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# Conformational energy (A-value) of the 4-phenyl-1,2,3-triazolyl group

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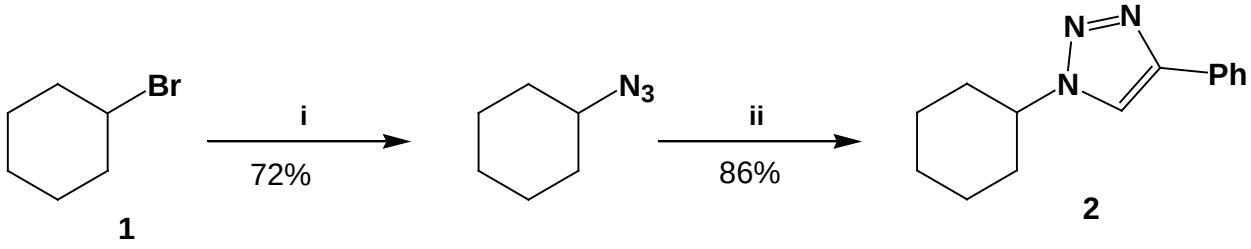
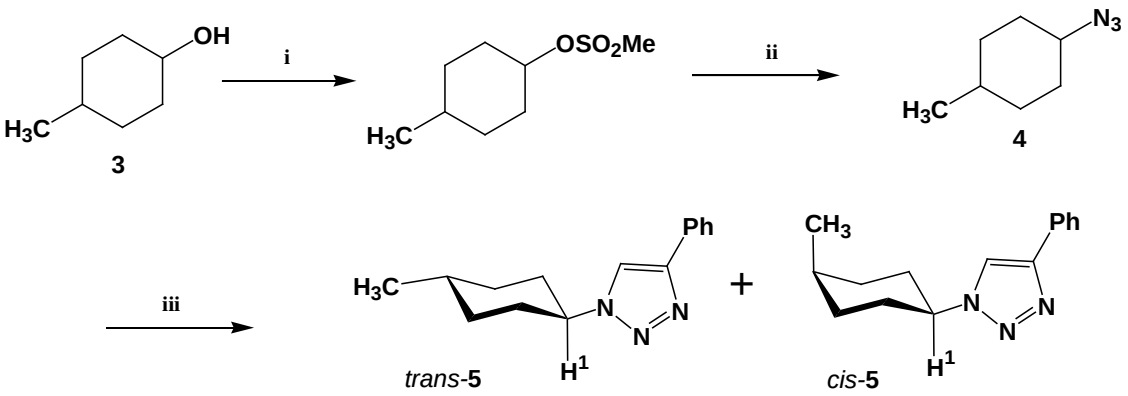
## Experimental

The chemicals were commercial (Sigma-Aldrich, VWR, TCI) and were used as purchased. Conventional techniques were used to purify all solvents prior to use. Column chromatography was performed on silica gel (40-75 μm, Sorbent Technologies). The reactions were monitored by TLC on silica gel 2.5 × 7.5 cm plates, Analtech Inc (eluent hexane/EtOAc; visualization by UV and staining with $I_2$).

$^1$H NMR and $^{13}$C NMR spectra were acquired on JEOL ECA-600 NMR spectrometer (600 MHz for $^1$H and 150 MHz for $^{13}$C) with spinning at room temperature. $^1$H-$^1$H-COSY and $^1$H-$^{13}$C-HMQC techniques were used to assign the signals. High-resolution mass spectra (HRMS) were obtained on a JEOL AccuTOF time-of-flight mass spectrometer (Peabody, MA) coupled with an Ionsense DART open-air ionization source (Saugus, MA).




**Scheme S1**. *Reagents and conditions:* i, $NaN_3$, DMSO, 189 °C, 12-24 h; ii, PhC≡CH, $CuSO_4 \cdot 5H_2O$, ascorbic acid, $H_2O$, 1,4-dioxane, room temperature, 4 h.




**Scheme S2**. *Reagents and conditions:* i, MsCl, pyridine, 0 °C, 3 h; ii, $NaN_3$, DMSO, 189 °C, 48 h; iii, PhC≡CH, $CuSO_4 \cdot 5H_2O$, ascorbic acid, $H_2O$, 1,4-dioxane, room temperature, 8 h.

**4-Methylcyclohexyl methanesulfonate.** 4-Methylcyclohexanol **3** (2.5 g, 2.7 mL, 20 mmol) was dissolved in pyridine (25 mL) and cooled in an ice bath (0-5 $^oC$). Methanesulfonyl chloride (1.85 mL, 24 mmol) was then added in small portions with constant stirring. The reaction was completed in 3 h (monitored by TLC). Ether (30 mL) and water (7 mL) were added, and the organic layer was washed successively with 2 N HCl, 5% $NaHCO_3$, and water and dried for 12 h over anhydrous $Na_2SO_4$. The organic solution was filtered, and the solvent was removed by rotary evaporation to give 2.89 g (75%) of the crude mesylate as a colorless oil containing both *cis* and *trans* isomers that could not be separated by column chromatography (*cis*:*trans*: = 1:3): $R_f$: 0.39 (hexane:EtOAc, 10:1). ***trans*-Isomer**: $^1H$ NMR (600 MHz, $CDCl_3$): δ 0.86 (s, 3H; $CH_3$), 1.01 (m, 2H; H3, H5), 1.24 (m, 1H; H4), 1.27 (m, 2H; H3, H5), 1.77 (m, 2H; H2eq, H6eq), 2.09 (m,2H; H2ax, H6ax), 2.97 (m, 3H; $CH_3$), 4.55 (m, 1H; H1). $^{13}C$ NMR (150 MHz, $CDCl_3$): δ 20.21 ($CH_3$), 25.68 (C2), 25.87 (C6), 28.64 (C3), 28.78 (C5), 32.64 (C4), 35.06 ($CH_3$).

