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QUANTITATIVE AND QUALITATIVE PREDICTIONS OF 4-AZIDO 2H-1,2,3- TRIAZOLES CYTOTOXICITY IN RELATION TO HUMAN BREAST CANCER CELL LINES

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Abstract. In the presented article, from this BC CLC-Pred web-application (Pass Online) has used for quantitative and qualitative predictions of substance cytotoxicity in relation to human nine breast cancer cell lines (T47D, ZR-75-1, MX1, Hs-578T, MCF7-DOX, MCF7, Bcap37, MCF7R, BT-20) for previously synthesized triazoles. Based on the obtained results, it was determined that the nature, strength, number and position of the functional groups in the aromatic ring in the molecule have a significant impact on the results. Thus, triazoles with electron donor groups showed higher activity than those with electroacceptor groups and at the same time, it was observed that the increase in the number of these groups had a positive effect on the activity. The position of functional groups in the aromatic ring, the presence or absence of conjugation in the compound and the effect of steric factors on biological activity are reflected in this article. Also, although the functional groups are of the same nature, depending on their strength (taking into account the mesomeric and electromeric effects), the number and types of active cells change, which in turn leads to interesting results.

Keywords: *BC CLC-Pred, QSAR, triazole, breast cancer cell.*

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1. Introduction

Compounds containing the triazole fragment are known to be used in medicine as medicinal preparations against a number of diseases. This is the main component, for example of anti-cancer (Sathish *et al*., 2013; Shaaban *et al*., 2010; Sunil *et al*., 2009), anti-microbial (against fungi and bacteria) (Gumrukcuoglu *et al*., 2007; Bhovi *et al*., 2005; Kagoshima *et al*., 2010), anti-histamine (anti-allergy) (Alagarsamy *et al*., 2009), cytotoxic (anti-cancer cell activity) (Silva *et al*., 2009; Rani *et al*., 2010), convulsant activity (used in the treatment of epilepsy and a number of diseases) (Guan *et al*., 2007; Wagle *et al*., 2009; Catarzi *et al*., 2004), analgesic activity (against pain) (Tozkoparan *et*

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al., 2002; Siddiqui *et al*., 2010), anti-inflammatory (against swelling and inflammation) (Goyal *et al*., 2010; Bhalgat *et al*., 2014) anti-mycotic (against fungal infection or against diseases caused by fungi) (Wujec *et al*., 2004) etc. medicinal preparations. In addition, compounds containing the triazole fragment, given the molecular weight, the number of rotatable bonds in the molecule, the number of donor-acceptor bonds, the number of acceptor hydrogen bonds and the octanol/water ratio meet the requirements of the RO5 rule in medicinal chemistry (Atakishiyeva *et al*., 2023; Abdullayeva *et al*., 2024; Yousuf *et al*., 2022). Taking this into account, the interest in their synthesis is increasing day by day. There are a number of methods known in the literature, some of which are not compatible with medicinal chemistry in terms of conditions and time.

At the same time, it does not mean that a number of compounds carrying a triazole fragment, the efficiency of the synthesis method and the use of their homologues in the treatment of the diseases will show biological activity. With these nuances in mind alone, synthetics prefer in silico studies to know whether substances are likely to exhibit biological activity beforehand. Swiss ADME (Mishra *et al*., 2019; Mahantesh *et al*., 2020; Trpathi *et al*., 2019), CADD (Computer Aided Drug Design) (Rentzsch *et al*., 2019; Zhao *et al*., 2020), Molecular Docking (Jakhar *et al*., 2020; Yuriev *et al*., 2013), QSAR (Quantitative Structure-Activity Relationship) (Tropsha, 2010; Cherkasov *et al*., 2014; Muratov *et al*., 2020) are examples of them.

For quantitative and qualitative prediction of cytotoxicity of previously synthesized triazoles (compound 1-18) (Shastin *et al*., 2018; Maharramov *et al*., 2023) against human breast cancer cell lines BC CLC-Pred (Lagunin *et al*., 2024) web application was used in the presented article. The ability to simultaneously quantitatively and qualitatively predict IC50 and IG50 values for nine breast cancer cell lines (T47D, ZR-75-1, MX1, Hs-578T, MCF7-DOX, MCF7, Bcap37, MCF7R, BT-20) was provided for us by BC CLC-Pred web application.

Let's analyze the nine breast cancer cell lines mentioned above one by one:

1. T47D - Represents invasive ductal breast carcinoma. Breast ducts refer to the passages through which milk flows from the mammary glands to the nipple. Invasive ductal breast carcinoma is breast cancer that occurs when healthy cells growing in the lining of the milk ducts change and invade the breast tissue outside the duct walls. This first group includes - luminal A- (ER+, PR±, HER2-). Estradiol, a hormone that is abundant in the cells doesn't regulate progesterone receptors. The resistance of cells to estrogens and antiestrogens is high.

