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Synthesis, spectral studies and molecular docking analysis of some aryl hydrazide derivatives

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Four series of aryl hydrazides have been synthesized using potassium hydrogen phthalate-assisted condensation by stirring aryl hydrazines with various substituted benzaldehydes and acetophenones at room temperature. The yield of this condensation is more than 85%. The influence of solvent on the yield has been studied. These hydrazides have been characterized by their physical constants, UV, IR, NMR, and mass spectral data. The characteristic spectral frequencies have been correlated with Hammett substituent constants and Swain Lupton's parameters using single and multi-regression analysis. From the statistical analysis results, the spectral quantitative structure-activity relationships have been assessed. The ligand-protein interaction ability of these hydrazines have been examined using molecular docking analysis.

Keywords: Aryl hydrazides, Potassium phthalate, Spectral correlation, Molecular docking

Nitrogen-containing compounds have been known to have tremendous potential in various fields of organic chemistry. The nitrogen-containing organic compounds, provide great biological properties, the nitrogen atoms can act as donors and find applications in the construction of supramolecular blocks. Hydrazine derivatives constitute a versatile class of compounds in organic chemistry. The compounds containing the hydrazone group possess a wide range of biological activities[1-6]. Organic chemistry is probably the most active and important field of heterocyclic chemistry at the moment, due to its extreme applicability to both biochemistry and petro-chemistry where the prime concern is the synthesis of new organic molecules[7-9]. The chemical properties of hydrazines have been widely investigated because of their chelating capability and their pharmacological applications[10] in several research fields. Heterocyclic hydrazines constitute an important class of biologically active drug molecules that have attracted the attention of medicinal chemists due to their anti-tubercular activity. Various synthetic methods with a variety of catalysts were reported for the synthesis of tosylhydrazines. Noda and Tanimori reported the solvent-free aqueous phase synthetic technique for the synthesis of various tosylhydrazines[11]. Keith and Gomez reported the synthesis of various tosylhydrazines by Mitsunobu reaction[12]. Various allylic hydrazones were synthesized by the diene and arylhydrazine in the presence of (*R*)-DTBM-Segphos-Pd(0) catalyst[13]. Chan *et al.*, reported the utilization of Rose Bengal catalyzed photochemical coupling of substituted 2-cycano-1-phenyl bromides with aryl hydrazine for the synthesis of various N-alkyl

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hydazones[14]. Various aryl tosylhydrazines were synthesized by the reduction of tosylhydrazines with pyridine-borne catalyst was reported by Kikugawa and Kawase[15]. Toth *et al.*,[16] reported the synthesis of anhydro-aldose tosylhydrazines from G-glycosy lmethyl carbenes. Spectral correlations were utilized for the prediction of geometry and configuration of organic compounds. The *s-cis* and *s-trans* conformers of the enones were assigned by infrared spectroscopy. The *E* and *Z* configurations of alkene derivatives were predicted by ^{1}H NMR spectroscopy. The characteristic spectral frequencies were utilized for the study of structure-activity relationships. Mayavel *et al.*, studied the spectral correlations and molecular docking of some bioactive *E*-imines[17]. Nalini *et al.*, studied the spectral QSAR and antifungal activities of some 2-(4-substituted phenyl)-imidazole-5-benzo ketones[18]. The spectral correlation study of some 3-((*E*)-3-substituted phenylacryloyl)benzonitriles was reported by Kamalkkannan *et al.*,[19] Manikandan *et al.*, studied the effect of substituents on the spectral frequencies of some (2-(*p*-substituted phenyl)-1H-benzo[d]imidazol-5-yl)methanones and (*E*)-N′-1-(substituted benzylidene) benzo hydrazides[20,21]. The presence of –HN-N=CH- group is responsible for their biological activities and they are more significantly considered in the development of novel drugs[22,23]. Hydrazine compounds contain and they have wide range of biological activities like anti-microbial[24,25], anti-analgesic[26], anti-inflammatory[27], anti-platelet[28], anti-tumoral activities[29], antiviral[30], antimalarial[31], anticancer[32], anti-tubercular[33], anticonvulsant[34], antiviral[35], antioxidant[36], anticancer[37], neuro-protective[38], herbicidal[39], antiproliferative[40], anti-convulsant[41] and anti-HIV[42] activities. The heterocyclic compounds containing hydrazone functionality play an important role in deciding the extent of their pharmacological properties[43]. Molecular docking analysis was utilized to find the ligand-protein interaction abilities in the drug molecules[44,45]. Numerous reports are available for the molecular docking analysis of various hydrazones along with bioactivities[17,46,47]. Raczuk *et al.*, investigated the molecular docking analysis of doxylamine-based hydrazine[48]. Molecular docking analysis of phthalidyl sulfonohydrazones was investigated by Ghosh *et al.*,[49] The protein-ligand interaction ability energy of aryl hydrazine and hydrazines was determined by molecular docking analysis and was reported by Gohil *et al.*,[50] In this research work authors synthesized various tosylhydrazines by thionyl chloride catalyzed condensation of tosylhydrazines and various acetophenones at RT stirring conditions. These tosylhydrazines were utilized for the study of the investigations of spectral correlations and molecular docking analysis.

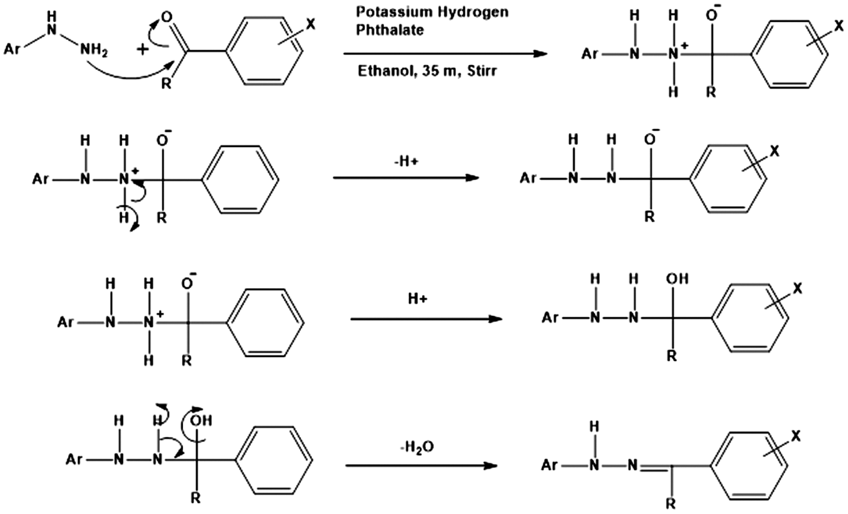
Results and Discussion

Authors made an effort to synthesize some hydrazide by condensation of aryl hydrazine with carbonyl compounds in the presence of potassium hydrogen phthalate under stirring at RT. As described in the experimental section, all hydrazides were synthesized and their yields are more than 85%. Here the electron-donating substituents gave more yields than the electron-withdrawing substituents. This condensation follows well-known nucleophilic addition followed by the removal of water afforded the hydrazides. The mechanistic pathway of this condensation is illustrated in Scheme 1. The first step is the hydrazine nucleophile attack to the carbonyl carbon, nitrogen gets a positive charge, and an oxide ion formed. The second step is the removal of a proton and the positive charge of the nitrogen atom was neutralized. The third step is the protonation of oxide ion to form hydroxide. The fourth step is the loss of water through β-elimination to afforded the hydrazide.

Influence of solvent

In this study, authors investigated the effect of influence on the yields of hydrazides **32-41** with a variety of solvents such as acetonitrile, ethanol, methanol, dioxane, dichloromethane, and dihydrofuran. The obtained yields with the solvents are given in Table 1. From Table 1, solvents like ethanol and methanol medium of the reaction gave more than 80% yields. The solvents such as acetonitrile, dioxane, dichloromethane, and tetrahydrofuran gave less than 80% yields. Overall, in all solvent mediums, the methyl substituents gave higher yields (72-84%). The aprotic solvents such as ethanol and methanol enhance the reactivity of the yields.

