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Ultrasonic-Assisted Synthesis of Pyrazolo[3,4-*d*]pyrimidin-4-ol Tethered with 1,2,3-Triazoles and Their Anticancer Activity

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Abstract—In the presents work synthesis and characterization of new heterocyclic derivatives containing pyrazolo[3,4-*d*]pyrimidine linkage with 1,4-disubstituted-1,2,3-triazoles via methylene-oxy group. The selected synthesized compounds were tested for their *in-vitro* anticancer activity against various cancer cell lines. Synthesis of compounds was done under ultrasonic-assisted Huisgen 1,3-dipolar cycloaddition reaction with good yields. Some of the newly synthesized compounds demonstrated good to moderate anticancer activity, most of compounds shows activity against renal cancer cell lines.

Keywords: pyrazolo[3,4-d]pyrimidin-4-ol,1,4-disubstituted-1,2,3-triazole derivatives, in-vitro anticancer screening, ultrasonic-assisted mild reaction conditions

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INTRODUCTION

Nitrogen-containing heterocyclic compounds are widely distributed in nature including amino acids, purines, pyrimidines and many other natural products. The purine is fused heterocyclic ring containing pyrimidine and imidazole ring, the chemical composition of purine is related to pyrazolopyrimidine. Pyrazolopyrimidine is a fused nitrogen containing heterocyclic ring system which considered as privileged core skeleton in the biologically active compounds and like a bioisostere of natural purine. Several pyrazolopyrimidine derivatives received great attention due to their biological and pharmacological activities [1–3]. In the current work on pyrazolo[3,4-*d*]pyrimidines are reported to encompass pharmacological potential as antiviral, [4] antimicrobial, [5, 6] antitumor [7–9], Parkinson's disease [10], skin cancer cell lines (G-361) [11], CNS cancer (SF-268) [12] and human leukemia (HL-60) [13]. Numerous compounds bearing this moiety are also well known for various therapeutic effects.

1,2,3-Triazole is a five-member heterocyclic ring contains three nitrogen and two carbon atoms. Mainly two isomeric forms of triazole have existed namely 1,2,3-triazole and 1,2,4-triazole. Generally disubstituted-1,2,3-triazole are further subdivided into two class, namely 1,4-disubstituted-1,2,3-triazoles and 1,5-disubstituted-1,2,3-triazoles. 1,5-Disubstituted triazoles have been synthesized using different catalysts and methos like RuAAC [14] and Nickel(II) [15]. 1,4-Disubstituted triazoles have been synthesized using Cu(I) catalysed click reaction. Previously many synthetic routes were reported for the synthesis of 1,4-disubstituted-1,2,3-triazole using cycloaddition reaction of 1,3-dipolar organic azide and terminal alkyne in the presence of Cu(I) catalyst [16–19].

Over the past few years, 1,4-disubstituted-1,2,3-triazoles have been an important class of compounds, due to their widely pharmacology activities and key intermediate in many industrial application such as agrochemical [20, 21], additives [22], pigment [23, 24], metal chelators [25], photostabilizers [26, 27] and corrosion inhibitors [28, 29]. The 1,2,3-triazole heterocycles are well-known privilege medicinal scaffolds because of their significant biological activity. A few examples are shown in Fig. 1, including antimicrobial [30–32], antiallergic [33], anti-HIV [34], antitubercular [35–37] and antitumor agents [38]. To the best of our knowledge and literature review, very few biological active hybrid molecules reported containing both pyrazolopyrimidine and 1,2,3-triazole skeleton (Fig. 2). Compound (**a**, **b**) are used as key intermediates in constructing the cross-linked deoxyoligonucleotides duplex [39]. 3,6-Dimethyl-1-phenyl-5-((1-aryl-1*H*-1,2,3-triazol-4-yl)-methyl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-4(5*H*)-ones (**c**) were reported for moderate anticancer activity against HCT-116, MCF-6 cell lines at 100 μM concentration and for 5-lipoxygenase inhibition activities [40]. 5-((1-(3-chlorophenyl)-1*H*-1,2,3-triazol-4-yl)methyl)-1-phenyl-1,5-dihydro-4*H*-pyrazolo[3,4-*d*]pyrimidin-4-one (**d**) were reported for their potent anticancer activity against C6 rat and U87 human glioma cell lines 10 μM concentration [41].

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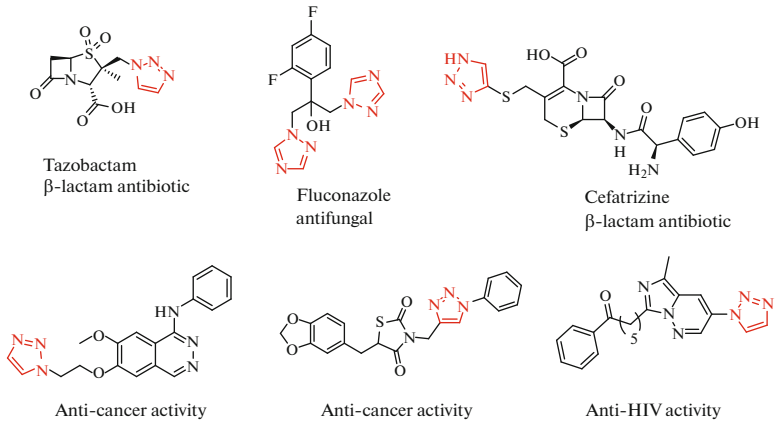


Fig. 1. Marketed drug and biologically active 1,2,3-triazole containing molecules.

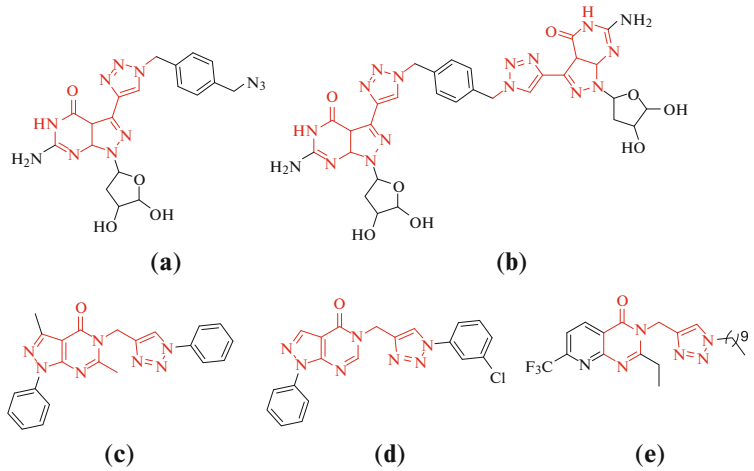


Fig. 2. Biologically active pyrazolopyrimidine and triazole containing hybrid compounds.

