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Article

Synthesis and Phytotoxic Activity of 1,2,3-Triazole Derivatives

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Uma série de treze derivados triazólicos contendo grupos benzila-halogenados foi sintetizada utilizando-se como etapa chave a cicloadição azida-alcino catalisada por Cu(I) (CuAAC), transformação comumente descrita como reação *click*. A atividade biológica destes compostos foi avaliada, e verificou-se que estes compostos interferem na germinação e no crescimento radicular (brotos e raízes) das espécies *Allium cepa* (cebola), modelo de monocotiledônea, e *Cucumis sativus* (pepino) e *Lactuca sativa* (alface), modelos de dicotiledôneas. Os compostos apresentaram atividade predominantemente inibitória com relação às espécies avaliadas principalmente na concentração de 10^{-4} mol L^{-1}, sendo que alguns deles foram tão ativos quanto o 2,4-D (ácido 2,4-diclorofenoxiacético), o controle positivo.

Thirteen triazole derivatives bearing halogenated benzyl substituents were synthesized using the Cu-catalyzed azide-alkyne cycloaddition (CuAAC), a leading example of the click chemistry approach, as the key step. The biological activity of the compounds was evaluated, and it was found that these compounds interfere with the germination and radicle growth (shoots and roots) of two dicotyledonous species, *Lactuca sativa* and *Cucumis sativus*, and one monocotyledonous species, *Allium cepa*. The compounds showed predominantly inhibitory activity related to the evaluated species mainly at the concentration of 10^{-4} mol L^{-1}. Some of them presented inhibitory activity comparable to 2,4-D (2,4-dichlorophenoxyacetic acid), used as positive control.

Keywords: herbicides, 1,2,3-triazoles, click chemistry, phytotoxicity

Introduction

Weeds can be defined in several ways, for example, as plants that grow where humans do not wish them to be. Vegetable species that grow in the wrong place, in the wrong quantity or at the wrong time can also be considered weeds. Another definition of a weed is a species whose utility has not been identified.[1-4] More often than not, weeds interfere with human activities such as agriculture. Weeds compete with crops for nutrients, water and physical space, and may harbor insect and disease pests. Thus, weeds are capable of greatly reducing both crop quality and yield, and therefore, weed control is highly desirable.[5,6]

Although there are several ways to weed, the use of chemicals (known as herbicides or weed killers) is currently the most cost efficient and reliable weed control method utilized by farmers.[1-3] Currently, there are several active compounds available to control weeds, but it is still necessary to identify new herbicides to overcome weed resistance problems resulting from pressure of selection.[7-10] In addition, due to the public's concerns about the environment, modern herbicides should have a favorable combination of properties, such as a high level of herbicidal activity, a low application rate, crop tolerance and low toxicity to mammals.

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In the search and development for new herbicides as well as other agrochemicals and pharmaceuticals, heterocyclic compounds play an important role. The heterocyclic core is frequently part of the pharmacophore responsible for the observed biological activity.[11,12] The heterocyclic portion of a compound can have beneficial effects in terms of its physicochemical properties, conferring lipophilicity and solubility values in the optimal range for uptake and bioavailability. Moreover, heterocycles are ideal bioisosteres of other homocyclic rings, heterocyclic rings and several different functional groups. In many cases, this bioisosterism can result in compounds with improved biological efficacy.[12-14] Nitrogen-containing heterocycles are representatives of this class of organic compounds that stand out due to their abundance in nature and great significance in biochemistry. These structural subunits exist in many natural compounds such as vitamins, hormones, antibiotics and alkaloids, in addition to being found in pharmaceuticals, herbicides, dyes and many other compounds.[14] Triazoles are one of the most studied classes of nitrogen heterocycles. Triazole derivatives have a wide range of applications and are used as explosives, drugs and agrochemicals. The 1,2,4-triazole core has been found to be an integral part of therapeutically interesting compounds that display significant antibacterial, central nervous system (CNS) stimulative, sedative, antifungal and antitumor activities.[14] It is also worth to mention that all triazole derivatives are synthetic.[15]

Another class of organic compounds widely employed as pesticides is the halogen-containing heterocycles. These compounds are generally more polar than their homocyclic analogs and possess lower *n*-octanol-water partition coefficients. Consequently, halogen-containing heterocycles are often more environmentally mobile. In addition to their use as pesticides, halogen-containing heterocycles have also been used as pharmaceuticals, dyes and explosives.

The past 30 years have witnessed a period of significant expansion in the research and development of halogenated compounds to be used as agrochemicals.[16-18] The primary advantages of using these compounds are their economic viability and high efficacy. This high efficacy makes these compounds environmentally safe and user friendly because they are used at very low concentrations. Interestingly, there has been an increase in the number of commercial products containing mixed-halogen compounds. The extrapolation of the current trend indicates that an increase in the number of fluorine-substituted agrochemicals throughout the twenty-first century is to be expected. QSAR (quantitative structure-activity relationship) studies have shown that fluorinated benzyl moieties with fragments such as $CHF_2O–$ or $CF_3O–$ are very active; therefore, the synthesis of compounds containing these fragments is a primary goal of modern agrochemistry.[19]

Because of the importance of heterocycles and halogens in the development of new agrochemicals and as well as our interest in the chemistry of triazoles[20-23] and in the preparation of bioactive compounds that can be used as new active ingredients to control weeds,[24-27] our group synthesized novel 1,2,3-triazoles bearing halogenated benzyl moieties, and then, evaluated their phytotoxic activities.

Experimental

Materials and methods

All of the solvents used were purified by distillation. Commercially available benzyl alcohol, 4-fluorobenzyl alcohol, 4-chlorobenzyl alcohol, 4-bromobenzyl alcohol, 4-iodobenzyl alcohol, 3,4-difluorobenzyl alcohol, 4-(trifluoromethyl)benzyl alcohol, 4-(trifluoromethoxy) benzyl alcohol, 5-bromo-2-chlorobenzyl alcohol, 2,4,6-trichlorobenzyl alcohol, pent-4-yn-1-ol, prop-2-yn-1-ol, triethylamine, methanesulfonyl chloride, sodium ascorbate, sodium azide and copper(II) sulfate were purchased from Aldrich (USA) and utilized without further purification. The ^1H and ^{13}C nuclear magnetic resonance (NMR) spectra were recorded on a Bruker Avance DPX 200 spectrometer at 200 MHz using $CDCl_3$ as the solvent and TMS (tetramethylsilane) as the internal standard, unless otherwise stated. The NMR data are presented as follows: chemical shift, δ in ppm, multiplicity, number of protons, proton assignments and *J* in Hz. Multiplicities are indicated by the following abbreviations: s (singlet), d (doublet), dd (double doublet), t (triplet), m (multiplet), qn (quintet) and brs (broad signal). Mass spectra were recorded on a Shimadzu GC MS-QP5050A instrument using direct insertion along with the electrospray ionization method and a quadrupole analyzer. Infrared spectra were recorded on a Spectra One Perkin-Elmer spectrophotometer, fitted with a Paragon ATR accessory. Melting points were determined using an MQAPF-301 melting point apparatus (Microquimica, Brazil) and are uncorrected. The progress of the reactions was monitored by thin layer chromatography (TLC). Column chromatography was performed over silica gel (60-230 mesh).

Synthesis

4-Fluorobenzyl methanesulfonate (**2b**)

To a 50 mL round bottom flask, 4-fluorobenzyl alcohol (126 mg, 1 mmol), dichloromethane (5 mL) and

triethylamine (280 μL, 2.0 mmol) were added, and the mixture was cooled to −50 °C. Subsequently, methanesulfonyl chloride (120 μL, 1.4 mmol) was added to the flask, and the mixture was stirred vigorously. The reaction was complete after 30 min. After completion, the organic layer was washed with 1% aqueous HCl (15 mL) followed by saturated aqueous $NaHCO_3$ (5 mL), dried over Na_2SO_4, and concentrated under reduced pressure. This procedure afforded compound **2b** in a 95% yield (193 mg, 0.95 mmol).

Sulfonates **2a**, **2c**-**2j** (Figure 1) and **6** (Figure 2) were synthesized in yields ranging from 77 to 100% using a procedure similar to that described for compound **2b**. The spectroscopic data for these compounds are available in the Supplementary Information (SI) section.

1-(Azidomethyl)-4-fluorobenzene (**3b**)

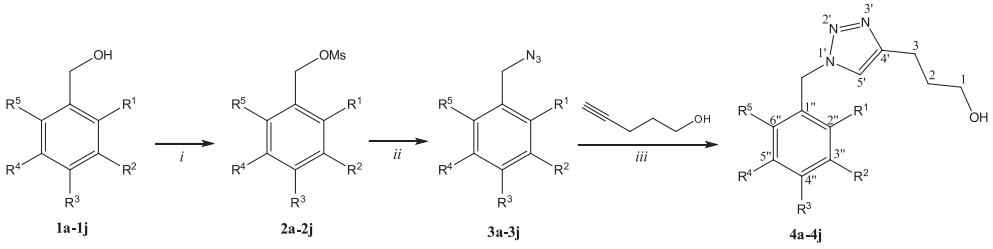
Mesylated compound **2b** (157 mg, 0.77 mmol) was added to a 50 mL round bottom flask containing 5 mL of DMSO (dimethyl sulfoxide) and 200 mg (3.1 mmol) of sodium azide. The reaction mixture was stirred at room temperature for 15 h. After this period of time, 15 mL of dichloromethane were added to the flask. The resulting organic layer was washed with 15 mL of saturated aqueous NaCl solution. After separation, the organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure to afford compound **3b** in a 91% yield (106 mg).

Azides **3a**, **3c**-**3j** (Figure 1) and **7** (Figure 2) were synthesized in yields ranging from 72 to 99% using a procedure similar to that described for compound **3b**. The spectroscopic data of the azides are available in the SI section.

3-[1'-(4"-Fluorobenzyl)-1',2',3'-triazol-4'-yl]propan-1-ol (**4b**)

A total of 93 mg (0.62 mmol) of the azide derivative **3b** was added to a 10 mL round bottom flask containing 1 mL of dichloromethane, 1 mL of water, 30.7 mg (0.12 mmol, 20 mol%) of $CuSO_4.5H_2O$, 48.8 mg (0.24 mmol, 40 mol%) of sodium ascorbate and 55 μL of pent-4-yn-1-ol. The resulting reaction mixture was vigorously stirred at room temperature for 24 h. Subsequently, the mixture was extracted with 15 mL of CH_2Cl_2, and the resulting material obtained after solvent removal was purified by silica gel column chromatography. The product was eluted with 100 mL of dichloromethane, 100 mL of dichloromethane/ethyl acetate (1:1 v/v), 100 mL of ethyl acetate and 100 mL of ethyl acetate/methanol (9:1 v/v). The procedure described afforded compound **4b** with a 71% yield (103 mg, 0.44 mmol).

Compounds **4a**, **4c**-**4j** (yield ranging from 44 to 90%), **5a** (87% yield), **5b** (49% yield) and **8** (87% yield) were



	Mesylate		Azide		1,2,3-Triazole	
	Compound	Yield / %	Compound	Yield / %	Compound	Yield / %
$R^1 = R^2 = R^3 = R^4 = R^5 = H$	**2a**	100	**3a**	85	**4a**	79
$R^1 = R^2 = R^4 = R^5 = H$, $R^3 = F$	**2b**	95	**3b**	91	**4b**	71
$R^1 = R^2 = R^4 = R^5 = H$, $R^3 = Cl$	**2c**	91	**3c**	93	**4c**	73
$R^1 = R^2 = R^4 = R^5 = H$, $R^3 = Br$	**2d**	99	**3d**	96	**4d**	55
$R^1 = R^2 = R^4 = R^5 = H$, $R^3 = I$	**2e**	90	**3e**	85	**4e**	90
$R^1 = R^2 = R^4 = R^5 = H$, $R^3 = OCF_3$	**2f**	100	**3f**	99	**4f**	44
$R^1 = R^2 = R^4 = R^5 = H$, $R^3 = CF_3$	**2g**	77	**3g**	81	**4g**	80
$R^1 = R^4 = R^5 = H$, $R^2 = R^3 = Br$	**2h**	93	**3h**	72	**4h**	74
$R^1 = Cl$, $R^2 = R^3 = R^5 = H$, $R^4 = Br$	**2i**	98	**3i**	92	**4i**	64
$R^1 = R^3 = R^5 = Cl$, $R^2 = R^4 = H$	**2j**	99	**3j**	92	**4j**	67

Figure 1. Preparation of compounds **4a**-**4j**. Reagents and conditions: (*i*) MsCl, Et_3N, CH_2Cl_2, −50 ºC, 30 min; (*ii*) NaN_3, DMSO, r.t., 15 h; and (*iii*) pent-4-yn-1-ol, NaAsc (40 mol%), $CuSO_4.5H_2O$ (20 mol%), CH_2Cl_2/H_2O (50% v/v), r.t., 24 h.

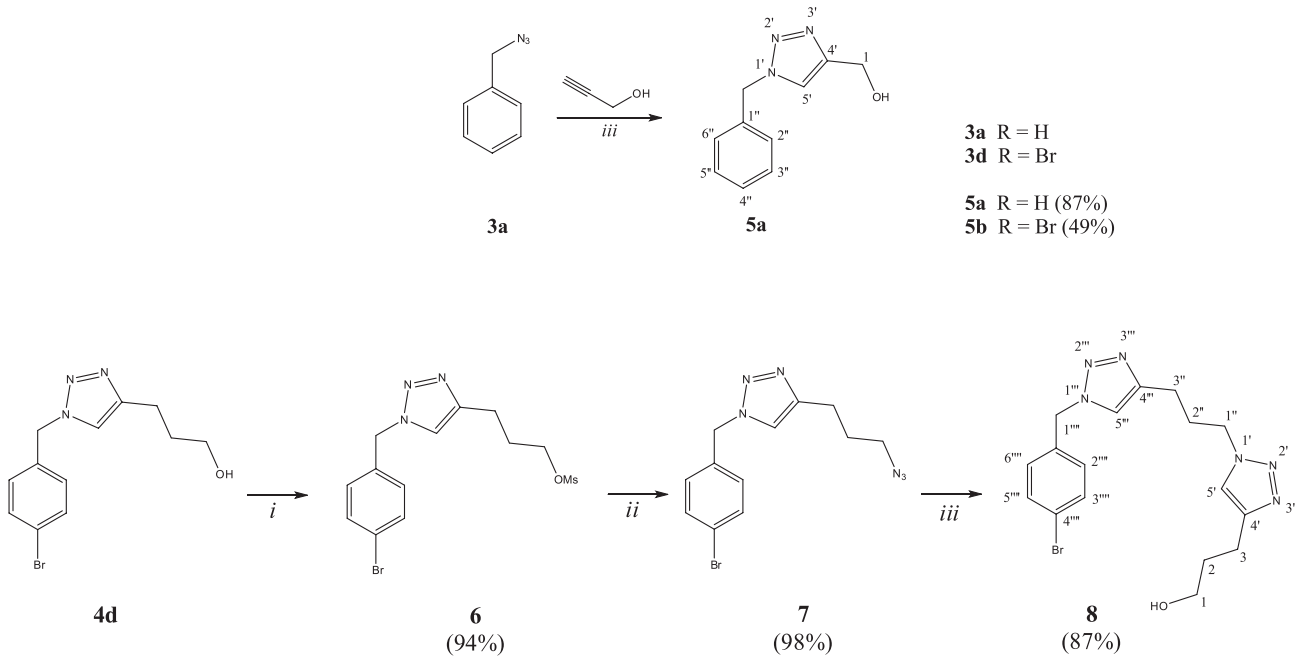


Figure 2. Preparation of compounds **5a**, **5b** and **8**. Reagents and conditions: (*i*) MsCl, Et_3N, CH_2Cl_2, –50 ºC, 30 min; (*ii*) NaN_3, DMSO, r.t., 15 h; and (*iii*) pent-4-yn-1-ol, NaAsc (40 mol%), $CuSO_4.5H_2O$ (20 mol%), CH_2Cl_2/H_2O (50% v/v), r.t., 24 h. Yields are given in parentheses.

prepared from the corresponding azides using a procedure similar to that described for compound **4b**. The compounds were purified by column chromatography using a typical eluotropic sequence (dichloromethane, ethyl acetate and methanol), and the yields are presented in Figures 1 and 2. The structures of the triazoles are supported by the spectroscopic and spectrometric data available in the SI section.

Biological assays

The evaluation of the phytotoxic activities of compounds **4a**-**4j**, **5a**, **5b** and **8** was performed using an adaptation of the methodology described by Macías *et al.*[28] The bioassays used Petri dishes (90 mm diameter) with one sheet of Whatman No. 1 filter paper as a substrate. The target species were *Allium cepa* (onion) as the model monocotyledonous plant and *Lactuca sativa* (lettuce) and *Cucumis sativus* (cucumber) as the dicotyledonous species. The plants were germinated and grown in aqueous solutions. The compounds to be assayed were dissolved in DMSO at different concentrations, and these solutions were diluted with distilled water, so that, the desired test concentrations (10^{-4}, 10^{-6} and 10^{-8} mol L^{-1}) were obtained. This procedure facilitated the dissolution of the assayed compounds. Twenty five commercial seeds of each target species were placed in each Petri dish. The appropriate treatment, or the negative control (aqueous solution containing DMSO but no test compound), was added (10 mL) to each Petri dish. Three replicates were used for each target species. After the addition of the seeds and the aqueous solutions (10 mL), the Petri dishes were sealed with parafilm to create closed-system models. The seeds were incubated at 25 °C in a controlled environment growth chamber in the absence of light. The bioassays lasted 5 days for the dicot model species and 7 days for the monocot model species (onion). After the growth period, the plants were frozen at −10 °C for 24 h to prevent growth during the measurement process. This process facilitated the handling of the plants and allowed the more accurate measurement of radicle elongation. The shoot and root lengths of each radicle were measured manually to the nearest millimeter, using a ruler. The germination rate was obtained by the direct counting of the number of seeds that germinated, but not necessarily developed. Seeds were considered to have germinated if a radicle protruded at least 1 mm. All treatments were replicated three times in a completely randomized design. The percent inhibition or stimulation of radicle growth (root and shoot) was calculated in relation to the radicle growth of the negative control using the following equation:

$$G\,(\%) = \left(\frac{S - C}{C}\right) 100 \qquad (1)$$

where S corresponds to the average value of germination or the radicle (root and shoot) length and C corresponds to the average growth of the negative control. When using this

equation, stimulatory effects correspond to values above the graphic base line, and inhibitory effects correspond to values below this line (Figures 3-6). Errors were estimated using the derivative method. *L. sativa*, *C. sativus* and *A. cepa* seeds (TOPSEED brand) were purchased from Agristar do Brasil, Petropólis city, Rio de Janeiro State, Brazil. The commercial herbicide 2,4-D (2,4-dichlorophenoxyacetic acid) was used as positive control.

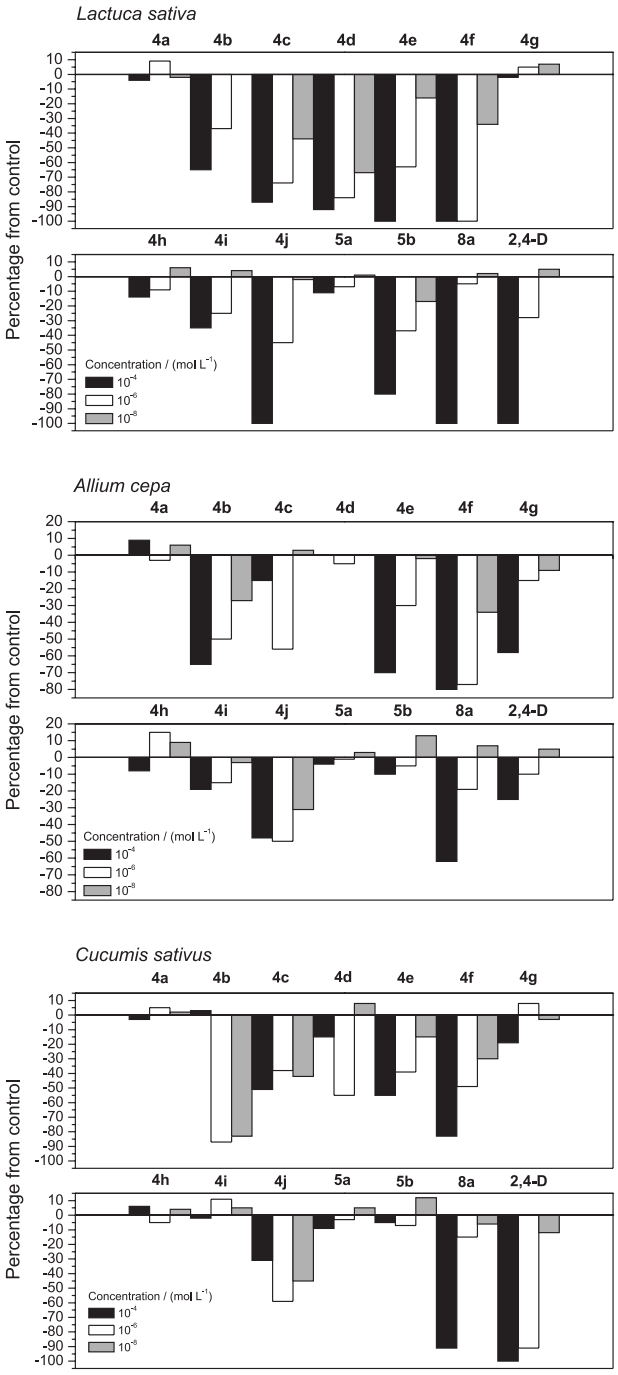


Figure 3. Effects of compounds **4a**-**4j**, **5a**, **5b**, **8** and 2,4-D on the germination of *L. sativa*, *A. cepa*, and *C. sativus*, relative to the negative control.

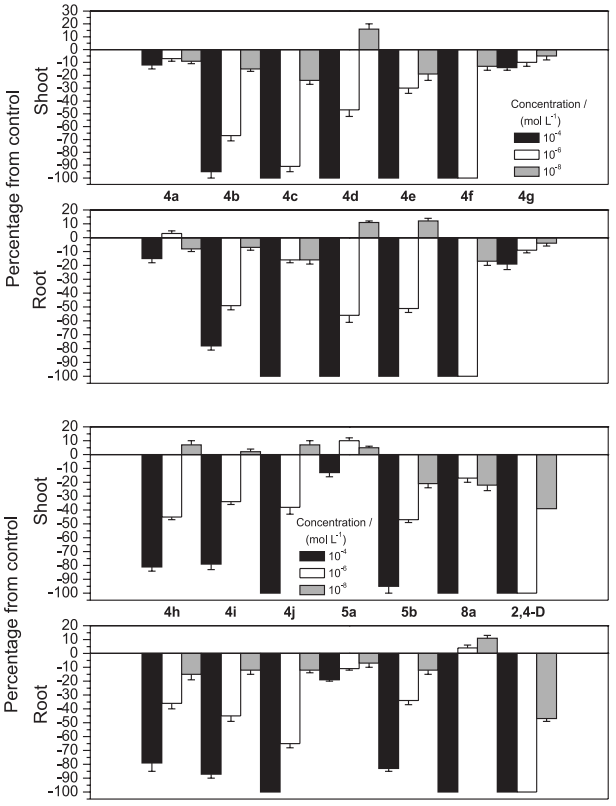


Figure 4. Effects of compounds **4a**-**4j**, **5a**, **5b**, **8** and 2,4-D on the shoot and root lengths of *L. sativa*, relative to the negative control.

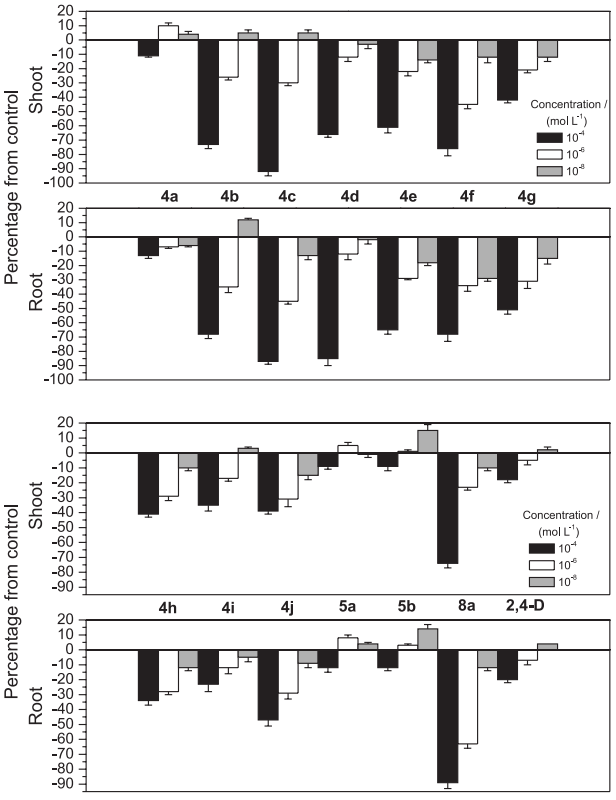


Figure 5. Effects of compounds **4a**-**4j**, **5a**, **5b**, **8** and 2,4-D on the shoot and root lengths of *A. cepa*, relative to the negative control

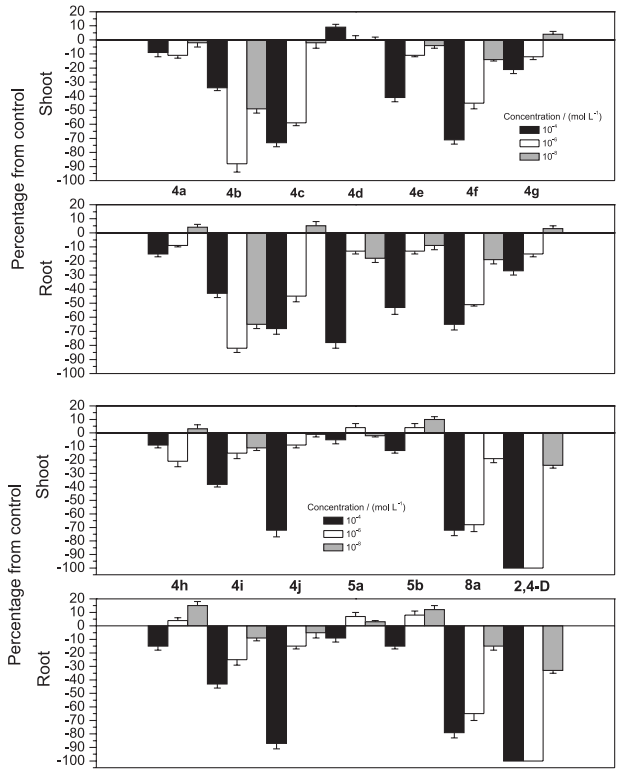


Figure 6. Effects of compounds **4a**-**4j**, **5a**, **5b**, **8** and 2,4-D on the shoot and root lengths of *C. sativus*, relative to negative the control.

Cluster analysis

The cluster analysis was performed using Statistica® software (version 5.0), and the clusters were generated on the basis of the activity parameters for the three concentrations. Data were statistically analyzed using Welch's test, with significance set at 0.01 and 0.05. Results are expressed as percentage differences to control. Zero represents control, positive values represent stimulation of the studied parameter, and negative values represent inhibition. Once the germination and growth data were acquired, cluster analysis was used to group compounds with similar phytotoxicity behaviors and associate them with their molecular structure. Complete linkage was used as an amalgamation rule and the distance measurement was based on squared euclidean distances, given by the equation below:

$$d(x,y) = \sum (x_i - y_i)^2 \quad (2)$$

where $d(x,y)$ is the squared euclidean distance (i-dimensional), i represents the number of variables, and x and y the observed values. Regression analyses were performed using the Microsoft Excel 2010 (Microsoft Corporation, USA) and Graph Pad Prism® (version 4).[29]

Results and Discussion

Synthesis of triazole derivatives

The compounds **4a**-**4j** were prepared in three steps as outlined in Figure 1.

Commercially available benzylic alcohols were initially converted into their corresponding mesylates **2a**-**2j** by the straightforward reaction with methanesulfonyl chloride.[30] Nucleophilic substitution reactions between sodium azide and the mesylates yielded azides **3a**-**3j**.[31] Cu-catalyzed azide-alkyne cycloaddition (CuAAC), a leading example of the click chemistry approach,[32] between compounds **3a**-**3j** and pent-4-yn-1-ol afforded the chemicals **4a**-**4j** in yields ranging from 44 to 90% (Figure 1). The click reaction is a very reliable method to prepare 1,2,3-triazoles. The conditions of the click reactions used to prepare **4a**-**4j** were similar to those reported by Iehl *et al.*,[33] who have shown that the reaction time should be approximately 2 h. However, in the present study, the product formation was not observed within less than 20 h. The best results were observed for a period of 24 h at room temperature. It is necessary caution when manipulating any kind of azide, organic and inorganic, due to the risk of explosion caused by mechanic shock, electrical spark as well as heating.[34,35]

A second set of compounds, **5a**, **5b** and **8**, was prepared as depicted in Figure 2.

Chemicals **5a** and **5b** were obtained, respectively, from azides **3a** and **3d** and were synthesized to evaluate the influence of shortening the triazole side chain on the compound biological activity (compound **5a** compared with **4a** and compound **5b** compared with **4d**). The aim of the preparation of triazole **8** was to evaluate the impact of the presence of two triazole rings on the phytotoxic activity (*vide infra*).

Evaluation of the phytotoxic activity of triazoles

The strategies employed for the discovery of new chemicals to control weeds (and other agrochemicals) are similar to those used for the discovery of bioactive compounds in the pharmaceutical industry and involve the assessment of the activity of extracts and pure compounds in a given biological system.[36] Preliminary laboratory bioassays need to be fast, economical and relevant to the system in question, in addition to being useful to establish the potential activity of a pure compound or an extract. Bioassays should also be followed by studies in greenhouses and fields to determine whether the initial observations are reproducible on a larger

scale.[37,38] The most widely used bioassay to evaluate the phytotoxicity of a synthesized compound is one that monitors the germination and growth of plants (root and shoot) of given species such as *Lactuca sativa* (lettuce), *Raphanus sativus* L. (radish), *Lepidium sativum* (cress), *Cucumis sativus* (cucumber) and *Allium cepa* (onion), among other species, primarily due to their high sensitivity and fast germination rates. Weeds, which would be the ideal candidates for this initial assessment to identify potential herbicides, are used for testing only after activity is observed against the species mentioned above. This is because weeds generally have low germination rates.[31,39]

The effects of 1,2,3-triazoles **4a**-**4j**, **5a**, **5b** and **8** on the germination and radicle growth (shoot and root) of the species *Lactuca sativa* (lettuce), *Cucumis sativus* (cucumber) and *Allium cepa* (onion) were evaluated at three different concentrations (10^{-4}, 10^{-6} and 10^{-8} mol L^{-1}) and the results are shown in Figures 3-6.

With respect to germination (Figure 3), the most pronounced effects were observed on *L. sativa*. Compounds **4b**-**4f**, **4j**, **5b** and **8** significantly inhibited the germination relative to the negative control. At 10^{-4} mol L^{-1}, triazoles **4d**, **4e**, **4f**, **4j** and **8** exhibited inhibitory activities greater than 90%. Regarding *A. cepa*, compound **4f** was the most efficient in inhibiting germination (ca. −80% at 10^{-4} and 10^{-6} mol L^{-1}). Some compounds were more effective inhibiting the germination than the positive control (2,4-D), especially on lettuce and onion.

For *C. sativus*, fluorinated **4f** strongly inhibited the germination at the highest concentration (−85%). The germination of *C. sativus* was also strongly inhibited by **4b** at 10^{-6} and 10^{-8} mol L^{-1}, and **8** at 10^{-4} mol L^{-1} (Figure 3).

The effects of compounds **4a**-**4j**, **5a**, **5b** and **8** on the radicle growth (shoot and root) of the evaluated species are presented in Figures 4-6. As general trend, the triazole derivatives had inhibitory effects on the tested species. In addition, the halogenated compounds had, in general, superior effects relative to those of their non-halogenated counterparts (compounds **4a** and **5a**), demonstrating the beneficial effects of the presence of halogen atoms on the biological activity of the evaluated compounds.

The growth of the shoots and roots of *L. sativa* was strongly inhibited (higher than 60%) by the majority of the test compounds at a concentration of 10^{-4} mol L^{-1}, as shown in Figure 4. Exceptions to this generalization were the derivatives **4a**, **4g** and **5a**, which can be considered inactive against this species. Interestingly, although the derivative **4f**, which contains a trifluoromethoxyphenyl group, inhibited the radicle growth of *L. sativa* by 100% at the highest concentration and retained this effect at 10^{-6} mol L^{-1}, the derivative **4g**, which contains a trifluoromethylphenyl group, was almost inactive. Only compound **4f** was as phytotoxic as the positive control, 2,4-D at the concentration of 10^{-4} and 10^{-6} mol L^{-1}.

The effects of the triazole derivatives on *A. cepa* are outlined in Figure 5. The growth of the shoots and roots of this monocotyledonous species was strongly inhibited by compounds **4b**-**4f** and **8** at 10^{-4} mol L^{-1}, with compound **8** being the most potent (−89%). With the exception of compounds **4a**, **5a** and **5b**, all of the synthesized compounds presented superior phytotoxic effects in the development of the onion root and shoot than the positive control, 2,4-D. This is not a surprisingly result since this commercial agrochemical is used as a selective herbicide controlling dicot species and preserving monocot ones.

The effects of compounds **4a**-**4j**, **5a**, **5b** and **8** on *C. sativus* were also evaluated (Figure 6). In this experiment, the most phytotoxic compound was the triazole **4b**, which caused almost 90% inhibition of the shoot development and 84% inhibition of the root development at a concentration of 10^{-6} mol L^{-1}. None of the synthesized compound was as phytotoxic as the positive control on the cucumber root and shoot development.

According to Macías *et al.*,[28,29] the compounds tested in standard bioassays tend to have inhibitory effect only at the highest concentrations; at lower concentrations, their inhibitory effect usually decreases and may sometimes reach a stimulatory effect. This growth stimulation at lower concentrations was observed for compounds **4d**, **4e**, **4h**, **4j**, **5a** and **8**, on the lettuce (Figure 4); for compounds **4b**, **4c**, **4i**, **5a** and **5b**, on the onion (Figure 5); and **4g**, **4h**, **5a** and **5b**, against cucumber (Figure 6).

Cluster analysis

To obtain a better understanding of the relationship between biological activity and the structural features of the evaluated compounds, cluster analysis was performed on the basis of biological activity values (root and shoot growth) for all of the concentrations tested (Figure 7).

Based on activity, the assayed compounds can be divided into three groups (G1, G2 and G3). The composition of each group was as follows: G1 is composed of chemicals with low activity, **4a**, **5a** and **4g**; G2 contains compounds **4h**, **4i**, and **5b**; and G3 contains compounds **4b**-**4f**, **4j** and **8**.

The compounds belonging to G1 do not possess a halogen directly attached to the benzyl ring. The compounds in G2 contain triazoles with two halogen atoms attached to the aromatic ring and one triazole with a shorter aliphatic side chain (**5b**). With the exception of **4f**, the compounds in G3 are derivatives containing one

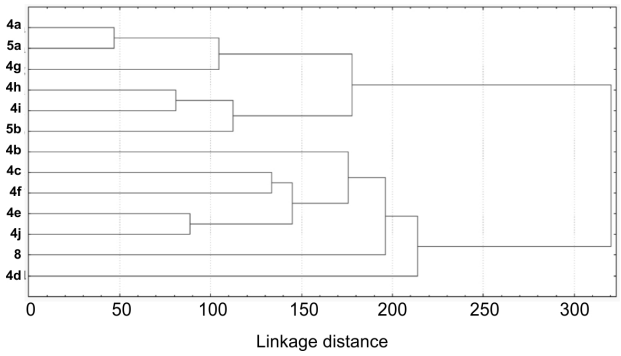


Figure 7. Cluster analysis of compounds **4a**-**4j**, **5a**, **5b** and **8** according to their biological profiles.

halogen attached to position 4'', or to position 4'''', in case of **8** (see Figures 1 and 2 for numbering), with compound **4b**, which has a fluorine substituent, being the most potent among all of the synthesized triazoles. Compound **8**, which has a bromine attached to position 4'''', was found to be one of the most active compounds. This result points to the fact that the presence of a second triazole ring possibly has a favorable impact in terms of biological activity. Further studies will be carried out to prove such hypothesis.

Conclusions

In summary, thirteen 1,2,3-triazoles were synthesized, purified and fully characterized. The conditions employed were satisfactory, and thus, the formation of side products was not observed. The phytotoxicity of these compounds was investigated against two dicotyledonous species, *Lactuca sativa* and *Cucumis sativus*, and one monocotyledonous species, *Allium cepa*. The products exhibited predominantly inhibitory activity on the target species, and they were more selective for the dicotyledonous species, in particular for lettuce. Some of them were more phytotoxic than the positive control (2,4-D), especially on lettuce and onion. The comparison of the activities of products **4b**-**4j** with the activities of compound **4a**, which was synthesized to evaluate the influence of the absence of a halogen substituent on phytotoxic activity, revealed that the halogenated products were much more active. The same relationship was observed when comparing the phytotoxicity of derivatives **5a** and **5b**. These products were synthesized to evaluate the influence of shortening the chain length on phytotoxic activity. Again, it was confirmed that the presence of a halogen substituent on product **5b** was necessary for appreciable phytotoxic activity. It was also noted an appreciable similarity between the phytotoxic activities of compounds **4b** and **5b**, and thus, confirming that the length of the triazole side chain does not have an important effect on phytotoxic activity.

The most significant results were observed for the fluorinated derivatives (**4b** and **4f**), and the chlorinated derivatives (**4c** and **4j**), and at some concentrations, these compounds inhibited lettuce germination by up to 100%. These compounds also inhibited the growth of shoots and roots by approximately 60% for all target species at a concentration of 10^{-4} mol L^{-1}.

Considering these results, these compounds seem worthy of further investigation and could be exploited for the design of new ones endowed with herbicidal activity. Synthetic efforts are under way in our laboratories to prepare and biologically evaluate new derivatives. The results will be submitted soon.

Supplementary Information

A list of all spectroscopic data is available free of charge at http://jbcs.sbq.org.br as a PDF file.

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Supplementary Information

Synthesis and Phytotoxic Activity of 1,2,3-Triazole Derivatives

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Benzyl methanesulfonate (**2a**)

Colorless liquid; yield 100%; IR (ATR) ν/cm^{-1} 3064, 3031, 2866, 1496, 1454, 1357, 1172, 1071, 1025, 967, 934, 912, 734; ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.85 (s, 3H, –C$\underline{H}_3$), 5.17 (s, 2H, benzylic), 7.03-7.38 (m, 5H, H2/H3/H4/H5/H6); ^{13}C NMR (50 MHz, $CDCl_3$) δ 37.6 (–$\underline{C}H_3$), 71.5 (benzylic), 128.5 (C4), 128.6 (C2/C6), 129.00 (C3/C5), 133.3 (C1).

4-Fluorobenzyl methanesulfonate (**2b**)

Colorless liquid; yield 95%; IR (ATR) ν/cm^{-1} 3017, 2931, 2855, 1508, 1156, 1061, 1043, 1010, 824, 779; ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.88 (s, 3H, –C$\underline{H}_3$), 5.11 (s, 2H, benzylic), 6.05-7.03 (m, 2H, H3/H5), 7.28-7.36 (m, 2H, H2/H6); ^{13}C NMR (50 MHz, $CDCl_3$) δ 37.6 (–$\underline{C}H_3$), 70.8 (benzylic), 115.6 (d, *J* 21.7 Hz, C3/C5), 129.4 (d, *J* 2.9 Hz, C1), 130.8 (d, *J* 8.5 Hz, C2/C6), 162.9 (d, *J* 246.4 Hz, C4).

4-Chlorobenzyl methanesulfonate (**2c**)

Yellow solid; m.p. 124 °C; yield 91%; IR (ATR) ν/cm^{-1} 1488, 1340, 1087, 1009, 805, 782; ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.94 (s, 3H, –C$\underline{H}_3$), 5.17 (s, 2H, benzylic), 7.33 (m, 4H, H2/H3/H5/H6); ^{13}C NMR (50 MHz, $CDCl_3$) δ 37.9 (–$\underline{C}H_3$), 70.6 (benzylic), 128.9 (C3/C5), 130.0 (C2/C6), 132.0 (C1), 135.0 (C4).

4-Bromobenzyl methanesulfonate (**2d**)

White solid; m.p. 153 °C; yield 99%; IR (ATR) ν/cm^{-1} 2838, 1485, 1342, 1122, 1067, 1033, 960, 793; ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.95 (s, 3H, –C$\underline{H}_3$), 5.17 (s, 2H, benzylic), 7.28 (d, 2H, *J* 8.4 Hz, H2/H6), 7.51 (d, 2H, *J* 8.4 Hz, H3/H5); ^{13}C NMR (50 MHz, $CDCl_3$) δ 38.2 (–$\underline{C}H_3$), 70.6 (benzylic), 123.5 (C4), 130.4 (C2/C6), 132.0 (C3/C5), 132.6 (C1).

4-Iodobenzyl methanesulfonate (**2e**)

Yellow solid; m.p. 181 °C; yield 90%; IR (ATR) ν/cm^{-1} 3039, 3018, 2941, 1485, 1402, 1333, 1167, 1057, 1009, 994, 950, 801, 753; ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.94 (s, 3H, –C$\underline{H}_3$), 5.14 (s, 2H, benzylic), 7.13 (d, 2H, *J* 8.0 Hz, H2/H6), 7.70 (d, 2H, *J* 8.0 Hz, H3/H5); ^{13}C NMR (50 MHz, $CDCl_3$) δ 38.2 (–$\underline{C}H_3$), 70.6 (benzylic), 95.4 (C4), 130.5 (C2/C6), 133.1 (C1), 137.2 (C3/C5).

4-(Trifluoromethoxy)benzyl methanesulfonate (**2f**)

Colorless liquid; yield 100%; IR (ATR) ν/cm^{-1} 2863, 1509, 1361, 1151, 1251, 1196, 1213, 1107, 1018, 961, 920, 813, 711; ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.94 (s, 3H, –C$\underline{H}_3$), 5.19 (s, 2H, benzylic), 7.20 (d, 2H, *J* 8.0 Hz, H3/H5), 7.42 (d, 2H, *J* 8.0 Hz, H2/H6); ^{13}C NMR (50 MHz, $CDCl_3$) δ 37.9 (–$\underline{C}H_3$), 70.4 (benzylic), 120.4 (q, *J* 256 Hz, –$\underline{C}F_3$), 121.2 (C3/C5), 130.4 (C2/C6), 132.4 (C1), 149.7 (C4).

4-(Trifluoromethyl)benzyl methanesulfonate (**2g**)

Colorless liquid; yield 77%; IR (ATR) ν/cm^{-1} 3039, 3018, 2941, 1333, 1109, 1020, 922, 801, 753; ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.97 (s, 3H, –C$\underline{H}_3$), 5.23 (s, 2H, benzylic), 7.47 (d, 2H, *J* 8.2 Hz, H2/H6), 7.57 (d, 2H, *J* 8.2 Hz, H3/H5); ^{13}C NMR (50 MHz, $CDCl_3$) δ 37.4 (–$\underline{C}H_3$), 70.2 (benzylic), 123.9 (q, *J* 270 Hz, –$\underline{C}F_3$), 125.2 (C3/C5), 128.7 (C2/C6), 131.3 (q, *J* 17 Hz, C4), 137.8 (C1).

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3,4-(Difluoro)benzyl methanesulfonate (**2h**)

Yellow liquid; yield 93%; IR (ATR) ν/cm^{-1} 3029, 2943, 1520, 1438, 1350, 1170, 1213, 1118, 1055, 952, 926, 812, 779, 735; ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.95 (s, 3H, –C$\underline{H}_3$), 5.10 (s, 2H, benzylic), 7.07-7.23 (m, 2H, H2/H5/H6); ^{13}C NMR (50 MHz, $CDCl_3$) δ 37.6 (–$\underline{C}H_3$), 70.0 (benzylic), 117.1-118.0 (m, C2/C5), 124.9-125.1 (m, C6), 130.7-130.9 (m, C1), 150.0 (dd, *J* 15 Hz, 250 Hz, C4), 150.4 (dd, *J* 15 Hz, 250 Hz, C3).

5-Bromo-2-chlorobenzyl methanesulfonate (**2i**)

Yellow solid; m.p. 207 °C; yield 98%; IR (ATR) ν/cm^{-1} 2849, 1447, 1398, 1346, 1169, 1043, 972, 806, 761; ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.03 (s, 3H, –C$\underline{H}_3$), 5.18 (s, 2H, benzylic), 7.17 (d, 1H, *J* 8.0 Hz, H3), 7.34 (d, 1H, *J* 8.0 Hz, H4), 7.53 (s, 1H, H6); ^{13}C NMR (50 MHz, $CDCl_3$) δ 37.5 (–$\underline{C}H_3$), 67.5 (benzylic), 120.4 (C5), 130.9 (C4), 132.2 (C2), 132.6 (C3), 133.1 (C6), 133.3 (C1).

