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N^2-Selective Iodofunctionalization of Olefins with *NH*-1,2,3-Triazoles to provide N^2-Alkyl-Substituted 1,2,3-Triazoles

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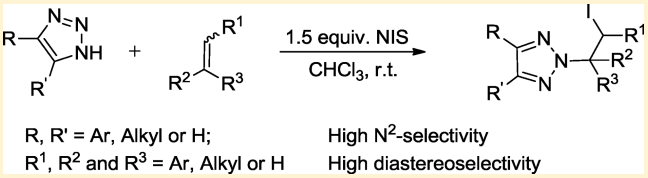
Supporting Information

ABSTRACT: A new method was developed to synthesize N^2-alkyl-substituted 1,2,3-triazole through *N*-iodosuccinimide (NIS) mediated iodofuctionalization reaction of the alkene group with bi-, mono-, and unsubstituted *NH*-1,2,3-triazoles. The favored *N*-1 type hydrogen bond between the iodonium ion intermediate and 1,2,3-triazole was supposed to be generated, which gave the desired N^2-alkyl triazole with a high N^2-selectivity.



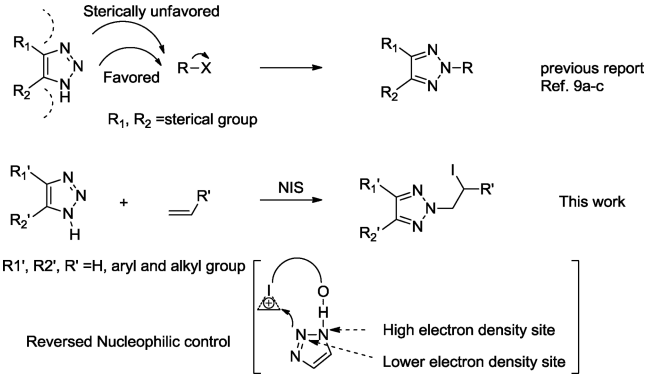
INTRODUCTION

The 1,2,3-triazole group is an important structural element in a broad range of organic molecules utilized in biological science,[1] medicinal chemistry,[2] and material science.[3] Since the discovery of "click chemistry" at the beginning of this century,[4] a number of methods have been developed to provide reliable means for the assembly of diversely N^1-substituted triazoles, for example: 1,4-disubstituted (copper(I)-catalyzed)[5] and 1,5-disubstituted (ruthenium(II)-catalyzed)[6] 1,2,3-triazoles, under the mild conditions and with excellent regioselectivity. Comparably, the synthesis of N^2-substituted 1,2,3-triazoles is far less explored. Considerable recent efforts have been made toward the preparation of N^2-aryl[7] and N^2-allyl-1,2,3-triazoles[8] with high N^2-selectivity through the palladium-catalyzed coupling reaction by using suitable bulky phosphine ligands.[7c,8c] Despite these achievements, however, there is still no general method for the synthesis of N^2-alkyl-1,2,3-triazoles, which could accommodate a broad range of triazole substitutions and provide coupling adducts with a high N^2-selectivity.[9]

The usual strategy to get N^2-alkyl-1,2,3-triazoles, which involves the nucleophilic substitution of alkylating reagents with unsubstituted *NH*-1,2,3-triazoles, is not effective because of the regioselectivity problem.[9] Recently, the N^2-selective alkylation reactions of alkyl halides with 1,2,3-triazoles have been achieved by incorporating C-4- and C-5-substituents on the hetero-arenes,[9a−c] of which the synthetic utilities were thus restricted by the substrate's steric requirements (Scheme 1). In 2014, our group developed a new synthetic route for the N^2-selective coupling of 1,2,3-triazoles with indoles or pyrroles through an *N*-iodophthalimide (or *N*-iodosuccinimide) mediated iodofunctionalization/elimination process,[10] in which the favored N^1-type intermolecular hydrogen bonding connection during the transition state provides the coupling adduct with a high N^2-selectively. We want to extend this reaction to the olefin's transformation.

The 1,2-halo functionalization of olefins, for example, haloamination, is one of the most important transformations in organic chemistry,[11] whereas employing triazoles as the nucleophiles in halo-mediated olefin conversion has seldom been explored before.[12] In the previous studies, N^2-alkyl-substituted triazole derivatives have been reported to exhibit a good degree of antiherpetic, antiarrhythmic, antiviral activities;[13] therefore, developing new strategies to build up an N^2-alkyl triazole entity would be of great interest. In this paper we will report the first example of iodofunctionalization of olefins with 1,2,3-triazoles, as the reaction depicted in Scheme 1, to produce N^2-alkyl-substituted 1,2,3-triazoles with high N^2-selectivity and high diastereoselectivity.

Scheme 1. Strategy for the Synthesis of N^2-Alkyl-Substituted Triazoles



RESULTS AND DISCUSSION

The reaction of *NH*-1,2,3-triazole **1a** and 4-*tert*-butylstyrene **2a** was chosen as the model system for our initial exploration. In a preliminary trial, as shown in Table 1, a solution of 0.1 mmoL of **1a** and 2 equiv of **2a** was treated with 1.5 equiv of NIS in DCM, and 30 min later the desired N^2-substituted triazole **3a**

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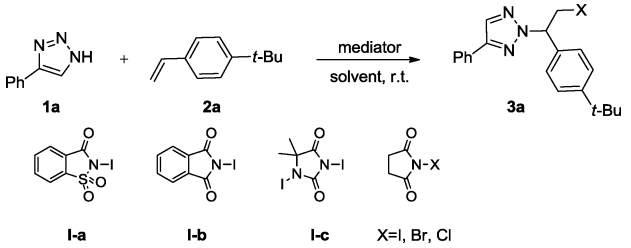
Table 1. Optimization of the Halogenation-Mediated Reaction of Triazole 1a with Olefin 2a[a]



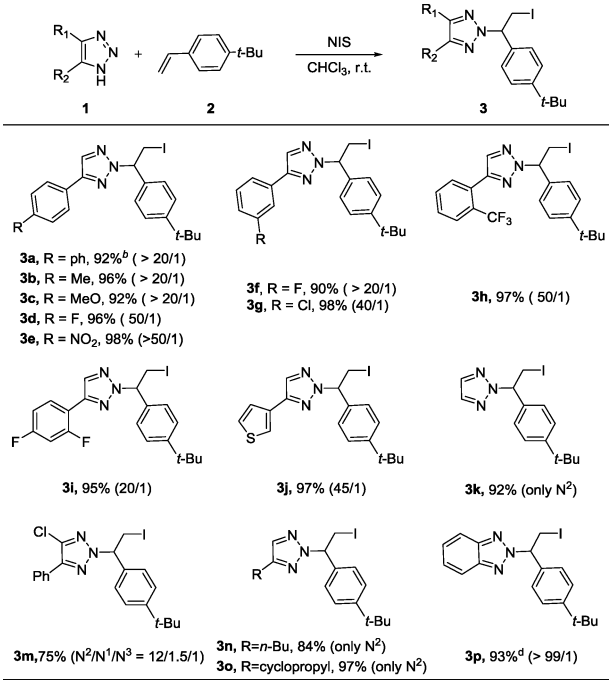
	mediator	sol./time (h)	yield (%)[b]	N^2/N^1
1	NIS	DCM (0.5)	90	20/1
2	I_2	DCM (1)	25	5/1
3	ICl	DCM (1)	trace	ND
4	$PhI(OAc)_2$	DCM (1)	NR	
5	**I-a**	DCM (1)	NR	
6	**I-b**	DCM (0.5)	85%(6/1)	6/1
7	**I-c**	DCM (0.5)	81%(6/1)	6/1
8	NBS	DCM (0.5)	22%	3/1
9	NCS	DCM (0.5)	trace	ND
10	NIS	$CHCl_3$	92%	>20/1
11	NIS	DCE	83%	15/1
12	NIS	toluene	76%	12/1
13	NIS	THF	10%	1/1
14	NIS	CH_3NO_2	35%	4/1
15	NIS	DMF	ND	
16	NIS	MeOH	ND	
17	NIS	H_2O	46%	4/1

[a]Unless otherwise noted, the reactions were carried out at 0.1 mmol scale in 2 mL of solvent at rt. [b]Isolated yields of N^2-selective coupling product. [c]N^2/N^1 ratio was determined by ^1H NMR of the reaction mixture. ND = not determined, NR = no reaction.

was readily obtained in 90% yield with a high N^2/N^1 regioselectivity (Table 1, entry 1). Performance of the other iodination reagents, such as I_2, ICl, $PhI(OAc)_2$, and three NIS analogues **I-a**, **I-b**, and **I-c**, was inferior to that of NIS (Table 1, entries 2−7). The halo counterparts NBS and NCS were fruitless too (Table 1, entries 8 and 9). The examination of several solvents proved that chloroform was the best reaction medium (Table 1, entries 10−13). The polar solvents, either aprotic THF, CH_3NO_2, DMF, or protic CH_3OH, gave no reaction or very low transformation, possibly due to NIS's destabilization in these milieus (Table 1, entries 14−16). However, H_2O could be utilized as the solvent, giving the alkyl triazole **3a** in a moderate yield (Table 1, entry 17).

