Chapter III

Section B

Sulfonated graphene oxide (GO) catalyzed one-pot synthesis of substituted pyrazole

III.B.1. Introduction

The dihydropyranopyrazole compounds are versatile building blocks and structural units of a wide variety of therapeutic agents. Pyranopyrazoles, are ubiquitous in many biologically active heterocyclic compounds and has attracted much consideration because of its wide range of activity like antimicrobial [1], antitumor [2], anticancer [3], anticoagulant [4], diuretic, anti-inflammatory [5,6], inhibition of human Chk1 kinase activities [7] antifungal, antidepressant and so on [8]. Some important Pharmaceutical agents and drug molecules containing dihydropyranopyrazole ring in their core structure were shown in (Figure III.B.1).

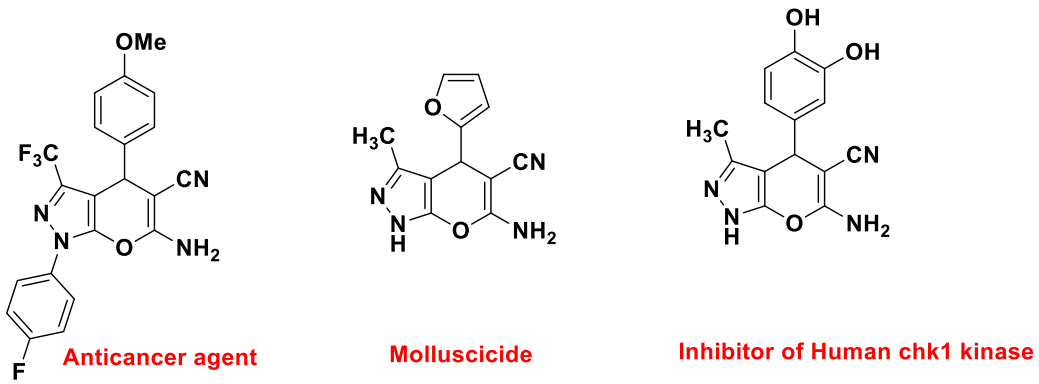
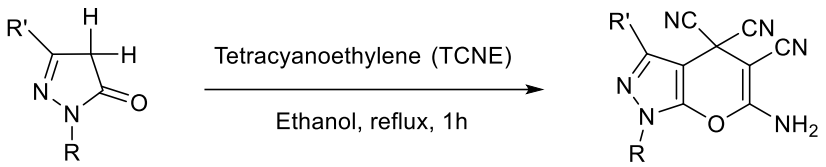


Figure III.B.1. *Some biologically active pyranopyrazoles*.

III.B.2. Background and objectives

In 1973 Junek *et al.* reported the first synthesis of pyranopyrazole from the reaction between 3-methyl-1-phenylpyrazolin-5-one and tetracyanoethylene (TCNE) (Scheme III.B.1) [9]. 5-Pyrazolones (5 mmol) reacted with TCNE in ethanol solution at refluxed conditions. 5-Pyrazolones were proved to be very reactive substrates towards TCNE. They observed that 3-phenyl-5-pyrazolone and 3-ethoxycarbonyl-1-phenyl-5-pyrazolone gave the cyclizing addition

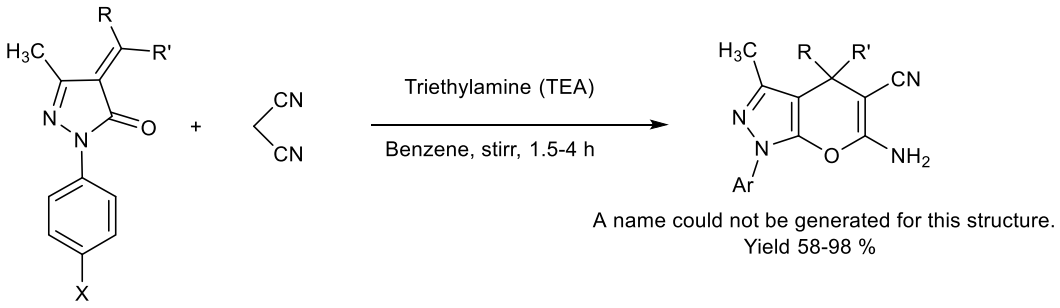
product pyrano-pyrazoles whereas it was not possible to react 2,3-dimethyl-1-phenyl-5-pyrazolone (antipyrine) with TCNE.



R= H, C_6H_5
R'= C_6H_5, $CO_2C_2H_5$

Scheme III.B.1. *Synthesis of pyranopyrazole from pyrazolone and tetracyanoethylene (TCNE).*

In 1980, Tacconi *et al.* reported a new route to the synthesis of pyranopyrazoles (Scheme III.B.2) [10]. Malononitrile is well-known to react with *α,β*-unsaturated carbonyls in the presence of different bases to form Knoevenagel or Michael adducts.



A name could not be generated for this structure.
Yield 58-98 %

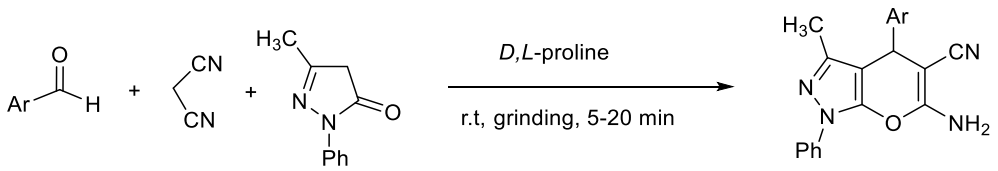
X= H, NO_2, R= H, CH_3
R'= CH_3, Ph, *p*-CH_3-C_6H_4, *p*-NO_2-C_6H_4, *p*-Cl-C_6H_4, 3,4-$C_6H_3Cl_2$

Scheme III.B.2. *The synthesis of pyranopyrazole from pyrazolone and malononitrile*

They added malononitrile to the suspension of 4-arylidene (4-alkylidene)-5-pyrazolone in benzene solution in presence of triethylamine base

and then stirred for 1.5-4 hrs. Herein, benzene is proved to be far better than methanol or ethanol solvent and triethylamine must be used instead of sodium ethylate or piperidine.

In 1983, Sharanin Yu *et al.* have developed first one-pot three-component reaction of pyrazolone, aldehyde, and malononitrile to synthesize pyranopyrazole in presence of ethanol using triethylamine as the catalyst [11]. Recently, the use of the grinding method has found application in organic synthesis. This method is more efficient and selective compared with traditional methods [12-14]. In 2007, Guo *et al.* synthesized 1,4-dihydropyranopyrazoles by a grinding method using D,L-Proline under the solvent-free condition at room temperature (Scheme III.B.3) [15]. Proline is a bifunctional abundant molecule that is inexpensive and readily available in both enantiomeric forms. These two functional groups help it to act as both acid and base and also facilitates the chemical transformations in concert, similar to the enzymatic catalysis [16].



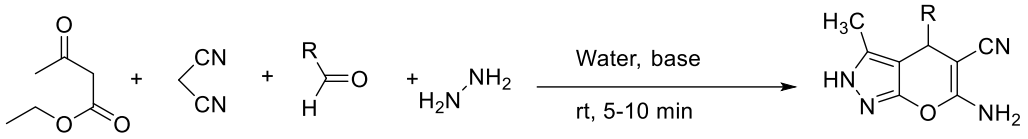
Ar= C_6H_5, 4-ClC_6H_4, 3-ClC_6H_4, 2-ClC_6H_4, 4-$NO_2C_6H_4$
3-$NO_2C_6H_4$, 4-BrC_6H_4, 2,4-ClC_6H_3, 4-$CH_3C_6H_4$, 4-OHC_6H_4
4-$CH_3OC_6H_4$

Yield 85-99 %

Scheme III.B.3. *Proline catalyzed synthesis of pyranopyrazole using the grinding method.*

In 2008, Vasuki *et al.* developed an environmentally benign four-component pathway for the synthesis of pyranopyrazoles using catalytic amounts of bases such as piperidine, pyrrolidine, morpholine, and triethylamine at room temperature (Scheme III.B.4) [17]. The maximum yield (94%) of the target product was obtained in presence of piperidine and water as the solvent

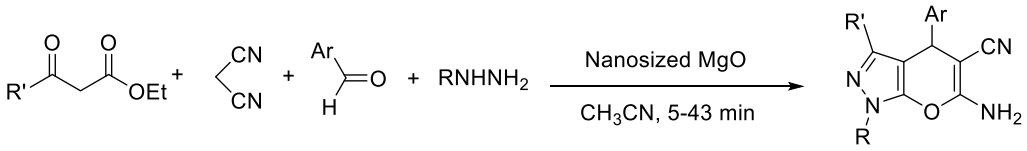
provided the best yield compared to common organic solvents. However, the reaction between benzaldehyde, hydrazine hydrate, ethyl acetoacetate, and malononitrile resulted in the corresponding pyranopyrazole without the need for a base.



