SYNTHESIS OF (±)-2β-HYDROXY-6α-ACETOXYNORTROPANE

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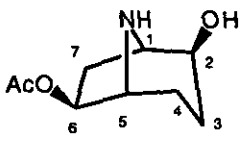
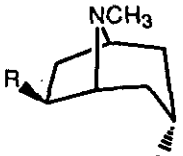
Abstract- 8-Benzyl-6α-chloro-6β-carbonitrile-2,2-ethylenedioxy-8-azabicyclo-[3.2.1]oct-3-ene (8) and its C(6) epimer (9) were hydrolyzed to afford 6-ketone (10). Reduction of the ketone (10) with sodium borohydride gave predominantly 6α-ol (14). 2-Ketone (20), obtained from 14 by deprotection followed by hydrogenation and acetylation, was reduced with sodium borohydride to give 2β-ol 21 as the major epimer. Nortropane (24) was prepared from 21 by debenzylation.

Baogongteng A (1), isolated from the Chinese medicine herb *Erycibe obtusifolia* Benth,[2] also named as Erycibe Alkaloid II, is a nortropane alkaloid with cholinergic activity. It has been used clinically in the treatment of glaucoma and its pharmacological activity on heart function has also been reported.[3,4] Other Compounds that have similar structure and biological activities have also been isolated from Chinese herbs.[5-7] The reported chemical synthesis of racemic baogongteng A from (±)-6β-acetoxy-tropan-3-one lacked selectivity and afforded low yields, thus being of little practical value.[8] Although C(2)-desoxy analoges were recently disclosed,[9-12] epimers of 1 with 2α- and/or 6α- configuration are unknown, and their synthesis and pharmacological activities are worthy of stusying. Baogongteng A has a free hydroxy group at C(2) and an acetoxy group at C(6), whereas many other tropane alkaloids, such as atropine (2), anisodamine (3), scopolamine (4) and anisodine (5), have oxygenated functions at C(3). The alkaloids represented by 1 require a route to the 2,6-dioxygenated tropane skeleton and the well-known Robinson-Schopf's[13] and Noyori's[14] methods to the construction of tropane ring seem not suitable. Katritzky and co-workers have found that 1,3-dipolar cycloaddition of 3-hydroxypyridinium betaines (6) with dipolarophiles such as acrylonitrile and acrylates gave 8-azabicyclo[3.2.1]oct-3-en-2-ones(7).[15] Some application of Katrizky reaction to the synthesis of 2-tropanols and monofluorinated 2-tropanol were published recently.[16,17] However, application of this method to naturally occurring tropane alkloids has not been accomplished yet, probably owing to the difficulty to convert nitrile or carboxyl group at C(6) position of the cycloadducts into the desired function group. We were interested

in applying this cycloaddition to the synthesis of tropane alkaloids having the oxygenated function at the C(2) and C(6) position, and investigated the conversion of chloro nitrile into oxygenated function at C(6) position in the Katrizky cycloadducts. The results of the investigation which led to an effective route to prepare 6α-epimer of baogongteng A are described in this paper.