2. ZR-75-1 - Represents invasive ductal breast carcinoma. This first group includes - luminal A- (ER+, PR±, HER2-). Low invasiveness, positive expression of CK8, CK18, CK19, negative expression of vimentin are characteristics of it. High levels of the mucin MUC-1 mRNA, low levels of MUC-2 mRNA are produced by these cells, but do not express the MUC-3 gene.

3. MX1 - Represents infiltrating breast carcinoma. It is the most common type of breast cancer. It starts inside the milk ducts and spreads to the healthy cells outside the ducts. Estrogen receptor negative (ER-) is given as a characteristic feature. Cancer cells that are negative for estrogen receptors do not need estrogen to grow, which means that they will continue to grow, not stop growing, even when treated with drugs that block the release of estrogen. This is also called ER negative.

4. Hs-578T - Represents invasive ductal breast carcinoma. Also known as triple negative breast cancer (ER–, PR–, HER-2–). Triple-negative breast cancer is a type of cancer that does not have receptors for estrogen and progesterone hormones in the cells.

5. MCF7-DOX - Represents invasive ductal breast carcinoma. A type of drug-resistant MCF7 cell line is even 15-20 times more resistant to Doxorubicin (DOX)-induced cytotoxicity (killing cancer cells).

6. MCF7 - Represents invasive ductal breast carcinoma. This first group, includes luminal A- (ER+, PR±, HER2-). These cells are quite large and known for their slow growth. Only these cells are recognized as the most suitable for in vitro studies by scientists, because they have a number of favorable properties. Note that TNF-alpha (tumor necrosis factor alpha) inhibits the proliferation of MCF7 cells.

7. Bcap37 - Represents breast carcinoma. Breast cancer cells start inside the milk ducts. The in situ form, that is, the earliest form, does not pose a serious threat to life and can be detected in its early stages. Note that cancer cells can make surrounding healthy breast cells sick. This in turn creates tumors that lead to stratification and eventually thickening.

8. MCF7R - Represents invasive ductal breast carcinoma. A derivative of the drug-resistant MCF7 cell line. It is highly resistant to doxorubicin and tamoxifen.

9. BT-20 – Represents invasive ductal breast carcinoma. Also known as triple negative breast cancer (ER, PR–, HER-2–). It is TNF-alpha that inhibits the proliferation of BT-20 cells.

In the written article, in addition to the effect of triazoles against the 9 breast cancer cells listed above, we also investigated the effect of the nature, strength, number and position of the functional groups in aromatic ring in the compounds.

2. Materials and Methods

Considering that the compounds containing the triazole fragment show high biological activity, targets prediction of triazoles (compound 1-18) (Shastin *et al*., 2018; Maharramov *et al*., 2023) was performed through BC CLC-Pred. MILES, MOL file or Marvin Javascript - 3 formats of compound structures were imported in the panel box and submitted to predict quantitative and qualitative predictions for the nine breast cancer cell lines.

Quantitative and qualitative predictions of substance cytotoxicity in relation to human breast cancer cell lines for synthesized triazoles were done by using of BC CLC-Pred web-application. The BC CLC-Pred web-application can be accessible freely by following the link https://www.way2drug.com/bc/.

3. Results and Discussion

For synthesized triazoles quantitative and qualitative predictions of substance cytotoxicity in relation to human breast cancer cell lines are given in the presented article. There are 3 main factors for this:

1. Electron distribution i.e the nature of functional groups
2. Steric factors, i.e. the position of functional groups in the aromatic ring
3. Number of functional groups

Based on this, 18 previously synthesized triazoles were selected. First, the cytotoxicity of 4-azido-2,5-diphenyl-2H-1,2,3-triazole, which does not have any functional group in the aromatic ring, was predicted by the program.

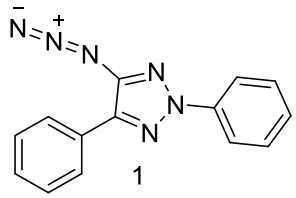

Figure 1. 4-azido-2,5-diphenyl-2H-1,2,3-triazole

First, the obtained results are reflected in the table.

Name	Classification				Quantitative			
	IC50		GI50		pIC50		pGI50	
	Value	AD	Value	AD	Value	AD	Value	AD
Bcap37	inactive	+						
BT-20	inactive	+	Active	+			6.1238	+
Hs-578T	active	+	Inactive	+				
MCF7			Inactive	+	4.9001	+6	4.7030	+
MCF7-DOX	active	+			6.4506	+		
MCF7R	inactive	+			4.7856	+		
MX-1	inactive	+			5.9874	+		
T47D	inactive	+	Inactive	+	4.8354	+	5.4599	+
ZR-75-1	inactive	+	Inactive	+	5.0542	+	5.7530	+

First, for clarity, let's give a general interpretation of the table. The first column contains names of nine breast cancer cell lines. IC50 and GI50 values for a given substance are given and in the AD cell + is given if the compound of interest belongs to the field of application, otherwise – IC50 is a quantitative measure that reflects the amount of a certain inhibitory substance required to interfere with a biological process. GI50 is a biomarker for cancer and other benign tumor diseases. The GI50 value is 50% inhibition of growth and is similar to IC50, but the main difference is that it is used to measure the concentration of a compound needed to inhibit the growth of cancer or other benign tumor cells by 50% in vitro.