The synthesized hydrazides are characterized by their earlier reported physical constants, microanalysis and spectroscopic data. These data are well agreeable and supported for the formation of hydrazides.



Scheme 1 — The mechanistic pathway for the synthesis of hydrazide by potassium hydrogen phthalate assisted condensation of aryl hydrazine and carbonyl compounds

Table 1 — Influence of solvents on the yields of hydrazides (**32-41**)

Entry	X	ACN	EtOH	MeOH	DO	DCM	THF
32	H	76	89	86	79	68	70
33	4-Br	75	87	84	76	63	69
34	4-F	69	85	80	74	64	68
35	2-OH	73	86	81	75	65	65
36	3-OH	74	86	82	76	62	69
37	4-OH	75	87	84	74	64	69
38	4-I	76	86	80	75	63	68
39	4-CH_3	84	93	91	82	72	76
40	3-NO_2	72	85	81	70	64	66
41	4-NO_2	70	84	80	71	65	64

ACN: Acetonitrile, EtOH: Ethanol, MeOH: Methanol, DO: Dioxane, DCM: Dichloromethane, THF: Tetrahydrofuran

Spectral correlation study on N'-(1-(substituted phenyl) ethylidene)benzene sulfono hydrazides (32-41)

In the present study, the spectral linearity of synthesized N'-(1-(substituted phenyl) ethylidene) benzenesulfonohydrazide **(32-41)** has been studied for evaluating the substituent effects. The spectral data observed for the tosylhydrazines, UV λ_{max} (nm), infrared stretches (ν, cm^{-1}) C=N, $SO_{2(symm)}$, $SO_{2(asymm)}$, N-H, the proton chemical shifts δ (ppm) of N-H, CH_3, C-CH_3 and carbon chemical shifts of C=N, CH_3, C-CH_3 are correlated with various substituent constants[17-21].

UV spectral study

The measured absorption maxima (λ_{max}, nm) values of the synthesized N'-(1-(substituted phenyl) ethylidene) benzenesulfonohydrazide **(32-41)** compounds have been correlated with Hammett substituent constants and *F* and *R* parameters using single and multi-linear regression analysis[17-21]. The results of the statistical analysis are presented in Table 2. Hammett equation employed for the correlation analysis, involving the absorption maxima is as shown below in equation (1).

$$\lambda = \rho\sigma + \lambda_o \qquad \dots (1)$$

where λ_o is the frequency for the parent member of the series.

From Table 2, it is evident that the UV absorption maximum λ_{max} (nm) values of all N'-(1-(substituted phenyl) ethylidene) benzenesulfonohydrazide **(32-41)** compounds have shown poor correlations (r < 0.900) with Hammett substituent constants and *F* and *R* parameters. This is attributed to the weak polar, inductive, field and resonance effects of substituents for predicting the reactivity on the UV absorption

Table 2 — The results of statistical analysis of ultraviolet absorption maxima ($\lambda_{max,}$ nm), infrared absorptions (ν, cm^{-1}) and NMR chemical shifts (δ, ppm) of N'-(1-(substituted phenyl) ethylidene) benzenesulfonohydrazide compounds with Hammett constants σ, σ^+, σ_I, σ_R and *F* and *R* parameters

Frequency	Const.	r	I	ρ	s	N	Correlated derivatives
Correlation of infrared stretches							
C=N	σ	0.885	1522.70	–8.082	17.31	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	σ^+	0.800	1521.72	–0.192	17.62	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	σ_I	0.855	1533.78	–34.925	15.14	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	σ_R	0.813	1523.74	9.894	17.40	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	F	0.856	1535.31	–35.008	14.92	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	R	0.832	1524.93	8.824	17.13	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
N-H	σ	0.811	3211.11	–6.585	23.35	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	σ^+	0.804	3210.25	–1.745	23.48	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	σ_I	0.853	3227.01	–48.380	19.92	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	σ_R	0.823	3215.00	22.979	22.58	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	F	0.856	3229.39	–49.173	19.47	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	R	0.825	3214.91	12.659	22.74	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
SO$_{2Symm}$	σ	0.812	1183.10	1.866	6.14	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	σ^+	0.800	1183.32	–0.017	6.19	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	σ_I	0.855	1178.75	13.246	5.16	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	σ_R	0.826	1182.13	–5.830	5.97	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	F	0.856	1177.96	13.813	4.96	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	R	0.853	1182.04	–3.518	5.97	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
SO$_{2Asymm}$	σ	0.817	1326.06	29.155	65.13	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	σ^+	0.807	1329.88	8.309	66.17	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	σ_I	0.856	1279.21	146.040	54.63	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	σ_R	0.817	1321.19	–41.154	65.33	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	F	0.860	1271.45	149.837	52.85	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	R	0.820	1318.85	–29.584	64.90	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
Correlation of proton NMR chemical shifts							
N-H	σ	0.844	7.244	0.034	0.02	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	σ^+	0.873	7.249	0.037	0.02	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	σ_I	0.824	7.238	0.029	0.03	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	σ_R	0.833	7.256	0.037	0.02	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	F	0.823	7.237	0.027	0.03	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	R	0.867	7.264	0.045	0.02	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
C-H (Ar-CH$_3$)	σ	0.827	2.372	0.067	0.09	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	σ^+	0.854	2.384	0.088	0.08	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	σ_I	0.826	2.343	0.109	0.09	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	σ_R	0.819	2.395	0.068	0.09	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	F	0.829	2.339	0.107	0.09	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	R	0.906	2.430	0.136	0.07	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
C-H(CH$_3$)	σ	0.845	1.338	0.341	0.26	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	σ^+	0.827	1.384	0.137	0.29	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$

(*Contd.*)

Table 2 — The results of statistical analysis of ultraviolet absorption maxima (λ_{max}, nm), infrared absorptions (ν, cm^{-1}) and NMR chemical shifts (δ, ppm) of N'-(1-(substituted phenyl) ethylidene) benzenesulfonohydrazide compounds with Hammett constants σ, σ^+, σ_I, σ_R and *F* and *R* parameters

Frequency	Const.	r	I	ρ	s	N	Correlated derivatives
	σ_I	0.839	1.221	0.459	0.27	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH_3, 3-NO_2, 4-NO_2
	σ_R	0.836	1.459	0.386	0.28	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH_3, 3-NO_2, 4-NO_2
	F	0.832	1.239	0.362	0.28	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH_3, 3-NO_2, 4-NO_2
	R	0.823	1.436	0.154	0.29	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH_3, 3-NO_2, 4-NO_2
Correlation of C-13 NMR chemical shifts							
C=N	σ	0.808	152.47	8.329	5.76	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH_3, 3-NO_2, 4-NO_2
	σ^+	0.800	153.72	7.076	5.10	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH_3, 3-NO_2, 4-NO_2
	σ_I	0.824	150.71	8.013	6.34	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH_3, 3-NO_2, 4-NO_2
	σ_R	0.850	155.95	12.147	5.71	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH_3, 3-NO_2, 4-NO_2
	F	0.844	151.81	4.297	6.57	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH_3, 3-NO_2, 4-NO_2
	R	0.812	156.10	7.245	5.74	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH_3, 3-NO_2, 4-NO_2
C-C (Ar-CH_3)	σ	0.814	22.71	–1.133	3.09	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH_3, 3-NO_2, 4-NO_2
	σ^+	0.842	22.50	–2.203	2.83	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH_3, 3-NO_2, 4-NO_2
	σ_I	0.811	23.07	–1.443	3.11	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH_3, 3-NO_2, 4-NO_2
	σ_R	0.823	22.05	–2.587	3.04	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH_3, 3-NO_2, 4-NO_2
	F	0.813	23.17	–1.531	3.10	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH_3, 3-NO_2, 4-NO_2
	R	0.870	20.86	–4.723	2.21	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH_3, 3-NO_2, 4-NO_2
C-C(CH_3)	σ	0.814	14.34	–0.537	1.51	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH_3, 3-NO_2, 4-NO_2
	σ^+	0.807	14.28	0.176	1.52	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH_3, 3-NO_2, 4-NO_2
	σ_I	0.821	14.72	–1.275	1.49	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH_3, 3-NO_2, 4-NO_2
	σ_R	0.831	14.42	0.715	1.51	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH_3, 3-NO_2, 4-NO_2
	F	0.836	14.91	–1.632	1.46	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH_3, 3-NO_2, 4-NO_2
	R	0.830	14.52	0.681	1.49	10	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH_3, 3-NO_2, 4-NO_2

r = Correlation coefficient; I = Intercept; ρ = Slope; s = Standard deviation; n = Number of correlated derivatives