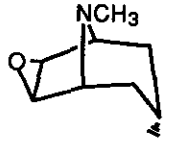


1: Baogongteng A



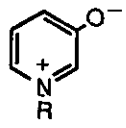
OOCCH(CH2OH)Ph

2: R = H, Atropine
3: R = OH, Anisodamine

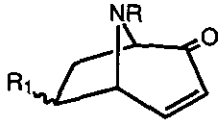


OOCCPh(CH2OH)R

4: R = H, Scopolamine
5: R = OH, Anisodine

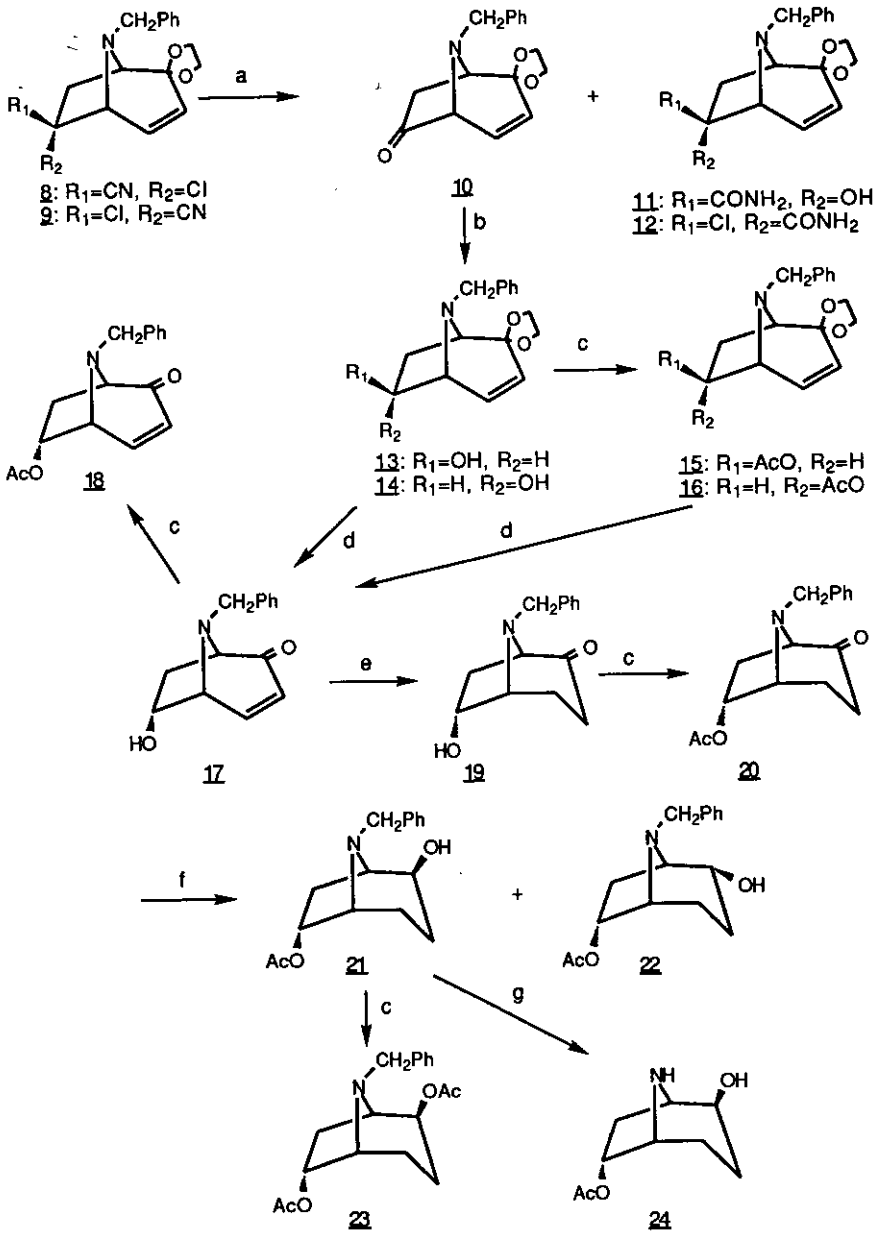


6: 3-hydroxypyridium
R = CH3, PhCH2, etc.



7: R = CH3, PhCH2, etc.
R1 = CO2CH3, CN, etc.

The 6-chloro nitriles (8 and 9), which were prepared from the cycloaducts of 1-benzyl-3-oxidopyridinium and 2-chloroacrylonitrile and the C(6)-stereochemistry studies with HETCOR and HETCOLOC nmr techniques have been established,[18] were hydrolyzed in *tert*-butanol with potassium hydroxide to afford 6-ketone (10) as the major product (35 % yield). Big differences in rates of hydrolysis were observed between the 6-chloro nitrile epimers (8 and 9). The 6α-nitrile (9) was found to hydrolyze more rapidly and to give chloro amide (12) as the major product (41 %) accompanied with the desired ketone (10) (35 %). On the other hand the 6β-nitrile (8) hydrolyzed relatively slowly giving only a small amount of hydroxy amide (11) with 10 as the major product. The ketone (10) was reduced with sodium borohydride in ethanol to give 6α-ol (14) as the major epimer. The epimers 14 and 13 (7:1) were separated by preparative tlc. The C(6)-stereochemistry of 13 and 14 was elucidated by ^{1}H-nmr spectroscopy by comparison with their acetates (16 and 15). For 6α-ol (14), the C(6)-H$_\beta$ signal is a multiplet indicating that C(6)-H$_\beta$ coupled to C(5)-H, C(7)-H$_\beta$ and C(7)-H$_\alpha$. For 6β-ol (13), although C(6)-H$_\alpha$ signal overlapped with those of methylene protons of PhCH$_2$, OCH$_2$CH$_2$O and C(5)-H signal overlapped with that of C(1)-H, and their coupling to other protons was difficult to identify, the C(7)-H$_\beta$ signal was identified as a doublet of doublets and coupling of C(7)-H$_\beta$ to C(6)-H$_\alpha$ was not found. The C(7)-H$_\alpha$ signal of 6β-ol (13) was also a doublet of doublets, but $J_{7\alpha,6\alpha}$ (7.4 Hz) was obviously larger than $J_{7\alpha,6\beta}$ (4.8 Hz) of 6α-ol (14). For acetates (16 and 15), the C(6)-H signals could be compared directly. The C(6)-H$_\beta$ signal of 16 was a mutiplet similar to that of 6α-ol (14), but the C(6)-Hα signal of 15, which was located downfield compared to that of 6β–ol (13) and separated with the signals of other protons, was a doublet of doublets and no coupling of C(6)-H$_\alpha$ with C(5)-H was observed.



