The Claisen Rearrangement. III.[1] *para* Claisen Rearrangement to Nitrogen in Allyl 3-Substituted 4-Quinolyl Ethers

YASUO MAKISUMI

Shionogi Research Laboratory, Shionogi and Company, Ltd., Fukushima-ku, Osaka, Japan

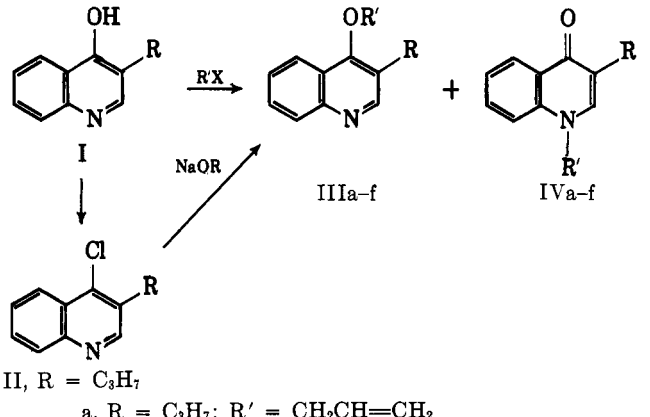
Received November 17, 1964

Thermal rearrangement of allyl 3-substituted 4-quinolyl ethers affords the corresponding N-allyl-4(1H)-quinolones in quantitative yields by migration of an allyl group to the *para* ring-nitrogen atom. The present investigation provides evidence that this rearrangement proceeds through a dienone-type intermediate with double inversion of a migrating group.

Although it has been known that, on heating, lactim ethers of aromatic heterocycles undergo rearrangement to isomeric and stable lactam forms with migration of an alkyl group to the *ortho* or *para* ring-nitrogen atom, Claisen rearrangement to a *para* ring-nitrogen atom is, to our knowledge, unreported.[2] However, a possibility of *para* Claisen rearrangement to the ring-nitrogen atom in allyl 3-substituted 4-quinolyl ethers was expected from the result of the preceding work[1] that allyl 4-quinolyl ethers readily undergo *ortho* Claisen rearrangement. It was of interest to determine whether rearrangement of allyl 3-substituted 4-quinolyl ethers is a Claisen rearrangement or a lactim ether lactam isomerization such as had been reported for 4-alkoxyquinolines.[3]

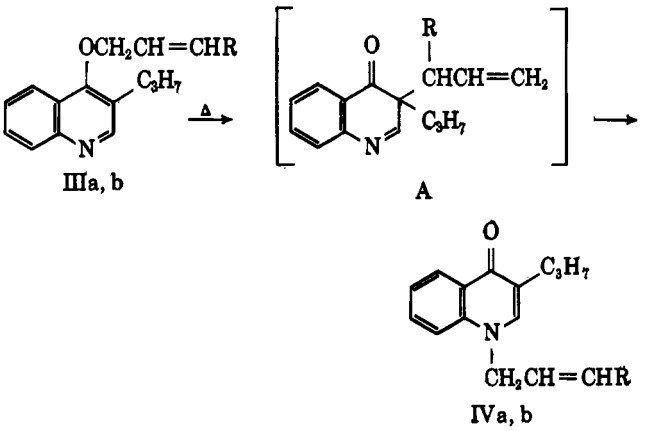
For this purpose, allyl and crotyl ethers (IIIa and IIIb) of 3-propyl-4-quinolinol (I, R = C_3H_7) were prepared by the two routes shown in Chart I and subjected to rearrangement reaction. Alkylation of I, R = C_3H_7, with allylic bromides in the presence of sodium ethoxide resulted in the formation of two kinds of the alkylated products: the allylic ethers, identical with IIIa and IIIb obtained by reaction of 4-chloro-3-propylquinoline (II) with sodium allylic oxides, and N-allylic 3-propyl-4(1H)-quinolones (IVa and IVb). The structures of IVa and IVb were confirmed by spectral analyses. Both of the compounds showed absorption shapes characteristic for the 4(1H)-quinolone nucleus in the ultraviolet spectrum[1,4] (see Table I) and exhibited carbonyl bands at 1630 cm.$^{-1}$ corresponding to those of the 1-alkyl-4(1H)-quinolones in the infrared spectrum.[1,5] The allylic group of IIIb and IVb was confirmed to be the crotyl group from the absorption of the —CH=CH— group. The fact that O- and N-α-methylallyl products were not formed in the alkylation with crotyl bromide rules out any possible allylic rearrangement in the process. Moreover, Chart I summarizes the syntheses of four additional allylic ethers IIIc–f and of the N-allylic 4(1H)-quinolones IVc–f relevant to the study of their rearrangements.

