

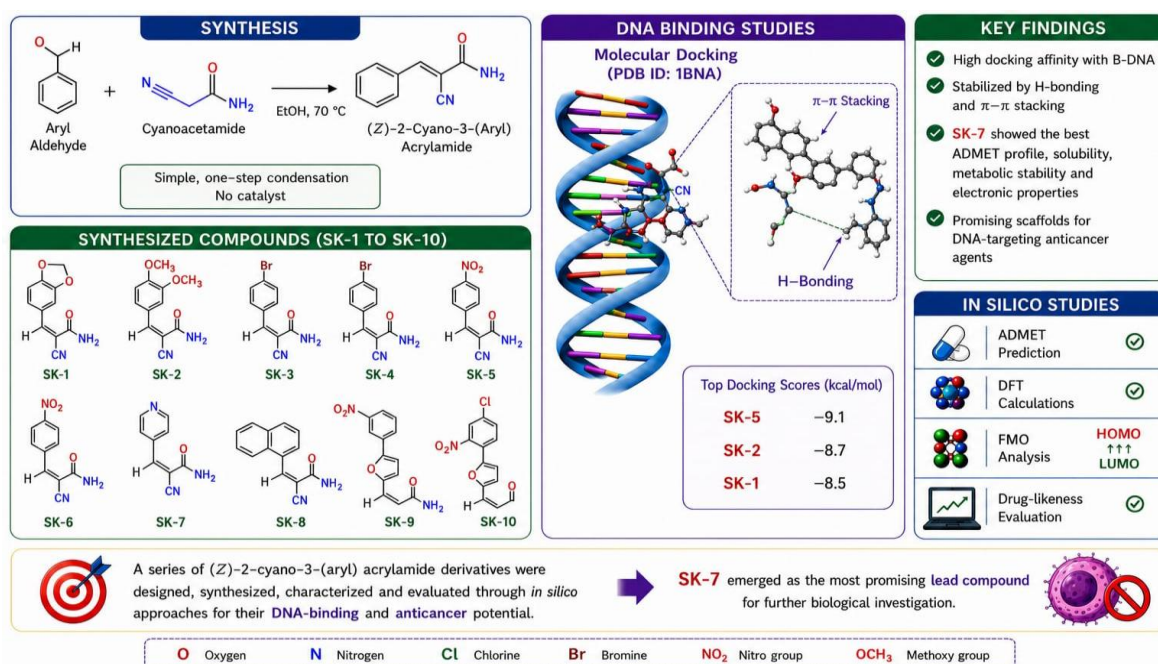
Synthesis, Spectroscopic Characterization, and Computational Study of New (Z)-2-Cyano-3-(Arylfuran) Acrylamide Derivatives as Promising DNA-Targeting Anticancer Agents

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Abstract: A new group of (Z)-2-cyano-3-aryl furan) acrylamide analogs were developed, synthesized and tested as anticancer agents. The synthesis of the compounds was performed by using a convenient two-step protocol using readily available anilines as starting material via aryl furfural intermediates, then condensed with cyan acetamide. The FT-IR and NMR spectroscopy were used to elucidate the structure. Molecular docking was performed against B-DNA (PDB ID: 1BNA) and the compounds SK-5, SK-2 and SK-1 showed docking scores of -9.1, -8.7 and -8.5 kcal/mol respectively. The hydrogen bonding and π - π stacking within the DNA helix were the main forces that stabilized the binding interactions. Pharmacokinetic and electronic properties were assessed with comprehensive *in silico* studies, such as the ADMET prediction, density functional theory (DFT) calculations, and frontier molecular orbital (FMO) analysis. Compound SK-7 was most favorable regarding its drug-like profile as it had the best solubility, stability in metabolism and electronic properties. These results demonstrate the promise of (Z)-2-cyano-3- (aryl furan) acryl amide derivatives as promising scaffolds to further develop DNA-targeting anticancer agents.

Keywords: Anticancer agents, DNA interaction, Molecular docking, Cyan acrylamide, ADMET, DFT



INTRODUCTION

Cancer continues to be a major cause of death in the world, and more effective and selective therapeutic agents should be developed continuously. Heterocyclic compounds have been historically important as vital scaffolds in medicinal chemistry because of their structural and biological variability. (Sung et al., 2021). Of these, furan-based derivatives have been of significant interest because of their wide range of biological activities, such as anticancer, antimicrobial, and anti-inflammatory activities. They have distinctive electronic properties that enable them to interact with biological macromolecules (Kerru, Gummidi, Maddila, Gangu, & Jonnalagadda, 2020)). Also, compounds derived out of furfural can be made using renewable biomass, increasing their sustainability and synthetic attractiveness (Lin, Han, Han, and Yang, 2021).

Another pharmacophore that is extensively used in drug design is cyan acetamide. Its bifunctional character allows the formation of structurally diverse molecules, which have important biological activity, most of which are associated with interactions with nucleic acids, including DNA. (Tantawy et al., 2024). DNA is a highly developed anticancer therapy target, and small molecules can disrupt replication and transcription by binding to the groove or intercalating into the DNA (Barqi et al., 2023).

DNA itself is one of the most attractive chemotherapy targets with the small molecule being able to inhibit important biological processes by non-covalent binding like intercalation or groove-binding (Aymami, Nunn, and Neidle, 1999). In this regard, the use of computational methods like molecular docking and ADMET prediction has become an essential part of drug discovery at an early stage, whereby a candidate molecule can be quickly screened before experimental validation (Ferreira, Dos Santos, Oliva, & Andricopulo, 2015). This has been complemented in silico ADMET profiling wherein, at early-stage triage, the scientists are able to forecast and prioritize compounds with good pharmacokinetic and safety profiles to improve development pipeline and thereby minimizing late-stage attrition (Pires, Blundell, & Ascher, 2015).

Armed with these principles, we theorized that strategic molecular hybridization of bioactive furan heterocycles with the multifunctional cyan acetamide pharmacophore would result in the production of new chemical entities, the DNA-binding specificities of which are enhanced and by which have potential anticancer uses. In the current research, we assumed that a furan skeleton could be hybridized with a cyan acrylamide moiety, leading to the development of new compounds with a high DNA-binding specificity and anticancer capacity. To confirm this hypothesis, a set of (Z)-2-cyano-3- (aryl furan) acrylamides were prepared and thoroughly analyzed by spectroscopic and computational methods. The combined strategy allowed the discovery of potential lead candidates, especially SK-7 compound, that can undergo further biological studies.

MATERIAL AND METHODS

Chemistry

Analytical grade reagents and solvents were used without further purification. TLC was done on silica gel plates (Merck 60 F254). Determination of melting points was done on a Gallen Kamp apparatus and was uncorrected. KBr pellets were used to record FT-IR spectra. The

^1H NMR was recorded at 300 and 500 MHz in CDCl_3 or $\text{DMSO}-d_6$ and tetramethyl silane (TMS) was used as an internal standard. The chemical shifts (δ) are reported in ppm.

Synthesis of Aryl Furfurals

Synthesis of aryl furfurals was achieved by diazotizing substituted anilines and then reacting with furfural. Diazonium salt was produced in situ by the reaction of NaNO_2 and HCl at 0°C temperature and then the furfural was reacted with the diazonium salt in the presence of CuCl_2 . The products obtained were recrystallized and washed with ethanol.

Synthesis of (Z)-2-Cyano-3-Aryl Acrylamides

The aryl aldehyde (0.01 mol) and cyan acetamide (0.01 mol) were stirred in ethanol as a solvent and catalytic amount of triethylamine at room temperature. A solid product was obtained in the reaction and filtered, washed using ethanol and recrystallized. The spectroscopic analysis was used to verify all compounds.

Preparation of Aryl Furfurals

Compound 1: (Z)-3-(benzo[d][1,3]dioxol-5-yl)-2-cyanoacrylamide (SK-1)

Yield: 1.48 gm (68%), Melting point: $153-155^\circ\text{C}$, IR ($\nu\text{-cm}^{-1}$): 3474.0, 3369.8, 3331.2, 2214.4, 1674.3, 1575.9, 1493.0, 1346.7, 1385.0, 1373.4, 1260.6, 1113.0, 1030.6, 958.7, 922.0, 810.0, 761.9, 657.8, ^1H NMR (400 MHz, $\text{DMSO}-d_6$): δ = 6.18(s, 2H, OCH_2O), 7.13(d, 1H, ArH, $J=8.15\text{Hz}$), 7.60(d, 1H, ArH, $J=8.15\text{Hz}$), 7.65(s, 1H, ArH), 7.72(s, 1H, NH_2), 7.83(s, 1H, NH_2), 8.08(s, 1H, Ar-CH).

Compound 2: (Z)-2-cyano-3-(3,4-dimethoxyphenyl) acrylamide (SK-2)

Yield: 1.78 gm (76%), Melting point: $172-173^\circ\text{C}$, IR ($\nu\text{-cm}^{-1}$): 3389.1, 3188.5, 2222.1, 1714.8, 1587.4, 1275.0, 1248, 1143.8, 1020.4, 954.8, 850.6, 792.8, 661.6, ^1H NMR (400 MHz, $\text{DMSO}-d_6$): δ =3.81(s, 3H, OCH_3), 3.86(s, 3H, OCH_3), 7.18(d, 1H, ArH, $J=8.53$), 7.57(d, 1H, ArH, $J=2.04\text{Hz}$), 7.59(s, 2H, NH_2), 7.68(s, 1H, Ar-CH), 8.12(s, 1H, ArH).

Compound 3: (Z)-3-(2-bromophenyl)-2-cyanoacrylamide (SK-3)

Yield: 2.21 gm (88%), Melting point: $188-189^\circ\text{C}$, IR ($\nu\text{-cm}^{-1}$): 3462.4, 3136.4, 2216.3, 1697.4, 1599.1, 1464.1, 1367.6, 1209.4, 1030.0, 927.8, 777.4, 733.2, 711.8, 679.0, ^1H NMR (400 MHz, CDCl_3): δ = 5.70(s, 1H, NH_2), 6.18(s, 1H, NH_2), 7.23(t, 1H, ArH, $J=1.62\text{Hz}$), 7.34(t, 1H, ArH, $J=0.83\text{Hz}$), 7.58(dd, 1H, ArH, $J=7.98, 1.21\text{Hz}$), 7.95(dd, 1H, ArH, $J=7.82, 1.60\text{Hz}$), 8.57(s, 1H, Ar-CH).

Compound 4: (Z)-3-(3-bromophenyl)-2-cyanoacrylamide (SK-4)

Yield: 2.29 gm (92%), Melting point: $136-137^\circ\text{C}$, IR ($\nu\text{-cm}^{-1}$): 3568.5, 3331.2, 3325.4, 3159.5, 2214.4, 1693.6, 1593.3, 1552.8, 1471.8, 1413.9, 1369.7, 1346.4, 1263.4, 1197.9, 1176.3,

775.4, 673.2, 652.0, 603.8, ^1H NMR (400 MHz, MeOD): δ =7.55(t, 1H, ArH, J =1.24Hz), 7.79(dd, 1H, ArH, J =1.75, 0.701Hz), 7.79(s, 1H, NH_2), 7.81(d, 1H, ArH, J =1.10Hz), 7.95(s, 1H, NH_2), 8.12(t, 1H, ArH, J =1.70Hz), 8.18(s, 1H, Ar-CH), ^{13}C NMR (125 MHz, MeOD): δ =8.23, 46.80, 107.10, 115.60, 122.87, 128.70, 130.58, 132.48, 134.89, 149.98.

Compound 5: (Z)-2-cyano-3-(3-nitrophenyl) acrylamide (SK-5)

Yield: 1.06 gm (50%), Melting point: 169-171°C, IR ($\nu\text{-cm}^{-1}$): 3470, 3366, 3321, 2211, 1672, 1570, 1483, 1342, 1384, 1371, 1254, 1110, 1020, 957, 920, 811, 762, 655, ^1H NMR (400 MHz, DMSO- d_6): δ =7.88(t, 1H, ArH, J =8.04Hz), 7.91(s, 1H, NH_2), 8.03(s, 1H, NH_2), 8.40(m, 2H, ArH), 8.42(dd, 1H, ArH, J =2.30, 0.85Hz), 8.79(t, 1H, ArH, J =2.03Hz).

Compound 6: (Z)-2-cyano-3-(4-nitrophenyl) acrylamide (SK-6)

Yield: 1.49 gm (69%), Melting point: 200-202 °C, IR ($\nu\text{-cm}^{-1}$): 3467, 3363, 3328, 2216, 1677, 1570, 1494, 1349, 1376, 1365, 1258, 1109, 1025, 956, 930, 800, 765, 652, ^1H NMR (400 MHz, DMSO- d_6): δ =7.94(s, 1H, NH_2), 8.08(s, 1H, NH_2), 8.15(dd, 2H, ArH, J =7.01, 1.71Hz), 8.32(s, 1H, Ar-CH), 8.41(dd, 2H, ArH, J =7.00, 1.951Hz).