a: KOH/*tert*-C_4H_9OH; b: $NaBH_4/C_2H_5$ OH; c: Ac_2O/pyridine; d: HCl/acetone;
e: H_2, 10 % Pd-C/CH_3OH; f: $NaBH_4$/THF; g: $Pd(OH)_2$-C/CH_3OH

Cleavage of the ketal moiety of 16 under mild condition, in acetone at room temperature with *p*-toluenesulfonic acid,[19] was unsuccessful. With concentrated HCl at room temperature, 16 was hydrolyzed to produce 17. Ketone (17) was also obtained from 14 under the same conditions. The desired acetate (18) was obtained from 17 on acetylation. Reduction of the α, β-unsaturated ketone (18) with sodium borohydride in ethanol resulted in a mixture of saturated and unsaturated 2-ol isomers which were difficult to separate and analyze. Unsaturated ketone (17) was hydrogenated over 10 % Pd-C to give saturated ketone (19). Acetylation of 19 afforded acetate (20). Reduction of 20 with sodium borohydride in THF afforded 2β-ol (21) and 2α-ol (22) (7:3) which could be separated by preparative tlc. The sharp absorption at 3470 cm^{-1} for 21 compared to the broader one at 3404 cm^{-1} for 22 in their ir spectra suggested that 21 has an intramolecular hydrogen bond, which required the hydroxyl group in 21 to be β-configuration. The ^{1}H-nmr spectra showed that for 21, the C(2)-H_α signal overlapped with that of methylene protons of $PhCH_2$, but for its acetate (23), the C(2)-H_α signal separated with other signals and was a broad singlet with $W_{1/2}$=9.0 Hz , and its shape was similar to that of the acetate of baogongteng A.[3] The nortropane (24) was obtained from 21 by catalytic debenzylation over $Pd(OH)_2$-C with hydrogen.

Reduction of ketone (10) with the stereoselective reducing agent lithium tri-*tert*-butoxyaluminium hydride failed to raise the β-epimer ratio in the products. So the steric hindrance about the carbonyl was not the chief factor determing the relative amount of epimers obtained in the reduction. Maybe coordination of the lone electron pair of the tropane nitrogen with boron or aluminum of reduced agents facilitates the approach from the " β " side, so the 6α-OH epimer is the favored product. Reduction of ketone (10) with sodium in 3-pentanol / toluene [20] gave 6β-ol (17) exclusively, but the yield was only 10% probably due to the unstability of ketone (10) under strong basic condition. The β-stereoselective reduction of 10 is still being studied of which success would greatly facilitate the synthesis of (±)-baogongteng A. Synthesis of the optically active natural alkaloid requires resolution of one of the chemical precusors as accomplished recently in a related series of tropines.[11]

ACKNOWLEDGEMENT

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EXPERIMENTAL

Melting point (uncorrected): Fisher-Johns apparatus; ir spectra (cm^{-1}): PE 577 instrument; ^{1}H-nmr(δ): JEOL FX 90Q and Varian VXR 300 spectrometers ($CDCl_3$ as solvent, TMS as internal standard); ms

(m/z) for electron-impact (EI ms): VG20-25 mass spectrometer; thin-layer chromatography plates: 0.8% CMC, 0.4% NaOH, and silica gel GF_{254}; Column chromatography: silica gel 200-300 mesh; Solvent systems for tlc: (a) cyclohexane : ethyl acetate=1:1; (b) cyclohexane : ethyl acetate=4:1. Either iodine (I_2) or ultroviolet lamp was used to visualize tlc plates. All compounds described here are racemic mixtures.

