

Synthesis of New 1-Benzyl-4-(((2-Ethyl-2-Methylchroman-4-yl)oxy)methyl)-1H-1,2,3-Triazoles and 4-(((2-Ethyl-2-Methylchroman-4-yl)oxy)methyl)-1-Phenyl-1H-1,2,3-Triazoles

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ABSTRACT

A new series of 1-benzyl-4-(((2-ethyl-2-methylchroman-4-yl)oxy)methyl)-1H-1,2,3-triazoles, 4-(((2-ethyl-2-methylchroman-4-yl)oxy)methyl)-1-phenyl-1H-1,2,3-triazoles were synthesized by the reaction of 2-ethyl-2-methyl-4-(prop-2-yn-1-yloxy)chroman and substituted benzyl/phenyl azides. The products were purified by column chromatography and structures of these compounds are established by IR, ¹H-NMR, ¹³C-NMR and mass spectral data.

Keywords: Chromanone, Triazoles.

INTRODUCTION

1,2,3-Triazoles constitute an important class of nitrogen heterocycles in the field of organic and medicinal chemistry. Medicinally, they have been shown to possess a wide range of diverse pharmacological properties such as antituberculosis,¹ antibacterial,^{2,3} antimalarial,⁴ antiepileptic,⁵ antileishmanial,⁶ antiallergic,⁷ antifungal,^{8,9} anticancer^{10,11} and anti-HIV¹² activities. Triazoles have been utilized as

proton transport facilitators,¹³ glycoside cluster arrays,^{14,15} spacers or linkers to dendrimers,^{16,17} DNA cleaving agents,¹⁸ structural components in hyper branched polymers¹⁹ and most importantly in liquid crystals.²⁰ In the present article, we report the synthesis of new 1-benzyl-5-(((2,2-dimethylchroman-4-yl)oxy)methyl)-1H-1,2,3-triazoles derivatives.

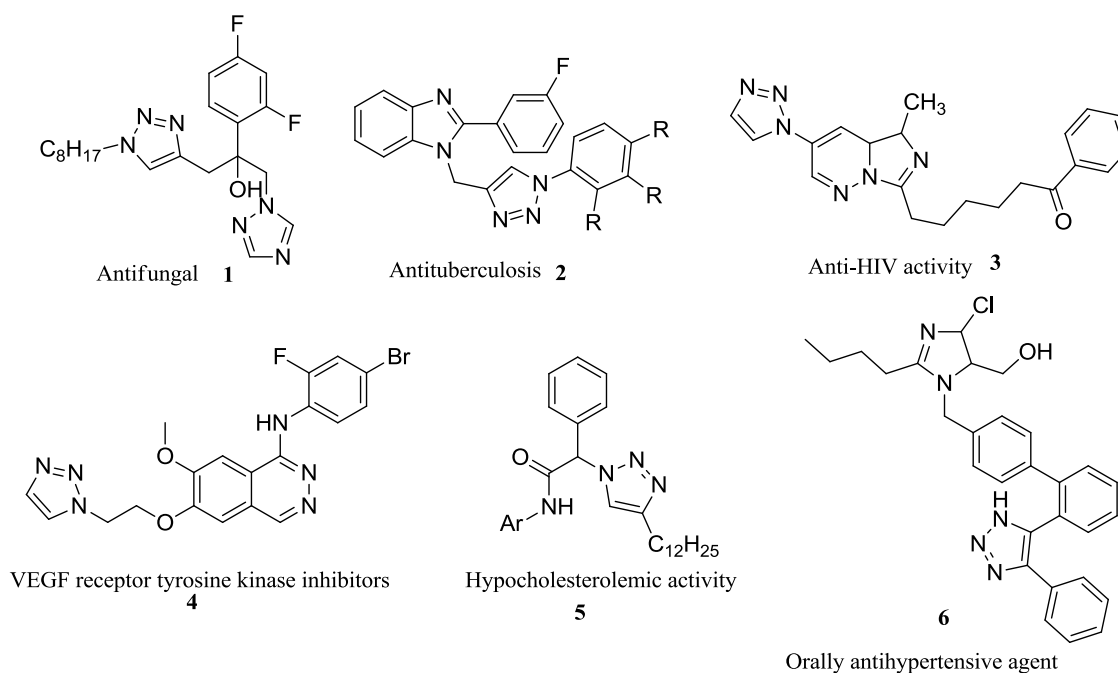


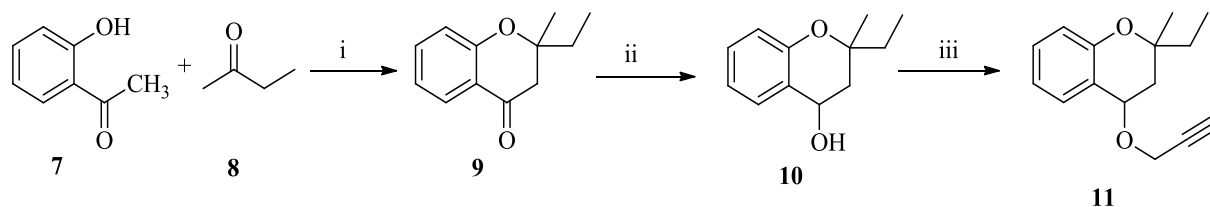
Fig. 1: 1,2,3-Triazole containing molecules with different biological activities