Then, with the optimized reaction conditions in hand, we examined the scope of this transformation by synthesizing a series of N^2-alkyl 1,2,3-triazoles. As shown in Table 2, various *NH*-1,2,3-triazoles were explored by using 4-*tert*-butylstyrene **2a** as the reactants. First, phenyl-substituted *NH*-1,2,3-triazoles were investigated, which afforded the desired coupling adducts in high yields with excellent N^2-regioselectivities (**3a**−**3i**, Table 2). No obvious electro-effect or site preference (*para*-, *meta*-, and *ortho*-substitution) was observed. It was notable that the reaction of **2a** with *p*-nitrophenyl triazole (**1e**) could be completed in 1−2 min, giving **3e** in 98% isolated yield and with a selectivity of N^2/N^1 > 50/1. Similarly, the reactions of electron-rich thiophenyl-substituted *NH*-1,2,3-triazole **1j** and unsubstituted *NH*-1,2,3-triazole **1k** went very smoothly (**3j**−**3k**, Table 2). 4,5-Disubstituted *NH*-1,2,3-triazoles **1m** provided the corresponding coupling adducts in a slightly reduced yield (**3m**,

Table 2. NIS-Mediated Reaction of 4-*tert*-Butylstyrene 2a with Various *NH*-1,2,3-Triazoles[a,b,c]



[a]Unless otherwise noted, the reactions were carried out at 0.1 mmol scale in 2 mL of chloroform at rt with the addition of 1.5 equiv of NIS (**1**/**2a** = 1/2). [b]Isolated yields of N^2-selective coupling product. [c]N^2/N^1 ratio, which was shown inside the parentheses below the structures, was determined by ^1H NMR of the reaction mixture. [d]The reaction temperature was 65 °C.

Table 2). Aliphatic *NH*-1,2,3-triazoles, including cyclopropyl and *n*-butyl substituents, were also tested, giving **3n** and **3o** in good to excellent yields without forming the N^1-coupling adduct (**3n**−**3o**, Table 2). Benzotriazole **1p**'s reaction must be performed at an elevated temperature (65 °C). Notably the N^2-coupling adduct **3p** could be obtained in 93% yield with a selectivity of N^2/N^1 > 99/1.[14]

Then, iodofunctionalization reactions of *p*-nitrophenyl *NH*-1,2,3-triazole **1e** with various olefins were explored. At first, several *para*-substituted styrenes were investigated. As shown in Table 3, both electro-rich and electro-deficient substituents did not affect the yields of the desired N^2-(2′-iodoalkyl)-triazole products (**4a**−**4d**, Table 3). The free phenol group and acetyl amine group were tolerated, which gave slightly reduced reaction yields (**4e**−**f**, Table 3). The reaction of 1,1-disubstituted olefin (2-phenyl propene **2h**) worked very well, giving **4h** in 90% yield with a N^2/N^1 selectivity of 15/1 (**4h**, Table 3). The cycloalkenes were then tested, in which cyclohexadiene and indene's reactions went smoothly (**4i**−**j**, Table 3). One C═C double bond was iodofunctionalized in cyclohexadiene's reaction (**4i**, Table 3). The vinyl ether **2k** and cyclic 3,4,6-tri-*O*-acetyl-D-galactal **2m** were also examined. A N^2-1,2,3-triazolyl glycoside **4m** could be obtained in moderated yield with excellent N^2/N^1 selectivity. Moreover, the free hydroxyl group in cinnamyl alcohol could be tolerated, giving **4n** in 60% yield with a N^2/N^1 selectivity of 50/1. Compound **4m**'s absolute stereochemistry was confirmed by its NOESY spectrum,[15a]

Next, the reactions of **1e** with aliphatic olefins were explored to elucidate olefin's regioselectivity in this iodo-mediated

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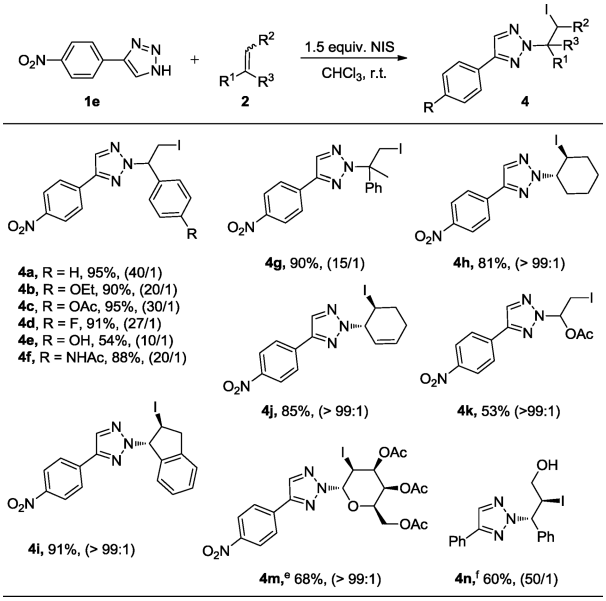
Table 3. NIS-Mediated Reaction of *p*-Nitrophenyl Triazole 1e with Various Olefins[a,b,c,d]



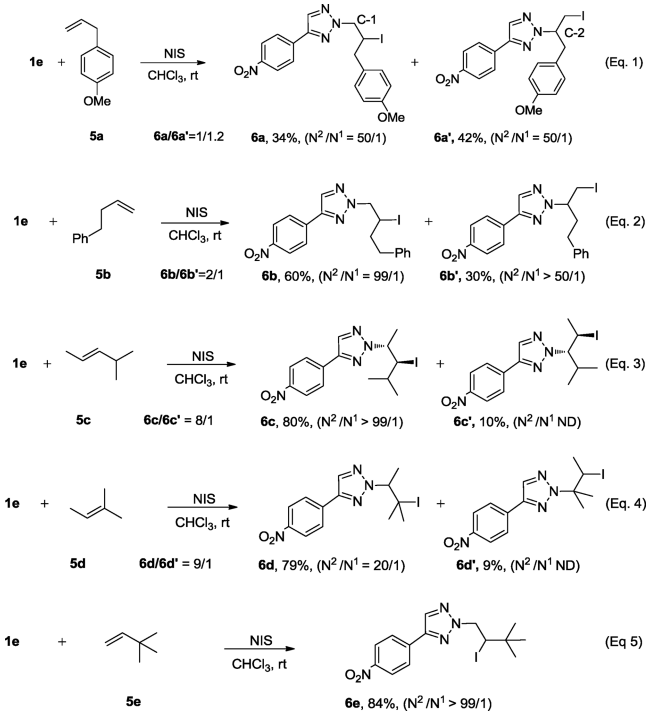
[a]Unless otherwise noted, the reactions were carried out at 0.1 mmol scale in 2 mL of chloroform at rt with the addition of 1.5 equiv of NIS (**1e**/**2** = 1/2). [b]Isolated yields of N^2-selective coupling product. [c]N^2/N^1 ratio, which was shown inside the parentheses below the structures, was determined by ^{1}H NMR of the reaction mixture. [d]Product **4h**–**j**,**4i**, and **4n**′s structure only show their relative configuration. [e]Product **4m**′s absolute stereochemistry was shown herein. [f]*NH*-1,2,3-triazole **1a** was utilized as the substrate.

transformation. In the reaction of **1e** with *p*-methoxy allylbenzene **5a**, the iodofunctionalization products **6a** and **6a**′ were obtained in total 76% yield with a ratio of **6a**/**6a**′ = 1/1.2. We consider that the nonclassical carbocation (Scheme 2, eq 1, C-2 position) could be stabilized by *β*-position *p*-methoxyphenyl group's homoconjugation,[16] which overrides internal C-2 carbon's unfavored steric hindrance and enhances the yield of product **6a**′ (Scheme 2, eq 1). As expected, when 4-phenyl-1-butene **5b** was utilized, the C-1 alkyl triazole **6b** was obtained as the major product (Scheme 2, eq 2). The similar steric effect was also observed in the reactions of **1e** with (*E*)-4-methyl-2-pentene **5c**, 2-methyl-2-butene **5d**, and *tert*-butylethylene **5e** (Scheme 2, eqs 3–5).

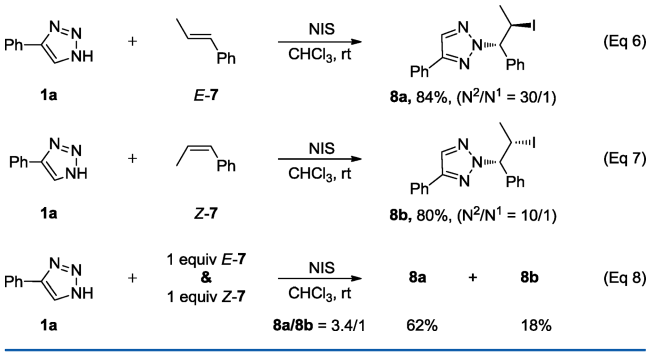
Except for the steric and electronic factors mentioned above, the olefin's *E*/*Z* configuration could affect its iodofunctionalization reaction. As shown in Scheme 3, when **1a** was treated with (*E*)-**7** and (*Z*)-**7** separately in the condition of 1.5 equiv of NIS in chloroform, two diastereomers **8a** and **8b** could be obtained in good yields and with a high stereospecificity. In the competitive reaction of **1a** with 1 equiv of (*E*)-**7** and 1 equiv of (*Z*)-**7**, the anticonfiguration product **8a** was obtained as the major product with a ratio of **8a**/**8b** = 3.4/1, showing that (*E*)-**7**′s reaction is faster than that of (*Z*)-**7**. The low reactivity of (*Z*)-**7** might be owing to its poor conjugation of the double bond with the *cis*-phenyl group. **8a**′s relative stereochemistry was confirmed by its X-ray structure, in which the triazole group connects with the alkyl group at the N^2 nitrogen atom.[15]

Then, we turn to explore the iodofunctionalization reaction of the other unsaturated substrates, such as alkyne, allene, and multifunctionalized olefins. As shown in Scheme 4, the reaction of phenyl triazole **1a** with phenyl acetylene afforded N^2-

