Syntheses of Benzomorphan and Related Compounds. Part 1. Synthesis of *N*-Substituted-1,2,3,4,5,6-hexahydro-8-hydroxy-2,6-methano-6,11-dimethyl-3-benzazocine [Studies on the Syntheses of Heterocyclic Compounds. Part CCLXXXII (1)]

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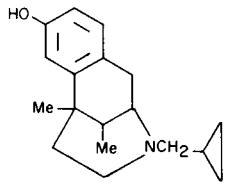
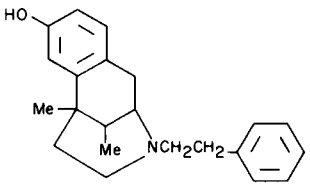
A modified synthesis of pentazocine, 1,2,3,4,5,6-hexahydro-8-hydroxy-2,6-methano-6,11-dimethyl-3-(3-methyl-2-butenyl)-3-benzazocine (III), has been achieved and catalytic hydrogenation has been found to be effective for the debenzylation of quaternary ammonium salts.

There has been reported a number of syntheses of benzomorphan derivatives, among which are cyclazocine (3) (I), phenazocine (4) (II) and pentazocine (5) (III), all well known as analgesic agents. In particular the latter compound, 1,2,3,4,5,6-hexahydro-8-hydroxy-2,6-methano-6,11-dimethyl-3-(3-methyl-2-butenyl)-3-benzazocine (III), has been found to be an effective analgesic agent without addiction. Therefore, a simplified alternate synthesis of III was investigated. We hereby wish to report the results of this investigation.



I



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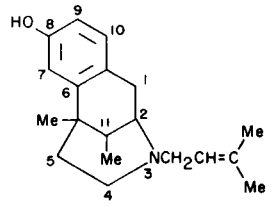


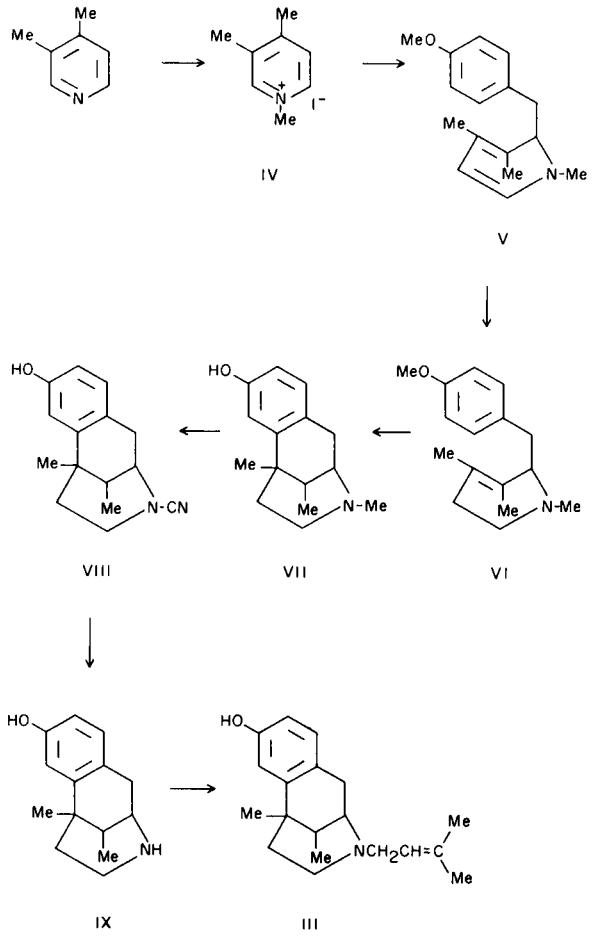
III

The *N*-substituted derivatives of 1,2,3,4,5,6-hexahydro-8-hydroxy-2,6-methano-6,11-dimethyl-3-benzazocine (IX) have been previously synthesized by condensation of IX with halides (5), and a representative synthetic method for this key compound (IX) is shown in Scheme I. In this case the *N*-methyl derivative (VII) was converted in poor yield into the compound (IX) by the von Braun reaction.

