

Synthesis of potential anti-*Trypanosoma cruzi* azole-naftifine analogues by azide–alkyne click reaction

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1. Equipment

The ^1H and ^{13}C nuclear magnetic resonance (NMR) spectra were recorded on a Bruker Avance DPX 200 spectrometer at 200 MHz. Mass spectra were recorded on a Shimadzu GC MS-QP5050A instrument using direct insertion along with the electrospray ionization method and a quadrupole analyzer. The IR spectra were obtained by the ATR spectrophotometer model Prestige-21, Shimadzu. Melting points were determined using an MQAPF-301 melting point apparatus (Microquimica, Brazil) and are uncorrected.

2. Synthesis of benzyl methanesulfonates

In a 10 ml round bottom flask, the corresponding alcohol **1** (1 mmol) was suspended in dichloromethane (5 ml), and triethylamine (2.0 mmol) was added. The mixture was cooled to $-50\text{ }^\circ\text{C}$ (using ethyl acetate bath). Methanesulfonyl chloride (1.4 mmol) was added to the flask at a rate of 21 μmol per minute using syringe pump on vigorous stirring. The reaction was complete after 30 min. The organic layer was washed with water (15 ml), 1% aqueous HCl (15 ml) followed by saturated aqueous NaHCO_3 (5 ml), dried over Na_2SO_4 , and concentrated under reduced pressure.

3. Synthesis of derivatives of organic azides **2a-j**

In a 50 ml round bottom flask, mesylate (1.25 mmol) from the previous step was suspended in DMSO (7 ml). Sodium azide (2.5 mmol, 0.5 ml of 0.5 M solution in DMSO) was added. The mixture was stirred at room temperature for 15 h. After this time, water (15 ml) was added, and the mixture was extracted with ethyl acetate (3 x 20 ml). The organic phases were combined, dried over sodium sulfate and the solvent was removed under reduced pressure. The crude material was purified by column chromatography using as eluent 4: 1 hexane: AcOEt to afford compounds **2a-j** in 70–99% yields.

4. Synthesis of propargylamines 3a,b

In a 50 ml flask, acetonitrile (10 ml) and KOH (0.6 mmol) were heated to 80 °C on stirring until a clear solution formed. Thereafter, *N*-methyl-*N*-(1-naphthylmethyl)amine hydrochloride or *N*-methyl-*N*-(9-anthracenylmethyl)amine (0.3 mmol) was added followed by the addition of propargyl bromide (0.4 mmol). After 3 h, water (10 ml) was added followed by extraction with ethyl acetate (3 x 15 ml). The organic phases were combined, dried over sodium sulfate and the solvent was removed. The crude material was purified by silica gel column chromatography, affording the desired propargylamines **3a,b**.

N-methyl-*N*-(1-naphthylmethyl)-*N*-propargylamine **3a**. Yield 85%. IR (KBr): $\nu = 3294, 2940, 2838, 2366, 1510, 1124, 1026, 798$ and 648 cm^{-1} . $^1\text{H NMR}$ (CDCl_3 , 200 MHz) $\delta = 8.23\text{-}8.27$ (m, 1H), $7.70\text{-}7.80$ (m, 2H), $7.30\text{-}7.51$ (m, 4H), 3.29 (d, $J = 2.0 \text{ Hz}$, 2H), 2.34 (s, 3H), 2.27 (t, $J = 2.0 \text{ Hz}$, 1H). $^{13}\text{C NMR}$ (CDCl_3 , 50 MHz) $\delta = 134.1, 133.8, 132.5, 128.3, 128.1, 127.5, 125.8, 125.6, 125.0, 124.6, 78.5, 73.6, 57.9, 44.8, 41.8$. 9l: Yield 89%. IR (KBr): $\nu = 3300, 3100, 2900, 2850, 2350$ and 1480 cm^{-1} . $^1\text{H NMR}$ (CDCl_3 , 200 MHz) $\delta = 8.44\text{-}8.56$ (m, 3H), $8.00\text{-}8.05$ (m, 2H), $7.44\text{-}7.59$ (m, 4H), 4.58 (s, 2H), 3.47 (d, $J = 2.0 \text{ Hz}$, 2H), 2.47 (s, 4H). $^{13}\text{C NMR}$ (CDCl_3 , 50 MHz) $\delta = 126.6, 124.9, 124.1, 122.8, 120.9, 120.0, 74.5, 68.8, 46.5, 40.4, 36.7$.

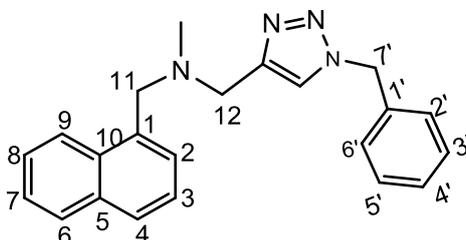
5. Synthesis ofazole-nafitifine analogues 4 by azide-alkyne click reaction

The appropriate azide **2** (2.0 mmol) was added into a 5 ml round bottom flask containing dichloromethane (1 ml), water (1 ml), of $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ (0.4 mmol), sodium ascorbate (0.8 mmol) and propargylic amine **3** (2.0 mmol). The mixture was stirred at room temperature (25 °C) for 5 h and then was extracted with CH_2Cl_2 (3x15 ml). The organic layer was washed with a mixture in the ratio of 1: 1 of solution 50% w/v EDTA and concentrated NH_4OH . The material obtained after solvent removal was purified by silica gel column chromatography eluting with ethyl acetate to give compounds **4a-t** in 55-98% yields.