R= C_6H_5, 4-Me-C_6H_4, 4-MeO-C_6H_4, 4-NO_2-C_6H_4, 4-Cl-C_6H_4
4-OH-C_6H_4, 4-F-C_6H_4, 2-MeO-C_6H_4, 3-MeO-C_6H_4, 3-NO_2-C_6H_4,
3-Pyridinyl, 4-Pyridinyl, 2-Furanyl, 2-Thiophenyl, Isopropyl

Scheme III.B.4. *The base-mediated four-component protocol for the synthesis of pyranopyrazoles in an aqueous medium at room temperature.*

In 2011, Babaie *et al.* reported a four-component route for the generation of pyranopyrazoles from hydrazine hydrate or phenyl hydrazine, ethyl 3-alkyl3-oxo propanoate, aldehydes, and malononitrile in the presence of nanosized magnesium oxide (MgO) as a highly effective heterogeneous base catalyst (Scheme III.B.5) [18]. The same group in 2010 studied the Knoevenagel condensations of aldehydes with malononitrile in the presence of magnesium oxide (MgO) catalyst and found that the rate of the reactions was very fast. Mechanistically, the synthesis of pyranopyrazole initially involves the formation of arylidene malononitrile in quantitative yield by the Knoevenagel addition of malononitrile to the aldehyde and nanosized magnesium oxide (MgO) catalyzes all the steps as an efficient heterogeneous catalyst.

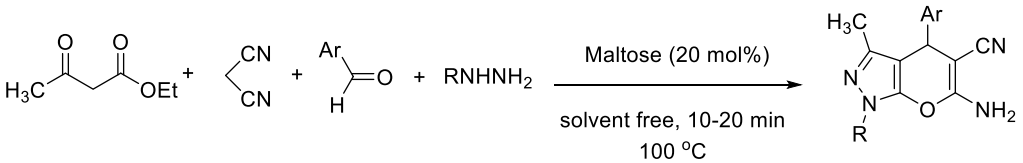


R= H, Ph
R'= CH_3, Propyl, *iso*-propyl
Ar= C_6H_5, 2-ClC_6H_4, 4-Cl-C_6H_4, 3-BrC_6H_4, 4-$NO_2C_6H_4$
4-$CH_3OC_6H_4$, 2,4-$Cl_2C_6H_3$

Yield 88-97 %

Scheme III.B.5. *Nanosized MgO catalyzed synthesis of pyranopyrazole.*

In 2013, Kangani *et al.* developed a simple and efficient one-pot four-component synthesis of 1,4-dihydropyranopyrazoles using maltose as an inexpensive and non-toxic catalyst (Scheme III.B.6) [19]. The reaction proceeds smoothly under solvent-free thermal conditions to produce the target product. Solvent-free reactions not only reduce the pollution but also the reaction handling cost by simplifying the experimental procedure and work-up [20]. This procedure has the advantages such as operational simplicity, non-hazardous catalyst, high yield, short reaction time, and minimum pollution of the environment.



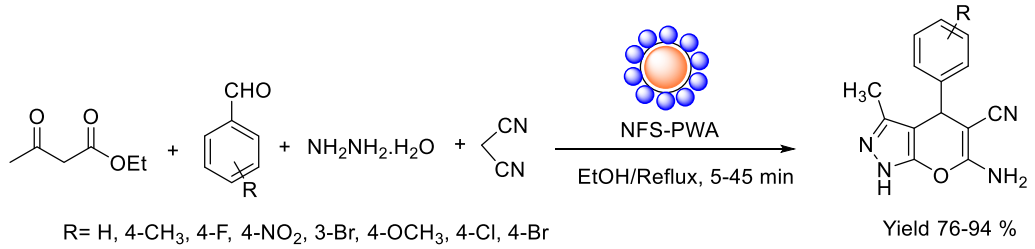
R= H, Ph
Ar= C_6H_5, 4-$N(CH_3)_2C_6H_4$,2-$NO_2C_6H_4$, 4-$NO_2C_6H_4$, 3-$NO_2C_6H_4$,
2-ClC_6H_4, 4-ClC_6H_4, 4-MeC_6H_4, 2,5-$(CH_3O)_2C_6H_3$, 4-OHC_6H_4, 2,4-$Cl_2C_6H_3$

Yield 74-98 %

Scheme III.B.6. *Synthesis of 1,4-dihydropyrano[2,3-c]pyrazoles in the presence of maltose as a biodegradable catalyst.*

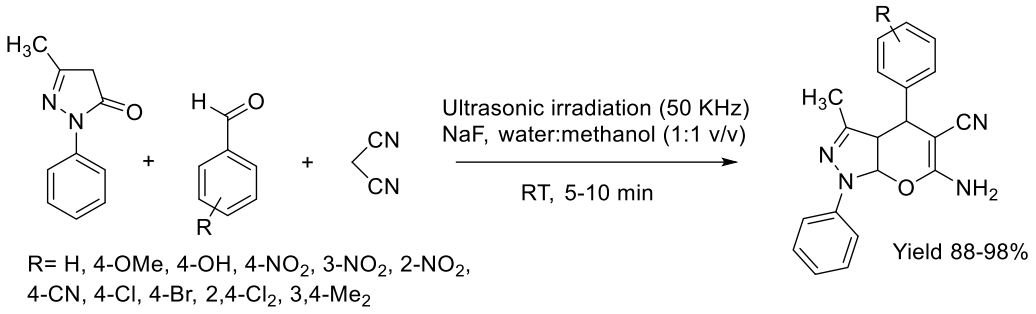
Among the solid acids, Heteropolyacid (HPA) has unique properties and its acidity is much higher than that of the mineral acids. Moreover, HPA is capable of activating substrates by protonation and sometimes is more effective

than traditional acid catalysts. The high solubility of HPA makes some difficulties to separate it from the reaction mixture. Thus immobilization of HPA on the supports having high surface area facilitates their separation and use as heterogeneous catalyst in organic transformation [21-23]. In 2015, Maleki *et al.* prepared chemical support of Keggin ($H_3PW_{12}O_{40}$) heteropolyacid (HPA) on silica-coated $NiFe_2O_4$ magnetic nanoparticles ($NiFe_2O_4@SiO_2$– $H_3PW_{12}O_{40}$ or NFS–PWA) and investigated its catalytic activity for the synthesis of pyranopyrazol (Scheme III.B.7) [24].



Scheme III.B.7. *$NiFe_2O_4@SiO_2$–$H_3PW_{12}O_{40}$ or NFS–PWA catalyzed synthesis of pyranopyrazole.*

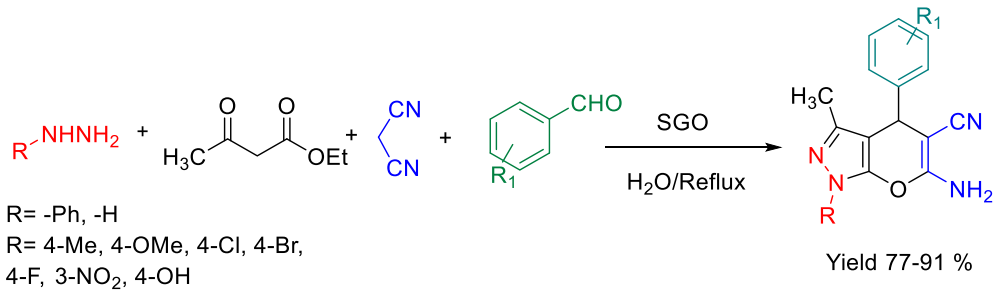
In 2018, Konakanchi *et al*. employed sodium fluoride (NaF) as an efficient catalyst for the one-pot three-component synthesis of series of dihydropyrano [2,3-c]pyrazoles (Scheme III.B.8) [25]. The best yield of the target product was obtained using ultrasonic irradiation (50 kHz) in presence of water:methanol (1:1 v/v) at 25 ^oC bath temperature. The increase in the product yield under ultrasonication may be due to the cavitation effect [26]. They obtained a wide variety of substituted 1,4-dihydropyranopyrazoles in good to excellent yield (88–98%) in 5–10 min utilizing the optimized condition.



Scheme III.B.8. *NaFcatalyzed one-pot three-component synthesis of pyranopyrazole.*

III.B.3. Present work: Result and discussion

Previously, GO and its derivative sulfonated graphene oxide (SGO) has been used as an efficient carbocatalyst in hydration, oxidation, Aza-Michael addition, condensation, hydrolysis of cellulose and hydration of alkynes.[27-29] Among metal free catalysts, sulfonated graphene oxide (SGO) is a highly air-stable, environmentally friendly acid catalyst for use in various chemical reactions.



