Accepted Manuscript

Recyclable palladium catalyst on grapheme oxide for the C-C/C-N Cross-Coupling Reactions of Heteroaromatic Sulfonates

Quanlu Yang, Zhengjun Quan, Shang Wu, Baoxin Du, Mingming Wang, Peidong Li, Yinpan Zhang, Xicun Wang

PII: S0040-4020(15)01000-5

DOI: 10.1016/j.tet.2015.06.103

Reference: TET 26939

To appear in: *Tetrahedron*

Received Date: 20 April 2015

Revised Date: 26 June 2015

Accepted Date: 29 June 2015

Please cite this article as: Yang Q, Quan Z, Wu S, Du B, Wang M, Li P, Zhang Y, Wang X, Recyclable palladium catalyst on grapheme oxide for the C-C/C-N Cross-Coupling Reactions of Heteroaromatic Sulfonates, *Tetrahedron* (2015), doi: 10.1016/j.tet.2015.06.103.

Graphical Abstract

Recyclable palladium catalyst on grapheme oxide for the C-C/C-N Cross-Coupling Reactions of Heteroaromatic Sulfonates

Leave this area blank for abstract info.

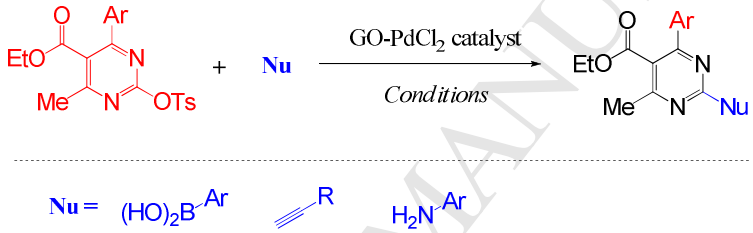
Quanlu Yang,[a, b] Zhengjun Quan,*[a] Shang Wu,[a, c] Baoxin Du,[a] Mingming Wang,[b] Peidong Li,[b] Yinpan Zhang,[b] Xicun Wang*[a]

[a] *Laboratory of Eco-Environment-Related Polymer Materials, Ministry of Education; Key Laboratory of Polymer Materials, College of Chemistry and Chemical Engineering, Northwest Normal University, Lanzhou, Gansu 730070, P. R. China*

E-mail: wangxicun@nwnu.edu.cn, quanzhengjun@hotmail.com

[b] *College of Chemical Engineering, Lanzhou University of Arts and Science, Beimiantan 400, Lanzhou, Gansu 730000, P. R. China*

[c] *College of Chemical Engineering, Northwest University for Nationalities, Lanzhou, Gansu 730030, P. R. China*



Tetrahedron
journal homepage: www.elsevier.com

Recyclable palladium catalyst on grapheme oxide for the C-C/C-N Cross-Coupling Reactions of Heteroaromatic Sulfonates

Quanlu Yang,[a, b] Zhengjun Quan,*[a] Shang Wu,[a, c] Baoxin Du,[a] Mingming Wang,[b] Peidong Li,[b] Yinpan Zhang,[b] Xicun Wang*[a]

[a] *Laboratory of Eco-Environment-Related Polymer Materials, Ministry of Education; Key Laboratory of Polymer Materials, College of Chemistry and Chemical Engineering, Northwest Normal University, Lanzhou, Gansu 730070, P. R. China*
E-mail: wangxicun@nwnu.edu.cn, quanzhengjun@hotmail.com
[b] *College of Chemical Engineering, Lanzhou University of Arts and Science, Beimiantan 400, Lanzhou, Gansu 730000, P. R. China*
[c] *College of Chemical Engineering, Northwest University for Nationalities, Lanzhou, Gansu 730030, P. R. China*

ARTICLE INFO

Article history:
Received
Received in revised form
Accepted
Available online

Keywords:
C-C coupling
C-N coupling
Nitrogen heterocycles
GO
Heterogeneous catalyst

ABSTRACT

A well-defined heterogeneous palladium catalyst, graphene oxide grafted with $PdCl_2$, was prepared and found to be an effective catalyst for the C-C, C-N coupling of hetero aryl sulfonates with aryl boronic acids, terminal alkynes, amines, respectively, leading to the desired coupling products in moderate to excellent yields. The catalyst was characterized by XRD, IR, SEM, TEM, XPS and ICP. It is worthy noting that this catalyst offers a number of advantages such as high stability and negligible metal leaching. It also retains good activity for at least five successive runs without any additional activation treatment, showing a better performance than the well-known commercial Pd/C catalysts. This approach would be very useful from a practical viewpoint.

1. Introduction

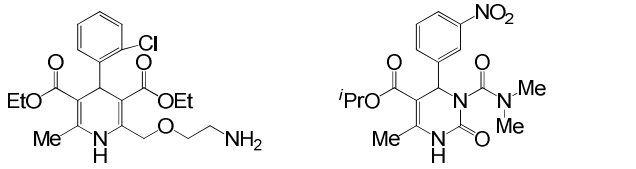
During the past decades, homogeneous palladium(II) catalysis was used as one of the most efficient tactics for carbon–carbon and carbon–heteroatom bond formations. Coupling reactions like the Heck-, Suzuki-, and Buchwald- type provided one-step methods for the assembling of complex structures. [1-7]

Palladium (Pd) catalyzed C-C and C-N coupling reactions have been of strategic importance since they offer fast reaction rates, high turnover frequency, good selectivity, and high production yield in various synthetic protocols. [8-14] Heteroaromatic compounds are important constituents of a wide range of natural products, pharmaceuticals, and fine chemicals, hence methods for their functionalization are of high interest. [15-20] In the Pd-catalyzed Suzuki coupling reactions, aryl sulfonates are a class of interesting and practical alternatives to aryl halides, because they are more easily to handle and usually less expensive than the corresponding aryl halides. However, aryl sulfonates are generally less reactive in the metal-catalyzed coupling reactions than the corresponding aryl chlorides, and thus, much harsher reaction conditions were adopted accordingly. [21-30]

Despite the remarkable utility of Pd catalysts in organic synthesis, the use of homogenous Pd catalysts has been limited to a narrow application area since their high cost and the difficulties to purify and reuse after chemical reactions. [31-33] Tedious separation and recycling of the palladium catalyst are major drawbacks of the homogeneous catalysts. [34] Immobilization of homogeneous catalysts onto a solid surface can be a method of reformation, which may facilitate the separation of the catalyst from the reaction products, and make the reutilization of the catalyst possible in multiple subsequent cycles. For decades, enormous efforts in this field were made to immobilize known catalysts onto various separable organic, inorganic or hybrid supporters, [35-45] such as activated carbon, [46] polymers, [47-49] glass polymer composites, [50] zeolites, [51] silica, [52-55] molecular sieves, [56-58] clays, [59-62] carbon nano tubes, [63] zinc ferrite, [64] graphene, [65] and sulfonated graphene. [66] Unfortunately, the supported Pd complex catalysts often suffer from reduced activity, inferior selectivity, and other problems such as metal leaching and high preparation complexity.

Recently, for catalysis studies, chemically exfoliated graphene oxide (GO) [67-80] has attracted extensive attention in heterocatalysis due to their unique two-dimensional structures, huge surface areas, tunable electrical properties and other excellent properties. [81, 82] Many transition metals, such as Ag, [83] Pd, [84-88] Pt, [89, 90] and Au, [91] were surported on GO and prepared as heterocatalysts for organic reactions.

Heterobiaryl compounds, with prevalent structural motifs in many pharmaceuticals and other biologically active molecules, have been a focus for all the time in the development of heterocyclic synthesis. [92] In particular, organic molecules with pyrimidine scaffolds are widely used in medication [93] and also as important precursors in the synthesis of other derivatives. [94-97] In 1990s, derivatives of the dihydropyrimidinthione (DHPM) were found their potential value as calcium antagonists (Figure 1), α_{1a}-antagonists, hypotensor, anticarcinogen, etc. [94, 98-100] Hence increasing efforts were devoted upon the synthesis of the DHPM derivatives and their reactivity.



(a) Amlodipine (b) Dihydropyrimidine calcium channel blocker

Figure 1. (a) Amlodipine, a calcium channel blocker of dihydropyridine [101]; (b) Dihydropyrimidine calcium channel blockers [98-100].

More recently, we have developed an approach to C2-substituted and functionalized pyrimidines, by cross coupling reactions of pyrimidin-2-yl sulfonates under mild conditions and rapid procedures [102-104]. Nonetheless, this homogenous palladium catalysis owned numerous drawbacks, especially, like high cost, and non-reusability. Based on the pioneering works in this area, herein, we report a facile and efficient method to immobilize Pd (II) complexes on GO in aqueous suspension. We found that this catalyst can afford high catalytic activities for the C-C and C-N cross-coupling reactions of pyrimidin-2-yl sulfonates with arylboronic acids, terminal alkynes and aniline. The catalyst has been found to be stable and recyclable in these systems, and the conversions in the case of a variety of substrates have been found to be good in its presence.

2. Results and discussion

2.1 Synthesis and characterization of the catalyst

GO was prepared by chemical oxidation and exfoliation of natural graphite under acidic conditions according to the improved Hummer's method. [105] Subsequently, 1.0 g the GO and 0.2 g $PdCl_2$ were mixed with 20 mL of de-ionized water, stirred at r.t. for 3 h. Despite the low solubility of $PdCl_2$ in water, cation exchange took place overnight. The suspension was separated by centrifugation, washed with de-ionized water (3 × 20 mL) and acetone (3 × 20 mL), dried in a vacuum oven at 40 ^oC for 4 h and gently powdered was obtained. The palladium content in GO-$PdCl_2$ was determined by means of inductively coupled plasma equipped with atomic emission spectrometry (ICP-AES) and amounted to be 2.86 wt % (0.27mmol/g).

In order to understand the structural properties of graphite, GO and GO-$PdCl_2$, XRD measurements were performed (Figure 2). The graphite powder presents a typical sharp diffraction peak at 2θ = 26.3°, which is characteristic for (002) reflection in graphite, corresponding d-spacing of 0.33 nm .Upon oxidation, A broad peak at 2θ = 9.3° was observed with a d-spacing of 0.95 nm, corresponding to the (002) reflection of GO. The increase in d-spacing is due to the insertion of H_2O molecules and various oxygen functional groups in the AB-stacked graphite sheets. [106-108] In GO-$PdCl_2$, the intensity of the peak at 9.3° significantly decreased, and an obvious peak at 2θ = 21.4° appeared. It is reasonable to consider that the reduced peak intensity in GO resulted from Pd^{2+} was conjugated onto the GO with surface oxygen. The peak at 2θ = 39.8°is characteristic for Pd (II) with face centered cubic structure, suggesting that the Pd is composed of crystalline nanostructures on graphene.

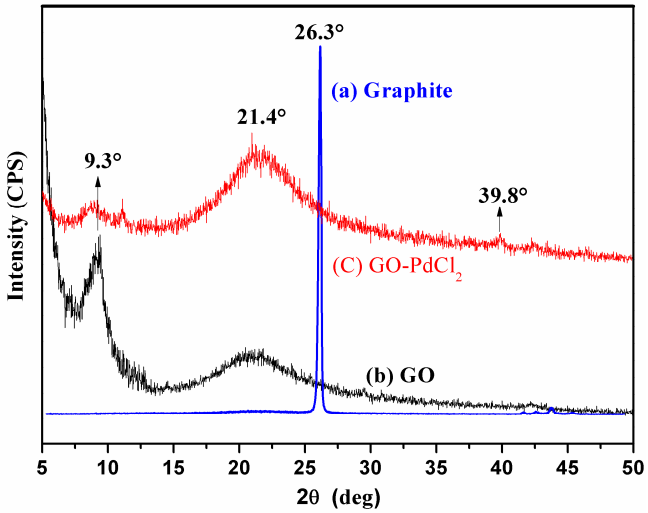


Figure 2. The XRD spectra of (a) Graphite, (b) GO, (c) GO-$PdCl_2$.

Figure 3 shows the FTIR spectra of graphite, GO, and GO-$PdCl_2$. It can be seen that the obvious change was existed in graphite and graphite oxide. After being oxidized, the peak at 3400cm^{-1} became broadened, which was the typical stretching vibration peak of –OH in –COOH. 1720 cm^{-1} and 1398 cm^{-1} that are ascribed to the C=O stretching vibrations of COOH groups and the O–H deformation vibrations of tertiary C–OH, 1625 cm^{-1} that are related to the O–H deformation vibrations of H_2O groups, 1049 cm^{-1} and 868 cm^{-1} that are indexed to the characteristic peaks of epoxy groups and peroxide groups.[107-108] The results provided direct evidences for the successful oxidation of graphite. For GO-$PdCl_2$, the peak corresponding to oxygen functional groups significantly decreased or disappeared. This is relatively consistent with the XRD data, where the Pd^{2+} reacts with surface oxygen, and the corresponding XRD peak intensity was reduced.

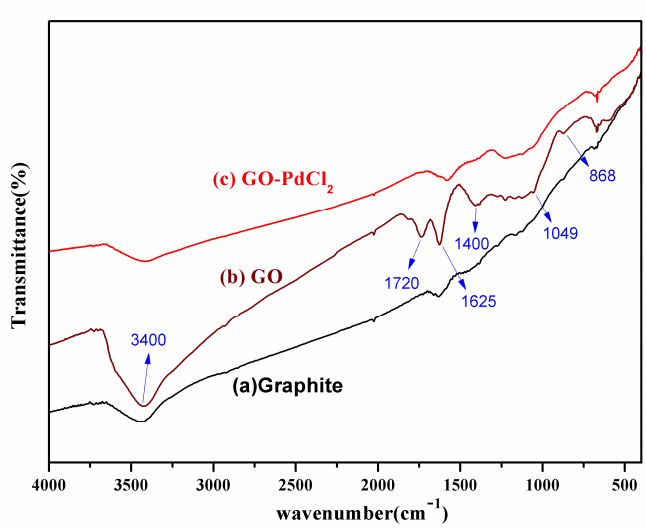


Figure 3. The FTIR spectra of (a) Graphite, (b) GO, (c) GO-$PdCl_2$.

We examined the detailed electronic configurations of GO-$PdCl_2$ complex using X-ray photoelectron spectroscopy (XPS) measurements. (Figure 4) The peaks at 342.80 eV and 337.43 eV were assigned to the binding energy of $Pd_{3d3/2}$ and $Pd_{3d5/2}$ in

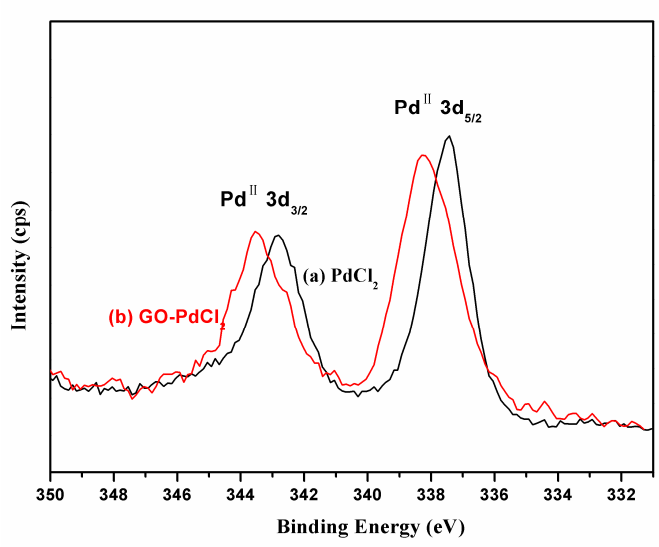


Figure 4. The XPS spectra of (a) GO, (b) GO-$PdCl_2$.

$PdCl_2$ respectively; it was found to 0.75 eV and 0.87 eV decrease in GO-$PdCl_2$ complex, which are originated from $Pd_{3d3/2}$ and $Pd_{3d5/2}$ of Pd^{II}. The results show the coordination or ionic bonds are formed in $PdCl_2$ with GO.

The morphologies of the Graphite, GO and GO-$PdCl_2$ were found out by scanning electron microscopy (SEM-EDX) and transmission electron microscopy (TEM). The SEM (Figure 5) and TEM (Figure 6) image (a, Figure 5; a, Figure 6) indicated stacking of multilayer in Graphite structure. After being oxidized, the sheet morphology with typical wrinkle of GO is clearly observed in the TEM and SEM images of GO (b, Figure 5; b, Figure 6). And then in Figure 5 (c) and Figure 6 (c), no obvious aggregated Pd particle on the surface of GO was observed. Furthermore, the EDS mapping images (d, Figure 5) revealed that a homogeneous distribution of Pd on GO, and then the EDX of GO and GO-$PdCl_2$ was texted (e and f, Figure 5); the presence of oxygen elements was confirmed, which indicated the successful oxidization of the graphite (e, Figure 5), and Figure 5 (f) revealed that the presence of Pd on the surface of GO. This is relatively consistent with the XRD and FTIR data.

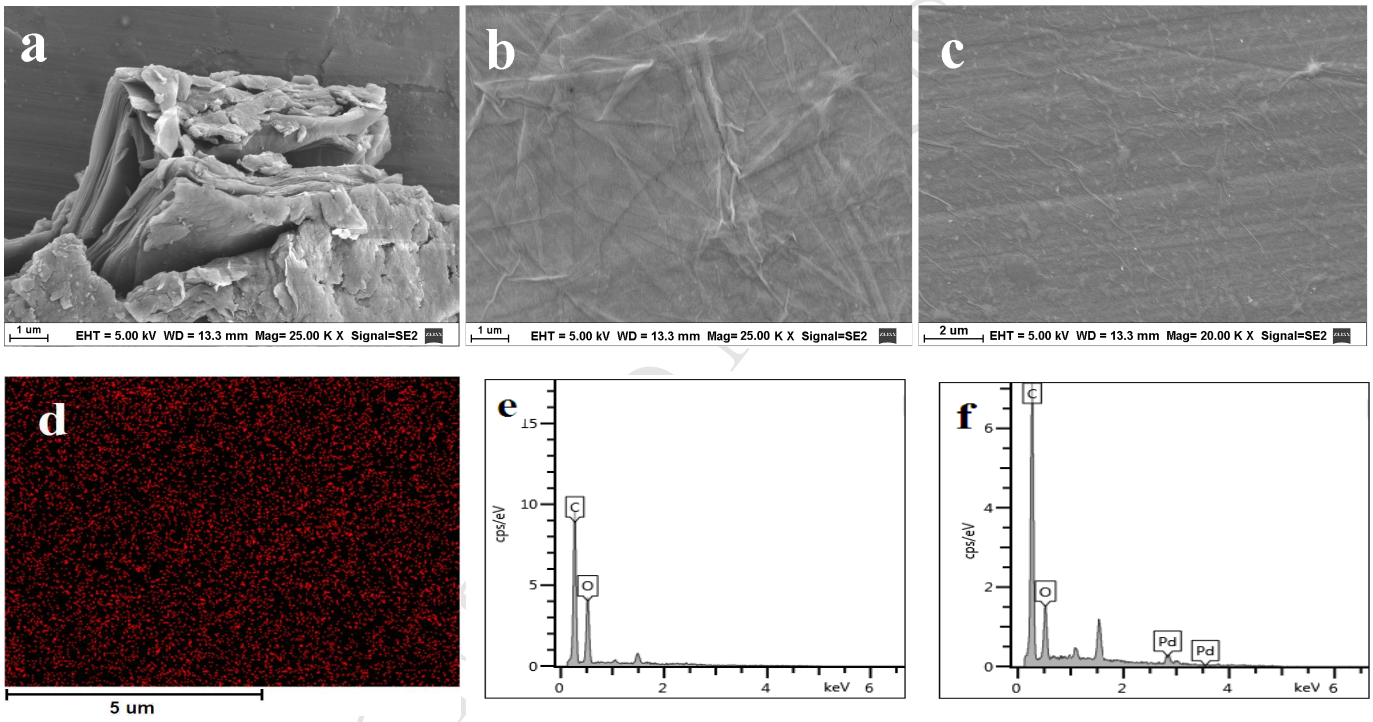


Figure 5. SEM image of (a) Graphite, (b) GO, (c) GO-$PdCl_2$, (d) the corresponding EDS mapping of Pd; and the EDX spectrum of (e) GO, (f) GO-$PdCl_2$.

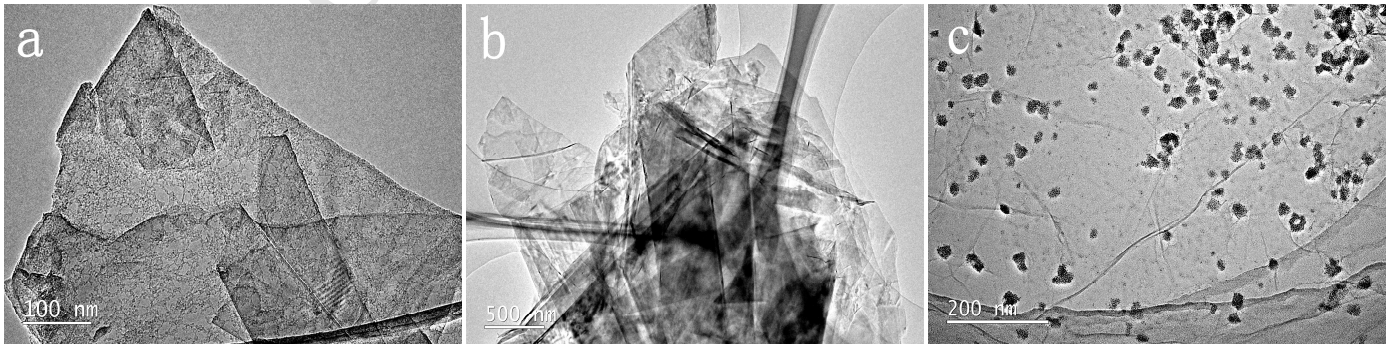
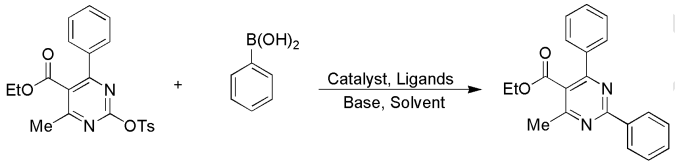


Figure 6. TEM image of (a) Graphite, (b) GO, (c) GO-$PdCl_2$.

2.2 Coupling reactions of pyrimidin-2-yl sulfonates with arylboronic acids

The catalytic performance of the prepared catalyst was systematically examined through Suzuki coupling reactions. As a model, the coupling reaction of ethyl 4-methyl-6-phenyl-2-(tosyloxy)pyrimidine-5-carboxylate (**1a**) with phenylboronic acid (**2a**) was studied (Table 1). Firstly, 1,4-dioxane was chosen as the solvent, and the ligands as well as the bases were evaluated, respectively (entries 1-7). It seems that PPh_3 and K_3PO_4 were the suitable ligand and base to give the corresponding coupling product **3a** in 87% yield (entry 2). The yield declined when 2,2'-oxybis(2,1-phenylene)bis(diphenylphosphane) (DPE-Phos) was used as the ligand (entry 1). However, an increase in the cross coupling reactivity was observed with $CsCO_3$ as base under similar conditions (entry 5). Other bases including NaOAc, TBAB, K_2CO_3 and NaF provided poor conversion (entries 3-4, 6-8). Further optimization of conditions was achieved for the solvent. Among the different solvents that were studied, low yields were obtained in toluene, CH_3CN and CCl_4 (entries 8-10). In the controlling experiments, no reaction occurred without ligand or GO, indicating their indispensible roles in the reaction. (entries 14, 15). Tests upon the catalyst amount suggested that 20 mg of the GO-$PdCl_2$ catalyst was enough to afford the high yield of the product (compare entry 2 with entry 11, 12). More catalyst added did not obviously accelerate the reaction in further (entry 13). Thereby, the appropriate condition is optimized as pyrimidin-2-yl sulfonate **1a** (0.25 mmol), arylboronic acid **2a** (0.375 mmol), K_3PO_4 (2.0 equiv.), PPh_3 (20 mol %), 20 mg of GO-$PdCl_2$ catalyst (Pd 2.86 wt %), stirred in 5 mL 1,4-dioxane at 110 °C for 18 h.

Table 1. Optimized conditions for the coupling of pyrimidin-2-yl sulfonates with arylboronic acids [a].



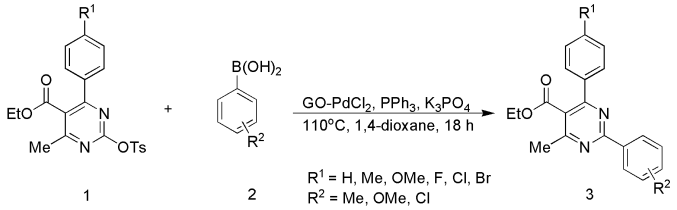
Entry	Catalyst	Base	Ligand	Solvent	Yield [b]
1	GO-$PdCl_2$ (20 mg)	K_3PO_4	DPE-Phos	dioxane	72%
2	GO-$PdCl_2$ (20 mg)	K_3PO_4	PPh_3	dioxane	87%
3	GO-$PdCl_2$ (20 mg)	NaOAc	PPh_3	dioxane	10%
4	GO-$PdCl_2$ (20 mg)	TBAB	PPh_3	dioxane	trace
5	GO-$PdCl_2$ (20 mg)	Cs_2CO_3	PPh_3	dioxane	52%
6	GO-$PdCl_2$ (20 mg)	K_2CO_3	PPh_3	dioxane	---
7	GO-$PdCl_2$ (20 mg)	NaF	PPh_3	dioxane	---
8	GO-$PdCl_2$ (20 mg)	K_3PO_4	PPh_3	toluene	8%
9	GO-$PdCl_2$ (20 mg)	K_3PO_4	PPh_3	CH_3CN	trace
10	GO-$PdCl_2$ (20 mg)	K_3PO_4	PPh_3	CCl_4	---
11	GO-$PdCl_2$ (10 mg)	K_3PO_4	PPh_3	dioxane	63%
12	GO-$PdCl_2$ (15 mg)	K_3PO_4	PPh_3	dioxane	71%
13	GO-$PdCl_2$ (30 mg)	K_3PO_4	PPh_3	dioxane	89%
14	GO (20 mg)	K_3PO_4	DPE-Phos	dioxane	---
15	GO-$PdCl_2$ (20 mg)	K_3PO_4	---	dioxane	---

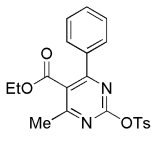
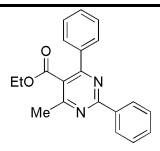
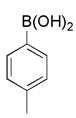
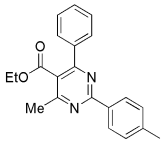
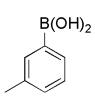
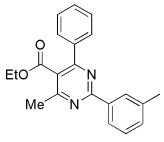
[a] Reaction condition: **1a** (0.25 mmol), **2a** (1.5 equiv.), ligands (20 or 6 mol %), base (2.0 equiv.), catalyst (Pd 2.86 wt %), solvent (5 mL), 110 °C, 18 h.
[b] Isolated yield of **3a** by column chromatography.

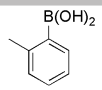
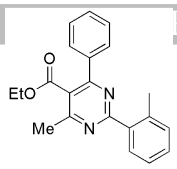
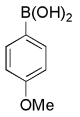
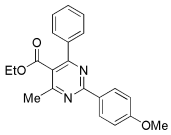
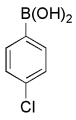
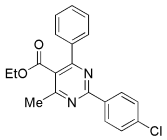
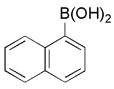
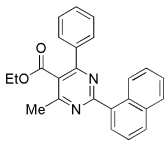
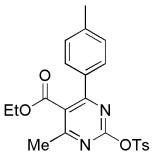
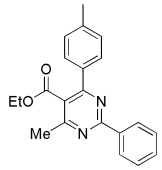
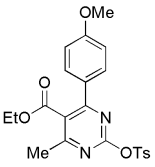
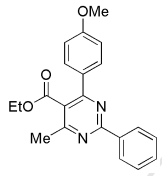
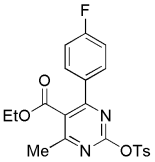
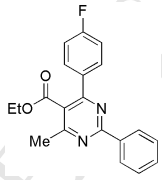
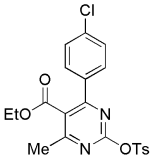
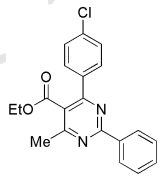
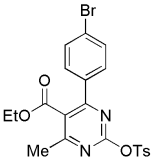
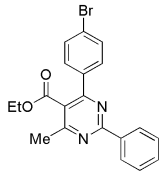
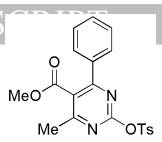
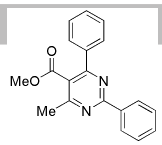
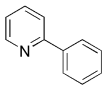
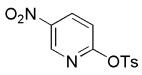
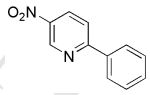
To expand the scope of substrates, we further examined the GO-Pd catalyst for the Suzuki coupling reactions of various pyrimidin-2-yl sulfonates (**1**) with different phenylboronic acids (**2**) under the optimized conditions (Table 2). Notably, there was not any obvious trend or difference in reactivity between the systems of varied electronic effects. Arylboronic acids with electron-donating (Me- and MeO-) and electron-withdrawing groups (Cl-) were well tolerated (entries 2-6), and satisfactory yields were obtained. Additionally, the arylboronic acids with either *p*-substituted (entry 2) or *m*-substituted (entry 3) methyl group afforded the cross-coupling products in 85% and 88% yields, respectively. On the other hand, sterically hindered substituents on the arylboronic acids impacted on the reaction. For example, the reactions involving 2-methylphenylboronic acid (**2d**) gave the corresponding product **3d** only in 72% yield (entry 4). As expected, electron-deficient 1-naphthylboronic acid **2g** was also a suitable reaction partner (entry 7).

In addition to arylboronic acids, several pyrimidin-2-yl sulfonates were used as starting compounds in the reaction. These substituted pyrimidin-2-yl sulfonates, bearing fluoro, chloro, bromation, methyl, and methoxyl groups, were smoothly converted to the corresponding products in high yields (entries 8-15). Fortunately, the catalytic system can be used for selective coupling of sulfonates groups keeping halogen functionalities intact with only **3j, 3k, 3l** produced, respectively (entries 10-12). To our delight, all reactions took place smoothly with the desired coupling products **3** isolated in moderate to excellent yields. Additionally, sulfonates of pyridine derivatives were also tested under this catalytic system, leading to moderated yields for the corresponding products **3n** and **3o** (entry 14, 15).

Table 2. Suzuki coupling reactions of pyrimidin-2-yl sulfonates with arylboronic acids [a].



Entry	Sulfonate	Arylboronic acid	Product	Yield[b]
1	 **1a**	 **2a**	 **3a**	**87%**
2	**1a**	 **2b**	 **3b**	**85%**
3	**1a**	 **2c**	 **3c**	**88%**

4	1a	 2d	 3d	72%
5	1a	 2e	 3e	86%
6	1a	 2f	 3f	92%
7	1a	 2g	 3g	96%
8	 1b	2a	 3h	83%
9	 1c	2a	 3i	87%
10	 1d	2a	 3j	91%
11	 1e	2a	 3k	88%
12	 1f	2a	 3l	81%
13	 1g	2a	 3m	82%
14	 1h	2a	 3n	68%
15	 1i	2a	 3o	76%

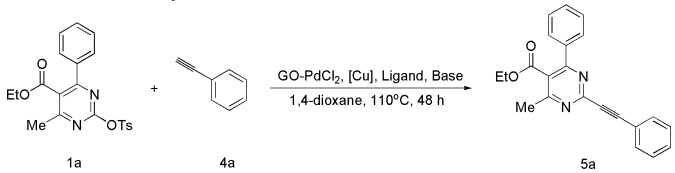
[a] Reaction conditions: **1** (0.25 mmol), **2** (1.5 equiv.), PPh_3 (20 mol %), GO-$PdCl_2$ (20 mg, Pd 2.1 mol %), K_3PO_4 (2.0 equiv.), stirred in 5 mL 1,4-dioxane at 110 °C, 18 h.

[b] Isolated Yield of product **3**.

2.3 Coupling reactions of pyrimidin-2-yl sulfonates with terminal alkynes

Subsequently, as a model reaction, the coupling reaction of pyrimidin-2-yl sulfonate (**1a**) with phenyl acetylene (**4a**) was studied. Firstly, the reaction conditions were studied (Table 3). Our previous optimized conditions [89] were applied to the bimetallic catalytic system, using a combination of GO-$PdCl_2$ (20 mg, Pd 2.86 wt %) and CuI (10 mol%), PPh_3 (10 mol%), and Et_3N (2.0 equiv.) in 1.4-dioxane (5 mL) at 110 °C for 48 h. Unfortunately, it provided poor yield of product **5a** (entry 1). Further study showed that this low yield remained when copper (I) thiophenecarboxylate (CuTC) was adopted instead of CuI (entry 2). And then, the choice of ligand was critical to the success of the reaction, when 2-(dicyclohexylphosphino)-2',4',6'-triisopropylbiphenyl (X-Phos) was screened as ligand, 38% of conversion was detected (entry 3). Finally, to our delight, the yield was dramatically increased to 86 % when K_3PO_4 was chosen as a base (entry 5).

