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Research Article

ISOLATED AND SYNTHESIS OF SYNTHETIC ANALOGUES OF FORSKOLIN

DR. A.L.V. RAMANA REDDY*, T.BHUPAL REDDY, DR. G.CHANDRASEKHAR, DR.C.NAGESWARA REDDY

Department of Chemistry, Govt Degree College Kodur (RS) YSR Kadapa District, A.P, India. Email: Aramanasvu@gmail.com

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ABSTRACT

1-Propargyloxy-forskolin **(1**) on reaction with different substituted azides (**2a-e**) gave 1,4-disubstituted triazol-forskolins (**3a-e**) and 1-propargyl-6-acetyl-7-deacetyl-forskloin(**4**) on reaction with different alkyl azides (**2a-e**) in presence of $CuSO_4.5H_2O$ and sodium ascorbate in water gave 1,4-disubstituted triazol-forskolins (**5a-e)** in good yields.

Keywords: 1-Propargyloxy-forskolin, 1-propargyl-6-acetyl-7-deacetyl-forskloin, $CuSO_4.5H_2O$

INTRODUCTION

Coleus forskohlii know as phashanabedi (telugu) a medicinal plant found in the Indian subcontinent is widely used in the Indian system of medicine. Forskolin a major diterpenoid isolated from the roots of Coleus forskohlii, directly activates the enzyme adenyl cyclase thereby increasing the intracellular level of cAMP and leading to various physiological effects. It has hypertensive, positive intoropic, and intraocular pressure lowering activity, anti glaucoma cardiovascular and ant obesity activity.

With a view to synthesize novel triazole substituted forskolins, the click reaction strategy has been adopted. It was planned to introduce a propargyl moiety (CH_2-C=H) at the C-1 OH of forskolin, since it was earlier reported that the order of OH reactivity is OH-1>OH-6>OH-9. In view of the presence of several functional groups and three free hydroxyls, we expected problems of regiomers formation, elimination and rearrangements in the first step of the semi synthetic work on forskolin, The resulting O-CH_2-C=C-H moiety is proposed to be reacted with a wide range of alkyl azides(R-N_3) under the click reaction conditions to give regioselectively 1, 4-disubstituted 1,2,3-triazols.

RESULTS AND DISCUSSION

Synthesis of -6-acetyl-7-deacetyl-1,4-disubstituted 1,2,3-triazolo -forskolins (6a-e)

1-Propargyl-6-acetyl-forskolin **(4)** on reaction with different alkyl azides **(2a-e)** in presence of $CuSO_4.5H_2O$ and sodium acerbate in water:t-butanol (1:1) medium gave 1,4-disubstituted triazolo-forskolins **(6a-e).** N-butyl-phthalimido-1,2,3-triazolo-7-deacetyl-6-acetyl-1,4-disubstituted-forskolin **(6a)** its IR peaks at 3458 cm^{-1} (OH), at 1735 cm^{-1} (CO,ester), 1708 cm^{-1} (CO, ketone) and 1685 cm^{-1} (CO, amide). In the ^1H NMR the triazol ring proton appeared at δ7.43 as singlet, the pthalimide protons appeared as δ 7.84 N-CH_2 at δ 4.39. The protons of the 7-deacetyl-6-acetyl forskolin moiety are δ 6.79 (s, 9-OH) δ 6.12 (dd, H-14), δ 5.80 (d, H-7), δ 5.12 (dd, H-15 trans), δ 4.90 (dd, H-15 cis) δ 2.07 (6a-$OCOCH_3$) δ 1.54 (s,8-CH_3), δ 1.40 (s, 10-CH_3), δ 1.36 (s,13-CH_3) , δ 1.08 (s, 4e-CH_3) and δ 1.08 (s, 4a-CH_3).