***cis*-Isomer**: $^1H$ NMR (600 MHz, $CDCl_3$): δ 0.88 (s, 3H; $CH_3$), 1.01 (m, 2H; H3, H5), 1.31 (m, 3H; H4, H3, H5), 1.75 (m, 2H; H2eq, H6eq), 2.00 (m,2H; H2ax, H6ax), 2.98 (m, 3H; $CH_3$), 4.92 (m, 1H; H1). $^{13}C$ NMR (150 MHz, $CDCl_3$): δ 20.21 ($CH_3$), 26.34(C2), 26.87 (C6), 27.02 (C3), 28.04 (C5), 32.51 (C4), 35.13 ($CH_3$). HRMS: $C_8H_{17}O_3S^+$ $[M+H]_{cal}$ *m/z* 193.0893; $[M+H]_{exp}$ *m/z* 193.0881

**General procedure for Azides via $S_N2$ substitution.** The corresponding cycloalkyl halide or mesylate (2 mmol) was dissolved in DMSO (20 mL), $NaN_3$ (3 mmol) was added, and the reaction mixture was refluxed gently for 24 h while the consumption of the halide or mesylate was monitored by TLC. Reaction was allowed to cool to room temperature and quenched with $H_2O$ (30 mL) at 0-5$^oC$. Reaction round bottom flask was placed in an ice bath; diethyl ether (50 mL) was added, and this was stirred for 3 hours. The organic solution was separated and washed with $H_2O$ (20 mL) at 0-5$^oC$ and brine (20 mL). The organic solution was separated and dried for 12 h over anhydrous $Na_2SO_4$ and filtered. The solvent was removed by rotary evaporator to give the crude product.

**Azidocyclohexane** was obtained as yellow oil: 0.182 g (72%) without purification. $R_f$ 0.32 (hexane:EtOAc, 10:1). $^1H$ NMR (600 MHz, $CDCl_3$): δ 1.34 (m, 6H; H3, H3, H4, H4, H5, H5), 1.77 (m, 2H; H2ax, H6ax), 1.90 (m, 2H; H2eq, H6eq), 3.31 (m, 1H; H1). $^{13}C$ NMR (150 MHz, $CDCl_3$): δ 24.32 (C3, C5), 25.35 (C4), 31.69 (C2, C6), 60.00 (C1). HRMS: $C_{16}H_{12}N_3^+$ $[M+H]_{cal}$ *m/z* 126.1015; $[M+H]_{exp}$ *m/z* 126.1031.

**1-Azido-4-methylcyclohexane (4)** was obtained as yellow oil: 0.209 g (75%), with both *cis* and *trans* isomers of the product that could not be separated by column chromatography (*cis*:*trans*: = 3:1): $R_f$ 0.31 (hexane:EtOAc, 19:1). *trans*-**4**: $^1H$ NMR (600 MHz, $CDCl_3$): δ 0.71 (s, 3H; $CH_3$), 0.93 (m,1H, H4), 1.32 (m, 4H; H3, H3, H5, H5), 1.56 (m, 2H; H2ax, H6ax), 1.91 (m, 2H; H2eq, H6eq), 3.84 (m, 1H; H1). $^{13}C$ NMR (150 MHz, $CDCl_3$): δ 26.38 (C3), 26.42 (C5), 26.49 ($CH_3$), 30.18 (C2, C6), 42.17 (C4), 57.02 (C1). *cis*-**4**: $^1H$ NMR (600 MHz, $CDCl_3$): δ 0.77 (s, 3H; $CH_3$), 0.96 (m,1H, H4), 1.14 (m, 2H; H3, H5), 1.32 (m, 2H; H3, H5), 1.53 (m, 2H; H2ax, H6ax), 1.91 (m, 2H; H2eq, H6eq), 3.99 (m, 1H; H1). $^{13}C$ NMR (150 MHz, $CDCl_3$): δ 26.33 (C3), 26.42 (C5), 26.49 ($CH_3$), 30.24 (C2), 30.54 (C6), 42.05 (C4), 57.57 (C1). HRMS: $C_7H_{14}N_3$ $^+[M+H]_{cal}$ *m/z* 140.1171; $[M+H]_{exp}$ *m/z* 140.1199.

**General procedure for synthesis of triazoles through copper catalyzed click reactions.**

Salt $CuSO_4.5H_2O$ (10 mmol) was dissolved in $H_2O$ (7 mL). Azide (1 mmol), alkyne (1.2 mmol) and ascorbic acid (3 mmol) were dissolved in a mixture of $H_2O$ (3 mL) and 1,4-dioxane (2 mL). The $CuSO_4$ solution was added to this mixture and stirred for 8 hours while checking for completion with TLC. After completion, the mixture was washed with $CHCl_3$ (2×20 mL) and dried with anhydrous $Na_2SO_4$ for 12 hours. The organic solution was filtered and the solvent was removed by rotary evaporator to give the crude product.