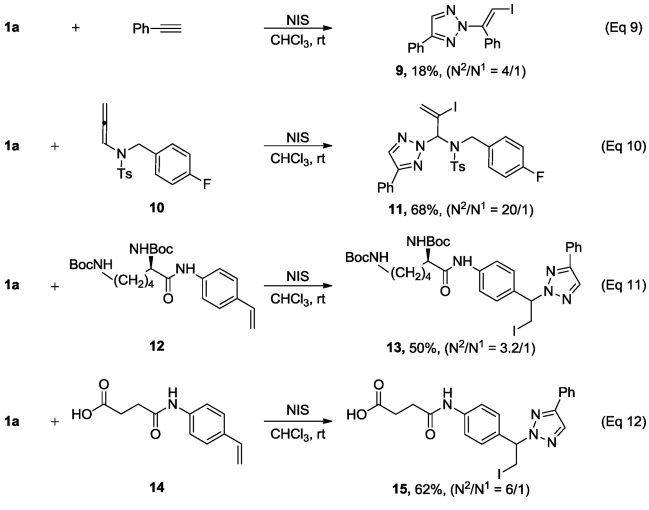
Scheme 2. Alkyl Olefin's Regioselectivity in the Iodofunctionalization Reaction



Scheme 3. Effect of Olefin's Configuration on the Reaction



Scheme 4. Iodofunctionalization Reaction of Other Unsaturated Substrates



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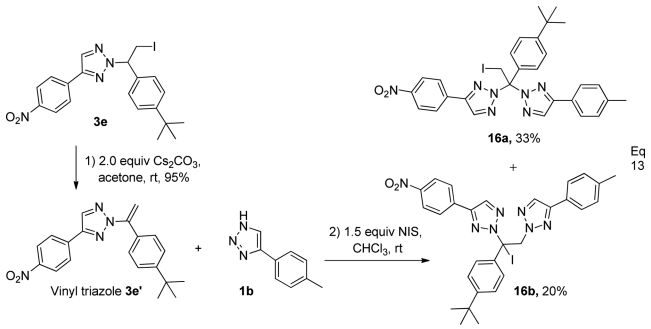
selective vinyl triazole **9** in low yield (Scheme 4, eq 9), while *N*-allenoamide **10** gave allylic triazole **11** in 68% yield with a ratio of N^2/N^1 = 20/1 (Scheme 4, eq 10). In the reactions of the functionalized olefins, in which a protected L-lysine group and a succinic acid group were incorporated, N^2-alkyl triazoles **13** and **15** were readily obtained in moderate yields with reduced N^2/N^1 selectivities.

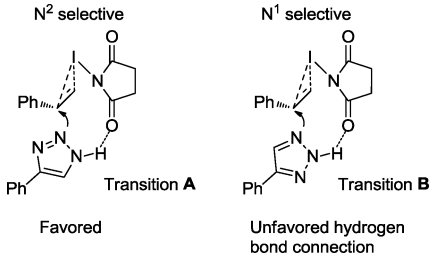
Then, further derivation of the obtained N^2-alkylated triazoles was then performed. When **3e** was treated with 2.0 equiv of Cs_2CO_3 in acetone at rt, a N^2-vinyl triazole product **3e′** was obtained in 95% yield, which could be transformed into two bis(triazole)-functionalized molecules through the second step NIS-mediated iodofunctionalization.[17] 1,1-Bis(triazole) compound **16a** and 1,2-bis(triazole) compound **16b** could be obtained in moderate yields (Scheme 5).

Scheme 5. Further Derivation of 3e to Give Bis(triazole) Molecules 16a and 16b



Based on our previous research, a plausible mechanism was proposed.[10] As shown in Scheme 6, due to the relatively lower

Scheme 6. Plausible Mechanism to Provide N^2-Selective Alkyl Triazole Product



electron density at the internal nitrogen (*N*-2) by comparison with two terminal nitrogens (*N*-1 and *N*-3),[18] the *N*-1 type hydrogen bond in transition A would be favored, in which the *N*-2 internal nitrogen atom attacks the three-membered iodonium ion from the opposite direction, giving N^2-selective alkyl triazole product as the major product. Olefin's regioselectivity could be rationalized by the steric and electronic factors. A compact transition state, which involves one olefin, one *NH*-1,2,3-triazole, and one NIS molecules, was depicted in Scheme 6. However, a relatively loose transition state involving two or more NIS molecules cannot be excluded.[19] Moreover, in **4m**′s preparation, the stereochemistry of the iodo indicates that the iodonium intermediate takes places in the more hindered face of the glycal, with an axial acetyl at the 4-position. In this particular case, the axial 4-OAc might direct the formation of the iodonium salts in the same face.

In conclusion, we have developed an efficient method to synthesize N^2-alkyl-substituted 1,2,3-triazole through NIS-mediated iodofunctionalization of olefin with *NH*-1,2,3-triazoles. Aryl/alkyl olefins and bi/mono/unsubstituted triazoles were employed to provide a series of N^2-(2-iodoalkyl)-1,2,3-triazoles with high N^2-selectivities and high diastereoselectivities.

EXPERIMENTAL SECTION

General Conditions. All reactions were conducted under open air at room temperature. $CHCl_3$ was obtained by fresh distillation over calcium hydride. Commercial reagents were used as supplied or purified by standard techniques where necessary. Substrates **1a**−**1o** were synthesized according to the reported method.[20] Column chromatography was performed using 200−300 mesh silica with the proper solvent system according to TLC analysis using UV light to visualize the reaction components. Unless otherwise noted, nuclear magnetic resonance spectra were recorded on a 400 MHz spectrometer. NMR data were reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, and brs = broad singlet), coupling constant in Hz, and integration. Chemical shifts for ^{13}C NMR spectra were recorded in parts per million from tetramethylsilane using the central peak of deuterochloroform (77.0 ppm) as the internal standard. IR spectra were recorded on an FTIR spectrometer (KBr) and reported in reciprocal centimeters (cm^{-1}). HRMS data were recorded on an orbitrap MS analyzer by using ESI ionization with 100,000 (fwhm) maximum resolution.

*General Procedure for NIS-Mediated Iodofunctionalization of 4-^{t}Butylstyrene **2a** with NH-1,2,3-Triazole **1a**.* To a suspension of **1a** (0.1 mmol) and 4-*tert*-butylstyrene **2a** (0.2 mmol) in $CHCl_3$ (4 mL) was added NIS (0.15 mmol) in one portion. Ten mins later, the reaction mixture was diluted with 20 mL of EtOAc and was then washed with saturated aqueous $Na_2S_2O_3$ (3 × 5 mL), distilled water (3 × 5 mL), and brine (10 mL). The organic phase was dried over anhydrous sodium sulfate, filtered, and concentrated in vacuo. Purification of the crude product through chromatography (petroleum/EtOAc = 80/1 as the eluent) afforded **3a** (39.6 mg, 92% yield) as a white solid.

*2-(1-(4-tert-Butylphenyl)-2-iodoethyl)-4-phenyl-2H-1,2,3-triazole (**3a**).* Obtained as a yellow solid in 92% yield (39.6 mg): M.P. 106 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.93 (s, 1 H), 7.84 (d, J = 8.5 Hz, 2 H), 7.44 (t, J = 7.3 Hz, 2 H), 7.38−7.34 (m, 5 H), 5.93 (dd, J = 10.8, 4.8 Hz, 1 H), 4.26 (t, J = 10.7 Hz, 1 H), 3.82 (dd, J = 10.6, 4.7 Hz, 1 H), 1.30 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.0, 148.0, 134.9, 131.4, 130.4, 128.9, 128.5, 126.4, 126.1, 126.0, 70.9, 34.7, 31.2, 5.7. IR (neat) 2962, 2902, 2868, 1473, 1460, 1363, 1267, 1176, 837, 767, 692, 605 cm^{-1}. HRMS (ESI) Calcd for $C_{20}H_{23}IN_3$ $[M + H]^+$: 432.0931; Found: 432.0928.

*2-(1-(4-tert-Butylphenyl)-2-iodoethyl)-4-p-tolyl-2H-1,2,3-triazole (**3b**).* Obtained as a white solid in 96% yield (42.7 mg): M.P. 114 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.90 (s, 1 H), 7.72 (d, J = 8.1 Hz, 2 H), 7.41−7.34 (m, 4 H), 7.24 (d, J = 8.0 Hz, 2 H), 5.92 (dd, J = 10.8, 4.8 Hz, 1 H), 4.24 (t, J = 10.7 Hz, 1 H), 3.81 (dd, J = 10.6, 4.8 Hz, 1 H), 2.39 (s, 3 H), 1.29 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.9, 148.0, 138.4, 135.0, 131.2, 129.5, 127.5, 126.4, 126.0, 125.9, 70.8, 34.7, 31.2, 21.4, 5.8. IR (neat) 2962, 2927, 2904, 2866, 1514, 1485, 1415, 1363, 1315, 1267, 1178, 1107, 819, 605 cm^{-1}. HRMS (ESI) Calcd for $C_{21}H_{25}IN_3$ $[M + H]^+$: 446.1088; Found: 446.1083.