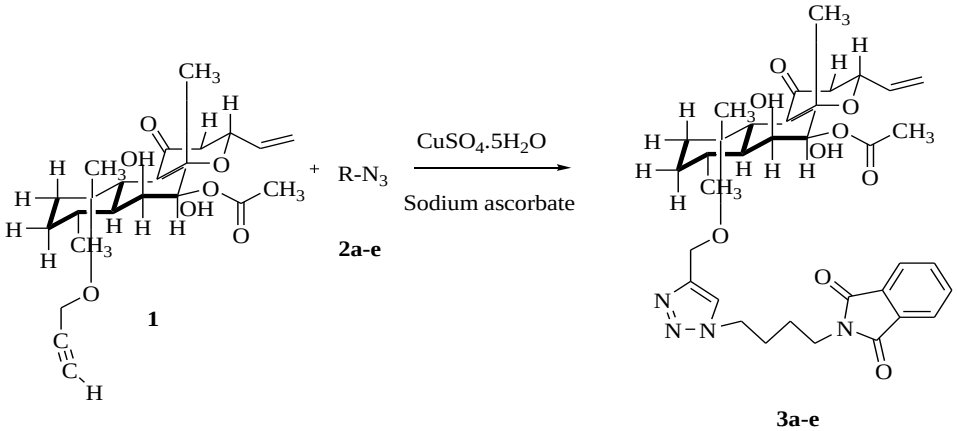
In ^{13}C NMR the carbon signal assignments for the phthalimido triazole moiety as δ 147.1 (C-4'), δ 122.4(C-5') δ 168.1(CO) and the carbon signal assignment for the 7-deacetyl-6-acetyl forskolin moiety δ 206.3 (CO), δ 170.3 (OCO) δ 143.7 (C-14), δ 109.7(C-15) δ 32.6(4a-CH_3), δ 30.7 (13-CH_3), δ 25.5(4e-CH_3) , δ 21.3 ($COCH_3$), δ 20.4 (8-CH_3) and δ 19.7 (10-CH_3).

MATERIAL AND METHODS

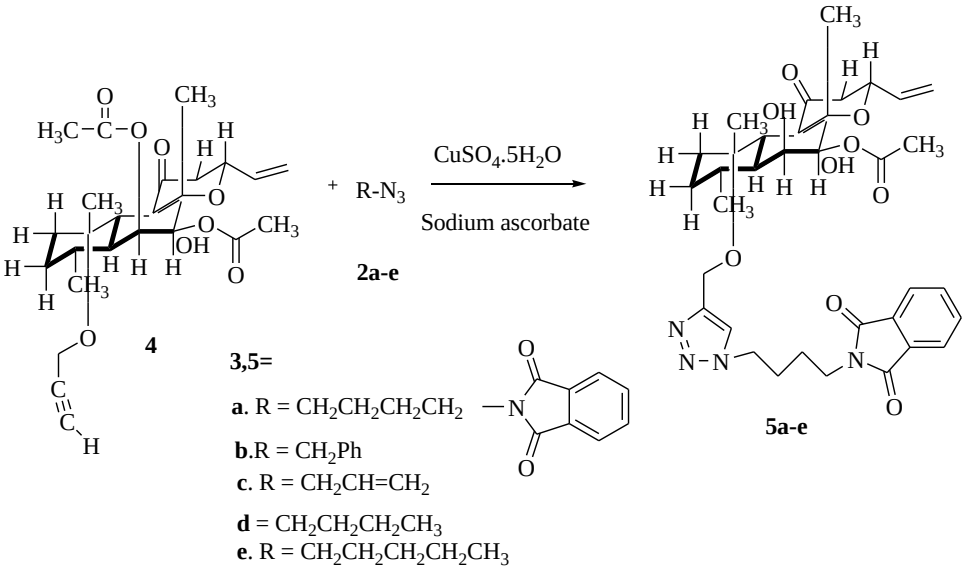
General: Melting points were determined on a Polmon instrument (model no. MP-96).IR spectra were recorded on Perkin-Elmer 337 spectrometer, and ^1H NMR (400 MHz) and ^{13}C NMR (100.6 MHz) were recorded on a Varian Gemini 200 spectrometer using TMS as internal standard (chemical shifts values were described in ppm δ). Mass spectra were recorded on a VG micromass LCMS 2010 instrument.