**1-Cyclohexyl-4-phenyl-1*H*-1,2,3-triazole (2)** was isolated as white crystals with a yield of 0.175 g (85%) after column chromatography (silica gel; hexane:EtOAc, 10:1). $R_f$ 0.62 (hexane:EtOAc, 10:1). $^1$H NMR (600 MHz, $CD_3OD$): δ 1.35 (m, 1H; H4ax), 1.55 (m, 2H; H3ax,H5ax), 1.80 (m, 1H; H4eq), 1.92 (m, 4H; H2ax,H6ax,H3eq,H5eq), 2.22 (m, 2H; H2eq, H6eq), 4.53 (tt, *J* = 11.7, 3.9 Hz, 1H; H1), 7.33 (m, 1H; phenyl), 7.43 (m, 2H; phenyl), 7.82 (m, 2H; phenyl), 8.36 (s, 1H; triazolyl). $^{13}$C NMR (150 MHz, $CD_3OD$): 25.31 (C3), 25.86 (C5), 26.01 (C4), 31.13(C2), 31.95 (C6), 59.34 (C1), 125.34, 126.91 (2CH; phenyl), 127.91 (CH; phenyl), 129.00 (C; phenyl), 129.18 (CH; triazolyl), 148.17 (C; triazolyl). HRMS: $C_{14}H_{18}N_3$ $[M+H]_{cal}$ *m/z* 228.1495; $[M+H]_{exp}$ *m/z* 228.1520.

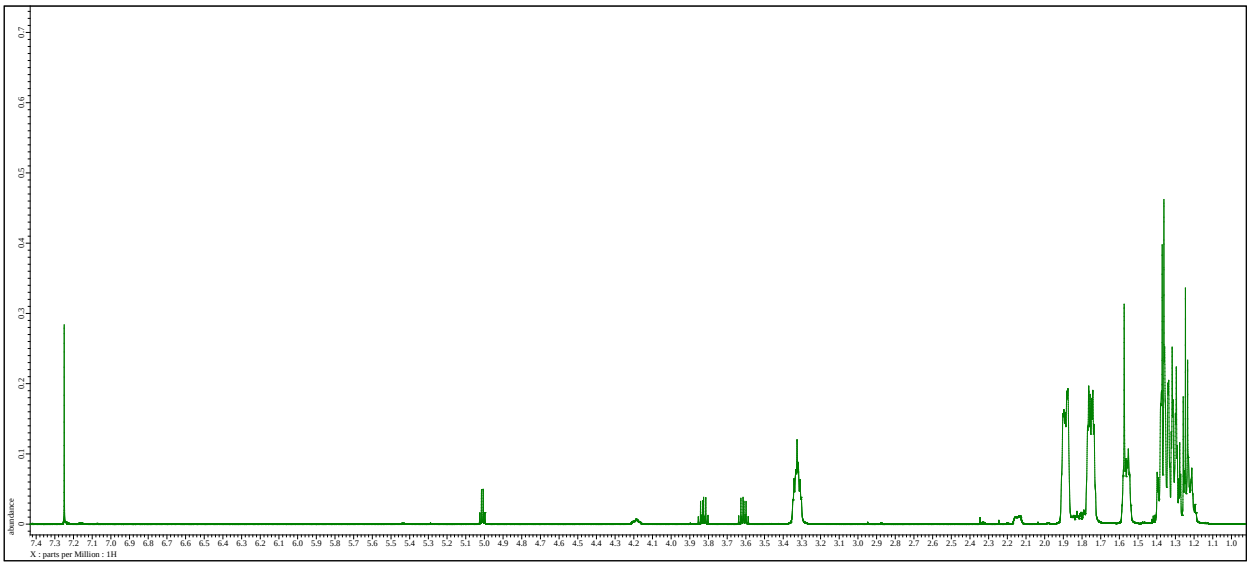
**1-(4-Methylcyclohexyl)-4-phenyl-1*H*-1,2,3-triazole (***trans*-**5** and *cis*-**5**, 1:3**)**. Final column chromatography (silica gel; hexane:EtOAc, 7:3) yielded a mixture of both isomers as colorless oil (0.291 mg, 82%). $R_f$ 0.50 for *cis*-**5** and 0.49 for *trans*-**5** (hexane:EtOAc, 7:3).

***trans*-5:** $^1$H NMR (600 MHz, $CDCl_3$): δ 0.89 (t, *J* = 7.1 Hz, 3H; $CH_3$), 1.62(m, 2H; H3ax,H5ax), 1.80 (m, 1H; H4), 1.95 (m, 2H; H3eq, H5eq), 2.07 (m, 2H; H2ax,H6ax), 2.34 (m, 2H; H2eq, H6eq), 4.62 (m, 1H; H1), 7.29 (m, 3H; phenyl), 7.33(m, 2H; phenyl), 7.92 (s, 1H; triazolyl). $^{13}$C NMR (150 MHz, $CDCl_3$): δ 14.12 ($CH_3$), 32.22 (C4), 34.69 (C2, C6), 35.26 (C3, C5), 61.21 (C1), 119.53, 126.23, 126.99, 127.01 (CH; phenyl), 127.31 (CH, triazolyl), 128.52 (C; phenyl), 145.36 (C; triazolyl). HRMS: $C_{15}H_{20}N_3$ $[M+H]_{cal}$ *m/z* 242.1652; $[M+H]_{exp}$ *m/z* 242.1664