Table 3. Optimization of the conditions of pyrimidin-2-yl sulfonates with terminal alkynes [a].



1a 4a 5a

Entry	[Cu]	Base	Ligands	Yield [b]
1	CuI	Et_3N	PPh_3	7%
2	CuTC	Et_3N	PPh_3	8%
3	CuTC	Et_3N	X-Phos	38%
4	CuTC	K_2CO_3	X-Phos	56%
5	CuTC	K_3PO_4	X-Phos	86%

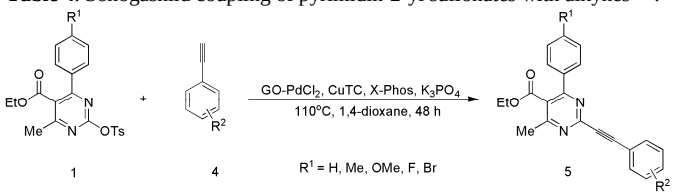
[a] Reaction condition: **1a** (0.25 mmol), **4a** (0.38 mmol), GO-$PdCl_2$ (20 mg, Pd 2.1 mol %), CuTC (10 mol %), K_3PO_4 (2.0 equiv.), X-Phos (6 mol %), 1,4-dioxane (5 mL), 110 °C, 48 h.

[b] Isolated yield of **5a** by column chromatography.

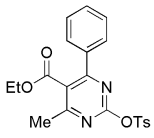
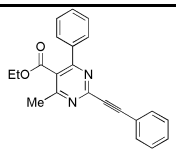
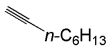
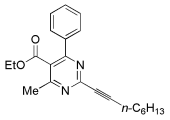
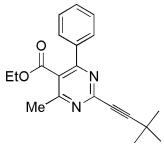
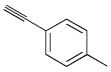
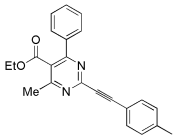
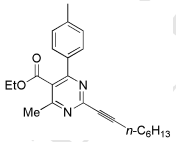
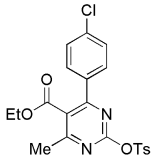
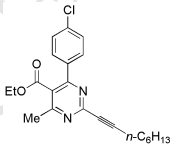
On the basis of the results described above, we can conclude that GO-$PdCl_2$ can be a fine catalyst for this type of Sonogashira coupling reactions between pyrimidin-2-yl sulfonates and terminal alkynes. To extend the scope of this reaction system, more substrates were examined under the optimized conditions (**Table 4**). The catalysts displayed nearly 100% selectivity to the

products. As the similar result with Suzuki reaction, the PPh_3 (as ligand) (entry 6) gives the most efficient N-arylation Sonogashira reaction is relatively insensitive to the electronic characteristics of the substituent groups. And all substrates can be converted into the corresponding products in excellent yields.

Table 4. Sonogashira coupling of pyrimidin-2-yl sulfonates with alkynes [a].



1 4 5

Entry	Sulfonate	Alkyne	Product	Yield [b]
1	 **1a**	 **4a**	 **5a**	**86%**
2	**1a**	 **4b**	 **5b**	**87%**
3	**1a**	 **4c**	 **5c**	**89%**
4	**1a**	 **4d**	 **5d**	**84%**
5	**1b**	**4b**	 **5e**	**66%**
6	 **1e**	**4b**	 **5f**	**89%**

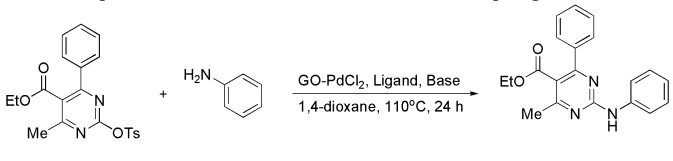
[a] Reaction conditions: **1** (0.25 mmol), **4** (1.5 equiv.), GO-$PdCl_2$ (20 mg, Pd 2.1 mol %), CuTC (10 mol%), K_3PO_4 (2.0 equiv.), X-Phos (6 mol %), 1,4-dioxane (5 mL), 110 °C, 48 h.

[b] Isolated yield of product **5**.

2.4 C-N Coupling reactions of pyrimidin-2-yl sulfonates with anilines

In addition to C-C coupling, anilines were used as nucleophiles in the C-N coupling reactions. The catalytic activity was investigated in the model reaction of pyrimidin-2-yl sulfonate (**1a**) with aniline (**6a**) (Table 5). The controlling experiments and the effect of varying base, and ligand on conversions suggest that the combination of K_3PO_4 (as base) and PPh_3 (as ligand) (entry 6) gives the most efficient N-arylation product **7a** (81% yield in 24 h).

Table 5. Optimization of the conditions of the C-N coupling reactions [a].



1a 6a 7a

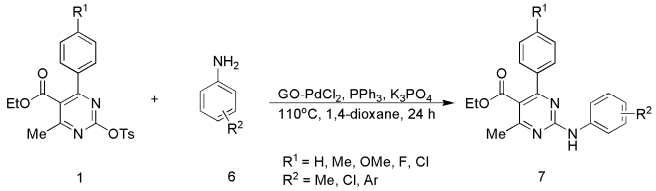
Entry	Base	Ligands	Yield [b]
1	DBU	PPh_3	0%
2	Et_3N	PPh_3	0%
3	K_2CO_3	PPh_3	0%
4	Cs_2CO_3	PPh_3	0%
5	K_3PO_4	-	44%
6	K_3PO_4	PPh_3	81%

[a] Reaction condition: **1a** (0.25 mmol), **6a** (0.38 mmol), GO-$PdCl_2$ (20 mg, Pd 2.1 mol %), PPh_3 (20 mol %),, K_3PO_4 (2.0 equiv.), 1,4-dioxane (5 mL), 110 °C, 24 h.

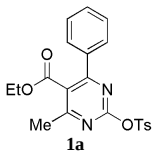
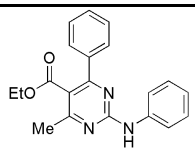
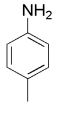
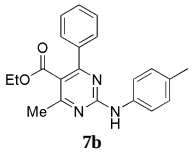
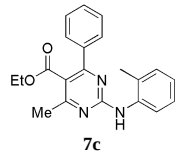
[b] Isolated yield of **7a** by column chromatography.

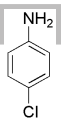
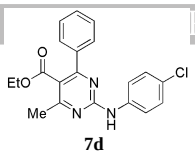
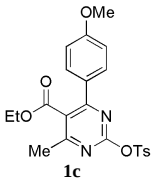
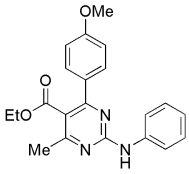
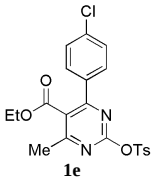
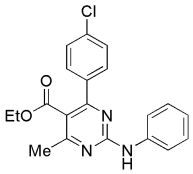
To evaluate the scope of C-N catalytic system, we investigated the coupling reactions by treating various pyrimidin-2-yl sulfonates with different anilines (Table 6). High catalytic activities were observed for the pyrimidin-2-yl sulfonates and both electron-rich and electron-poor anilines, affording the corresponding N-arylation compounds in good to excellent yields (entries 2-4). In particular, *o*-toluidine, which has discernible steric- encumbrance, afforded the corresponding product **7c** in low yields (entry 3). For all the anilines examined, the reaction tolerated a variety of anilines containing an electron-withdrawing group (Cl) (entry 6) as well as an electron-donating group (OMe) (entry 5) on the phenyl ring, and gave similar yields.

Table 6. Scope of the C-N coupling reactions [a].



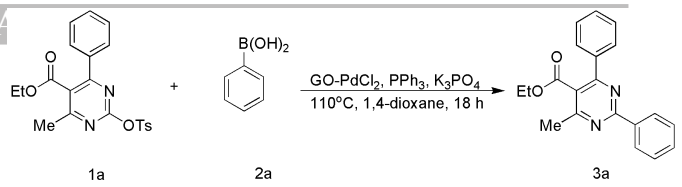
1 6 7

Entry	Sulfonate	Arylboronic acid	Product	Yield[b]
1	 **1a**	 **6a**	 **7a**	**81%**
2	**1a**	 **6b**	 **7b**	**79%**
3	**1a**	 **6c**	 **7c**	**49%**

4	1a	 6d	 7d	82%
5	 1c	6a	 7e	78%
6	 1e	6a	 7f	88%

[a] Reaction conditions: Reaction conditions: **1** (0.25 mmol), **6** (1.5 equiv.), PPh_3 (20 mol %), GO-$PdCl_2$ (20 mg, Pd 2.1 mol %), K_3PO_4 (2.0 equiv.), stirred in 5 mL 1,4-dioxane at 110 °C, 24 h.

[b] Isolated yield of product **7**.



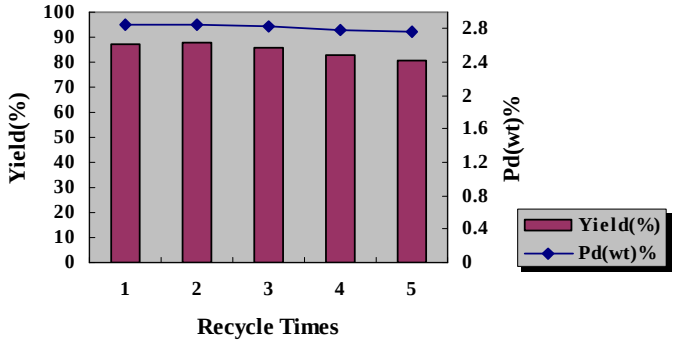


Figure 7. Recycling test of GO-$PdCl_2$ for Suzuki reaction.

2.5 Recycling of the catalyst

An important point concerning the use of heterogeneous catalysts is its lifetime, particularly for industrial and pharmaceutical applications. The recycling experiments were performed with the Suzuki coupling reaction between ethyl 4-methyl-6-phenyl-2-(tosyloxy)pyrimidine-5-carboxylate (**1a**) and phenylboronic acid (**2a**) as the model substrates, under the same reaction conditions as described above. After completion of each running, the mixture was cooled to room temperature, and then the catalyst was separated by centrifugation, and was washed, dried and replaced in the reaction vessel to be used in the sequential running. The reaction progress was monitored by TLC, and the conversion and product selectivity were observed by GC analysis (Figure 7).

The catalyst was used repeatedly for 5 times and then was examined by ICP-AES analysis within very narrow scope (2.86% to 2.75%) to observe its palladium content. Only 128 parts per billion palladium was detected in the reaction phase, (ICP-MS) indicating quite a slender metal leaching of the catalyst during the reactions. (Figure 7).

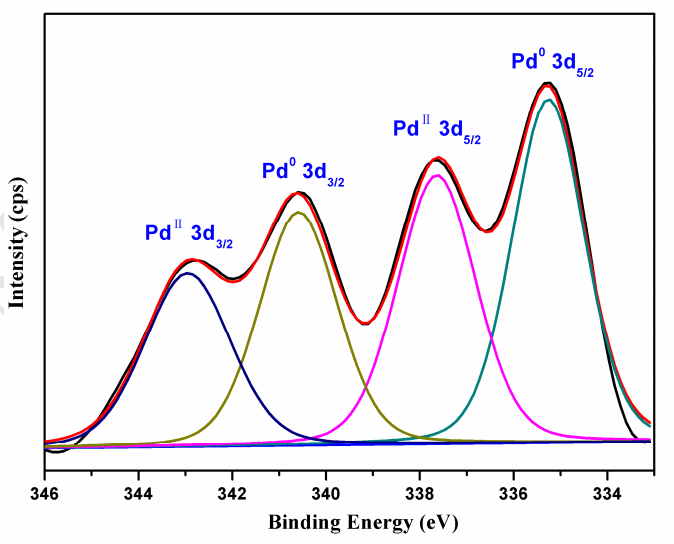


Figure 8. XPS spectra of the reused wool-Pd complex catalyst.

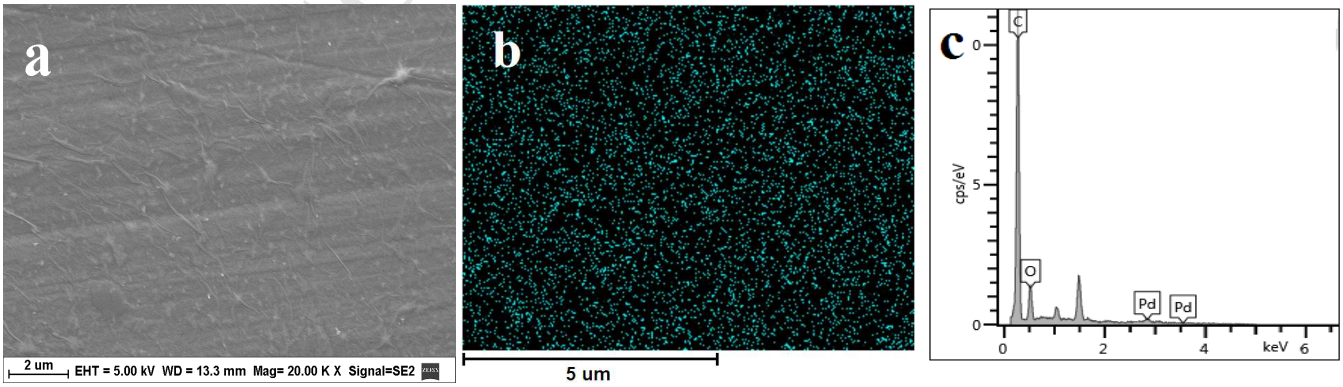


Figure 9. (a) SEM image of the reused catalyst (after the Suzuki reaction), (b) the corresponding EDS mapping of Pd, (c) the corresponding EDX spectrum.

To further investigate the reused catalyst, XPS was employed to characterize. Figure 8 showed the Pd 3d spectrum of the reused catalyst. It can be seen that a doublet for two chemically different Pd entities, with peak binding energies of 335.22 eV (Pd $3d_{5/2}$) and 340.60 eV (Pd $3d_{3/2}$), which confirmed the presence of Pd^0 in the reused catalyst. The XPS results indicated that Pd (0) was formed during the catalytic reaction. This was in an agreement with the previous report. [40]

Subsequently, the reused catalyst was again examined by SEM-EDX, and the image indicated that the surface morphology of the recycled catalyst did not show any significant change even after 5 reaction cycles (Figure 9), showing a good stability of the GO-$PdCl_2$ catalyst during the Suzuki coupling reaction.

2.6 Hot filtration test

In order to further evaluate the palladium leaching of the GO-$PdCl_2$ catalyst as well as the catalytic contributions of the leached palladium, we carried out the hot filtration tests upon the C-C coupling reaction. The test was operated between the coupling reaction of **1a** and **2a** under standard conditions. The reaction mixture was stirred for 6 hours and filtered in order to remove the heterogeneous catalyst (the conversion is 37%); then the mixture was stirred for another 18 hours. However, no further reaction was detected. This result indicated that any leaching of active species into solution was insignificant.

3. Conclusion

We have achieved the preparation of a reactive, selective, and recyclable GO-$PdCl_2$ catalyst. This catalyst exhibited high enrichment towards the reactants as well as excellent activity for a wide scope of C-C/C-N cross-coupling reactions. In addition, the GO-$PdCl_2$ showed an improved stability in the coupling reactions of pyrimidin-2-yl sulfonates with arylboronic acids, terminal alkynes and aryl amines. Further exploration of the heterogeneous catalyst developed by the organic reaction in other useful catalytic transformations is actively undergoing in our laboratory.

4. Experimental section

4.1 Chemicals

All starting materials and reagents were commercially available and used without further purification unless otherwise noted. Solvents were purified and dried by standard methods prior to use. All products have been previously reported and characterized. All known products gave satisfactory analytical data corresponding to the reported literature values.

4.2 Apparatus

All reactions were conducted under nitrogen atmosphere with a dual-manifold Schlenk tube and in oven-dried glassware unless otherwise noted. All NMR spectra are recorded on MERCURY (400 MHz for ^{1}H NMR, 100 MHz for ^{13}C NMR) spectrometers; chemical shifts are expressed in ppm (δunits) relative to TMS signal as internal reference in $CDCl_3$. Gas chromatography (GC) analysis was performed on a Shimadezu GC-2010 equipped with a 15 m × 0.53 mm × 1.5 μm RTX-1 capillary column and a oxyhydrogen flame detector. ICP-AES were measured on IRIS Advantage. XPS measurement was recorded on PHI5702 photoelectron spectrometer. Binding energy was referred to C_{1s} (284.80 eV). FTIR spectroscopy patterns were obtained on an FT/IR-660 Plus system (Jasco, Tokyo, Japan). The samples were mixed with KBr powders and pressed into a disk suitable for FTIR measurement. The morphologies of the catalyst were examined with field emission scanning electron microscopy (FE-SEM, Ultra Plus, Carl Zeiss). Elemental analysis of the photocatalyst was conducted by an energy-dispersive X-ray spectrometer (EDX) attached to the scanning electron microscope. Column chromatography was generally performed on silica gel (200–300 mesh) and TLC analyses were conducted on silica gel GF254 plates.

4.3 General procedures for the Suzuki coupling reactions of pyrimidin-2-yl sulfonates with arylboronic acids

Pyrimidin-2-yl sulfonate **1** (0.25 mmol), arylboronic Acid **2** (0.375 mmol), K_3PO_4 (2.0 equiv.), PPh_3 (20 mol %), 20 mg of GO-$PdCl_2$ catalyst (Pd 2.86 wt %) were added to a 15 mL Schlenk tube, and was then evacuated and purged with nitrogen gas for four times sequentially; then 5 mL 1,4-dioxane in was added by a syringe under nitrogen atomosphere; the mixture was then stirred at 110 ^{o}C for 18 h. After completion, the catalyst was separated by centrifugation, and the mixture was cooled to room temperature, quenched by addition of saturated aqueous NH_4Cl (3 mL), and extracted with diethyl ether (3 × 5 mL). The organic solvents were combined and washed with aqueous NaOH (2 mmol/ mL, 2 mL), brine, and then dried with anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography with a mixture of ethyl acetate and petroleum ether as eluent. The product was analyzed by GC-MS or NMR analysis. The conversion and selectivity were determined using GC analysis. All the prepared compounds are known and were compared with authentic samples. [89]

*4.3.1 Ethyl 4-methyl-2,6-diphenylpyrimidine-5-carboxylate (**3a**).* White solid; m.p. 66-67 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.62- 8.59 (dd, *J* = 2.8 Hz, 6.4 Hz, 2H), 7.81-7.79 (m, 2H), 7.54-7.52 (m, 6H), 4.28-4.22 (q, *J* = 7.2 Hz, 2H), 2.75 (s, 3H), 1.14-1.10 (t, J= 7.2 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ= 168.52, 165.40, 163.72, 163.69, 138.22, 137.1, 131.12, 130.01, 128.73, 128.58, 128.52, 128.49, 123.41, 61.8, 22.90, 13.68 ppm.

*4.3.2 Ethyl 4-methyl-6-phenyl-2-p-tolylpyrimidine-5-carboxylate (**3b**).* White solid; m.p. 61-63 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.49-8.47 (d, *J* = 8.2 Hz, 2H), 7.79-7.77 (m, 2H), 7.54-7.46 (m, 3H), 7.33-7.31 (d, *J* = 8.1 Hz, 3H), 4.26-4.21 (q, *J* = 7.2 Hz, 2H), 2.72 (s, 3H), 2.46 (s, 3H), 1.12-1.10 (t, *J* = 7.2 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.52, 165.34, 163.68, 163.61, 141.49, 138.33, 134.42, 130.01, 129.33, 128.72, 128.54, 128.48, 123.12, 61.83, 22.72, 21.61, 13.70 ppm.

*4.3.3 Ethyl 4-methyl-6-phenyl-2-m-tolylpyrimidine-5-carboxylate (**3c**).* White solid; m.p. 69- 71 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.27-8.29 (d, *J* = 7.4 Hz, 2H), 7.69-7.67 (dd, *J* = 6.5 Hz, 3.1 Hz, 2H), 7.42-7.39 (m, 3H), 7.33-7.29(t, *J* = 7.9 Hz, 1H), 7.25-7.23(t, *J* = 7.5 Hz, 1H), 4.16-4.11 (q, *J* = 7.2 Hz, 2H), 2.62 (s, 3H), 2.38 (s, 3H), 1.02-0.99 (t, *J* = 7.2 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.42, 165.31, 163.84, 163.28, 138.22, 138.14, 137.02, 131.79, 129.91, 129.14, 128.53, 128.42, 125.83, 123.33, 61.67, 22.90, 21.53, 13.59 ppm.

*4.3.4 Ethyl 4-methyl-6-phenyl-2-o-tolylpyrimidine-5-carboxylate (**3d**).* White solid; m.p. 77-78 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87-7.79 (m, 1H), 7.73-7.57 (m, 2H), 7.46- 7.33 (m, 3H), 7.32-7.19 (m, 3H), 4.16 (q, *J* = 7.2 Hz, 2H), 2.63 (s, 3H), 2.55 (s, 3H), 1.03 (t, *J* = 7.2 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.36, 166.75, 165.00, 163.12, 137.93, 137.62, 137.45, 131.31, 130.55, 129.97, 129.65, 128.48, 128.39, 125.93, 122.77, 61.86, 22.78, 21.32, 13.66 ppm.

*4.3.5 Ethyl 2-(4-methoxyphenyl)-4-methyl-6-phenylpyrimidine-5-carboxylate (**3e**).* White solid; m.p. 57-59 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.49-8.39 (m, 2H), 7.72-7.60 (m, 2H), 7.46-7.32 (m, 3H), 6.95-6.85 (m, 2H), 4.11 (q, *J* = 7.2 Hz, 2H), 3.79 (s, 3H), 2.59 (s, 3H), 0.99 (t, *J* = 7.2 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.54, 165.23, 163.53, 163.40, 162.13,

141.51, 138.41, 134.4, 130.34, 129.82, 128.39, 122.57, 113.79, 61.63, 55.33, 22.84, 13.63 ppm.

*4.3.6 Ethyl 2-(4-chlorophenyl)-4-methyl-6-phenylpyrimidine-5-carboxylate (**3f**).* White solid; m.p. 84-86 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.51-8.36 (m, 2H), 7.80-7.56 (m, 2H), 7.52-7.29 (m, 5H), 4.13 (q, *J* = 7.2 Hz, 2H), 2.61 (s, 3H), 1.01 (t, *J* = 7.2 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.25, 165.48, 163.63, 162.64, 138.04, 137.29, 135.59, 130.00, 129.96, 128.70, 128.44, 128.41, 123.52, 61.80, 22.80, 13.64 ppm.

*4.3.7 Ethyl 4-methyl-2-(naphthalen-1-yl)-6-phenylpyrimidine-5-carboxylate (**3g**).* White solid; m.p. 83-85 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.62-8.60 (m, 1H), 8.06 (dd, *J* = 7.2, 1.2 Hz, 1H), 7.89 (d, *J* = 8.2 Hz, 1H), 7.87-7.80 (m, 1H), 7.77-7.65 (m, 2H), 7.59-7.31 (m, 6H), 4.18 (q, *J* = 7.2 Hz, 2H), 2.69 (s, 3H), 1.05 (t, *J* = 7.2 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.26, 166.35, 165.29, 163.53, 137.85, 135.41, 134.05, 130.96, 130.73, 130.06, 129.58, 128.55, 128.42, 126.85, 125.85, 125.70, 125.16, 123.18, 109.69, 61.93, 22.86, 13.67 ppm.

*4.3.8 Ethyl 4-methyl-2-phenyl-6-p-tolylpyrimidine-5-carboxylate (**3h**).* White solid; m.p. 66-67 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.60-8.38 (m, 2H), 7.60 (d, *J* = 8.1 Hz, 2H), 7.46-7.35 (m, 3H), 7.23-7.17 (m, 2H), 4.16 (q, *J* = 7.2 Hz, 2H), 2.60 (s, 3H), 2.34 (s, 3H), 1.06 (t, *J* = 7.2 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.63, 165.14, 163.59, 163.34, 140.23, 137.23, 135.30, 130.91, 129.17, 128.58, 128.44, 128.41, 123.14, 61.72, 22.81, 21.38, 13.73 ppm.

*4.3.9 Ethyl 4-(4-methoxyphenyl)-6-methyl-2-phenylpyrimidine-5-carboxylate (**3i**).* Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.54-8.43 (m, 2H), 7.77-7.62 (m, 2H), 7.45-7.36 (m, 3H), 6.88 (d, *J* = 8.8 Hz, 2H), 4.15 (q, *J* = 7.2 Hz, 2H), 3.72 (s, 3H), 2.56 (s, 3H), 1.05 (t, *J* = 7.2 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.72, 164.98, 163.36, 162.53, 161.17, 137.14, 130.82, 130.32, 130.01, 128.44, 128.36, 122.68, 113.80, 61.66, 55.24, 22.71, 13.73 ppm.

*4.3.10 Ethyl 4-(4-fluorophenyl)-6-methyl-2-phenylpyrimidine-5-carboxylate (**3j**).* White solid; m.p. 85- 86 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.46 (dd, *J* = 6.8, 3.0 Hz, 2H), 7.77-7.62 (m, 2H), 7.48-7.33 (m, 3H), 7.11-7.06 (m, 2H), 4.16 (q, *J* = 7.2 Hz, 2H), 2.61 (s, 3H), 1.06 (t, *J* = 7.2 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.33, 165.46, 165.20, 163.65, 162.71, 162.28, 136.97, 134.28, 131.10, 130.58, 130.50, 128.58, 128.50, 123.16, 115.66, 115.44, 61.84, 22.82, 13.74 ppm.

*4.3.11 Ethyl 4-(4-chlorophenyl)-6-methyl-2-phenylpyrimidine-5-carboxylate (**3k**).* White solid; m.p. 83-84 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.52-8.41 (m, 2H), 7.69-7.59 (m, 2H), 7.47-7.34 (m, 5H), 4.16 (q, *J* = 7.2 Hz, 2H), 2.62 (s, 3H), 1.07 (t, *J* = 7.2 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.15, 165.55, 163.66, 162.31, 136.81, 136.56, 136.36, 131.20, 129.85, 128.73, 128.63, 128.52, 123.19, 61.92, 22.79, 13.74 ppm.

*4.3.12 Ethyl 4-(4-bromophenyl)-6-methyl-2-phenylpyrimidine-5-carboxylate (**3l**).* White solid; m.p. 87-89 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.50 (m, 2H), 7.78 (d, *J* = 8.4 Hz, 2H), 7.47-7.37 (m, 5H), 4.19 (q, *J* = 7.2 Hz, 2H), 2.63 (s, 3H), 1.06 (t, *J* = 7.2 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.52, 165.39, 163.06, 137.14, 137.00, 131.02, 128.94, 128.87, 128.60, 128.49, 127.78, 127.18, 127.16, 123.22, 61.82, 22.88, 13.72 ppm.

*4.3.13 Methyl 4-methyl-2,6-diphenylpyrimidine-5-carboxylate (**3m**).* White solid; m.p. 123-125 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.57-8.55 (m, 2H), 7.77-7.76 (m, 2H), 7.51-7.48 (m, 6H), 3.72 (s, 3H), 2.68 ppm (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.03, 165.46, 163.77, 163.40, 138.10, 137.10, 131.06, 130.07, 128.63, 128.54, 128.49, 128.35, 123.00, 52.53, 22.89 ppm.

*4.3.14 2-Phenylpyridine (**3n**).* Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.62 (d, *J* = 4.6 Hz, 1H), 7.97-7.87 (m, 2H), 7.73-7.59 (m, 2H), 7.42-7.32 (m, 3H), 7.24-7.12 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.33, 149.50, 139.17, 136.85, 128.97, 128.72, 126.88, 122.08, 120.59 ppm.

*4.3.15 5-nitro-2-phenylpyridine (**3o**).* White solid; m.p. 121-122 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.45 (d, *J* = 2.4 Hz, 1H), 8.47 (dd, *J* = 8.8, 2.7 Hz, 1H), 8.12-8.02 (m, 2H), 7.87 (d, *J* = 8.8 Hz, 1H), 7.57-7.46 (m, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.29, 145.16, 142.82, 136.98, 131.90, 130.88, 129.10, 127.66, 120.00 ppm.

4.4 General procedures for the Sonogashira coupling reactions of pyrimidin-2-yl sulfonates with terminal alkynes

Pyrimidin-2-yl sulfonate **1** (0.25 mmol), terminal alkyne **4** (0.375 mmol), K_3PO_4 (2.0 equiv.), PPh_3 (20 mol %), 20 mg of GO-$PdCl_2$ catalyst (Pd 2.86 wt %) and CuTC (10 mol %) were added to a Schlenk tube. The tube containing the mixture of substrates was evacuated and purged with nitrogen gas for four times. Then, 5 mL 1,4-dioxane was added by a syringe under nitrogen atomosphere, and the reaction mixture was stirred at 110 °C for 48 h. After completion, the catalyst was separated by centrifugation, the mixture was cooled to room temperature, quenched by addition of saturated aqueous NH_4Cl (3 mL), and extracted with diethyl ether (3 × 5 mL). The organic solvents were combined and washed with aqueous NaOH (2 mmol/mL, 2 mL), brine, and then dried with anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography with a mixture of ethyl acetate and petroleum ether as eluent. The product was analyzed by GC-MS or NMR analysis. The conversion and selectivity were determined using GC analysis. All the prepared compounds are known and were compared with authentic samples. [89]

*4.4.1 Ethyl 4-methyl-6-phenyl-2-(phenylethynyl)pyrimidine-5-carboxylate (**5a**).* White solid; m.p. 161-162 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.70-7.66 (m, 4H), 7.48-7.39 (m, 3H), 7.38-7.27 (m, 3H), 4.22- 4.17 (q, *J* = 8.0 Hz,, 2H), 2.67 (s, 3H), 1.06 (t, *J* = 8.0 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 167.53, 165.59, 164.08, 152.38, 137.19, 132.85, 132.54, 130.40, 130.01, 129.91, 129.52, 128.75, 126.53, 128.38, 128.17, 124.19, 121.25, 88.53, 88.09, 61.98, 22.47, 13.48 ppm.

*4.4.2 Ethyl 4-Methyl-2-(oct-1-ynyl)-6-phenylpyrimidine-5-carboxylate (**5b**).* Yellow oil. ^{1}H NMR (400 MHz, CDCl3): δ = 7.63–7.49 (m, 2H), 7.47–7.28 (m, 3 H), 4.10 (q, *J* = 7.2 Hz, 2 H), 2.54 (s, 3 H), 2.40 (t, *J* = 7.3 Hz, 2 H), 1.65–1.53 (m, 2 H), 1.43–1.33 (m, 2 H),1.28–1.19 (m, 4 H), 0.97 (t, *J* = 7.2 Hz, 3 H), 0.81 (t, *J* = 6.7 Hz, 3H) ppm. ^{13}C NMR (100 MHz, CDCl3): δ = 167.58, 165.39, 163.91,152.27, 137.18, 130.06, 128.44, 128.25, 123.95, 91.65, 79.93, 61.87,31.25, 28.70, 27.89, 22.52, 22.43, 19.41, 13.99, 13.53 ppm.

*4.4.3 Ethyl 2-(3,3-Dimethylbut-1-ynyl)-4-methyl-6-phenylpyrimidine-5-carboxylate (**5c**).* White solid; m.p. 98-99 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.57-7.36 (m, 2H), 7.46-7.25 (m, 3H), 4.10 (q, *J* = 7.2 Hz, 2H), 2.54 (s, 3H), 1.30 (s, 9H), 0.97 (t, *J* = 7.2 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 167.61, 165.29, 163.90, 152.51, 137.33, 129.99, 128.43, 128.29, 123.94, 98.45, 78.87, 61.82, 30.38, 27.90, 22.52, 13.54. ppm.

*4.4.4 Ethyl 4-Methyl-6-phenyl-2-(p-tolylethynyl)pyrimidine-5-carboxylate (**5d**).* Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.65-7.56 (m, 2H), 7.51 (d, *J* = 8.0 Hz, 2H), 7.45-7.33 (m, 3H), 7.10 (d, *J* = 7.9 Hz, 2H), 4.12 (q, *J* = 7.2 Hz,, 2H), 2.58 (s, 3H), 2.30 (s, 3H), 0.99 (t, *J* = 7.2 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 167.57, 165.54, 164.05, 152.47, 140.17, 137.20, 132.65, 130.16, 129.13, 128.54, 128.29, 124.00, 118.09, 89.07, 87.66, 61.96, 22.61, 21.63, 13.58 ppm.

