



SUPPLEMENTARY MATERIAL TO
**Synthesis of novel menthol derivatives containing 1,2,3-triazole
group and their *in vitro* antibacterial activities**

MOHADESEH KARBASI¹, PEYMAN SALEHI^{1*}, ATOUSA ALIAHMADI²,
MORTEZA BARARJANIAN¹ and FARZANEH ZANDI²

¹Department of Phytochemistry, Medicinal Plants and Drugs Research Institute, Shahid Beheshti University, G. C., Evin, 1983963113 Tehran, Iran and ²Department of Biology, Medicinal Plants and Drugs Research Institute, Shahid Beheshti University, G. C., Evin, 1983963113 Tehran, Iran

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(1-(2-(RS(4-Fluoro-3-nitrophenylamino)(cyano)methyl)phenyl)-1H-1,2,3-triazol-4-yl)methyl(1R,2S,5R)-2-isopropyl-5-methylcyclohexyl succinate (**6a₁**)

Yield: 70 % , white powder; M.p.: 106 – 109 °C; IR(KBr, cm⁻¹): 3448.9, 2926.2, 2362.7, 1729.5, 1616.3, 1540.9; ¹H NMR (300 MHz, CDCl₃), (δ, ppm): mixture of two isomers 7.97 (s, 2H, H_T), 7.90 - 7.83 (m, 2H, H_{Ar}), 7.71 - 7.61 (m, 4H, H_{Ar}), 7.53 - 7.44 (m, 2H, H_{Ar}), 7.39 - 7.32 (m, 2H, H_{Ar}), 7.21 - 7.08 (m, 2H, H_{Ar}), 7.02 - 6.94 (m, 2H, H_{Ar}), 5.77 (d, *J* = 9.2 Hz, 1H, -CH-CN, one isomer), 5.76 (d, *J* = 9.2 Hz, 1H, -CH-CN, another isomer), 5.35 - 5.26 (m, 4H, -O-CH₂-C_{Triazole}), 5.17 (d, *J* = 9.2 Hz, 1H, NH, one isomer), 5.16 (d, *J* = 9.2 Hz, 1H, NH, another isomer), 4.71 - 4.61 (m, 2H, -CH-O-), 2.63 (s, 8H, -CO-CH₂-CH₂-CO-), 1.99 - 1.86 (m, 2H, CH), 1.87 - 1.80 (m, 2H, CH), 1.77 - 1.61 (m, 4H, CH₂), 1.45 - 1.35 (m, 2H, CH), 1.36 - 1.28 (m, 2H, CH), 1.24 - 0.90 (m, 6H, CH), 0.89 - 0.86 (m, 12H, 4CH₃), 0.71 (dd, *J* = 6.9 Hz, 6H, 2CH₃). ¹³C-NMR (75 MHz, CDCl₃), (δ, ppm): 172.32, 172.05, 149.80 (d, *J* = 257 Hz), 143.97, 140.85, 137.29, 135.36, 131, 27, 130.97, 130.48, 128.56, 126.54, 125.75, 121.72, 119.56, 116.31, 110.90, 74.79, 57.50, 47.60, 46.88, 40.78, 34.14, 31.37, 29.29, 29.04, 26.21, 23.37, 21.99, 20.37, 16.29. MS (ESI): [M+H]⁺ C₃₁H₃₅FN₆O₆ calcd 607.66, found 607.70.

(1-(2-(RS(3,4-Dichlorophenylamino)(cyano)methyl)phenyl)-1H-1,2,3-triazol-4-yl)methyl(1R,2S,5R)-2-isopropyl-5-methylcyclohexyl succinate (**6a₂**)

Yield: 68 % , cream powder; M.p.: 106 - 108 °C; IR (KBr, cm⁻¹): 3444.4, 2924.5, 2357.2, 1733.1, 1632.7; ¹H NMR (300 MHz, CDCl₃), (δ, ppm): mixture of two isomers 7.93 (m, 1H, H_{Triazole}), 7.86 - 7.83 (m, 1H, H_{Ar}), 7.68 - 7.61 (m,

* Corresponding author. E-mail: p-salehi@sbu.ac.ir

2H, H_{Ar}), 7.52- 7.43 (m, 1H, H_{Ar}), 7.25 (s, 1H, H_{Ar}), 6.80 (d, $J = 2.9$ Hz, 1H, H_{Ar}), 6.56 (dd, $J = 8.9, 2.9$ Hz, 1H, H_{Ar}), 5.69 (d, $J = 9.4$ Hz, 1H, -CH-CN), 5.31 (s, 2H, H -O-CH₂-C_{Triazol}), 4.81 (d, $J = 9.3$, 1H, -NH-), 4.67 (td, $J = 11.0, 4.6$ Hz, 1H, -CH-O-), 2.62 (s, 4H, -CO-CH₂CH₂-CO-), 2.00 - 1.90 (m, 1H, CH-Me₂), 1.87-1.74 (m, 1H, CH-CHO), 1.67 (s, 2H, CH₂), 1.46 - 1.38 (m, 1H, CH), 1.37 - 1.27 (m, 1H, CH), 1.14-0.94 (m, 3H, CH), 0.87 (d, $J = 6.8$ Hz, 6H, 2CH₃), 0.76 (d, $J = 6.9$ Hz, 3H, CH₃). ¹³C-NMR (75 MHz, CDCl₃), (δ, ppm): 172.3, 171.9, 143.8, 143.7, 135.3, 133.1, 131.0, 130.1, 130.2, 128.9, 126.6, 125.7, 123.5, 116.6, 116.3, 114.3, 74.8, 57.5, 47.2, 46.9, 40.8, 34.1, 31.4, 29.3, 29.0, 26.2, 23.4, 22.0, 20.7, 16.3. MS (ESI): [M+H]⁺ C₃₁H₃₅Cl₂N₅O₄ calcd 613.55, found 613.58.