Values of IC50 and IG50 were transferred to molar concentration and logarithmic view of pIC50 and pIG50 values. If the pIC50 and pGI50 values are higher than 6, it is given as active, otherwise inactive. Active means predicts cell line cytotoxicity for paclitaxel used in the treatment of breast cancer. Paclitaxel is a type of chemotherapy. It is a treatment for a number of different types of cancer.

For compound 1 - 4-azido-2,5-diphenyl-2H-1,2,3-triazole, which has no functional groups in the aromatic rings, only the BT-20 cell line has a value of 6.1238 and it shows activity.

Then, the cytotoxicity of triazole derivatives bearing an electrondonor group was predicted with reference to the principle of electron distribution. Here, 9 pre-synthesized triazoles (compounds 2-10) were selected taking into account the nature, strength (mesomeric effect, inductive effect), position and number of the functional group directly attached to the aromatic ring. General information about the synthesized 2H-1,2,3-triazole-based physiologically active compounds, as well as quantitative and qualitative predictions of substances cytotoxicity in relation to human breast cancer cell lines, can be obtained from the supplementary material.

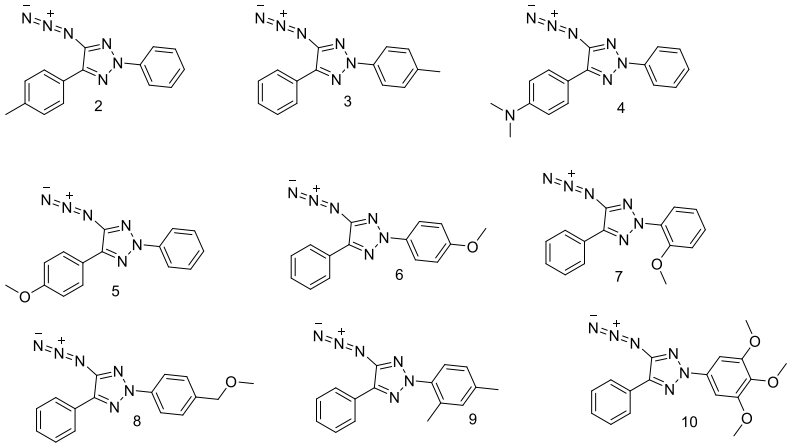

Figure 2. 4-azido 2H-1,2,3-triazoles containing an electron-donating group

A general interpretation of the results shows that triazoles bearing a methyl group, regardless of the aromatic ring on which the methyl group is located, have GI50 values below 6, resulting in no activity. The increase in the number of methyl groups does not have a strong effect on the activity and shows only a slight activity against ZR-75-1 cancer cells. 4-(5-azido-2-phenyl-2H-1,2,3-triazol-4-yl)-N,N-dimethylaniline bearing p-dimethylamine group shows activity against BT-20 and T47D cells. BT-20 shows activity against ZR-75-1 cells in combination with triazoles (compound 5.6) containing 4-methoxy benzaldehyde group. For compound 7, this activity is only against BT-20 cells. From here, the fundamental influence of steric factors on biological activity is clearly visible. If there is an ethoxy group, we can observe its activity against ZR-75-1 cells only.

The main conclusion from the above is that the strength of functional groups in compounds, that is, positive inductive and positive mesomeric effect, affects biological activity. And at the same time, the number of functional groups plays an important role. Thus, as the number of methoxy groups in the compound increases (compound 10), the number of cells showing activity also increases (BT-20, ZR-75-1, MCF-7). That is, compound 10, 4-azido-5-phenyl-2-(3,4,5-trimethoxyphenyl)-2H-1,2,3-triazole, shows the best results, which means that it can be used in various breast cancer cell lines against paclitaxel as a compound with a high potential to detect broad-spectrum cytotoxicity.

Taking into account the above positive results, 8 triazoles bearing electron acceptor groups were selected in order to investigate the effect of electron distribution in the

molecule on biological activity. The general formulas of selected triazoles are reflected below.