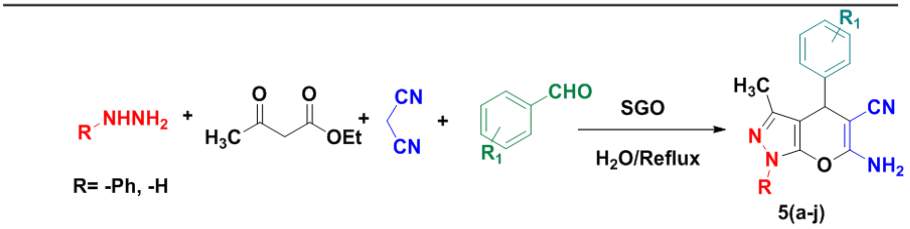
Scheme III.B.9. *SGO catalyzed one-pot four-component synthesis of pyranopyrazole.*

The versatility and the catalytic performance of the catalyst SGO were observed in one pot-four component synthesis of 1,4-dihydropyranopyrazoles (Scheme

III.B.9) using hydrazine hydrate/phenylhydrazine, aromatic aldehyde, malononitrile, ethyl acetoacetate, and the results are summarised below.

III.B.3.1. Result and discussion

Table III.B.1. Optimization of reaction condition for the synthesis of 1,4-dihydropyranopyrazoles[a]



Entry	Time (min)	solvent	Catalyst amount(mg)	Yield(%)
1	120	No solvent	20	<50
2	60	EtOH /Reflux	20	55
3	60	DMF/Reflux	20	45
4	60	CH_3CN/Reflux	20	40
5	120	DCM/Reflux	20	<40
6	120	THF/Reflux	20	<30
7	60	H_2O/Reflux	20	65
8	**60**	**H_2O/Reflux**	**30**	**91**
9	60	H_2O/Reflux	50	94
10	60	H_2O/Reflux	10	<50
11	120	H_2O/r.t	40	<40[b]

[a]Reaction of phenylhydrazine (1.5 mmol), ethyl acetoacetate (1 mmol), malononitrile (1 mmol), 4-bromo benzaldehyde (1 mmol), and SGO-1 with a varying amount at refluxed conditions.

[b]Room temperature reaction

To examine the feasibility of the reaction and to optimize the reaction parameters, a model reaction was carried out using phenylhydrazine, ethyl acetoacetate, malononitrile, and 4-bromo benzaldehyde as the starting components. Different solvents EtOH, DMF, DCM, CH_3CN, THF (Table III.B.1, entry 2-6) were implemented to get the desired product in high yield, but H_2O, the green solvent was proved to be more appropriate for this reaction (Table III.B.1, entry 8). However, the temperature has a considerable effect on

the reaction, as can be seen from (Table III.B.1, entry 11) that room-temperature reaction exerted less than 40 % yield.

Investigating the catalytic efficiency of synthesized SGO-1, it was compared with GO and SGO-2, but SGO-1 afforded the desired product with a high yield. Other Lewis acids were also employed to get the desired product. The results indeed showed that high yield was only achieved in the presence of SGO-1 (Table III.B.2, entry 3)

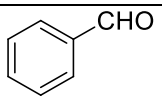
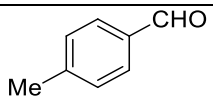
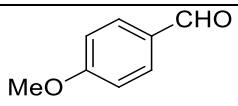
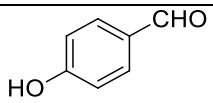
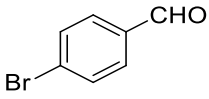
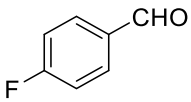
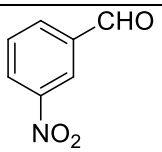
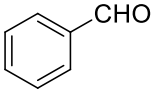
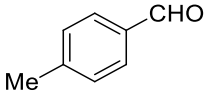
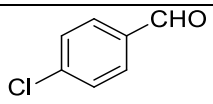
Table III.B.2. Comparison of the efficiency of the present catalyst with a different catalytic system[a].

Entry	Condition	Catalyst	Yield(%)
1	No solvent	-	<30
2	H_2O/Reflux	GO	78[b]
3	**H_2O/Reflux**	**SGO-1**	**91[c]**
3	H_2O/Reflux	SGO-2	85
4	H_2O/Reflux	Al_2O_3	<40
5	H_2O/Reflux	$FeCl_3$	70
6	H_2O/Reflux	$ZnCl_2$	<50

[a]Reaction of phenylhydrazine (1.5 mmol), ethyl acetoacetate (1 mmol), malononitrile (1 mmol), 4-bromo benzaldehyde (1 mmol), catalyst 30 mg at the refluxed condition in water.
[b]GO was prepared by Modified hummers method,
[c]SGO-1 by Tours method.

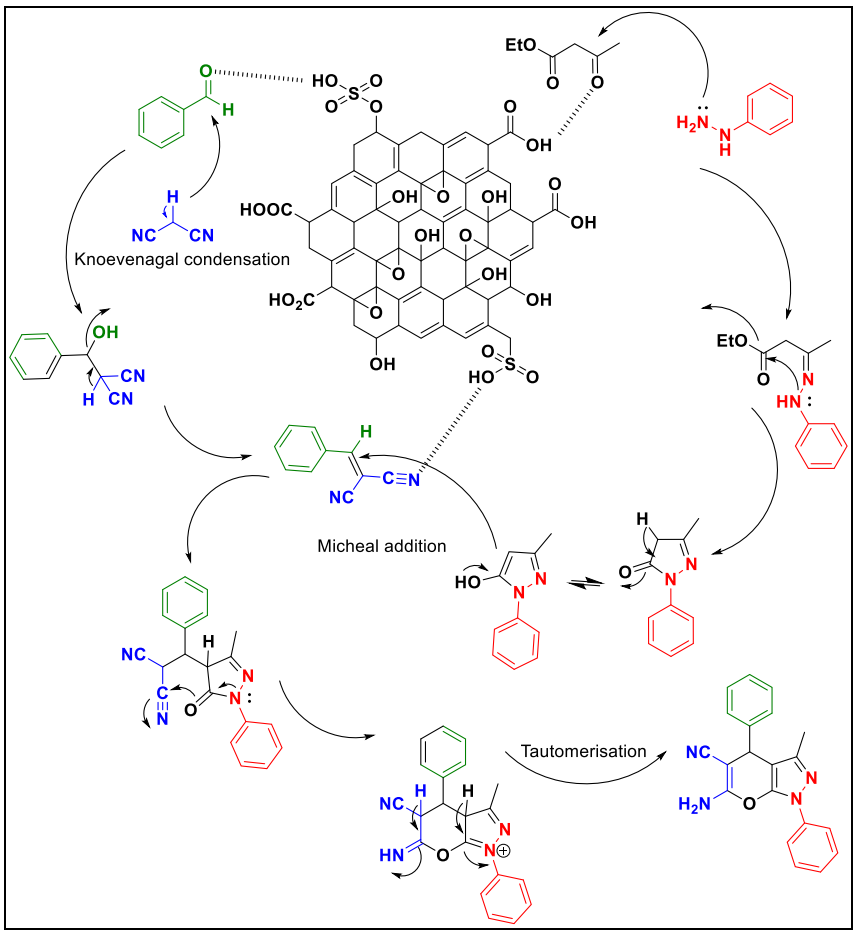
After optimizing the reaction parameters, the versatility of the reaction was examined by varying different aromatic aldehydes and the results were summarized in Table III.B.3. Aldehydes with electron-withdrawing groups, however, exerted the desired product with a high yield and quicken the entire process (Table III.B.3, entry 5, 6, 7, 10). As an extension of our present work we have replaced phenylhydrazine with hydrazine hydrate and the results were satisfactory as shown in (Table III.B.3, entry 8-10).

Table III.B.3. Synthesis of different substituted 1,4-dihydropyranopyrazoles[a].

Entry	Product	R	Aldehyde	Time	Yield	Mp (°C)	
						Found	Reported
1	5a	-Ph		60	80	169-170	170-172
2	5b	-Ph		60	82	180-182	180-182
3	5c	-Ph		60	84	175-176	177-179
4	5d	-Ph		60	83	197-198	195-197
5	5e	-Ph		50	89	180-182	180-182
6	5f	-Ph		50	91	177-178	174-177
7	5g	-Ph		60	88	188-190	190-191
8	5h	-H		50	77	240-241	240-242
9	5i	-H		50	80	203-205	205-207
10	5j	-H		50	88	231-232	231-233

[a]Reaction of R-$NHNH_2$(1.5 mmol), ethyl acetoacetate (1 mmol), malononitrile (1 mmol), aromatic benzaldehyde (1 mmol), 30 mg of SGO atthere fluxed condition in H_2O.

III.B.3.2. Mechanism



Scheme III.B.10. *A plausible route for the synthesis of 1,4-dihydropyrano[2,3-c]pyrazoles.*

A plausible mechanism for the synthesis of 1,4-dihydropyranopyrazoles using SGO was shown here (Scheme III.B.10). At first, 5-methyl-2-phenyl-2,4-dihydro-3*H*-pyrazole-3-one was formed by the condensation of phenylhydrazine and ethyl acetoacetate. Subsequently, knoevenagal condensation between

aromatic aldehyde and malononitrile exerted 2-benzylidenemalonitrile. Afterthat, pyrazolone and benzylidenemalononitrile participated in Micheal addition followed by cyclization. Finally, the desired 1,4-dihydropyranopyrazole was obtained through tautomerization in the last step of the reaction mechanism.