(1-(3-(RS(4-fluoro-3-nitrophenylamino)(cyano)methyl)phenyl)-1H-1,2,3-triazol-4-yl)methyl(1R,2S,5R)-2-isopropyl-5-methylcyclohexyl succinate (6b₁)

Yield: 85 %, white powder; 59-62 °C; IR (KBr, cm⁻¹): 3446.99, 2926.28, 2359.09, 1734.28, 1622.52, 1542.80. ¹H NMR (300 MHz, CDCl₃), (δ, ppm): mixture of two isomers 8.14 (s, 1H, H_{Tr}), 8.06 (s, 1H, H_{Ar}), 7.77 (d, $J = 8.0$ Hz, 1H, H_{Ar}), 7.71 (d, $J = 8.1$ Hz, 1H, H_{Ar}), 7.63 (dd, 7.9 Hz 1H, H_{Ar}), 7.52 - 7.44 (m, 1H, H_{Ar}), 7.23 - 7.12 (m, 1H, H_{Ar}), 7.10 - 6.97 (m, 1H, H_{Ar}), 5.66 (d, $J = 8.6$ Hz, 1H, -HC-CN), 5.40 - 5.18 (m, 3H, -O-CH₂-C_{Triazole}, -NH-), 4.66 (td, $J = 10.9, 4.4$ Hz, 1H, -CH-O-), 2.78 - 2.50 (m, 4H, -CO-CH₂-CH₂-CO-), 1.97 - 1.88 (m, 1H, CH), 1.86 - 1.78 (m, 1H, CH), 1.69 - 1.61 (m, 2H, CH₂), 1.45 - 1.39 (m, 1H, CH), 1.37-1.31 (m, 1H, CH), 1.12-0.89 (m, 3H, CH), 0.87 (d, $J = 7.0$ Hz, 3H, CH₃), 0.86 (d, $J = 6.4$ Hz, 3H, CH₃), 0.71 (d, $J = 6.9$ Hz, 3H, CH₃). ¹³C-NMR (75 MHz, CDCl₃), (δ, ppm): 172.3, 171.9, 149.5 (d, $J = 256.5$ Hz), 143.9, 141.2, 137.5, 137.4, 135.3, 131.0, 127.6, 122.2, 121.4, 121.2, 119.5, 119.3, 110.4, 74.8, 57.6, 49.6, 46.9, 40.8, 34.1, 31.3, 29.3, 29.1, 26.2, 23.3, 21.9, 20.7, 16.3. MS (ESI): [M+H]⁺ C₃₁H₃₆FN₆O₆ calcd 607.66, found 607.68.

(1-(3-(RS(4-Ethylphenylamino)(cyano)methyl)phenyl)-1H-1,2,3-triazol-4-yl)methyl(1R,2S,5R)-2-isopropyl-5-methylcyclohexyl succinate (6b₃)

Yield: 70 %, white powder; M.p.: 53 - 55 °C; IR(KBr, cm⁻¹): 3424.5, 2923.8, 2358.7, 1731.5, 1614.7; ¹H NMR (300 MHz, CDCl₃), (δ, ppm): mixture of two isomers 8.12 (s, 1H, H_{Triazole}), 8.03 (s, 1H, H_{Ar}), 7.82 (d, $J = 8.1$ Hz, 1H, H_{Ar}), 7.74 (d, $J = 8.0$ Hz, 1H, H_{Ar}), 7.63 (dd, $J = 8.0$ Hz, 1H, H_{Ar}), 7.13 (d, $J = 8.6$ Hz, 2H, H_{Ar}), 6.75 (d, $J = 8.6$ Hz, 2H, H_{Ar}), 5.54 (br s, 1H, -CH-CN), 5.41 - 5.27 (m, 2H, -O-CH₂-C_{Triazole}), 4.69 (td, $J = 10.8, 4.4$ Hz, 1H, -CH-O-), 4.18 (br s, 1H, -NH), 2.74 - 2.62 (m, 4H, -CO-CH₂-CH₂-CO-), 2.60 (q, $J = 7.6$ Hz, 2H, CH₂), 1.99 - 1.91 (m, 1H, CH), 1.90 - 1.80 (m, 1H, CH), 1.71 - 1.60 (m, 2H, CH₂), 1.49 - 1.40 (m, 1H, CH), 1.39 - 1.32 (m, 1H, CH), 1.22(t, $J = 7.6$ Hz, 3H, CH₃), 1.11-0.91 (m, 3H, CH), 0.89 (d, $J = 7.0$ Hz, 3H, CH₃), 0.88 (d, $J = 6.4$ Hz, 3H, CH₃), 0.74 (d, $J = 6.9$ Hz, 3H, CH₃). ¹³C-NMR (75 MHz, CDCl₃), (δ, ppm): 172.3, 171.8, 143.8, 142.1, 137.5, 136.5, 136.4, 130.7, 128.9, 127.4, 122.0, 121.2,