2,4,6-Trichlorobenzyl methanesulfonate (**2j**)

Yellow solid; m.p. 242 °C; yield 99%; IR (ATR) ν/cm^{-1} 1484, 1447, 1346, 1305, 1044, 858; ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.03 (s, 3H, –C$\underline{H}_3$), 5.32 (s, 2H, benzylic), 7.26 (s, 2H, H3/H5); ^{13}C NMR (50 MHz, $CDCl_3$) δ 37.3 (–$\underline{C}H_3$), 65.3 (benzylic), 127.3 (C1), 128.5 (C3/C5), 136.5 (C4), 137.5 (C2/C6).

3-[1'-(4"-Bromobenzyl)-1',2',3'-triazol-4'-yl]propyl methanesulfonate (**6**)

White solid; 231 °C; yield 94%; IR (ATR) ν/cm^{-1} 3123, 2942, 1489, 1409, 1336, 1069, 1041, 773; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.89 (t, 2H, *J* 5.8 Hz, H3), 2.95 (s, 3H, –C$\underline{H}_3$), 3.65 (qn, 2H, *J* 5.8 Hz, H2), 4.14 (t, 2H, *J* 5.8 Hz, H1), 5.35 (s, 2H, benzylic), 7.04 (d, 2H, *J* 7.8 Hz, H2"/H6"), 7.35 (d, 2H, *J* 7.8 Hz, H3"/H5"), 7.39 (s, 1H, H5'); ^{13}C NMR (50 MHz, $CDCl_3$) δ 21.9 (C3), 28.3 (C2), 37.0 (–$\underline{C}H_3$), 53.1 (benzylic), 69.1 (C1), 121.6 (C5'), 122.4 (C4"), 129.6 (C2"/C6"), 131.9 (C3"/C5"), 133.8 (C1"), 146.2 (C4').

1-(Azidomethyl)benzene (**3a**)

Colorless liquid; yield 85%; IR (ATR) ν/cm^{-1} 2925, 2872, 2092, 1588, 1484, 1059, 1006, 786; ^{1}H NMR (200 MHz, $CDCl_3$) δ 4.26 (s, 2H, benzylic), 7.09-7.26 (m, 5H, H2/H3/H4/H5/H6); ^{13}C NMR (50 MHz, $CDCl_3$) δ 54.8 (benzylic), 128.4 (C4), 128.3 (C3/C5), 128.9 (C2/C6), 135.5 (C1).

1-(Azidomethyl)-4-fluorobenzene (**3b**)

Colorless liquid; yield 91%; IR (ATR) ν/cm^{-1} 2931, 2880, 2093, 1601, 1508, 1221; ^{1}H NMR (200 MHz, $CDCl_3$) δ 4.30 (s, 2H, benzylic), 7.09-7.30 (m, 4H, H2/H3/H5/H6); ^{13}C NMR (50 MHz, $CDCl_3$) δ 53.9 (benzylic), 115.6 (d, *J* 21.5 Hz, C3/C5), 130.0 (d, *J* 8.2 Hz, C2/C6), 131.4 (d, *J* 2.5 Hz, C1), 162.6 (d, *J* 245.0 Hz, C4).

1-(Azidomethyl)-4-chlorobenzene (**3c**)

Yellow liquid; yield 93%; IR (ATR) ν/cm^{-1} 2930, 2877, 2092, 1491, 1090, 838, 796; ^{1}H NMR (200 MHz, $CDCl_3$) δ 4.30 (s, 2H, benzylic), 7.24 (d, 2H, *J* 7.5 Hz, H2/H6), 7.36 (d, 2H, *J* 7.5 Hz, H3/H5); ^{13}C NMR (50 MHz, $CDCl_3$) δ 53.9 (benzylic), 128.9 (C3/C5), 129.4 (C2/C6), 134.0 (C1), 134.1 (C4).

1-(Azidomethyl)-4-bromobenzene (**3d**)

Yellow liquid; yield 96%; IR (ATR) ν/cm^{-1} 3046, 2929, 2875, 2091, 1592, 1488, 1070, 1011, 834, 791; ^{1}H NMR (200 MHz, $CDCl_3$) δ 4.30 (s, 2H, benzylic), 7.18 (d, 2H, *J* 8.4 Hz, H2/H6), 7.51 (d, 2H, *J* 8.4 Hz, H3/H5); ^{13}C NMR (50 MHz, $CDCl_3$) δ 53.9 (benzylic), 122.2 (C4), 129.7 (C2/C6), 131.9 (C3/C5), 134.4 (C1).

1-(Azidomethyl)-4-iodobenzene (**3e**)

Yellow liquid; yield 85%; IR (ATR) ν/cm^{-1} ν/cm^{-1} 3026, 2931, 2912, 2857, 2120, 1585, 1481, 1058, 1007, 830, 796; ^{1}H NMR (200 MHz, $CDCl_3$) δ 4.29 (s, 2H, benzylic), 7.06 (d, 2H, *J* 8.2 Hz, H2/H6), 7.71 (d, 2H, *J* 8.2 Hz, H3/H5); ^{13}C NMR (50 MHz, $CDCl_3$) δ 54.2 (benzylic), 94.1 (C4), 130.0 (C2/C6), 135.1 (C1), 137.9 (C3/C5).

1-(Azidomethyl)-4-(trifluoromethoxy)benzene (**3f**)

Yellow liquid; yield 99%; IR (ATR) ν/cm^{-1} 2098, 1509, 1251, 1195, 1213, 1153, 1107, 1018, 1107, 1019, 847, 777; ^{1}H NMR (200 MHz, $CDCl_3$) δ 4.36 (s, 2H, benzylic), 7.25 (d, 2H, *J* 8.4 Hz, H3/H5), 7.36 (d, 2H, *J* 8.4 Hz, H2/H6); ^{13}C NMR (50 MHz, $CDCl_3$) δ 54.0 (benzylic), 120.7 (q, *J* 256 Hz, –$\underline{C}F_3$), 121.4 (C3/C5), 129.7 (C2/C6), 134.4 (C1), 149.2 (C4).

1-(Azidomethyl)-4-(trifluoromethyl)benzene (**3g**)

Colorless liquid; yield 81%; IR (ATR) ν/cm^{-1} 2091, 1488, 1245, 1196, 1070, 1011, 1107, 834, 791; ^{1}H NMR (200 MHz, $CDCl_3$) δ 4.37 (s, 2H, benzylic), 7.40 (d, 2H, *J* 8.0 Hz, H2/H6), 7.61 (d, 2H, *J* 8.0 Hz, H3/H5); ^{13}C NMR (50 MHz, $CDCl_3$) δ 53.8 (benzylic), 124.1 (q, *J* 270 Hz, –$\underline{C}F_3$), 125.5 (C3/C5), 128.1 (C2/C6), 130.2 (q, *J* 32 Hz, C4), 139.6 (C1).

1-(Azidomethyl)-3,4-(difluoro)benzene (**3h**)

Yellow liquid; yield 72%; IR (ATR) ν/cm^{-1} 2095, 1517, 1435, 1251, 1195, 1286, 1210, 1116, 779; ^{1}H NMR

(200 MHz, $CDCl_3$) δ 4.31 (s, 2H, benzylic), 7.00-7.23 (m, 2H, H2/H5/H6); ^{13}C NMR (50 MHz, $CDCl_3$) δ 53.6 (benzylic), 116.9-117.8 (m, C2/C5), 124.2-124.3 (m, C6), 132.6-132.8 (m, C1), 149.7 (m, C4), 152.5 (m, C3).

1-(Azidomethyl)-5-bromo-2-chlorobenzene (**3i**)

Yellow liquid; yield 92%; IR (ATR) ν/cm^{-1} 2097, 1459, 1391, 1043, 811; ^1H NMR (200 MHz, $CDCl_3$) δ 5.18 (s, 2H, benzylic), 7.21 (d, 1H, *J* 8.2 Hz, H3), 7.36 (d, 1H, *J* 8.2 Hz, H4), 7.53 (s, 1H, H6); ^{13}C NMR (50 MHz, $CDCl_3$) δ 51.6 (benzylic), 120.7 (C5), 130.9 (C4), 131.2 (C2), 132.3 (C3), 132.9 (C6), 135.4 (C1).

1-(Azidomethyl)-2,4,6-(trichloro)benzene (**3j**)

Yellow solid; m.p. 215 °C; yield 92%; IR (ATR) ν/cm^{-1} 2094, 1579, 1548, 1071, 853; ^1H NMR (200 MHz, $CDCl_3$) δ 4.60 (s, 2H, benzylic), 7.34 (s, 2H, H3/H5); ^{13}C NMR (50 MHz, $CDCl_3$) δ 51.6 (benzylic), 128.4 (C1), 130.3 (C3/C5), 135.3 (C4), 136.8 (C2/C6).

1-(Azido)-3-[1'-(4"-bromobenzyl)-1',2',3'-triazol-4'-yl]propyl (**7**)

White solid; m.p. 242 °C; yield 98%; IR (ATR) ν/cm^{-1} 3193, 3114, 2921, 2857, 2096, 1483, 1398, 1056, 1006, 797; ^1H NMR (200 MHz, $CDCl_3$) δ 1.80 (qn, 2H, *J* 5.6 Hz, H2), 2.69 (t, 2H, *J* 5.6 Hz, H3), 3.23 (t, 2H, *J* 5.8 Hz, H1), 5.36 (s, 2H, benzylic), 7.04 (d, 2H, *J* 7.8 Hz, H2''/H6''), 7.35 (d, 2H, *J* 7.8 Hz, H3''/H5''), 7.20 (s, 1H, H5'); ^{13}C NMR (50 MHz, $CDCl_3$) δ 22.7 (C3), 28.5 (C2), 50.7 (benzylic), 53.4 (C1), 121.1 (C5'), 122.8 (C4''), 129.7 (C2''/C6''), 132.3 (C3''/C5''), 134.0 (C1''), 147.3 (C4').

3-(1'-Benzyl-1',2',3'-triazol-4'-yl)propan-1-ol (**4a**)

White solid; m.p. 215-220 °C; yield 79%; IR (ATR) ν/cm^{-1} 3293, 2972, 2880, 1379, 1087, 1045; ^1H NMR (200 MHz, $CDCl_3$) δ 1.85 (brs, 2H, H2), 2.74 (brs, 2H, H3), 3.62 (brs, 2H, H1), 5.42 (s, 2H, benzylic), 7.18-7.25 (brs, 4H, H2''/H3''/H5''/H6''), 7.29 (s, 1H, H5'); ^{13}C NMR (50 MHz, $CDCl_3$) δ 22.0 (C3), 32.0 (C2), 54.0 (benzylic), 61.3 (C1), 121.2 (C5'), 128.0 (C2''/C6''), 128.6 (C4''), 129.1 (C3''/C5''), 134.8 (C1''), 148.4 (C4'); HRMS (ESI) *m/z* 218.1258 ([M + H], $C_{12}H_{16}N_3O$), 240.1080 ([M + Na], $C_{12}H_{15}N_3ONa$).

3-[1'-(4"-Fluorobenzyl)-1',2',3'-triazol-4'-yl]propan-1-ol (**4b**)

White solid; m.p. 216-217 °C; yield 71%; IR (ATR) ν/cm^{-1} 3274, 3112, 3062, 2943, 2873, 1549, 1419, 1091, 1052, 821, 786; ^1H NMR (200 MHz, $CDCl_3$) δ 1.89 (qn, 2H, *J* 6 Hz, H2), 2.77 (t, 2H, *J* 6 Hz, H3), 3.65 (t, 2H, *J* 6 Hz, H1), 4.64 (brs, 1H, –O<u>H</u>), 5.45 (s, 2H, benzylic), 6.95-7.04 (m, 2H, H3''/H5''), 7.21-7.28 (m, 2H, H2''/H6''), 7.42 (s, 1H, H5'); ^{13}C NMR (50 MHz, $CDCl_3$) δ 21.7 (C3), 31.9 (C2), 52.9 (benzylic), 60.9 (C1), 115.6 (d, $J_{C\text{-}F}$ 22 Hz, C3''/C5''), 121.0 (C5'), 127.6 (d, $J_{C\text{-}F}$ 8 Hz, C2''/C6''), 130.7 (d, $J_{C\text{-}F}$ 3 Hz, C1''), 147.9 (C4'), 162.4 (d, $J_{C\text{-}F}$ 246 Hz, C4''); HRMS (ESI) *m/z* 236.1165 ([M + H], $C_{12}H_{15}FN_3O$), 258.0982 ([M + Na], $C_{12}H_{14}FN_3ONa$).

3-[1'-(4"-Chlorobenzyl)-1',2',3'-triazol-4'-yl]propan-1-ol (**4c**)

White solid; 230-235 °C; yield 73%; IR (ATR) ν/cm^{-1} 3297, 3115, 3063, 2938, 2866, 1492, 1434, 1033, 907, 761; ^1H NMR (200 MHz, $CDCl_3$) δ 1.72 (qn, 2H, *J* 6.4 Hz, H2), 2.61 (t, 2H, *J* 6.4 Hz, H3), 3.48 (t, 2H, *J* 6.4 Hz, H1), 4.35 (brs, 1H, –O<u>H</u>), 5.27 (s, 2H, benzylic), 7.02 (d, 2H, *J* 8.3 Hz, H2''/H6''), 7.11 (d, 2H, *J* 8.3 Hz, H3''/H5''), 7.31 (s, 1H, H5'); ^{13}C NMR (50 MHz, $CDCl_3$) δ 21.9 (C3), 31.9 (C2), 53.2 (benzylic), 61.1 (C1), 121.2 (C5'), 128.7 (C3''/C5''), 129.1 (C2''/C6''), 133.3 (C1''), 134.0 (C4''), 147.8 (C4'); HRMS (ESI) *m/z* 252.0875 ([M + H], $C_{12}H_{15}ClN_3O$), 274.0700 ([M + Na], $C_{12}H_{14}ClN_3ONa$).

3-[1'-(4"-Bromobenzyl)-1',2',3'-triazol-4'-yl]propan-1-ol (**4d**)

White solid; 237-240 °C; yield 55%; IR (ATR) ν/cm^{-1} 3278, 3133, 2942, 1489, 1430, 1046, 1011, 795, 764; ^1H NMR (200 MHz, $CDCl_3$) δ 1.88 (qn, 2H, *J* 6.8 Hz, H2), 2.77 (t, 2H, *J* 6.8 Hz, H3), 3.64 (t, 2H, *J* 6.8 Hz, H1), 4.48 (brs, 1H, –O<u>H</u>), 5.42 (s, 2H, benzylic), 7.11 (d, 2H, *J* 8.3 Hz, H2''/H6''), 7.35 (s, 1H, H5'), 7.45 (d, 2H, *J* 8.3 Hz, H3''/H5''); ^{13}C NMR (50 MHz, $CDCl_3$) δ 21.9 (C3), 31.9 (C2), 53.2 (benzylic), 61.1 (C1), 121.2 (C5'), 122.6 (C4''), 129.6 (C2''/C6''), 132.1 (C3''/C5''), 133.9 (C1''), 148.2 (C4'); HRMS (ESI) *m/z* 296.0389 ([M + H], $C_{12}H_{15}BrN_3O$), 318.0218 ([M + Na], $C_{12}H_{14}BrN_3ONa$.

3-[1'-(4"-Iodobenzyl)-1',2',3'-triazol-4'-yl]propan-1-ol (**4e**)

White solid; m.p. 238-241 °C; yield 90%; IR (ATR) ν/cm^{-1} 3253, 3113, 3062, 2944, 2925, 1548, 1484, 1051, 1008, 758; ^1H NMR (200 MHz, $CDCl_3$) δ 1.87 (brs, 2H, H2), 2.76 (brs, 2H, H3), 3.63 (brs, 2H, H1), 4.34 (brs, 1H, –O<u>H</u>), 5.40 (s, 2H, benzylic), 6.97 (d, 2H, *J* 7.9 Hz, H2''/H6''), 7.37 (s, 1H, H5'), 7.62 (d, 2H, *J* 7.9 Hz, H3''/H5''); ^{13}C NMR (50 MHz, $CDCl_3$) δ 21.8 (C3), 31.8 (C2), 53.1 (benzylic), 60.9 (C1), 94.6 (C4''), 121.2 (C5'), 129.6 (C2''/C6''), 134.4 (C1''), 137.8 (C3''/C5''), 148.0 (C4'); HRMS (ESI) *m/z* 344.0239 ([M + H], $C_{12}H_{15}IN_3O$), 366.0070 ([M + Na], $C_{12}H_{14}IN_3ONa$).

3-[1'-(4"-Trifluoromethoxybenzyl)-1',2',3'-triazol-4'-yl] propan-1-ol (**4f**)

White solid; m.p. 215-220 °C; yield 44%; IR (ATR) ν/cm^{-1} 3292, 3119, 3072, 2946, 2931, 1511, 1232, 1199, 1214, 1162, 1046, 1021, 842, 777; ^1H NMR (200 MHz,

$CDCl_3$) δ 1.90 (brs, 2H, H2), 2.80 (brs, 2H, H3), 3.66 (brs, 2H, H1), 3.98 (brs, 1H, –O<u>H</u>), 5.49 (s, 2H, benzylic), 7.19 (d, 2H, *J* 8.0 Hz, H3''/H5''), 7.30 (d, 2H, *J* 8.0 Hz, H2''/H6''), 7.39 (brs, 1H, H5'); ^{13}C NMR (50 MHz, $CDCl_3$) δ 22.00 (C3), 32.04 (C2), 53.08 (benzylic), 61.3 (C1), 120.4 (q, $J_{C\text{-}F}$ 256.0 Hz, –O<u>C</u>F_3), 121.3 (C3''/C5''), 121.3 (C4' or C4''), 129.5 (C2''/C6''), 133.7 (C5'), 149.1 (C1''), 149.1 (C4' or C4''); HRMS (ESI) *m/z* 302.1084 ([M + H], $C_{13}H_{15}F_3N_3O_2$), 324.0911 ([M + Na], $C_{13}H_{14}F_3N_3O_2Na$).

3-[1'-(4"-Trifluoromethylbenzyl)-1',2',3'-triazol-4'-yl]propan-1-ol (**4g**)

White solid; m.p. 216-220 °C; yield 80%; IR (ATR) ν/cm^{-1} 3342, 2946, 1219, 1163, 1066, 1018, 822, 779; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.87 (qn, 2H, *J* 6.4 Hz, H2), 2.78 (t, 2H, *J* 6.4 Hz, H3), 3.15 (brs, 1H, –O<u>H</u>), 3.64 (t, 2H, *J* 6.4 Hz, H1), 5.53 (s, 2H, benzylic), 7.31 (brs, 1H, H5'), 7.32 (d, 2H, *J* 7.9 Hz, H2''/H6''), 7.58 (d, 2H, *J* 7.9 Hz, H3''/H5''); ^{13}C NMR (50 MHz, $CDCl_3$) δ 22.0 (C3), 32.1 (C2), 53.5 (benzylic), 61.5 (C1), 121.4 (C5'), 123.7 (q, $J_{C\text{-}F}$ 247.0 Hz, –<u>C</u>F_3), 126.1 (C3''/C5''), 130.9 (q, *J* 31 Hz, C4''), 128.4 (C2''/C6''), 138.9 (C1''), 148.5 (C4'); HRMS (ESI) *m/z* 286.1124 ([M + H], $C_{13}H_{15}F_3N_3O$), 308.0982 ([M + Na], $C_{13}H_{14}F_3N_3ONa$).

3-[1'-(3",4"-Difluorobenzyl)-1',2',3'-triazol-4'-yl]propan-1-ol (**4h**)

Yellow solid; m.p. 215-219 °C; yield 74%; IR (ATR) ν/cm^{-1} 3358, 2936, 1519, 1286, 1214, 1114, 1054, 781; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.88 (qn, 2H, *J* 7.0 Hz, H2), 2.77 (t, 2H, *J* 7.0 Hz, H3), 3.67 (t, 2H, *J* 7.0 Hz, H1), 5.40 (s, 2H, benzylic), 6.95-7.11 (m, 2H, H2''/H5''/H6''), 7.49 (s, 1H, H5'); ^{13}C NMR (50 MHz, $CDCl_3$) δ 21.7 (C3), 31.85 (C2), 52.9 (benzylic), 60.9 (C1), 117.0 (d, $J_{C\text{-}F}$ 17 Hz, C2''), 117.9 (d, $J_{C\text{-}F}$ 17 Hz, C5''), 120.8 (C4'), 124.0 (dd, $J_{C\text{-}F}$ 4 Hz, 7 Hz, C6''), 123.1 (C5'), 131.7 (t, $J_{C\text{-}F}$ 5 Hz, C1''), 150.0 (dd, $J_{C\text{-}F}$ 250 Hz, 15 Hz, C4''), 150.5 (dd, $J_{C\text{-}F}$ 250 Hz, 14 Hz, C3''); HRMS (ESI) *m/z* 254.1066 ([M + H], $C_{12}H_{14}F_2N_3O$), 276.0902 ([M + Na], $C_{12}H_{13}F_2N_3ONa$).

3-[1'-(5"-Bromo-2"-chlorobenzyl)-1',2',3'-triazol-4'-yl]propan-1-ol (**4i**)

White solid; m.p. 237-239 °C; yield 64%; IR (ATR) ν/cm^{-1} 3363, 3124, 2950, 1472, 1045, 807; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.81 (brs, 2H, H2), 2.71 (brs, 2H, H3), 3.57 (brs, 2H, H1), 4.08 (brs, 1H, –O<u>H</u>), 5.43 (s, 2H, benzylic), 7.10-7.35 (m, 2H, H3''/H4''/H6''), 7.39 (s, 1H, H5'); ^{13}C NMR (50 MHz, $CDCl_3$) δ 21.9 (C3), 31.9 (C2), 50.6 (benzylic), 61.1 (C1), 120.9 (C5''), 131.1 (C4''), 132.6 (C3''), 132.0 (C2''), 132.9 (C6''), 134.5 (C1''), 148.1 (C4'); HRMS (ESI) *m/z* 331.9966 ([M + H], $C_{12}H_{14}BrClN_3O$), 353.9776 ([M + Na], $C_{12}H_{13}BrClN_3ONa$).

3-[1'-(2",4",6"-Trichlorobenzyl)-1',2',3'-triazol-4'-yl]propan-1-ol (**4j**)

Yellow solid; m.p. 242-246 °C; yield 67%; IR (ATR) ν/cm^{-1} 3341, 3131, 2949, 1581, 1549, 1071, 869; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.89 (brs, 2H, H2), 2.78 (brs, 2H, H3), 3.17 (brs, 1H, –O<u>H</u>), 3.67 (brs, 2H, H1), 5.76 (s, 2H, benzylic), 7.20-7.40 (m, 2H, H3''/H5''/H5'); ^{13}C NMR (50 MHz, $CDCl_3$) δ 22.1 (C3), 32.1 (C2), 48.5 (benzylic), 61.7 (C1), 121.1 (C5'), 128.8 (C3''/C5''), 128.8 (C1''), 136.3 (C4''), 137.4 (C2''/C6''), 147.7 (C4'); HRMS (ESI) *m/z* 320.0102 ([M + H], $C_{12}H_{13}Cl_3N_3O$), 341.9944 ([M + Na], $C_{12}H_{13}Cl_3N_3ONa$).

(1'-Benzyl-1',2',3'-triazol-4'-yl)methanol (**5a**)

White solid; m.p. 215-220 °C; yield 87%; IR (ATR) ν/cm^{-1} 3253, 3116, 3064, 1489, 1038, 1011; ^{1}H NMR (200 MHz, $CDCl_3$) δ 4.11 (brs, 1H, –O<u>H</u>), 4.67 (s, 2H, H1), 5.43 (s, 2H, benzylic), 7.30 (brs, 5H, H2''/H3''/H4''/H5''/H6''), 7.43 (s, 1H, H5'); ^{13}C NMR (50 MHz, $CDCl_3$) δ 54.3 (benzylic), 56.1 (C1), 122.0 (C5'), 128.2 (C2''/C6''), 128.9 (C4''), 129.2 (C3''/C5''), 134.6 (C1''), 148.4 (C4'); HRMS (ESI) *m/z* 190.0939 ([M + H], $C_{10}H_{12}N_3O$), 212.0767 ([M + Na], $C_{10}H_{11}N_3ONa$).

[1'-(4"-Bromobenzyl)-1',2',3'-triazol-4'-yl]methanol (**5b**)

White solid; m.p. 222-224 °C; yield 49%; IR (ATR) ν/cm^{-1} 3253, 3116, 3064, 1489, 1038, 1011; ^{1}H NMR (200 MHz, $CDCl_3$) δ 4.26 (brs, 1H, –O<u>H</u>), 4.65 (s, 2H, H1), 5.43 (s, 2H, benzylic), 7.11 (d, 2H, *J* 8.4 Hz, H2''/H6''), 7.42 (d, 2H, *J* 8.4 Hz, H3''/H5''), 7.63 (s, 1H, H5'); ^{13}C NMR (50 MHz, $CDCl_3$) δ 53.1 (benzylic), 55.3 (C1), 122.2 (C5'), 122.5 (C4''), 129.5 (C2''/C6''), 131.9 (C3''/C5''), 133.5 (C1''), 148.2 (C4'); HRMS (ESI) *m/z* 268.1549 ([M + H], $C_{10}H_{10}BrN_3O$).

3-(1'-{3"-[1'"-(4'"-Bromobenzyl)-1'",2'",3'"-triazol-4'"-yl]propyl}-1',2',3'-triazol-4'-yl)propan-1-ol (**8**)

White solid; m.p. 240-245 °C; yield 87%; IR (ATR) ν/cm^{-1} 3329, 3138, 3115, 2949, 2873, 1489, 1431, 1048, 1006, 796; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.87 (qn, 2H, *J* 6.8 Hz, H2), 2.15 (qn, 2H, *J* 6.8 Hz, H2''), 2.58 (t, 2H, *J* 6.8 Hz, H3''), 2.70 (t, 2H, *J* 6.8 Hz, H3), 3.58 (t, 2H, *J* 6.8 Hz, H1), 4.12 (brs, 1H, –O<u>H</u>), 4.27 (t, 2H, *J* 6.8 Hz, H1''), 5.36 (s, 2H, benzylic), 7.05 (d, 2H, *J* 7.6 Hz, H2''''/H6''''), 7.33 (d, 2H, *J* 7.6 Hz, H3''''/H5''''), 7.38 (brs, 2H, H5'/H5'''); ^{13}C NMR (50 MHz, $CDCl_3$) δ 21.9 (C3), 22.2 (C3''), 29.5 (C2''), 32.0 (C2), 49.0 (C1''), 53.2 (benzylic),

61.1 (C1), 121.5 (C5'/C5'''), 122.6 (C4''''), 129.61 (C2''''/C6''''), 132.1 (C3''''/C5''''), 133.8 (C1''''), 146.5 (C4'), 147.5 (C4'''); HRMS (ESI) *m/z* 405.1080 ([M + H], $C_{17}H_{22}BrN_6O$), 427.0853 ([M + Na], $C_{17}H_{22}BrN_6ONa$).

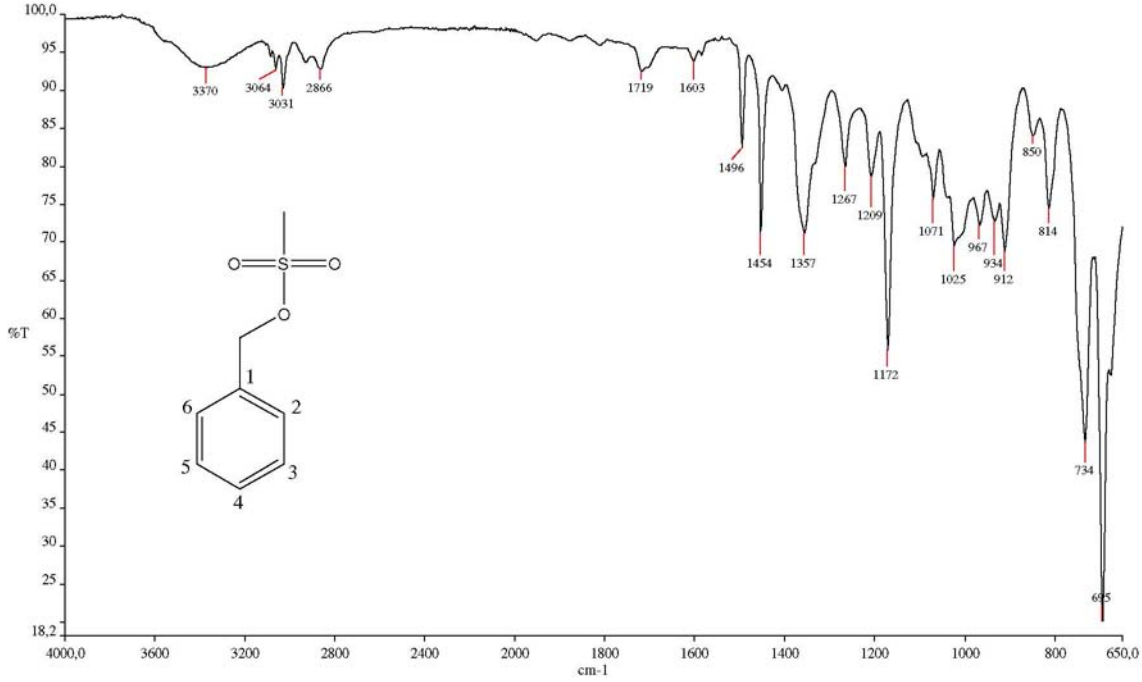

Figure S1. IR (ATR) spectrum of benzyl methanesulfonate (**2a**).

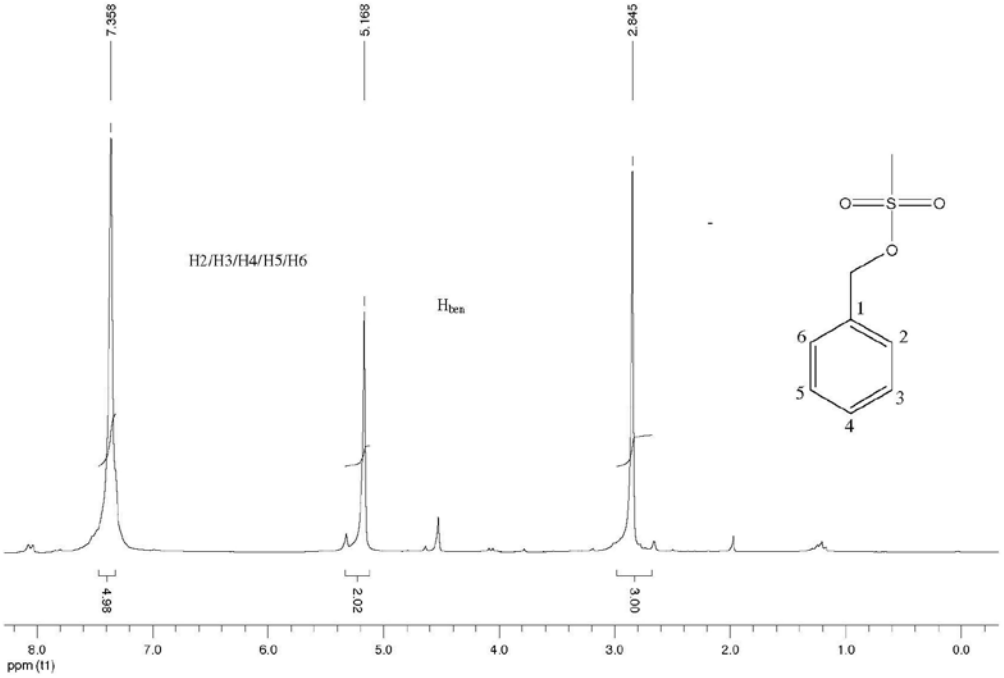

Figure S2. ^{1}H NMR spectrum (200 MHz, $CDCl_3$) of benzyl methanesulfonate (**2a**).

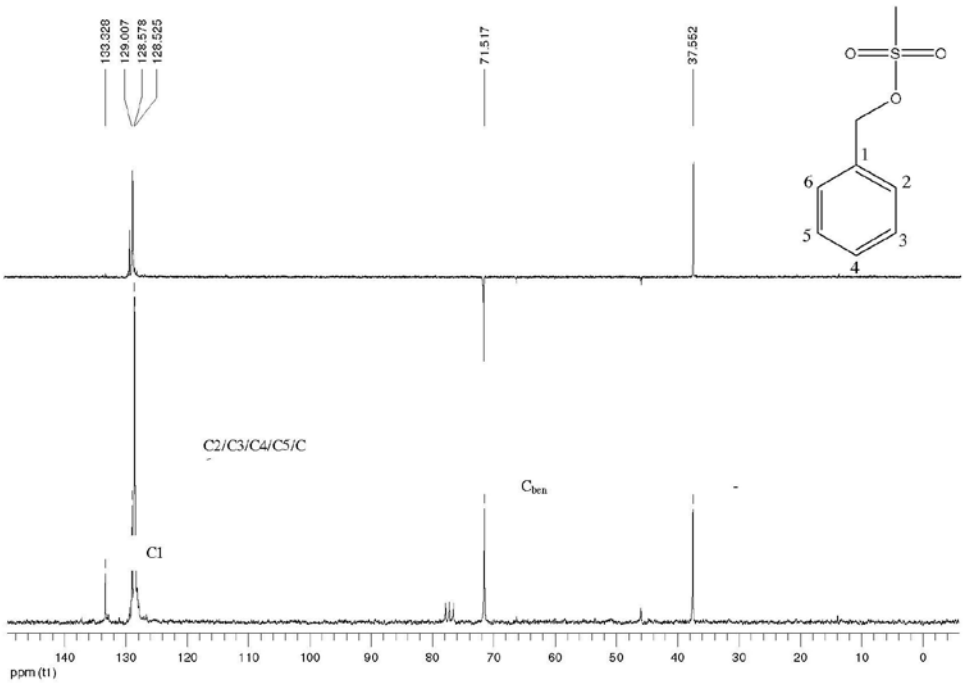

Figure S3. ^{13}C NMR and DEPT-135 spectrum (50 MHz, $CDCl_3$) of benzyl methanesulfonate (**2a**).

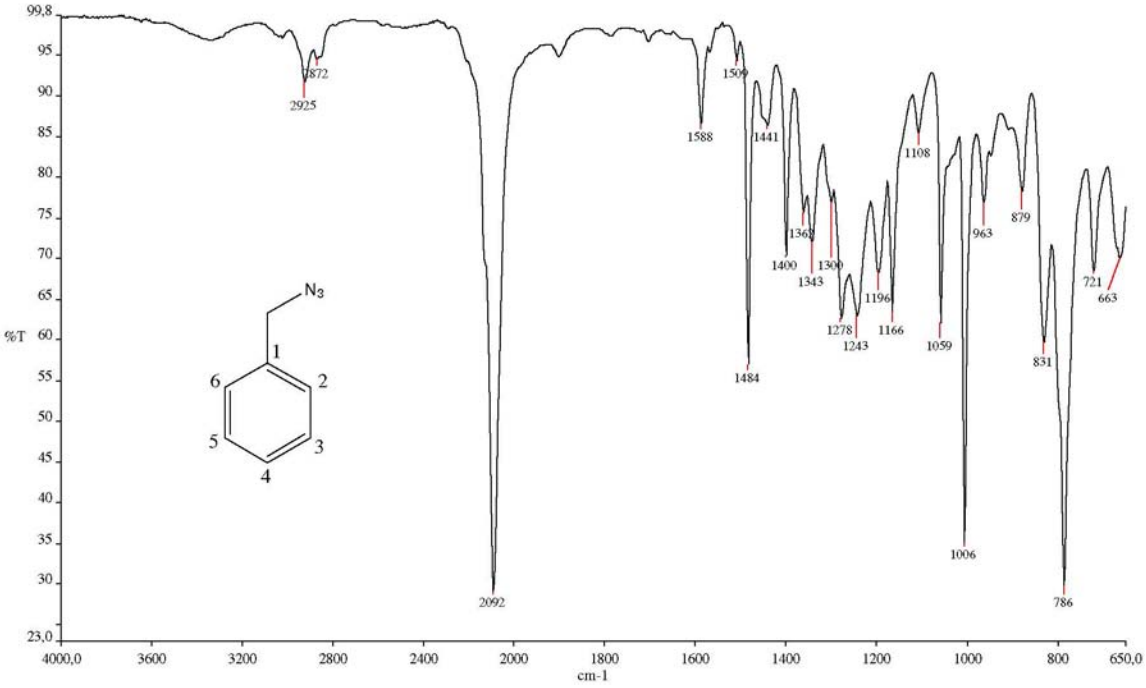

Figure S4. IR (ATR) spectrum of 1-(azidomethyl)benzene (**3a**).

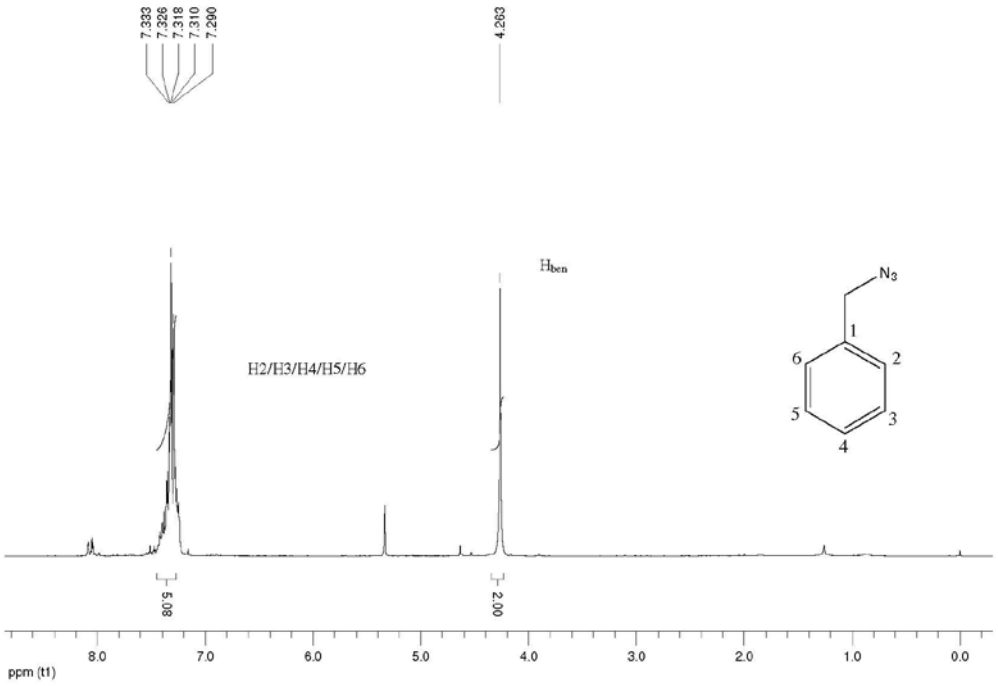

Figure S5. ^{1}H NMR spectrum (200 MHz, $CDCl_3$) of 1-(azidomethyl)benzene (**3a**).

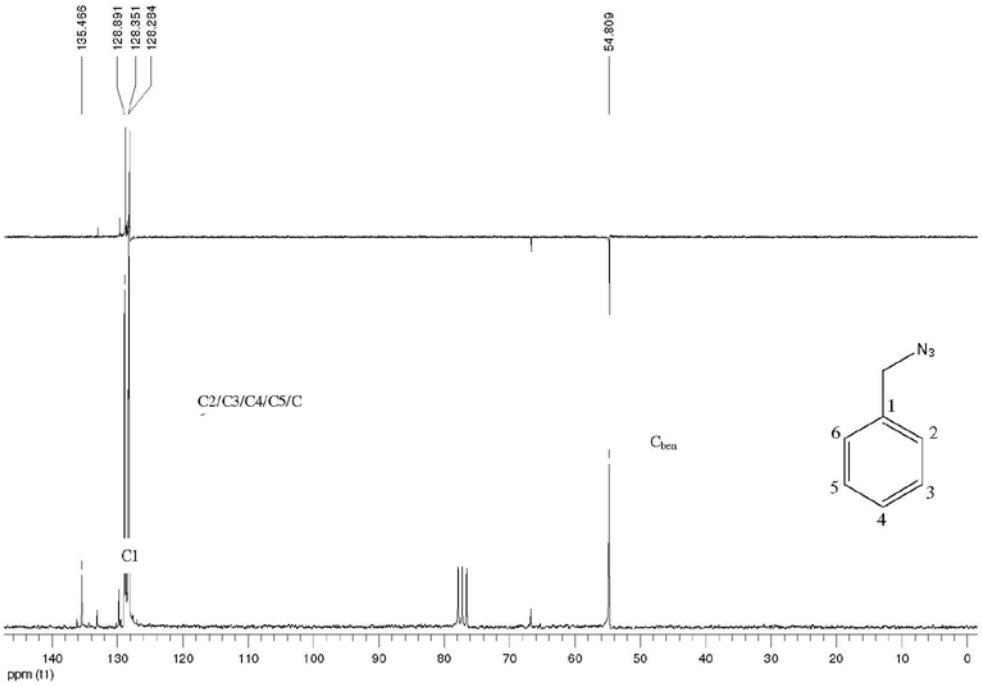

Figure S6. ^{13}C NMR and DEPT-135 spectrum (50 MHz, $CDCl_3$) of 1-(azidomethyl)benzene (**3a**).

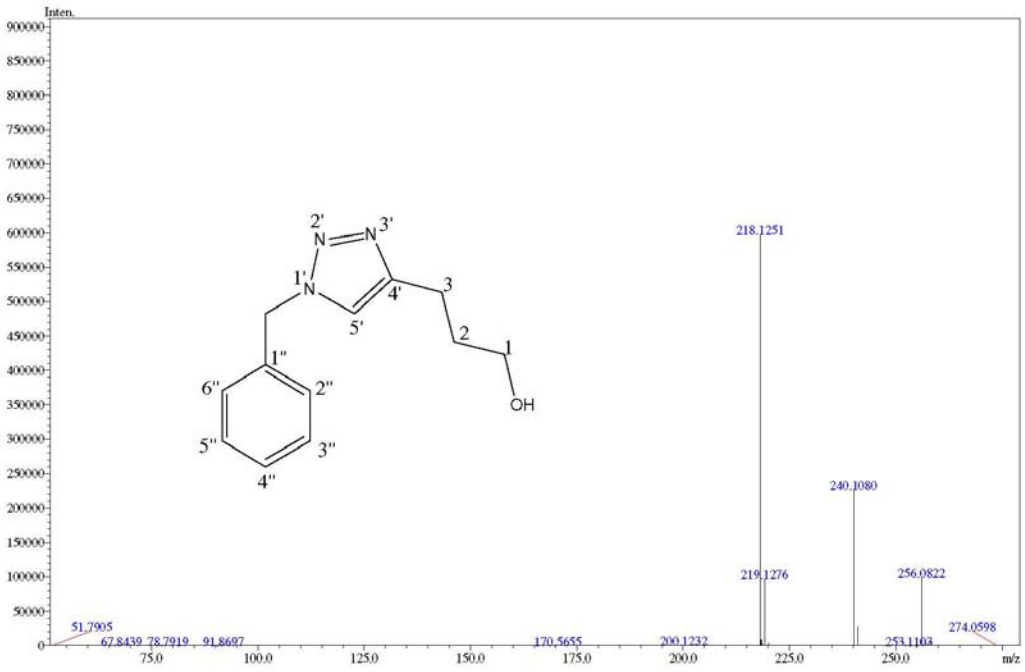

Figure S7. HRMS spectrum of 3-(1'-benzyl-1',2',3'-triazol-4'-yl)propan-1-ol (**4a**).

