Supplementary Information

Methylene resonance and conjugation effects in 3-(4-bromophenyl)-5-(substituted phenyl)-4,5-dihydroisoxazoles: Synthesis, spectral QSAR studies, *in silico* and *in vitro* activities evaluation

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Table S1- Results of statistical analysis of IR and NMR spectral data of 3-(4-bromophenyl)-5-substituted phenyl-4,5-dihydroisoxazole derivatives (**1-8**) with Hammett substituent constants σ, σ^{+}, σ_I, σ_R, F and R parameters

Table S2- Multi-Regression analysis results and its equations

Compounds 1-8: NMR spectra of compounds1-8.

In IR spectral correlations, the structure parameter Hammett equation, as stated in equation (1)[22], is applied in this correlation.

$$\nu = \rho\sigma + \nu_o \quad \ldots (1)$$

where ν_0 is the frequency for the parent member of the series.

The NMR correlation study utilized the Hammett equation[23], as given in equation (2).

$$\delta = \rho\sigma + \delta_o \quad \ldots (2)$$

where δ_o is the chemical shift (ppm) for the parent member of the series.

Table S1- Results of statistical analysis of IR and NMR spectral data of 3-(4-bromophenyl)-5-substituted phenyl-4,5-dihydroisoxazole derivatives (**1-8**) with Hammett substituent constants σ, σ^+, σ_I, σ_R, F and R parameters

Freq.	Const.	r	I	ρ	s	n	Correlated derivatives
νC=N	σ	0.117	1634.33	-10.13	31.49	8	H, 3-Cl, 4-Cl, 2-F, 4-F, 4-CH_3, 3-NO_2, 4-NO_2
	σ^+	0.161	1634.33	-11.84	31.30	8	H, 3-Cl, 4-Cl, 2-F, 4-F, 4-CH_3, 3-NO_2, 4-NO_2
	σ_I	0.006	1631.78	-0.69	31.71	8	H, 3-Cl, 4-Cl, 2-F, 4-F, 4-CH_3, 3-NO_2, 4-NO_2
	σ_R	0.156	1628.86	-18.66	31.32	8	H, 3-Cl, 4-Cl, 2-F, 4-F, 4-CH_3, 3-NO_2, 4-NO_2
	F	0.050	1629.29	4.86	31.67	8	H, 3-Cl, 4-Cl, 2-F, 4-F, 4-CH_3, 3-NO_2, 4-NO_2
	R	0.177	1628.09	-18.17	31.21	8	H, 3-Cl, 4-Cl, 2-F, 4-F, 4-CH_3, 3-NO_2, 4-NO_2
δH_a	σ	0.919	3.299	0.170	0.063	8	H, 3-Cl, 4-Cl, 2-F, 4-F, 4-CH_3, 3-NO_2, 4-NO_2

	σ^+	0.917	3.302	0.166	0.052	8	H, 3-Cl, 4-Cl, 2-F, 4-F, 4-CH_3, 3-NO_2, 4-NO_2
	σ_I	0.956	3.278	0.171	0.073	6	3-Cl, 4-Cl, 2-F, 4-F, 3-NO_2, 4-NO_2
	σ_R	0.925	3.359	0.086	0.086	7	H, 3-Cl, 4-Cl, 4-F, 4-CH_3, 3-NO_2, 4-NO_2
	F	0.960	3.273	0.164	0.070	6	3-Cl, 4-Cl, 2-F, 4-F, 3-NO_2, 4-NO_2
	R	0.918	3.357	0.054	0.087	6	H, 3-Cl, 4-Cl, 4-CH_3, 3-NO_2, 4-NO_2
δH_b	σ	0.807	3.852	0.056	0.288	8	H, 3-Cl, 4-Cl, 2-F, 4-F, 4-CH_3, 3-NO_2, 4-NO_2
	σ^+	0.837	3.800	0.247	0.268	8	H, 3-Cl, 4-Cl, 2-F, 4-F, 4-CH_3, 3-NO_2, 4-NO_2
	σ_I	0.823	3.775	0.230	0.281	8	H, 3-Cl, 4-Cl, 2-F, 4-F, 4-CH_3, 3-NO_2, 4-NO_2
	σ_R	0.848	3.793	-0.529	0.252	8	H, 3-Cl, 4-Cl, 2-F, 4-F, 4-CH_3, 3-NO_2, 4-NO_2
	F	0.845	3.687	0.397	0.258	8	H, 3-Cl, 4-Cl, 2-F, 4-F, 4-CH_3, 3-NO_2, 4-NO_2
	R	0.851	3.777	-0.481	0.247	8	H, 3-Cl, 4-Cl, 2-F, 4-F, 4-CH_3, 3-NO_2, 4-NO_2
δH_c	σ	0.856	5.816	-0.790	0.420	8	H, 3-Cl, 4-Cl, 2-F, 4-F, 4-CH_3, 3-NO_2, 4-NO_2
	σ^+	0.845	5.743	-0.539	0.454	8	H, 3-Cl, 4-Cl, 2-F, 4-F, 4-CH_3, 3-NO_2, 4-NO_2
	σ_I	0.831	5.816	-0.549	0.484	8	H, 3-Cl, 4-Cl, 2-F, 4-F, 4-CH_3, 3-NO_2, 4-NO_2
	σ_R	0.850	5.458	-0.968	0.441	8	H, 3-Cl, 4-Cl, 2-F, 4-F, 4-CH_3,