CHART I



a, R = C_3H_7; R′ = $CH_2CH{=}CH_2$
b, R = C_3H_7; R′ = $CH_2CH{=}CHCH_3$
c, R = $CH_2CH{=}CH_2$; R′ = $CH_2CH{=}CHCH_3$
d, R = $CH(CH_3)CH{=}CH_2$; R′ = $CH_2CH{=}CH_2$
e, R = $CH_2CH{=}CH_2$; R′ = $CH_2C(CH_3){=}CH_2$
f, R = $CH_2C(CH_3){=}CH_2$; R′ = $CH_2CH{=}CH_2$

Rearrangement of the allyl ether IIIa at 200° without solvent afforded a sole product in an almost quantitative yield. This product was proved to be identical with IVa by infrared spectral comparison. Analogously, when IIIb was heated at 200°, IVb was quantitatively obtained as a sole rearrangement product. Thus, it was confirmed that allyl 3-substituted 4-quinolyl ethers readily undergo rearrangement to give 3-substituted 1-allyl-4(1H)-quinolones in quantitative yields by migration of the allyl group to the *para* ring-nitrogen atom.



It has been established that the *para* Claisen rearrangement[6] proceeds through a dienone intermediate with double inversion of a migrating allyl group.

In order to determine whether rearrangement of the ethers IIIa and IIIb proceeds by a mechanism

(1) Part II: Y. Makisumi, *Chem. Pharm. Bull.* (Tokyo), **12**, 1424 (1964).
(2) It should be noted that the author observed *para* Claisen rearrangement to nitrogen in the studies of "out-of-ring" Claisen rearrangement [see Y. Makisumi, *Tetrahedron Letters*, **No. 13**, 699 (1964); **No. 25**, 1635 (1964)].
(3) M. Conrad and L. Limpach, *Ber.*, **20**, 948 (1887); M. Conrad and F. Eckhardt, *ibid.*, **22**, 73 (1889); H. Meyer, *Monatsh.*, **27**, 259, 265 (1906).
(4) G. W. Ewing and E. A. Steck, *J. Am. Chem. Soc.*, **68**, 2181 (1946).
(5) A. R. Katritzky, "Physical Methods in Heterocyclic Chemistry," Vol. II, Academic Press Inc., New York, N. Y., 1963, p. 263, and references cited therein.
(6) For an excellent recent review of the Claisen rearrangement, see S. J. Rhoads, "Molecular Rearrangements," Vol. I, P. de Mayo, Ed., Interscience Publishers, Inc., New York, N. Y., 1963, p. 655.

TABLE I

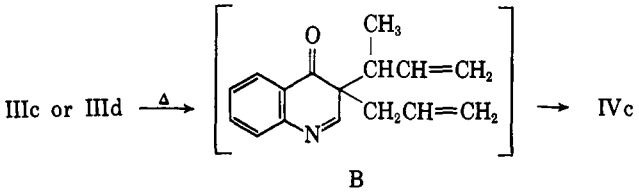
ULTRAVIOLET SPECTRA OF 4(1H)-QUINOLONES

Compd.	λ_{max}, mμ (log ε)					
IVa	213 (4.34)	245.5(4.35)	282 (3.31)[a]	292.5(3.44)	331.5(4.10)	345.5(4.18)
IVb	213 (4.39)	246 (4.39)	282.5(3.35)[a]	292.5(3.47)	331.5(4.14)	346 (4.19)
IVc	212.5(4.43)	245.5(4.41)	282 (3.39)[a]	293 (3.51)	331.5(4.13)	344.5(4.19)
IVd	213 (4.42)	245.5(4.45)	282 (3.43)[a]	292 (3.57)	330 (4.17)	344.5(4.24)
IVe	212.5(4.40)	246 (4.40)	282 (3.43)[a]	292 (3.54)	330.5(4.14)	344.5(4.22)
IVf	214 (4.41)	246 (4.40)	283 (3.40)[a]	293 (3.52)	330.5(4.13)	345 (4.18)