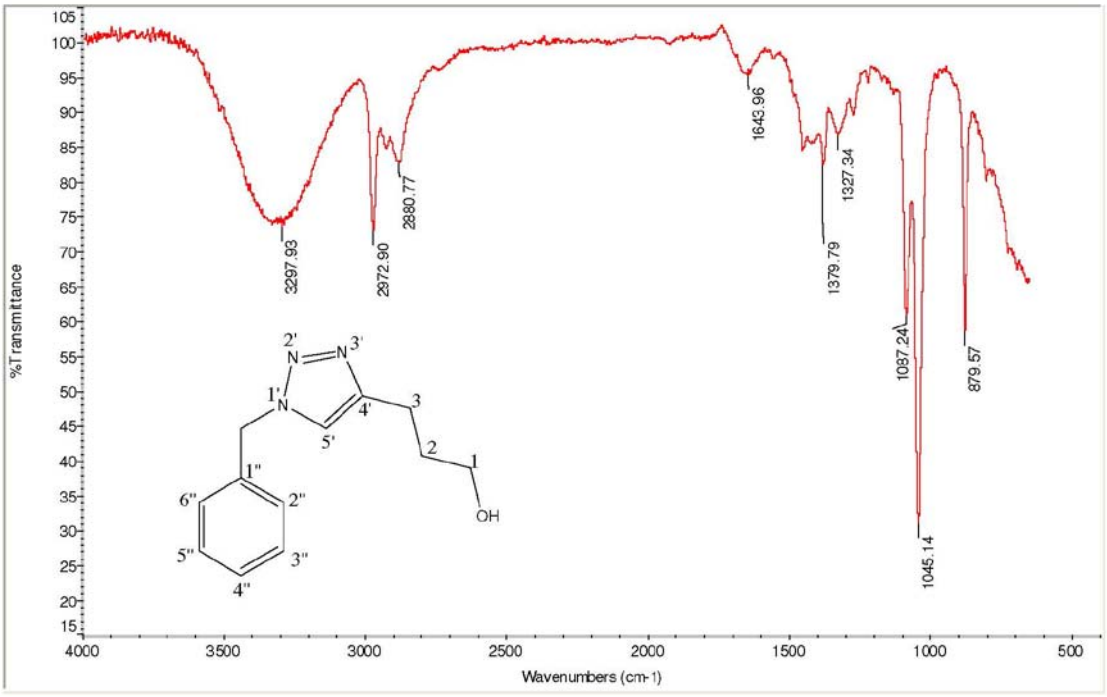

Figure S8. IR (ATR) spectrum of 3-(1'-benzyl-1',2',3'-triazol-4'-yl)propan-1-ol (**4a**).

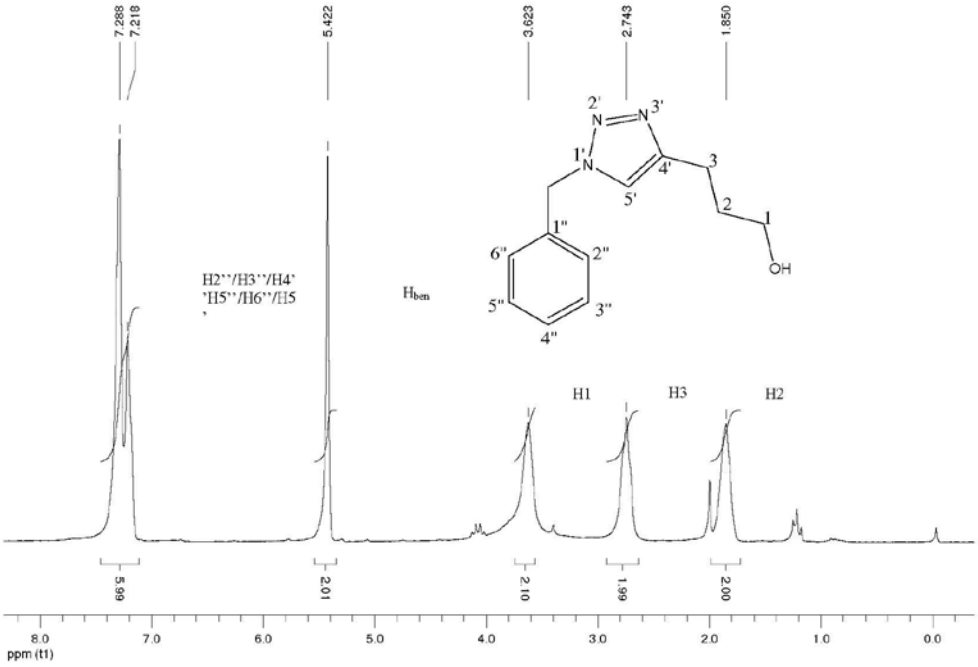

Figure S9. [1]H NMR spectrum (200 MHz, $CDCl_3$) of 3-(1'-benzyl-1',2',3'-triazol-4'-yl)propan-1-ol (**4a**).

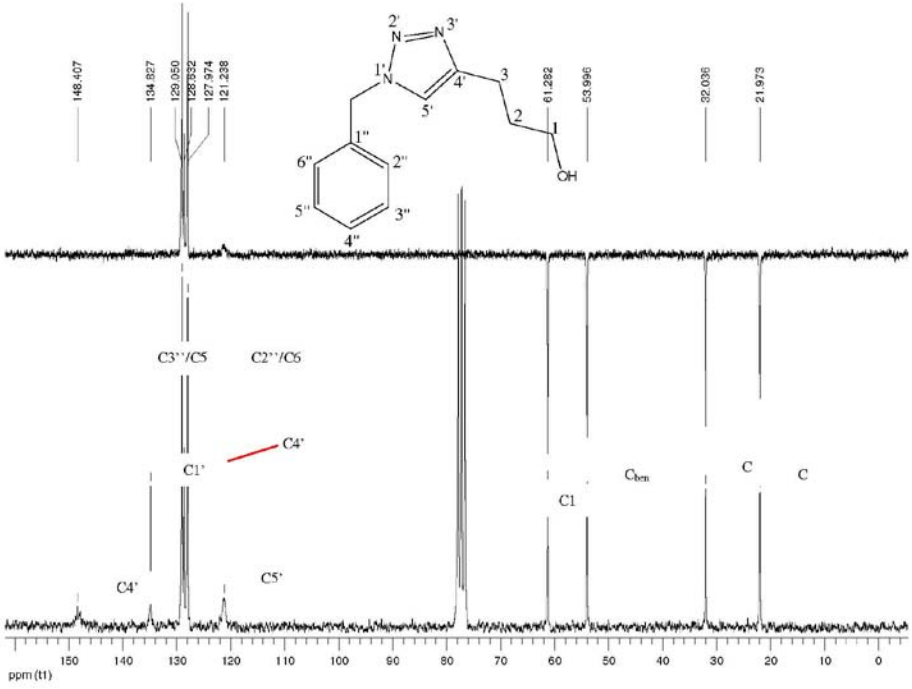

Figure S10. [13]C NMR and DEPT-135 spectrum (50 MHz, $CDCl_3$) of 3-(1'-benzyl-1',2',3'-triazol-4'-yl)propan-1-ol (**4a**).

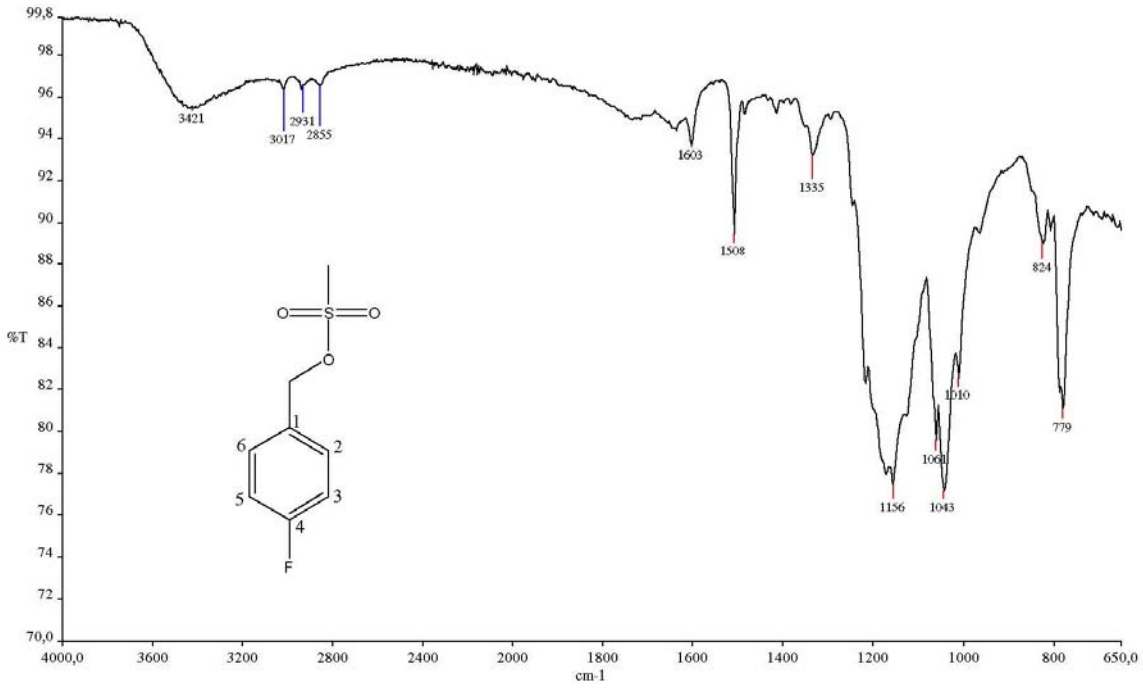

Figure S11. IR (ATR) spectrum of 4-fluorobenzyl methanesulfonate (**2b**).

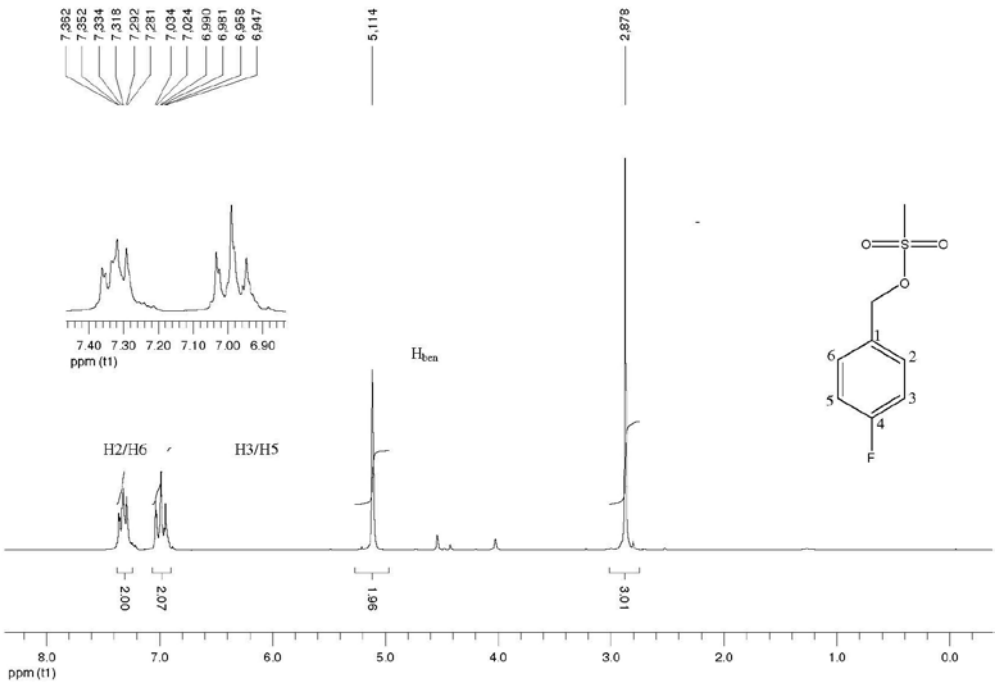

Figure S12. ^{1}H NMR spectrum (200 MHz, $CDCl_3$) of 4-fluorobenzyl methanesulfonate (**2b**).

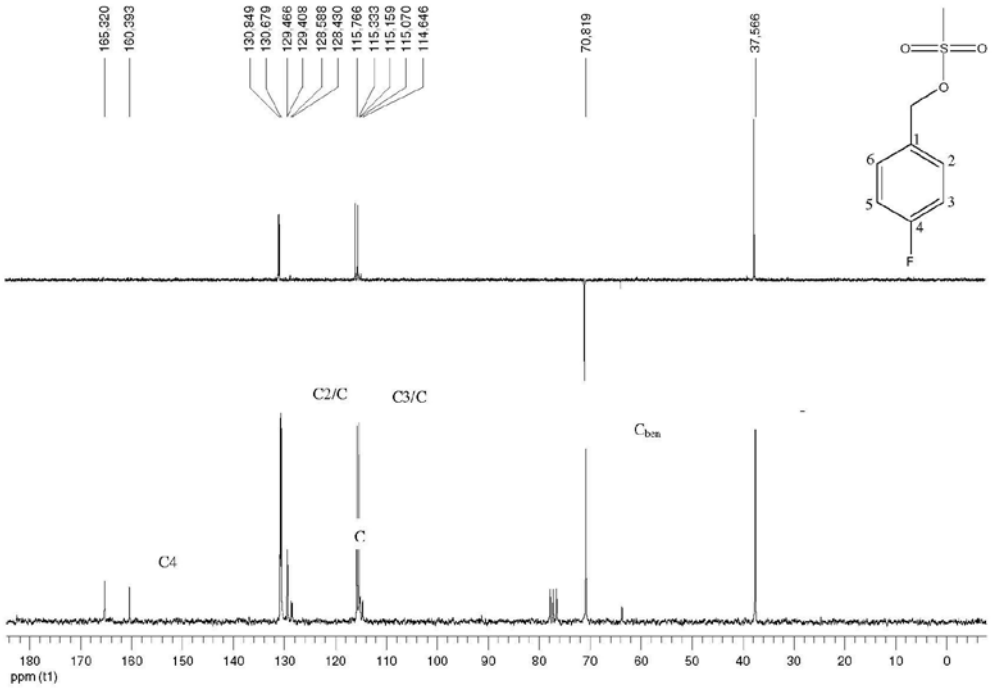

Figure S13. ^{13}C NMR and DEPT-135 spectrum (50 MHz, $CDCl_3$) of 4-fluorobenzyl methanesulfonate (**2b**).

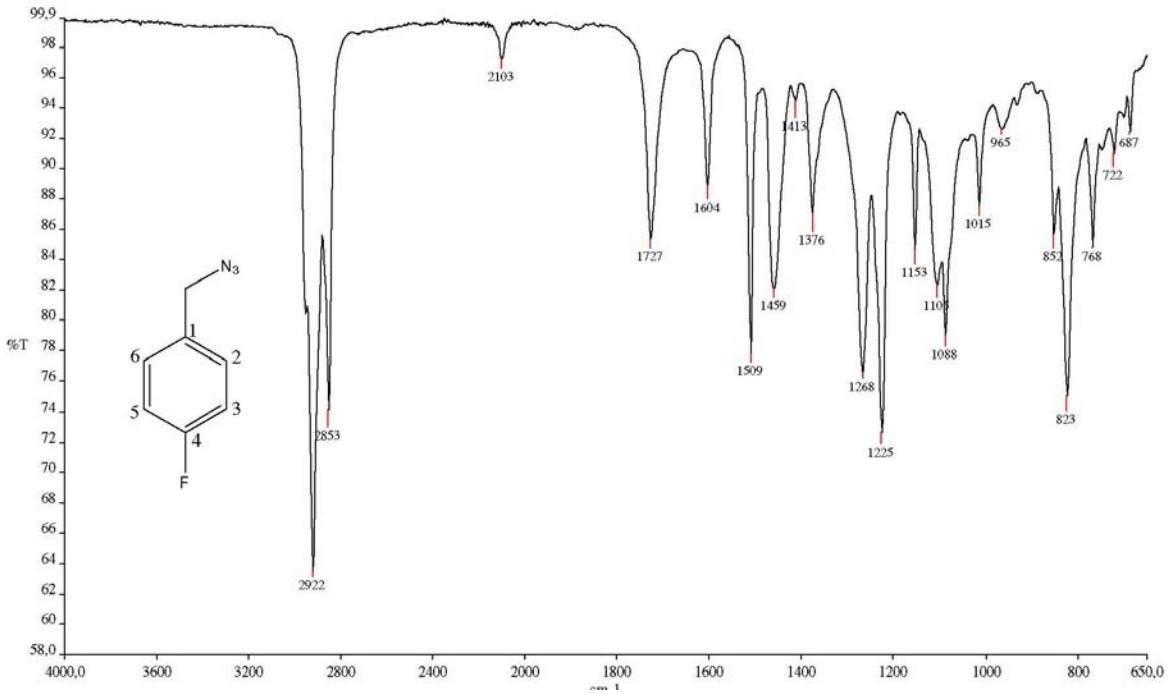

Figure S14. IR (ATR) spectrum of 1-(azidomethyl)-4-fluorobenzene (**3b**).

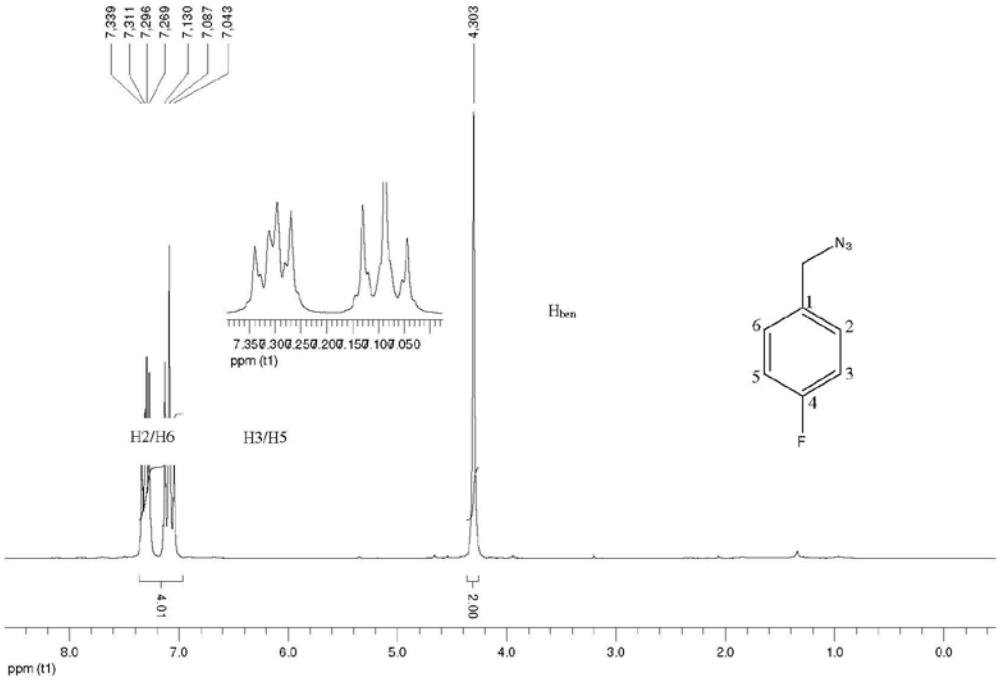

Figure S15. ^{1}H NMR spectrum (200 MHz, $CDCl_3$) of 1-(azidomethyl)-4-fluorobenzene (**3b**).

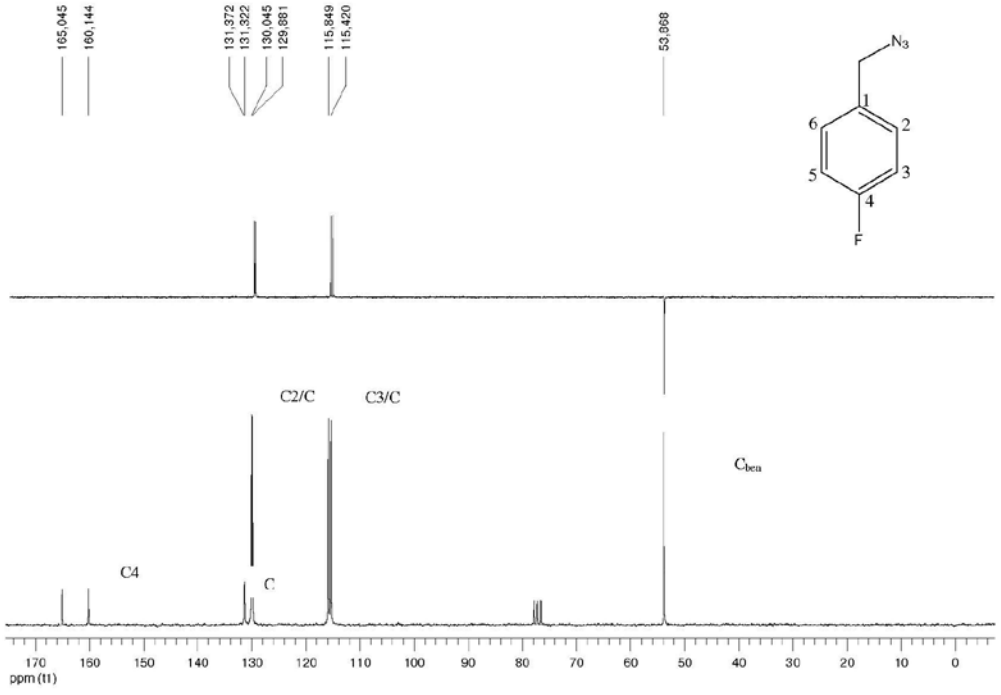

Figure S16. ^{13}C NMR and DEPT-135 spectrum (50 MHz, $CDCl_3$) of 1-(azidomethyl)-4-fluorobenzene (**3b**).

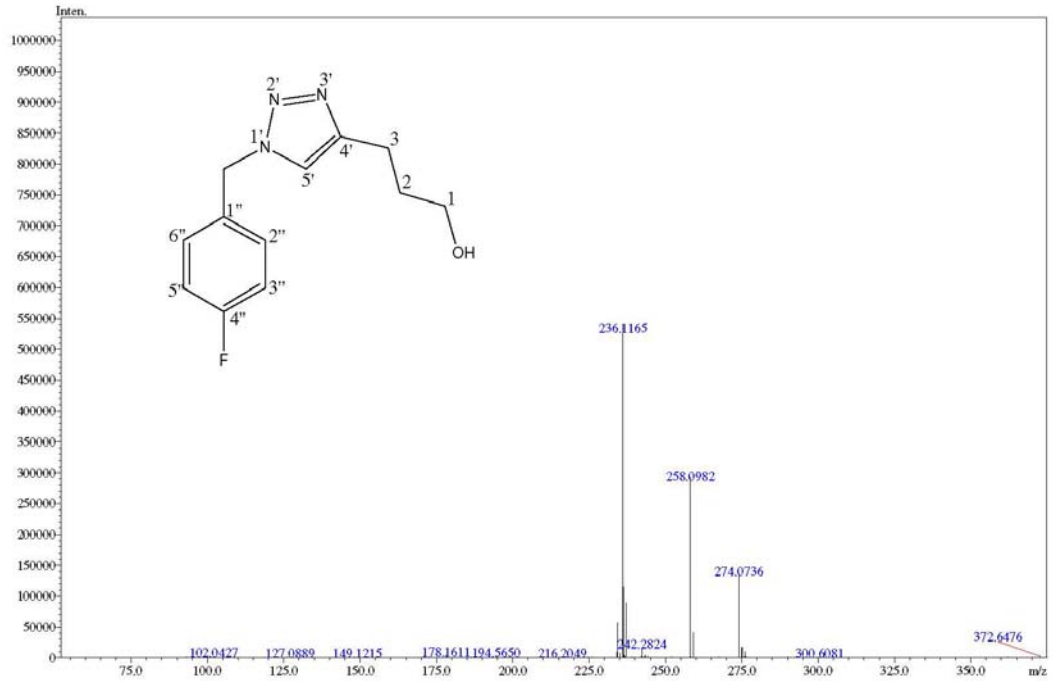

Figure S17. HRMS spectrum of 3-[1'-(4''-fluorobenzyl)-1',2',3'-triazol-4'-yl]propan-1-ol (**4b**).

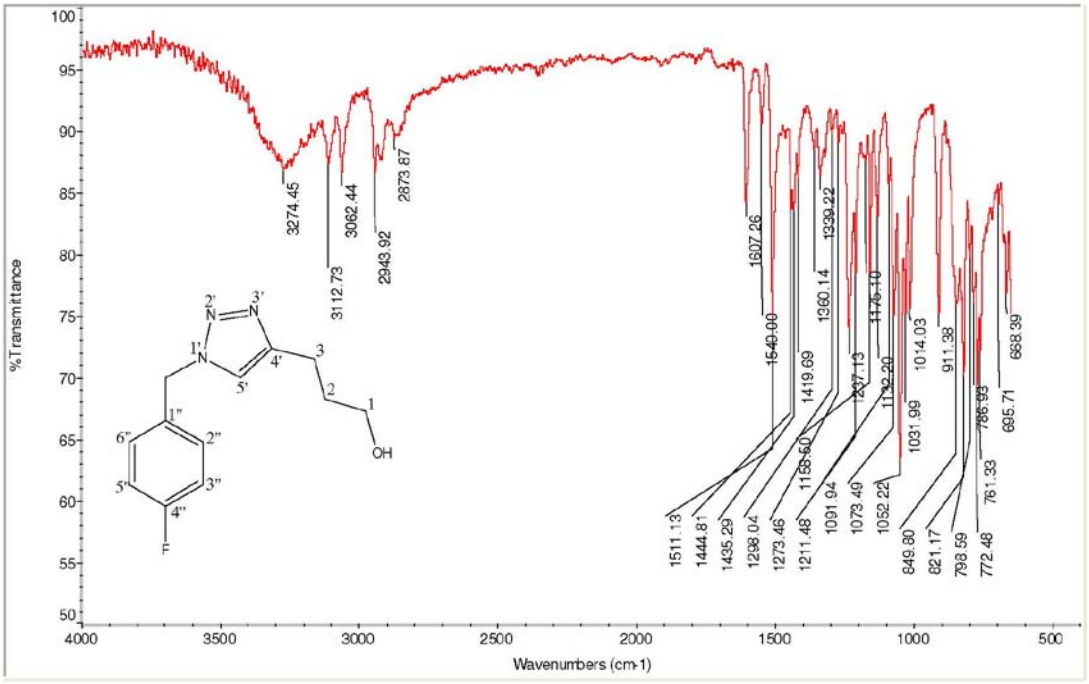

Figure S18. IR (ATR) spectrum of 3-[1'-(4''-fluorobenzyl)-1',2',3'-triazol-4'-yl]propan-1-ol (**4b**).

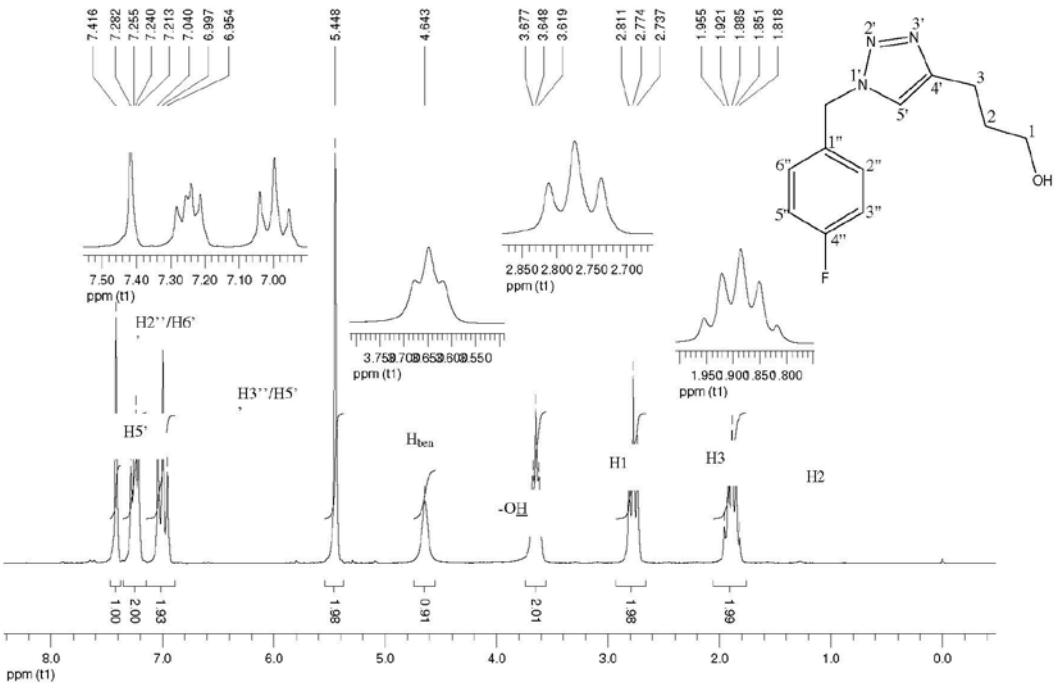

Figure S19. ^{1}H NMR spectrum (200 MHz, $CDCl_3$) of 3-[1'-(4''-fluorobenzyl)-1',2',3'-triazol-4'-yl]propan-1-ol (**4b**).

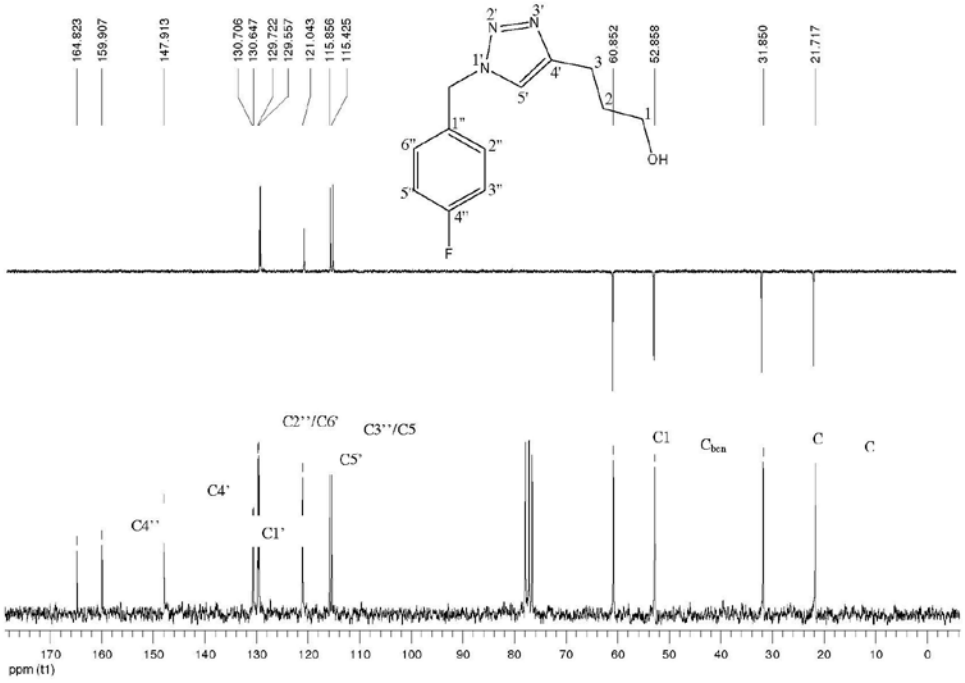

Figure S20. ^{13}C NMR and DEPT-135 spectrum (50 MHz, $CDCl_3$) of 3-[1'-(4''-fluorobenzyl)-1',2',3'-triazol-4'-yl]propan-1-ol (**4b**).

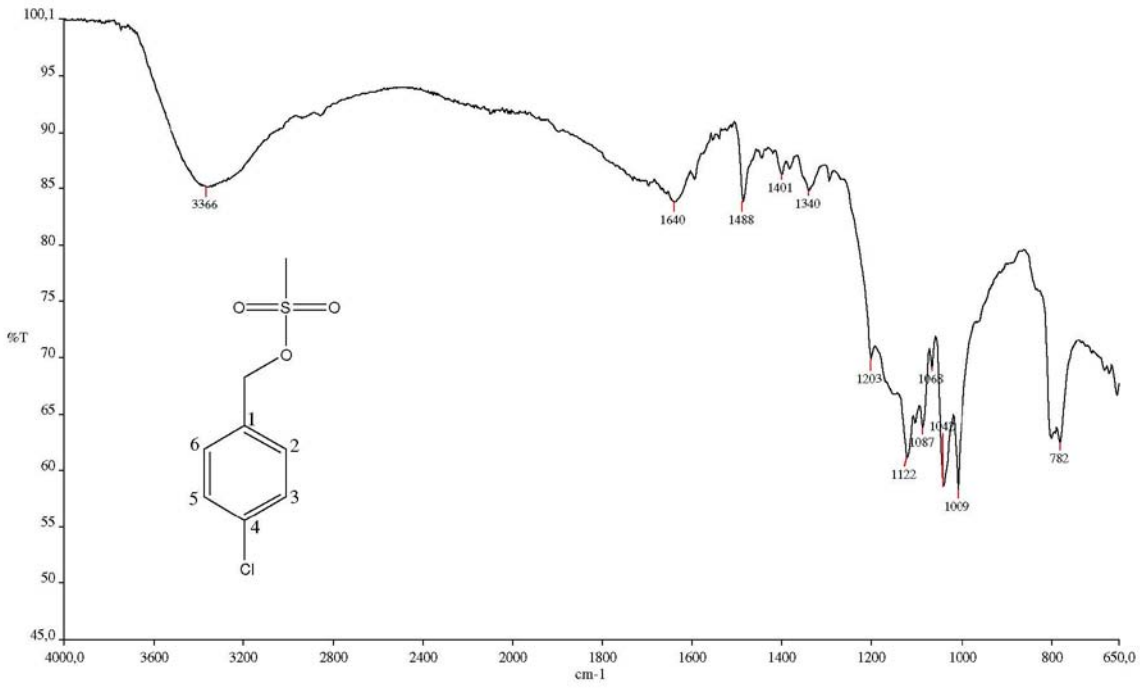

Figure S21. IR (ATR) spectrum of 4-chlorobenzyl methanesulfonate (**2c**).

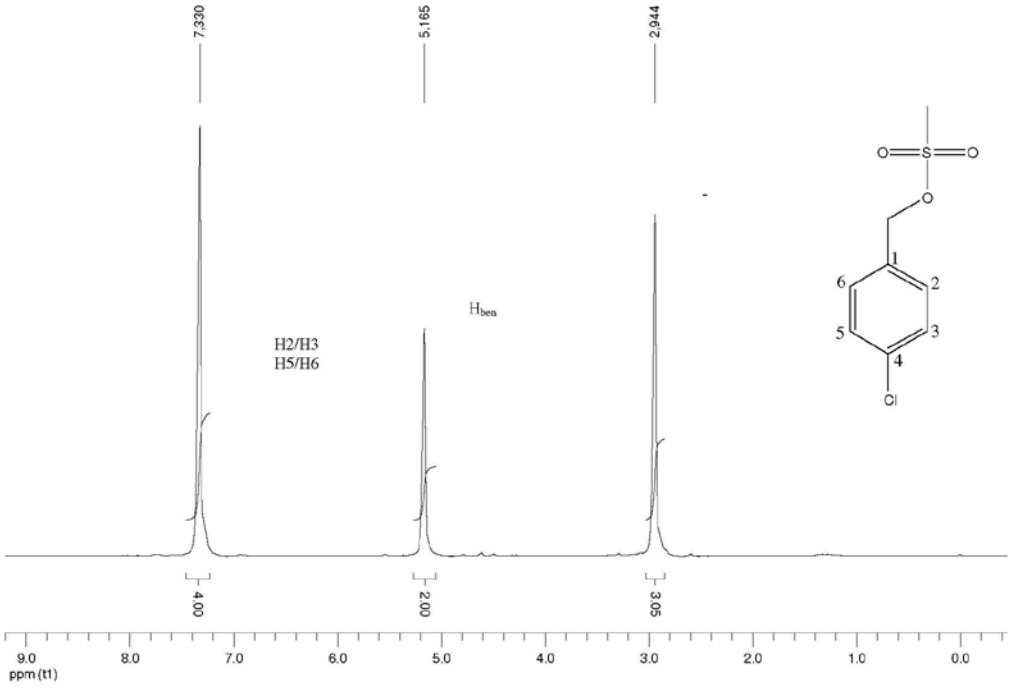

Figure S22. ^{1}H NMR spectrum (200 MHz, $CDCl_3$) of 4-chlorobenzyl methanesulfonate (**2c**).

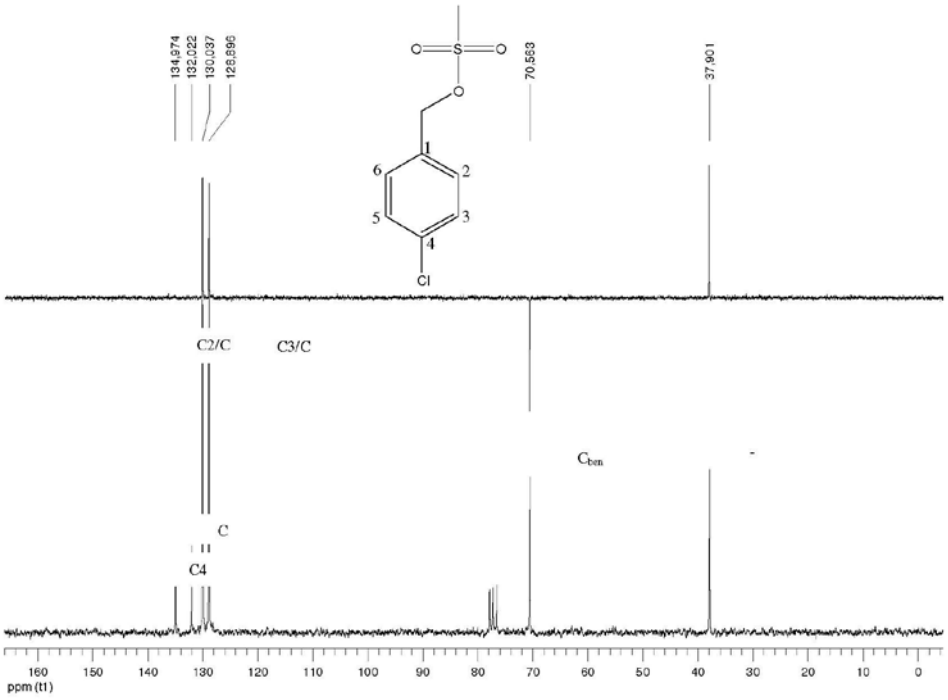

Figure S23. ^{13}C NMR and DEPT-135 spectrum (50 MHz, $CDCl_3$) of 4-chlorobenzyl methanesulfonate (**2c**).

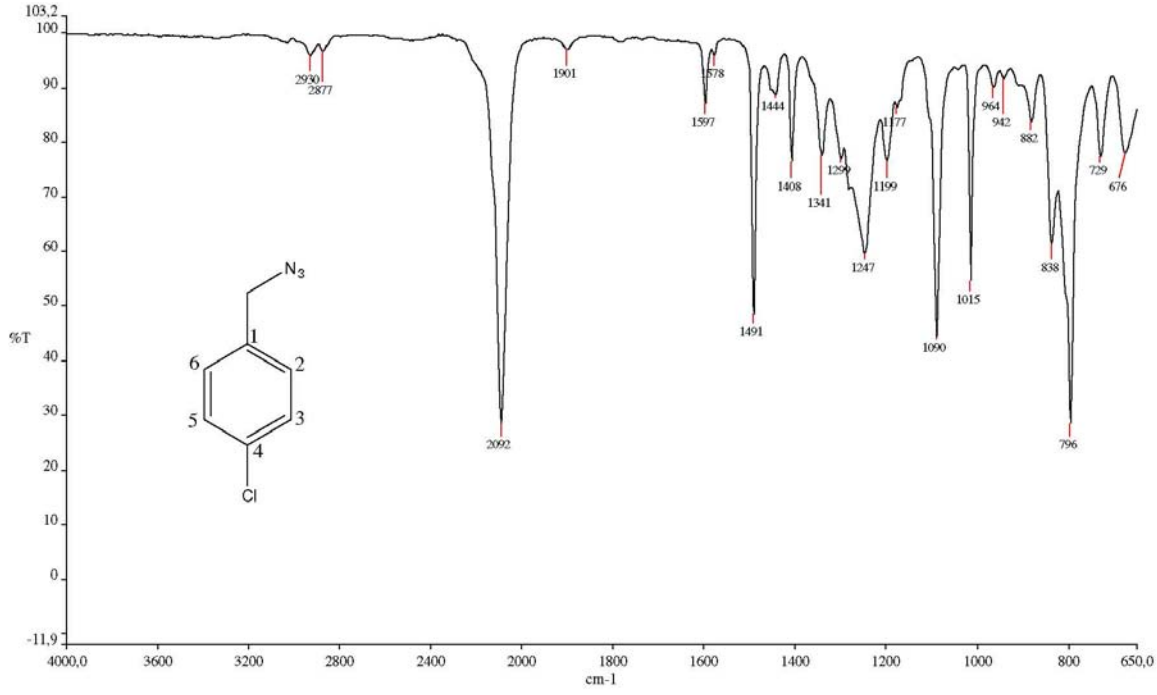

Figure S24. IR (ATR) spectrum of 1-(azidomethyl)-4-chlorobenzene (**3c**).

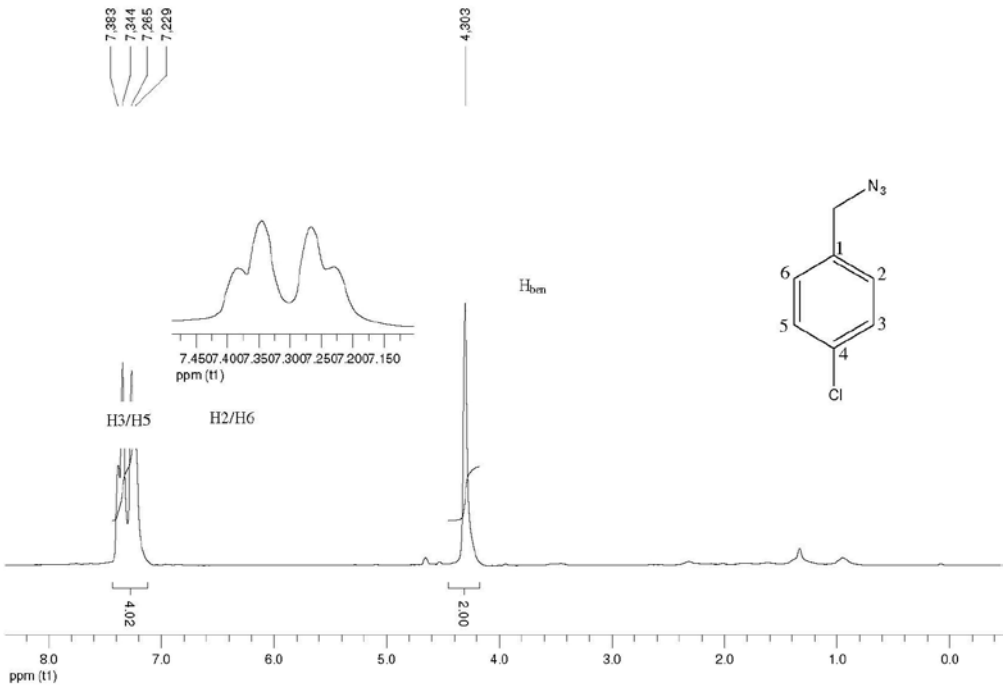

Figure S25. ^{1}H NMR spectrum (200 MHz, $CDCl_3$) of 1-(azidomethyl)-4-chlorobenzene (**3c**).

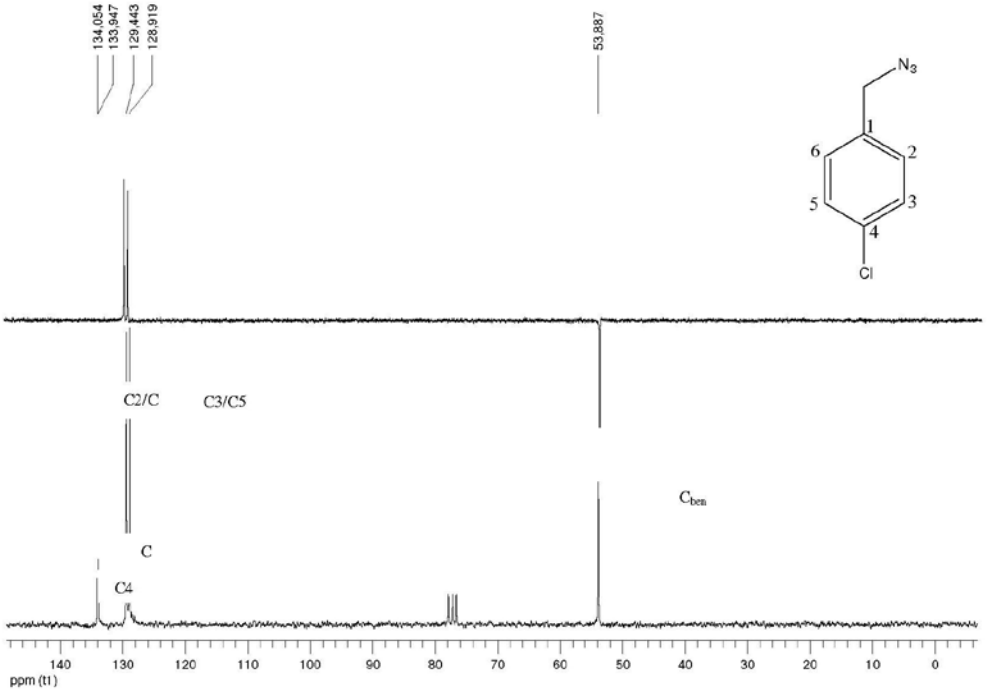

Figure S26. ^{13}C NMR and DEPT-135 spectrum (50 MHz, $CDCl_3$) of 1-(azidomethyl)-4-chlorobenzene (**3c**).