5. Characterization of azole-nafitifine analogues

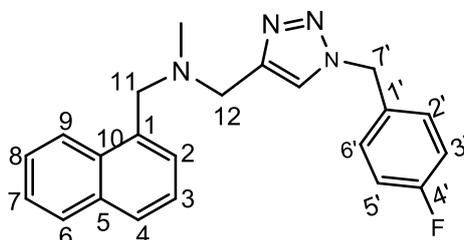
5.1 Analogues derived from naphthalene 4a-j

N-[(1-Benzyl-1*H*-1,2,3-triazol-4-yl)methyl]-*N*-methyl-*N*-(1-naphthylmethyl)amine 4a



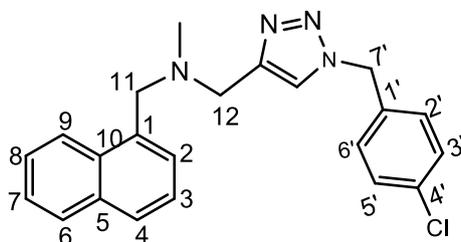
Yield: 90%. Yellow oil, $^1\text{H NMR}$ (200 MHz, CDCl_3 , δH (ppm), multiplicity, integration, J (Hz), attribution): 8.03 (d, 1H, $J = 6.0$ Hz, H9), 7.61-7.22 (m, 2H, H4 e H6), 7.11-7.34 (m, 10H, $\text{H}_{\text{triazole}}$, H2, H3, H7, H8, H2', H3', H4', H5', H6'), 5.35 (s, 2H, H7'), 3.83 (s, 2H, H11), 3.67 (s, 2H, H12), 2.13 (s, 3H, CH_3). $^{13}\text{C NMR}$ (50 MHz, CDCl_3): δC (ppm): 42.4 (CH_3), 52.5 (C12), 54.1 (C7'), 59.8 (C11), 122.7 ($\text{CH}_{\text{triazole}}$), 145.8 ($\text{C}_{\text{triazole}}$), 124.6, 125.2, 125.6, 125.9, 127.7, 128.0, 128.1, 128.5, 128.7, 129.1 ($\text{CH}_{\text{aromatic}}$), 132.5, 133.9, 134.4, 134.9 ($\text{C}_{\text{aromatic}}$). **HRMS (ESI):** m/z calculated – $[\text{M} + \text{H}]^+$: 343.1917; Found: 343.1907, Error: 3 ppm

N-{[1-(4-Fluorobenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}-*N*-methyl-*N*-(1-naphthylmethyl)amine 4b



Yield: 94%. Yellow oil, $^1\text{H NMR}$ (200 MHz, CDCl_3 , δH (ppm), multiplicity, integration, J (Hz), attribution): 8.17 (d, 1H, $J = 8.0$ Hz, H9), 7.75-7.82 (m, 2H, H4 e H6), 7.19-7.47 (m, 7H, $\text{H}_{\text{triazole}}$, H2, H3, H7, H8, H2', H6'), 7.03 (t, 2H, $J = 8.0$ Hz, H3' e H5'), 5.44 (s, 2H, H7'), 3.96 (s, 2H, H11), 3.80 (s, 2H, H12), 2.28 (s, 3H, CH_3). $^{13}\text{C NMR}$ (50 MHz, CDCl_3): δC (ppm): 42.5 (CH_3), 52.5 (C12), 53.3 (C7'), 59.9 (C11), 122.6 ($\text{CH}_{\text{triazole}}$), 146.0 ($\text{C}_{\text{triazole}}$), 116.1 ($^2J_{\text{CF}} = 22.0$ Hz, C3'/C5'), 162.8 ($^1J_{\text{CF}} = 246.5$ Hz, C4'), 129.9 ($^3J_{\text{CF}} = 8.5$ Hz, C2'/C6'), 124.6, 125.2, 125.6, 125.8, 127.6, 128.1, 128.5, ($\text{CH}_{\text{aromatic}}$), 130.8, 132.5, 133.9, 134.5, ($\text{C}_{\text{aromatic}}$); **HRMS (ESI):** m/z calculated – $[\text{M} + \text{H}]^+$: 361.1823; Found: 361.1780; Error: 12 ppm

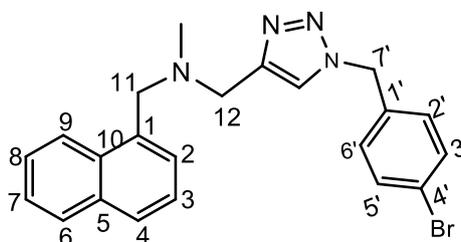
N-{[1-(4-Chlorobenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}-*N*-methyl-*N*-(1-naphthylmethyl)amine 4c



Yield: 94%. Yellow oil, $^1\text{H NMR}$ (200 MHz, CDCl_3 , δH (ppm), multiplicity, integration, J (Hz), attribution): 8.13 (d, 1H, $J = 8.0$ Hz, H9), 7.73-7.84 (m, 2H, H4 e H6), 7.14-7.49 (m, 7H, $\text{H}_{\text{triazole}}$, H2, H3, H7, H8, H2', H6'), 7.13 (d, 2H, $J = 8.0$ Hz, H3' e H5'), 5.44 (s, 2H, H7'), 3.94 (s, 2H, H11), 3.77 (s, 2H, H12), 2.26 (s, 3H, CH_3).