Compound 7: (Z)-2-cyano-3-(pyridin-4-yl) acrylamide (SK-7)

Yield: 1.65 gm (95%), Melting point: 208-210 °C, IR ($\nu\text{-cm}^{-1}$): 3427.7, 3028.4, 2216.3, 1697.4, 1599.1, 1415.8, 1361.8, 1005.0, 974.1, 806.3, 779.3, ^1H NMR (250 MHz, DMSO- d_6): δ =7.80(d, 2H, ArH, J =5.60Hz), 7.96(s, 1H, NH_2), 8.09(s, 1H, NH_2), 8.20(s, 1H, Ar-CH), 8.82(d, 2H, ArH, J =5.00Hz), ^{13}C NMR (125 MHz, DMSO- d_6): δ =111.98, 115.92, 123.39, 139.56, 148.71, 151.17, 162.36.

Compound 8: (Z)-2-cyano-3-(naphthalen-1-yl) acrylamide (SK-8)

Yield: 1.99 gm (90%) Melting point: 176-177 °C IR ($\nu\text{-cm}^{-1}$): 3402.6, 3167.3, 2222.1, 1693.6, 1591.3, 1381.1, 1352.1, 1244.1, 947.1, 808.2, 783.1, 765.4, 727.2, 669.3, 632.7, ^1H NMR (400 MHz, Acetone- d_6): δ = 7.23(s, 1H, NH_2), 7.45(s, 1H, NH_2), 7.67(m, 3H, ArH), 8.06(dd, 1H, ArH, J =8.63, 1.56Hz), 8.18(m, 3H, ArH), 9.04(s, 1H, Ar-CH).

Compound 9: (Z)-2-cyano-3-(5-(3-nitrophenyl) furan-2-yl) acrylamide (SK-9)

Yield: 2.20 gm (78%), Melting point: 258-260 °C, IR ($\nu\text{-cm}^{-1}$): 3467, 3377, 3325, 2216, 1678, 1570, 1490, 1341, 1380, 1371, 1269, 1109, 1021, 913, 811, 754, 650, ^1H NMR (400 MHz, DMSO- d_6): δ =7.46(d, 1H, Furan, J =3.60Hz), 7.62(d, 1H, Furan, J =3.60Hz), 7.72(s, 1H, NH_2), 7.82(t, 2H, ArH, J =8.00Hz), 8.02(s, 1H, Ar-CH), 8.27(dd, 2H, ArH, J =8.0Hz), 8.70(s, 1H, NH_2).

Compound 10: (Z)-3-(5-(4-chloro-2-nitrophenyl) furan-2-yl)-2-cyanoacrylamide (SK-10)

Yield: 2.71 gm (85%), Melting point: 209-210 °C, IR ($\nu\text{-cm}^{-1}$): 3465, 3360, 3321, 2210, 1664, 1570, 1499, 1341, 1385, 1370, 1245, 1121, 950, 933, 811, 769, 658, ^1H NMR (400 MHz, DMSO-

d₆): δ =7.14(d, 1H, Furan, J=3.60Hz), 7.46(d, 1H, Furan, J=3.60Hz), 7.73(s, 1H, NH₂), 7.85(s, 1H, NH₂), 7.96(d, 2H, ArH, J=4.40Hz), 8.22(s, 1H, Ar-CH).

The synthesis of compounds (SK.1-8) was carried out by treatment of aromatic aldehydes with cyanoacetamide in basic condition. While in compounds SK.9 and SK.10 in first step aryl furfurals were prepared through the diazotization reaction of arylamines with furfural. These intermediates were then refluxed with cyanoacetamide to yield the desired derivatives.

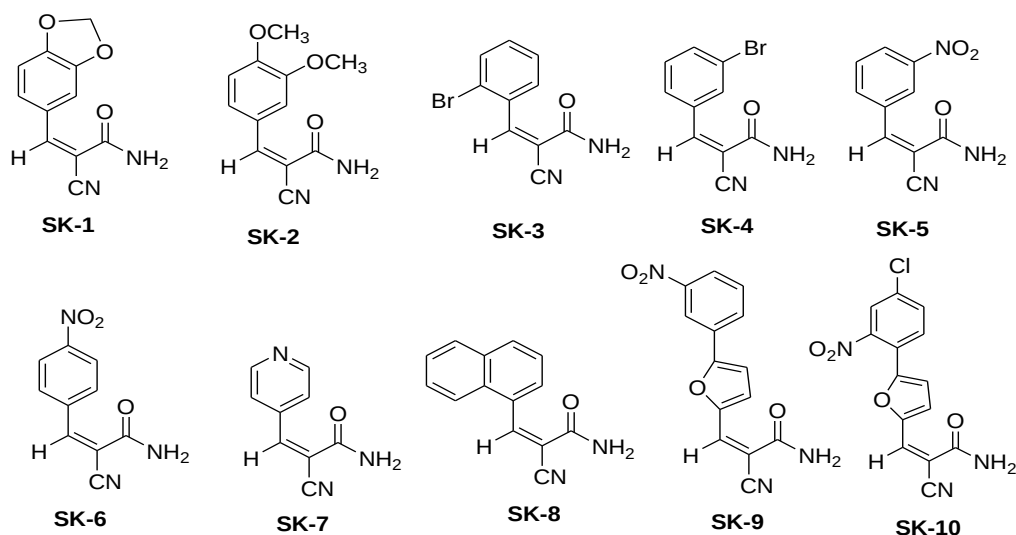


Figure 1: Structural representations of all the key functional groups in SK-1-10

COMPUTATIONAL STUDY

In Silico ADMET Analysis

To determine the pharmacokinetic and safety profile of the synthesized (Z)-2-cyano-3-(aryl furan) acrylamide derivatives (SK-1SK-10), a thorough analysis was conducted in silico ADMET. Absorption, distribution, metabolism, excretion, and toxicity parameters have been analyzed to select those compounds that have good drug-like characteristics and low safety risks. This assessment is important in the prioritization of lead candidates before experimental pharmacological research.

Absorption Properties

The calculated aqueous solubility rates show that most derivatives have moderate solubility, which is in line with aromatic heterocyclic structures. Interestingly, SK-7 has the highest solubility (-0.944), which implies better dissolution behavior that can increase oral bioavailability. SK-9 and SK-10, on the other hand, have reduced solubility, potentially restricting absorption in physiological settings. The prediction of Caco-2 permeability values indicates that most of the compounds can be transported efficiently by the membrane with SK-3 and SK-4 demonstrating higher values of permeability. Most derivatives have an intestinal absorption exceeding 75, which implies good oral absorption potential. The high permeability and satisfactory absorption combine to indicate the relevance of several

candidates to be taken orally. Interactions between efflux transporters were also tested to determine the possible restrictions on intracellular drug accumulation. All the derivatives are not expected to block P-glycoprotein, making it unlikely that transporter-mediated drug-drug interactions will occur. SK-9 is, however, classified as a P-glycoprotein substrate, and this could affect its retention within the cell and its therapeutic effect. SK-7, on the other hand, lacks P-glycoprotein liability, which helps in long-term intracellular exposure.

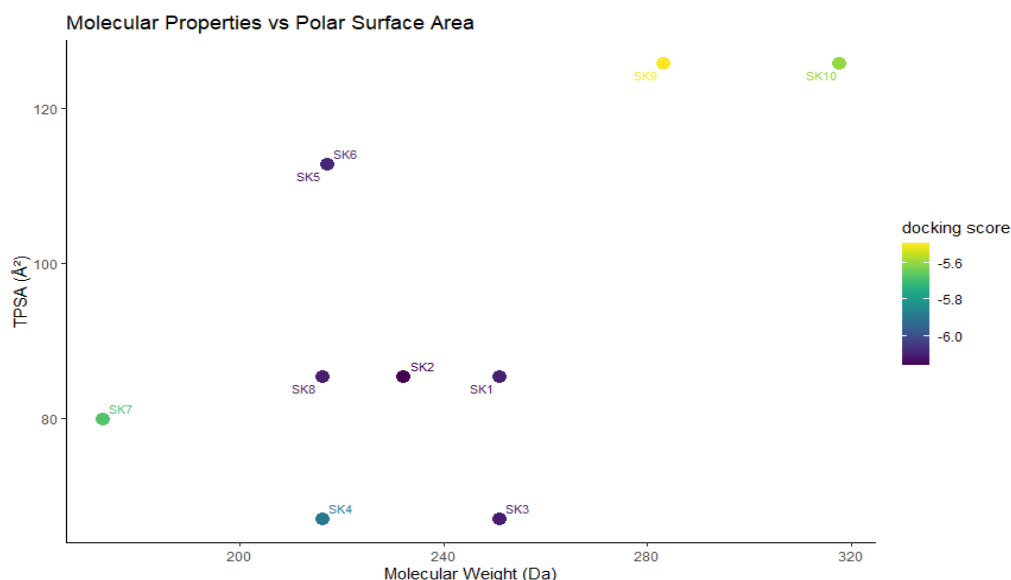


Figure 2: Comparison of physicochemical properties of SK ligands. The influence of the structure changes on lipophilicity, solubility and molecular flexibility.

Distribution Characteristics

The fraction unbound values predicted show moderate plasma protein binding through the series. SK-7 has the highest unbound fraction, indicating more availability of free drug to interact biologically.

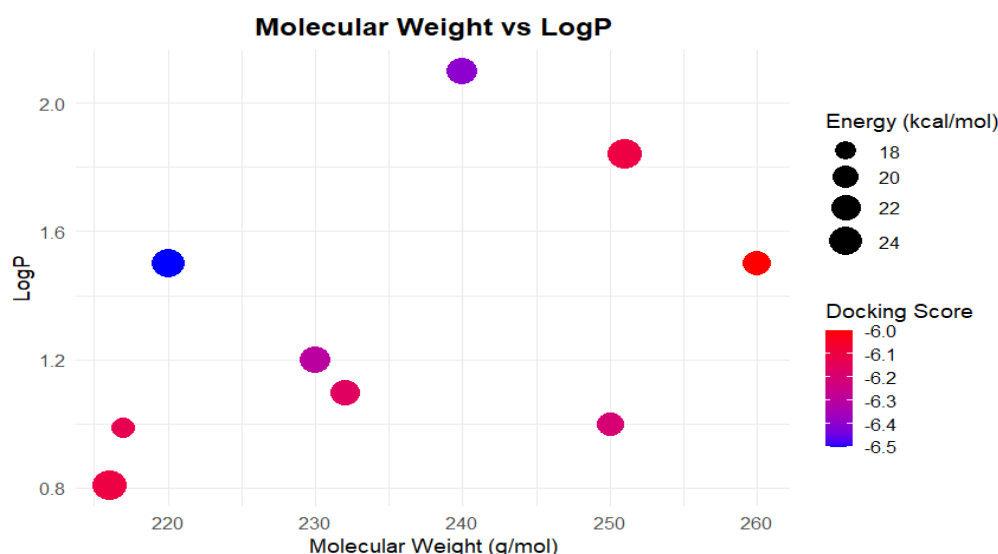


Figure 3: Comparison of SK ligand molecular properties (MW, LogP, TPSA, surface area) with a focus on the structure -property relationships

It is a desirable property of anticancer agents, in which the high concentration in the target location is required. The distribution values indicate that there is no excessive tissue accumulation and the volume is balanced. Although certain derivatives exhibit a bit higher distribution tendency, SK-7 has an ideal distribution profile, which minimizes the chances of off-target tissue exposure. All the derivatives exhibit low anticipated blood-brain barrier and central nervous system permeability. This attribute is desirable in non-CNS anticancer agents, since it reduces the likelihood of neurological adverse effects, and improves peripheral tumor specificity.

Metabolic Stability

Interaction profiling on cytochrome P450 shows that all the compounds are not substrates of CYP2D6, which decreases the likelihood of fast metabolic elimination. The SK-9 and SK-10 are the predicted CYP3A4 substrates, indicating the possibility of metabolically interaction. Most derivatives prevent CYP1A2, but SK-7 is the only derivative which does not prevent CYP1A2, which is a distinct metabolic benefit. In general, SK-7 has the most desirable metabolic profile with the least liabilities of enzymes.

Excretion Profile

The values of predicted total clearance indicate that there is an acceptable elimination behavior in the series of compounds. SK-7 exhibits good clearance, which could lower systemic accretion and concomitant toxicity risks. All the compounds are not noted as renal OCT2 substrates, meaning that there is a low risk of the possibility of transporter-mediated renal toxicity.

