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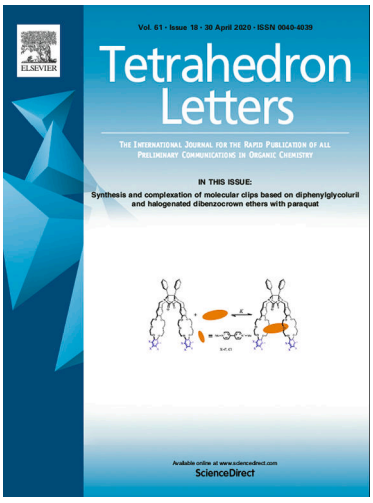

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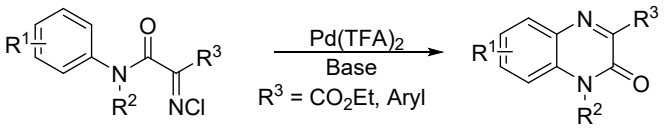

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Ligand-free Pd(II)-catalyzed Cyclization of α-Chloroimino-*N*-arylamides to Synthesis of Quinoxalin-2(1*H*)-ones

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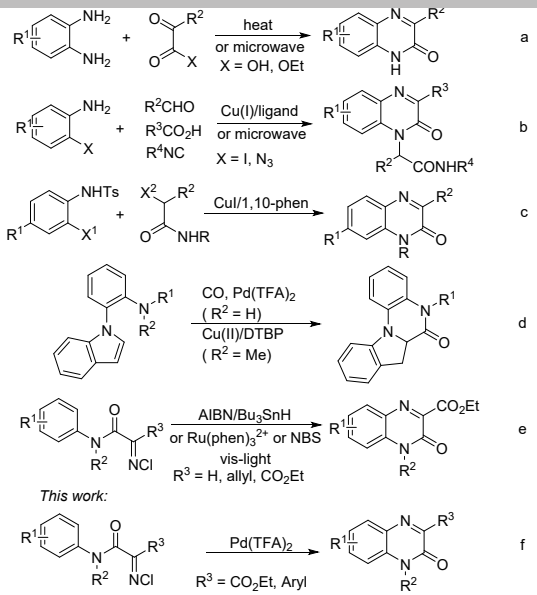
ABSTRACT

A ligand-free Pd(II)-catalyzed synthesis of quinoxalin-2(1*H*)-ones has been developed. $Pd(TFA)_2$ can induce ethyl 2-(*N*-arylcarbamoyl)-2-chloroiminoacetates to undergo Cyclization to afford quinoxalin-2(1*H*)-one products in high yields in the presence of Na_2CO_3. This catalytic system is also effective to convert α-aryl-α-chloroimino-*N*-arylamides to the corresponding quinoxalin-2(1*H*)-one products via tandem N-Cl cleavage and *N*-arylation in moderate yields. The reaction described herein constitutes simple and effective approach towards quinoxalin-2(1*H*)-one derivatives.

Introduction

As an important pharmacophore and useful heterocyclic scaffold, quinoxalin-2(1*H*)-one derivatives have attracted considerable attention due to their significant bioactive and medicinal activities in the past decades [1-6]. Quinoxalin-2(1*H*)-one derivatives exhibit wide pharmaceutical properties, including anticancer [2], anti-HIV [3], anti-Toxoplasma [4], antimicrobial [5] and protein kinase inhibitory [6]. Moreover, quinoxalin-2(1*H*)-one derivatives are useful synthetic intermolecules which could prepare for complex organic compounds [7].