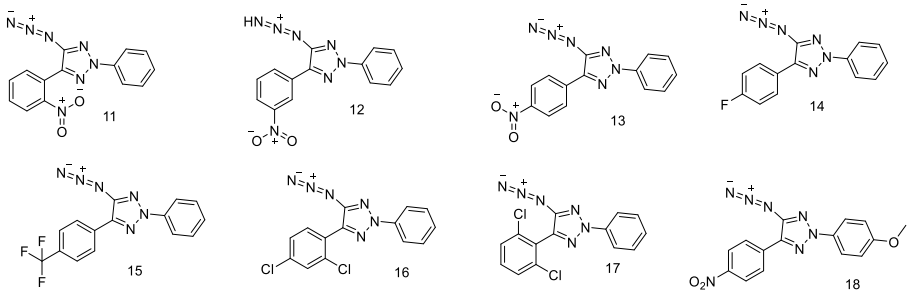

Figure 3. 4-azido 2H-1,2,3- triazoles bearing an electronacceptor group

If we look at the initial prediction of compounds 11-13, it was determined that the nitro group shows activity against BT-20 cells with its location in ortho and para positions, but it does not show any activity in the meta position, which can be explained by the addition of the functional group to aromatic compounds. Regardless of the number of compounds containing fluorine atoms (compound 14,15) does not affect the biological activity in any way, while compounds containing chlorine atoms (compound 16,17) regardless of their position, we observe that they show activity only against ZR-75-1 cells. Both electron-donor and electron-acceptor groups (compound 18) show activity against both BT-20 and T47-D cells and the effect of the electron-donor group on the activity is clearly observed here.

4. Conclusion

These results show us that in addition to carrying the triazole fragment, the electron distribution in the compound, steric factors, whether the functional groups create attachment in the compound also affect the activity. As a result, the fact that the methoxy group, which is a strong electron-donating group, is in the para and ortho positions in the aromatic ring and its number increases, proves once again what we said.

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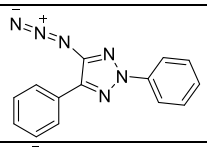
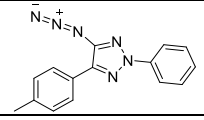
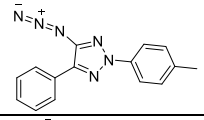
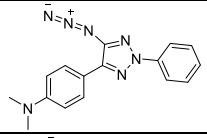
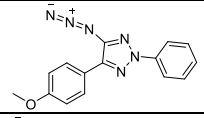
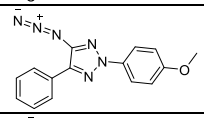
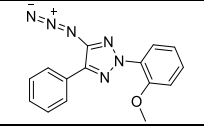
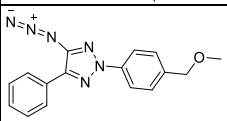
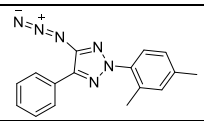
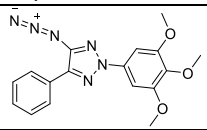
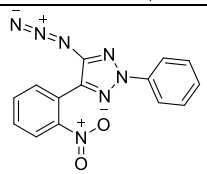
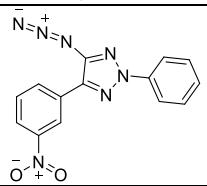
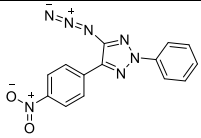
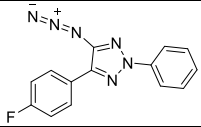
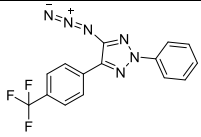
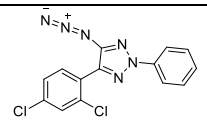
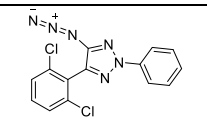
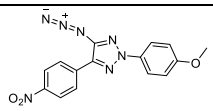
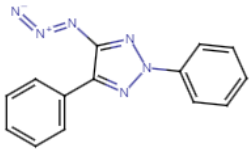
Table 1. Overview of the presented 4-azido 2H-1,2,3-triazoles