In our work, the quaternary ammonium salts (XVI and XVII) of 3-benzyl-1,2,3,4,5,6-hexahydro-8-hydroxy-2,6-methano-6,11-dimethyl-3-benzazocine (XIVa), which was synthesized from 3,4-lutidine in five steps, were reductively debenzylated to give the *N*-substituted-1,2,3,4,5,6-hexahydro-8-hydroxy-2,6-methano-6,11-dimethyl-3-benzazocines, III and VII, respectively. 1-Benzyl-3,4-dimethylpyridinium chloride (X), which was obtained by quaternization of 3,4-lutidine with benzyl chloride, was reacted with 4-methoxybenzyl chloride in the presence of magnesium *via* the Grignard reaction to give 1-benzyl-1,2-dihydro-2-(4-methoxybenzyl)-3,4-dimethylpyridine (XI). Thin layer chromatography (6) of XI showed two spots, but, due to its instability, the reduction of XI with sodium borohydride was carried out without purification to give 1-benzyl-1,2,5,6-tetrahydro-2-(4-methoxybenzyl)-3,4-dimethylpyridine (XII). Compound XII was purified in the form of salts such as the hydrochloride, m.p. 152-154°, the oxalate and the picrate. The NMR spectrum (δ) of XII showed a singlet at 3.58, due to the methylene protons of the *N*-benzyl group, a singlet at 3.77 due to the methoxyl group, and a pair of doublets (A_2B_2 type) at 6.66 and 7.08 ppm with J = 9.1 cps due to aromatic protons of the 4-methoxybenzyl group.

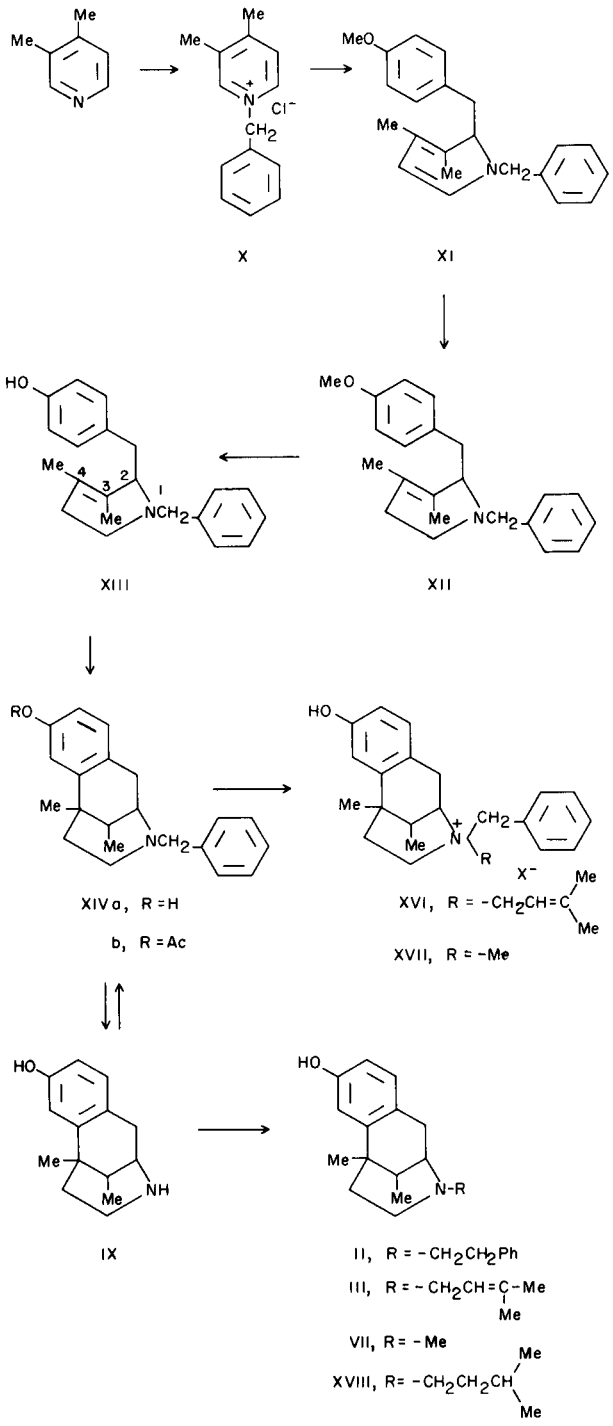
When compound XII was refluxed with 48% hydrobromic acid for 30-40 hours (8), the expected cyclization