Toxicity Assessment

Several of the derivatives are predicted to be mutagenic by AMES toxicity but SK-1, SK-2, SK-7, and SK-8 are AMES-negative, indicating the better genotoxic safety of these compounds. Notably, the compounds are all predicted not to inhibit hERG I and II channels, thus the potential risk of cardiotoxicity is low. Human maximum tolerated doses values are estimated to be good with SK-7 having good safety margin. All the derivatives are hepatotoxic. Some compounds are observed to have skin sensitization, but SK-7 shows an acceptable profile in the predicted safety limits. Also, aquatic toxicity tests show SK-7 has less toxicity to the environment than some other derivatives. They were assessed based on equal consideration of the absorption, distribution, metabolism, excretion, and toxicity parameters resulting in SK-7 as the most promising lead compound of the synthesized derivatives. Its high aqueous solubility, good oral absorption, no efflux liability, optimum plasma protein binding, good metabolic clearance, effective clearance and no significant toxicity are all contributing factors to its development as a prospective anticancer agent. The results are a strong indication that SK-7 needs to be experimentally validated and biologically tested.

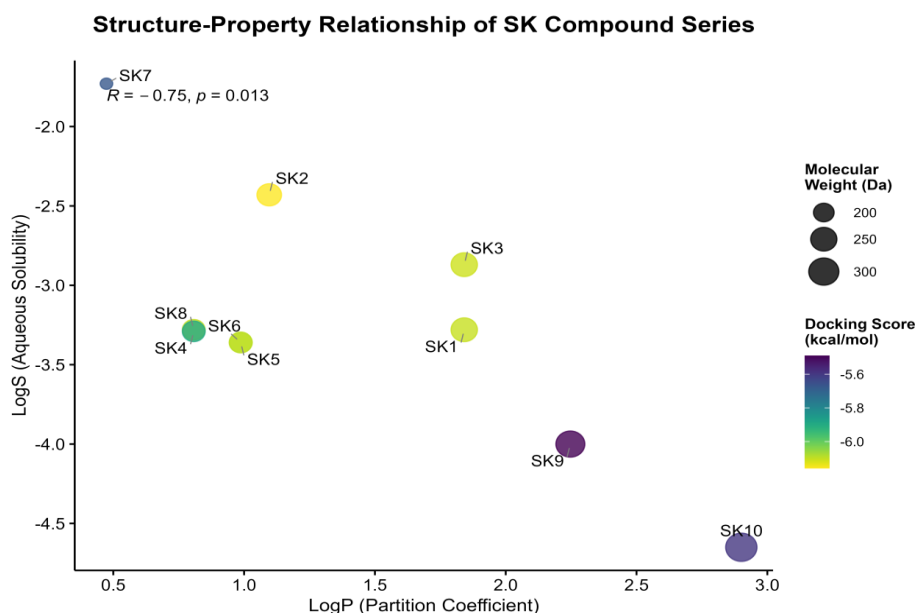


Figure 4: Physicochemical characterization of SK derivatives and comparing them regarding tendencies of lipophilia and structural effect

A physicochemical, ADMET, and molecular docking analysis was conducted in silico to determine the drug-likeness and binding efficacy of SK1-SK10 ligands.

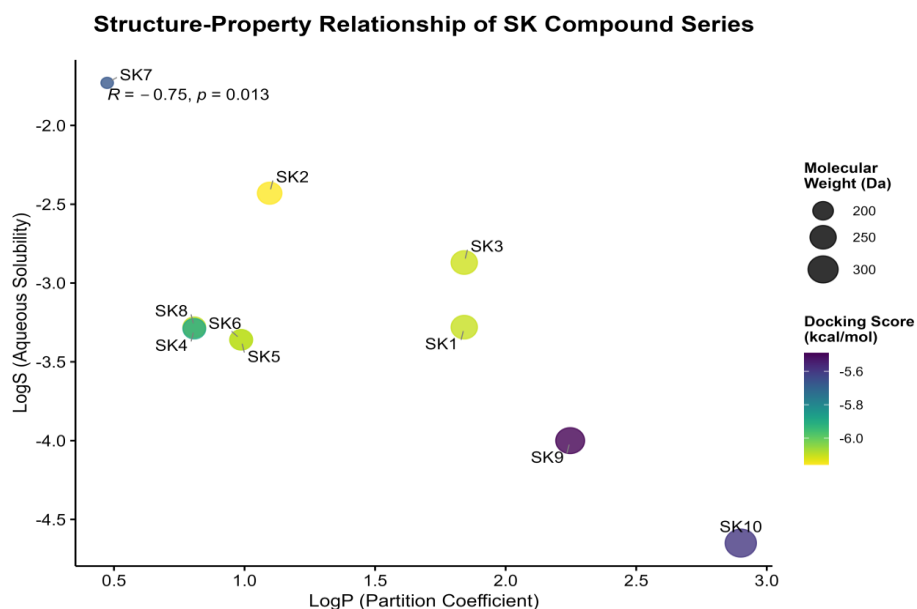


Figure 5: Together with the summary of molecular descriptors which are applied to quantify the solubility and flexibilities of SK ligands

Standard computational tools were used to compute key descriptors, such as molecular weight, lipophilicity (LogP), topological polar surface area (TPSA), rotatable

bonds, solubility (Log S), skin permeability (log Kp), and docking scores, and docking was done against the target protein (PDB ID: 2O8B). The overall characteristics of the ligands include moderate molecular weights, low to moderate lipophilicity, and reasonable TPSA values, indicating good oral bioavailability. The results of docking show that the scores of bindings are always negative throughout the series, which indicates that the interaction between the ligand and proteins is stable and SK1, SK2, SK3, and SK5 exhibit rather higher binding affinities. The SK9 and SK10 compounds are less lipophilic and have higher molecular weights but still have reasonable docking scores due to an increased surface area and polar functionality. Together with positive physicochemical profiles, reasonable permeability estimates, and positive docking energies, the series of drugs can be characterized as drug-like with some of the best compromises in terms of binding affinity and pharmacokinetic properties to provide further anticancer development.

Table 1: Determined in advance properties of ADMET of SK-1 using SK-10 with an overview of the absorption, distribution, metabolism, excretion and toxicity behavior.

		SK-1	SK-2	SK-3	SK-4	SK-5	SK-6	SK-7	SK-8	SK-9	SK-10
Property	Model Name	Predicted Value	Predicted Value	Predicted Value	Predicted Value	Predicted Value	Predicted Value	Predicted Value	Predicted Value	Predicted Value	Predicted Value
Absorption	Water solubility	-2.169	-2.72	-2.229	-2.346	-2.506	-2.416	-0.944	-2.169	-3.071	-3.651
	Caco2 permeability	0.579	0.654	0.907	1.019	-0.001	0.027	0.805	0.579	0.88	0.793
	Intestinal absorption (human)	69.683	69.996	93.94	94.851	80.337	80.391	76.141	69.683	87.385	88.653
	Skin Permeability	-3.079	-2.926	-2.261	-2.306	-2.56	-2.554	-3.483	-3.079	-2.699	-2.704
	P-glycoprotein substrate	No	No	No	No	No	No	No	No	Yes	No
	P-glycoprotein I inhibitor	No	No	No	No	No	No	No	No	No	No
Distribution	P-glycoprotein II inhibitor	No	No	No	No	No	No	No	No	No	No
	VDss (human)	-0.165	-0.187	-0.01	0.043	0.028	-0.019	-0.405	-0.165	0.006	-0.002
	Fraction unbound (human)	0.336	0.372	0.293	0.324	0.238	0.24	0.568	0.336	0.115	0.113
	BBB permeability	-0.344	-0.388	-0.116	-0.143	-0.463	-0.474	-0.157	-0.344	-0.664	-0.88
	CNS permeability	-2.575	-2.921	-2.215	-2.822	-2.589	-2.588	-2.906	-2.575	-2.382	-2.28
Metabolism	CYP2D6 substrate	No	No	No	No	No	No	No	No	No	No
	CYP3A4 substrate	No	No	No	No	No	No	No	No	Yes	Yes
	CYP1A2 inhibitor	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
	CYP2C19 inhibitor	No	No	No	No	No	No	No	No	No	Yes
	CYP2C9 inhibitor	No	No	No	No	No	No	No	No	No	Yes
	CYP2D6 inhibitor	No	No	No	No	No	No	No	No	No	No
	CYP3A4 inhibitor	No	No	No	No	No	No	No	No	No	No
Excretion	Total Clearance	0.166	0.392	-0.042	-0.107	0.359	0.732	0.763	0.166	0.509	0.054
	Renal OCT2 substrate	No	No	No	No	No	No	No	No	No	No
Toxicity	AMES toxicity	No	No	Yes	Yes	Yes	Yes	No	No	Yes	Yes
	Max. tolerated dose (human)	0.782	1.373	0.734	0.887	0.372	0.421	1.135	0.782	0.256	0.298
	hERG I inhibitor	No	No	No	No	No	No	No	No	No	No
	hERG II inhibitor	No	No	No	No	No	No	No	No	No	No
	Oral Rat Acute Toxicity (LD50)	2.002	2.103	2.348	2.241	2.23	2.221	2.267	2.002	2.442	2.536
	Oral Rat Chronic Toxicity (LOAEL)	1.512	2.099	1.001	1.001	1.482	1.49	2.77	1.512	1.473	1.424
	Hepatotoxicity	No	No	No	No	No	No	No	No	No	No
	Skin Sensitisation	No	No	Yes	Yes	Yes	No	Yes	No	No	No
	T.Pyiformis toxicity	0.822	0.692	1.125	1.159	1.142	1.151	-0.348	0.822	1.378	1.309
	Minnow toxicity	1.293	1.153	1.051	0.818	0.999	1.214	2.036	1.293	0.297	-0.557

Density Functional Theory (DFT) Geometry Optimization

Density Functional Theory Geometry Optimization. All the synthesized (Z)-2-cyano-3-(aryl furan) acrylamide derivatives (SK-1 - SK-10) were optimized completely with the Density Functional Theory at the B3LYP/6-31++G (d, p) level. This hybrid functional with a diffuse and polarized basis set is long known to be successful in the accurate description of heteroatom-rich organic systems, conjugated π -framework interactions, and hydrogen-bonding interactions. The geometry optimization was done without use of symmetry constraints to make sure that the optimized structures converged to the actual energy minima and none of the imaginary frequencies were detected, which proves the stability of the optimized structures.

Optimized Bond Length Analysis

The optimum C-C bond lengths in the aryl and furan rings are at a range of 1.37-1.42 Å, which is in line with the delocalized aromatic nature in all derivatives. The relatively similar values of bonds like C2-C1, C3-C2 and C4-C3 reflect that planarity and conjugation are maintained along the molecular backbone.

Table 2: Computed length of SK derivatives (in Å) on B3LYP/6-31++G (d, p) level of theory.

