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NORTROPANE ALKALOIDS FROM THE LEAVES OF *ERYTHOXYLUM MOONII*

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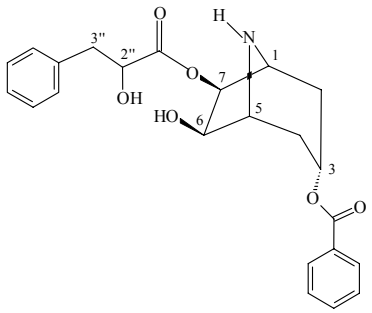
Abstract – Four new nortropane alkaloids have been isolated from the leaves of *Erythroxylum moonii* and identified as nortropane-3α-6β-7β-triol 3-benzoate 7-(2′-hydroxy-3′-phenylpropanoate) (**1**), nortropane-3α-7β-diol 7-*trans*-cinnnamate 3-propanoate (**2**), nortropane-3α-7β-diol 7-benzoate 3-(2′-methylpropanoate) (**3**), and nortropane-3α-7β-diol 3-(2′-methylpropanoate) 7-*cis*-(3′′,4′′,5′′-trimethoxycinnamate) (**4**). Additionally, five known bases are characterized as tropane-3α-7β-diol 7-benzoate (**5**), tropane-3α-7β-diol 3-phenylacetate (**6**), tropane-3α-7β-diol 3-benzoate (**7**), tropane-3α-6β-7β-triol 3-benzoate (**8**), and tropane-3α-yl 3-(3′,4′,5′-trimethoxybenzoate) (**9**). The structures for the compounds are proposed on the basis of spectroscopic evidences.

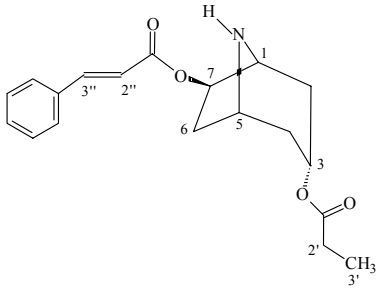
Tropane alkaloids is a class of naturally occurring compounds that display a diverse range of biological activities and are used in a variety of medicinal indications.[1] Representative examples of this class of compound include scopolamine, atropine, hyoscyamine and cocaine. Recently a pharmacological interest has been aroused in polyhydroxynortropane alkaloids (calystegines), which have inhibitory effect on β-glucosidase and α-galactosidase enzymes.[2] Pervilleines, new tropane bases from *E. pervillei,* are reported to partially circumvent the multidrug-resistant (MDR) tumour cells in mammals.[3] Various tropane derivatives are also finding application as novel imaging agents.[4] The family Erythroxylaceae has proved to be a rich source of tropane alkaloids.[5] In our preliminary work, the methanol extract of *Erythroxylum moonii* showed antifungal activity against certain pathogenic fungi and led to the isolation of new dimeric and monomeric tropane alkaloids.[6,7] In this paper, we describe the isolation and structure

elucidation of four new nortropane alkaloids, namely nortropane-3α-6β-7β-triol 3-benzoate 7-(2′-hydroxy-3′- phenylpropanoate) (**1**), nortropane-3α-7β-diol 7-*trans*-cinnnamate 3-propanoate (**2**), nortropane-3α-7β-diol 7-benzoate 3-(2′-methylpropanoate) (**3**), and nortropane-3α-7β-diol 3-(2′-methylpropanoate) 7-*cis*-(3′′,4′′,5′′-trimethoxycinnamate) (**4**) along with five known tropane bases. The structures of the compounds are elucidated by the application of spectroscopic techniques.[8,9] The ^{1}H and ^{13}C NMR spectral assignments have been assigned using COSY, HMBC and HMQC experiments. The C-3,C-7 notation is used for tropane alkaloids where the choice between the C-3,C-6 and C-3,C-7 notations is arbitrary.[5] The same principle is applied to C-3,C-6,C-7 trisubstituted tropane alkaloids.