№	Sturucture	Name	Molecular formula	Molecular weight	Smile notation
1		4-azido-2,5-diphenyl-2H-1,2,3-triazole	C14H10N6	262.27g/mol	[N-]=[N+]=NC1=NN(N=C1C1=CC=CC=C1)C1=CC=CC=C1
2		4-azido-2-phenyl-5-(p-tolyl)-2H-1,2,3-triazole	C15H12N6	276.30 g/mol	CC1=CC=C(C=C1)C1=NN(N=C1N=[N+]=[N-])C1=CC=CC=C1
3		4-azido-5-phenyl-2-(p-tolyl)-2H-1,2,3-triazole	C14H12N6	276.30 g/mol	CC1=CC=C(C=C1)N1N=C(N=[N+]=[N-])C(=N1)C1=CC=CC=C1
4		4-(5-azido-2-phenyl-2H-1,2,3-triazol-4-yl)-N,N-dimethylaniline	C16H15H7	305.34 g/mol	CN(C)C1=CC=C(C=C1)C1=NN(N=C1N=[N+]=[N-])C1=CC=CC=C1
5		4-azido-5-(4-methoxyphenyl)-2-phenyl-2H-1,2,3-triazole	C15H12N6O	292.30 g/mol	COC1=CC=C(C=C1)C1=NN(N=C1N=[N+]=[N-])C1=CC=CC=C1
6		4-azido-2-(4-methoxyphenyl)-5-phenyl-2H-1,2,3-triazole	C15H12N6O	292.30 g/mol	COC1=CC=C(C=C1)N1N=C(N=[N+]=[N-])C(=N1)C1=CC=CC=C1
7		4-azido-2-(2-methoxyphenyl)-5-phenyl-2H-1,2,3-triazole	C15H12N6O	292.30 g/mol	COC1=C(C=CC=C1)N1N=C(N=[N+]=[N-])C(=N1)C1=CC=CC=C1
8		4-azido-2-(4-(methoxymethyl)phenyl)-5-phenyl-2H-1,2,3-triazole	C14H12N6	306.32 g/mol	CCOC1=CC=C(C=C1)N1N=C(N=[N+]=[N-])C(=N1)C1=CC=CC=C1
9		4-azido-2-(2,4-dimethylphenyl)-5-phenyl-2H-1,2,3-triazole	C16H14N6	290.33 g/mol	CC1=CC(C)=C(C=C1)N1N=C(N=[N+]=[N-])C(=N1)C1=CC=CC=C1
10		4-azido-5-phenyl-2-(3,4,5-trimethoxyphenyl)-2H-1,2,3-triazole	C17H16N6O3	352.35 g/mol	COC1=CC(=CC(OC)=C1OC)N1N=C(N=[N+]=[N-])C(=N1)C1=CC=CC=C1
11		4-azido-5-(2-nitrophenyl)-2-phenyl-2H-1,2,3-triazole	C14H9N7O2	307.08 g/mol	[N-]=[N+]=NC1=NN(N=C1C1=C(C=CC=C1)N(=O)=O)C1=CC=CC=C1
12		4-azido-5-(3-nitrophenyl)-2-phenyl-2H-1,2,3-triazole	C14H9N7O2	307.08 g/mol	[N-]=[N+]=NC1=NN(N=C1C1=CC(=CC=C1)N(=O)=O)C1=CC=CC=C1

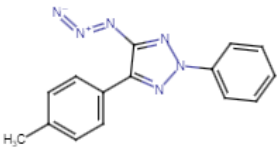
13		4-azido-5-(4-nitrophenyl)-2-phenyl-2H-1,2,3-triazole	C14H9N7O2	307.08 g/mol	[N-]=[N+]=NC1=NN(N=C1C1=CC=C(C=C1)N(=O)=O)C1=CC=CC=C1
14		4-azido-5-(4-fluorophenyl)-2-phenyl-2H-1,2,3-triazole	C14H9FN6	280.26 g/mol	FC1=CC=C(C=C1)C1=NN(N=C1N=[N+]=[N-])C1=CC=CC=C1
15		4-azido-2-phenyl-5-(4-(trifluoromethyl)phenyl)-2H-1,2,3-triazole	C15H9F3N6	330.27 g/mol	FC(F)(F)C1=CC=C(C=C1)C1=NN(N=C1N=[N+]=[N-])C1=CC=CC=C1
16		4-azido-5-(2,4-dichlorophenyl)-2-phenyl-2H-1,2,3-triazole	C14H8Cl2N6	331.16 g/mol	ClC1=CC(Cl)=C(C=C1)C1=NN(N=C1N=[N+]=[N-])C1=CC=CC=C1
17		4-azido-5-(2,6-dichlorophenyl)-2-phenyl-2H-1,2,3-triazole	C14H8Cl2N6	331.16 g/mol	ClC1=CC=CC(Cl)=C1C1=NN(N=C1N=[N+]=[N-])C1=CC=CC=C1
18.		4-azido-2-(4-methoxyphenyl)-5-(4-nitrophenyl)-2H-1,2,3-triazole	C15H11N7O3	337.29 g/mol	COC1=CC=C(C=C1)N1N=C(N=[N+]=[N-])C(=N1)C1=CC=C(C=C1)N(=O)=O

Compound 1.