III.B.3.3. Conclusion

In conclusion, an efficient carbocatalyst SGO is employed for the synthesis of substituted pyranopyrazoles from commercially available aldehydes. Sulfonated graphene oxide (SGO) acts as heterogeneous acid catalyst and itself is capable to furnish the desired 6-Amino-3-methyl-4-phenyl-1,4-[2,3-c]pyrazole-5-carbonitriles with excellent yield. It can be envisioned that such a cheap and robust solid acid catalyst SGO holds great potential for a wide range of acid-catalysed reactions.

III.B.4. Experimental section

III.B.4.1. General information

The reactions were monitored by TLC [carried out on Merck silica gel (60 F254) by using UV light as visualizing agent]. NMR spectra of all the products were taken in $CDCl_3$/DMSO-d_6 (TMS as an internal standard) using a Bruker AV-300 spectrometer operating for ^{1}H at 300 MHz and for ^{13}C at 75 MHz. ^{1}H NMR spectroscopic data are represented as follows: chemical shift (ppm), multiplicity (s = singlet, d= doublet, t = triplet, dd = doublet of doublets, m = multiplet, brs = broad), integration, coupling constants in Hertz (Hz). ^{13}C NMR spectroscopic data are reported in ppm. Coupling constants were reported as J values in Hertz (Hz).The chemicals and reagents were purchased from Merck, Spectrochem, and Sigma-Aldrich.

III.B.4.2. General procedure for the preparation of the catalyst

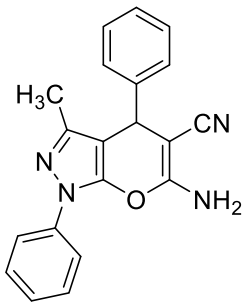
SGO-1 and SGO-2 were prepared by the Tours method according to the literature. In brief, 9:1 mixture of concentrated H_2SO_4/H_3PO_4 (360:40 ml) was taken in a beaker, after that graphite powder (3.0 g) was added slowly to it taking the whole system in an ice bath to keep the temperature below 20 ^oC. $KMnO_4$ (9.0 g) was then added slowly in portions to the solutions. Afterward, the reaction mixture was heated to 50 ^oC and stirred for 12 h. After the reaction, the mixture was centrifuged (5000 rpm for 30 min), and the supernatant was decanted away. The remaining solid material was then washed with water successively, 30% HCl and ethanol to remove the remaining salt. The solid obtained was then dried to obtain the powdered graphene oxide [29]. In SGO-2 9.0 g of $KMnO_4$ is only replaced by 18 g.

III.B.4.3. General procedure for the synthesis of 6-Amino-3-methyl-4-phenyl-1,4-[2,3-c]pyrazole-5-carbonitriles

In a 25-mL round-bottomed flask phenyl hydrazine/hydrazine hydrate (1.5 mmol), ethyl acetoacetate (1 mmol), aromatic aldehyde (1 mmol), malononitrile (1 mmol), and SGO (0.03 g) were refluxed at water medium for appropriate period of time. The progress of the reaction was monitored by TLC and after completion of the reaction, the ice-cold water was added to the reaction mixture. Then, the precipitated organic product was decanted, washed with water and recrystallized from proper solvents to give pure products.After that, the catalyst was recovered by centrifugation and washed with ethanol and dried. All the products are known, and their melting point was found to be identical to those reported in the literature.

III.B.4.4. Spectral data of various pyranopyrazole derivatives

5a.6-Amino-3-methyl-1,4-diphenyl-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (Table III.B.3, entry 1) [19]

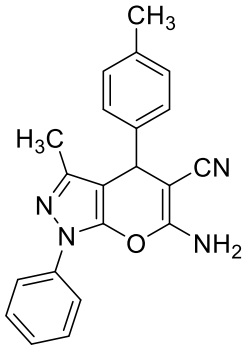


^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 1.76 (s, 3H), 4.66 (s, 1H), 7.20-7.49 (m, 10H), 7.76-7.78 (d, 2H, *J*= 8Hz);

^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm) 12.58, 36.74, 58.16, 98.65, 119.98, 126.19, 127.06, 127.79, 128.54, 129.35, 143.62, 143.88, 145.27, 159.43.

IR (KBr, cm^{-1}) bands 3469, 3332, 2197, 1654, 1514, 1384, 753.

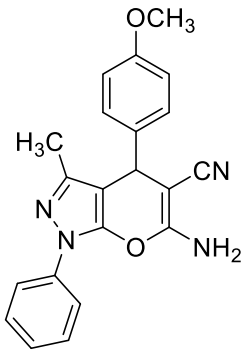
5b.6-Amino-3-methyl-1-phenyl-4-(*p*-tolyl)-1,4-dihydropyrano[2,3c]pyrazole-5-carbonitrile (Table III.B.3, entry 2) [19]



^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 1.81 (s, 3H), 2.22 (s, 3H), 4.89 (s, 1H), 7.08-7.44 (m, 9H), 7.68-7.70 (d, 2H, *J*=8Hz);

^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm) 12.17, 21.60, 60.33, 99.48, 121.05, 126.11, 127.66, 129.25, 129.39, 129.48, 135.39, 137.84, 139.68, 146.81, 160.05.

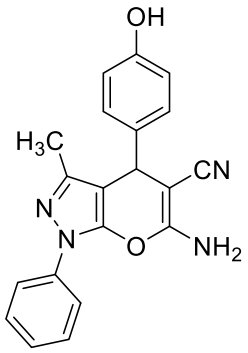
5c.6-amino-4-(4-methoxyphenyl)-3-methyl-1-phenyl-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (Table III.B.3, entry 3)[19]



^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 1.92 (s, 3H), 3.95 (s, 3H), 4.38 (s, 1H), 7.15-7.90 (m, 11H);

^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm) 12.52, 58.16, 60.326, 98.65, 119.98, 126.19, 127.06, 127.79, 128.43, 129.35, 137.54, 143.62, 143.98, 145.27, 159.54.

5d.6-amino-4-(4-hydroxyphenyl)-3-methyl-1-phenyl-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (Table III.B.3, entry 4) [19]

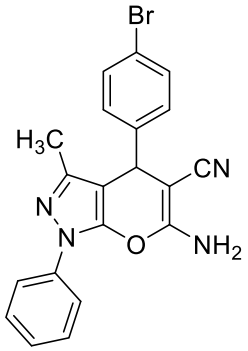


^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 2.30 (s, 1H), 4.94 (s, 1H), 6.59-6.64 (t, 2H), 6.78 (s, 1H), 7.16-7.19 (t, 2H), 7.35-7.39 (t, 4H), 7.62-7.64 (d, 2H, *J*=8Hz);

^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm) 12.19, 33.41, 56.21, 99.48, 112.41, 115.71, 120.18, 121.13, 126.10, 129.48, 133.85, 145.41, 146.73, 147.73, 159.27;

IR (KBr, cm^{-1}) bands 3527, 3314, 2178, 1724, 1589, 814, 753.

5e.6-amino-4-(4-bromophenyl)-3-methyl-1-phenyl-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (Table III.B.3, entry 5)[19]

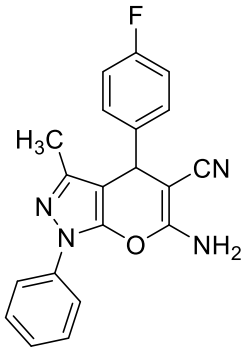


^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 2.17 (s, 3H), 4.92 (s, 1H), 7.17-7.69 (m, 11 H);

^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm) 12.11, 33.18, 58.16, 99.41, 119.59, 121.11, 126.20, 129.47, 130.10, 131.49, 131.65, 143.62, 143.88, 145.27, 159.43;

IR (KBr, cm^{-1}) bands 3320, 2919, 1598, 1503, 1293, 1157, 752.

5f.6-amino-4-(4-fluorophenyl)-3-methyl-1-phenyl-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (Table III.B.3, entry 6) [19]

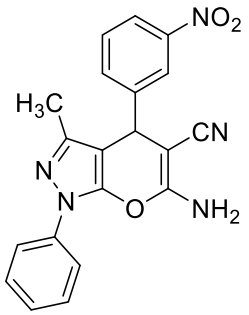


^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 2.30 (s, 1H), 4.94 (s, 1H), 7.05-7.44 (m, 9H), 7.67-7.69 (d, 2H, *J*=8Hz);

^{13}C NMR (400 MHz, DMSO-d_6) δ (ppm) 12.50, 33.02, 58.16, 99.41, 115.17, 115.38, 121.11, 129.47, 129.61, 138.78, 145.19, 146.87, 148.34, 159.43;

IR(KBr, cm^{-1}) bands 3330, 2918, 1567, 1498, 1071, 751.

