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m-CHLOROPERBENZOIC ACID OXIDATION OF CORYNANTHE-TYPE INDOLE ALKALOID, MITRAGYNINE, AFFORDED UNUSUAL DIMERIZATION PRODUCTS

Hayato Ishikawa, Mariko Kitajima, and Hiromitsu Takayama*

Graduate School of Pharmaceutical Sciences, Chiba University; 1-33 Yayoi-cho, Inage-ku, Chiba 263-8522, Japan; takayama@p.chiba-u.ac.jp

Abstract – The *m*-chloroperbenzoic acid oxidation of a Corynanthe-type indole alkaloid, mitragynine (**1**), in the presence of trifluoroacetic acid produced unusual dimeric compounds (**3** and **4**), both of which had a linkage between the C-7 and C-12' positions in the indole part of the starting material.

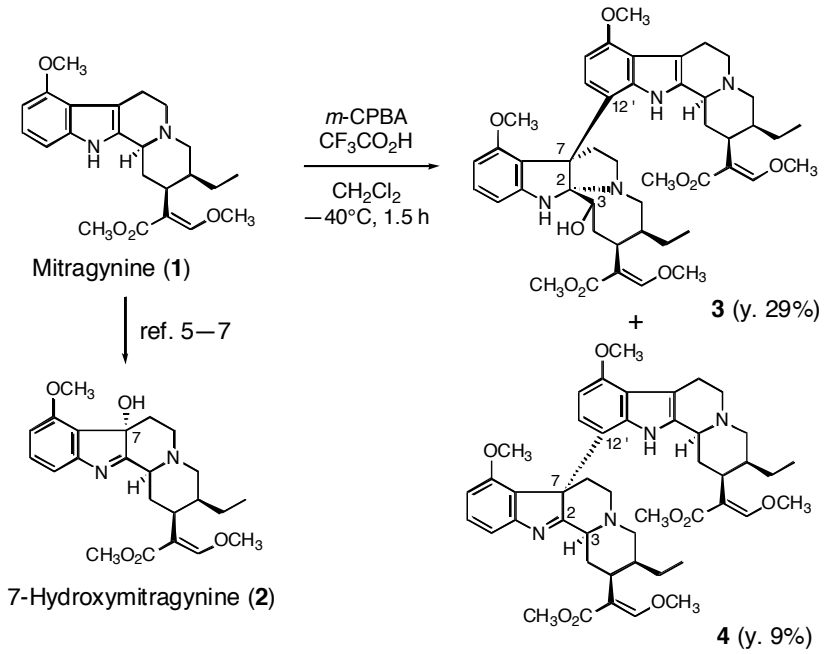
INTRODUCTION

In our recent chemical and pharmacological study[1] on the rubiaceous plant, *Mitragyna speciosa*, which has been traditionally used in tropical countries as a substitute for opium,[2] we have found that 7-hydroxymitragynine (**2**),[3] a minor constituent of this plant, exhibited highly potent opioid agonistic property *in vitro* and *in vivo* experiments in mice.[4] In particular, **2** displayed efficient antinociception when administered orally to mice in the tail-flick and hot plate tests, exhibiting superior advantage over morphine as regards the ability to induce antinociception *via* oral administration. Inspired by this result, we investigated[5−7] the preparation of **2** from mitragynine (**1**), a major component of *M. speciosa*.[3, 8] Gueller and Borschberg have reported an efficient procedure for transforming Aristotelia-type indole alkaloids into 7-hydroxyindolenine derivatives using *m*-chloroperbenzoic acid (*m*-CPBA) in the presence of trifluoroacetic acid.[9] When we applied this method to mitragynine (**1**), a Corynanthe-type indole alkaloid, unexpected dimerization products were obtained. We describe herein the structures and the possible mechanisms for the formation of these compounds.

RESULTS AND DISCUSSION

The *m*-CPBA oxidation of indole alkaloids possessing two nitrogen atoms, i.e., aromatic and aliphatic amino groups, in the molecule generally gives the *N*-oxide derivatives of the alkylamino part.