8-Benzyl-2,2-ethylenedioxy-8-azabicyclo[3.2.1]oct-3-en-6-one (10), 8-Benzyl-2,2-ethylenedioxy-6α-hydroxy-8-azabicyclo[3.2.1]oct-3-en-6β-amide (11), and 8-Benzyl-2,2-ethylenedioxy-6β-chloro-8-azabicyclo[3.2.1]oct-3-en-6α-amide (12)

3.90 g (12.3 mmol) of 8 was dissolved in 50 ml of *tert*-butanol and 1.69 g (30.1 mmol) of potassium hydroxide and 5 ml of water was added. The solution was refluxed with stirring under nitrogen for 24 h. The reaction solution was treated with 50 ml of 5 % $NaHCO_3$ aqueous solution and extracted with ether (2 X 50 ml). The combined ether layers were dried over Na_2SO_4. After the removal of solvent under reduced pressure, 3.31 g of light brown syrup was obtained. The syrup was chromatographed on a silica gel column (ether : petroleum ether=1:1). 0.48 g (1.5 mmol) of 8 (Rf=0.71) was recovered as white crystals. 1.20 g (4.43 mmol, 36 %) of 10 (Rf=0.49) as a colorless syrup and 0.40 (1.27 mmol, 10%) of 11 (Rf=0.26) as white prisms were obtained sequently. Under the same reaction conditions (8 h, tlc showed the completion of reaction) and workup, 0.91 g (3.35 mmol, 35 %) of 10 and 1.32 g (3.95 mmol, 41.3 %) of 12 were obtained from 3.03 g (9.75 mmol) of 9.

10: Ir (film): 1751, 1601, 1493 cm^{-1}; ms (m/z): 271 (M^+); ^{1}H-nmr: δ 7.40 (m, 5H, Ph), 6.08 (dd, J=10.1, 4.4 Hz, 1H, C4-H), 5.86 (dd, J=10.1, 1.8 Hz, 1H, C3-H), 4.20-3.84 (m, 6H, OCH_2CH_2O, $PhCH_2$), 3.52-3.40 (m, 2H, C1-H, C5-H), 2.80-2.00 (m, 2H, C7-H) ppm.

11 : mp148-149 °C (EtOH); ir (KBr): 3315, 1650, 1494 cm^{-1}; ms (m/z): 316 (M^+); ^{1}H-nmr: δ 7.96, 5.27 (NH_2), 7.26 (s, 5H, Ph), 6.06 (dd, J=10.1, 4.4 Hz, 1H, C4-H), 5.87 (dd, J=9.6, 1.8 Hz,1H, C3-H), 4.31 (s, 1H, OH), 4.20-3.80 (m, 6H, OCH_2CH_2O, $PhCH_2$), 3.27 (m, 2H, C1-H, C5-H), 2.60-2.10 (m, 2H, C7-H_2) ppm. Anal Calcd for $C_{17}H_{20}N_2O_4$: C, 64.53; H, 6.37; N, 8.86. Found: C, 64.22; H, 6.32; N, 8.59.

12: mp135-137.5 °C (AcOEt); ir (KBr): 3430, 3329, 3186, 1699, 1679, 1382 cm^{-1}; ms (m/z): 334 (M^+); ^{1}H-nmr: δ 7.49-7.27 (m, 5H, Ph), 5.88 (dd, J=9.6, 4.4 Hz,1H, C4-H), 5.72 (dd, J=9.6, 1.8 Hz,1H, C3-H), 4.24-3.79 (m, 6H, OCH_2CH_2O, $PHCH_2$), 5.95-5.65 (m, 2H, NH_2), 4.39 (t, J=7.9, 4.4 Hz, 2H, C1-H, C5-H), 3.27 (d, J=15.3 Hz, 1H, C7-H_α), 2.59 (dd, J=15.3, 7.9 Hz, 1H, C7-H_β) ppm. Anal Cacld for $C_{17}H_{21}N_2O_3Cl$: C, 60.96; H, 6.32; N, 8.37. Found : C, 70.01; H, 6.40; N, 8.44.