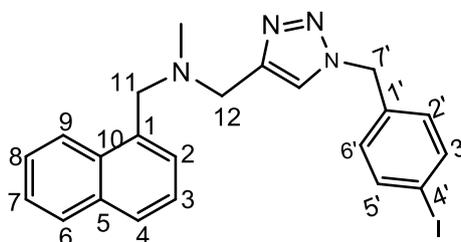
$^{13}\text{C NMR}$ (50 MHz, CDCl_3): δC (ppm): 42.5 (CH_3), 52.5 (C12), 53.3 (C7'), 59.8 (C11), 122.6 ($\text{CH}_{\text{triazole}}$), 146.1 ($\text{C}_{\text{triazole}}$), 124.6, 125.2, 125.7, 125.9, 127.7, 128.1, 128.5, 129.3, 129.4 ($\text{CH}_{\text{aromatic}}$), 132.5, 133.4, 133.9, 134.4, 134.7 ($\text{C}_{\text{aromatic}}$). **HRMS (ESI):** m/z calculated – $[\text{M} + \text{H}]^+$: 377.1528; Found: 377.1492; Error: 9 ppm.

***N*-{[1-(4-Bromobenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}-*N*-methyl-*N*-(1-naphthylmethyl)amine 4d**



Yield: 68%. Yellow solid, **M.p:** 74.0 – 75.5 °C, $^1\text{H NMR}$ (200 MHz, CDCl_3 , δH (ppm), multiplicity, integration, J (Hz), attribution): 8.16 (d, 1H, $J = 6.0$ Hz, H9), 7.76-7.87 (m, 2H, H4 e H6), 7.27-7.51 (m, 7H, $\text{H}_{\text{triazole}}$, H2, H3, H7, H8, H2', H6'), 7.12 (d, 2H, $J = 8.0$ Hz, H3' e H5'), 5.45 (s, 2H, H7'), 3.96 (s, 2H, H11), 3.80 (s, 2H, H12), 2.13 (s, 3H, CH_3). $^{13}\text{C NMR}$ (50 MHz, CDCl_3): δC (ppm): 42.3 (CH_3), 52.4 (C12), 53.3 (C7'), 59.7 (C11), 122.5 ($\text{CH}_{\text{triazole}}$), 145.9 ($\text{C}_{\text{triazole}}$), 124.4, 125.1, 125.5, 125.7, 127.5, 128.0, 128.4, 129.5, 132.2 ($\text{CH}_{\text{aromatic}}$), 122.7, 132.3, 133.8, 134.2 ($\text{C}_{\text{aromatic}}$). **HRMS (ESI):** m/z calculated – $[\text{M} + \text{H}]^+$: 421.1022; Found: 421.1019, Error: 0.7 ppm

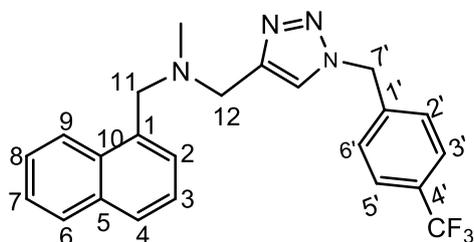
***N*-{[1-(4-Iodobenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}-*N*-methyl-*N*-(1-naphthylmethyl)amine 4e**



Yield: 93%. Yellow solid **M.p:** 102.3 – 103.4 °C $^1\text{H NMR}$ (200 MHz, CDCl_3 , δH (ppm), multiplicity, integration, J (Hz), attribution): 8.12 (d, 1H, $J = 8.0$ Hz, H9), 7.63-7.83 (m, 2H, H4 e H6), 7.30-7.41 (m, 5H, $\text{H}_{\text{triazole}}$, H2, H3, H7, H8), 7.63-7.83 (m, 4H, H4, H6, H2', H6'), 6.94 (d, 2H, $J = 8.0$ Hz, H3' e H5'), 5.38 (s, 2H, H7'), 3.93 (s, 2H, H11), 3.76 (s, 2H, H12), 2.25 (s, 3H, CH_3). $^{13}\text{C NMR}$ (50 MHz, CDCl_3): δC (ppm): 42.5 (CH_3), 52.5 (C12), 53.6 (C7'), 59.8 (C11), 122.4 ($\text{CH}_{\text{triazole}}$), 146.2 ($\text{C}_{\text{triazole}}$), 124.5,

125.1, 125.6, 125.7, 127.4, 128.0, 128.4, 129.7, 138.2 (CH_{aromatic}), 94.3, 132.5, 133.9, 134.5 (C_{aromatic}). **HRMS (ESI):** *m/z* calculated – [M + H]⁺: 469.0884; Found: 469.0861; Error: 5 ppm.

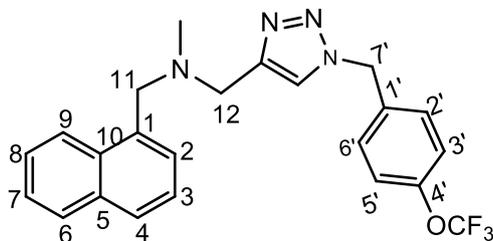
***N*-Methyl-1-(1-naphthylmethyl)-*N*-{[1-(4-trifluoromethylbenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}amine 4f**



Yield: 73%. Yellow solid, **M.p:** 69.5 – 70.1 °C, **¹H NMR** (200 MHz, CDCl₃, δH (ppm), multiplicity, integration, J (Hz), attribution): 8.17 (m, 1H, H₉), 7.75-7.86 (m, 2H, H₄, H₆), 7.30-7.63 (m, 9H, H_{2'}, H_{3'}, H_{5'}, H_{6'}, H₂, H₃, H₇, H₈, H_{triazole}), 5.54 (s, 2H, H_{7'}), 3.98 (s, 2H, H₁₁), 3.81 (s, 2H, H₁₂), 2.29 (s, 3H, CH₃).