[a] Shoulder.

involving dienone-type intermediate A or by that[1,7,8] involving the cleavage of the ether bond and the consecutive intermolecular alkylation with an allylic fragment such as has been observed in isomerization of lactim ethers of heterocycles to isomeric lactam forms, the rearrangements of crotyl 3-allyl-4-quinolyl ether (IIIc) and allyl 3-(1-methylallyl)-4-quinolyl ether (IIId) were examined. If a dienone-type intermediate were involved, rearrangement of the crotyl ether IIIc would lead by way of the intermediate B not only to the 4(1H)-quinolone IVc in which the crotyl group had migrated to a *para* position of the pyridine ring but also to the 4(1H)-quinolone IVd in which an allyl group appeared in the *para* position and the crotyl group remained in the *ortho* position as a 1-methylallyl group by its inversion. Similarly, the allyl ether IIId should give rise to a mixture of the 4(1H)-quinolones IVc and IVd.

Rearrangement of the crotyl ether IIIc was examined by heating at 200° without solvent. Careful investigation of the reaction mixture showed that IIIc rearranged to the expected IVc in a quantitative yield with formation of no detectable amount of the other expected product IVd. Rearrangement of the allyl ether IIId also gave a single product, identical with IVc, in a quantitative yield.

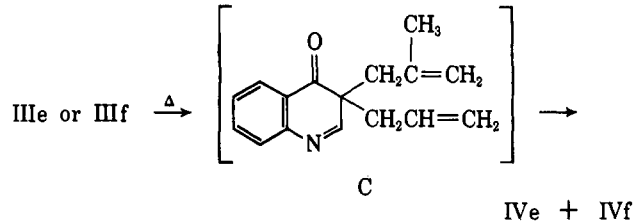


B

Although IVd was not detectable in both rearrangement reactions, these results show the probability that the migration of an allylic group to a *para* ring-nitrogen atom would proceed through the dienone-type intermediate, 3-allyl-3-(1-methylallyl)-4(3H)-quinolone (B), with double inversion of a migrating allylic group. Since migration of an allylic group to an *ortho* position is inevitably associated with inversion, it may be assumed that a 1-methylallyl group migrates more readily than an unsubstituted allyl group.[9] It may be considered that this preferential migration of the 1-methylallyl group is based on the following two reasons. First, the inductive effect of the α-methyl group of an allyl group would accelerate migration of the 1-methylallyl group in comparison with an unsubstituted allyl group. Secondly, a steric requirement in a dienone-type intermediate would promote migration of a more crowded group, a 1-substituted allyl group, than an unsubstituted allyl group to be stabilized by relief of steric strain.

If these electronic and steric effects of an α-substituent in an allyl group are inevitable, a β-substituted allyl group, which is almost unaffected by such effects, would migrate to a ring nitrogen at a nearly equal rate as that of an unsubstituted allyl group. Then, it is expected that rearrangement of methallyl 3-allyl-4-quinolyl ether (IIIe) would lead by way of the intermediate C to a mixture of 1-methallyl-3-allyl-4(1H)-quinolone (IVe) and 1-allyl-3-methallyl-4(1H)-quinolone (IVf), and then allyl 3-methallyl-4-quinolyl ether (IIIf) also should give rise to a mixture of IVe and IVf.

The rearrangements of the ethers IIIe and IIIf were carried out by heating the ether without solvent at 200°. A quinolone product obtained in a quantitative yield from the methallyl ether IIIe was confirmed to be a mixture of IVe and IVf by infrared spectral analysis. N.m.r. spectral analysis showed that this product was a mixture of IVe and IVf in the proportion of about 1:1. The allyl ether IIIf also completely rearranged to give a mixture of IVe and IVf in the same proportion of 1:1 that was observed in the reaction of the methallyl ether IIIe.



