Notes

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Zen-ichi Horii, Chuzo Iwata, and Yasumitsu Tamura : Studies on Ergot Alkaloids and Related Compounds. XI.*1 Synthesis of *trans*- and *cis*-4-Methyl-1,2,3,4, 4*a*,5,6,10*b*-octahydrobenzo[*f*]quinoline.

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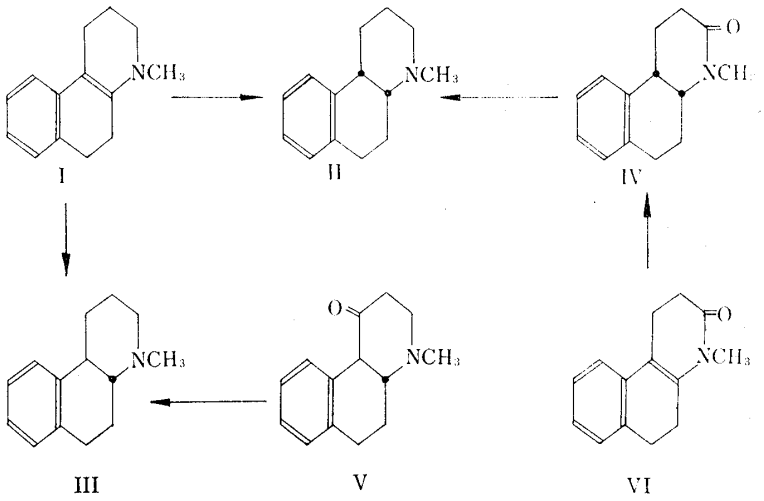
Previously, Nelson, Ladbury and Hsi[1] have reported that the hydrogenation of 4-methyl-1,2,3,4,5,6-hexahydrobenzo[*f*]quinoline (I) or the sodium borohydride reduction of the perchlorate of I gives only one stereoisomer of 4-methyl-1,2,3,4,4*a*,5,6,10*b*-octahydrobenzo[*f*]quinoline, and the stereochemistry of this isomer in the ring-fusion is tentatively assigned *cis* as shown by structure (II). Later, Masamune and Koshi[2] have obtained both II and its *trans* isomer (III) *via* the reductions of benzo[*f*]quinoline, and assigned their stereochemistries, from comparison of the behaviors of both isomers towards the Hofmann's exhaustive methylation, which accord with the assignment given by Nelson, *et al.* The methods of Masamune, *et al.* are, however, of little preparative value, because of their poor yields. The present paper describes methods for the preparation of II and III starting from I, 4-methyl-1,2,5,6-tetrahydrobenzo[*f*]quinolin-3(4*H*)-one (VI),[3] and 4-methyl-3,4,4*a*,5,6,10*b*-hexahydrobenzo[*f*]quinolin-1(2*H*)-one (V).[4] The results prove the stereochemistries of IV and V as well as II and III.



I II IV

III V VI

Birch reduction[5] of I with lithium and liquid ammonia gave a 70% yield of an oily III, characterized as a methiodide, m.p. 240° (decomp.) (lit.,[2] m.p. 238~240°). The infrared spectrum of the free base (III) was shown to be identical, throughout the range, with that of III reported by Masamune, *et al.*[2]

*1 Part X : This Bulletin, **12**, 1405 (1964).

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1) N. A. Nelson, J. E. Ladbury, R. S. P. Hsi : J. Am. Chem. Soc., **80**, 6633 (1958).

2) T. Masamune, M. Koshi : Bull. Chem. Soc. Japan, **32**, 1005 (1959); T. Masamune, M. Ohno, M. Koshi, S. Ohuchi, T. Iwadare : J. Org. Chem., **29**, 1419 (1964).

3) Z. Horii, C. Iwata, Y. Tamura, N. A. Nelson, G. H. Rasmusson : J. Org. Chem., **29**, 2768 (1964).

4) Z. Horii, C. Iwata, M. Ito, Y. Tamura : Yakugaku Zasshi, **84**, 1220 (1964).

5) A. J. Birch, H. Smith : Quart. Rev., **12**, 17 (1958).

Clemmensen reduction[6] of the aminoketone (V) carried out by refluxing a conc. hydrochloric acid solution in the presence of amalgamated zinc for 32 hours gave a 30% yield of III, which was characterized and identified in the same manner as described above for the Birch reduction product.