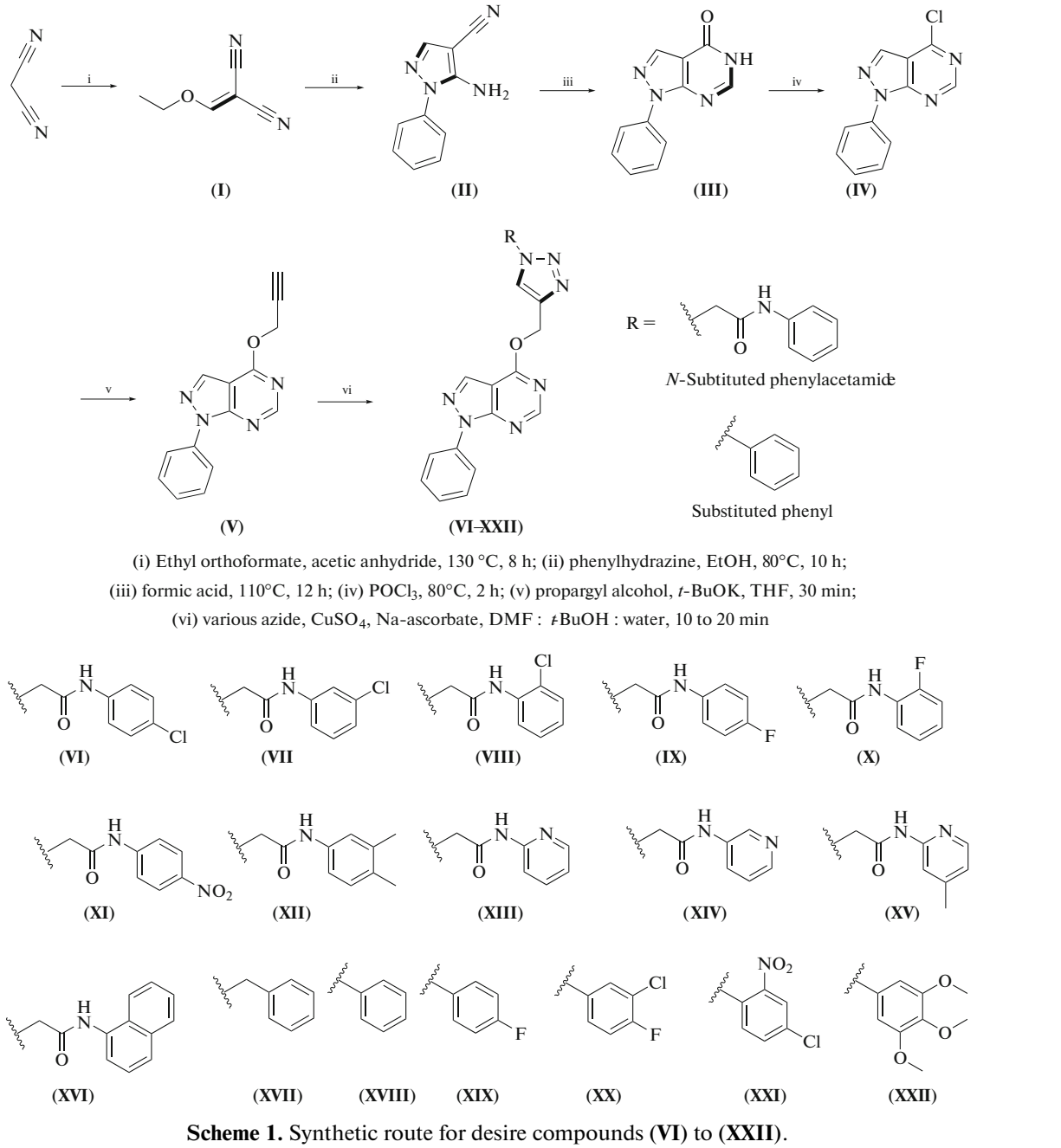
Compound (**e**) showed potent activity against pancreatic cancer cell lines (Fig. 2) [42].

Our efforts focused on the synthesize of biologically active new 1,2,3-triazole derivatives attached to pyrazolo[3,4-*d*]pyrimidine linkage with methyleneoxy ether. Based on all above-mentioned literature and extension of our studies on the development of new triazole derivatives, we have developed the ultrasonic-assisted mediated synthesis of new derivatives of 1,2,3-triazole containing pyrazolopyrimidine using 1,3-dipolar cycloaddition reaction of substituted azides and alkynes in the presence of Cu(I) catalysed, the synthesized compounds have been screening for their *in-vitro* anticancer activity against various types of cancer and their different cell lines.

RESULTS AND DISCUSSION

Chemistry

We have initially examined the synthesis of title compounds were carried out by both conventional and ultrasonic-assisted method, according to result it's clear that ultrasonic approach to be extremely fast, providing to excellent yield (82–94%) have been without further purification. The preparation of 2-(ethoxymethylene) malononitrile (**I**) according to previously reported reaction of malononitrile, triethyl orthoformate and acetic anhydride [43, 44], then Michael addition of phenylhydrazine on (**I**) to give 5-amino-1-phenyl-1*H*-pyrazole-4-carbonitrile (**II**) [44, 45]. The resulting aminocyanopyrazole (**II**) was given intermolecular condensation reaction through refluxing in formic acid to afford 1-phenyl-1,5-dihydro-4*H*-pyrazolo[3,4-*d*]pyrimidin-4-one (**III**) [45, 46], further pyrazolo[3,4-*d*]pyrimidin-4-one (**III**) was heated in phosphorus oxychloride to afforded 4-chloro-1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidine (**IV**) [45–47]. Resulting chloro pyrazolo[3,4-*d*]pyrimidine (**IV**) react with propargyl alcohol in the presence of potassium tert-butoxide to afforded 1-phenyl-4-(prop-2-yn-1-yloxy) -1*H*-pyrazolo[3,4-*d*]pyrimidine (**V**). The synthesis of desire triazole compounds using Copper(I)-catalyzed azide-alkyne cycloaddition (CuAAC) reaction of the terminal alkyne (**V**) react with various aromatic or aliphatic azide in the presence of Cu(I) to afforded desired triazole compounds (**VI–XXII**). The synthesized targeted compounds carried out as outlined in Scheme 1.



Scheme 1. Synthetic route for desire compounds **(VI)** to **(XXII)**.

Therefore, the protocol of the ultrasonic mediated reactions was reduced significant energy and fulfil the green chemistry approaches. Moreover, the ultrasonic reaction is faster, easier and more reliable compared to conventional methods, thus a variety of compounds were synthesized by these type of approaches, but only some reports are available for the click chemistry by using ultrasonic irradiation method in organic chemistry/drug discovery. Based on previously reported ultrasonic-assisted method is a great role in synthetic organic chemistry, so we are promoted to use this type of mild reaction conditions for the synthesis of desired compounds, which was prepared from cycloaddition reaction of azide and terminal alkyne in the presence of Cu(II) catalyst and Sodium ascorbate as a co-catalyst.

