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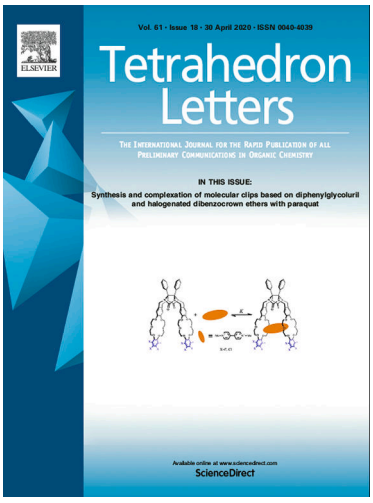

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Direct C-H arylation of quinoxalinones with aryl acylperoxides under catalyst-free condition

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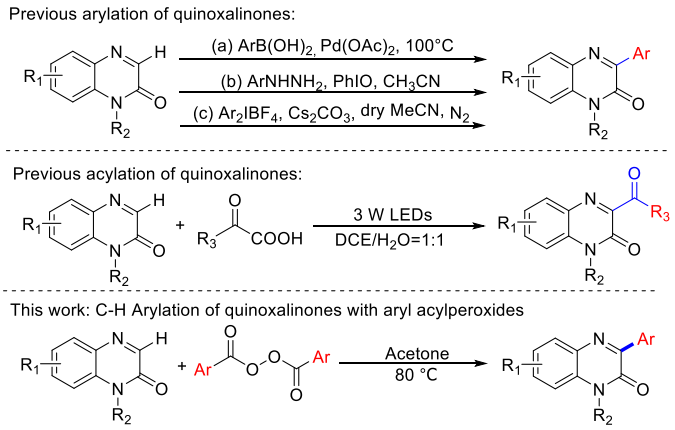
ABSTRACT

A simple and novel method for the direct C-H arylation of quinoxalinones with aryl acylperoxides has been developed. This reaction proceeded smoothly through a radical process under catalyst-free condition, giving the target products in moderate good yields. Such strategy provides a simple and green alternative for the synthesis of 3-arylquinoxalinones.

Introduction

Quinoxalinone derivatives are widely distributed in natural products, pharmaceuticals, bioactive compounds and function materials [1]. In particular, 3-functional quinoxalinones are well known for their superior biological and pharmacological effects and outstanding chemical properties, such as aldose reductase inhibitors [2], antitumor agents [3], stearoyl coenzyme A desaturases [4] and semiconductors [5]. Therefore, the synthesis of 3-functional quinoxalinones has received more extensive attention. The traditional method to access 3-substituted quinoxalinones is the cyclization of 1, 2-diaminobenzene with 1, 2-dicarbonyls and its derivatives [6]. However, such transformations often require high temperature and harsh reaction conditions. Direct C3-H functionalization of quinoxalinones has subsequently emerged as a useful tool for the construction of such compounds. So far, a series of cross-coupling reactions including C-C coupling [7], C-O coupling [8], C-N coupling [9], C-CF_3 coupling [10], C-S coupling [11], C-P coupling [12] have been realized using quinoxalinones and the corresponding partners as starting materials. Among them, the construction of C3-C bond of quinoxalinones with arylating reagents is particularly important due to their widely application in new drug research and discovery. In 2013, Alami and co-workers realized C3-arylation of quinoxalinones using arylboronic acids as arylating reagent (Scheme 1a) [13]. Despite the wide range of substrates and good yields, notable palladium catalyst was inevitably used, increasing synthetic cost. Besides, Lee successfully synthesized 3-arylquinoxalinones using arylhydrazines arylating reagents in the presence of strong oxidant PhIO (Scheme 1b) [14]. The same year, Zhang reported direct C-H arylation of quinoxalinones with diaryliodonium salts in the presence of Cs_2CO_3 under N_2 atmosphere (Scheme 1c) [15]. Although various arylating reagents have been created in these reactions for the construction of the construction of C3-C bond of quinoxalinones, complicated preparation process still limited their application.

Very recently, He and co-works reported a green and environmentally friendly decarboxylative acylation of quinoxalinones without any metal, photocatalyst or oxidant [16]. Such transformation encouraged us to consider using aryl carboxylic acid derivatives as starting materials to achieve C-H



Scheme 1. The C3-H functionalization of quinoxalinones.

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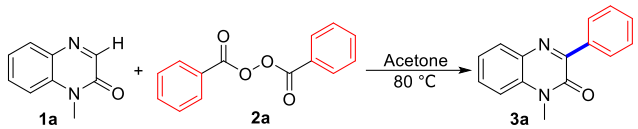
Table 1. Optimization of reaction conditions.

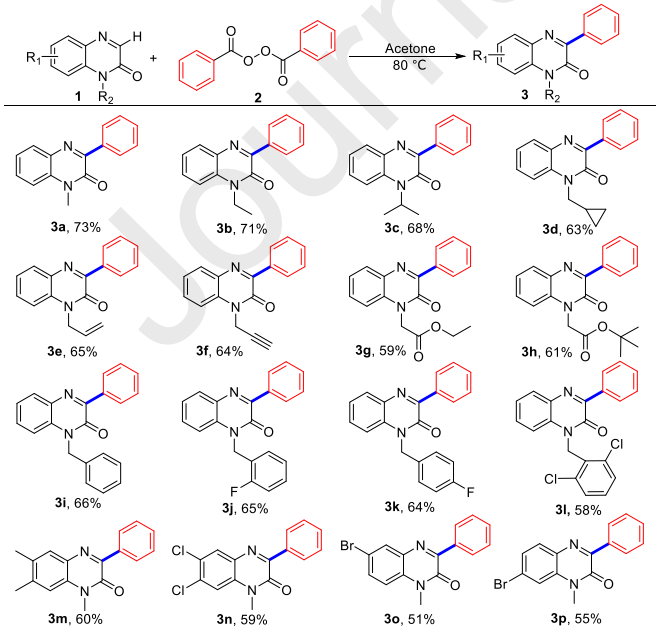


Entry	Temp. (°C)	Solvent	2a (x)	Yield (%)[b]
1	80	DCE	2	60
2	80	CH_3CH_2OH	2	18
3	80	MeCN	2	23
4	80	Acetone	2	72
5	80	THF	2	32
6	80	H_2O	2	trace
7	80	Acetone/H_2O = 1:1	2	66
8	100	Acetone	2	71
9	60	Acetone	2	55
10	80	Acetone	1.5	73
11	80	Acetone	1	51
12[c]	80	Acetone	1.5	42
13[d]	80	Acetone	1.5	67
14[e]	80	Acetone	1.5	72
15[f]	80	Acetone	1.5	70

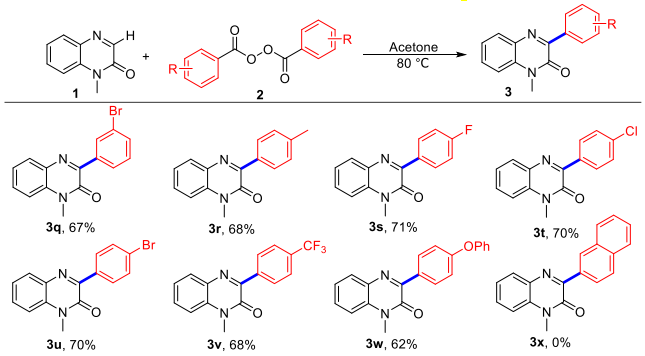
[a] Reaction conditions: **1a** (0.2 mmol), **2a** (x equiv.), solvent (2.0 mL), 12 h. [b] Isolated yields. [c] The reaction was performed for 6 h. [d] The reaction was performed for 24 h. [e] The reaction was performed under N_2 atmosphere. [f] The reaction was performed under O_2 atmosphere.

arylation of quinoxalinones. Aryl acylperoxides are commonly used as radical initiators in polymerization based on their decomposition to aryl radical under the condition of heat or visible light [17]. Besides, aryl acylperoxides could be easily synthesized from the readily available aryl carboxylic acids [18].

Table 2. Substrate scope of quinoxalinones. [a,b]



[a] Reaction conditions: **1** (0.2 mmol), **2a** (1.5 equiv), acetone (2.0 mL), 80 °C, 12 h. [b] Isolated yields.



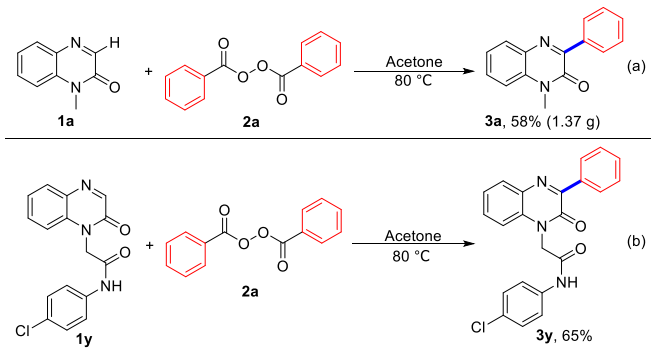
[a] Reaction conditions: **1** (0.2 mmol), **2a** (1.5 equiv), acetone (2.0 mL), 80 °C, 12 h. [b] Isolated yields.

Herein, we demonstrated a strategy for the direct C-H arylation of quinoxalinones using aryl acylperoxides as arylating reagent under catalyst-free condition, providing a simple and green alternative for the synthesis of 3-arylquinoxalinones. To the best of our knowledge, such methodology has never been reported yet.

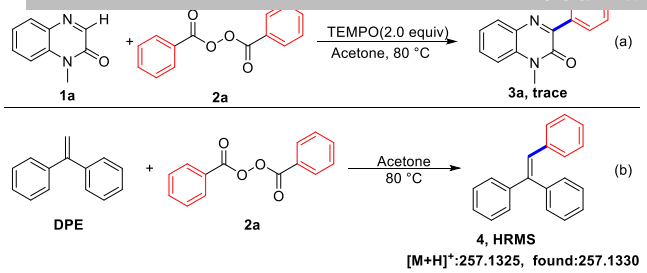
Results and discussion

In the beginning, we chose quinoxalinone (**1a**) and dibenzoyl peroxide (BPO) (**2a**) as starting substrates to screen the reaction condition. Target product (**3a**) was obtained in 60% yield when the reaction was performed in DCE at 80 °C for 12 hours (Table 1, entry 1). Subsequently, various solvents including CH_3CH_2OH, MeCN, acetone, THF, H_2O and mixture of acetone and H_2O were studied (Table 1, entries 2-7), and the product yield was increased to 72% when acetone was used as solvent (Table 1, entry 4). The influence of temperature on the reaction yield was then investigated. The reaction yield was lowered no matter that the temperature was increased (100 °C) or decreased (60 °C, Table 1, entries 8-9). The amount of BPO was also affected the reaction yield, and the highest yield can be obtiand when 1.5 equivalents of BPO was added into the reaction system (Table 1, entries 10-11). Further studies on reaction time and atmosphere could not enhance the product yield (Table 1, entries 12-15).

Under the optimized conditions, the transformations were further carried out to investigate the substrate scope of quinoxalinones with BPO (Table 2). The quinoxalinones with *N*-substituted alkyl groups such as methyl, ethyl, isopropyl, cyclopropylmethyl gave the corresponding products (**3a-d**) in 63%-73% yields. It was worth mentioning that the alkenyl, alkynyl and ester groups, which can be further modified, were also compatible, providing the corresponding products (**3e-h**) in 59%-65% yields. The benzyl group with electron-donating or electron-withdrawing groups can undergo the reaction smoothly,



Scheme 2. Method application.

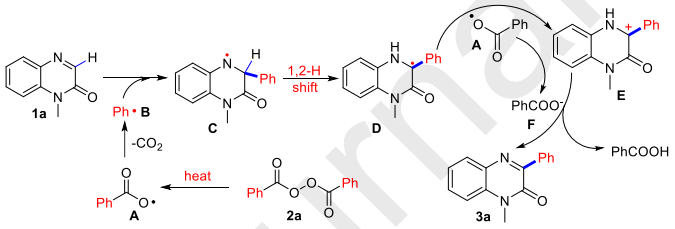


Scheme 3. Control experiments.

yielding the products (**3i-l**) in 58-66% yields. In addition, the quinoxalinones bearing methyl, chloro and bromo on benzene ring could also be transformed into the corresponding products in moderate yields (**3m**-**3p**). From the above experimental results, it can be seen that the reaction has good functional group tolerance for quinoxalinones. Subsequently, the substrate scope of aryl acyl peroxide derivatives was studied (Table 3). The product yields were acceptable by employing aryl acyl peroxides with electron-donating or electron-withdrawing groups (**3q-w**). However, probably because of steric hindrance effect, the corresponding product (**3x)** is not obtained when using naphthalene containing acyl peroxides as arylating reagent.