SK-1	Bond length (Å)	SK-2	Bond length (Å)	SK-3	Bond length (Å)	SK-4	Bond length (Å)	SK-5	Bond length (Å)
C6C5	1.398	C2C1	1.389	C2C1	1.386	C2C1	1.392	C2C1	1.395
C1C6	1.382	C3C2	1.409	C3C2	1.418	C3C2	1.411	C3C2	1.413
O12C6	1.39	C4C3	1.418	C4C3	1.414	C4C3	1.416	C4C3	1.41
C4C5	1.37	C5C4	1.383	C5C4	1.389	C5C4	1.382	C5C4	1.384
O13C5	1.406	C6C1	1.398	C6C1	1.395	C6C1	1.396	C6C1	1.393
C2C1	1.396	C7C3	1.453	C7C3	1.457	C7C3	1.461	C7C3	1.463
C3C4	1.423	O15C5	1.392	Br13C2	1.937	Br13C5	1.93	N15C5	1.465
C14O12	1.488	O17C6	1.38	H16C1	1.081	H16C1	1.083	H18C1	1.083
C7C3	1.454	H19C1	1.082	H17C4	1.082	H17C2	1.08	H19C2	1.081
H17C1	1.08	H20C2	1.08	H18C5	1.083	H18C4	1.083	H20C4	1.081
H18C2	1.084	H21C4	1.083	H19C6	1.084	H19C6	1.082	H21C6	1.08
H19C4	1.081	C8C7	1.369	C8C7	1.367	C8C7	1.365	C8C7	1.363
H23C14	1.091	H12C7	1.089	H12C7	1.086	H12C7	1.089	H12C7	1.089
H24C14	1.091	C9C8	1.502	C9C8	1.508	C9C8	1.507	C9C8	1.509
C8C7	1.369	C13C8	1.427	C14C8	1.43	C14C8	1.428	C13C8	1.429
H20C7	1.089	N10C9	1.366	N10C9	1.364	N10C9	1.364	N10C9	1.362
C9C8	1.503	O11C9	1.248	O11C9	1.247	O11C9	1.246	O11C9	1.246
C15C8	1.427	C16O15	1.479	N15C14	1.168	N15C14	1.168	N14C13	1.168
N10C9	1.365	C18O17	1.464	H20N10	1.014	H20N10	1.014	O16N15	1.282
O11C9	1.247	N14C13	1.169	H21N10	1.013	H21N10	1.013	O17N15	1.284
N16C15	1.169	H22N10	1.013	-	-	-	-	H22N10	1.014
H21N10	1.014	H23N10	1.013	-	-	-	-	H23N10	1.013
H22N10	1.013	H24C16	1.09	-	-	-	-	-	-
-	-	H25C16	1.089	-	-	-	-	-	-
-	-	H26C16	1.097	-	-	-	-	-	-
-	-	H27C18	1.09	-	-	-	-	-	-
-	-	H28C18	1.095	-	-	-	-	-	-
-	-	H29C18	1.096	-	-	-	-	-	-
SK-6	Bond length (Å)	SK-7	Bond length (Å)	SK-8	Bond length (Å)	SK-9	Bond length (Å)	SK-10	Bond length (Å)
C2C1	1.39	C2C1	1.393	C6C5	1.398	C2C1	1.449	C2C1	1.462
C3C2	1.404	C3C2	1.401	C1C6	1.382	C3C2	1.413	C3C2	1.423
C4C3	1.404	C4C3	1.401	O13C6	1.39	C7C2	1.399	C7C2	1.415
C5C4	1.39	C5C4	1.393	C4C5	1.37	C4C3	1.393	C4C3	1.386
C6C1	1.391	N6C1	1.35	O14C5	1.406	C5C4	1.394	C5C4	1.389
C7C3	1.488	C7C3	1.488	C2C1	1.396	C6C7	1.387	C6C7	1.398
N15C6	1.462	H15C1	1.084	C3C4	1.423	O8C1	1.385	O8C1	1.401
H18C1	1.08	H16C2	1.082	C15O13	1.488	C11C1	1.383	C11C1	1.389
H19C2	1.083	H17C4	1.082	C7C3	1.454	C9O8	1.392	C9O8	1.383
H20C4	1.083	H18C5	1.084	H18C1	1.08	C10C11	1.42	C10C11	1.416
H21C5	1.08	C8C7	1.345	H19C2	1.084	C12C9	1.419	C12C9	1.42
C8C7	1.344	H12C7	1.089	H20C4	1.081	N20C6	1.465	C18C5	1.82
H12C7	1.089	C9C8	1.52	H23C15	1.091	H23C3	1.085	N21C7	1.464
C9C8	1.522	C13C8	1.425	H24C15	1.091	H24C4	1.083	H24C3	1.084
C13C8	1.424	N10C9	1.363	C8C7	1.369	H25C5	1.08	H25C4	1.082
N10C9	1.362	O11C9	1.237	H12C7	1.089	H26C7	1.08	H26C6	1.078
O11C9	1.238	N14C13	1.167	C9C8	1.503	H27C10	1.077	H27C10	1.077
N14C13	1.167	H19N10	1.014	C16C8	1.427	H28C11	1.076	H28C11	1.069
O16N15	1.284	H20N10	1.013	N10C9	1.365	C13C12	1.366	C13C12	1.366
O17N15	1.284	-	-	O11C9	1.247	H14C12	1.087	H14C12	1.087
H22N10	1.014	-	-	N17C16	1.169	C15C13	1.515	C15C13	1.514
H23N10	1.013	-	-	H21N10	1.014	C18C13	1.423	C19C13	1.423
-	-	-	-	H22N10	1.013	N16C15	1.369	N16C15	1.367
-	-	-	-	-	-	O17C15	1.24	O17C15	1.241
-	-	-	-	-	-	N19C18	1.169	N20C19	1.169
-	-	-	-	-	-	O21N20	1.284	O22N21	1.282
-	-	-	-	-	-	O22N20	1.283	O23N21	1.283
-	-	-	-	-	-	H29N16	1.013	H29N16	1.014
-	-	-	-	-	-	H30N16	1.012	H30N16	1.013

This is a structural property necessary to π -electron delocalization that is critical in DNA intercalation and electronic communication in anticancer agents. It is interesting to

note that compounds SK-3, SK-4, and SK-7 exhibit more consistent aromatic bond lengths, possibly indicating a greater conjugation stability than more substituted analogues of SK-9 and SK-10, in which additional substituents cause slight increases in bond lengths. The bond lengths of the C $\equiv$ N-C linkage and acryl amide structure indicate a high degree of conjugation between the cyano group and the olefinic linkage and amide group. The lengths of the N3C bonds (~1.161.17 Å) in all the compounds are a sign of partial double-bond character due to resonance delocalization. This is an essential step towards ensuring the molecular rigidity that is commonly known to have enhanced DNA-binding affinity. SK-7 has the highest homogeneous N-C and C=O associated bond lengths, which suggests the best electron delocalization of the acrylamide fragment. The C-O and C-N bond lengths of furan oxygen and amide nitrogen atoms are within reasonable ranges (1.24-1.49 Å), which proves correct structural assignment and effective involvement of heteroatoms in conjugation. The presence of substituent effects can be observed in the presence of halogenated derivatives: Br-C bonds in SK-3 and SK-4 (~1.93 Å); Cl-C bonds in SK-10 (~1.82 Å). These long bonds are indicative of heavier atoms, which mildly distort local geometry and can affect the electronic distribution and steric interactions with biological targets. The optimized N-H and C-H bond lengths are always between 1.01-1.10 Å, which means that the positioning of hydrogen is stable. These hydrogen atoms play a part in the possible intermolecular hydrogen bonding with DNA bases or phosphate groups. Notably, SK-7 has well-balanced hydrogen bond geometries, which facilitate intramolecular stability and intermolecular recognition. SK-7 is the most optimized derivative based on detailed analysis of DFT geometry. Its bond length distribution is indicative of high conjugation, small steric strain and optimum orientation of functional groups as pertains to DNA interaction. The maintained planarity and a balance of heteroatom involvement imply SK-7 would most effectively stack and hydrogen bond with nucleic acid targets through π -pile and hydrogen bonding. The geometry optimization procedure by DFT ascertains that all the synthesized (Z)-2-cyano-3-(aryl furan) acrylamide derivatives have stable, well-defined, molecular structures. The differences in bond lengths between the series bring out the importance of type and position of substituents on molecular geometry. Of all the compounds that have been studied, SK-7 has the best structural properties, which justifies its use as the lead compound in further DNA interaction investigations and anticancer research.

Frontier Molecular Orbital (FMO) Analysis

Frontier molecular orbital (FMO) analysis is a powerful method to study the electronic properties, chemical reactivity, and charge-transfer of molecular systems. This paper has determined the HOMO and LUMO energies of SK-1 to SK-10 at DFT level and the energy gaps between them (ΔE_{Gap}) to determine their electronic stability and reactivity. HOMO energy is proportional to the electron-donating capacity of a molecule and LUMO energy the electron-accepting capacity. The decreased HOMOLUMO energy gap usually correlates with increased chemical reactivity, increased intramolecular charge transfer (ICT) and better nonlinear optical (NLO) response. The HOMO and LUMO energies of the studied systems, as indicated in Table X, are between -7.306 eV and -5.897 eV and -3.308 eV -2.045 eV respectively. SK-10 has the lowest energy gap (3.118 eV) of all the systems, which indicates easy electronic excitation and high charge-transfer properties. This narrow band gap means more polarizability and electronic responsiveness, which are good properties of optoelectronic and NLO use. Conversely, SK-7 exhibits the highest energy gap (4.537 eV),

which means it is more kinetically stable and less reactive. Further systems like SK-5 and SK-6, which have a comparatively deeper HOMO and a greater band gap, also exhibit enhanced electronic stability by being less donative of electrons. Interestingly, SK-1 and SK-8 have the same HOMO and LUMO energies, which leads to almost similar energy gaps (about 3.744 eV). This resemblance implies similar electrical structures and reactivity patterns of these two systems. In the meantime, SK-9, which has a moderate band gap of 3.508 eV, offers a compromise between stability and reactivity and thus is a possible candidate in charge-transfer-driven applications. In general, the downward pattern in the HOMO-LUMO energy gap of SK-7 to SK-10 reflects the upward trend in the intramolecular charge-transfer efficiency in the series. These results prove that molecular modification can have a great impact on the electronic structure and can be used strategically to modify the optoelectronic and nonlinear optical properties of the investigated systems. The analysis of quantum chemical descriptors is based on the analysis of quantum chemical descriptors. The frontier molecular orbital energies give quantum chemical descriptors that are useful in assessing the intrinsic reactivity, stability and charge-transfer properties of molecular systems. Global reactivity indices, including ionization potential (IP), electron affinity (EA), electronegativity (χ), chemical potential (μ), chemical hardness (η), softness (S) and electrophilicity index (ω) were assessed of SK-1 to SK-10 using conceptual DFT formalism. The ionization potential is the measure of how difficult it is to remove electrons in a molecule. Of the systems studied, SK-5 shows the highest IP (7.306 eV), which means that it has a high ability to retain electrons and better electronic stability. SK-2 on the other hand exhibits the least IP (5.897 eV), which implies a relatively easy donation of electrons. The electron affinity values show the opposite trend, and SK-10 has the highest EA (3.308 eV), which shows that it is highly susceptible to accepting electrons and engaging in a charge transfer process. Electronegativity (χ) is a number that describes the ability of a molecule to attract electrons in general. The χ values are highest in SK-2 to SK-5 with SK-5 having the highest electronegativity (5.123 eV), which correlates with the deep HOMO and large ionization potential. The negative values of chemical potential (μ) of all systems are a confirmation of thermodynamic stability and lower values (especially of SK-5 and SK-10) of μ are an indication of stronger electron-withdrawing nature.

Table 3: SK-1 to SK-10 values of HOMO, LUMO, and the energy gap which are electronic properties obtained by DFT.

System	HOMO EH (eV)	LUMO EL (eV)	ΔE_{Gap} (eV)
SK-1	-5.93752748	-2.19323884	3.74428864
SK-2	-5.89725461	-2.04548093	3.85177368
SK-3	-6.76067233	-2.48548927	4.27518306
SK-4	-6.75849542	-2.50970742	4.248788
SK-5	-7.30626090	-2.93964754	4.36661336
SK-6	-7.03142576	-2.64603653	4.38538923
SK-7	-6.65618055	-2.11949594	4.53668461
SK-8	-5.93752748	-2.19323880	3.74428868
SK-9	-6.31059577	-2.80277420	3.50782157
SK-10	-6.42597211	-3.30781778	3.11815433

The most important parameters in the study of molecular stability and reactivity are chemical hardness (η) and softness (S). SK-10 is the hardest (1.559 eV) and the softest (0.321 eV) which means that it is more electronically flexible and more reactive. In contrast, SK-7 is the hardest (2.268 eV) which means that it is more resistant to charge redistribution and more stable kinetically. Electrophilicity index (ω) is a measure of the electron-accepting strength of a system which is a product of chemical potential and hardness. SK-10 exhibits the most electrophilicity value (7.59 eV), which implies a strong tendency to receive electrons and a strong intramolecular nature of charge transfer. Other systems including SK-5 and SK-9 also exhibit rather large ω values and could make good contenders in optoelectronic and nonlinear optical applications.

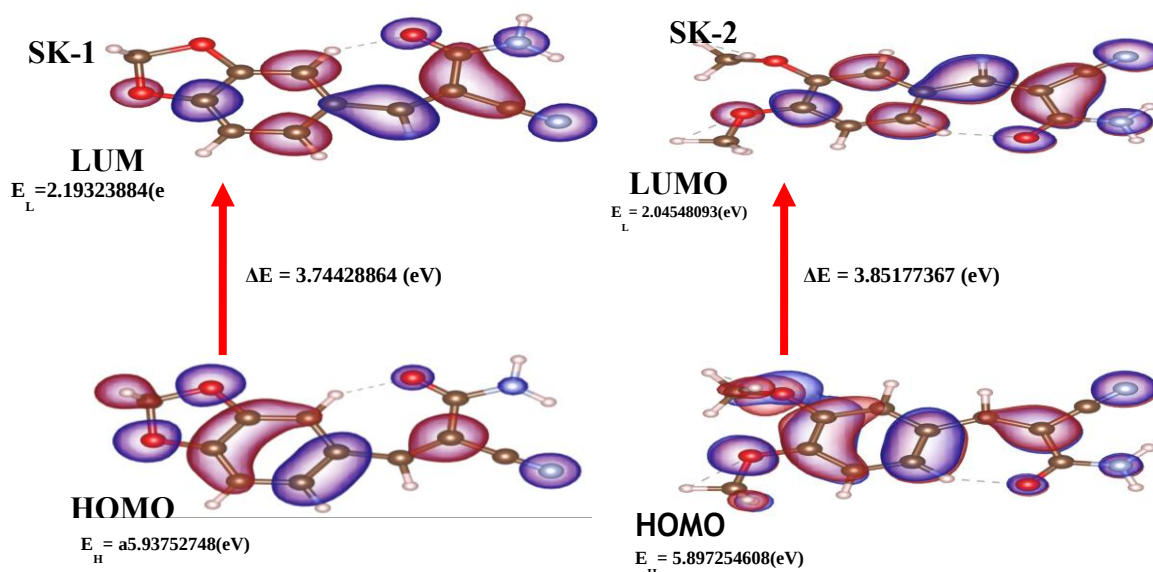


Figure 6: A HOMO-LUMO energy gap comparison of SK-1 and SK-2 demonstrating the influence of the change in the structure on the electronic stability.