I. General procedure for the synthesis of 1,4-disubstituted-1,2,3-triazole-forskolins(3a-e)

l-Propargyloxy-forskolin **(1**) (0.29,0.45mmol) and N-butylazido-phthalimide**(2a)** (0.10g, 0.45 mmol) were suspended in a 1: 1 mixure of water and tert-butylalcohol (5 mL), Sodium ascorbate (0.3mmol) was added, followed by copper (II) sulfate pentahydrate (7.5 mg, 0.03 mmol). The heterogeneous mixture was stirred vigorously overnight, at which point it cleared and TLC analysis indicated complete consumption of the reactants. The reaction mixture was diluted with water (50 mL), cooled in ice, and the white precipitate was collected by filtration. After washing the precipitate with cold water (2 x 25 mL), it was dried under vacuum to afford (0.27g, 87%) of pure product **3a** as white powder, mp 170 ºC.



Scheme 1



Scheme 2

i). [1-(4- phthalimidobutyl)-1H-1,2,3-triazol-4-yl] methoxy-1-forskolin (3a)

IR (KBr): 3458 cm^{-1}(OH), 1735 cm^{-1}(OCO), 1708 cm^{-1}(CO); 1685 cm^{-1} (NCO).

^{1}H NMR (400 MHz,): δ 7.83(dd, J=5.8Hz,5" ,4"-H),7.71(dd, J=5.8 Hz,6",5"-H).7.43 (s,5'-H),6.79 (s,9-OH),5-94(dd, J=17.2Hz,10.4 Hz,H-14),5.50(d, J=4.0 Hz,H-7),5.16 (dd, J=17.2 Hz, J=1.2Hz,H-15), 4.86 (dd, J=10.4 Hz, J=l.2 Hz, H-15),4.68 (d, J=12.0 Hz,1H,OCH_2), 4.42(d, J=12.0 Hz, lH, OCH_2), 4.40 (m, H-6), 4.38 (t, J= 6.8 Hz, N-CH_2),4.32 (br,H-l), 3.23 (d,J=l6.0 Hz, lH,H-12), 2.32(d, J=16.0 Hz,1H,H-12), 2.19(d, J=l.62 Hz,H-5), 2.12(s,$COCH_3$), 1.95 (m, CH_2, H-2,6-OH), 1.74(m,4H,CH_2,H-2,H-3),l.62 (s,8-CH_3), 1.44 (s, 10-CH_3), l.28 (s, l3-CH_3),l.24 (s,4e-CH_3),1.09 (d, J=13.2 Hz, H-3), 0.98(s,4a-CH_3).

^{13}C NMR (l00.6 MHz): 207.0 (CO),169.3 (OCO),168.1 (NCO),146.9(C-4'),143.8(C-14),133.8(C-5'',4"),132.1(C-6a,2a),123.1 (C.6",3")122.4 (C.5'),109.5(C-15),83.2 (c-9), 82.2 (C-8), 81..2 (C-7), 76.6 (C-13),75.3 (C-1), 69.8 (C-6), 62.l (OCH2),49.4 (C-12),49.3 (l'-CH2),43.8 (C-10), 43.7 (C-5),36.8 (1"-CH_2),36.4 (C-3), 34.1 (C-4), 32.7 (4a,-CH_3), 31.2 (13-CH_3),27.3 (1'-CH_2-CH_2),25.5 (4e-CH_3), 24.1 (C-2),23.9 (1"-CH_2-CH_2), 20.9 ($COCH_3$), 20.5 (8-CH3), 20.0 (10-CH_3).

DIP MS: m/z 693[M+H], 715[M+Na].

Employing the similar procedure as mentioned for **3a,** compounds **3b-e** were obtained from **1** and **5b-e** obtained from **4** as solids.

ii) (1 -Benzyl- 1H- 1,2,3-triazol-4-yl) methoxy-1-forskolin (3b):

White solid, mp 73 ºC, 90% yield.

IR (KBr): 3326 cm^{-1}(OH), 1734cm^{-1}(OCO), 1712 cm^{-1}(CO).