*4.4.5 Ethyl 4-Methyl-2-(oct-1-ynyl)-6-p-tolylpyrimidine-5-carboxylate (**5e**).* Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.48 (dd, *J* = 8.2, 2.0 Hz, 2 H), 7.18–7.14 (m, 2H), 4.13 (dd, *J* = 7.2, 2.9 Hz, 2H), 2.52 (d, *J* = 2.5 Hz, 3 H), 2.42–2.37 (m, 2H), 2.31 (d, *J* = 2.6 Hz, 3H), 1.64–1.54 (m, 2 H), 1.38 (dd, *J* = 13.1,

6.4 Hz, 2H),1.28–1.16 (m, 4H), 1.05–1.01 (m, 3H), 0.82–0.79 (m, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.83, 165.15, 163.72, 152.25,140.42, 134.27, 129.17, 128.28, 123.80, 91.41, 80.03, 61.86, 31.27,28.71, 27.92, 22.50, 22.45, 21.35, 19.43, 14.00, 13.64 ppm.

*4.4.6 Ethyl 4-(4-Chlorophenyl)-6-methyl-2-(oct-1-ynyl)pyrimidine-5-carboxylate (**5f**).* Brown oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.58–7.45 (m, 2H), 7.42–7.31 (m, 2H), 4.11–4.17 (m, 2H), 2.54 (d, *J* = 1.2 Hz, 3H), 2.40 (t, *J* = 7.3 Hz, 2H), 1.65–1.54 (m, 2H), 1.43–1.34 (m, 2H), 1.28–1.19 (m, 4H), 1.07–1.03 (m, 3H), 0.85–0.76(m, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.43, 165.64,162.59, 152.33, 136.52, 135.59, 129.73, 128.75, 123.84, 92.04, 79.86,62.07, 31.27, 29.65, 28.72, 27.90, 22.56, 22.45, 19.44, 14.01,13.67 ppm.

4.5 General procedures for the C-N coupling reactions of pyrimidin-2-yl sulfonates with anilines

Pyrimidin-2-yl sulfonate **1** (0.25 mmol), anilines **6** (0.375 mmol), K_3PO_4 (2.0 equiv.), PPh_3 (20 mol %), 20 mg of GO-$PdCl_2$ catalyst (Pd 2.86 wt %) were added to a 15 mL Schlenk tube, and was then evacuated and purged with nitrogen gas for four times sequentially; then 5 mL 1,4-dioxane in was added by a syringe under nitrogen atomosphere; the mixture was then stirred at 110 °C for 24 h until the reaction was completed. After cooling the mixture to room temperature, the catalyst was separated by centrifugation, and the liquid was quenched with saturated NH_4Cl aqueous solution (3 mL), and extracted with ethoxyethane (3 × 5 mL). The organic solvents were combined and washed with aqueous NaOH (2 mmol/mL, 2 mL), brine, and then dried with anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography, eluting with a mixture of ethyl acetate and petroleum ether. The product was analyzed by GC-MS or NMR analysis. The conversion and selectivity were determined using GC analysis. All the prepared compounds are known and were compared with authentic samples. [88, 90]

*4.5.1 Ethyl 4-methyl-6-phenyl-2-(phenylamino)pyrimidine-5-carboxylate (**7a**).* Colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.71 (s, 1H), 7.61-7.45 (m, 4H), 7.38-7.27 (m, 3H), 7.18 (t, *J* = 7.9 Hz, 2H), 6.92 (dd, *J* = 11.4, 4.2 Hz, 1H), 4.00 (q, *J* = 7.1 Hz, 2H), 2.46 (s, 3H), 0.87 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 168.41, 167.17, 165.73, 158.71, 139.01, 138.52, 129.60, 128.71, 128.23, 127.96, 122.57, 119.16, 116.93, 61.19, 22.88, 13.46 ppm.

*4.5.2 Ethyl 4-methyl-6-phenyl-2-(p-tolylamino)pyrimidines-5-carboxylate (**7b**).* Brown oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (s, 1H), 7.64-7.56 (m, 2H), 7.50 (dd, *J* = 8.3, 1.5 Hz, 2H), 7.42 (dd, *J* = 4.3, 2.6 Hz, 3H), 7.10 (d, *J* = 7.5 Hz, 2H), 4.12-4.06 (m, 2H), 2.55 (d, *J* = 1.8 Hz, 3H), 2.30 (s, 3H), 0.99-0.95 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ =168.48, 167.17, 165.76, 158.79, 138.62, 136.38, 132.19, 129.55, 129.22, 128.21, 127.96, 119.42, 116.64, 61.15, 22.91, 20.70, 13.47 ppm.

*4.5.3 Ethyl 4-methyl-6-phenyl-2-(o-tolylamino)pyrimidine-5-carboxylate (**7c**).* Brown oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.07 (d, *J* = 8.1 Hz, 1H), 7.61-7.46 (m, 2H), 7.35 (dd, *J* = 5.1, 1.8 Hz, 3H), 7.20-7.10 (m, 2H), 6.97 (dd, *J* = 8.5, 11.1 Hz, 2H), 4.02 (q, *J* = 7.1 Hz, 2H), 2.47 (s, 3H), 2.26 (s, 3H), 0.91 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 168.51, 167.26, 165.88, 159.09, 138.59, 136.98, 130.40, 129.63, 128.30, 127.99, 126.50, 121.51, 117.02, 61.23, 22.92, 18.16, 13.53 ppm.

*4.5.4 Ethyl 2-(4-chlorophenylamino)-4-methyl-6-phenylpyrimidine-5-carboxylate (**7d**).* Colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ =7.97 (s, 1H), 7.71-7.57 (m, 2H), 7.56-7.47 (m, 2H), 7.41 (d, *J* = 5.8 Hz, 3H), 7.24-7.17 (m, 2H), 4.11 (q, *J* = 7.1 Hz, 2H), 2.55 (s, 3H), 0.98 (dd, *J* = 7.7, 6.6 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.28, 167.24, 165.70, 158.53, 138.30, 137.63, 129.75, 128.60, 128.29, 127.95, 127.32, 120.40, 117.25, 61.30, 22.88, 13.52 ppm.

*4.5.5 Ethyl 4-(4-methoxyphenyl)-6-methyl-2-(phenylamino)pyrimidine-5-carboxylate (**7e**).* Claybank oil, ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.56 (d, *J* = 10.1 Hz, 1H), 7.34 (d, *J* = 8.5 Hz, 4H), 7.06-6.95 (m, 2H), 6.72 (t, *J* = 7.4 Hz, 1H), 6.68-6.61 (m, 2H), 3.88 (q, *J* = 7.1 Hz, 2H), 3.52 (s, 3H), 2.24 (s, 3H), 0.80 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 168.90, 166.83, 164.88, 161.05, 158.78, 139.26, 130.80, 129.77, 128.75, 122.55, 119.27, 116.67 , 113.75, 61.30, 55.28, 22.83, 13.75 ppm.

*4.5.6 Ethyl 4-(4-chlorophenyl)-6-methyl-2-(phenylamino)pyrimidine-5-carboxylate (**7f**).* White solid, m.p. 129-130 °C, ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.54 (s, 1H), 7.46-7.27 (m, 4H), 7.19-7.14 (m, 2H), 7.09-7.04 (m, 2H), 6.87-6.75 (m, 1H), 3.98-3.86 (m, 2H), 2.42-2.26 (m, 3H), 0.92- 0.74 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 168.38, 167.60, 164.61, 158.92, 139.08, 137.15, 136.02, 129.62, 128.93, 128.65, 122.98, 119.50, 116.97, 61.52, 23.12, 13.78 ppm.

Acknowledgements

This work was financially supported by National Natural Science Foundation of China (Nos. 21362032, 21362031 and 21464013), the Natural Science Foundation of Gansu Province (No. 1208RJYA083), and the Scientific and Technological Innovation Engineering program of Northwest Normal University (No. nwnu-kjcxgc-03-64).

References and notes

1. Mizoroki, T.; Mori K.; Ozaki, A. *Bull. Chem. Soc. Jpn*. **1971**, *44*, 581–584.
2. Heck, R. F.; Nolley, J. P. *J. Org. Chem*. **1972**, *37*, 2320–2322.
3. Lundgren, R. J.; Sappong-Kumankumah, A.; Stradiotto, M. *Chem. Eur. J.* **2010**, *16*, 1983–1991.
4. Miyaura, N.; Suzuki, A. *Chem. Rev*. **1995**, *95*, 2457–2483.
5. Fors, B. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **2010**, *132*, 15914–15917.
6. Culkin, D. A.; Hartwig, J. F. *Acc. Chem. Res.* **2003**, *36*, 234–245.
7. Muci, A. R.; Buchwald, S. L. *Top. Curr. Chem.* **2002**, *219*, 131–209.
8. Ramakrishnan, A.; Dumbuya, K.; Ofili, J.; Steinruck, H. P.; Gottfried, J. M.; Schwieger, W. Appl. Clay Sci. **2011**, *51*, 8–14.
9. G. Cahiez, O. Gager, A. Moyeux, T. Delacroix, *Adv. Synth. Catal.* **2012**, *354*, 1519–1528.
10. Wang, Z.-Y.; Chen, G.-Q.; Shao, L.-X. *J. Org. Chem.* **2012**, *77*, 6608–6614.
11. T. Abe, T. Mino, K. Watanabe, F. Yagishita, M. Sakamoto, *Eur. J. Org. Chem.* **2014**, 3909–3916.
12. Djakovitch, L.; Koehler, K. *J. Am. Chem. Soc.* **2001**, *123*, 5990–5999.
13. Stokes, B. J.; Opra, S. M.; Sigman, M. S. *J. Am. Chem. Soc.* **2012**, *134*, 1408–11411.
14. Cívicos, J. F.; Alonso, D. A.; Nájera, C. *Adv. Synth. Catal.* **2012**, *354*, 2771–2776.
15. Roth, H. J.; Kleemann, A. In *Pharmaceutical Chemistry, Volume 1: Drug Synthesis*; John Wiley and Sons: New York, **1988**.
16. Sha, F.; Huang, X. *Angew. Chem., Int. Ed.* **2009**, *48*, 3458–3461.
17. Movassaghi, M.; Hill, M. D.; Ahmad, O. K. *J. Am. Chem. Soc.* **2007**, *129*, 10096–10097.
18. Karpov, A. S.; Merkul, E.; Rominger, F.; Müller, T. J. J. *Angew. Chem., Int. Ed.* **2005**, *44*, 6951–6956.
19. Bagley, M. C.; Glover, C.; Merritt, E. A. *Synlett* **2007**, 2459–2482.
20. Hill, M. D.; Movassaghi, M. *Chem. Eur. J.* **2008**, *14*, 6836–6844.
21. Limmert, M. E.; Roy, A. H.; Hartwig, J. F. J. Org. Chem. **2005**, *70*, 9364–9370.
22. Roy, A. H.; Hartwig, J. F. *J. Am. Chem. Soc.* **2003**, 125, 8704–8705.
23. Wilson, D. A.; Wilson, C. J.; Moldoveanu, C.; Resmerita, A.-M.; Corcoran, P.; Hoang, L. M.; Rosen, B. M.; Percec, V. *J. Am. Chem. Soc.* **2010**, *132*, 1800–1801.

24. Gao, C.-Y.; Yang, L.-M. *J. Org. Chem.* **2008**, *73*, 1624–1627.
25. Ackermann, L.; Althammer, A. *Org. Lett.* **2006**, *8*, 3457–3460.
26. Xie, X.-M.; Ni, G.; Ma, F.-F.; Ding, L.-N.; Xu, S.; Zhang, Z.-G. *Synlett* **2011**, 955–958.
27. Zhang, J.-L.; Chen, X.-R.; Hu, T.-J.; Zhang, Y.; Xu, K.-L.; Yu, Y.-P.; Huang, *J. Catal. Lett.* **2010**, *139*, 56–60.
28. Zhou, J.-R.; Fu, G. C. *J. Am. Chem. Soc.* **2003**, *125*, 12527–12530.
29. Fan, S.-L.; Yang, J.; Zhang, X.-G. *Org. Lett.* **2011**, *13*, 4374–4377.
30. So, C. M.; Kwong, F. Y. *Chem. Soc. Rev.* **2011**, *40*, 4963–4972.
31. Yi, C. Y.; Hua, R. M. *Catal. Comm.* **2006**, *7*, 377–379.
32. Michalik, J.; Narayana, M.; Kevan, L. *J. Phys. Chem.* **1985**, *89*, 4553–4560.
33. Sachtler, W. M. H.; Cavalcanti, F. A. P.; Zhang, Z. *Catal. Lett.* **1991**, *9*, 261–271.
34. Arun, V.; Sridevi, N.; Robinson, P. P.; Manju, S.; Yusuff, K. K. M. *J. Mol. Catal. A: Chem.* **2009**, *4*, 191–198.
35. Borah B. J., Dutta D. K. *J. Mol. Catal. A* **2013**, *366*, 202–209.
36. Fang M., Fan G., Li F. *Catal. Lett.* **2014**, *144*, 142–150.
37. Xue, L.; Jia, B.; Tang, L.; Ji, X. F.; Huang, M. Y.; Jiang, Y. Y. *Polym. Adv. Technol.* **2004**, *15*, 346–349.
38. Wang, S.; Zhang, Z.; Chi, C.; Wu, G.; Ren, J.; Wang, Z.; Huang, M.; Jiang, Y. *React. & Funct. Polym.* **2008**, *68*, 424–430.
39. Ranjbar-Mohammadi, M.; Hajir Bahrami, S.; Arami, M. *J. Appl. Polym. Sci.*, **2013**, *129*, 707–713.
40. Wu, S.; Ma, H. C.; Jia, X. J.; Zhong, Y. M.; Lei, Z. Q. *Tetrahedron* **2011**, *67*, 250–256.
41. Ma, H.-C.; Cao, W.; Bao, Z.-K.; Lei, Z.-Q. *Catal. Sci. Technol.* **2012**, *2*, 2291–2296.
42. Ma, H.-C.; Wang, F.; Cao, W.; Bao, Z.-K.; Ma, Y.; Yang, Z.-W.; Lei, Z.-Q. *Chin. J. Catal.* **2012**, *33*, 1594–1600.
43. Cotugno, P.; Casiello, M.; Nacci, A.; Mastrorilli, P.; Monopoli, A. *J. Organomet. Chem.*, **2014**, *752*, 1–5.
44. Cirtiu, C. M.; Dunlop-Briere, A. F.; Moores, A. *Green Chem.*, **2011**, *13*, 288–293.
45. Kumbhar, A.; Jadhav, S.; Kamble, S.; Rashinkar, G.; Salunkhe, R. *Tetrahedron Lett.*, **2013**, *54*, 1331–1337.
46. Zhao, F.; Bhanage, B. M.; Shirai, M.; Arai, M. *Chem. Eur. J.* **2000**, *6*, 843–848.
47. Gallon, B. J.; Kojima, R. W.; Kaner, R. B.; Diaconescu, P. L. *Angew. Chem., Int. Ed.* **2007**, *46*, 7251–7254.
48. Hagio, H.; Sugiura, M.; Kobayashi, S. *Org. Lett.* **2006**, *8*, 375–378.
49. Liu, G. Hou, M.; Song, J.; Jiang, T.; Fan, H.; Zhang, Z.; Han, B. *Green Chem.*, **2010**, *12*, 65–69.
50. Mennecke, K.; Cecilia, R.; Glasnov, T. N.; Gruhl, S.; Vogt, C.; Feldhoff, A.; Vargas, M. A. L.; Kappe, C. O.; Kunz, U.; Kirschning, A. *Adv. Synth. Catal.* **2008**, *350*, 717–730.
51. Djakovitch, L.; Koehler, K. *J. Am. Chem. Soc.* **2001**, *123*, 5990–5999.
52. Bedford, R. B.; Singh, U. G.; Walton, R. I.; Williams, R. T.; Davis, S. A. *Chem. Mater.* **2005**, *17*, 701–707.
53. S. P. Prakash, K. R. Gopidas, *ChemCatChem* **2014**, *6*, 1641–1651.
54. C. Mateos, J. A. Rincon, B. Martn-Hidalgo, J. Villanueva, *Tetrahedron Lett.* **2014**, *55*, 3701–3705.
55. Jin, M. J.; Taher, A.; Kang, H. J.; Choi, M.; Ryoo, R. *Green Chem.* **2009**, *11*, 309–313.
56. Emmez, E.; Yang, B.; Shaikhutdinov, S.; Freund, H. -J. *J. Phys. Chem. C.* **2014**, *118*, 29034–29042.
57. Carretero-Genevrier, A.; Oro-Sole, J.; Gazquez, J.; Magen, C.; Miranda, L.; Puig, T.; Obradors, X.; Ferain, E.; Sanchez, C.; Rodriguez-Carvajal, J.; Mestres, N. *Chem. Mater.* **2014**, *26*, 1019–1028.
58. Doherty, C. M.; Buso, D.; Hill, A. J.; Furukawa, S.; Kitagawa, S.; Falcaro, P. *Acc. Chem. Res.* **2014**, *47*, 396–405.
59. Ramchandani, R. K.; Uphade, B. S.; Vinod, M. P.; Wakharkar, R. D.; Choudhary, V. R.; Sudalai, A. *Chem. Commun.* **1997**, 2071–2072.
60. Arundhathi, R.; Damodara, D.; Mohan, K. V.; Kantam, M. L.; Likhara, P. R. *Adv. Synth. Catal.*, **2013**, *355*, 751–756.
61. Indra, A.; Gopinath, C. S.; Bhaduri, S.; Lahiri, G. K. *Catal. Sci. Technol.*, **2013**, *3*, 1625–1633.
62. Hassinea, A.; Sebtia, S.; Solhyb, A.; Zahouily, M. *Appl. Catal. A-Gen.*, **2013**, *450*, 13–18.
63. Singh, A. S.; Patil, U. B.; Nagarkar, J. M. *Catal. Commun.* **2013**, *35*, 11–16.
64. Chen, X. C.; Hou, Y. Q.; Wang, H.; Gao, Y.; He, J. H. *J. Phys. Chem. C* **2008**, *118*, 8172–8176.
65. Siamaki, A. R.; Khder, A. E. R. S.; Abdelsayed, V.; El-Shall, M. S.; Gupton, B. F. *J. Catal.* **2011**, *279*, 1–11.
66. Wang; Hu, J.; Han, Y.; Zhou, M.; Jiang, Y. X.; Sun, P. *Catal. Sci. Technol.* **2012**, *2*, 332–2340.
67. Chua C. K., Pumera M. *Chem. Soc. Rev.* **2014**, *43*, 291–312.
68. Qu, K. G.; Wu, L.; Ren, J. S.; Qu, X. G. *Appl. Mater. Interfaces*, **2012**, *4*, 5001–5009.
69. Nie, R. F.; Shi, J. J.; Du, W. C.; Hou, Z. Y. *Appl. Catal. A-Gen.*, **2014**, *473*, 1–6.
70. Feng, Y.S. *Tetrahedron*, **2014**, *70*, 5249–5253.
71. DelRae, H.; Harold, H. K. *Top. Catal.*, **2014**, *57*, 762–773.
72. Bai, L. S. *Tetrahedron Lett.*, **2014**, *55*, 4545–4548.
73. Jia, H. P.; Dreyer, D. R.; Bielawski, C. W. *Tetrahedron*, **2011**, *67*, 4431–4434.
74. Meyer J. C., Geim A. K., Katsnelson M. I., Novoselov K. S., Booth T. J., Roth S. *Nature* **2007**, *446*, 60–63.
75. Blandez, J. F.; Primo, A. *Angew. Chem. Int. Ed.*, **2014**, *126*, 12789–12794.
76. Guo, X.; Hao, C.; Jin, G.; Zhu, H. Y.; Guo, X. Y. *Angew. Chem. Int. Ed.*, **2014**, *126*, 2004–2008.
77. Wang, X. Z.; .Chen, W. F; Yan, L. F. *Mater. Chem. Phys.* **2014**, *148*, 103–109.
78. Park, J. H. *Tetrahedron Lett.*, **2014**, *55*, 3426–3430.
79. Verma, S.; Verma, D.; Jain, S. L. *Tetrahedron Lett.*, **2014**, *58*, 2406–2409.
80. Huang, H.; Huang, J.; Liu, Y. M.; He, H. Y.; Cao, Y.; Fan, K. N. *Green Chem.*, **2012**, *14*, 930–938.
81. Dreyer D. R., Park S., Bielawski C. W., Ruoff R. S. *Chem. Soc. Rev.* **2010**, *39*, 228–240.
82. Tan, R.; Li, C.; Luo, J.; Kong, Y.; Zheng, W.; Yin, D. *J. Catal.* **2013**, *298*, 138–147.
83. Lightcap, I. V.; Kosel, T. H.; Kamat, P. V. *Nano Lett.* **2010**, *10*, 577–583.
84. Scheuermann, G. M.; Rumi, L.; Steurer, P.; Bannwarth, W.; Mülhaupt, R. *J. Am. Chem. Soc.* **2009**, *131*, 8262–8270.
85. Richmond, M. K.; Scott, S. L.; Alper, H. *J. Am. Chem. Soc.* **2001**, *123*, 10521–10525.
86. Hu, Z. L.; Aizawa, M.; Wang, Z. M.; Yoshizawa, N.; Hatori, H. *Langmuir* **2010**, *26*, 6681–6688.
87. Li, Y.; Fan, X.; Qi, J.; Ji, J.; Wang, S.; Zhang, G.; Zhang, F. *Nano Res.* **2010**, *3*, 429–437.
88. Santra, S.; Hota, P. K.; Bhattacharyya, R.; Bera, P.; Ghosh, P.; Mandal, S. K. *ACS Catal.* **2013**, *3*, 2776–2789.
89. Dong, L. F.; Gari, R. R. S.; Li, Z.; Craig, M. M.; Hou, S. F. *Carbon* **2010**, *48*, 781–787.
90. Li, Y. J.; Gao, W.; Ci, L. J.; Wang, C. M.; Ajayan, P. M. *Carbon* **2010**, *48*, 1124–1130.
91. Kamat, P. V. *J. Phys. Chem. Lett.* **2010**, *1*, 520–527.
92. Hughes, R. A.; Moody, C. J. *Angew. Chem. Int. Ed.* **2007**, *46*, 7930–7954.
93. Kappe, C. O. *Eur. J. Med. Chem.* **2000**, *35*, 1043–1052.
94. Kappe, C. O. *Tetrahedron* **1993**, *49*, 6937–6963.
95. Kappe, C. O. *Acc. Chem. Res.* **2000**, *33*, 879–888.
96. Kappe, C. O.; Stadler, *A. Org. React.* **2004**, *63*, 1–117.
97. Singh, K.; Arora, D.; Singh, K.; Singh, S. *Mini-Rev. Med. Chem.* **2009**, *9*, 95–106.
98. Atwal, K. S.; Rovnyak, G. C.; Schwartz, J.; Moreland, S.; Hedberg, A.; Gougoutas, J. Z.; Malley, M. F.; Floyd, D. M. *J. Med. Chem.* **1990**, *33*, 1510–1515.
99. Atwal, K. S.; Swanson, B. N.; Unger, S. E.; Floyd, D. M.; Moreland, S.; Hedberg, A.; O'Reilly, B. C. *J. Med. Chem.* **1991**, *34*, 806–811.
100. Rovnyak, G. C.; Atwal, K. S.; Hedberg, A.; Kimball, S. D.; Moreland, S.; Gougoutas, J. Z.; O'Reilly, B. C.; Schwartz, J.; Malley, M. F. *J. Med. Chem.* **1992**, *35*, 3254–3263.
101. Bellemann, P. *Innovative Approaches In Drug Research*, Elsevier: Amsterdam, **1986**, pp. 23-46.
102. Wang, X.-C.; Yang, G.-J.; Quan, Z.-J.; Ji, P.-Y.; Liang, J.-L.; Ren, R.-G. *Synlett* **2010**, 1657–1660.
103. Quan, Z.-J.; Jing, F.-Q.; Zhang, Z.; Da, Y.-X.; Wang, X.-C. *Eur. J. Org. Chem.* **2013**, 7175–7183.
104. Quan, Z.-J.; Jing, F.-J.; Zhang, Z.; Da, Y.-X.; Wang, X.-C. *Chin. J. Chem.* **2013**, *31*, 1495–1502.
105. Marcano, D. C.; Kosynkin, D. V.; Berlin, J. M. *ACS Nano* **2010**, *4*, 4806–4814.

106. Zhang, Y. H.; Tang, Z. R.; Fu, X. Z.; Xu, Y. J. *ACS Nano* **2010**, *4*, 7303–7314.
107. Lee K. H.; Han S. W.; Kwon, K. Y.; Park, J. B. *J. Colloid Interf. Sci*. **2013**, *403*, 127-133.
108. Li, S. S.; Hu, Y. Y.; Feng, J. J.; Lv, Z. Y.; Chen, J. R.; Wang, A. J. *Int. J. hydrogen Energ.* **2014**, *39*, 3730-3738.

Recyclable palladium catalyst on grapheme oxide for the C-C/C-N Cross-Coupling Reactions of Heteroaromatic Sulfonates

SUPPORTING INFORMATION

Quanlu Yang,[a, b] Zhengjun Quan,*[a] Shang Wu,[a, c] Baoxin Du,[a] Mingming Wang,[b] Peidong Li,[b] Yinpan Zhang,[b] Xicun Wang*[a]

a Laboratory of Eco-Environment-Related Polymer Materials, Ministry of Education; Key Laboratory of Polymer Materials, College of Chemistry and Chemical Engineering, Northwest Normal University, Lanzhou, Gansu 730070, P. R. China

E-mail: wangxicun@nwnu.edu.cn, quanzhengjun@hotmail.com

b College of Chemical Engineering, Lanzhou University of Arts and Science, Beimiantan 400, Lanzhou, Gansu 730000, P. R. China

c College of Chemical Engineering, Northwest University for Nationalities, Lanzhou, Gansu 730030, P. R. China

Contents

1. General

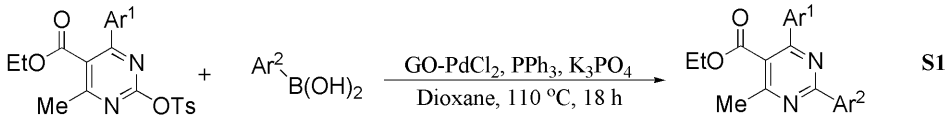
All starting materials and reagents were commercially available and used without further purification unless otherwise noted. Solvents were purified and dried by standard methods prior to use. All products have been previously reported and characterized. All known products gave satisfactory analytical data corresponding to the reported literature values.

All reactions were conducted under nitrogen atmosphere with a dual-manifold Schlenk tube and in oven-dried glassware unless otherwise noted. All NMR spectra are recorded on MERCURY (400 MHz for ^{1}H NMR, 100 MHz for ^{13}C NMR) spectrometers; chemical shifts are expressed in ppm (δunits) relative to TMS signal as internal reference in $CDCl_3$. Gas chromatography (GC) analysis was performed on a Shimadezu GC-2010 equipped with a 15 m × 0.53 mm × 1.5 μm RTX-1 capillary column and a oxyhydrogen flame detector. ICP-AES were measured on IRIS Advantage. XPS measurement was recorded on PHI5702 photoelectron spectrometer. Binding energy was referred to C_{1s} (284.80 eV). FTIR spectroscopy patterns were obtained on an FT/IR-660 Plus system (Jasco, Tokyo, Japan). The samples were mixed with KBr powders and pressed into a disk suitable for FTIR measurement. The morphologies of the catalyst were examined with field emission scanning electron microscopy (FE-SEM, Ultra Plus, Carl Zeiss). Elemental analysis of the photocatalyst was conducted by an energy-dispersive X-ray spectrometer (EDX) attached to the scanning electron microscope. Column chromatography was generally performed on silica gel (200–300 mesh) and TLC analyses were conducted on silica gel GF254 plates.

2. Experimental details and characterization data for all compounds

2.1 The GO-$PdCl_2$ was prepared following these procedures: GO was prepared by chemical oxidation and exfoliation of natural graphite under acidic conditions according to the improved Hummer's method. [1] Subsequently, 1.0 g the GO and 0.2 g $PdCl_2$ were mixed with 20 mL of de-ionized water, stirred at r.t. for 3 h. Despite the low solubility of $PdCl_2$ in water, cation exchange took place overnight. The suspension was separated by centrifugation, washed with de-ionized water(3 × 20 mL) and acetone (3 × 20 mL), dryed in a vacuum oven at 40 ^oC for 4 h and gently powdered was obtained. The palladium content in GO-$PdCl_2$ was determined by means of inductively coupled plasma equipped with atomic emission spectrometry (ICP-AES) and amounted to be 2.86 wt %.

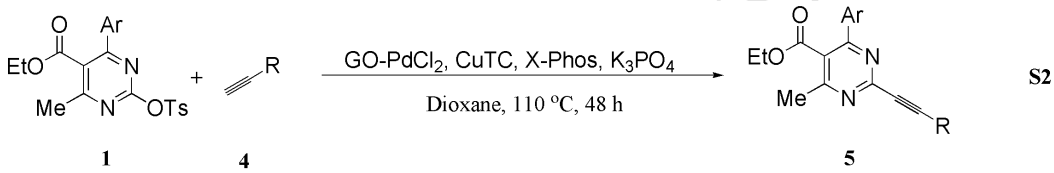
2.2 General procedures for the Suzuki coupling reactions of pyrimidin-2-yl sulfonates with arylboronic acids (eq S1). Pyrimidin-2-yl sulfonate **1** (0.25 mmol), arylboronic Acid **2** (0.375 mmol), K_3PO_4 (2.0 equiv.), PPh_3 (20 mol %), 20 mg of GO-$PdCl_2$ catalyst (Pd 2.86 wt %) were added to a 15 mL Schlenk tube, and was then evacuated and purged with nitrogen gas for four times sequentially; then 5 mL 1,4-dioxane in was added by a syringe under nitrogen atomosphere; the mixture was then stirred at 110 ^oC for 18 h. After completion, the catalyst was separated by centrifugation, the mixture was cooled to room temperature, quenched by addition of saturated aqueous NH_4Cl (3 mL), and extracted with diethyl ether (3 × 5 mL). The organic solvents were combined and washed with aqueous NaOH (2 mmol/ mL, 2 mL), brine, and then dried with anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography with a mixture of ethyl acetate and petroleum ether as eluent. The product was analyzed by GC-MS or NMR analysis. The conversion and selectivity were determined using GC analysis. All the prepared compounds are known and were compared with authentic samples.



1 **2** **3** **S1**

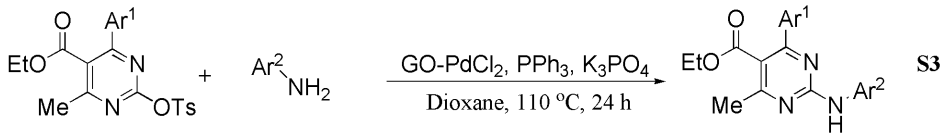
2.3 General procedures for the Sonogashira coupling reactions of pyrimidin-2-yl sulfonates with terminal alkynes (eq S2). Pyrimidin-2-yl sulfonate **1** (0.25 mmol), terminal alkyne **4** (0.375 mmol), K_3PO_4 (2.0 equiv.), PPh_3 (20 mol %), 20 mg of GO-$PdCl_2$ catalyst (Pd 2.86 wt %) and CuTC (10 mol %) were added to a Schlenk tube. The tube containing the

mixture of substrates was evacuated and purged with nitrogen gas for four times. Then, 5 mL 1,4-dioxane was added by a syringe under nitrogen atomosphere, and the reaction mixture was stirred at 110 °C for 48 h. After completion, the catalyst was separated by centrifugation, the mixture was cooled to room temperature, quenched by addition of saturated aqueous NH_4Cl (3 mL), and extracted with diethyl ether (3 × 5 mL). The organic solvents were combined and washed with aqueous NaOH (2 mmol/mL, 2 mL), brine, and then dried with anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography with a mixture of ethyl acetate and petroleum ether as eluent. The product was analyzed by GC-MS or NMR analysis. The conversion and selectivity were determined using GC analysis. All the prepared compounds are known and were compared with authentic samples.



1 4 5 S2

2.4 General procedures for the C-N coupling reactions of pyrimidin-2-yl sulfonates with anilines (eq S3). Pyrimidin-2-yl sulfonate **1** (0.25 mmol), anilines **6** (0.375 mmol), K_3PO_4 (2.0 equiv.), PPh_3 (20 mol %), 20 mg of GO-$PdCl_2$ catalyst (Pd 2.86 wt %) were added to a 15 mL Schlenk tube, and was then evacuated and purged with nitrogen gas for four times sequentially; then 5 mL 1,4-dioxane in was added by a syringe under nitrogen atomosphere; the mixture was then stirred at 110 ^oC for 24 h until the reaction was completed. After cooling the mixture to room temperature, the catalyst was separated by centrifugation, and the liquid was quenched with saturated NH_4Cl aqueous solution (3 mL), and extracted with ethoxyethane (3 × 5 mL). The organic solvents were combined and washed with aqueous NaOH (2 mmol/mL, 2 mL), brine, and then dried with anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography, eluting with a mixture of ethyl acetate and petroleum ether. The product was analyzed by GC-MS or NMR analysis. The conversion and selectivity were determined using GC analysis. All the prepared compounds are known and were compared with authentic samples.