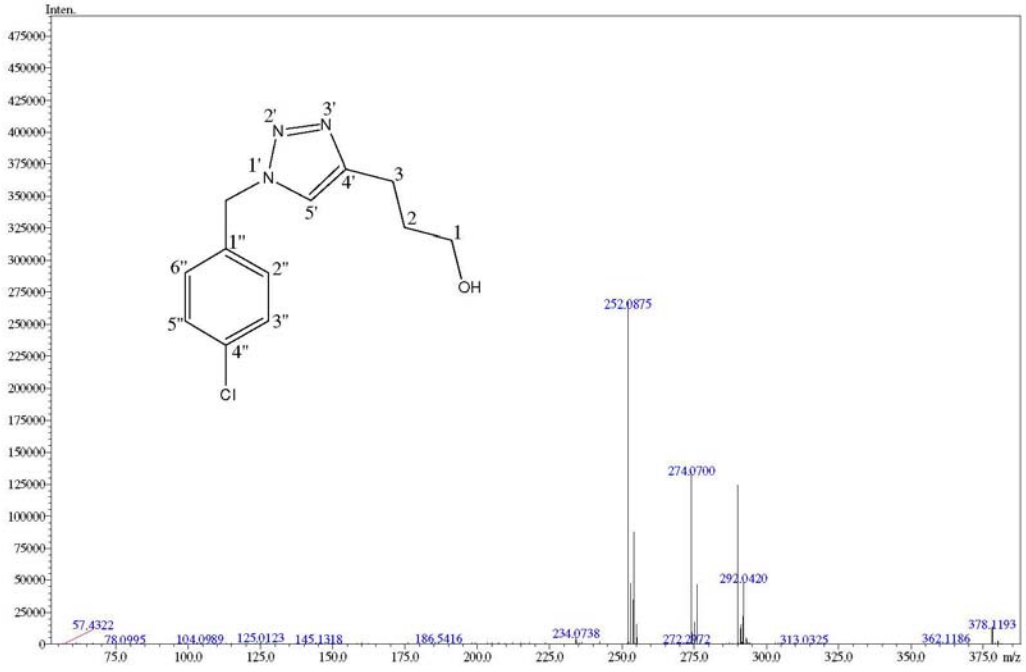

Figure S27. HRMS spectrum of 3-[1'-(4''-chlorobenzyl)-1',2',3'-triazol-4'-yl]propan-1-ol (**4c**).

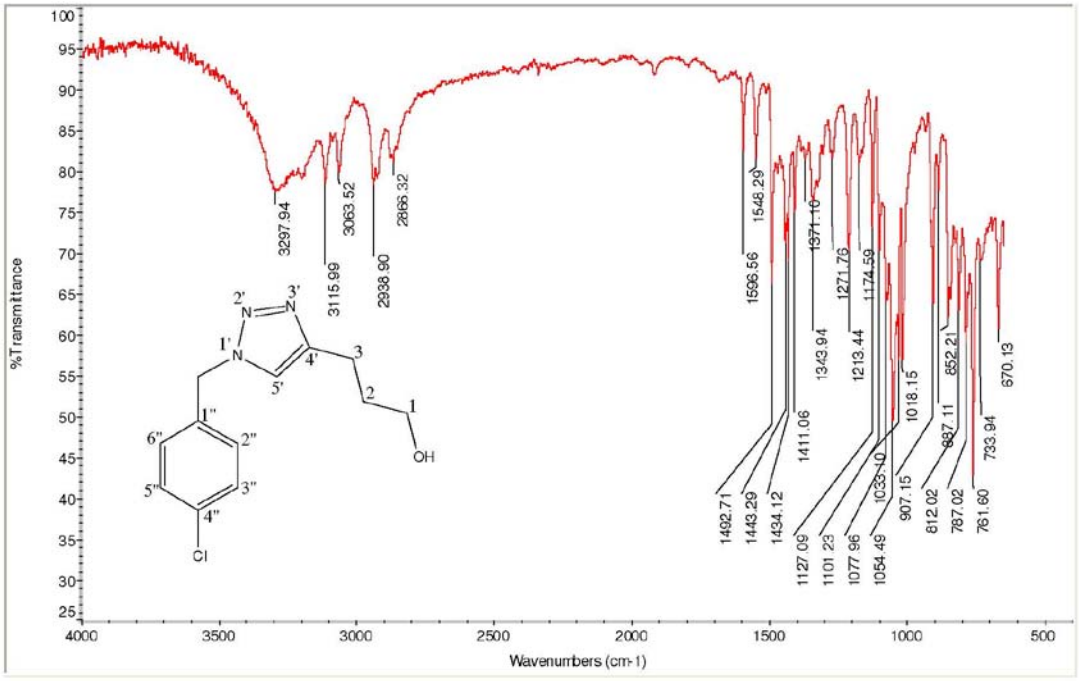

Figure S28. IR (ATR) spectrum of 3-[1'-(4''-chlorobenzyl)-1',2',3'-triazol-4'-yl]propan-1-ol (**4c**).

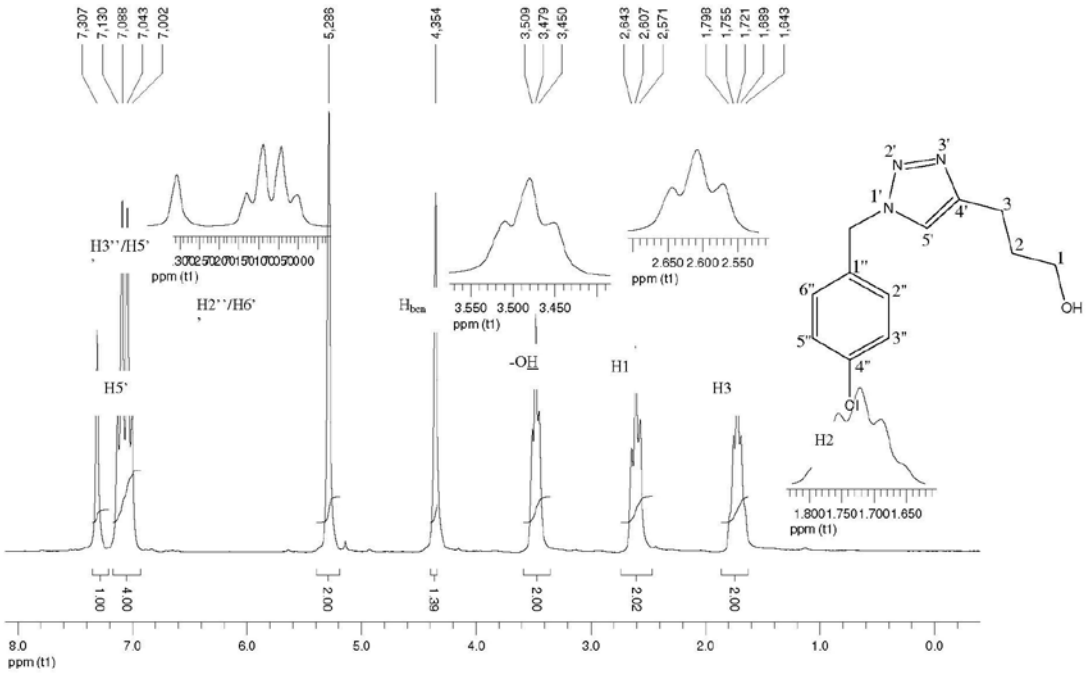

Figure S29. ^{1}H NMR spectrum (200 MHz, $CDCl_3$) of 3-[1'-(4''-chlorobenzyl)-1',2',3'-triazol-4'-yl]propan-1-ol (**4c**).

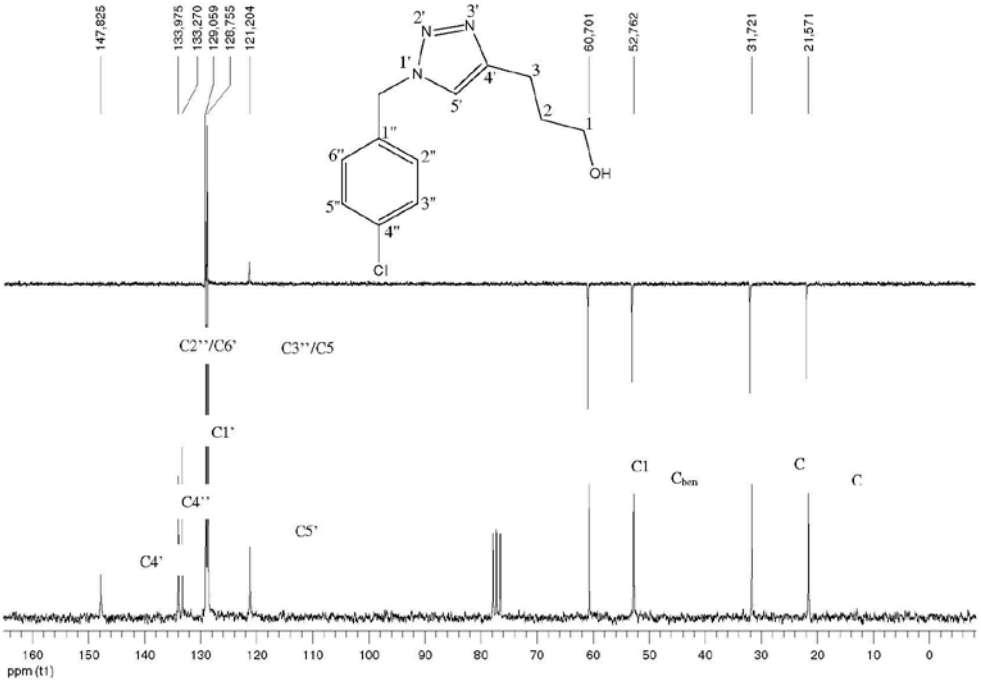

Figure S30. ^{13}C NMR and DEPT-135 spectrum (50 MHz, $CDCl_3$) of 3-[1'-(4''-chlorobenzyl)-1',2',3'-triazol-4'-yl]propan-1-ol (**4c**).

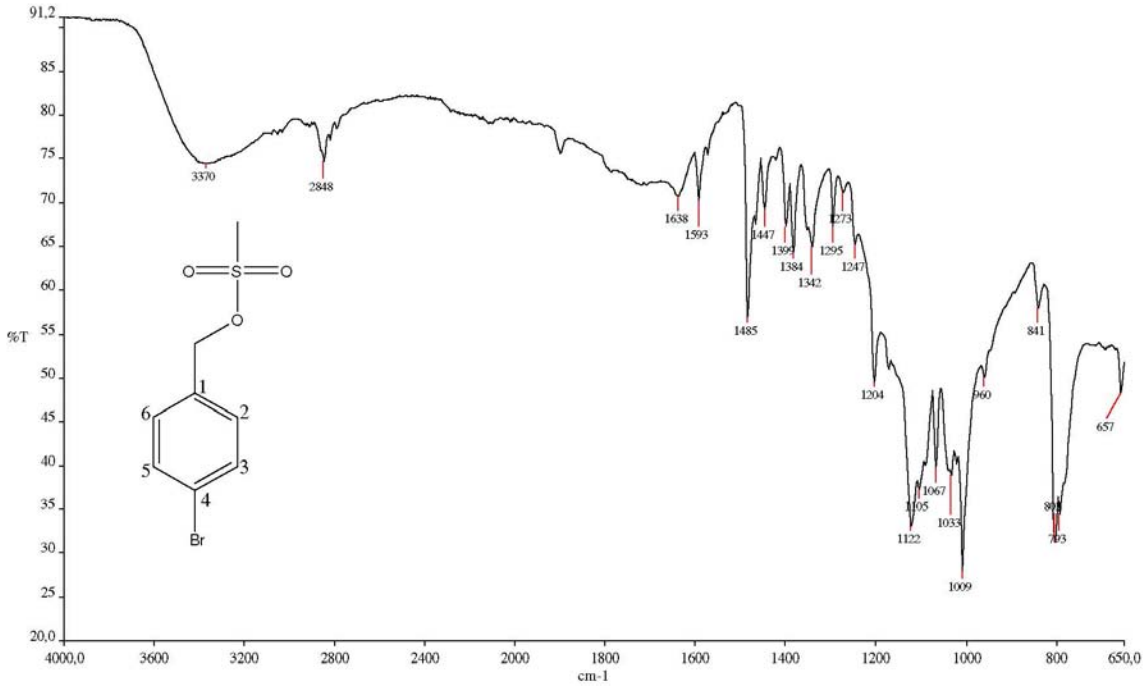

Figure S31. IR (ATR) spectrum of 4-bromobenzyl methanesulfonate (**2d**).

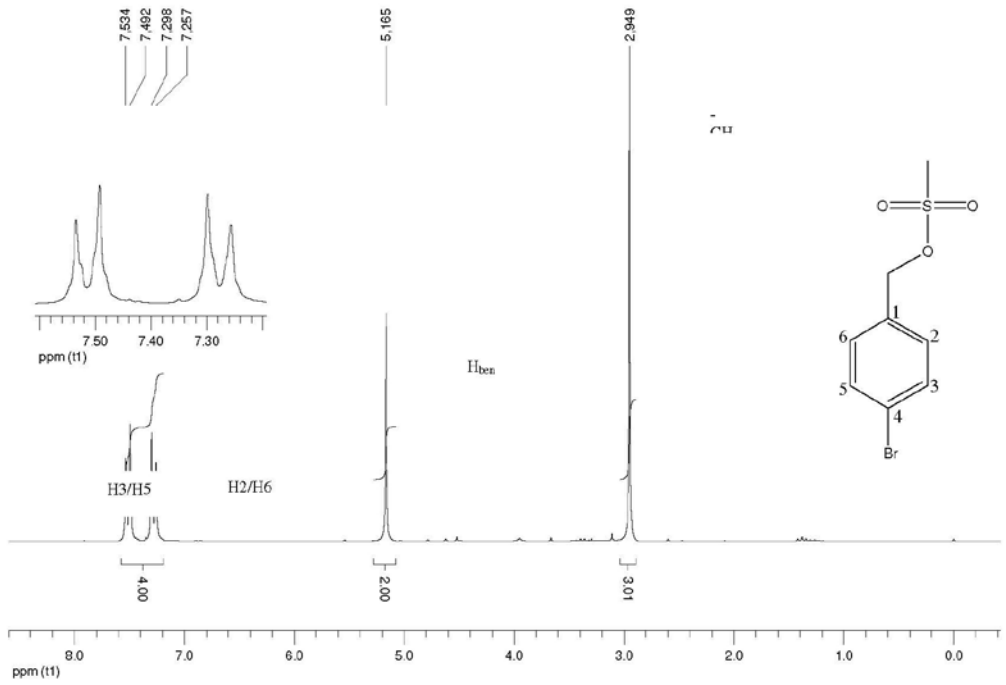

Figure S32. ^{1}H NMR spectrum (200 MHz, $CDCl_3$) of 4-bromobenzyl methanesulfonate (**2d**).

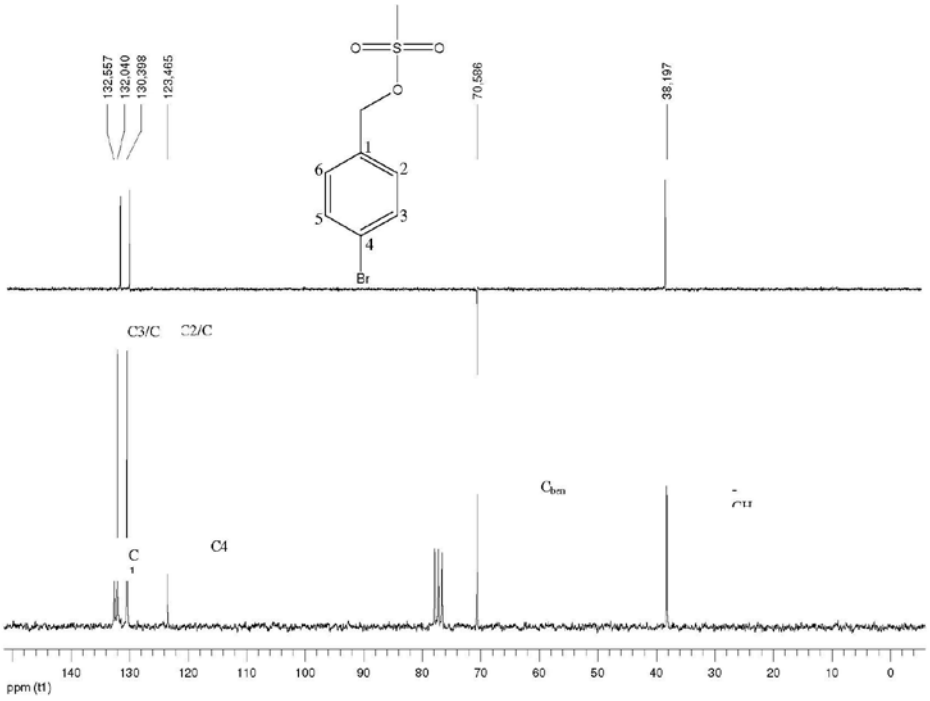

Figure S33. ^{13}C NMR and DEPT-135 spectrum (50 MHz, $CDCl_3$) of 4-bromobenzyl methanesulfonate (**2d**).

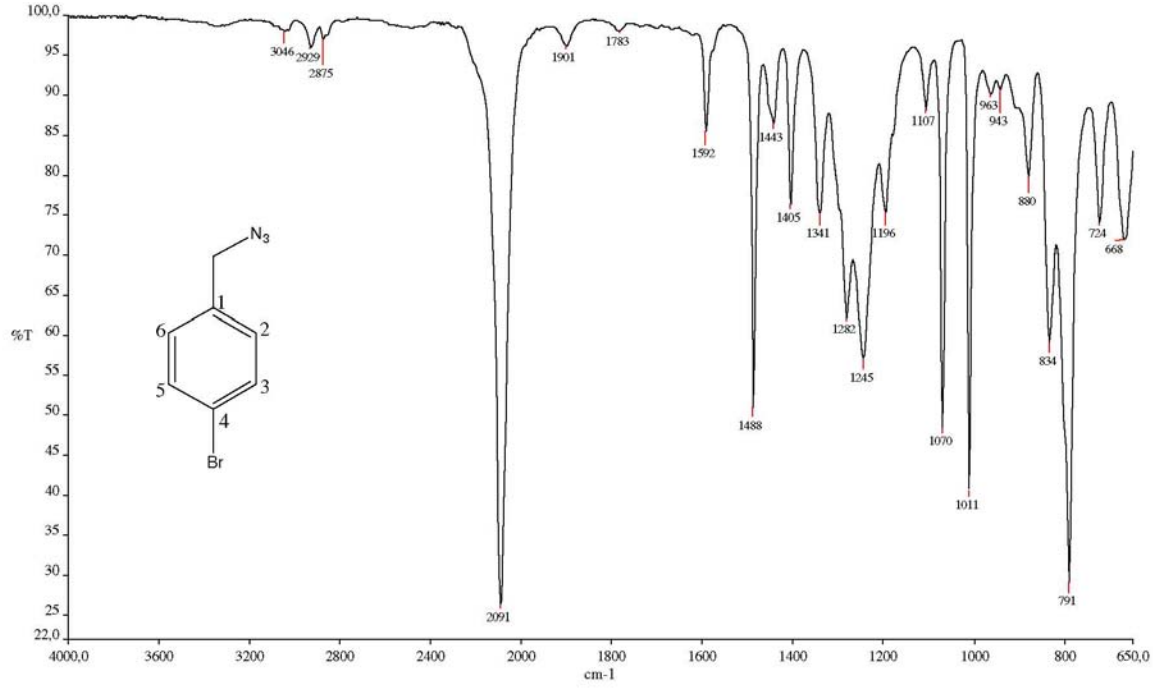

Figure S34. IR (ATR) spectrum of 1-(azidomethyl)-4-bromobenzene (**3d**).

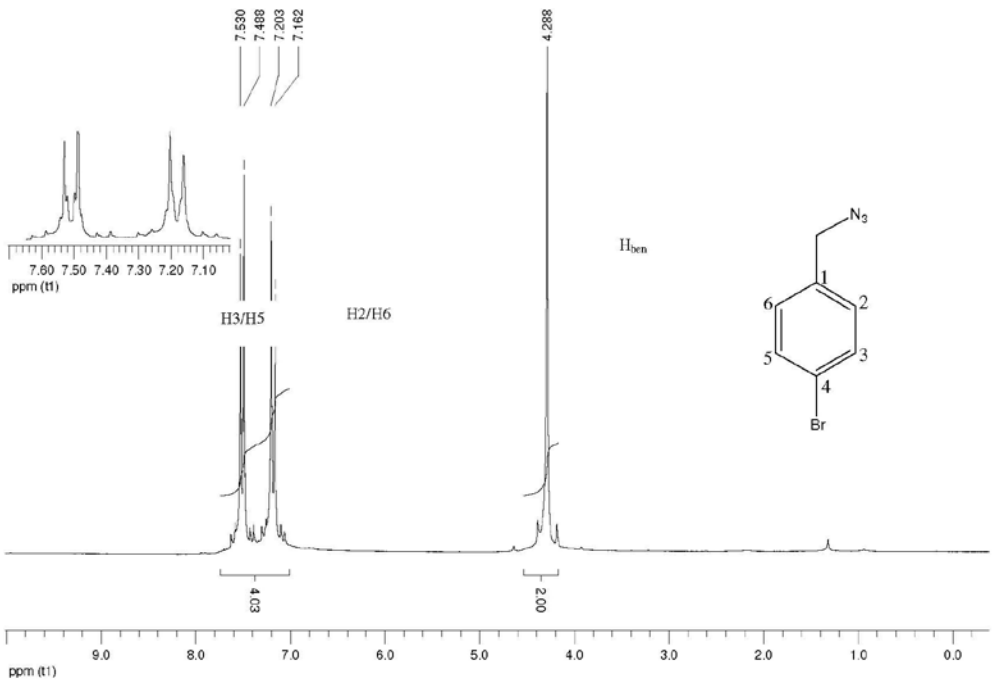

Figure S35. ^{1}H NMR spectrum (200 MHz, $CDCl_3$) of 1-(azidomethyl)-4-bromobenzene (**3d**).

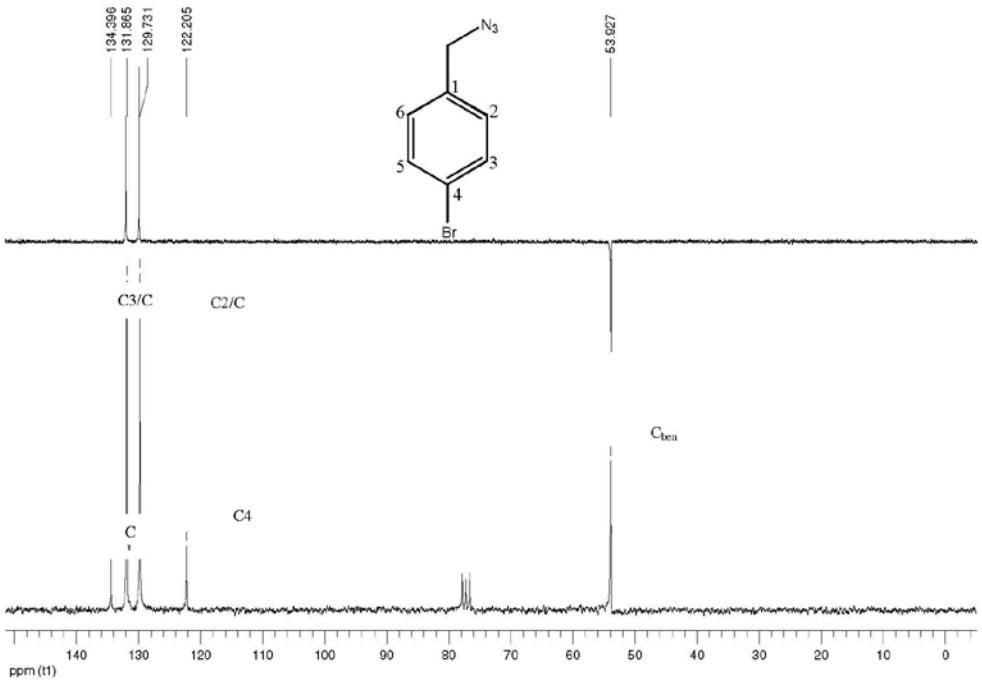

Figure S36. ^{13}C NMR and DEPT-135 spectrum (50 MHz, $CDCl_3$) of 1-(azidomethyl)-4-bromobenzene (**3d**).

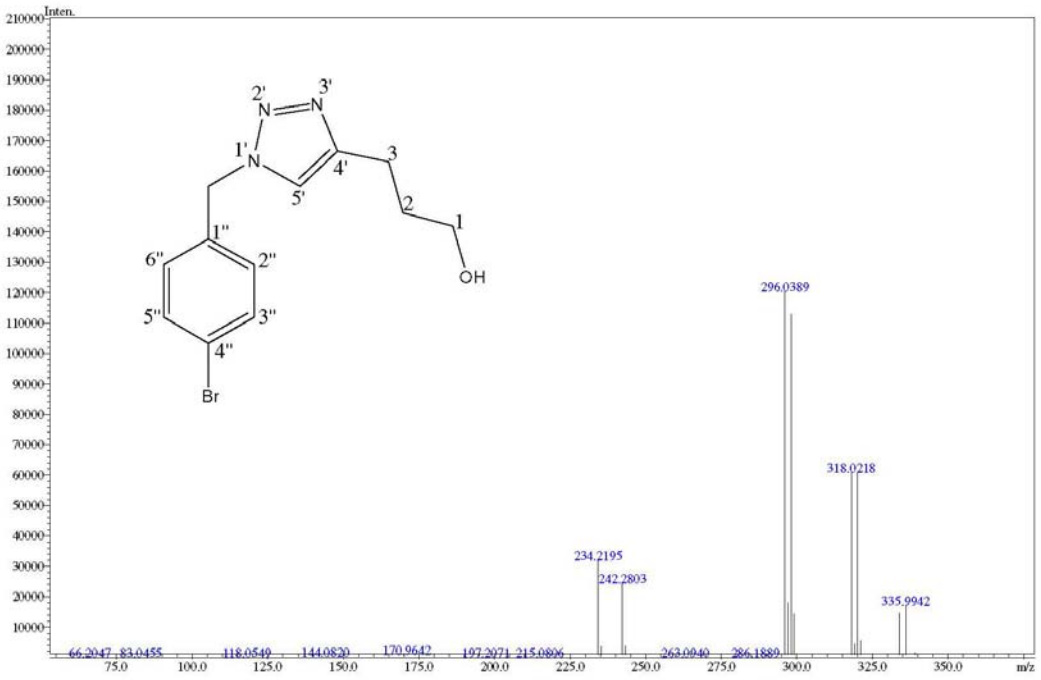

Figure S37. HRMS spectrum of 3-[1'-(4''-bromobenzyl)-1',2',3'-triazol-4'-yl]propan-1-ol (**4d**).

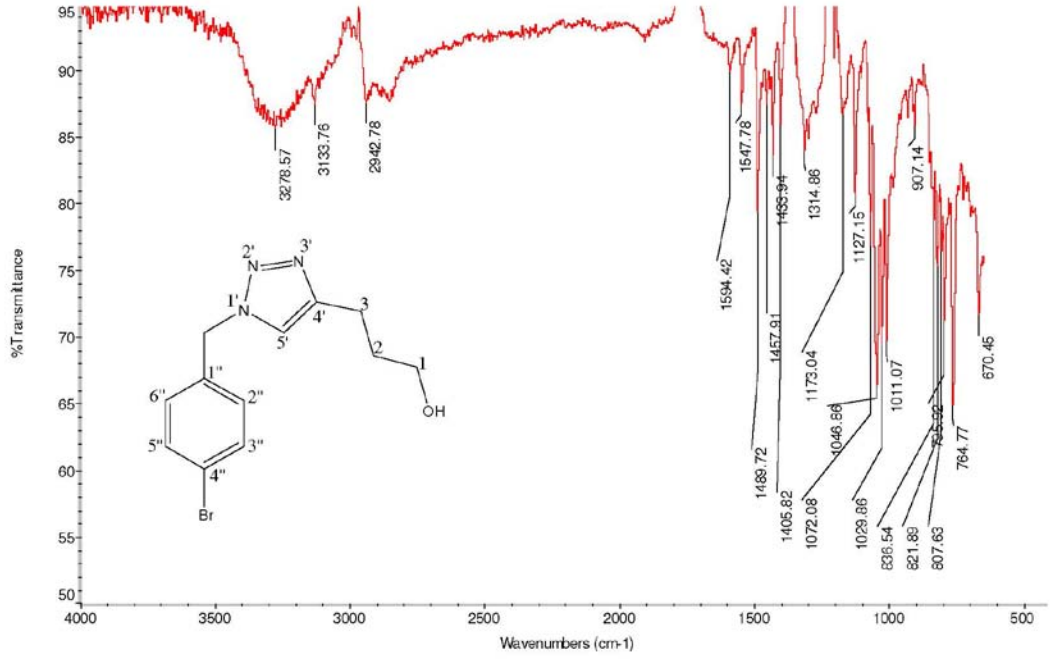

Figure S38. IR (ATR) spectrum of 3-[1'-(4''-bromobenzyl)-1',2',3'-triazol-4'-yl]propan-1-ol (**4d**).

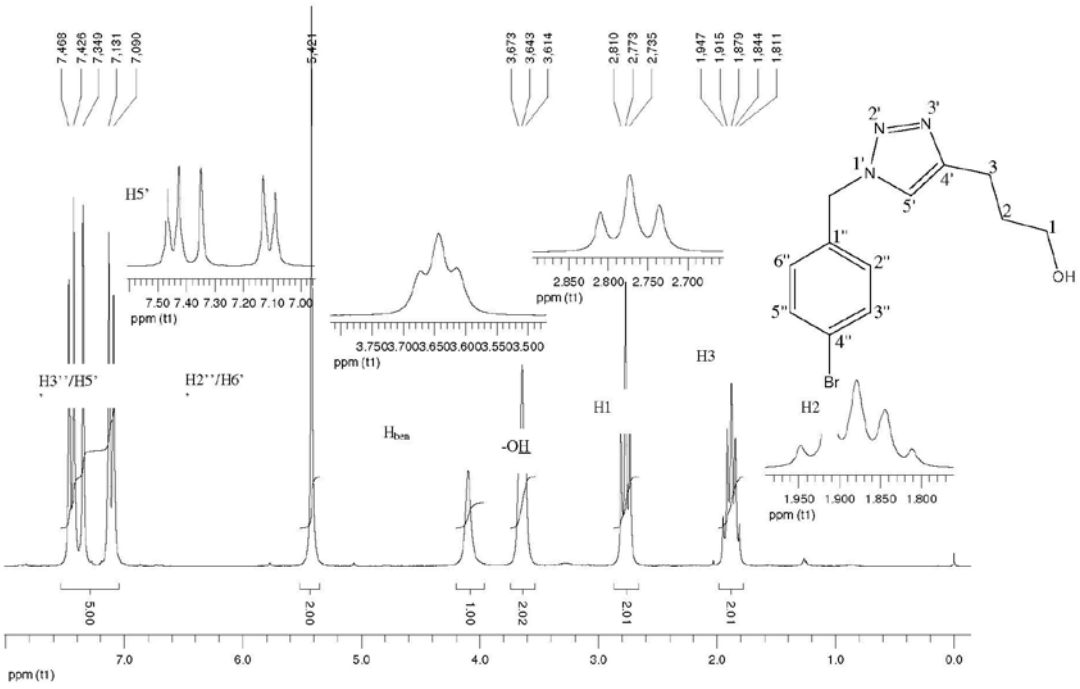

Figure S39. ^{1}H NMR spectrum (200 MHz, $CDCl_3$) of 3-[1'-(4''-bromobenzyl)-1',2',3'-triazol-4'-yl]propan-1-ol (**4d**).

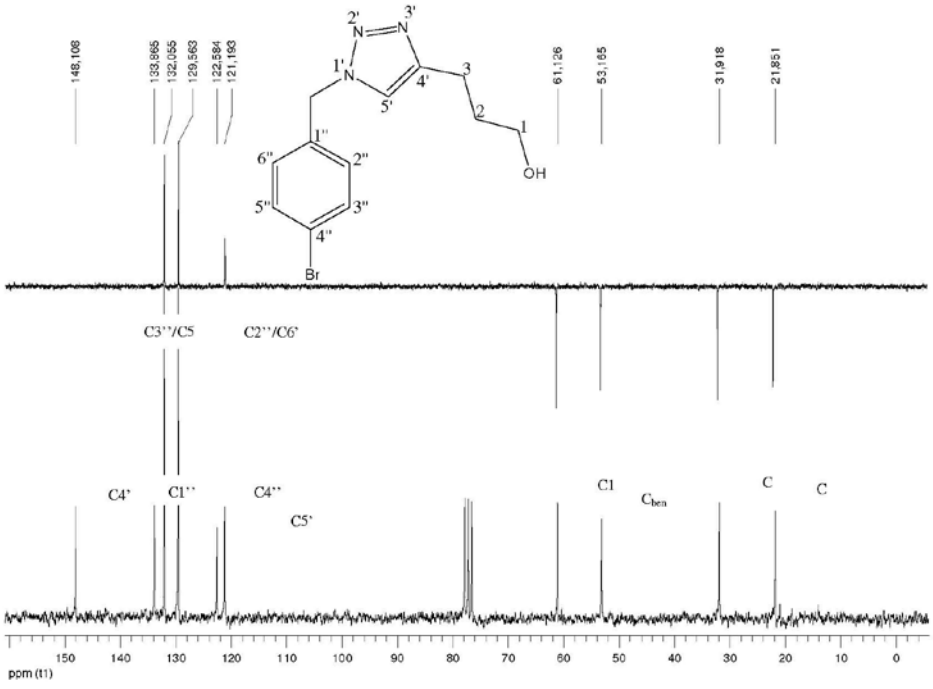

Figure S40. ^{13}C NMR and DEPT-135 spectrum (50 MHz, $CDCl_3$) of 3-[1'-(4''-bromobenzyl)-1',2',3'-triazol-4'-yl]propan-1-ol (**4d**).

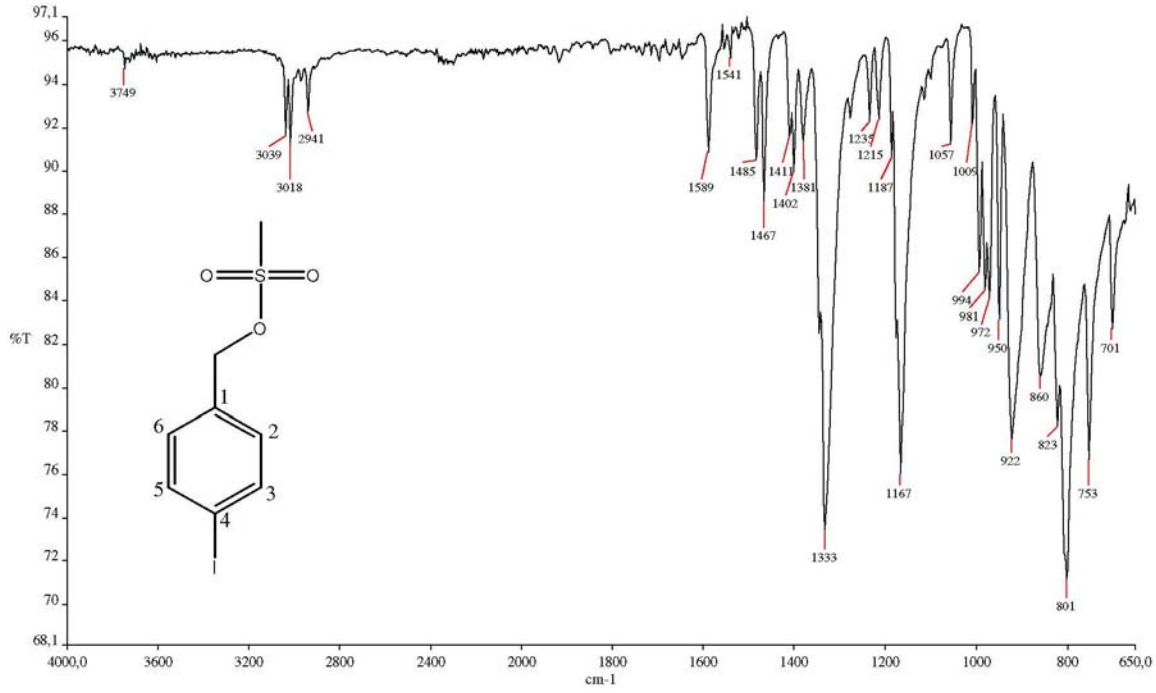

Figure S41. IR (ATR) spectrum of 4-iodobenzyl methanesulfonate (**2e**).

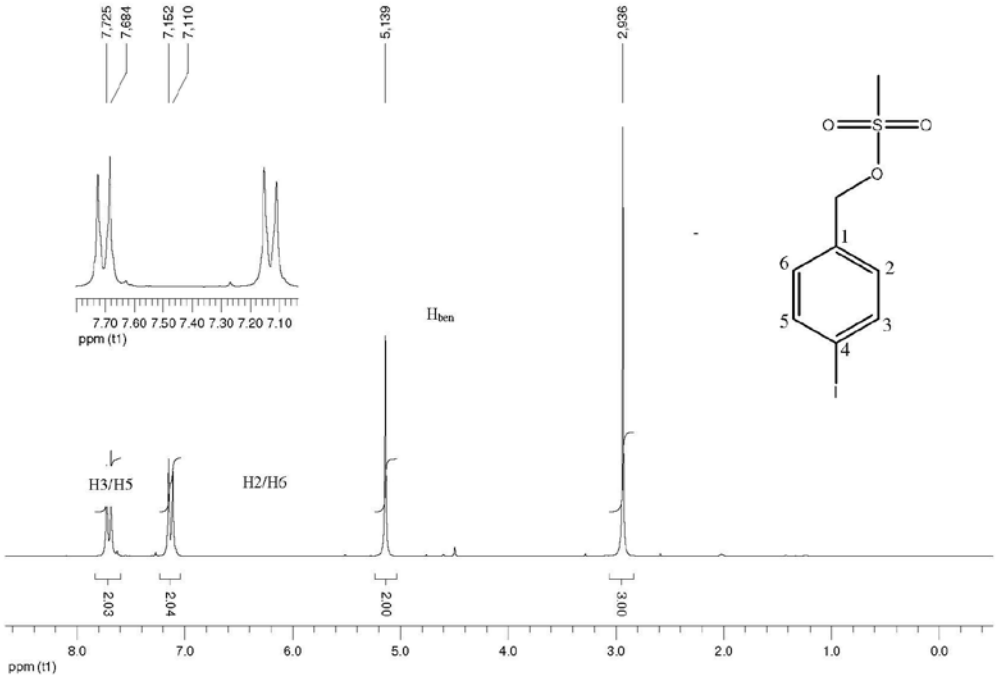

Figure S42. ^{1}H NMR spectrum (200 MHz, $CDCl_3$) of 4-iodobenzyl methanesulfonate (**2e**).

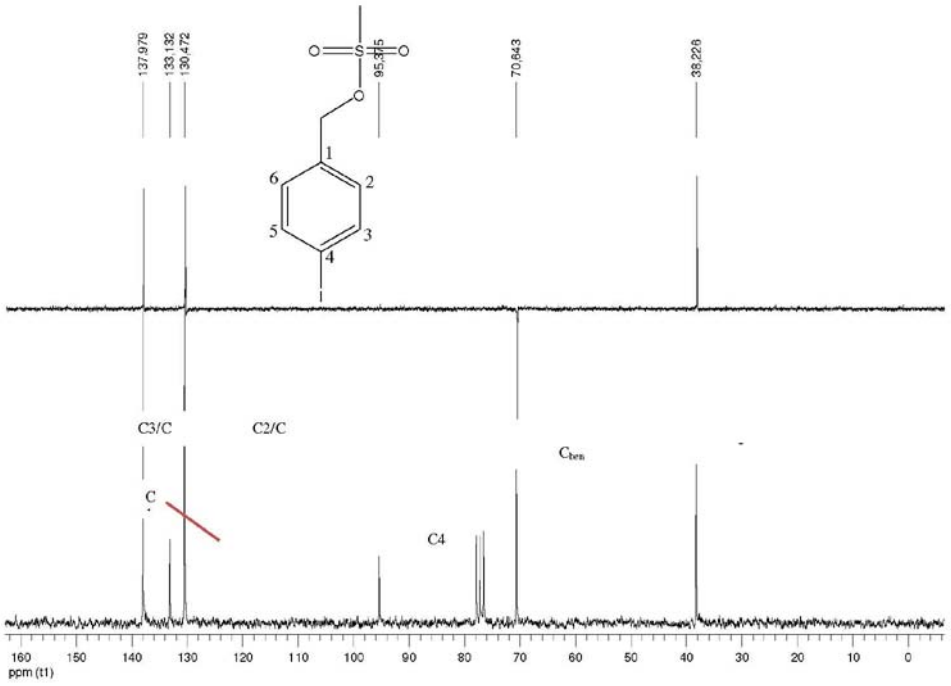

Figure S43. ^{13}C NMR and DEPT-135 spectrum (50 MHz, $CDCl_3$) of 4-iodobenzyl methanesulfonate (**2e**).

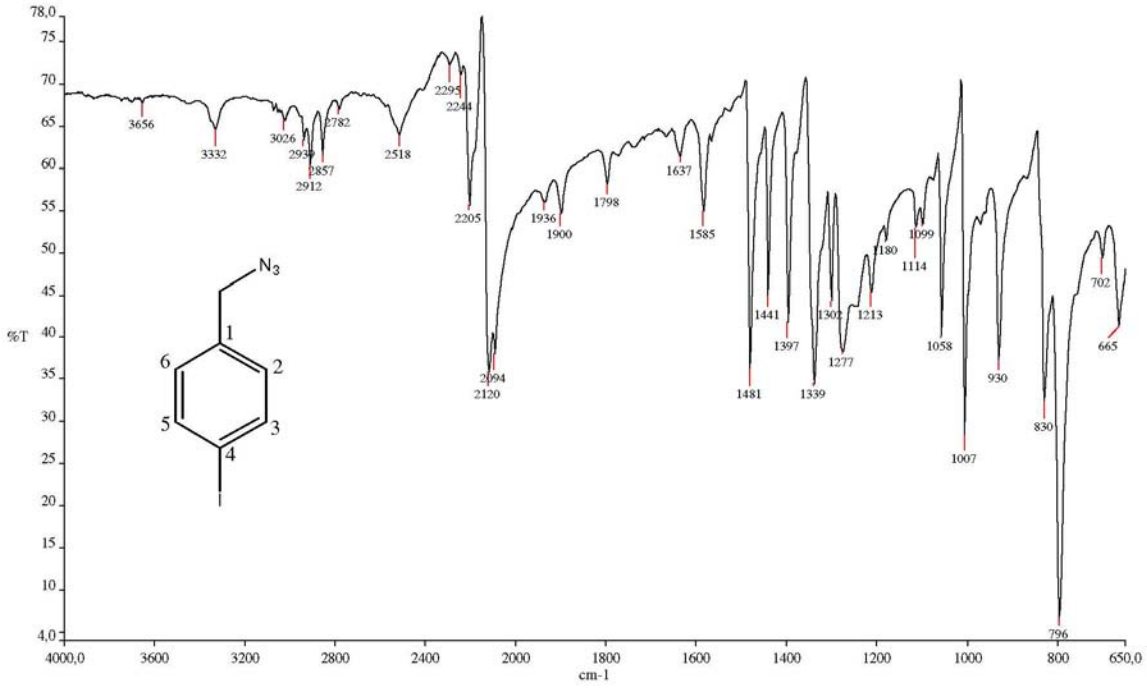

Figure S44. IR (ATR) spectrum of 1-(azidomethyl)-4-iodobenzene (**3e**).

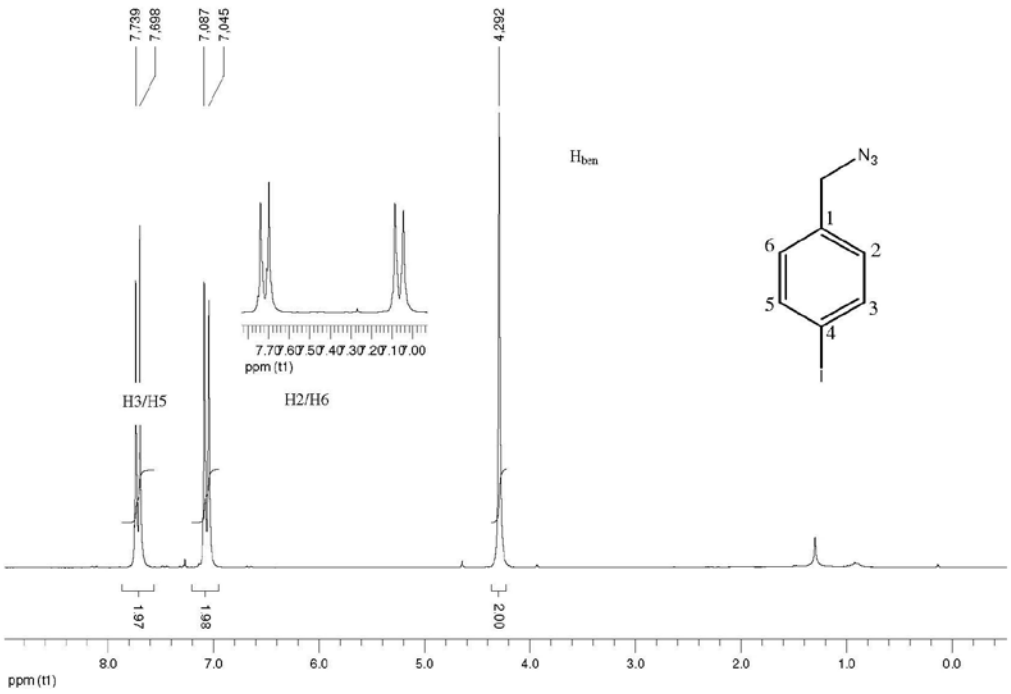

Figure S45. ^{1}H NMR spectrum (200 MHz, $CDCl_3$) of 1-(azidomethyl)-4-iodobenzene (**3e**).