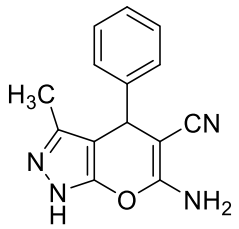
5g.6-amino-4-(3-nitrophenyl)-3-methyl-1-phenyl-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (Table III.B.3, entry 7) [19]



^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 2.33 (s, 1H), 5.13 (s, 1H), 7.18-7.73 (m, 10H), 8.07 (s, 1H);

^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm) 12.40, 33.42, 58.167, 98.31, 121.19, 121.75, 122.29, 126.28, 129.51, 130.25, 134.89, 145.19, 146.87, 148.34, 158.43.

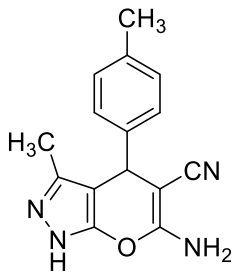
5h. 6-amino-3-methyl-4-phenyl-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (Table III.B.3, entry 8) [19]



^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 2.10 (s, 1H), 5.33 (s, 1H), 7.16-7.80 (m, 7H), 11.45 (brs, 1H);

^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm) 11.81, 33.32, 58.167, 98.71, 121.10, 126.23, 129.47, 130.11, 131.49, 131.62, 143.65, 143.88, 159.43.

5i. 6-amino-3-methyl-4-(p-tolyl)-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (Table III.B.3, entry 9) [19]

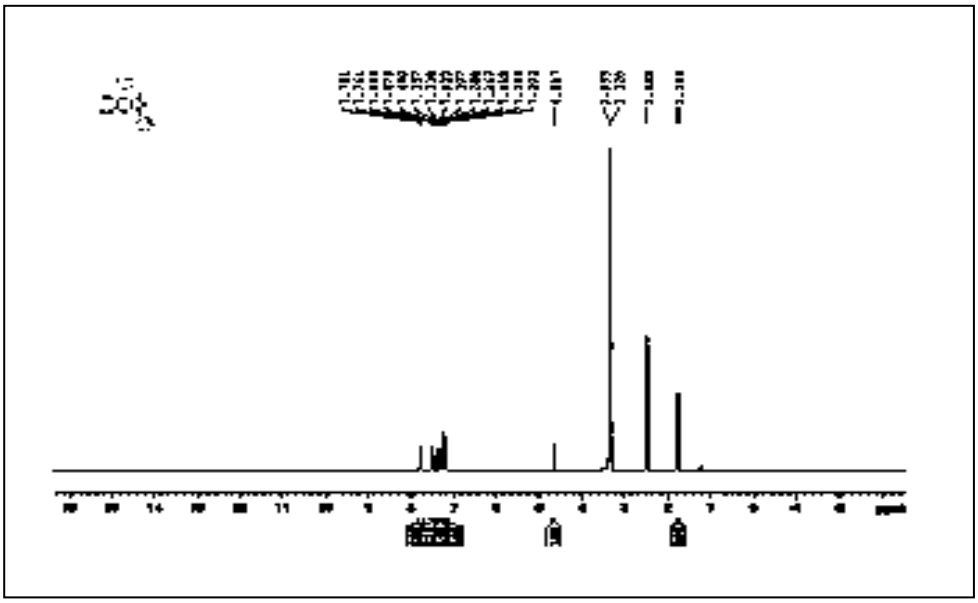


^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 1.67 (s, 3H), 2.20 (s, 3H), 5.62 (s, 1H), 7.30-7.49 (m, 5H), 7.76-7.78 (d, 2H, *J*=7.6Hz), 11.45 (brs, 1H);

^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm) 13.392, 21.234, 33.508, 58.301, 98.311, 117.990, 120.226, 124.864, 128.793, 134.764, 138.784, 148.202, 159.411.

III.B.4.4. Scanned copies of ^{1}H and ^{13}C NMR spectra of synthesised compounds

Figure III.B.2. *Scanned copy of ^{1}H and ^{13}C NMR spectra of 6-Amino-3-methyl-1,4-diphenyl-1,4-dihydropyrano[2,3c]pyrazole-5-carbonitrile*



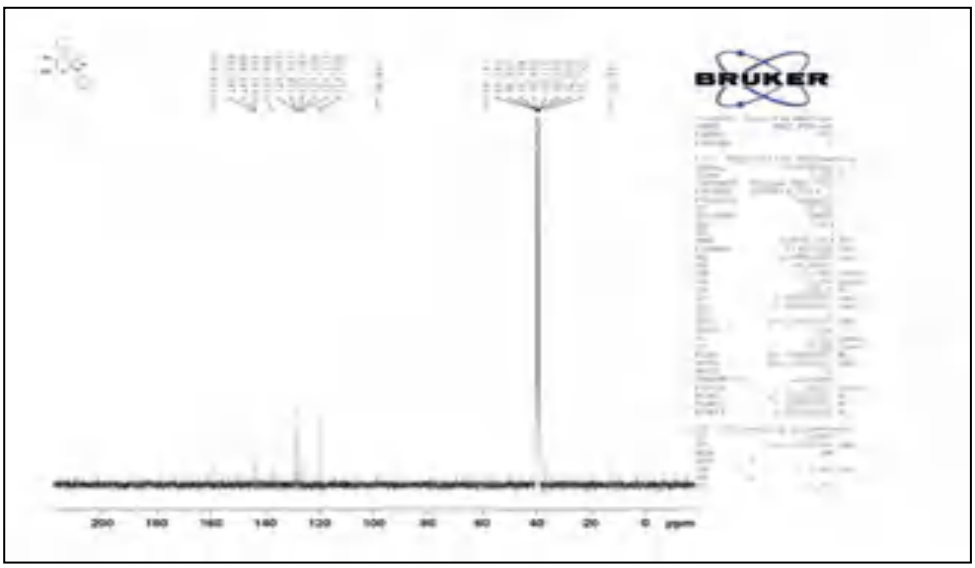
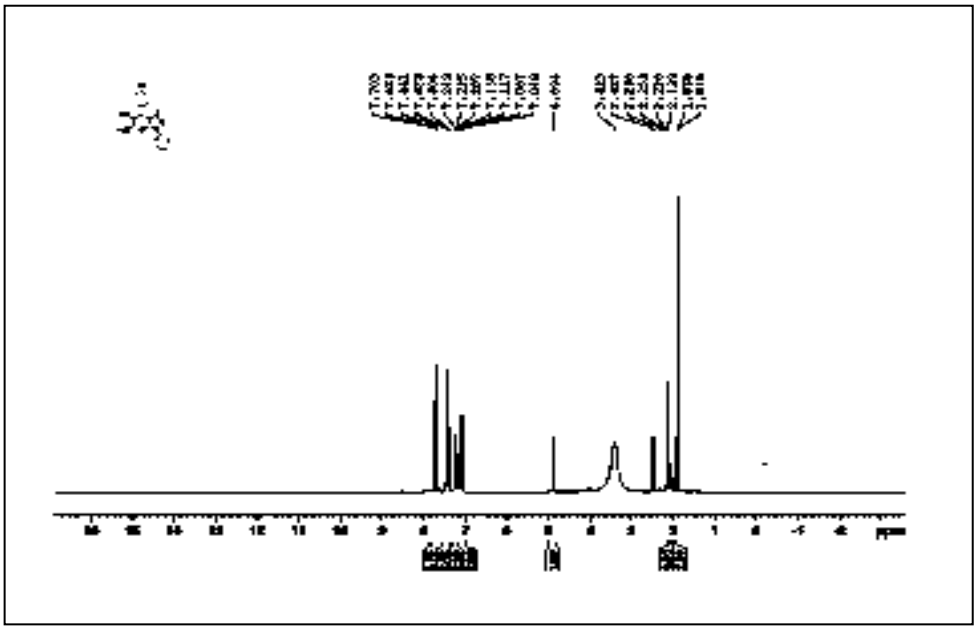


Figure III.B.3. *Scanned copy of ^{1}H and ^{13}C NMR spectra of 6-Amino-3-methyl-1-phenyl-4-(p-tolyl)-1,4-dihydropyrano[2,3c]pyrazole-5-carbonitrile*