							3-NO_2, 4-NO_2.
	F	0.818	5.729	-0.295	0.501	8	H, 3-Cl, 4-Cl, 2-F, 4-F, 4-CH_3, 3-NO_2, 4-NO_2
	R	0.847	5.448	-0.785	0.448	8	H, 3-Cl, 4-Cl, 2-F, 4-F, 4-CH_3, 3-NO_2, 4-NO_2
δC=N	σ	0.808	154.250	0.868	3.927	8	H, 3-Cl, 4-Cl, 2-F, 4-F, 4-CH_3, 3-NO_2, 4-NO_2
	σ^+	0.824	155.092	-2.187	3.825	8	H, 3-Cl, 4-Cl, 2-F, 4-F, 4-CH_3, 3-NO_2, 4-NO_2
	σ_I	0.806	154.836	-0.850	3.932	8	H, 3-Cl, 4-Cl, 2-F, 4-F, 4-CH_3, 3-NO_2, 4-NO_2
	σ_R	0.851	155.574	7.648	3.376	8	H, 3-Cl, 4-Cl, 2-F, 4-F, 4-CH_3, 3-NO_2, 4-NO_2
	F	0.827	155.996	-3.312	3.787	8	H, 3-Cl, 4-Cl, 2-F, 4-F, 4-CH_3, 3-NO_2, 4-NO_2
	R	0.853	155.757	6.738	3.340	8	H, 3-Cl, 4-Cl, 2-F, 4-F, 4-CH_3, 3-NO_2, 4-NO_2
δCH_2	σ	0.947	43.033	-0.937	0.289	8	H, 3-Cl, 4-Cl, 2-F, 4-F, 4-CH_3, 3-NO_2, 4-NO_2
	σ^+	0.963	42.950	-0.656	0.347	8	H, 3-Cl, 4-Cl, 2-F, 4-F, 4-CH_3, 3-NO_2, 4-NO_2
	σ_I	0.947	43.066	-0.732	0.394	6	3-Cl, 4-Cl, 2-F, 4-F, 3-NO_2, 4-NO_2
	σ_R	0.968	42.608	-1.154	0.327	6	H, 3-Cl, 4-Cl, 4-CH_3, 3-NO_2, 4-NO_2
	F	0.853	42.993	-0.489	0.419	8	H, 3-Cl, 4-Cl, 2-F, 4-F, 4-CH_3, 3-NO_2, 4-NO_2.
	R	0.960	42.603	-0.894	0.352	6	H, 3-Cl, 4-Cl, 4-CH_3, 3-NO_2, 4-NO_2

δC-X	σ	0.922	140.858	8.162	13.040	6	H, 3-Cl, 4-Cl, 4-CH_3, 3-NO_2, 4-NO_2
	σ^+	0.927	140.825	8.467	12.867	7	H, 3-Cl, 4-Cl, 2-F, 4-CH_3, 3-NO_2, 4-NO_2
	σ_I	0.963	131.526	28.863	10.364	8	H, 3-Cl, 4-Cl, 2-F, 4-F, 4-CH_3, 3-NO_2, 4-NO_2
	σ_R	0.950	139.538	-25.523	11.534	6	H, 3-Cl, 4-Cl, 2-F, 4-F, 4-CH_3,
	F	0.994	127.564	34.334	7.215	8	H, 3-Cl, 4-Cl, 2-F, 4-F, 4-CH_3, 3-NO_2, 4-NO_2
	R	0.957	138.508	-24.719	10.96	6	H, 3-Cl, 4-Cl, 2-F, 4-F, 4-CH_3

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

Table S2. Multi-Regression analysis results and its equations

νC=N Regressions

$\nu C{=}N\ (cm^{-1}) = 1629.29\ (\pm 23.80) - 1.082\ (\pm 47.81)\ \sigma_I - 18.68\ (\pm 52.77)\ \sigma_R$

($R = 0.916$, n = 8, $P > 90\%$) … (3)

$\nu C{=}N\ (cm^{-1}) = 1628.42\ (\pm 22.88) - 0.84\ (\pm 45.01)\ F - 18.$

($R = 0.920$, n = 8, $P > 90\%$) … (4)

δ $H_{a,\ b,\ and\ c}$ Regressions

$\delta H_a\ (ppm) = 3.294\ (\pm 0.052) + 0.173\ (\pm 0.106)\ \sigma_I + 0.090\ (\pm 0.117)\ \sigma_R$

($R = 0.967$, n = 8, $P > 95\%$) … (5)

$\delta H_a\ (ppm) = 3.270\ (\pm 0.044) + 0.202\ (\pm 0.087)\ F + 0.124 (\pm 0.092)\ R$

($R = 0.988$, n = 8, $P > 96\ \%$) … (6)

$\delta H_b (ppm) = 3.705\ (\pm 0.185) + 0.220\ (\pm 0.372)\ \sigma_I - 0.524 (\pm 0.411)\ \sigma_R$

(R =0.901, n = 8, *P* >90 %) … (7)

δH_b (ppm) = 3.669 (±0.170) +0.278 (±0.334) F - 0.385(±0.354) R

(R =0.943, n = 8, *P* >90 %) … (8)

δH_c(ppm) = 5.686(±0.310) -0.570 (±0.623) σ_I -0.982(±0.687) σ_R

(R =0.903, n = 8, *P* >90%) … (9)

δH_c(ppm) = 5.682 (± 0.299) - 0.602 (±0.588) F -0.993 (±0.622) R

(R =0.913, n = 8, *P* >90%) … (10)

δC=N Regressions

δC=N(ppm) = 155.85(±2.561) –0.693(±5.145) σ_I + 7.631(±5.678) σ_R

(R =0.941, n = 8, *P* > 90 %) … (11)

δC=N(ppm) = 156.292(±2.429) –1.375(±4.779) F + 6.262(±5.056) R

(R =0.934, n = 8, *P* > 90 % … (12)

δCH_2(ppm) =42.91 (±0.183) –0.756(±0.368) σ_I – 1.173(±0.406) σ_R

(R =0.972, n = 8, *P* > 96%) … (13)