*2-(1-(4-tert-Butylphenyl)-2-iodoethyl)-4-(4-methoxyphenyl)-2H-1,2,3-triazole (**3c**).* Obtained as a white solid in 92% yield (42.4 mg): M.P. 95 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.85 (s, 1 H), 7.75 (d, J = 8.8 Hz, 2 H), 7.39−7.34 (m, 4 H), 6.96 (d, J = 8.9 Hz, 2 H), 5.90 (dd, J = 10.7, 4.8 Hz, 1 H), 4.24 (t, J = 10.6 Hz, 1 H), 3.84 (s, 3 H), 3.81 (dd, J = 10.6, 4.8 Hz, 1 H), 1.29 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.9, 151.9, 147.8, 135.0, 130.8, 127.4, 126.4, 125.9, 123.1, 114.3, 70.8, 55.4, 34.7, 31.2, 5.8. IR (neat) 2960, 2904, 2866, 2835, 2339, 1614, 1485, 1463, 1288, 1251, 1174, 1031, 975, 881, 831, 738, 607, 530 cm^{-1}. HRMS (ESI) Calcd for $C_{21}H_{25}IN_3O$ $[M + H]^+$: 462.1037; Found: 462.1033.

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*2-(1-(4-tert-Butylphenyl)-2-iodoethyl)-4-(4-fluorophenyl)-2H-1,2,3-triazole (**3d**).* Obtained as a yellow solid in 96% yield (43.1 mg): M.P. 74 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (s, 1 H), 7.81−7.78 (m, 2 H), 7.39−7.34 (m, 4 H), 7.12 (t, J = 8.7 Hz, 2 H), 5.90 (dd, J = 10.8, 4.6 Hz, 1 H), 4.24 (t, J = 10.7 Hz, 1 H), 3.80 (dd, J = 10.6, 4.7 Hz, 1 H), 1.29 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.8 (d, $^1J_{F-C}$ = 246.2 Hz), 152.0, 147.1, 134.8, 131.1, 127.8 (d, $^3J_{F-C}$ = 8.1 Hz), 126.6, 126.4, 126.0, 115.8 (d, $^2J_{F-C}$ = 21.6 Hz), 70.9, 34.7, 31.2, 5.6. IR (neat) 2962, 2904, 2868, 1483, 1363, 1267, 1232, 1176, 833 cm^{-1}. HRMS (ESI) Calcd for $C_{20}H_{22}FIN_3$ [M + H]$^+$: 450.0837; Found: 450.0829.

*2-(1-(4-tert-Butylphenyl)-2-iodoethyl)-4-(4-nitrophenyl)-2H-1,2,3-triazole (**3e**).* Obtained as a yellow solid in 98% yield (46.7 mg): M.P. 124 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.30 (d, J = 8.9 Hz, 2 H), 8.03 (s, 1 H), 7.99 (d, J = 8.9 Hz, 2 H), 7.41−7.35 (m, 4 H), 5.94 (dd, J = 11.0, 4.6 Hz, 1 H), 4.25 (t, J = 10.9 Hz, 1 H), 3.82 (dd, J = 10.7, 4.6 Hz, 1 H), 1.29 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.3, 147.6, 145.8, 136.6, 134.4, 132.3, 126.6, 126.4, 126.1, 124.3, 71.4, 34.7, 31.2, 5.3. IR (neat) 2960, 2927, 2868, 1604, 1344, 1309, 1267, 1178, 1109, 852, 839, 738, 605 cm^{-1}. HRMS (ESI) Calcd for $C_{20}H_{22}IN_4O_2$ [M + H]$^+$: 477.0782; Found: 477.0779.

*2-(1-(4-tert-Butylphenyl)-2-iodoethyl)-4-(3-fluorophenyl)-2H-1,2,3-triazole (**3f**).* Obtained as a white solid in 90% yield (40.4 mg): M.P. 91 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92 (s, 1 H), 7.60−7.54 (m, 2 H), 7.42−7.35 (m, 5 H), 7.05 (td, J = 8.4, 2.4 Hz, 1 H), 5.92 (dd, J = 10.8, 4.7 Hz, 1 H), 4.24 (t, J = 10.7 Hz, 1 H), 3.81 (dd, J = 10.6, 4.7 Hz, 1 H), 1.30 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.2 (d, $^1J_{F-C}$ = 244.1 Hz), 152.1, 146.9, 134.7, 132.5 (d, $^3J_{F-C}$ = 8.3 Hz), 131.5, 130.4 (d, $^3J_{F-C}$ = 8.3 Hz), 126.4, 126.0, 121.7, 115.4 (d, $^2J_{F-C}$ = 21.0 Hz), 113.0 (d, $^2J_{F-C}$ = 22.8 Hz), 71.1, 34.7, 31.2, 5.5. IR (neat) 2962, 2902, 2868, 1618, 1589, 1479, 1267, 1224, 1174, 881, 864, 786, 605 cm^{-1}. HRMS (ESI) Calcd for $C_{20}H_{22}FIN_3$ [M + H]$^+$: 450.0842; Found: 450.0859.

*1-(4-tert-Butylphenyl)-2-iodoethyl)-4-(3-chlorophenyl)-2H-1,2,3-triazole (**3g**).* Obtained as a yellow solid in 98% yield (45.6 mg): M.P. 74 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91 (s, 1 H), 7.84−7.83 (m, 1 H), 7.68 (td, J = 7.4, 1.5 Hz, 1 H), 7.41−7.31 (m, 6 H), 5.91 (dd, J = 10.9, 4.7 Hz, 1 H), 4.24 (t, J = 10.8 Hz, 1 H), 3.80 (dd, J = 10.6, 4.7 Hz, 1 H), 1.29 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.1, 146.7, 134.9, 134.7, 132.1, 131.5, 130.1, 128.5, 126.4, 126.1, 126.0, 124.1, 71.1, 34.7, 31.2, 5.5. IR (neat) 2962, 2866, 1732, 1571, 1467, 1365, 1267, 1176, 1018, 993, 881, 837, 786, 767, 605 cm^{-1}. HRMS (ESI) Calcd for $C_{20}H_{22}ClIN_3$ [M + H]$^+$: 466.0541; Found: 466.0537.

*2-(1-(4-tert-Butylphenyl)-2-iodoethyl)-4-(2-(trifluoromethyl)-phenyl)-2H-1,2,3-triazole (**3h**).* Obtained as yellow oil in 97% yield (48.4 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 (s, 1 H), 7.79 (d, J = 7.9 Hz, 1 H), 7.73 (d, J = 7.7 Hz, 1 H), 7.62 (d, J = 7.4 Hz, 1 H), 7.52 (d, J = 7.7 Hz, 1 H), 7.40 (d, J = 8.6 Hz, 2 H), 7.36 (d, J = 8.6 Hz, 2 H), 5.95 (dd, J = 10.9, 4.6 Hz, 1 H), 4.23 (t, J = 10.8 Hz, 1 H), 3.81 (dd, J = 10.6, 4.7 Hz, 1 H), 1.31 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.1, 145.4, 134.7, 134.1, 132.0, 131.8, 129.5, 128.7, 128.2 (d, $^2J_{F-C}$ = 19.6 Hz), 126.4, 126.0, 123.9 (d, $^1J_{F-C}$ = 272.0 Hz), 71.1, 34.7, 31.2, 5.7. IR (neat) 2962, 2904, 2870, 1365, 1315, 1267, 1174, 1109, 837, 765, 740 cm^{-1}. HRMS (ESI) Calcd for $C_{21}H_{22}F_3IN_3$ [M + H]$^+$: 500.0805; Found: 500.0797.

*2-(1-(4-tert-Butylphenyl)-2-iodoethyl)-4-(2,4-difluorophenyl)-2H-1,2,3-triazole (**3i**).* Obtained as a white solid in 95% yield (44.4 mg): M.P. 67 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07−8.01 (m, 2 H), 7.40−7.34 (m, 4 H), 7.00−6.89 (m, 2 H), 5.93 (dd, J = 10.8, 4.7 Hz, 1 H), 4.24 (t, J = 10.8 Hz, 1 H), 3.81 (dd, J = 10.6, 4.7 Hz, 1 H), 1.30 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.8 (d, $^1J_{F-C}$ = 260.9 Hz), 160.0 (d, $^1J_{F-C}$ = 239.4 Hz), 152.1, 141.8, 134.7, 133.7 (d, $^2J_{F-C}$ = 11.4 Hz), 129.5 (dd, $^3J_{F-C}$ = 9.2, 5.2 Hz), 126.4, 126.0, 114.8 (d, $^3J_{F-C}$ = 9.6 Hz), 112.0 (d, $^2J_{F-C}$ = 21.3 Hz), 104.4 (t, $^2J_{F-C}$ = 25.4 Hz), 71.0, 34.7, 31.2, 5.5. IR (neat) 2962, 2868, 1624, 1598, 1450, 1363, 1296, 1267, 1139, 1105, 1080, 848, 817, 607 cm^{-1}. HRMS (ESI) Calcd for $C_{20}H_{21}F_2IN_3$ [M + H]$^+$: 468.0743; Found: 468.0743.

*2-(1-(4-tert-Butylphenyl)-2-iodoethyl)-4-(thiophen-3-yl)-2H-1,2,3-triazole (**3j**).* Obtained as a yellow oil in 97% yield (42.4 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 (s, 1 H), 7.66−7.65 (m, 1 H), 7.49 (d, J = 5.0 Hz, 1 H), 7.40−7.33 (m, 5 H), 5.90 (dd, J = 10.8, 4.8 Hz, 1 H), 4.23 (t, J = 10.6 Hz, 1 H), 3.81 (dd, J = 10.6, 4.8 Hz, 1 H), 1.29 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.0, 144.1, 134.9, 131.7, 131.5, 126.4, 126.1, 125.9, 121.8, 70.8, 34.7, 31.3, 5.7. IR (neat) 2960, 2902, 2866, 1579, 1514, 1415, 1334, 1267, 1178, 856, 837, 786, 705, 605 cm^{-1}. HRMS (ESI) Calcd for $C_{18}H_{21}IN_3S$ [M + H]$^+$: 438.0493; Found: 438.0495.