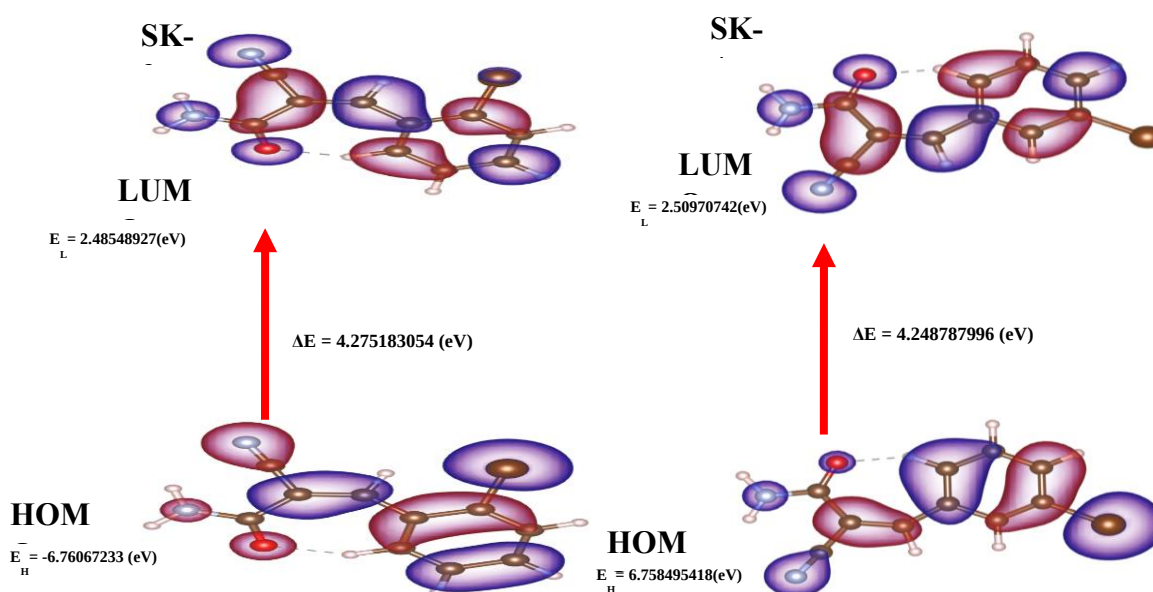


Figure 7: Comparison between HOMO-LUMO energy gaps of SK-3 and SK-4 which measure the variations in the electronic reactivity.

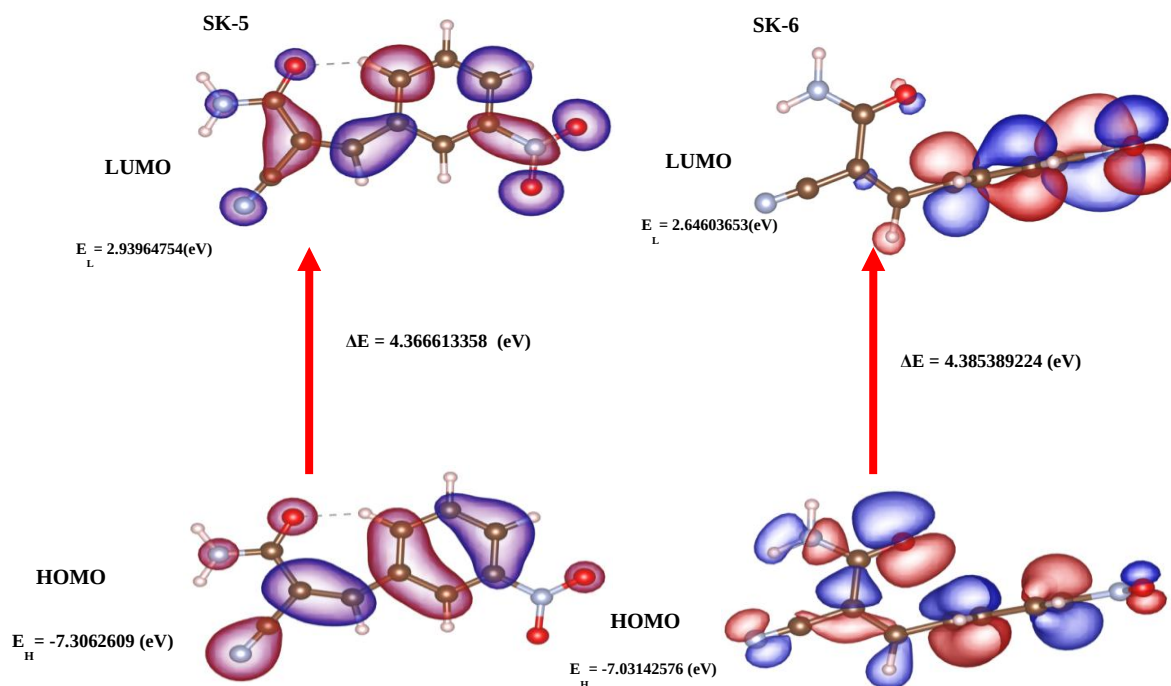


Figure 8: Direct comparison of HOMO-LUMO energy gap of SK-5 and SK-6 that demonstrates the electronic behavior in relation to structure

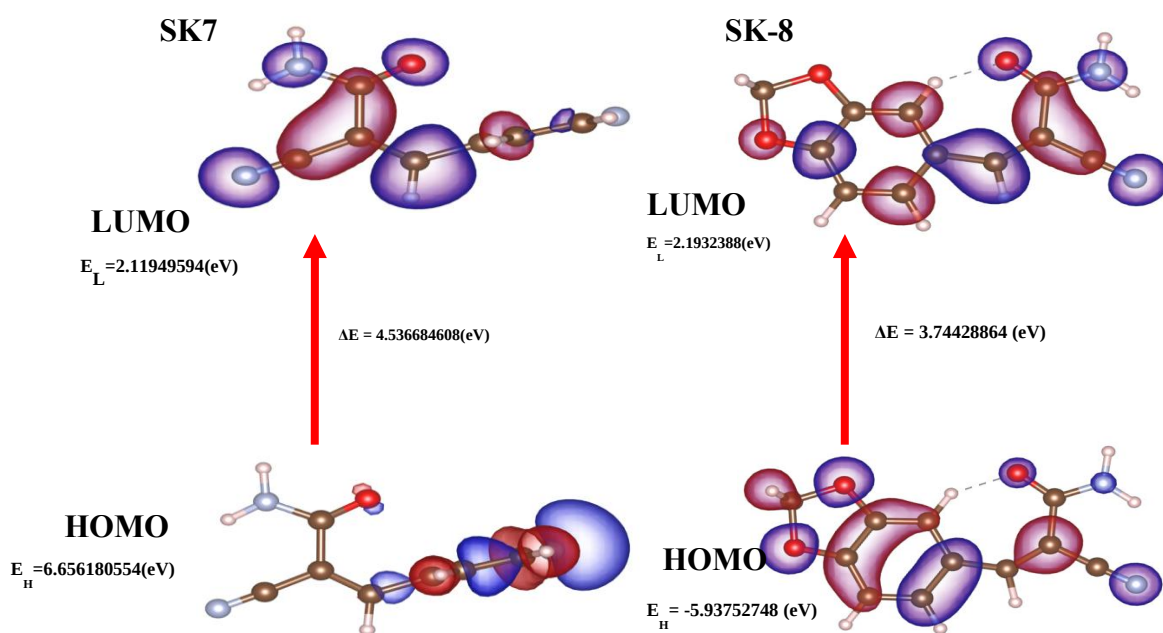


Figure 9: SK-7 and SK-8 HOMO-LUMO energy gaps are compared to indicate the variation in the stability of the molecules.

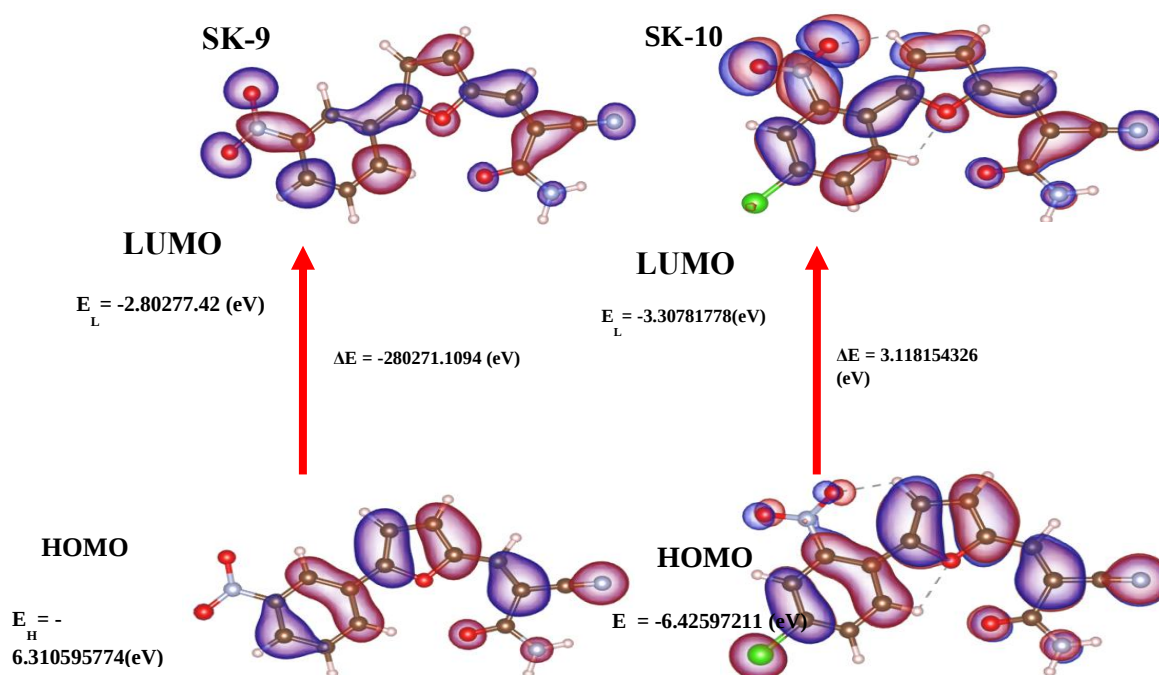


Figure 10: Comparison of HOMO-LUMO energy gap between SK-9 and SK-10 which are difference in the reactivity of the two structures because of the structural changes

Quantum Chemical Descriptors Analysis

The frontier molecular orbital energies give quantum chemical descriptors that are useful in assessing the intrinsic reactivity, stability and charge-transfer properties of molecular systems. Global reactivity indices, including ionization potential (IP), electron affinity (EA), electronegativity (χ), chemical potential (μ), chemical hardness (η), softness (S) and electrophilicity index (ω) were assessed of SK-1 to SK-10 using conceptual DFT formalism. The ionization potential is the measure of how difficult it is to remove electrons in a molecule. Of the systems studied, SK-5 shows the highest IP (7.306 eV), which means that it has a high ability to retain electrons and better electronic stability. SK-2 on the other hand exhibits the least IP (5.897 eV), which implies a relatively easy donation of electrons. The electron affinity values show the opposite trend, and SK-10 has the highest EA (3.308 eV), which shows that it is highly susceptible to accepting electrons and engaging in a charge transfer process. Electronegativity (χ) is a number that describes the ability of a molecule to attract electrons in general. The χ values are highest in SK-2 to SK-5 with SK-5 having the highest electronegativity (5.123 eV), which correlates with the deep HOMO and large ionization potential. The negative values of chemical potential (μ) of all systems are confirmation of thermodynamic stability and lower values (especially of SK-5 and SK-10) of μ are an indication of stronger electron-withdrawing nature. The most important parameters in the study of molecular stability and reactivity are chemical hardness (η) and softness (S). SK-10 is the hardest (1.559 eV) and the softest (0.321 eV) which means that it is more electronically flexible and more reactive. In contrast, SK-7 is the hardest (2.268 eV) which means that it is more resistant to charge redistribution and more stable kinetically. Electrophilicity index (ω) is a measure of the electron-accepting strength of a system which is a product of chemical potential and hardness. SK-10 exhibits the most electrophilicity value (7.59 eV), which implies a strong tendency to receive electrons and a strong

intramolecular nature of charge transfer. Other systems including SK-5 and SK-9 also exhibit rather large ω values and could make good contenders in optoelectronic and nonlinear optical applications.