RESULTS AND DISCUSSION

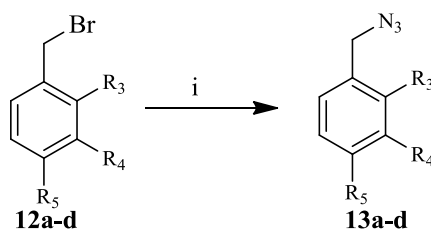
Synthesis of 1-benzyl-5-(((2,2-dimethylchroman-4-yl)oxy)methyl)-1H-1,2,3-triazoles

The reaction of 2-hydroxy acetophenone (**7**) with acetone, 2-butanone (**8a-b**) in the presence of piperidine resulted in 2-ethyl-2-

methylchroman-4-one²¹ (**9a-b**). These chromanone on reduction with NaBH₄ led to 2-ethyl-2-methylchroman-4-ol²² (**10a-b**). 2-ethyl-2-methylchroman-4-ol on alkylation with propargylbromide in the presence of NaH in THF led to 2-ethyl-2-methyl-4-(prop-2-yn-1-yloxy)chroman²³ (**11a-b**).

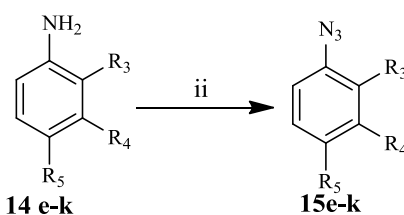


Reagents and conditions: i. piperidine, EtOH ii. NaBH₄, CH₃OH iii. NaH, Propargyl bromide, dry THF Benzyl bromide on reaction with sodium azide in DMF solvent led to benzyl azides and aniline dissolved in con HCl reacted with NaNO₂ followed by reaction with NaN₃ furnish phenyl azides²⁴.



- a= R₃=R₄=R₅=H
 b= R₃=R₄=H, R₅=Cl
 c= R₃=R₅=Cl, R₄=H
 d= R₃=H, R₄=R₅=Cl

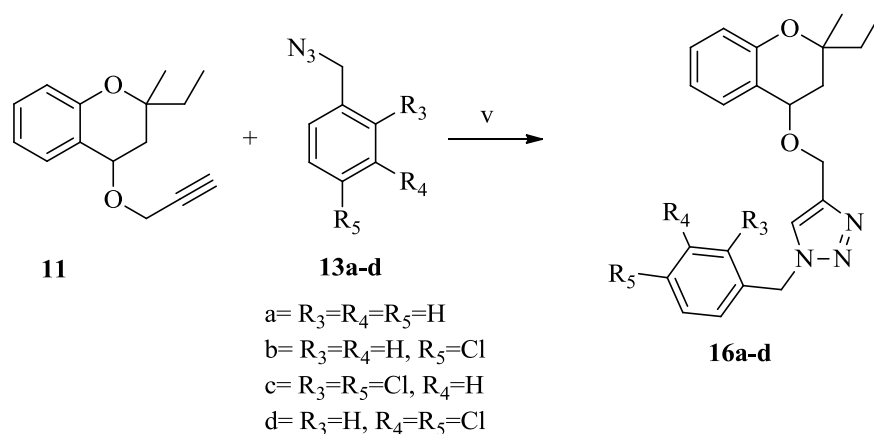
Reagents and conditions: NaN₃, DMF, rt, 6 h



- e=R₃=R₄=R₅=H i=R₃=R₅=H R₄=Cl
 f=R₃=R₄=H, R₅=Br j=R₃=R₅=H R₄=OCH₃
 g=R₃=R₄=H, R₅=Cl k=R₃=Cl, R₄=R₅=H
 h=R₃=R₄=H, R₅=F

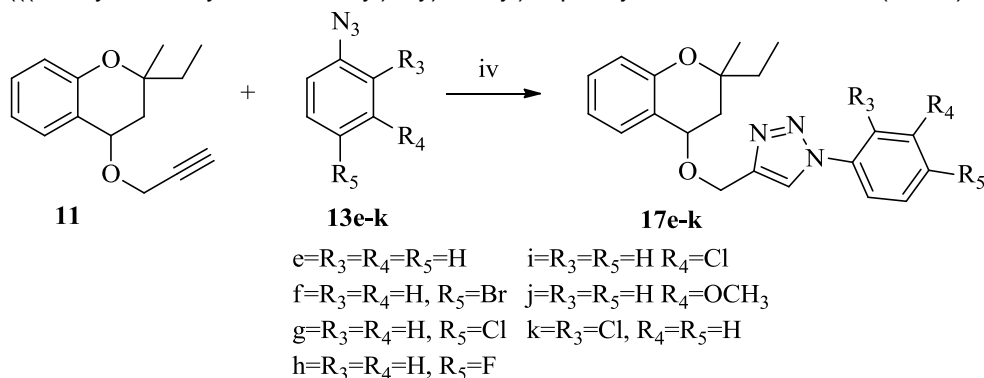
Reagents and conditions: Con HCl, NaNO₂, NaN₃

2-ethyl-2-methyl-4-(prop-2-yn-1-yloxy)chroman (**11**) reacted with different benzyl azides (**13a-dk**) furnish 1-benzyl-4-(((2-ethyl-2-methylchroman-4-yl)oxy)methyl)-1H-1,2,3-triazole²⁴ (**16a-d**).