In order to prove the application value of such method, the gram-scale synthesis of 3-arylquinoxalinones was carried out, the target product was obtained in 58% yield (Scheme 2a). Then, the antitumor drug **3y** can be successfully synthesized in good yield by the reaction of **1y** with peroxide **2a** [19], which implied that such method has a great potential in the preparation of some quinoxalone drug skeletons (Scheme 2b).

To find out the reasonable mechanism of this transformation, the control experiments were carried out (Scheme 3). First of all, we added 2.0 equivalents of 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) to the reaction system, the target product was not generated, which indicated that a free radical mechanism was involved in the reaction. For further verify this



Scheme 4. Plausible mechanism.

assumption, the DPE trapping reagent was used to capture free radicals, and the corresponding product **4** was successfully detected by HRMS.

Based on the above results and literatures [20], the plausible mechanism of this reaction was stated in Scheme 4. Initially, BPO (**2a**) was thermally decomposed to benzoyloxyl radicals (**A**). Among them, a part of the benzoyloxyl radicals (**A**) were converted into phenyl radicals (**B**) by releasing CO_2. Then, the phenyl radicals (**B**) attack the C3-position of quinoxalinones to produce intermediates **C**. After a 1,2-H shift and benzoyloxyl radical capture single electron and proton to produce the product **3a** with the generation of benzoic acid.

Conclusion

In conclusion, we have established a method for the direct C-H arylation of quinoxalinones with aryl acylperoxides under h of synthesizing 3-arylquinoxalinones under simple and green conditions, which improved the possibility of practical application in the later stage.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.catcom.xxx.

References

[1] (a) R. E. TenBrink, W. B. Im, V. H. Sethy, A. H. Tang, D. B. Carter, J. Med. Chem., 37 (1994), 758-768;
(b) A. Carta, S. Piras, G. Loriga, G. Paglietti, Mini-Rev. Med. Chem., 6 (2006), 1179-1200;
(c) X. Li, K. Yang, W. Li, W. Xu, Drugs Future, 31 (2006), 979−989;
(d) L. Shi, J. Zhou, J. Wu, J. Cao, Y. Shen, H. Zhou, X. Li, Bioorg. Med. Chem., 24 (2016), 1840-1852.

[2] X. Qin, X. Hao, H. Han, S. Zhu, Y. Yang, B. Wu, S. Hussain, S. Parveen, C. Jing, B. Ma, C. Zhu, J. Med. Chem., 58 (2015), 1254-1267.

[3] S. A. M. El-Hawash, N. S. Habib, M. A. Kassem, Arch. Pharm., 339 (2006), 564-571.

[4] D. O. Koltun, E. Q. Parkhill, N. I. Vasilevich, A. I. Glushkov, T. M. Zilbershtein, A. V. Ivanov, A. G. Cole, I. Henderson, N. A. Zautke, S. A. Brunn, N. Mollova, K. Leung, J. W. Chisholm, J. Zablocki, Bioorg. Med. Chem. Lett., 2009, 19, 2048-2052.

[5] J. Quinn, C. Guo, L. Ko, B. Sun, Y. He, Y. Li, RSC Adv., 6 (2016), 22043-22051.

[6] Z. Xu, A. Y. Shaw, J. Dietrich, A. P. Cappelli, G. Nichol, C. Hulme, Mol. Diversity, 16 (2012), 73-79.

[7] (a) A. Carrër, J.-D. Brion, M. Alami, S. Messaoudi, Adv. Synth. Catal., 356 (2014), 3821;
(b) B. Ramesh, C. R. Reddy, G. R. Kumar, B. V. S. Reddy, Tetrahedron Lett., 59 (2018), 628-631;
(c) L. Yang, P. Gao, X.-H. Duan, Y.-R. Gu, L.-N. Guo, Org. Lett., 20 (2018), 1034-1037;
(d) H. Zhang, J. Xu, M. Zhou, J. Zhao, P. Zhang, W. Li, Org. Biomol. Chem., 17 (2019), 10201-10208;
(e) Z. Wei, S. Qi, Y. Xu, H. Liu, J. Wu, H. Li, C. Xia, G. Duan, Adv. Synth. Catal., 361 (2019), 5490-5498.

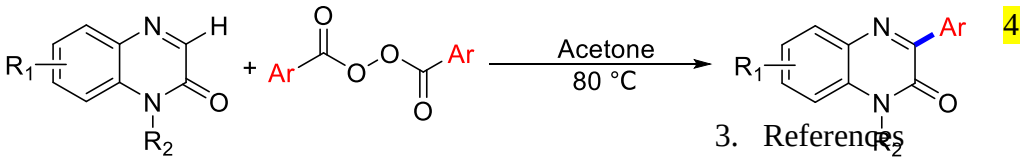
[8] (a) J. Zhou, P. Zhou, T. Zhao, Q. Ren and J. Li, Adv. Synth. Catal., 361 (2019), 5371;
(b) J. Xu, H. Yang, H. Cai, H. Bao, W. Li, P. Zhang, Org. Lett., 21 (2019) , 4698-4702.

[9] (a) G. Abhishek, S. D. Mahesh, J. Nidhi, J. Org. Chem., 82 (2017), 4784-4792;
(b) W. Wei, L. Wang, P. Bao, Y. Shao, H. Yue, D. Yang, X. Yang, X. Zhao, H. Wang, Org. Lett., 20 (2018), 7125-7130.

[10] (a) G. Hong, J. Yuan, J. Fu, G. Pan, Z. Wang, L. Yang, Y. Xiao, P. Mao, X. Zhang, Org. Chem. Front., 6 (2019), 1173-1182;
(b) L. Wang, Y. Zhang, F. Li, X. Hao, H.-Y. Zhang, J. Zhao, Adv. Synth. Catal., 360 (2018), 3969-3977.

[11] (a) L.-Y. Xie, Y.-L. Chen, L. Qin, Y. Wen, J.-W. Xie, J.-X. Tan, Y. Huang, Z. Cao, W.-M. He, Org. Chem. Front., 6 (2019), 3950-3955;
(b) Q.-H. Teng, Y. Yao, W.-X. Wei, H.-T. Tang, J.-R. Li, Y.-M. Pan, Green Chem., 21 (2019), 6241-6245.

[12] L.-B. Qu, ChemistrySelect, 4 (2019), 11066-11070;
(b) K.-J. Li, Y.-Y. Jiang, K. Xu, C.-C. Zeng, B.-G. Sun, Green Chem., 21 (2019), 4412-4421.
[13] A. Carrër, J.-D. Brion, S. Messaoudi, M. Alami, Org. Lett., 15 (2013), 5606-5609.
[14] S. Paul, J. H. Ha, G. E. Park, Y. R. Lee, Adv. Synth. Catal., 359 (2017), 1515-1521.
[15] K. Yin, R.-H. Zhang, Org. Lett., 19 (2017), 1530-1533.
[16] L.-Y. Xie, Y.-S. Bai, X.-Q. Xu, X. Peng, H.-S. Tang, Y. Huang, Y.-W. Lin, Z. Cao, W.-M. He, Green Chem., 22 (2020), 1720-1725.
[17] A. R. H. Ali, N. Sébastien, M. Vincent, R. Jean, Polym. Chem., 11 (2020),
[18] (a) N. Zhu, J. Zhao, H. Bao, Chem. Sci., 8 (2017), 2081-2085;
(b) X. Yao, X. Weng, K. Wang, H. Xiang, X. Zhou, Green Chem., 20 (2018), 2472-2476;
(c) V. Botla, N. Pillia, C. Malapaka, Green Chem., 21 (2019), 1735-1742.
[19] J. Yuan, S. Liu, L. Qu, Adv. Synth. Catal., 359 (2017), 4197-4207.
[20] (a) X.-H. Yao, X. Weng, K.-X. Wang, H-F. Xiang, X.-G. Zhou, Green Chem., 20 (2018), 2472-2476;
(b) C. Jin, X. Zhang, B. Sun, Z.-Y. Yan, T.-W. Xu, Synlett, 30 (2019), 1585-1591.



Direct C-H arylation of quinoxalinones with aryl acylperoxides under catalyst -free condition

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Supporting Information

Table of contents

1. Experimental section

General Information

All the chemicals were obtained commercially and used without any prior purification. All products were isolated by short chromatography on a silica gel (200-300 mesh) column using petroleum ether (60-90°C) and ethyl acetate. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Advance 500 spectrometer at ambient temperature with $CDCl_3$ or DMSO as solvent and tetramethylsilane (TMS) as the internal standard. Melting points were determined on an X-5 Data microscopic melting point apparatus. Analytical thin layer chromatography (TLC) was performed on Merk precoated TLC (silica gel 60 F254) plates. Compounds for HRMS were analyzed by positive mode electrospray ionization (ESI) using Agilent 6530 QTOF mass spectrometer.

Ge… arylquinoxalinones 3

1 (0.2 mmol), **2** (0.3 mmol) and acetone (2 mL) were added to a 15 mL pressure tube. The reaction mixture was heated at 80 °C for 12 h. Then, the mixture was cooled down to room temperature, and quenched with ethyl acetate-sodium hydrogen carbonate solution. The organic layer was dried with anhydrous $MgSO_4$ and distilled under reduced pressure. The crude product was further purified by silica gel column chromatography (PE/EA = 10:1) to afford product **3**.

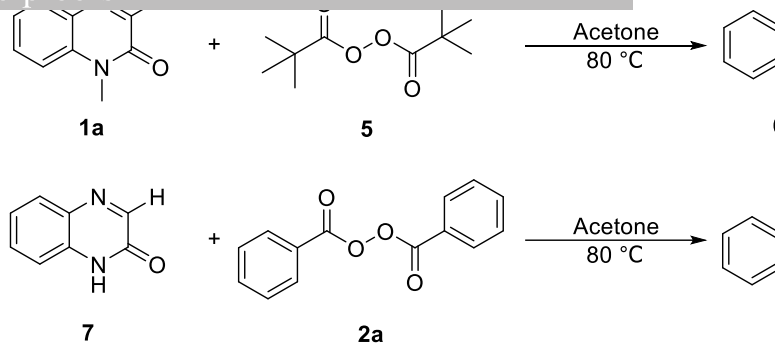
General procedure for gram-scale synthesis of product 3a

1a (10 mmol), **2a** (15 mmol) and acetone (50 mL) were added to a 200 mL round bottom flask. The reaction mixture was heated at 80 °C for 12 h. Then, the mixture was cooled down to room temperature, and quenched with ethyl acetate-sodium hydrogen carbonate solution. The organic layer was dried with anhydrous $MgSO_4$ and distilled under reduced pressure. The crude product was further purified by silica gel column chromatography (PE/EA = 10:1) to afford product **3a**.

General procedure for control experiments

(a): 1a (0.2 mmol), **2a** (0.3 mmol), TEMPO (0.4 mmol) and acetone (2 mL) were added to a 15 mL pressure tube. The reaction mixture was heated at 80 °C for 12 h. Then, the mixture was cooled down to room temperature, and product **3aa** was barely detectable.
(b): 2a (0.2 mmol), DPE (0.4 mmol) and acetone (2 mL) were added to a 15 mL pressure tube. The reaction mixture was heated at 80 °C for 12 h. Then, the corresponding product **4** was successfully detected by HRMS.

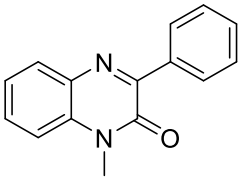
Reaction with alkyl acyl peroxides or *N*-unsubstituted quinoxalinones



(a): 1a (0.2 mmol), **5** (0.3 mmol) and acetone (2 mL) were added to a 15 mL pressure tube. The reaction mixture was heated at 80 °C for 12 h. Product **6** was barely generated.
(b): 7 (0.2 mmol), **2a** (0.3 mmol) and acetone (2 mL) were added to a 15 mL pressure tube. The reaction mixture was heated at 80 °C for 12 h. Product **8** was barely generated.
The experimental results prove that the reaction does not apply to alkyl acyl peroxides or is carried out with *N*-unsubstituted quinoxalinones.

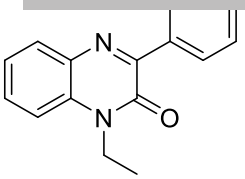
2. Characterization of the products

1-Methyl-3-phenylquinoxalin-2(1*H*)-one (3a)[1]



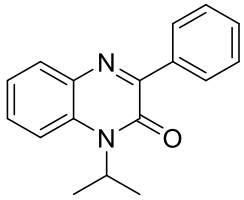
The product was obtained as yellow solid in 73% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 (dd, J = 6.6, 3.0 Hz, 2H), 7.94 (dd, J = 8.0, 1.0 Hz, 1H), 7.59 – 7.55 (m, 1H), 7.50 – 7.47 (m, 3H), 7.37 (t, J = 7.6 Hz, 1H), 7.33 (d, J = 8.4 Hz, 1H), 3.77 (s, 3H).