Table 4: SK-Ligands reactivity quantifiers based on DFT calculations e.g., IP, EA, hardness, softness and electrophilicity

System	IP	EA	χ	μ	η	S	ω
SK-1	5.938	2.193	4.065	-4.0654	1.872	0.27	4.4
SK-2	5.897	2.046	3.971	-3.9714	1.926	0.26	4.1
SK-3	6.761	2.486	4.623	-4.6231	2.138	0.23	5
SK-4	6.759	2.51	4.634	-4.6341	2.124	0.24	5.1
SK-5	7.306	2.94	5.123	-5.1230	2.183	0.23	6
SK-6	7.031	2.646	4.839	-4.8387	2.193	0.23	5.3
SK-7	6.656	2.12	4.388	-4.3878	2.268	0.22	4.3
SK-8	5.938	2.193	4.065	-4.0654	1.872	0.27	4.4
SK-9	6.311	2.803	4.557	-4.5567	1.754	0.29	5.9
SK-10	6.426	3.308	4.867	-4.8669	1.559	0.32	7.6

Molecular Electrostatic Potential (MESP) Analysis

Analysis Molecular electrostatic potential (MESP) analysis provides a graphical and numerical analysis of charge distribution of a molecule and is useful in the discovery of electrophilic and nucleophilic reactive sites. The MESP surfaces of the systems under study were mapped onto the optimized geometries with the aim of correlating the electrostatic characteristics with the calculated quantum descriptors. Regions of negative electrostatic potential (red) in any system are largely concentrated around electronegative atoms (oxygen and other heteroatom-containing functional groups) pointing to favored sites of electrophilic attack. On the other hand, the positive potential areas (blue) are primarily spread across hydrogen atoms and electron-deficient carbon centers, which are also good locations to form nucleophilic interactions. The long neutral (green) bands above the conjugated structures indicate that there is a successful π -delocalization, which facilitates intramolecular charge transfer. More electrophilic and soft molecules, like SK-10 and SK-9, are more polarized in their MESP maps, with strong separation of charges between donor and acceptor regions. Such an increase in electrostatic asymmetry supports the flow of charges along the molecular backbone, which agrees with their reduced hardness and increased electrophilicity indices. Conversely, harder and less soft systems like SK-7 have quite smooth potential distribution, which indicates poorer charge-transferability and higher electronic stability. Overall, the MESP analysis supports the tendencies of global reactivity descriptors, which proves that the change in the molecular modification has a great impact on the charge distribution, reactivity, and electronic response. The close relationship between MESP characteristics and quantum descriptors also confirms the appropriateness of such systems in application in need of effective charge transfer and nonlinear optical activity.

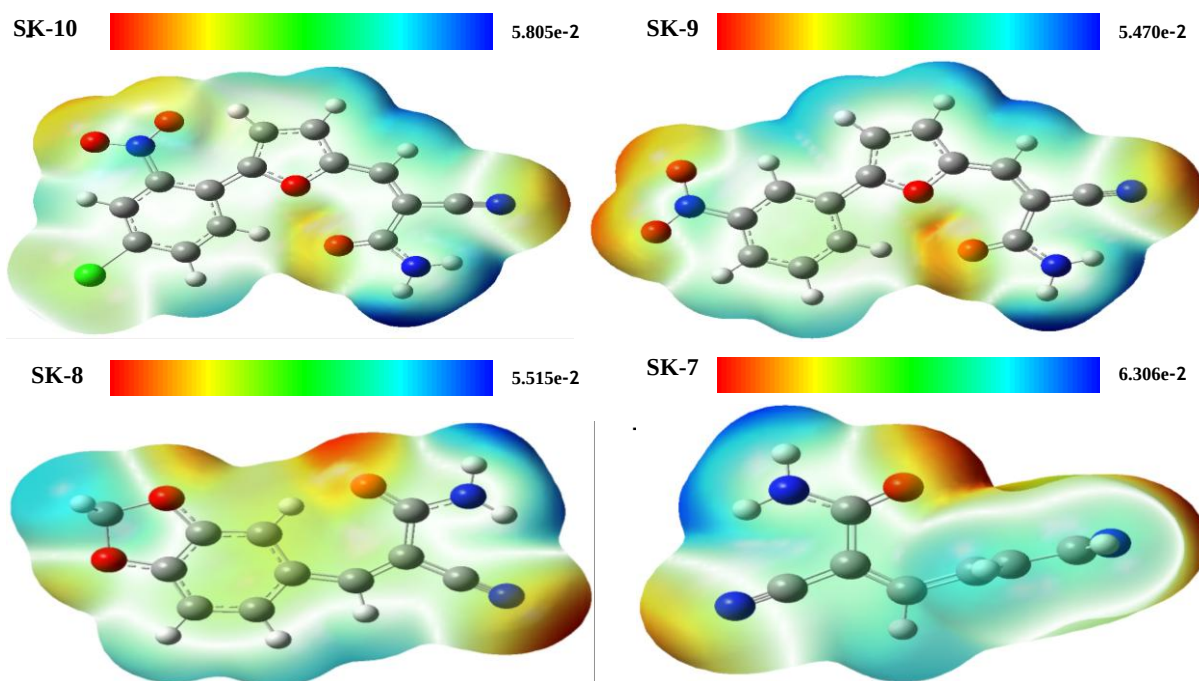


Figure 11: Let SK-7 to SK-10 Which of these structures are electron rich/ electron deficient?

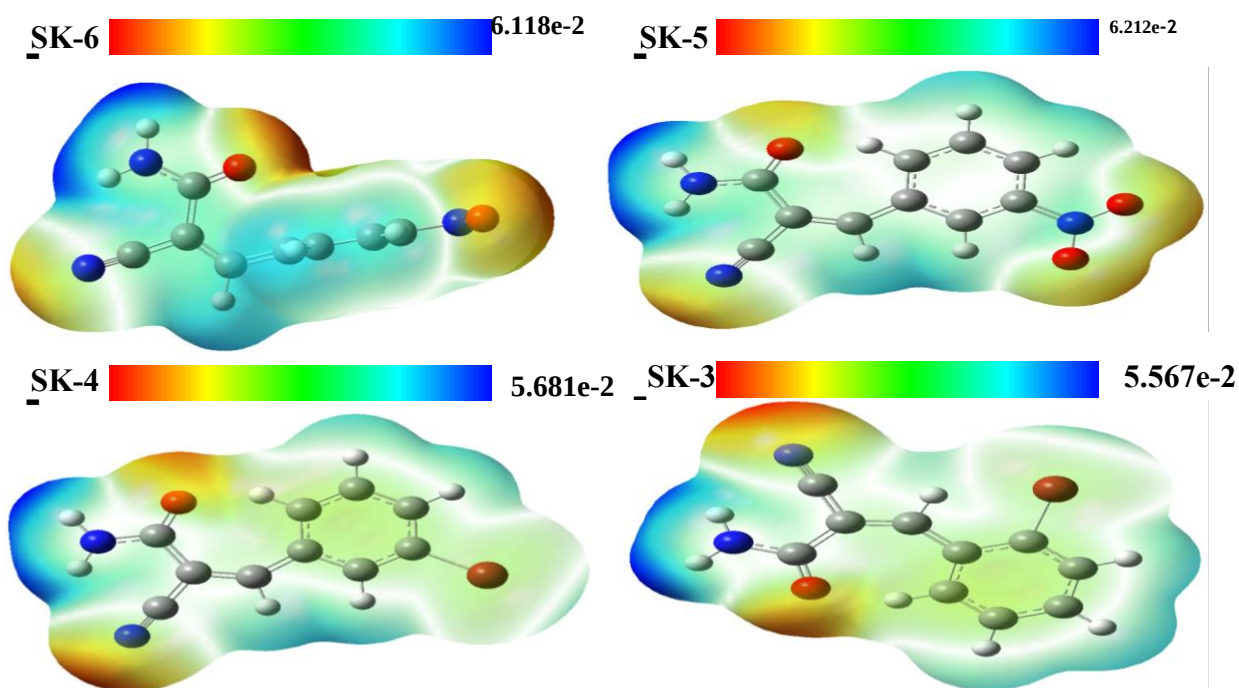


Figure 12: MESP distribution of SK-3 to SK-6 with the focus on the distribution of charges or the detailed pattern of it and the reactive sites

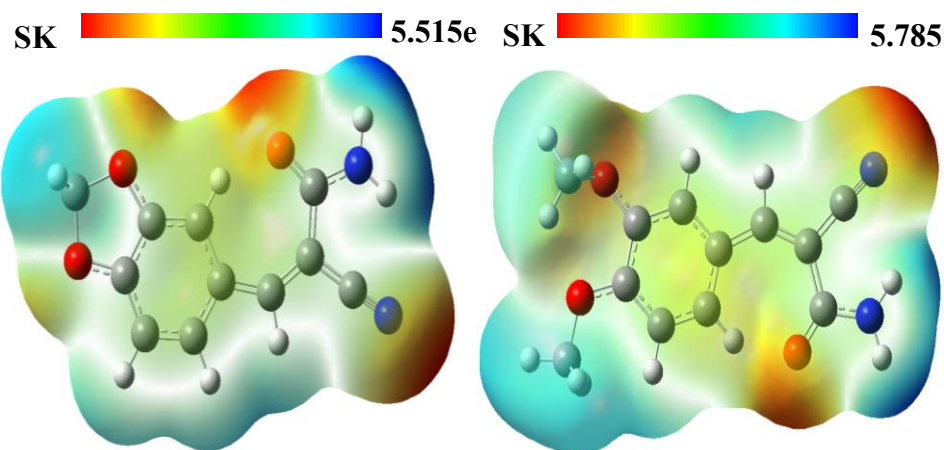


Figure 13: MESP image of SK-1 and SK-2 with electrons that are spatially distributed

Molecular Docking Analysis

Molecular Docking Analysis The molecular docking analysis was performed using the method of comparative molecular docking.

Comparative Molecular Docking Analysis

Molecular docking was used to clarify the binding characteristics of the synthesized derivatives (SK-1 SK-10) in the active site of the target protein (PDB ID: 2O8B). In general, a stable binding environment with a well-defined and reproducible interaction pattern is observed, with all compounds adopting a stable conformation in the binding pocket. Throughout the series, the hydrogen bonding with GLY674, ASN653, and GLN681 appears as a leading anchoring pattern, which mainly occurs via the amide and Cyano groups. These interactions offer a stable polar scaffold that stabilizes the position of ligands in the active site. Simultaneously, most derivatives are shown to be π - π stacked with TYR815, which once again highlights the importance of aromatic interactions in improving binding affinity. Although the first derivatives SK-1, SK-4 and SK-7 are balanced in terms of hydrogen bonding and π - π interactions, subsequent derivatives are increasingly enriched in hydrophobic and π - π interactions. Specifically, SK-5 and SK-6 introduce more π -cation interactions with TYR815 which helps to stabilize the solution with more electrostatic interactions. SK-9 and SK-10 exhibit the most interactive profiles, with a high degree of π - to π -stacking with TYR815 and PHE650, and π -alkyl contacts with ILE648 and VAL642 and other hydrophobic residues. This increased interaction network implies more accommodation in the hydrophobic areas of the binding pocket. It is interesting to note that SK-10 has the strongest binding mode in a series, which combines hydrogen bonding with strong π -cation, 1-cation, 1-cation interaction, 1-cation, 1-cation interaction, and 1-cation, 1-cation interaction. This cooperative interaction behavior implies that there is better stabilization of binding compared with other derivatives. The trends in docking are consistent with optimized molecular geometries and affirm a structure-binding correlation where an increase in aromaticity and substituent-controlled hydrophobicity leads to protein-binding. To conclude, docking analysis shows that the moderate and highly stabilized binding progressively increase throughout the series, with SK-9 and SK-10 being the most promising

ones. These results are molecular-length justifications to their additional testing in anticancer and DNA-interaction research

Docking of SK-1 with PDB ID: 2O8B

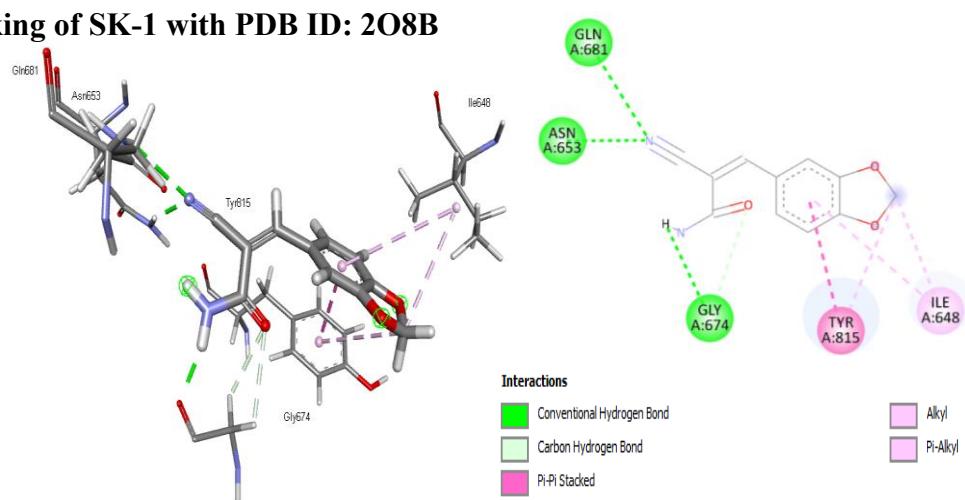


Figure 14: Assessment of the physicochemical property of SK ligands with emphasis laid on the differences on the molecular property based on structure.