Reagents and conditions: v. CuSO₄·5H₂O, Sodium ascorbate, DMF

2-ethyl-2-methyl-4-(prop-2-yn-1-yloxy)chroman (**11**) reacted with substituted phenyl azides (**13e-k**) furnish 4-(((2-ethyl-2-methylchroman-4-yl)oxy)methyl)-1-phenyl-1H-1,2,3-triazole ²⁴ (**17e-k**).



Reagents and conditions: iv. CuSO₄·5H₂O, Sodium ascorbate, DMF

CONCLUSION

We have synthesized novel 1-benzyl-4-(((2-ethyl-2-methylchroman-4-yl)oxy)methyl)-1H-1,2,3-triazoles, 4-(((2-ethyl-2-methylchroman-4-yl)oxy)methyl)-1-phenyl-1H-1,2,3-triazoles in excellent yields employing click chemistry approach.

Experimental section

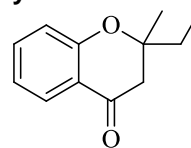
General remarks

Air or/and moisture sensitive reactions were carried out in anhydrous solvents under an argon atmosphere in an oven or flame-dried glassware. All anhydrous solvents were distilled prior to use: THF from Na and benzophenone; CH₂Cl₂, DMSO from CaH₂. Commercial reagents were used without purification. Column chromatography was carried out by using ACME silica gel (60-120 mesh).

Infrared spectra were recorded on Perkin-Elmer 683 spectrometer. ¹H and ¹³C NMR spectra were recorded on a Varian Unity-500 or Varian INOVA 400 MHz or a Bruker-300 spectrometer. Chemical shifts (δ) are given in ppm relative to TMS and coupling constants

(J) in Hz. The following abbreviations are used to designate signal multiplicity: s = singlet, d = doublet, dd = doublet of doublet, t = triplet, td = triplet of doublet, q = quartet, m = multiplet, br = broad. Mass spectra were obtained on an Exactive Thermo Scientific Orbit rap Mass Spectrometer.

2-ethyl-2-methylchroman-4-one (9)



To a stirred solution of 2-hydroxyacetophenone (2 g, 14.7mmol) and butan-2-one (1.165 g, 16.17mmol) in methanol (10 mL), pyrrolidine (1.17 g, 13.4mmol) was added at room temperature. The reaction mixture was refluxed for 2-3 h. The completion of the reaction was monitored by TLC. The reaction mixture was quenched by crushed ice and extracted with ethyl acetate. The organic layer was washed by brine (2 × 15 mL) and dried over anhydrous sodium sulfate, and the solvent was removed under pressure to obtain the crude products. The obtained residues

were purified by column chromatography on silica gel, pet ether and ethylacetate elutes were used.

Physical state: yellow liquid

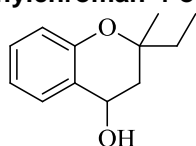
IR: 2975, 2930, 1689, 1601, 1571, 1452, 1370, 1324, 1301, 1253, 1205, 1165, 1112, 768 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 0.95(t, 3H), 1.38(s, 3H), 1.68(m, 2H), 2.61(dd, $J=16.4$ Hz, 16.4 Hz, 2H), 6.91(m, 2H), 7.43(m, 1H), 7.82(dd, $J=1.7, 1.7$ Hz, 1H).

^{13}C NMR (100 MHz, CDCl_3): δ 192.8, 159.9, 136.1, 126.4, 120.5, 118.3, 81.4, 47.0, 32.0, 23.3, 7.9 ppm.

ESI-MS: 191 $[\text{M}+\text{H}]^+$.

2-Ethyl-2-methylchroman-4-ol (10)



To a stirred solution of 2,2-dimethylchromanone (2 g, 1eq., 11.36mmol) in absolute ethanol was treated with NaBH_4 (0.516 g, 1.2 eq.) and stirred at room temperature 2 h. The reaction mixture was then quenched with 3 mL H_2O , then 3 mL brine, extracted with EtOAc (4x3 mL). The organic layers were combined, dried over Na_2SO_4 , filtered, and then evaporated to dryness. The resulting residue was purified by column chromatography (silica gel, ethyl acetate: pet ether) as eluent (1.82 g) 90% yield.

Physical state: yellow liquid.