Some limited study performed in order to establish an effective and mild reaction conditions for the synthesis of compounds (**VI–XXII**). Initially, we perform reaction at conventional method in the presences of Cu(I) catalysed in various solvents or mixture of solvents, based on previously reported conventional method shown in Table 1 entry 1 to 7. In order to shorter reaction time as well as mild reaction conditions, the reaction performs under the ultrasonic irradiation using Digital ultrasonic cleaner to gave lower yield at first 5 to 10 minutes but good yield observed at

Table 1. Optimization of reaction conditions for the synthesis of compound **VI**

Entry	Solvent	Catalyst	Time, h	Yield, %
(I)	MeOH	$CuSO_4$, Na-ascorbate	12	37[a]
(II)	DMF : MeOH (1 : 1)	$CuSO_4$, Na-ascorbate	12	52[a]
(III)	DMF : *t*-BuOH (1 : 1)	$CuSO_4$, Na-ascorbate	8	65[a]
(IV)	**DMF : *t*-BuOH : Water (1 : 1 : 1)**	**$CuSO_4$, Na-ascorbate**	**6**	**84[a]**
(V)	DMF : Water (1 : 1)	$CuSO_4$, Na-ascorbate	8	62[a]
(VI)	BuOH : Water (1 : 1)	$CuSO_4$, Na-ascorbate	8	72[a]
(VII)	Water	$CuSO_4$, Na-ascorbate	12	18[a]
(VIII)	**DMF : *t*-BuOH : Water (1 : 1 : 1)**	**$CuSO_4$, Na-ascorbate**	**20 min**	**94[b]**
(IX)	DMF : *t*-BuOH : Water (1 : 1 : 1)	CuI (10%)	20 min	75[b]
(X)	DMF : *t*-BuOH : Water (1 : 1 : 1)	CuBr (10%)	30 min	67[b]

[a]Conventional method; [b]ultrasonic-assisted method at room temperature.

20 minutes shown in Table 1 entry 8 to 10. Based on all the above trial reaction, the model reaction conditions for preparation of targeted compounds using ultrasonic irradiation and DMF : *t*-BuOH : water (1 : 1 : 1) as a solvent (Table 1, entry 4 and 8) to achieve good yields, shorter reaction times and no required any purification.

All the newly synthesized compounds were characterized by using FT-IR, ^{1}H NMR, ^{13}C NMR and mass spectrometry analysis. In particular ^{1}H NMR spectrum of targeted compounds, we observed singlet peak at δ 10.101–11.125 ppm due to presence of aliphatic amide proton (–CONH) in compounds (**VI**) to (**XVI**), in the compound (**XI**) the –CONH peak moved in high deshilded region due to $-NO_2$ group and also shown one singlet peak in deshielded region for the –CH proton of triazole ring, in aliphatic azide (**VI**) to (**XVI**) shown at around δ 8.38 ppm, in aromatic azide (**XVIII**) to (**XXII**) the –CH peck move in deshilded region around δ 9.00 ppm. The aliphatic $-CH_2$ between triazole ring and amide bond is shown singlet at δ 5.364–5.594 ppm (**VI**) to (**XVI**), in compound **XVII** $-CH_2$ peck shightly move in deshilded region due to attched with phenyl ring. Another singlet of methylene-oxy $-CH_2$ observed at δ 5.376–5.847 ppm more deshielded due to directly attached with electronic withdrawing group. In ^{13}C NMR spectrum, show deshielded peak at δ 164 ppm for the presence of C=O bond in compounds (**VI**) to (**XVI**), the another peck in deshilded region at 162 ppm show C–O bond of pyrimidne ring.the fused aromatic carbon of pyrazolopyrimidine ring shown at δ103 ppm due to electronic rich. The both aliphatic $-CH_2$ carbon are shown around δ52–60 ppm. In deshilded region compound (**IX**), (**X**), (**XIX**) and (**XX**) shown doublet of C–F coupling. In the FT-IR spectral data, we observed sharp peak of N–H stretching value at 3250–3380 cm^{-1} in compounds (**VI**) to (**XVI**), C–H stretching of aliphatic CH_2 shown peak near 3080 cm^{-1} and C–H bending observed near 1360–1450 cm^{-1}. The C=O stretching of amide bond shown peak around 1600–1720 cm^{-1} in compounds (**VI**) to (**XVII**), in compound (**XVII**) C=O stretching shown at 1604 cm^{-1} due to presence of benzylic amine. In mass spectrometry we observed molecular ion peak with natural abundance and their related fragmentation pattern, in all mass spectrum data we observed most stable fragment of compounds cleavage from ether bond between triazole ring and pyrazolopyrimidine ring it's observed at *m/z* 211.9.

The spectral data and physical parameter of newly synthesized triazole derivatives (**VI**) to (**XXII**) are well-characterized with the assigned structure of compounds, ^{1}H and ^{13}C NMR, mass and FT-IR spectra of the compounds are given in supplementary material and are in good agreement with the proposed structure of the compounds.

BIOLOGICAL EVALUATION

In Vitro Anticancer Screening of the Synthesized Compounds

In previously reported studies of pyrazolo[3,4-*d*]pyrimidine link with triazole molecules, it gives promising anticancer activity (Fig. 2, compound **c** and **d**), in these compound presence of amide bond in pyrazolo[3,4-*d*]pyrimidin-4-one. Due to the fact that we have design hybrid pyrazolopyrimidine containing triazole molecules linked with methylene-oxy group and addition of aliphatic amide group to improve the biological activity. In our current in vitro anticancer primary screening studies, some compounds found as a moderated anticancer agent against different cancer cell lines. Primary in vitro anticancer screening, com-

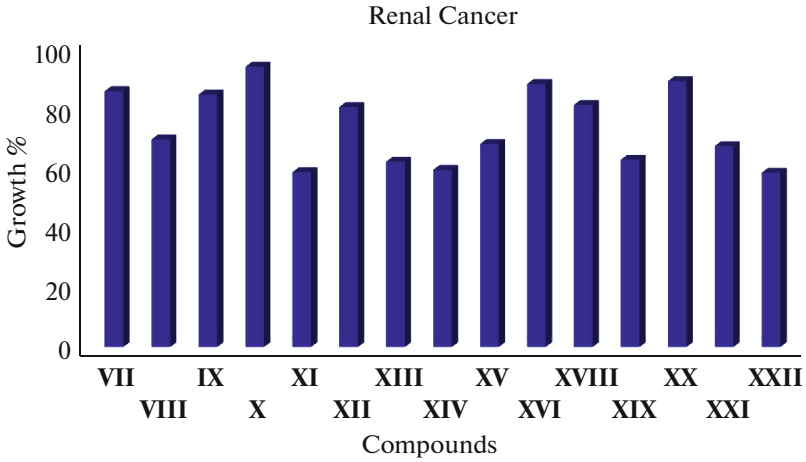


Fig. 3. In vitro anticancer screening data of synthesized compounds against renal cancer cell line.

pound (**XVIII**) give good activity against breast cancer (T-47D), (**XIV**) give moderate activity against Non-Small Cell Lung Cancer (HOP-92), Ovarian Cancer (OVCAR-8) and Renal Cancer (SN12C), (**XI**) and (**XXI**) give moderate activity against Renal Cancer (A498) and (**XXII**) also give moderate activity against Renal Cancer (UO-31). Pyrazolopyrimidine-triazole compounds give good activities against different type of cancer, these type hybrid compound given multiple action of mechanism, [48] based on literature plausible action of mechanism reported as mTOR inhibitors, [41] exhibiting antiproliferative effect against cells, inhibited cancer cell migration and induce cell cycle arrest at G1 phase [49]. Most of all synthesized compounds show moderate anticancer activity against renal cancer cell line, the graph of a renal cancer cell line are shown in Fig. 3. The compounds (**XI**), (**XIII**), (**XIV**), (**XIX**) and (**XXII**) give moderate activity and some compounds moderated active against more than one cancer cell line, some compounds are given less activity or non-active against 60-cell line. The mean graph plot of GI_{50} values are given in Table 2, and one-dose graph given in the supplementary material.