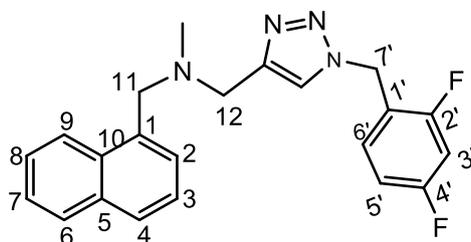
¹³C NMR (50 MHz, CDCl₃): δC (ppm): 42.3 (CH₃), 52.4 (C₁₂), 53.3 (C_{7'}), 59.8 (C₁₁), 122.7 (CH_{triazole}), 146.1 (C_{triazole}), 130.8 (²J_{CF} = 32.5 Hz, C_{4'}), 123.7 (¹J_{CF} = 270.5 Hz, CF₃), 124.4, 125.1, 125.5, 125.7, 126.0, 126.4, 127.5, 128.0, 128.4 (CH_{aromatic}), 125.9, 132.3, 133.8, 138.7 (C_{aromatic}). **HRMS (ESI):** *m/z* calculated – [M + H]⁺: 411.1791, Found: 411.1763, Error: 6 ppm.

***N*-Methyl-1-(1-naphthylmethyl)-*N*-{[1-(4-trifluoromethoxybenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}amine 4g**



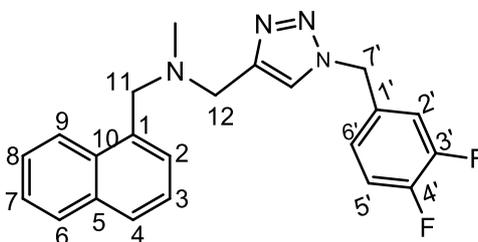
Yield: 88%. Yellow solid, **M.p:** 66.7 – 67.3 °C, **¹H NMR** (200 MHz, CDCl₃, δH (ppm), multiplicity, integration, J (Hz), attribution): 8.17 (d, 1H, J = 8.0 Hz, H₉), 7.76-7.82 (m, 2H, H₄ e H₆), 7.25-7.45 (m, 9H, H_{triazole}, H₂, H₃, H₇, H₈, H_{2'}, H_{3'}, H_{5'}, H_{6'}), 5.49 (s, 2H, H_{7'}), 3.99 (s, 2H, H₁₁), 3.82 (s, 2H, H₁₂), 2.29 (s, 3H, CH₃). **¹³C NMR** (50 MHz, CDCl₃): δC (ppm): 42.6 (CH₃), 52.6 (C₁₂), 53.6 (C_{7'}), 60.0 (C₁₁), 122.7 (CH_{triazole}), 146.3 (C_{triazole}), 121.6, 124.6, 125.3, 125.7, 125.9, 127.7, 128.2, 128.6, 129.6 (CH_{aromatic}), 132.6, 133.7, 134.0, 134.5, 149.5 (C_{aromatic}). **HRMS (ESI):** *m/z* calculated – [M + H]⁺: 427.1740, Found: 427.1745, Error: 1 ppm.

***N*-{[1-(2,4-Difluorobenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}-*N*-methyl-*N*-(1-naphthylmethyl)amine 4h**



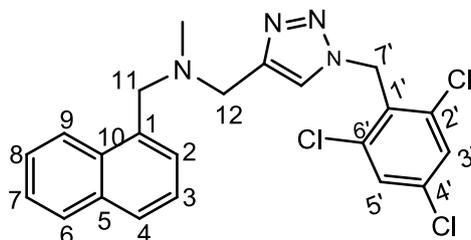
Yield: 85%. Yellow oil, $^1\text{H NMR}$ (200 MHz, CDCl_3 , δH (ppm), multiplicity, integration, J (Hz), attribution): 8.18-8.20 (m, 1H, H9), 7.75-7.86 (m, 2H, H4 e H6), 6.81-7.48 (m, 8H, $\text{H}_{\text{triazole}}$, H2, H3, H7, H8, H3', H5', H6'), 5.49 (s, 2H, H7'), 3.96 (s, 2H, H11), 3.80 (s, 2H, H12), 2.27 (s, 3H, CH_3). $^{13}\text{C NMR}$ (50 MHz, CDCl_3): δC (ppm): 42.3 (CH_3), 52.4 (C12), 46.9 (C7'), 59.8 (C11), 122.6 ($\text{CH}_{\text{triazole}}$), 145.9 ($\text{C}_{\text{triazole}}$), 118.3, 132.3, 133.8, 134.3 ($\text{C}_{\text{aromatic}}$), 104.2, 112.3, 115.7, 124.4, 125.1, 125.5, 125.7, 127.5, 127.9, 128.4, 129.7, 131.5 ($\text{CH}_{\text{aromatic}}$). **HRMS (ESI):** m/z calculated – $[\text{M} + \text{H}]^+$: 379.1729, Found: 379.1704, Error: 7 ppm

***N*-{[1-(3,4-Difluorobenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}-*N*-methyl-*N*-(1-naphthylmethyl)amine 4i**