1 **6** **7** **S3**

2.5 Procedures for the hot filtration test. Pyrimidin-2-yl sulfonate **1a** (0.25 mmol), phenel boronic acid **2a** (0.375 mmol), K_3PO_4 (2.0 equiv.), PPh_3 (20 mol %), 20 mg of GO-$PdCl_2$ catalyst (Pd 2.86 wt %) were added to a 15 mL Schlenk tube, and was then evacuated and purged with nitrogen gas for four times sequentially; then 5 mL 1,4-dioxane in was added by a syringe under nitrogen atomosphere; the mixture was then stirred at 110 ^oC for 6 h. Sample was taken from the mixture, and was analyzed by HPLC. The mixture was then filtrated to remove the catalyst, and was stirred at 110 ^oC for another 18 h. Finally the mixture was analyzed by HPLC. As a result, 37% of product **3a** was detected by HPLC, and this proportion remained after the catalyst was removed, suggesting that no reaction occurred without the catalyst.

Referrences

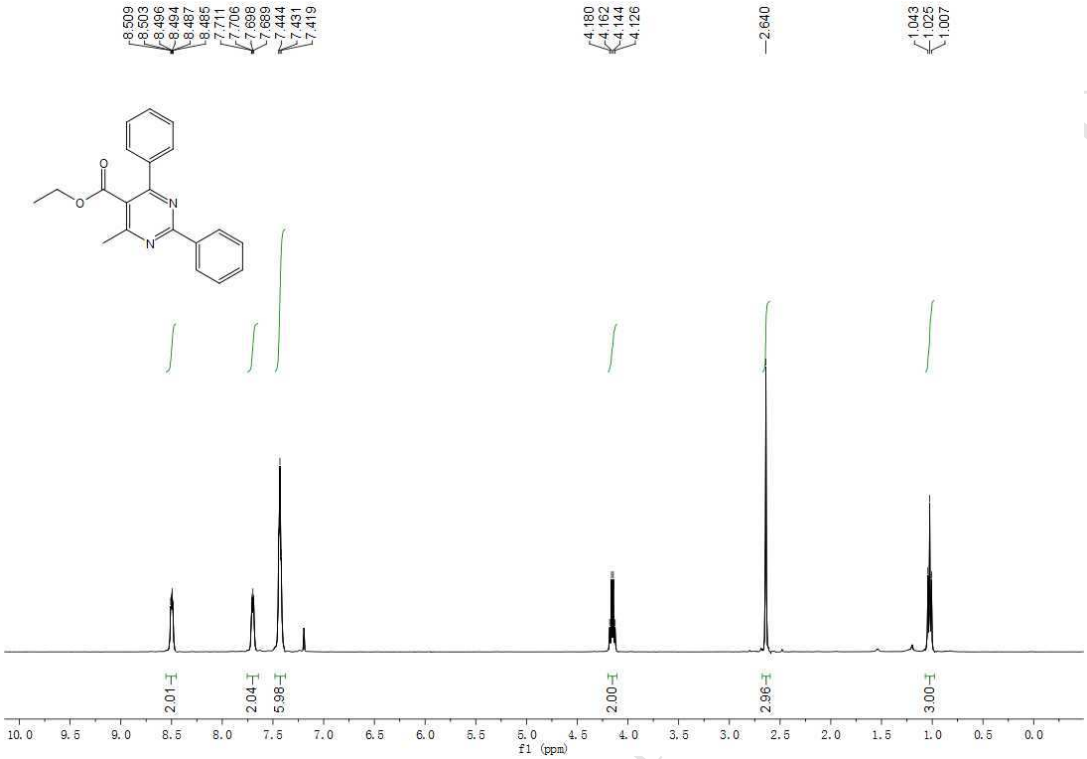
1 D. C. Marcano, D. V. Kosynkin, J. M. Berlin, ACS Nano 2010, 4, 4806-4814.

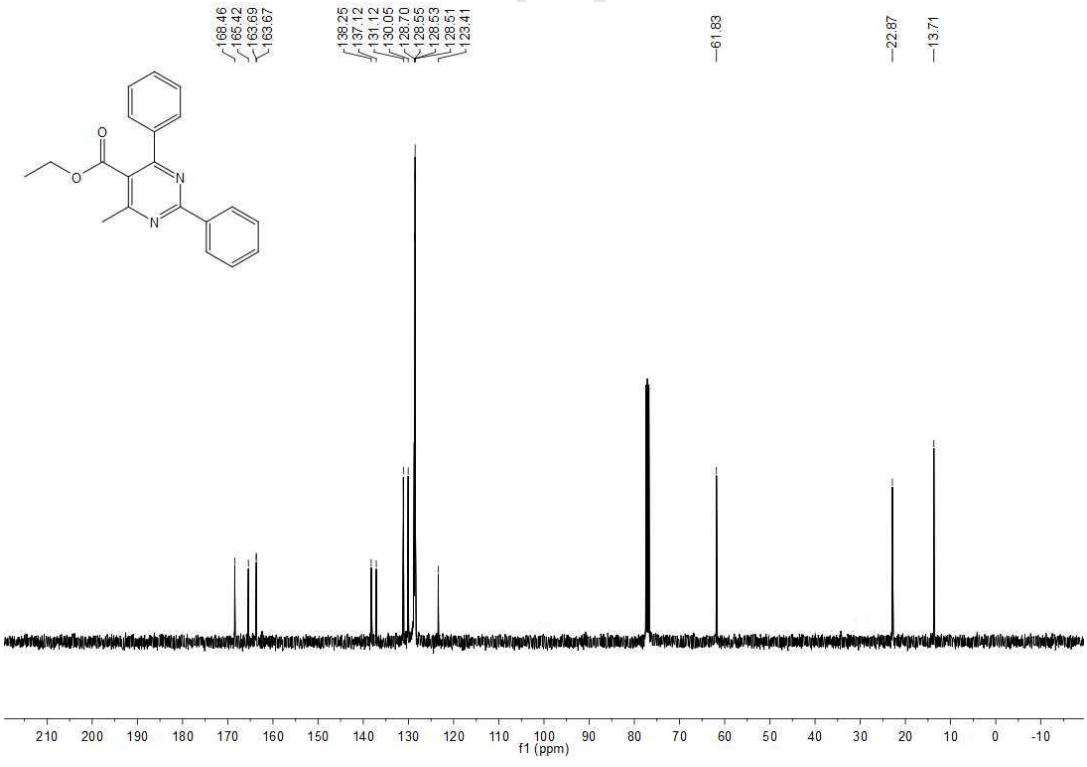
2 Zheng-Jun Quan, Fu-Qiang Jing, Zhang Zhang, Yu-Xia Da, Xi-Cun Wang, *Eur. J. Org. Chem.* **2013**, 7175–7183.

3 Zhengjun Quan, Fuqiang Jing, Zhang Zhang, Yuxia Da, and Xicun Wang, *Chin. J. Chem.* **2013**, *31*, 1495-1502.

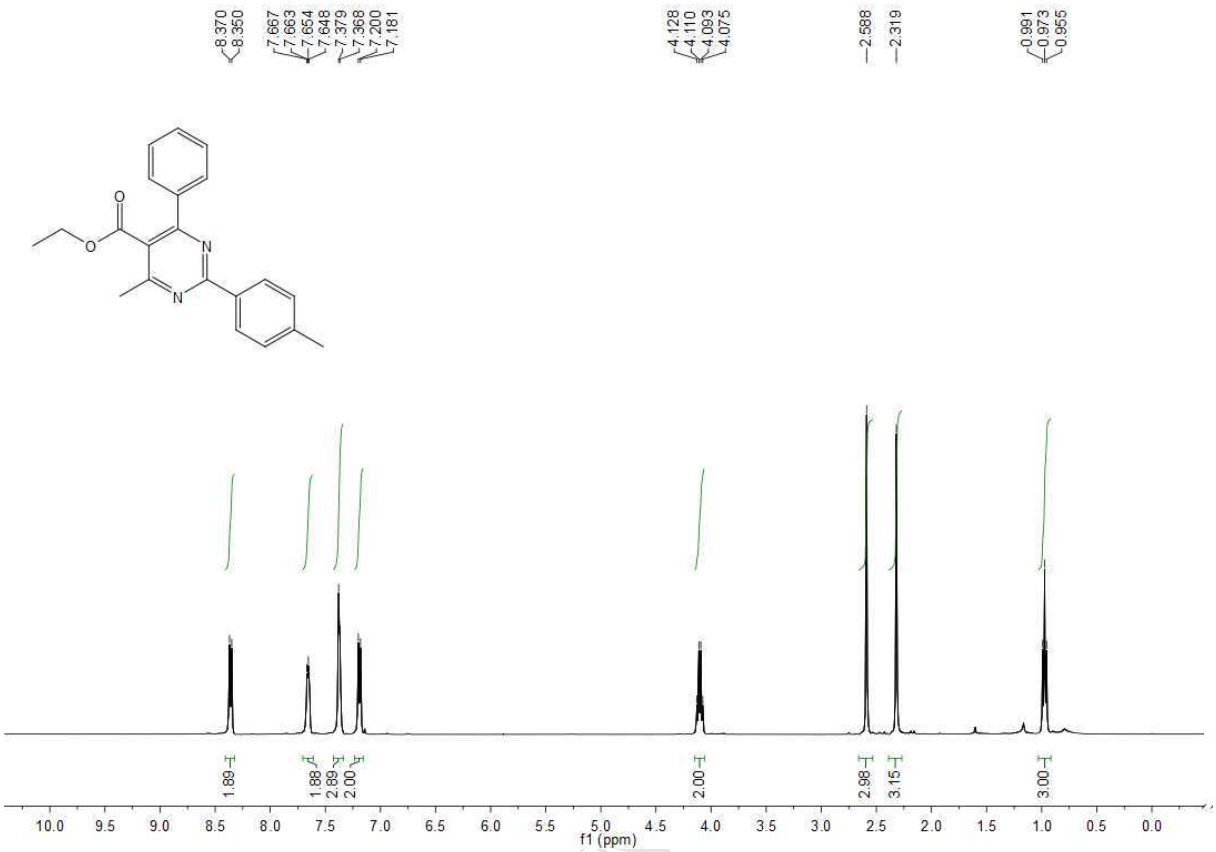
Copies of the NMR Spectra for Products

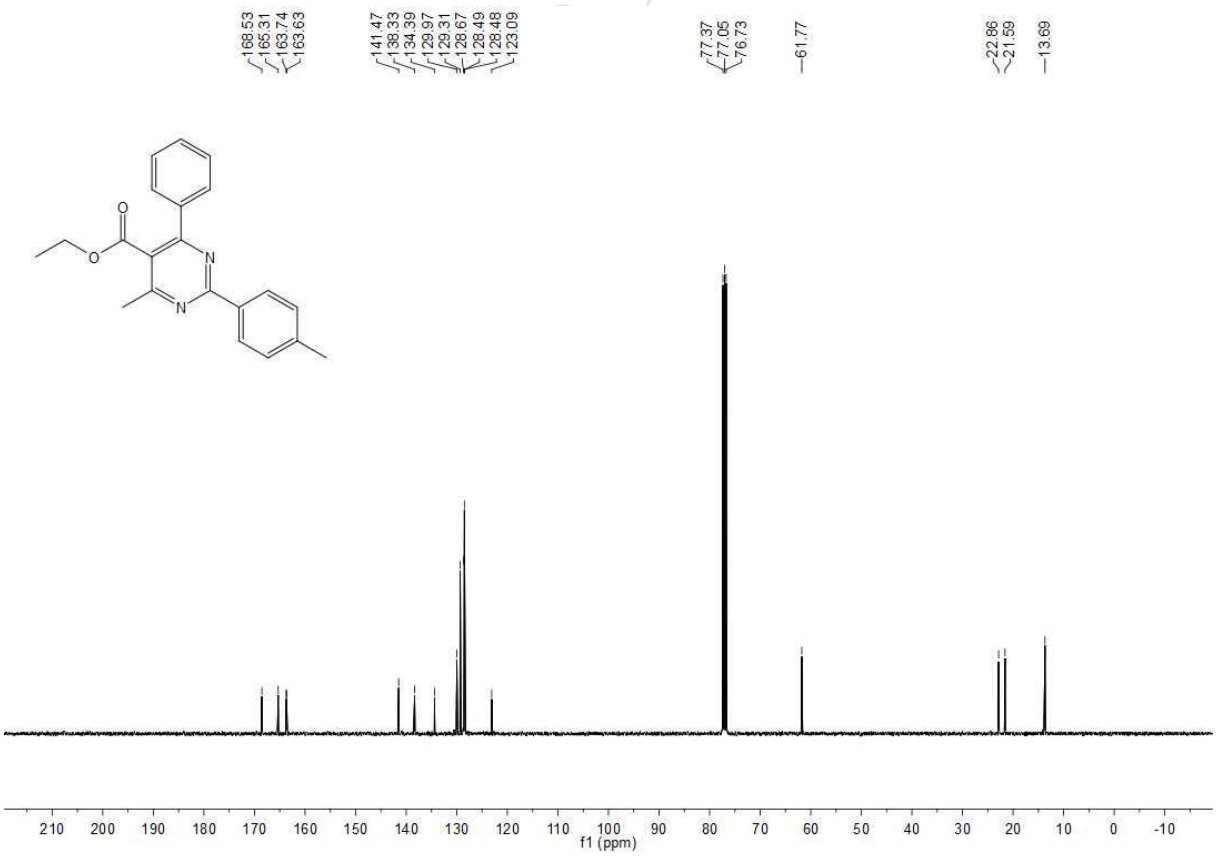
Ethyl 4-methyl-2,6-diphenylpyrimidine-5-carboxylate (3a)



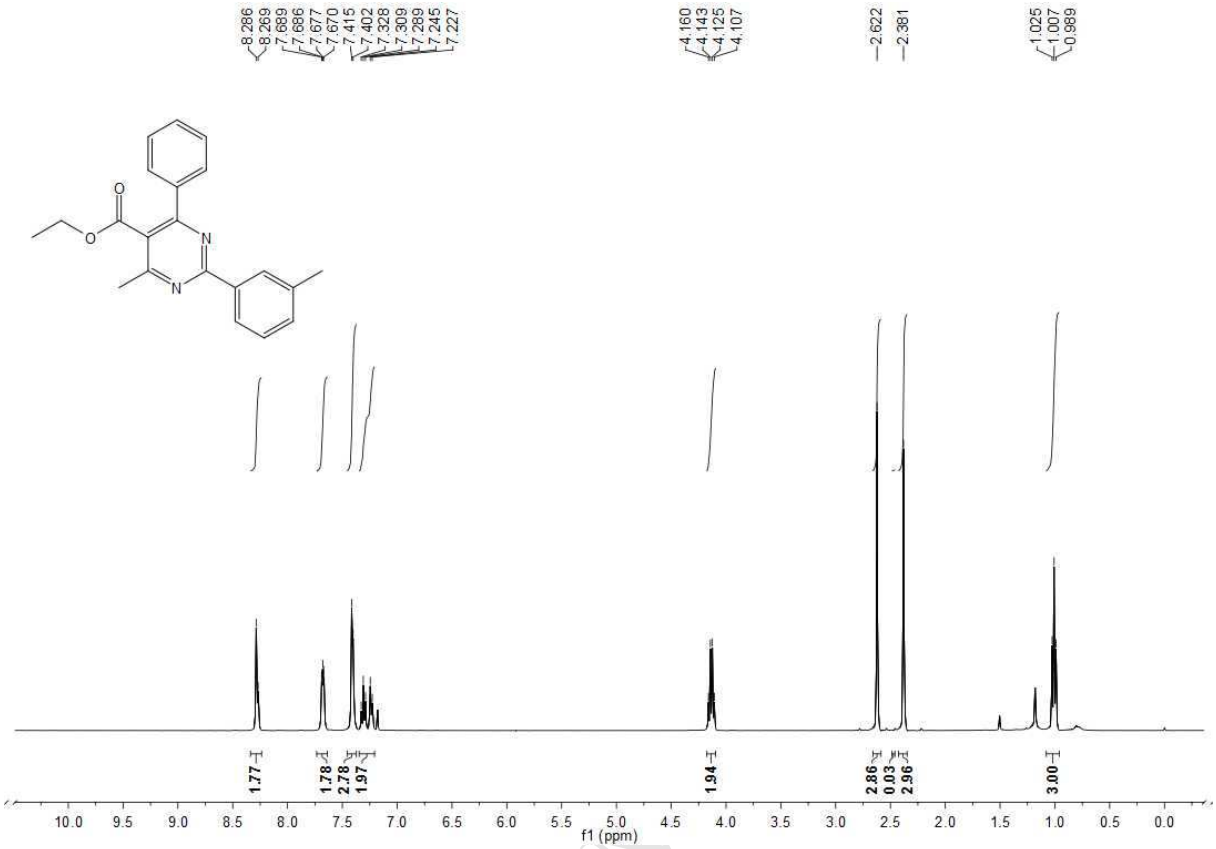


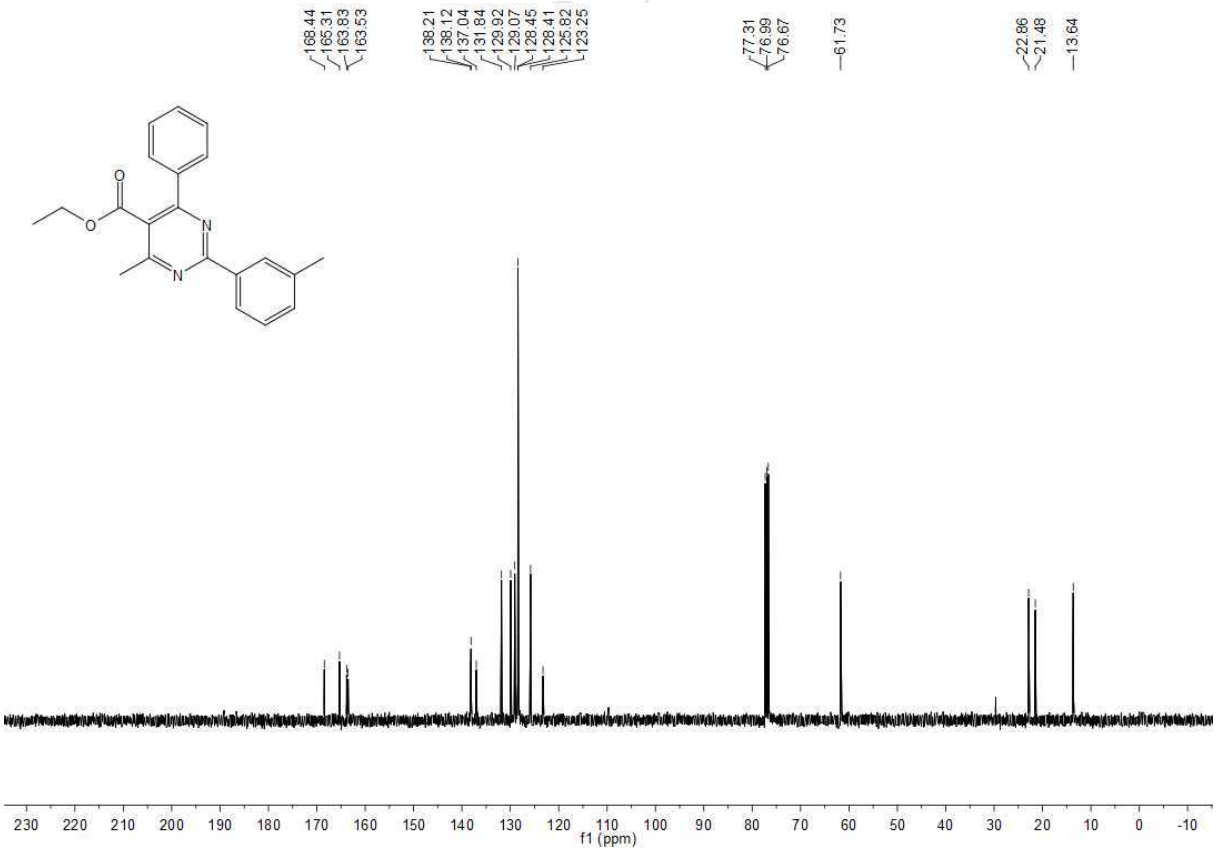
Ethyl 4-methyl-6-phenyl-2-p-tolylpyrimidine-5-carboxylate (3b)



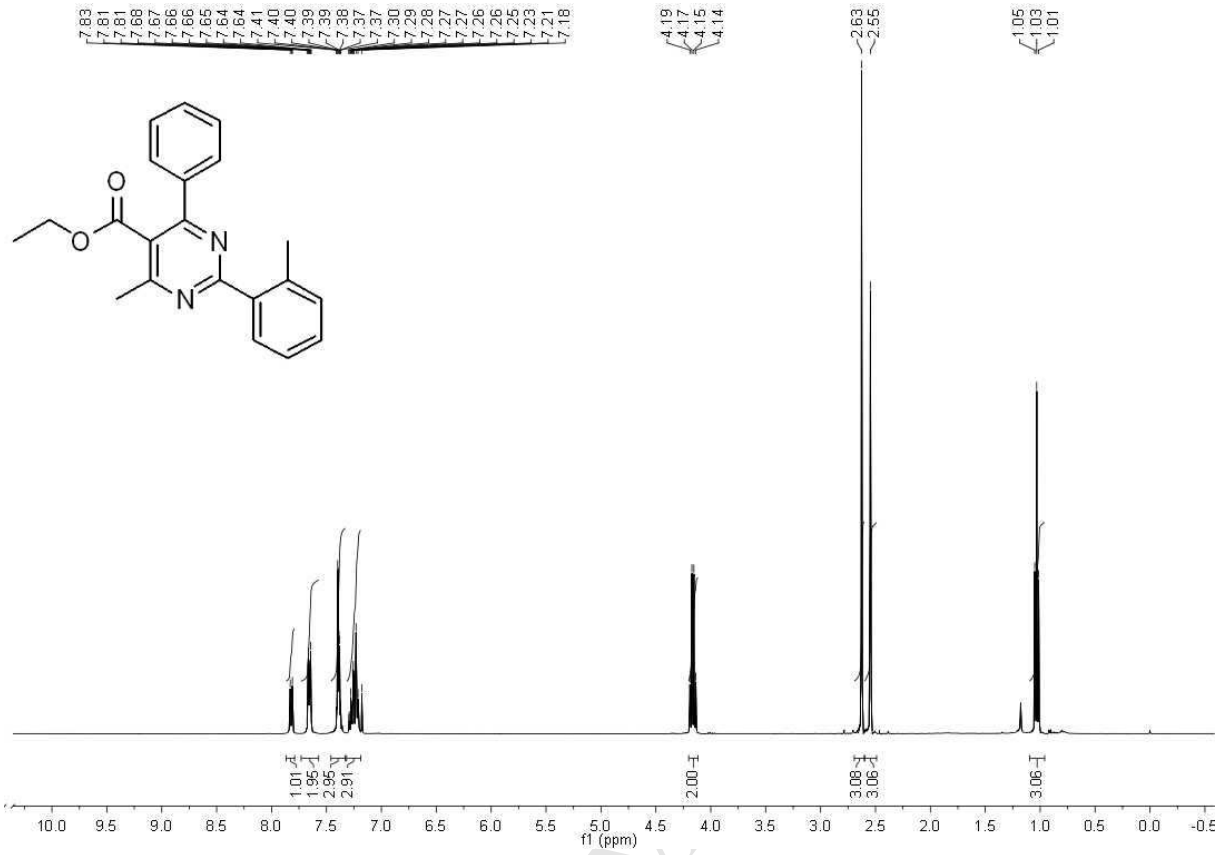


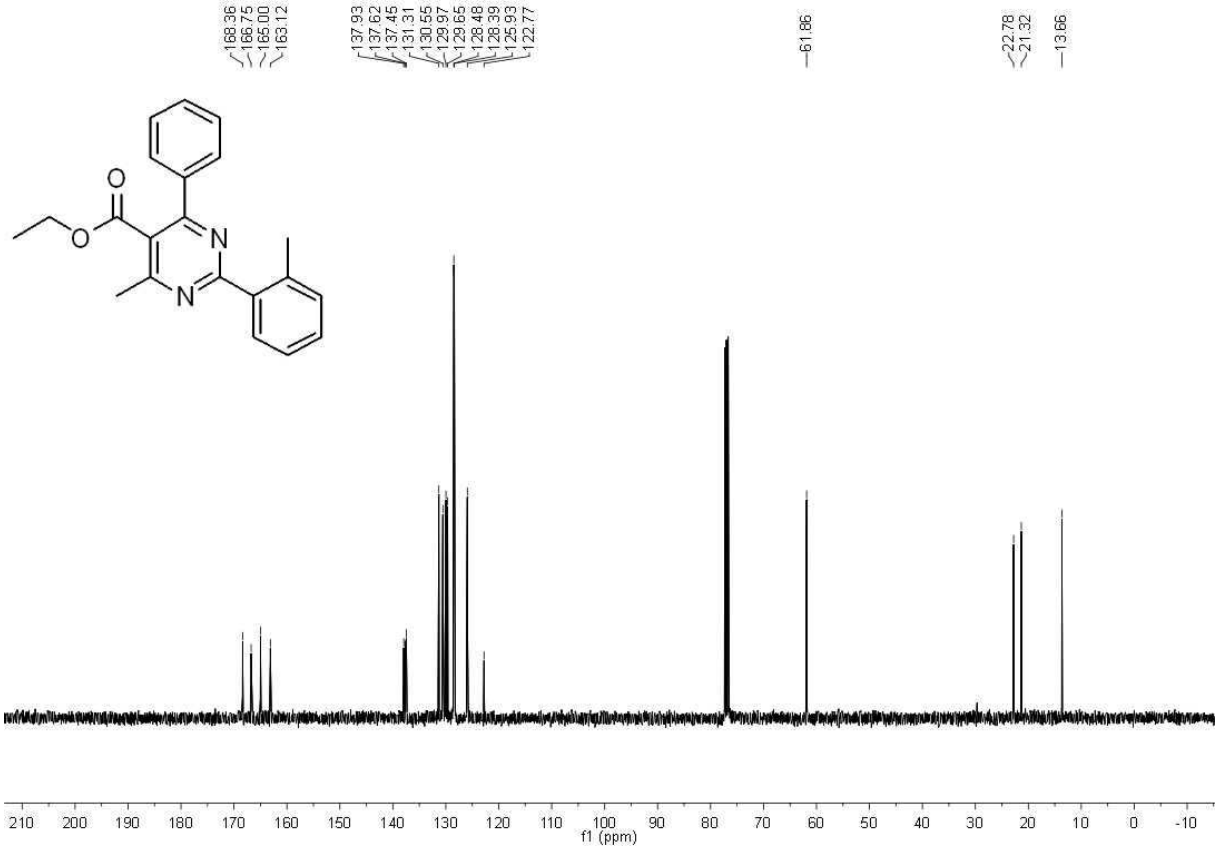
Ethyl 4-methyl-6-phenyl-2-m-tolylpyrimidine-5-carboxylate (3c)



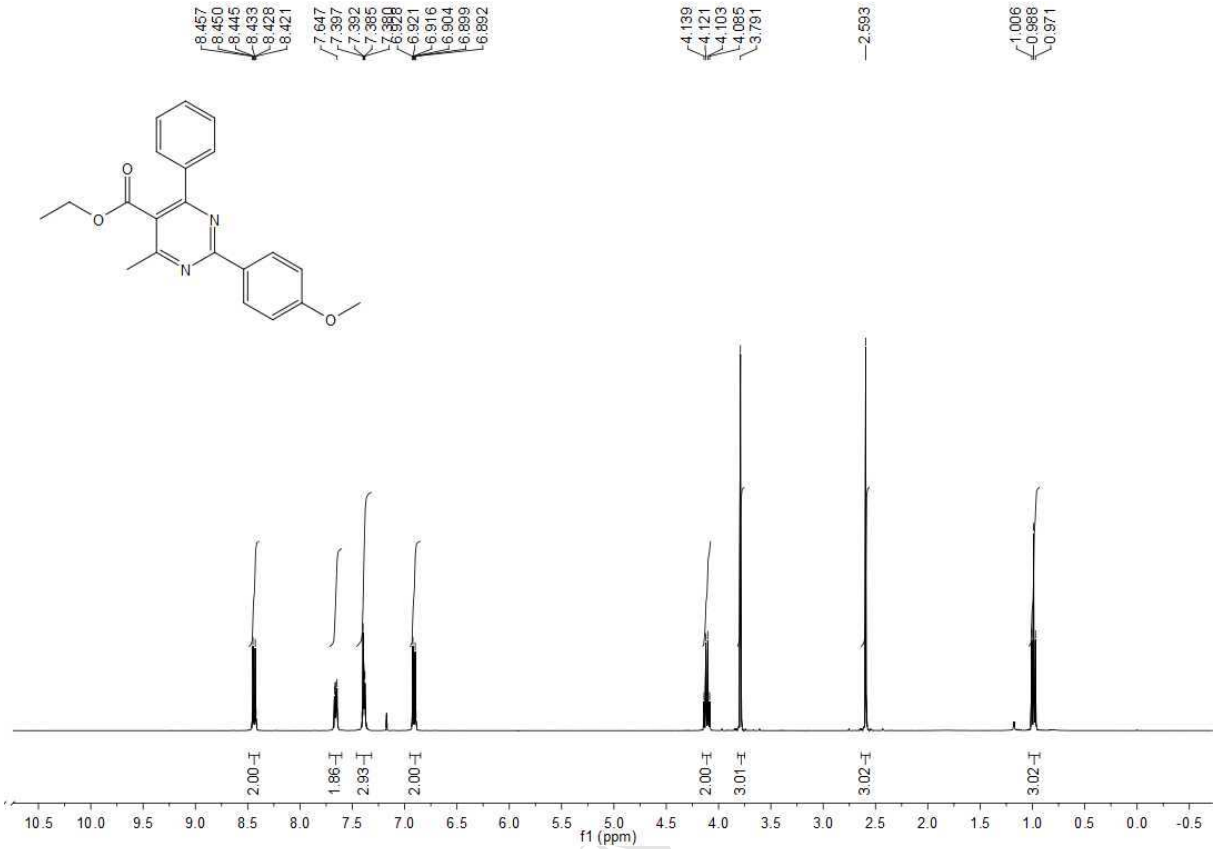


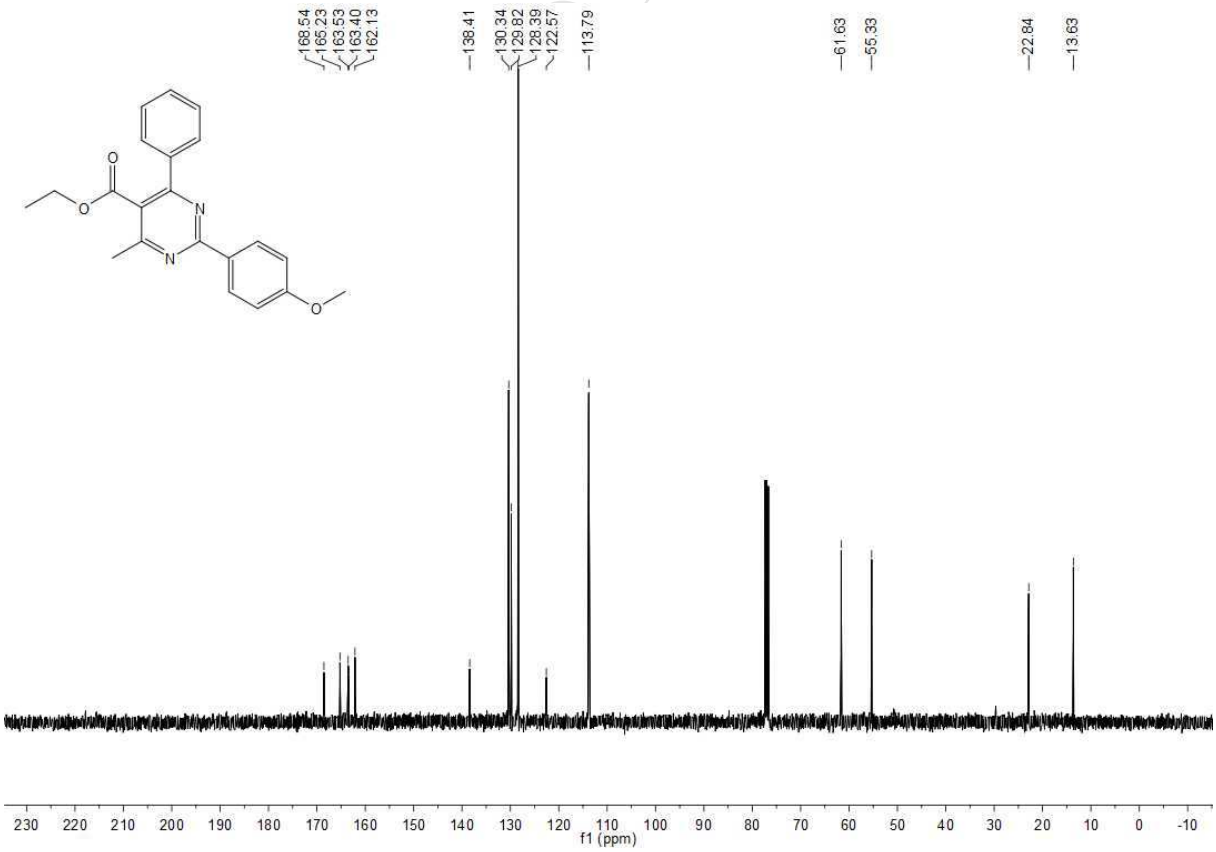
Ethyl 4-methyl-6-phenyl-2-o-tolylpyrimidine-5-carboxylate (3d)