Scheme 1

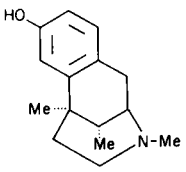


and demethylation occurred to give 3-benzyl-1,2,3,4,5,6-hexahydro-8-hydroxy-2,6-methano-6,11-dimethyl-3-benzazocine (XIVa). The NMR spectrum (δ) of XIIa revealed the methyl protons of the C_{11}-position as a doublet at 0.78 with J = 7.5 cps, a singlet at 1.26 due to the methyl group of the C_6-position, the methylene protons of the *N*-benzyl group as a singlet at 3.69, and the aromatic protons as an ABX type signal (J_{ortho} = 7.7 cps, J_{meta} = 2.3 cps) at 6.47-7.02 ppm. This fact revealed that cyclization had occurred at the position *meta* to the hydroxyl group to give the compound (XIVa) which was also characterized as its acetyl derivative (XIVb). In the above reaction the demethylated intermediate (XIII) of the cyclized compound (XIVa) was separated as the hydrobromide, m.p. 212-213°. The IR spectrum of the hydrobromide showed an absorption due to the hydroxyl group at 3320 cm^{-1}. In the NMR (δ) spectrum of XIII, the signal due to the methoxyl group, which was observed at 3.77 in the case of compound (XII), has disappeared and a hydroxyl signal was shown at 5.20 ppm. Furthermore, four aromatic protons were observed as a pair of doublets (A_2B_2 type) with J = 7.5 cps at 6.67 and 7.02 ppm. Further treatment of XIII with hydrobromic acid gave XIVa, showing that cyclization of XII had proceeded through compound XIII.

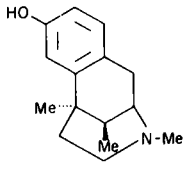
Scheme 2



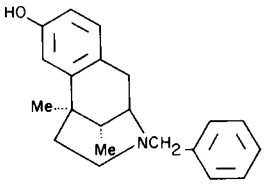
The presence of two diastereoisomers differing in configuration at the C_{11}-position were anticipated, but our sample is believed to be compound XIVa having the 11-α-methyl conformation for the following reasons. It was assumed that the predominant conformer resulting from the above cyclization is the one with the 11-methyl substituent oriented away from the nitrogen, namely, axial for the hydroxyaromatic ring, as shown in XIVa-α. This assumption is similar to the analogy with the morphinan synthesis (9) and also depends upon the "*trans rule*" (10) of the addition to olefinic bonds, namely, to the 3,4-double bond of XIII, Fullerton. *et al.* (11) reported that in case of two diastereoisomers (A and B) of 1,2,3,4,5,6-hexahydro-8-hydroxy-3,6,11-trimethyl-3-benzazocine, the methyl signal at the C_{11}-position was observed as a doublet in a field 25 cps higher than that observed at the C_6-position in conformer A, whereas the signal at the C_{11}-position of B shifted to a lower field and both signals at the C_6- and C_{11}-positions overlapped each other. The former fact corresponded to the NMR spectral data of our sample. Thus the configuration at the 11-methyl-substituent of XIVa has been confirmed as XIVa-α type compound. In this case the other conformer (XIVa-β) has not been isolated.



