Tetrahedron Letters No.25, pp. 1635-1640, 1964. Pergamon Press Ltd.
Printed in Great Britain.

THE MECHANISM OF THE CLAISEN REARRANGEMENT TO A *META* SIDE CHAIN

Yasuo Makisumi

Shionogi Research Laboratory, Shionogi & Co., Ltd.
Fukushima-ku, Osaka, Japan

(Received 5 May 1964)

IN the previous paper on the thermal rearrangement of 3-substituted 2-alkyl-4-quinolyl allyl ethers (1), it was reported that migration of the allyl group to the α-carbon (the active methyl or methylene group) of the *meta*-alkyl side chain occurs in a good yield, along with the migration to the *para*-ring nitrogen. It was assumed that both types of rearrangement would proceed by a mechanism involving a double inversion of the migrating allyl group *via* the same dienone-type intermediate and would compete in the second six-membered cyclic stages having a different orientation of the migrating allyl group. We wish to report on some evidence for the above suggested mechanism.

2-Methyl-3-allyl-4-crotyloxyquinoline (Ia), b.p$_{0.1}$ 135-136°; picrate, m.p. 129-130°, was prepared from 2-methyl-3-allyl-4-quinolinol by the action of crotyl bromide in the presence of a base. Heating Ia at 200° for 30 min. without solvent afforded an 84% yield of 1-crotyl-2-methyl-3-allyl-4(1*H*)-quinolone (II), m.p. 86-86.5°; $\nu_{max}^{CHCl_3}$ 1620 (C=O*), 965 (CH=CH), and 995 and 912 (CH=CH$_2$) cm^{-1},

---

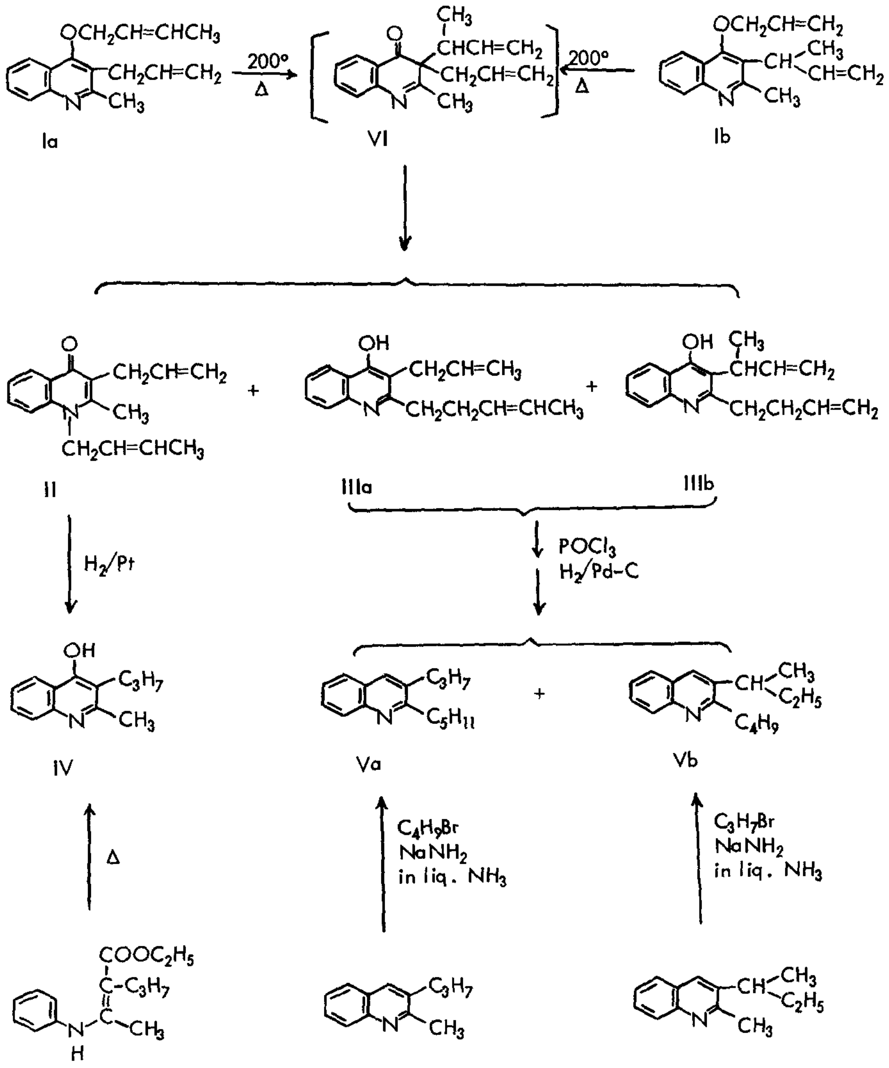
* The carbonyl absorption in the 1-alkyl-4(1*H*)-quinolones appears at around 1620 cm^{-1}. See refs. 1 and 2.