The lactam (IV) has been prepared by the hydrogenation of 4-methyl-1,2,5,6-tetrahydrobenzo[*f*]quinolin-3(4*H*)-one (VI) in a previous paper.[3] The stereochemistry of IV seems most probably to be *cis* in the ring fusion, although it has not been mentioned. Reduction of the lactam (IV) with lithium aluminum hydride in boiling ether gave a 60% yield of an oily II, characterized as the methiodide, m.p. 294~295° (decomp.) (lit.,[1,2] m.p. 295° (decomp.)). The infrared spectrum of the free base (II) was shown to be identical, throughout the range, with that of II prepared by Nelson, *et al.* and also by Masamune, *et al.*

Since it is generally accepted that Birch reduction gives a thermodynamically stable isomer, while hydrogenation gives a *cis*-addition product, the stereochemistries of II and III are reasonably interpreted by the above reactions, and also are consistent with those assigned by Masamune, *et al.* and Nelson, *et al.* The establishment of the stereochemistries of II and III would prove the structures of IV and V.

Reduction of I with sodium borohydride in methanol at room temperature for 7 hours gave a mixture of II and III in 50% yield.

Experimental*3

***trans*-4-Methyl-1,2,3,4,4*a*,5,6,10*b*-octahydrobenzo[*f*]quinoline (III)**——a) Birch reduction of the enamine (I): A solution of 160 mg. of the enamine (I)[1] in 10 ml. of anhyd. Et_2O was added to a stirred solution of 100 mg. of Li in 250 ml. of liq. NH_3. The blue solution was stirred for 5 hr. and then 5 g. of NH_4Cl was added. After NH_3 was allowed to evaporate, H_2O and Et_2O were added to the residue. The Et_2O layer was separated and the aqueous layer was extracted with Et_2O. The combined Et_2O solution was washed with H_2O, dried over anhyd. Na_2SO_4 and evaporated. Distillation of the residual oil gave 150 mg. of a crude III, b.p_2 140~150° (bath temperature). Chromatography of the crude product on Al_2O_3 using benzene as eluent gave 120 mg. (70%) of III. This product was identified with III reported by Masamune, *et al.*[2] by comparison of the IR spectrum of the free base and melting point of the methiodide.

The methiodide of III was recrystallized from EtOH, m.p. 240° (decomp.) (lit.[2] m.p. 238~240°). *Anal.* Calcd. for $C_{14}H_{19}N \cdot CH_3I$: C, 52.48; H, 6.46; N, 4.08. Found: C, 52.36; H, 6.47; N, 3.98.

b) Clemmensen reduction of the *trans*-aminoketone (V): A solution of 1 g. of the *trans*-aminoketone (V)[4] in 8 ml. of conc. HCl was refluxed in the presence of 5 g. of amalgamated Zn for 24 hr. Further 5 g. of amalgated Zn and 10 ml. of conc. HCl were added, and the mixture was refluxed for an additional 8 hr. The liquid was decanted from the excess of metal and washed repeatedly by shaking with AcOEt. The HCl solution was basified with Na_2CO_3 and extracted with Et_2O. The Et_2O extract was washed with H_2O, dried over anhyd. $MgSO_4$ and evaporated. Distillation of the residual oil gave 300 mg. (30%) of III, b.p_2 140~150° (bath temperature). This product was identified with III prepared in a) by comparison of the IR spectrum of the free base and melting point of the methiodide.

The methiodide of III was recrystallized from EtOH, m.p. 240°.[2] *Anal.* Calcd. for $C_{14}H_{19}N \cdot CH_3I$: C, 52.48; H, 6.46; N, 4.08. Found: C, 52.58; H, 6.39; N, 4.28.

***cis*-4-Methyl-1,2,3,4,4*a*,5,6,10*b*-octahydrobenzo[*f*]quinoline (II)**——To a stirred solution of 180 mg. of the *cis*-lactam (IV)[3] in 54 ml. of anhyd. Et_2O was added 200 mg. of $LiAlH_4$. The mixture was heated under reflux for 5 hr. before decomposing the excess hydride by addition of AcOEt and then aq. KOH. The Et_2O layer was separated and the aqueous layer was extracted with Et_2O. The combined Et_2O solution was washed with H_2O, dried over anhyd. Na_2SO_4 and evaporated. Distillation of the residual oil gave 50 mg. (60%) of II, b.p_3 150~160° (bath temperature). This product was identified with II reported by Nelson, *et al.*[1] and Masamune, *et at.*[2] by comparison of the IR spectrum of the free base and melting point of the methiodide.

The methiodide of II was recrystallized from EtOH, m.p. 294~295° (decomp.) (lit.[1] m.p. 295° (decomp.)). *Anal.* Calcd. for $C_{14}H_{19}N \cdot CH_3I$: C, 52.48; H, 6.46; N, 4.08. Found: C, 52.40; H, 6.45; N, 4.00.