*2-(1-(4-tert-Butylphenyl)-2-iodoethyl)-2H-1,2,3-triazole (**3k**).* Obtained as a white solid in 92% yield (32.7 mg): M.P. 68 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (s, 2 H), 7.37 (d, J = 8.4 Hz, 2 H), 7.30 (d, J = 8.5 Hz, 2 H), 5.92 (dd, J = 10.8, 4.7 Hz, 1 H), 4.21 (t, J = 10.8 Hz, 1 H), 3.79 (dd, J = 10.6, 4.7 Hz, 1 H), 1.29 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.0, 134.8, 134.5, 126.3, 125.9, 70.7, 34.7, 31.2, 5.6. IR (neat) 2962, 2905, 2866, 1510, 1418, 1333, 1111, 962, 835, 816, 573 cm^{-1}. HRMS (ESI) Calcd for $C_{14}H_{19}IN_3$ [M + H]$^+$: 356.0618; Found: 356.0612.

*2-(1-(4-tert-Butylphenyl)-2-iodoethyl)-4-chloro-5-phenyl-2H-1,2,3-triazole (**3m**).* Obtained as a white solid in 75% yield (34.9 mg): M.P. 83 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96 (d, J = 7.4 Hz, 2 H), 7.47 (t, J = 7.0 Hz, 2 H), 7.42−7.36 (m, 5 H), 5.82 (dd, J = 10.8, 4.8 Hz, 1 H), 4.20 (t, J = 10.8 Hz, 1 H), 3.78 (dd, J = 10.7, 4.8 Hz, 1 H), 1.30 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.3, 143.1, 134.2, 133.7, 128.9, 128.7, 127.1, 126.4, 126.0, 71.7, 34.7, 31.2, 4.8. IR (neat) 2962, 2902, 2866, 1460, 1404, 1346, 1205, 1178, 1014, 835, 694 cm^{-1}. HRMS (ESI) Calcd for $C_{20}H_{22}ClIN_3$ [M + H]$^+$: 466.0541; Found: 466.0539.

*4-Butyl-2-(1-(4-tert-butylphenyl)-2-iodoethyl)-2H-1,2,3-triazole (**3n**).* Obtained as a yellow solid in 84% yield (34.5 mg): M.P. 67 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 (s, 1 H), 7.36 (d, J = 8.5 Hz, 2 H), 7.29 (d, J = 8.4 Hz, 2 H), 5.81 (dd, J = 10.8, 4.8 Hz, 1 H), 4.16 (t, J = 10.7 Hz, 1 H), 3.75 (dd, J = 10.5, 4.8 Hz, 1 H), 2.70 (t, J = 7.6 Hz, 2 H), 1.69−1.62 (m, 2 H), 1.43−1.34 (m, 2 H), 1.29 (s, 9 H), 0.93 (t, J = 7.3 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.8, 149.0, 135.1, 133.0, 126.3, 125.8, 70.4, 34.6, 31.4, 31.2, 25.3, 22.3, 13.8, 6.0. IR (neat) 2962, 2929, 2868, 1516, 1413, 1363, 1267, 1178, 1024, 881, 837, 750, 603 cm^{-1}. HRMS (ESI) Calcd for $C_{18}H_{27}IN_3$ [M + H]$^+$: 412.1244; Found: 412.1238.

*2-(1-(4-tert-Butylphenyl)-2-iodoethyl)-4-cyclopropyl-2H-1,2,3-triazole (**3o**).* Obtained as a white solid in 97% yield (38.3 mg): M.P. 72 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37−7.35 (m, 3 H), 7.28 (d, J = 8.4 Hz, 2 H), 5.78 (dd, J = 10.7, 4.8 Hz, 1 H), 4.14 (t, J = 10.6 Hz, 1 H), 3.74 (dd, J = 10.6, 4.8 Hz, 1 H), 1.99−1.92 (m, 1 H), 1.29 (s, 9 H), 0.99−0.94 (m, 2 H), 0.82−0.78 (m, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.8, 151.1, 135.1, 131.4, 126.4, 125.8, 70.4, 34.6, 31.3, 8.2, 6.8, 5.9. IR (neat) 2962, 2904, 2868, 1537, 1462, 1415, 1363, 1321, 1269, 1178, 1012, 879, 835, 738, 605 cm^{-1}. HRMS (ESI) Calcd for $C_{17}H_{23}IN_3$ [M + H]$^+$: 396.0931; Found: 396.0927.

*2-(1-(4-tert-Butylphenyl)-2-iodoethyl)-2H-benzo[d][1,2,3]triazole (**3p**).* Obtained as a white solid in 93% yield (37.7 mg): M.P. 79 °C. ^{1}H NMR (400 MHz, CDCl3): δ 7.91−7.89 (m, 2 H), 7.43−7.35 (m, 6 H), 6.18 (dd, J = 10.6, 4.8 Hz, 1 H), 4.40 (t, J = 10.6 Hz, 1 H), 3.92 (dd, J = 10.8, 5.0 Hz, 1 H), 1.27 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.3, 144.3, 134.4, 126.6, 126.0, 118.4, 72.6, 34.7, 31.2, 5.1. IR (neat) 2962, 2902, 2868, 1512, 1415, 1321, 1269, 1228, 1178, 1109, 893, 829, 749, 605 cm^{-1}. HRMS (ESI) Calcd for $C_{18}H_{21}IN_3$ [M + H]$^+$: 406.0775; Found: 406.0766.

*2-(2-Iodo-1-phenylethyl)-4-(4-nitrophenyl)-2H-1,2,3-triazole (**4a**).* Obtained as a white solid in 95% yield (39.9 mg): M.P. 77 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.30 (d, J = 8.9 Hz, 2 H), 8.03 (s, 1 H), 7.98 (d, J = 8.9 Hz, 2 H), 7.45−7.42 (m, 2 H), 7.41−7.35 (m, 3H), 5.96 (dd, J = 10.7, 4.9 Hz, 1 H), 4.25 (t, J = 10.7 Hz, 1 H), 3.84 (dd, J = 10.7, 4.8 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.6, 145.9, 137.4, 136.5, 132.2, 129.2, 129.1, 126.7, 126.6, 124.3, 71.6, 5.0. IR (neat) 3062, 3032, 2960, 2926, 2848, 1604, 1340, 1309, 1178, 1111, 977, 877, 852, 736, 702, 567 cm^{-1}. HRMS (ESI) Calcd for $C_{16}H_{14}IN_4O_2$ [M + H]$^+$: 421.0156; Found: 421.0151.

*2-(1-(4-Ethoxyphenyl)-2-iodoethyl)-4-(4-nitrophenyl)-2H-1,2,3-triazole (**4b**).* Obtained as yellow oil in 90% yield (41.8 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.28 (d, J = 8.8 Hz, 2 H), 8.01 (s, 1 H), 7.97 (d, J = 8.8 Hz, 2 H), 7.37 (d, J = 8.7 Hz, 2 H), 6.87 (d, J = 8.7 Hz, 2 H),

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5.90 (dd, J = 10.6, 5.0 Hz, 1 H), 4.22 (t, J = 10.6 Hz, 1 H), 4.00 (dd, J = 14.0, 7.0 Hz, 2 H), 3.80 (dd, J = 10.6, 5.0 Hz, 1 H), 1.39 (t, J = 7.0 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.5, 147.5, 145.8, 136.6, 132.2, 129.3, 128.0, 126.6, 124.3, 114.9, 71.1, 63.6, 14.8, 5.5. IR (neat) 2980, 2929, 2875, 1606, 1515, 1344, 1305, 1251, 1178, 1045, 852, 736, 567 cm^{-1}. HRMS (ESI) Calcd for $C_{18}H_{18}IN_4O_3$ $[M + H]^+$: 465.0418; Found: 465.0416.

*4-(2-Iodo-1-(4-(4-nitrophenyl)-2H-1,2,3-triazol-2-yl)ethyl)-phenylacetate (**4c**).* Obtained as a white solid in 95% yield (45.4 mg): M.P. 106 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.29 (d, J = 8.9 Hz, 2 H), 8.02 (s, 1 H), 7.97 (d, J = 8.8 Hz, 2 H), 7.47 (d, J = 8.6 Hz, 2 H), 7.10 (d, J = 8.6 Hz, 2 H), 5.95 (dd, J = 10.7, 4.8 Hz, 1 H), 4.22 (t, J = 10.8 Hz, 1 H), 3.80 (dd, J = 10.7, 4.8 Hz, 1 H), 2.29 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.3, 151.1, 147.6, 146.0, 136.4, 134.8, 132.4, 128.0, 126.6, 124.3, 122.3, 70.9, 21.2, 4.8. IR (neat) 2954, 2924, 2852, 1764, 1606, 1517, 1369, 1344, 1309, 1201, 1168, 912, 854, 736 cm^{-1}. HRMS (ESI) Calcd for $C_{18}H_{16}IN_4O_4$ $[M + H]^+$: 479.0211; Found: 479.0207.