Several versatile methods have been developed for the construction of quinoxalin-2(1*H*)-one. The traditional synthetic route was based on the condensation of *o*-phenylenediamines with α-ketone acids or with their related derivatives, such as α-aldehyde acid, α-ketone acid ester or oxazolones [8] (Scheme 1a). During the past few years, transition metal-catalyzed intra- and inter-molecular C-N bonds formation have been developed as fundamental methods for preparation of quinoxalin-2(1*H*)-ones [9-11]. One of the transition metal-catalyzed synthesis approaches to quinoxalin-2(1*H*)-ones is Ugi multi-component reaction followed by reductive cyclization [9] (Scheme 1b). More elaborate approach that involves transition-metal-catalyzed intra- and inter-molecular *N*-arylation have received considerable attention [10] (Scheme 1c). Other strategies such as copper catalyzed intramolecular oxidative coupling that starts from *o*-indolyl-*N*,*N*-dimethylarylamines [11] and palladium catalyzed oxidative carbonylation of C_2 C(sp2)-H bond of 2-(1*H*-indol-1-yl)anilines [12] have been reported (Scheme 1d). Recently, the radical cyclization constitutes effective method for the synthesis of quinoxalin-2(1*H*)-one. Spagnolo et al. [13] Zhang et al. [14] and Yu et al. [15] developed the cyclization of α-(aminocarbonyl)iminyl radical which would be useful intermediate towards quinoxalin-2(1*H*)-one derivatives under AIBN-promoted or visible light-induced conditions, respectively (Scheme 1e). Although these reactions would provide relatively simple and straightforward means for the synthesis of quinoxalin-2(1*H*)-ones, the reported procedures require hazardous reagents, harsh conditions and suffer from competition from other pathways [8,13-15]. Therefore, the development of more convenient and efficient route towards quinoxalin-2(1*H*)-one derivatives is still desirable. Herein, we demonstrate an efficient ligand-free palladium-catalyzed transformation of α-chloroimino-*N*-arylamides to synthesize quinoxalin-2(1*H*)-ones via cyclization with expanded scope of substrates at C_3 position on the scaffold (Scheme 1f).

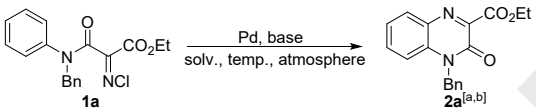


Scheme 1 Synthetic strategies of quinoxalin-2(*1H*)-ones

Results and Discussion

We chose 2-(*N*-arylcarbamoyl)-2-chloroiminoacetate **1a** as the model substrate and began to our investigation into the optimal reaction conditions (Table 1). Initially, the target product **2a** was isolated in 40% yield when the cyclization of compound **1a** was

Table 1. Optimization of reaction conditions.



Entry	Pd catalyst (equiv)	Base (equiv)	Solvent	Temperature (℃)	Atmosphere	Product [Yield (%)]
1	$Pd(TFA)_2$(0.2)	Cs_2CO_3(2.0)	DCE	80	Ar	40
2	$Pd(TFA)_2$(0.2)	K_2CO_3(2.0)	DCE	80	Ar	45
3	$Pd(TFA)_2$(0.2)	K_3PO_4(2.0)	DCE	80	Ar	65
4	$Pd(TFA)_2$(0.2)	$NaHCO_3$(2.0)	DCE	80	Ar	80
5	$Pd(TFA)_2$(0.2)	Na_2HPO_4(2.0)	DCE	80	Ar	75
6	$Pd(TFA)_2$(0.2)	Na_2CO_3(2.0)	DCE	80	Ar	82
7	$Pd(TFA)_2$(0.2)	TEA(2.0)	DCE	80	Ar	53
8	$Pd(TFA)_2$(0.1)	Na_2CO_3(2.0)	DCE	80	Ar	55
9	$Pd(TFA)_2$(0.15)	Na_2CO_3(2.0)	DCE	80	Ar	69
10	$Pd(TFA)_2$(0.2)	Na_2CO_3(1.0)	DCE	80	Ar	72
11	$Pd(TFA)_2$(0.2)	Na_2CO_3(1.5)	DCE	80	Ar	75
12	$Pd(TFA)_2$(0.2)	Na_2CO_3(2.0)	$PhCH_3$	80	Ar	----[c]
13	$Pd(TFA)_2$(0.2)	Na_2CO_3(2.0)	THF	80	Ar	55
14	$Pd(TFA)_2$(0.2)	Na_2CO_3(2.0)	DMF	80	Ar	78
15	$Pd(TFA)_2$(0.2)	Na_2CO_3(2.0)	DCE	80	Air	74
16	***$Pd(TFA)_2$(0.2)***	***Na_2CO_3(2.0)***	***DCE***	***100***	***Ar***	***85***
17	$Pd(TFA)_2$(0.2)	Na_2CO_3(2.0)	DCE	120	Ar	74
18	$Pd(OAc)_2$(0.2)	Na_2CO_3(2.0)	DCE	100	Ar	40
19	$PdCl_2(PPh_3)_2$(0.2)	Na_2CO_3(2.0)	DCE	100	Ar	----[d]
20	$Pd(TFA)_2$(0.2)	----	DCE	100	Ar	25
21	----	Na_2CO_3(2.0)	DCE	100	Ar	trace[e]
22	----	----	DCE	100	Ar	N.R.[f]