1-Ethyl-3-phenylquinoxalin-2(1*H*)-one (3b)[1]



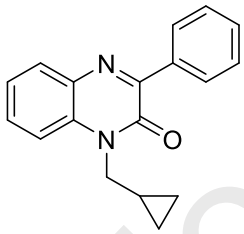
The product was obtained as yellow solid in 71% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.34 – 8.29 (m, 2H), 7.97 (d, J = 7.8 Hz, 1H), 7.57 (t, J = 7.7 Hz, 1H), 7.49 (d, J = 3.2 Hz, 3H), 7.39 – 7.34 (m, 2H), 4.40 (q, J = 7.1 Hz, 2H), 1.43 (t, J = 7.1 Hz, 3H).

1-Isopropyl-3-phenylquinoxalin-2(1*H*)-one (3c)



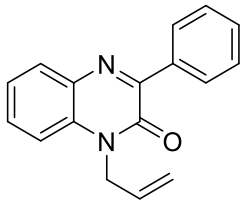
The product was obtained as yellow liquid in 68% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (d, J = 7.9 Hz, 2H), 8.07 (d, J = 8.2 Hz, 1H), 7.83 (d, J = 7.4 Hz, 1H), 7.64 (t, J = 7.6 Hz, 1H), 7.55 (t, J = 7.6 Hz, 1H), 7.53 – 7.47 (m, 3H), 5.70 – 5.63 (m, 1H), 1.48 (d, J = 6.2 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.06 (s), 146.77 (s), 140.08 (s), 138.65 (s), 136.35 (s), 130.54 (s), 129.79 (s), 129.53 (s), 128.94 (s), 128.11 (s), 126.63 (s), 126.45 (s), 69.59 (s), 21.90 (s). HRMS (ESI+): Calculated for: $C_{17}H_{16}N_2O$ $[M+H]^+$ 265.1336, Found 265.1328.

1-(Cyclopropylmethyl)-3-phenylquinoxalin-2(1*H*)-one (3d)[2]



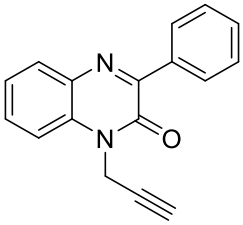
The product was obtained as yellow solid in 63% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.33 – 8.27 (m, 2H), 7.97 (d, J = 7.9 Hz, 1H), 7.57 (t, J = 7.8 Hz, 1H), 7.48 (m, 4H), 7.36 (t, J = 7.6 Hz, 1H), 4.29 (d, J = 7.0 Hz, 2H), 1.37 – 1.30 (m, 1H), 0.61 (t, J = 4.4 Hz, 2H), 0.57 (m, 2H).

1-Allyl-3-phenylquinoxalin-2(1*H*)-one (3e)[1]



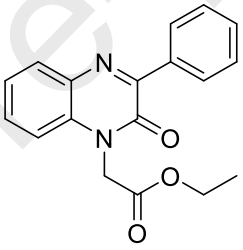
yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.33 (m, 2H), 7.96 (d, J = 8.0 Hz, 1H), 7.53 (t, J = 7.8 Hz, 1H), 7.48 (d, J = 3.0 Hz, 3H), 7.36 (t, J = 7.6 Hz, 1H), 7.31 (d, J = 8.4 Hz, 1H), 5.99 (m, 1H), 5.29 (m, 1H), 5.22 (m, 1H), 4.98 (d, J = 3.9 Hz, 2H).

3-Phenyl-1-(prop-2-yn-1-yl)quinoxalin-2(1*H*)-one (3f)[1]



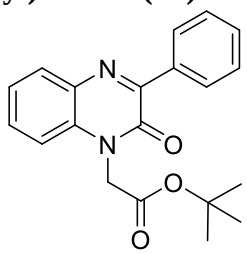
The product was obtained as yellow solid in 64% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.36 – 8.30 (m, 2H), 7.96 (d, J = 8.0 Hz, 1H), 7.60 (t, J = 7.8 Hz, 1H), 7.51 – 7.46 (m, 4H), 7.40 (t, J = 7.6 Hz, 1H), 5.12 (d, J = 1.3 Hz, 2H), 2.31 (d, J = 4.8 Hz, 1H).

Ethyl 2-(2-oxo-3-phenylquinoxalin-1(2*H*)-yl)acetate (3g)[3]



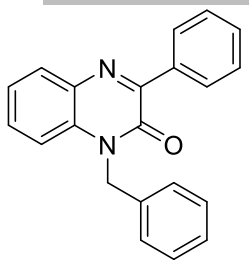
The product was obtained as yellow solid in 59% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.36 – 8.30 (m, 2H), 7.96 (d, J = 8.0 Hz, 1H), 7.52 (t, J = 7.1 Hz, 1H), 7.49 (dd, J = 8.5, 5.9 Hz, 3H), 7.36 (t, J = 7.6 Hz, 1H), 7.10 (d, J = 8.4 Hz, 1H), 5.08 (s, 2H), 4.26 (q, J = 7.1 Hz, 2H), 1.28 (t, J = 7.1 Hz, 3H).

Tert-butyl 2-(2-oxo-3-phenylquinoxalin-1(2*H*)-yl)acetate (3h)[4]



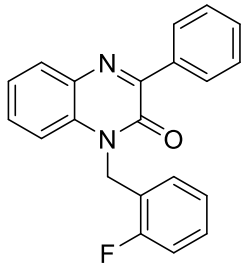
The product was obtained as yellow solid in 61% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.33 – 8.28 (m, 2H), 7.95 (d, J = 8.0 Hz, 1H), 7.52 (t, J = 7.8 Hz, 1H), 7.47 (d, J = 6.6 Hz, 3H), 7.35 (t, J = 7.6 Hz, 1H), 7.09 (d, J = 8.4 Hz, 1H), 4.99 (s, 2H), 1.47 (s, 9H).

1-E



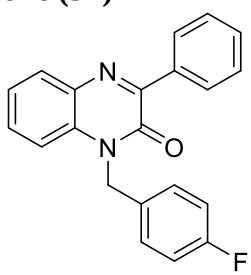
The product was obtained as yellow solid in 66% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.40 – 8.36 (m, 2H), 7.96 (d, J = 8.0 Hz, 1H), 7.52 – 7.49 (m, 3H), 7.45 (t, J = 7.1 Hz, 1H), 7.35 – 7.27 (m, 7H), 5.58 (s, 2H).

1-(2-Fluorobenzyl)-3-phenylquinoxalin-2(1*H*)-one (3j)



The product was obtained as yellow solid in 65% yield. M. P. 140–141 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.37 (m, 2H), 7.96 (d, J = 8.0 Hz, 1H), 7.48 (m, 4H), 7.33 (t, J = 7.6 Hz, 1H), 7.27 (d, J = 8.5 Hz, 1H), 7.24 (m, 1H), 7.15 – 7.06 (m, 2H), 7.01 (t, J = 7.5 Hz, 1H), 5.62 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.40 (d, J = 245.8 Hz), 154.95 (s), 154.11 (s), 135.95 (s), 133.37 (s), 132.47 (s), 130.65 (s), 130.54 (s), 130.52 (s), 129.67 (s), 129.47 (d, J = 8.2 Hz), 128.60 (d, J = 3.5 Hz), 128.16 (s), 124.73 (d, J = 3.5 Hz), 123.99 (s), 122.45 (d, J = 13.9 Hz), 115.56 (d, J = 21.4 Hz), 113.99 (s), 39.58 (d, J = 5.3 Hz). ^{19}F NMR (471 MHz, $CDCl_3$) δ -118.25 (s). HRMS (ESI+): Calculated for: $C_{21}H_{15}FN_2O$ $[M+H]^+$ 331.1241, Found 331.1244.

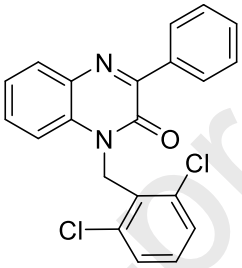
1-(4-Fluorobenzyl)-3-phenylquinoxalin-2(1*H*)-one (3k)



The product was obtained as yellow solid in 64% yield. M. P. 109–110 °C. ^{1}H NMR (500 MHz,

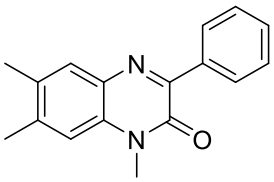
1H), 7.49 (m, 3H), 7.45 (d, J = 7.2 Hz, 1H), 7.33 (t, J = 7.6 Hz, 1H), 7.31 – 7.24 (m, 3H), 7.00 (t, J = 8.6 Hz, 2H), 5.51 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.25 (d, J = 246.4 Hz), 154.75 (s), 154.23 (s), 135.93 (s), 133.41 (s), 132.60 (s), 131.14 (d, J = 3.2 Hz), 130.73 (s), 130.52 (s), 130.37 (s), 129.65 (s), 128.89 (d, J = 8.2 Hz), 128.15 (s), 123.93 (s), 115.90 (d, J = 21.7 Hz), 114.12 (s), 45.49 (s). ^{19}F NMR (471 MHz, $CDCl_3$) δ -114.34 (s). HRMS (ESI+): Calculated for: $C_{21}H_{15}FN_2O$ $[M+H]^+$ 331.1241, Found 331.1239.

1-(2,6-Dichlorobenzyl)-3-phenylquinoxalin-2(1*H*)-one (3l)



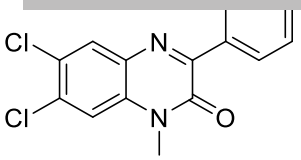
The product was obtained as yellow solid in 58% yield. M. P. 167–168 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.32 (d, J = 4.3 Hz, 2H), 7.93 (m, 1H), 7.50 (d, J = 7.7 Hz, 3H), 7.43 – 7.37 (m, 1H), 7.31 (m, 3H), 7.19 (m, 2H), 5.91 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.38 (s), 153.98 (s), 136.12 (s), 135.51 (s), 133.54 (s), 132.47 (s), 131.08 (s), 130.66 (s), 130.38 (s), 130.03 (s), 129.53 (s), 129.48 (s), 129.36 (s), 128.14 (s), 123.66 (s), 114.25 (s), 42.26 (s). HRMS (ESI+): Calculated for: $C_{21}H_{14}Cl_2N_2O$ $[M+H]^+$ 381.0556, Found 381.0550.

1,6,7-Trimethyl-3-phenylquinoxalin-2(1*H*)-one (3m)[3]



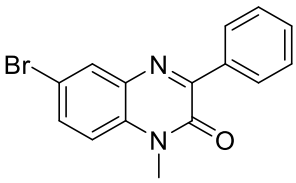
The product was obtained as yellow solid in 60% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.29 (d, J = 7.7 Hz, 2H), 7.71 (s, 1H), 7.49 – 7.44 (m, 3H), 7.09 (s, 1H), 3.74 (s, 3H), 2.43 (s, 3H), 2.36 (s, 3H).

6,7-Dichloro-1-methyl-3-phenylquinoxalin-2(1*H*)-one (3n)[3]



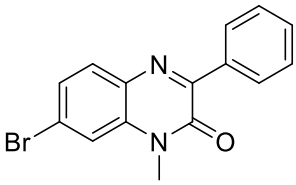
The product was obtained as yellow solid in 59% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.29 (d, J = 8.3 Hz, 2H), 7.99 (s, 1H), 7.48 (t, J = 7.9 Hz, 3H), 7.39 (s, 1H), 3.69 (s, 3H).

6-Bromo-1-methyl-3-phenylquinoxalin-2(1*H*)-one (3o)[3]



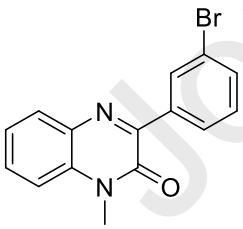
The product was obtained as yellow solid in 51% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.33 – 8.27 (m, 2H), 7.77 (d, J = 8.4 Hz, 1H), 7.50 – 7.44 (m, 5H), 3.72 (s, 3H).

7-Bromo-1-methyl-3-phenylquinoxalin-2(1*H*)-one (3p)[3]



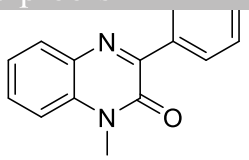
The product was obtained as yellow solid in 55% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.31 (dd, J = 7.6, 2.1 Hz, 2H), 8.09 (d, J = 2.2 Hz, 1H), 7.64 (dd, J = 8.9, 2.3 Hz, 1H), 7.49 (dd, J = 6.0, 4.7 Hz, 3H), 7.20 (d, J = 8.9 Hz, 1H), 3.74 (s, 3H).