The UV spectrum of compound (**1**) showed the absorption maxima at 276.3, 265.9 and 229.9 nm, indicating the presence of aromatic rings. The alkaloid showed IR spectral absorptions due to hydroxyl group (ν_{max} at 3470 cm^{-1}), olefinic CH (ν_{max} at 3000 cm^{-1}) and ester carbonyls (ν_{max} at 1730, 1723 cm^{-1}). The HREI-MS afforded the M^+ at *m/z* 411.1676 (calcd 411.1681) corresponding to the molecular formula $C_{23}H_{25}NO_6$. The MS spectrum showed a significant ion (**1a**) at *m/z* 203 [M − C(6)HOH-C(7)HOCOCH(OH)$CH_2C_6H_5$]$^+$ together with pyridinium and related ions at *m/z* 82 $[C_5H_8N]^+$, 81 $[C_5H_7N]^+$ and 80 $[C_5H_6N]^+$, indicating the nortropane-3,6,7-triol skeleton, esterified at C-3 with an acid (acylium ion at *m/z* 105).[8,10] The presence of ions at *m/z* 121 $[C_6H_5CO_2]^+$, 105 $[C_6H_5CO]^+$ and 77 $[C_6H_5]^+$, were consistent with a benzoyloxy substitution. The fragments appeared at *m/z* 165 $[C_6H_5CH_2CH(OH)COO]^+$, 149 $[C_6H_5CH_2CH(OH)CO]^+$ and 77 $[C_6H_5]^+$ suggested the 2-hydroy-3-phenylpropanoic acid involvement at C-7 of the nortropane nucleus. The ^{1}H-NMR spectrum showed an ester substitution at C-3 and the orientation of the C-3 proton was deduced to be equatorial (β) on the basis of coupling constants (dd, δ 5.16, $J_{3eq,\ 2ax} = J_{3eq,\ 4ax}$ = 4.5 Hz).[8,11] The C-6 and C-7 α (endo) protons were appeared at δ 4.70 (d, $J_{6en,\ 7en}$ = 8.0 Hz) and 5.72 (d, $J_{7en,\ 6en}$ = 8.0 Hz), respectively.[8] In tropane alkaloids where there are *exo* substituents at C-6 and C-7, the remaining *endo* protons showed coupling of *ca*. J = 0 Hz with the vicinal bridgehead protons due to a dihedral angle close to 90º (bridgehead and *endo* protons).[8] The methine C-2′′ proton of 2-hydroy-3-phenylpropanoyloxy moiety was observed at δ 4.39 as a double doublet ($J_{2'',\ 3b''}$ = 6.7 Hz, $J_{2'',\ 3a''}$ = 5.6 Hz), while C-3′′ methylene protons showed signals at δ 2.98 (H-3a′′) and 3.15 (H-3b′′). The ^{13}C-NMR spectrum (Table 1) showed ester carbonyl carbon signals at δ 173.9 (C-1′′) and 165.7 (C-1′). The C-3 was appeared at δ 66.3, while C-6 and C-7 methine carbon showed resonances at δ 76.7 and 81.0, respectively. The position of 2′-hydroxy-3′-phenylpropanoyl and benzoyl residues were further confirmed by the clear long-range hetronuclear correlation peaks between carbonyl carbons resonated at δ 173.9 and 165.7 of the acyl moieties with H-7 and H-3 signals of the nortropane nucleus, respectively. On the basis of this spectroscopic data, structure (**1**) was assigned to the new compound.