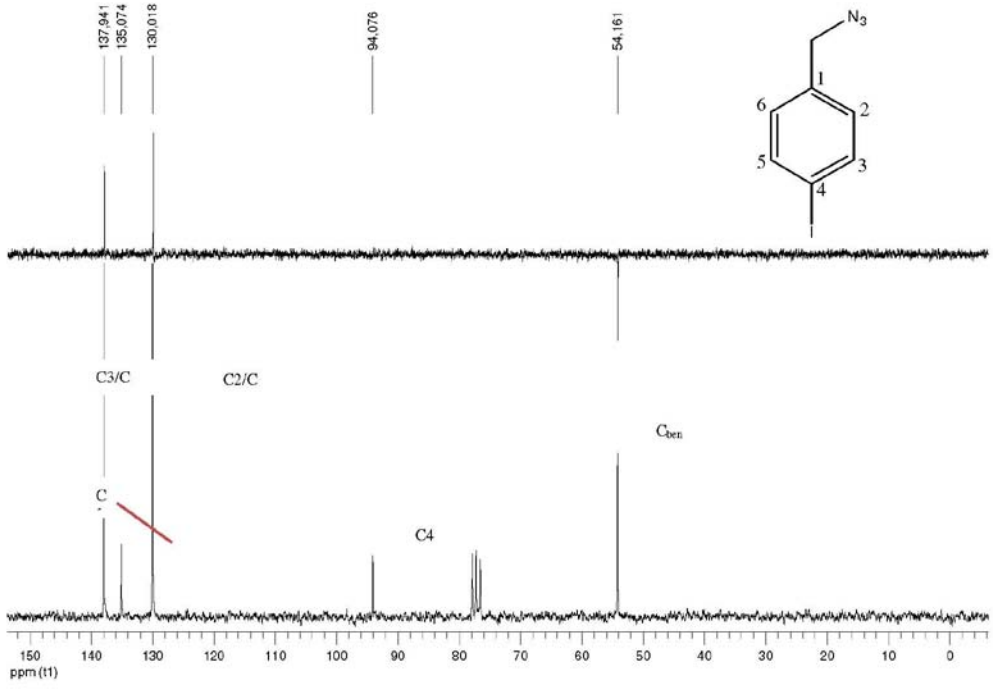

Figure S46. ^{13}C NMR and DEPT-135 spectrum (50 MHz, $CDCl_3$) of 1-(azidomethyl)-4-iodobenzene (**3e**).

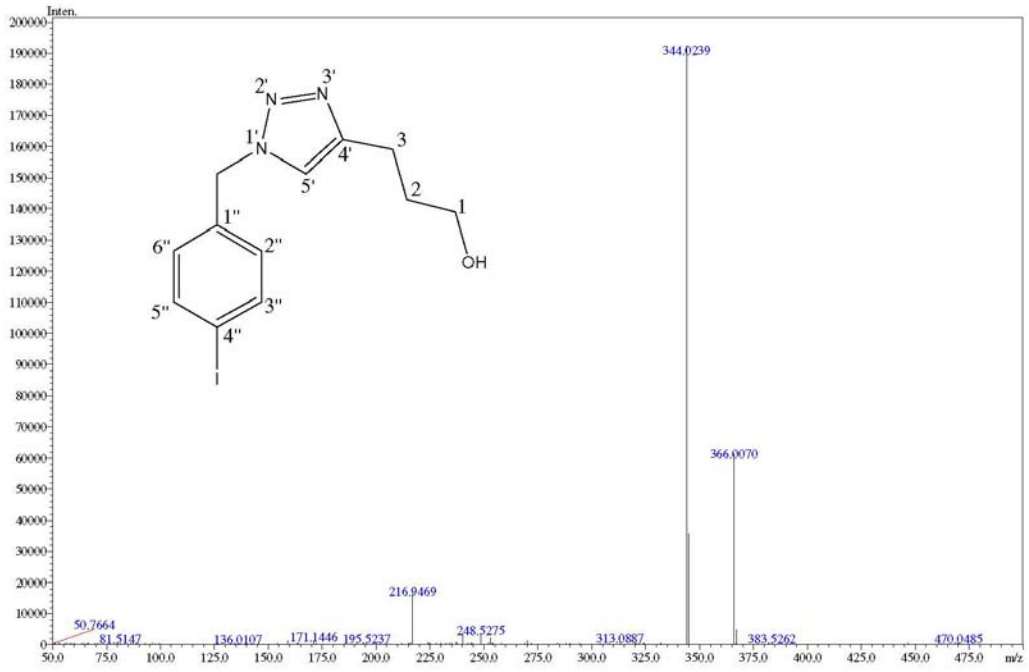

Figure S47. HRMS spectrum of 3-[1'-(4''-iodobenzyl)-1',2',3'-triazol-4'-yl]propan-1-ol (**4e**).

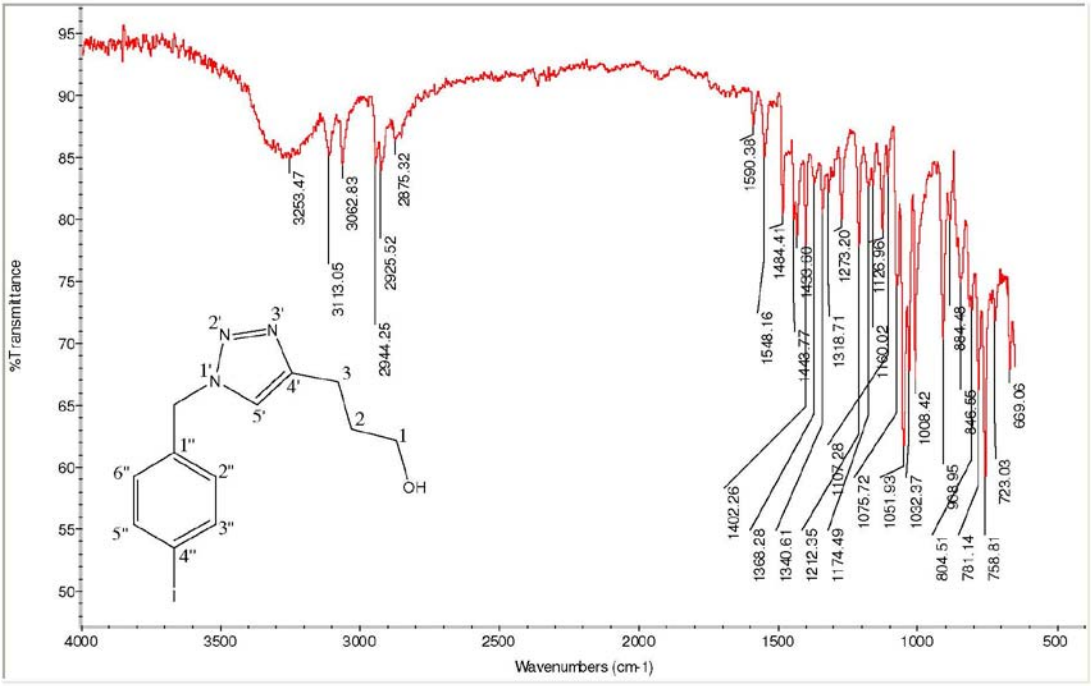

Figure S48. IR (ATR) spectrum of 3-[1'-(4''-iodobenzyl)-1',2',3'-triazol-4'-yl]propan-1-ol (**4e**).

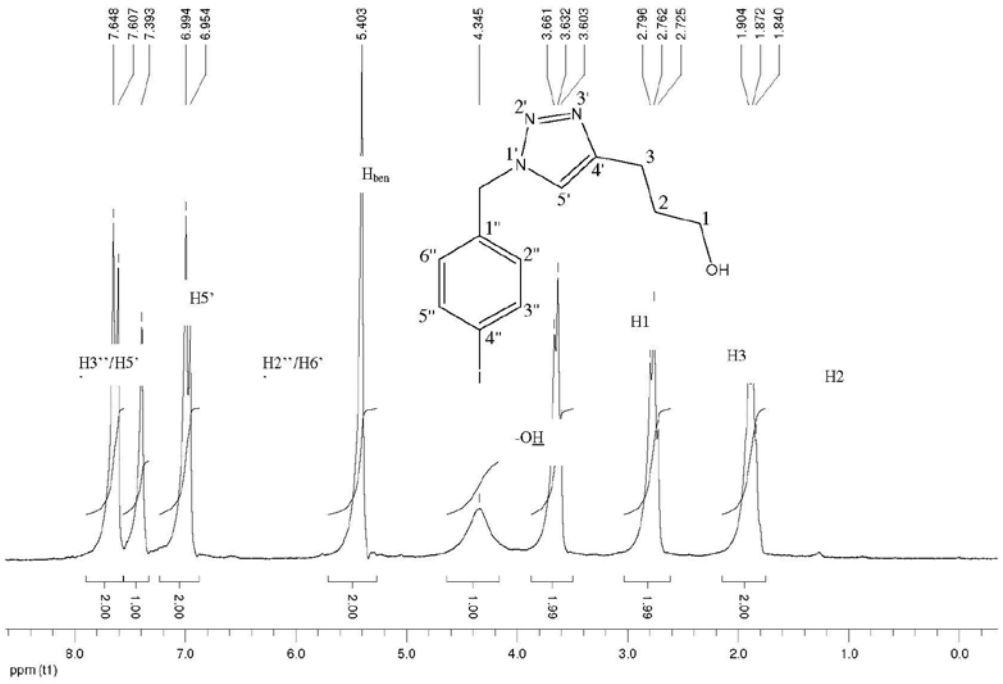

Figure S49. ^{1}H NMR spectrum (200 MHz, $CDCl_3$) of 3-[1'-(4''-iodobenzyl)-1',2',3'-triazol-4'-yl]propan-1-ol (**4e**).

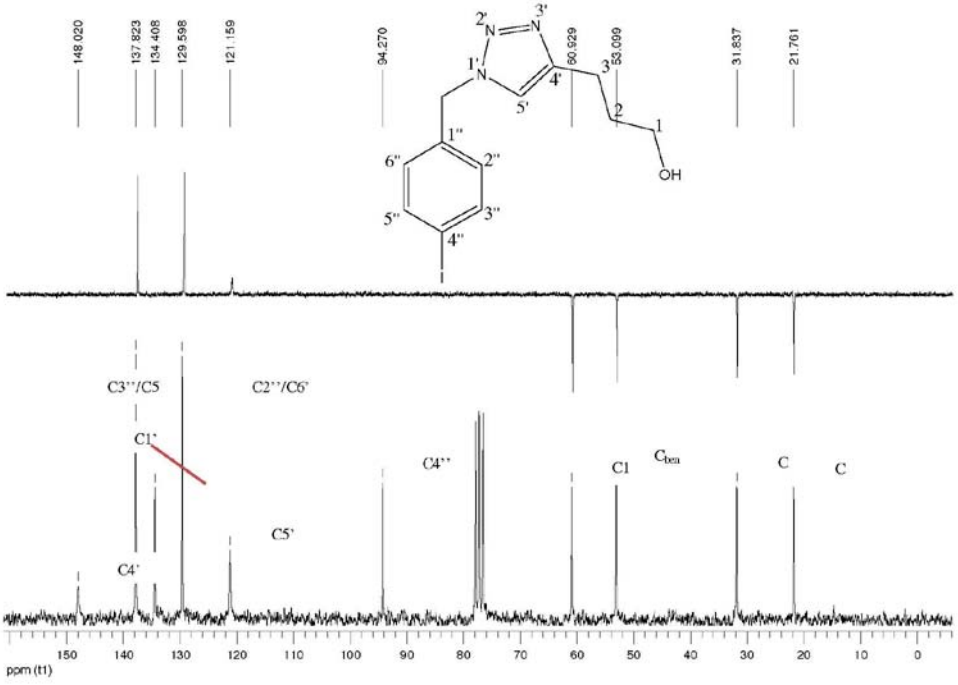

Figure S50. ^{13}C NMR and DEPT-135 spectrum (50 MHz, $CDCl_3$) of 3-[1'-(4''-iodobenzyl)-1',2',3'-triazol-4'-yl]propan-1-ol (**4e**).

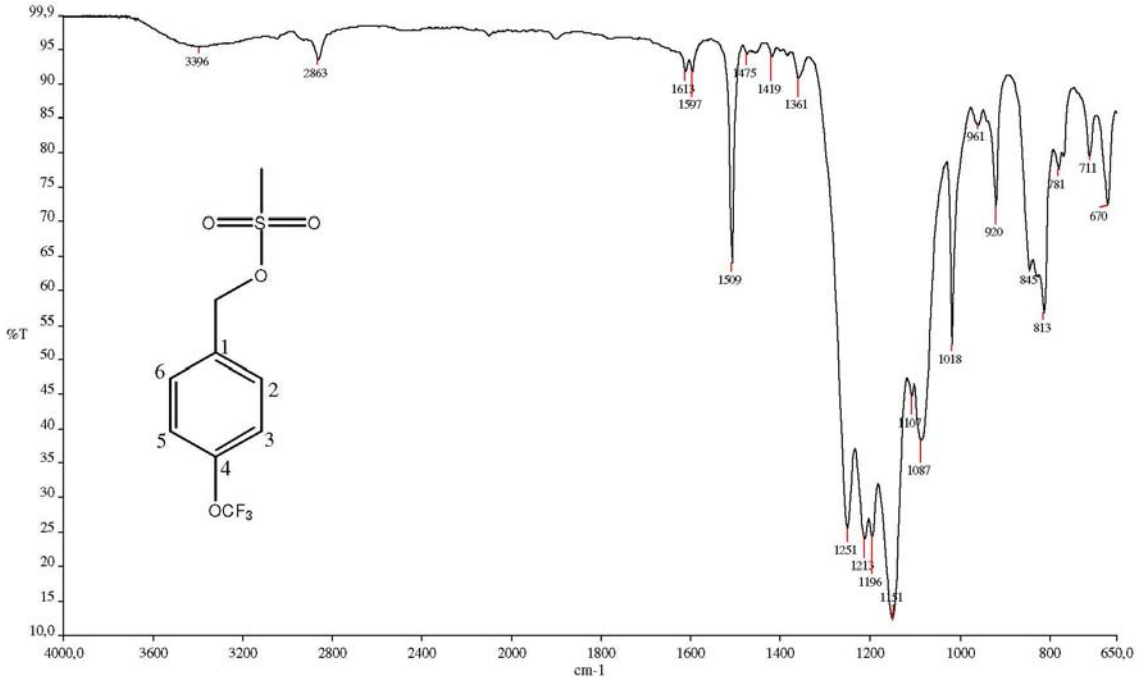

Figure S51. IR (ATR) spectrum of 4-(trifluoromethoxy)benzyl methanesulfonate (**2f**).

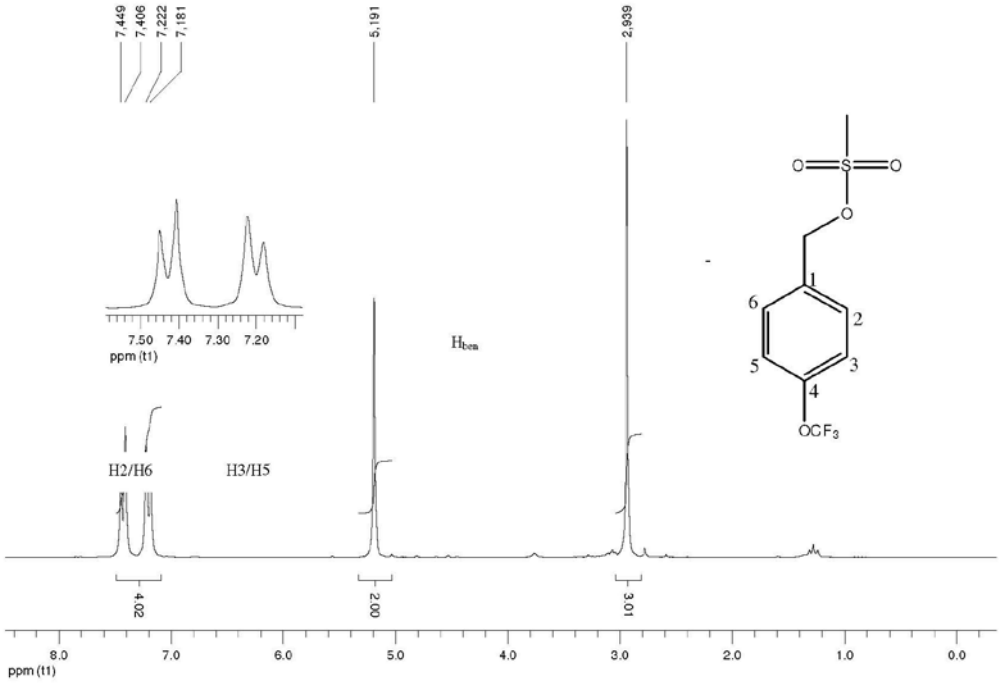

Figure S52. ^{1}H NMR spectrum (200 MHz, $CDCl_3$) of 4-(trifluoromethoxy)benzyl methanesulfonate (**2f**).

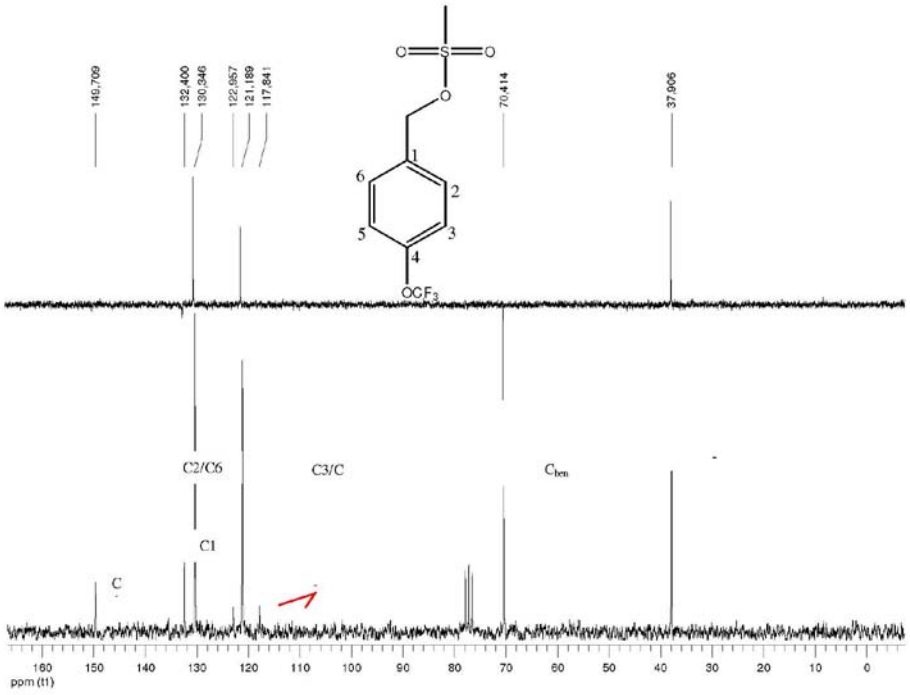

Figure S53. ^{13}C NMR and DEPT-135 spectrum (50 MHz, $CDCl_3$) of 4-(trifluoromethoxy)benzyl methanesulfonate (**2f**).

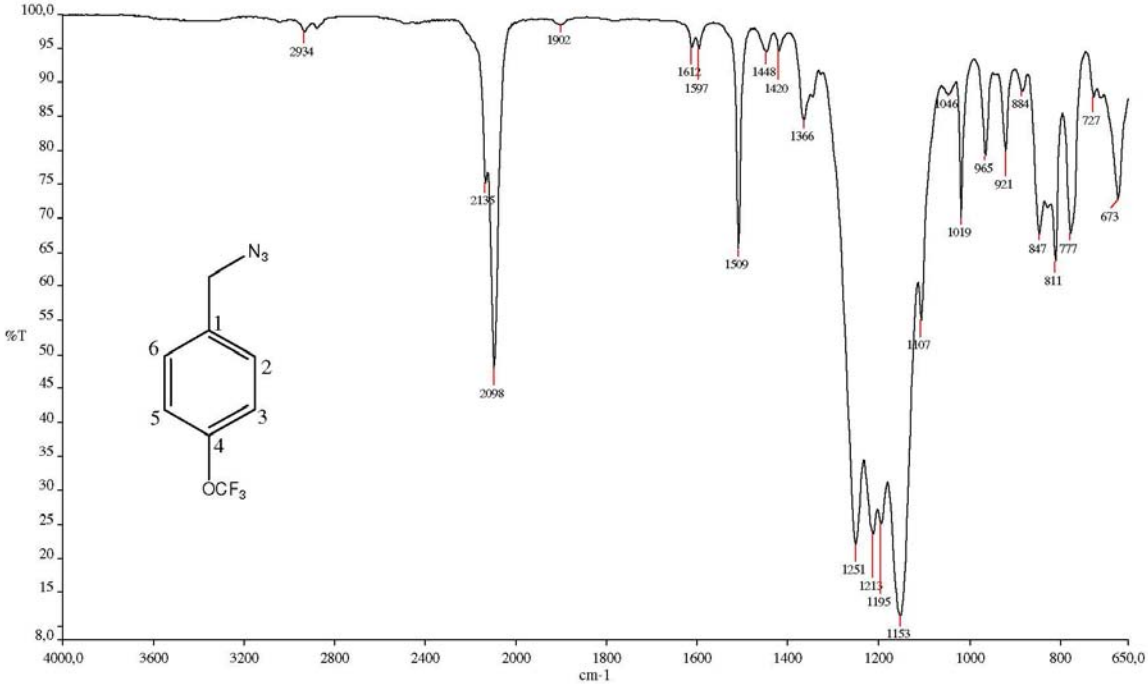

Figure S54. IR (ATR) spectrum of 1-(azidomethyl)-4-(trifluoromethoxy)benzene (**3f**).

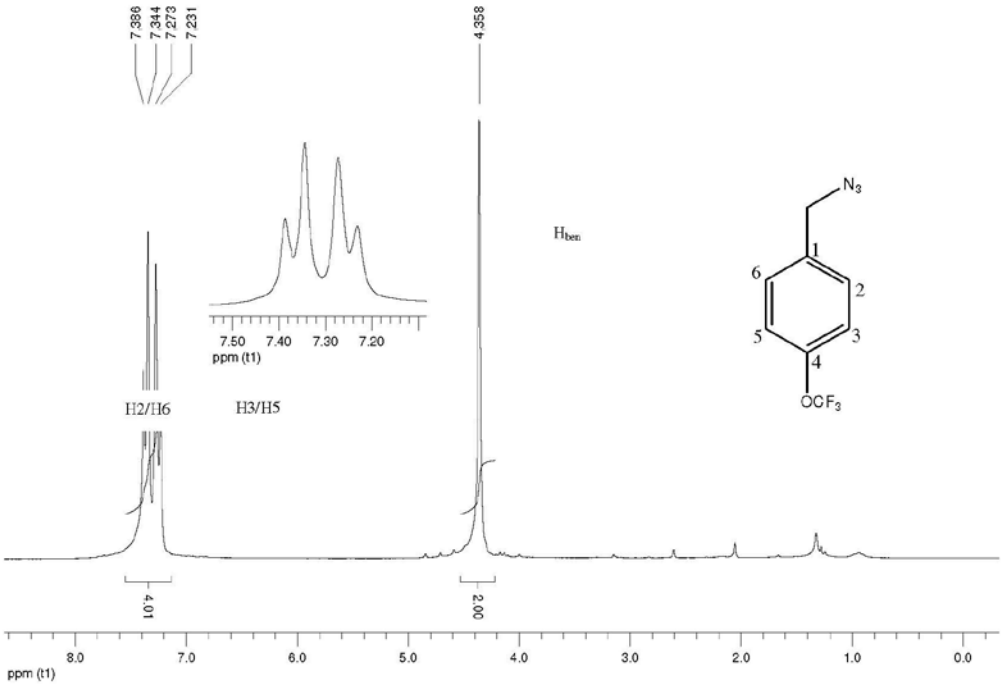

Figure S55. ^{1}H NMR spectrum (200 MHz, $CDCl_3$) of 1-(azidomethyl)-4-(trifluoromethoxy)benzene (**3f**).

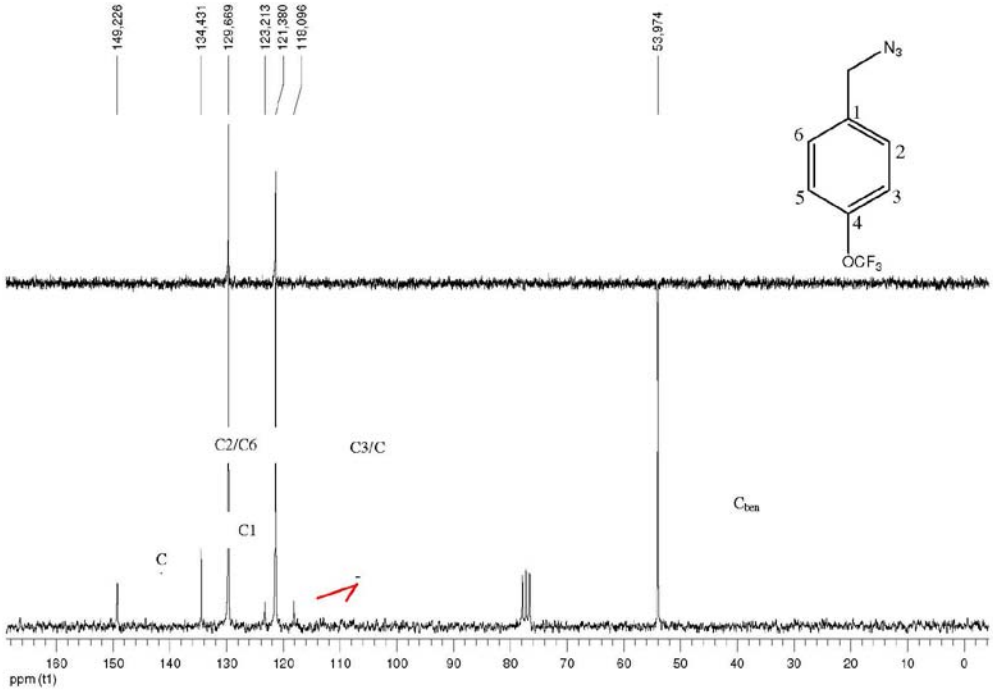

Figure S56. ^{13}C NMR and DEPT-135 spectrum (50 MHz, $CDCl_3$) of 1-(azidomethyl)-4-(trifluoromethoxy)benzene (**3f**).

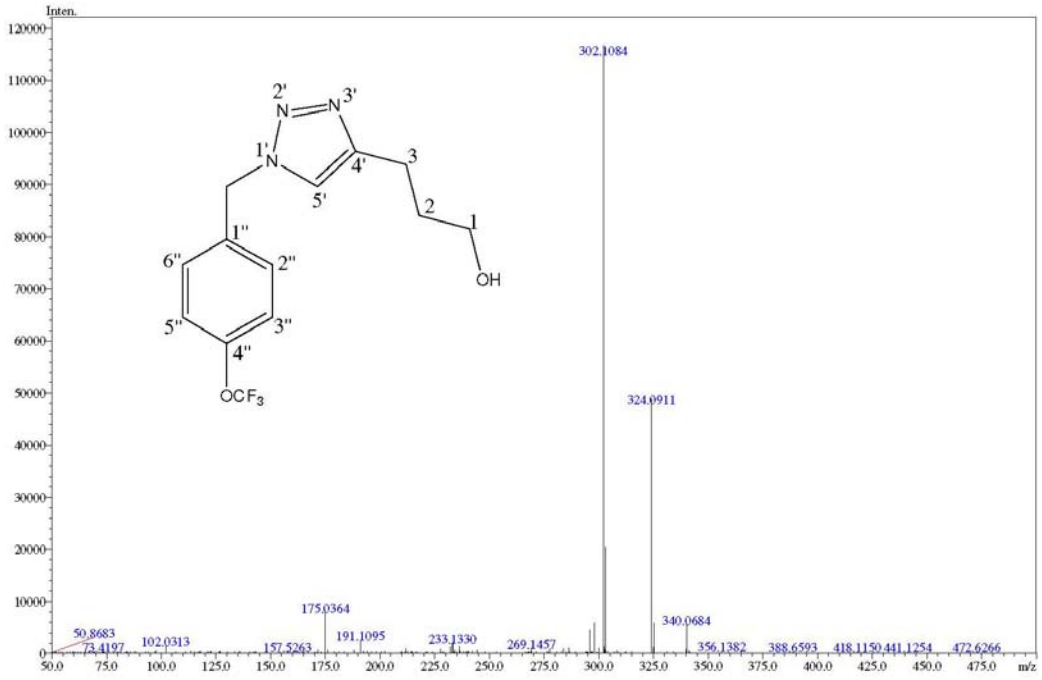

Figure S57. HRMS spectrum of 3-[1'-(4''-trifluoromethoxybenzyl)-1',2',3'-triazol-4'-yl]propan-1-ol (**4f**).

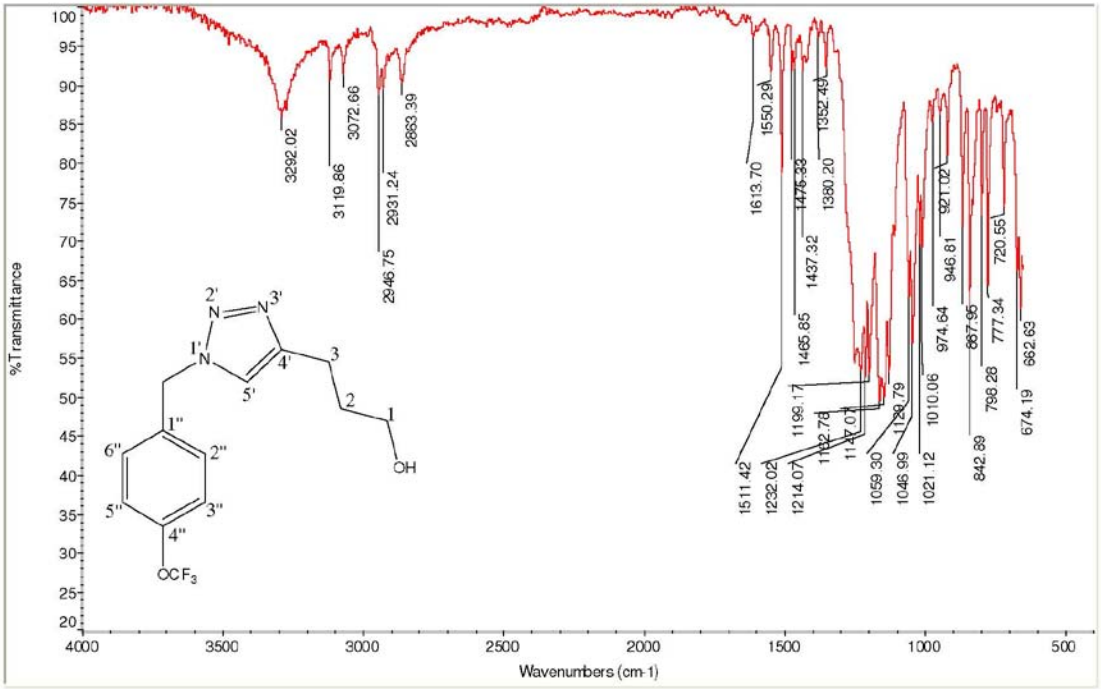

Figure S58. IR (ATR) spectrum of 3-[1'-(4''-trifluoromethoxybenzyl)-1',2',3'-triazol-4'-yl]propan-1-ol (**4f**).

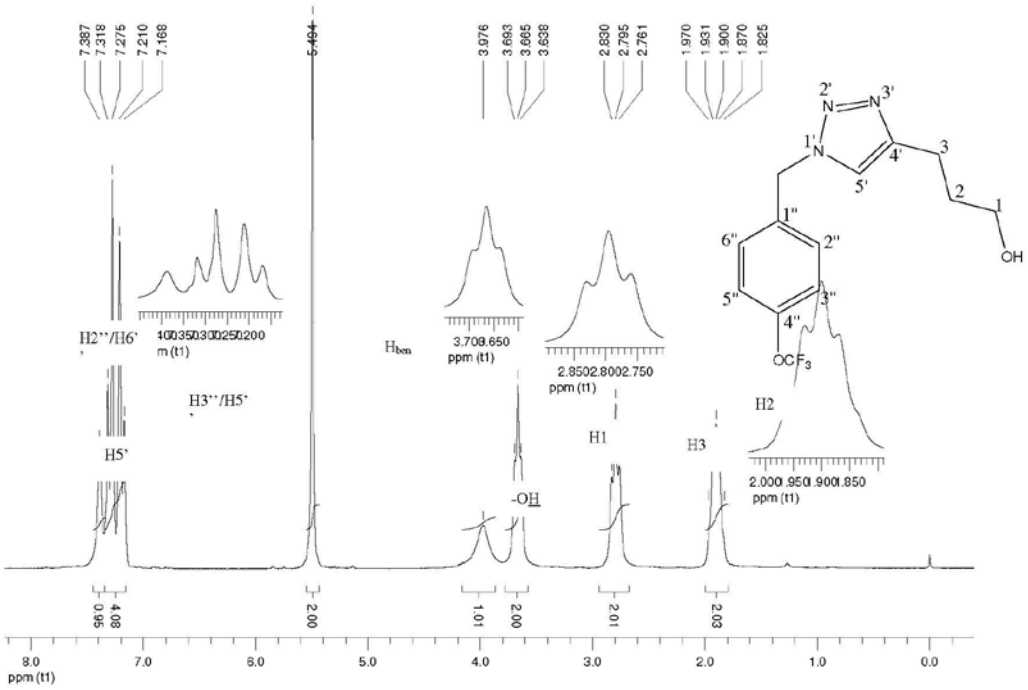

Figure S59. ^{1}H NMR spectrum (200 MHz, $CDCl_3$) of 3-[1'-(4''-trifluoromethoxybenzyl)-1',2',3'-triazol-4'-yl]propan-1-ol (**4f**).

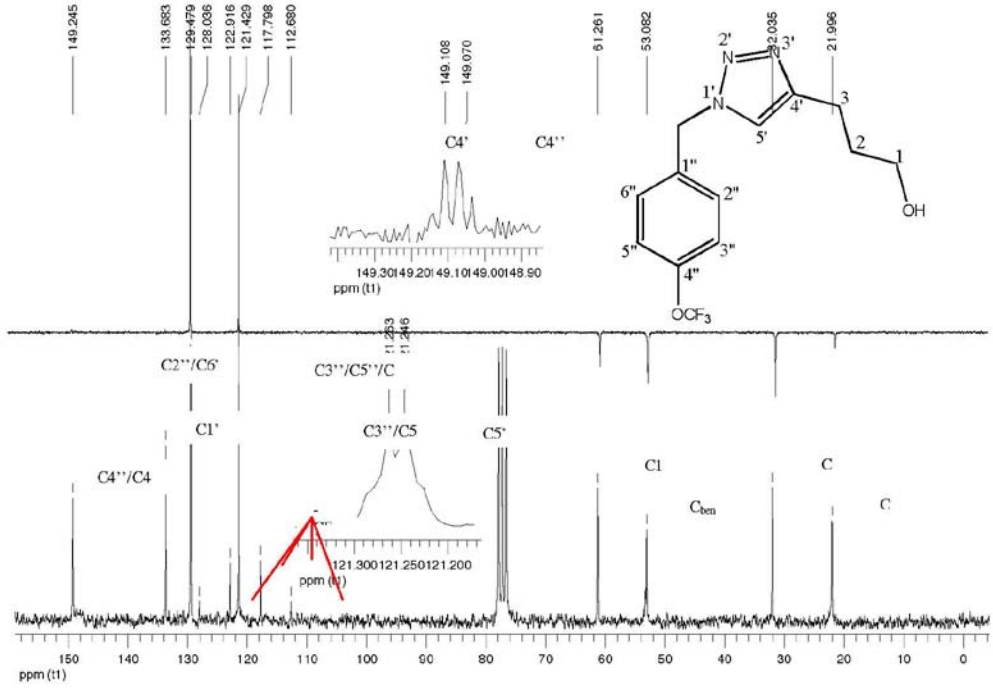

Figure S60. ^{13}C NMR and DEPT-135 spectrum (50 MHz, $CDCl_3$) of 3-[1'-(4''-trifluoromethoxybenzyl)-1',2',3'-triazol-4'-yl]propan-1-ol (**4f**).

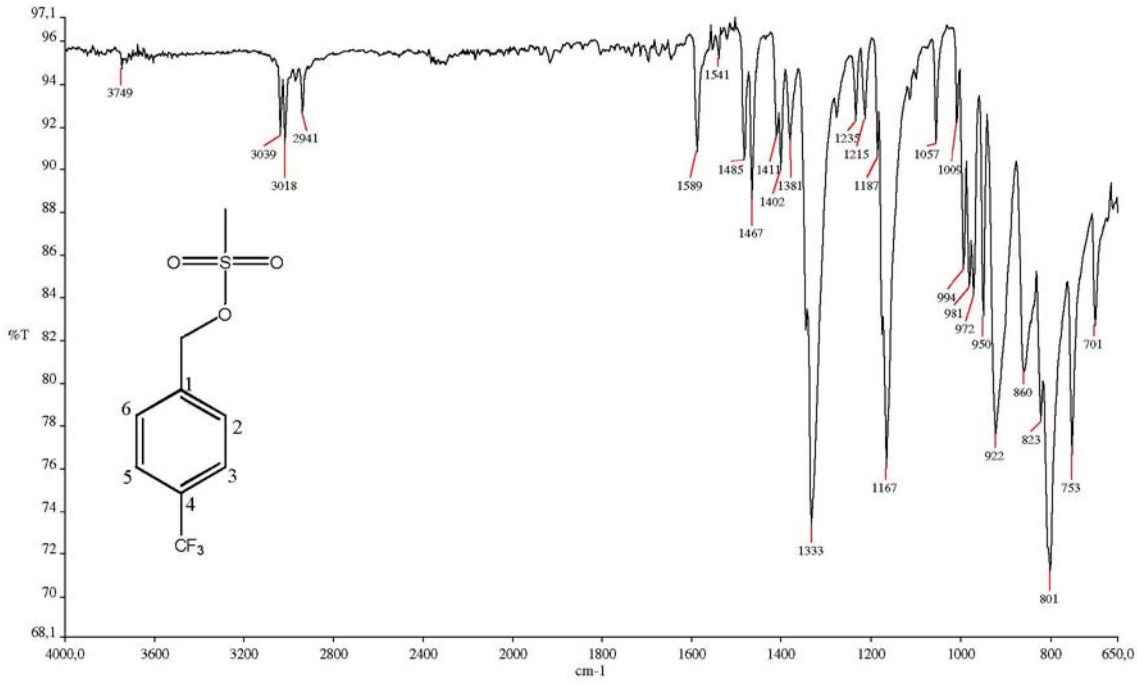

Figure S61. IR (ATR) spectrum of 4-(trifluoromethyl)benzyl methanesulfonate (**2g**).

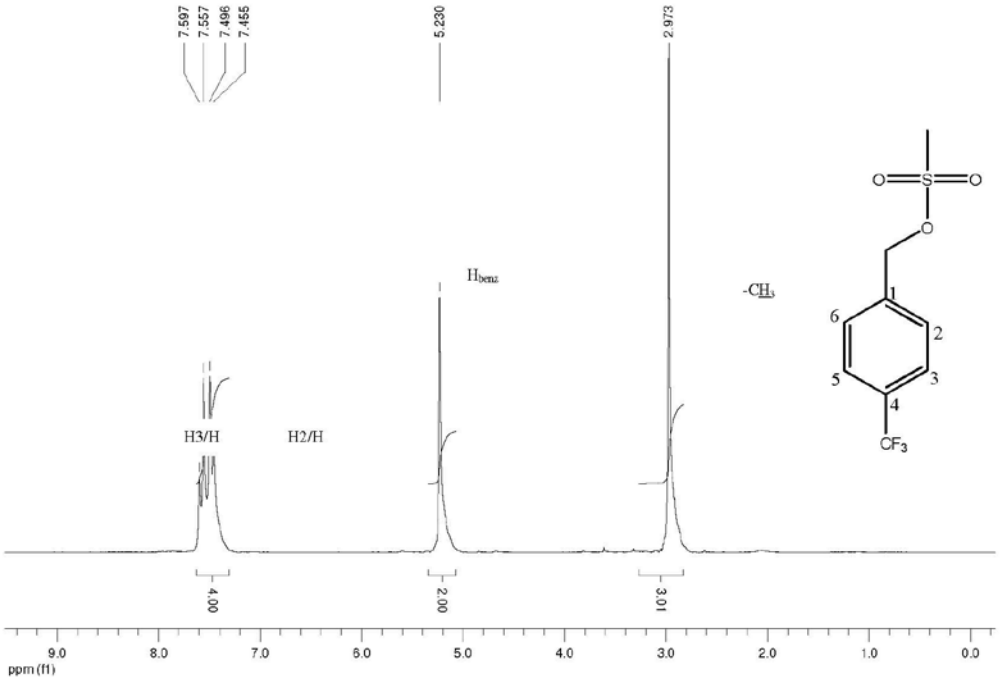

Figure S62. ^{1}H NMR spectrum (200 MHz, $CDCl_3$) of 4-(trifluoromethyl)benzyl methanesulfonate (**2g**).

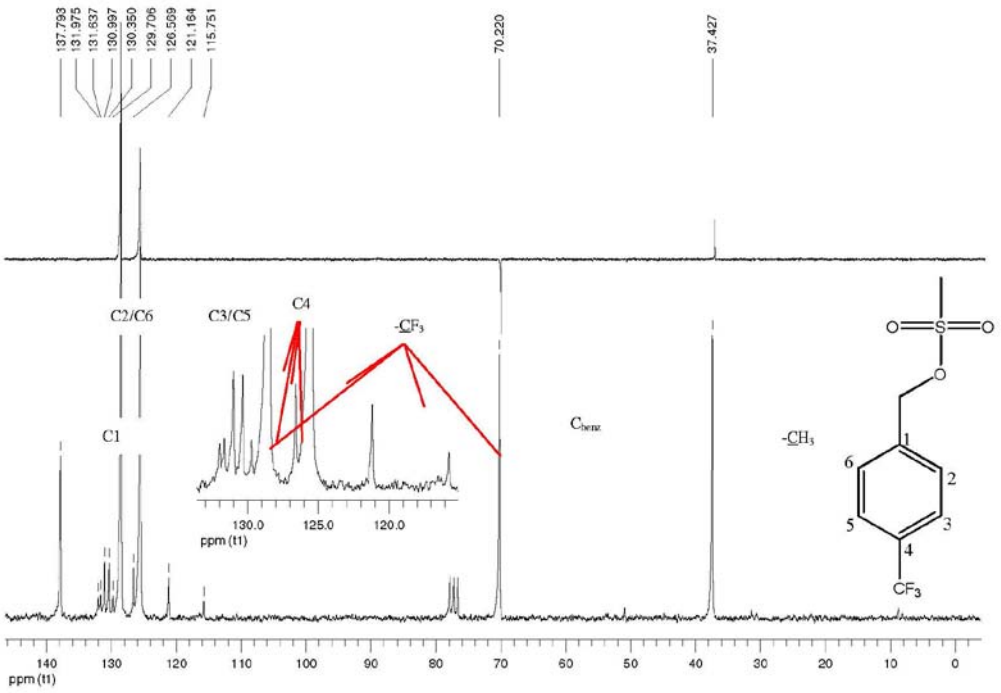

Figure S63. ^{13}C NMR and DEPT-135 spectrum (50 MHz, $CDCl_3$) of 4-(trifluoromethyl)benzyl methanesulfonate (**2g**).