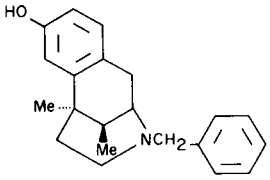
A



B



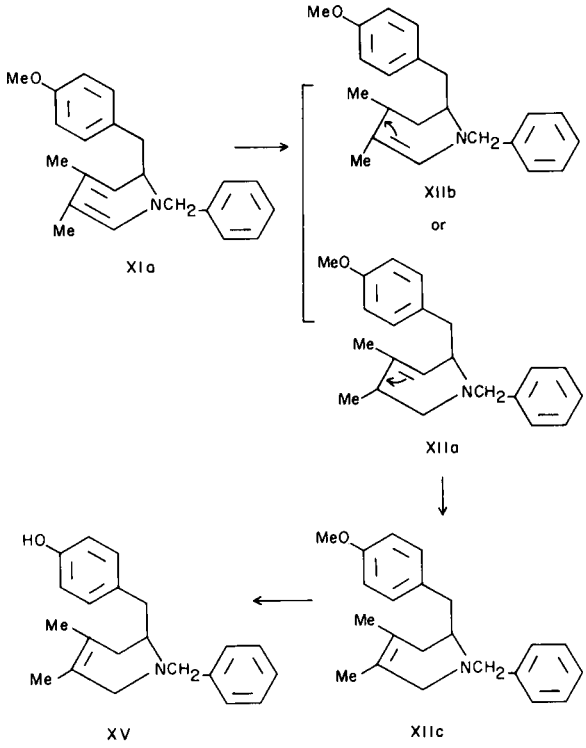
XIVa-α



XIVa-β

Grignard reaction of X, followed by reduction with sodium borohydride, afforded the pure compound XII successfully, and a second compound having the same composition as XII was separated from the filtrate as the hydrochloride, m.p. 198-200°. Treatment of XII with 48% hydrobromic acid gave colorless needles, m.p. 274-275° (dec.) as the hydrobromide, and microanalysis revealed that this compound has the same composition as XIVa. The NMR (δ) spectrum showed no methoxyl signal, a broad signal at 4.60 and four aromatic protons as a pair of doublets (A_2B_2 type) at 6.75 and 7.00 ppm. These facts revealed that no cyclization had occurred and one methoxyl group had been demethylated. Thus, Grignard reaction of X gave the compound XIa, in which the 4-methoxybenzyl group appeared to have been introduced into the C_6-position. Reduction of XIa, followed by migration of the double bond of XIIa or XIIb, would give the more stable compound XIIc. This migration is supported by the fact that the two methyl protons were shown as a singlet as well as the compound XII, and no cyclization had occurred in case of XIIc which gives the compound XV.

Scheme 3



Catalytic hydrogenation of the hydrochloride of XIVa in the presence of 10% palladium-charcoal gave the 1,2,3,4,5,6-hexahydro-8-hydroxy-2,6-methano-6,11-dimethyl-3-benzazocine (IX) in 90% yield, which was identical with an authentic sample (prepared by demethylation of VII *via* von Braun reaction) on mixed m.p. test and IR spectral comparison. The reaction of IX, which was obtained by reduction of XIVa, with 3-methyl-2-butenyl bromide (12) according to Archer's method (5) also gave our expected pentazocine (III). The same treatment of IX with phenethyl bromide also gave the

phenazocine (II). On the other hand the reaction of IX with benzyl bromide in the presence of sodium bicarbonate gave the *N*-benzyl derivative XIVa, which was then reacted with 3-methyl-2-butenyl bromide to give 3-benzyl-1,2,3,4,5,6-hexahydro-8-hydroxy-2,6-methano-6,11-dimethyl-3-(3-methyl-2-butenyl)-3-benzazocinium bromide (XVI) as a colorless powder. In this case the hydrobromide of XIVa was obtained in addition to our expected quaternary ammonium salt (XVI), perhaps due to the decomposition of the labile 3-methyl-2-butenyl bromide (12).

Finally, reductive debenzylation of XVI was investigated. A number of examples (13) regarding the debenzylation by catalytic hydrogenation of *N*-benzyl derivatives of tertiary amines are well known, but attempts to remove the *N*-benzyl group of the quaternary ammonium salts has been barely examined (14). Therefore, after about 1 molar equivalent of hydrogen had been absorbed, we looked for evidence that XVI had been catalytically debenzylated to the pentazocine (III). The IR, UV, NMR spectra and TLC of III were superimposable on those of the sample which had been obtained from the reaction of IX with 3-methyl-2-butenyl bromide. In this case the dihydropentazocine (XVIII) was also formed as a by-product. Catalytic hydrogenation of XVI in the presence of Raney Ni also gave a mixture of III and XVIII. Furthermore, catalytic hydrogenation of the methiodide (XVII), prepared by methylation of XIVa with methyl iodide, in the presence of 10% palladium-charcoal gave 1,2,3,4,5,6-hexahydro-8-hydroxy-2,6-methano-3,6,11-trimethyl-3-benzazocine (VII) in good yield, which was identical with an authentic sample obtained according to May's method (11, 15) (*cf.* Scheme 1), on mixed m.p. test and IR spectral comparison.