δCH_2 (ppm) =42.936 (±0.170) – 0.857(±0.334) F – 1.194(±0.353) R

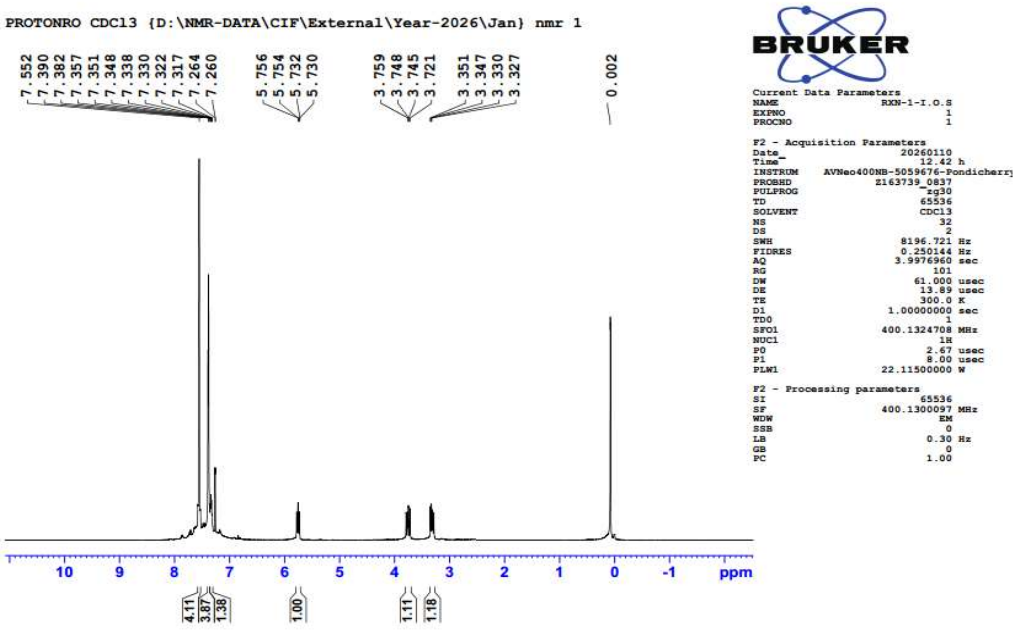
(R =0.969, n = 8, *P* > 96%) … (14)

δC-X(ppm) =128.226 (±6.080) +28.354(±12.213) σ_I – 24.814(±13.479) σ_R

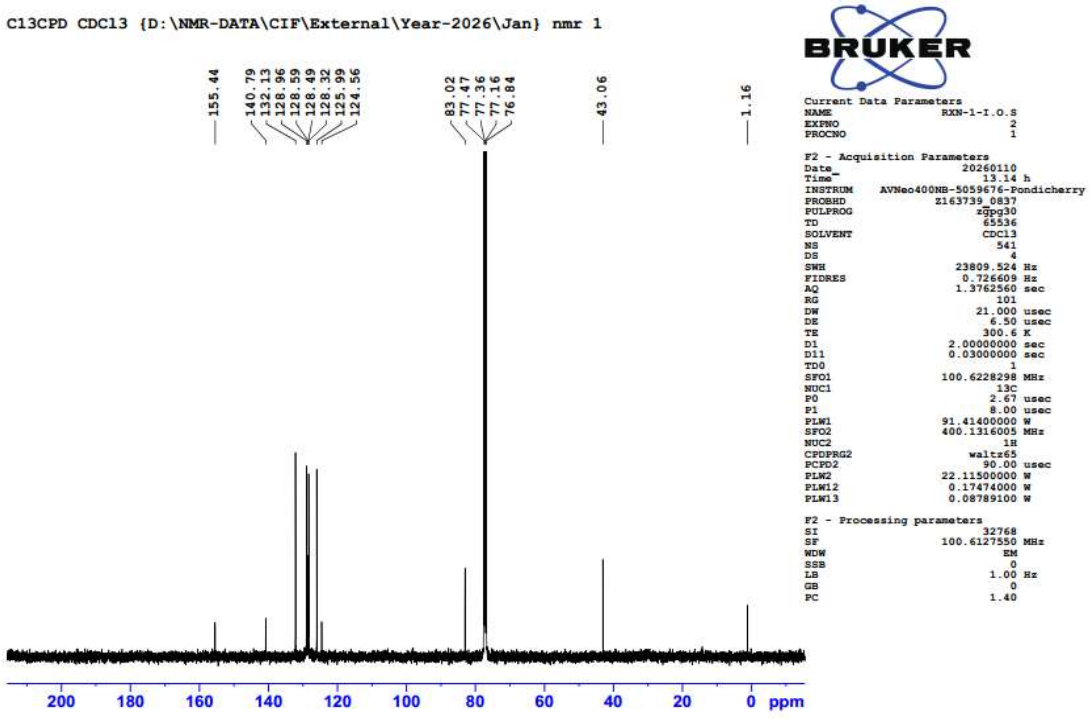
(R =0.965, n = 8, *P* > 95 %) … (15)