Yield: 55%. Yellow oil, $^1\text{H NMR}$ (200 MHz, CDCl_3 , δH (ppm), multiplicity, integration, J (Hz), attribution): 8.12-8.17 (m, 1H, H9), 7.76-7.86 (m, 2H, H4 e H6), 6.98-7.48 (m, 8H, $\text{H}_{\text{triazole}}$, H2, H3, H7, H8, H2', H5', H6'), 5.43 (s, 2H, H7'), 4.05 (s, 2H, H11), 3.86 (s, 2H, H12), 2.31 (s, 3H, CH_3). $^{13}\text{C NMR}$ (50 MHz, CDCl_3): δC (ppm): 42.3 (CH_3), 52.2 (C12), 52.8 (C7'), 59.7 (C11), 122.7 ($\text{CH}_{\text{triazole}}$), 145.9 ($\text{C}_{\text{triazole}}$), 116.8, 117.7, 124.1, 124.4, 125.1, 125.5, 125.7, 127.6, 128.0, 128.4 ($\text{CH}_{\text{aromatic}}$), 131.7, 132.3, 133.8, 134.0, 147.7, 152.7 ($\text{C}_{\text{aromatic}}$). **HRMS (ESI):** m/z calculated – $[\text{M} + \text{H}]^+$: 379.1729, Found: 379.1698, Error: 12 ppm.

***N*-Methyl-1-(1-naphthylmethyl)-*N*-{[1-(2,4,6-trichlorobenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}amine 4j**

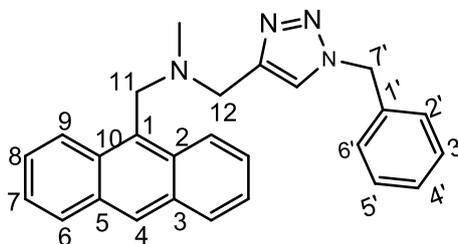


Yield: 75%. Yellow oil, $^1\text{H NMR}$ (200 MHz, CDCl_3 , δH (ppm), multiplicity, integration, J (Hz), attribution): 8.13-8.17 (m, 1H, H9), 7.76-7.86 (m, 2H, H4 e H6), 7.42-7.48 (m, 7H, $\text{H}_{\text{triazole}}$, H2, H3, H7, H8, H3' e H5'), 5.78 (s, 2H, H7'), 3.98 (s, 2H, H11), 3.81 (s, 2H, H12), 2.28 (s, 3H, CH_3). $^{13}\text{C NMR}$ (50 MHz, CDCl_3): δC (ppm): 42.5 (CH_3), 52.4 (C12), 48.4 (C7'), 59.8 (C11), 122.3 ($\text{CH}_{\text{triazole}}$), 145.5 ($\text{C}_{\text{triazole}}$), 124.5, 125.1, 125.5, 125.7, 127.6, 128.0, 128.4, 128.9 ($\text{CH}_{\text{aromatic}}$), 132.4, 133.8, 134.5, 136.2,

137.3 (C_{aromatic}). **HRMS (ESI):** m/z calculated – [M + H]⁺: 445.0748, Found: 445.0714, Error: 7 ppm.

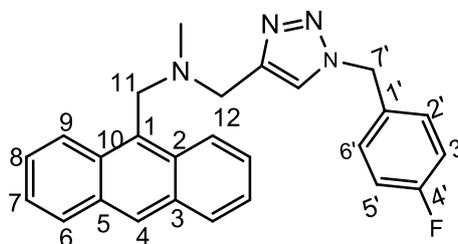
5.2 Analogues derived from anthracene 4k-t

N-(9-Anthracenylmethyl)-*N*-[(1-benzyl-1*H*-1,2,3-triazol-4-yl)methyl]-*N*-methylamine 4k



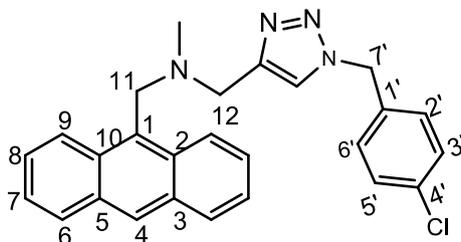
Yield: 88%. Yellow solid **M.p:** 139.1 – 140.2 °C **¹H NMR** (200 MHz, CDCl₃, δH (ppm), multiplicity, integration, J (Hz), attribution): 8.23-8.26 (m, 3H, H₆, H₄), 7.83-7.87 (m, 2H, H₉), 7.11-7.33 (m, 10H, H₂', H₆', H₃', H₅', H₄', H₇, H₈, H_{triazole}), 5.35 (s, 2H, H₇'), 4.38 (s, 2H, H₁₁), 3.77 (s, 2H, H₁₂), 2.14 (s, 3H, CH₃). **¹³C NMR** (50 MHz, CDCl₃): δC (ppm): 42.0 (CH₃), 52.8 (C₁₂), 53.0 (C₁₁), 54.0 (C₇'), 122.6 (CH_{triazole}), 146.0 (C_{triazole}), 124.8, 125.7, 127.5, 127.9, 128.6, 129.0, 129.0 (CH_{aromatic}), 129.9, 131.2, 131.3, 134.8 (C_{aromatic}). **HRMS (ESI):** m/z calculated – [M + H]⁺: 393.2079, Found: 393.2070, Error: 2 ppm.