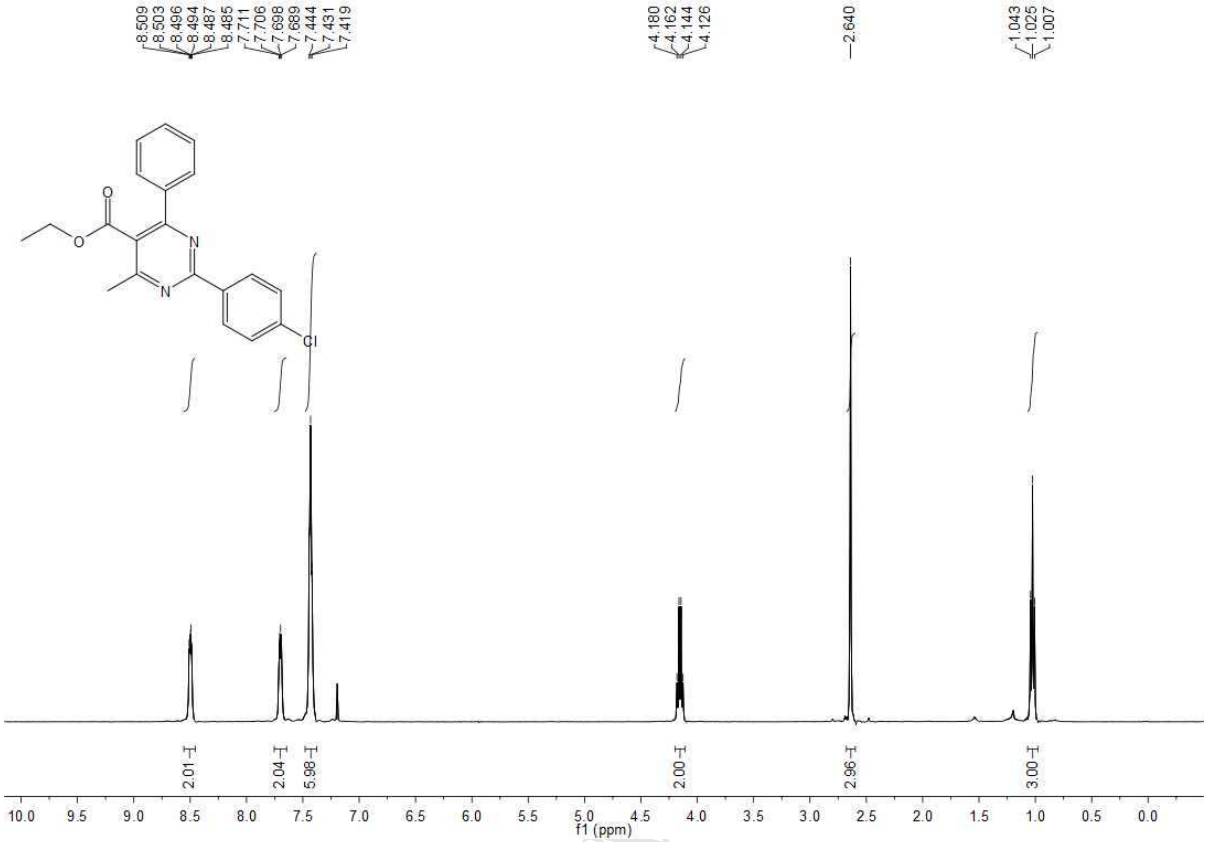


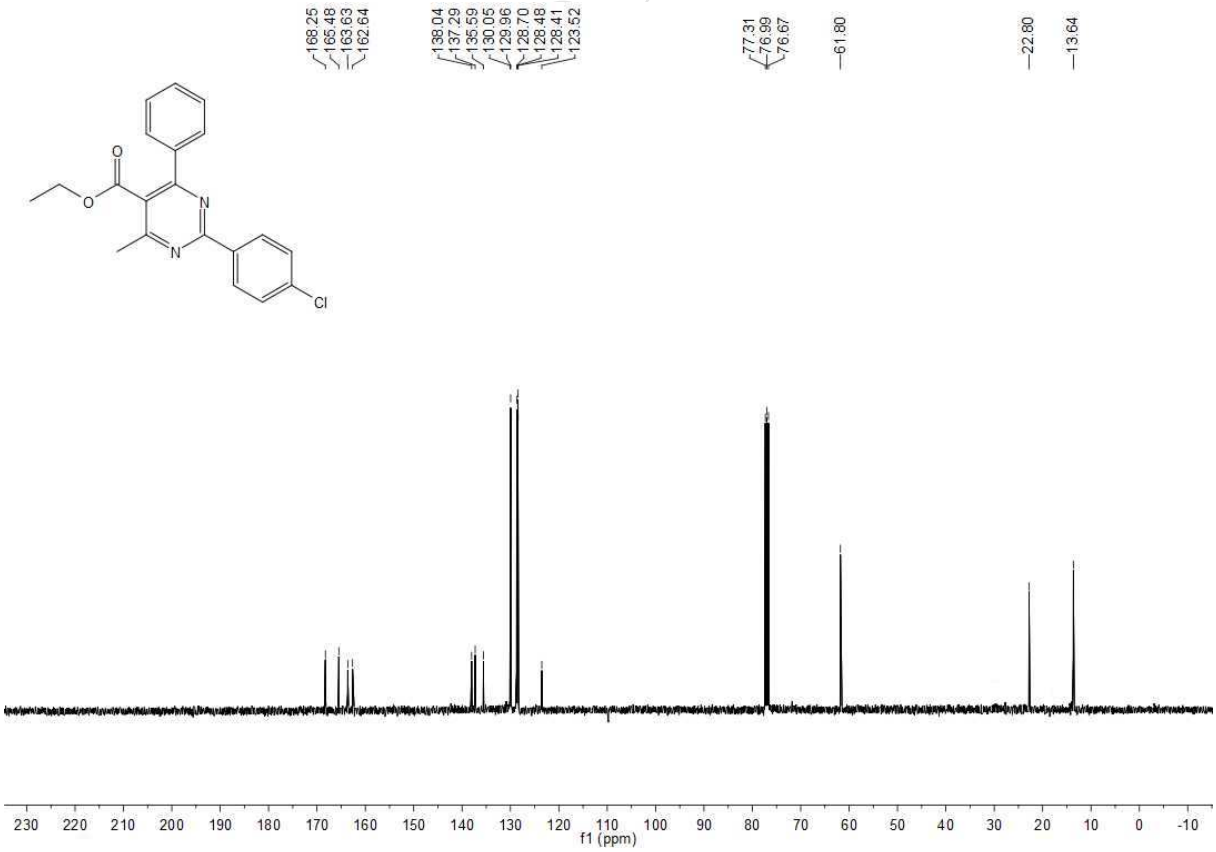
Ethyl 2-(4-methoxyphenyl)-4-methyl-6-phenylpyrimidine-5-carboxylate (3e)



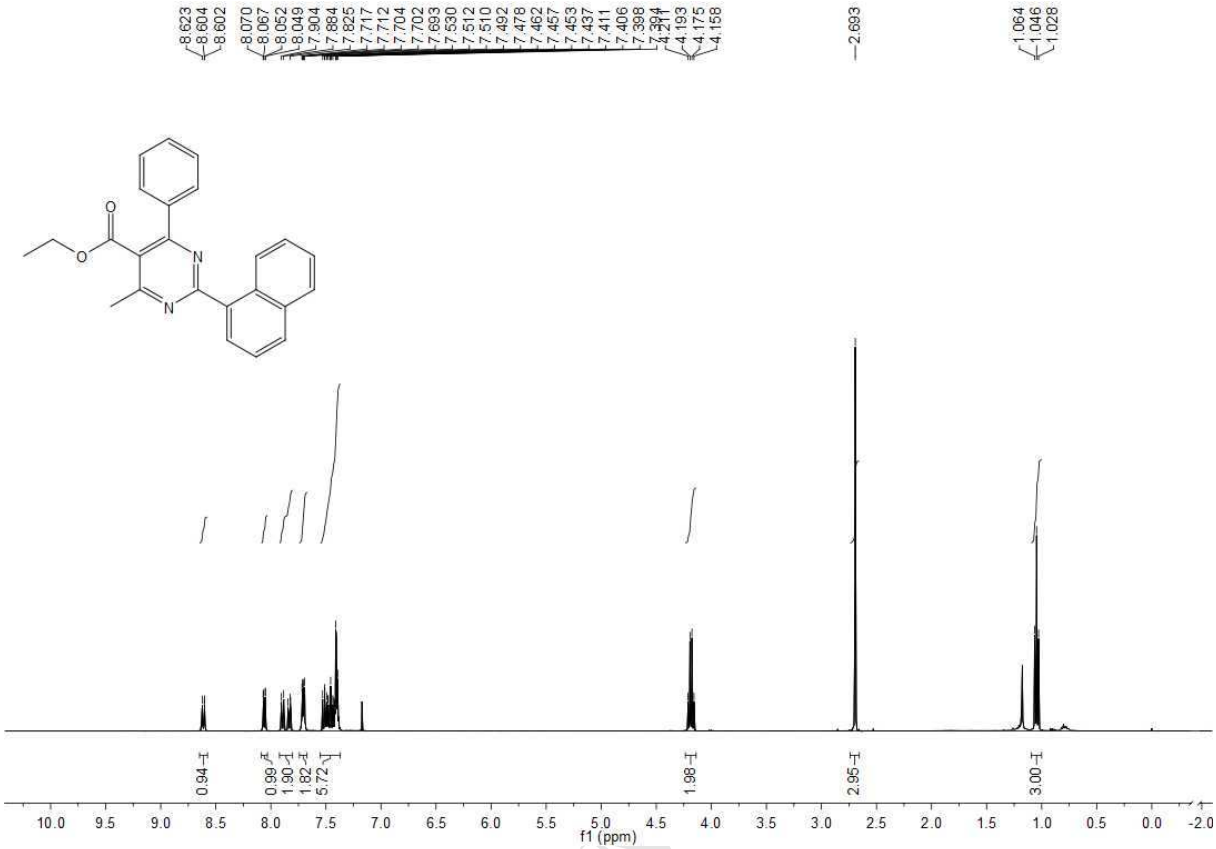


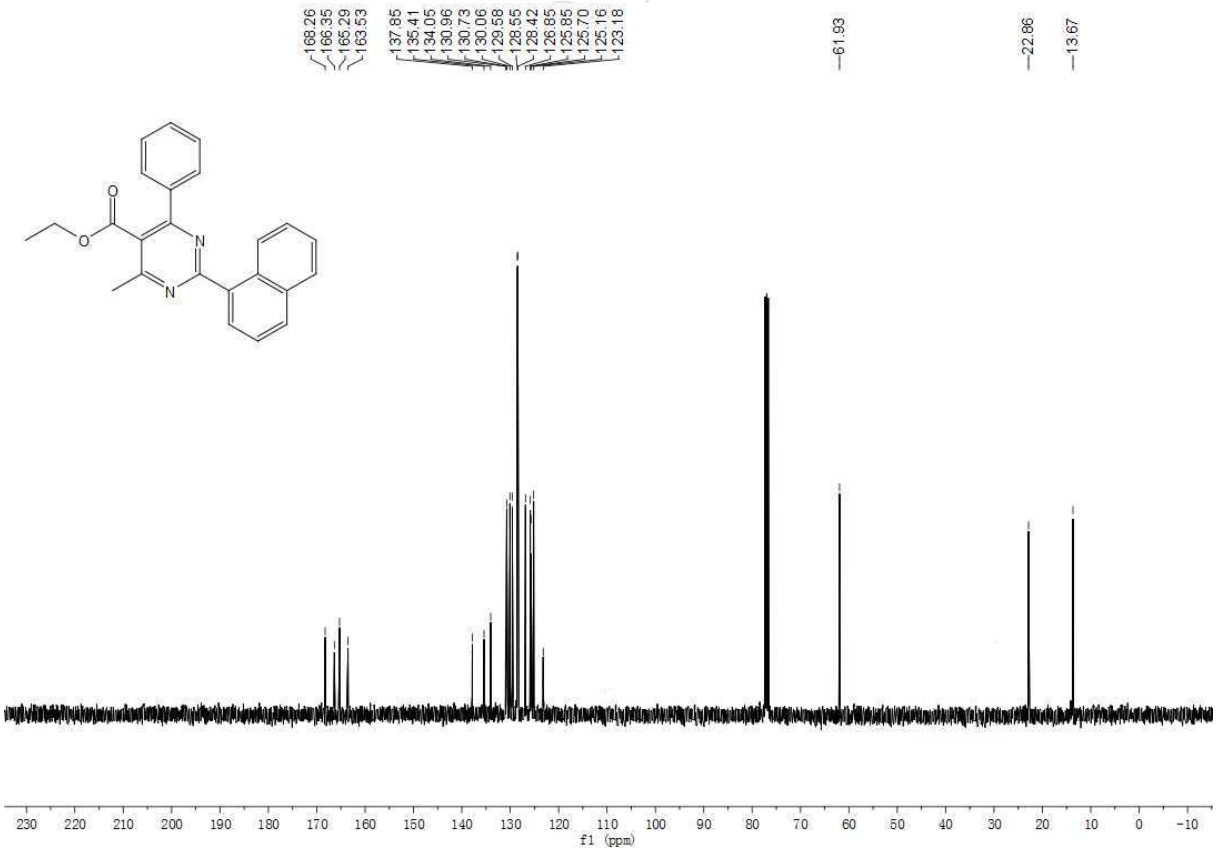
Ethyl 2-(4-chlorophenyl)-4-methyl-6-phenylpyrimidine-5-carboxylate (3f)



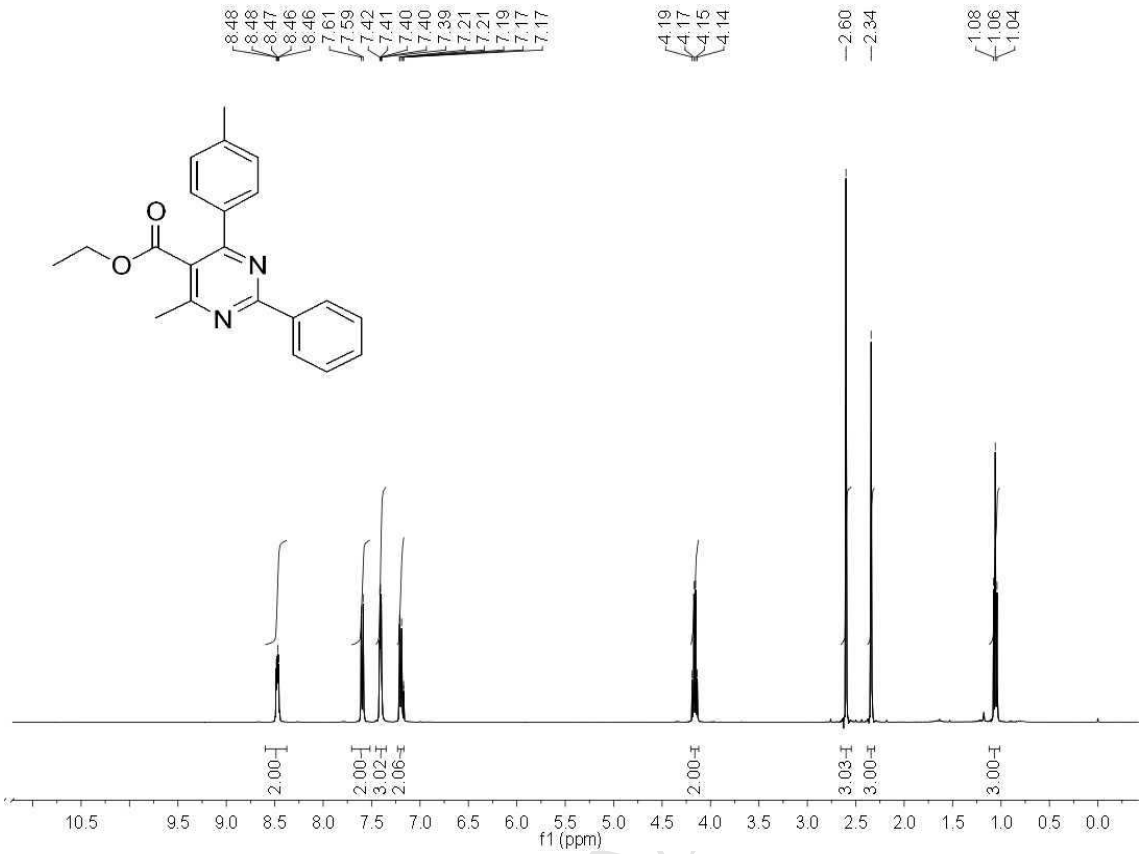


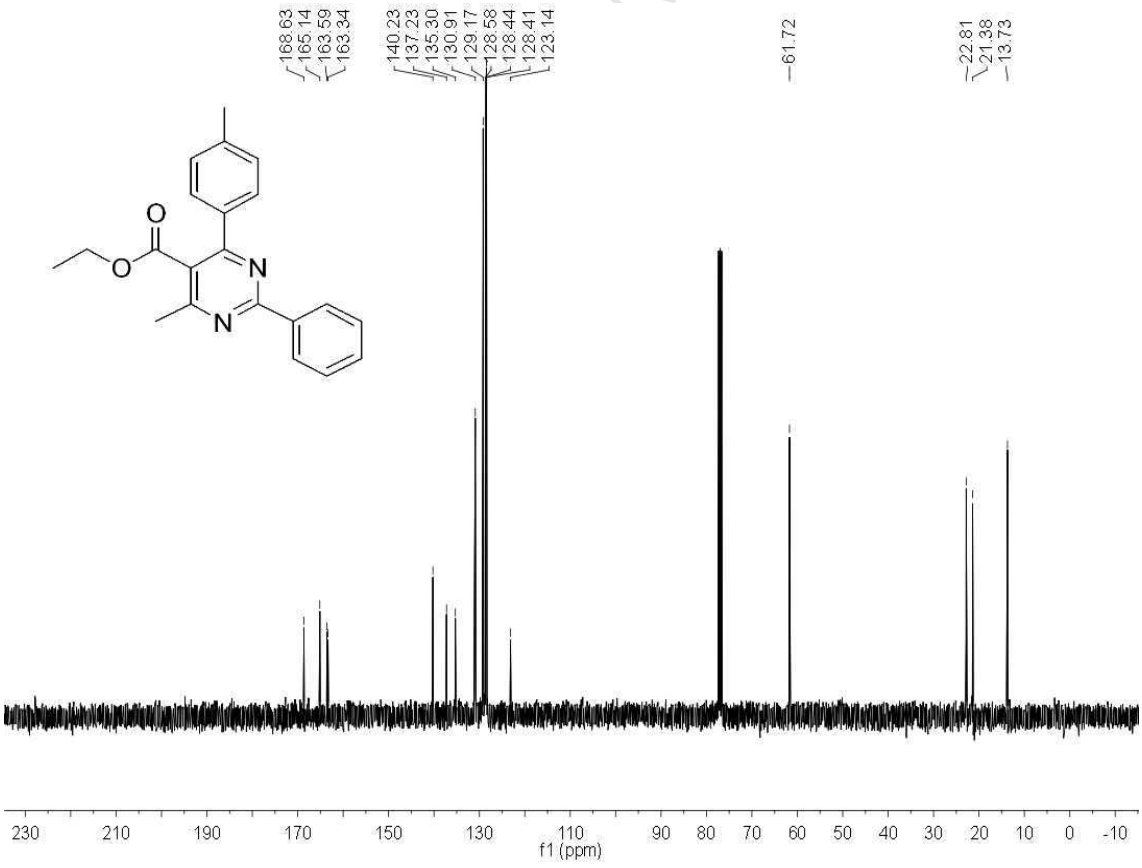
Ethyl 4-methyl-2-(naphthalen-1-yl)-6-phenylpyrimidine-5-carboxylate (3g)



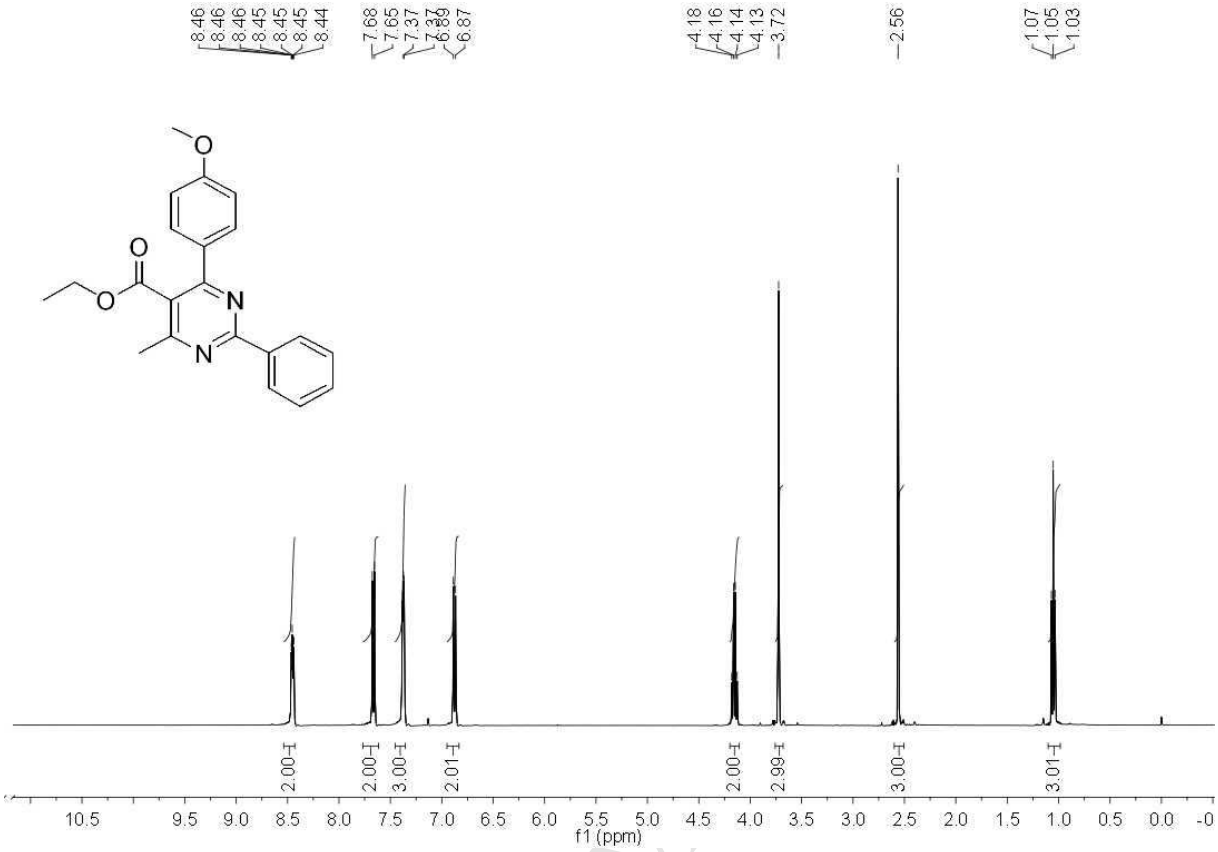


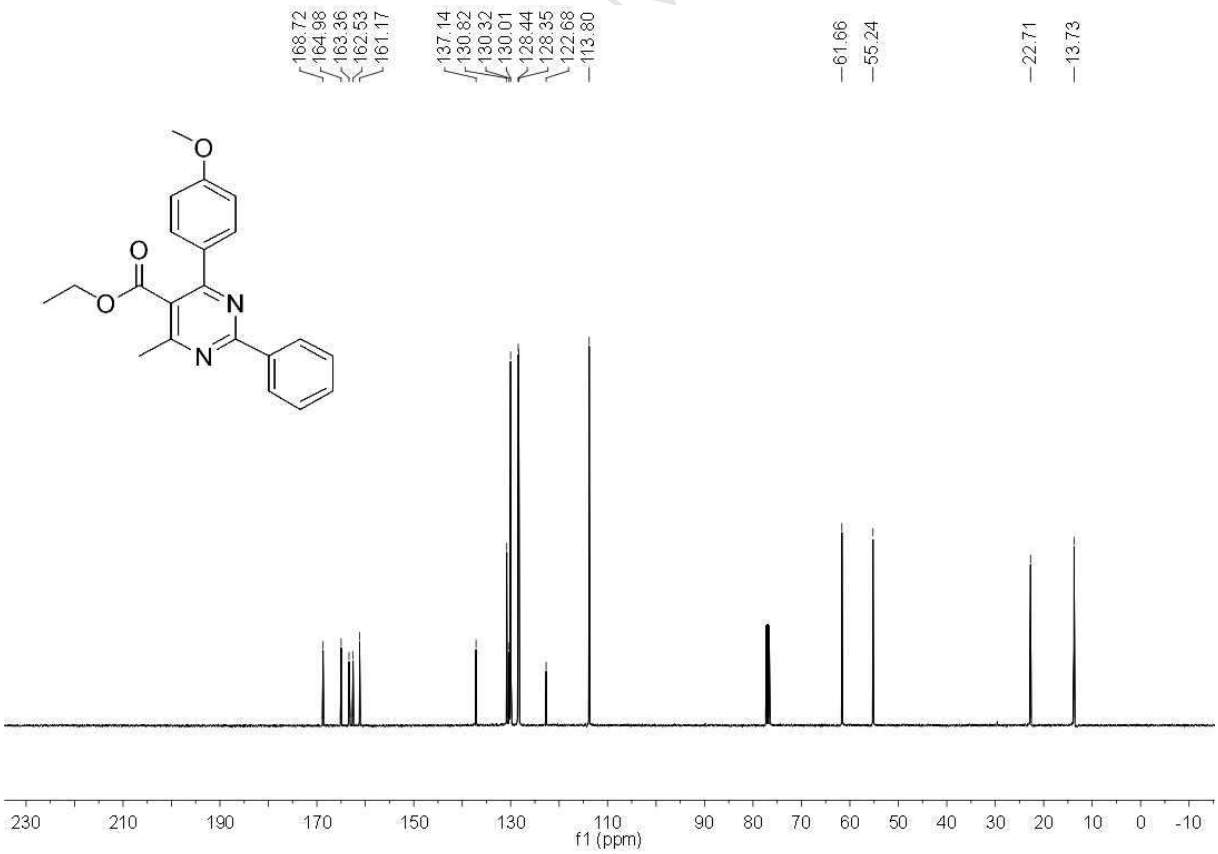
Ethyl 4-methyl-2-phenyl-6-p-tolylpyrimidine-5-carboxylate (3h)



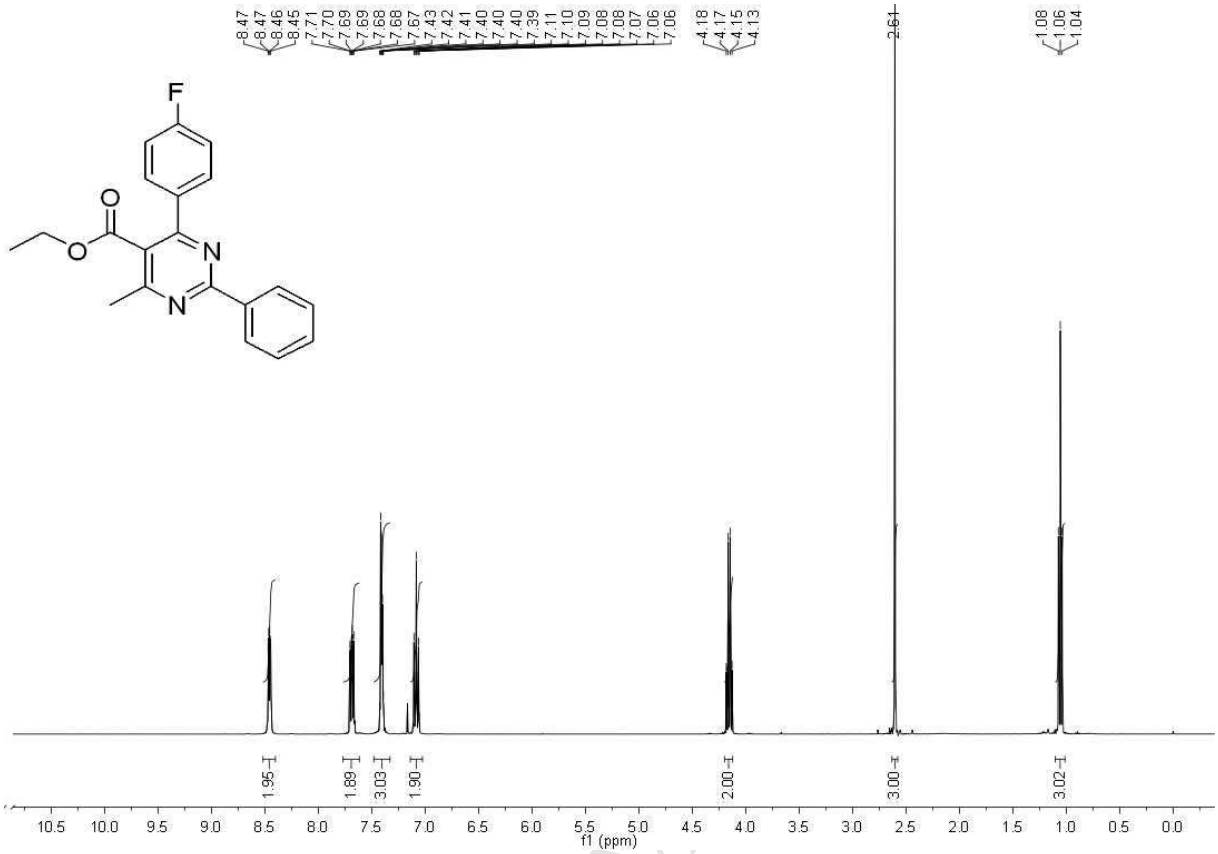


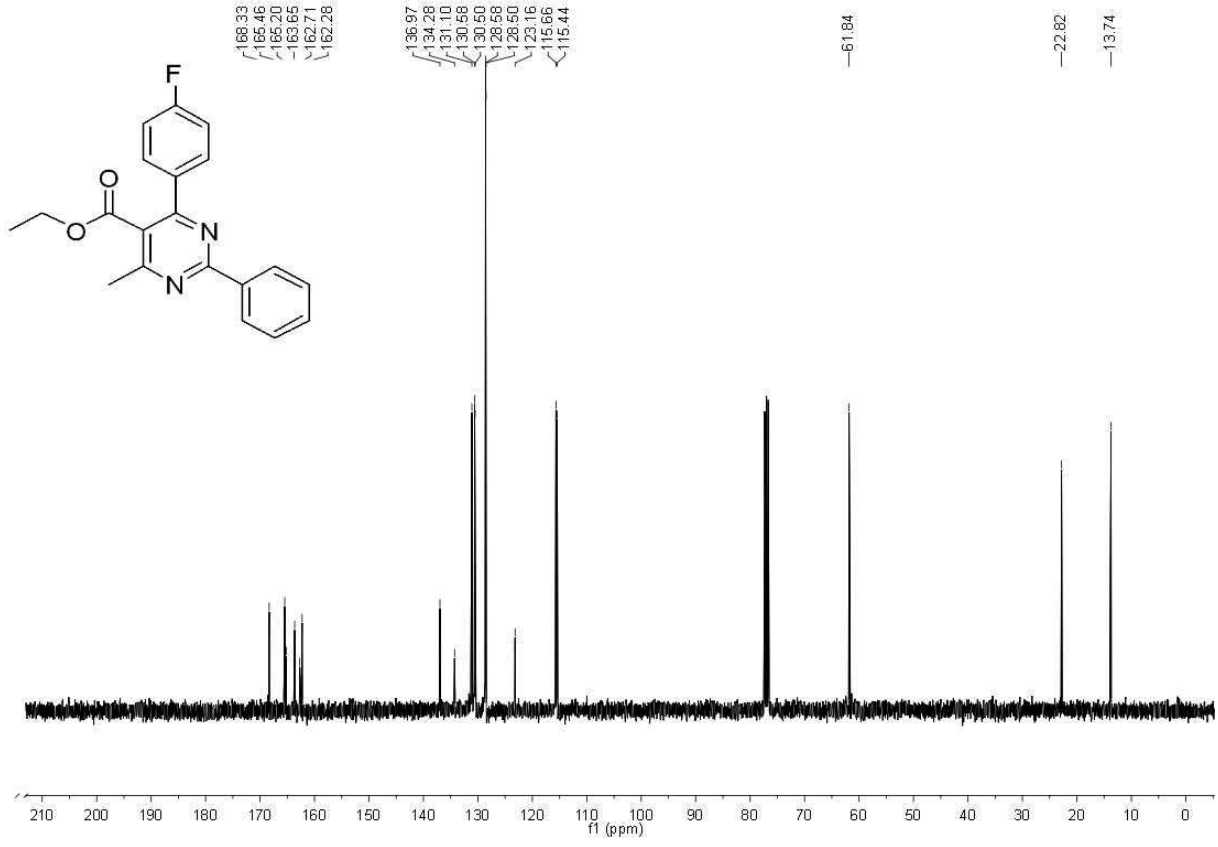
Ethyl 4-(4-methoxyphenyl)-6-methyl-2-phenylpyrimidine-5-carboxylate (3i)



