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 Hsi¹⁾ 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 Koshi²⁾ 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 (V),³⁾ and 4-methyl-3,4,4*a*,5,6,10*b*-hexahydrobenzo[*f*]quinolin-1(2*H*)-one (VI).⁴⁾ The results prove the stereochemistries of IV and V as well as II and III.

Birch reduction⁵⁾ 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⁾

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Clemmensen reduction⁶⁾ 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-1,2,3,4,4a,5,6,10b-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. Et₂O was added to a stirred solution of 100 mg. of Li in 250 ml. of liq. NH₃. The blue solution was stirred for 5 hr. and then 5 g. of NH₄Cl was added. After NH₃ was allowed to evaporate, H₂O and Et₂O were added to the residue. The Et₂O layer was separated and the aqueous layer was extracted with Et₂O. The combined Et₂O solution was washed with H₂O, dried over anhyd. Na₂SO₄ 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 Al₂O₃ 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 C₁₄H₁₉N·CH₃I: 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 Na₂CO₃ and extracted with Et₂O. The Et₂O extract was washed with H₂O, dried over anhyd. MgSO₄ 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 C₁₄H₁₉N·CH₃I: C, 52.48; H, 6.46; N, 4.08. Found: C, 52.58; H, 6.39; N, 4.28.

***cis*-4-Methyl-1,2,3,4,4a,5,6,10b-octahydrobenzo[*f*]quinoline (II)**—To a stirred solution of 180 mg. of the *cis*-lactam (IV)³⁾ in 54 ml. of anhyd. Et₂O was added 200 mg. of LiAlH₄. The mixture was heated under reflux for 5 hr. before decomposing the excess hydride by addition of AcOEt and then aq. KOH. The Et₂O layer was separated and the aqueous layer was extracted with Et₂O. The combined Et₂O solution was washed with H₂O, dried over anhyd. Na₂SO₄ 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 al.*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 C₁₄H₁₉N·CH₃I: 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.

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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 NaBH₄. 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. Na₂CO₃. The basic solution was extracted with Et₂O. The Et₂O extract was washed with H₂O, dried over anhyd. Na₂SO₄ and evaporated. Chromatography of the residual oil on Al₂O₃ 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-1,2,3,4,4a,5,6,10b-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-3,4,4a,5,6,10b-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-1,2,4a,5,6,10b-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.

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4-Nitrochinolin-N-oxyd ist wegen seiner mutagenischen,¹⁾ carcinogenischen²⁾ und carzinostatischen³⁾ 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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