CONCLUSIONS

In a summary, the present work we developed a simple, rapid and effective synthesis of pyrazolopyrimidine triazole derivative from 1,3-dipolar cycloaddition reaction of alkyne with various aromatic and aliphatic azide using Cu(II) catalyst in the presence of Sodium ascorbate. The use of ultrasonic irradiation method effectively shorter reaction time and higher yield compared to the conventional method. In the in vitro anti-cancer screening, some compounds were given moderate to good anti-cancer activity against 60-human cell line and some compounds react as less active or non-active against cancer cell line.

EXPERIMENTAL

Materials and Methods

All purchased chemicals used without further purification. Reactions were monitored by thin-layer chromatography (TLC) on silica gel-G plates (G60 F254). Ultrasonic irradiation experiments were carried out in Digital ultrasonic cleaner (LMUC-12). Melting points were determined using an open capillary melting point apparatus. FT-IR data were recorded on a Shimadzu FT-IR-8400 instrument in cm^{-1} (KBr). NMR spectra were recorded on a Bruker Avance 400 MHz spectrometer (400 MHz for ^1H NMR and 101 MHz for ^{13}C NMR) in deuterated solvents like DMSO-d_6 and $CDCl_3$ with respect to tetramethylsilane as a standard. NMR data predated using MestReNova, ^1H NMR chemical shifts are designated using the following abbreviations as well as their combinations: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad signal, coupling constants in Hz. Mass spectra were recorded on a Shimadzu GC-MS-QP-2010 mass spectrometer in ESI (70 eV) model using direct inlet probe technique and m/z is reported in atomic units per elementary charge.

The selected synthesized compounds were evaluated for in vitro anti-cancer activity at National Cancer Institute (NCI) Bethesda, Maryland, USA. under the Development Therapeutic Program DTP. They evaluated for anti-cancer activity against 60 different human cell line of different type of cancer like Leukemia, Non-Small Cell Lung, Colon, CNS, Melanoma, Ovarian, Renal, Prostate and Breast cancer. In a primary screening of compounds tested only one dose against 60-cell lines at 10^{-5} M concentration and 75 μL volume. The one-dose data was reported as a mean graph of the percent growth of treated cells and the One-dose assay is growth relative to the no-drug control, and relative to the time zero number of cells. This

Table 2. In vitro anticancer screening of synthesized compounds

Entry	Yield, %	60 cell line assay in one dose at 1×10^{-5} M concentration		
		active cell lines	mean growth %	growth of most sensitive cell
(VI)	94	–	–	–
(VII)	87	Leukemia (MOLT-4)	95.17	–25.05
(VIII)	92	Renal Cancer (A498)	95.96	–29.83
(IX)	94	Leukemia (SR)	91.64	–31.12
(X)	82	Leukemia (RPMI-8226)	98.00	–13.33
(XI)	**85**	**Renal Cancer (A498)**	**91.92**	**–40.88**
(XII)	90	CNS Cancer (SNB–75)	89.09	–34.17
(XIII)	82	Renal Cancer (UO–31)	94.11	–37.33
(XIV)	**87**	**Non–Small Cell Lung Cancer (HOP-92)**		**–40.90**
		Ovarian Cancer (OVCAR-8)	**93.71**	–36.56
		Renal Cancer (SN12C)		**–40.10**
(XV)	84	Renal Cancer (UO-31)	91.84	–31.37
(XVI)	92	Ovarian Cancer (OVCAR-4)	94.35	–23.06
(XVII)	90	–	–	–
(XVIII)	**92**	**Breast Cancer (T-47D)**	**100.85**	**–73.56**
(XIX)	94	Renal Cancer (TK-10)	98.16	–36.64
(XX)	88	Non–Small Cell Lung Cancer (NCI-H522)	102.77	–27.39
(XXI)	84	Renal Cancer (A498)	99.66	–32.07
(XXII)	**85**	**Renal Cancer (UO-31)**	**90.73**	**–41.04**

allows the detection of both growth inhibition (values between 0 and 100) and lethality (values less than 0).

Synthesis procedure of 2-(ethoxymethylene) malononitrile (I). This compound synthesis to accourding literature [43, 44], yield 47.34%, mp 66–68°C, exact mass: 122.05.

Synthesis procedure of 5-amino-1-phenyl-1*H*-pyrazole-4-carbonitrile (II). This compound synthesis to accourding literature [44, 45], yield 87.53%, mp 132–134°C, exact mass: 184.07.

Synthesis procedure of 1-phenyl-1,5-dihydro-4*H*-pyrazolo[3,4-*d*]pyrimidin-4-one (III). This compound synthesis to accourding literature [45, 46], Yield 72.04%, mp > 250°C, exact mass: 212.07.

Synthesis procedure of 4-chloro-1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidine (IV). This compound synthesis to accourding literature [45–47], yield 93.31%, mp 134–136°C, exact mass: 230.04.

Synthesis procedure of 1-phenyl-4- (prop-2-yn-1-yloxy)-1*H*-pyrazolo[3,4-*d*]pyrimidine (V). To a solution of propargyl alcohol (2.33 g, 41.73 mmol) in 50 mL dry THF under nitrogen atmosphere and stirred solution under cooling. Then after added portion-wise potassium tert-butoxide (5.07 g, 45.21 mmol) and the resulting reaction mixture was stirred for 20 minutes at same temperature. Then after solution of 4-chloro-1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidine (**IV**) (8.0 g, 34.78 mmol) in dry THF was added drop wise and after addition the reaction mixture was stirred for 30 minutes room temperature. The reaction monitored by TLC, after completion of the reaction solvent remove under reduced pressure, then after water was added and product was extract using pet. ether, combine organic layer and dry using sodium sulphate, solvent remove under reduced pressure to afford light yellow colour solid product (7.8 g, yield 89.66%, mp 82–86°C, exact mass: 250.09).

General synthetic process for substituted 2-chloro-*N*-phenylacetamide derivatives. To a solution of various aniline (1.0 equiv) in acetone were added chloroacetyl chloride (1.1 equiv) and reaction mixture stirred at room temperature for 2–3 h, reaction was monitored by TLC, after completion of reaction mixture poured in cold water, the separated solid product collected and washed with cold water and dry in vacuum filter to afford 2-chloro-*N*-phenylacetamide derivatives.

General synthetic process for substituted 2-azido-*N*-phenylacetamide derivatives. To a solution of 2-chloro-*N*-phenylacetamide derivatives (1.0 equiv) in DMF were added sodium azide (3.0 equiv) and reaction mixture stirred at room temperature for 10–12 h, reaction was monitored by TLC, after complication of reaction mixture poured in cold water, the separated solid collected and washed with cold water and dry in vacuum filter to afford 2-azido-*N*-phenylacetamide derivatives.