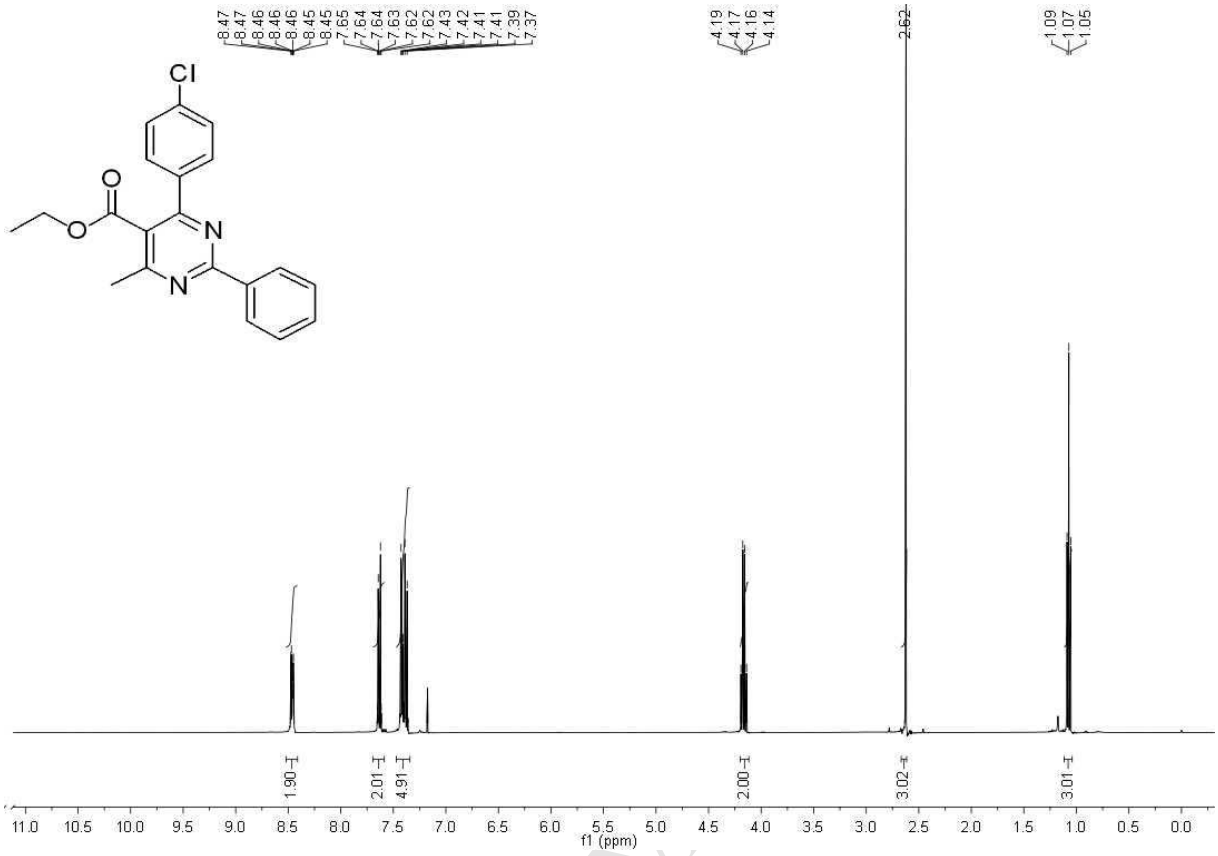


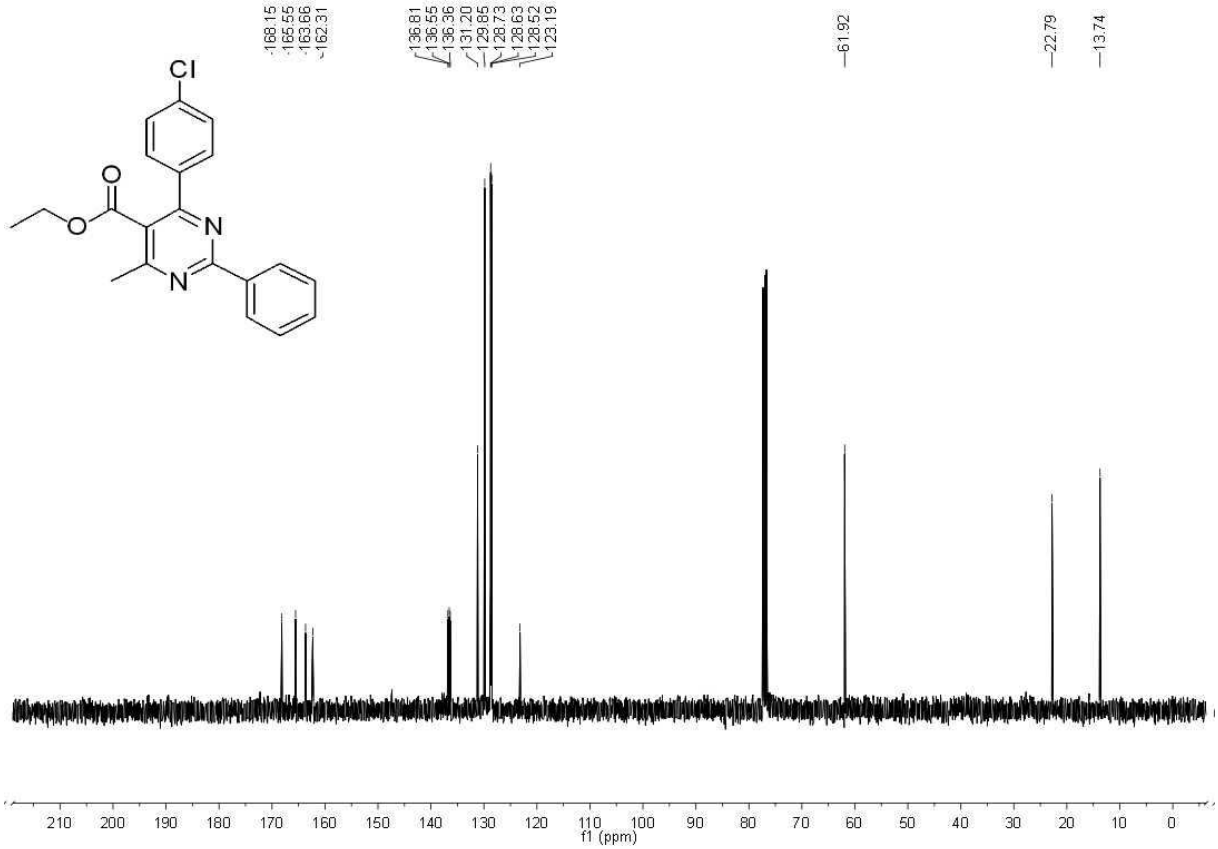
Ethyl 4-(4-fluorophenyl)-6-methyl-2-phenylpyrimidine-5-carboxylate (3j)



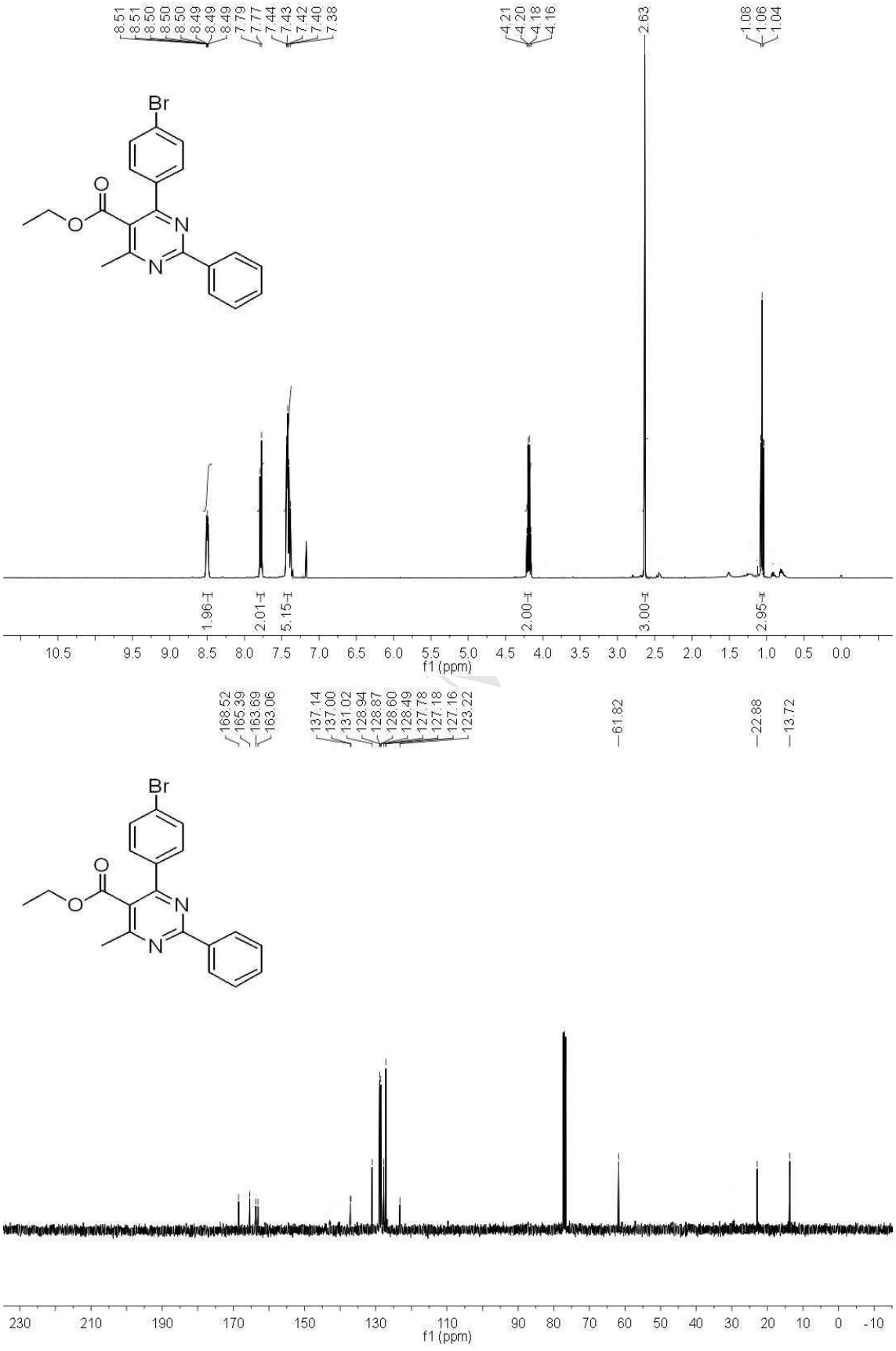


Ethyl 4-(4-chlorophenyl)-6-methyl-2-phenylpyrimidine-5-carboxylate (3k)

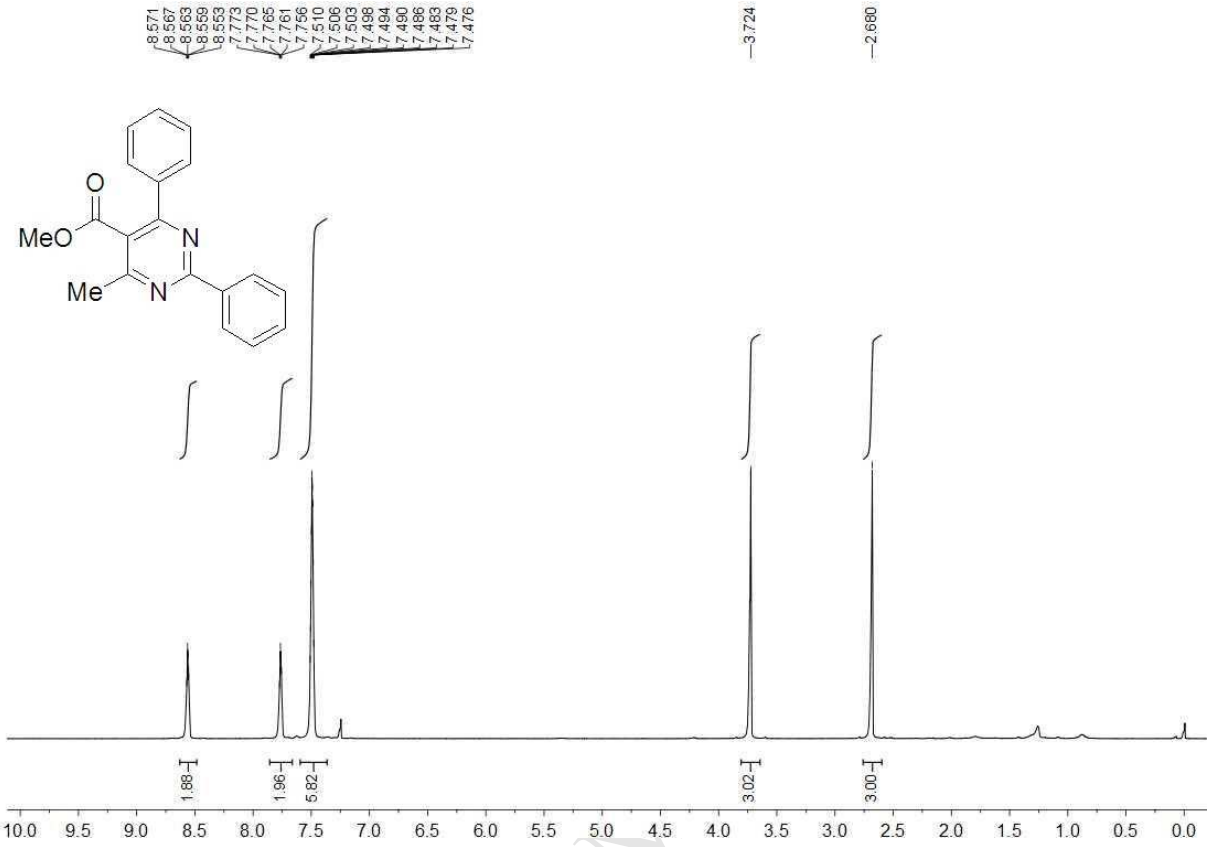


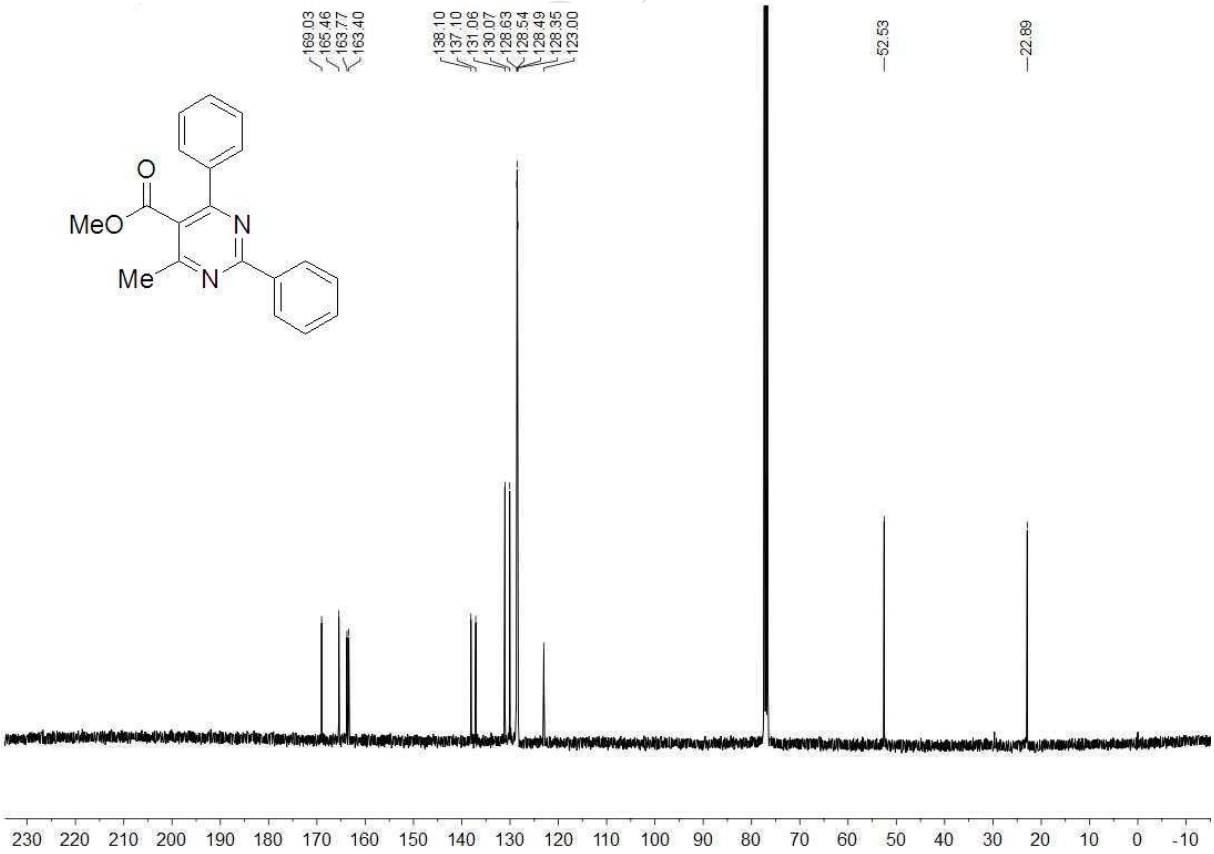


Ethyl 4-(4-bromophenyl)-6-methyl-2-phenylpyrimidine-5-carboxylate (3l)

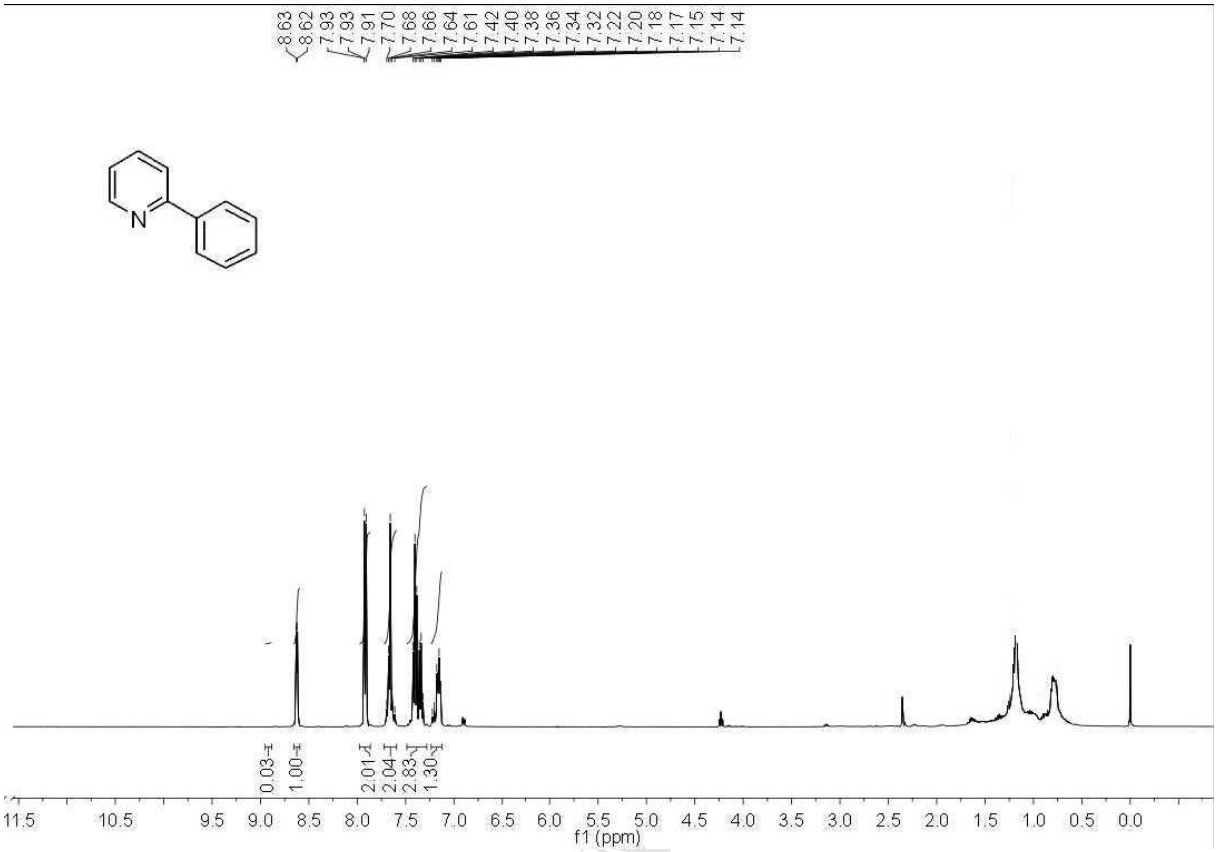


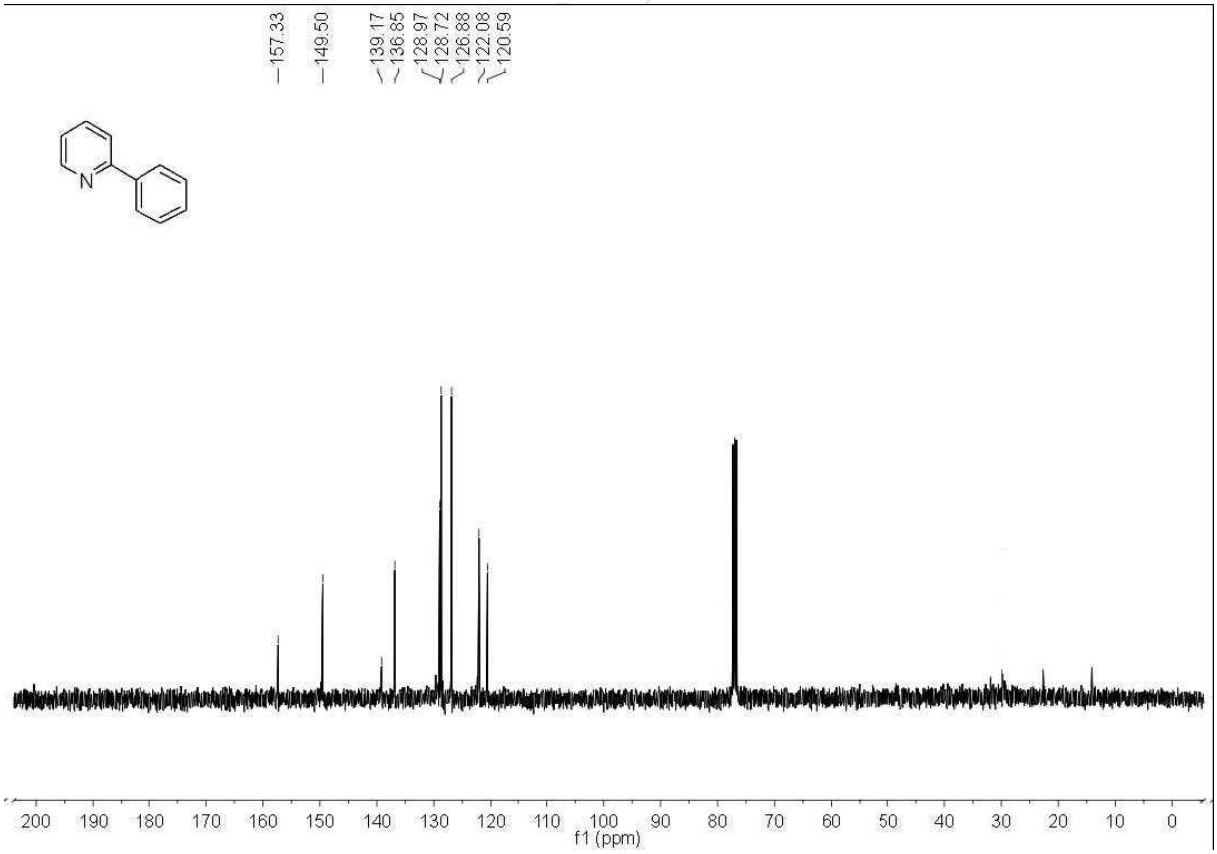
Methyl 4-methyl-2,6-diphenylpyrimidine-5-carboxylate (3m)



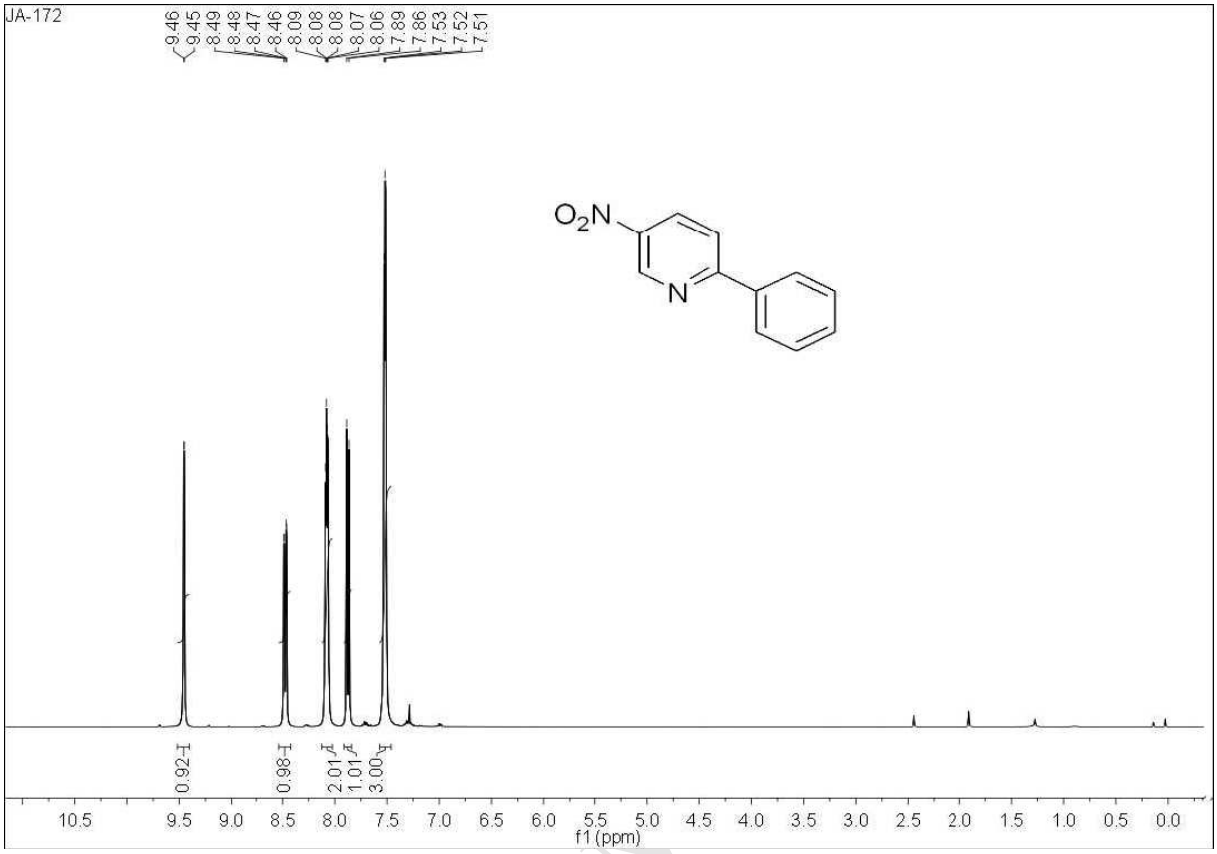


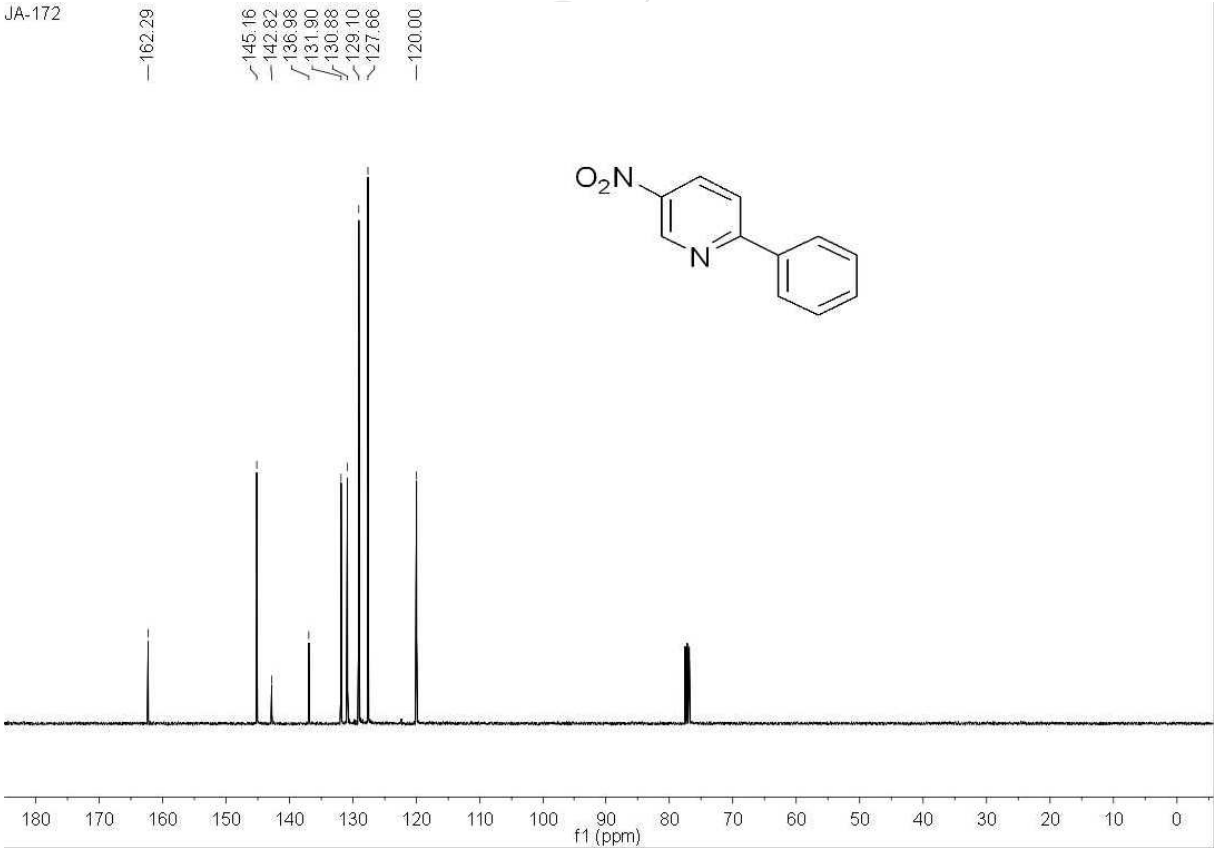
2-Phenylpyridine (3n)