N-(9-Anthracenylmethyl)-*N*-{[1-(4-fluorobenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}-*N*-methylamine 4l



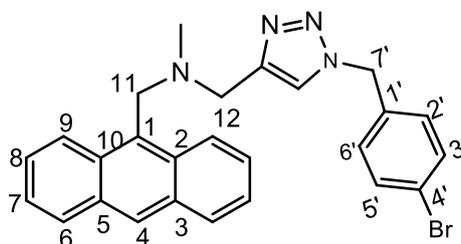
Yield: 80%. Yellow solid, **M.p:** 138.7 – 139.8 °C, **¹H NMR** (200 MHz, CDCl₃, δH (ppm), multiplicity, integration, J (Hz), attribution): 8.37-8.40 (m, 3H, H₄, H₆), 7.96-8.01 (m, 2H, H₉), 6.99-7.48 (m, 9H, H₂', H₆', H₃', H₅', H₇, H₈, H_{triazole}), 5.42 (s, 2H, H₇'), 4.51 (s, 2H, H₁₁), 3.89 (s, 2H, H₁₂), 2.28 (s, 3H, CH₃). **¹³C NMR** (50 MHz, CDCl₃): δC (ppm): 42.1 (CH₃), 52.6 (C₁₂), 53.1 (C₁₁), 53.2 (C₇'), 122.4 (CH_{triazole}), 146.2 (C_{triazole}), 162.7 (¹J_{CF} = 265.5 Hz, C₄'), 116.0 (²J_{CF} = 21.5 Hz, C₄'), 129.84 (³J_{CF} = 8.5 Hz, C₄'), 124.8, 125.7, 127.5, 128.9, 129.7, (CH_{aromatic}), 130.6, 130.6, 131.2, 131.3 (C_{aromatic}). **HRMS (ESI):** m/z calculated – [M + H]⁺: 411.1985, Found: 411.1957, Error: 7 ppm.

N-(9-Anthracenylmethyl)-*N*-{[1-(4-chlorobenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}-*N*-methylamine 4m



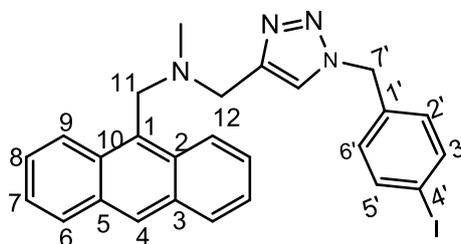
Yield: 75%. Yellow solid, **M.p:** 137.4 – 139.1 °C, $^1\text{H NMR}$ (200 MHz, CDCl_3 , δH (ppm), multiplicity, integration, J (Hz), attribution): 8.41 (m, 3H, H4, H6), 7.98-7.80 (m, 2H, H9), 7.16-7.46 (m, 9H, H2', H6', H3', H5', H7, H8, $\text{H}_{\text{triazole}}$), 5.46 (s, 2H, H7'), 4.52 (s, 2H, H11), 3.88 (s, 2H, H12), 2.29 (s, 3H, CH_3). $^{13}\text{C NMR}$ (50 MHz, CDCl_3): δC (ppm): 42.2 (CH_3), 52.6 (C12), 53.0 (C11), 53.2 (C7'), 122.5 ($\text{CH}_{\text{triazole}}$), 146.4 ($\text{C}_{\text{triazole}}$), 124.8, 125.7, 127.6, 129.0, 129.3 ($\text{CH}_{\text{aromatic}}$), 129.9, 131.2, 131.4, 133.3, 134.7 ($\text{C}_{\text{aromatic}}$). **HRMS (ESI):** m/z calculated – $[\text{M} + \text{H}]^+$: 427.1689, Found: 427.1653, Error: 8 ppm.

***N*-(9-Anthracenylmethyl)-*N*-{[1-(4-bromobenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}-*N*-methylamine 4n**



Yield: 93%. Yellow solid, **M.p:** 141.9 – 142.3 °C, $^1\text{H NMR}$ (200 MHz, CDCl_3 , δH (ppm), multiplicity, integration, J (Hz), attribution): 8.35-8.39 (m, 4H, H4, H6), 7.96-8.00 (m, 3H, H9), 7.07-7.48 (m, 9H, H2', H6', H3', H5', H7, H8, $\text{H}_{\text{triazole}}$), 5.41 (s, 2H, H7'), 4.52 (s, 2H, H11), 3.89 (s, 2H, H12), 2.28 (s, 3H, CH_3). $^{13}\text{C NMR}$ (50 MHz, CDCl_3): δC (ppm): 42.0 (CH_3), 52.6 (C12), 53.0 (C11), 53.3 (C7'), 122.7 ($\text{CH}_{\text{triazole}}$), 146.0 ($\text{C}_{\text{triazole}}$), 124.7, 124.8, 125.7, 127.6, 129.0, 129.5, 132.2, 134.0 ($\text{CH}_{\text{aromatic}}$), 127.1, 131.2, 131.3, 133.7 ($\text{C}_{\text{aromatic}}$). **HRMS (ESI):** m/z calculated – $[\text{M} + \text{H}]^+$: 471.1184, Found: 471.1176, Error: 2 ppm.