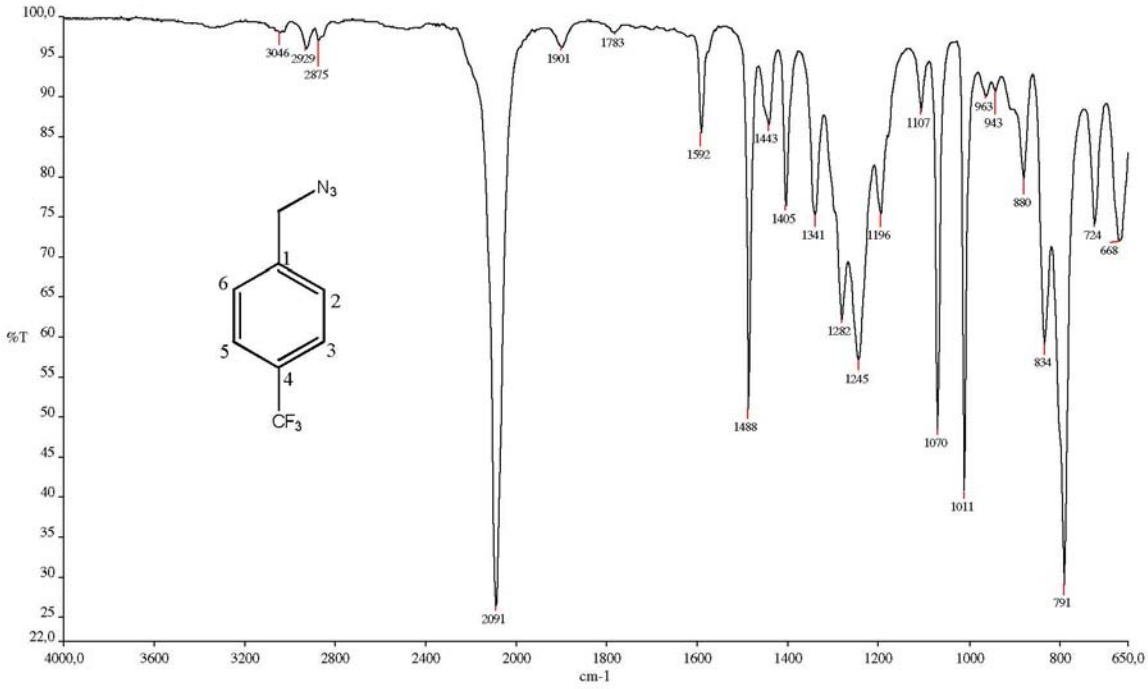

Figure S64. IR (ATR) spectrum of 1-(azidomethyl)-4-(trifluoromethyl)benzene (**3g**).

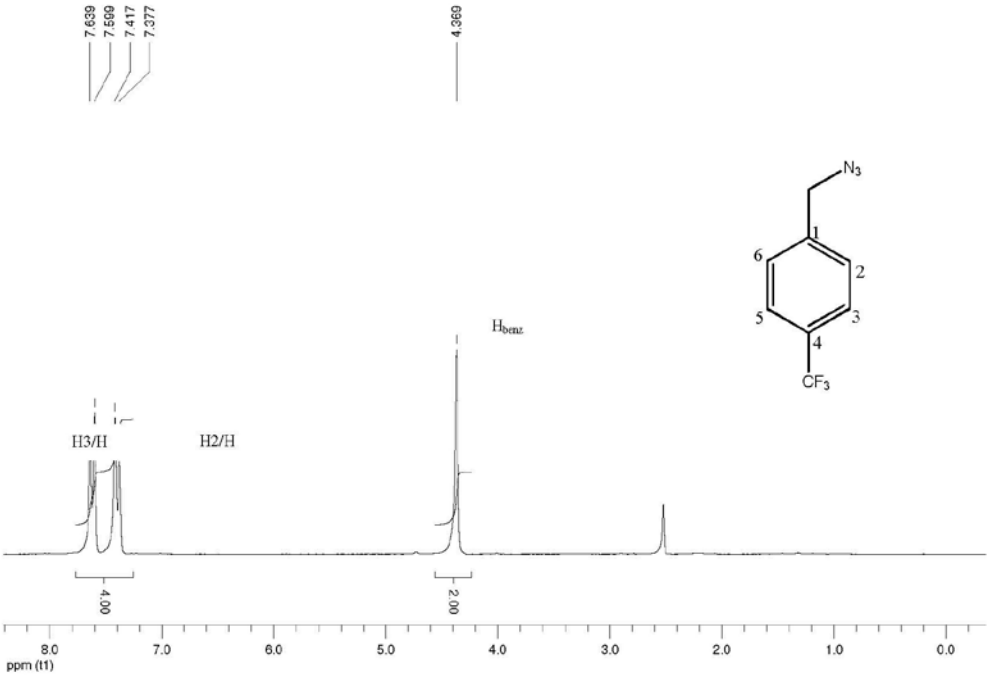

Figure S65. [1]H NMR spectrum (200 MHz, $CDCl_3$) of 1-(azidomethyl)-4-(trifluoromethyl)benzene (**3g**).

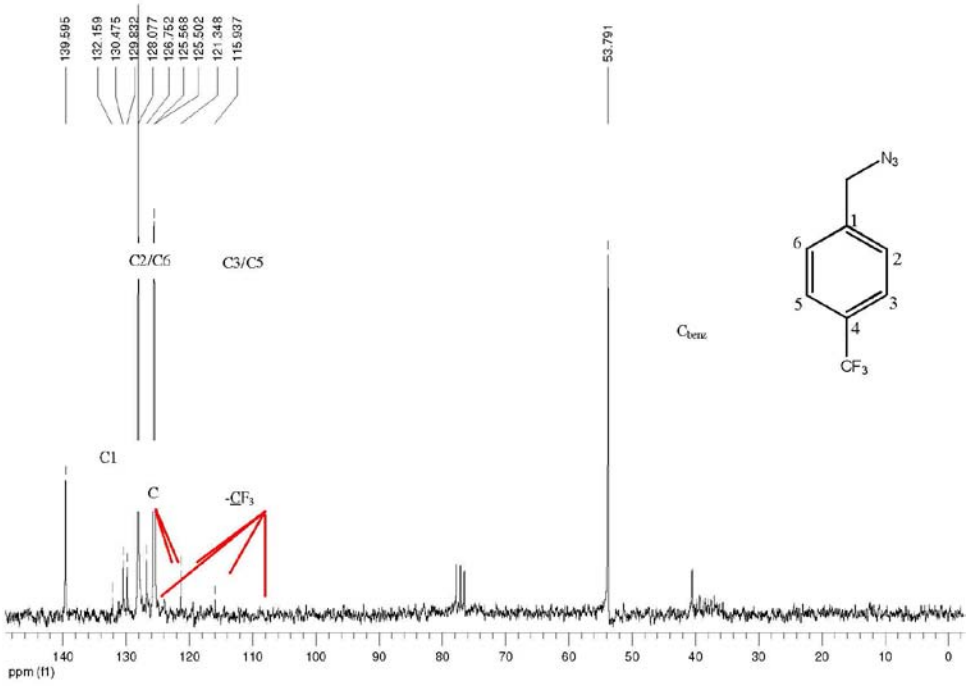

Figure S66. [13]C NMR and DEPT-135 spectrum (50 MHz, $CDCl_3$) of 1-(azidomethyl)-4-(trifluoromethyl)benzene (**3g**).

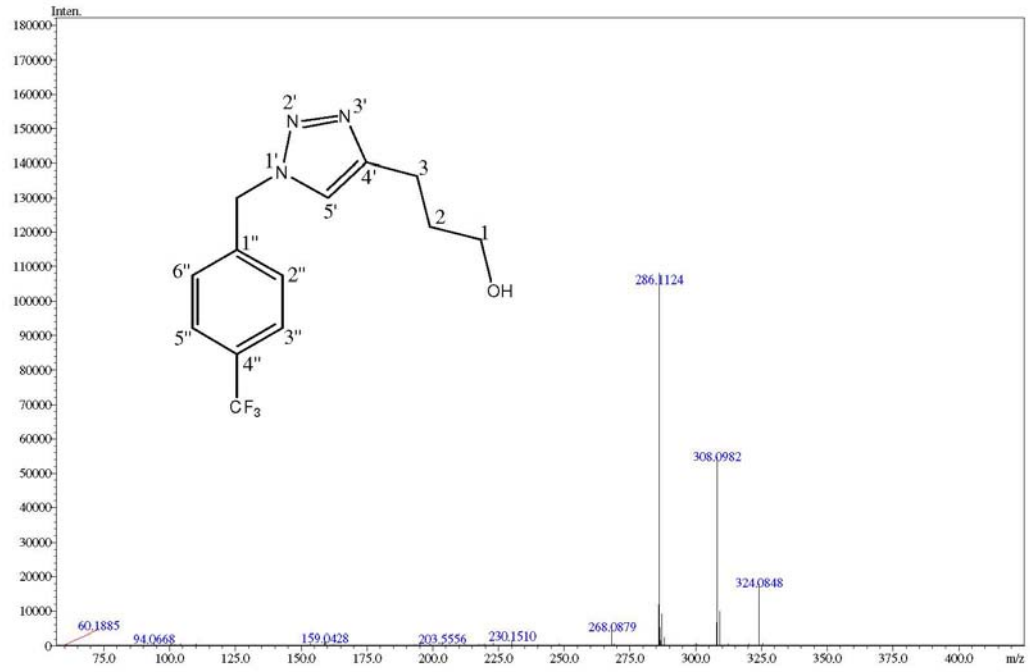

Figure S67. HRMS spectrum of 3-[1'-(4''-trifluoromethylbenzyl)-1',2',3'-triazol-4'-yl]propan-1-ol (**4g**).

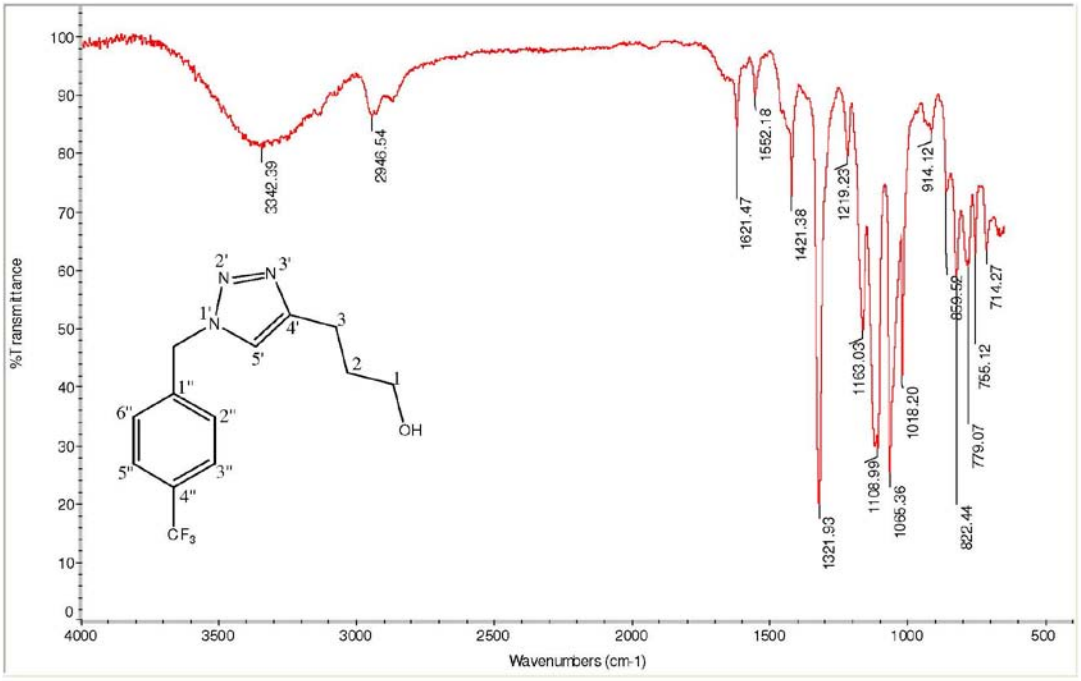

Figure S68. IR (ATR) spectrum of 3-[1'-(4''-trifluoromethylbenzyl)-1',2',3'-triazol-4'-yl]propan-1-ol (**4g**).

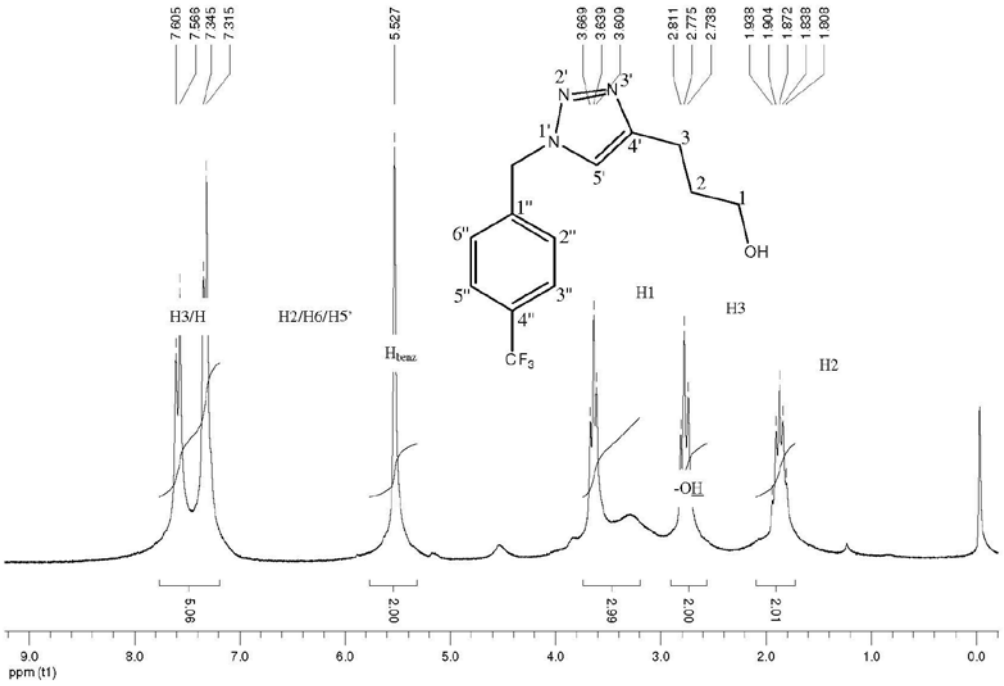

Figure S69. ^{1}H NMR spectrum (200 MHz, $CDCl_3$) of 3-[1'-(4''-trifluoromethylbenzyl)-1',2',3'-triazol-4'-yl]propan-1-ol (**4g**).

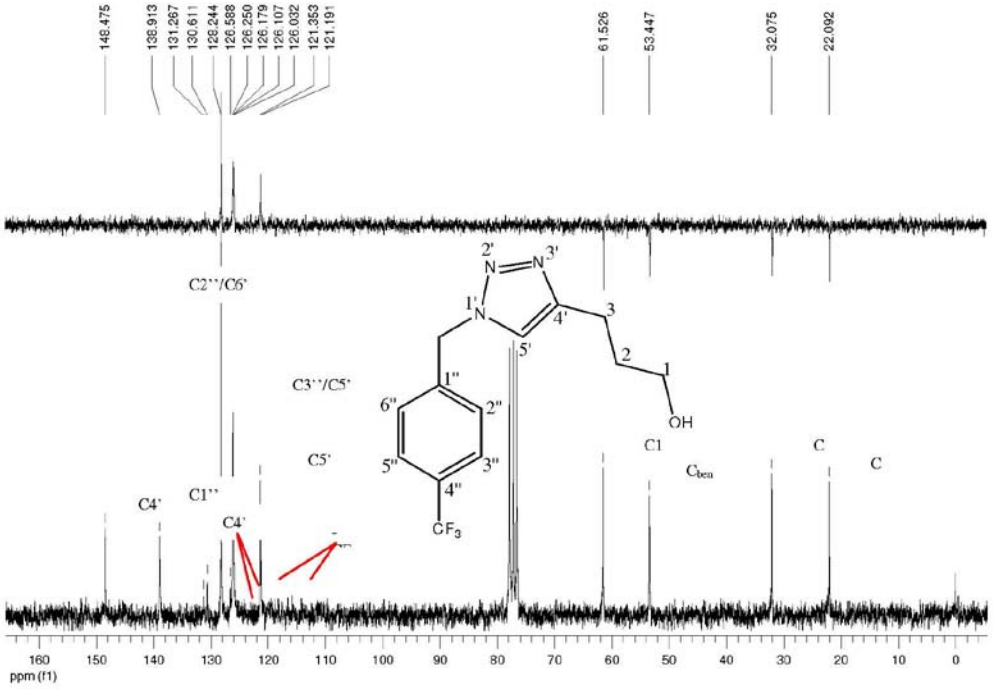

Figure S70. ^{13}C NMR and DEPT-135 spectrum (50 MHz, $CDCl_3$) of 3-[1'-(4''-trifluoromethylbenzyl)-1',2',3'-triazol-4'-yl]propan-1-ol (**4g**).

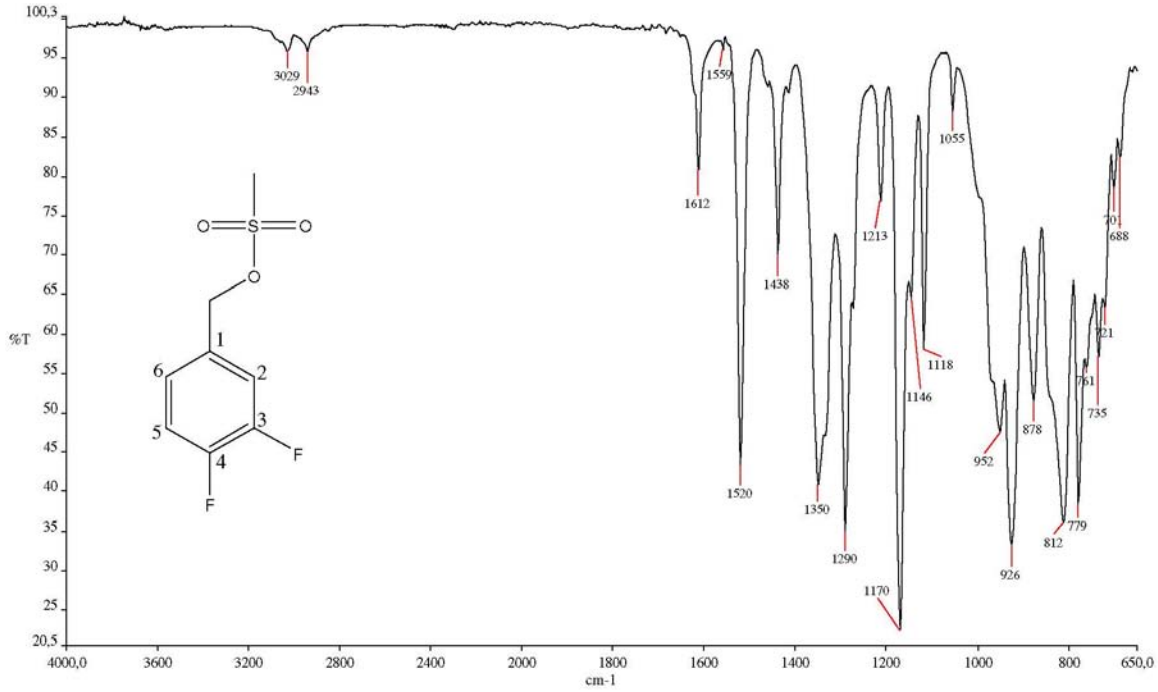

Figure S71. IR (ATR) spectrum of 3,4-(difluoro)benzyl methanesulfonate (**2h**).

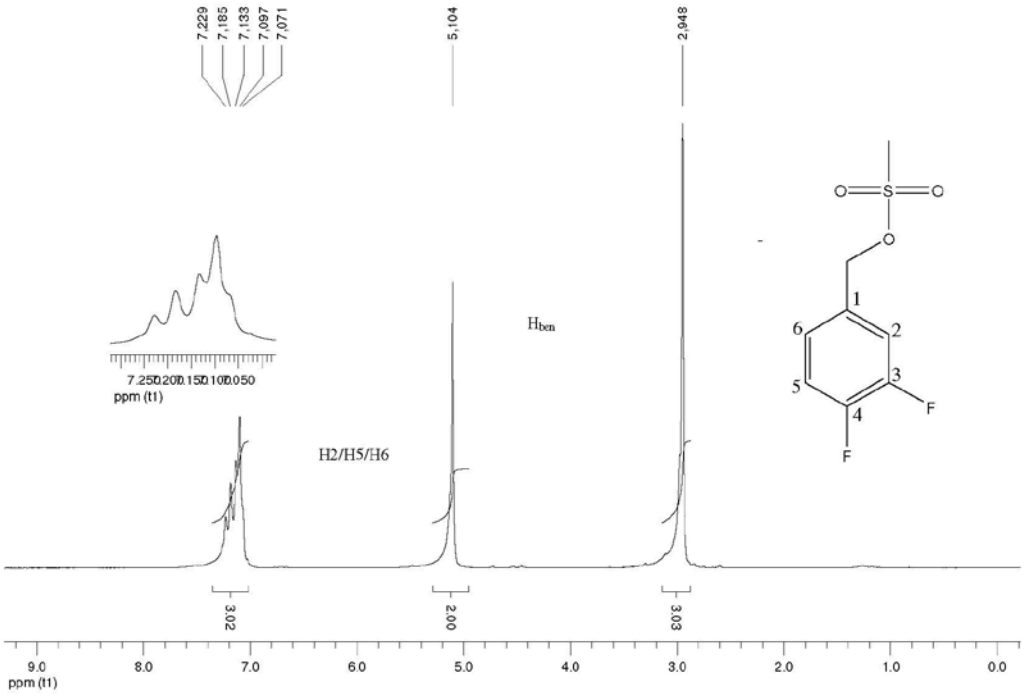

Figure S72. ^{1}H NMR spectrum (200 MHz, $CDCl_3$) of 3,4-(difluoro)benzyl methanesulfonate (**2h**).

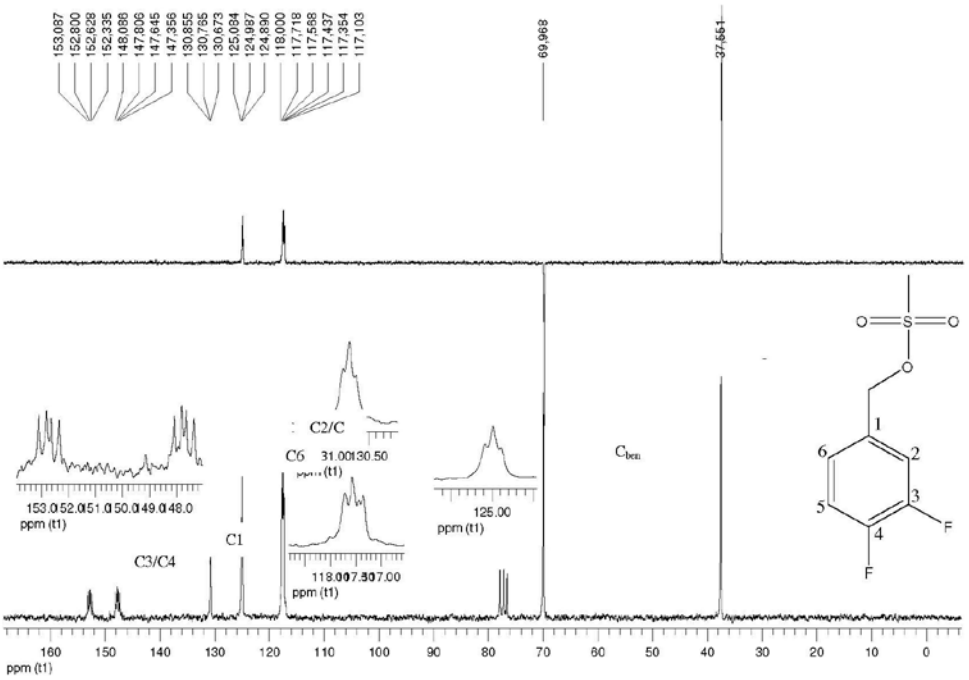

Figure S73. ^{13}C NMR and DEPT-135 spectrum (50 MHz, $CDCl_3$) of 3,4-(difluoro)benzyl methanesulfonate (**2h**).

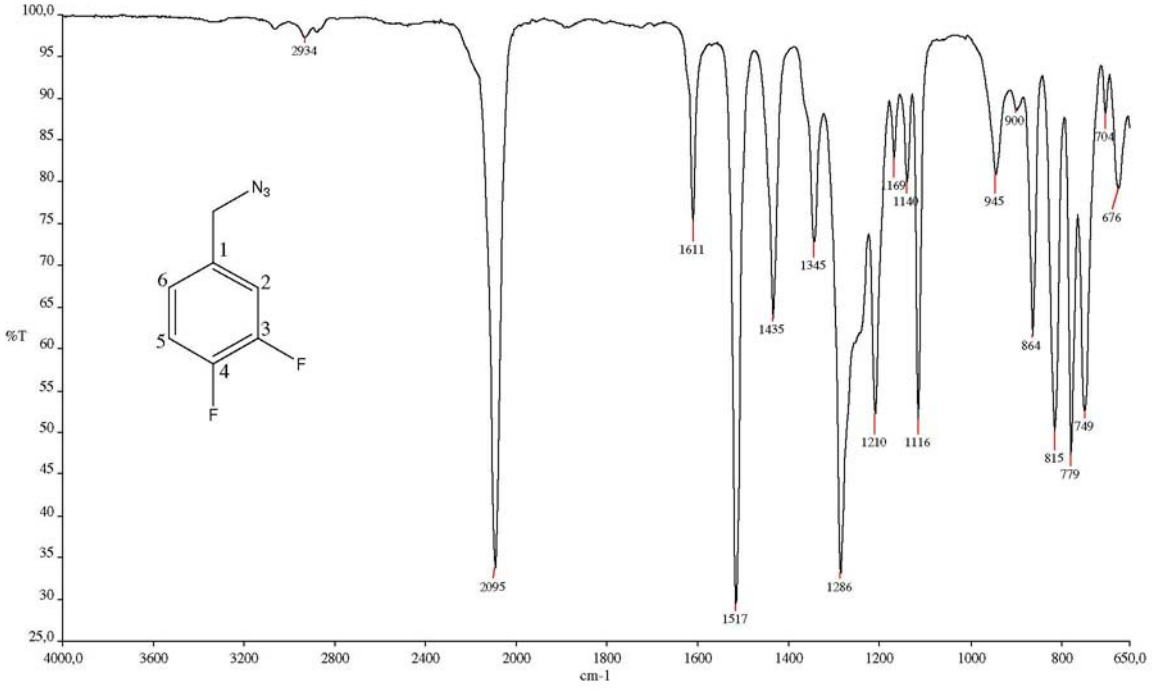

Figure S74. IR (ATR) spectrum of 1-(azidomethyl)-3,4-(difluoro)benzene (**3h**).

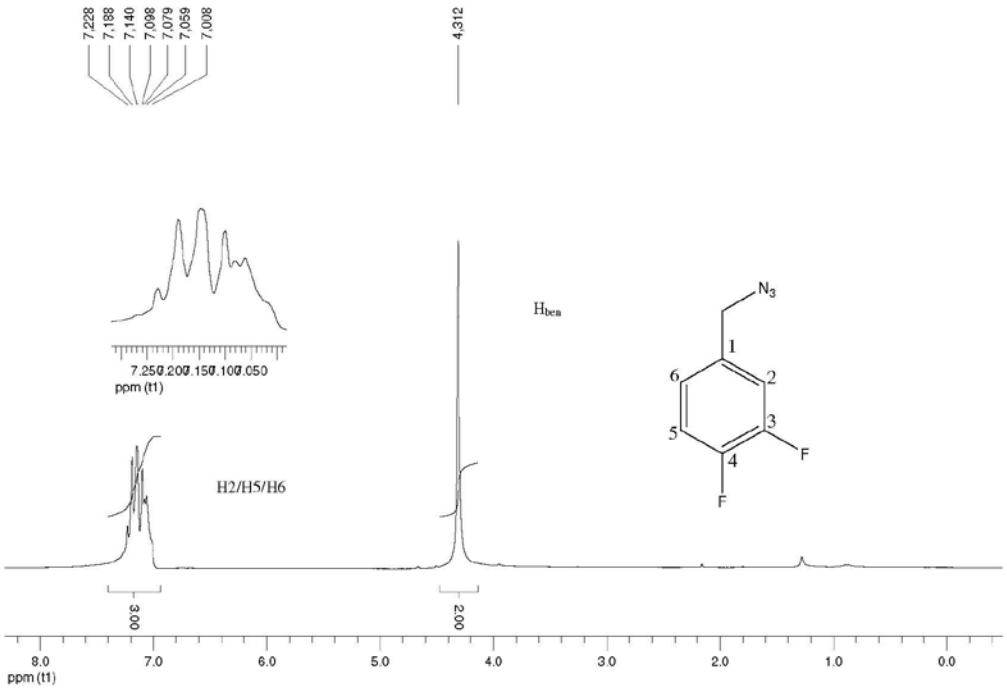

Figure S75. ^{1}H NMR spectrum (200 MHz, $CDCl_3$) of 1-(azidomethyl)-3,4-(difluoro)benzene (**3h**).

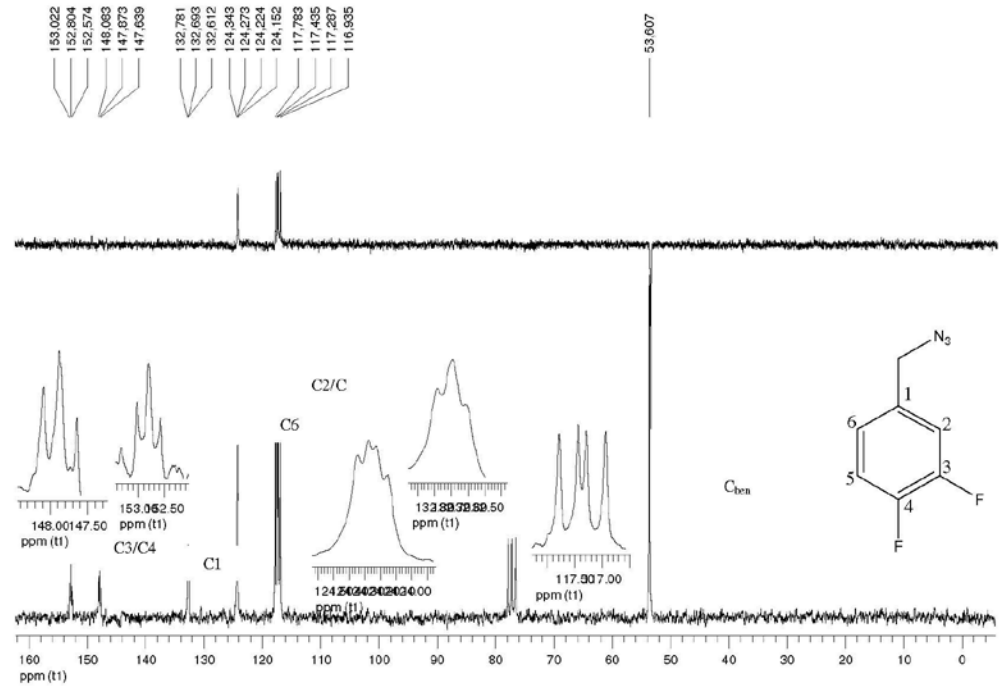

Figure S76. ^{13}C NMR and DEPT-135 spectrum (50 MHz, $CDCl_3$) of 1-(azidomethyl)-3,4-(difluoro)benzene (**3h**).

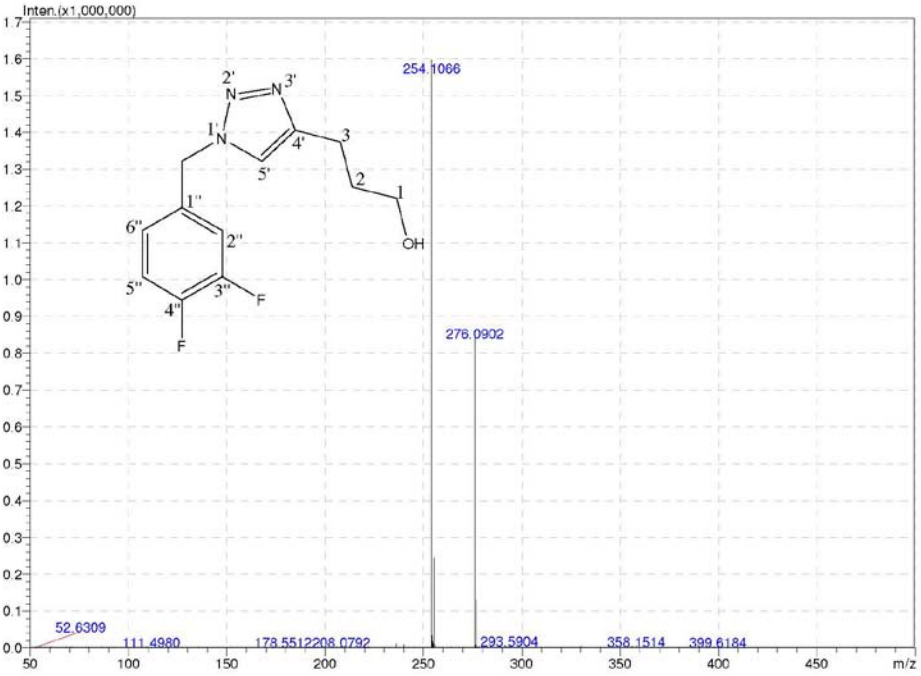

Figure S77. HRMS spectrum of 3-[1'-(3'',4''-difluorobenzyl)-1',2',3'-triazol-4'-yl]propan-1-ol (**4h**).

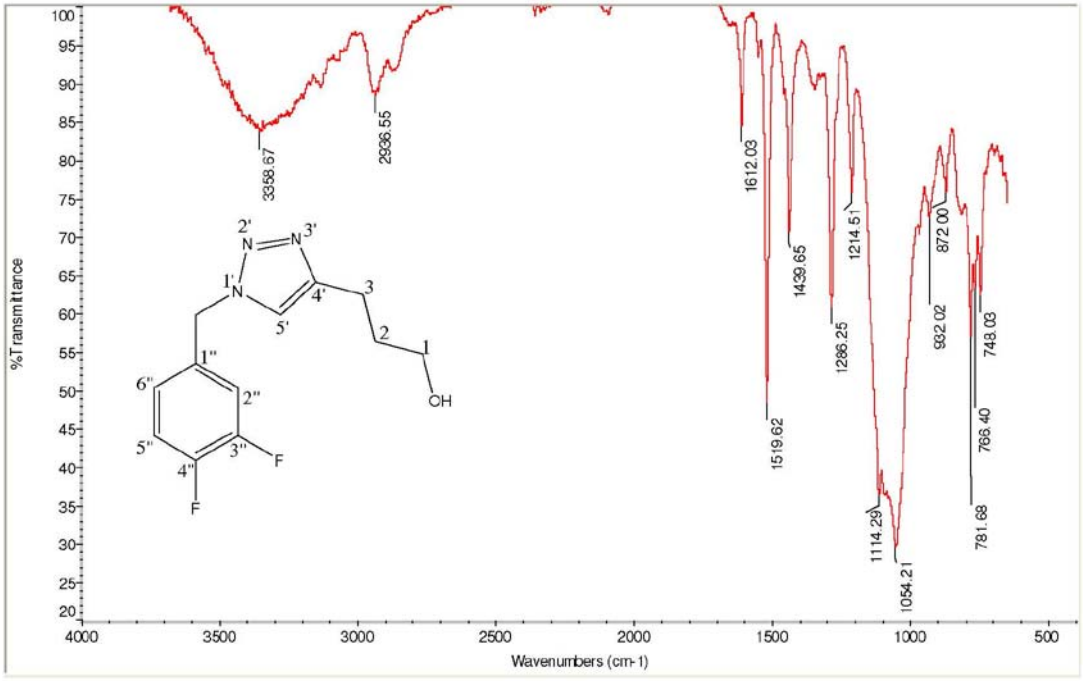

Figure S78. IR (ATR) spectrum of 3-[1'-(3'',4''-difluorobenzyl)-1',2',3'-triazol-4'-yl]propan-1-ol (**4h**).

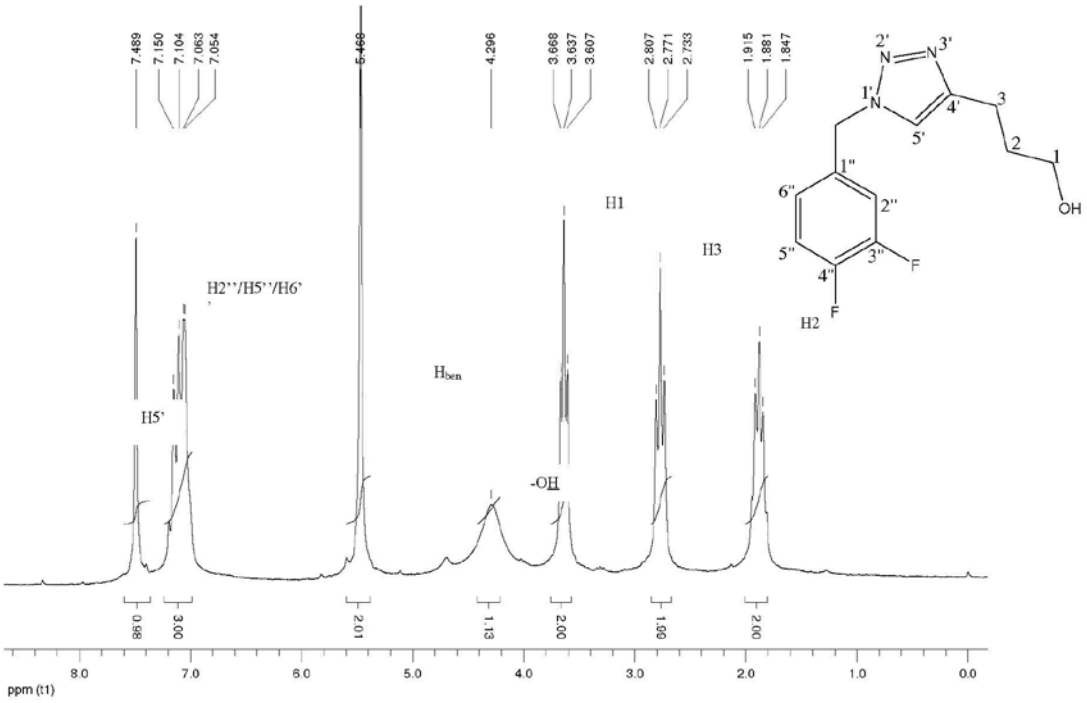

Figure S79. ^{1}H NMR spectrum (200 MHz, $CDCl_3$) of 3-[1'-(3'',4''-difluorobenzyl)-1',2',3'-triazol-4'-yl]propan-1-ol (**4h**).

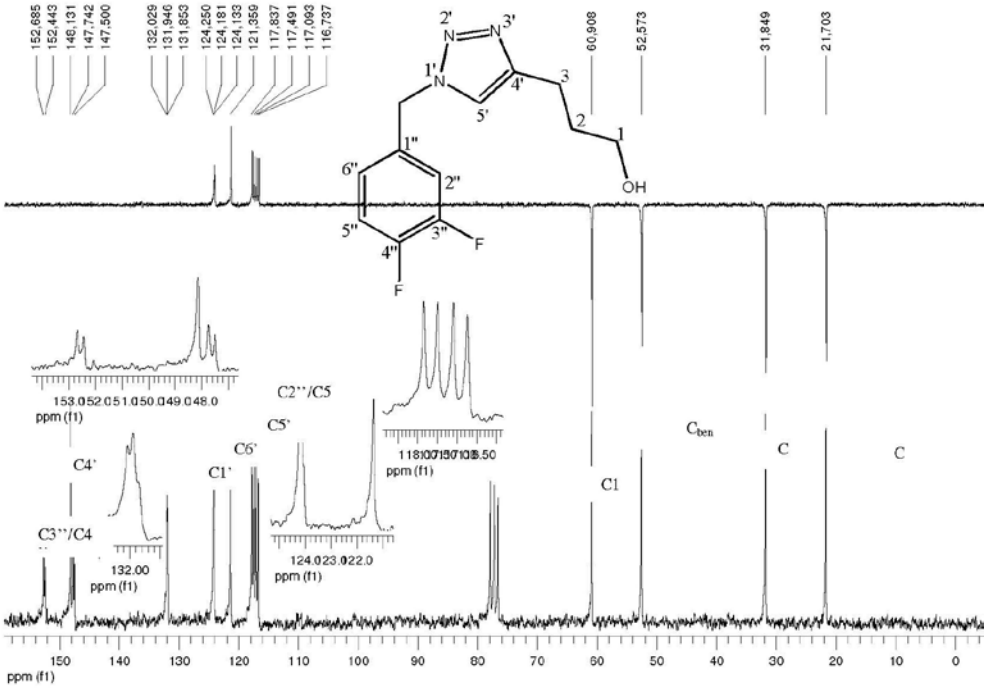

Figure S80. ^{13}C NMR and DEPT-135 spectrum (50 MHz, $CDCl_3$) of 3-[1'-(3'',4''-difluorobenzyl)-1',2',3'-triazol-4'-yl]propan-1-ol (**4h**).

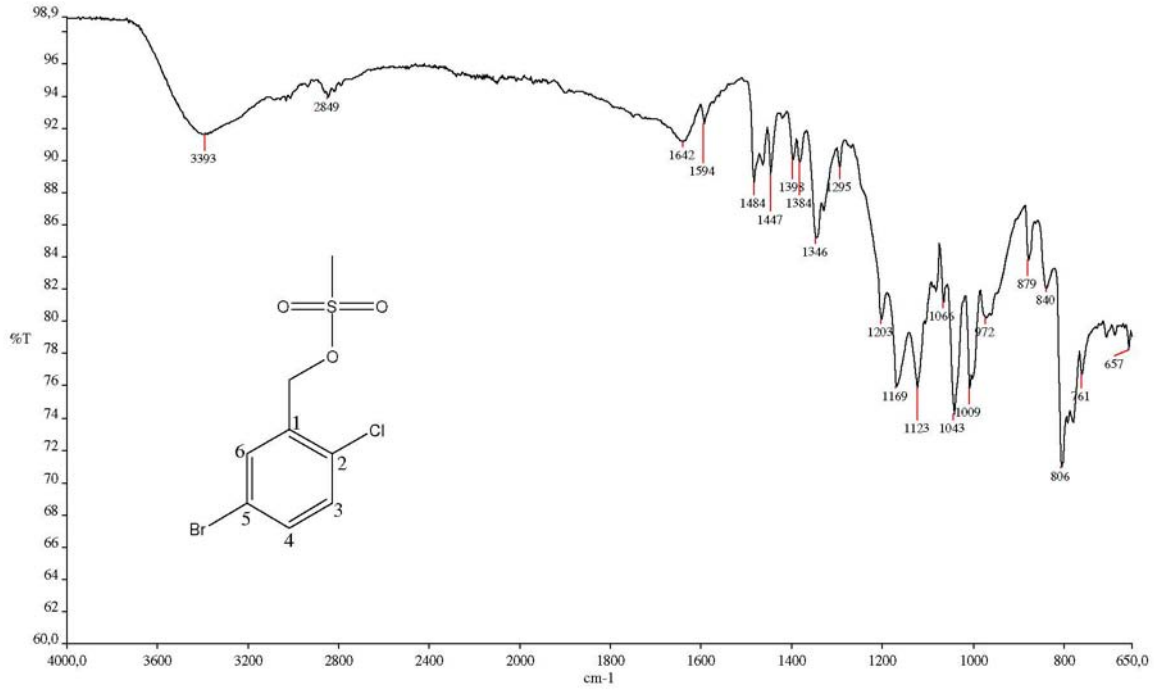

Figure S81. IR (ATR) spectrum of 5-bromo-2-chlorobenzyl methanesulfonate (**2i**).