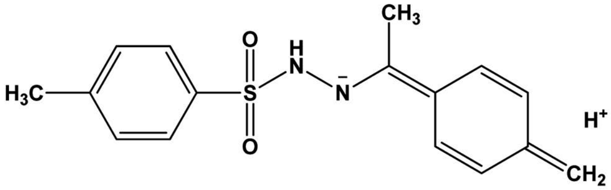


Fig. 1 — The resonance-conjugative structure

through resonance as per the conjugative structure as shown in Fig. 1.

All the correlations have shown positive ρ values except the *R* parameter. This indicates the operation of normal substituent effect with respect to UV absorption maximum (λ_{max}, nm) values in all N'-(1-(substituted phenyl) ethylidene) benzenesulfonohydrazide compounds.

All the single parameter correlations failed for the UV absorption maximum (λ_{max}, nm) values with Hammett constants and *F* and *R* parameters, it is decided to go for multi-regression analysis with Swain-Lupton's[51] parameters. While seeking the multi-regression analysis there is satisfactory correlations are observed as shown in the following equations (2) and (3).

$$\lambda max(nm) = 277.65(\pm 9.237)+11.594(\pm 1.085)\sigma_I+2.246(\pm 0.379)\,\sigma_R \quad \ldots (2)$$

$$(r = 0.924\ n = 10, P > 90\%)$$

$$\lambda max\ (nm) = 276.70(\pm 9.270) + 6.128(\pm 1.985)F-5.802(\pm 0.279)\,R \quad \ldots (3)$$

$$(r = 0.923, n = 10, P > 90\%)$$

IR spectral correlation study

In infrared spectral correlations, the Hammett equation employed for the correlation analysis, involving the absorption maxima is as shown below in equation (4).

$$\nu = \rho\sigma + \nu_o \qquad \dots (4)$$

where υ_o is the frequency for the parent member of the series.

The measured infrared frequencies (ν, cm^{-1}) such as N-H, $SO_{2(symm)}$, $SO_{2(asymm)}$, and C=N values are correlated[17-21] with Hammett substituent constants and *F* and *R* parameters using single and multi-linear regression analysis. The results of the statistical correlation analysis are presented in Table 2.

Correlation of ν N-H (cm^{-1})

From Table 2, it is evident that the IR frequency ν N-H(cm^{-1}) values of all N'-(1-(substituted phenyl) ethylidene) benzenesulfonohydrazide **(32-41)** compounds have shown poor correlations (r < 0.900) with Hammett substituent constants and *F* and *R* parameters. This is attributed to the weak polar, inductive, field and resonance effects of substituents for predicting the reactivity on the IR frequency νN-H(cm^{-1}) through resonance as per the conjugative structure as shown in Fig. 1.

All the correlations have shown positive ρ values except σ_R constant and *R* parameter. This indicates the operation of normal substituent effect with respect to IR frequency νN-H (cm^{-1}) values in all N'-(1-(substituted phenyl) ethylidene) benzenesul fonohydrazide **(32-41)** compounds.

Correlation of $SO_{2(symm)}$ stretches

From Table 2, it is evident that the IR frequency $\nu SO_{2\,symm}$(cm^{-1}) values of all N'-(1-(substituted phenyl) ethylidene)benzenesulfonohydrazide **(32-41)** compounds have shown poor correlations (r < 0.900) with Hammett substituent constants and *F* and *R* parameters. This is attributed to the weak polar, inductive, field and resonance effects of substituents for predicting the reactivity on the IR frequency νSO_{2symm}(cm^{-1}) through resonance as per the conjugative structure as shown in Fig. 1. All the correlations have shown positive ρ values except σ^+, σ_R constants and *R* parameter. This indicates the operation of normal substituent effect with respect to IR frequency νSO_{2symm}(cm^{-1}) values in all N'-(1-(substituted phenyl) ethylidene) benzenesul fonohydrazide **(32-41)** compounds.

Correlation of $SO_{2(asymm)}$ stretches

From Table 2, it is evident that the IR frequency $\nu SO_{2(asymm)}$ (cm^{-1}) values of all N'-(1-(substituted phenyl) ethylidene)benzenesulfonohydrazide **(32-41)** compounds have shown poor correlations (r < 0.900) with Hammett substituent constants and *F* and *R* parameters. This is attributed to the weak polar, inductive, field and resonance effects of substituents for predicting the reactivity on the IR frequency all N'-(1-(substituted phenyl) ethylidene) benzenesul fonohydrazide **(32-41)** $SO_{2\ (asymm)}$ (cm^{-1}) through resonance as per the conjugative structure as shown in Fig. 1. All the correlations have shown positive ρ values except σ_R constant and *R* parameter. This indicates the operation of normal substituent effect with respect to IR frequency $\nu SO_{2(asymm)}$(cm^{-1}) values in all substituted N'-(1-(substituted phenyl) ethylidene) benzenesul fonohydrazide **(32-41)** compounds. All the single parameter correlations failed for the infrared frequencies (cm^{-1}) of νN-H, $\nu SO_{2(symm)}$, $\nu SO_{2(asymm)}$ with Hammett constants and *F* and *R* parameters, it is decided to go for multi-regression analysis with Swain-Lupton's[51] parameters. While seeking the multi regression analysis there is satisfactory correlations are observed as shown in the following equations (5) to (10).

$$\nu N\text{-}H(cm^{-1}) = 3237.45(\pm 12.683)-57.670(\pm 6.202)\,\sigma_I + 35.495(\pm 3.861)\,\sigma_R \quad \dots (5)$$
$$(r = 0.967,\ n = 10,\ P > 95\%)$$

$$\nu N\text{-}H(cm^{-1}) = 3235.99\,(\pm 13.215)-51.726(\pm 2.639)\,F+15.452(\pm 1.654)\,R \quad \dots (6)$$
$$(r = 0.963,\ n = 10,\ P > 95\%)$$

$$\nu SO_{2(symm)}(cm^{-1}) = 1176.03(\pm 3.286) +15.662(\pm 6.789)\,\sigma_I-9.229(\pm 1.183)\,\sigma_R \quad \dots (7)$$
$$(r = 0.968,\ n = 10,\ P > 95\%)$$

$$\nu SO_{2(symm)}(cm^{-1}) = 1176.12(\pm 3.320)+ 14.524(\pm 6.441)F -4.302(\pm 1.681)\,R \quad \dots (8)$$
$$(r = 0.967,\ n = 10,\ P > 95\%)$$

$$\nu SO_{2(asymm)}(cm^{-1}) = 1256.48(\pm 36.762) +166.256 (\pm 75.950)\,\sigma_I -77.237(\pm 6.163)\,\sigma_R \quad \dots (9)$$
$$(r = 0.956,\ n = 10,\ P > 95\%)$$

$$\nu SO_{2(asymm)}(cm^{-1}) = 1255.22(\pm 36.376) +156.118 (\pm 7.573)\,F-38.011(\pm 4.336)\,R \quad \dots (10)$$
$$(r = 0.966,\ n = 10,\ P > 95\%)$$

NMR spectral study

In nuclear magnetic resonance spectra, the proton and the ^{13}C chemical shifts (δ) depend on the electronic environment of the nuclei concerned. The assigned chemical shifts (ppm) have been correlated with reactivity parameters using Hammett equation[17-21] in the form of

$$\delta = \rho\sigma + \delta_o \qquad \text{... (11)}$$

where δ_o is the frequency for the parent member of the series.