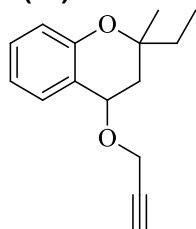
IR: 3194, 2963, 1608, 1582, 1482, 1224, 1034, 1017, 750 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.43 (dt, $J = 33.1, 16.6$ Hz, 1H), 7.18 (t, $J = 7.7$ Hz, 1H), 7.06 – 6.67 (m, 2H), 2.35 – 1.95 (m, 1H), 1.94 – 1.53 (m, 5H), 1.35 (d, $J = 29.6$ Hz, 2H), 1.26 (s, 1H), 0.97 (dt, $J = 21.7, 7.5$ Hz, 3H) ppm.

^{13}C NMR (100 MHz, CDCl_3): δ 153.2, 129.1, 127.8, 127.4, 124.7, 120.1, 117.1, 78.0, 77.3, 77.1, 76.6, 63.4, 63.1, 40.5, 40.1, 34.5, 30.8, 25.4, 23.0, 8.0 ppm.

ESI-MS: 193 $[\text{M}+\text{H}]^+$.

2-ethyl-2-methyl-4-(prop-2-yn-1-yloxy)chroman (11)



To a solution of 2,2-dimethylchroman-4-ol(550 mg, 1.09 mmol) in dry THF (5 mL) was added solid NaH (60%, 123 mg, 3.08 mmol) at 0 °C under argon. The reaction mixture was stirred at room temperature for 1h. Then propargyl bromide (283 μL , 3.33 mmol) was added. The reaction mixture was stirred for 3 h at room temperature. Then it was quenched with sat.aq. NH_4Cl at 0 °C and extracted with ethyl acetate. The combined organic layers were washed with H_2O and brine, dried over Na_2SO_4 . After concentration under vacuum, the residue was purified by flash chromatography using hexane/ethyl acetate as an eluent to give 2,2-dimethyl-4-(prop-2-yn-1-yloxy)chroman(576 mg, yield 97%) as colorless oil³⁴.

Physical state: yellow liquid.

IR: 3440, 1632, 1526, 1480, 1453, 1376, 1300, 1241, 1186, 1031, 750 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.45 – 7.36 (m, 1H), 7.21 – 7.13 (m, 1H), 6.94 – 6.86 (m, 1H), 6.83 – 6.75 (m, 1H), 4.84–4.74 (m, 1H), 4.39 – 4.24 (m, 2H), 2.49 (t, $J = 2.4$ Hz, 1H), 2.12 (ddd, $J = 36.7, 13.7, 5.7$ Hz, 1H), 2.02 – 1.93 (m, 1H), 1.81 – 1.60 (m, 2H), 1.33 (d, $J = 44.4$ Hz, 3H), 0.96 (t, $J = 7.5$ Hz, 3H) ppm.

^{13}C NMR (100 MHz, CDCl_3) δ 153.6, 129.3, 128.9, 128.5, 119.9, 117.2, 80.1, 74.5, 69.6, 69.2, 55.5, 35.5, 32.2, 24.8, 8.0 ppm.

ESI-MS: 253 $[\text{M}+\text{Na}]^+$.

Synthesis of benzyl azides (13a-d)

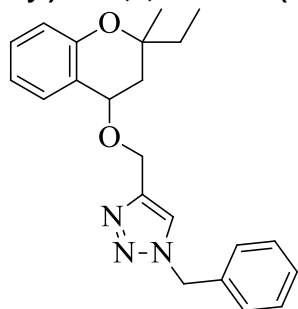
Sodium azide (715 mg, 11.0 mmol) was dissolved in 20 mL DMSO and benzyl bromide (1.71 g, 1.19 mL, 10 mmol) was added to the solution. The reaction mixture was stirred for 2 h at room temperature. 200 mL H_2O were added and after cooling to room temperature, the aqueous solution was extracted with diethyl ether (3x100 mL). The combined organic layers were washed with water (2x100 mL) and brine (100 mL). After drying over Na_2SO_4 the ether was removed under reduced pressure to yield the pure azide in a yield⁴⁹ of 90% as colourless oil. These are used without characterization.

Synthesis of phenyl azides (15e-k)

The aniline (1 g, 10.7 mmol) was suspended in 30 mL hydrochloric acid (17%) at room temperature and then ethanol was added until a clear solution was obtained. The solution was cooled to 0 °C and NaNO_2 (1.1 g, 1.5 eq.) was added in small portions. After stirring at 0 °C for 15-30 min. NaN_3 (1.05 g, 1.5 eq.) was slowly added and the mixture was stirred for additional 2 h at room temperature. The reaction mixture was extracted with diethyl ether (3x80 mL) and the combined organic

fractions were washed with saturated NaHCO_3 solution (3x50 mL) and with brine (50 mL). After drying over Na_2SO_4 the ether was removed under reduced pressure and the desired azides were used without further purification and characterization.