Thus, a simplified synthesis of pentazocine has been successfully accomplished and catalytic hydrogenation has been revealed to be effective in the case of debenzylation of quaternary ammonium salts.

EXPERIMENTAL

1-Benzyl-3,4-dimethylpyridinium chloride (X).

A mixture of 10 g. of 3,4-lutidine, 11.8 g. of benzyl chloride and 15 ml. of dry benzene was refluxed on a water-bath for 3 hours. After cooling, the crystals which separated were collected by filtration and recrystallized from isopropanol-ether to give 18.4 g. (83.6%) of X as very hygroscopic colorless needles, m.p. 156-158°.

Anal. Calcd. for $C_{14}H_{16}ClN \cdot 1.5H_2O$: N, 5.40. Found: N, 5.26.

1-Benzyl-1,2,5,6-tetrahydro-2-(4-methoxybenzyl)-3,4-dimethylpyridine (XII).

To a stirred mixture of 3 g. of metallic magnesium, a small amount of iodine and 100 ml. of dry ether was added dropwise a solution of 7 g. of 4-methoxybenzyl chloride in 50 ml. of dry ether at room temperature over a period of 1.5 hours, and the mixture was then refluxed for 30 minutes. Excess magnesium was removed by decantation from the solution which was then added in one portion to a suspension of 3.5 g. of X in 50 ml. of dry ether and the mixture was heated under reflux for 2.5 hours. After cooling, the reaction mixture was poured into 50 ml. of 20% ammonium chloride solution. The ethereal layer which separated, was extracted with 10% hydrochloric acid solution, made basic with concentrated ammonia and extracted with ether. The extract was washed with water, dried over potassium carbonate and evaporated to give 4 g. (83.7%) of 1-benzyl-1,2-dihydro-2-(4-methoxybenzyl)-3,4-dimethylpyridine (XI) as a dark reddish oil.

The above oil (XI) was used in the following reaction without purification because of its instability. To a stirred solution of 3.75 g. of XI in 30 ml. of methanol was added a mixture of 2.35 g. of sodium hydroxide, 5 ml. of water and 4.44 g. of sodium borohydride and the mixture was refluxed for 0.5 hour. After removal of the methanol, 50 ml. of water was added to the above residue and the solution was extracted with ether. The extract was washed with water, dried over potassium carbonate and evaporated to afford an oil, which was distilled *in vacuo* to give 2.3 g. of a pale yellow oil, b.p. 175-178° (0.2 mm.). This oil was purified by thin layer chromatography using petroleum ether-ether (3:1), resulting in two spots, R_f 0.69 and R_f 0.56, which were detected with iodine vapor. Recrystallization of the oxalate from isopropanol gave 2.42 g. (46.9%) of XII as colorless needles, m.p. 158-160°, which showed one spot of R_f 0.69. NMR δ (in deuteriochloroform), 1.63 (6H, singlet, C_3- and C_4-CH_3), 3.58 (2H, singlet, $\geq NCH_2C_6H_5$), 3.77 (3H, singlet, OCH_3), 6.66 and 7.08 (4H, a pair of doublets with A_2B_2 type, J = 9.1 cps, aromatic protons).

Anal. Calcd. for $C_{22}H_{27}NO \cdot C_2H_2O_4$: C, 70.05; H, 7.10. N, 3.40. Found: C, 69.69; H, 6.64; N, 3.90.

Compound XII was also characterized as the hydrochloride (from isopropanol-ether) and picrate (from ethanol) giving colorless needles, m.p. 152-154°, and yellow needles, m.p. 115-118°, respectively.

The above filtrate, from which the oxalate of XII had been removed by filtration, was basified with 10% sodium hydroxide solution and extracted with chloroform. The extract was washed with water, dried over potassium carbonate, and evaporated to give a brown oil, whose thin layer chromatography (6) gave a pale brown oil having R_f 0.56. NMR δ (in deuteriochloroform), 1.57 (6H, singlet, C_3- and C_4-CH_3), 3.73 (5H, singlet, OCH_3 and $\geq N$-$CH_2C_6H_5$), 6.75 and 7.00 (4H, a pair of doublets with A_2B_2 type, J = 8.2 cps, aromatic protons). Recrystallization of the hydrochloride from isopropanol-ether gave colorless prisms, m.p. 198-200°.