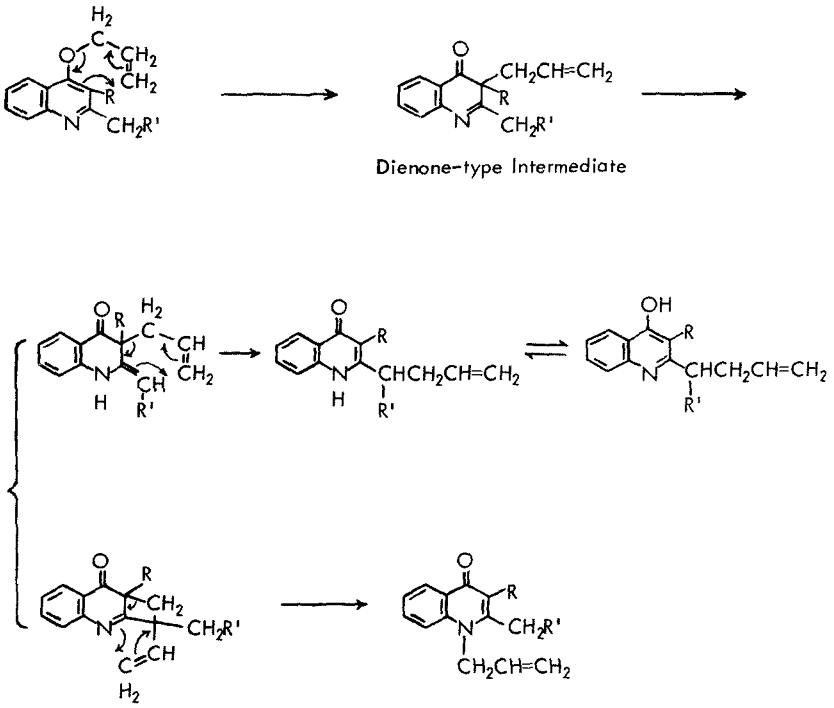
and a 13% yield of a mixture (III) of 2-(3-pentenyl)-3-allyl-4-quinolinol (IIIa) and 2-(3-butenyl)-3-(1-methylallyl)-4-quinolinol (IIIb). The ultraviolet spectrum of II showed an absorption curve [λ_{max}^{EtOH} mμ (log ε): 243.5 (4.45), 250.5 (4.42), 328 (4.12), and 341.5 (4.16)] which is characteristic for the 4(1*H*)-quinolone nucleus. The n.m.r. spectrum of II substantiated the above assigned structure. Moreover, catalytic hydrogenation of II over Adams' catalyst gave 2-methyl-3-propyl-4-quinolinol (IV), m.p. 279-280°, which was identical with an authentic sample prepared by ring-closure of ethyl 2-propyl-3-anilinocrotonate (3).

Although attempts to isolate the respective components of the mixture (III) failed, analysis of its recrystallized crystals, m.p. 213-222°, showed the empirical formula of $C_{17}H_{19}ON$ with infrared absorption [ν_{max}^{Nujol} 3272 (NH[*]), 1640 (C=O[*]), 965 (CH=CH), and 989 and 907 ($CH=CH_2$) cm^{-1}] . Chlorination of the mixture (III) with phosphoryl chloride followed by catalytic reduction over palladium-carbon afforded a colorless oil (V). Its picrate, m.p. 118-123°, was analysed as a monopicrate of the formula, $C_{17}H_{23}N$, corresponding to a mixture of 2-pentyl-3-propylquinoline (Va) and 2-butyl-3-*sec*-butylquinoline (Vb). The standard compounds of Va and Vb were synthesized by an equivocal method (1, 4); Va, b.$p_{0.3}$ 134-135; picrate, m.p. 139-140°, was prepared by butylation of 2-methyl-3-propylquinoline with butyl bromide in liquid ammonia in the presence of sodium amide. Similarly, Vb, b.$p_{0.15}$ 131-132°; picrate, m.p. 145-146°, was also prepared by propylation of 2-methyl-3-*sec*-butylquinoline with propyl bromide. Gas chromatography of the oil (V) showed two components with areas in the ratio of 1 : 4.5. The major component