δC-X(ppm) =126.886(±4.295) +29.889(±8.449) F – 14.373(±8.939) R

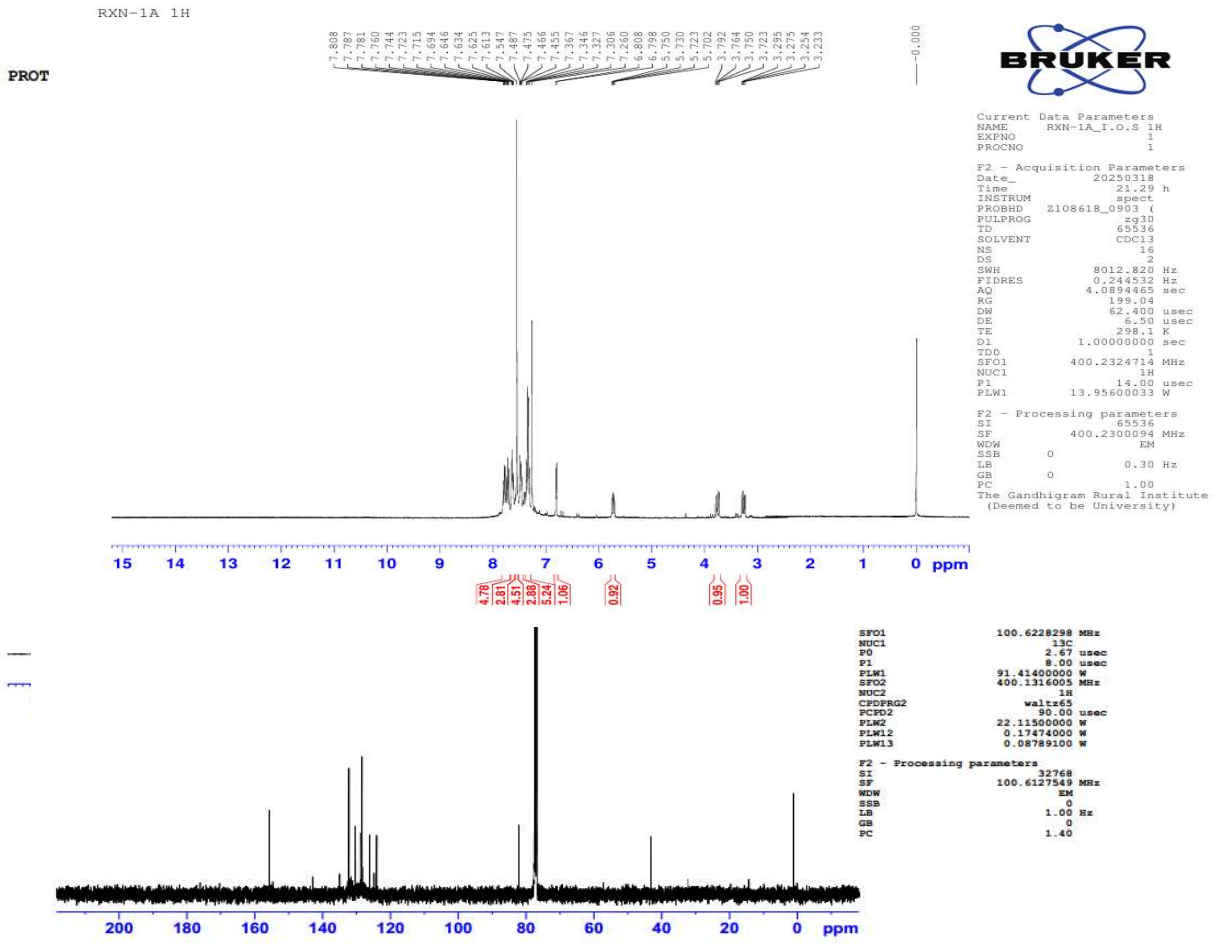
(R =0.998, n = 8, *P* > 97%) … (16)



Compound 1. ^{1}H NMR sp^^t^^um of 3-(4-bromophenyl)-4,5-dihydro-5-phenylisoxazole



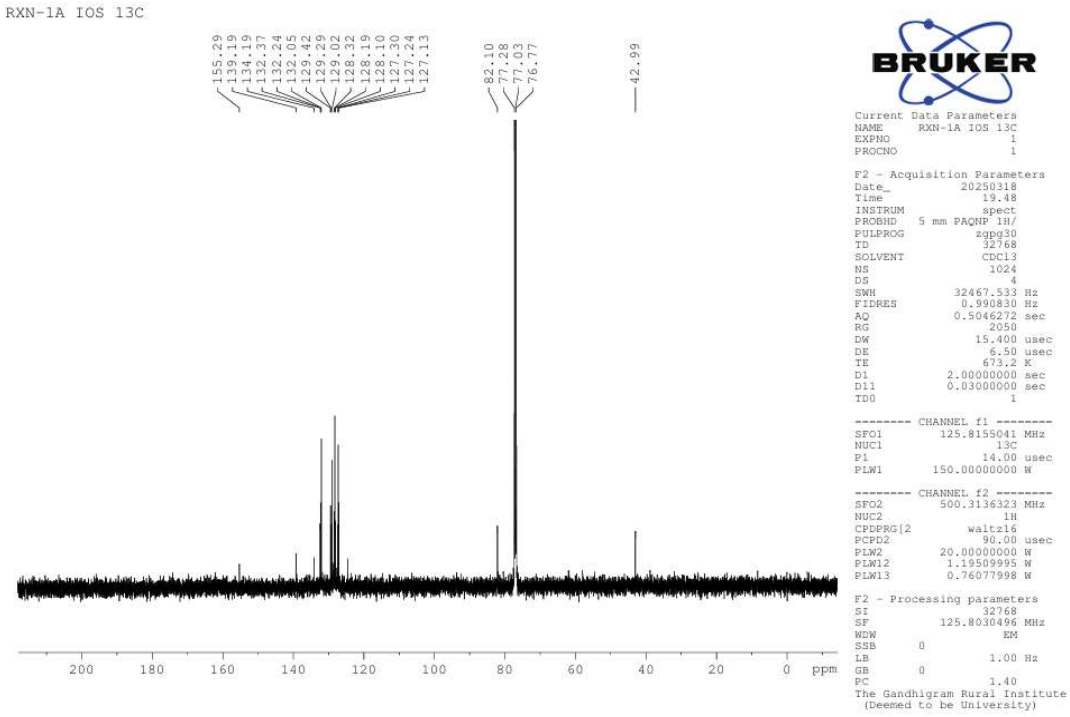
Compound 1. ^{13}CNMR spectrum of 3-(4-bromophenyl)-4,5-dihydro-5-phenylisoxazole



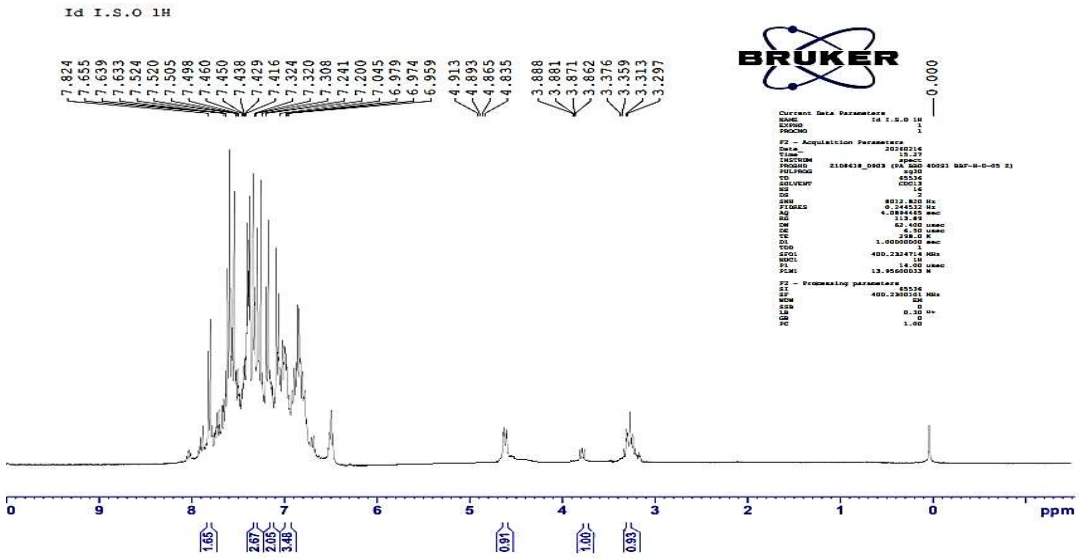
Compound 2. ^{1}H NMR spectrum of 3-(4-bromophenyl)-5-(3-chlorophenyl)-4,5-dihydroisoxazole