Mitragynine (**1**) afforded an N_b-oxide derivative under conventional conditions (one equivalent of *m*-CPBA in methylene chloride).[6] To prevent this kind of reaction, Gueller and Borschberg devised a condition for *m*-CPBA oxidation by adding trifluoroacetic acid that protected the lone electron pair of the N_b by protonation, thereby succeeding in the oxidation of the indole part preferentially to yield 7-hydroxyindolenine derivative in good yield.[9] The application of this protocol (*m*-CPBA, TFA, CH_2Cl_2, −40°C, 1.5 h) to mitragynine (**1**), however, resulted in the isolation of two products having unusual structures. (Scheme 1) The structure of major product (**3**) obtained in 29% yield was inferred from spectroscopic data and the chemical reaction as described below. The minor product isolated in 9% yield was proved to be compound (**4**), which was formed by hypervalent iodine {phenyliodine(III) bis(trifluoroacetate)} oxidation of mitragynine (**1**).[5]



Scheme 1

The molecular formula ($C_{46}H_{60}N_4O_9$) determined from the high-resolution FABMS spectrum and the ^{13}C-NMR spectrum implied that **3** had a dimeric structure. The ^{1}H- and ^{13}C-NMR spectra of **3** clearly showed the presence of two sets of fundamental structural units in the starting material (**1**), i.e., two β-methoxyacylic acid methyl ester residues, two ethyl groups, and two 9-methoxy groups on the aromatic ring. Furthermore, the UV absorption bands (298, 244 (sh), 229, and 218 nm) and the ^{13}C-NMR spectrum that disclosed twenty sp^2 carbons and twenty-six sp^3 carbons including one characteristic aminoacetal carbon (δ 93.6) indicated that **3** contained one indolic and one indoline chromophore. In the ^{1}H-NMR spectrum, a set of three aromatic protons at δ 6.28 (1H, doublet, *J*=7.6 Hz), δ 6.27 (1H, doublet, *J*=7.6 Hz), and δ 7.00 (1H, doublet of doublet, J_1=J_2=7.6 Hz), which are the same as those of **1**, and a set of *ortho*-coupled protons at δ 6.40 (1H, doublet, *J*=8.3 Hz) and δ 7.15 (1H, doublet, *J*=8.3 Hz) were

observed. These indicated that one of the two units was intact as regards the substituent mode on the benzene ring and the other unit had a substituent at the C-10 or C-12 position. In the ^{1}H-detected heteronuclear multiple-bond correlation (HMBC) spectrum (Figure 1), connectivities were observed between the two *ortho*-coupled protons (δ 6.40 and 7.15) and an aromatic carbon (δ 153.9), that could be assigned as C-9' based on its chemical shift, as well as between the *ortho*-coupled proton (δ 7.15) and a quaternary carbon (δ 54.5) that could be assigned as C-7 based on the fact that this carbon showed HMBC cross-peaks with the protons at N_a, C-5 and C-6. These findings indicated the presence of a bridge between C-7 in the indoline part and C-12' on the indole ring of another unit. In the indoline part of the dimeric structure, three characteristic signals in the ^{13}C-NMR spectrum, i.e., δ 93.6, 70.5, and 54.5, were observed compared with those in mitragynine (**1**). These chemical shifts were very similar to those (see Figure 1) of a known indole alkaloid, N_b-demethylechitamine (**5**),[10] which contained a 3-hydroxy-pyrrolidinoindoline residue in the molecule.