1



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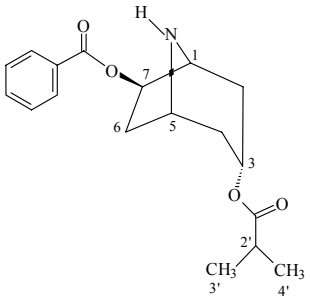

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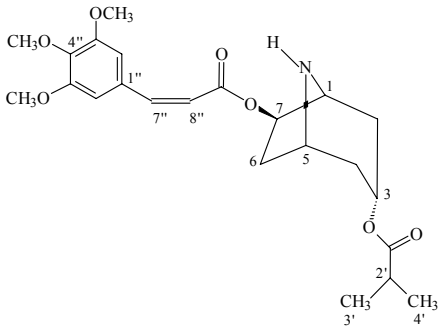

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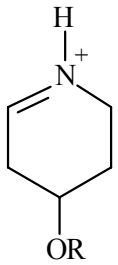
The HREI-MS spectrum of nortropane-3α-7β-diol 7-*trans*-cinnnamate 3-propanoate (**2**) gave molecular ion at *m/z* 329.1626 (calcd 329.1627) corresponding to molecular formula $C_{19}H_{23}NO_4$. The base peak at *m/z* 57 $[CH_3CH_2CO]^+$ together with ions at *m/z* 73 $[CH_3CH_2COO]^+$ indicated the presence of propanoyloxy moiety. The attachment of propanoic acid at C-3 was established by an ion (**2a**) observed at *m/z* 155 [M – $C(6)H_2$-$C(7)HOCOCH{=}CHC_6H_5]^+$, resulted from the cleavages of C-7/C-1 and C-6/C-5 bonds.[11] The characteristic ions of cinnamoyloxy group were observed at *m/z* 147 $[C_6H_5CH{=}CHCOO]^+$, 131 $[C_6H_5CH{=}CHCO]^+$, 103 $[C_6H_5CH{=}CH]^+$ and 77 $[C_6H_5]^+$.[6] The ^{1}H-NMR spectral signal at δ 5.28 was a double doublet ($J_{3eq,\,2ax} = J_{3eq,\,4ax}$ = 5.5 Hz), consistent with a 3α-ester function.[8] The attachment of cinnamoyl ester at C-7 was evident from a characteristic multiplet (a one-proton double doublet) at δ 5.94 ($J_{7en,\,6en}$ = 8.3 Hz, $J_{7en,\,6ex}$ = 3.3 Hz) due to C-7 α (*endo*) proton.[8] The absence of a three-proton singlet due to the *N*-methyl protons and the presence of a one-proton multiplet at δ 3.17 (*N*-H) indicated the presence of a nortropane nucleus. The cinnamic acid residue gave signals for *trans*-alkene protons at δ 6.59 (d, *J* = 15.9 Hz, $COC\underline{H}{=}CHC_6H_5$) and 7.67 (d, *J* = 15.9 Hz, $COCH{=}C\underline{H}C_6H_5$). The ^{13}C-NMR spectrum showed resonances for ester carbonyl carbons at δ 174.3 (C-1′, propanoyloxy moiety) and 167.1 (C-1′′, cinnamoyloxy residue). The methine carbons signals appeared at δ 78.9, 67.7, 62.9 and 58.7, were assigned to C-7, C-3, C-1 and C-5 of the nortropane residue, respectively. The C-2′′ and C-3′′ (*trans*-alkene carbons of cinnamoyl moiety) showed resonance signals at δ 118.3 and 146.6, respectively. These spectroscopic observations led to the structure **2** for this new tropane base.