3-(3-Bromophenyl)-1-methylquinoxalin-2(1*H*)-one (3q)[3]



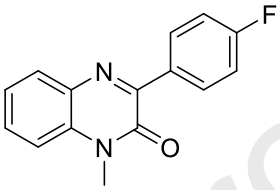
The product was obtained as yellow solid in 67% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.51 (t, J = 1.6 Hz, 1H), 8.33 (d, J = 7.9 Hz, 1H), 7.94 (d, J = 8.0 Hz, 1H), 7.59 (t, J = 8.2 Hz, 2H), 7.37 (m, 3H), 3.77 (s, 3H).

1-Methyl-3-(p-tolyl)quinoxalin-2(1*H*)-one (3r)[3]



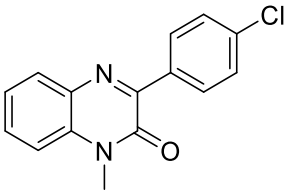
The product was obtained as yellow solid in 68% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.25 (d, J = 7.7 Hz, 2H), 7.93 (d, J = 7.8 Hz, 1H), 7.54 (t, J = 7.6 Hz, 1H), 7.37 – 7.33 (m, 1H), 7.30 (t, J = 7.9 Hz, 3H), 3.75 (s, 3H), 2.42 (s, 3H).

3-(4-Fluorophenyl)-1-methylquinoxalin-2(1*H*)-one (3s)[3]



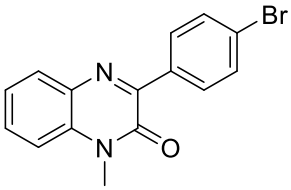
The product was obtained as yellow solid in 71% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.42 – 8.36 (m, 2H), 7.92 (d, J = 7.0 Hz, 1H), 7.57 (t, J = 7.8 Hz, 1H), 7.37 (t, J = 7.6 Hz, 1H), 7.33 (d, J = 8.4 Hz, 1H), 7.15 (t, J = 8.7 Hz, 2H), 3.76 (s, 3H). ^{19}F NMR (471 MHz, $CDCl_3$) δ -109.98 (s).

3-(4-Chlorophenyl)-1-methylquinoxalin-2(1*H*)-one (3t)[3]



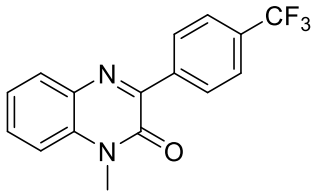
The product was obtained as yellow solid in 70% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.34 (d, J = 8.6 Hz, 2H), 7.93 (m, 1H), 7.59 (t, J = 7.1 Hz, 1H), 7.45 (d, J = 8.6 Hz, 2H), 7.38 (t, J = 7.2 Hz, 1H), 7.34 (d, J = 8.4 Hz, 1H), 3.77 (s, 3H).

3-(4-Bromophenyl)-1-methylquinoxalin-2(1*H*)-one (3u)[3]



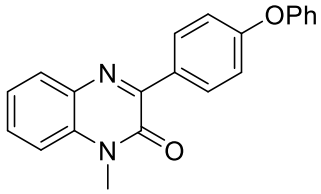
The product was obtained as yellow solid in 70% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.26 (d, J = 8.7 Hz, 2H), 7.92 (d, J = 8.0 Hz, 1H), 7.58 (m, 3H), 7.37 (t, J = 7.6 Hz, 1H), 7.32 (d, J = 8.4 Hz, 1H), 3.75 (s, 3H).

1-Methyl-3-(4-(trifluoromethyl)phenyl)quinoxalin-2(1*H*)-one (3v)[3]



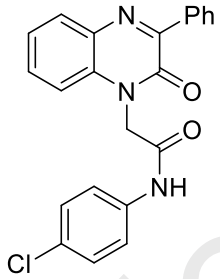
The product was obtained as yellow solid in 68% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.46 (d, J = 8.2 Hz, 2H), 7.95 (d, J = 8.0 Hz, 1H), 7.72 (d, J = 8.2 Hz, 2H), 7.60 (t, J = 7.8 Hz, 1H), 7.39 (t, J = 7.6 Hz, 1H), 7.34 (d, J = 8.4 Hz, 1H), 3.77 (s, 3H). ^{19}F NMR (471 MHz, $CDCl_3$) δ -62.80 (s).

1-Methyl-3-(4-phenoxyphenyl)quinoxalin-2(1*H*)-one (3w)[5]



The product was obtained as yellow solid in 62% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.38 (d, J = 8.8 Hz, 2H), 7.93 (d, J = 8.0 Hz, 1H), 7.55 (t, J = 7.8 Hz, 1H), 7.37 (m, 3H), 7.32 (d, J = 8.3 Hz, 1H), 7.15 (t, J = 7.4 Hz, 1H), 7.09 (d, J = 8.7 Hz, 4H), 3.76 (s, 3H).

***N*-(4-chlorophenyl)-2-(2-oxo-3-phenylquinoxalin-1(2*H*)-yl)acetamide (3y)[6]**

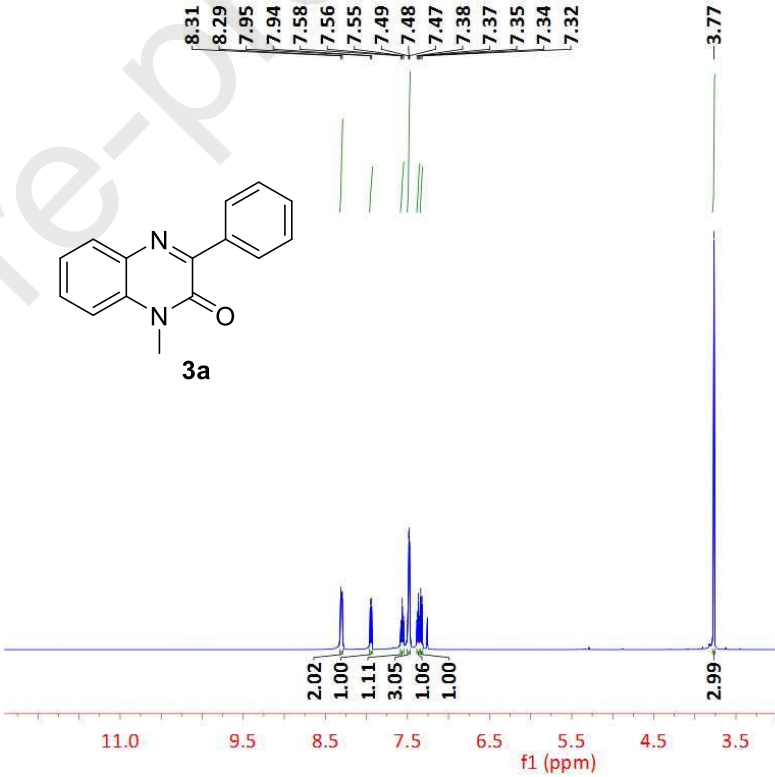


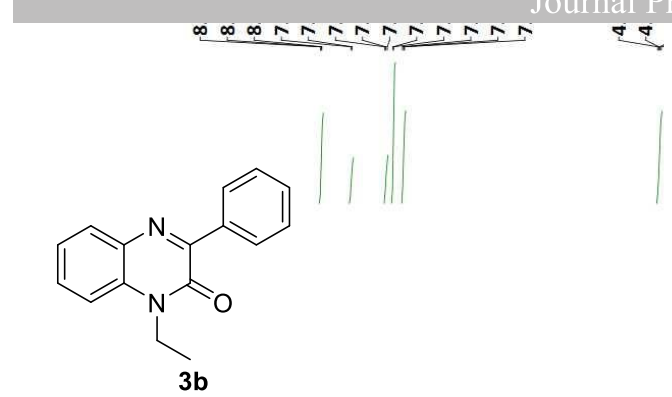
The product was obtained as yellow solid in 65% yield. ^{1}H NMR (500 MHz, DMSO) δ 10.65 (s, 1H), 8.29 – 8.26 (m, 2H), 7.94 (d, J = 7.9 Hz, 1H), 7.63 (dd, J = 8.0, 3.8 Hz, 3H), 7.58 (d, J = 7.8 Hz, 1H), 7.52 (dd, J = 7.1, 4.6 Hz, 3H), 7.43 (t, J = 7.5 Hz, 1H), 7.38 (d, J = 8.9 Hz, 2H), 5.22 (s, 2H).

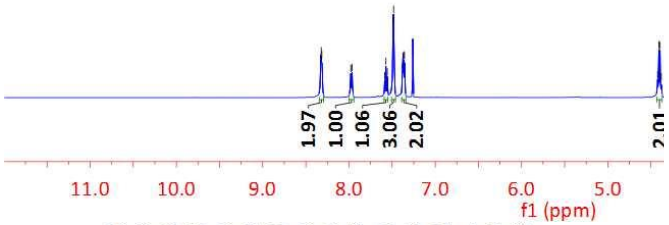
3. References

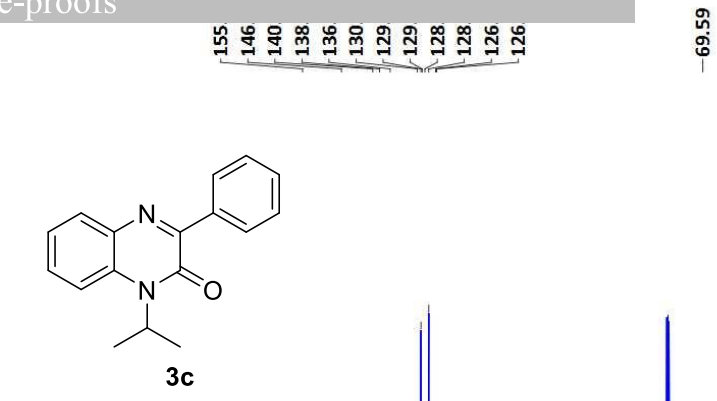
[1] B. D. Nibedita, B. Mayurakhi, B. Gakul, RSC Adv., 10 (2020), 3615–3624.
Synthesis, 45 (2013), 459–462.
[3] K. Yin, R. Zhang, Org. Lett., 19 (2017), 1530−1533.
[4] L. Wang, P. Bao, W. Liu, S. Liu, C. Hu, H. Yue, D. Yang, W. Wei, J. Org. Chem., 38 (2018), 3189-3196.
[5] B. Ramesh, C. R. Reddy, G. R. Kumar, B. V. S. Reddy, Tetrahedron Lett., 59 (2018), 628.
[6] J. Yuan, S. Liu, L. Qu, Adv. Synth. Catal., 359 (2017), 4197–4207.