C

IVe + IVf

The results reported here are consistent, thus, with a mechanism of rearrangement by way of a dienone intermediate in which the allylic group migrating from the ether must be bonded to an *ortho* carbon in such a manner as to become equivalent to an allylic group originally in that position.

Experimental

Melting points were determined using a Kofler hot stage and are uncorrected. The infrared spectra were recorded in chloroform solution and the ultraviolet spectra were run in ethanol solution. The n.m.r. spectra were obtained in deuteriochloroform solution with a Varian A-60 spectrometer, using tetramethylsilane as an internal standard.

3-Propyl-4-quinolinol (I, R = C_3H_7).—A solution of 5.55 g. (0.03 mole) of 3-allyl-4-quinolinol[1] (I, R = $CH_2CH{=}CH_2$) in 100 ml. of ethanol was hydrogenated over 0.6 g. of 10% palladium on charcoal at room temperature and 1.0 equiv. of hydrogen

(7) K. B. Wiberg, T. M. Shryne, and R. R. Kintner, *J. Am. Chem. Soc.*, **79**, 3160 (1957).

(8) Y. Makisumi, *Chem. Pharm. Bull.* (Tokyo), **11**, 851, 859 (1963).

(9) The earlier observations[10,11] concerning the case of migration of α-substituted allyl groups should be noted.

(10) S. J. Rhoads, R. Raulins, and R. Reynolds, *J. Am. Chem. Soc.*, **75**, 2531 (1953).

(11) E. N. Marvell and R. Teranishi, *ibid.*, **76**, 6165 (1954).

was absorbed. The catalyst was filtered off and the solvent was removed under reduced pressure. The residue was recrystallized from benzene to afford 5.23 g. (95%) of colorless pillars, m.p. 171–172°.

Anal. Calcd. for $C_{12}H_{13}NO$: C, 76.97; H, 7.00; N, 7.48. Found: C, 76.76; H, 6.90; N, 7.57.

4-Chloro-3-propylquinoline (II).—A mixture of 2.0 g. of I (R = C_3H_7) and 6 ml. of phosphorus oxychloride was refluxed for 2 hr. The excess phosphorus oxychloride was removed under reduced pressure and the residual sirup was poured into ice–water. The solution was made alkaline with 15% sodium hydroxide solution and extracted with ether. The ethereal extract was washed with water and dried over magnesium sulfate. Upon removal of the solvent, 2.2 g. of an oily residue was left, which was distilled to give 1.98 g. (90%) of II as a colorless oil, b.p. 114–115° (0.09 mm.).

Anal. Calcd. for $C_{12}H_{12}ClN$: C, 70.07; H, 5.88; N, 6.81. Found: C, 70.15; H, 5.93; N, 6.78.

The picrate had m.p. 154–155° (from ethanol).

Anal. Calcd. for $C_{12}H_{12}ClN \cdot C_6H_3N_3O_7$: C, 49.69; H, 3.47; N, 12.88. Found: C, 49.95; H, 3.56; N, 13.06.

4-Allyloxy-3-propylquinoline (IIIa).—To a solution of 350 mg. (0.015 g.-atom) of sodium dissolved in 20 ml. of allyl alcohol was added 2.06 g. (0.01 mole) of II. The mixture was heated under reflux for 5 hr. After cooling, the precipitated sodium chloride was filtered off and the filtrate was evaporated under reduced pressure. The residue was dissolved in ether, washed with water, and dried over magnesium sulfate. Evaporation of the solvent gave 1.75 g. of an oil, which was chromatographed on alumina. Elution with benzene afforded 1.49 g. (72.3% recovery) of the unchanged material (II). Elution with chloroform gave 195 mg. (8.6%) of IIIa as a colorless oil, b.p. 117–118° (0.4 mm.), after distillation.

Anal. Calcd. for $C_{15}H_{17}NO$: C, 79.29; H, 7.54; N, 6.16. Found: C, 79.31; H, 7.63; N, 6.09.

The picrate had m.p. 143–144° (from ethanol).

Anal. Calcd. for $C_{15}H_{17}NO \cdot C_6H_3N_3O_7$: C, 55.26; H, 4.42; N, 12.28. Found: C, 55.16; H, 4.38; N, 12.31.