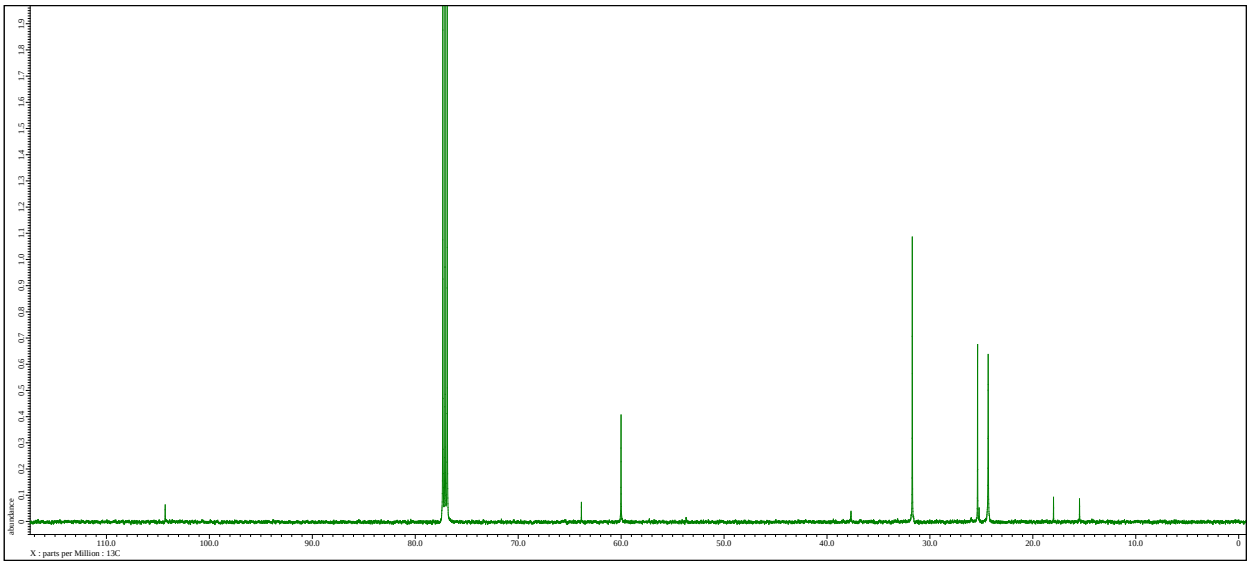
***cis*-5:** $^1$H NMR (600 MHz, $CDCl_3$): δ 0.82 (t, *J* = 7.1 Hz, 3H; $CH_3$), 1.75 (m, 2H; H3ax,H5ax), 1.80 (m, 1H; H4), 1.93(m, 2H; H3eq, H5eq), 2.11 (m, 2H; H2ax,H6ax), 2.59(m, 2H; H2eq, H6eq), 4.61 (m, 1H; H1), 7.15 (m, 3H; phenyl), 7.23 (m, 2H; phenyl), 7.78 (s, 1H; triazolyl). $^{13}$C NMR (150 MHz, $CDCl_3$): δ 14.12 ($CH_3$), 32.22 (C4), 34.69 (C2, C6), 35.26 (C3, C5), 61.21 (C1), 121.28 (CH; triazolyl), 119.53, 126.23, 126.99, 127.01 (CH; phenyl), 127.31 (CH, triazolyl), 128.52 (C; phenyl), 145.36 (C; triazolyl). HRMS: $C_{15}H_{20}N_3$ $[M+H]_{cal}$ *m/z* 242.1652; $[M+H]_{exp}$ *m/z* 242.1684.

## Images of $^{1}H$ and $^{13}C$ NMR and MS spectra

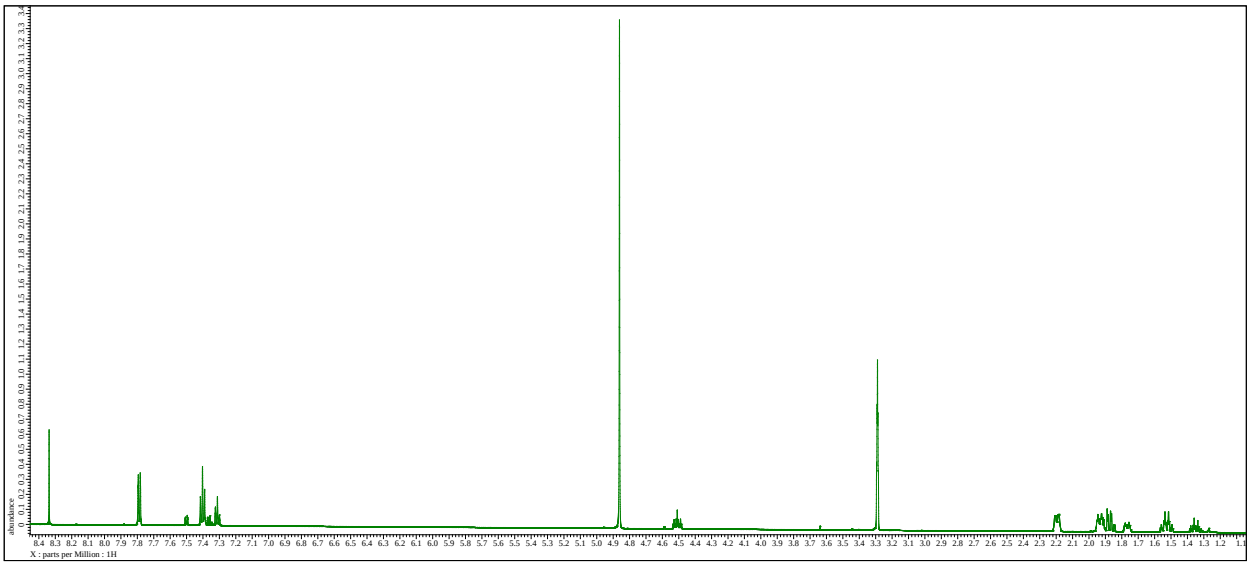
### Azidocyclohexane ($^{1}H$ NMR, $CDCl_3$)