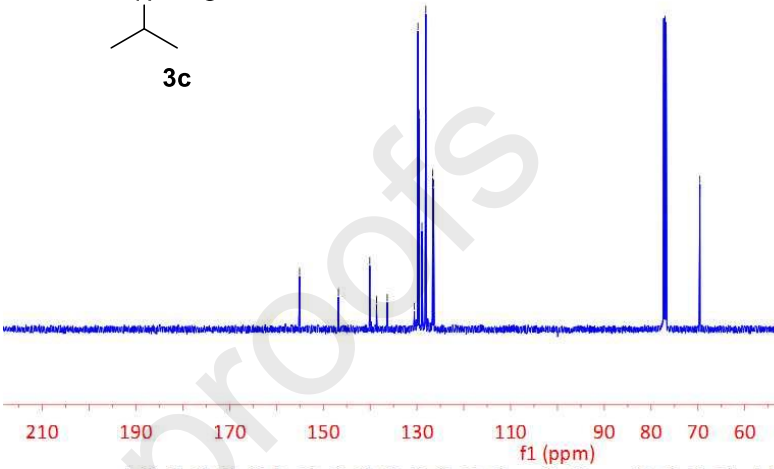
4. Copies of NMR

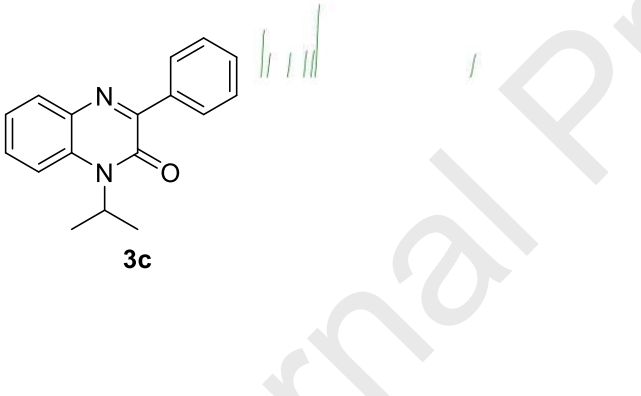


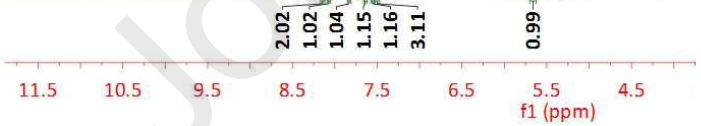


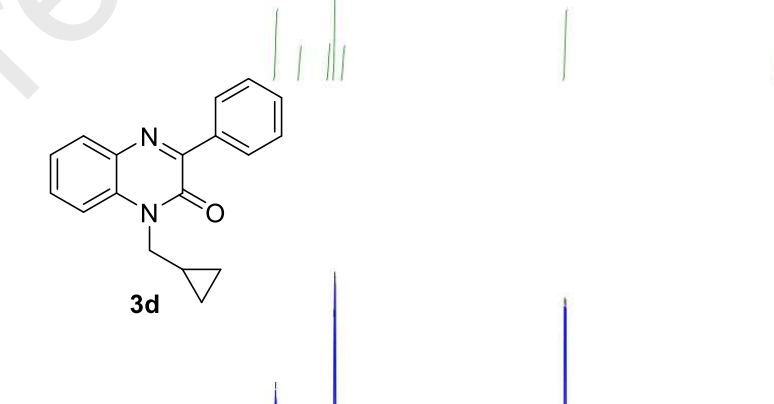


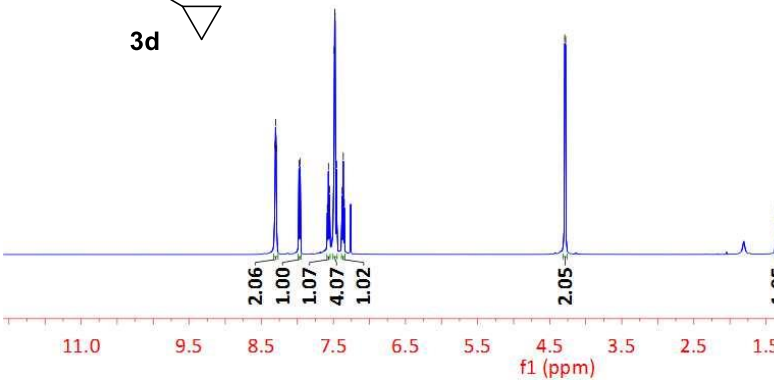


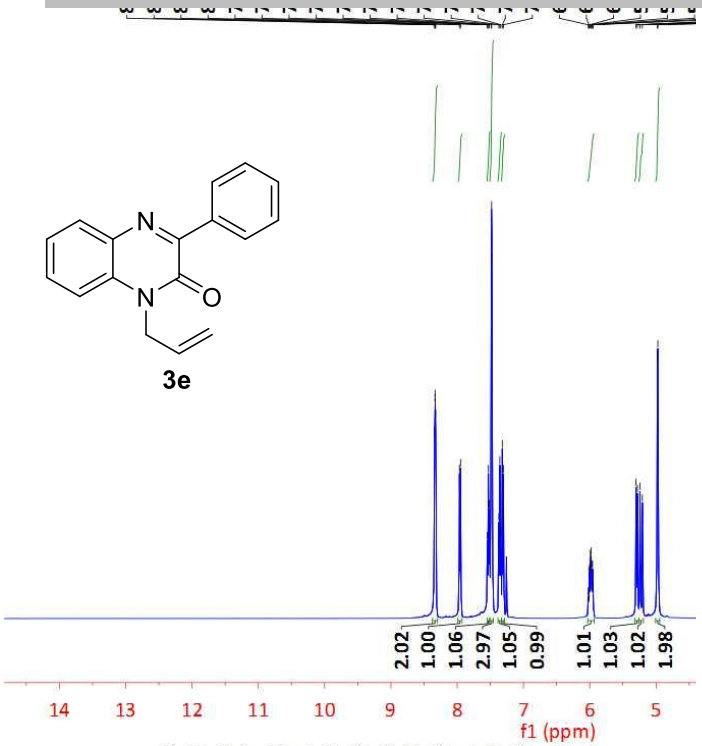


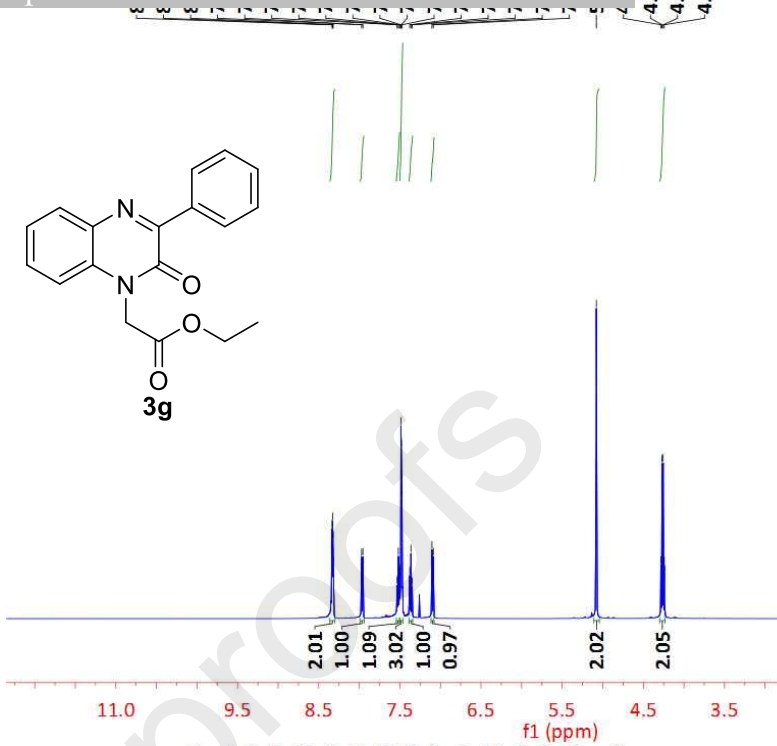


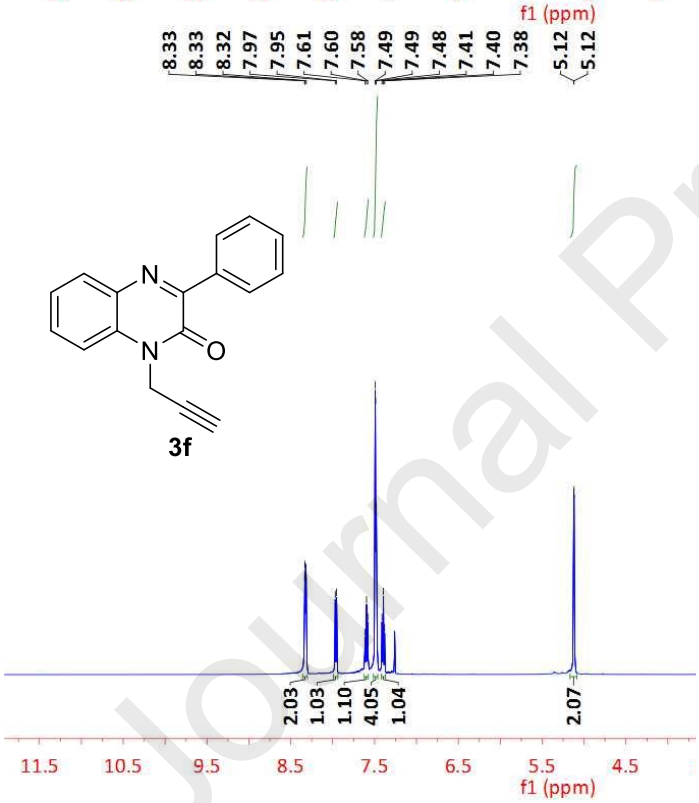


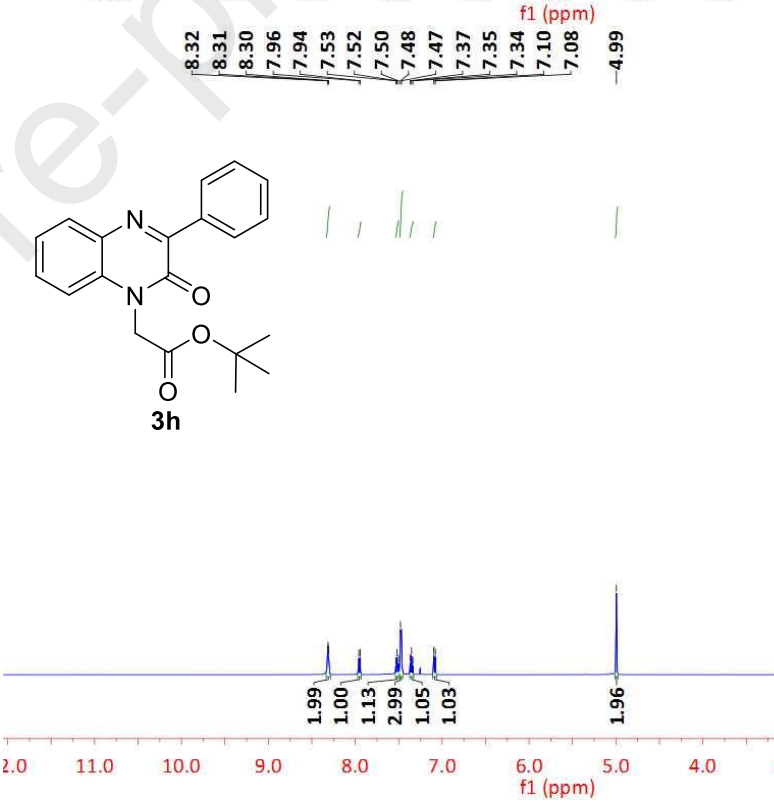