Compound 2 .^{13}C NMR spectrum of 3-(4-bromophenyl)-5-(3-chlorophenyl)-4,5-dihydroisoxazole

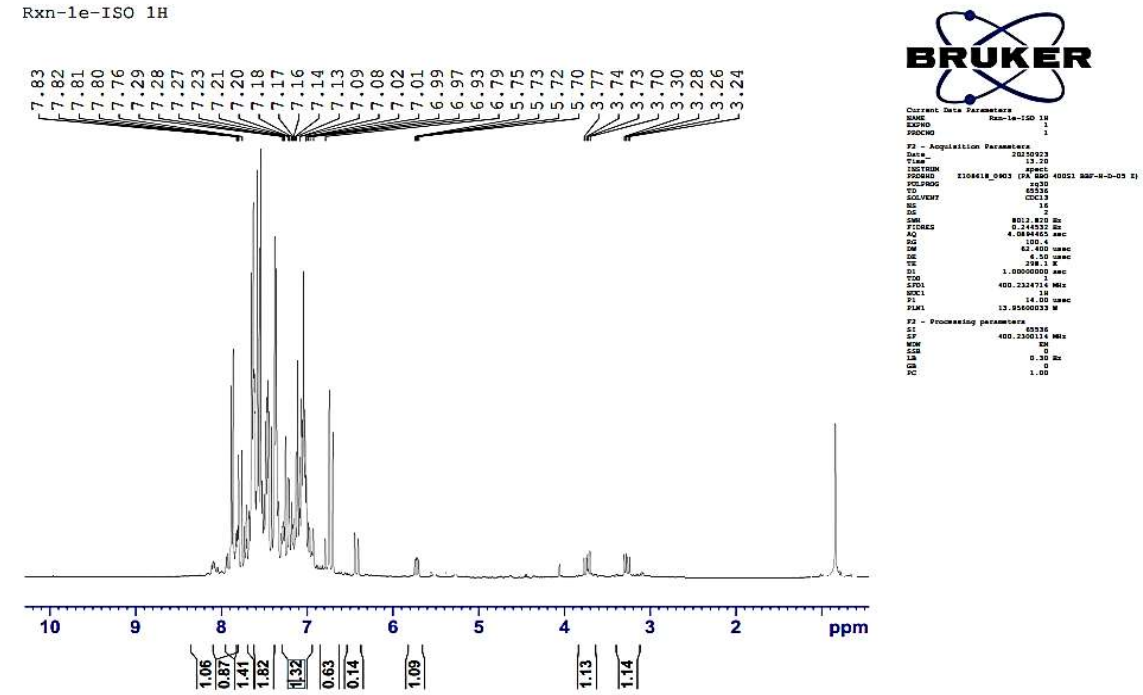
Compound 3. ^{1}H NMR spectrum of 3-(4-bromophenyl)-5-(4-chlorophenyl)-4,5-dihydroisoxazole

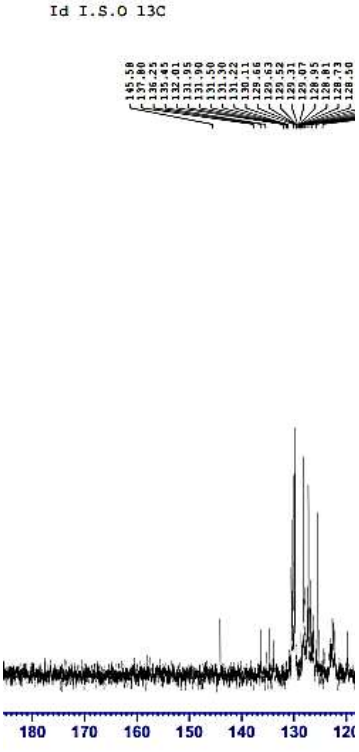


Compound 3. ^{13}C NMR spectrum of 3-(4-bromophenyl)-5-(4-chlorophenyl)-4,5-dihydroisoxazole



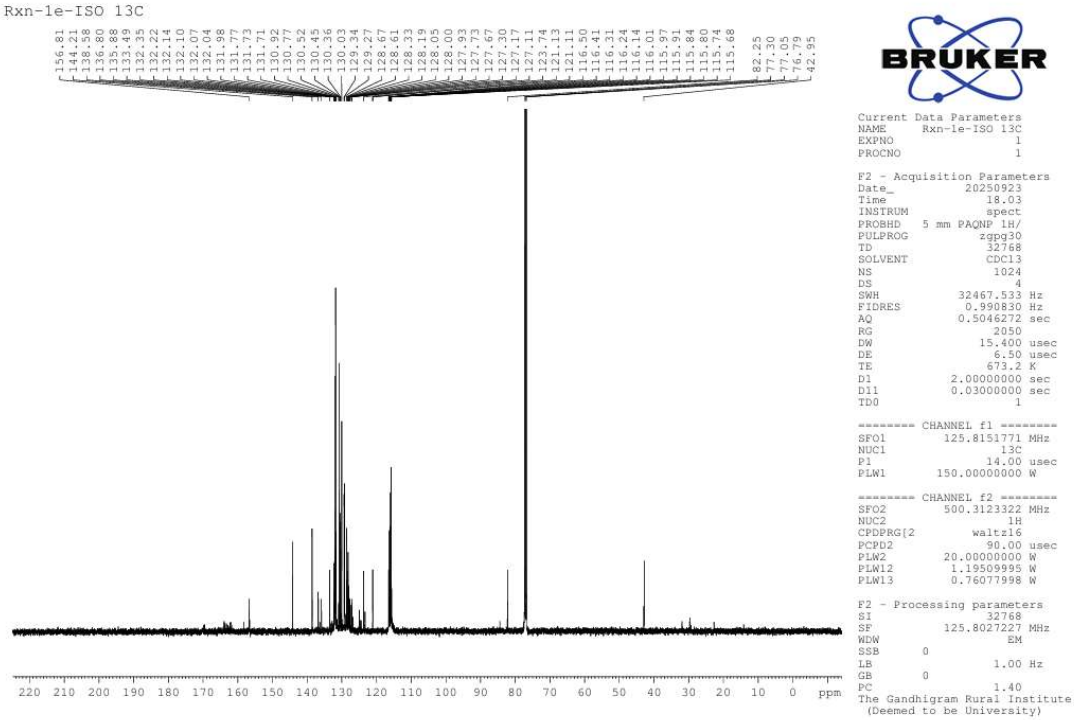
Compound 4. ^{1}H NMR spectrum of 3-(4-bromophenyl)-5-(2-fluorophenyl)-4,5-dihydroisoxazole