4-Crotyloxy-3-propylquinoline (IIIb).—II (2.06 g., 0.01 mole) was added to a solution of 350 mg. (0.015 g.-atom) of sodium dissolved in 20 ml. of crotyl alcohol. The mixture was refluxed for 5 hr. Work-up of the reaction mixture as for the preparation of IIIa gave 260 mg. (10.8%) of IIIb, b.p. 118–119° (0.15 mm.), ν_{max} 966 cm.$^{-1}$ (—CH=CH—).

Anal. Calcd. for $C_{16}H_{17}NO$: C, 79.63; H, 7.94; N, 5.80. Found: C, 79.52; H, 7.99; N, 5.75.

The picrate had m.p. 128–129° (from ethanol).

Anal. Calcd. for $C_{16}H_{17}NO \cdot C_6H_3N_3O_7$: C, 56.17; H, 4.71; N, 11.91. Found: C, 56.00; H, 4.82; N, 11.80.

4-Allyloxy-3-propylquinoline (IIIa) and 1-Allyl-3-propyl-4(1H)-quinolone (IVa).—To a solution of 250 mg. (0.011 g.-atom) of sodium in 20 ml. of absolute ethanol was added 1.87 g. (0.01 mole) of I (R = C_3H_7). To this was added 1.33 g. (0.011 mole) of allyl bromide. The mixture was refluxed for 5 hr. The precipitated sodium bromide was filtered off and the solvent was removed under reduced pressure. The residue was dissolved in ether, washed with 5% sodium hydroxide solution and water, and dried over magnesium sulfate. Evaporation of the solvent gave 2.18 g. of a crude product, which was chromatographed on alumina. Elution with benzene–chloroform (3:1) afforded 450 mg. (19%) of a colorless oil which was found to be identical by infrared spectrum with IIIa prepared from II. Elution with ethyl acetate gave 1.43 g. (63%) of IVa as a colorless oil, b.p. 180–181° (0.3 mm.), on distillation: ν_{max} 1631 (C=O), 990, and 927 (—CH=CH_2) cm.$^{-1}$. The ultraviolet spectrum showed the 4(1H)-quinolone nucleus (Table I).

Anal. Calcd. for $C_{15}H_{17}NO$: C, 79.29; H, 7.54; N, 6.16. Found: C, 79.35; H, 7.63; N, 6.02.

The picrate had m.p. 115–116° (from ethanol).

Anal. Calcd. for $C_{15}H_{17}NO \cdot C_6H_3N_3O_7$: C, 55.26; H, 4.42; N, 12.28. Found: C, 55.42; H, 4.57; N, 12.50.

4-Crotyloxy-3-propylquinoline (IIIb) and 1-Crotyl-3-propyl-4-(1H)-quinolone (IVb).—To a solution of 1.87 g. (0.01 mole) of I (R = C_3H_7) and sodium ethoxide [prepared from 250 mg. (0.011 g.-atom) of sodium] in 20 ml. of absolute ethanol, was added 1.5 g. (0.011 mole) of crotyl bromide. The mixture was refluxed for 5 hr. Work-up of the reaction mixture as described above gave 1.85 g. of a crude product, which was chromatographed on alumina. Elution with benzene–chloroform (2:1) afforded 430 mg. (18%) of a colorless oil which was found to be identical by infrared spectrum with IIIb prepared from II. Elution with ethyl acetate gave 1.34 g. (55.6%) of IVb as a colorless oil, b.p. 195–196° (0.4 mm.), on distillation: ν_{max} 1630 (C=O) and 965 (—CH=CH—) cm.$^{-1}$. The ultraviolet spectrum showed the 4(1H)-quinolone nucleus (Table I).

Anal. Calcd. for $C_{16}H_{19}NO$: C, 79.63; H, 7.94; H, 5.80. Found: C, 79.48; H, 8.07; N, 5.69.

The picrate had m.p. 128–129° (from ethanol).

Anal. Calcd. for $C_{16}H_{19}NO \cdot C_6H_3N_3O_7$: C, 56.17; H, 4.71; N, 11.91. Found: C, 55.93; H, 4.82; N, 11.80.