General synthetic process for substituted Azidobenzene derivatives. Take a RBF and charge with various aniline derivatives (1.0 equiv) dissolved in 6 N HCl solution and stir for 15 minutes were drop wise added solution of sodium nitrite (1.5 equiv) at 0–5°C temperature and reaction mixture stirred for 45 minutes at same temperature. Then solution of sodium azide (1.5 equiv) was added under cooling and reaction mixture stirred at room temperature for 4–6 h. Reaction monitor by TLC, after completion of reaction mixture was poured in water and extract with ethyl acetate. The organic layer combine and dry over sodium sulphate and solvent remove under reduce pressure to afford azidobenzene derivatives.

General synthetic procedure for *N*-substituted aryl-2-(4-(((1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-yl)oxy)methyl)-1*H*-1,2,3-triazole-1-yl) acetamides (VI to XVI). To an equimolar mixture of 1-phenyl-4-(prop-2-yn-1-yloxy)-1*H*-pyrazolo[3,4-*d*]pyrimidine (**V**) and substituted 2-azido-*N*-arylacetamide in RBF were added DMF : *t*-BuOH : H_2O (1 : 1 : 1) and catalytic amount of sodium ascorbate and aqueous copper sulphate solution, resulting reaction mixture was placed in ultrasonic for 15 to 25, the reaction was monitor by TLC. After completion of the reaction, the reaction mixture poured in cold water, collected the separated solid and washed with ammonium chloride solution to remove copper than after further washed with water and small amount of methanol and dry over vacuum, to afford (**VI**) to (**XVI**) (yield 82–94%).

***N*-(4-Chlorophenyl)-2-(4-(((1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-yl)oxy)methyl)-1*H*-1,2,3-triazol-1-yl) acetamide (VI).** Yield: 94%, Tan solid, mp: 204–206°C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ 10.66 (1H, s, H29 –CONH), 8.80 (1H, s, H10 pyrimidine), 8.56 (1H, s, H13 pyrazole), 8.38 (1H, s, H19 triazole), 8.20 (2H, d, J = 8.0 Hz, Ar–H), 7.61 (4H, t, J = 7.7 Hz, Ar–H), 7.47–7.36 (3H, m, Ar–H), 5.78 (2H, s, H22 $-OCH_2$), 5.39 (2H, s, H32 $-COCH_2$). ^{13}C NMR (101 MHz, DMSO) δ 164.35 (C30 C=O), 162.80 (C12 C–O), 155.83 (C8), 154.22 (C10), 141.33, 138.31, 137.32, 133.12, 129.32, 128.84, 127.33, 127.16, 126.85, 121.00, 120.72, 103.50 (C7), 59.89 (C22 $-OCH_2$), 52.17 (C32 $-CH_2$). FT-IR data (ν, cm^{-1}): 3255.95, 3093.92, 2955.04, 1674.27, 1604.83, 1550.82, 1496.81, 1435.09, 1319.35, 1242.2, 1172.76, 1095.6, 1057.03, 979.87, 895, 825.56, 748.41, 686.68, 648.1, 563.23, 501.51, 424.35. Mass (*m*/*z*): exact mass: 460.12, found mass: 459.70.

***N*-(3-Chlorophenyl)-2-(4-(((1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-yl) oxy) methyl)-1*H*-1,2,3-triazol-1-yl) acetamide (VII).** Yield: 87%, Brown solid, mp: 194–196°C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ 10.72 (1H, s, H29 –CONH), 8.81 (1H, s, H10 pyrimidine), 8.56 (1H, s, H13 pyrazole), 8.38 (1H, s, H19 triazole), 8.24–8.15 (2H, m, Ar–H), 7.78 (1H, t, J = 2.1 Hz, Ar–H), 7.66–7.56 (2H, m, Ar–H), 7.52–7.33 (3H, m, Ar–H), 7.16 (1H, dd, J = 8.1 Hz, 2.2 Hz, Ar–H), 5.78 (2H, s, C22 $-OCH_2$), 5.40 (2H, s, H32 $-COCH_2$). ^{13}C NMR (101 MHz, DMSO) δ 164.63 (C30 C=O), 162.81 (C12 C–O), 155.84 (C8), 154.23 (C10), 141.35, 139.77, 138.31, 133.16, 133.12, 130.67, 129.33, 127.17, 126.86, 123.51, 121.01, 118.66, 117.59, 103.50 (C7), 59.89 (C22 $-OCH_2$), 52.18 (C32 $-CH_2$) FT-IR data (ν, cm^{-1}): 3309.96, 3093.92, 2955.04, 1681.98, 1597.11, 1550.82, 1435.09, 1357.93, 1319.35, 1234.48, 1172.76, 1095.6, 979.87, 895, 786.98, 756.12, 686.68, 632.67, 547.8, 439.78. Mass (*m*/*z*): exact mass: 460.12, found mass: 459.70.

***N*-(2-Chlorophenyl)-2-(4-(((1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-yl) oxy) methyl)-1*H*-1,2,3-triazol-1-yl)acetamide (VIII).** Yield: 92%, Off-white solid, mp: 162–164°C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ 10.10 (1H, s, H29 –CONH), 8.80 (1H, s, H10 pyrimidine), 8.54 (1H, s, H13 pyrazole), 8.38 (1H, s, H19 triazole), 8.19 (2H, d, J = 88.0 Hz, Ar–H), 7.74 (1H, d, J = 8.0 Hz, Ar–H), 7.60 (2H, t, J = 7.7 Hz, Ar–H), 7.53 (1H, d, J = 7.9 Hz, Ar–H), 7.41 (1H, t, J = 7.4 Hz, Ar–H), 7.35 (1H, t, J = 7.6 Hz, Ar–H), 7.23 (1H, t, J = 7.8 Hz, Ar–H), 5.78 (2H, s, H22 $-OCH_2$), 5.49 (2H, s, H32 $-COCH_2$). ^{13}C NMR (101 MHz, DMSO) δ 164.84 (C32 C=O), 162.80 (C12 C–O), 155.83 (C8), 154.22 (C10), 141.34, 138.31, 134.09, 133.12, 129.62, 129.32, 127.55, 127.21, 126.85, 126.74, 126.26, 125.89, 121.00, 103.50 (C7), 59.89 (C22 $-OCH_2$), 51.92 (C32 $-CH_2$). FT-IR data (ν, cm^{-1}): 3255.95, 3086.21, 1921.16, 1689.7, 1604.83, 1550.82, 1442.8, 1311.64, 1226.77, 1165.04, 1103.32, 1057.03, 979.87, 887.28, 748.41, 648.1, 563.23, 455.22. Mass (*m*/*z*): exact mass: 460.12, found mass: 459.80.