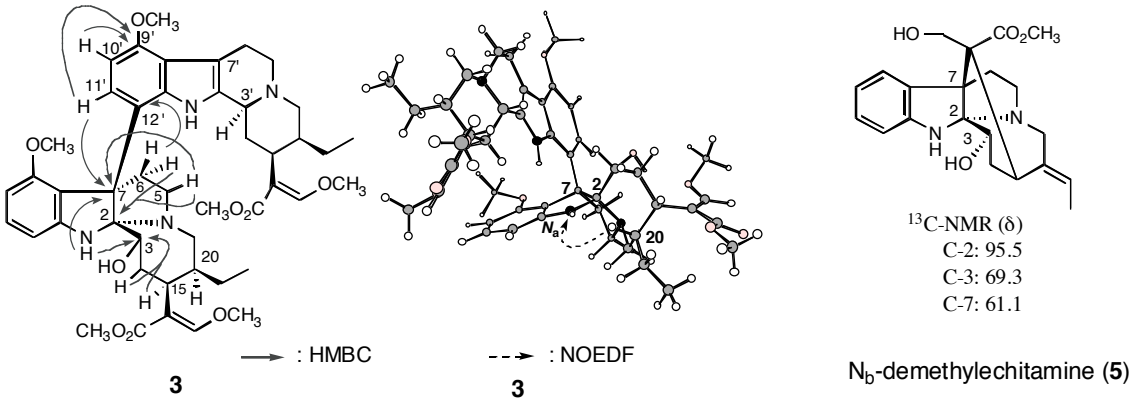
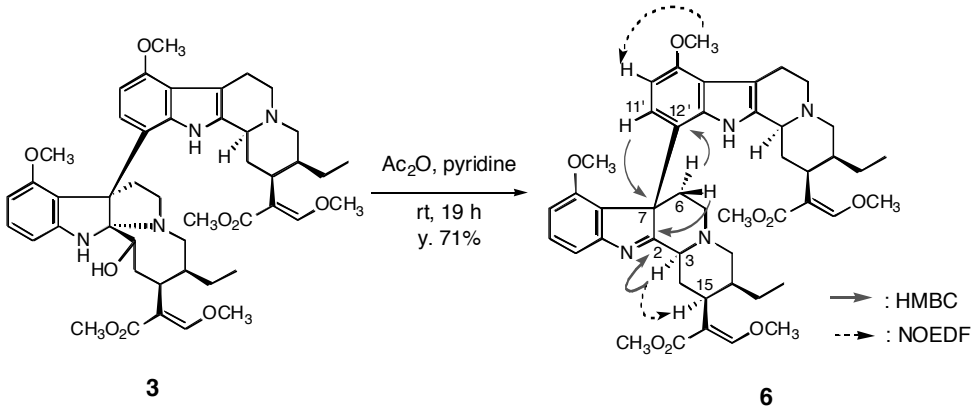


Figure 1

The presence of this function was supported by the HMBC cross-peaks between the quaternary aminoacetal carbon (δ 93.6) and the protons at N_a, C-5, C-6, and C-14, and between the secondary hydroxyl carbon (δ 70.5) and the protons at N_a, C-14, and C-15. The remaining part of dimer (**3**) was revealed to have the structure of mitragynine itself, except for a substituent at C-12', based on the reasons mentioned above and on the comparison of the ^{13}C-NMR spectra of **3** and **1**. To elucidate the stereochemistry of the newly formed chiral centers in **3**, differential nuclear Overhauser effect (NOEDF) experiments were carried out. The clear NOE observed between H-20 and N_a-H, as shown in Figure 1, indicated that the N_b group was attached to the C-2 position from the α-side, implying a C2(*R*) configuration. This finding suggested that the substituent (an indole ring) at C-7 was attached from the β-side, because the bicyclo[3.3.0]octane ring system could only assume the *cis*-fused form. However, significant information of the stereochemistry of the secondary hydroxyl group at C-3 could not be

obtained from the NOEDF experiments. Thus, we attempted to prepare the acetyl derivative of **3**. Under conventional conditions (acetic anhydride in pyridine at room temperature), we obtained an unexpected compound (**6**) in 71% yield. (Scheme 2)



3 **6**

Scheme 2

The molecular formula ($C_{46}H_{58}N_4O_8$) determined from the high-resolution FAB-MS spectrum and the ^{1}H-NMR spectrum indicated that **6** was not the acetate derivative but the dehydration product. The UV absorption bands and the ^{1}H- and ^{13}C-NMR spectra were very similar with thoses of **4** and the molecular formula was identical to that of **4**. In particular, the aminoacetal carbon in **3** disappeared and instead, a characteristic indolenine carbon (δ 191.3) was observed in the ^{13}C-NMR spectrum. The HMBC cross-peaks between the imine carbon (δ 191.3) and the protons at C-3 and C-6 supported the indolenine structure. The stereochemistry of the newly formed chiral center at C-3 was deduced to be *S* from the observation of NOE between H-3 and H-15. (Scheme 2) From these data, the structure of the dimeric compound was deduced to be formula (**6**), which was an epimer of **4** at the C-7 position. Actually, in the CD spectra, both compounds displayed the opposite Cotton sign in the 200—260 nm region, as shown in Figure 2.