[a] The reaction was performed on a 0.2 mmol sacle.
[b] Isolated yield.
[c] The starting material was decomposed.
[d] 70% starting material recovered after 36 hrs.
[e] **2a** was trace and 75% starting material recovered.
[f] No reaction took place.
$Pd(TFA)_2$: palladium(II) trifluoroacetate; DCE: 1,2-dichloroethane; TEA : triethylamine

ium trifluoroacetate ($Pd(TFA)_2$, 0.2 equiv.) as catalyst and Cs_2CO_3 (2.0 equiv.) as base under argon atmosphere (Table 1, entry 1). Encouraged by this result, we screened a series of inorganic base (K_2CO_3, K_3PO_4, $NaHCO_3$, Na_2HPO_4, Na_2CO_3) in DCE at 80 °C oil bath under argon atmosphere, the desired product **2a** was received in 82% yield in the presence of Na_2CO_3, but other bases were not as efficient as Na_2CO_3 (Table 1, entries 2-6). With TEA (triethylamine) as base, **2a** was produced in 53% yield (Table 1, entry 7). Then we tried to reduce the amounts of $Pd(TFA)_2$ (0.10 and 0.15 equiv.) and Na_2CO_3 (1.0 and 1.5 equiv.). However, the yield was decreased when the amounts were reduced (Table 1, entries 8-11). The reaction exhibited a large solvent effect: the model material **1a** was decomposed in toluene (Table 1, entry 12), the yield of **2a** was significantly decreased in THF (Table 1, entry 13), and DMF led to a slightly lower yield compared with DCE (Table 1, entry 14). Air was found to have a small influence on the reaction (Table 1, entry 15). Afterwards, the reaction was carried out at different temperatures (Table 1, entries 16 and 17) and the best yield (85%) was achieved at 100 °C oil bath (Table 1, entry 16). Replacing $Pd(TFA)_2$ with other palladium catalysts, such as $Pd(OAc)_2$ and $PdCl_2(PPh_3)_2$, resulted in a decrease in the yields (Table 1, entries 18 and 19). Finally, the base was necessary in this transformation and the yield was only 25% in the absence of the Na_2CO_3 (Table 1, entry 20). In the condition control experiment, in the absence of Pd(II) catalyst, only trace of product was obtained (< 5%, Table 1, entry 21). When the catalyst and base were removed, no reaction took place (Table 1, entry 22).

With the previous optimized conditions, we then investigated the substrate scope of the current protocol, and the results were illustrated in Scheme 2. As shown, substrates bearing a substituent at the *para*-position of the *N*-phenyl ring was first investigated, *N*-chloroimines compounds **1** with both electron-donating groups (Me, **1b**; MeO, **1c**; and Ph, **1d**) and electron-withdrawing groups (F, **1e**; Cl, **1f**; Br, **1g**; I, **1h**; and CF_3, **1i**) underwent smooth transformation and delivered the corresponding products (**2b**–**2i**) in good to excellent yields and showed the potential application in further chemical transformations (**2e**–**2i**). For *meta*-substitution **1j**-**1n**, irrespective of its electronic character, could be tolerated in general and

