, $J=5.5$ Hz, C-2-H), 3.70 (3H, s, OMe), 4.03 (1H, m, CH–Me), 4.73 and 5.13 (2H, each m, $CH=CH_2$), 6.07 (1H, ddd, $J=5.5$, 10, 18 Hz, $CH-CH=CH_2$. Double d, $J=10$, 18 Hz, on irradiation at δ 4.03), 6.43 (1H, d, $J=3$ Hz, Ar–H), 6.60 (1H, d, $J=3$ Hz, Ar–H). Picrate: mp 157.5—158 °C (ethanol–chloroform). *Anal.* Calcd for $C_{21}H_{24}N_4O_8$: C, 54.78; H, 5.25; N, 12.17%. Found: C, 54.76; H, 5.35; N, 12.17%. This product **8d** was also obtained from **6d**. The treatment of **6d** (51 mg) with sodium cyanoborohydride (52 mg), 37% formalin (0.2 ml) and acetic acid (0.1 + 0.05 ml) in acetonitrile (4 ml), and subsequent purification of the crude product (56 mg) by column chromatography (silica gel 1.1 g, benzene), gave **6d** in 99% yield; this product was identical with the above specimen by GLC and NMR comparisons.

Rearrangement of 4f ($X=BF_4$) under Reaction Condition B——The crude product (350 mg) was subjected to Kugelrohr distillation at 108 °C/4 mmHg, giving 205 mg (57.8% yield) of **3b**. The distillation residue (140 mg) was separated by preparative TLC (silica gel, chloroform). Besides **3b** (13 mg), 27 mg of rearrangement product was isolated; it was homogeneous on TLC but was found to be a mixture of two products (21.6 and 78.2%) by GLC analysis. These two products have essentially the same fragmentation patterns in GC-MS. Major component: MS *m/z*: 245 (M^+, base). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1410, 1085, 885, 860. NMR δ: 1.73 (6H, br s, $=CMe_2$), 1.93 (2H, m, C-3-H), 2.76 (2H, t, $J=6.5$ Hz, C-4-H), 2.84 (3H, s, N–Me), 3.10 (2H, t, $J=5.5$ Hz, C-2-H. Singlet when irradiated at δ 1.93), 3.26 (2H, d, $J=8$ Hz, $Ar-CH_2-CH=$. Broad s on irradiation at δ 5.30). 3.73 (3H, s, OMe), 5.30 (1H, mt, $J=7$ Hz, $Ar-CH_2-CH=CMe_2$. Triplet, $J=7$ Hz when irradiated at δ 1.73), 6.47 (1H, s, Ar–H), 6.50 (1H, s, Ar–H).

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