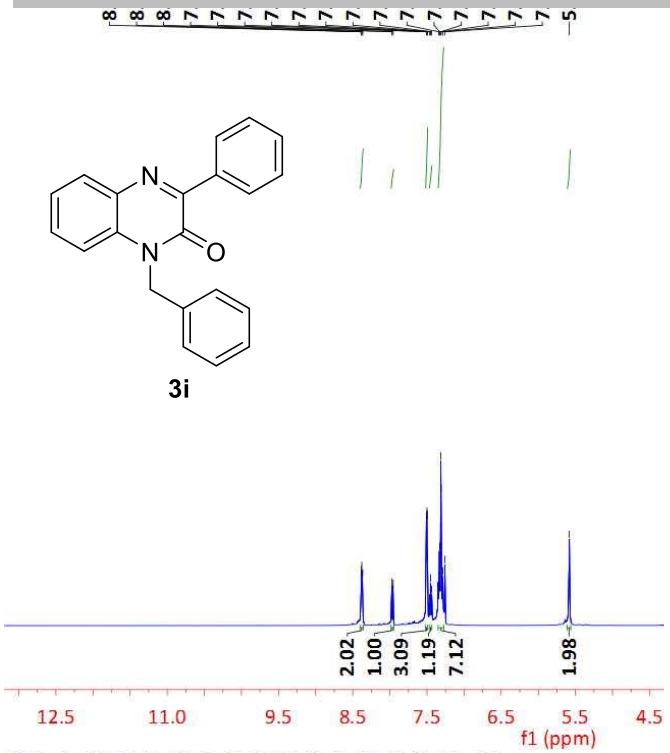


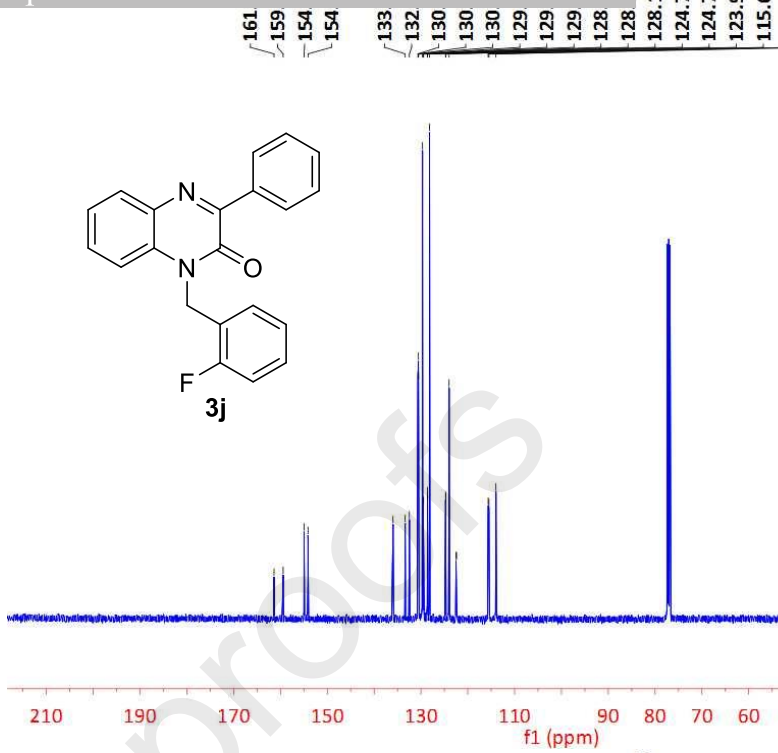


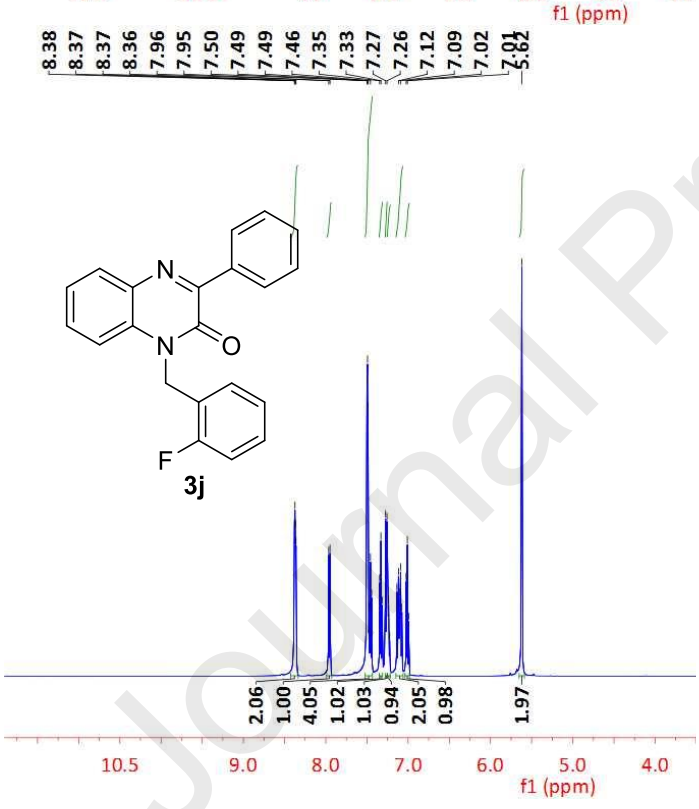


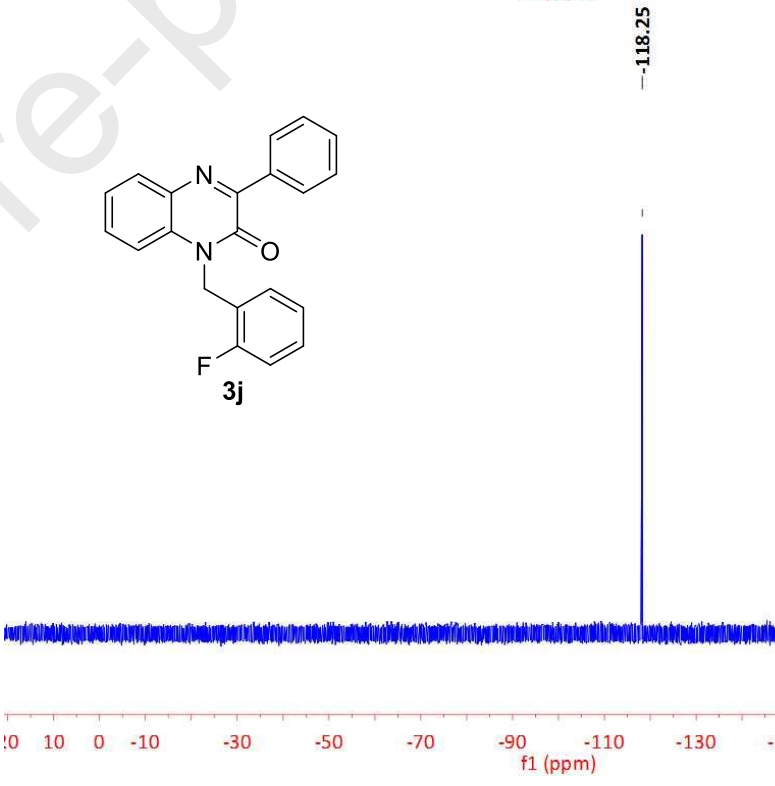


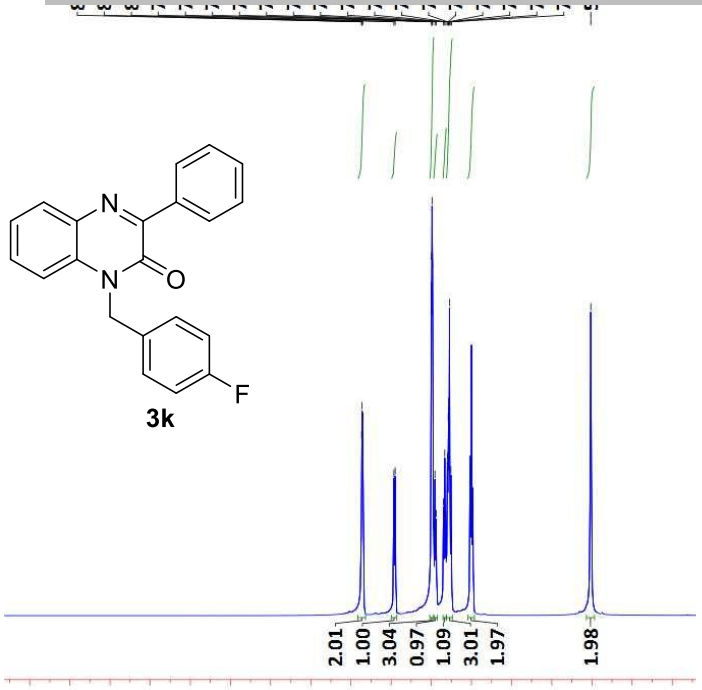


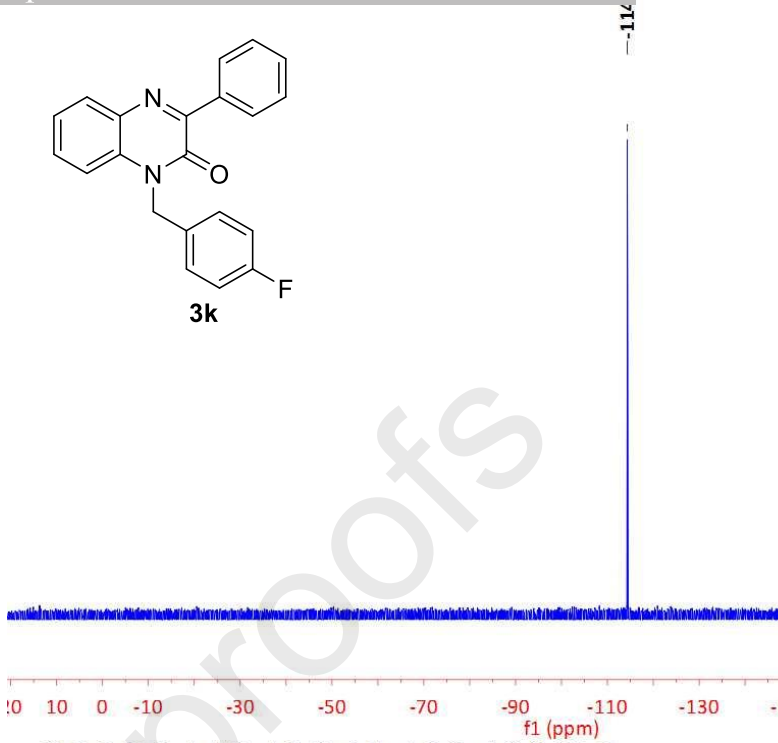


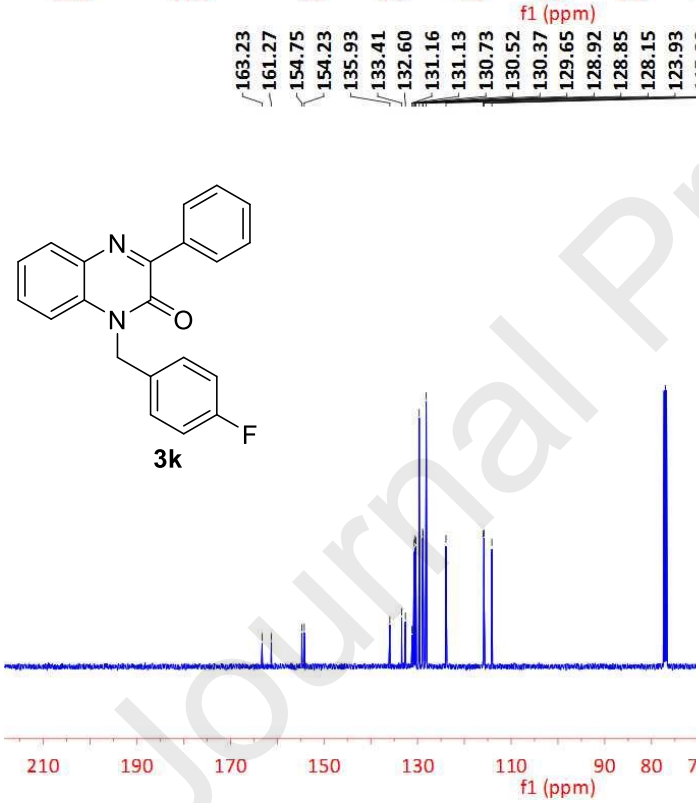


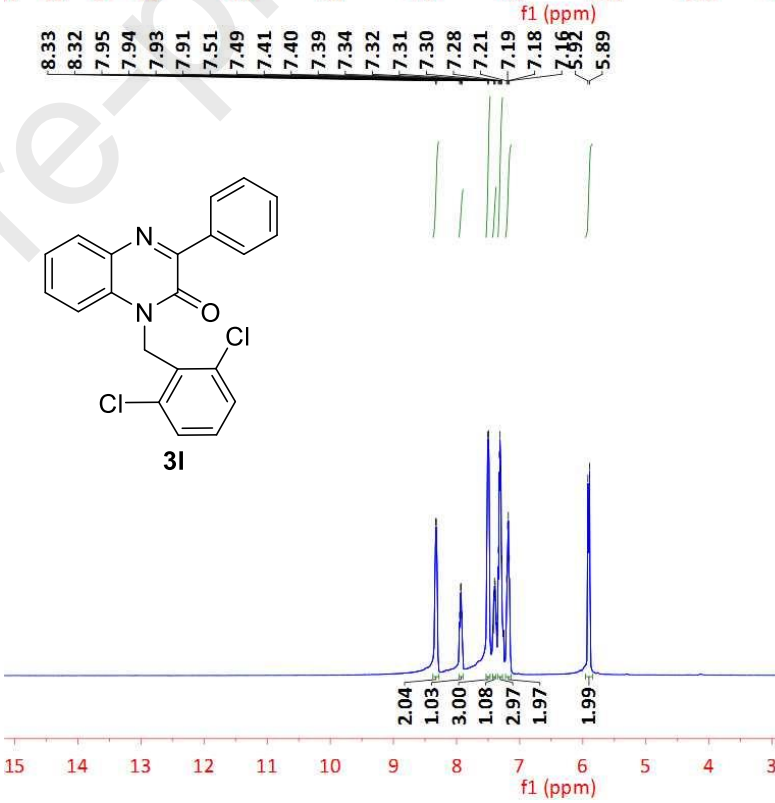


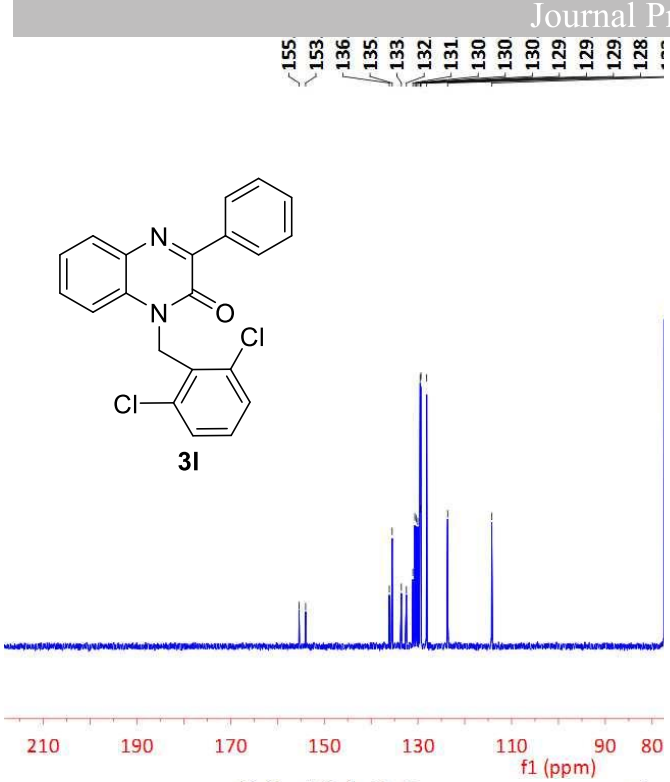