***N*-(4-Fluorophenyl)-2-(4-(((1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-yl)oxy)methyl)-1*H*-1,2,3-triazol-1-yl) acetamide (IX).** Yield: 94%, Tan solid, mp: 194–196°C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ 10.59 (1H, s, H29 –CONH), 8.81 (1H, s, H10 pyrimidine), 8.56 (1H, s, H13 pyrazole), 8.38 (1H, s, H19 triazole), 8.24–8.15 (2H, m, Ar–H), 7.66–7.56 (4H, m, Ar–H), 7.42 (1H, t, J = 7.4 Hz, Ar–H), 7.19 (2H, t, J = 8.9 Hz, Ar–H), 5.78 (2H, s, H22 $-OCH_2$), 5.38 (2H, s, H32 $-COCH_2$). ^{13}C NMR (101 MHz, DMSO) δ 164.09 (C30 C=O), 162.81 (C12 C–O), 159.39 (C28 C–F), 157.01 (C28 C–F), 155.84 (C8), 154.23 (C10), 141.31, 138.31, 134.77, 134.74, 133.13, 129.33, 127.16, 126.86, 121.01, 120.93, 115.63, 115.41, 103.50 (C7), 59.90 (C22 $-OCH_2$), 52.12 (C32 $-CH_2$). FT-IR data (ν, cm^{-1}): 3263.66, 3093.92, 2955.04, 1674.27, 1604.83, 1550.82, 1512.24, 1435.09, 1319.35, 1226.77, 1165.04, 1095.6, 1057.03, 979.87, 895, 840.99, 786.98, 756.12, 686.68, 563.23, 516.94. Mass (*m*/*z*): exact mass: 444.15, found mass: 443.70.

***N*-(2-Fluorophenyl)-2-(4-(((1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-yl) oxy) methyl)-1*H*-1,2,3-triazol-1-yl)acetamide (X).** Yield: 82%, Tan solid, M.P.: 188–190°C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ 10.38 (1H, s, H29 –CONH), 8.80 (1H, s, H10 pyrimidine),

8.56 (1H, s, H13 pyrazole), 8.39 (1H, s, H19 triazole), 8.19 (2H, d, J = 8.0 Hz, Ar–H), 7.91 (1H, td, J = 4.8, 4.3, 2.2 Hz, Ar–H), 7.60 (2H, t, J = 7.9 Hz, Ar–H), 7.42 (1H, t, J = 7.4 Hz, Ar–H), 7.36–7.25 (1H, m, Ar–H), 7.25–7.13 (1H, m, Ar–H), 5.78 (2H, s, H22 $-OCH_2$), 5.48 (2H, s, H32 $-COCH_2$). ^{13}C NMR (101 MHz, DMSO) δ 164.77 (C30 C=O), 162.80 (C12 C–O), 155.83 (C8), 154.64 (C24 C–F), 154.22 (C10), 152.20 (C24 C–F), 141.32, 138.31, 133.12, 129.32, 127.20, 126.84, 125.73, 125.65, 125.46, 125.34, 124.48, 123.73, 120.99, 115.70, 115.51, 103.49 (C7), 59.89 (C22 $-OCH_2$), 51.97 (C32 $-CH_2$). FT-IR data (ν, cm^{-1}): 3255.95, 3086.21, 1928.88, 1674.27, 1604.83, 1550.82, 1496.81, 1435.09, 1357.93, 1327.07, 1219.05, 1172.76, 1095.6, 1057.03, 972.16, 941.29, 887.28, 794.7, 756.12, 686.68, 578.66, 462.93. Mass (m/z): exact mass: 444.15, found mass: 443.80.

***N*-(4-Nitrophenyl)-2-(4-(((1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-yl) oxy)methyl)-1*H*-1,2,3-triazol-1-yl)acetamide (XI).** Yield: 85%, White solid, mp: 206–208°C; ^1H NMR (DMSO-d_6, 400 MHz) δ 11.12 (1H, s, H29 –CONH), 8.81 (1H, s, H10 pyrimidine), 8.56 (1H, s, H13 pyrazole), 8.40 (1H, s, H19 triazole) 8.26 (2H, d, J = 8.8 Hz, Ar–H), 8.20 (2H, d, J = 8.0 Hz, Ar–H), 7.84 (2H, d, J = 8.8 Hz, Ar–H), 7.61 (2H, t, J = 7.8 Hz, Ar–H), 7.42 (1H, t, J = 7.4 Hz, Ar–H), 5.79 (2H, s, H22 $-OCH_2$), 5.48 (2H, s, C32 $-COCH_2$). FT-IR data (ν, cm^{-1}): 3309.96, 3101.64, 1913.45, 1720.56, 1604.83, 1558.54, 1504.53, 1442.8, 1342.5, 1257.63, 1172.76, 1103.32, 979.87, 848.71, 756.12, 686.68, 640.39, 493.79. Mass (m/z): exact mass: 471.14, found mass: 470.90.

***N*-(3,4-Dimethylphenyl)-2-(4-(((1-phenyl-1*H*-pyrazolo[3,4-*d*]Pyrimidin-4-yl)oxy)methyl)-1*H*-1,2,3-triazol-1-yl)acetamide (XII).** Yield: 90%, Brown solid, mp: 166–168°C; ^1H NMR (DMSO-d_6, 400 MHz) δ 10.46 (1H, s, H29 –CONH), 8.80 (1H, s, H10 pyrimidine), 8.56 (1H, s, H13 pyrazole), 8.38 (1H, s, H19 triazole), 8.20 (2H, d, J = 8.0 Hz, Ar–H), 7.60 (2H, t, J = 7.8 Hz, Ar–H), 7.47–7.35 (2H, m, Ar–H), 7.31 (1H, dd, J = 8.1, 2.3 Hz, Ar–H), 7.07 (1H, d, J = 8.2 Hz, Ar–H), 5.78 (2H, s, H22 $-OCH_2$), 5.36 (2H, s, H32 $-COCH_2$), 2.17 (6H, d, J = 7.4 Hz, H33 H34 $-CH_3$). FT-IR data (ν, cm^{-1}): 3309.96, 3093.92, 1681.98, 1604.83, 1550.82, 1504.53, 1435.09, 1357.93, 1319.35, 1226.77, 1165.04, 1103.32, 1057.03, 972.16, 887.28, 817.85, 756.12, 632.67, 547.8, 501.51, 439.78. Mass (m/z): exact mass: 454.19, found mass: 454.

2-(4-(((1-Phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-yl)oxy)methyl)-1*H*-1,2,3-triazol-1-yl)-*N*-(pyridin-2-yl)acetamide (XIII). Yield: 82%, White solid, mp: 162–164°C; ^1H NMR (DMSO-d_6, 400 MHz) δ 11.07 (1H, s, H29 –CONH), 8.80 (1H, s, H10 pyrimidine), 8.55 (1H, s, H13 pyrazole), 8.40 (1H, s, H19 triazole), 8.38–8.35 (1H, m, Ar–H), 8.24–8.15 (2H, m, Ar–H), 8.01 (1H, d, J = 8.3 Hz, Ar–H), 7.81 (1H, td, J = 7.9, 2.0 Hz, Ar–H), 7.60 (2H, t, J = 7.9 Hz, Ar–H), 7.41 (1H, t, J = 7.4 Hz, Ar–H), 7.15 (1H, dd, J = 7.4, 4.8 Hz, Ar–H), 5.78 (2H, s, H22 $-OCH_2$), 5.48 (2H, s, H32 $-COCH_2$). FT-IR data (ν, cm^{-1}): 3302.24, 3140.22, 3047.63, 1689.7, 1597.11, 1550.82, 1435.09, 1303.92, 1234.48, 1165.04, 1095.6, 1057.03, 979.87, 895, 779.27, 686.68, 648.1, 563.23, 509.22. Mass (m/z): exact mass: 427.15, found mass: 426.90.