---

[*] Although the 4-quinolinols can exist in either the lactim or lactam form, it is known that these compounds show the latter form in neutral medium and solid state. The lactam carbonyl absorption appears at around 1640 cm^{-1}. See refs. 1 and 2.


Ia
200°
Δ
VI
200°
Δ
Ib
II
IIIa
IIIb
H2/Pt
POCl3
H2/Pd-C
IV
Va
Vb
Δ
C4H9Br
NaNH2
in liq. NH3
C3H7Br
NaNH2
in liq. NH3



was shown to be identical with Va by introducing an authentic sample and noting which peak was enhanced. Similarly, the minor component was identical with Vb. The infrared spectral analysis of the oil (V) showed that V is a mixture of Va and Vb.

2-Methyl-3-(1-methylallyl)-4-allyloxyquinoline (Ib), b.p$_{0.15}$ 136-137°; picrate, m.p. 133-134°, was prepared from 2-methyl-3-(1-methylallyl)-4-quinolinol (5) by the action of allyl bromide. Analogous rearrangement of Ib under the same conditions as above gave an 83.5% yield of II and a 14% yield of a mixture (III') of IIIa and IIIb. The major product of this rearrangement reaction was identical with II obtained from Ia by mixed melting point and infrared spectral comparison. The minor product

(III') having an empirical formula, $C_{17}H_{19}ON$, showed an almost identical infrared spectrum with that of the mixture (III) obtained by rearrangement of Ia. The mixture (III') was also converted by the same way as above into an oil (V') which formed a monopicrate of the formula, $C_{17}H_{23}N$. Gas chromatography of the oil (V') showed two components (relative areas, 1 : 4.3) which were respectively identified with authentic samples Vb and Va. The oil (V') showed the infrared spectrum corresponding to a mixture of Va and Vb.

These results demonstrate that the thermal rearrangement of Ia and Ib proceed through the same intermediate, 2-methyl-3-allyl-3-(1-methylallyl)-4(3*H*)-quinolone (VI). Thus, it was evident that in the thermal rearrangement of 3-substituted 2-alkyl-4-quinolyl allyl ethers, migration of the allyl group to the α-carbon (the active methyl or methylene group) of the *meta*-alkyl side chain and to the *para*-ring nitrogen proceeds by a mechanism involving a double inversion of the migrating allyl group *via* the same dienone-type intermediate and compete with each other in the second six-membered cyclic stages having a different orientation of the migrating allyl group. It was therefore proved that the migration reaction of an allyl group to a *meta*-side chain is an extensive reaction of the Claisen rearrangement (6).

For all the compounds described, satisfactory elemental analysis were obtained.

Acknowledgements. The author is grateful to Prof. Emeritus E. Ochiai and Dr. K. Takeda and Dr. H. Kano of this Laboratory for their interest in this work.

REFERENCES

1. Y. Makisumi, Tetrahedron Letters No. 13, 699 (1964).
2. For example, see A. R. Katritzky, Physical Methods in Heterocyclic Chemistry Vo. II, p. 263. Academic Press, New York and London (1963) and references cited therein.
3. R. Gillis, F. Lions and E. Ritchie, J. Proc. Roy. Soc. N. S. Wales **73**, 258 (1940).
4. F. W. Bergstrom, J. Am. Chem. Soc., **53**, 3027, 4065 (1931).
5. Y. Makisumi, Chem. & Pharm. Bull. (Tokyo) in press.
6. For excellent reviews on this subject see D. S. Tarbell, Organic Reactions, Ed. by R. Adams, Vo. II, p. 1. John Wiley & Sons, Inc., New York (1944); D. J. Cram, Steric Effect in Organic Chemistry, Ed. by M. S. Newman, p. 295. John Wiley & Sons, Inc., New York (1956); E. S. Gould, Mechanism and Structure in Organic Chemistry, p. 644. Henry Holt & Co., Inc., New York (1959).