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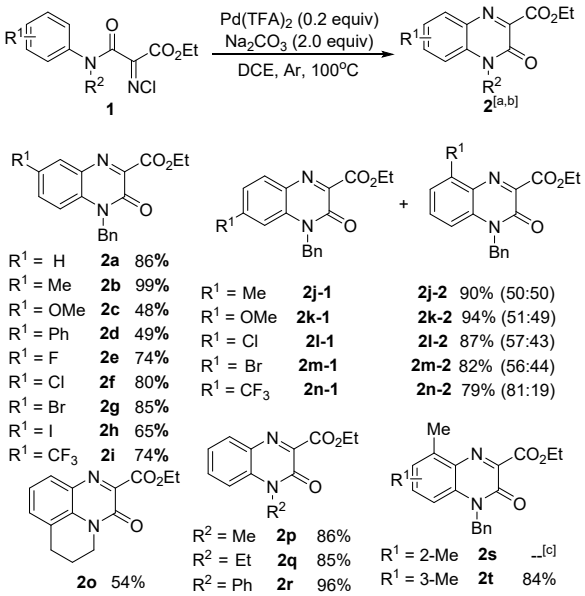
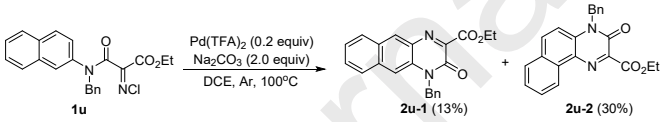
that the sterically less hindered one was the major product, which was different from our previous studies [15,16]. Unfortunately, *ortho*-substitution **1s** was incompetent to be converted to the



[a] Reaction conditions: A mixture of **1** (0.5 mmol), $Pd(TFA)_2$ (0.1 mmol) and Na_2CO_3 (1.0 mmol) in 5 mL of anhydrous DCE was stirred at 100 °C.
[b] Isolated yield.
[c] The substrate was decomposed.

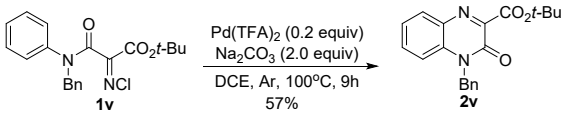
Scheme 2. $Pd(TFA)_2$-catalyzed cyclization of 2-(*N*-arylcarbamoyl)-2-chloroiminoacetates **1.**

To further explore the effect of the electronic nature of the substrate, this method was then applied to compound **1u** and the result was summarized in Scheme 3. As shown, the substrate **1u** could afford two regioisomers with the sterically hindered one **2u-2** being more favored and indicate that Pd(II)-catalyzed intramediate was electrophilic and favored to attack on the more electron-rich position of *N*-aryl ring.



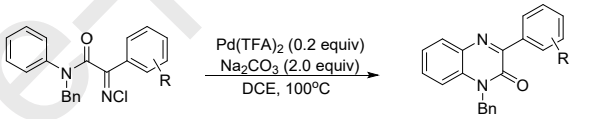
Scheme 3. Reaction showing effect of the electronic nature of **1u**.

The optimal conditions with $Pd(TFA)_2$ as catalyst was then applied to *tert*-butyl group substituted *N*-chloroimines compound **1v**, the reaction also worked well and provided the cyclization product **2v** in 57% yield (Scheme 4). The $–CO_2t$-Bu group would be easy to hydrolysis and decarboxylation, and **2v** could be further functionalization at C_3 position on the scaffold.



Scheme 4. The reactions of **1v** under standard conditions.

We next examined the applicability of this $Pd(TFA)_2$-catalyzed system to the reaction of α-aryl-α-chloroimine-*N*-arylamides **3**, and the results were summarized in Scheme 5. Unfortunately, our initial experiment showed trace of desired cyclization compound **4a** [17] was obtained and **3a** was decomposed under previous optimal conditions. We assumed that for the reaction of **3** to take place, the α-position of **3** had to be an electron-withdrawing group. It was likely that electron-withdrawing groups were more beneficial for palladium coordinating with the nitrogen atom to form electrophilic intermediates [16a]. Indeed, compound **3b** that contained CF_3 group at the *para*-position of α-phenyl ring was converted smoothly to the quinoxalin-2(1*H*)-one product **4b** in moderate yield (50%), the yield was slightly higher (56%) under air atmosphere. However, a mixture was obtained and the yield of **4b** was decreased when the reaction was performed under neat oxygen atmosphere (Scheme 5).