1-benzyl-4-(((2-ethyl-2-methylchroman-4-yl)oxy)methyl)-1H-1,2,3-triazole (16a)



To a solution of 2,2-dimethyl-4-(prop-2-yn-1-yloxy)chroman (0.2g, 1 eq.) in DMF was added 4-chloro benzyl azide (0.17 g, 1.1 eq.) to this solution aq solution of copper sulphate and sodium ascorbate was added and stirred for 10 h at room temperature. After completion of reaction monitored by TLC cold water was added and extracted with ethylacetate (3x50 mL). Organic fractions are dried over Na_2SO_4 and concentrated and purified by column chromatography by eluting with pet ether and ethylacetate.

Physical state: colourless liquid.

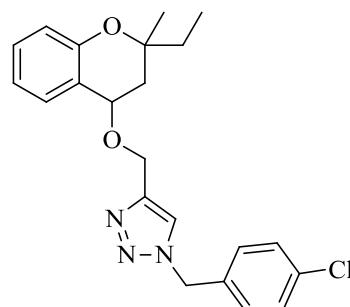
IR: 3128, 3089, 2922, 2874, 2358, 2335, 1615, 1590, 1561, 1472, 1451, 1380, 1329, 1216, 1130, 1110, 1090 cm^{-1} .

^1H NMR (500 MHz, CDCl_3) δ 7.49 (d, $J=6.2$ Hz, 1H), 7.38 (m, 3H), 7.28 (m, 3H), 7.16 (m, 1H), 6.85 (t, 1H), 6.78 (m, 1H), 5.53 (d, $J=1.8$ Hz, 2H), 4.83 (m, 2H), 4.69 (m, 1H), 2.17 (dd, $J=5.9, 5.7$ Hz, 1H), 1.99 (dd, $J=4.7, 4.2$ Hz, 1H), 1.68 (m, 2H), 1.26 (m, 3H), 0.92 (t, 3H) ppm.

^{13}C NMR (100 MHz, CDCl_3) δ 153.5, 146.1, 134.5, 129.2-128.0, 122.3, 119.8, 117.2, 70.4, 70.1, 62.1, 54.1, 35.7, 33.6, 24.9, 8.0 ppm.

ESI-MS: 364 $[\text{M}+\text{H}]^+$.

1-(4-chlorobenzyl)-4-(((2-ethyl-2-methylchroman-4-yl)oxy)methyl)-1H-1,2,3-triazole (16b)



Physical state: colourless liquid.

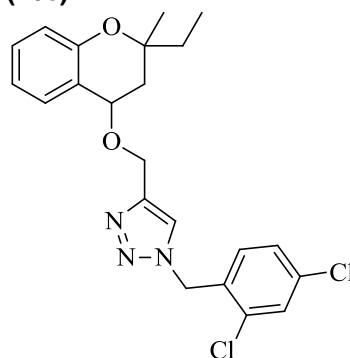
IR: 3124, 3087, 2918, 2870, 2355, 1591, 1548, 1482, 1337, 1212, 1125, 1107, 1091 cm^{-1} .

^1H NMR (500 MHz, CDCl_3) δ 7.49 (d, $J=7.3$ Hz, 1H), 7.35 (d, $J=8.3$ Hz, 2H), 7.28 (m, 1H), 7.22 (m, 2H), 7.16 (m, 1H), 6.85 (t, 1H), 6.79 (m, 1H), 5.50 (d, $J=2.2$ Hz, 2H), 4.84 (m, 2H), 4.70 (m, 1H), 2.18 (dd, $J=5.7, 5.6$ Hz, 1H), 1.99 (dd, $J=4.7, 4.2$ Hz, 1H), 1.77-1.54 (m, 2H), 1.26 (m, 3H), 0.95 (t, 3H) ppm.

^{13}C NMR (100 MHz, CDCl_3) δ 153.6, 146.3, 113.0, 131.4, 129.3-129.1, 128.6, 128.1, 122.2, 119.8, 117.3, 70.5, 70.3, 62.1, 53.4, 35.6, 33.6, 24.9, 8.0 ppm.

ESI-MS: 398 $[\text{M}+\text{H}]^+$.

1-(2,4-dichlorobenzyl)-4-(((2-ethyl-2-methylchroman-4-yl)oxy)methyl)-1H-1,2,3-triazole (16c)



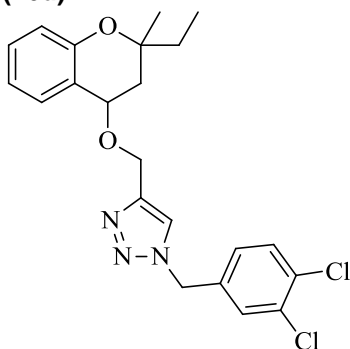
Physical state: yellow liquid.

IR: 3128, 3091, 2922, 2874, 2359, 2337, 1615, 1596, 1574, 1470, 1290, 1268, 1216, 1130, 1107, 1087 cm^{-1} .

^1H NMR (500 MHz, CDCl_3) δ 7.59 (d, $J=3.9$ Hz, 1H), 7.45 (d, $J=2.0$ Hz, 1H), 7.23 (m, 2H), 7.13 (m, 1H), 6.82 (m, 1H), 6.77 (m, 1H), 5.63 (s, 2H), 4.71 (m, 2H), 4.63 (m, 1H), 1.94 (m, 2H), 1.68 (m, 2H), 1.26 (m, 3H), 0.92 (t, 3H) ppm.