Anal. Calcd. for $C_{22}H_{27}NO \cdot HCl$: C, 73.82; H, 7.90. Found: C, 73.56; H, 8.23.

3-Benzyl-1,2,3,4,5,6-hexahydro-8-hydroxy-2,6-methano-6,11-dimethyl-3-benzazocine (XIVa).

(a) From Compound XII.

A mixture of 9 g. of the oxalate of XII and 200 ml. of 48% hydrobromic acid was heated under reflux in an oil-bath at 160-180° for 30 hours. After 5 hours' refluxing, an intermediate (XIII) began to separate as the hydrobromide. After cooling, the reaction mixture was basified with 28% ammonia and extracted with chloroform. The extract was washed with water, dried over potassium carbonate, and evaporated to give a caramel-like compound, whose hydrochloride was recrystallized from isopropanol

to afford 4.28 g. (57.0%) of XIVa as colorless needles, m.p. 268-270° (dec.). The free base was obtained and recrystallized from acetone to give colorless plates, m.p. 153-154°; NMR δ (deuteriochloroform), 0.78 (3H, doublet, J = 7.5 cps, C_{11}-CH_3), 1.26 (3H, singlet, C_6-CH_3), 3.69 (2H, singlet, ≥NC$H_2C_6H_5$), 5.08 (1H, broad singlet, OH), 6.47-7.02 (3H, ABX type, J_{ortho} = 7.7 cps, J_{meta} = 2.3 cps, aromatic protons).

Anal. Calcd. for $C_{21}H_{25}NO$·HCl: C, 73.36; H, 7.56; N, 4.07. Found: C, 73.21; H, 7.61; N, 4.37.

Recrystallization of the intermediate XIII from methanol-ether gave 1-benzyl-1,2,5,6-tetrahydro-2-(4-methoxybenzyl)-3,4-dimethylpyridine as colorless needles, m.p. 212-213°; infrared λ max (potassium bromide), cm^{-1}, 3330 (OH), 2750-2400 (≥N^+H), δ max 743, 700 (monosubstituted benzene); NMR δ (in deuteriochloroform) of free base, 1.58 (3H, singlet, C_3- or C_4-CH_3), 1.62 (3H, singlet, C_3- or C_4-CH_3), 3.59 (2H, singlet, ≥NC$H_2C_6H_5$), 5.20 (1H, singlet, OH), 6.67 and 7.02 (4H, a pair of doublets with A_2B_2 type, J = 7 cps, aromatic protons).

Anal. Calcd. for $C_{21}H_{25}NO$·HBr: C, 64.94; H, 6.75; N, 3.61. Found: C, 65.18; H, 7.04; N, 3.70.

The hydrochloride (from ethanol-ether) gave colorless prisms, m.p. 216-217°.

(b) From Compound IX.

A mixture of 0.45 g. of IX, 8 ml. of ethanol, 0.35 g. of sodium bicarbonate, and 0.39 g. of benzyl bromide was refluxed on a water-bath for 5 hours and the ethanol was distilled off. A mixture of the resultant residue and 50 ml. of ether was extracted with 100 ml. of 5% hydrochloric acid solution. The acidic aqueous extract was made basic with concentrated ammonia and extracted again with chloroform. The extract was washed with water, dried over sodium sulfate, and evaporated to give a caramel-like substance, whose recrystallization from acetone afforded 0.35 g. (55.1%) of XIVa as colorless plates, m.p. 153-154°. This was identical with the sample obtained from compound XII.

8-Acetoxy-2-benzyl-1,2,3,4,5,6-hexahydro-2,6-methano-6,11-dimethyl-3-benzazocine (XIVb).

A mixture of 2.7 g. of XIVa and 2 ml. of acetic anhydride was refluxed in an oil-bath at 145° for 1 hour. After removal of acetic anhydride, the mixture was made basic with 10 ml. of 10% sodium hydroxide solution and extracted with chloroform. The extract was washed with water, dried over potassium carbonate, and evaporated to give an oil, whose distillation *in vacuo* afforded 2.75 g. (88.4%) of XIVb as a pale yellow oil, b.p. 200-205° (0.07 mm.); infrared ν max (liquid) cm^{-1}, 1765 ($COCH_3$); NMR δ (in deuteriochloroform), 0.79 (3H, doublet, J = 7.1 cps, C_{11}-CH_3), 1.33 (3H, singlet, C_6-CH_3), 2.22 (3H, singlet, COCH_3), 3.63 (2H, singlet, ≥NC$H_2C_6H_5$), 6.73-7.15 (3H, ABX type pattern, J_{ortho} = 6.3 cps, J_{meta} = 1.5 cps, aromatic protons).