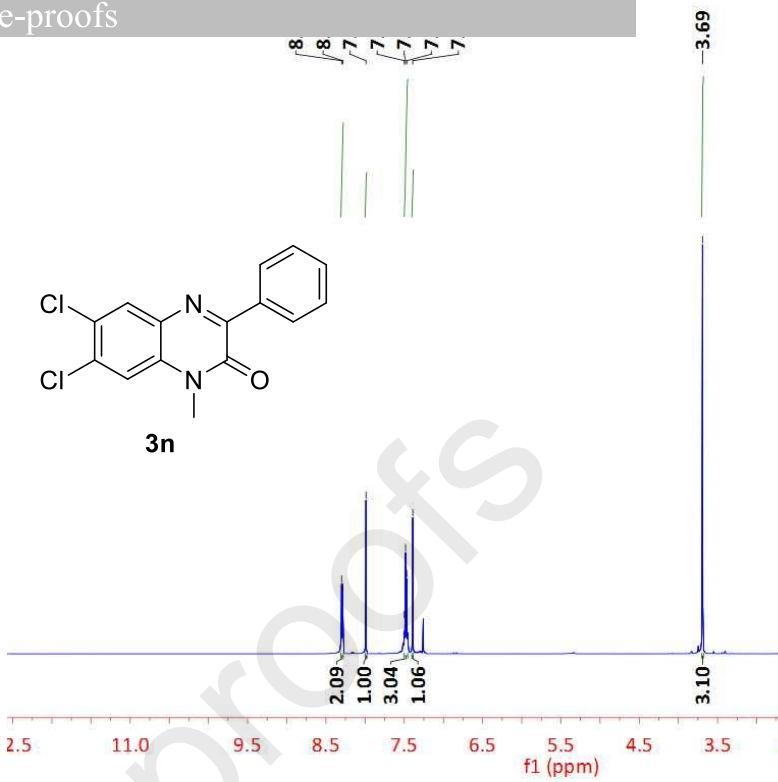


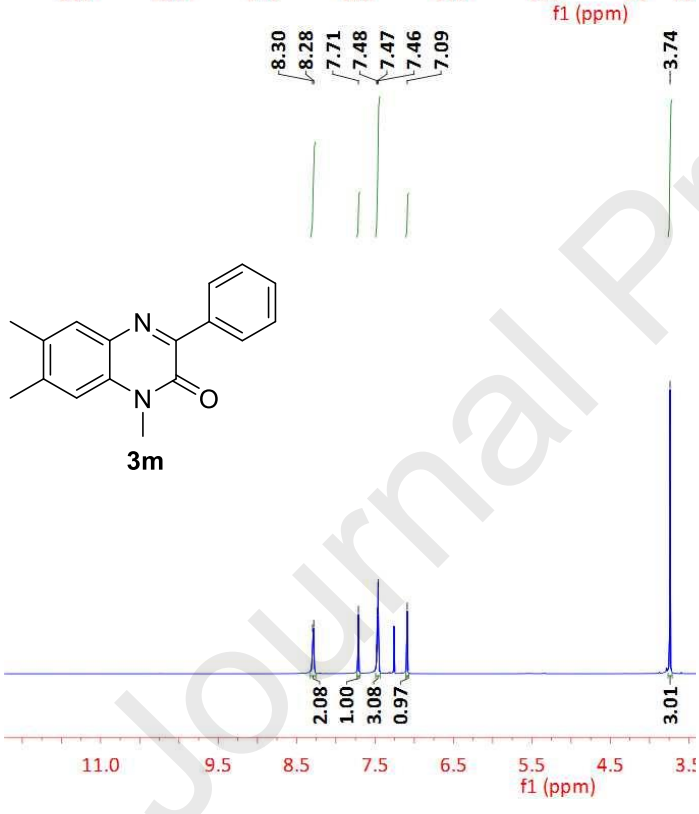


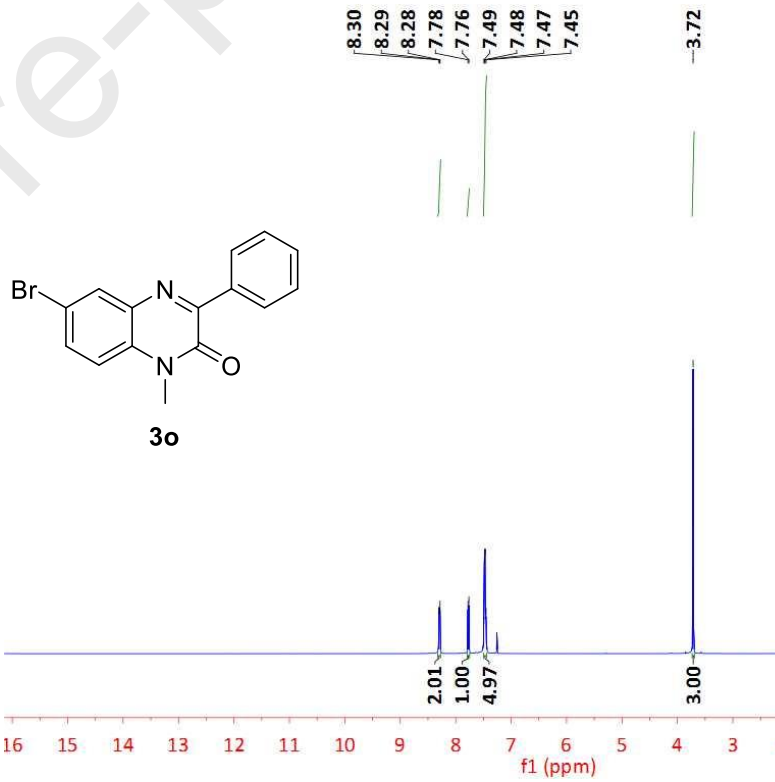


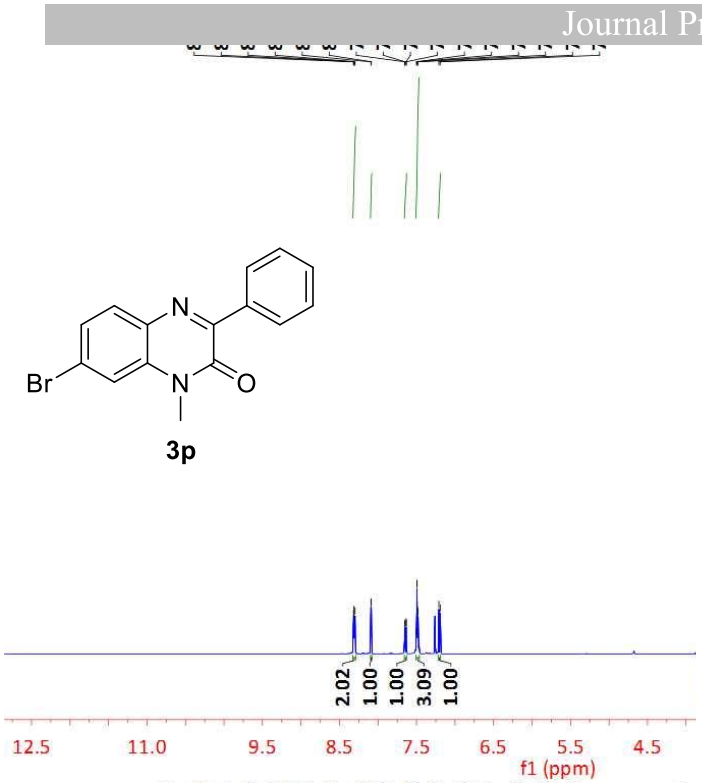


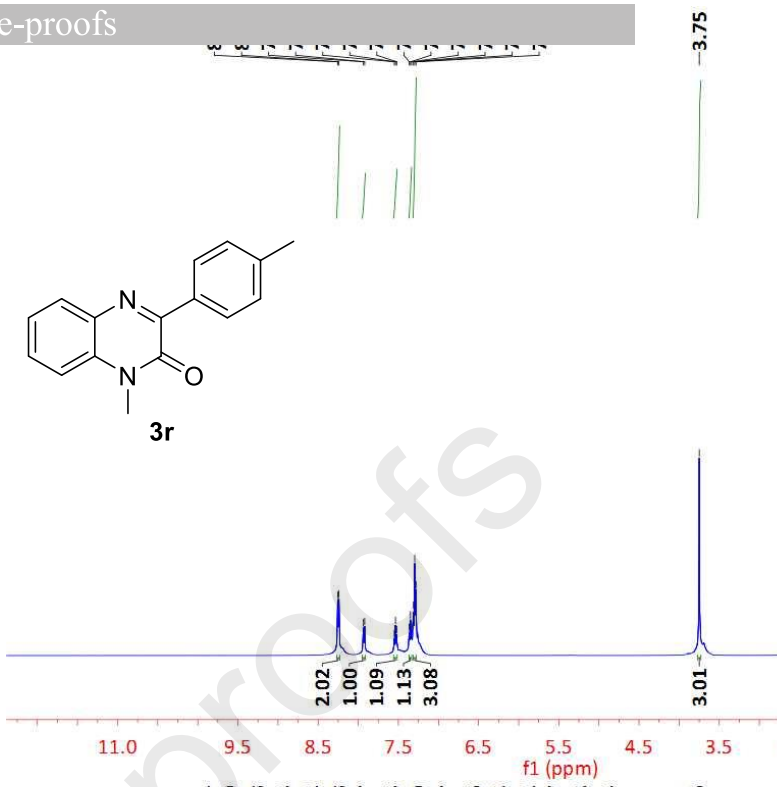


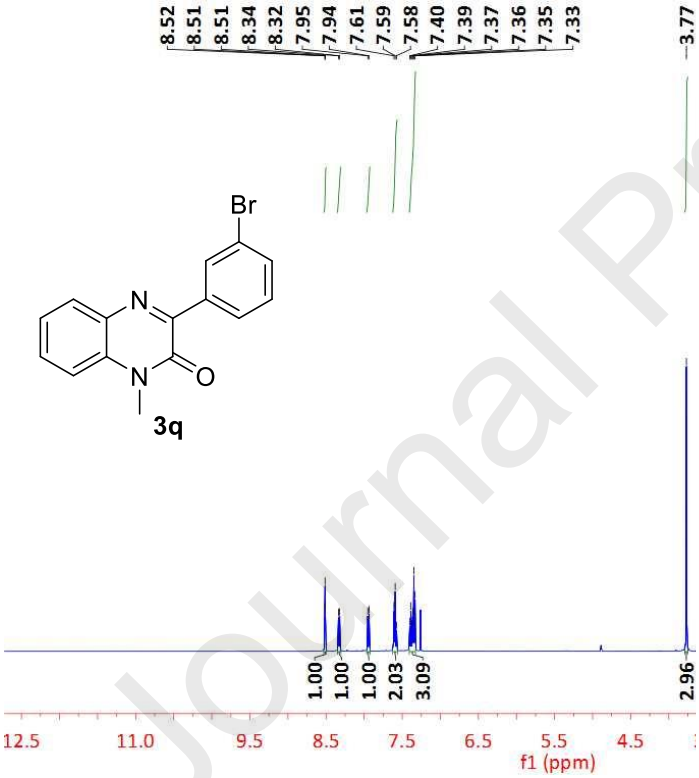


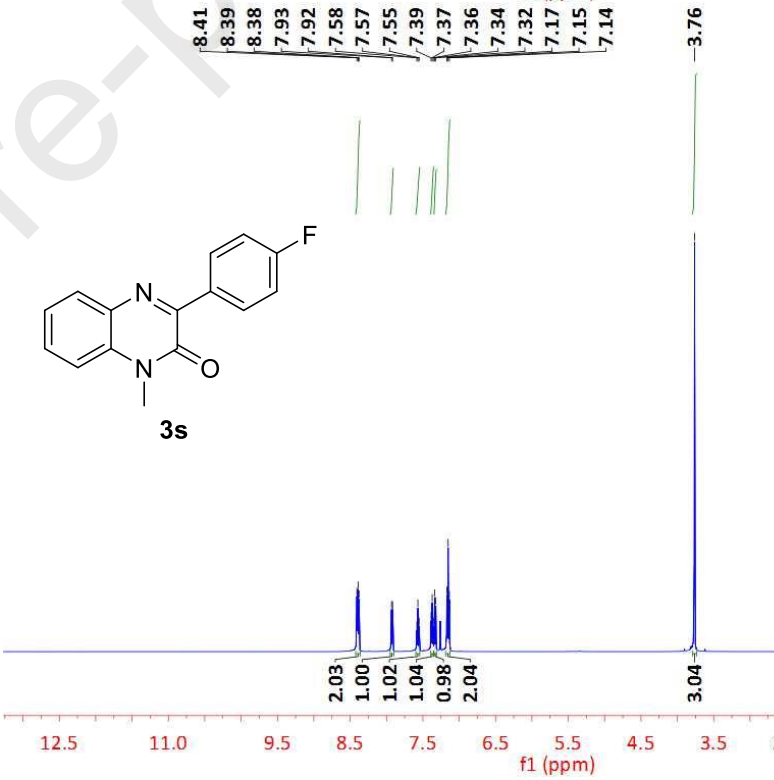


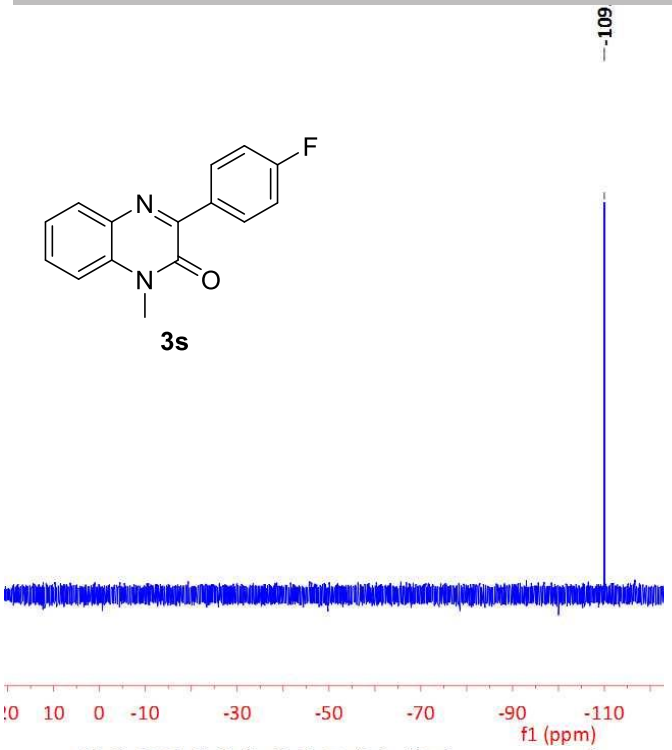


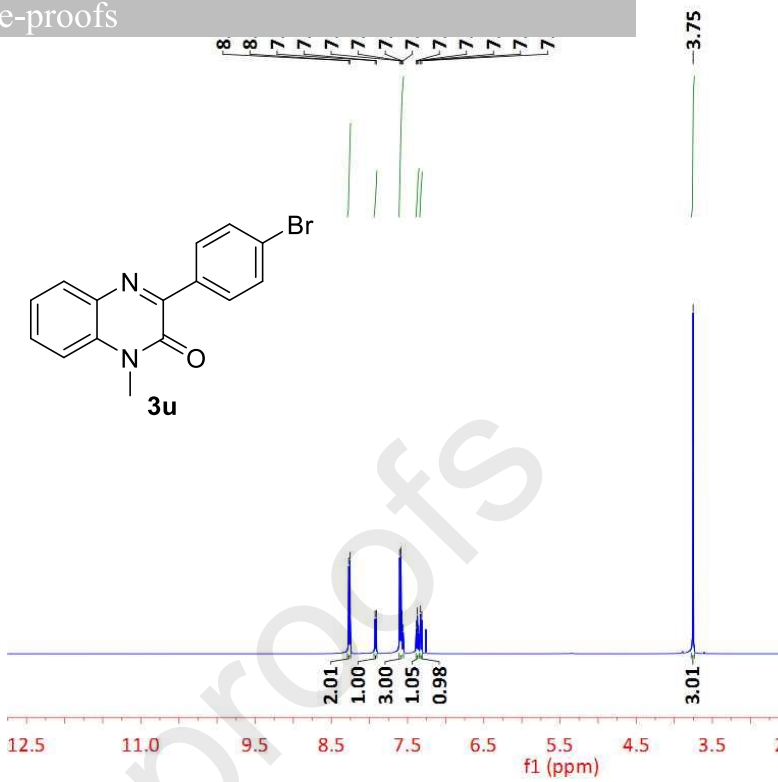