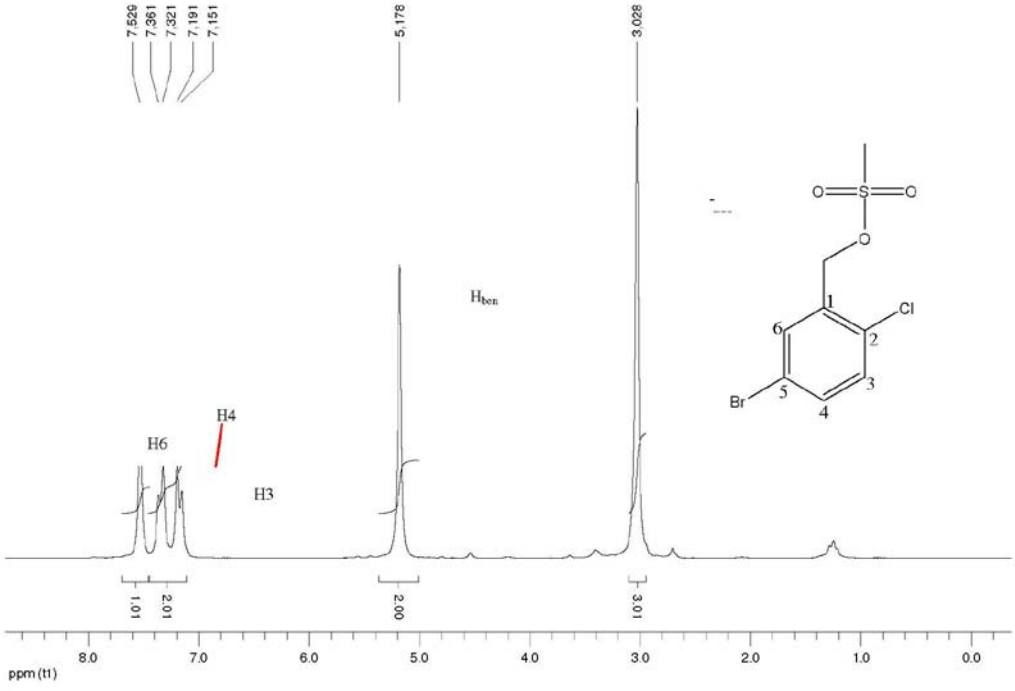

Figure S82. ^{1}H NMR spectrum (200 MHz, $CDCl_3$) of 5-bromo-2-chlorobenzyl methanesulfonate (**2i**).

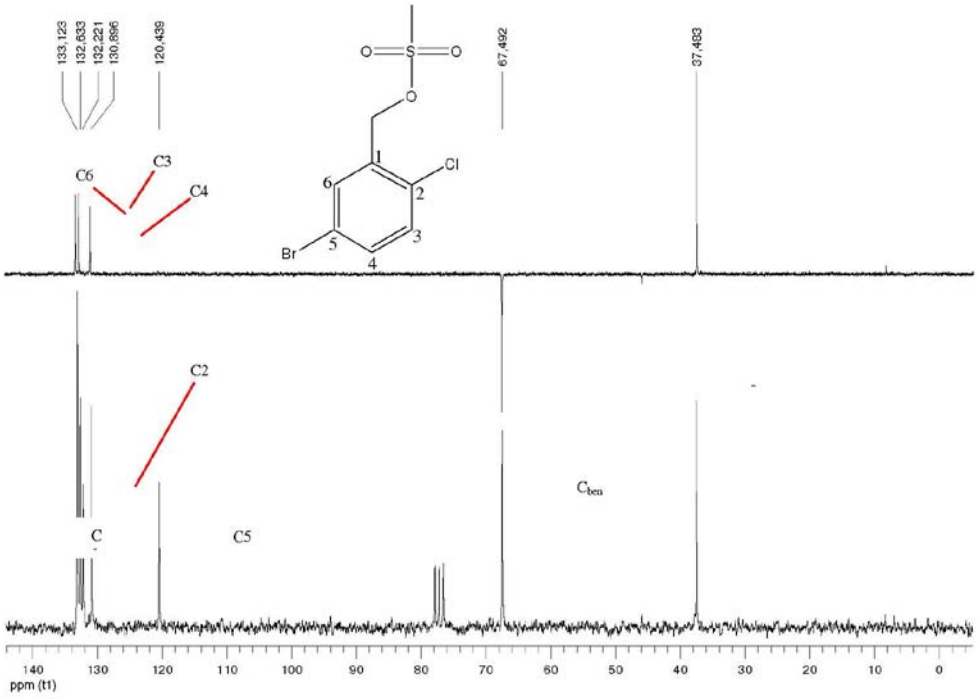

Figure S83. ^{13}C NMR and DEPT-135 spectrum (50 MHz, $CDCl_3$) of 5-bromo-2-chlorobenzyl methanesulfonate (**2i**).

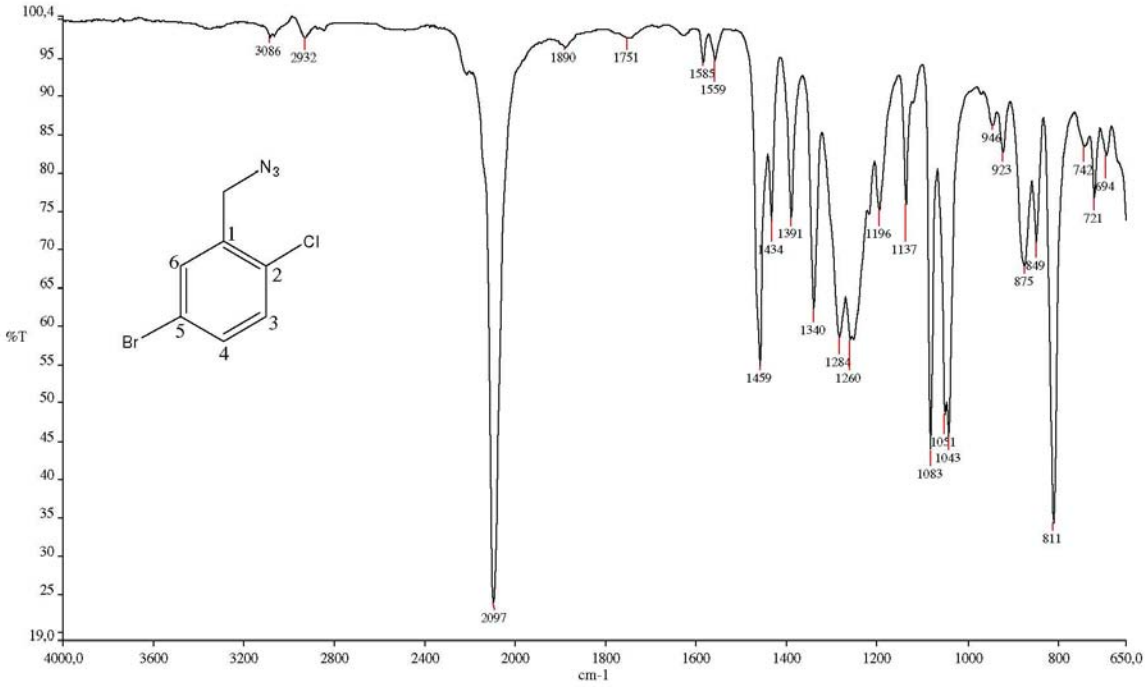

Figure S84. IR (ATR) spectrum of 1-(azidomethyl)-5-bromo-2-chlorobenzene (**3i**).

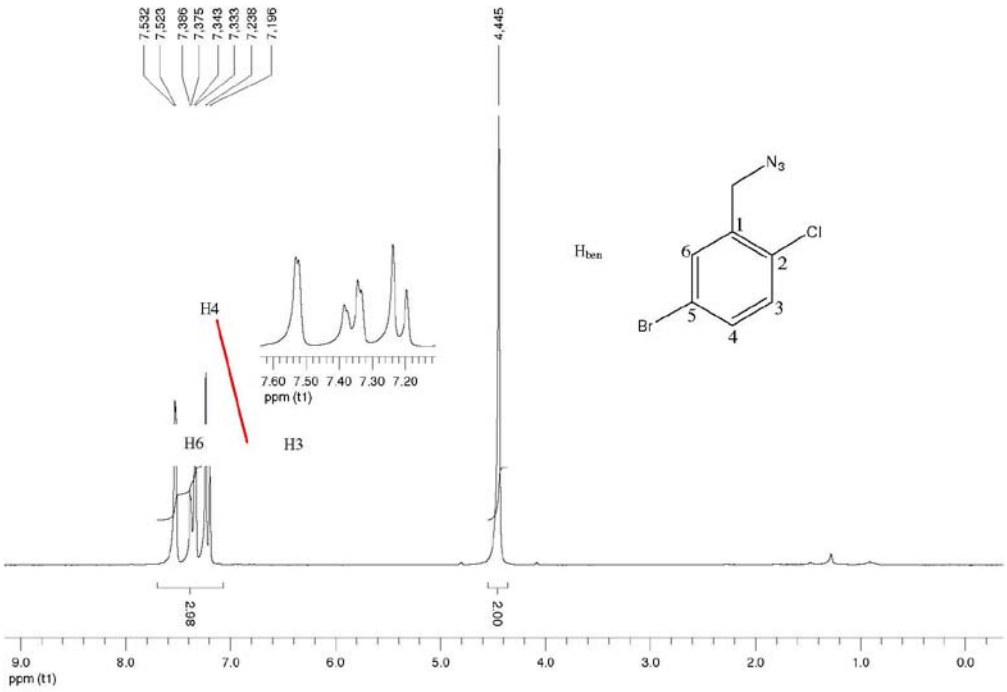

Figure S85. ^{1}H NMR spectrum (200 MHz, $CDCl_3$) of 1-(azidomethyl)-5-bromo-2-chlorobenzene (**3i**).

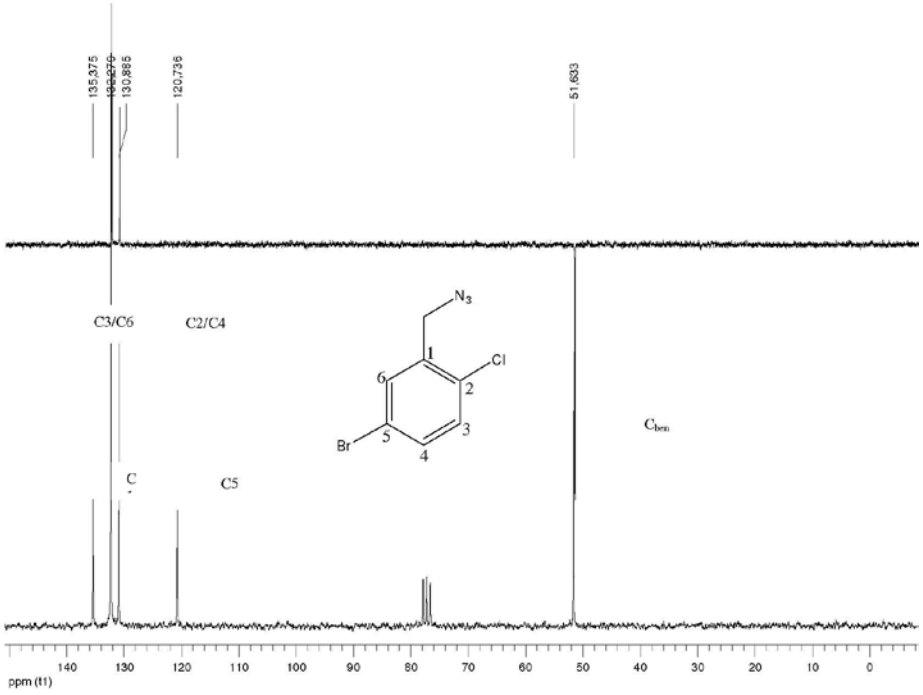

Figure S86. ^{13}C NMR and DEPT-135 spectrum (50 MHz, $CDCl_3$) of 1-(azidomethyl)-5-bromo-2-chlorobenzene (**3i**).

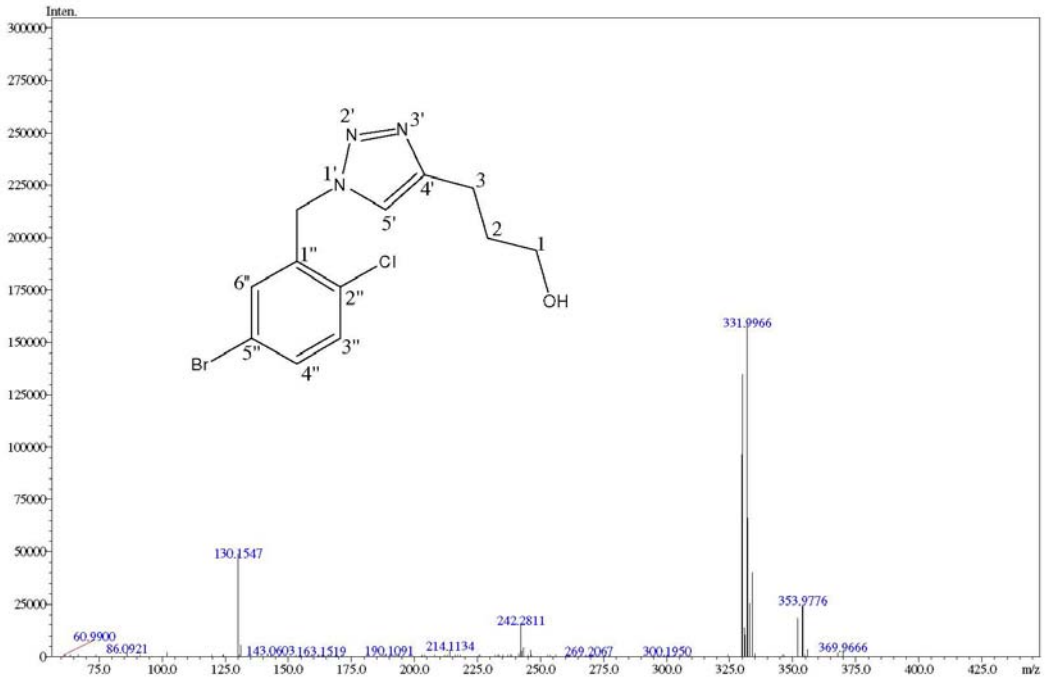

Figure S87. HRMS spectrum of 3-[1'-(5''-bromo-2''-chlorobenzyl)-1',2',3'-triazol-4'-yl]propan-1-ol (**4i**).

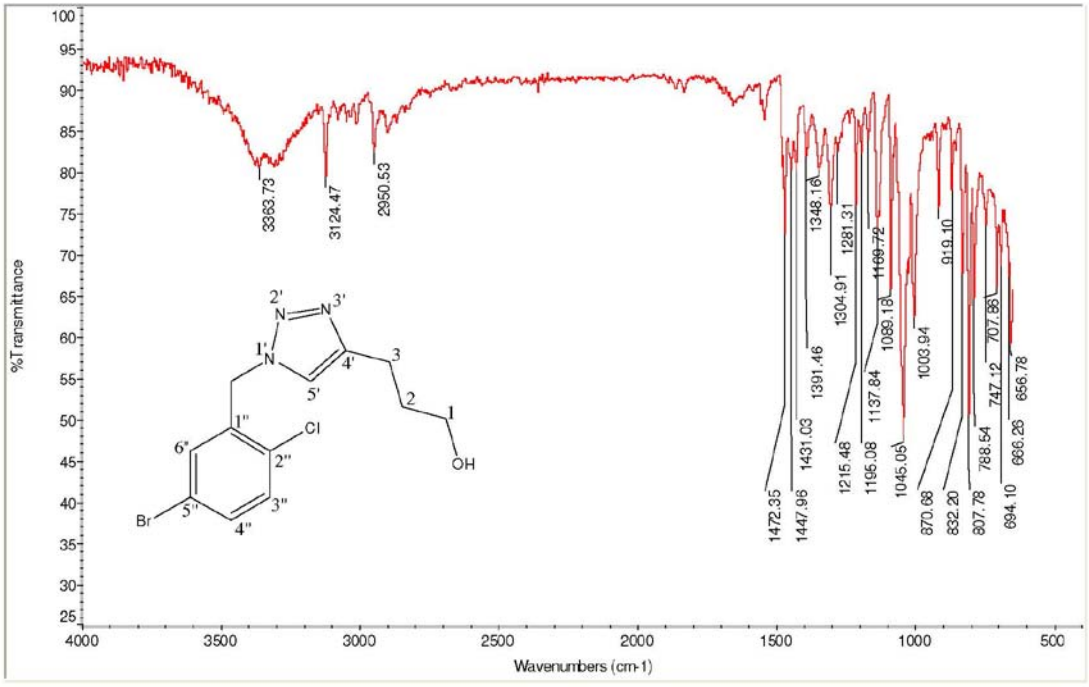

Figure S88. IR (ATR) spectrum of 3-[1'-(5''-bromo-2''-chlorobenzyl)-1',2',3'-triazol-4'-yl]propan-1-ol (**4i**).

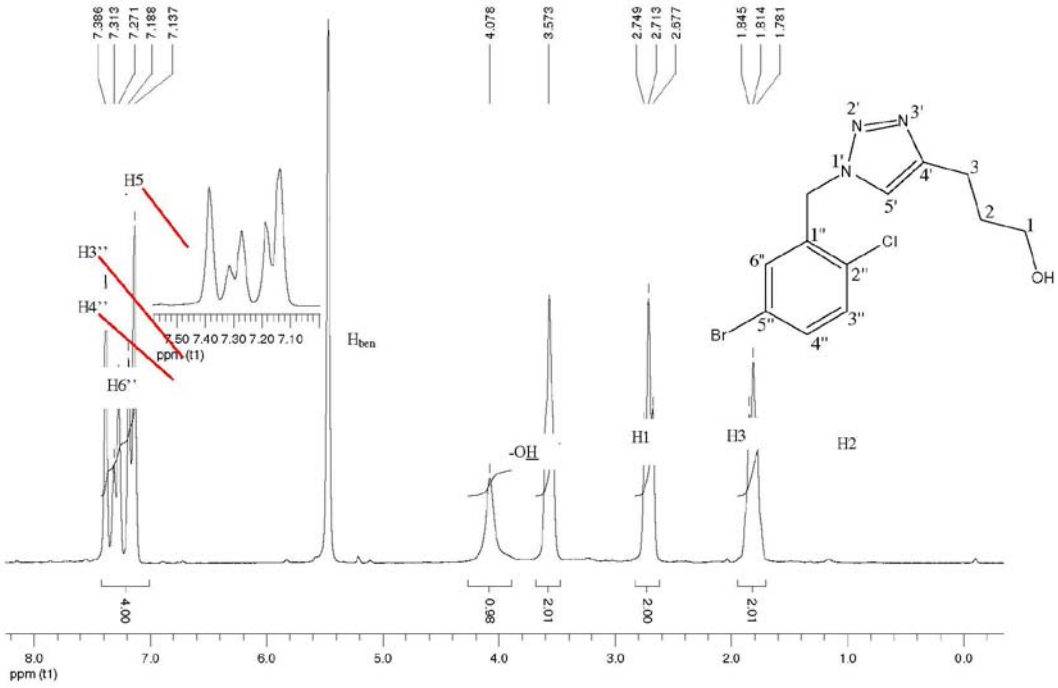

Figure S89. [1]H NMR spectrum (200 MHz, $CDCl_3$) of 3-[1'-(5''-bromo-2''-chlorobenzyl)-1',2',3'-triazol-4'-yl]propan-1-ol (**4i**).

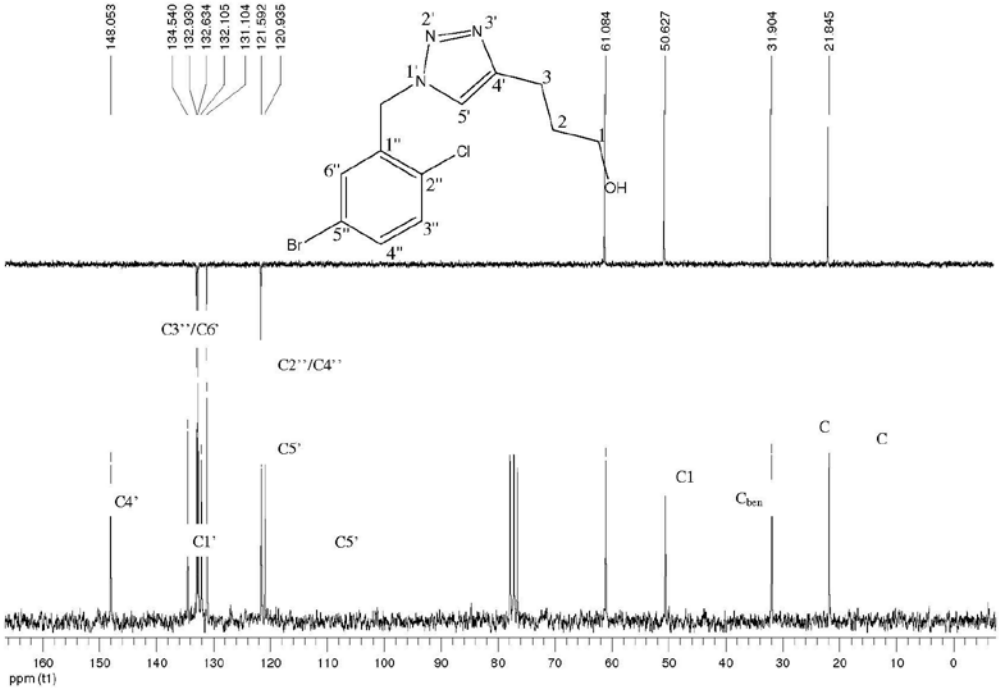

Figure S90. [13]C NMR and DEPT-135 spectrum (50 MHz, $CDCl_3$) of 3-[1'-(5''-bromo-2''-chlorobenzyl)-1',2',3'-triazol-4'-yl]propan-1-ol (**4i**).

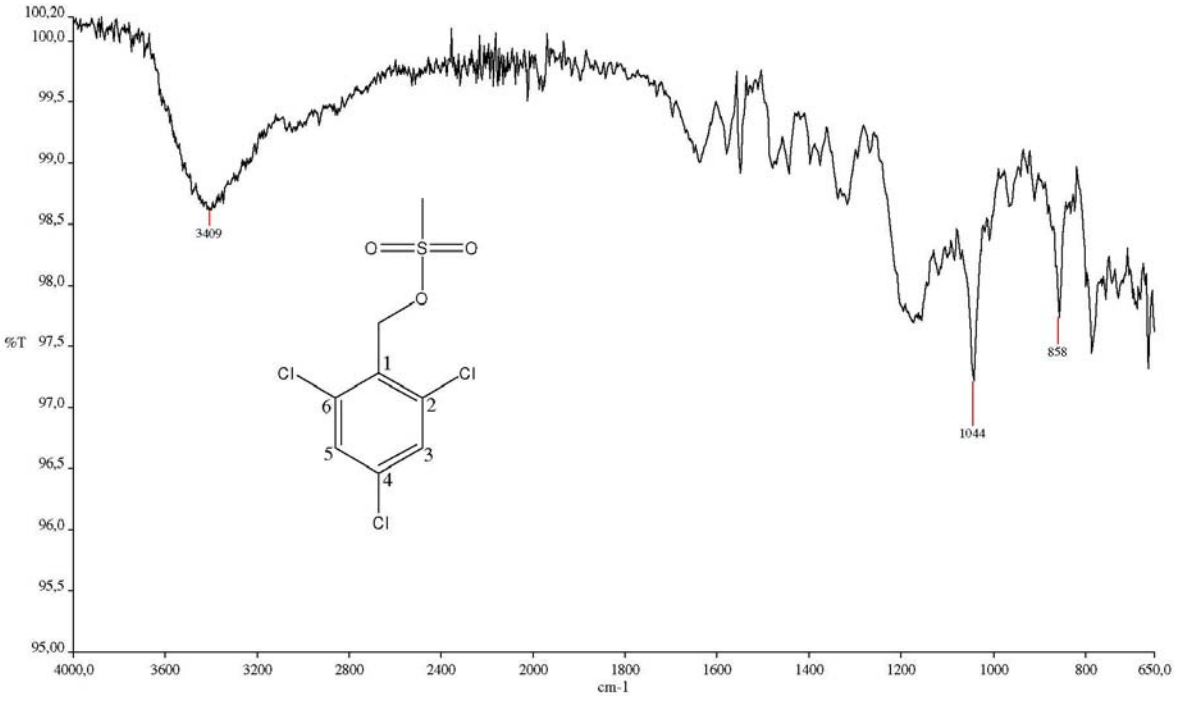

Figure S91. IR (ATR) spectrum of 2,4,6-trichlorobenzyl methanesulfonate (**2j**).

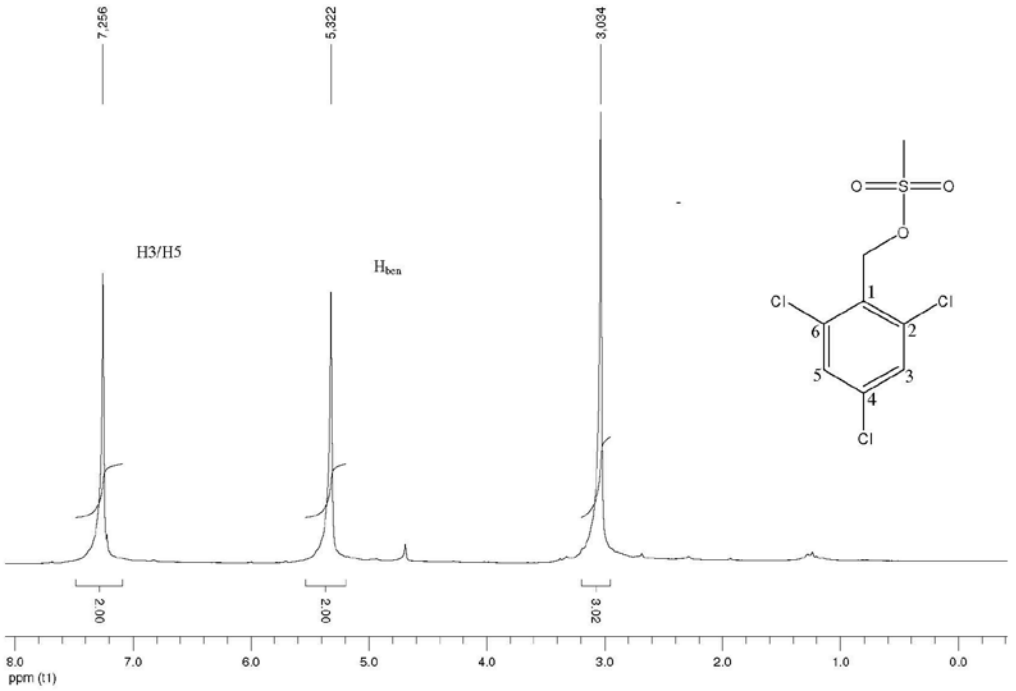

Figure S92. ^{1}H NMR spectrum (200 MHz, $CDCl_3$) of 2,4,6-trichlorobenzyl methanesulfonate (**2j**).

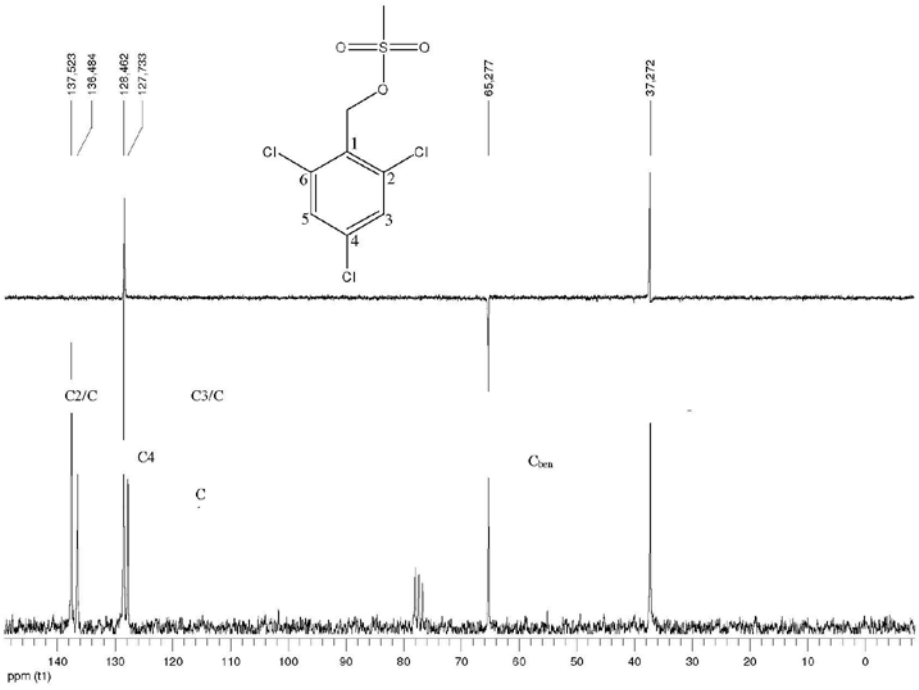

Figure S93. ^{13}C NMR and DEPT-135 spectrum (50 MHz, $CDCl_3$) of 2,4,6-trichlorobenzyl methanesulfonate (**2j**).

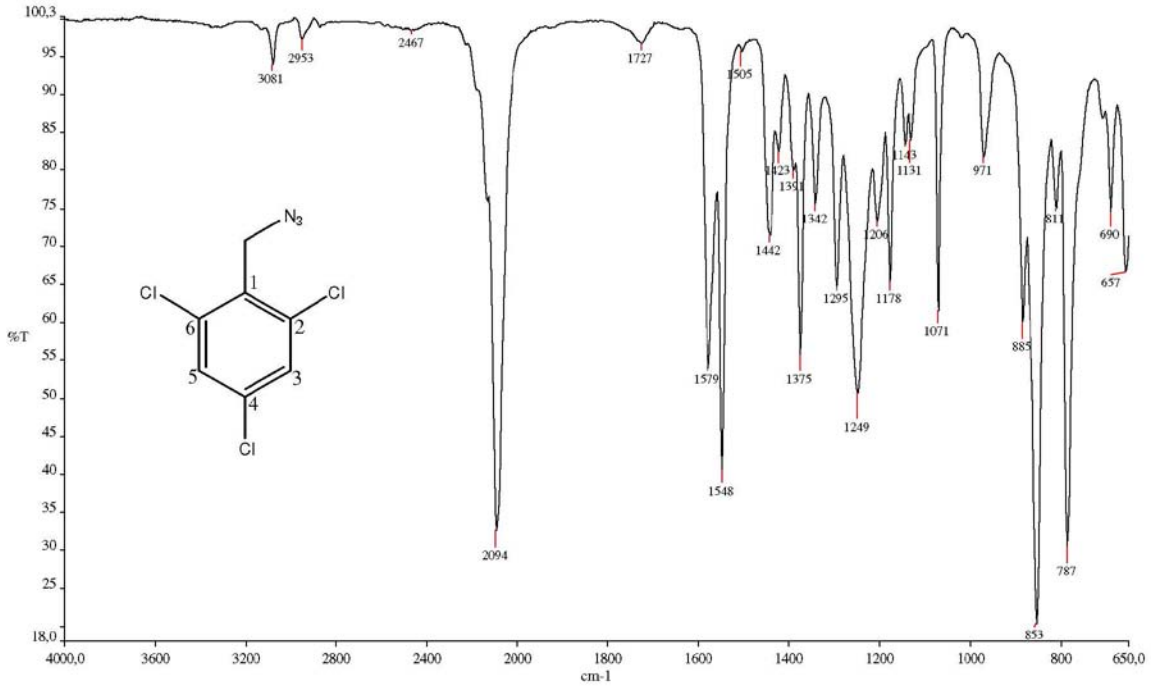

Figure S94. IR (ATR) spectrum of 1-(azidomethyl)-2,4,6-trichlorobenzene (**3j**).

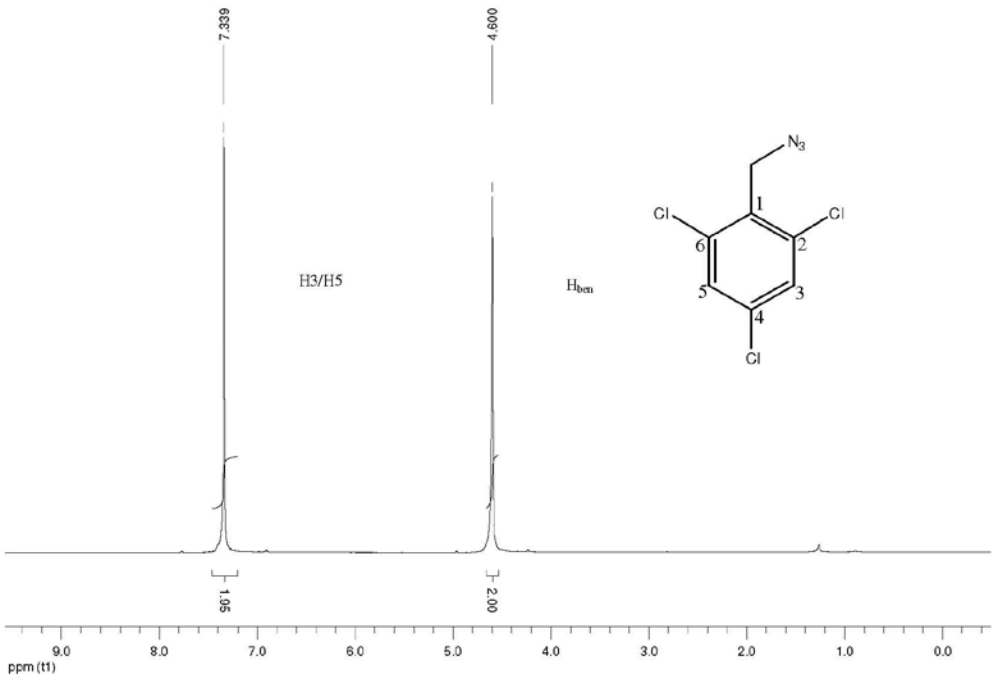

Figure S95. ^{1}H NMR spectrum (200 MHz, $CDCl_3$) of 1-(azidomethyl)-2,4,6-trichlorobenzene (**3j**).

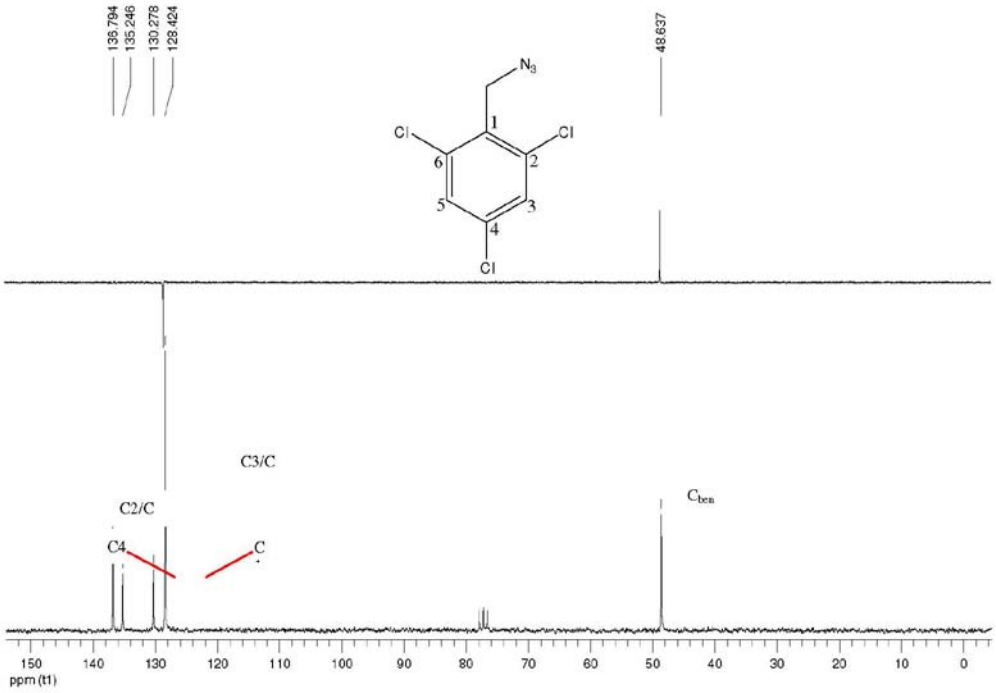

Figure S96. ^{13}C NMR and DEPT-135 spectrum (50 MHz, $CDCl_3$) of 1-(azidomethyl)-2,4,6-trichlorobenzene (**3j**).

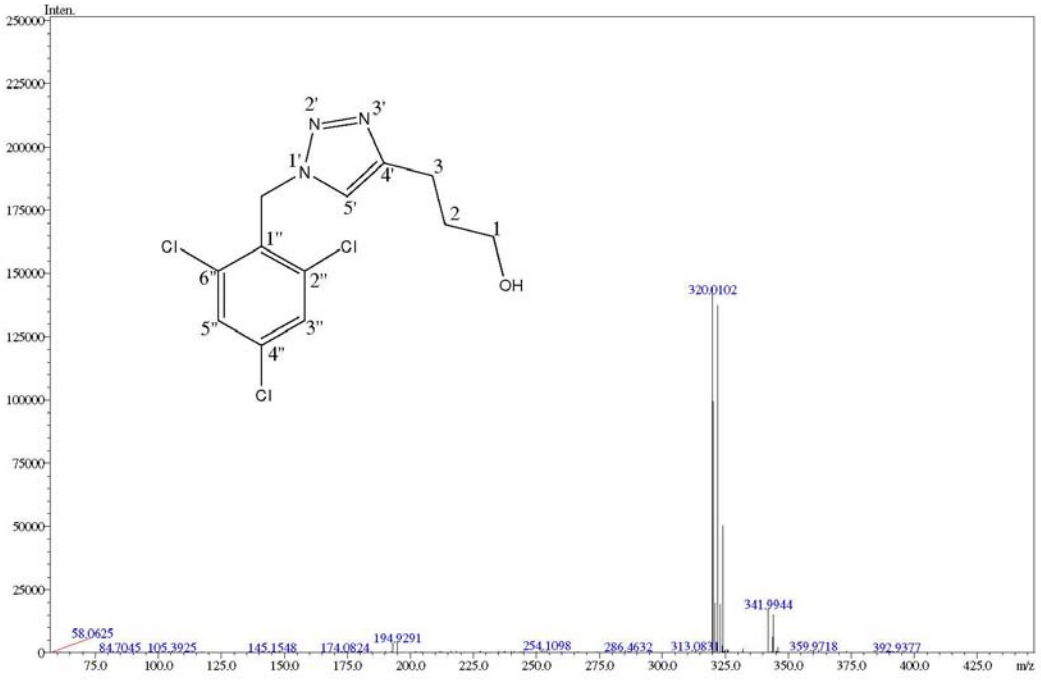

Figure S97. HRMS spectrum of 3-[1'-(2'',4'',6''-trichlorobenzyl)-1',2',3'-triazol-4'-yl]propan-1-ol (**4j**).

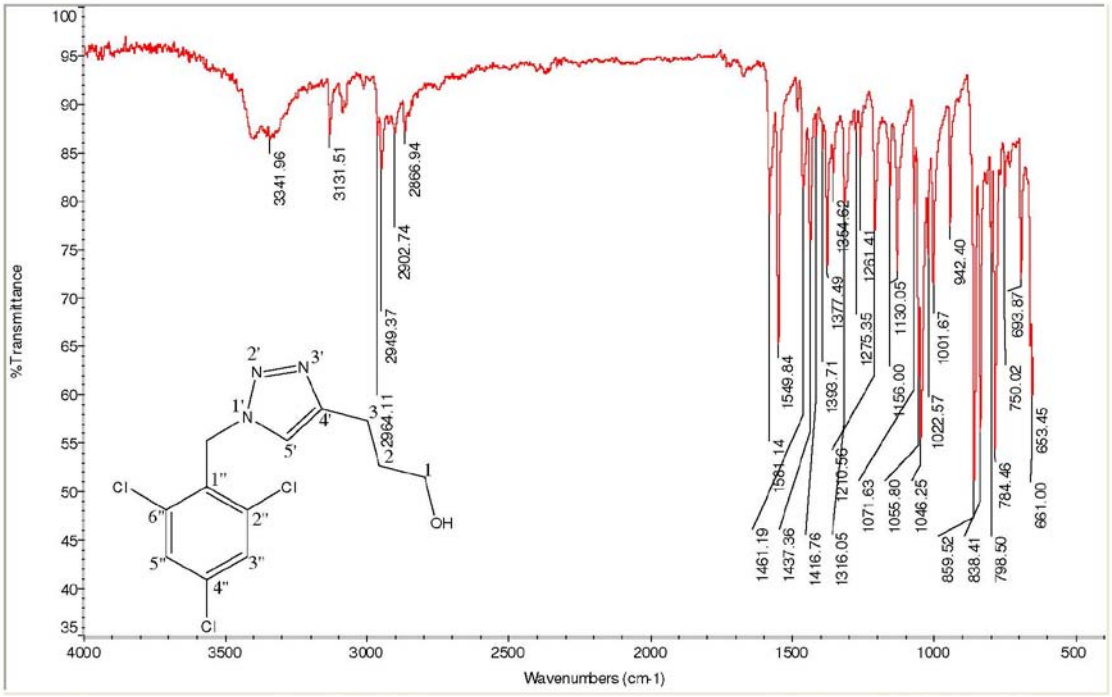

Figure S98. IR (ATR) spectrum of 3-[1'-(2'',4'',6''-trichlorobenzyl)-1',2',3'-triazol-4'-yl]propan-1-ol (**4j**).

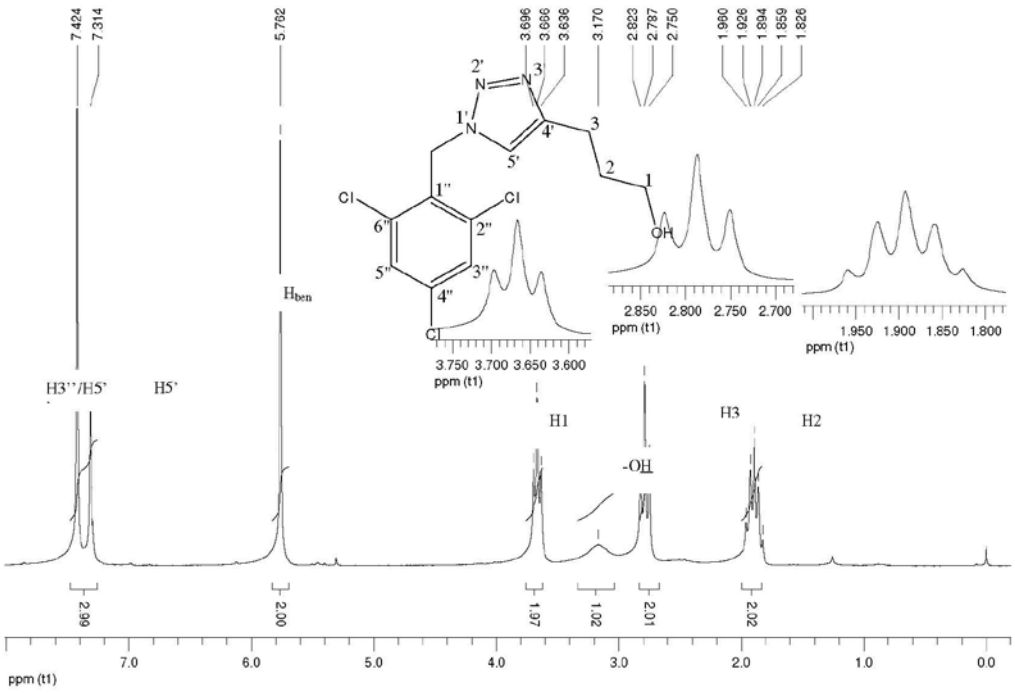

Figure S99. ^{1}H NMR spectrum (200 MHz, $CDCl_3$) of 3-[1'-(2'',4'',6''-trichlorobenzyl)-1',2',3'-triazol-4'-yl]propan-1-ol (**4j**).

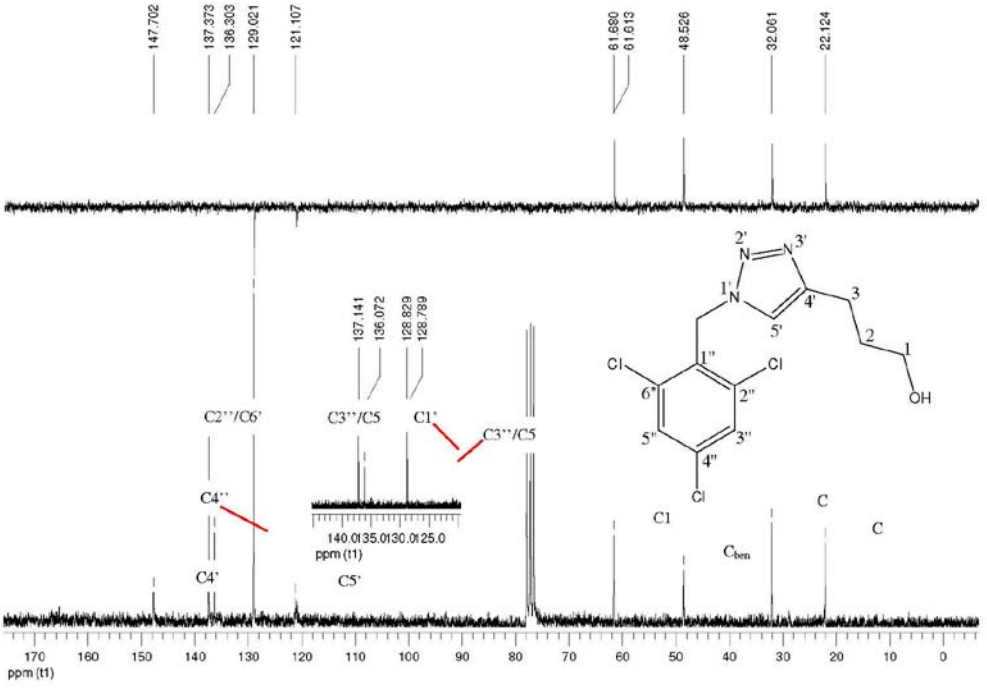

Figure S100. ^{13}C NMR and DEPT-135 spectrum (50 MHz, $CDCl_3$) of 3-[1'-(2'',4'',6''-trichlorobenzyl)-1',2',3'-triazol-4'-yl]propan-1-ol (**4j**).