^{1}H NMR Spectral Correlations of N-H chemical shifts

From Table 2, the assigned N-H chemical shifts (δ ppm) values of N'-(1-(substituted phenyl) ethylidene) benzenesulfonohydrazide **(32-41)** compounds have shown poor correlations ($r < 0.900$) with Hammett substituent constants and *F* and *R* parameters. This is attributed to the weak polar, inductive, field and resonance effects of substituents predicting the reactivity on the chemical shifts through resonance as per the conjugative structure as shown in Fig. 1. All the correlations have shown positive ρ values. This indicates the operation of normal substituent effect with respect to NMR spectral values (ppm) values in all substituted N'-(1-(substituted phenyl) ethylidene) benzenesul fonohydrazide **(32-41)** compounds.

^{1}H NMR Spectral Correlations of C-H(Ar-CH$_3$) chemical shifts

From Table 2, the assigned C-H(Ar-CH$_3$) chemical shifts (δ, ppm) values of N'-(1-(substituted phenyl) ethylidene)benzenesulfonohydrazide **(32-41)** compounds have shown poor correlations ($r < 0.900$) with Hammett substituent constants and *F* and *R* parameters. This is attributed to the weak polar, inductive, field, and resonance effects of substituents predicting the reactivity on the chemical shifts through resonance as per the conjugative structure as shown in Fig. 1. All the correlations have shown positive ρ values. This indicates the operation of normal substituent effect with respect to NMR spectral values (ppm) values in all N'-(1-(substituted phenyl) ethylidene)benzenesulfonohydrazide **(32-41)** compounds.

^{1}H NMR Spectral Correlations of C-H(C-CH$_3$)

From Table 2, the assigned C-H(C-CH$_3$) chemical shifts (δ, ppm) values of N'-(1-(substituted phenyl) ethylidene) benzenesulfonohydrazide **(32-41)** compounds have shown poor correlations ($r < 0.900$) with Hammett substituent constants and *F* and *R* parameters. This is attributed to the weak polar, inductive, field and resonance effects of substituents predicting the reactivity on the chemical shifts through resonance as per the conjugative structure as shown in Fig. 1. All the correlations have shown positive ρ values. This indicates the operation of normal substituent effect with respect to NMR spectral values (ppm) values in all N'-(1-(substituted phenyl) ethylidene) benzenesulfonohydrazide **(32-41)** compounds.

All the single parameter correlations failed for the ^{1}H NMR spectral chemical shifts values with Hammett constants and *F* and *R* parameters, it is decided to go for multi regression analysis with Swain-Lupton's[51] parameters. While seeking the multi-regression analysis there is satisfactory correlations are observed as shown in the following equations (12) to (17).

$$\delta\text{N-H(ppm)} = 7.240(\pm0.021) + 0.021(\pm0.003)\sigma_I + 0.032(\pm0.009)\,\sigma_R \qquad \text{… (12)}$$

$$(r = 0.937,\ n = 10,\ P > 90\%)$$

$$\delta\text{N-H(ppm)} = 7.256(\pm0.016) + 0.020(\pm0.001)F + 0.043(\pm0.018)\,R \qquad \text{… (13)}$$

$$(r = 0.969,\ n = 10,\ P > 95\%)$$

$$\delta\text{Ar-CH}_3\text{(ppm)} = 2.357(\pm0.068) + 0.096(\pm0.041)\sigma_I + 0.047(\pm0.028)\,\sigma_R \qquad \text{… (14)}$$

$$(r = 0.931,\ n = 10,\ P > 90\%)$$

$$\delta\text{Ar-CH}_3\text{(ppm)} = 2.395(\pm0.052) + 0.085(\pm0.001)F + 0.131(\pm0.057)\,R \qquad \text{… (15)}$$

$$(r = 0.968,\ n = 10,\ P > 95\%)$$

$$\delta\text{C-H(CH}_3\text{)(ppm)} = 1.311(\pm0.194) + 0.379(\pm0.002)\,\sigma_I + 0.304(\pm0.005)\sigma_R \qquad \text{… (16)}$$

$$(r = 0.947,\ n = 10,\ P > 90\%)$$

$$\delta\text{C-H(CH}_3\text{)(ppm)} = 1.297(\pm0.204) + 0.339\,(\pm0.096)F + 0.136(\pm0.026)R \qquad \text{… (17)}$$

$$(r = 0.938,\ n = 10,\ P > 90\%)$$

^{13}C NMR Spectral Correlation

^{13}C NMR Spectral Correlations of C=N

From Table 2, the assigned C=N chemical shifts (δ ppm) values of N'-(1-(substituted phenyl) ethylidene)benzenesulfonohydrazide **(32-41)** compoundds have shown poor correlations ($r < 0.900$) with Hammett substituent constants and *F* and *R* parameters. This is attributed to the weak polar, inductive, field and resonance effects of substituents predicting the reactivity on the chemical shifts through resonance as per the conjugative structure as shown in Fig. 1. All the correlations have shown positive ρ values. This indicates the operation of normal substituent effect with respect to NMR spectral values (ppm) values in all N'-(1-(substituted phenyl) ethylidene) benzenesulfonohydrazide **(32-41)** compounds.

^{13}C NMR Spectral Correlations of C-C(Ar-CH$_3$)

From Table 2, the assigned C-C(Ar-CH$_3$) chemical shifts (δ ppm) values of (*E*)-2-(1-phenylethylidene)-1-tosylhydrazine compounds have shown poor correlations ($r < 0.900$) with Hammett substituent constants and *F* and *R* parameters. This is attributed to the weak polar, inductive, field and resonance effects of substituents predicting the reactivity on the chemical shifts through resonance as per the conjugative structure as shown in Fig. 1. All the correlations have shown negative ρ values. This indicates the operation of reverse substituent effect with respect to NMR spectral values (ppm) values in all N'-(1-(substituted phenyl) ethylidene) benzenesulfonohydrazide **(32-41)** compounds.

^{13}C NMR Spectral Correlations of C-C(C-CH$_3$)

From Table 2, the assigned C-C(C-CH$_3$) chemical shifts (δ ppm) values of (*E*)-2-(1-phenylethylidene)-1-tosylhydrazine compounds have shown poor correlations ($r < 0.900$) with Hammett substituent constants and *F* and *R* parameters. This is attributed to the weak polar, inductive, field and resonance effects of substituents predicting the reactivity on the chemical shifts through resonance as per the conjugative structure as shown in Fig. 1. All the correlations have shown positive ρ values except σ, σ_I, and *F* parameters. This indicates the operation of normal substituent effect with respect to NMR spectral values (ppm) in all N'-(1-(substituted phenyl) ethylidene) benzenesulfonohydrazide **(32-41)** compounds.