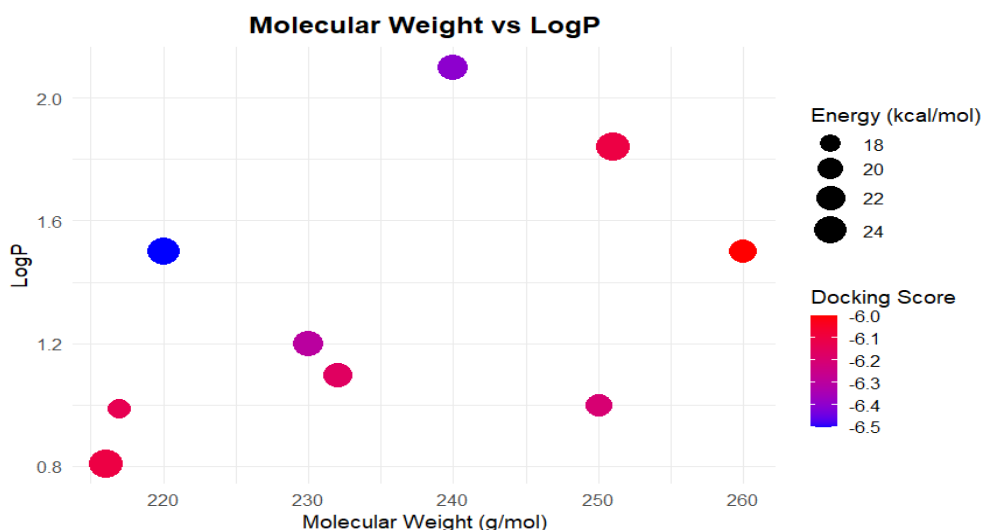


Figure 15: SK-1 docking to the target protein (PDB: 2O8B) which has discharge hdischargedinding, 9 -bonds with the proteins and hydrophobic contacts.

Docking of SK-2 with PDB ID: 2O8B

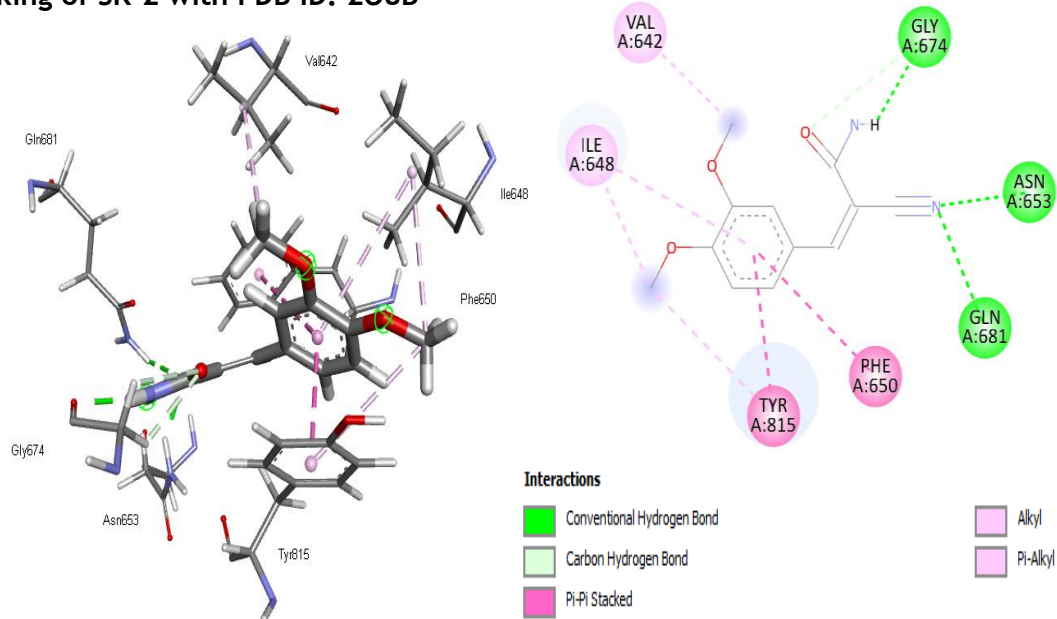


Figure 16: Key binding interactions (2D- and 3D docking interactions of the ligand in the 2O8B active site).

Docking of SK-3 with PDB ID: 2O8B

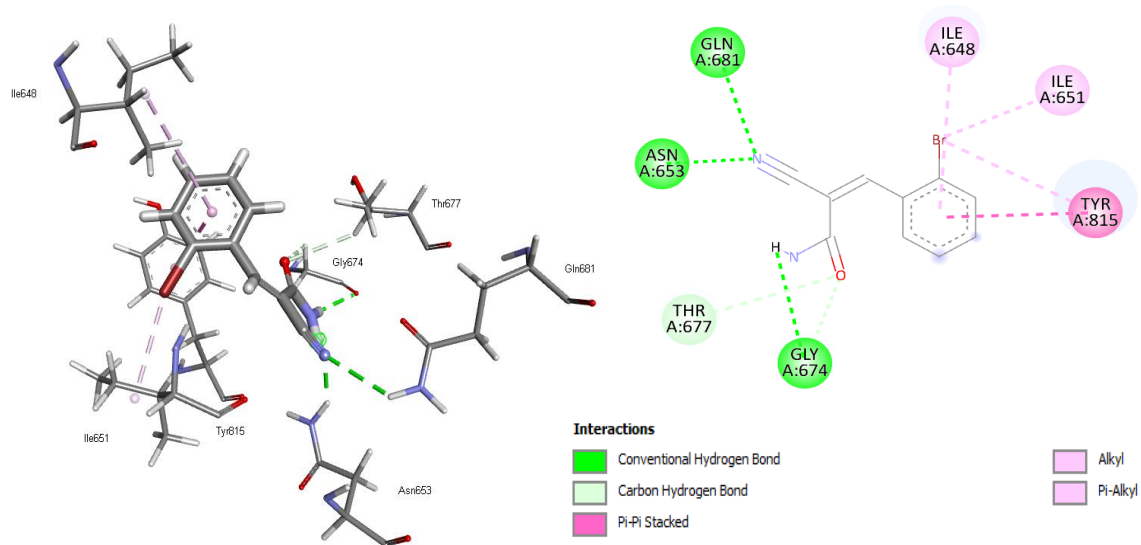


Figure 17: Reactions with 2O8B are binding interactions and are also familiar with the existence of hydrogen bonds, π - stacking and hydrophobic interactions

Docking of SK-4 with PDB ID: 2O8B

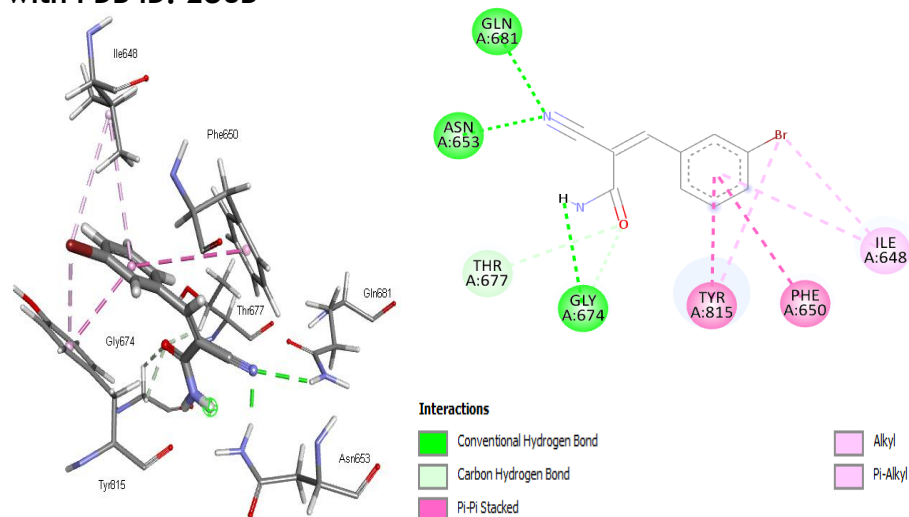


Figure 18: Summary of SK-4 docking profile in the active site of 2O8B highlighting the key intermolecular interactions

Docking of SK-5 with PDB ID: 2O8B

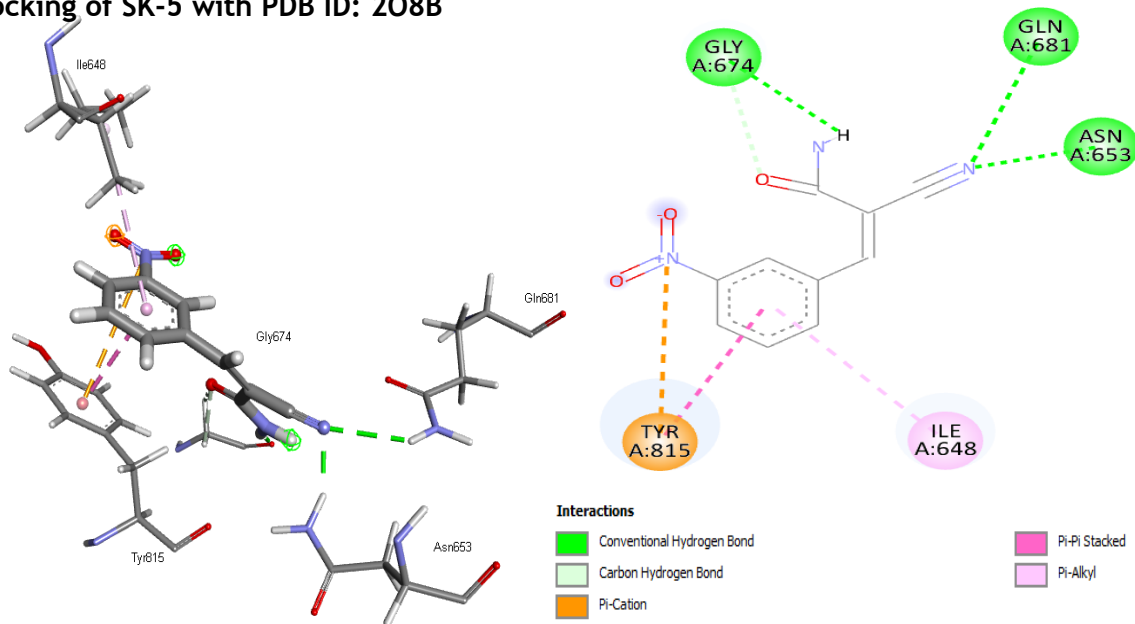


Figure 19: SK-5 binding interactions with 2O8B which exhibit hydrogen bonding, cation (pi), and Hydrophobic interactions.