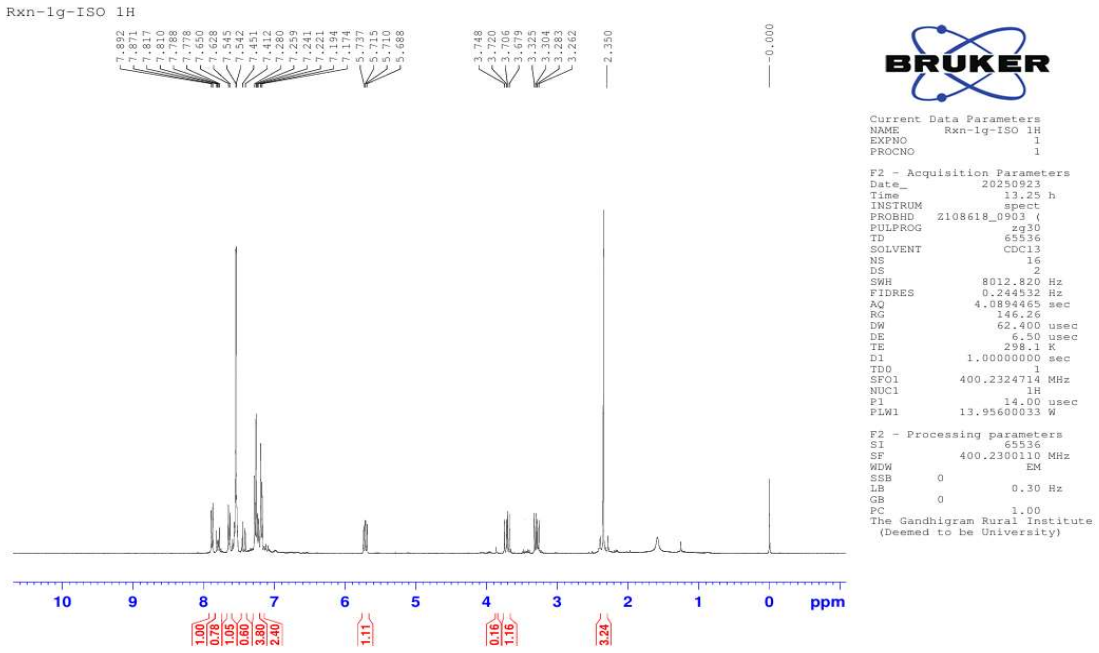


Compound 4. ^{13}C NMR spectrum of 3-(4-bromophenyl)-5-(2-fluorophenyl)-4,5-dihydroisoxazole

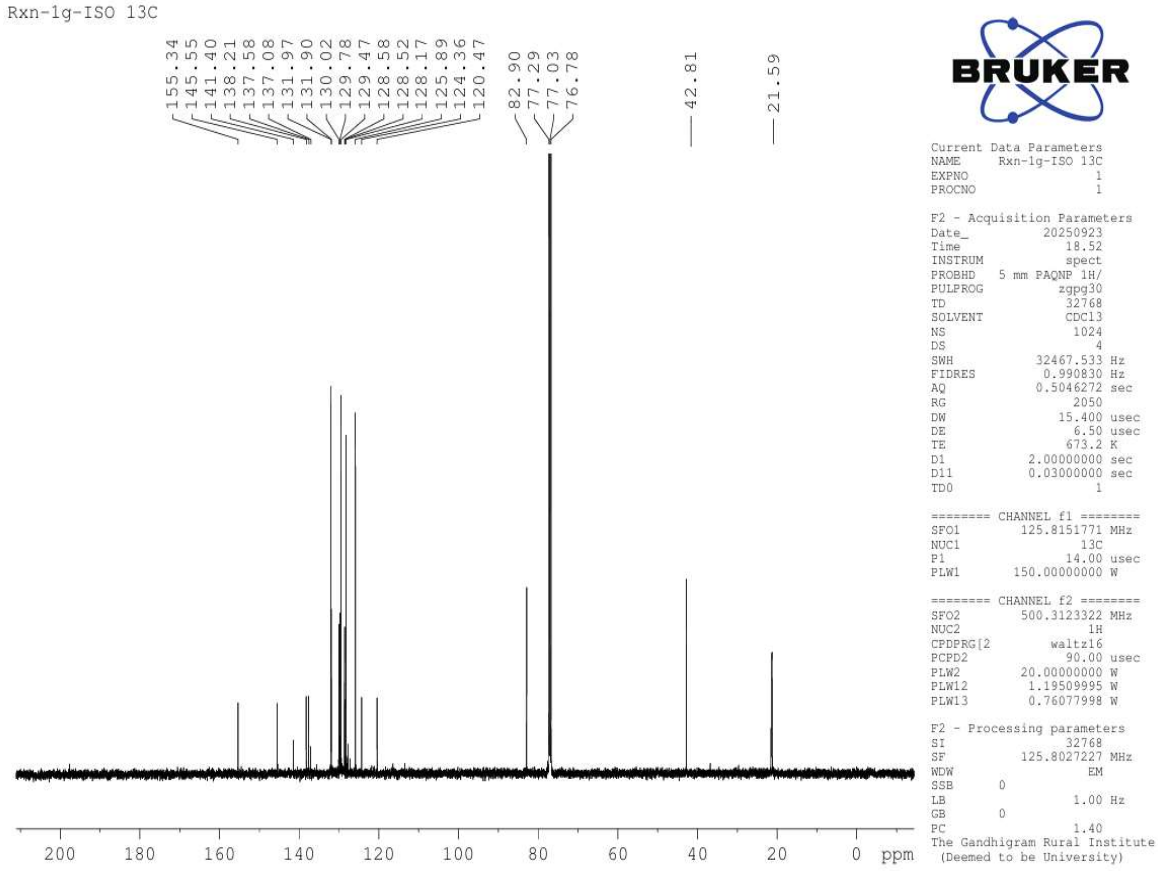
Compound 5. ^{1}H NMR spectrum of 3-(4-bromophenyl)-5-(4-fluorophenyl)-4,5-dihydroisoxazole