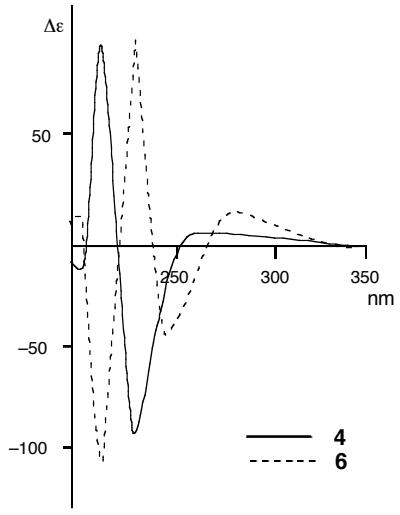
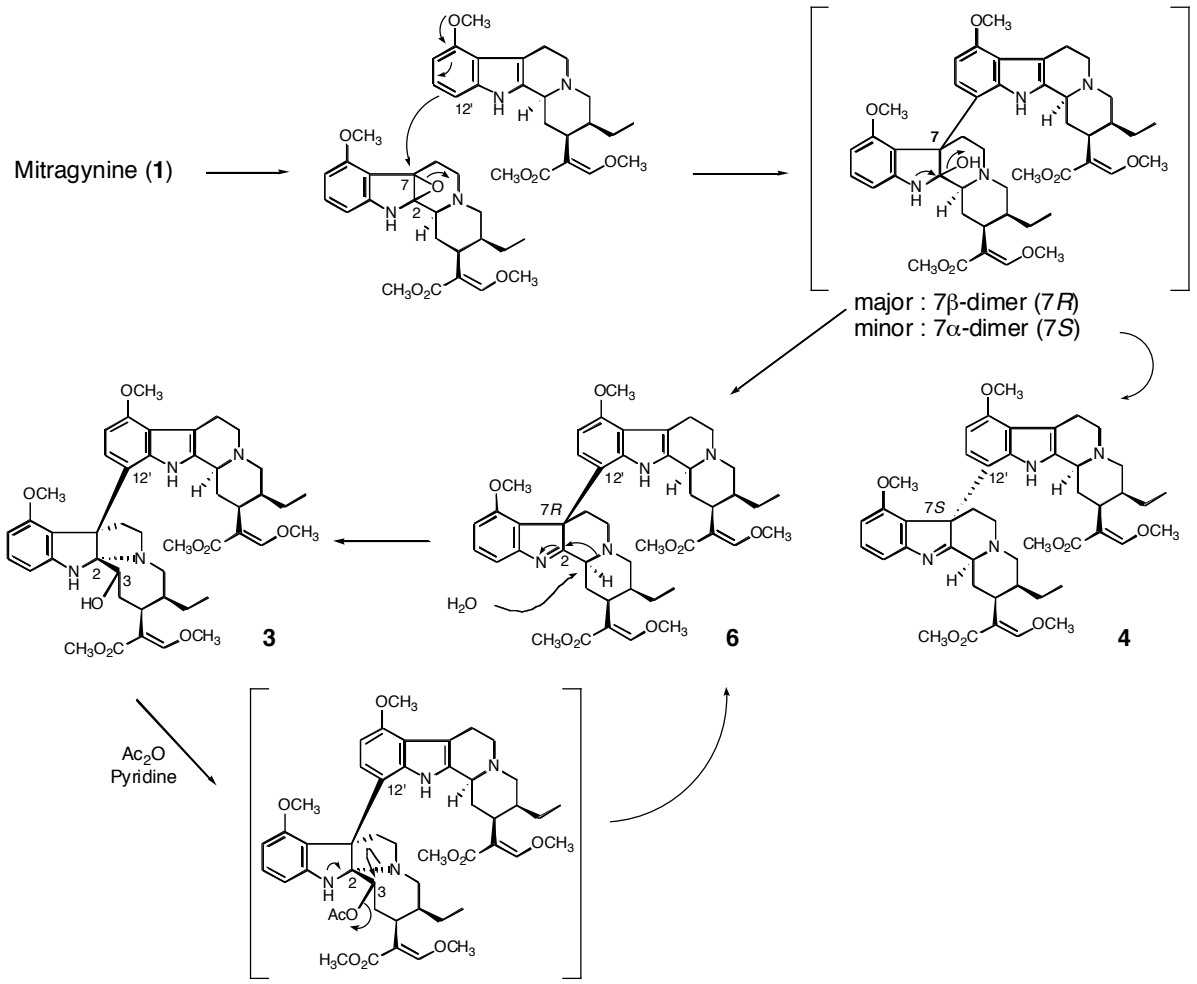