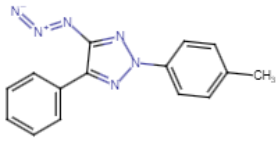
Name	Classification				Quantitative			
	IC50		GI50		pIC50		pGI50	
	Value	AD	Value	AD	Value	AD	Value	AD
Bcap37	inactive	+						
BT-20	inactive	+	active	+			6.1238	+
Hs-578T	active	+	inactive	+				
MCF7			inactive	+	4.9001	+	4.7030	+
MCF7-DOX	active	+			6.4506	+		
MCF7R	inactive	+			4.7856	+		
MX-1	inactive	+			5.9874	+		
T47D	inactive	+	inactive	+	4.8354	+	5.4599	+
ZR-75-1	inactive	+	inactive	+	5.0542	+	5.7530	+

Compound 2



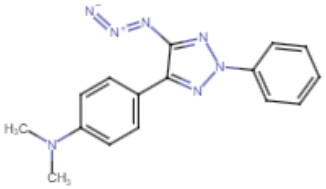
Name	Classification				Quantitative			
	IC50		GI50		pIC50		pGI50	
	Value	AD	Value	AD	Value	AD	Value	AD
Bcap37	inactive	+						
BT-20	inactive	+	inactive	+			5.9510	+
Hs-578T	inactive	+	inactive	+				
MCF7			inactive	+	4.9860	+	4.9732	+
MCF7-DOX	active	+			5.9239	+		
MCF7R	inactive	+			4.9683	+		
MX-1	inactive	+			5.9983	+		
T47D	inactive	+	inactive	+	4.1432	+	5.4677	+
ZR-75-1	inactive	+	inactive	+	4.9762	+	5.9024	+

Compound 3.



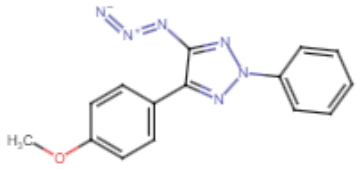
Name	Classification				Quantitative			
	IC50		GI50		pIC50		pGI50	
	Value	AD	Value	AD	Value	AD	Value	AD
Bcap37	inactive	+						
BT-20	inactive	+	inactive	+			5.9489	+
Hs-578T	active	+	inactive	+				
MCF7			inactive	+	5.0137	+	4.9732	+
MCF7-DOX	active	+			5.9037	+		
MCF7R	inactive	+			4.9802	+		
MX-1	inactive	+			5.9931	+		
T47D	inactive	+	inactive	+	4.1432	+	5.4680	+
ZR-75-1	inactive	+	inactive	+	4.9714	+	5.8690	+

Compound 4



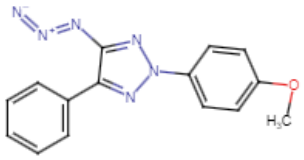
Name	Classification				Quantitative			
	IC50		GI50		pIC50		pGI50	
	Value	AD	Value	AD	Value	AD	Value	AD
Bcap37	inactive	+						
BT-20	inactive	+	active	+			6.2429	+
Hs-578T	inactive	+	inactive	+				
MCF7			inactive	+	5.2350	+	5.0644	-
MCF7-DOX	active	+			6.2473	+		
MCF7R	inactive	+			4.8677	+		
MX-1	active	+			6.2363	+		
T47D	inactive	+	active	+	4.5645	-	5.2452	-
ZR-75-1	active	+	inactive	+	6.0484	+	5.7469	+

Compound 5.



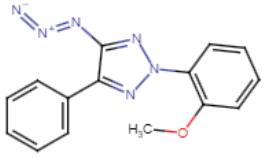
Name	Classification				Quantitative			
	IC50		GI50		pIC50		pGI50	
	Value	AD	Value	AD	Value	AD	Value	AD
Bcap37	inactive	+						
BT-20	inactive	+	active	+			5.9941	+
Hs-578T	inactive	+	inactive	+				
MCF7			inactive	+	5.6087	+	6.2507	-
MCF7-DOX	active	+			6.4196	+		
MCF7R	inactive	+			4.8545	+		
MX-1	inactive	+			6.4020	+		
T47D	active	+	inactive	+	6.0500	-	5.9412	+
ZR-75-1	inactive	+	active	+	5.6583	+	6.1069	+

Compound 6.



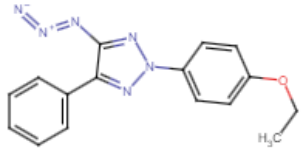
Name	Classification				Quantitative			
	IC50		GI50		pIC50		pGI50	
	Value	AD	Value	AD	Value	AD	Value	AD
Bcap37	inactive	+						
BT-20	inactive	+	active	+			5.9703	+
Hs-578T	inactive	+	inactive	+				
MCF7			inactive	+	5.5070	+	6.2507	-
MCF7-DOX	active	+			6.4022	+		
MCF7R	inactive	+			4.9256	+		
MX-1	active	+			6.4624	+		
T47D	active	+	inactive	+	6.0500	-	5.9418	+
ZR-75-1	inactive	+	active	+	5.6484	+	6.1006	+

Compound 7.