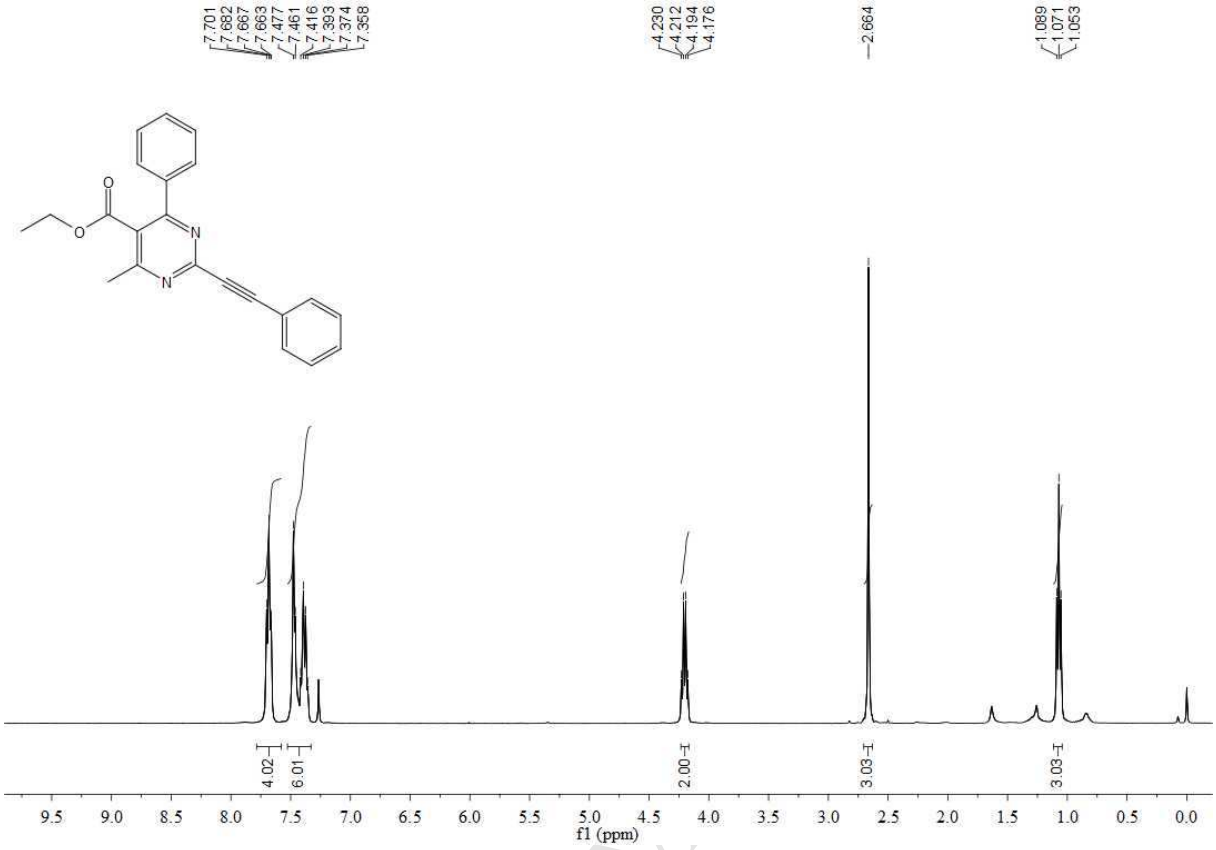


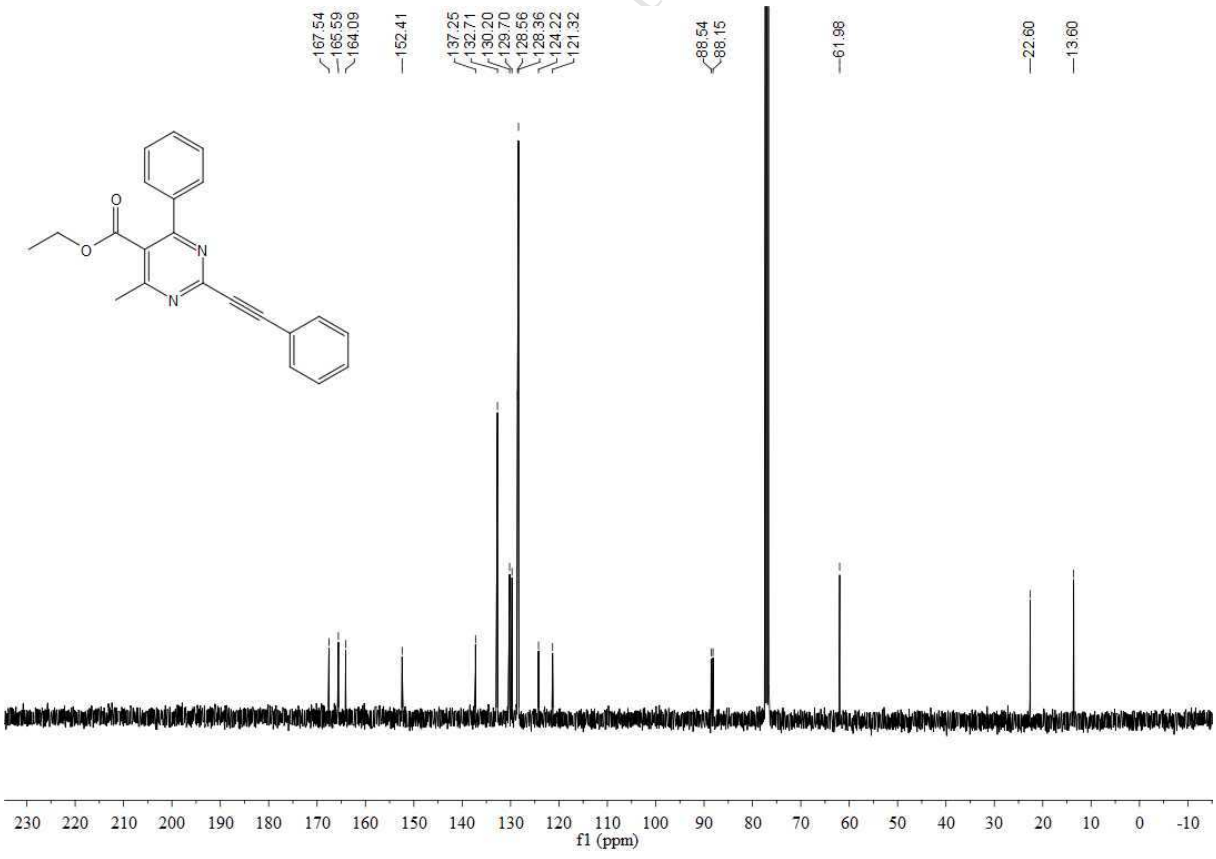
5-nitro-2-phenylpyridine (3o)



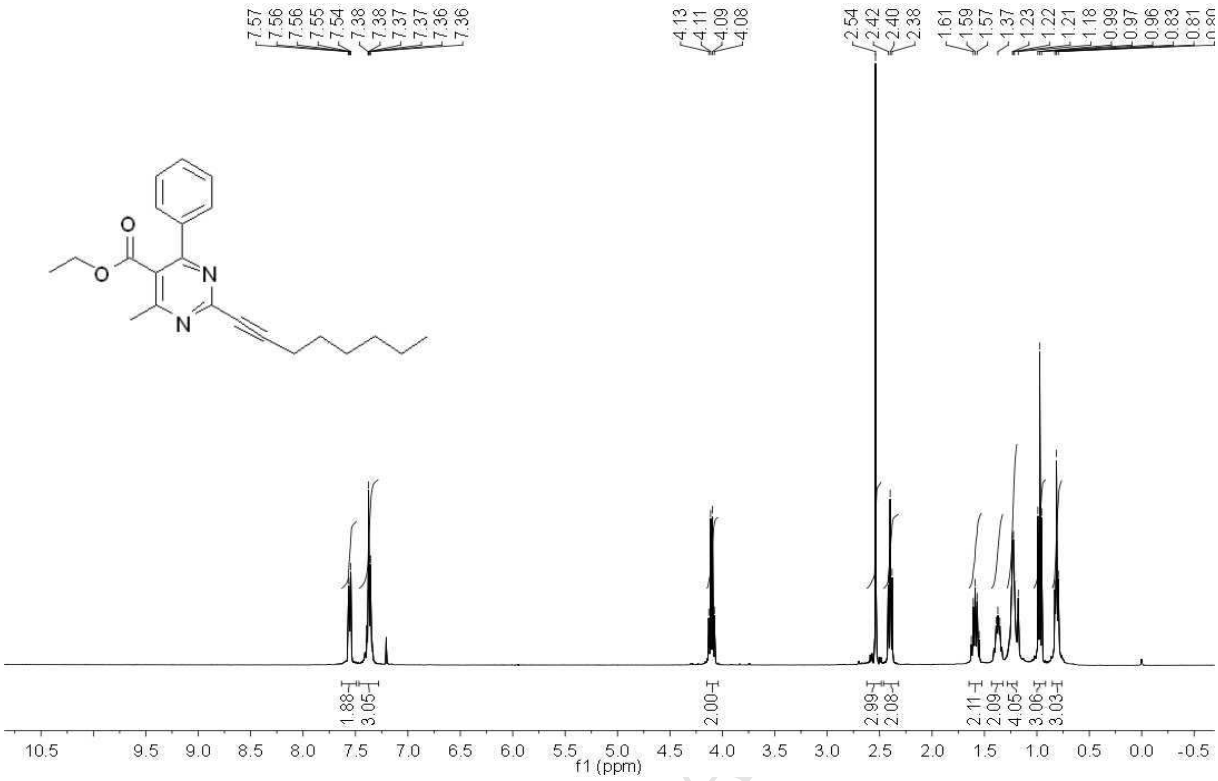


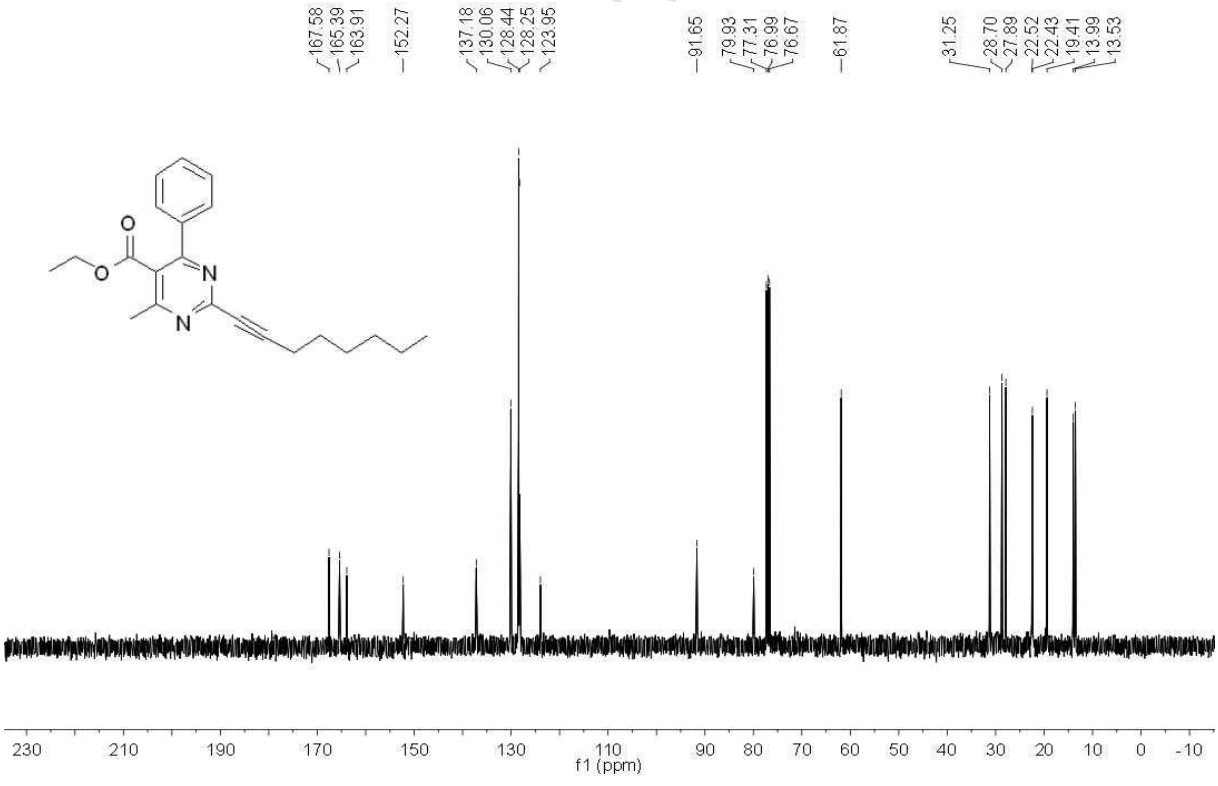
Ethyl 4-methyl-6-phenyl-2-(phenylethynyl)pyrimidine-5-carboxylate (5a)



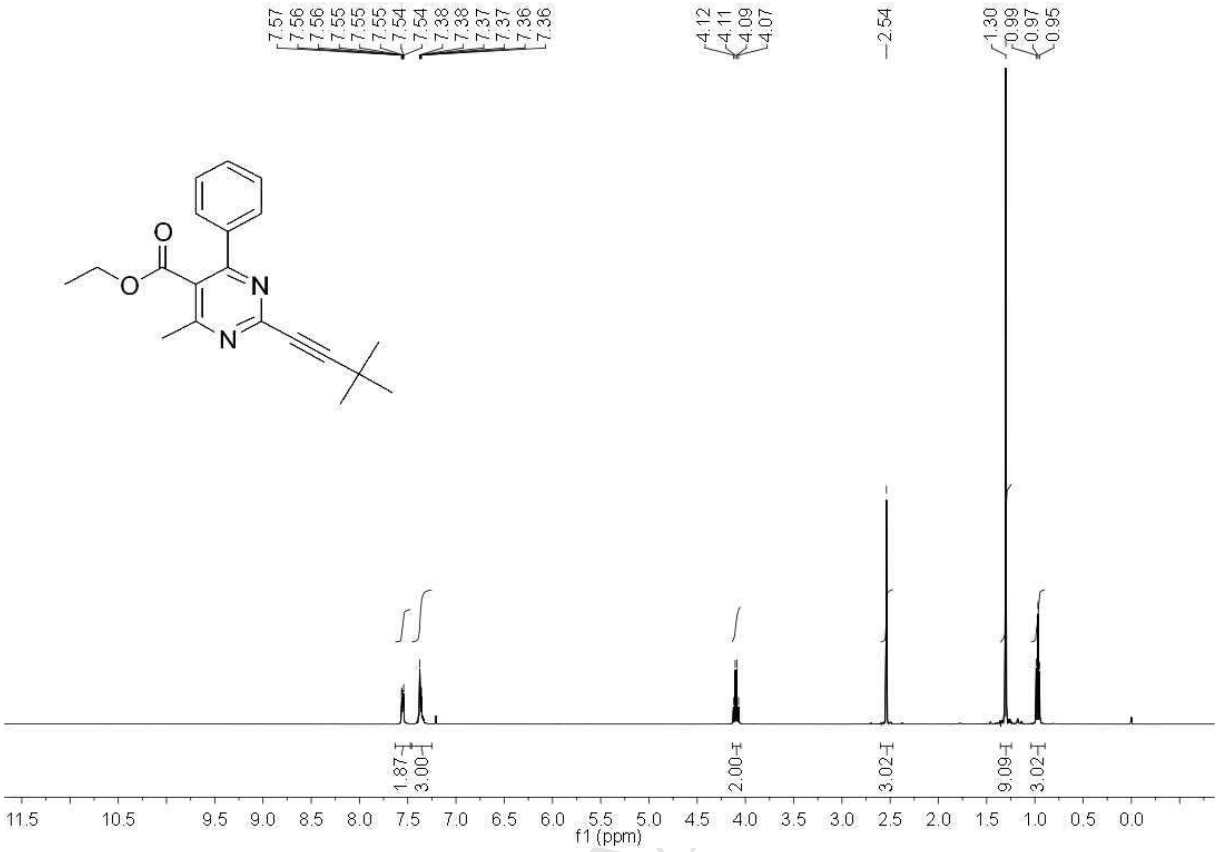


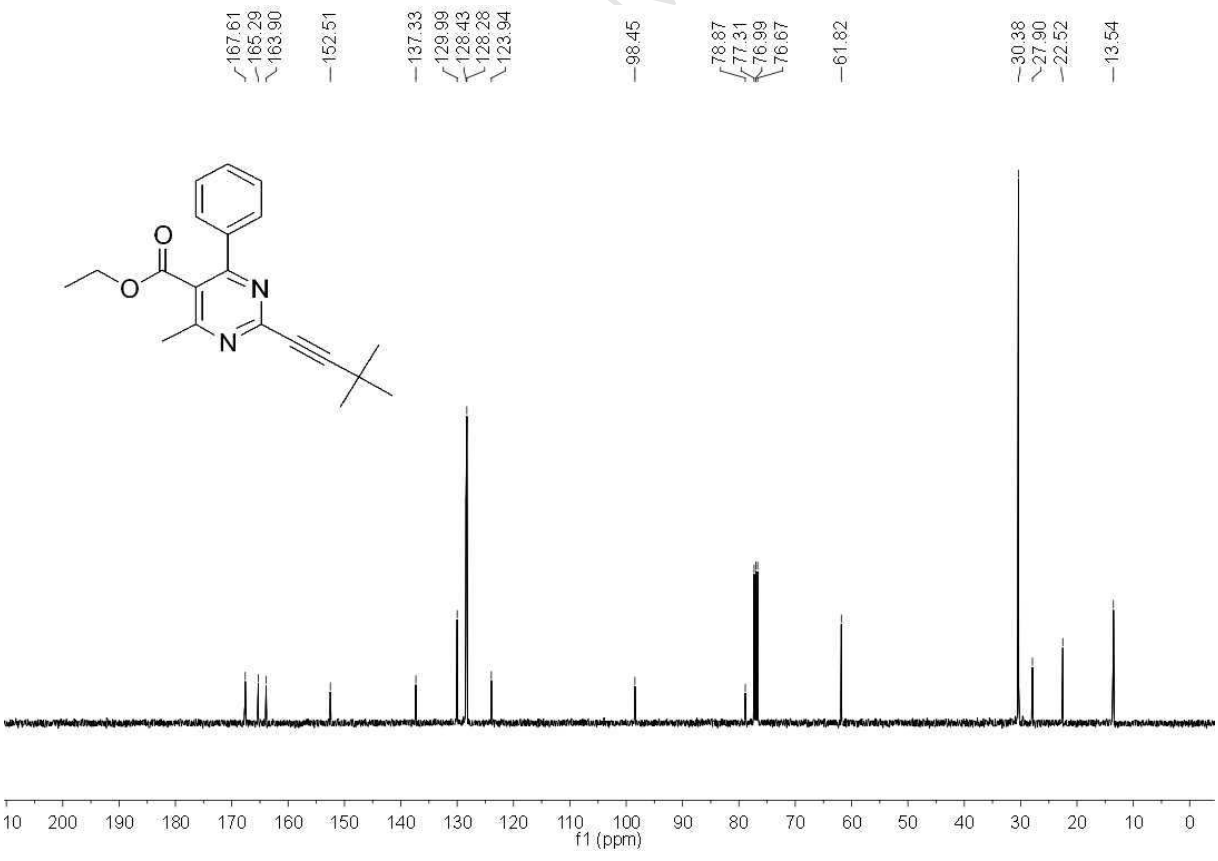
Ethyl 4-Methyl-2-(oct-1-ynyl)-6-phenylpyrimidine-5-carboxylate (5b)



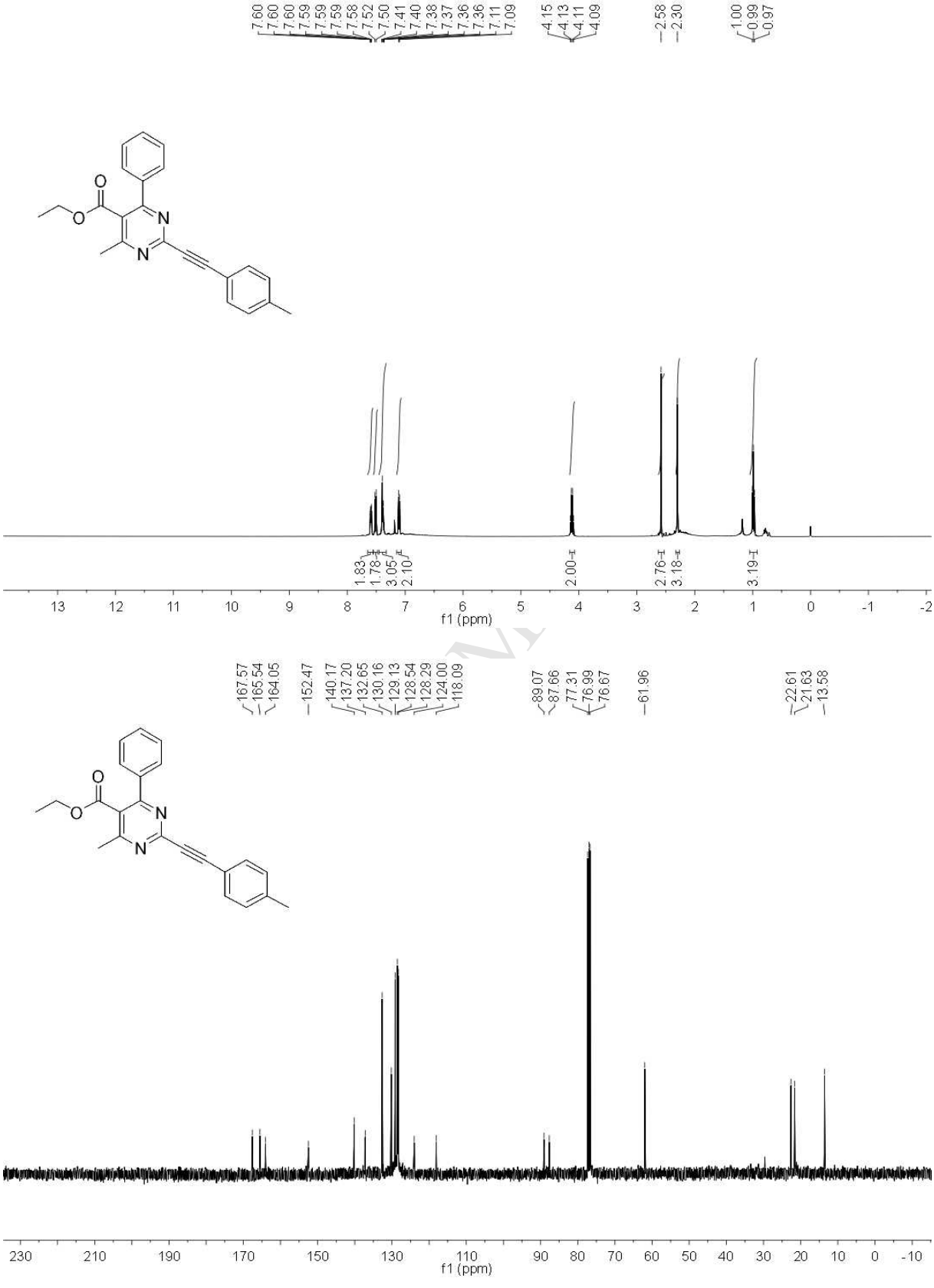


Ethyl 2-(3,3-Dimethylbut-1-ynyl)-4-methyl-6-phenylpyrimidine-5-carboxylate (5c)

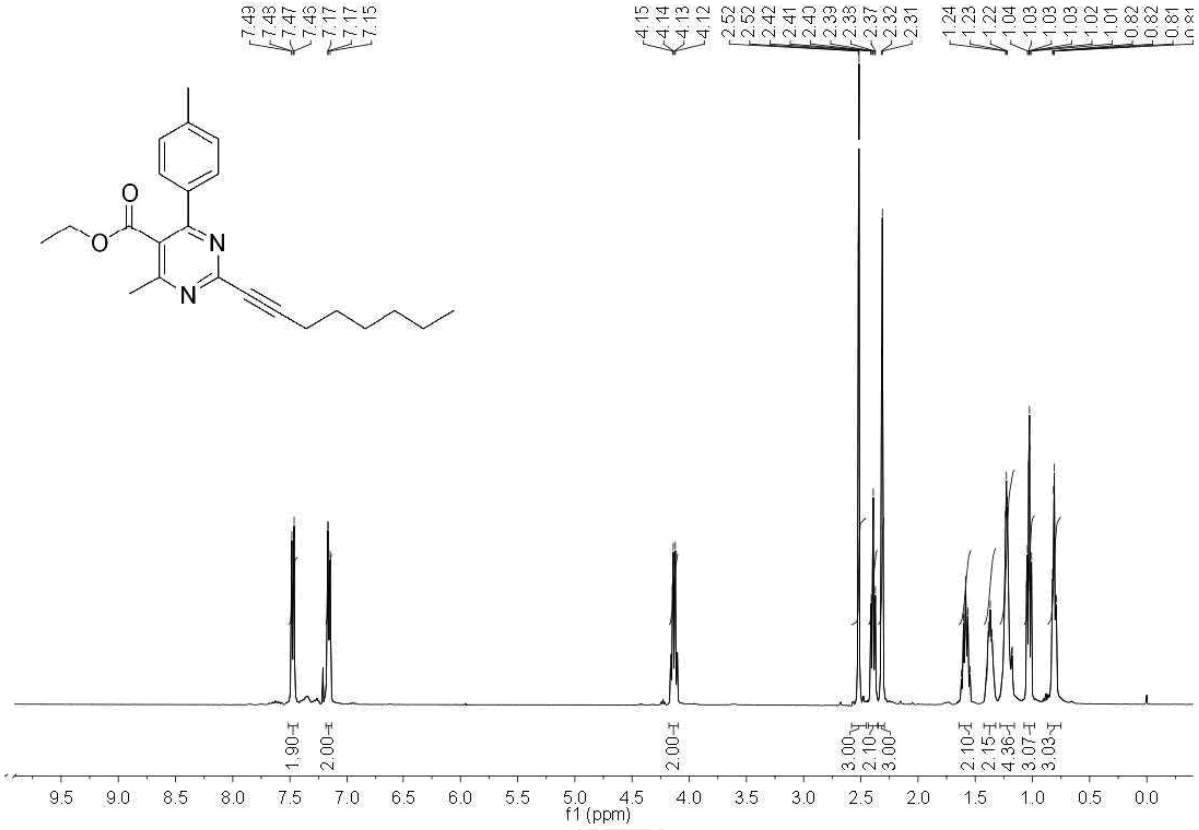


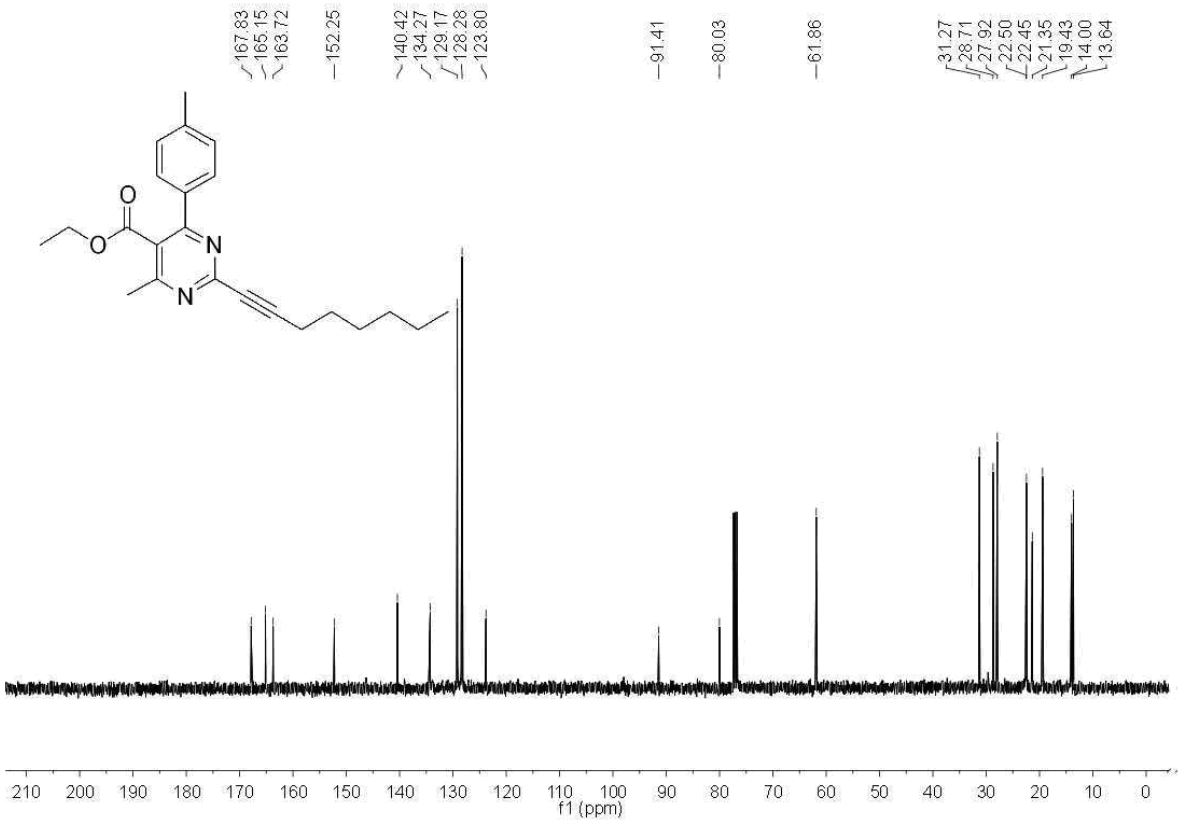


Ethyl 4-Methyl-6-phenyl-2-(p-tolylethynyl)pyrimidine-5-carboxylate (5d)

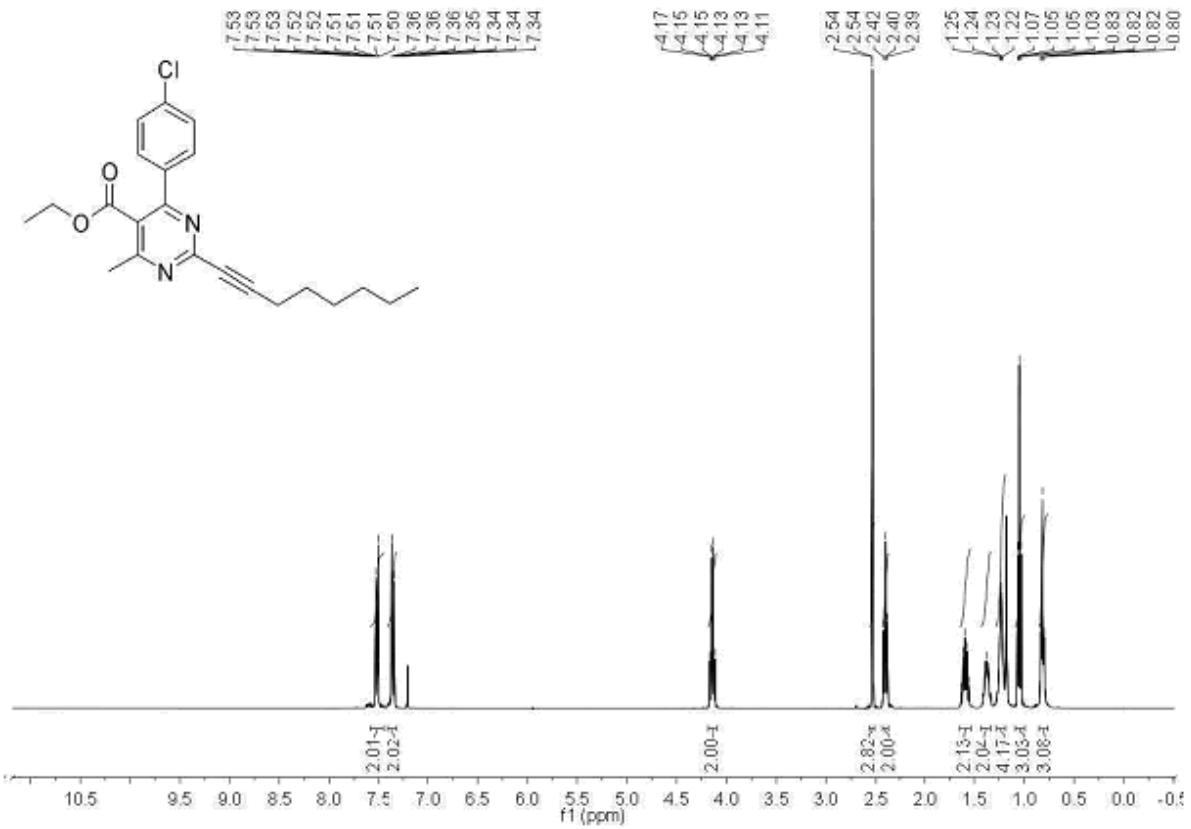


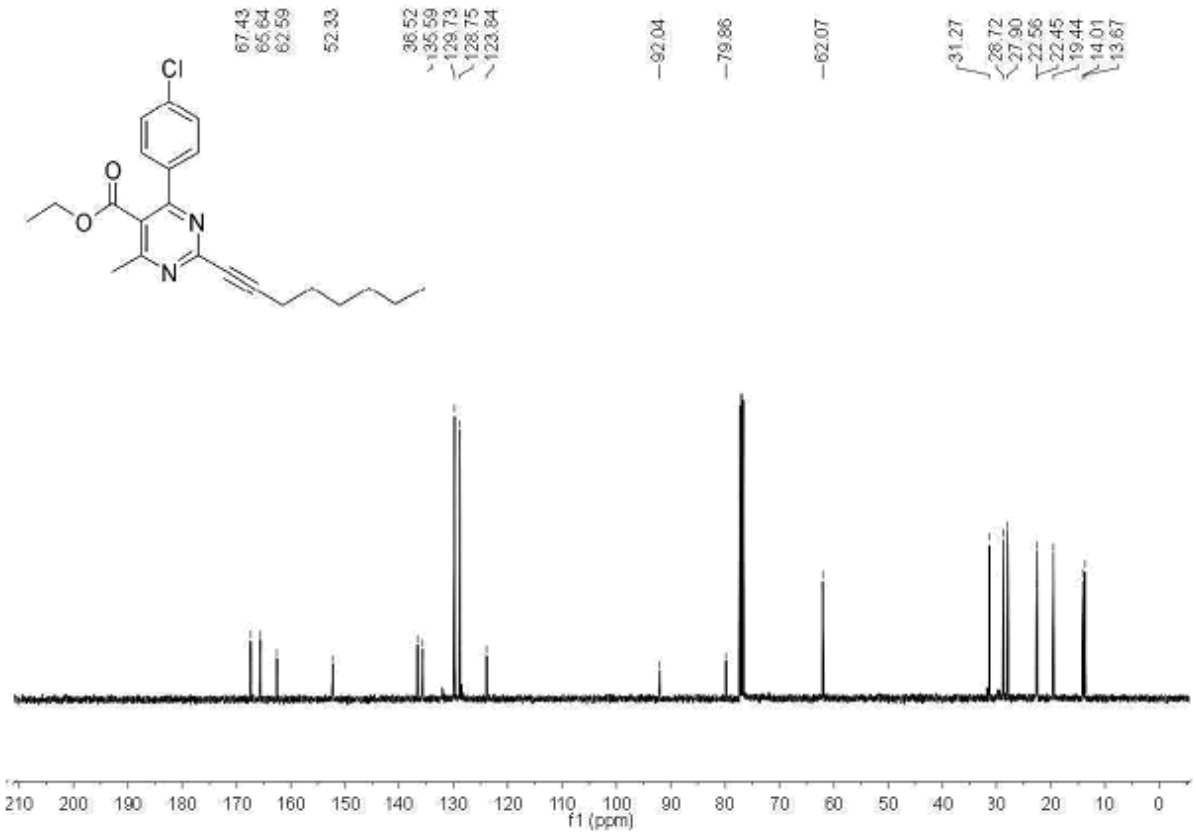
Ethyl 4-Methyl-2-(oct-1-ynyl)-6-p-tolylpyrimidine-5-carboxylate (5e)