119.2, 117.8, 114.7, 74.7, 57.7, 50.1, 46.9, 40.8, 34.1, 31.3, 29.3, 29.1, 27.9, 26.2, 23.3, 22.0, 20.7, 16.3, 15.8. MS (ESI): $[M+H]^+$ $C_{33}H_{41}N_5O_4$ calcd 572.72, found 572.75.

(1-(3-(RS(4-Bromophenylamino)(cyano)methyl)phenyl)-1H-1,2,3-triazol-4-yl)methyl(1R,2S,5R)-2-isopropyl-5-methylcyclohexyl succinate (6b₄)

Yield: 70 % , white powder; M.p.: 53 – 55 °C; IR(KBr, cm^{-1}): 3423.7, 2925.3, 1730.8, 1602.5; 1H NMR (300 MHz, $CDCl_3$), (δ , ppm): mixture of two isomers 8.13 (s, 1H, $H_{Triazol}$), 8.03 (s, 1H, H_{Ar}), 7.79 (d, $J = 8.1$ Hz, 1H, H_{Ar}), 7.68 (d, $J = 8.0$ Hz, 1H, H_{Ar}), 7.63 (dd, $J = 7.8$ Hz 1H, H_{Ar}), 7.38 (d, $J = 8.8$ Hz, 2H, H_{Ar}), 6.68 (d, $J = 8.8$ Hz, 2H, H_{Ar}), 5.54 (s, 1H, -CH-CN), 5.40 - 5.26 (m, 2H, -O-CH₂-C_{Triazol}), 4.68 (td, $J = 10.9, 4.4$ Hz, 1H, -CH-O-), 4.52 (br s, 1H, -NH-), 2.73 - 2.58 (m, 4H, -CO-CH₂CH₂CO), 2.00 - 1.91 (m, 1H, CH), 1.88 - 1.79 (m, 1H, CH), 1.73 - 1.59 (m, 2H, CH₂), 1.44 - 1.38 (m, 1H, CH), 1.37 - 1.24 (m, 1H, CH), 1.12 - 0.91 (m, 3H, CH), 0.88 (d, $J = 7.0$ Hz, 3H, CH₃), 0.87 (d, $J = 6.4$ Hz, 3H, CH₃), 0.73 (d, $J = 6.9$ Hz, 3H, CH₃). ^{13}C -NMR (75 MHz, $CDCl_3$), (δ , ppm): 172.3, 171.9, 143.9, 143.3, 137.5, 135.8, 132.4, 130.9, 127.4, 122.1, 121.4, 119.3, 117.3, 116.0, 112.6, 74.8, 57.7, 49.6, 46.9, 40.8, 34.1, 31.3, 29.3, 29.1, 26.2, 23.3, 22.0, 20.7, 16.3 ppm. MS (ESI): $[M+Na]^+$ $C_{31}H_{36}BrN_5O_4$ calcd 645.54 found 645.59.

(1-(3-(RS(4-Cyanobenzylamino)(cyano)methyl)phenyl)-1H-1,2,3-triazol-4-yl)methyl(1R,2S,5R)-2-isopropyl-5-methylcyclohexyl succinate (6b₅)

Yield: 65 % , cream powder; M.p.: 59 – 62 °C; IR(KBr, cm^{-1}): 3432.7, 2926.1, 2368.1, 1734.4, 1610.6; 1H NMR (300 MHz, $CDCl_3$), (δ , ppm): mixture of two isomers 8.13 (s, 1H, $H_{Triazole}$), 8.04 (s, 1H, H_{Ar}), 7.79 (d, $J = 7.9$ Hz, 1H, H_{Ar}), 7.71 (d, $J = 8.0$ Hz, 1H, H_{Ar}), 7.64 (dd, $J = 7.8$ Hz, 1H, H_{Ar}), 7.53 (d, $J = 8.7$ Hz, 2H, H_{Ar}), 6.81 (d, $J = 8.7$ Hz, 2H, H_{Ar}), 5.66 (d, $J = 8.0$ Hz, 1H, -CH-CN), 5.45 - 5.21 (m, 3H, -O-CH₂-C_{Triazole}, -NH-), 4.67 (td, $J = 10.8, 4.4$ Hz, 1H, -CH-O-), 2.73 - 2.56 (m, 4H, -CO-CH₂-CH₂-CO-), 1.97 - 1.89 (m, 1H, CH), 1.87 - 1.80 (m, 1H, CH), 1.71 - 1.61 (m, 2H, CH₂), 1.49 - 1.41 (m, 1H, CH), 1.38 - 1.32 (m, 1H, CH), 1.05 - 0.92 (m, 3H, CH), 0.87 (d, $J = 7.0$ Hz, 3 H, CH₃), 0.86 (d, $J = 6.4$ Hz, 3H, CH₃), 0.72 (d, $J = 6.9$ Hz, 3H, CH₃). ^{13}C -NMR (75 MHz, $CDCl_3$), (δ , ppm): 172.3, 171.9, 147.9, 143.9, 137.5, 135.2, 133.8, 130.9, 127.5, 122.1, 121.4, 119.5, 119.3, 116.9, 113.9, 102.1, 74.8, 57.6, 48.6, 46.8, 40.7, 34.1, 31.3, 29.2, 29.0, 26.2, 23.3, 22.0, 20.7, 16.3. MS (ESI): $[M+H]^+$ $C_{32}H_{36}N_6O_4$ calcd 569.68, found 569.75.