3-Allyl-4-crotyloxyquinoline (IIIc) and 3-allyl-1-crotyl-4(1H)-quinolone (IVc) were prepared by alkylation of 1.85 g. (0.01 mole) of I (R = $CH_2CH=CH_2$) with crotyl bromide in the same way as above and isolated by chromatography on alumina. Elution with benzene–chloroform (2:1) afforded 700 mg. (29.3%) of IIIc as a colorless oil: b.p. 125° (0.2 mm.); infrared spectrum, 966 (—CH=CH—), 993, and 920 (—CH=CH_2) cm.$^{-1}$, and no C=O band.

Anal. Calcd. for $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85. Found: C, 80.24; H, 7.18; N, 5.68.

The picrate had m.p. 138° (from ethanol).

Anal. Calcd. for $C_{16}H_{17}NO \cdot C_6H_3N_3O_7$: C, 56.41; H, 4.30; N, 11.96. Found: C, 56.20; H, 4.39; N, 11.90.

Elution with ethyl acetate gave 1.26 g. (52.7%) of IVc as a colorless oil: b.p. 166° (0.04 mm.); ν_{max} 1630 (C=O), 964 (—CH=CH—), 996, and 917 (—CH=CH_2) cm.$^{-1}$. The ultraviolet spectrum showed the 4(1H)-quinolone nucleus (Table I).

Anal. Calcd. for $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85. Found: C, 80.31; H, 7.14; N, 5.79.

4-Allyloxy-3-(1-methylallyl)quinoline (IIId) and 1-allyl-3-(1-methylallyl)-4(1H)-quinolone (IVd) were prepared by alkylation of 1.99 g. (0.01 mole) of 3-(1-methylallyl)-4-quinolinol[1] (I, R = $CH(CH_3)CH=CH_2$) with allyl bromide in the same way as above and isolated by chromatography on alumina. Elution with benzene afforded 412 mg. (17.2%) of IIId as a colorless oil: b.p. 115–116° (0.2 mm.); infrared spectrum, 978 and 922 (—CH=CH_2) cm.$^{-1}$ and no C=O band.

Anal. Calcd. for $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85. Found: C, 80.42; H, 7.21; N, 5.69.

The picrate had m.p. 166–166.5° (from ethanol).

Anal. Calcd. for $C_{16}H_{17}NO \cdot C_6H_3N_3O_7$: C, 56.41; H, 4.30; N, 11.96. Found: C, 56.21; H, 4.32; N, 11.90.

Elution with chloroform gave 1.57 g. (65.7%) of IVd as colorless prisms, m.p. 69–70°, on recrystallization from benzene–petroleum ether (b.p. 60–90°): ν_{max} 1628 (C=O), 988, and 921 (—CH=CH_2) cm.$^{-1}$. The ultraviolet spectrum showed the 4(1H)-quinolone nucleus (Table I).

Anal. Calcd. for $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85. Found: C, 80.56; H, 7.21; N, 5.82.

3-Allyl-4-methallyloxyquinoline (IIIe) and 3-allyl-1-methallyl-4(1H)-quinolone (IVe) were prepared by alkylation of 3.7 g. (0.02 mole) of I (R = $CH_2CH=CH_2$) with methallyl chloride in the same way as above and isolated by chromatography on alumina. Elution with benzene gave 899 mg. (18.8%) of IIIe as a colorless oil, b.p. 127–128° (0.15 mm.); the infrared spectrum had no C=O band.

Anal. Calcd. for $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85. Found: C, 80.46; H, 7.21; N, 5.79.

The picrate had m.p. 149.5° (from ethanol).

Anal. Calcd. for $C_{16}H_{17}NO \cdot C_6H_3N_3O_7$: C, 56.41; H, 4.30; N, 11.96. Found: C, 56.42; H, 4.46; N, 12.19.

Elution with chloroform afforded 2.51 g. (52.5%) of IVe as colorless prisms, m.p. 80.5–81.5°, on recrystallization from benzene–petroleum ether: ν_{max} 1630 (C=O), 996, 916 (—CH=CH_2), and 906 (>C=CH_2) cm.$^{-1}$. The ultraviolet spectrum showed the 4(1H)-quinolone nucleus (Table I). The n.m.r. spectrum showed a singlet at τ 8.24 (CH_3) and a doublet (J = 6.5 c.p.s.) centered at 6.54 (CH_2 at C-3).