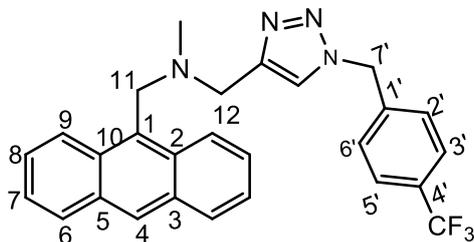
***N*-(9-Anthracenylmethyl)-*N*-{[1-(4-iodobenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}-*N*-methylamine 4o**



Yield: 93%. Yellow solid, **M.p:** 135.1 – 135.7 °C, $^1\text{H NMR}$ (200 MHz, CDCl_3 , δH (ppm), multiplicity, integration, J (Hz), attribution): 8.35-8.39 (m, 3H, H4, H6), 7.96-8.00 (m, 2H, H9), 7.29-7.45 (m, 8H, H2', H6', H7, H8, $\text{H}_{\text{triazole}}$), 6.93 (m, 2H, H3', H5'), 5.37 (s, 2H, H7'), 4.49 (s, 2H, H11), 3.87 (s, 2H, H12), 2.27 (s, 3H, CH_3). $^{13}\text{C NMR}$ (50 MHz, CDCl_3): δC (ppm): 42.5 (CH_3), 53.0 (C12), 53.5 (C11), 54.1 (C7'), 122.5 ($\text{CH}_{\text{triazole}}$), 146.2 ($\text{C}_{\text{triazole}}$), 124.7, 124.8, 125.7, 127.6, 129.0, 129.7, 138.1

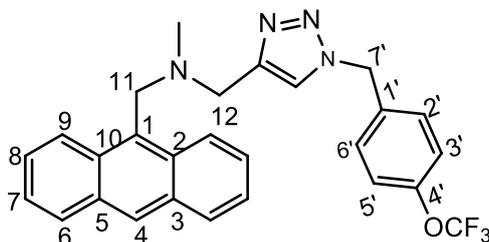
(CH_{aromatic}), 94.4, 131.2, 131.3, 134.4 (C_{aromatic}). **HRMS (ESI):** m/z calculated – [M + H]⁺: 519.1045, Found: 519.1050, Error: 1 ppm.

***N*-(9-Anthracenylmethyl)-*N*-methyl-*N*-{[1-(4-trifluoromethylbenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}amine 4p**



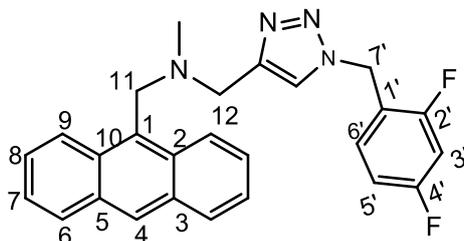
Yield: 76%. Yellow solid, **M.p:** 148.0 – 149.5°C, **¹H NMR** (200 MHz, CDCl₃, δH (ppm), multiplicity, integration, J (Hz), attribution): 8.39 (m, 3H, H4, H6), 7.99 (m, 2H, H9), 7.31-7.61 (m, 9H, H2', H6', H3', H5', H7, H8, H_{triazole}), 5.50 (s, 2H, H7'), 4.52 (s, 2H, H11), 3.89 (s, 2H, H12), 2.30 (s, 3H, CH₃). **¹³C NMR** (50 MHz, CDCl₃): δC (ppm): 42.1 (CH₃), 52.6 (C12), 53.1 (C7'), 53.2 (C11), 122.7 (CH_{triazole}), 146.5 (C_{triazole}), 126.0 (³J_{CF} = 3.5 Hz, C3'/C5'), 124.8, 125.7, 127.6, 128.0, 129.0 (CH_{aromatic}), 129.8, 131.2, 131.3, 138.7 (C_{aromatic}). **HRMS (ESI):** m/z calculated – [M + H]⁺: 461.1953, Found: 461.1957, Error: 0,8 ppm.

***N*-(9-Anthracenylmethyl)-*N*-methyl-*N*-{[1-(4-trifluoromethoxybenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}amine 4q**



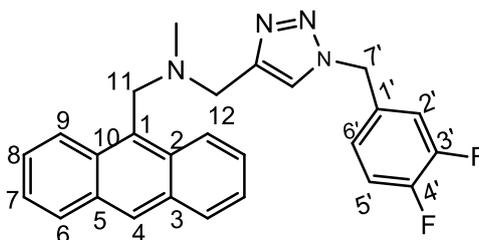
Yield: 96%. Yellow solid, **M.p:** 110.1 – 111.5°C, **¹H NMR** (200 MHz, CDCl₃, δH (ppm), multiplicity, integration, J (Hz), attribution): 8.30-8.39 (m, 3H, H4, H6), 7.78-7.98 (m, 2H, H9), 7.23-7.44 (m, 9H, H2', H6', H3', H5', H7, H8, H_{triazole}), 5.47 (s, 2H, H7'), 4.53 (s, 2H, H11), 3.90 (s, 2H, H12), 2.28 (s, 3H, CH₃). **¹³C NMR** (50 MHz, CDCl₃): δC (ppm): 42.0 (CH₃), 52.5 (C12), 52.9 (C7'), 53.1 (C11), 122.7 (CH_{triazole}), 146.0 (C_{triazole}), 124.7, 124.8, 125.7, 127.1, 127.7, 128.9, 129.4, 134.0 (CH_{aromatic}), 121.4, 131.2, 131.3, 133.4, 149.2 (C_{aromatic}). **HRMS (ESI):** m/z calculated – [M + H]⁺: 477.1902, Found: 477.1902, Error: 0 ppm.