*3 All melting points are uncorrected.

6) G. R. Clemo, J. G. Cook, R. Raper: J. Chem. Soc., **1938**, 1103.

Reduction of the Enamine (I) **with Sodium Borohydride**——To a stirred solution of 200 mg. of the enamine (I) in 30 ml. of MeOH was added 700 mg. of $NaBH_4$. The mixture was stirred at room temperature for 7 hr. before decomposing the excess hydride by addition of AcOH. The mixture was concentrated under reduced pressure on a water bath and the residue was basified with a saturated aq. Na_2CO_3. The basic solution was extracted with Et_2O. The Et_2O extract was washed with H_2O, dried over anhyd. Na_2SO_4 and evaporated. Chromatography of the residual oil on Al_2O_3 using benzene as eluent gave 40 mg. (20%) of II and 60 mg. (30%) of III. These products, II and III, were identified with the corresponding samples described above, by comparison of the IR spectra of the free bases and melting points of the methiodides.

Summary

trans-4-Methyl-1,2,3,4,4*a*,5,6,10*b*-octahydrobenzo[*f*]quinoline (III) was prepared by Birch reduction of 4-methyl-1,2,3,4,5,6-hexahydrobenzo[*f*]quinoline (I) and by Clemmensen reduction of *trans*-4-methyl-3,4,4*a*,5,6,10*b*-hexahydrobenzo[*f*]quinolin-1(2*H*)-one (V). The *cis* isomer (II) of III was prepared by lithium aluminum hydride reduction of *cis*-4-methyl-1,2,4*a*,5,6,10*b*-hexahydrobenzo[*f*]quinolin-3(4*H*)-one (IV).

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Eiji Ochiai und Hiroshi Mitarashi : Über 2-Äthylen-iminomethyl-4-nitrochinolin-N-oxyd.

(*ITSUU Laboratorium**1)

4-Nitrochinolin-N-oxyd ist wegen seiner mutagenischen,[1] carzinogenischen[2] und carzinostatischen[3] Wirkungen immer bemerkenswerter geworden. Es handelt sich bei der vorliegenden Mitteilung um einen Versuch, in 4-Nitrochinolin-N-oxyd ein Radikal mit einer vermutlich carzinostatischen Wirkung einzuführen.

Zu diesem Zweck wurde zuerst 2-Chlormethyl-4-nitrochinolin-N-oxyd (I) durch Nitrierung von 2-Chlormethylchinolin-N-oxyd (II)[4] hergestellt. I bildete Nadeln vom Schmp. 163°. Sein Ultraviolett Spektrum war mit demjenigen von 4-Nitrochinaldin-N-oxyd sehr ähnlich (Fig. 1) und beim Erhitzen in konz. Salzsäure entwickelten sich Nitrosengase, so daß seine Konstitution sichergestellt wurde. Nebenbei wurde ein isomeres Mononitroderivat als gelbe Nadeln vom Schmp. 139° in geringer Menge erhalten, dessen Konstitution noch nicht festgestellt wurde.

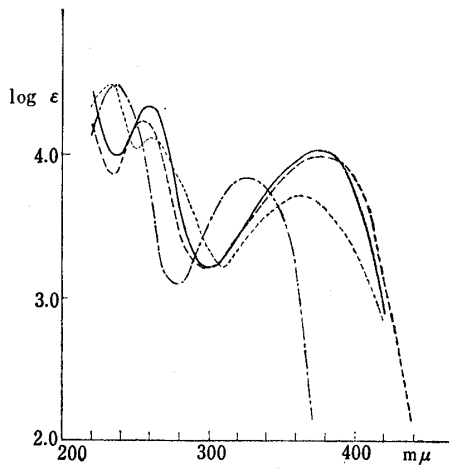

Fig. 1.

——— 4-Nitro-2-chlormethylchinolin-N-oxyd
– – – – – 4-Nitrochinaldin-N-oxyd
—•—•— 2-Chlormethylchinolin-N-oxyd
····· ?-Nitro-2-chlormethylchinolin-N-oxyd

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2) W. Nakahara, F. Fukuoka, T. Sugimura : Gann, **48**, 129 (1957); K. Mori : Gann, **52**, 265 (1961); **54**, 415 (1963).
3) S. Sakai, K. Minoda, G. Saito, S. Akagi, A. Ueno, F. Fukuoka : Gann, **46**, 605 (1955).
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