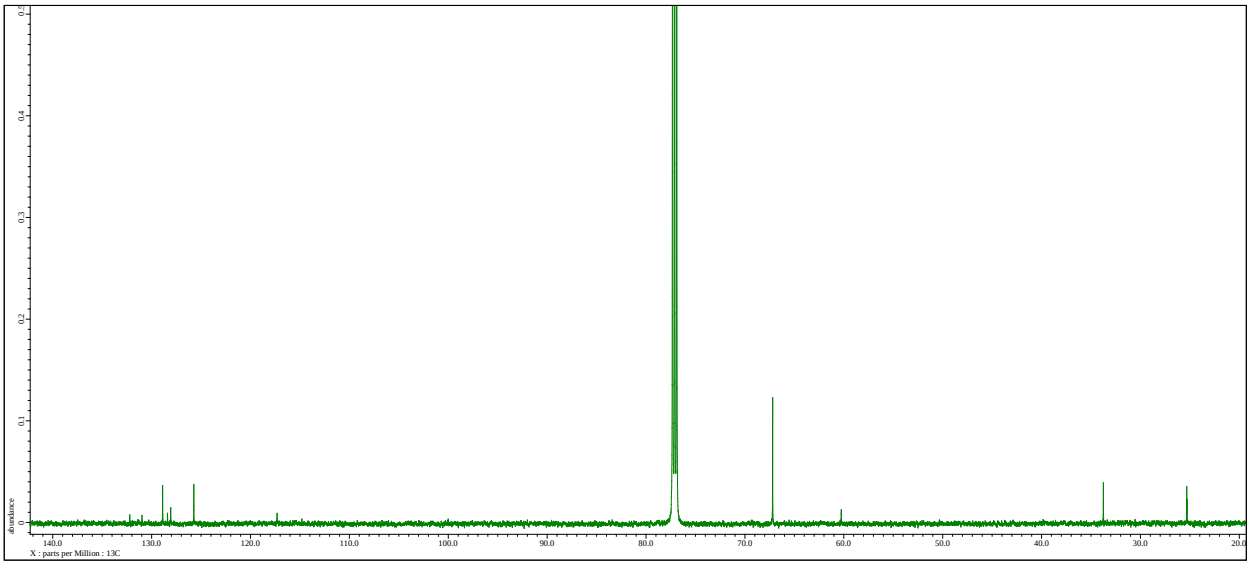

### Azidocyclohexane ($^{13}C$ NMR, $CDCl_3$)



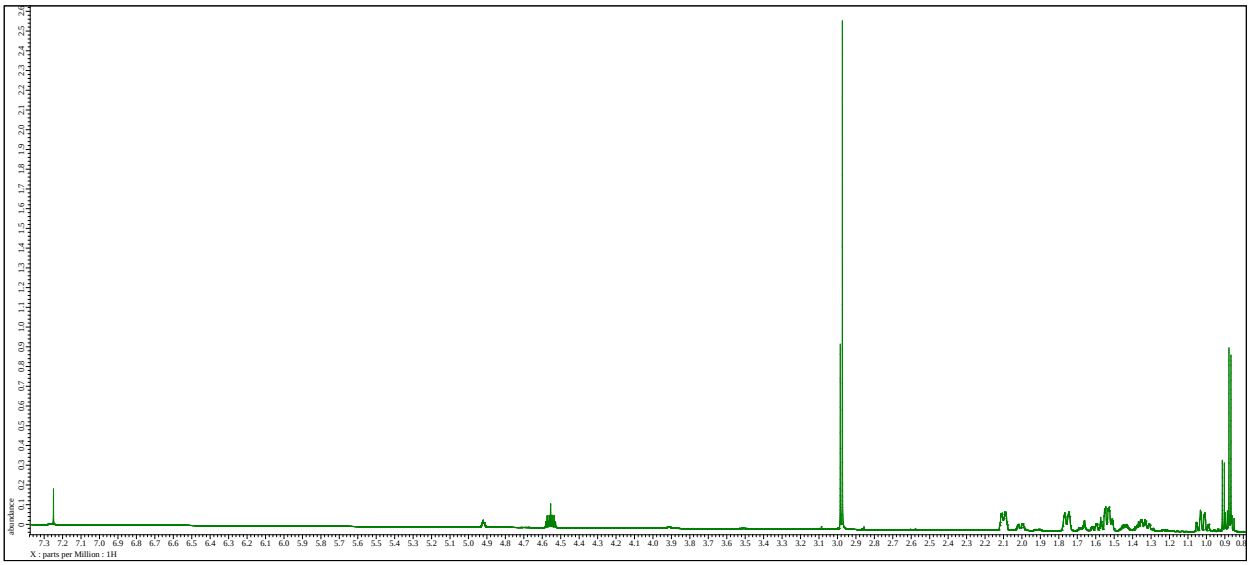
## 1-Cyclohexyl-4-phenyl-1*H*-1,2,3-triazole (2) ($^{1}$H NMR, $CD_3OD$)