No.	R	*m/z*
1a	PhCO	203
2a	CH_3CH_2CO	155
3a	$(CH_3)_2CHCO$	169

The compound (**3**) was obtained as an amorphous powder. The HREI-MS showed the molecular ion at *m/z* 317.1624 consistent with the molecular formula $C_{18}H_{23}NO_4$ (calcd 317.1627). In the EI-MS, the prominent ion (**3a**) at *m/z* 169 $[M - C(6)H_2\text{-}C(7)HOCOC_6H_5]^+$ along with pyridinium and related ions at *m/z* 82 $[C_5H_8N]^+$, 81$[C_5H_7N]^+$ and 80 $[C_5H_7N]^+$ indicated the nortropane-3,6-diol skeleton, esterified at C-3 with butanoic acid (acylium ion at *m/z* 71).[9,11] The significant peak at *m/z* 43 $[C_3H_7]^+$, obtained through α-cleavage of the acid moiety and the absence of a peak at *m/z* $[M - 28]^+$ resulting from a McLafferty rearrangement of *n*-butanoic acid moiety, established the presence of 2′-methylpropanoyl moiety. The ions observed at *m/z* 77 $[C_6H_5]^+$, 105 $[C_6H_5CO]^+$ and 121 $[C_6H_5O_2]^+$ demonstrated the esterifying group at C-7 to be benzoic acid. The ^{1}H-NMR spectrum displayed an upfield six-proton doublet at δ 1.13 ($J_{3',2'} = J_{4',2'}$ = 5.6 Hz), attributable to the terminal methyl protons of the 2′-methylpropanoyloxy moiety.[7] The C-3 methine proton of the nortropane nucleus appeared at δ 5.49 (dd, $J_{3eq,\,2ax} = J_{3eq,\,4ax}$ = 4.7 Hz), suggesting it to have β-configuration. Consequently the ester has the 3α-stereochemistry.[8] The presence of an ester at C-7 was inferred from a double doublet centred at δ 5.78 ($J_{7en,\,6en}$ = 7.6 Hz, $J_{7en,\,6ex}$ = 3.1 Hz) due to C-7 *endo* (α) proton.[8] The proton directly attached to the nitrogen atom was appeared as a one-proton multiplet at δ 3.02. The ^{13}C-NMR spectrum of compound (**3)** showed resonances for all eighteen carbon atoms in the molecule (see Table 1). The quaternary carbon signals were observed at δ 175.5 and 165.2 due to C-1′ and C-1′′ ester carbonyl carbons, respectively. The signals appeared at δ 81.0 and 66.3, were assigned to C-7 and C-3 of the nortropane residue, respectively. The positions of the benzoyloxy and 2′-methylpropanoyloxy residues were confirmed by the clear long-range heteronuclear correlation peaks between the carbonyl carbons of the isobutyryl (δ 175.5) and benzoyl (δ 165.2) moieties and H-3 (δ 5.49) and H-7 (δ 5.78) signals of the nortropane nucleus, respectively. The alkaloid (**3**) was thus characterized as nortropane-3α-7β-diol 7-benzoate 3-(2′-methylpropanoate).

Table 1: ^{13}C NMR spectral assignments of the new compounds

Carbon	1	2	3	4
C-1	63.7	62.9	64.1	63.1
C-2	35.3*	33.6	32.9	33.2
C-3	66.3	67.7	66.3	65.9
C-4	35.7*	34.4	33.7	35.2
C-5	63.7	58.7	61.2	60.4
C-6	76.7	35.9	36.5	36.2
C-7	81.0	78.9	81.0	79.4
Ester at C-3				
C=O	165.7	174.3	175.5	176.7
C-2′	—	27.6	33.9	34.8
C-3′	—	10.9	18.7	19.2
Ipso-C	130.7	—	—	—
Ortho-C	129.4	—	—	—
Meta-C	127.9	—	—	—
Para-C	136.1	—	—	—
Ester at C-7				
C=O	173.9	167.1	165.2	169.2
2′′	73.7	118.3	—	—
3′′	39.8	146.6	—	—
Ipso-C	137.5	134.9	131.0	124.8
Ortho-C	129.3*	130.3	129.9	107.3
Meta-C	129.6*	129.2	128.3	153.7
Para-C	126.2	131.4	135.5	139.3
C-7′′	—	—	—	143.5
C-8′′	—	—	—	120.3
OCH_3-3′′, OCH_3-5′′	—	—	—	56.3
OCH_3-4′′	—	—	—	60.1

Spectra were recorded at 125 MHz for **1**, **3** and **4**, and 100 MHz for **2** in $CDCl_3$ solutions. *Assignments are interchangeable.