^{13}C NMR (100 MHz, CDCl_3) δ 153.6, 140.6, 135.5, 134.1, 131.1, 131.0, 129.7, 129.3, 129.1, 128.7, 128.2, 127.9, 119.8, 117.3, 70.5, 70.2, 60.9, 50.8, 35.7, 33.6, 24.9, 8.0 ppm.

ESI-MS: 432 $[\text{M}+\text{H}]^+$.

1-(3,4-dichlorobenzyl)-4-(((2-ethyl-2-methylchroman-4-yl)oxy)methyl)-1H-1,2,3-triazole (16d)

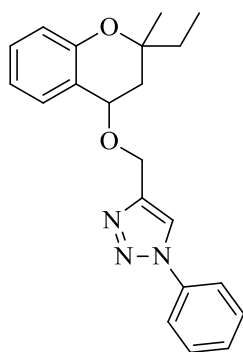
Physical state: brown liquid.

IR: 3132, 3092, 2991, 2918, 2871, 2359, 2058, 1636, 1604, 1561, 1471, 1451, 1400, 1366, 1331, 1281, 1210, 1190, 1110, 1086, 1048, 1030, 1003 cm^{-1} .

^1H NMR (500 MHz, CDCl_3) δ 7.52(d, $J=4.7$ Hz, 1H), 7.43(d, $J=8.3$ Hz, 1H), 7.37(s, 1H), 7.28(d, $J=7.3$ Hz, 1H), 7.09(m, 2H), 6.83(t, 1H), 6.77(d, $J=8.1$ Hz, 1H), 5.48(s, 2H), 4.76(m, 2H), 4.63(m, 1H), 2.08(m, 1H), 1.94(m, 1H), 1.62-1.59(m, 2H), 1.26(m, 3H), 0.92(t, 3H) ppm.

^{13}C NMR (100 MHz, CDCl_3) δ 153.6, 140.6, 135.5, 134.1, 131.1, 131.0, 129.7, 129.3, 129.1, 128.7, 128.2, 127.9, 119.8, 117.3, 70.5, 70.2, 60.9, 50.8, 35.7, 33.6, 24.9, 8.0 ppm.

ESI-MS: 454 $[\text{M}+\text{Na}]^+$.

4-(((2-ethyl-2-methylchroman-4-yl)oxy)methyl)-1-phenyl-1H-1,2,3-triazole (17e)

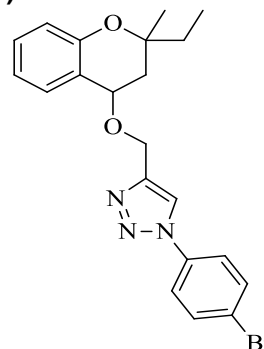
Physical state: colourless liquid

IR: 3130, 3089, 2994, 2922, 2875, 2358, 2057, 1632, 1604, 1558, 1490, 1306, 1274, 1130, 1112, 1095 cm^{-1} .

^1H NMR (500 MHz, CDCl_3) δ 8.00 (d, $J=7.2$ Hz, 1H), 7.72 (m, 2H), 7.50 (m, 2H), 7.35 (m, 2H), 7.14 (m, 1H), 7.86 (m, 1H), 6.78 (m, 1H), 4.84 (m, 2H), 4.71 (m, 1H), 2.15 (dd, $J=5.6, 5.8$ Hz, 1H), 2.01 (dd, $J=3.3, 3.9$ Hz, 1H), 1.59 (m, 2H), 1.40 (s, 1H), 1.29 (s, 2H), 0.94 (t, 3H) ppm.

^{13}C NMR (100 MHz, CDCl_3) δ 153.7, 146.4, 137.1, 134.6, 129.8, 129.7, 128.9, 128.8, 128.2, 128.1, 127.9, 122.4, 121.9, 120.6, 120.0, 117.3, 70.8, 70.5, 62.1, 54.2, 35.7, 33.8, 32.1, 8.1 ppm.

ESI-MS: 350 $[\text{M}+\text{H}]^+$.

1-(4-bromophenyl)-4-(((2-ethyl-2-methylchroman-4-yl)oxy)methyl)-1H-1,2,3-triazole(17f)

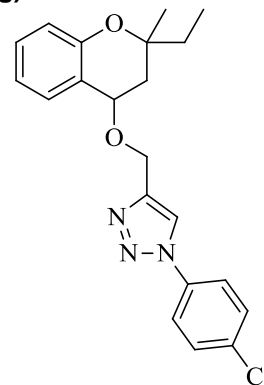
Physical state: brown liquid

IR: 3132, 3090, 2993, 2915, 2876, 2364, 1638, 1616, 1591, 1521, 1488, 1316, 1282, 1190, 1110, 1088, 1048, 1030, 1003 cm^{-1} .