Docking of SK-6 with PDB ID: 2O8B

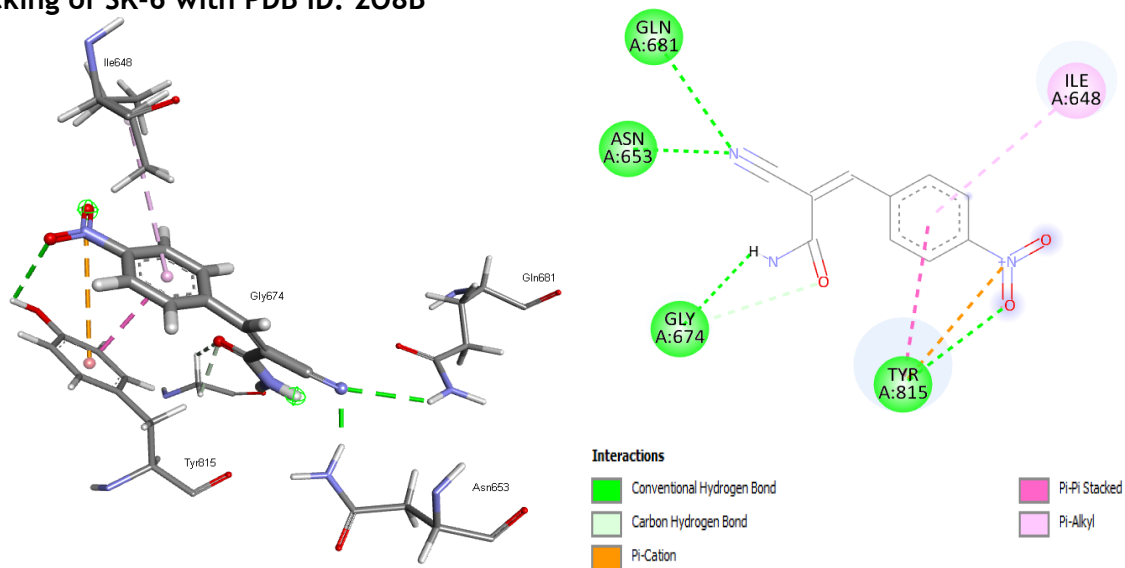


Figure 20: Mechanisms SK-6 is interacting with the target protein focusing on stabilizing non-covalent interactions.

Docking of SK-7 with PDB ID: 2O8B

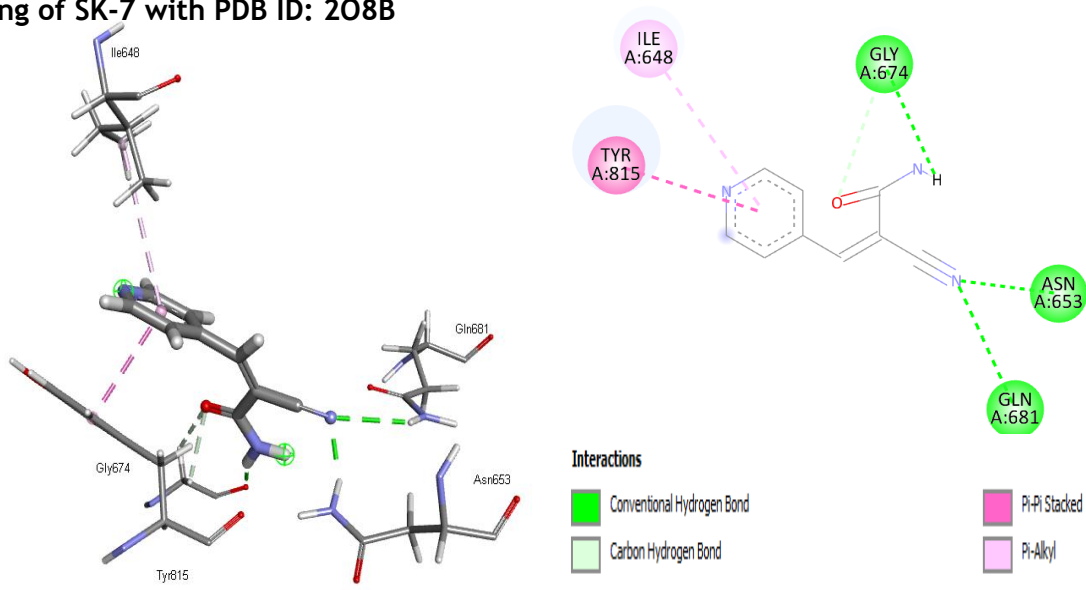


Figure 21: The mode of interaction of SK-7 in 2O8B shows the change in the key hydrogen bonding and hydrophobic effects.

Docking of SK-8 with PDB ID: 2O8B

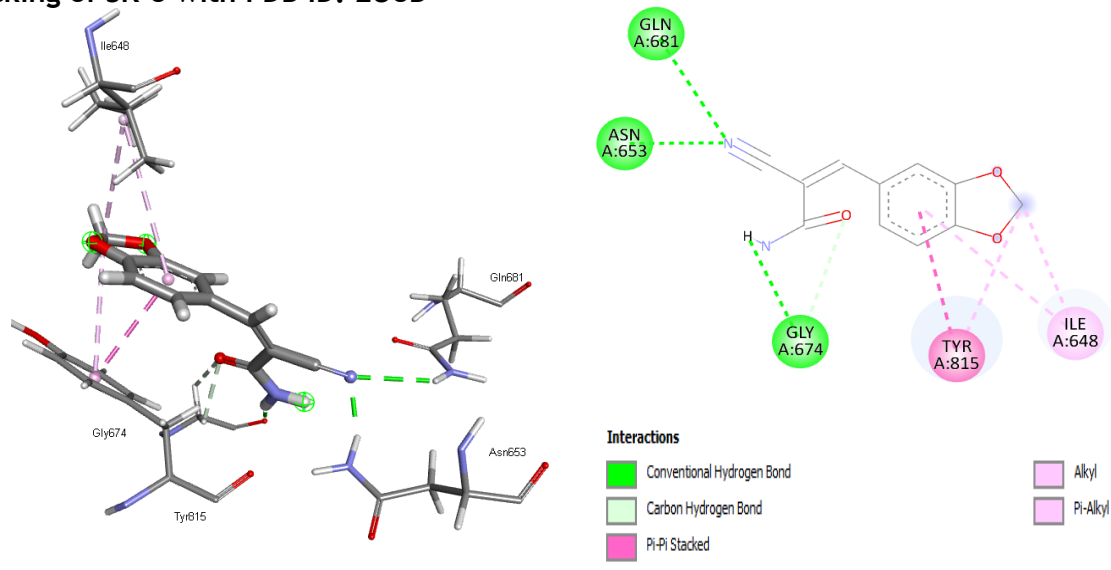


Figure 22: 2O8B interaction with SK-8 Docking interaction between SK-8 and 2O8B, illustrating significant stabilizing results

Docking of SK-9 with PDB ID: 2O8B

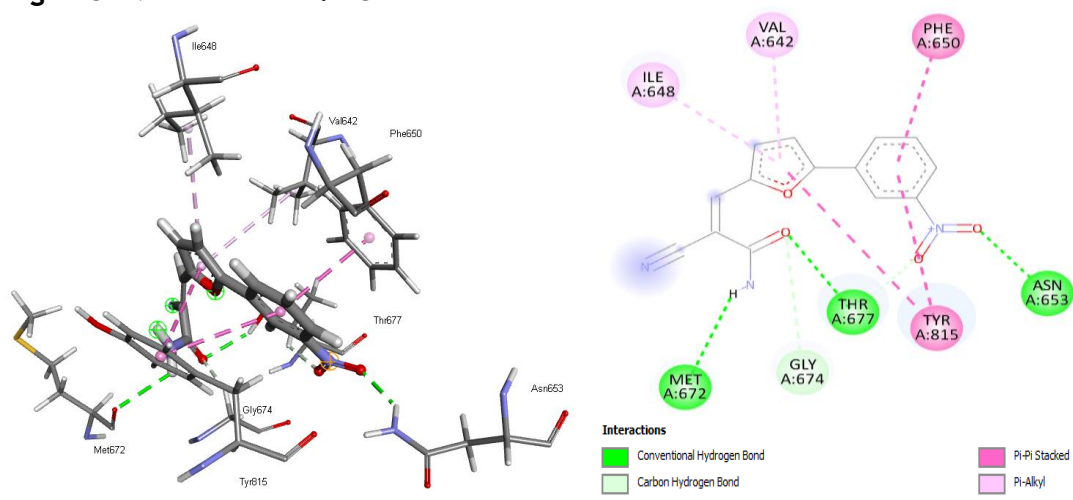


Figure 23: Reactions of SK-9 with 2O8B in an active site.

Docking of SK-10 with PDB ID: 208B

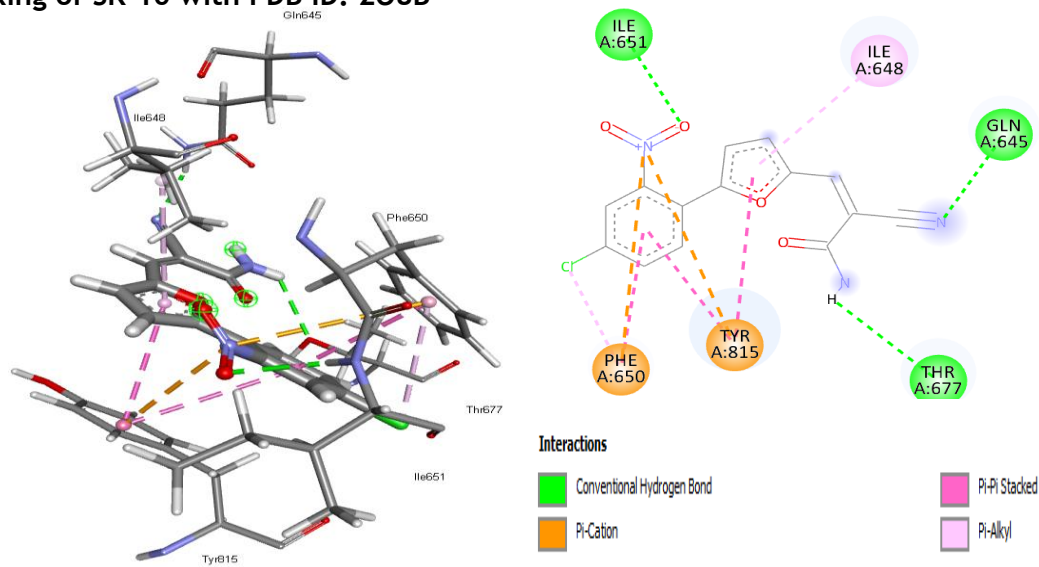


Figure 24: SK-10 interaction with 208B: SK-10PI interaction with 208B (residues) is π -cation interaction, 8 interaction, and hydrophobic interaction

Table 5: Summary of the physicochemical and pharmacokinetic and docking properties of SK ligands, including binding energy, the drug-likeness properties.

Ligands	Formula	Molecular Weight	Log P	Rotatable Bonds	Surface Area	MR	TPSA	Log S	log Kp (cm/s)	docking score	Energy
SK2	C ₁₂ H ₁₂ N ₂ O ₃	232.239	1.0961	4	99.053	61.79	85.34	-2.43	-6.97	-6.159	22.241
SK5	C ₁₀ H ₇ N ₃ O ₃	217.184	0.9871	3	90.749	57.63	112.7	-3.36	-6.64	-6.13	19.038
SK3	C ₁₀ H ₇ BrN ₂ O	251.083	1.8414	2	89.963	56.5	66.88	-2.87	-6.53	-6.109	16.452
SK1	C ₁₁ H ₈ N ₂ O ₃	251.083	1.8414	2	89.963	54.87	85.34	-3.28	-6.29	-6.103	25.493
SK8	C ₁₁ H ₈ N ₂ O ₃	216.196	0.8076	2	91.682	54.87	85.34	-3.28	-6.29	-6.103	25.493
SK6	C ₁₀ H ₇ N ₃ O ₃	217.184	0.9871	3	90.749	57.63	112.7	-3.36	-6.64	-6.088	20.249
SK4	C ₁₀ H ₇ BrN ₂ O	216.196	0.8076	2	91.682	56.5	66.88	-3.29	-6.23	-5.895	15.438
SK7	C ₉ H ₇ N ₃ O	173.175	0.4739	2	75.315	46.6	79.77	-1.73	-7.01	-5.674	17.163
SK10	C ₁₄ H ₈ ClN ₃ O ₄	317.688	2.9005	4	128.903	80.34	125.84	-4.65	-6.56	-5.596	23.712
SK9	C ₁₄ H ₉ N ₃ O ₄	283.243	2.2471	4	118.6	75.33	125.84	-4	-6.79	-5.49	18.18

CONCLUSION

An integrated computational approach was used to successfully synthesize and test a novel series of (Z)-2-cyano-3-(aryl furan) acrylamide derivatives. Molecular docking experiments showed good DNA-binding capabilities whereas ADMET and DFT showed good pharmacokinetic and electronic characteristics. SK-7 was the most balanced in the list of the synthesized compounds, that's why it is a good candidate to be further experimentally validated as an anticancer drug.

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