8-Benzyl-6β- and 6α-hydroxy-2,2-ethylenedioxy-8-azabicyclo [3.2.1]oct-3-enes (13 and 14)

0.91 g (3.36 mmol) of 10 was dissolved in 10 ml of ethanol and 0.13 g (3.35 mmol) of sodium borohydride was added. The mixture was allowed to stand at room temperature for 20 h. The bulk of solvent was removed under reduced pressure and water (10 ml) was added. Extraction of the aqueous phase with chloroform (3 X 10 ml) gave 0.89 g of colorless syrup on evaporation. The syrup was

separated by preparative tlc (ethyl acetate : petroleum ether=1:1) to afford 137 mg (0.50 mmol, 15 %) of 13 and 671 mg (2.46 mmol, 73.4 %) of 14 as colorless syrups.

13: Ir (film): 3433, 1604, 1494 cm^{-1}; ms (m/z): 273 (M^+); ^{1}H-nmr: δ 7.28 (m, 5H, Ph), 6.02 (dd, J=9.8, 4.8 Hz,1H, C4-H), 5.80 (dd, J=9.8, 1.8 Hz,1H, C3-H), 4.21-3.73 (m, 7H, C6-H$_\alpha$, OCH_2CH_2O, $PhCH_2$), 3.31 (t, J=4.8 Hz, 2H, C1-H, C5-H), 2.61 (s, 1H, OH), 2.49 (dd, J=14.4, 6.6 Hz, 1H, C7-H$_\beta$), 1.88 (dd, J=14.7, 7.4 Hz, 1H, C7-H$_\alpha$) ppm.

14: Ir (film): 3416, 1602, 1493 cm^{-1}; ms (m/z): 273 (M^+); ^{1}H-nmr: δ 7.28 (m, 5H, Ph), 6.02 (dd, J=9.8, 4.8 Hz, 1H, C4-H), 5.80 (dd, J=9.8, 1.8 Hz, 1H, C3-H), 4.46 (m, 1H, C6-H$_\beta$), 4.13-3.70 (m, 6H, CH_2CH_2O, $PhCH_2$), 3.41 (t, J=5.7, 4.8 Hz, 1H, C5-H), 3.06 (d, J=7.9 Hz, 1H, C1-H), 2.11 (s, 1H, OH), 2.58 (m, 1H, C7-H$_\beta$), 1.69 (dd, J=14.4, 4.8 Hz,1H, C7-H$_\alpha$) ppm.

8-Benzyl-6β- and 6α-acetoxy-2,2-ethylenedioxy-8-azabicyclo[3.2.1]oct-3-enes (15 and 16)

90 mg (0.33 mmol) of 13 was dissolved in 0.2 ml of acetic anhydride and 0.2 ml of pyridine. The solution was allowed to stand at room temperature for 23 h. The excess of acetic anhydride and pyridine was removed under reduced pressure. The residue was purified by passage through a short silica gel column eluted with ether to give 80 mg (0.25 mmol, 77 %) of 15 as light yellow oil.

15: Ir (film): 1733, 1604, 1494 cm^{-1} ; ms (m/z): 315 (M^+); ^{1}H-nmr: δ 7.41-7.19 (m, 5H, Ph), 6.01 (dd, J=9.6, 5.3 Hz, 1H, C4-H), 5.60 (dd, J=9.9, 1.8 Hz, 1H, C3-H), 4.93(dd, J=7.2, 1.8 Hz, 1H, C6-He), 4.01-3.81 (m, 6H, OCH_2CH_2O, $PhCH_2$), 2.56 (dd, J=14.7, 7.3 Hz, 1H, C7-H$_\beta$), 2 .09 (dd,J=13.6, 7.4 Hz, 1H, C7-H$_\alpha$), 2.05 (s, 3H, CH_3COO) ppm.

In a simiar way to the preparation of 15, 16 (73.2 %) was obtained from 14 as light yellow oil.

16: Ir (film): 1735, 1602, 1494 cm^{-1}; ms (m/z): 315 (M^+); ^{1}H-nmr: δ 7.28 (m, 5H, Ph), 5.92 (dd, J=9.8, 4.8 Hz, 1H, C4-H), 5.73 (dd, J=9.4, 1.8 Hz, 1H, C3-H), 5.16 (m, 1H, C6-H$_\beta$), 4.16-3.82 (m, 6H, OCH_2CH_2O, $PhCH_2$), 3.65 (t, J=5.7, 4.8 Hz, 1H, C5-H), 3.12 (dd, J=6.6, 0.9 Hz, 1H, C1-H), 2.63(ddd, J=14.2, 9.7, 6.6 Hz,1H, C7-H$_\beta$),1.99 (s, 3H, CH_3COO),1.88 (dd, J=14.2,4.8 Hz, 1H, C7-H$_\alpha$) ppm.