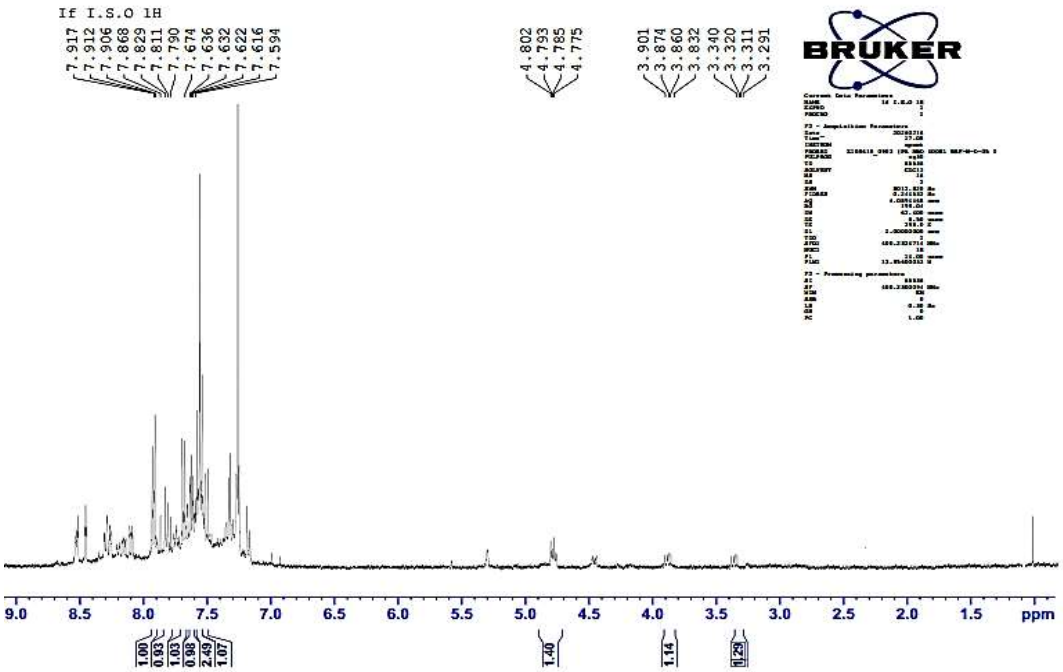
Compound 5. ^{13}C NMR spectrum of 3-(4-bromophenyl)-5-(4-fluorophenyl)-4,5-dihydroisoxazole



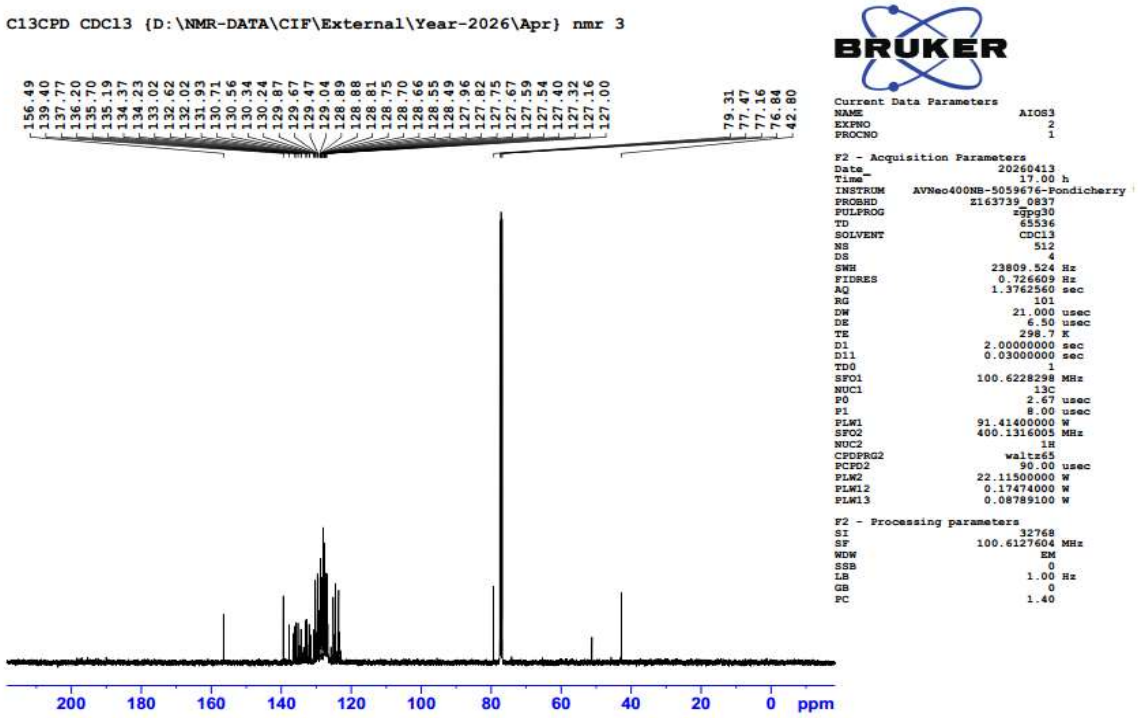
Compound 6. ^{1}H NMR spectrum of 3-(4-bromophenyl)-4,5-dihydro-5-p-tolylisoxazole