(1-(3-(SR(4-Tolylamino)(cyano)methyl)phenyl)-1H-1,2,3-triazol-4-yl)methyl(1R,2S,5R)-2-isopropyl-5-methylcyclohexyl succinate (6b₆)

Yield: 70 % , white powder; M.p.: 53 – 54 °C; IR(KBr, cm^{-1}): 3440.8, 2923.2, 1730.0, 1619.1; 1H NMR (300 MHz, $CDCl_3$), (δ , ppm): mixture of two isomers 8.13 (s, 1H, $H_{Triazole}$), 8.03 (s, 1H, H_{Ar}), 7.82 (d, $J = 7.9$ Hz, 1H, H_{Ar}), 7.73 (d, $J = 8.1$ Hz, 1H, H_{Ar}), 7.63 (dd, $J = 8.0$ Hz, 1H, H_{Ar}), 7.10 (d, $J = 8.3$ Hz, 2H, H_{Ar}),

6.72 (d, $J = 8.3$ Hz, 2H, H_{Ar}), 5.53 (br s, 1H, -CH-CN), 5.38-5.31 (m, 2H, -O-CH₂-C_{Triazole}), 4.68 (td, $J = 10.8, 4.3$ Hz, 1H, -CH-O-), 4.17 (br s, 1H, -NH-), 2.71 - 2.62 (m, 4H, -CO-CH₂CH₂-CO-), 2.29 (s, 3H, CH₃), 2.25 - 2.16 (m, 1H, CH), 1.98 - 1.80 (m, 1H, CH), 1.71 - 1.65 (m, 2H, CH₂), 1.49 - 1.40 (m, 1H, CH), 1.39 - 1.32 (m, 1H, CH), 1.14 - 0.92 (m, 3H, CH), 0.90 - 0.86 (m, 6H, 2CH₃), **0.74** (d, $J = 6.9$ Hz, 3H, CH₃). ¹³C-NMR (75 MHz, CDCl₃), (δ , ppm): 172.3, 171.8, 143.9, 141.9, 137.6, 136.4, 130.8, 130.2, 130.1, 127.5, 122.1, 121.3, 119.3, 117.8, 114.8, 74.7, 57.8, 50.2, 46.9, 40.8, 34.2, 31.4, 29.3, 29.1, 26.2, 23.4, 22.0, 20.8, 20.5, 16.3 ppm. MS (ESI): [M+H]⁺ C₃₂H₃₉N₅O₄ calcd 558.70, found 558.72.

(1-(3-(RS(4-Fluorophenylamino)(cyano)methyl)phenyl)-1H-1,2,3-triazol-4-yl)methyl(1R,2S,5R)-2-isopropyl-5-methylcyclohexyl succinate (6b7)

Yield: 70 %, yellow oil; IR (KBr, cm⁻¹): 3348.4, 2952.4, 1729.9, 1510.9, 1223.5, 1159.2; ¹H NMR (300 MHz, CDCl₃), (δ , ppm): mixture of two isomers 8.13 (s, 1H, $H_{Triazole}$), 8.04 (s, 1H, H_{Ar}), 7.81 (d, $J = 8.2$ Hz, 1H, H_{Ar}), 7.73 (d, $J = 8.1$ Hz, 1H, H_{Ar}), 7.63 (dd, $J = 7.9$ Hz, 1H, H_{Ar}), 7.05 - 6.92 (m, 2H, H_{Ar}), 6.81 - 6.69 (m, 2H, H_{Ar}), 5.50 (s, 1H, -CH-CN), 5.40 - 5.25 (m, 2H, -O-CH₂-C_{Triazole}), 4.68 (td, $J = 10.8, 4.3$ Hz, 1H, -CH-O-), 2.78 - 2.48 (m, 4H, -CO-CH₂-CH₂-CO-), 2.00 - 1.91 (m, 1H, CH), 1.89 - 1.79 (m, 1H, CH), 1.72 - 1.63 (m, 2H, CH₂), 1.48 - 1.39 (m, 1H, CH), 1.37 - 1.28 (m, 1H, CH), 1.08 - 0.91 (m, 3H, CH), 0.88 (d, $J = 7.0$ Hz, 3H), 0.87 (d, $J = 6.4$ Hz, 3H, CH₃), 0.73 (d, $J = 6.9$ Hz, 3H, CH₃). ¹³C-NMR (75 MHz, CDCl₃), (δ , ppm): 172.4, 171.9, 157.4 (d, $J = 237$ Hz), 143.8, 140.6, 137.4, 136.1, 130.7, 127.5, 122.1, 121.2, 119.2, 117.7, 116.2, 116.0, 74.7, 57.7, 50.4, 46.8, 40.7, 34.1, 31.3, 29.3, 29.0, 26.20, 23.3, 21.9, 20.7, 16.2 ppm. MS (ESI): [M+Na]⁺ C₃₁H₃₆FN₅O₄ calcd 584.64, found 584.68.