^{1}H NMR (400 MHz): δ 7.38 (s, 5'-H), 7.37 - 7.28 (m,1",2",3",4",5"-H),6.77 (s, 9-OH), 5.90 (dd, J=17.2 Hz, J=10.4 Hz, H-14), 5.52 (d, J=4.4 Hz, H-7),5.50 (s, N-CH_2), 5'16 (dd, J=17.2 Hz, J=1.6 Hz, H-15), 4.86 (dd, H=10.4 Hz, J=1.6 Hz, H-15), 4.68 (d, J=12.0 Hz ,1H, OCH_2), 4.40 (br, H-6), 4.40 (d,J=12.0 Hz, OCH_2),4.35 (d, J= 4.5 Hz, H-1), 3.17 (d, J=15.8 Hz, H-12),2.26 (d, J=15.8 Hz,H-12),2.18 (d, J=l.5 Hz, H-5), 2.15 (s, $COCH_3$) , l.63 (s, 8-CH_3),1.46 (s, 10-CH_3),1.29(s,13-CH_3),1.26 (s,4e-CH_3), 0.98 (s,4a-CH_3).

^{13}C NMR (100.6 MHz): 207.1 (CO), 169.4 (OCO), 146.8 (C-4'), 144.3 (C-14),134.5 (C-l'', 129.0 (C-5",3"), 128.6 (C-4")'128.0 (C-6",2")' 122.3 (C-5') ,109.6 (C-15),83.4 (C-9), 82.2 (C-8), 81.3 (C-7), 76.6 (C-13), 75.3 (C-1),69.8 (C-6),62.2 (OCH_2), 54.1(N-CH_2),49.2(C-12), 43.8 (C-5), 43.7 (C-10), 36.4 (C-3), 34.l (C-4), 32.7 (4a-CH_3).31.2 (l3-CH_3), 24.0 (4e-CH_3),23.9(C-2,20.9 ($COCH_3$), 20.5 (8-CH_3), 20.0 (10-CH_3).

DIP MS: m/z 582[M+H].

iii) (1-Allyl-1H-1,2,3-triazol-4 -yl) methoxy-1-forskolin (3c) :

White solid, mp 173 ºC, 82 %yield.

IR (KBr): 3329 cm^{-1}(OH), 1735 cm^{-1}(OCO), 1712cm^{-1}(CO).

^{1}H NMR (400 MHz): δ 7.45 (s, H-5'), 6.82 (s, 9-OH), 6.04-5.93 (m, H-14,-HC=), 5.53(d, J=3.2 Hz, H-7), 5.35 (m, =CH_2), 5.19 (d,J=17.2 Hz, H-15), 4.97 (d, J=5.6 Hz, N-CH_2), 4.90 d,J=10.4 Hz,H-15), 4.73 (d, J=12.0 Hz, lH,OCH_2),4.44 (m, 2H, H-6,OCH_2),4.37(br,H-l),3.24(d, J=16.0Hz, H-12),2.37(d, J=l6.0 Hz,H-12), 2.21(d, J=l.2Hz,H-),2.15(s,$COCH_3$),1.98 (m,H-2,6-OH),1.78 (d, J-14.4 Hz,H-2),1.67 (br, H-3, 8-CH_3), l.48 (s, 10-CH_3),1.33 (s,13-CH_3),1.27 (s,4e-CH_3), 1.12 (d, J=12.8 Hz,H-3), 1.01 (s, 4a-CH_3).

^{13}C NMR (100.6 MHz): 206.9 (CO),169.4 (OCO),146.9 (C-4)', 144.l (C-14),l3l.l (HC=),122.1 (=CH_2),120.0 (C-5'), 109.6 (C-15), 83.5 (C-9), 82.2 (C-13), 8l.2 (C-l),76.9(C-8),75.2(C-),69.8(C-6),62.2(OCH_2), 52.6(N-CH_2),49.3(C-12),43.8(C-5),43.7(C-10),36.4(C-3),34.1(C-4), 32.7(4a-CH_3),31.2(13-CH_3), 24.0(4e-CH_3),23.9(C-2), 20.9 ($COCH_3$), 20.5 (8-CH_3), 20.0 (10-CH_3).

DIP MS: m/z 532 [M+H].

iv (1-Butyl- 1H - 1,2,3-triazol-4-yl) methoxy -1-forskolin (3d) :

White solid, mp 59 ºC. 86 %yield.

IR (KBr): 3337 cm^{-1}(OH), 1734 cm^{-1}(OCO), 1713 cm^{-1}(CO).