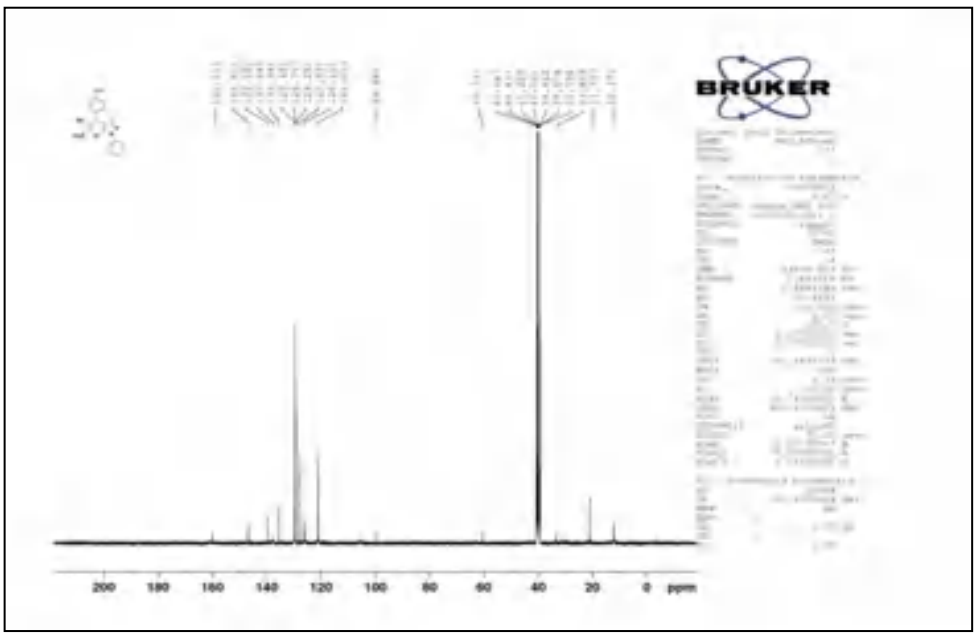
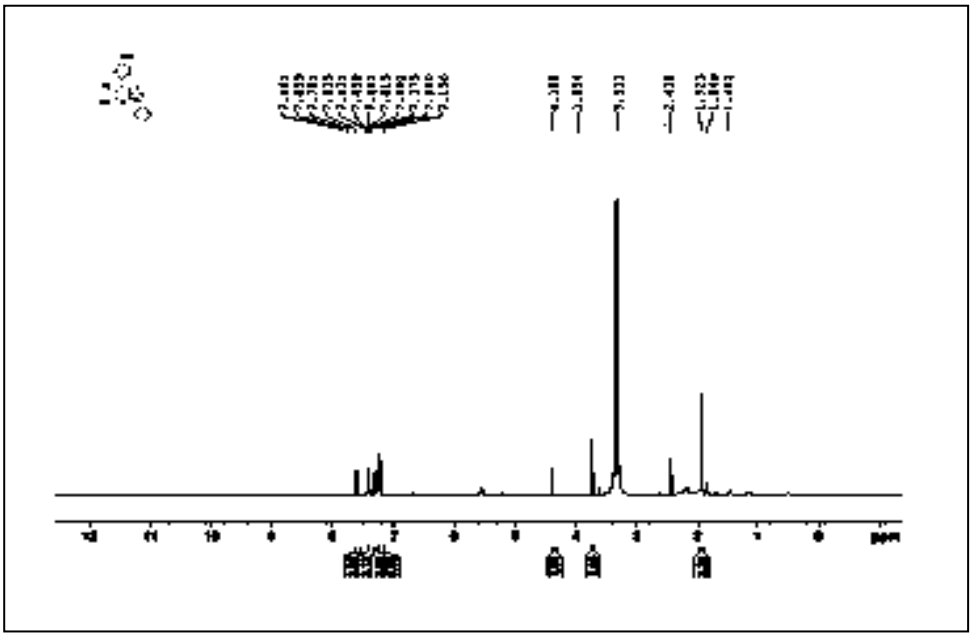


Figure III.B.4. *Scanned copy of ^{1}H and ^{13}C NMR spectra of 6-amino-4-(4-methoxyphenyl)-3-methyl-1-phenyl-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile*



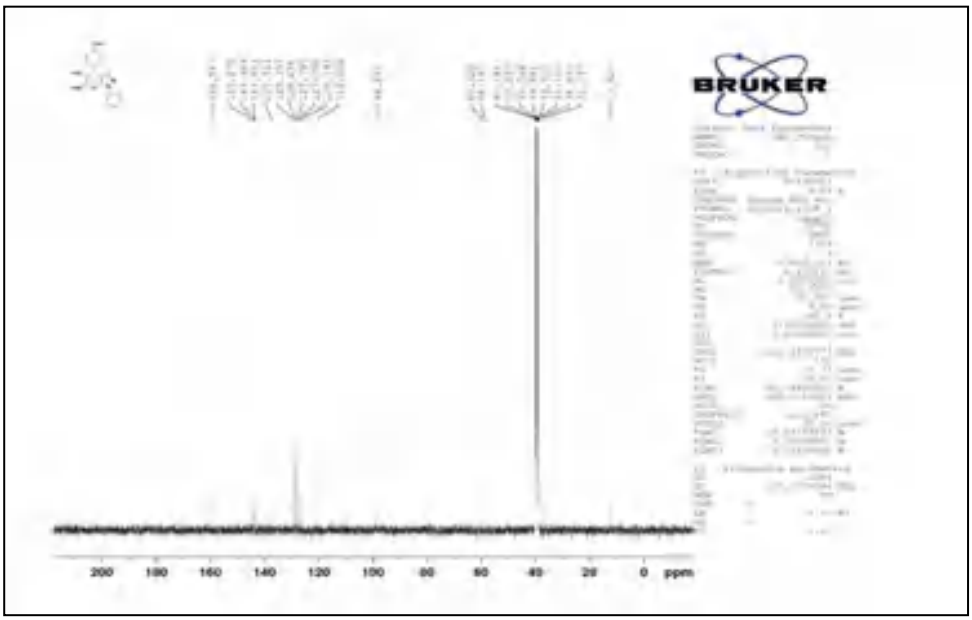
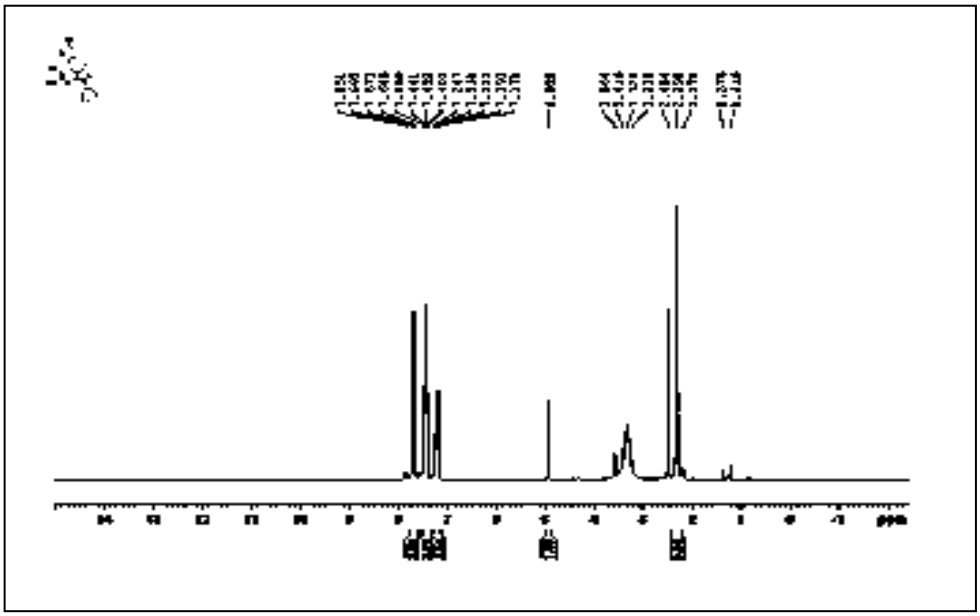


Figure III.B.5. *Scanned copy of ^{1}H and ^{13}C NMR spectra of 6-amino-4-(4-bromophenyl)-3-methyl-1-phenyl-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile*