All the single parameter correlations failed for the ^{13}C NMR spectral chemical shifts values with Hammett constants and *F* and *R* parameters, it is decided to go for multi-regression analysis with Swain-Lupton's[51] parameters. While seeking the multi-regression analysis there is satisfactory correlations are observed as shown in the following equations (18) to (23).

$$\delta C{=}N(\text{ppm}) = 153.95(\pm 4.069) + 5.125(\pm 1.408)\sigma_I + 11.035(\pm 1.657)\,\sigma_R \quad \ldots (18)$$

$$(r = 0.962,\ n = 10,\ P > 95\%)$$

$$\delta C{=}N(\text{ppm}) = 154.82(\pm 4.153) + 3.127(\pm 1.058)\,F + 7.076(\pm 1.605)\,R \quad \ldots (19)$$

$$(r = 0.947,\ n = 10,\ P > 90\%)$$

$$\delta C\text{-}C(Ar\text{-}CH_3)(\text{ppm}) = 22.36\ (\pm 2.219) - 0.811\ (\pm 0.085)\,\sigma_I - 2.411\ (\pm 1.175)\,\sigma_R \quad \ldots (20)$$

$$(r = 0.924,\ n = 10,\ P > 90\%)$$

$$\delta C\text{-}C(Ar\text{-}CH_3)(\text{ppm}) = 21.17(\pm 1.612) - 0.757(\pm 0.028)\,F - 4.682(\pm 1.788)R \quad \ldots (21)$$

$$(r = 0.970,\ n = 10,\ P > 95\%)$$

$$\delta C\text{-}C(CH_3)(\text{ppm}) = 15.02(\pm 1.069) - 1.551(\pm 0.008)\sigma_I + 1.052(\pm 0.011)\sigma_R \quad \ldots (22)$$

$$(r = 0.928,\ n = 10,\ P > 90\%)$$

$$\delta C\text{-}C(CH_3)(\text{ppm}) = 15.24(\pm 1.036) - 1.760(\pm 0.010)F + 0.776(\pm 0.149)R \quad \ldots (23)$$

$$(r = 0.931,\ n = 10,\ P > 90\%)$$

Results of molecular docking analysis

The docking results of different substituted azides **(1-41)** these synthesized ligands were docked with Ubiquitin-like protein activation complex protein inhibitor 2NVU and revealed the binding energy values ranging from -5.0 to -7.8kcal/mol. These binding energy values are listed in Table 3.

Table 3 — Binding energy values of azine compounds (**1-41**)

Entry	X	Binding energy (ΔG) kcal/mol
	(*E*)-N'-(substituted benzylidene)benzohydrazides	
1	H	–5.45
2	3-Br	–5.77
3	2-Cl	–5.75
4	4-Cl	–5.5
5	4-F	–5.01
6	3-OH	–5.9
7	4-OH	–5.1
8	4-CH$_3$	–5.05
9	2-NO$_2$	–5.0
10	3-NO$_2$	–5.4
	(*E*)-N'-(1-(substituted phenyl)ethylidene)benzohydrazides	
11	H	–5.48
12	4-Br	–7.8
13	4-F	–5.21
14	2-OH	–5.16
15	3-OH	–4.62
16	4-OH	–5.5
17	4-I	–6.01
18	4-OCH$_3$	–5.0
19	4-CH$_3$	–5.89

(*Contd.*)

Table 3 — Binding energy values of azine compounds (**1-41**) (*Contd.*)

Entry	X	Binding energy (ΔG) kcal/mol
20	2-NO_2	–5.48
21	4-NO_2	5.53
	(*E*)-N'-(substitutedbenzylidene)-4-methylbenzenesulfonohydrazides	
22	H	–6.45
23	3-Br	–5.66
24	2-Cl	–5.83
25	4-Cl	–5.88
26	4-F	–5.70
27	3-OH	–5.96
28	4-OH	–5.95
29	4-CH_3	–5.91
30	2-NO_2	–5.42
31	3-NO_2	–4.82
	(*E*)-N'-(1-(substituted phenyl)ethylidene)-4-methylbenzenesulfonohydrazides	
32	H	–5.83
33	4-Br	–5.98
34	4-F	–5.49
35	2-OH	–5.37
36	3-OH	–5.88
37	4-OH	–5.39
38	4-I	–5.61
39	4-CH_3	–5.86
40	3-NO_2	–5.35
41	4-NO_2	–5.05

The compound **2** shows binding energy values -5.77 kcal/mol and also shows amino acid residues such as one Hydrogen bond interaction GLN A:130 (Glutamine), two Hydrophobic bond interactions ALA A:487, VAL A:445 (Alanine, valine). The compound **6** shows binding energy values -5.9 kcal/mol and also shows amino acid residues such as two Hydrophobic bond interactions LEU C:112, LEU C:135 (Leucine), one Hydrogen bond interaction ASN C:140 (Asparagine). The compound **12** shows binding energy values -7.8kcal/mol and also shows amino acid residues such as three Hydrophobic bond interactions LEU C:137, LEU J:8, PRO C:44 (Leucine, Proline), three electrostatic bond interaction ASP C:67, LYS C:45, LYS J:6 (Aspartic acid, Lysine). The compound **17** shows binding energy values -6.01kcal/mol and also shows amino acid residues such as three electrostatic bond interactions GLU J:34, LYS J:11, LYS J:33 (Glutamic acid, Lysine). The compound **33** shows binding energy values -5.98kcal/mol and also shows amino acid residues such as five Hydrophobic bond interactions ALA C:49, ALA B:2345, LEU B:2162, LEU B:2435, PRO B:2344 (Alanine, Leucine, Proline). The compound **36** shows binding energy values -5.88kcal/mol and also shows amino acid residues such as one Hydrophobic bond interaction PHE B:2044 (Phenylalanine), one Hydrogen bond interaction GLN B:2043 (Glutamine), one electrostatic bond interaction ASP B:2047 (Aspartic acid). The compound **22** shows binding energy values -6.45kcal/mol and also shows amino acid residues such as two Hydrophobic bond interactions PRO A:282, LEU A:183 (Proline, Leucine), two Hydrogen bond interaction GLN A:280, THR A:278 (Glutamine, Threonine), one electrostatic bond interaction ASP A:186 (Aspartic acid). The compound **27** shows binding energy values -5.96kcal/mol and also shows amino acid residues such as two Hydrophobic bond interactions LEU A:180, LEU A:183 (Leucine), two Hydrogen bond interaction GLN A:280, THR A:274 (Glutamine, Threonine). The two- and three-dimensional docking poses of compounds are shown in Table 4.