^1H NMR (400 MHz, CDCl_3) δ 7.97(d, $J=9.6$ Hz, 1H), 7.61 (m, 4H), 7.34 (m, 1H), 7.15 (m, 1H), 6.87 (t, 1H), 6.79 (m, 1H), 4.83 (m, 2H), 4.71 (m, 1H), 2.15 (dd, $J=5.6, 5.8$ Hz, 1H), 2.01 (dd, $J=3.3, 3.9$, 1H), 1.62 (m, 2H), 1.39-1.29 (m, 3H), 0.95 (m, 3H) ppm.

^{13}C NMR (100 MHz, CDCl_3) δ 153.6, 146.7, 135.9, 132.8, 129.3, 129.2, 128.7, 128.2, 122.3, 121.8, 120.3, 119.9, 117.3, 70.8, 70.5, 62.0, 35.6, 33.7, 24.9, 8.0 ppm.

ESI-MS: 428 $[\text{M}+\text{H}]^+$.

1-(4-chlorophenyl)-4-(((2-ethyl-2-methylchroman-4-yl)oxy)methyl)-1H-1,2,3-triazole(17g)

Physical state: brown liquid.

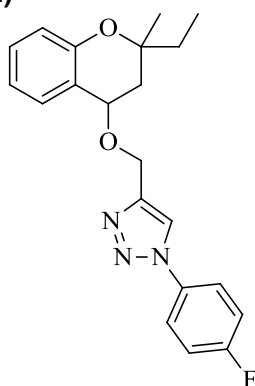
IR: 3446, 3116, 2972, 2925, 2778, 1604, 1560, 1502, 1481, 1361, 1324, 1268, 1222, 1131, 1053, 1023, 823 cm^{-1} .

^1H NMR (400 MHz, CDCl_3) δ 8.06(d, $J=9.6$ Hz, 1H), 7.56 (m, 2H), 7.49 (m, 2H) 7.25 (m, 1H), 6.98 (m, 1H), 6.96 (t, 1H), 6.93 (m 1H), 4.63 (m, 2H), 4.13 (m, 1H), 2.20 (dd, $J=5.6, 5.8$ Hz, 1H), 1.97 (dd, $J=3.3, 3.9$, 1H), 1.82 (m, 2H), 1.53 (m, 3H), 0.92 (m, 3H) ppm.

^{13}C NMR (100 MHz, CDCl_3) δ 153.3, 144.5, 134.9, 134.5, 128.7, 127.4, 126.5, 125.6, 122.3, 121.8, 120.3, 119.2, 112.3, 78.8, 78.5, 65.6, 37.6, 35.7, 26.1, 8.0 ppm.

ESI-MS: 384 $[\text{M}+\text{H}]^+$.

4-(((2-ethyl-2-methylchroman-4-yl)oxy)methyl)-1-(4-fluorophenyl)-1H-1,2,3-triazole(17h)



Physical state: yellow liquid

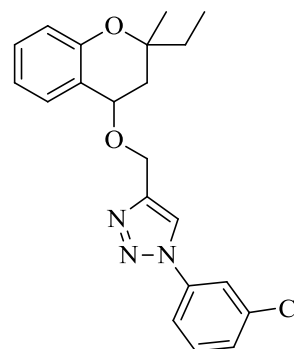
IR: 3126, 3085, 2978, 2924, 1606, 1513, 1486, 1454, 1370, 1274, 1222, 1208, 1124, 1105, 1040, 934, 826 cm^{-1} .

^1H NMR (400 MHz, CDCl_3): δ 8.06(d, $J=9.6$ Hz, 1H), 7.60 (m, 2H), 7.25 (m, 1H), 7.24 (m, 2H), 6.96 (m, 1H), 6.95 (t, 1H), 6.90 (m 1H), 4.63 (m, 2H), 4.21 (m, 1H), 2.20 (dd, $J=5.6, 5.8$ Hz, 1H), 1.98 (dd, $J=3.3, 3.9$, 1H), 1.81 (m, 2H), 1.52 (m, 3H), 0.92 (m, 3H) ppm.

^{13}C NMR (101 MHz, CDCl_3): δ 162.8, 153.1, 144.5, 132.6, 127.4, 126.6, 125.6, 122.5, 120.2, 119.3, 115.8, 112.3, 79.7, 78.5, 65.8, 37.6, 35.7, 26.1, 8.0 ppm.

ESI-MS: 368 $[\text{M}+\text{H}]^+$.

1-(3-chlorophenyl)-4-(((2-ethyl-2-methylchroman-4-yl)oxy)methyl)-1H-1,2,3-triazole(17i)



Physical state: yellow liquid.

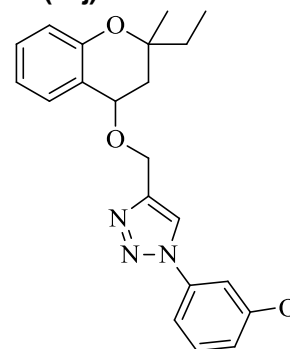
IR: 3447, 3118, 2974, 2929, 2781, 1605, 1564, 1504, 1482, 1363, 1325, 1269, 1224, 1133, 1052, 1025, 820 cm^{-1} .