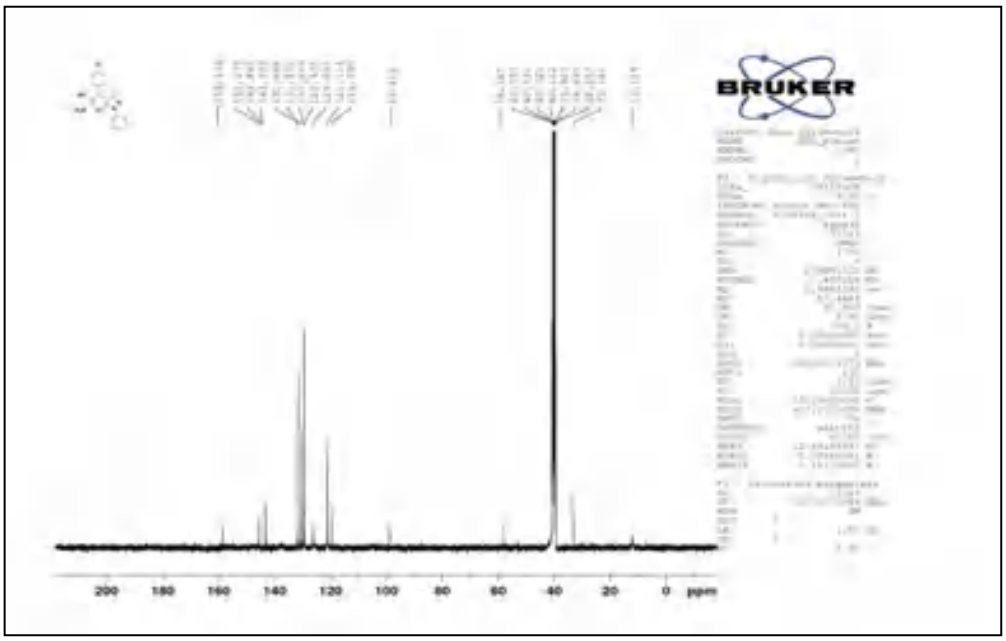
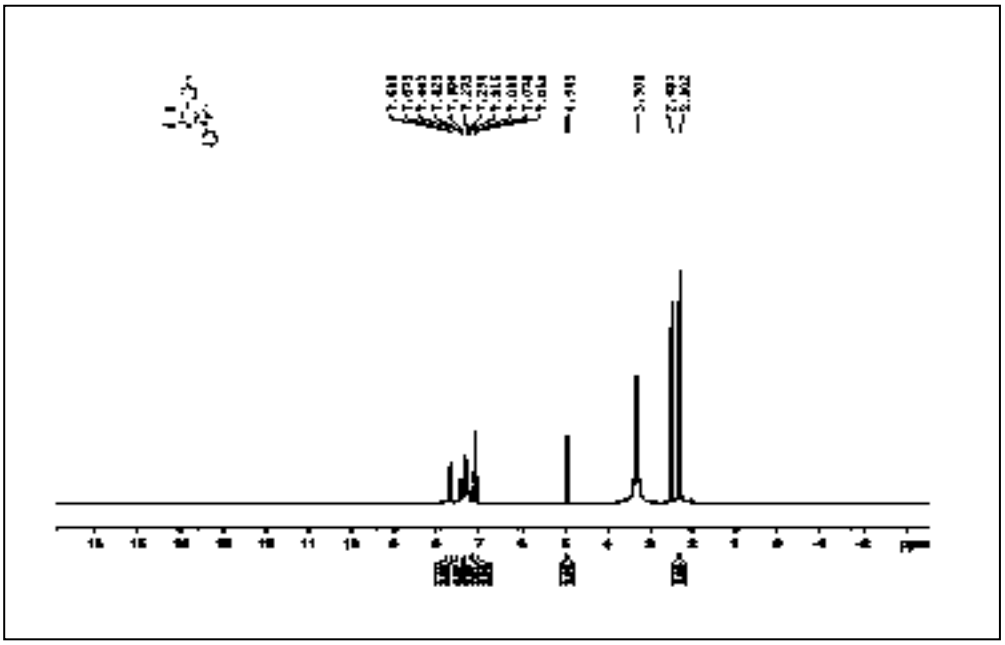


Figure III.B.6. *Scanned copy of ^{1}H and ^{13}C NMR spectra of 6-amino-4-(4-fluorophenyl)-3-methyl-1-phenyl-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile*



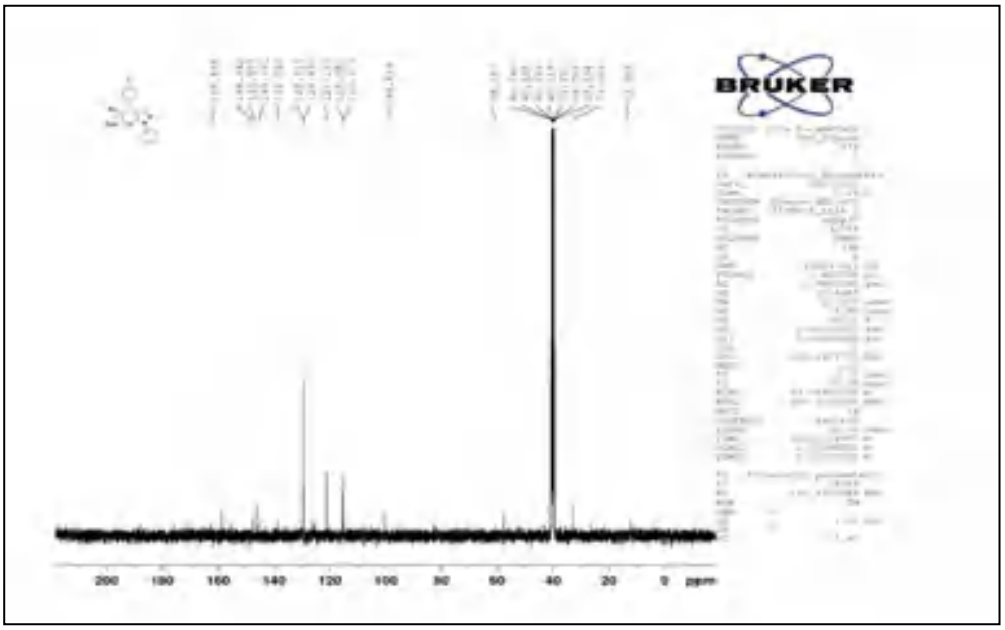
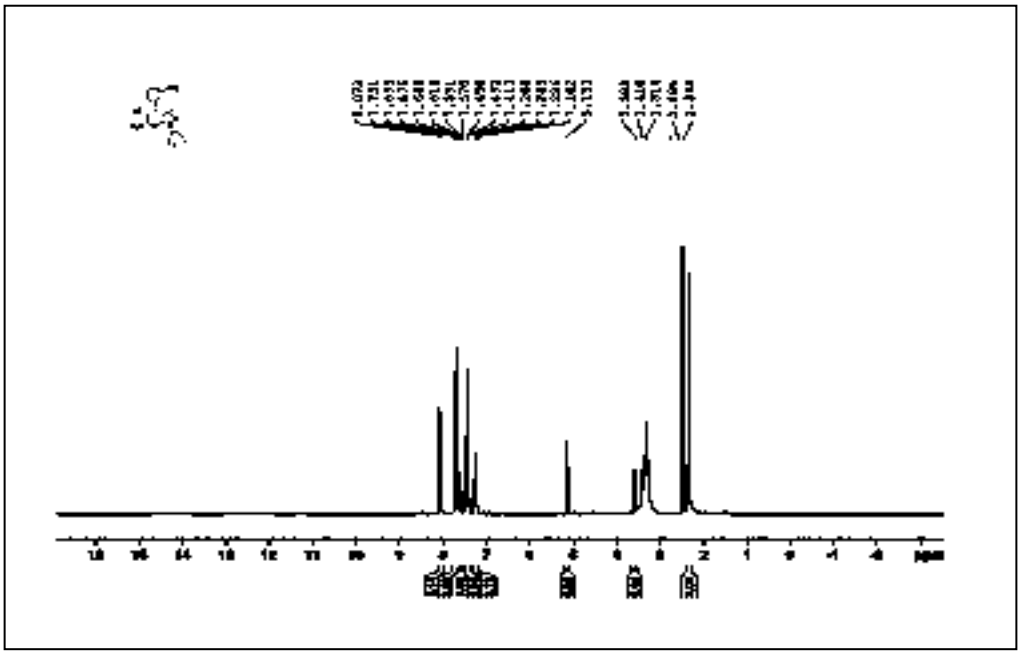


Figure III.B.7. *Scanned copy of ^{1}H and ^{13}C NMR spectra of 6-amino-4-(3-nitrophenyl)-3-methyl-1-phenyl-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile*