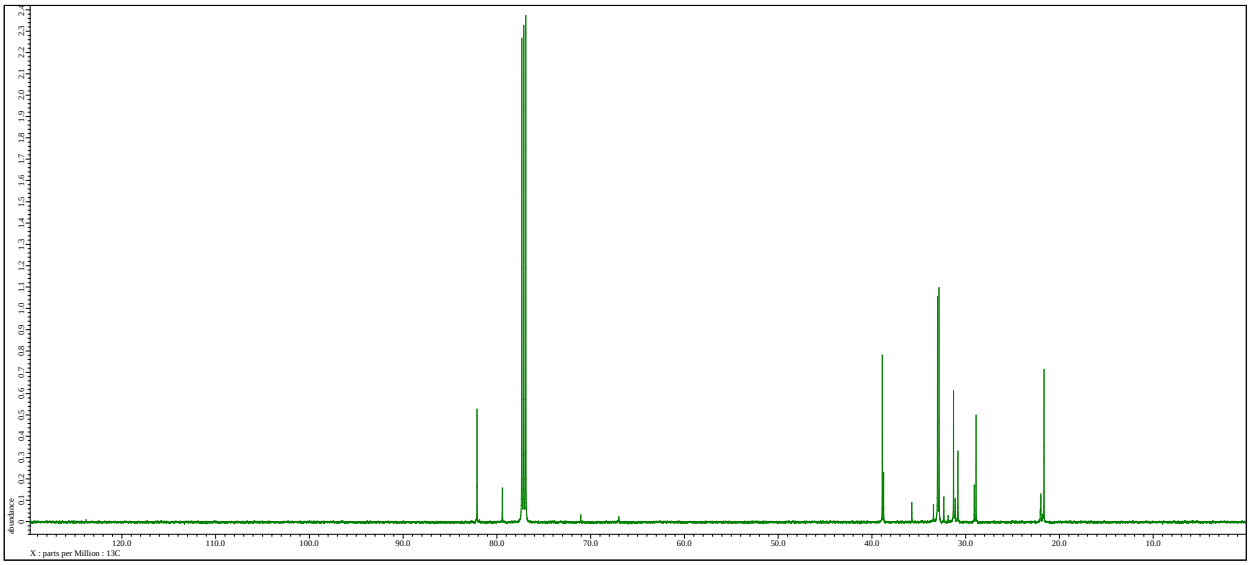

## 1-Cyclohexyl-4-phenyl-1*H*-1,2,3-triazole (2) ($^{13}$C NMR, $CD_3OD$)



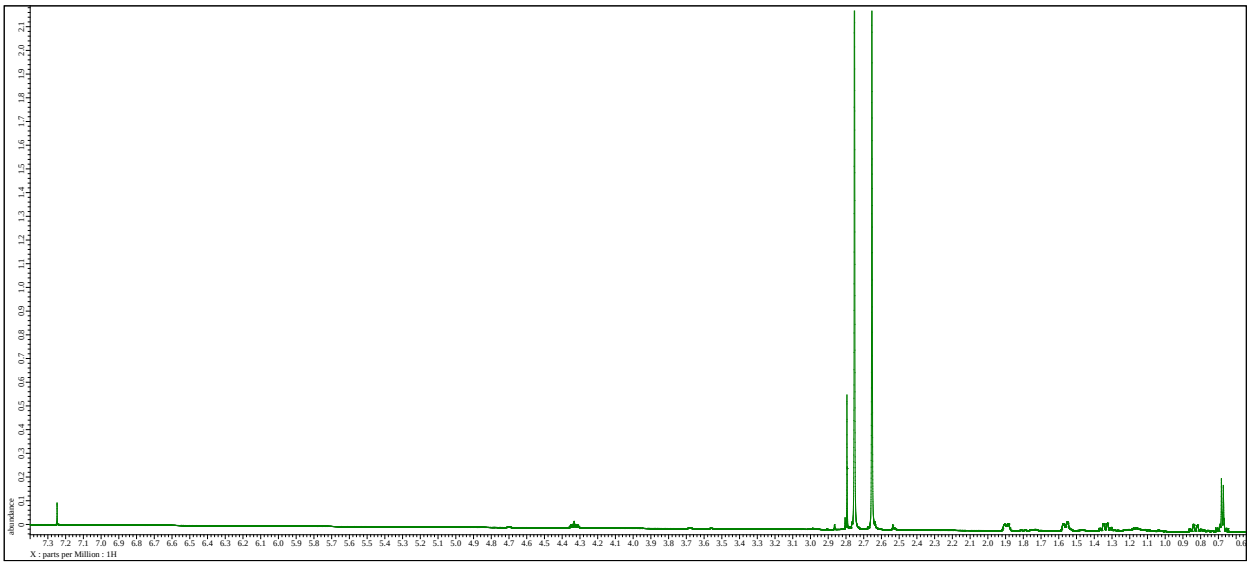
## 4-Methylcyclohexyl methanesulfonate ($^{1}$H NMR, $CDCl_3$)