^{1}H NMR (400 MHz): δ 7.40 (s, 5'-H), 6.83 (s, 9-OH), 5.96 (dd, J=17.2Hz, J=10.4 Hz,H-14), 5.52 (d, J=2.4 Hz, H-7), 5.18 (d, J=17.2 Hz, H-15), 4.87 (d,J=I0.4H2, H-15), 4-54 (d, J=12.0 Hz,1H, OCH_2), 4.43 (d, J=12.0 Hz, lH, OCH_2), 4.41(br, H-6),4.36 (br, H-1), 4.33 (t, J=7.2 Hz, N-CH_2), 3.23 (d, J=16.0 Hz, H-12), 2.36 (d, J=16.0 Hz, H-12), 2.20 (d, J=l-6 Hz, H-5), 2.13 (s, OCH_2),2.05-1.82 (m, H-2,6-OH), 1.75 (m, H-2,H-3),1.65 (s,8-CH_3), 1.47 (s, l0-CH_3), l.38 (m,5H),1.37 (s, l3-CH_3), 1.31 (s,4e-CH_3), 1.20-1.05 (m,4H),1.01 (s,4a,-CH_3),0.99(t, J= 6.2Hz, CH_3).

^{13}C NMR (100.6 MHz): 206.9 (CO),169.4 (OCO),146.9 (C-4'), 143.9 (C-14),22.1 (C-5'),109.5 (C-15), 83.5 (C-9), 82.2 (C-13),81.2 (C-1), 76.6 (C-8), 75.2 (C-7),69.8 (C-6), 62.3 (OCH_2), 50.0 (N-CH_2), 49.3 (C-12),43.8 (C-5),43.7 (C-10),36.4 (C-3),34.1 (C-4), 32.7 (N-CH_2-2),32.1 (4a-CH_3), 31.3 (13-CH_3),24.0 (4e-CH_3), 23.9 (C-2),20.8 ($COCH_3$),20.5 (N-CH_2-3), 20.0 (8-CH_3),19.6 (10-CH_3),13.2 (N-CH_3-4).

DIPMS: m/z 548[M+H].

v) (1 -Pentyl-1H- l ,2,3-triazol-4-yl) methoxy-l-forskolin (3e):

Light yellow solid, mp 125 ºC. 80 % yield.

IR (KBr): 3356 cm^{-1}(OH), 1748 cm^{-1} (OCO), 1715 cm^{-1}(CO).

^{1}H NMR (400 MHz): δ 7.40 (s,H-5'),6.83 (s, 9-OH), 5.97 (dd, J=17.2 Hz,10.4 Hz, H-l4),5.52 (d, J=4.0 Hz, H-7), 5.20 (dd, J=17.2 Hz,l.2 Hz, H-15), 4.87 (dd, J=10.4,1.2 Hz,H-15),4.70 (d, J=11.6 Hz, lH,OCH_2), 4.44 (d, J=l1.6 Hz,1H,OCH_2), 4.43 (d, J=2.4 Hz, H-6), 4.37 (m, H-1),4.31 (t, J=7.2 Hz, N-CH_2),3.22 (d, J=16.4 Hz, H-12),2.36 (d, J=16.4 Hz, H-12),2.20 (d, J=2.4 Hz, H-5), 2.14 (s,$COCH_3$), 2.02 (d, J=12.4 Hz,H-2), 1.91 (m, 4H), 1.75 (d, J=12.4 Hz, H-2), l.66 (m,CH_3,H-3),1.47 (s,10-CH_3), 1.34 (m, CH_2, CH), l.31 (s, 13-CH_3), 1.26 (s' 4"-CH), 1.10 (d,J=13.2 Hz,H-3),1.0 (s, 4a-CH_3), 0.91 (t, J=6.8 Hz, 3H).

^{13}C NMR (100.6MHz): δ 6206.9(CO),169.3(OCO),146.9(C-4'),143.9(C-14),122.0 (C-5'),109.5(C-15),83.5(C-9),82-2(C-13),81.2(C-l),75.2(C-9),69.8(C-8),69.7(C-6),62.3(OCH_2),50.2(N-CH_2-),49.3(C-12),43.8(C-5),43.7(C-10),36.4(C-3),34.1 (C-4), 32.7 (N-CH_2-2), 31.3 (4a-CH_3), 29.7 (N-CH_2-3),285 (4e-CH_3),24.0(13-CH_3),23.9(C-2),21.9(N-CH_2-4),20.9($COCH_3$),20.l(8-CH_3),19.9(10-CH_3),13.8(N-CH_3-5).