8-Benzyl-6α-hydroxy-8-azabicyclo[3.2.1]oct-3-en-2-one (17)

310 mg (0.98 mmol) of 16 was dissolved in 3 ml of acetone and 3 ml of concentrated HCl was added. The solution was allowed to stand at room temperature for 12 h and made basic by concentrated NH_4OH and extracted with chloroform (2 X 5 ml). The combined extracts were washed with water (2 X 10 ml), dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by passage through a short silica gel column (ethyl acetate : petroleum ether=1:1) to give 160 mg (0.7 mmol, 61.3 %) of 17 as yellow oil.

17: Ir (film): 3414, 1678, 1493 cm^{-1}; ms (m/z): 229 (M^+); ^{1}H-nmr: δ 7.28 (s, 5H, Ph), 6.93 (dd, J=9.6, 4.8 Hz, 1H, C4-H), 6.30 (dd, J=9.8, 4.8 Hz, 1H, C3-H), 4.83 (m, 1H, C6-H$_\beta$), 3.86 (t, J=5.3 Hz, 1H, C5-H), 3.78 (s, 2H, $PhCH_2$), 3.49 (d, J=8.3 Hz, 1H, C1-H), 2.89 (ddd, J=13.9, 8.8, 8.3 Hz, 1H, C7-H$_\beta$), 2.06 (s, 1H, OH), 1.43 (dd, J=14.4, 4.4 Hz, 1H, C7-H$_\alpha$) ppm.

8-Benzyl-6α-acetoxy-8-azabicyclo[3.2.1]oct-3-en-2-one (18)

In a similary way to the preparation of 15, 18 was obtained from 17 as a yellow oil, yield: 83.3 %.
18: Ir (film): 1735, 1688, 1604, 1494 cm^{-1} ; ms (m/z): 271 (M^+); ^{1}H-nmr: δ 7.25 (s, 5H, Ph), 6.76 (dd, J=9.8, 5.3 Hz, 1H, C4-H), 6.26 (dd, J=10.1, 1.8 Hz, 1H, C3-H), 5.36 (m, 1H, C6-Hβ), 4.03 (t, J=5.7, 5.3 Hz, 1H, C5-H), 3.75 (s, 2H, $PhCH_2$), 3.47 (d, J=8.3 Hz, 1H, C1-H), 2.88 (ddd, J=14.0, 8.6, 8.3 Hz, 1H, C7-Hβ), 1.99 (s, 3H, CH_3COO), 1.54 (dd, J=14.4, 4.5 Hz, 1H, C7-Hα) ppm.

8-Benzyl-6α-hydroxy-8-azabicyclo[3.2.1]octan-2-one (19)

260 mg (1.14 mmol) of 17 was dissolved in 15 ml of methanol and 50 mg of 10 % Pd-C was added. The mixture was stirred at room temperature under hydrogen until all the starting material disappeared. After the removal of the catalyst and solvent, 240 mg of light yellow syrup was obtained. The syrup was dissolved in ethyl acetate and filtered through a short silica gel column. The solvent was evaporated under reduced pressure to give 19 as a colorless syrup (190 mg, 0.82 mmol, 72 %).
19: Ir (film): 3427, 1700, 1602, 1492 cm^{-1}; ms (m/z): 231 (M^+); ^{1}H-nmr: δ 7.26 (s, 5H, Ph), 4.60 (m, 1H, C6-Hβ), 3.75 (s, 2H, $PhCH_2$), 3.62 (s, 1H, OH), 3.38-3.13 (m, 2H, C1-H, C5-H), 2.79-2.54 (m, 1H, C7-Hβ), 2.29-2.02 (m, 2H, C3-H_2), 1.50 (dd, J=14.4, 4.4 Hz, 1H, C7-Hα), 1.31-1.16 (m, 2H, C4-H_2) ppm.