2-(4-(((1-Phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-yl)oxy)methyl)-1*H*-1,2,3-triazol-1-yl)-*N*-(pyridin-3-yl)acetamide (XIV). Yield: 87%, White solid, mp: 168–170°C; ^1H NMR (DMSO-d_6, 400 MHz) δ 10.78 (1H, s, H29 –CONH), 8.81 (1H, s, H10 pyrimidine), 8.56 (1H, s, H13 pyrazole), 8.40 (1H, s, H19 triazole), 8.24–8.15 (2H, m, Ar–H), 8.03 (1H, d, J = 8.3 Hz, Ar–H), 7.66–7.55 (2H, m, Ar–H), 7.42 (2H, t, J = 7.4 Hz, Ar–H), 5.79 (2H, s, H22 $-OCH_2$), 5.44 (2H, s, H32 $-COCH_2$). FT-IR data (ν, cm^{-1}): 3379.4, 3255.95, 3063.06, 3009.05, 2283.79, 1936.6, 1890.3, 1705.13, 1604.83, 1489.1, 1427.37, 1319.35, 1226.77, 1157.33, 1095.6, 979.87, 895, 794.7, 756.12, 694.4, 648.1, 563.23, 509.22. Mass (m/z): exact mass: 427.15, found mass: 426.90.

***N*-(4-Methylpyridin-2-yl)-2-(4-(((1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-yl)oxy)methyl)-1*H*-1,2,3-triazol-1-yl)acetamide (XV).** Yield: 84%, White solid, mp: 180–182°C; ^1H NMR (DMSO-d_6, 400 MHz) δ 10.97 (1H, s, H29 –CONH), 8.81 (1H, s, H10 pyrimidine), 8.57 (1H, s, H13 pyrazole), 8.38 (1H, s, H19 triazole), 8.25–8.16 (3H, m, Ar–H), 7.87 (1H, s, Ar–H), 7.61 (2H, t, J = 7.9 Hz, Ar–H), 7.42 (1H, t, J = 7.4 Hz, Ar–H), 7.00 (1H, d, J = 5.2 Hz, Ar–H), 5.79 (2H, s, H22 $-OCH_2$), 5.45 (2H, s, H32 $-COCH_2$), 2.30 (3H, s, H33 $-CH_3$). FT-IR data (ν, cm^{-1}): 3302.24, 3147.93, 3070.78, 2962.76, 1890.3, 1681.98, 1604.83, 1558.54, 1504.53, 1458.23, 1419.66, 1350.22, 1319.35, 1211.34, 1165.04, 1095.6, 1049.31, 979.87, 887.28, 825.56, 756.12, 725.26, 686.68, 648.1, 601.81, 447.5. Mass (m/z): exact mass: 441.17, found mass: 440.90.

***N*-(Naphthalen-1-yl)-2-(4-(((1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-yl)oxy)methyl)-1*H*-1,2,3-triazol-1-yl)acetamide (XVI).** Yield: 92%, Light pink solid, mp: 198–200°C; ^1H NMR (DMSO-d_6, 400 MHz) δ 10.48 (1H, s, H29 –CONH), 8.81 (1H, s, H10 pyrimidine), 8.56 (1H, s, H13 pyrazole), 8.44 (1H, s, H19 triazole), 8.19 (3H, t, J = 8.8 Hz, Ar–H), 7.97 (1H, d, J = 7.7 Hz, Ar–H), 7.81 (1H, d, J = 8.2 Hz, Ar–H), 7.73 (1H, d, J = 7.5 Hz, Ar–H), 7.56 (5H, dq, J = 30.5, 7.9 Hz, Ar–H), 7.42 (1H, t, J = 7.5 Hz, Ar–H), 5.80 (2H, s, H22 $-OCH_2$), 5.59 (2H, s, H38 $-COCH_2$). FT-IR data (ν, cm^{-1}): 3471.98, 3279.1, 3086.21, 2955.04, 1928.88, 1674.27, 1604.83, 1550.82, 1504.53, 1435.09, 1319.35, 1219.05, 1165.04, 1095.6, 1057.03, 979.87, 887.28, 848.71, 786.98, 686.68, 578.66, 509.22. Mass (m/z): exact mass: 476.17, found mass: 475.80.

General synthetic procedure for 1-substituted aryl-4-((1-various substituted aryl-1*H*-1,2,3-triazol-4-yl) methoxy)-1*H*-pyrazolo[3,4-*d*]pyrimidines (XVII to XXII). To a 1-phenyl-4-(prop-2-yn-1-yloxy)-1*H*-pyrazolo[3,4-*d*]pyrimidine (5) (1.0 eq) and various azidoaryl (1.1 eq) in RBF were added DMF : *t*-BuOH : H_2O (1 : 1 : 1) and catalytic amount of Sodium ascorbate and aqueous copper sulphate solution, resulting reaction mixture was placed in ultrasonic for 10 to 15 minutes, the reaction was monitor by TLC. After completion of the reaction mixture poured in cold water, the separated solid collected and washed with ammonium chloride solution to remove copper than after further washed with water and small amount of methanol and dry over vacuum, to afford **XVII** to **XXII** (yield 84–94%).

***N*-Benzyl-2-(4-(((1-phenyl-1*H*-pyrazolo[3,4-*d*]-pyrimidin-4-yl)oxy)methyl)-1*H*-1,2,3-triazol-1-yl) acetamide (XVII).** Yield: 90%, Brown solid, mp: 122–124°C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ 8.78 (1H, s, H10 pyrimidine), 8.53 (1H, s, H13 pyrazole), 8.42 (1H, s, H19 triazole), 8.19 (2H, d, J = 8.0 Hz, Ar-H), 7.60 (2H, t, J = 7.8 Hz, Ar–H), 7.46–7.30 (5H, m, Ar–H), 7.23 (1H, s, Ar–H), 5.73 (2H, s, H22 $-OCH_2$), 5.64 (2H, s, C29 $-CH_2$). FT-IR data (ν, cm^{-1}): 3117.07, 3039.91, 2816.16, 1805.43, 1751.42, 1604.83, 1558.54, 1496.81, 1458.23, 1427.37, 1342.5, 1226.77, 1172.76, 1095.6, 1049.31, 979.87, 887.28, 840.99, 794.7, 756.12, 709.83, 655.82, 555.52, 486.08. Mass (*m*/*z*): exact mass: 483.15, found mass: 483.00.