(1-(4-(RS(4-Fluoro-3-nitrophenylamino)(cyano)methyl)phenyl)-1H-1,2,3-triazol-4-yl)methyl(1R,2S,5R)-2-isopropyl-5-methylcyclohexyl succinate (6c1)

Yield: 63 %, white powder; M.p.: 114 - 116 °C; IR (KBr, cm⁻¹): 3445.7, 2924.6, 2358.6, 1733.9, 1627.7; ¹H NMR (300 MHz, CDCl₃), (δ , ppm): mixture of two isomers 8.14 (s, 1H, $H_{Triazole}$), 7.82 (d, $J = 8.7$ Hz, 2H, H_{Ar}), 7.75 (d, $J = 8.7$ Hz, 2H, H_{Ar}), 7.55 - 7.42 (m, 1H, H_{Ar}), 7.25 - 7.16 (m, 1H, H_{Ar}), 7.09 - 7.01 (m, 1H, H_{Ar}), 5.61 (d, $J = 8.6$ Hz, 1H, -CH-CN), 5.38 - 5.24 (m, 2H, -O-CH₂-C_{Triazole}), 5.00 (d, $J = 8.6$ Hz, 1H, NH), 4.68 (td, $J = 10.9, 4.3$ Hz, 1H, -CH-O-), 2.76 - 2.55 (m, 4H, -CO-CH₂CH₂-CO-), 2.00 - 1.90 (m, 1H, CH), 1.88 - 1.78 (m, 1H, CH), 1.70 - 1.61 (m, 2H, CH₂), 1.46 - 1.38 (m, 1H, CH), 1.37 - 1.29 (m, 1H, CH), 1.14 - 0.90 (m, 3H, CH), 0.89 (d, $J = 7.0$ Hz, 3H, CH₃), 0.87 (d, $J = 6.4$ Hz, 3H, CH₃), 0.74 (d, $J = 6.9$ Hz, 3H, CH₃). ¹³C-NMR (75 MHz, CDCl₃), (δ , ppm): 172.4, 171.9, 149.6 (d, $J = 256.5$ Hz), 144.0, 141.2, 137.6, 137.3, 133.5, 128.8, 122.1, 121.1, 119.6, 119.3, 117.0, 110.4, 74.8, 57.7, 49.5, 46.9, 40.8, 34.1, 31.4, 29.1, 29.0, 26.2, 23.3, 21.9, 20.7, 16.3. MS (ESI): [M+H]⁺ C₃₁H₃₅FN₆O₆ calcd 607.66, found 607.69.

(1-(4-(RS(3,4-Dichlorophenylamino)(cyano)methyl)phenyl)-1H-1,2,3-triazol-4-yl)methyl(1R,2S,5R)-2-isopropyl-5-methylcyclohexyl succinate (**6c₂**):

Yield: 72 % , cream powder; M.p.: 100 – 102 °C; IR (KBr, cm⁻¹): 3434.11, 2927.53, 2366.45, 1730.02, 1602.00; ¹H NMR (300 MHz, CDCl₃), (δ, ppm): mixture of two isomers 8.13 (s, 1H, H_{Triazole}), 7.85 (d, *J* = 8.7 Hz, 2H, H_{Ar}), 7.76 (d, *J* = 8.7 Hz, 2H, H_{Ar}), 7.32 (d, *J* = 8.7 Hz, 1H, H_{Ar}), 6.91 (d, *J* = 2.7 Hz, 1H, H_{Ar}), 6.65 (dd, *J* = 8.7, 2.7 Hz, 1H, H_{Ar}), 5.53 (d, *J* = 8.7 Hz, 1H, -CH-CN), 5.38 - 5.28 (m, 2H, -O-CH₂-C_{Triazole}), 4.68 (td, *J* = 10.8, 4.4 Hz, 1H, -CH-O-), 4.5 (d, *J* = 8.7 Hz, 1H, NH), 2.71 - 2.61 (m, 4H, -CO-CH₂CH₂-CO), 1.98 - 1.91 (m, 1H, CH), 1.89 - 1.80 (m, 1H, CH), 1.72 - 1.63 (m, 2H, CH₂), 1.46 - 1.38 (m, 1H, CH), 1.38 - 1.30 (m, 1H, CH), 1.16 - 0.90 (m, 3H, CH), 0.89 (d, *J* = 7.0 Hz, 3H, CH₃), 0.88 (d, *J* = 6.4 Hz, 3H, CH₃), 0.74 (d, *J* = 6.9 Hz, 3H, CH₃). ¹³C-NMR (75 MHz, CDCl₃), (δ, ppm): 172.3, 171.9, 144.1, 143.9, 137.5, 133.9, 133.1, 130.9, 128.7, 123.1, 121.9, 121.0, 117.3, 115.9, 113.8, 74.8, 57.7, 49.2, 46.9, 40.8, 34.1, 31.8, 29.3, 29.10, 26.2, 23.4, 22.0, 20.7, 16.3. MS (ESI): [M+H]⁺ C₃₁H₃₅Cl₂N₅O₄ calcd 612.55, found 612.58.