***N*-(9-Anthracenylmethyl)-*N*-{[1-(2,4-difluorobenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}-*N*-methylamine 4r**



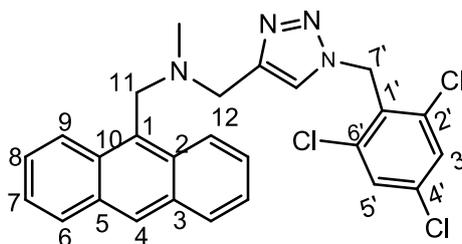
Yield: 98%. Yellow solid, **M.p:** 112.5 – 113.7 °C, **¹H NMR** (200 MHz, CDCl₃, δH (ppm), multiplicity, integration, J (Hz), attribution): 8.38 – 8.42 (m, 3H, H4, H6), 7.96–8.00 (m, 2H, H9), 6.80–7.48 (m, 9H, H6', H3', H5', H7, H8, H_{triazole}), 5.46 (s, 2H, H7'), 4.51 (s, 2H, H11), 3.89 (s, 2H, H12), 2.29 (s, 3H, CH₃). **¹³C NMR** (50 MHz, CDCl₃): δC (ppm): 42.1 (CH₃), 52.6 (C12), 46.9 (C7'), 53.1 (C11), 122.6 (CH_{triazole}), 146.1 (C_{triazole}), 104.2, 112.3, 116.2, 124.8, 125.6, 127.5, 128.9, 129.8 (CH_{aromatic}) 117.9, 118.3, 129.8, 131.2, 131.3 (C_{aromatic}). **HRMS (ESI):** *m/z* calculated – [M + H]⁺: 429.1891, Found: 429.1852, Error: 9 ppm.

***N*-(9-Anthracenylmethyl)-*N*-{[1-(3,4-difluorobenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}-*N*-methylamine 4s**



Yield: 82%. Yellow solid, **M.p:** 138.0 – 139.3 °C, **¹H NMR** (200 MHz, CDCl₃, δH (ppm), multiplicity, integration, J (Hz), attribution): 2.30 (s, 3H, CH₃), 3.88 (s, 2H, H12), 4.53 (s, 2H, H11), 5.41 (s, 2H, H7'), 6.98–7.48 (m, 8H, H2', H6', H5', H7, H8, H_{triazole}), 7.98–8.01 (m, 2H, H9), 8.41 (m, 3H, H4, H6). **¹³C NMR** (50 MHz, CDCl₃): δC (ppm): 42.1 (CH₃), 52.5 (C12), 52.8 (C7'), 53.2 (C11), 122.1 (CH_{triazole}), 146.1 (C_{triazole}), 116.9, 117.3, 117.8, 118.1, 124.0, 124.5, 125.7, 127.6, 129.0 (CH_{aromatic}), 129.9, 131.3, 131.3 (C_{aromatic}). **HRMS (ESI):** *m/z* calculated – [M + H]⁺: 429.1891, Found: 429.1851, Error: 9 ppm.

***N*-(9-Anthracenylmethyl)-*N*-methyl-*N*-{[1-(2,4,6-trichlorobenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}amine 4t**



Yield: 87%. Yellow solid, **M.p:** 124.2 – 125.7°C, **¹H NMR** (200 MHz, CDCl₃, δH (ppm), multiplicity, integration, J (Hz), attribution): 8.37–8.41 (m, 3H, H4, H6), 7.99–8.01 (m, 2H, H9), 7.28–7.49 (m, 7H, H3', H5', H7, H8, H_{triazole}), 5.77 (s, 2H, H7'), 4.55 (s, 2H, H11), 3.92 (s, 2H, H12), 2.29 (s, 3H, CH₃). **¹³C NMR** (50 MHz, CDCl₃): δC (ppm): 42.1 (CH₃), 52.7 (C12), 48.5 (C7'), 52.9 (C11), 122.6 (CH_{triazole}), 146.4 (C_{triazole}), 124.8, 124.8, 125.8, 127.7, 128.9, 129.0 (CH_{aromatic}), 131.3, 131.4, 131.2, 137.3 (C_{aromatic}). **HRMS (ESI):** *m/z* calculated – [M + H]⁺: 495.0910, Found: 495.0903, Error: 1 ppm.

Table S1 Crystal data and refinement parameters of compound **4e** reported in this study.

molecular formula		C ₂₂ H ₂₁ IN ₄
fw (g mol ⁻¹)		468.33
cryst syst		triclinic
space group		<i>P</i> -1
<i>Z</i> / <i>Z</i> '		2/1
<i>T</i> (K)		293(2)
unit cell dimensions	<i>a</i> (Å)	5.5291(4)
	<i>b</i> (Å)	12.9638(9)
	<i>c</i> (Å)	15.4547(11)
	α (°)	70.88(3)
	β (°)	84.50(4)
	γ (°)	77.72(5)
<i>V</i> (Å ³)		1022.3(3)
calculated density (mg m ⁻³)		1.521
absorption coefficient μ (mm ⁻¹)		1.580
θ range for data collection (°)		3.23 to 26.62
index ranges	<i>h</i>	-6 to 6
	<i>k</i>	-16 to 15
	<i>l</i>	-19 to 19
data collected		7101
unique reflections		4026
unique reflections with $I > 2\sigma(I)$		2639
symmetry factor (R_{int})		0.0312
completeness to θ_{max} (%)		94.3
<i>F</i> (000)		468
parameters refined		255
goodness-of-fit on F^2		1.258
final <i>R</i> factors for $I > 2\sigma(I)$		R1 = 0.0711
		wR2 = 0.2368
<i>R</i> factors for all data		R1 = 0.1003
		wR2 = 0.2491
largest diff. peak / hole (e/Å ³)		1.641 and -1.377
CCDC deposit number		1039072