Experimental Section

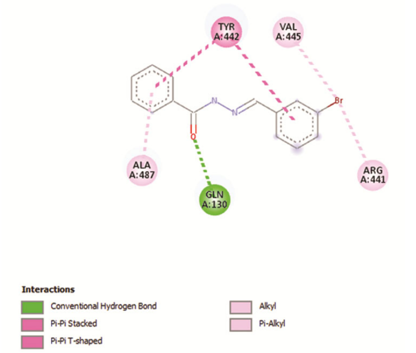
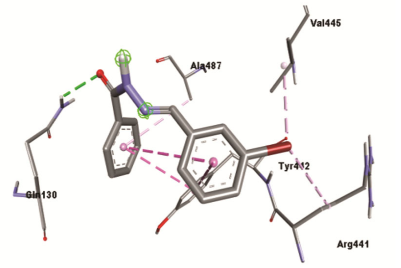
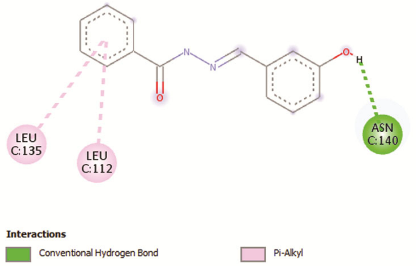
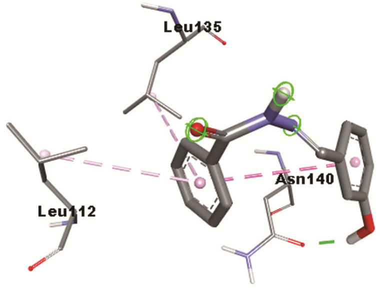
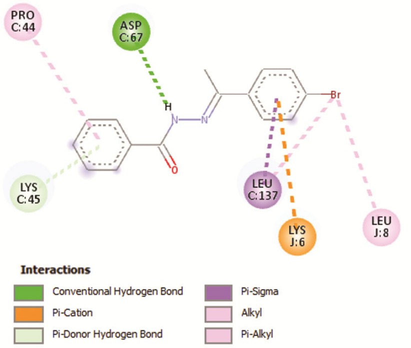
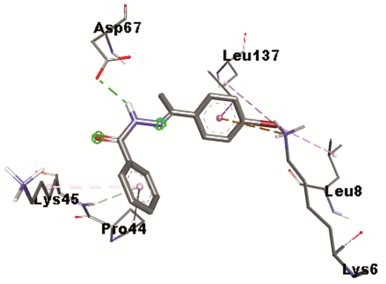
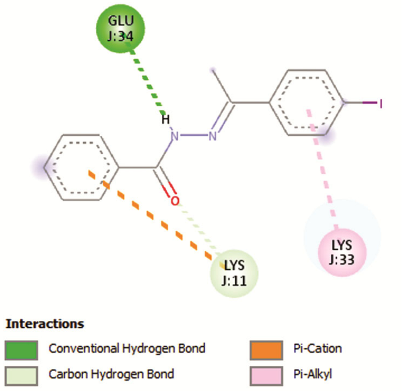
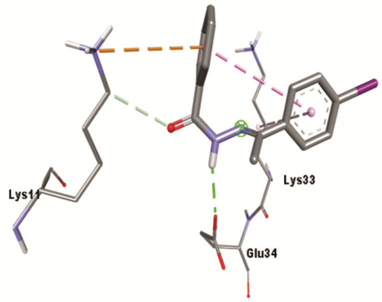
Materials and Methods

All chemicals are procured from the chemical company of Aldrich Bangalore. To detect the melting points of all prepared tosylhydrazines are found in Suntex melting point apparatus with capillary tubes. The ultraviolet spectra of the tosylhydrazines synthesized have been noted using a double beam-ELICO BL222 Bio-Spectrophotometer. Fourier transform infrared spectra (KBr, 4000-400 cm^{-1}) have been documented on the AVATAR-300 FT-IR spectrophotometer. The BRUKER-500MHz NMR spectrometers were used for noted proton and ^{13}C spectra in $CDCl_3$ solvent using tetramethylsilane as the internal standard. Micro analyses of all compounds were performed in the Thermofinnigan CHN analyzer.

General Procedure for synthesis of aryl hydrides

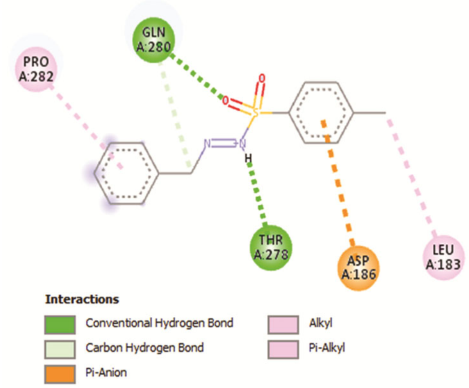
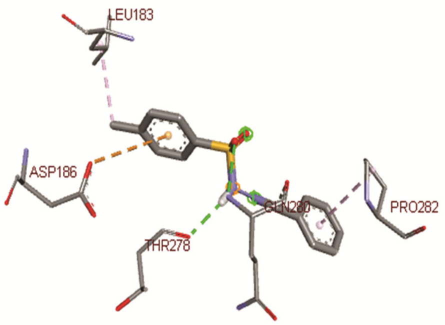
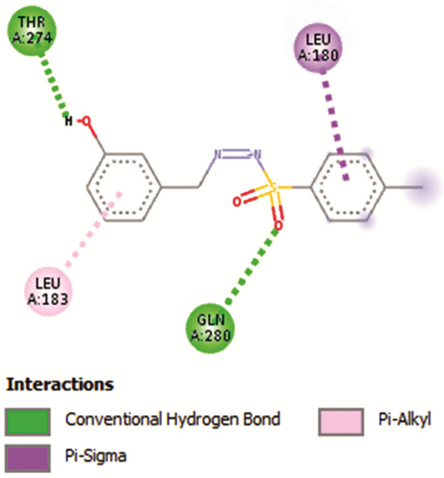
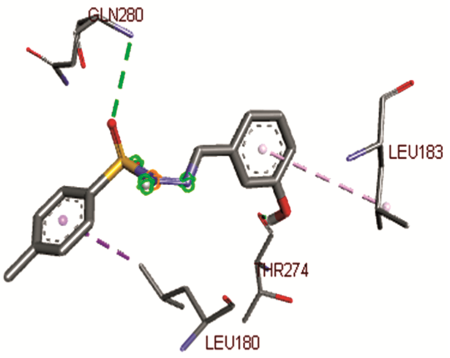
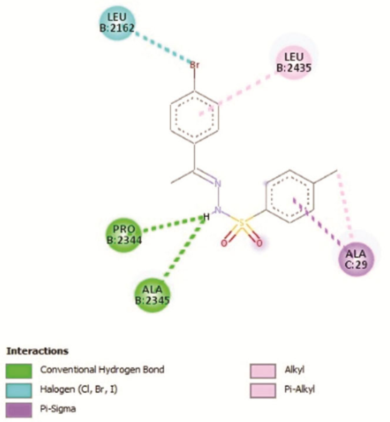
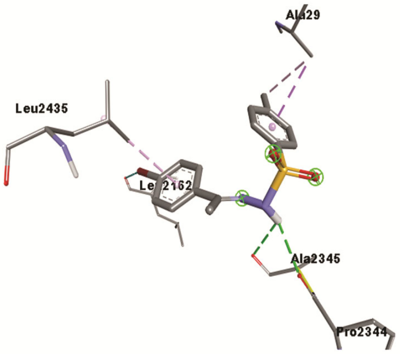
An equal molar volume of benzoyl hydrazine or tosylsulfonylhydrazine, substituted benzaldehyde or acetophenones, 3 mL of 5M potassium hydrogen phthalate and 20 mL of ethanol were stirred in a magnetic stirrer for 35 minutes (Scheme 2). The completion of the reaction was monitored by thin-layer chromatography, the mixture was allowed to

Table 4 — The 2D and 3D images of best-docked azine compounds

Entry	2D Image	3D Image	Binding energy (ΔG)kcal/mol
	(*E*)-N'-(substituted benzylidene)benzohydrazides		
2			–5.77
6			–5.9
	(*E*)-N'-(1-(substitutedphenyl)ethylidene)benzohydrazides		
12			–7.8
17			–6.01

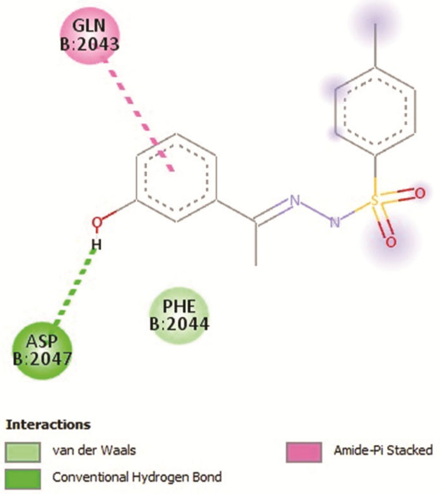
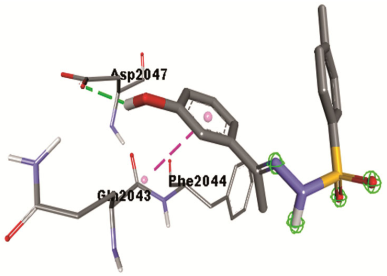
(*Contd.*)