Figure 2. CD spectra of compounds (**4**) and (**6**)

The possible mechanism for the formation of these dimeric compounds is depicted in Scheme 3. Under acidic conditions, *m*-CPBA preferentially reacts with the indole part in mitragynine (**1**) to yield the 2,7-epoxy intermediate,[11] which is subjected to electrophilic aromatic substitution in the presence of another mitragynine (**1**). The elimination of one water molecule from the resulting hemiaminoacetal intermediates affords dimers (**4**) and (**6**) possessing an indolenine residue. Although the reason is obscure, in the case of

β-isomer (**6**), further rearrangement occurs to give the echitamine-type compound (**3**) having a pyrrolidinoindoline chromophore. When **3** is treated with acetic anhydride in pyridine, the resulting 3-acetoxy group acts as a leaving group, promoting the reconstruction of the indolenine derivative (**6**).



Scheme 3

EXPERIMENTAL

General UV: recorded in MeOH on a JASCO V-560 instrument. ^{1}H and ^{13}C-NMR spectra: recorded on a JEOL JNM A-400, JNM A-500, JNM ECP-400, or JNM ECP-600 spectrometer; *J* values are given in Hz. EI-MS: direct probe insertion at 70 eV recorded on a JEOL JMS GC-mate spectrometer. FAB-MS: recorded on a JEOL JMS-HX110 mass spectrometer. CD: recorded on a JASCO J-720WI spectrometer. TLC: precoated Kieselgel 60 F_{254} plates (Merck, 0.25 mm thick). Column chromatography: Kieselgel 60 [Merck, 70-230 (for open chromatography)], aluminum oxide 90 [Merck, 70-230 (for open chromatography)].

m-CPBA oxidation of mitragynine (1)

To a stirred solution of mitragynine (**1**) (100.0 mg, 0.25 mmol) in dry CH_2Cl_2 (4.0 mL) was added trifluoroacetic acid (0.1 mL). After stirring for 5 min at –40°C under argon atmosphere, a solution of *m*-