(1-(4-(RS(4-Ethylphenylamino)(cyano)methyl)phenyl)-1H-1,2,3-triazol-4-yl)methyl(1R,2S,5R)-2-isopropyl-5-methylcyclohexyl succinate (**6c₃**)

Yield: 70 % , white powder; M.p.: 101 – 102 °C; IR(KBr, cm⁻¹): 3437.1, 2924.9, 2359.1, 1733.5, 1618.3; ¹H NMR (300 MHz, CDCl₃), (δ, ppm): mixture of two isomers 8.13 (s, 1H, H_{Triazole}), 7.85 (d, *J* = 8.9 Hz, 2H, H_{Ar}), 7.78 (d, *J* = 8.9 Hz, 2H, H_{Ar}), 7.12 (d, *J* = 8.9 Hz, 2H, H_{Ar}), 6.74 (d, *J* = 8.9 Hz, H_{Ar}), 5.53 (d, *J* = 8.9 Hz, 1H, -CH-CN), 5.40 - 5.26 (m, 2H, -O-CH₂-C_{Triazole}), 4.68 (td, *J* = 10.9, 4.3 Hz, 1H, -CH-O-), 4.22 (d, *J* = 8.8 Hz, 1H, NH), 2.72 - 2.64 (m, 4H, -CO-CH₂-CH₂-CO-), 2.59 (q, *J* = 7.7 Hz, 2H, CH₂), 1.97 - 1.90 (m, 1H, CH), 1.88 - 1.80 (m, 1H, CH), 1.71 - 1.63 (m, 2H, CH₂), 1.48 - 1.34 (m, 1H, CH), 1.35 - 1.20 (m, 1H, CH), 1.20 (t, *J* = 7.6 Hz, 3H, CH₃), 1.12 - 0.90 (m, 3H, CH), 0.9 (d, *J* = 6.9 Hz, 3H, CH₃), 0.87 (d, *J* = 6.4 Hz, 3H, CH₃), 0.74 (d, *J* = 6.8 Hz, 3H, CH₃). ¹³C-NMR (75 MHz, CDCl₃), (δ, ppm): 172.3, 171.9, 143.9, 142.2, 137.4, 136.5, 134.9, 128.9, 128.7, 121.9, 120.9, 117.9, 114.7, 74.8, 57.8, 49.9, 46.9, 40.8, 34.1, 29.3, 29.1, 28.0, 26.2, 23.4, 22.02, 20.7, 16.3, 15.8. MS (ESI): [M+Na]⁺ C₃₃H₄₁N₅O₄ calcd 594.70, found 594.71.

(1-(4-(RS(4-Bromophenylamino)(cyano)methyl)phenyl)-1H-1,2,3-triazol-4-yl)methyl(1R,2S,5R)-2-isopropyl-5-methylcyclohexyl succinate (**6c₄**)

Yield: 68 % , white powder; M.p.: 109 – 111 °C; IR (KBr, cm⁻¹): 3437.10, 2924.58, 2358.34, 1734.01, 1636.93; ¹H NMR (300 MHz, CDCl₃), (δ, ppm): mixture of two isomers 8.13 (s, 1H, H_{Triazole}), 7.85 (d, *J* = 8.8 Hz, 2H, H_{Ar}), 7.76 (d, *J* = 8.8 Hz, 2H, H_{Ar}), 7.37 (d, *J* = 8.8 Hz, 2H, H_{Ar}), 6.69 (d, *J* = 8.8 Hz, H_{Ar}), 5.53 (d, *J* = 8.7 Hz, 1H, -CH-CN), 5.40 - 5.28 (m, 2H, -O-CH₂-C_{Triazole}), 4.68 (td, *J* = 10.9, 4.4 Hz, 1H, -CH-O-), 4.44 (d, *J* = 8.7 Hz, 1H, NH), 2.73 - 2.59 (m, 4H, -CO-CH₂CH₂-CO-), 2.00 - 1.90 (m, 1H, CH), 1.89 - 1.79 (m, 1H, CH), 1.72 - 1.62

(m, 2H, CH₂), 1.47 - 1.36 (m, 1H, CH), 1.35 - 1.21 (m, 1H, CH), 1.12 - 0.90 (m, 3H, CH), 0.9 (d, *J* = 6.9 Hz, 3H, CH₃), 0.87 (d, *J* = 6.4 Hz, 3H, CH₃), 0.74 (d, *J* = 6.9 Hz, 3H, CH₃). ¹³C-NMR (75 MHz, CDCl₃), (δ, ppm): 172.3, 171.9, 143.9, 143.33, 137.5, 134.1, 132.4, 128.7, 121.9, 121.1, 117.4, 116.1, 112.6, 74.8, 57.8, 49.5, 46.9, 40.8, 34.1, 31.4, 29.3, 29.1, 26.2, 23.4, 22.0, 20.7, 16.3. MS (ESI): [M+H]⁺ C₃₁H₃₆BrN₅O₄ calcd 623.56, found 623.57.