DIP MS: m/z 562[M+H].

vi). [1-)4-phthalimidobutyl)-1H-1,2,3-triazol-4-yl] methoxy-1-(6-acetyl-7-deacetyl-forskolin (5a)

White solid, mp 147 ºC. 85 % yield.

IR (KBr): 3458 cm^{-1}(OH),1735 cm^{-1}(OCO),1708 cm^{-1}(CO), 1685 cm^{-1}(NCO).

^{1}H NMR (400 MHz): δ 7.84 (dd, J=5.6Hz, J= 2.8 Hz, 5",4"-H), 7.72 (dd, J=2.8Hz, J=5.6 Hz, 6",3"-H), 7.43 (s, 5'-H),6.85 (s, 9-OH), 6.12 (dd, J=17.2Hz, J=l0.4 Hz, H-14), 5.80 (t, J=Hz, H-7), 5.12 (dd,J=17.2 Hz, J=0.8Hz,H-15),4.90(dd, J=10.4 Hz,0.8 Hz,H-15),4.70(d, J=12.0Hz, lH,OCH_2), 4.44 (d, J=12.0 Hz,1H, OCH_2), 4.41 (m, H-6), 4.39 (t, J=6.8 Hz, 1"-CH_2), 4.28 (br,H-1), 3.73 (t, J=6.8Hz, l'-CH_2), 3.18 (d, J=16.8Hz, H-12), 2.40(d, J=16.8 Hz,H-12),2.30 (d, J=2.8Hz,H-5),2.20 (br, OH), 2.07 (s,$COCH_3$),1.94 (m ,l"-CH_2-CH_2,H-2),l.74(m, 1-CH_2-CH_2, H-2), 1.68 (d, J=l3.2Hz,H-3), 1.54(s,8-CH_3), 1.40 (s,10-CH_3), 1.36 (s,13-CH_3), 1.10 (d, J= 13.2Hz,H-3), 1.08 (s, 4e-CH_3),1.03 (s, 4a-CH_3).

^{13}C NMR(100.6 MHz): 206.3(CO),170.3(OCO),168.1(NCO),147.1(C-4'),143.7 (C-14),133.9 (C-5" ,4"),132.l (C-2a,6a),123.2 (C-3",6"),722.4 (5'), 109.7 (Cl5),83.1 (C-9),82.1 (C-8), 81.8 (C-6), 75.4(C-13),73.7 (C-1),71.3 (C-7), 62.1(OCH_2),49.5(C-l2),49.2 (1"-CH_2),44.l (C-10), 42.9 (C-5),36.8 (l'-CH_2),36.7 (C-3), 33.7 (C-4),32.6 (4a-CH_3),30.7 (13-CH_3),27.4 (l'-CH_2-CH_2), 25.5 (4e-CH_3), 23.1 (C-2), 22.8 (1"-CH_2-CH_2), 21.3 ($COCH_3$), 20.4 (8-CH_3),19.7 (10-CH_3).

DIP MS: m/z 693 [M+H].

vii) (1-Benzyl-1H-1,2,3-triazol-4-yl) methoxy- 1-(6-acetyl-7-deacetyl-forskolin) (5b):

White solid, mp 177 ºC. 84 %yield.

IR (KBr): 3342 cm-1(OH), 1732 cm-1(OCO), 1711cm-1(CO).