CPBA (44.0 mg, 0.18 mmol) in CH_2Cl_2 (1.0 mL) was added *via* a syringe. After stirring for 1.5 h at the same temperature, dimethyl sulfide (10 μL) was added to the reaction mixture and the cold mixture was poured into 28% NH_3 and H_2O and was extracted with $CHCl_3$ three times. The combined organic layer was washed with brine, dried over $MgSO_4$ and evaporated. The residue was separated by Al_2O_3 column chromatography (30% AcOEt/*n*-hexane) to give **3** (29.1 mg, 29%) and **4** (5.8 mg, 9%), both as amorphous powder. **3**: UV (MeOH) λ_{max}: 298, 244 (sh), 229, and 218 nm. ^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 9.54 (1H, br s, $N_{a'}$-H), 7.47 and 7.41 (each 1H, s, H-17 and H-17'), 7.15 (1H, d, *J*=8.3, H-11'), 7.00 (1H, dd, *J*=7.6 and 7.6, H-11), 6.40 (1H, d, *J*=8.3, H-10'), 6.28 (1H, d, *J*=7.6, H-10), 6.27 (1H, d, *J*=7.6, H-12), 3.83 (3H, s, 9'-OCH_3), 3.75 and 3.73 (each 3H, s, 17-OCH_3 and 17'-OCH_3), 3.72 and 3.66 (each 3H, s, 22-OCH_3 and 22'-OCH_3), 3.58 (3H, s, 9-OCH_3), 3.12 (1H, br d, *J*=14.0, H-6), 3.03 (2H, m, H-3' and H-6'), 2.95 (4H, m, H-6', H-15, H-21 and H-21'), 2.85 (1H, dd like, *J*=11.6 and 6.1, H-5'), 2.80 (2H, m, H-5 and H-15'), 2.70 (1H, m, H-14), 2.64 (1H, td like, *J*=12.3 and 5.3, H-6'), 2.48 (1H, td like, *J*=12.3 and 4.3, H-5'), 2.39 (1H, br d, *J*=8.6, H-21), 2.25 (1H, ddd, *J*=12.8, 12.8, and 12.8, H-14'), 2.10 (1H, t like, *J*=11.0, H-5), 2.05 (1H, m, H-3), 2.02 (1H, m, H-21'), 1.75 (2H, m, H-19 and H-19'), 1.63 (1H, m, H-14'), 1.56 (1H, m, H-20'), 1.52 (1H, m, H-20), 1.49 (1H, m, H-14), 1.20 (2H, m, H-19 and H-19'), 0.85 and 0.82 (each 3H, t, *J*=7.3, H_3-18 and H_3-18'). ^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: 169.3 and 169.2 (C-22 and C-22'), 160.5 and 160.3 (C-17 or C-17'), 157.9 (C-9), 153.9 (C-9'), 148.5 (C-13), 135.2 (C-13'), 133.4 (C-2'), 129.6 (C-11), 122.7 (C-11'), 118.4 (C-12'), 118.3 (C-8), 116.1 (C-8'), 111.9 and 111.5 (C-16 and C-16'), 106.5 (C-7'), 104.2 and 104.1 (C-10 and C-12), 99.2 (C-10'), 93.6 (C-2), 70.5 (C-3), 61.6 (C-3'), 61.34 and 61.29 (17-OCH_3 and 17'-OCH_3), 58.8 (C-21'), 57.8 (C-21), 55.3 (9-OCH_3), 55.1 (9'-OCH_3), 54.5 (C-7), 53.9 (C-5'), 53.7 (C-5), 51.30 and 51.27 (22-OCH_3 and 22'-OCH_3), 40.6 (C-20'), 40.4 (C-20), 39.9 (C-15'), 39.8 (C-15), 29.4 (C-14'), 28.6 (C-6), 24.7 (C-14), 23.9 (C-6'), 19.0 (C-19 and C-19'), 12.9 and 12.8 (C-18 and C-18'). FABMS (NBA) *m/z*: 813 [MH^+]. HR-FABMS (NBA): calcd for $C_{46}H_{61}N_4O_9$ [MH^+]: 813.4439, found: 813.4432. CD (0.17 mM, MeOH, 24°C), λnm (Δε): 290 (0), 272 (+2.5), 267 (0), 249 (–31.4), 240 (0), 232 (+77.0), 225 (0), 218 (–66.3), 203 (–0.5). **4**: UV (MeOH) λ_{max}: 297, 248 (sh), and 232 nm. ^{1}H-NMR (600 MHz, $CDCl_3$, —50°C) δ [ppm]: 7.43 and 7.40 (each 1H, s, H-17 and H-17'), 7.38 (1H, d, *J*=7.8, H-12), 7.34 (1H, d, *J*=7.7, H-11'), 7.24 (1H, t, *J*=7.8, H-11), 6.90 (1H, br s, $N_{a'}$-H), 6.59 (1H, d, *J*=7.8, H-10), 6.50 (1H, d, *J*=7.7, H-10'), 3.86 (3H, s, 9'-OCH_3), 3.79 and 3.58 (each 3H, s, 17-OCH_3 and 17'-OCH_3), 3.69 and 3.60 (each 3H, s, 22-OCH_3 and 22'-OCH_3), 3.57 (3H, s, 9-OCH_3), 3.45 (1H, br d, *J*=14.0, H-6), 3.00 (1H, m, H-6'), 2.95 (1H, m, H-21 or H-21'), 2.92 (1H, m, H-3'), 2.90 (1H, m, H-14), 2.87 and 2.78 (each 1H, m, H-15 and H-15'), 2.82 (1H, m, H-6'), 2.80 (1H, m, H-5'), 2.73 (2H, m, H-5), 2.57 (1H, br d, *J*=10.7, H-3), 2.38 (1H, q like, *J*=12.9, H-14'), 2.32 (1H, m, H-5'), 2.30 (1H, m, H-21 or H-21'), 2.20 (1H, br d, *J*=10.4, H-21 or H-21'), 1.68