*2-(1-(4-Fluorophenyl)-2-iodoethyl)-4-(4-nitrophenyl)-2H-1,2,3-triazole (**4d**).* Obtained as a white solid in 91% yield (39.9 mg): M.P. 79 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.30 (d, J = 8.9 Hz, 2 H), 8.02 (s, 1 H), 7.97 (d, J = 8.8 Hz, 2 H), 7.47–7.43 (m, 2 H), 7.07 (t, J = 8.6 Hz, 2 H), 5.93 (dd, J = 10.3, 5.3 Hz, 1 H), 4.20 (t, J = 10.7 Hz, 1 H), 3.81 (dd, J = 10.7, 5.2 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.0 (d, J = 247.2 Hz), 147.6, 146.0, 136.4, 133.2, 132.4, 128.7 (d, J = 8.4 Hz), 126.7, 124.3, 116.1 (d, J = 21.7 Hz), 70.7, 4.8. IR (neat) 1604, 1510, 1344, 1309, 1232, 1180, 977, 852, 839, 536, 501 cm^{-1}. HRMS (ESI) Calcd for $C_{16}H_{13}FIN_4O_2$ $[M + H]^+$: 439.0062; Found: 439.0056.

*4-(2-Iodo-1-(4-(4-nitrophenyl)-2H-1,2,3-triazol-2-yl)ethyl)phenol (**4e**).* Obtained as a white solid in 54% yield (23.5 mg): M.P. 202 °C. ^{1}H NMR (400 MHz, Methanol-d_4): δ 8.30 (d, J = 8.8 Hz, 2 H), 8.23 (s, 1 H), 8.09 (d, J = 8.8 Hz, 2 H), 7.29 (d, J = 8.6 Hz, 2 H), 6.75 (d, J = 8.6 Hz, 2 H), 5.91 (dd, J = 11.0, 4.6 Hz, 1 H), 4.22 (t, J = 10.8 Hz, 1 H), 3.87 (dd, J = 10.6, 4.6 Hz, 1 H). ^{13}C NMR (100 MHz, Methanol-d_4): δ 157.9, 147.5, 145.7, 136.6, 132.1, 128.6, 127.8, 126.3, 123.8, 115.2, 71.1, 4.4. IR (neat) 2954, 2922, 2852, 1604, 1514, 1334, 1309, 1172, 854, 835, 756 cm^{-1}. HRMS (ESI) Calcd for $C_{16}H_{13}IN_4NaO_3$ $[M + Na]^+$: 458.9925; Found: 458.9918.

*N-(4-(2-Iodo-1-(4-(4-nitrophenyl)-2H-1,2,3-triazol-2-yl)ethyl)-phenyl)acetamide (**4f**).* Obtained as a yellow solid in 88% yield (42.0 mg): M.P. 56 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.28 (d, J = 8.8 Hz, 2 H), 8.01 (s, 1 H), 7.97 (d, J = 8.8 Hz, 2 H), 7.51 (d, J = 8.5 Hz, 2 H), 7.48 (s, 1 H), 7.38 (d, J = 8.5 Hz, 2 H), 5.90 (dd, J = 10.5, 5.1 Hz, 1 H), 4.19 (t, J = 10.6 Hz, 1 H), 3.79 (dd, J = 10.7, 5.1 Hz, 1 H), 2.15 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.5, 147.6, 145.9, 138.7, 136.5, 133.0, 132.3, 127.5, 126.6, 124.2, 120.2, 71.0, 24.6, 5.0. IR (neat) 3305, 3194, 2916, 1668, 1602, 1515, 1413, 1344, 1317, 1263, 1182, 977, 852, 736 cm^{-1}. HRMS (ESI) Calcd for $C_{18}H_{17}IN_5O_3$ $[M + H]^+$: 478.0371; Found: 478.0358.

*2-(1-Iodo-2-phenylpropan-2-yl)-4-(4-nitrophenyl)-2H-1,2,3-triazole (**4g**).* Obtained as a white solid in 90% yield (39.1 mg): M.P. 82 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.30 (d, J = 8.8 Hz, 2 H), 8.08 (s, 1 H), 8.01 (d, J = 8.8 Hz, 2 H), 7.34–7.28 (m, 3 H), 7.02–7.00 (m, 2 H), 4.49 (d, J = 10.6 Hz, 1 H), 4.04 (t, J = 10.6 Hz, 1 H), 2.31 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.5, 141.7, 136.7, 132.1, 128.9, 128.3, 126.6, 125.0, 124.3, 69.9, 28.0, 16.0; IR (neat) 3061, 2991, 1943, 2852, 1606, 1381, 1303, 1182, 852, 748, 698, 574 cm^{-1}. HRMS (ESI) Calcd for $C_{17}H_{16}IN_4O_2$ $[M + H]^+$: 435.0305; Found: 435.0313.

*2-(2-Iodocyclohexyl)-4-(4-nitrophenyl)-2H-1,2,3-triazole (**4h**).* Obtained as a white solid in 81% yield (32.2 mg): M.P. 65 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.29 (d, J = 8.8 Hz, 2 H), 7.97 (d, J = 8.8 Hz, 2 H), 7.97 (s, 1 H), 4.76–4.60 (m, 2 H), 2.72–2.68 (m, 1 H), 2.26–2.17 (m, 2 H), 2.01–2.00 (m, 2 H), 1.71–1.67 (m, 1 H), 1.58–1.47 (m, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.5, 145.4, 136.8, 131.7, 126.5, 124.3, 71.7, 39.6, 34.4, 30.8, 27.8, 24.6. IR (neat) 2937, 2858, 1604, 1517, 1346, 1311, 1161, 1111, 970, 852 cm^{-1}. HRMS (ESI) Calcd for $C_{14}H_{16}IN_4O_2$ $[M + H]^+$: 399.0313; Found: 399.0308.

*2-(2-Iodo-2,3-dihydro-1H-inden-1-yl)-4-(4-nitrophenyl)-2H-1,2,3-triazole (**4i**).* Obtained as a white solid in 91% yield (38.5 mg): M.P. 86 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.29 (d, J = 8.8 Hz, 2 H), 8.04 (s, 1 H), 7.97 (d, J = 8.9 Hz, 2 H), 7.37–7.33 (m, 2 H), 7.25–7.21 (m, 1 H), 7.08 (d, J = 7.6 Hz, 1 H), 6.39 (d, J = 7.2 Hz, 1 H), 5.03 (q, J = 7.6 Hz, 1 H), 3.87 (dd, J = 16.2, 7.6 Hz, 1 H), 3.55 (dd, J = 16.2, 8.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.6, 146.2, 141.5, 138.7, 136.4, 132.7, 129.6, 127.8, 126.6, 124.6, 124.3, 123.9, 76.8, 43.7, 22.2. IR (neat) 2953, 2927, 2852, 1604, 1517, 1475, 1342, 1311, 1263, 1111, 852, 748 cm^{-1}. HRMS (ESI) Calcd for $C_{17}H_{14}IN_4O_2$ $[M + H]^+$: 433.0156; Found: 433.0153.

*2-(6-Iodocyclohex-2-enyl)-4-(4-nitrophenyl)-2H-1,2,3-triazole (**4j**).* Obtained as a white solid in 85% yield (33.7 mg): M.P. 76 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.29 (d, J = 8.8 Hz, 2 H), 8.00 (s, 1 H), 7.98 (d, J = 8.8 Hz, 2 H), 6.18–6.15 (m, 1 H), 5.70–5.67 (m, 1 H), 5.57–5.55 (m, 1 H), 4.83–4.78 (m, 1 H), 2.51–2.25 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.6, 145.9, 136.5, 132.2, 131.4, 126.6, 124.3, 123.1, 69.5, 32.8, 26.9, 25.9. IR (neat) 2920, 2839, 1604, 1517, 1338, 1311, 1139, 1111, 979, 852, 810 cm^{-1}. HRMS (ESI) Calcd for $C_{14}H_{14}IN_4O_2$ $[M + H]^+$: 397.0156; Found: 397.0156.

*2-Iodo-1-(4-(4-nitrophenyl)-2H-1,2,3-triazol-2-yl)ethyl Acetate (**4k**).* Obtained as a white solid in 53% yield (21.3 mg): M.P. 89 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.31 (d, J = 8.8 Hz, 2 H), 8.07 (s, 1 H), 8.01 (d, J = 8.8 Hz, 2 H), 7.17 (dd, J = 8.1, 5.9 Hz, 1 H), 3.95 (dd, J = 10.6, 8.2 Hz, 1 H), 3.80 (dd, J = 10.6, 5.8 Hz, 1 H), 2.16 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.6, 147.9, 146.9, 135.7, 133.3, 126.9, 124.4, 83.8, 20.6, 0.2. IR (neat) 2924, 2358, 2341, 1761, 1520, 1348, 1209, 1018, 852 cm^{-1}. HRMS (ESI) Calcd for $C_{12}H_{11}IN_4NaO_4$ $[M + Na]^+$: 424.9718; Found: 424.9712.

*N^2-(4-Nitrophenyl)-2H-1,2,3-triazol-2-yl glycoside **4m**.* Obtained as a white solid in 68% yield (40.0 mg): M.P. 166 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.32 (d, J = 8.5 Hz, 2 H), 8.08 (s, 1 H), 8.00 (d, J = 8.6 Hz, 2 H), 6.49 (d, J = 6.9 Hz, 1 H), 5.73 (t, J = 3.4 Hz, 1 H), 5.53 (t, J = 4.4 Hz, 1 H), 5.09 (dd, J = 6.8, 3.8 Hz, 1 H), 4.69 (dd, J = 12.3, 8.8 Hz, 1 H), 4.46–4.42 (m, 1 H), 4.26 (dd, J = 12.4, 4.0 Hz, 1 H), 2.22 (s, 3 H), 2.14 (s, 3 H), 2.04 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.7, 169.5, 169.2, 148.0, 146.9, 135.7, 133.3, 126.9, 124.4, 88.0, 72.8, 68.4, 65.7, 60.2, 29.7, 22.7, 20.9, 20.8, 14.1. IR (neat) 2953, 1750, 1521, 1371, 1346, 1228, 1111, 1072, 1049, 975, 854, 736, 704 cm^{-1}. HRMS (ESI) Calcd for $C_{20}H_{22}IN_4O_9$ $[M + H]^+$: 589.0426; Found: 589.0421.