The HREI-MS of compound (**4**) showed the molecular ion at *m/z* 433.2101 corresponding to the molecular formula $C_{23}H_{31}NO_7$ (calcd 433.2100). The MS signal (**3a**) appeared at *m/z* 169 [M – C(6)H_2-C(7)HOCOCH=$CHC_6H_2(OCH_3)_3$]$^+$ along with fragment ions at *m/z* 43 $[C_3H_7]^+$, 71 $[C_3H_7O]^+$, 87 $[C_3H_7O_2]^+$, and 82 $[C_5H_8N]^+$, indicated a 2′-methylpropanoyloxy substitution at C-3 of the nortropane nucleus.[9] The fragments observed at *m/z* 237 [OCOCH=$CHC_6H_2(OCH_3)_3$]$^+$, 221 [COCH=$CHC_6H_2(OCH_3)_3$]$^+$, 193 [CH=$CHC_6H_2(OCH_3)_3$]$^+$ and 167 $[C_6H_2(OCH_3)_3]^+$ showed the presence of trimethoxycinnamoyloxy moiety. The ^{1}H-NMR spectrum showed a six-proton doublet at δ 1.15 (d, $J_{3',2'}$ =

$J_{4',2'}$ = 5.8 Hz), was attributed to the two methyl groups protons of the 2′-methylpropanoyloxy moiety. The C-7 *endo* (α) proton was observed as a double doublet at δ 5.42 ($J_{7en, 6en}$ = 7.4 Hz, $J_{7en, 6ex}$ = 3.3 Hz), while the alpha (α) orientation of the ester group at C-3 was inferred by a double doublet at δ 5.35 ($J_{3eq, 2ax} = J_{3eq, 4ax}$ = 5.3 Hz) due to C-3 β (equatorial) proton.[8] The methoxy group singlets were observed at δ 3.89 (OCH_3-4′′) and 3.93 (OCH_3-3′′, OCH_3-5′′). The *cis*-olefinic protons of cinnamic acid showed resonance signals at δ 6.28 (COC<u>H</u>=CHC_6H_5, $J_{8'', 7''}$ = 12.5 Hz) and 7.43 (COCH=C<u>H</u>C_6H_5, $J_{7'', 8''}$ = 12.5 Hz).[7] The ^{13}C-NMR signals at δ 79.4 and 65.9 were assigned to ester-bearing C-7 and C-3 carbons of nortropane moiety, respectively. The C-7′′ and C-8′′ of the cinnamoyloxy moiety showed resonance signals at δ 143.5 and 120.3, respectively. The spectroscopic evidences led to structure (**4**) for the new alkaloid.

The other known bases isolated for the first time from the leaves of *E. moonii* are tropane-3α-7β-diol 7-benzoate (**5**),[12,13] tropane-3α-7β-diol 3-phenylacetate (**6**),[10] tropane-3α-7β-diol 3-benzoate (**7**),[14] tropane-3α-6β-7β-triol 3-benzoate (**8**),[12] and tropane-3α-yl 3-(3′,4′,5′-trimethoxybenzoate) (**9**).[11,13]

EXPERIMENTAL

Plant material and instrumentation were as previously described.[7]

Extraction and Isolation Procedures: The alkaloids were extracted from the ground leaves (4 kg) of *E. moonii* as previously described.[7] Purification of the alkaloids was carried out on preparative TLC plates using the solvent systems mentioned below: system A 93% $CHCl_3$/7% MeOH and ammonia vapor; system B 95% $CHCl_3$/5% MeOH with ammonia vapor.