(2H, m, H-19 and H-19'), 1.63 (1H, m, H-14), 1.54 (1H, m, H-6), 1.48 (3H, m, H-14', H-20 and H-20'), 1.10 (2H, m, H-19 and H-19'), 0.79 and 0.75 (each 3H, t, *J*=7.2, H_3-18 and H_3-18'). ^{13}C-NMR (150 MHz, $CDCl_3$, −50°C) δ [ppm]: 190.1 (C-2), 170.0 and 169.6 (C-22 and C-22'), 161.5 and 161.4 (C-17 and C-17'), 155.7 (C-9), 154.9 (C-13), 153.5 (C-9'), 134.3 (C-13'), 133.1 (C-2'), 130.2 (C-8), 129.5 (C-11), 121.5 (C-11'), 117.8 (C-7'), 114.0 (C-12), 110.86 and 110.84 (C-16 and C-16'), 110.80 (C-12'), 109.2 (C-10), 107.4 (C-8'), 99.1 (C-10'), 62.4 and 61.5 (17-OCH_3 and 17'-OCH_3), 62.3 (C-3), 61.0 (C-3'), 59.6 (C-7), 57.6 and 57.4 (C-21 and C-21'), 55.6 (9-OCH_3), 55.4 (9'-OCH_3), 53.8 (C-5'), 52.1 and 52.0 (22-OCH_3 and 22'-OCH_3), 51.2 (C-5), 40.4 and 40.3 (C-20 and C-20'), 39.5 and 38.4 (C-15 and C-15'), 32.4 (C-6), 29.1 (C-14'), 26.6 (C-14), 23.8 (C-6'), 19.1 and 19.0 (C-19 and 19'), 13.0 (C-18 and C-18'). FABMS (NBA) *m/z*: 795 [MH^+]. HR-FABMS (NBA): calcd for $C_{46}H_{59}N_4O_8$ [MH^+]: 795.4333, found: 795.4324. CD (0.20 mM, MeOH, 24°C), λnm (Δε): 310 (0), 305 (–0.9), 300 (0), 298 (+2.3), 292 (0), 287 (–1.1), 280 (0), 269 (+4.8), 260 (0), 234 (–139.0), 227 (0), 220 (+101.0), 208 (0).

Acetylation of Dimer (3)

To a stirred solution of **3** (20.0 mg, 0.025 mmol) in dry pyridine (0.6 mL) was added Ac_2O (0.6 mL, 6.36 mmol) at rt under argon atmosphere. After the reaction mixture was stirred for 19 h, it was poured into chilled water and extracted with $CHCl_3$ three times. The combined organic layer was washed with brine, dried over $MgSO_4$ and evaporated. The residue was purified by Al_2O_3 column chromatography (30% AcOEt/*n*-hexane) to give dimer (**6**) (14.2 mg, 71%) as an amorphous powder. **6**: UV (MeOH) λ_{max}: 297, 247 (sh), and 227 nm. ^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 7.42 and 7.14 (each 1H, s, H-17 and H-17'), 7.34 (1H, d, *J*=8.2, H-11'), 7.29 (1H, d, *J*=7.9, H-12), 7.20 (1H, dd, *J*=7.9, 7.9, H-11), 6.57 (1H, d, *J*=7.9, H-10), 6.49 (1H, br s, $N_{a'}$-H), 6.48 (1H, d, *J*=8.2, H-10'), 3.85 (3H, s, 9'-OCH_3), 3.73 and 3.52 (each 3H, s, 17-OCH_3 and 17'-OCH_3), 3.72 and 3.57 (each 3H, s, 22-OCH_3 and 22'-OCH_3), 3.65 (1H, m, H-6), 3.36 (3H, s, 9-OCH_3), 3.21 (1H, dd, *J*=13.4 and 2.5, H-3), 3.10 (1H, td like, *J*=9.8 and 4.2, H-5), 3.02 (1H, m, H-6'), 2.91~2.81 (6H, m, H-3', H-5', H-6', H-21, H-21', and H-15'), 2.72 (1H, dt, *J*=13.4 and 4.0, H-15), 2.42 (1H, m, H-5), 2.32 (2H, m, H-5' and H-21'), 2.22 (1H, br d, *J*=9.5, H-21), 1.96 (1H, ddd, *J*=13.1, 13.1, 13.1, H-14'), 1.60~1.50 (3H, m, H-6, H-20 and H-20'), 1.34 (1H, br d, *J*=13.4, H-14), 1.17 (1H, br d, *J*=13.1, H-14'), 1.11 and 0.88 (each 1H, m, H-19 and H-19'), 0.75 and 0.65 (each 1H, m, H-19 and H-19'), 0.79 (3H, t, *J*=7.3, H_3-18 or H_3-18'), 0.69 (3H, t, *J*=7.0, H_3-18 or H_3-18'). ^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: 191.3 (C-2), 169.23 and 169.15 (C-22 and C-22'), 160.32 and 160.22 (C-17 and C-17'), 156.2 (C-9), 156.0 (C-13), 153.3 (C-9'), 134.3 (C-13'), 132.6 (C-2'), 132.1 (C-8), 129.3 (C-11), 122.2 (C-11'), 117.3 (C-7'), 113.3 (C-12), 112.7 (C-12'), 111.6 and 110.9 (C-16 and C-16'), 108.8 (C-10), 106.1 (C-8'), 99.6 (C-10'), 66.0 (C-3), 61.3 and 61.2 (17-OCH_3 and 17'-OCH_3), 60.7 (C-3'), 58.9 (C-7), 57.8 (C-21'), 55.6 (9-OCH_3), 55.4 (9'-OCH_3), 55.1 (C-21), 53.8 (C-5'), 51.3 and 51.0 (22-OCH_3 and 22'-