Recrystallization of the hydrochloride from ethanol-ether gave colorless prisms, m.p. 165-166°.

Anal. Calcd. for $C_{23}H_{27}NO_2$·HCl: N, 3.63. Found: N, 3.87.

3-Benzyl-1,2,3,4,5,6-hexahydro-8-hydroxy-2,6-methano-6,11-dimethyl-3-(3-methyl-2-butenyl)-3-benzazocinium bromide (XVI).

A mixture of 3.07 g. of XIVa, 3 g. of 3-methyl-2-butenyl bromide, 2.8 g. of sodium bicarbonate, and 60 ml. of acetone was refluxed for 5 hours. After removal of the inorganic substance by filtration, the acetone was distilled off to give a residue which was dissolved in 30 ml. of chloroform. The solution was basified with 10% ammonia hydroxide and the chloroform layer was separated. The solvent was washed with water, dried over potassium carbonate, and evaporated to give a caramel-like substance, whose recrystallization from ethanol-ether afforded 2.06 g. (45.1%) of XVI as a colorless powder, m.p. 159-161°; infrared ν max (potassium bromide) 3490 and 3250 (OH and water of crystallization), 1665 (≻C=C≺).

Anal. Calcd. for $C_{26}H_{34}BrNO·H_2O$: C, 65.81; H, 7.64; N, 2.95. Found: C, 66.07; H, 7.51; N, 3.21.

3-Benzyl-1,2,3,4,5,6-hexahydro-8-hydroxy-2,6-methano-3,6,11-trimethyl-3-benzazocinium iodide (XVII).

A mixture of 3.07 g. of XIVa, 7.1 g. of methyl iodide, and 50 ml. of methanol was refluxed for 2 hours and the methanol was removed by distillation to give a residue, which solidified on being triturated with ether. Recrystallization from isopropanol gave 3.9 g. (86.6%) of XVII as colorless prisms, m.p. 217-218° (dec.).

Anal. Calcd. for $C_{22}H_{28}INO$: C, 58.80; H, 6.28; N, 3.12. Found: C, 58.82; H, 6.68; N, 3.01.

1,2,3,4,5,6-Hexahydro-8-hydroxy-2,6-methano-6,11-dimethyl-3-(3-methyl-2-butenyl)-3-benzazocine (III).

(a) A solution of 1.5 g. of XVI in 50 ml. of ethanol upon hydrogenation in the presence of 0.15 g. of 10% palladium charcoal, absorbed 0.7 molar equivalent of hydrogen (52 ml.) over a period of 5 minutes. After absorption of the above amount of hydrogen, the catalyst was removed by filtration and the solvent was evaporated in the presence of a few drops of concentrated ammonia to give an oil, whose solution in 30 ml. of ether was extracted with 10% hydrochloric acid solution. The preceding acidic solution was made basic with 10% ammonia and extracted with ether. The extract was washed with water, dried over potassium carbonate and evaporated to give 0.82 g. (87.4%) of an oil, which was purified by silicic acid (3 g.) chromatography. Removal of 60 ml. of the first ethereal eluate gave a mixture of XIVa, XVIII and III, which was further chromatographed using 200 ml. of ether-chloroform (95:5) as an eluant. Evaporation of the eluate (fractions 7-20, each 10 ml.), gave the pentazocine (5) (III), whose UV, IR, and NMR spectra and TLC were identical with those of an authentic sample (5); NMR δ (in deuteriochloroform), 0.84 (3H, doublet, J = 6.7 cps, C_{11}-CH_3), 1.30 (3H, singlet C_6-CH_3), 1.68 (6H, singlet, -CH_2CH=C(CH_3)$_2$), 1.20-3.35 (11H, multiplet, methylene and methine protons), 5.29 (1H, triplet, J = 7.5 cps, -CH_2CH=C(CH_3)$_2$), 6.41 (1H, singlet, OH), 6.49-7.00 (3H, ABX type pattern, J_{ortho} = 7.7 cps, J_{meta} = 2.3 cps, aromatic protons). UV λ max (methanol) (log ε), 282 mμ (3.30); infrared ν max (chloroform) cm^{-1}, 3600 (OH), 1670 (≻C=C≺); TLC, R_f 0.42 [benzene-chloroform-methanol (5:5:2), detected with iodine vapor].