Nortropane-3α-6β-7β-triol 3-benzoate 7-(2′-hydroxy-3′-phenylpropanoate) (1): Colorless semisolid; 4.1 mg, yield 1.02 x 10^{-4} %; R_f = 0.81 (system A); $[\alpha]^{25}_D$ +17.6° (c = 0.13, $CHCl_3$); IR ν_{max} ($CHCl_3$) 3470, 3000, 1730, 1723, 1625 cm^{-1}; UV λ_{max} (MeOH) 276.3 (log ε 2.91), 265.9 (log ε 2.41), 229.9 (log ε 3.99), 209.2 (log ε 3.93) nm; HREI-MS *m/z* observed (fragment, cacld) 411.1676 ($C_{23}H_{25}NO_6$, 411.1681); EI-MS (70 eV) *m/z* (rel. int. %) 411 (8), 306 (3), 290 (4), 262 (11), 246 (15), 208 (34), 203 (21), 165 (3), 149 (9), 121 (17), 105 (100), 98 (14), 82 (73), 81 (87), 80 (53), 77 (77), 57 (16). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 1.89 (1H, d, $J_{2eq, 2ax}$ = 15.9 Hz, H-2 *eq*), 1.94 (1H, d, $J_{4eq, 4ax}$ = 16.1 Hz, H-4 *eq*), 2.56 (1H, m, H-4 *ax*), 2.83 (1H, m, H-2 *ax*), 2.87 (1H, m, *N*-H), 2.98 (1H, dd, $J_{3a'', 3b''}$ = 13.9 Hz, $J_{3a'', 2''}$ = 5.6 Hz, H-3a′′), 3.15 (1H, dd, $J_{3b'', 3a''}$ = 13.9 Hz, $J_{3b'', 2''}$ = 6.7 Hz, H-3b′′), 3.63 (1H, br m, H-1), 3.79 (1H, br s, H-5), 4.39 (1H, dd, $J_{2'', 3b''}$ = 6.7 Hz, $J_{2'', 3a''}$ = 5.6 Hz, H-2′′), 4.70 (1H, d, $J_{6en, 7en}$ = 8.0 Hz, H-6 *endo*), 5.16 (1H, dd, $J_{3eq, 2ax} = J_{3eq, 4ax}$ = 4.5 Hz, H-3 *eq*), 5.72 (1H, d, $J_{7en, 6en}$ = 8.0 Hz, H-7 *endo*), 7.10 (3H, m, *para*-, *meta*-H′′), 7.23 (2H, m, *ortho*-H′′), 7.51 (2H, dd, $J_{m, o}$ = 8.3 Hz, $J_{m, p}$ = 7.1 Hz, *meta*-H′), 7.63 (1H, tt, $J_{p, m}$ = 7.1 Hz, $J_{p, o}$ = 1.1 Hz, *para*-H′), 8.07 (2H, dd, $J_{o, m}$ = 8.3 Hz, $J_{o, p}$ =1.1 Hz, *ortho*-H′). ^{13}C-NMR ($CDCl_3$, 125 MHz) δ: see Table 1.