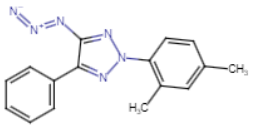
Name	Classification				Quantitative			
	IC50		GI50		pIC50		pGI50	
	Value	AD	Value	AD	Value	AD	Value	AD
Bcap37	inactive	+						
BT-20	inactive	+	active	+			5.9952	+
Hs-578T	inactive	+	inactive	+				
MCF7			inactive	+	5.3085	+	6.2757	-
MCF7-DOX	active	+			6.7138	+		
MCF7R	inactive	+			4.7861	+		
MX-1	inactive	+			6.3178	+		
T47D	active	+	inactive	+	6.1107	-	5.6363	+
ZR-75-1	inactive	+	inactive	+	5.5499	+	6.0879	+

Compound 8.



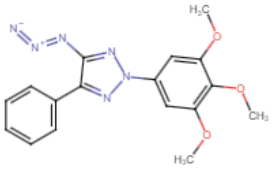
Name	Classification				Quantitative			
	IC50		GI50		pIC50		pGI50	
	Value	AD	Value	AD	Value	AD	Value	AD
Bcap37	inactive	+						
BT-20	inactive	+	inactive	+			5.5963	+
Hs-578T	inactive	+	inactive	+				
MCF7			inactive	+	5.6398	+	5.4338	-
MCF7-DOX	active	+			6.3075	+		
MCF7R	inactive	+			4.8911	+		
MX-1	active	+			6.3976	+		
T47D	inactive	+	inactive	+	4.8676	+	5.6135	-
ZR-75-1	inactive	+	active	+	5.2164	+	6.0087	+

Compound 9.



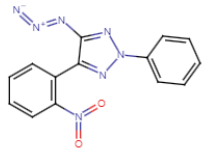
Name	Classification				Quantitative			
	IC50		GI50		pIC50		pGI50	
	Value	AD	Value	AD	Value	AD	Value	AD
Bcap37	inactive	+						
BT-20	inactive	+	inactive	+			5.9912	+
Hs-578T	active	+	inactive	+				
MCF7			inactive	+	5.0080	+	4.9746	-
MCF7-DOX	active	+			5.3292	+		
MCF7R	inactive	+			5.2518	+		
MX-1	active	+			6.1572	+		
T47D	inactive	+	inactive	+	4.5057	-	5.8261	+
ZR-75-1	inactive	+	active	+	5.0496	+	6.1415	+

Compound 10.



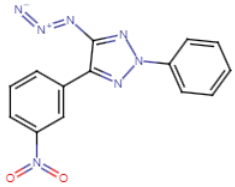
Name	Classification				Quantitative			
	IC50		GI50		pIC50		pGI50	
	Value	AD	Value	AD	Value	AD	Value	AD
Bcap37	inactive	+						
BT-20	active	+	active	+			6.3183	+
Hs-578T	inactive	+	inactive	+				
MCF7			active	+	5.8250	+	6.8005	+
MCF7-DOX	active	+			6.8244	+		
MCF7R	inactive	+			4.6538	+		
MX-1	inactive	+			6.1633	+		
T47D	active	+	inactive	+	6.1026	-	5.6990	+
ZR-75-1	active	+	active	+	6.6482	+	6.3588	+

Compound 11.



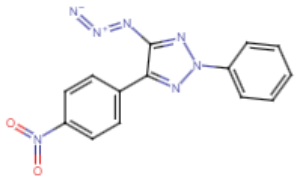
Name	Classification				Quantitative			
	IC50		GI50		pIC50		pGI50	
	Value	AD	Value	AD	Value	AD	Value	AD
Bcap37	inactive	+						
BT-20	inactive	+	active	+			6.2207	+
Hs-578T	active	+	inactive	+				
MCF7			inactive	+	5.1662	+	5.2478	+
MCF7-DOX	active	+			6.4288	+		
MCF7R	inactive	+			4.7763	+		
MX-1	inactive	+			6.0005	+		
T47D	inactive	+	inactive	+	4.5896	+	5.4902	-
ZR-75-1	inactive	+	inactive	+	5.5781	+	6.1252	+

Compound 12.



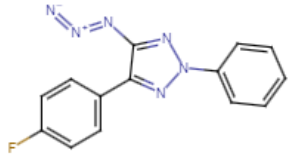
Name	Classification				Quantitative			
	IC50		GI50		pIC50		pGI50	
	Value	AD	Value	AD	Value	AD	Value	AD
Bcap37	inactive	+						
BT-20	inactive	+	inactive	+			6.1550	+
Hs-578T	inactive	+	inactive	+				
MCF7			inactive	+	5.1288	+	5.6546	+
MCF7-DOX	active	+			6.3353	+		
MCF7R	inactive	+			4.8929	+		
MX-1	inactive	+			5.7445	+		
T47D	inactive	+	inactive	+	4.7865	+	5.1345	+
ZR-75-1	inactive	+	inactive	+	5.4531	+	6.0962	+

Compound 13.