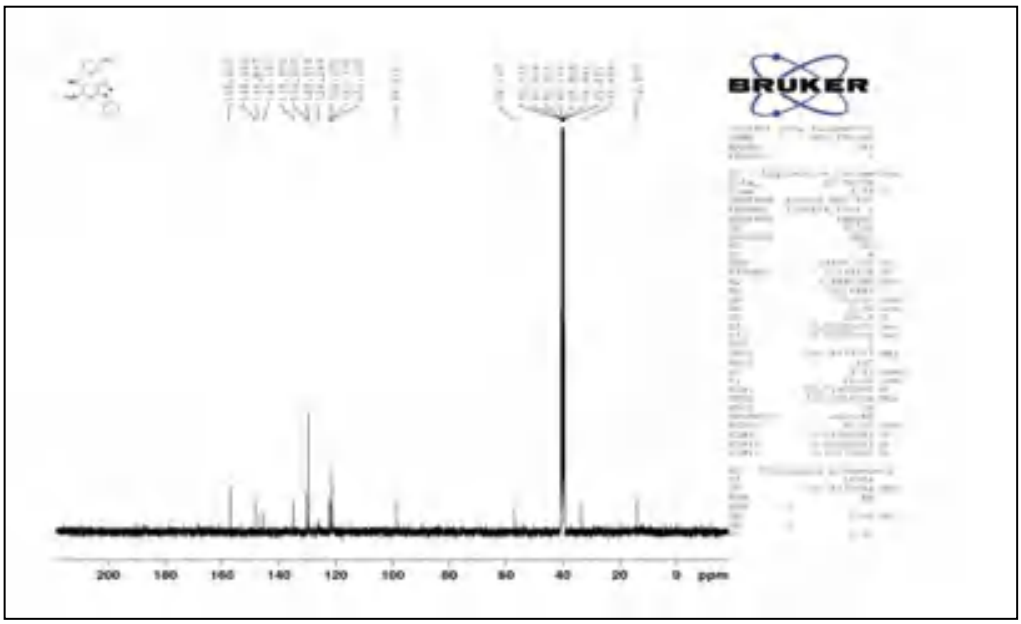
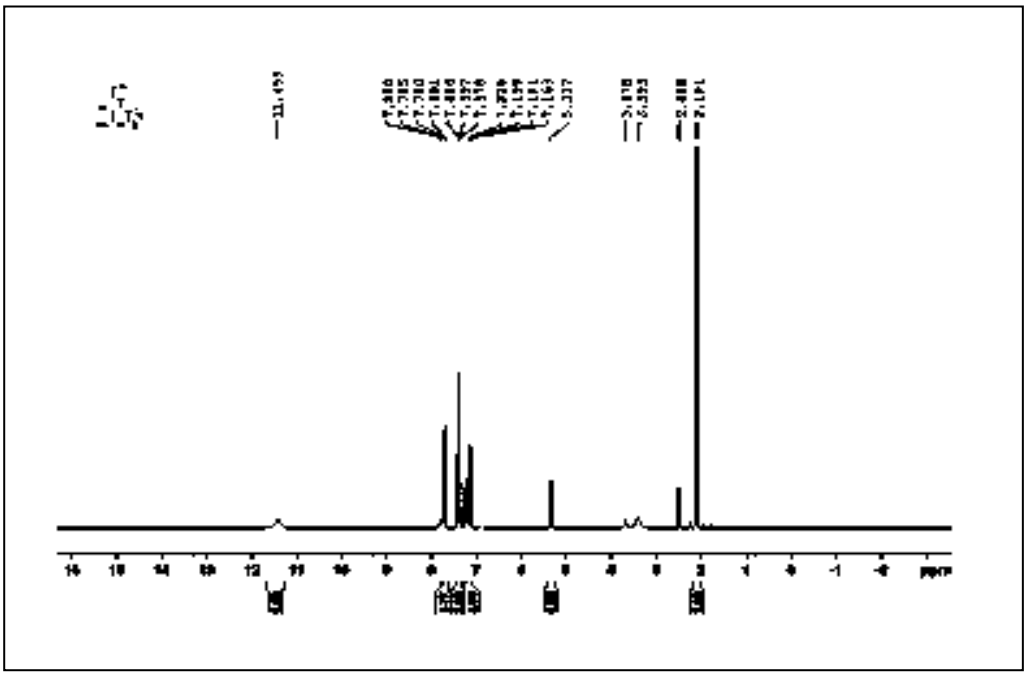


Figure III.B.8. *Scanned copy of ^{1}H and ^{13}C NMR spectra of 6-amino-3-methyl-4-phenyl-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile*



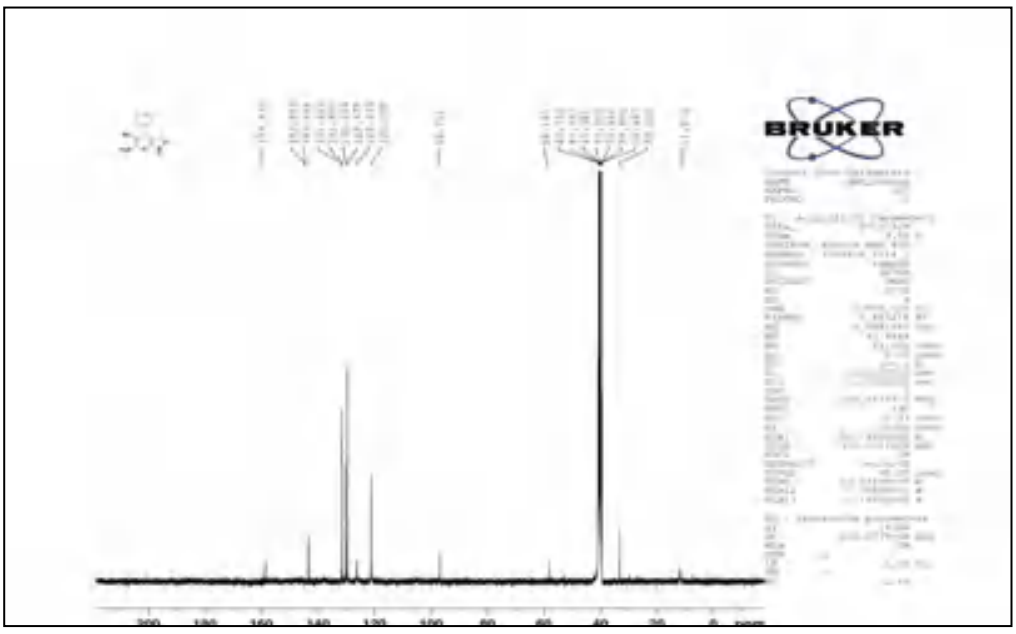
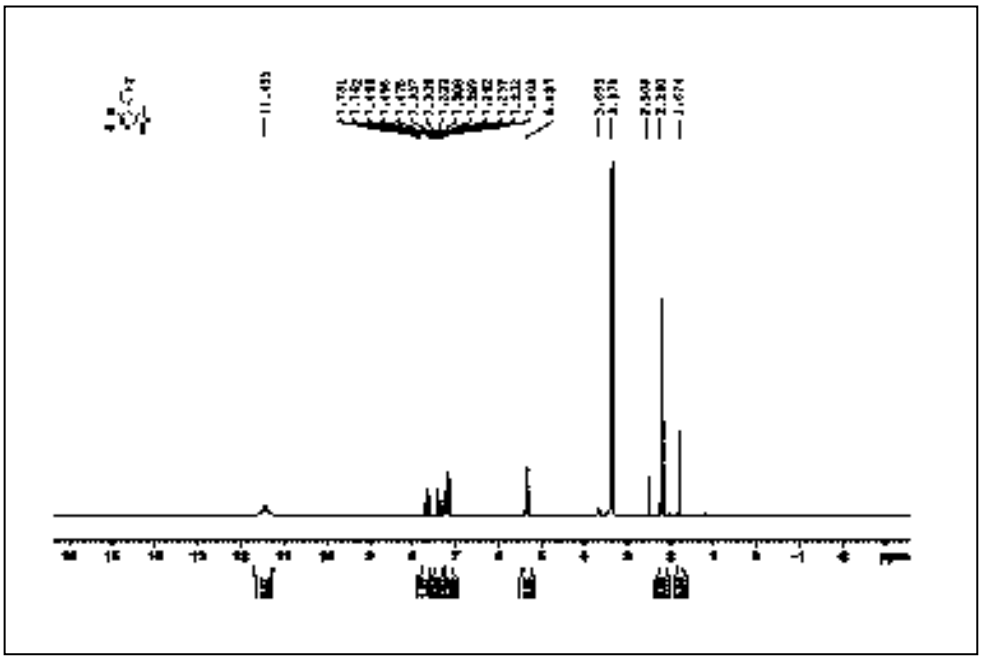
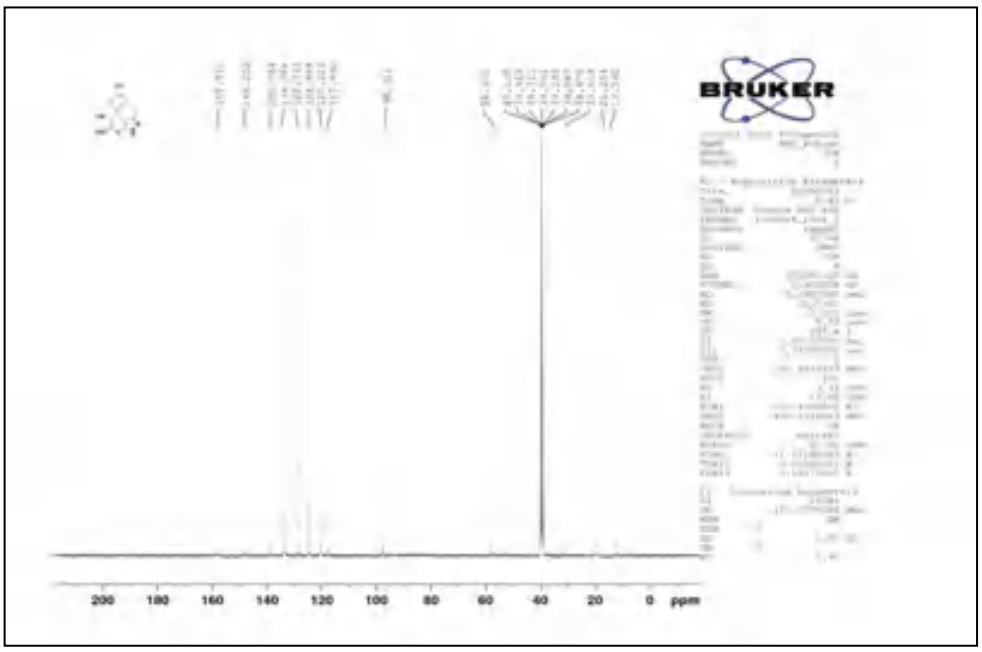


Figure III.B.9. *Scanned copy of ^{1}H and ^{13}C NMR spectra of 6-amino-3-methyl-4-(p-tolyl)-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile*





III.B.5. References

References are given in Bibliography under Chapter III, Section B