Evaporation of fractions 4-6 gave a residue, which was chromatographed on 1 g. of silicic acid to give 50 mg. of XVIII as a syrup. Since both the free base and the hydrochloride could not be crystallized, catalytic hydrogenation of III in the presence of 10% palladium charcoal was carried out to give the syrup, whose IR and NMR spectra were identical with the above sample (XVIII); NMR δ (in deuteriochloroform), 0.81 (3H, doublet, J = 7.4 cps, C_{11}-CH_3), 0.85 (6H, doublet, J = 5.5 cps, -CH_2CH(CH_3)$_2$), 1.28 (3H, singlet, C_6-CH_3), 5.54 (1H, singlet, OH), 6.47-6.98 (3H, ABX type pattern, J_{ortho} = 7.7 cps, J_{meta} = 2.3 cps, aromatic protons).

(b) A mixture of 3.8 g. of XVI, 100 ml. of ethanol, and 1 g. of triethylamine was hydrogenated in the presence of 5 ml. of Raney Nickel (16), 0.8 molar equivalent of hydrogen (167.5 ml.) being absorbed during 50 minutes. After removal of the catalyst, the excess of the reagents was distilled off to give 1.95 g. (82%) of an

oil, which was chromatographed on 35 g. of silicic acid using 200 ml. of ether to give a mixture of XIVa, XVIII and III. Further elution with 500 ml. of ether-chloroform (95:5) gave the pentazocine (III) from fractions 7-27 (each 25 ml.). Spectral data and TLC supported the structure of III.

1,2,3,4,5,6-Hexahydro-8-hydroxy-2,6-methano-3,6,11-trimethyl-3-benzazocine (VII).

A solution of 2 g. of XVII in 100 ml. of ethanol was hydrogenated in the presence of 1 g. of 10% palladium charcoal, one molar equivalent of hydrogen (95 ml.) being absorbed. After removal of the catalyst, the ethanol was distilled off to give a residue, which was basified with 10% ammonia and repeatedly extracted with chloroform. The extract was washed with water, dried over potassium carbonate, and evaporated to give a colorless powder, whose recrystallization from ethanol gave 0.91 g. (88.5%) of VII as colorless needles, m.p. 229-233°. This was identical with an authentic sample (11, 15) and no depression was observed on admixed melting point determination.

1,2,3,4,5,6-Hexahydro-8-hydroxy-2,6-methano-6,11-dimethyl-3-benzazocine (IX).

A solution of 10 g. of the hydrochloride of XIVa in 200 ml. of ethanol was hydrogenated in the presence of 10 g. of 30% palladium charcoal, 1 molar equivalent of hydrogen being absorbed over a period of 8 hours. After the catalyst had been removed by filtration and washed with ethanol, the filtrate and washings were combined and evaporated to give a solid, which was basified with 10% ammonia and extracted with 50 ml. of chloroform. The extract was washed with water, dried over potassium carbonate and evaporated to give a residue, whose recrystallization from acetone gave 5.7 g. (90.1%) of IX as colorless needles, m.p. 229-231°, identical with an authentic sample (11, 15).

Acknowledgements.

We thank Dr. H. Nada, Dr. T. Masuda, Dr. K. Morita, and Mr. Y. Sawa, Takeda Pharmaceutical Co. Ltd., for their helpful assistance and discussions and we also thank President A. Yanagisawa and Director O. Takagi of the Grelan Pharmaceutical Co. Ltd. for their assistance. We are also grateful to Miss R. Hasebe, Miss R. Kawakami, and Miss Y. Tadano, the Analytical Centre of Pharmaceutical Institute, School of Medicine, Tohoku University, for NMR determinations and microanalyses.

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Received December 21, 1968

Sendai, Japan (2) and Tokyo, Japan