OCH_3), 48.7 (C-5), 40.6 and 40.0 (C-20 and C-20'), 39.7 and 39.5 (C-15 and C-15'), 28.8 (C-14'), 28.3 (C-6 and C-14), 23.9 (C-6'), 19.1 and 18.4 (C-19 and 19'), 12.7 and 12.5 (C-18 and C-18'). FABMS (NBA) *m/z*: 795 [MH^+]. HR-FABMS (NBA): calcd for $C_{46}H_{59}N_4O_8$ [MH^+]: 795.4333, found: 795.4324. CD (0.12 mM, MeOH, 24°C), λnm (Δε): 320 (0), 290 (+12.6), 267 (0), 243 (–35.1), 238 (0), 232 (+66.6), 226 (0), 220 (–104.0), 205 (0).

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REFERENCES

1. H. Takayama, *Chem. Pharm. Bull.*, 2004, **52**, 916, and references cited therein.
2. K. L. R. Jansen and C. J. Prast, *J. Ethnopharmacol.*, 1988, **23**, 115, and references cited therein.
3. D. Ponglux, S. Wongseripipatana, H. Takayama, M. Kikuchi, M. Kurihara, M. Kitajima, N. Aimi, and S. Sakai, *Planta Med.*, 1994, **60**, 580.
4. K. Matsumoto, S. Horie, H. Ishikawa, H. Takayama, N. Aimi, D. Ponglux, and K. Watanabe, *Life Sciences*, 2004, **74**, 2143.
5. H. Ishikawa, H. Takayama, and N. Aimi, *Tetrahedron Lett.*, 2002, **43**, 5637.
6. H. Takayama, H. Ishikawa, M. Kurihara, M. Kitajima, N. Aimi, D. Ponglux, F. Koyama, K. Matsumoto, T. Moriyama, L. T. Yamamoto, K. Watanabe, T. Murayama, and S. Horie, *J. Med. Chem.*, 2002, **45**, 1949.
7. H. Takayama, H. Ishikawa, M. Kitajima, and N. Aimi, *Chem. Pharm. Bull.*, 2002, **50**, 960.
8. a) H. Takayama, M. Kurihara, M. Kitajima, I. M. Said, and N. Aimi, *Tetrahedron*, 1998, **54**, 8433. b) H. Takayama, M. Kurihara, M. Kitajima, I. M. Said, and N. Aimi, *J. Org. Chem.*, 1999, **64**, 1772. c) H. Takayama, M. Kurihara, M. Kitajima, I. M. Said, and N. Aimi, *Tetrahedron*, 2000, **56**, 3145. d) H. Takayama, H. Ishikawa, M. Kurihara, M. Kitajima, S. Sakai, N. Aimi, H. Seki, K. Yamaguchi, I. M. Said, and P. J. Houghton, *Tetrahedron Lett.,* 2001, **42**, 1741.
9. R. Gueller and H.-J. Borschberg, *Tetrahedron Asymmetry*, 1992, **3**, 1197.
10. N. Keawpradub, H. Takayama, N. Aimi, and S. Sakai, *Phytochemistry*, 1994, **37**, 1745.
11. T. Hino, H. Yamaguchi, K. Matsuki, K. Nakano, M. Sodeoka, and M. Nakagawa, *J. Chem. Soc., Perkin Trans. I*, 1983, 141.