(1-(4-(RS(4-Cyanobenzylamino)(cyano)methyl)phenyl)-1H-1,2,3-triazol-4-yl)methyl(1R,2S,5R)-2-isopropyl-5-methylcyclohexyl succinate (6c_s)

Yield: 70 % , cream powder; M.p.: 110 – 112 °C; IR(KBr, cm⁻¹): 3436.34, 2924.18, 2362.89, 1733.88, 1611.49; ¹H NMR (300 MHz, CDCl₃), (δ, ppm): mixture of two isomers 8.13 (s, 1H, H_{Triazole}), 7.86 (d, *J* = 8.7 Hz, 2H, H_{Ar}), 7.76 (d, *J* = 8.7 Hz, 2H, H_{Ar}), 7.54 (d, *J* = 8.7 Hz, 2H, H_{Ar}), 6.82 (d, *J* = 8.7 Hz, 2H, H_{Ar}), 5.63 (d, *J* = 8.0 Hz, 1H, -CH-CN), 5.42 - 5.23 (m, 3H, -O-CH₂-C_{Triazole}, -NH-), 4.68 (td, *J* = 10.9, 4.4 Hz, 1H, -CH-O-), 2.74 - 2.75 (m, 4H, -CO-CH₂CH₂-CO-), 2.01 - 1.89 (m, 1H, CH), 1.89 - 1.78 (m, 1H, CH), 1.72 - 1.59 (m, 2H, CH₂), 1.47 - 1.39 (m, 1H, CH), 1.39 - 1.29 (m, 1H, CH), 1.11 - 0.90 (m, 3H, CH), 0.87 (d, *J* = 6.9 Hz, 3H, CH₃), 0.86 (d, *J* = 6.4 Hz, 3H, CH₃), 7.3 (d, *J* = 6.9 Hz, 3H, CH₃). ¹³C-NMR (75 MHz, CDCl₃), (δ, ppm): 172.4, 171.9, 147.9, 144.0, 137.7, 133.9, 133.5, 128.8, 121.9, 121.1, 119.5, 116.9, 113.9, 102.3, 74.8, 57.7, 48.5, 46.9, 40.8, 34.1, 31.4, 29.3, 29.1, 26.2, 23.4, 22.0, 20.7, 16.3. MS (ESI): [M+H]⁺ C₃₂H₃₆N₆O₄ calcd 569.68, found 569.71.

(1-(2-Formylphenyl)-1H-1,2,3-triazol-4-yl)methyl(1R,2S,5R)-2-isopropyl-methylcyclohexyl succinate (5a)

Yield: 90 % , white powder, M.P: 76 - 78 °C. IR (KBr, cm⁻¹): 2927.30, 1730.91, 1601.86, 1158.25, ¹H NMR (300 MHz, CDCl₃), (δ, ppm): 9.94 (s, 1H, -CHO-), 8.14 (dd, *J* = 7.8 Hz, 1.3 Hz, 1H, H_{Ar}), 8.06 (s, 1H, H_{Triazole}), 7.79 - 7.65 (td, *J* = 7.6, 1.3 Hz, 1H, H_{Ar}), 7.70 (t, *J* = 7.4 Hz, 1H, H_{Ar}), 7.55 (d, *J* = 7.8 Hz, 1H, H_{Ar}), 5.41-5.32 (m, 2H, -O-CH₂-C_{Triazole}), 4.72 - 4.60 (m, 1H, -CH-O-), 2.71 - 2.60 (m, 4H, -CO-CH₂-CH₂-CO-), 1.97 - 1.90 (m, 1H, CH), 1.89 - 1.82 (m, 1H, CH), 1.71 - 1.62 (m, 2H, CH₂), 1.47 - 1.36 (m, 1H, CH), 1.39 - 1.29 (m, 1H, CH), 1.05 - 0.93 (m, 3H, CH), 0.87 (d, *J* = 7.0 Hz, 3H, CH₃), 0.86 (d, *J* = 6.6 Hz, 3H, CH₃), 0.73 (d, *J* = 6.9 Hz, 3H, CH₃) ppm. ¹³C-NMR (75 MHz, CDCl₃), (δ, ppm): 188.28, 172.19, 171.66, 143.71, 138.08, 134.57, 130.38, 130.10, 129.52, 125.75, 125.35, 74.67, 57.69, 46.94, 40.81, 34.17, 31.34, 29.33, 29.12, 26.26, 23.45, 21.94, 20.66, 16.31. MS (ESI): [M+H]⁺ C₂₄H₃₁N₃O₅ calcd 442.53, found 442.63.