Nortropane-3α-7β-diol 7-*trans*-cinnnamate 3-propanoate (2): White amorphous solid; 4.6 mg, yield 1.15 x 10^{-4} %; R_f = 0.59 (system A); $[\alpha]^{25}_D$ –23.1° (*c* = 0.31, MeOH); IR ν_{max} ($CHCl_3$) 3340, 2999, 1736, 1715, 1635 cm^{-1}; UV λ_{max} (MeOH) 279.6 (log ε 4.37) nm; HREI-MS *m/z* observed (fragment, cacld) 329.1626 ($C_{19}H_{23}NO_4$, 329.1627); EI-MS (70 eV) *m/z* (rel. int. %) 329 (9), 314 (5), 300 (3), 272 (18), 256 (6), 252 (11), 182 (31), 155 (39), 147 (28), 131 (37), 103 (26), 98 (3), 82 (35), 81 (43), 80 (29), 77 (72), 73 (25), 57 (100), 55 (42). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 0.96 (3H, t, $J_{3',2'}$ = 7.3 Hz, H-3′), 1.79 (1H, dd, $J_{2eq, 2ax}$ = 14.8 Hz, $J_{2eq, 1}$ = 2.5 Hz, H-2 *eq*), 1.85 (1H, dd, $J_{4eq, 4ax}$ = 14.7 Hz, $J_{4eq, 5}$ = 3.1 Hz, H-4 *eq*), 2.21 (1H, dd, $J_{4ax, 4eq}$ = 14.7 Hz, $J_{4ax, 5}$ = 3.1 Hz, H-4 *ax*), 2.43 (2H, m, H-2′ and H-6 *exo*), 2.57 (1H, dd, $J_{2ax, 2eq}$ = 14.8 Hz, $J_{2ax, 1}$ = 3.1 Hz, H-2 *ax*), 2.97 (1H, dd, $J_{6en, 6ex}$ = 14.7 Hz, $J_{6en, 7en}$ = 8.3 Hz, H-6 *endo*), 3.17 (1H, m, *N*-H), 3.57 (1H, br s, H-1), 3.72 (1H, m, H-5), 5.28 (1H, dd, $J_{3eq, 2ax} = J_{3eq, 4ax}$ = 5.5 Hz, H-3 *eq*), 5.94 (1H, dd, $J_{7en, 6en}$ = 8.3 Hz, $J_{7en, 6ex}$ = 3.3 Hz, H-7 *endo*), 6.59 (1H, d, $J_{2'', 3''}$ = 15.9 Hz, H-2′′), 7.23 (2H, dd, $J_{m, o}$ = 8.4 Hz, $J_{m, p}$ = 7.8 Hz, *meta*-H), 7.35 (1H, tt, $J_{p, m}$ = 7.8 Hz, $J_{p, o}$ = 1.1 Hz, *para*-H), 7.67 (1H, d, $J_{3'', 2''}$ = 15.9 Hz, H-3′′), 7.83 (2H, dd, $J_{o, m}$ = 8.4 Hz, $J_{o, p}$ =1.1 Hz, *ortho*-H); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ: see Table 1.

Nortropane-3α-7β-diol 7-benzoate 3-(2′-methylpropanoate) (3): Light brown amorphous powder; 5.5 mg, yield 1.37 x 10^{-4} %; R_f = 0.63 (system A); $[\alpha]^{25}_D$ –21.4° (*c* = 0.07, MeOH); IR ν_{max} ($CHCl_3$) 3360, 3010, 1740, 1720, 1620 cm^{-1}; UV λ_{max} (MeOH) 275.4 (log ε 2.87), 232.3 (log ε 4.07) nm; HREI-MS *m/z* observed (fragment, cacld) 317.1624 ($C_{18}H_{23}NO_4$, 317.1627); EI-MS (70 eV) *m/z* (rel. int. %) 317 (17), 274 (12), 246 (21), 240 (6), 230 (14), 212 (6), 196 (13), 169 (100), 148 (15), 121 (25), 109 (31), 108 (15), 105 (49), 98 (23), 87 (41), 82 (57), 81 (62), 80 (49), 77 (62), 71 (46), 43 (51). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 1.13 (6H, d, $J_{3',2'} = J_{4',2'}$ = 5.6 Hz, H-3′ and H-4′), 1.73 (1H, dd, $J_{2eq, 2ax}$ = 15.9 Hz, $J_{2eq, 1}$ = 2.5 Hz, H-2 *eq*), 1.89 (1H, dd, $J_{4eq, 4ax}$ = 14.7 Hz, $J_{4eq, 5}$ = 2.5 Hz, H-4 *eq*), 2.21 (1H, ddd, $J_{4ax, 4eq}$ = 14.7 Hz, $J_{4ax, 3eq}$ = 4.7 Hz, $J_{4ax, 5}$ = 3.1 Hz, H-4 *ax*), 2.43 (3H, m, H-2 *ax*, H-2′ and H-6 *exo*), 2.85 (1H, dd, $J_{6en, 6ex}$ = 15.7 Hz, $J_{6en, 7en}$ = 7.6 Hz, H-6 *endo*), 3.02 (1H, m, *N*-H), 3.56, (1H, br s, H-1), 3.79 (1H, m, H-5), 5.49 (1H, dd, $J_{3eq, 2ax} = J_{3eq, 4ax}$ = 4.7 Hz, H-3 *eq*), 5.78 (1H, dd, $J_{7en, 6en}$ = 7.6 Hz, $J_{7en, 6ex}$ = 3.1 Hz, H-7 *endo*), 7.49 (2H, dd, $J_{m, o}$ = 8.3 Hz, $J_{m, p}$ = 7.6 Hz, *meta*-H), 7.61 (1H, tt, $J_{p, m}$ = 7.6 Hz, $J_{p, o}$ = 1.1 Hz, *para*-H), 8.07 (2H, dd, $J_{o, m}$ = 8.3 Hz, $J_{o, p}$ =1.1 Hz, *ortho*-H). ^{13}C-NMR ($CDCl_3$, 125 MHz) δ: see Table 1.