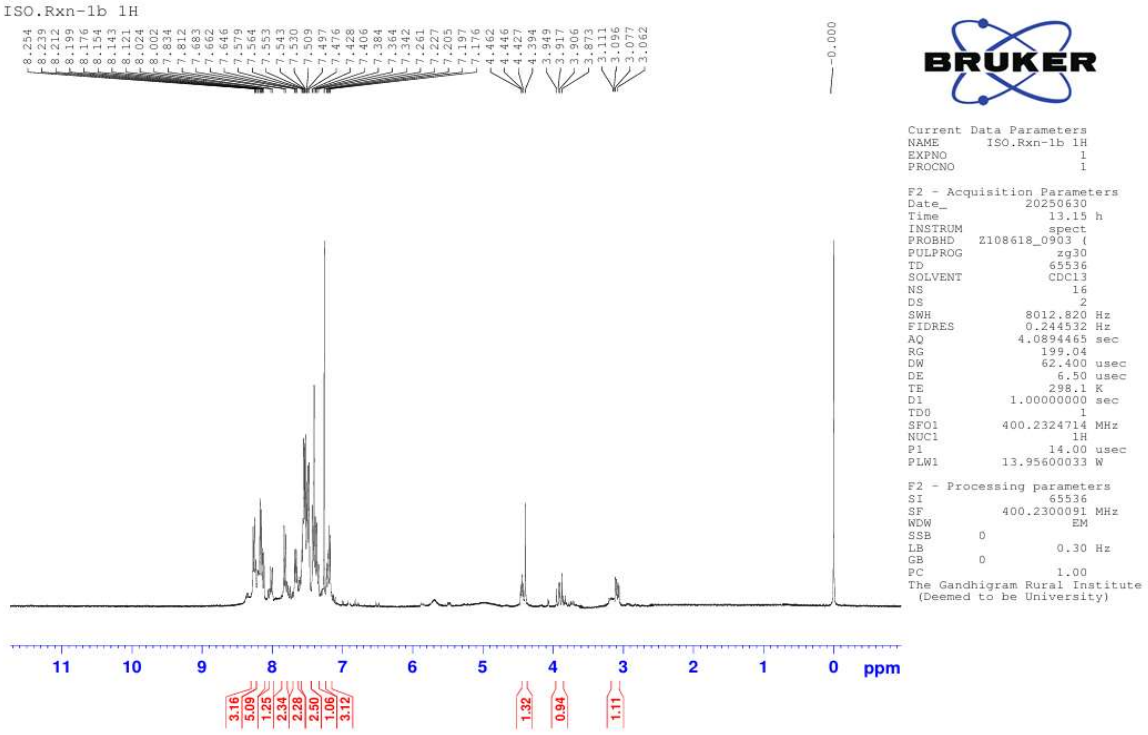
Compound 6. ^{13}C NMR spectrum of 3-(4-bromophenyl)-4,5-dihydro-5-p-tolylisoxazole



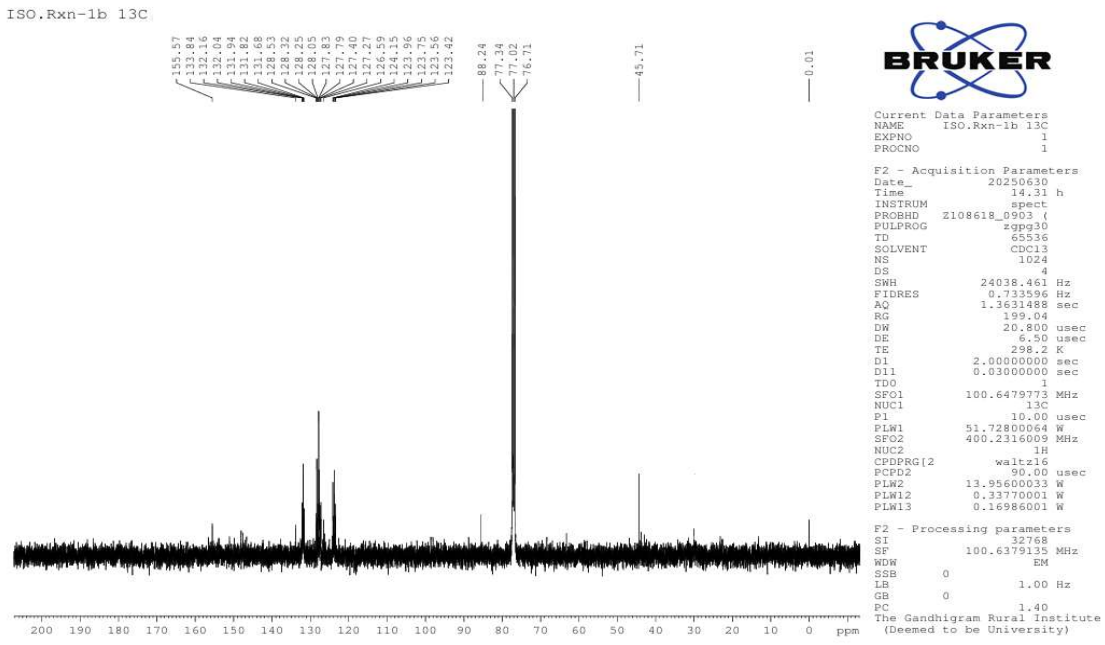
Compound 7. ^{1}H NMR spectrum of 3-(4-bromophenyl)-4,5-dihydro-5-(3-nitrophenyl) isoxazole



Compound 7. ^{13}C NMR spectrum of 3-(4-bromophenyl)-4,5-dihydro-5-(3-nitrophenyl) isoxazole



Compound 8. ^{1}H NMR spectrum of 3-(4-bromophenyl)-4,5-dihydro-5-(4-nitrophenyl) isoxazole



Compound 8. ^{1}H NMR spectrum of 3-(4-bromophenyl)-4,5-dihydro-5-(4-nitrophenyl) isoxazole