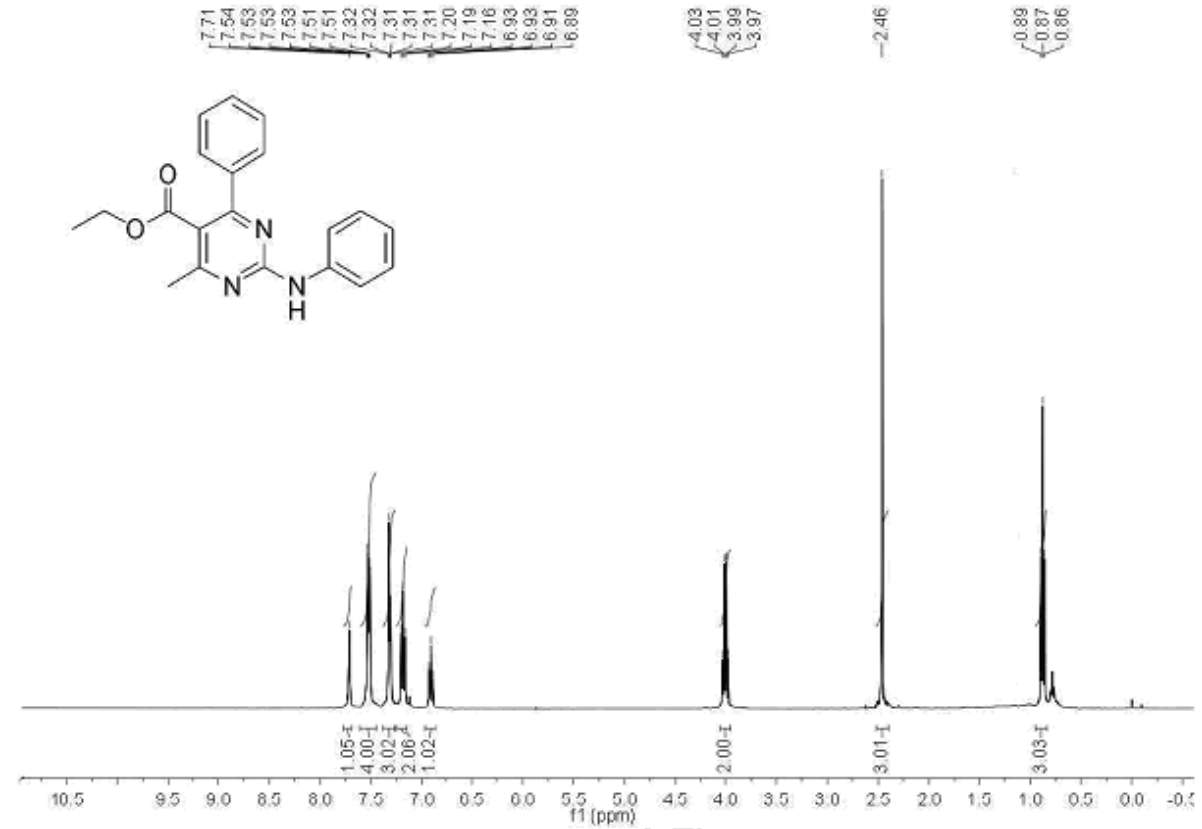


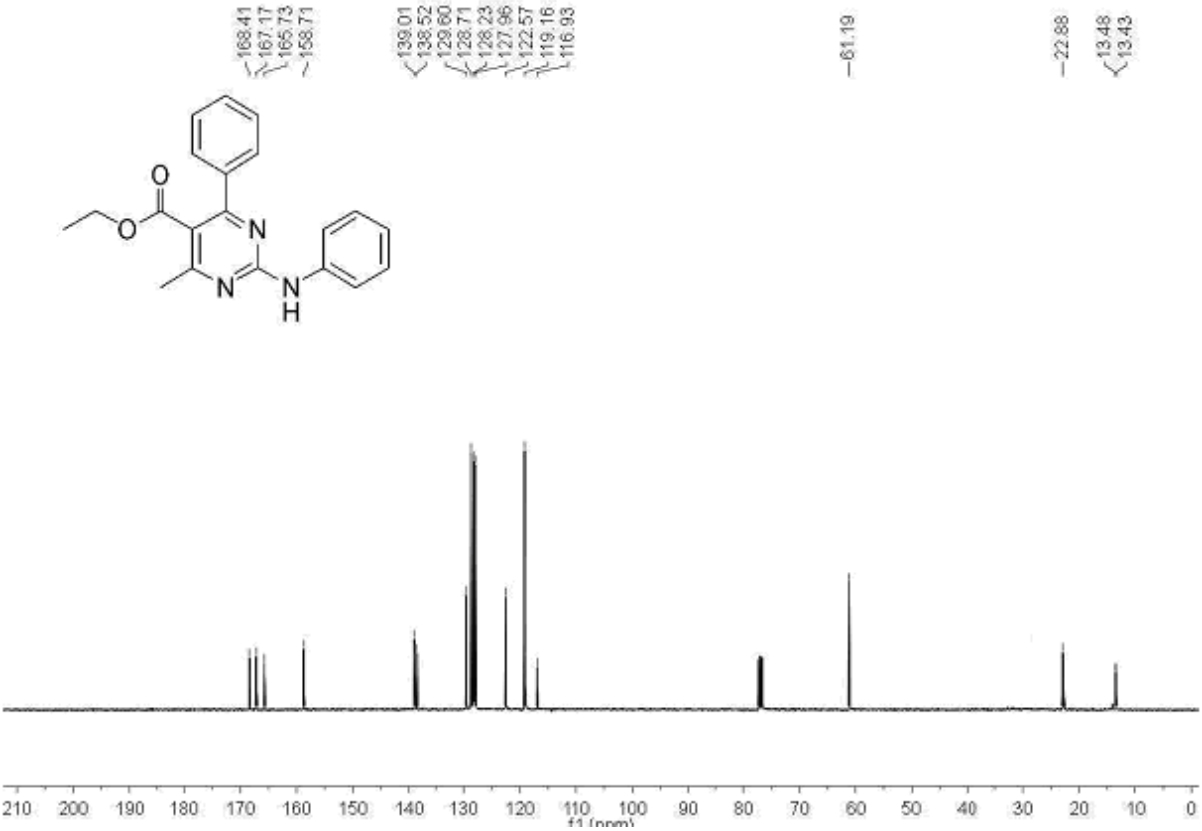
Ethyl 4-(4-Chlorophenyl)-6-methyl-2-(oct-1-ynyl)pyrimidine-5-carboxylate (5f)



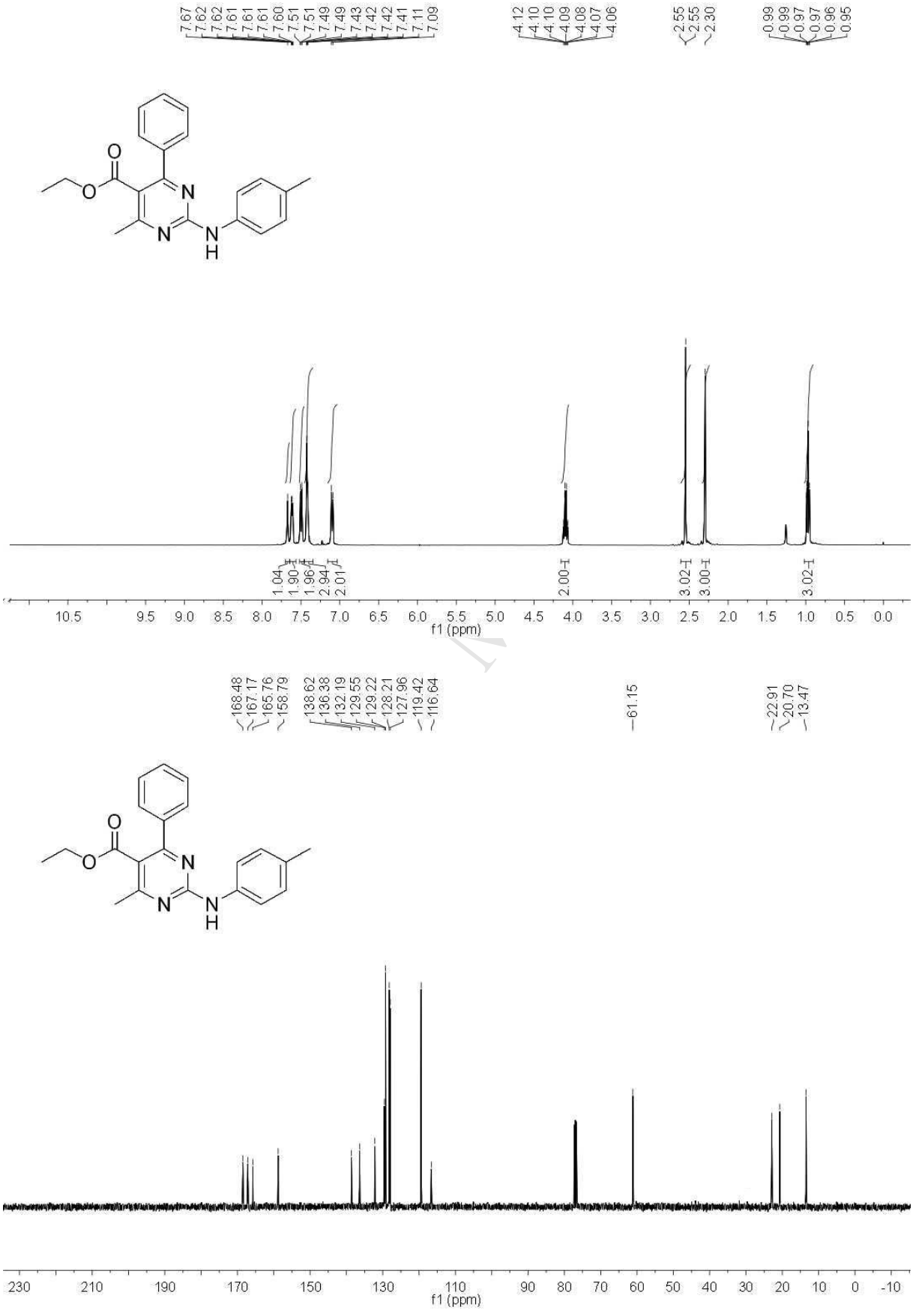


Ethyl 4-methyl-6-phenyl-2-(phenylamino)pyrimidine-5-carboxylate (7a)

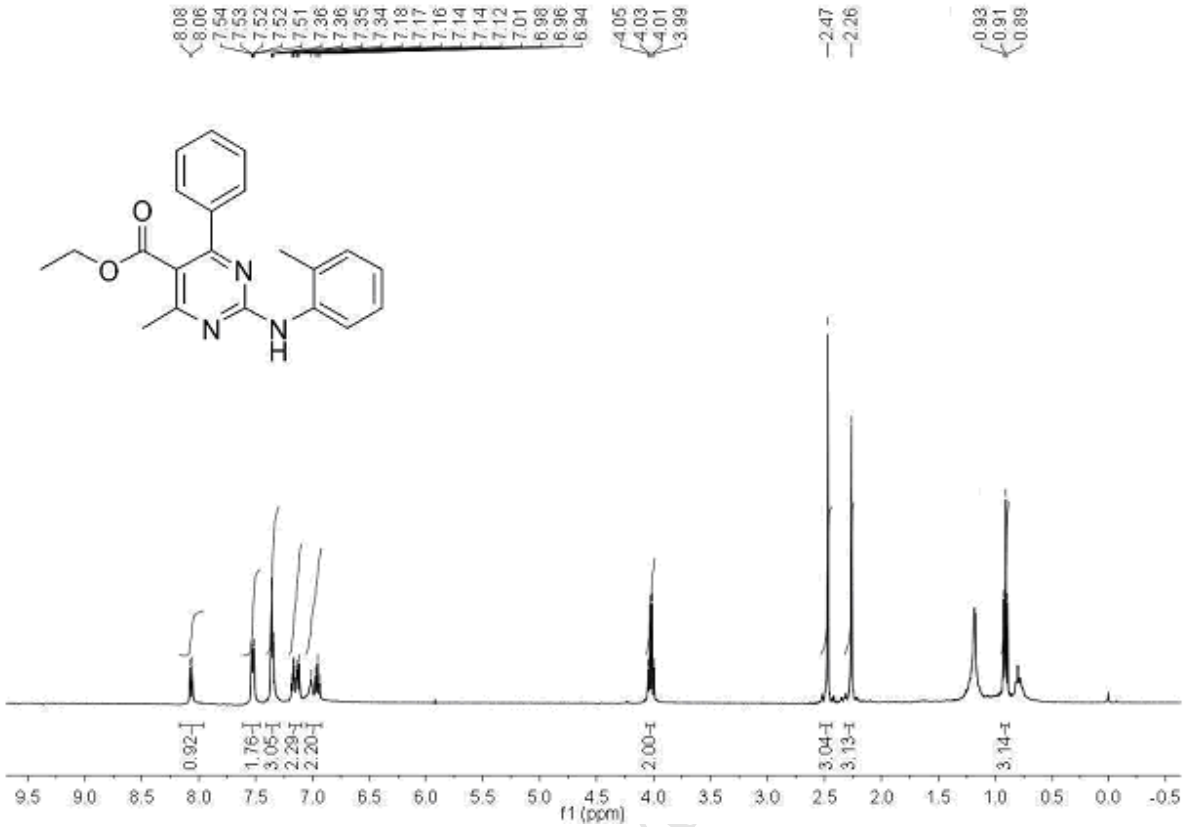


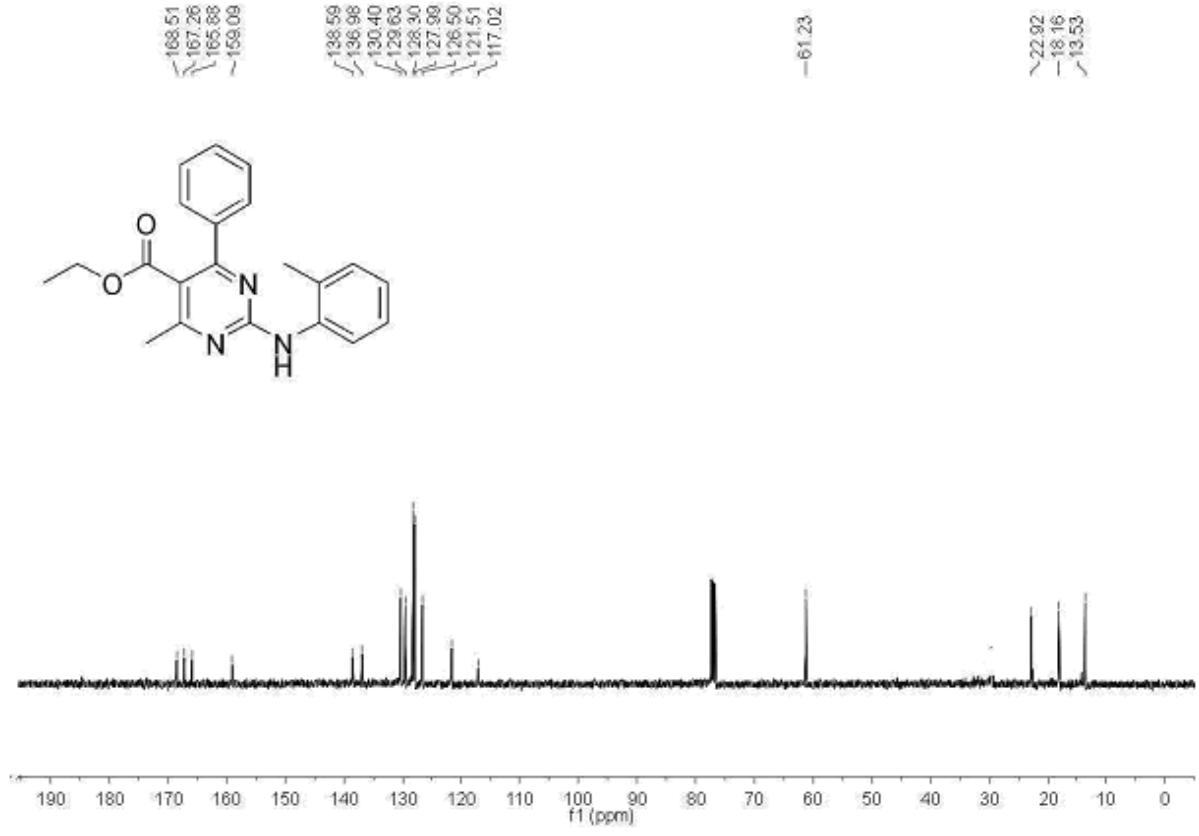


Ethyl 4-methyl-6-phenyl-2-(*p*-tolylamino)pyrimidines-5-carboxylate (7b)

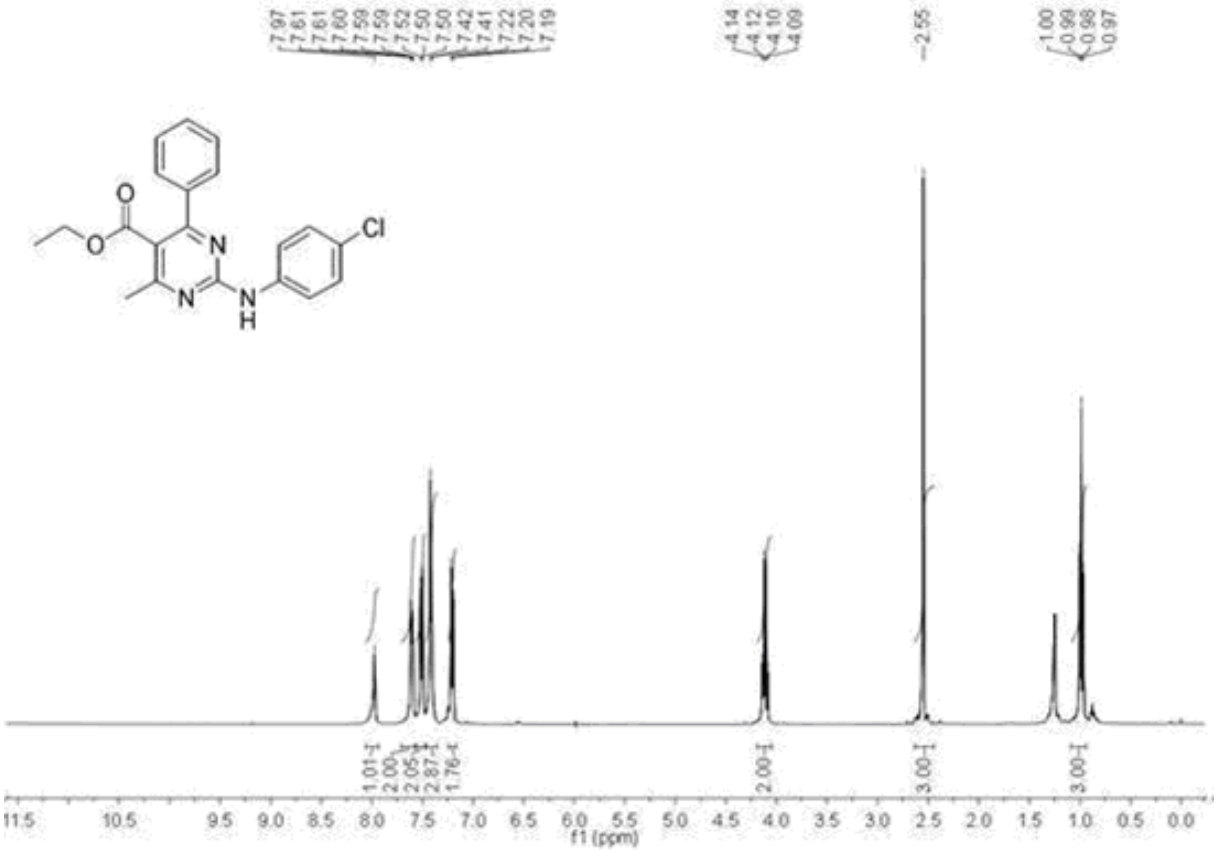


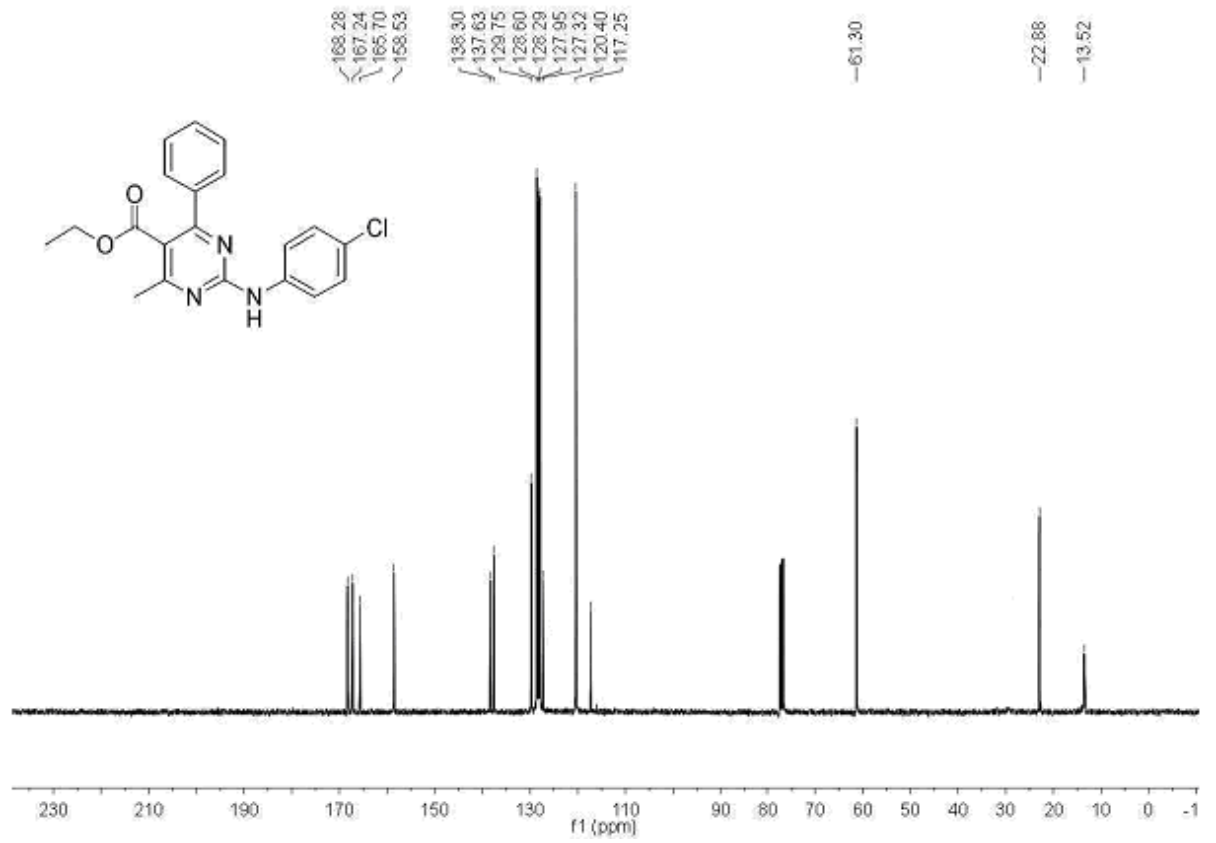
Ethyl 4-methyl-6-phenyl-2-(*o*-tolylamino)pyrimidine-5-carboxylate (7c)



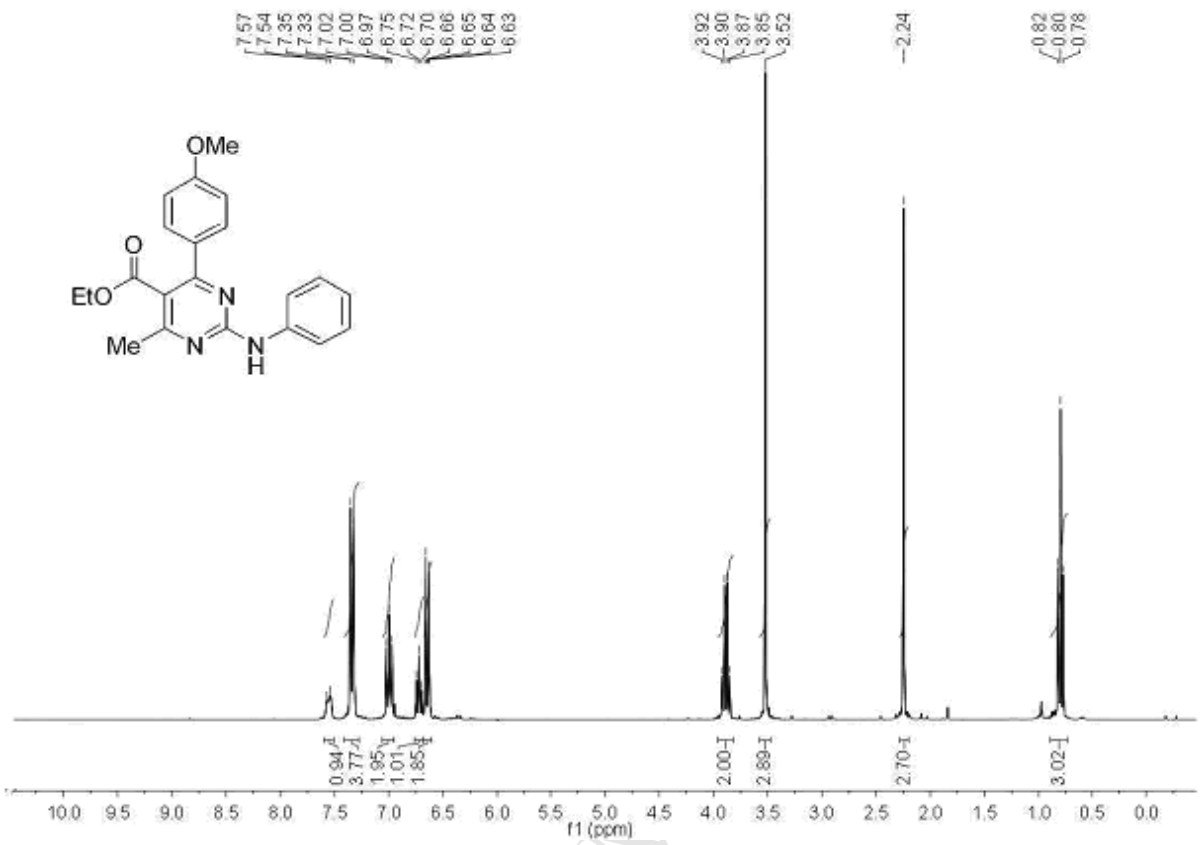


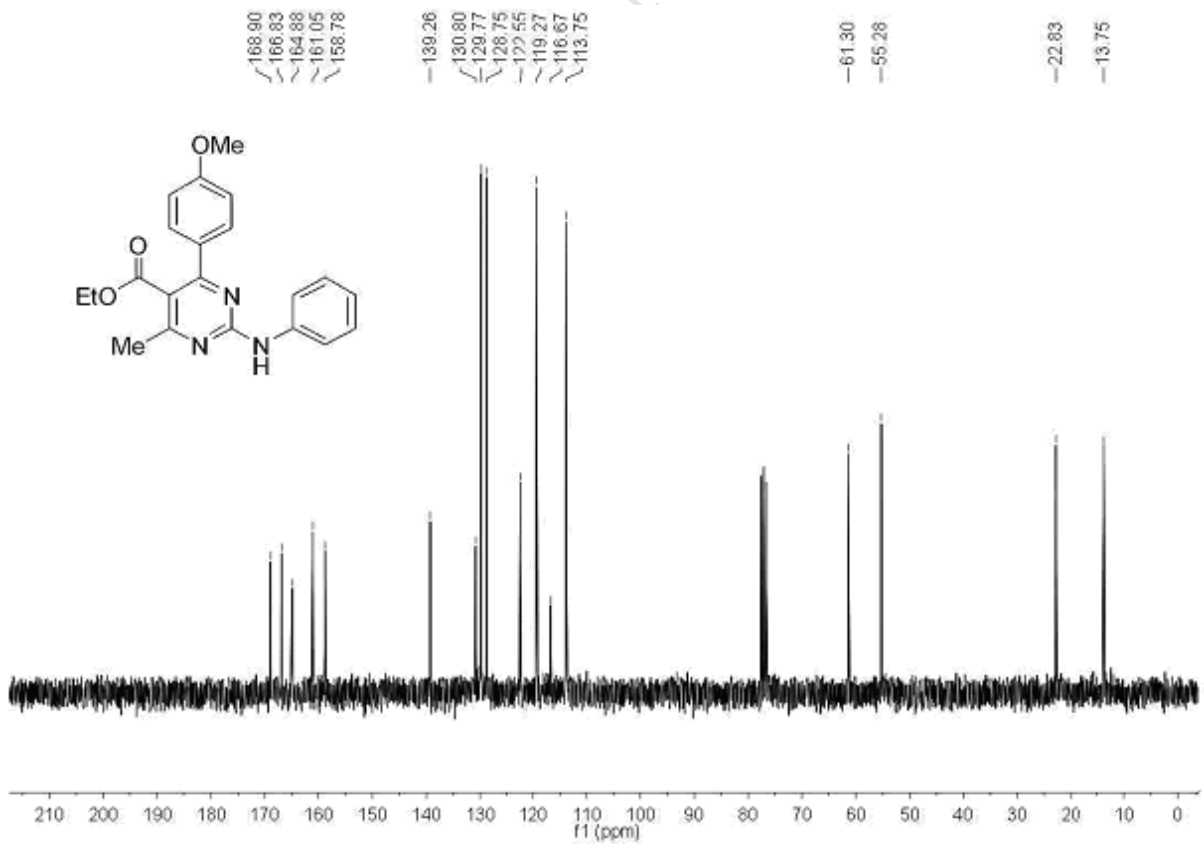
Ethyl 2-(4-chlorophenylamino)-4-methyl-6-phenylpyrimidine-5-carboxylate (7d)





Ethyl 4-(4-methoxyphenyl)-6-methyl-2-(phenylamino)pyrimidine-5-carboxylate (7e)





Ethyl 4-(4-chlorophenyl)-6-methyl-2-(phenylamino)pyrimidine-5-carboxylate (7f)