(2R,3S*)-2-Iodo-3-phenyl-3-(4-phenyl-2H-1,2,3-triazol-2-yl)-propan-1-ol (**4n**).* Obtained as a white solid in 60% yield (24.3 mg): M.P. 138 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (s, 1 H), 7.78 (d, J = 7.8 Hz, 2 H), 7.59 (d, J = 8.1 Hz, 2 H), 7.45–7.43 (m, 6 H), 6.12 (d, J = 10.6 Hz, 1 H), 5.15–5.11 (m, 1 H), 3.78–3.72 (m, 1 H), 3.51–3.45 (m, 1 H), 2.58 (t, J = 6.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.2, 137.1, 131.5, 129.9, 129.1, 128.9, 128.8, 128.7, 128.2, 126.0, 71.5, 64.9, 37.3. IR (neat) 2924, 1456, 1369, 1296, 1070, 767, 746, 694 cm^{-1}. HRMS (ESI) Calcd for $C_{17}H_{17}IN_3O$ $[M + H]^+$: 406.0411; Found: 406.0404.

*2-(2-Iodo-3-(4-methoxyphenyl)propyl)-4-(4-nitrophenyl)-2H-1,2,3-triazole (**6a**).* Obtained as a white solid in 34% yield (15.8 mg): M.P. 95 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.30 (d, J = 8.9 Hz, 2 H), 7.99 (s, 1 H), 7.96 (d, J = 8.8 Hz, 2 H), 7.16 (d, J = 8.6 Hz, 2 H), 6.86 (d, J = 8.6 Hz, 2 H), 4.90–4.75 (m, 3 H), 3.78 (s, 3 H), 3.23–3.11 (m, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.7, 147.6, 145.9, 136.4, 132.2, 130.2, 130.1, 126.5, 124.4, 114.0, 61.7, 55.3, 42.9, 30.0. IR (neat) 2835, 1606, 1514, 1338, 1305, 1249, 1178, 1031, 852 cm^{-1}. HRMS (ESI) Calcd for $C_{18}H_{18}IN_4O_3$ $[M + H]^+$: 465.0418; Found: 465.0416.

*2-(1-Iodo-3-(4-methoxyphenyl)propan-2-yl)-4-(4-nitrophenyl)-2H-1,2,3-triazole (**6a′**).* Obtained as a white solid in 42% yield (19.5 mg): M.P. 103 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.29 (d, J = 8.8 Hz, 2 H), 7.95 (d, J = 8.8 Hz, 2 H), 7.95 (s, 1 H), 7.00 (d, J = 8.5 Hz, 2 H), 6.78 (d, J = 8.6 Hz, 2 H), 4.99–4.92 (m, 1 H), 3.76 (s, 3 H), 3.72 (dd, J = 10.7, 8.8 Hz, 1 H), 3.65 (dd, J = 10.6, 4.8 Hz, 1 H), 3.38 (dd, J = 14.0, 7.8 Hz, 1 H), 3.29 (dd, J = 14.0, 6.8 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.7, 147.6, 145.6, 136.6, 131.9, 130.0, 127.9, 126.6, 124.3, 114.1, 68.9, 55.2, 40.4, 5.7. IR (neat) 2956, 2931, 2835, 1606, 1514, 1344, 1247, 1178, 1109, 1033, 977, 852, 819, 758 cm^{-1}. HRMS (ESI) Calcd for $C_{18}H_{18}IN_4O_3$ $[M + H]^+$: 465.0418; Found: 465.0416.

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*2-(2-Iodo-4-phenylbutyl)-4-(4-nitrophenyl)-2H-1,2,3-triazole (**6b**).* Obtained as a yellow solid in 60% yield (26.9 mg): M.P. 94 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.30 (d, J = 8.8 Hz, 2 H), 7.97 (s, 1 H), 7.94 (d, J = 8.8 Hz, 2 H), 7.29−7.25 (m, 2 H), 7.22−7.15 (m, 3 H), 4.93 (d, J = 13.9, 6.9 Hz, 1 H), 4.83 (d, J = 14.0, 8.0 Hz, 1 H), 4.56−4.49 (m, 1 H), 3.01−2.95 (m, 1 H), 2.76−2.69 (m, 1 H), 2.14−2.04 (m, 1 H), 1.99−1.90 (m, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.6, 145.9, 140.0, 136.3, 132.1, 128.6, 128.5, 126.5, 126.4, 124.3, 62.5, 38.3, 35.0, 28.9; IR (neat) 2926, 2854, 1604, 1519, 1338, 979, 852, 758, 700 cm^{-1}; HRMS (ESI) Calcd for $C_{18}H_{18}IN_4O_2$ $[M + H]^+$: 449.0469; Found: 449.0470.

*2-(1-Iodo-4-phenylbutan-2-yl)-4-(4-nitrophenyl)-2H-1,2,3-triazole (**6b′**).* Obtained as a white solid in 30% yield (13.4 mg): M.P. 97 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.32 (d, J = 8.9 Hz, 2 H), 8.02 (s, 1 H), 8.00 (d, J = 8.9 Hz, 2 H), 7.29 (t, J = 7.6 Hz, 2 H), 7.20 (t, J = 7.4 Hz, 1 H), 7.15 (d, J = 7.5 Hz, 2 H), 4.83−4.7 (m, 1 H), 3.72 (dd, J = 10.6, 8.7 Hz, 1 H), 3.59 (dd, J = 10.6, 5.0 Hz, 1 H), 2.56−2.49 (m, 3 H), 2.41−2.32 (m, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.7, 140.0, 136.6, 132.1, 128.6, 128.4, 126.6, 126.4, 124.3, 66.8, 36.7, 32.1, 6.0. IR (neat) 2924, 2854, 1604, 1517, 1344, 1311, 977, 852, 756, 702 cm^{-1}. HRMS (ESI) Calcd for $C_{18}H_{18}IN_4O_2$ $[M + H]^+$: 449.0469; Found: 449.0469.

*2-(3-Iodo-4-methylpentan-2-yl)-4-(4-nitrophenyl)-2H-1,2,3-triazole (**6c**).* Obtained as a colorless oil in 80% yield (32.0 mg). ^{1}H NMR (400 MHz, $CDCl_3$): major δ 8.29 (d, J = 8.8 Hz, 2 H), 7.99−7.95 (m, 3 H), 4.99−4.92 (m, 1 H), 4.54 (dd, J = 9.7, 3.5 Hz, 1 H), 1.91 (d, J = 6.6 Hz, 3 H), 0.93 (dd, J = 12.0, 6.3 Hz, 6 H), 0.40−0.36 (m, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.5, 145.3, 136.5, 131.7, 126.5, 124.3, 64.8, 51.3, 30.5, 23.8, 21.5, 19.9. IR (neat) 2964, 2931, 2873, 1604, 1517, 1346, 1338, 1303, 1111, 852 cm^{-1}. HRMS (ESI) Calcd for $C_{14}H_{18}IN_4O_2$ $[M + H]^+$: 401.0469; Found: 401.0470.

*2-(3-Iodo-3-methylbutan-2-yl)-4-(4-nitrophenyl)-2H-1,2,3-triazole (**6d**).* Obtained as a white solid in 79% yield (30.5 mg). ^{1}H NMR (400 MHz, $CDCl_3$): major δ 8.29 (d, J = 8.8 Hz, 2 H), 7.97 (d, J = 8.9 Hz, 2 H), 7.96 (s, 1 H), 4.93 (q, J = 7.0 Hz, 1 H), 1.92 (s, 3 H), 1.86 (s, 3 H), 1.79 (d, J = 7.08 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.5, 145.0, 136.9, 131.4, 126.5, 124.3, 69.1, 36.2, 26.3, 23.9, 23.8. IR (neat) 2991, 2927, 2868, 1604, 1517, 1344, 1296, 1111, 977, 852, 758, 594 cm^{-1}. HRMS (ESI) Calcd for $C_{13}H_{16}IN_4O_2$ $[M + H]^+$: 387.0313; Found: 387.0312.

*2-(2-Iodo-3,3-dimethylbutyl)-4-(4-nitrophenyl)-2H-1,2,3-triazole (**6e**).* Obtained as a colorless oil in 84% yield (33.6 mg). ^{1}H NMR (400 MHz, $CDCl_3$): major δ 8.29 (d, J = 8.7 Hz, 2 H), 7.98 (s, 1 H), 7.97 (d, J = 8.6 Hz, 2 H), 4.89−4.69 (m, 3 H), 1.23 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.5, 145.9, 136.5, 132.1, 126.5, 124.3, 60.2, 48.6, 35.1, 28.6. IR (neat) 2964, 2870, 1604, 1517, 1369, 1313, 1109, 977, 852 cm.; HRMS (ESI) Calcd for $C_{14}H_{18}IN_4O_2$ $[M + H]^+$: 401.0469; Found: 401.0468.