^{1}H NMR (400 MHz, $CDCl_3$): 7.37 (s, H-5'),7.37 -7.34 (m, 3",4",5" -H), 7.27 -7.24(m, 2", 6"-H), 6.67 (s, 9-OH), 6.06 (dd, J=17.2Hz,J=l0.4Hz, H-15), 5.76 (m, H-7), 5.49 (s, N-CH_2),5.07 (dd, J=17.3Hz,J=1.2Hz, H-15), 4.85(dd, J=10.4Hz, J=l.2Hz, H-15), 4.68 (d, J=12.0Hz, lH,OCH_2),4.39(d,J=l2.0Hz,1H,OCH_2),4.36 (br, H-6), 4.25 (m,H-l), 3.07 (d, J=16.8Hz,H-12).2.29 (d,J=16.8Hz, H-12), 2.27 (d,J=4.0Hz, H-5), 2.06 (s, $COCH_3$) , l.92 (d, J=13.2Hz,H-2),1.74 (D,J=13.2Hz,H-2),1.66 (m,H-3),1.52 (s, 8-CH_3), l.40 (s, 10-CH_3), 1.38 (s,13-CH_3), 1.05 (s, 4e-CH_3), 0.98 (s, 4a-CH_3).

C NMR (100.6 MHz): 206.4 (CO), 170.3 (OCO), 147.0 (C-5), l44.1 (C-14),134.5 (C-1),129.0 (C.3",5"),728.7 (C-4''),128.0 (C-2",6"),122.3 (C-4'), 109.7 (C-15),83.6 (C-9), 82.2 (C-13), 81.8 (C-l) ,75.4 (C-7),73.7 (C-8), 71.3 (C-6), 62.1(OCH_2), 54.1(N-CH_2), 49.2 (C-5), 44.1 (C-10), 42.9 (C-12),36.l (C-3), 33.7 (C-4),32.6 (4a-CH_3),30.6(c-13), 23.1 (4e-CH_3),22.8 (C-2),21.3 ($COCH_3$),20.4 (8-CH_3).

DIP MS: m/z 582[M+H]

viii) 1-Allyl- 1H- 1,2,3 triazol-4-yl) methoxy- 1 -(6-acetyl-7-deacetyl-forskolin) (5c):

Yellow solid, mp, 89 ºC.83 % yield.

IR (KBr): 3470 cm^{-1}(OH), 1735 cm^{-1}(OCO), 1715 cm^{-1} (CO).

^{1}H NMR (400 MHz): δ 7.42 (s, H-5'), 6.85 (s, 9-OH), 6.10 (m, H-14, -CH=), 5.80 (br,H-7),5.36 (m, =CH_2),5.11 (d, J=17.6 Hz, H-l5),4.95 (d, J= 5.2 Hz, N-CH_2),4.71 (d, J=10.8 Hz,H-15), 4.49 (d, J=12.0Hz,1H,OCH_2),4.42(m,H-6),4.36(m,H-1),3.17(d,J=16.8 Hz,H-12), 2.43 (d, 16.8 Hz, H-12), 2.28 (d,J=2.2Hz, H-5), 2.16 (s, $COCH_3$), l.55 (s, 8-CH_3), 1.48 (s, 10-CH_3),1.38 (d, J=13.0Hz, H-3),l.02 (s, 4e-CH_3), 0.97s, 4a-CH_3).

^{13}C NMR (l00.6 MHz): 206.7 (CO),169.5 (OCO), 147.l (C-4'), 143.9 (C-14), 131.1(C=), 122.2(=CH_2), 120.0(C-5'),109.6(C-15),83.4(C-9),82.1(C-13),81.8(C-l),75.4 (C-8), 73.6 (C-7),711 (C-6), 62-2 (OCH_2),52.5 (N-CH_2), 49.2 (C-12), 46.9 (C-10),42.9(C-5),36.7(C-3),34.5(C-4),32.6(4a-CH_3),30.7(13-CH_3),24.5(4e-CH_3),23.0(C-2), 20.8 ($COCH_3$), 20.4 (8-CH_3),19.7 (10-CH_3).

DIP MS: m/z 532 [M+H].

ix) 1 -Butyl- 1 H-1,2,3-triazol-4-yl) methoxy-1 -(6-acetyl-7-deacetyl-forskolin) (5d):

White solid, mp 79 ºC. 82 %yield.

IR (KBr): 3454 cm^{-1}(OH), 1741 cm^{-1} (OCO), 1714 cm^{-1}(CO).