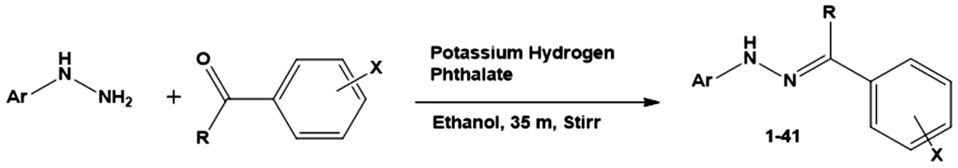
Table 4 — The 2D and 3D images of best-docked azine compounds (*Contd.*)

Entry	2D Image	3D Image	Binding energy (ΔG)kcal/mol
	(*E*)-N'-(substituted benzylidene)-4-methylbenzenesulfonohydrazide		
22			–6.45
27			–5.96
	(*E*)-N'-(1-(substituted phenyl)ethylidene)-4-methylbenzenesulfonohydrazides		
33			–5.98

(*Contd.*)

Table 4 — The 2D and 3D images of best-docked azine compounds (*Contd.*)

Entry	2D Image	3D Image	Binding energy (ΔG)kcal/mol
36			–5.88



Entry	Ar	R	X
1-10	Benzoyl	H	H, 3-Br, 2-Cl, 4-Cl, 4-F, 3-OH, 4-OH, 4-CH_3, 2-NO_2, 3-NO_2
11-21	Benzoyl	CH_3	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
22-31	Tosylsulfonyl	H	H, 3-Br, 2-Cl, 4-Cl, 4-F, 3-OH, 4-OH, 4-CH_3, 2-NO_2, 3-NO_2
32-41	Tosylsulfonyl	CH_3	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-CH_3, 3-NO_2, 4-NO_2

Scheme 2 — Synthesis of aryl hydrazides

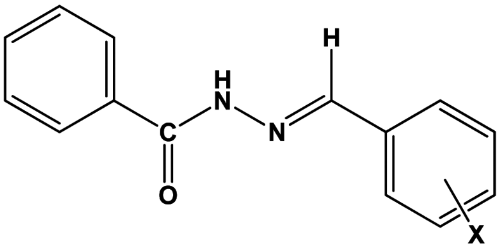
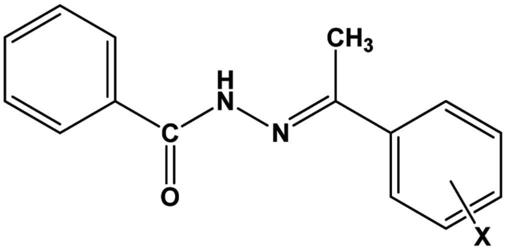
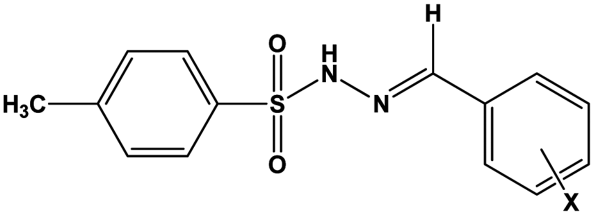
stand for 20 minutes. The product was filtered at the pump, washed with water and brine and dried well. The crude was recrystallized by absolute ethanol, dried and kept in a desiccator.

Synthesized aryl hydrazides are characterized by their physical constants, microanalysis and spectroscopic data. The physical constants, yields, time and microanalysis of the hydrazides are tabulated in Table 5. The infrared and NMR spectral frequencies of tosyl sulfonyl hydrazides (**32-41**) are tabulated in Table 6.

Molecular Docking analysis

The human protein related to breast cancer Ubiquitin-like protein activation complex (PDB ID: 2NVU) was downloaded from the online data established by the RCSB Protein Data Bank[44,45,52]. The ligand molecules were downloaded into pdb format using Chem Draw 3D software. The molecular docking of the selected ligands and protein was analyzed using Auto Dock Vina software (version 4.2). Likewise, the ligand molecules in pdb format were charged with Gasteiger-Marsili partial charges and converted into pdbqt format. The protein structure obtained from the Protein Data Bank (PDB) undertook the removal of water molecules. Later, polar hydrogen atoms were completely added to the PDB protein. Partial atomic Kollman charges were added. Lastly, the hydrogenated-charged proteins in the pdb files were successively transformed into the pdbqt format using Auto Dock Tools (version 1.5.7). Dissimilar-sized grid boxes at (X, Y and Z

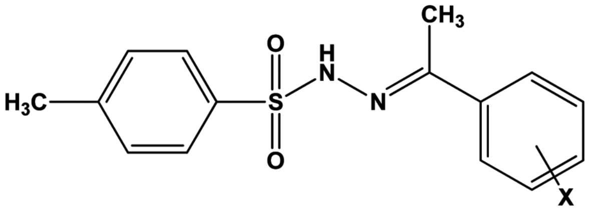
Table 5 — Physical constants, yields, time and microanalysis of the hydrazides

Entry	X	M.F.	M. W.	Time (m)	Yield (%)	m.p. (°C)
						
1	H	$C_{14}H_{12}N_2O$	224	22	92	166-167(165-166) (Ref. 20)
2	3-Br	$C_{14}H_{11}BrN_2O$	303	25	89	140-141(138-139) (Ref. 20)
3	2-Cl	$C_{14}H_{11}ClN_2O$	258	24	88	142-143(141-142) (Ref. 20)
4	4-Cl	$C_{14}H_{11}ClN_2O$	258	23	88	147-148(147-148) (Ref. 20)
5	4-F	$C_{14}H_{11}FN_2O$	242	29	85	150-151(149-150) (Ref. 20)
6	3-OH	$C_{14}H_{12}N_2O_2$	240	26	86	162-163(163-164) (Ref. 20)
7	4-OH	$C_{14}H_{12}N_2O_2$	240	26	85	162-163(161-162) (Ref. 20)
8	4-CH$_3$	$C_{15}H_{14}N_2O$	238	24	93	121-122(120-121) (Ref. 20)
9	2-NO$_2$	$C_{14}H_{11}N_3O_3$	269	35	87	172-173(173-174) (Ref. 20)
10	3-NO$_2$	$C_{14}H_{11}N_3O_3$	269	28	86	166-167(165-166) (Ref. 20)
						
11	H	$C_{15}H_{14}N_2O$	238	27	90	140-141(141-142) (Ref. 21)
12	4-Br	$C_{15}H_{13}BrN_2O$	316	24	89	145-146(146-147) (Ref. 21)
13	4-F	$C_{15}H_{13}FN_2O$	256	35	88	141-142(139-140) (Ref. 21)
14	2-OH	$C_{15}H_{14}N_2O_2$	254	26	87	135-136(134-135) (Ref. 21)
15	3-OH	$C_{15}H_{14}N_2O_2$	254	27	87	121-122(119-120) (Ref. 21)
16	4-OH	$C_{15}H_{14}N_2O_2$	254	26	85	169-170(168-169) (Ref. 21)
17	4-I	$C_{15}H_{13}IN_2O$	364	32	86	183-184(182-183) (Ref. 21)
18	4-OCH$_3$	$C_{16}H_{16}N_2O_2$	268	25	93	141-142(142-143) (Ref. 21)
19	4-CH$_3$	$C_{16}H_{16}N_2O$	252	25	91	137-138(138-139) (Ref. 21)
20	3-NO$_2$	$C_{16}H_{16}N_3O_3$	283	34	86	109-110(108-109) (Ref. 21)
21	4-NO$_2$	$C_{16}H_{16}N_3O_3$	283	31	85	135-136(136-137) (Ref. 21)
						