^1H NMR (500 MHz, CDCl_3) δ 8.01 (d, $J = 9.9$ Hz, 1H), 7.80 (dd, $J = 4.4, 2.1$ Hz, 1H), 7.65 (ddd, $J = 7.9, 3.1, 1.9$ Hz, 1H), 7.50 – 7.41 (m, 2H), 7.37 (ddd, $J = 12.7, 7.9, 1.2$ Hz, 1H), 7.20 – 7.15 (m, 1H), 6.92 – 6.87 (m, 1H), 6.83 – 6.79 (m, 1H), 4.97 – 4.84 (m, 2H), 4.79 – 4.71 (m, 1H), 2.20 (ddd, $J = 28.2, 13.6, 5.7$ Hz, 1H), 2.09 – 2.01 (m, 1H), 1.85 – 1.67 (m, 2H), 1.41 – 1.30 (m, 3H), 0.98 (ddd, $J = 9.6, 6.6, 4.5$ Hz, 3H) ppm.

^{13}C NMR (100 MHz, CDCl_3): δ 153.1, 144.4, 132.8, 132.6, 132.3, 130.0, 129.8, 128.6, 127.5, 126.7, 125.8, 120.3, 119.4, 112.3, 79.6, 78.4, 37.7, 35.4, 26.3, 8.0 ppm.

ESI-MS: 383 $[\text{M}+\text{H}]^+$.

4-(((2-ethyl-2-methylchroman-4-yl)oxy)methyl)-1-(3-methoxyphenyl)-1H-1,2,3-triazole(17j)



Physical state: brown liquid.

IR: 3124, 3085, 2971, 2925, 1604, 1594, 1586, 1473, 1386, 1218, 1201, 1126, 1104, 1047, 936, 829 cm^{-1} .

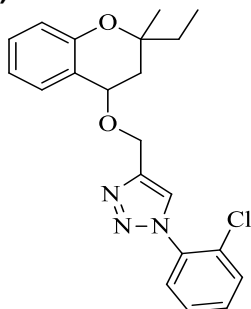
^1H NMR (500 MHz, CDCl_3) δ 7.78 – 7.73 (m, 2H), 7.38 (dd, $J = 16.0, 7.6$ Hz, 1H), 7.19 (dd, $J = 10.1, 4.7$ Hz, 1H), 6.98 (d, $J = 8.5$ Hz, 2H), 6.91 (t, $J = 7.4$ Hz, 1H), 6.81 (dd, $J = 7.9, 3.5$ Hz, 1H), 6.56 (d, $J = 6.6$ Hz, 1H), 4.84 – 4.68 (m, 3H), 3.86 (s, 3H), 2.14 (ddd, $J = 34.1, 13.6, 5.8$ Hz, 1H), 2.07 – 1.98 (m, 1H), 1.82 –

1.62 (m, 2H), 1.41 – 1.28 (m, 3H), 0.97 (dt, $J = 9.7, 7.5$ Hz, 3H) ppm.

^{13}C NMR (100 MHz, CDCl_3) δ 160.5, 153.6, 146.3, 138.0, 130.5, 129.3, 129.2, 128.7, 120.6, 119.9, 117.3, 114.6, 112.4, 106.3, 70.7, 62.1, 61.9, 55.6, 35.7, 33.7, 23.6, 8.0 ppm.

ESI-MS: 402 $[\text{M}+\text{Na}]^+$.

1-(2-chlorophenyl)-4-(((2-ethyl-2-methylchroman-4-yl)oxy)methyl)-1H-1,2,3-triazole(17k)



Physical state: yellow liquid.

IR: 3443, 3118, 2970, 2923, 2779, 1602, 1558, 1504, 1486, 1359, 1323, 1269, 1225, 1130, 1055, 1020, 813 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 8.03 (d, $J = 8.2$ Hz, 1H), 7.75 – 7.55 (m, 2H), 7.50 – 7.43 (m, 2H), 7.41 – 7.33 (m, 1H), 7.20 – 7.09 (m, 1H), 6.88 (td, $J = 7.5, 1.1$ Hz, 1H), 6.80 (ddd, $J = 8.2, 3.8, 1.1$ Hz, 1H), 5.00 – 4.86 (m, 2H), 4.81 – 4.67 (m, 1H), 2.19 (ddd, $J = 31.2, 13.6, 5.8$ Hz, 1H), 2.05 (ddd, $J = 13.4, 7.6, 2.8$ Hz, 1H), 1.84 – 1.60 (m, 2H), 1.35 (d, $J = 52.1$ Hz, 3H), 0.97 (td, $J = 7.5, 5.9$ Hz, 3H) ppm.

^{13}C NMR (100 MHz, CDCl_3): δ 153.6, 144.5, 134.9, 130.7, 129.3, 129.2, 128.7, 128.6, 128.3, 127.9, 127.7, 124.5, 119.9, 117.3, 70.6, 62.0, 61.9, 35.8, 33.7, 24.9, 8.0 ppm.

ESI-MS: 383 $[\text{M}+\text{H}]^+$.

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