Anal. Calcd. for $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85. Found: C, 80.23; H, 7.23; N, 5.91.

4-Allyloxy-3-methallylquinoline (IIIf) and 1-Allyl-3-methallyl-4(1H)-quinolone (IVf).—These were prepared by alkylation of 1.99 g. (0.01 mole) of 3-methallyl-4-quinolinol[1] (I, R = $CH_2C(CH_3)=CH_2$) with allyl bromide in the same way as above and isolated by chromatography on alumina. Elution with benzene gave 540 mg. (22.6%) of IIIf as a colorless oil, b.p. 127–128° (0.15 mm.); the infrared spectrum had no C=O band.

Anal. Calcd. for $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85. Found: C, 80.13; H, 7.18; N, 6.05.

The picrate had m.p. 131.5–132.5° (from ethanol).

Anal. Calcd. for $C_{16}H_{17}NO \cdot C_6H_3N_3O_7$: C, 56.41; H, 4.30; N, 11.96. Found: C, 56.39; H, 4.38; N, 12.03.

Elution with chloroform afforded 1.39 g. (58.2%) of IVf as colorless plates, m.p. 72–73°, on recrystallization from benzene–petroleum ether: ν_{max} 1630 (C=O), 984, 927 (—CH=CH_3), and 895 (>C=CH_2) cm.$^{-1}$. The ultraviolet spectrum showed the 4(1H)-quinolone nucleus (Table I). The n.m.r. spectrum showed singlets at τ 8.24 (CH_3) and 6.67 (CH_2 at C-3).

Anal. Calcd. for $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85. Found: C, 80.14; H, 7.36; N, 5.89.

Rearrangement of 4-Allyloxy-3-propylquinoline (IIIa).—The allyl ether IIIa (200 mg.) was heated without solvent at 200° for 30 min. Thin layer chromatography of the reaction product on an alumina plate showed a single spot, indicating an identical R_f value with that of IVa. Chromatography on alumina afforded 192 mg. (96%) of a colorless oil, which had an infrared spectrum identical with that of IVa, and no other product was detectable. The picrate had m.p. 115–116° and showed no depression of the melting point on admixture with the picrate of IVa.

Rearrangement of 4-Crotyloxy-3-propylquinoline (IIIb).—The rearrangement of 300 mg. of IIIb was conducted at 200° for 30 min. The composition of the reaction mixture was investigated by thin layer chromatography and a single spot, identical with that of IVb, appeared. Careful chromatography on alumina gave 290 mg. (97%) of a colorless oil, identical with IVb by infrared spectrum, and any other product was not detectable. The picrate had m.p. 128–129° and showed no depression of melting point on admixture with that of IVb.

Rearrangement of 3-Allyl-4-crotyloxyquinoline (IIIc).—The crotyl ether IIIc (600 mg.) was heated without solvent at 200° for 30 min. The composition of the reaction mixture was investigated by thin layer chromatography and a single spot, indicating an identical R_f value with that of IVc, appeared. Chromatography on alumina gave 570 mg. (95%) of a colorless oil, identical with IVc by infrared spectrum, and any amount of IVd was not detectable.

Rearrangment of 4-Allyloxy-3-(1-methylallyl)quinoline (IIId).—The rearrangement of 300 mg. of IIId was examined by the same method as that for IIIc. An almost quantitative amount of IVc and no detectable amounts of IVd were obtained.

Rearrangement of 3-Allyl-4-methallyloxyquinoline (IIIe).—The methallyl ether IIIe (500 mg.) was heated without solvent at 200° for 30 min. After cooling, the reaction mixture was dissolved in chloroform and chromatographed on alumina. Gradient elution with benzene, chloroform, and ethyl acetate gave 480 mg. of a semisolidified product. A typical analysis of this product is given below.

Anal. Calcd. for $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85. Found: C, 80.38; H, 7.19; N, 5.86.

The infrared spectrum of the product was identical with that of a mixture (about 1:1) of the two pure 4(1H)-quinolones IVe and IVf. The n.m.r. spectrum showed signals corresponding to those of a mixture of IVe and IVf.