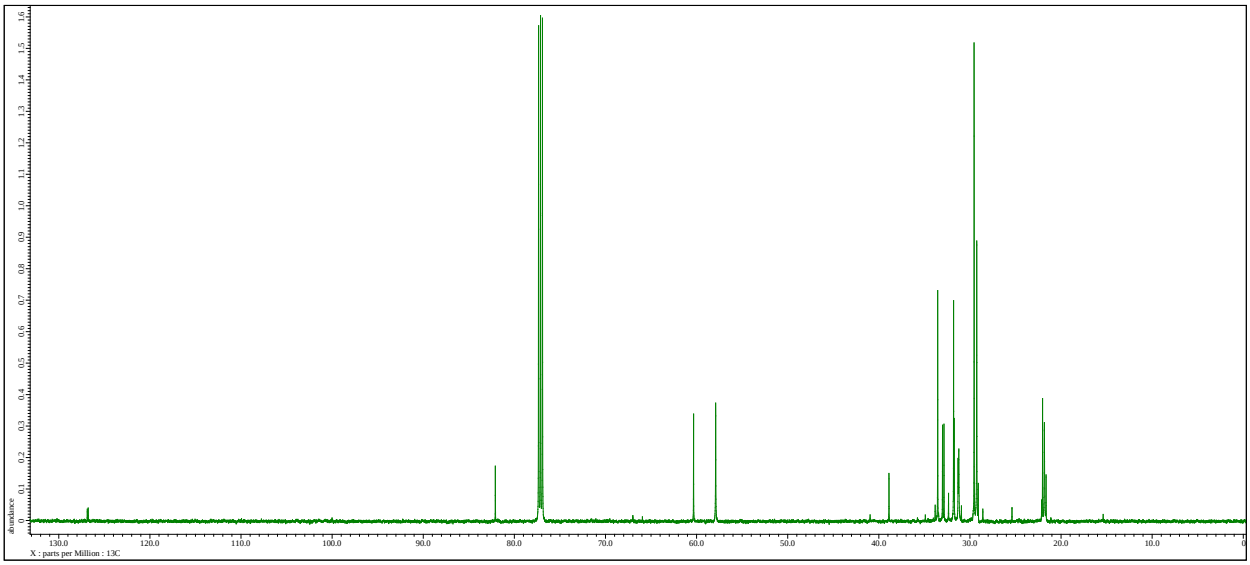

## 4-Methylcyclohexyl methanesulfonate ($^{13}$C NMR, $CDCl_3$)



## 1-Azido-4-methylcyclohexane (4) ($^{1}$H NMR, $CDCl_3$)

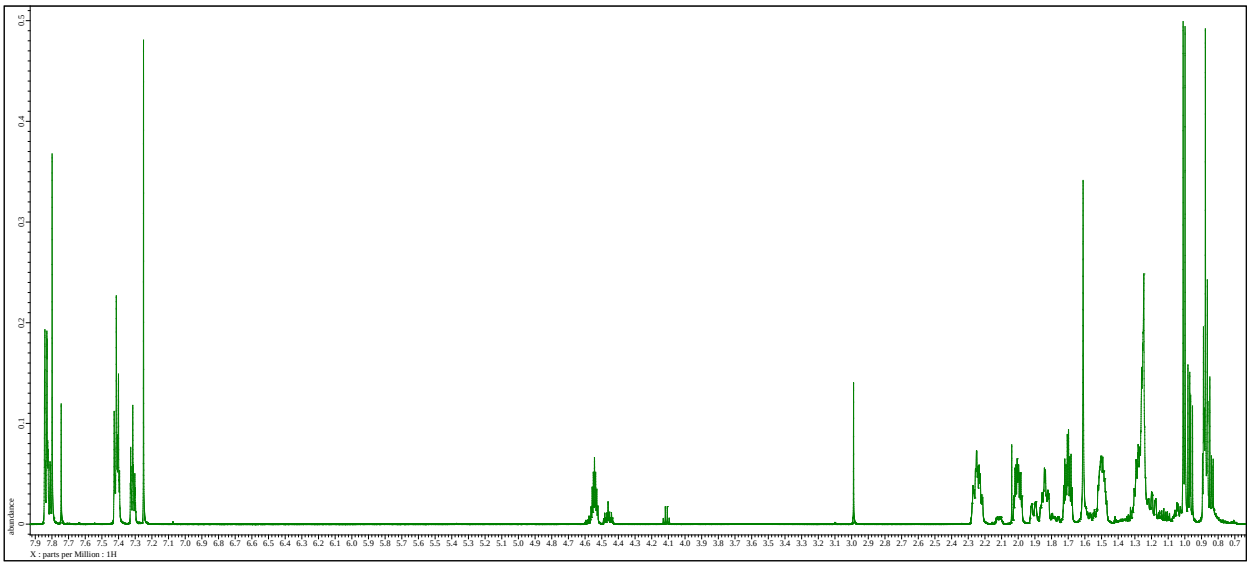



## 1-Azido-4-methylcyclohexane (4) ($^{13}$C NMR, $CDCl_3$)



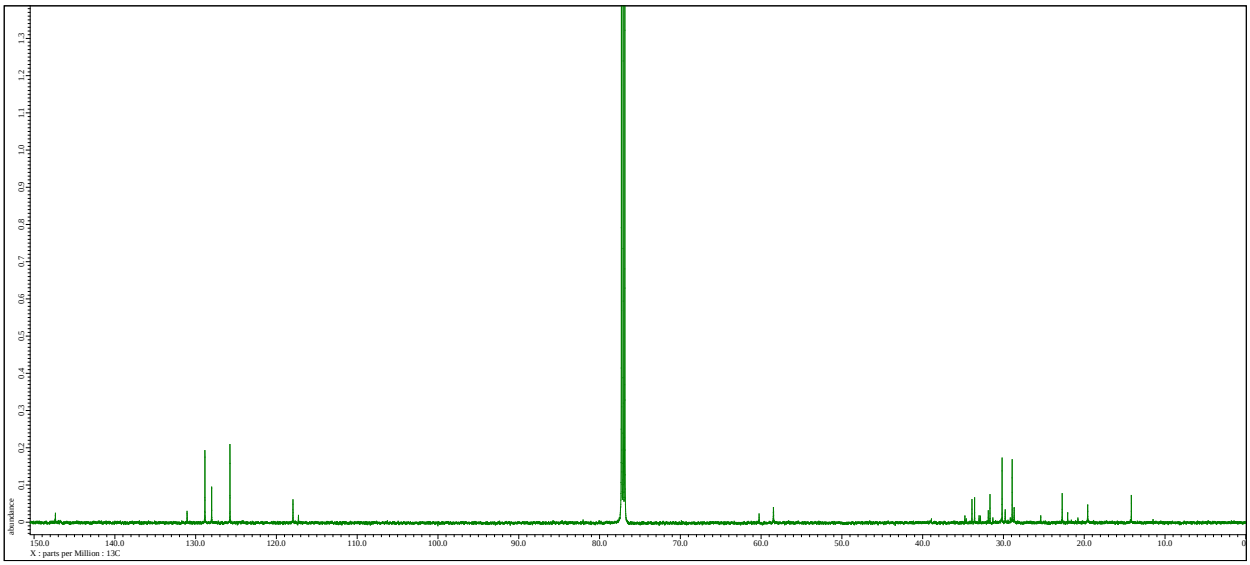