2-((1S,2S*)-2-Iodo-1-phenylpropyl)-4-phenyl-2H-1,2,3-triazole (**8a**).* Obtained as a white solid in 84% yield (32.7 mg): M.P. 72 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 (s, 1 H), 7.80 (d, J = 8.6 Hz, 2 H), 7.64 (d, J = 8.3 Hz, 2 H), 7.45−7.33 (m, 6 H), 5.83 (d, J = 10.8 Hz, 1 H), 5.08−5.00 (m, 1 H), 1.84 (d, J = 6.8 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.8, 135.8, 131.2, 130.4, 129.0, 128.8, 128.5, 127.5, 126.1, 77.7, 26.8, 26.0. IR (neat) 3034, 2924, 2866, 1456, 1296, 1139, 97, 844, 765, 738, 690, 590 cm^{-1}. HRMS (ESI) Calcd for $C_{17}H_{17}IN_3$ $[M + H]^+$: 390.0462; Found: 390.0457.

2-((1R,2R*)-2-Iodo-1-phenylpropyl)-4-phenyl-2H-1,2,3-triazole (**8b**).* Obtained as a white solid in 80% yield (31.1 mg): M.P. 67 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 (s, 1 H), 7.83 (d, J = 8.4 Hz, 2 H), 7.58 (d, J = 7.9 Hz, 2 H), 7.43 (t, J = 7.8 Hz, 2 H), 7.39−7.33 (m, 4 H), 5.74 (d, J = 11.1 Hz, 1 H), 5.23−5.15 (m, 1 H), 1.83 (d, J = 7.0 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.8, 137.8, 131.3, 130.2, 129.0, 128.9, 128.6, 128.5, 128.2, 126.0, 76.5, 25.9, 25.6. IR (neat) 3034, 2924, 2866, 1475, 1456, 1367, 1317, 1151, 1070, 975, 848, 767, 754, 561 cm^{-1}. HRMS (ESI) Calcd for $C_{17}H_{17}IN_3$ $[M + H]^+$: 390.0462; Found: 390.0458.

*(Z)-2-(2-Iodo-1-phenylvinyl)-4-phenyl-2H-1,2,3-triazole (**9**).* Obtained as a yellow solid in 18% yield (6.7 mg): M.P. 65 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 (s, 1 H), 7.82 (d, \J = 7.2 Hz, 2 H), 7.53−7.26 (m, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.9, 145.1, 134.6, 132.8, 130.2, 129.7, 129.5, 129.1, 129.0, 128.5, 126.2, 72.4. IR (neat) 3073, 3035, 2922, 2384, 1476, 1393, 1339, 1265, 988, 895, 768, 716, 692 cm^{-1}. HRMS (ESI) Calcd for $C_{16}H_{13}IN_3$ $[M + H]^+$: 374.0149; Found: 374.0149.

*N-(4-Fluorobenzyl)-N-(2-iodo-1-(4-phenyl-2H-1,2,3-triazol-2-yl)-allyl)-4-methylbenzenesulfonamide (**11**).* Obtained as a white solid in 68% yield (40.0 mg): M.P. 97 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77 (s, 1 H), 7.64 (d, J = 8.3 Hz, 2 H), 7.46−7.39 (m, 3 H), 7.36 (d, J = 8.3 Hz, 2 H), 7.31−7.26 (m, 3 H), 6.97 (d, J = 8.1 Hz, 2 H), 6.86 (d, J = 8.7 Hz, 2 H), 6.05−6.03 (m, 2 H), 4.92 (d, J = 16.0 Hz, 1 H), 4.85 (d, J = 16.0 Hz, 1 H), 2.15 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.2 (d, J = 244.4 Hz), 148.1, 143.7, 136.0, 132.0, 131.7, 131.5, 131.1, 129.4, 129.1, 129.0, 128.9, 126.6 (d, J = 121.0 Hz), 114.7 (d, J = 21.3 Hz), 100.7, 82.2, 48.9, 21.3. IR (neat) 2955, 2924, 1510, 1356, 1290, 1223, 1266, 1090, 1041, 816, 770 cm^{-1}. HRMS (ESI) Calcd for $C_{25}H_{23}FIN_4O_2S$ $[M + H]^+$: 589.0565; Found: 589.0558.

*tert-Butyl(5R)-6-(4-(2-iodo-1-(4-phenyl-2H-1,2,3-triazol-2-yl)-ethyl)phenylamino)-6-oxohexane-1,5-diyldicarbamate (**13**).* Obtained as a yellow solid in 50% yield (35.9 mg): M.P. 89 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.65 (br, 1 H), 7.91 (s, 1 H), 7.81−7.80 (m, 2 H), 7.52−7.49 (m, 2 H), 7.42 (t, J = 8.0 Hz, 2 H), 7.36−7.33 (m, 3 H) 5.89−5.85 (m, 1 H), 5.27 (br, 1 H), 4.67−4.64 (m, 1 H), 4.21−4.15 (m, 2 H), 3.80−3.75 (m, 1 H), 3.10−3.07 (m, 2 H), 1.91−1.89 (m, 1 H), 1.73−1.59 (m, 1 H), 1.50−1.45 (m, 4 H), 1.42 (s, 18 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.7, 156.3, 148.0, 138.5, 133.4, 131.4, 130.3, 128.9, 128.5, 127.5, 126.1, 120.0, 79.4, 70.5, 31.2, 29.6, 28.5, 28.3, 22.6, 5.4; IR (neat) 3313, 3201, 2976, 2931, 2864, 1674, 1606, 1514, 1365, 1251, 1168, 736 cm^{-1}. HRMS (ESI) Calcd for $C_{32}H_{44}IN_6O_5$ $[M + H]^+$: 719.2412; Found: 719.2414.

*4-(4-(2-Iodo-1-(4-phenyl-2H-1,2,3-triazol-2-yl)ethyl)phenylamino)-4-oxobutanoic Acid (**15**).* Obtained as a yellow solid in 62% yield (30.3 mg): M.P. 116 °C. ^{1}H NMR (400 MHz, CD_3OD): δ 8.09 (s, 1 H), 7.86 (d, J = 8.4 Hz, 2 H), 7.57 (d, J = 8.6 Hz, 2 H), 7.45−7.34 (m, 5 H), 5.94 (dd, J = 10.8, 4.7 Hz, 1 H), 4.22 (t, J = 10.6 Hz, 1 H), 3.91 (dd, J = 10.6, 4.8 Hz, 1 H), 2.66 (s, 4 H). ^{13}C NMR (100 MHz, CD_3OD): δ 174.9, 171.5, 148.0, 139.1, 133.4, 131.1, 130.2, 128.5, 128.2, 127.0, 125.6, 119.7, 70.6, 30.9, 28.5, 4.2. IR (neat) 2980, 2933, 1732, 1714, 1666, 1608, 1516, 1450, 1409, 1373, 1246, 1182, 1045, 839 cm^{-1}. HRMS (ESI) Calcd for $C_{20}H_{20}IN_4O_3$ $[M + H]^+$: 491.0575; Found: 491.0565.

*2-(1-(4-tert-Butylphenyl)-2-iodo-1-(4-(4-nitrophenyl)-2H-1,2,3-triazol-2-yl)ethyl)-4-p-tolyl-2H-1,2,3-triazole (**16a**).* Obtained as a white solid in 33% yield (20.9 mg): M.P. 210 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.28 (d, J = 8.8 Hz, 2 H), 8.08 (s, 1 H), 7.98 (d, J = 9.0 Hz, 2 H), 7.96 (s, 1 H), 7.70 (d, J = 8.1 Hz, 2 H), 7.42 (d, J = 8.6 Hz, 2 H), 7.23 (d, J = 8.0 Hz, 2 H), 7.18 (d, J = 8.6 Hz, 2 H), 5.06 (d, J = 11.0 Hz, 1 H), 5.02 (d, J = 11.0 Hz, 1 H), 2.38 (s, 3 H), 1.34 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.7, 148.8, 147.8, 146.3, 139.1, 135.9, 133.5, 133.1, 132.5, 129.6, 128.0, 127.0, 126.7, 126.2, 125.0, 124.3, 87.4, 34.7, 31.2, 21.4, 12.2. HRMS (ESI) Calcd for $C_{29}H_{28}IN_7NaO_2$ $[M + Na]^+$: 656.1241; Found: 656.1240.

*2-(1-(4-tert-Butylphenyl)-1-iodo-2-(4-p-tolyl-2H-1,2,3-triazol-2-yl)ethyl)-4-(4-nitrophenyl)-2H-1,2,3-triazole (**16b**).* Obtained as a white solid in 20% yield (12.7 mg): M.P. 197 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.31 (d, J = 8.8 Hz, 2 H), 8.13 (s, 1 H), 8.04 (s, 1 H), 7.99 (d, J = 8.8 Hz, 2 H), 7.70 (d, J = 8.1 Hz, 2 H), 7.41 (d, J = 8.6 Hz, 2 H), 7.20 (d, J = 8.0 Hz, 2 H), 6.98 (d, J = 8.6 Hz, 2 H), 5.22 (d, J = 11.2 Hz, 1 H), 4.93 (d, J = 11.2 Hz, 1 H), 2.36 (s, 3 H), 1.34 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.4, 148.0, 147.8, 146.7, 138.5, 135.5, 134.4, 133.5, 129.5, 127.1, 127.0, 125.7, 125.5, 124.4, 121.0, 85.2, 34.8, 31.2, 21.3, 10.7. IR (neat) 2961, 2361, 2344, 1605, 1522, 1338, 1267, 978, 918, 853, 822, 750 cm^{-1}. HRMS (ESI) Calcd for $C_{29}H_{28}IN_7NaO_2$ $[M + Na]^+$: 656.1241; Found: 656.1249.

■ ASSOCIATED CONTENT

Supporting Information

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4m′s NOESY spectral data and copies of ^{1}H and ^{13}C NMR spectra for all new compounds (PDF)
Compound **8a**′s X-ray structure and its cif file (CIF)

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Notes

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