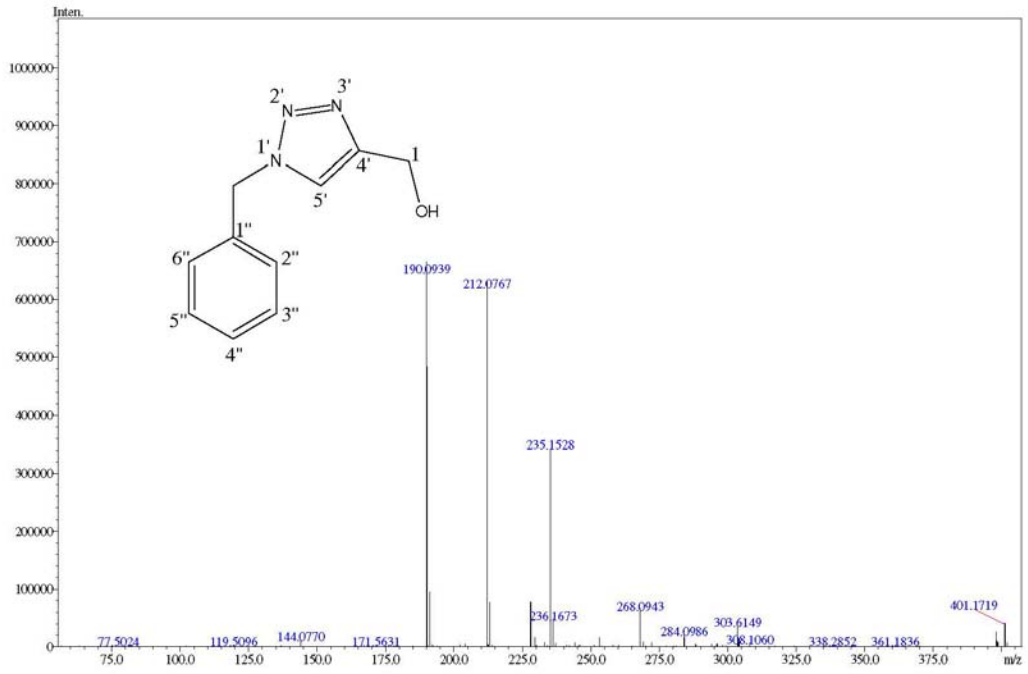

Figure S101. HRMS spectrum of (1'-benzyl-1',2',3'-triazol-4'-yl)methanol (**5a**).

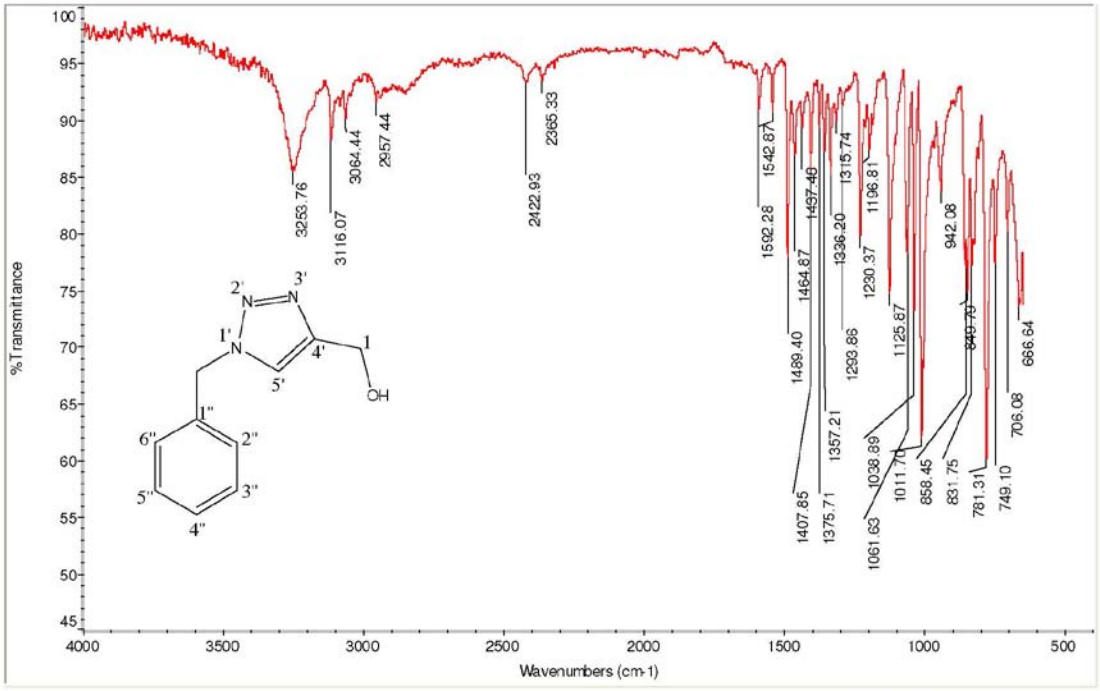

Figure S102. IR (ATR) spectrum of (1'-benzyl-1',2',3'-triazol-4'-yl)methanol (**5a**).

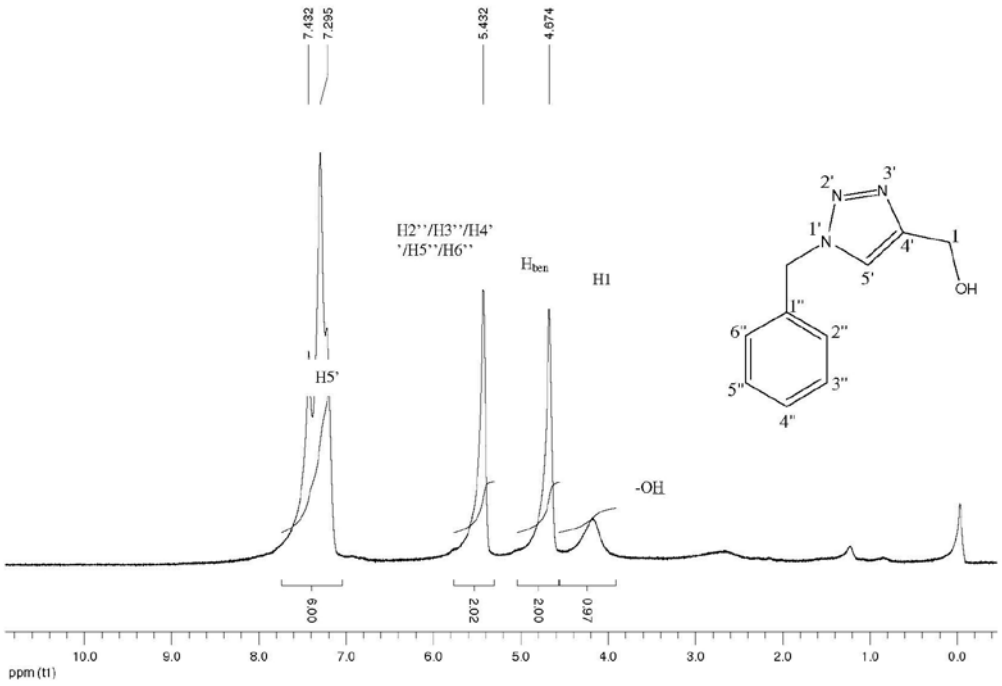

Figure S103. ^{1}H NMR spectrum (200 MHz, $CDCl_3$) of (1'-benzyl-1',2',3'-triazol-4'-yl)methanol (**5a**).

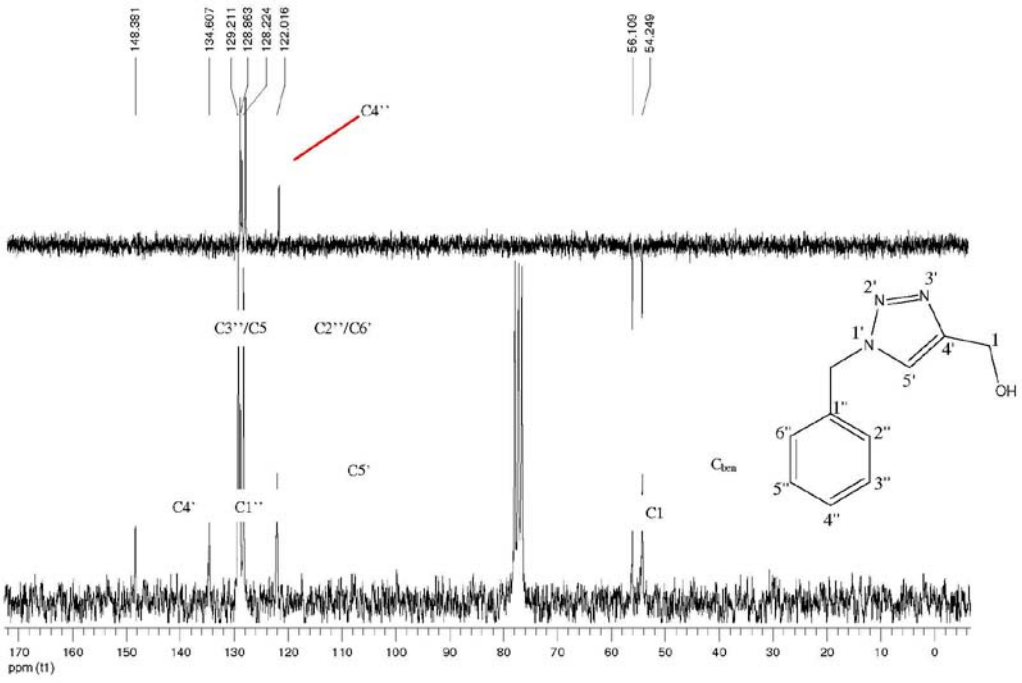

Figure S104. ^{13}C NMR and DEPT-135 spectrum (50 MHz, $CDCl_3$) of (1'-benzyl-1',2',3'-triazol-4'-yl)methanol (**5a**).

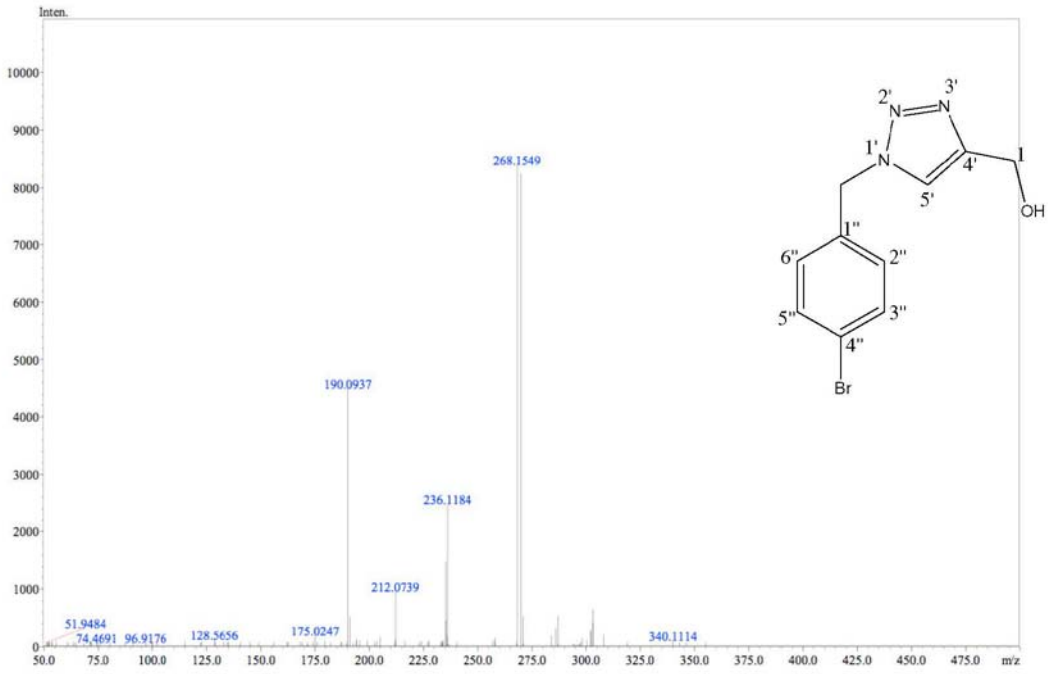

Figure S105. HRMS spectrum of [1'-(4''-bromobenzyl)-1',2',3'-triazol-4'-yl]methanol (**5b**).

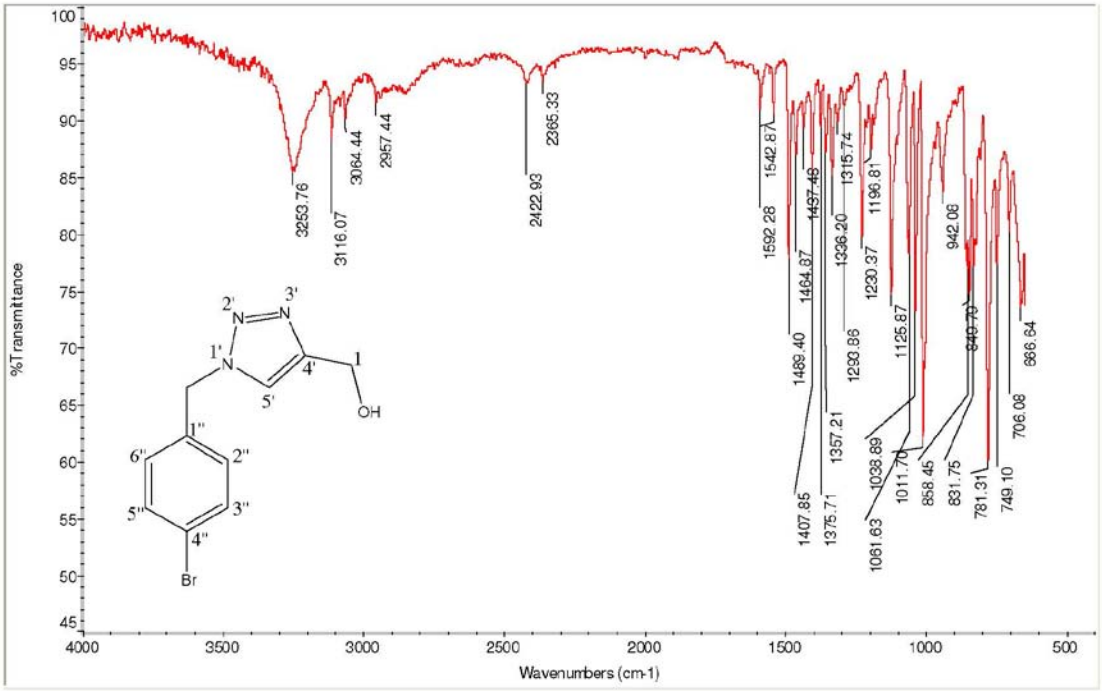

Figure S106. IR (ATR) spectrum of [1'-(4''-bromobenzyl)-1',2',3'-triazol-4'-yl]methanol (**5b**).

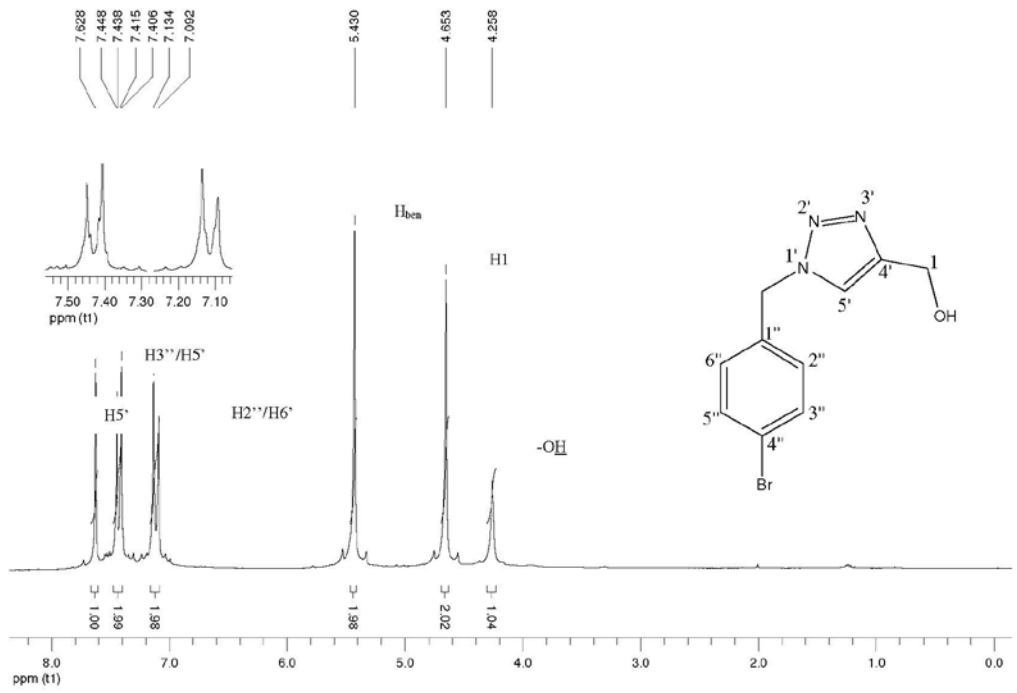

Figure S107. ^{1}H NMR spectrum (200 MHz, $CDCl_3$) of [1'-(4''-bromobenzyl)-1',2',3'-triazol-4'-yl]methanol (**5b**).

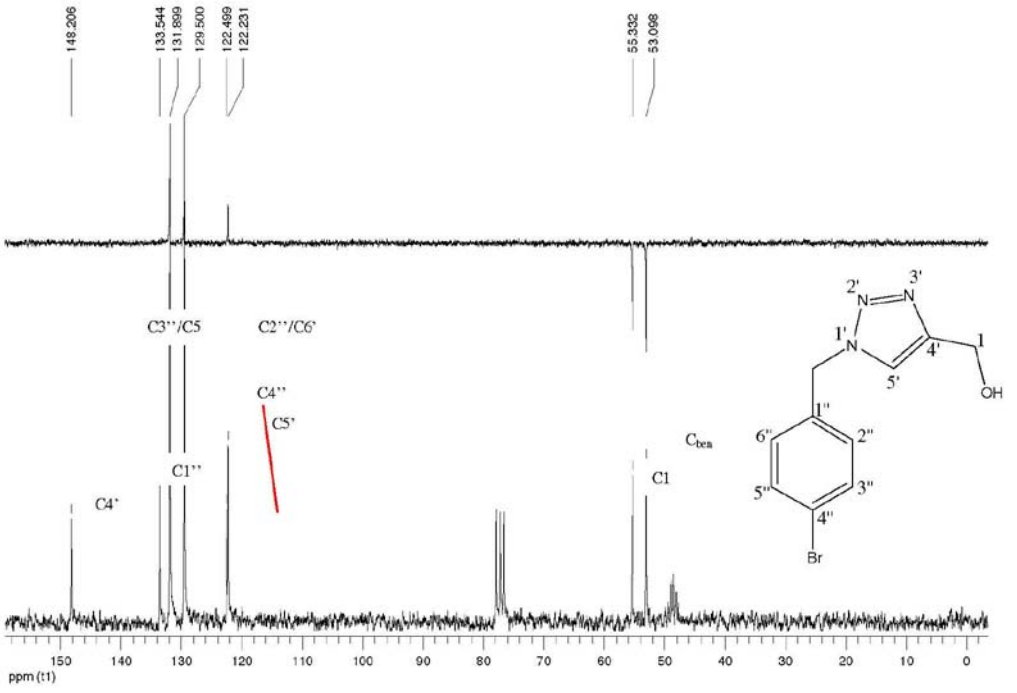

Figure S108. ^{13}C NMR and DEPT-135 spectrum (50 MHz, $CDCl_3$) of [1'-(4''-bromobenzyl)-1',2',3'-triazol-4'-yl]methanol (**5b**).

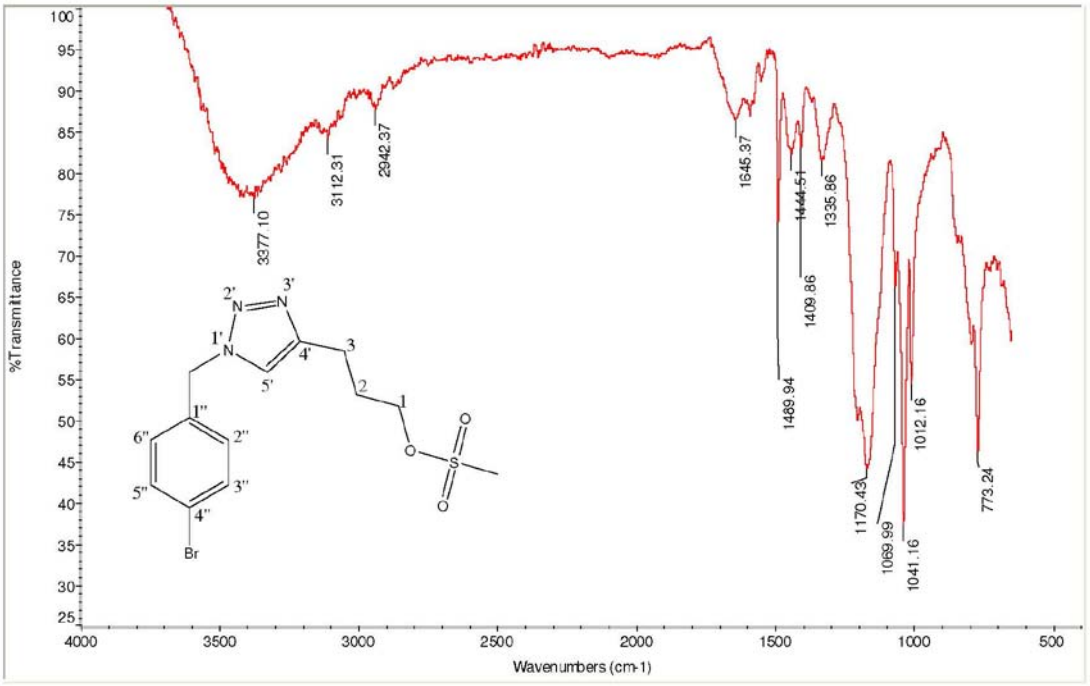

Figure S109. IR (ATR) spectrum of 3-[1'-(4''-bromobenzyl)-1',2',3'-triazol-4'-il]propyl methanesulfonate (**6a**).

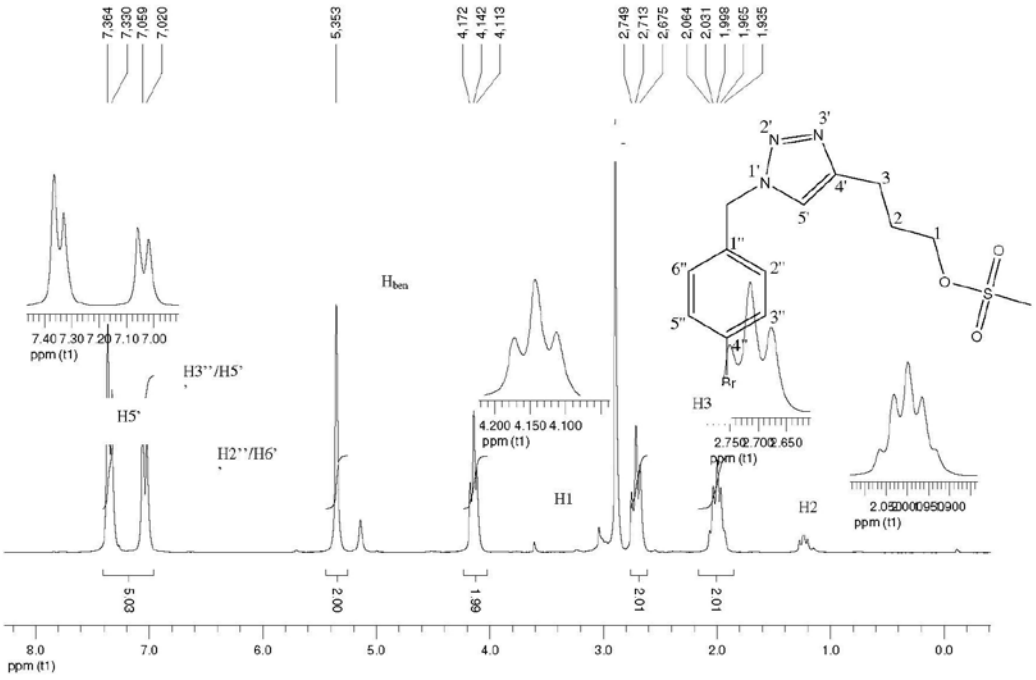

Figure S110. ^{1}H NMR spectrum (200 MHz, $CDCl_3$) of 3-[1'-(4''-bromobenzyl)-1',2',3'-triazol-4'-il]propyl methanesulfonate (**6a**).

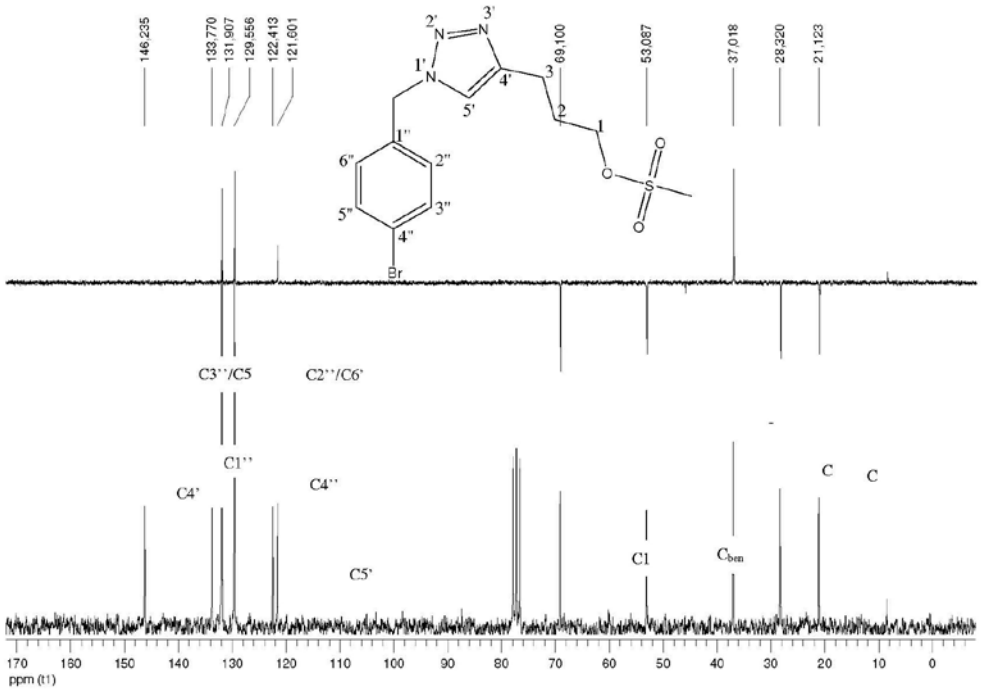

Figure S111. ^{13}C NMR and DEPT-135 spectrum (50 MHz, $CDCl_3$) of 3-[1'-(4''-bromobenzyl)-1',2',3'-triazol-4'-il]propyl methanesulfonate (**6a**).

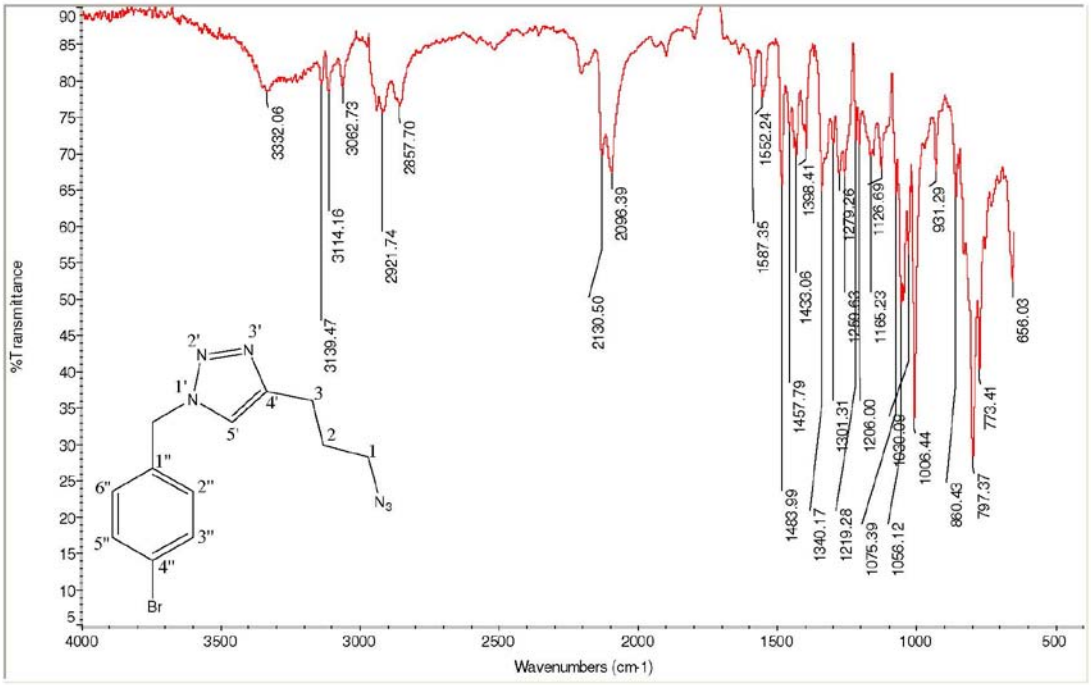

Figure S112. IR (ATR) spectrum of 1-(azido)-3-[1'-(4''-bromobenzyl)-1',2',3'-triazol-4'-il]propyl (**7a**).

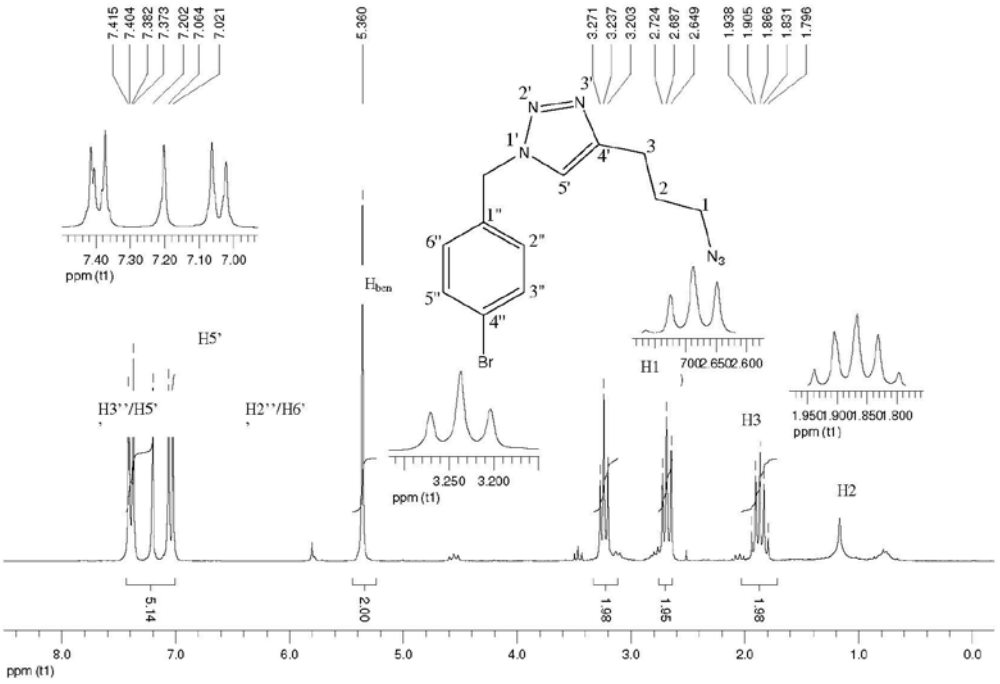

Figure S113. ^{1}H NMR spectrum (200 MHz, $CDCl_3$) of 1-(azido)-3-[1'-(4''-bromobenzyl)-1',2',3'-triazol-4'-il]propyl (**7a**).

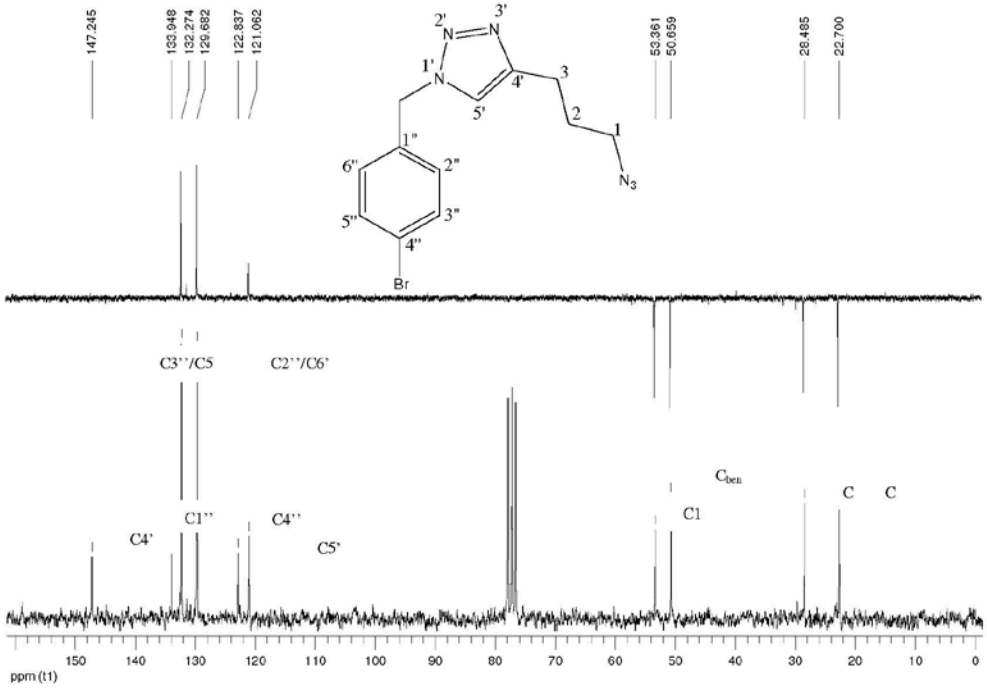

Figure S114. ^{13}C NMR and DEPT-135 spectrum (50 MHz, $CDCl_3$) of 1-(azido)-3-[1'-(4''-bromobenzyl)-1',2',3'-triazol-4'-il]propyl (**7a**).

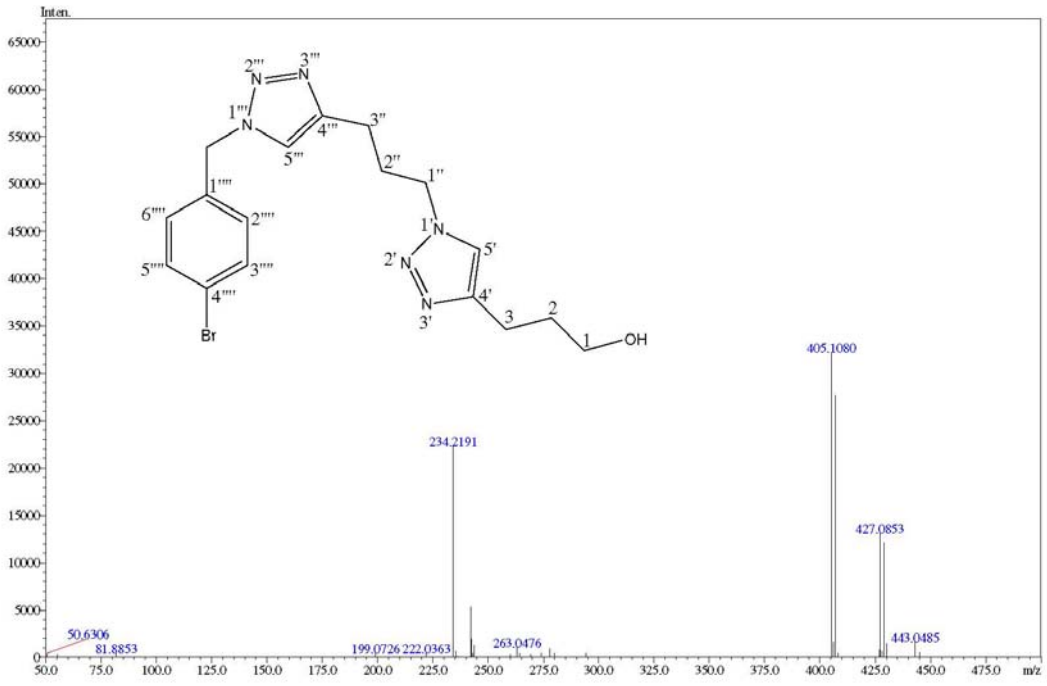

Figure S115. HRMS spectrum of 3-(1'-{3''-[1'''-(4''''-bromobenzyl)-1''',2''',3'''-triazol-4'''-yl]propyl}-1',2',3'-triazol-4'-yl)propan-1-ol (**8a**).

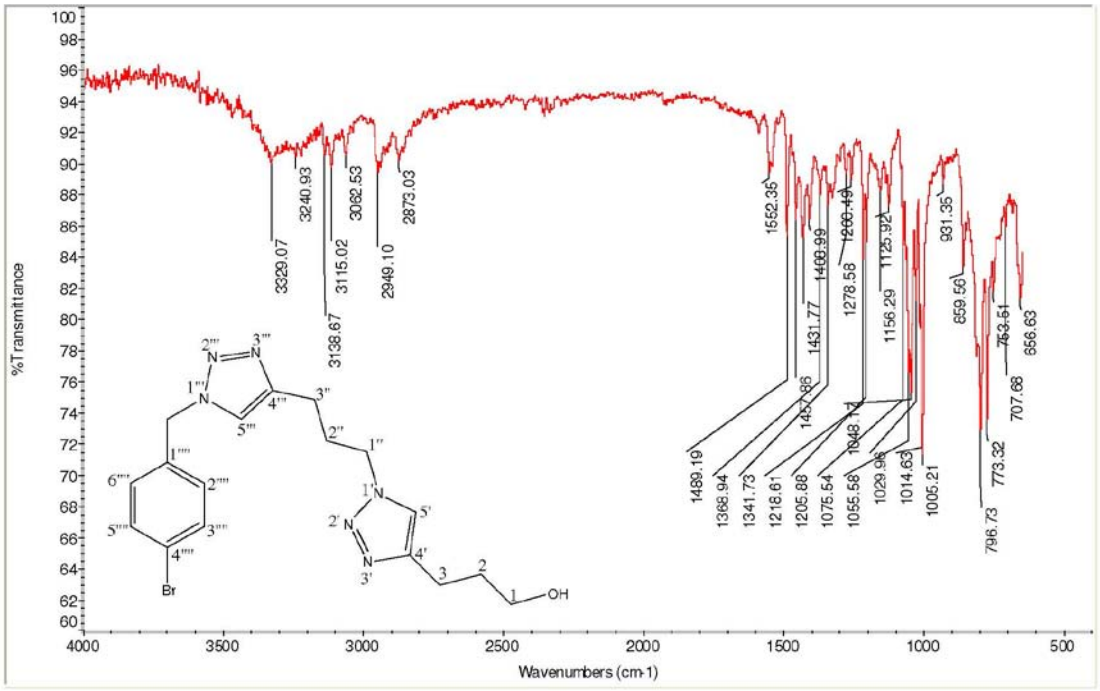

Figure S116. IR (ATR) spectrum of 3-(1'-{3''-[1'''-(4''''-bromobenzyl)-1''',2''',3'''-triazol-4'''-yl]propyl}-1',2',3'-triazol-4'-yl)propan-1-ol (**8a**).

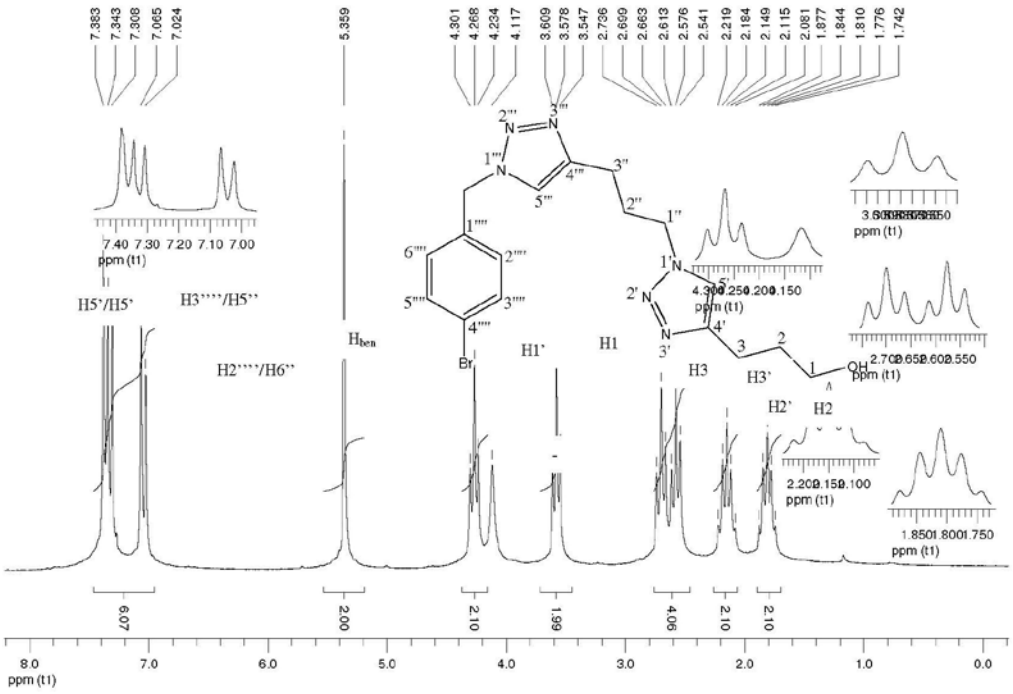

Figure S117. [1]H NMR spectrum (200 MHz, $CDCl_3$) of 3-(1'-{3''-[1'''-(4''''-bromobenzyl)-1''',2''',3'''-triazol-4'''-yl]propyl}-1',2',3'-triazol-4'-yl) propan-1-ol (**8a**).

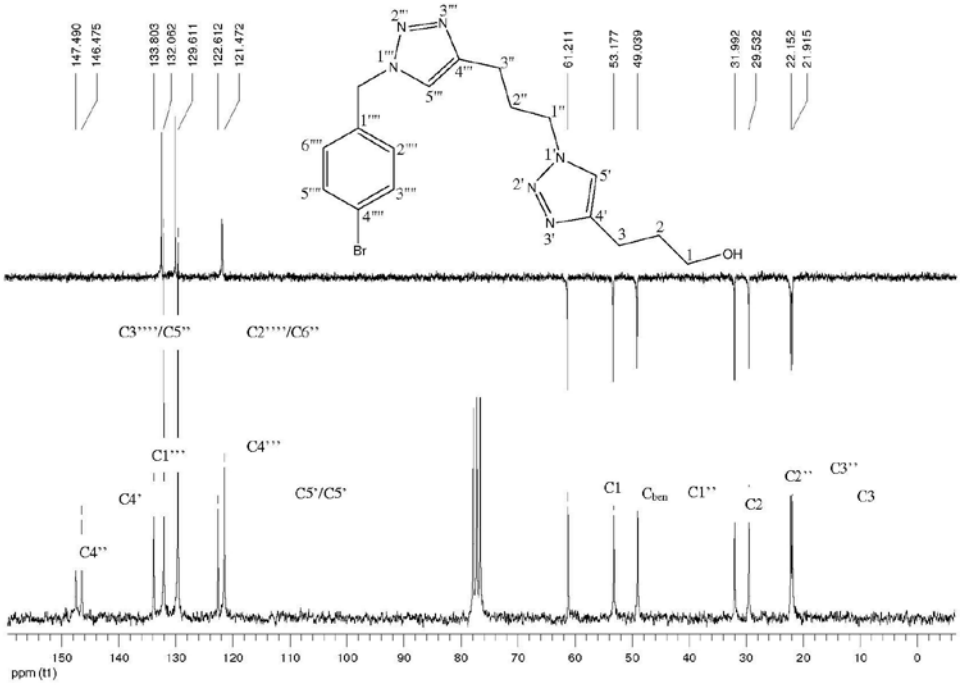

Figure S118. [13]C NMR and DEPT-135 spectrum (50 MHz, $CDCl_3$) of 3-(1'-{3''-[1'''-(4''''-bromobenzyl)-1''',2''',3'''-triazol-4'''-yl]propyl}-1',2',3'-triazol-4'-yl)propan-1-ol (**8a**).