**1-(4-Methylcyclohexyl)-4-phenyl-1*H*-1,2,3-triazole (*trans*-5 and *cis*-5)**

**($^{1}$H NMR, $CDCl_3$)**

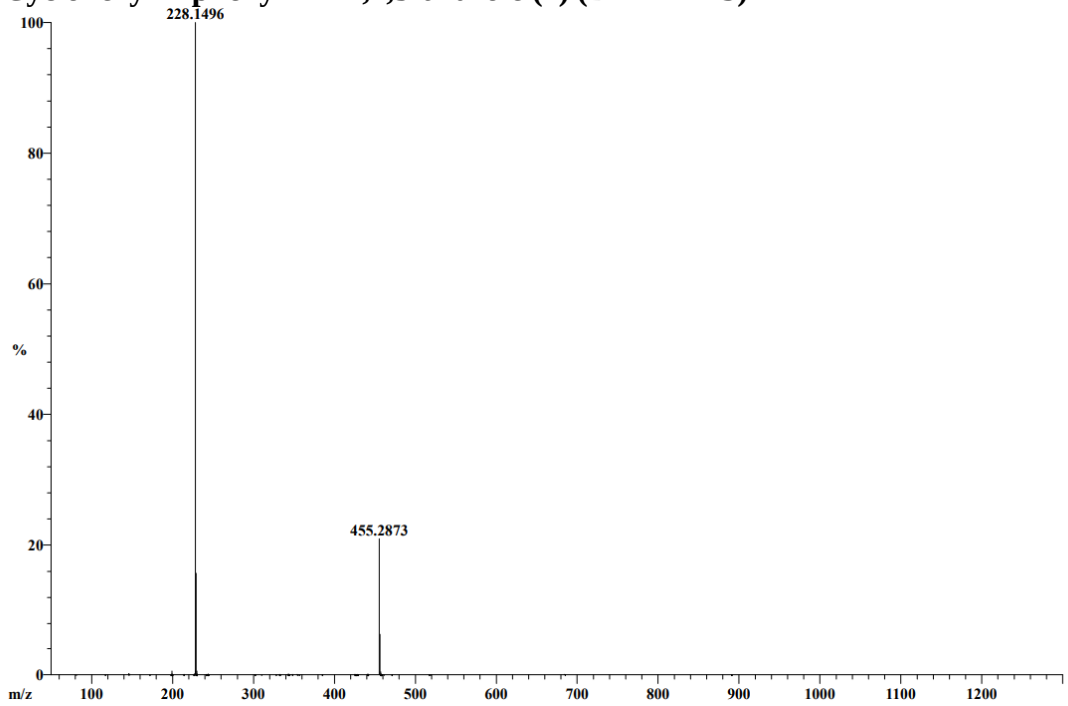


**1-(4-Methylcyclohexyl)-4-phenyl-1*H*-1,2,3-triazole (*trans*-5 and *cis*-5)**

**($^{13}$C NMR $CDCl_3$)**



**1-Cyclohexyl-4-phenyl-1*H*-1,2,3-triazole (2) (DART-MS)**




**1-(4-Methylcyclohexyl)-4-phenyl-1*H*-1,2,3-triazole (*trans*-5 and *cis*-5) (DART-MS)**