22	H	$C_{14}H_{14}N_2O_2S$	274	25	93	99-100(98-99) (Ref. 24)
23	3-Br	$C_{14}H_{13}BrN_2O_2S$	353	26	89	134-135(135-136) (Ref. 24)
24	2-Cl	$C_{14}H_{13}ClN_2O_2S$	308	26	88	122-123(124-125) (Ref. 24)

(*Contd.*)

Table 5 — Physical constants, yields, time and microanalysis of the hydrazides (*Contd.*)

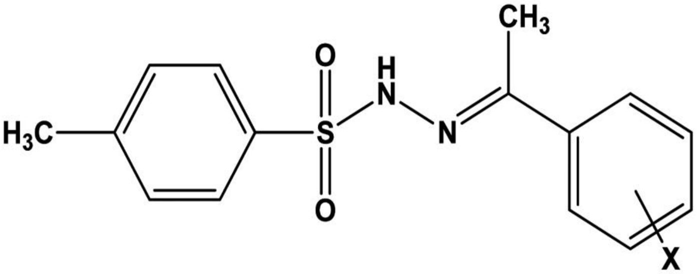
Entry	X	M.F.	M. W.	Time (m)	Yield (%)	m.p. (°C)
25	4-Cl	$C_{14}H_{13}ClN_2O_2S$	308	28	90	120-121(118-119) (Ref. 24)
26	4-F	$C_{14}H_{13}FN_2O_2S$	292	32	85	125-126(124-125) (Ref. 24)
27	3-OH	$C_{14}H_{14}N_2O_3S$	290	35	86	127-128(129-130) (Ref. 24)
28	4-OH	$\mathrm{C14H14N2O_3S}$	290	35	87	129-130(127-128) (Ref. 24)
29	4-CH_3	$C_{15}H_{16}N_2O_2S$	288	30	94	128-129(127-128) (Ref. 24)
30	2-NO_2	$C_{14}H_{13}N_3O_4S$	319	34	86	123-124(122-123) (Ref. 24)
31	3-NO_2	$C_{14}H_{13}N_3O_4S$	319	33	86	111-112(110-111) (Ref. 24)



32	H	$C_{15}H_{16}N_2O_2S$	288	26	89	142-143(141-142) (Ref. 25)
33	4-Br	$C_{15}H_{15}BrN_2O_2S$	366	27	87	100-101(99-100) (Ref. 25)
34	4-F	$C_{15}H_{15}FN_2O_2S$	306	29	85	63-64(61-62) (Ref. 25)
35	2-OH	$C_{15}H_{16}N_2O_3S$	304	28	86	114-115(112-113) (Ref. 25)
36	3-OH	$C_{15}H_{16}N_2O_3S$	304	30	86	133-134(132-133) (Ref. 25)
37	4-OH	$C_{15}H_{16}N_2O_3S$	304	34	87	148-149(147-148) (Ref. 25)
36	4-I	$C_{15}H_{15}IN_2O_2S$	413	28	86	131-132(129-130) (Ref. 25)
39	4-CH_3	$C_{16}H_{18}N_2O_2S$	302	25	93	120-121(118-119) (Ref. 25)
40	3-NO_2	$C_{15}H_{15}N_3O_4S$	333	34	85	138-139(137-138) (Ref. 25)
41	4-NO_2	$C_{15}H_{15}N_3O_4S$	333	30	87	126-127(125-126) (Ref. 25)

Table 6 — The ultraviolet maximum absorptions (λ max), FT-IR frequencies (ν, cm-1), and NMR Chemical shifts (δ, ppm) of tosyl hydrazides (32-41)

Entry	X	UV	IR				
			CH	SO2 (sym)	SO2 (assym)	NH	C=N



32	H	263.6	2899.01	1166.91	1361.72	3271.29	1568.11
33	4-Br	296.4	2897.08	1186.24	1371.35	3188.31	1519.93
34	4-F	263.7	2918.30	1186.23	1373.36	3201.87	1519.92
35	2-OH	278.9	2918.30	1184.25	1373.35	3203.73	1519.94
36	3-OH	296.3	2918.30	1184.27	1303.84	3203.72	1519.90
37	4-OH	284.8	2962.66	1184.23	1342.43	3207.65	1515.13
38	4-I	276.0	2910.58	1186.26	1342.42	3205.63	1514.15
39	4-CH3	280.2	2974.23	1184.24	1342.41	3207.64	1515.23
40	3-NO2	276.4	2991.59	1186.28	1342.44	3205.61	1514.10
41	4-NO2	296.6	2995.45	1184.26	1342.47	3207.66	1510.89

(*Contd.*)

Table 6 — The ultraviolet maximum absorptions (λ max), FT-IR frequencies (ν, cm-1), and NMR Chemical shifts (δ, ppm) of tosyl hydrazides (32-41) (*Contd.*)

Entry	X	UV			IR		
			CH	SO2 (sym)	SO2 (assym)	NH	C=N
				^{1}H NMR			
		Ar-CH3	NH	NC-CH3	Ar-H		X
32	H	2.431	7.261	1.253	7.267-7.943		
33	4-Br	2.416	7.263	1.255	6.930-7.956		
34	4-F	2.435	7.265	1.253	7.268-8.336		
35	2-OH	2.468	7.252	1.232	7.257-7.992		2.462
36	3-OH	2.431	7.264	1.201	7.234-7.982		2.534
37	4-OH	2.143	7.192	1.342	7.263-7.928		3.814
38	4-I	2.351	7.191	1.575	7.261-7.922		
39	4-CH3	2.319	7.242	1.263	7.267-7.927		2.210
40	3-NO2	2.413	7.260	1.275	7.287-7.935		
41	4-NO2	2.415	7.269	2.134	7.194-7.870		
				^{13}C NMR			
		Ar-CH3	N=C	NC-CH3	Ar-C	Cipso	X
32	H	21.66	149.60	13.35	128.23-131.89	129.21	–
33	4-Br	21.63	163.52	16.94	128.11-130.63	126.07	–
34	4-F	21.66	149.25	13.24	123.67-144.65	149.24	–
35	2-OH	21.45	160.56	15.46	127.92-148.36	131.07	–
36	3-OH	21.66	149.39	13.31	126.56-145.86	132.01	–
37	4-OH	30.95	149.63	13.27	127.79-144.11	113.67	–
38	4-I	21.64	144.77	14.12	123.97-136.17	151.44	–
39	4-CH3	21.75	155.83	16.41	123.65-144.67	135.03	27.03
40	3-NO2	21.63	160.85	13.34	121.27-144.66	138.96	–
41	4-NO2	21.64	151.43	13.35	122.06-134.95	134.15	–

dimensions) were created for PDB protein. The help of hydrophobic, intramolecular hydrogen, ionic bonds and Van der Waals interactions between ligand and protein interactions were used to calculate free binding energy (ΔG). Moreover, after the determination of docking scores for protein and ligand docking, the one with the highest negative energy was chosen for the 2- and 3-dimensional docking poses by using Discovery Studio Visualization.

Conclusions

Some substituted aryl hydrazides were synthesized by the condensation of aryl hydrazine with substituted benzaldehyde in RT stirring method. In this condensation, the obtained yield was more than 85%. The purities of synthesized hydrazide were examined by comparing the data already reported in the literature. The present characterization data of these hydrazides are well agreeable with the earlier data and these are well supported for the formation of compounds. The characteristic spectral frequencies of hydrazides **(32-41)** were correlated with Hammett substituent constants and *F* and *R* parameters. From the results of statistical analyses, the effects of substituent on the spectral data have been predicted. Some of the single linear correlations gave poor correlations with all Hammett sigma substituents constants, *F* and *R* parameters. While seeking the multi-regression analyses, they showed satisfactory correlations. The ligand-protein interaction ability study of synthesized aryl hydrazides was carried out through molecular docking analysis. From the docking study, the hydrazides **2, 6, 12, 17, 22, 27, 33** and **36** have shown good ligand-protein binding energy.

Acknowledgment

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