^{1}H NMR (400 MHz): 7.40 (s, H-5'),6.87 (s, 9-OH), 6.13 (dd, J=17.6Hz,10.8 Hz ,H-15), 5.79 (s, OH-7), 5.30 (d, J=2.4Hz, H-7),5.11(d, J=l7.6 Hz,H-75),4.92 (d, J=l0.8 Hz, H-I5), 4.71 (d, J=l0.4 Hz,1H, OCH_2), 4.41(d, J=10.4 Hz,1H, OCH_2), 4.32 (m, N-CH_2), 4.32(m, H-l), 3.17 (d, J=I6.8 Hz, H-12), 2.44 (d, J=16.8 Hz, H-12), 2.29 (d, J=2.4 Hz, H-5), 2.07(s,$COCH_3$), 1.90 (d, J=12.8 Hz,H-2e), 1.72 (m, H-2, H-3), 1.63(s,8-CH_3), 1.41(s, 10-CH_3), 1.39 (m,CH_2,CH_3),1.20-1.05 (m,4H), l.03(s,CH_3),0.98(t, J=5.4 Hz,N-CH_3-4).

^{13}C NMR (100.6 MHz) 206.4 (CO), 170.4 (OCO), 147.0 (C-4'),143.6 (C-14)122.2(C-5'), 109.7 (C-15), 83.3(C-9),82.5(C-13),81.8(C-1),75.3(C-8),73.7(C-7),71.3 (C-6), 62.2 (OCH_2), 50.0 (N-CH_2-1), 49.2 (C-12) 44.l (C-10), 42.8 (C-5), 36.6(C-3),33.7 (C-4), 32.9 (N-CH_2_2), 32.0 (4a-CH_3), 30.6 (N-CH_2-3),24.7 (13-CH_3), 23.0 (4e-CH_3),22.8 (C-2),2 1 .4 ($COCH_3$), 20.8 (8-CH_3), 19.7 (10-CH_3), 13.2 (N-CH_3-5).

DIP MS: m/z 548[M+H].

x) (1 -pentyl -1H-1,2,3-triazol-4-yl) methoxy-1-(6-acetyl-7-deacetyl-forskolin) (5e):

White solid, mp 109 ºC. 80 % yield.

IR (KBr): 3326 cm^{-1}(OH), 1734 cm^{-l} (OCO), l7l0cm^{-1}(CO).

^{1}H NMR (400 MHz) δ 7.39 (s, 1H, H-5'), 6.89 (s, 9-OH), 6.13 (dd, J= 17.2 Hz, J= l0.4 Hz,H-14), 5.81(q, J= 4.4Hz, H-7), 5.11 (dd,J=17.2Hz, J= l.0Hz, H-15), 4.92 (dd, J= l0.8Hz,J=1.0Hz, H-15), 4.ll (d,J=11.6Hz,1H, OCH_2),4.44 (d,J=11.6Hz,lH, OCH_2), 4.43 (m,H-6),4.31(br,H-l), 4.28 (t, J=7.0 Hz,N-CH_2),3.18(d,J=16.8 Hz,H-12),2.45(d,J=16.8 Hz, H-12),2.30 (d,J=2.8 Hz,H-5),2.08 (s, $COCH_3$), 1.87-1.93 (m, 3H), l.56 (s, 8-CH_3, 1 .42(s,10-CH_3), 1.38(s, l3-CH_3), 1.30-1.33 (m,4H)', 1.03(s,4e-CH_3),0.98(s,4a-CH_3), 0.90 (t, 6.4Hz, CH_3),

^{13}C NMR (100.6 MHz) 206.3 (CO), 170.3 (OCO), 147.1 (C-4), 143.6 (C-14),122.1 (C-5),109.7 (C-15), 83.3 (C-9), 82.1 (C-13), 81.8 (C-1), 75.4 (C-8), 73.7 (C-7),71.3 (C-6), 62.3 (OCH_2), 50.3 (N-CH_2-l),49.2 (C-12),44.1 (C-10)', 42.9 (C-5),36.7 (C-3),33.7 (C-4), 32.6 (4a-CH_3),30.7 (N-CH_2-3),29.8 (13-CH_3), 28.5 (N-CH_2-2), 23.l (4e-CH_3),22.8 (C-2), 21.9(N-CH_2-4), 21.4($COCH_3$),20.4(8-CH_3),19.8(10-CH_3).

DIP MS: m/z 562[M+H].

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