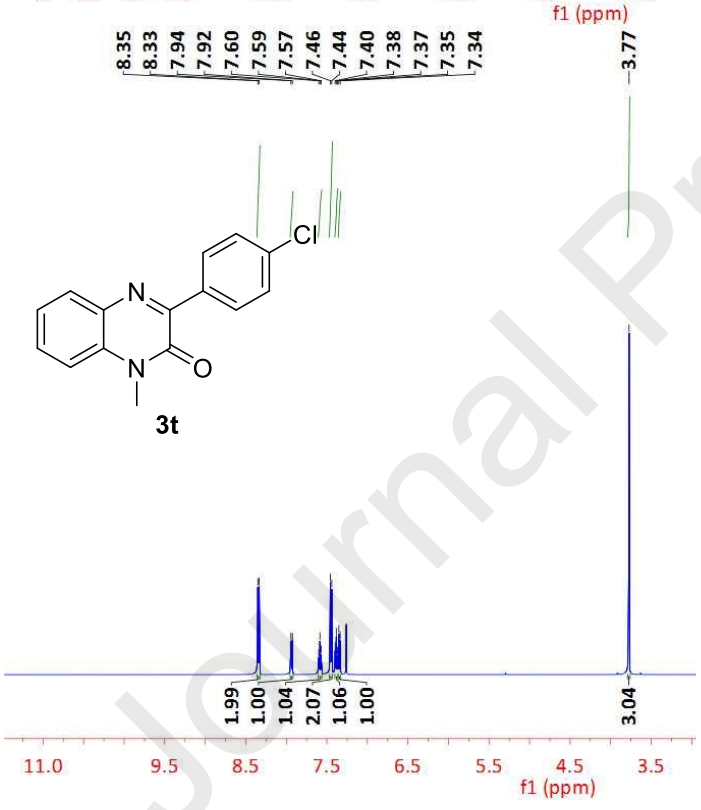


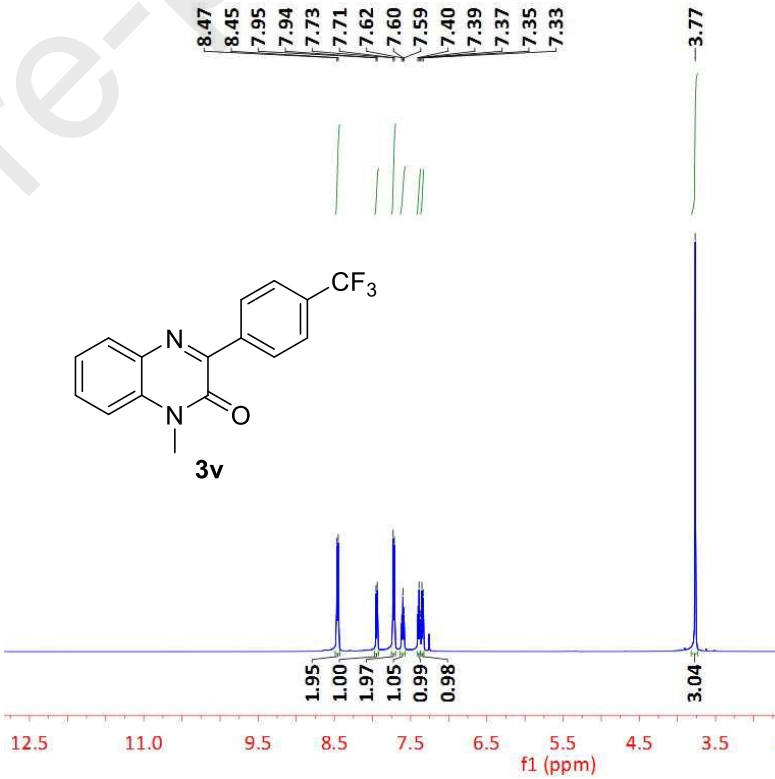


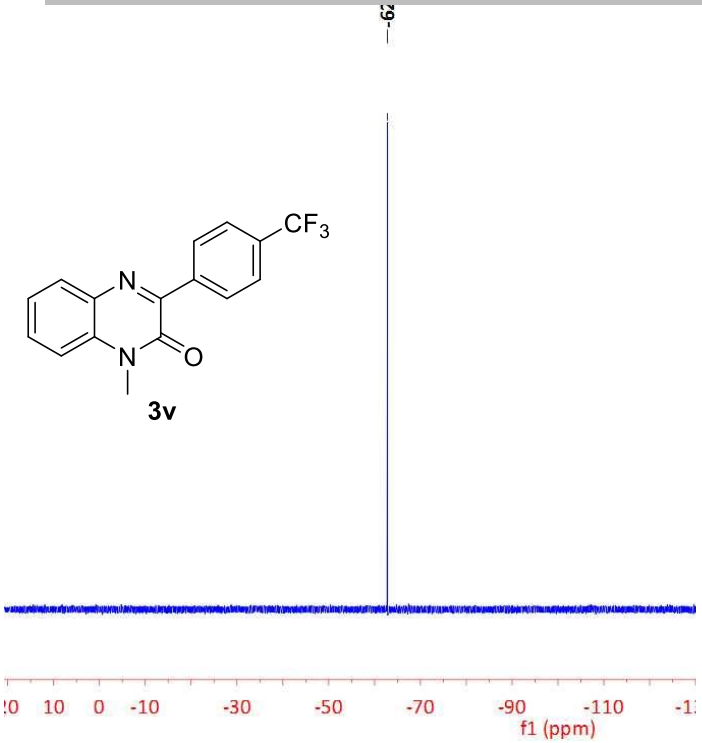


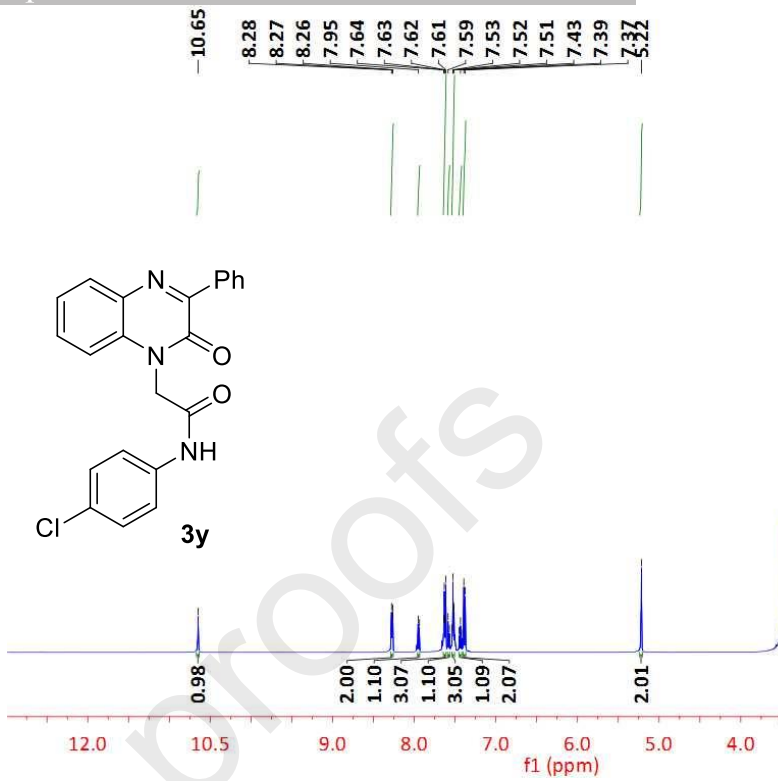


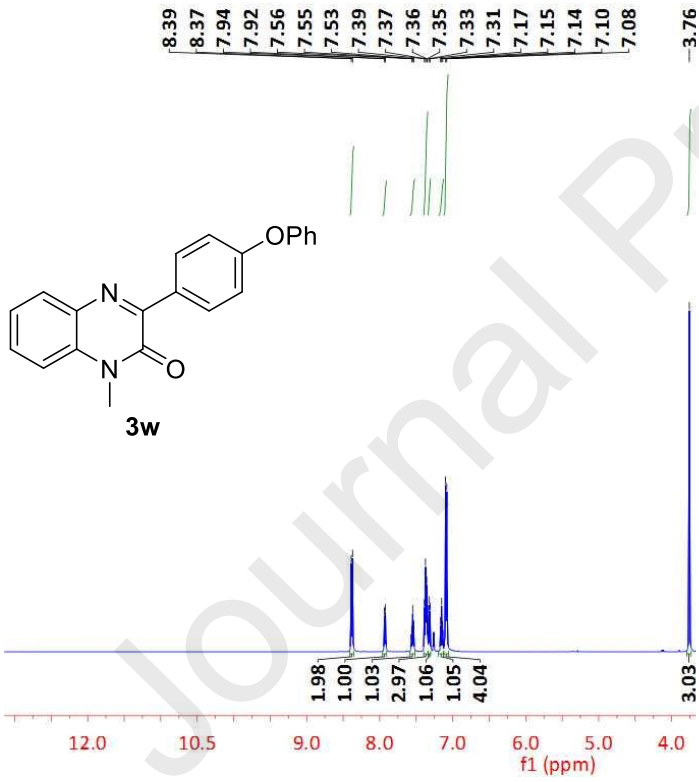












1. Catalyst-free arylation
2. Cheap and available arylating reagent
3. 24 examples with moderate-to-good yields

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.