Rearrangement of 4-Allyloxy-3-methallylquinoline (IIIf).—The rearrangement of 400 mg. of IIIf was conducted in the same way as for IIIe described above. There was obtained 380 mg. of the 4(1H)-quinolone product, which was completely identical with that obtained from IIIe by infrared and n.m.r. spectra.

Computation of the Compositions of the Rearrangement Products from the N.m.r. Spectra.—Compositions of the product obtained from IIIe were calculated from n.m.r. spectra of 10% solutions of the unknowns and the two pure 4(1H)-quinolones IVe and IVf in deuteriochloroform. The proton signals of the CH_2 group at τ 6.54 and 6.67 were used. The product was determined to be a mixture of IVe and IVf in the proportion of about 1:1 on the basis of the relative integrated intensities of both signals. The product obtained from IIIf showed proton signals of the same proportion of IVe and IVf as those of the product from IIIe in n.m.r. spectrum.

Acknowledgment.—The author is sincerely grateful to Professor E. Ochiai, Dr. K. Takeda, and Dr. H. Kano for their encouragement, and to Dr. H. Tanida for his helpful discussions.

The Claisen Rearrangement. IV.[1] "Out-of-Ring" Claisen Rearrangement to the Active Methylene Group of a *meta* Side Chain in Allyl 4-Quinolyl Ethers[2]

YASUO MAKISUMI

Shionogi Research Laboratory, Shionogi and Company, Ltd., Fukushima-ku, Osaka, Japan

Received November 17, 1964

Thermal rearrangement of allyl 2,3-dialkyl-4-quinolyl ethers (Ia–c) affords good yields of the corresponding 2-(3-butenyl)-4(1H)-quinolones (IIa–c) formed by attachment of the allyl group to the active methylene group at C-2, along with small amounts of 1-allyl-2,3-dialkyl-4(1H)-quinolones (IIIa–c) and the tricyclic compounds (IVa–c) formed by the intramolecular ring closure of the former products (IIa–c). The formation of IIa–c is explicable by a sequence of two consecutive cyclic transition states, the last of which involves a tautomerism of the imine–enamine variety.

The Claisen rearrangement maintains importance among organic reactions as an excellent prototype of a thermally induced, intramolecular isomerization.[3]

In 1926, Claisen and Tietze[4] reported a second type of rearrangement of substituted phenyl allyl ethers. Unlike the then known rearrangements of allyl phenyl ethers in which the migrating allyl group eventually becomes attached directly to the aromatic nucleus, this rearrangement proceeds in such manner that the allyl residue becomes attached, not to the benzene ring, but to the β-carbon of an *o*-propenyl side chain.[5]

It has been demonstrated that the *para* Claisen rearrangement yields products which are consistent with the proposal of Hurd and Pollack[6] involving a double inversion and results suggest that this rearrangement proceeds through a dienone intermediate. An interesting similarity of a mechanism of the rearrangement of an allyl residue to an *o*-propenyl side chain to that of the *para* Claisen rearrangement was reported by Lauer[7] and Schmid.[8]

(1) Part III: Y. Makisumi, *J. Org. Chem.*, **30**, 1986 (1965).

(2) A preliminary report of this work was published in *Tetrahedron Letters*, **No. 13**, 699 (1964).

(3) For an excellent recent review of the Claisen rearrangement, see S. J. Rhoads, "Molecular Rearrangements," P. de Mayo, Ed., Interscience Publishers, Inc., New York, N. Y. 1963, p. 655.

(4) L. Claisen and E. Tietze, *Ann.*, **449**, 81 (1926).

(5) It should be noted that Nickon observed the allyl migration to the β-carbon of a *p*-propenyl side chain [see A. Nickon and B. R. Aaronoff, *J. Org. Chem.*, **27**, 3379 (1962); **29**, 3014 (1964)].

(6) C. D. Hurd and M. A. Pollack, *ibid.*, **3**, 550 (1939).

(7) W. M. Lauer and D. M. Wujciak, *J. Am. Chem. Soc.*, **78**, 5601 (1956).

(8) K. Schmid, P. Fahrini, and H. Schmid, *Helv. Chim. Acta*, **39**, 708 (1956).