Nortropane-3α-7β-diol 3-(2′-methylpropanoate) 7-*cis*-(3′′,4′′,5′′-trimethoxycinnamate) (4): Colorless semisolid; 4.0 mg, yield 1.00 x 10^{-4} %; R_f = 0.48 (system B); $[\alpha]^{25}_D$ –25.2° (*c* = 0.07, $CHCl_3$); IR ν_{max} ($CHCl_3$) 3340, 3015, 1725, 1710, 1615 cm^{-1}; UV λ_{max} (MeOH) 326.2 (log ε 4.43) nm; HREI-MS *m/z* observed (fragment, cacld) 433.2101 ($C_{23}H_{31}NO_7$, 433.2100); EI-MS (70 eV) *m/z* (rel. int. %) 433 (7), 362 (4), 346 (4), 264 (7), 237 (3), 226 (5), 221 (3), 212 (5), 196 (13), 193 (10), 169 (10), 167 (3), 109 (23), 108 (14), 98 (90), 97 (18), 87 (18), 82 (23), 81 (17), 71 (100), 57 (48), 43 (48). ^{1}H-NMR ($CDCl_3$, 500 MHz) δ:

1.15 (6H, d, $J_{3',2'} = J_{4',2'}$ = 5.8 Hz, H-3′ and H-4′), 2.02 (1H, d, $J_{2eq,2ax}$ = 14.4 Hz, H-2 *eq*), 2.16 (1H, d, $J_{4eq,4ax}$ = 14.7 Hz, H-4 *eq*), 2.57 (3H, m, H-4 ax, H-6 *exo* and H-2′), 2.83 (1H, m, H-2 *ax*), 2.91 (1H, dd, , $J_{6en,6ex}$ = 14.2 Hz, $J_{6en,7en}$ = 7.4 Hz, H-6 *endo*), 3.03 (1H, m, *N*-H), 3.39 (1H, br s, H-1), 3.52 (1H, m, H-5), 3.89 (3H, s, OCH_3-4′′), 3.93 (6H, s, OCH_3-3′′ and OCH_3-5′′), 5.35 (1H, dd, $J_{3eq,2ax} = J_{3eq,4ax}$ = 5.3 Hz, H-3 *eq*), 5.42 (1H, dd, $J_{7en,6en}$ = 7.4 Hz, $J_{7en,6ex}$ = 3.3 Hz, H-7 *endo*), 6.28 (1H, d, $J_{8'',7''}$ = 12.5 Hz, H-8′′), 7.21 (2H, s, H-2′′ and H-6′′), 7.43 (1H, d, $J_{7'',8''}$ = 12.5 Hz, H-7′′). ^{13}C-NMR ($CDCl_3$, 100 MHz) δ: see Table 1.

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