Name	Classification				Quantitative			
	IC50		GI50		pIC50		pGI50	
	Value	AD	Value	AD	Value	AD	Value	AD
Bcap37	inactive	+						
BT-20	inactive	+	active	+			6.1396	+
Hs-578T	inactive	+	inactive	+				
MCF7			inactive	+	5.2406	+	6.9216	-
MCF7-DOX	active	+			6.3209	+		
MCF7R	inactive	+			4.9164	+		
MX-1	inactive	+			5.6264	+		
T47D	inactive	+	inactive	+	4.0663	+	5.1241	+
ZR-75-1	inactive	+	inactive	+	5.4331	+	5.9508	+

Compound 14.



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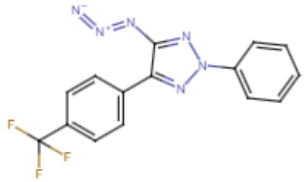
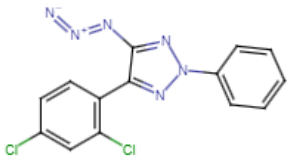
Name	Classification				Quantitative			
	IC50		GI50		pIC50		pGI50	
	Value	AD	Value	AD	Value	AD	Value	AD
Bcap37	inactive	+						
BT-20	inactive	+	inactive	+			5.8759	+
Hs-578T	inactive	+	inactive	+				
MCF7			inactive	+	4.9841	+	4.8302	+
MCF7-DOX	active	+			5.7338	+		
MCF7R	inactive	+			4.8619	+		
MX-1	inactive	+			5.6518	+		
T47D	inactive	+	inactive	+	4.2768	-	5.0390	+
ZR-75-1	inactive	+	inactive	+	5.2210	+	5.6898	+

Compound 15.



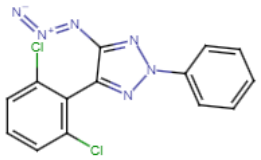
Name	Classification				Quantitative			
	IC50		GI50		pIC50		pGI50	
	Value	AD	Value	AD	Value	AD	Value	AD
Bcap37	inactive	+						
BT-20	inactive	+	inactive	+			5.6222	+
Hs-578T	inactive	+	inactive	+				
MCF7			inactive	+	5.1138	+	4.7792	+
MCF7-DOX	active	+			6.0962	+		
MCF7R	inactive	+			5.3437	+		
MX-1	inactive	+			5.8729	+		
T47D	inactive	+	inactive	+	4.0672	-	5.4837	+
ZR-75-1	inactive	+	inactive	+	4.9772	+	5.9722	+

Compound 16.



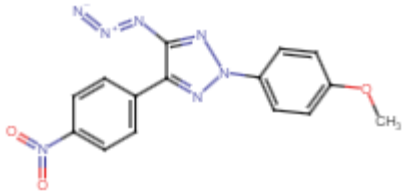
Name	Classification				Quantitative			
	IC50		GI50		pIC50		pGI50	
	Value	AD	Value	AD	Value	AD	Value	AD
Bcap37	inactive	+						
BT-20	inactive	+	inactive	+			5.9224	+
Hs-578T	inactive	+	inactive	+				
MCF7			inactive	+	4.9335	+	5.1165	+
MCF7-DOX	active	+			5.2480	+		
MCF7R	inactive	+			5.1699	+		
MX-1	inactive	+			5.5218	+		
T47D	inactive	+	inactive	+	4.4019	+	5.7115	+
ZR-75-1	inactive	+	active	+	5.1516	+	6.5194	+

Compound 17.



Name	Classification				Quantitative			
	IC50		GI50		pIC50		pGI50	
	Value	AD	Value	AD	Value	AD	Value	AD
Bcap37	inactive	+						
BT-20	inactive	+	inactive	+			5.9765	+
Hs-578T	inactive	+	inactive	+				
MCF7			inactive	+	4.9794	+	5.0126	+
MCF7-DOX	active	+			5.7766	+		
MCF7R	inactive	+			5.3127	+		
MX-1	inactive	+			5.8171	+		
T47D	inactive	+	inactive	+	4.2017	+	5.2984	+
ZR-75-1	inactive	+	active	+	5.2999	+	6.7043	+

Compound 18.



Name	Classification				Quantitative			
	IC50		GI50		pIC50		pGI50	
	Value	AD	Value	AD	Value	AD	Value	AD
Bcap37	inactive	+						
BT-20	inactive	+	active	+			5.9122	+
Hs-578T	inactive	+	inactive	+				
MCF7			inactive	+	5.6848	+	5.3030	+
MCF7-DOX	active	+			6.1779	+		
MCF7R	inactive	+			4.8348	+		
MX-1	inactive	+			5.8123	+		
T47D	inactive	+	active	+	4.6932	+	5.9683	-
ZR-75-1	active	+	inactive	+	5.9248	+	6.1242	+