8-Benzyl-6α-acetoxy-8-azabicyclo[3.2.1]octan-2-one (20)

In a similary way to the preparation of 15, 20 was obtained from 19 as a colorless syrup, yield: 73 %.
20: ir (film): 1739,1234 cm^{-1}; ms (m/z): 273 (M^+); ^{1}H-nmr: δ 7.27 (s, 5H, Ph), 5.38 (m, 1H, C6-Hβ), 3.76 (s,2H, $PhCH_2$), 3.57-3.50 (m, 1H, C5-H), 3.23 (d, J=8.3 Hz,1H, C1-H), 2.92-2.56 (m, 1H, C7-Hβ), 2.43-2.14 (m, 2H, C3-H_2), 2.06 (s, 3H, CH_3COO),1.98 (m, 2H, C4-H_2),1.66 (dd, J=14.4, 4.4 Hz, C7-Hα) ppm.

8-Benzyl-6β-acetoxy-8-azabicyclo [3.2.1] octan-2β- and 2α-ols (21 and 22)

In a similary way to the preparation of 13 and 14, 21 (70 mg, 0.25 mmol, 53 %) and 22 (30 mg, 0.09 mmol, 23 %) were obtained from 24 (130 mg, 0.48 mmol) as colorless syrups.
21: Ir (film): 3470, 1737, 1246 cm^{-1}; ms (m/z): 275 (M^+); ^{1}H-nmr: δ 7.30 (s, 5H, Ph), 5.44 (m, 1H, C6-Hβ), 3.57 (m, 3H, C2-Hα, $PhCH_2$), 3.35 (t, J=5,7, 5.3 Hz,1H, C5-H), 3.10 (d, J=8.3 Hz, 1H, C1-H), 2.85-2.48 (m, 2H, C7-Hβ, OH), 2.06 (s, 3H, CH_3COO), 2.00-1.29 (m, 5H, C7-Hα, C3-H_2, C4-H_2) ppm.
22: Ir (film): 3408, 1732, 1246 cm^{-1}; ms (m/z): 275 (M^+); ^{1}H-nmr: δ 7.30 (s, 5H, Ph), 5.40 (m, 1H, C6-Hβ), 4.12-3.92 (m, 1H, C2-Hβ), 3.72 (s, 2H, $PhCH_2$), 3.40-3.20 (m, 1H, C5-H), 3.18-3.00 (m, 1H, C1-H), 2.66-2.28(m, 2H, C7-Hβ, OH), 2.07 (s, 3H, CH_3COO), 2.00-1.60 (m, 5H, C7-Hα, C3-H_2, C4-H_2) ppm.

8-Benzyl-2β, 6α-diacetoxy-8-azabicyclo[3.2.1]octane (23)

In a similary way to the preparation of 15, 23 was obtained from 21 as a colorless syrup, yield: 91 %.
23: Ir (film): 1735, 1242, 1040 cm^{-1}; ms (m/z): 317 (M^+); ^{1}H-nmr: δ 7.30 (m, 5H, Ph), 5.38 (m, 1H, C6-Hβ), 4.76 (br s, 1H, C2-Hα), 3.72 (m, 2H, $PhCH_2$), 3.43 (br.d., J=5.3 Hz,1H, C5-H), 3.25 (br d, J=8.3 Hz, 1H, C1-H), 2.62 (ddd, J=14.0, 8.6, 8.3 Hz, 1H, C7-Hβ), 2.06 (s, 6H, 2XCH_3COO), 2.00-1.26 (m, 5H, C7-Hα, C3-H_2, C4-H_2) ppm.

6α-Acetoxy-8-azabicyclo[3.2.1]octan-2β-ol (24) (2β-Hydroxy-6α-acetoxynortropane)

80 mg (0.29 mmol) of 21 was dissolved in 8 ml of methanol and 30 mg of $Pd(OH)_2$ -C was added. The

mixture was stirred at room temperature under hydrogen until all the starting material disappeared. After the removal of catalyst and solvent, 24 was obtained quantitatively as colorless needles.
24: mp 125-128 °C; ir(KBr): 3291, 3053, 1730, 1240 cm^{-1}; ms (m/z): 185 (M^+); ^{1}H-nmr: δ 5.12 (m, 1H, C6-H_β), 3.65 (br s, 1H, C2-H_α), 3.50 (m, 1H, C5-H), 3.40 (m, 1H, C1-H), 3.04-2.63 (m, 2H, NH, OH). 2.46-2.14 (m, 1H, C7-H_β), 2.08 (s, 3H, CH_3COO), 1.94-1.24 (m, 5H, C7-H_α, C3-H_2, C4-H_2) ppm.
Anal Calcd for $C_9H_{15}NO_3$: C, 58.37; H, 8.16; N, 7.56. Found: C, 58.15; H, 8.48; N, 7.42.

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