1-Phenyl-4-((1-phenyl-1*H*-1,2,3-triazol-4-yl) methoxy)-1*H*-pyrazolo[3,4-*d*]pyrimidine (XVIII). Yield: 92%, White solid, mp: 122–124°C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ 9.04 (1H, s, H19 triazole), 8.81 (1H, s, H10 pyrimidine), 8.57 (1H, s, H13 pyrazole), 8.24–8.13 (2H, m, Ar–H), 7.98–7.90 (2H, m, Ar–H), 7.67–7.56 (4H, m, Ar–H), 7.52 (1H, t, J = 7.4 Hz, Ar–H), 7.42 (1H, t, J = 7.4 Hz, Ar–H), 5.85 (2H, s, H22 $-OCH_2$). ^{13}C NMR (101 MHz, DMSO) δ 162.71 (C12 C–O), 155.85 (C8), 154.23 (C10), 142.83, 138.30, 136.46, 133.14, 129.89, 129.31, 128.84, 126.83, 123.61, 120.96, 120.23, 103.53 (C7), 59.78 (C22 $-CH_2$). FT-IR data (ν, cm^{-1}): 3132.5, 3086.21, 2962.76, 1959.74, 1898.02, 1805.43, 1597.11, 1558.54, 1504.53, 1435.09, 1350.22, 1319.35, 1234.48, 1165.04, 1095.6, 1049.31, 979.87, 902.72, 848.71, 763.84, 686.68, 632.67, 547.8, 516.94. Mass (*m*/*z*): exact mass: 369.13, found mass: 368.80.

4-((1-(4-Fluorophenyl)-1*H*-1,2,3-triazol-4-yl) methoxy)-1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidine (XIX). Yield: 94%, Gray solid, mp: 136–138°C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ 9.01 (1H, s, H19 triazole), 8.81 (1H, s, H10 pyrimidine), 8.57 (1H, s, H13 triazole), 8.23–8.16 (2H, m, Ar–H), 8.03–7.93 (2H, m, Ar–H), 7.65–7.56 (2H, m, Ar–H), 7.53–7.44 (2H, m, Ar–H), 7.46–7.37 (1H, m, Ar–H), 5.84 (2H, s, H22 $-OCH_2$). ^{13}C NMR (101 MHz, DMSO) δ 162.93 (C28 C–F), 162.70 (C12 C–O), 160.48 (C28 C–F), 155.85 (C8), 154.24 (C10), 142.84, 138.30, 133.13, 133.04, 133.01, 129.32, 126.84, 123.83, 122.67, 122.58, 120.96, 116.85, 116.62, 103.52 (C7), 59.75 (C22 $-OCH_2$). FT-IR data (ν, cm^{-1}): 3124.79, 3078.49, 2962.76, 1898.02, 1604.83, 1558.54, 1512.24, 1450.52, 1357.93, 1234.48, 1165.04, 1103.32, 1049.31, 987.59, 902.72, 833.28, 786.98, 756.12, 686.68, 648.1, 601.81, 532.37, 493.79. Mass (*m*/*z*): exact mass: 483.12, found mass: 486.70.

4-((1-(3-Chloro-4-fluorophenyl)-1*H*-1,2,3-triazol-4-yl)methoxy)-1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidine (XX). Yield: 88%, White solid, mp: 152–154°C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ 9.06 (1H, s, H19 triazole), 8.81 (1H, s, H10 pyrimidine), 8.56 (1H, s, H13 pyrazole), 8.25 (1H, dd, J = 6.4, 2.7 Hz, Ar–H), 8.23–8.15 (2H, m, Ar–H), 8.00 (1H, m, Ar–H), 7.70 (1H, t, J = 9.0 Hz, Ar–H), 7.66–7.56 (2H, m, Ar–H), 7.47–7.37 (1H, m, Ar–H), 5.85 (2H, s, H22 $-OCH_2$). ^{13}C NMR (101 MHz, DMSO) δ 162.67 (C12 C–O), 158.16 (C28 C–F), 155.85 (C8), 155.70 (C28 C–F), 154.24 (C10), 143.03, 138.30, 133.47, 133.43, 133.11, 129.32, 126.86, 123.92, 122.55, 121.13, 121.05, 120.96, 120.84, 120.65, 118.24, 118.02, 103.52 (C7), 59.68 (C22 $-CH_2$). FT-IR data (ν, cm^{-1}): 3433.41, 3155.65, 3109.35, 2114.05, 1874.87, 1604.83, 1558.54, 1504.53, 1458.23, 1427.37, 1388.79, 1327.07, 1242.2, 1172.76, 1095.6, 1018.45, 979.87, 941.29, 879.57, 825.56, 756.12, 717.54, 686.68, 648.1, 501.51. Mass (*m*/*z*): exact mass: 421.09, found mass: 420.70.

4-((1-(4-Chloro-2-nitrophenyl)-1*H*-1,2,3-triazol-4-yl)methoxy)-1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidine (XXI). Yield: 82%, White solid, mp: 172–174°C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ 8.95 (1H, s, H19 triazole), 8.80 (1H, s, H10 pyrimidine), 8.57 (1H, s, H13 pyrazole), 8.43 (1H, d, J = 2.3 Hz, Ar–H), 8.20 (2H, d, J = 8.0 Hz, Ar–H), 8.09 (1H, dd, J = 8.6, 2.4 Hz, Ar–H), 7.98 (1H, d, J = 8.6 Hz, Ar–H), 7.61 (2H, t, J = 7.8 Hz, Ar–H), 7.42 (1H, t, J = 7.4 Hz, Ar–H), 5.87 (2H, s, H22 $-OCH_2$). FT-IR data (ν, cm^{-1}): 3441.12, 3109.35, 1735.99, 1651.12, 1604.83, 1550.82, 1504.53, 1442.8, 1357.93, 1319.35, 1249.91, 1165.04, 1111.03, 1033.88, 995.3, 902.72, 840.99, 794.7, 763.84, 694.4, 640.39, 547.8, 516.94, 447.5. Mass (*m*/*z*): exact mass: 448.07, found mass: 447.70.

1-Phenyl-4-((1-(3,4,5-trimethoxyphenyl)-1*H*-1,2,3-triazol-4-yl)methoxy)-1*H*-pyrazolo[3,4-*d*]pyrimidine (XXII). Yield: 85%, White solid, M.P.: 146–148°C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ 9.05 (1H, s, H19 triazole), 8.82 (1H, s, H10 pyrimidine), 8.57 (1H, s, H13 pyrazole), 8.24–8.16 (2H, m, Ar–H), 7.61 (2H, dd, J = 8.6, 7.4 Hz, Ar–H), 7.47–7.38 (1H, m, Ar–H), 7.24 (2H, s, Ar–H), 5.85 (2H, s, H22 $-OCH_2$), 3.89 (6H, s, C32, C34 $-CH_3$), 3.72 (3H, s, C33 $-CH_3$). FT-IR data (ν, cm^{-1}): 3456.55, 3109.35, 2831.6, 2106.34, 1998.32, 1928.88, 1597.11, 1504.53, 1450.52, 1350.22, 1288.49, 1234.48, 1165.04, 1126.47,

1041.6, 1003.02, 902.72, 864.14, 771.55, 694.4, 640.39, 524.66. Mass (m/z): exact mass: 459.17, found mass: 459.00.

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COMPLIANCE WITH ETHICAL STANDARDS

This article does not contain any studies involving human participants performed by any of the authors and does not contain any studies involving animals performed by any of the authors.

Conflict of Interests

The authors declare that they have no conflicts of interest.

SUPPLEMENTARY MATERIALS

In a supplementry material we cover ^{1}H NMR spectra, ^{13}C NMR spectra mass spectra, FT-IR spectra, one-dose graph of anticancer activity.

Supplementary materials are available for this article at https://doi.org/10.1134/S1068162020050106 and are accessible for authorized users.

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