(1-(3-Formylphenyl)-1H-1,2,3-triazol-4-yl)methyl(1R,2S,5R)-2-isopropyl-5-methylcyclohexyl succinate (5b)

Yield: 80 % , yellow oil, IR (KBr, cm⁻¹): 2951.69, 1732.41, 1228.82, 1157.42, ¹H NMR (300 MHz, CDCl₃), (δ, ppm): 10.10 (s, 1H, -CHO-), 8.27 - 8.23 (m, 1H, H_{Ar}), 8.21 (s, 1H, H_{Triazole}), 8.13 - 8.05 (m, 1H, H_{Ar}), 8.01 - 7.92 (m, 1H, H_{Ar}), 7.74 (t, *J* = 7.8 Hz, 1H, H_{Ar}), 5.40 - 5.31 (m, 2H, -O-CH₂-C_{Triazole}), 4.68

(td, $J = 10.9, 4.4$ Hz, 1H, -CH-O-), 2.72 - 2.61(m, 4H, -CO-CH₂-CH₂-CO), 1.96 - 1.92 (m, 1H, CH), 1.86 - 1.82 (m, 1H, CH), 1.69 - 1.62 (m, 2H, CH₂), 1.47 - 1.39 (m, 1H, CH), 1.38 - 1.30 (m, 1H, CH), 1.08 - 0.93(m, 3H, CH), 0.87 (d, $J = 7.0$ Hz, 3H, CH₃), 0.86 (d, $J = 6.6$ Hz, 3H, CH₃), 0.73 (d, $J = 6.9$ Hz, 3H, CH₃) ppm. ¹³C-NMR (75 MHz, CDCl₃), (δ , ppm): 190.79, 172.25, 171.79, 144.07, 137.72, 137.52, 130.71, 129.97, 125.77, 121.96, 120.33, 74.64, 57.74, 46.85, 40.75, 34.10, 31.29, 29.29, 29.07, 26.17, 23.32, 21.94, 20.68, 16.25. MS (ESI): [M+H]⁺ C₂₄H₃₁N₃O₅ calcd 442.53, found 422.58.

(1-(4-Formylphenyl)-1H-1,2,3-triazol-4-yl)methyl(1R,2S,5R)-2-isopropyl-5-methylcyclohexyl succinate (5c)

Yield: 75 %, white powder, M.P: 80 - 81 °C. IR (KBr, cm⁻¹): 2924.08, 1735.64, 1628.80, 1159.27, 1H NMR (300 MHz, CDCl₃), (δ , ppm): 10.03 (s, 1H, -CHO-), 8.21 (s, 1H, HTriazole), 8.02 (d, $J = 8.6$ Hz, 2H, HAr), 7.95 (d, $J = 8.6$ Hz, 2H, HAr), 5.36 - 5.25 (m, 2H, -O-CH₂-CTriazole), 4.62 (td, $J = 10.8, 4.3$ Hz, 1H, -CH-O-), 2.67 - 2.57 (m, 4H, -CO-CH₂-CH₂-CO), 1.93 - 1.84 (m, 1H, CH), 1.83 - 1.74 (m, 1H, CH), 1.65 - 1.56 (m, 2H, CH₂), 1.44 - 1.34 (m, 1H, CH), 1.35 - 1.24 (m, 1H, CH), 1.03 - 0.86 (m, 3H, CH), 0.83 (d, $J = 7.0$ Hz, 3H, CH₃), 0.81 (d, $J = 6.4$ Hz, 3H, CH₃), 0.68 (d, $J = 6.9$ Hz, 3H, CH₃) ppm. ¹³C-NMR (75 MHz, CDCl₃), (δ , ppm): 190.70, 172.28, 171.82, 144.25, 140.80, 136.01, 131.34, 121.90, 120.45, 74.70, 57.74, 46.87, 40.78, 34.11, 31.35, 29.30, 29.09, 26.20, 23.36, 21.97, 20.70, 16.27. MS (ESI): [M+H]⁺ C₂₄H₃₁N₃O₅ calcd 442.53, found 442.60.

(1R,2S,5R)-2-Isopropyl-5-methylcyclohexyl prop-2-yl succinate (3)

Yield: 80 %, brown liquid, IR (KBr, cm⁻¹): 3289, 2952, 1738, 1375, 1157, 995, 672. 1H NMR (300 MHz, CDCl₃), (δ , ppm): 4.78 - 4.62 (m, 3H, -CH-O- and C Acetylene -CH₂), 2.75 - 2.59 (m, 4H, -CO-CH₂-CH₂-CO-), 2.49 (t, $J = 2.5$ Hz, 1H, H Acetylene), 2.02 - 1.93 (m, 1H, CH), 1.93 - 1.78 (m, 1H, CH), 1.75 - 1.58 (m, 2H, CH₂), 1.54 - 1.41 (m, 1H, CH), 1.40 - 1.25 (m, 1H, CH), 1.19 - 0.92 (m, 3H, CH₂), 0.90 (d, $J = 6.9$ Hz, 3H, CH₃), 0.89 (d, $J = 7.1$ Hz, 3H, CH₃), 0.75 (d, $J = 6.9$ Hz, 3H, CH₃) ppm. ¹³C-NMR (75 MHz, CDCl₃), (δ , ppm): 171.52, 171.49, 75.00, 74.63, 52.14, 46.93, 40.79, 34.19, 31.35, 29.26, 28.98, 26.19, 23.37, 22.00, 20.75, 16.27. MS (ESI): [M+Na]⁺ C₁₇H₂₆O₄ calcd 317.37, found 317.37.