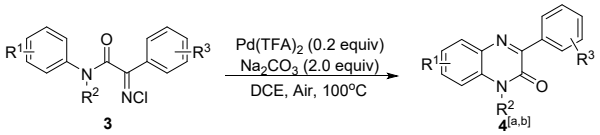


[a] The reactions were carried out in 0.2 mmol scale in DCE.
[b] Isolated yield under Argon atmosphere.
[c] Isolated yield under Air atmosphere.
[d] Isolated yield under oxygen atmosphere

Scheme 5. The reactions of **3a** and **3b** under standard and modified conditions.

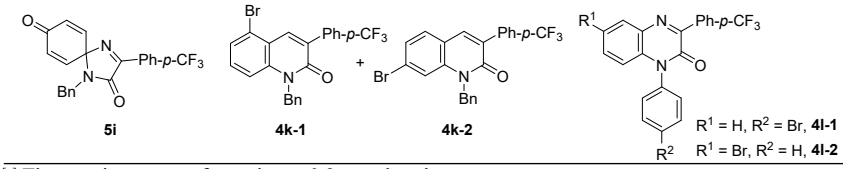
We investigated the substrate scope of the modified conditions, and the results are illustrated in Table 2. First, **3b**–**3h** were tested under air atmosphere, the reactions underwent smoothly and gave corresponding products **4b**–**4h** with moderate yields (Table 2, entries 2-7). In the case of **3i**, except for desired compound **4i**, azaspirocyclohexadienone **5i** was obtained in 31% yield (Table 2, entry 8). The substrates-bearing methyl (**3j**) and bromine (**3k**) on the *meta*-position of *N*-phenyl ring also proceeded with moderate yields and two regioisomers were obtained (**4j** and **4k**), with the sterically more hindered one **4k** being the major product (Table 2, entry 10). Notably, two expected products were isolated in the reaction of **3l**, **4l-1** was favored due to the electronic nature of the substituent (Table 2, entry 11), which was in accordance with the **1u** (Scheme 3).

Table 2 $Pd(TFA)_2$-catalyzed cyclization of **3** under air atmosphere.



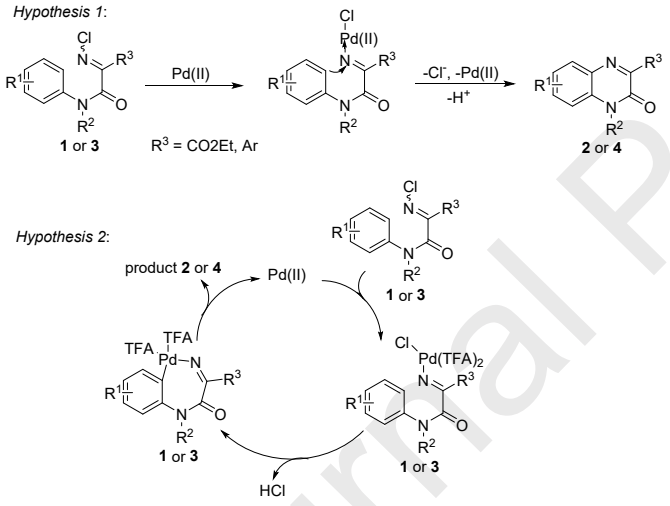
Entry	**3**	R^1	R^2	R^3	Product/Yield (%)
1	**3b**	H	Bn	*p*-CF_3	**4b**/56
2	**3c**	H	Bn	*p*-Cl	**4c**/48
3	**3d**	H	Bn	*p*-NO_2	**4d**/39
4	**3e**	H	Bn	*m*-CF_3	**4e**/50
5	**3f**	H	Et	*p*-CF_3	**4f**/56
6	**3g**	H	Ph	*p*-CF_3	**4g**/47
7	**3h**	*p*-F	Bn	*p*-CF_3	**4h**/59
8[c]	**3i**	*p*-MeO	Bn	*p*-CF_3	**4i**/31+**5i**/37

10	**3k**	*m*-Br	Bn	*p*-CF_3	**4k-1**+**4k-2**(56:44)/57
11	**3l**	*p*-Br	Ph	*p*-CF_3	**4l-1**+**4l-2**(62:38)/50



[a] The reaction was performed on a 0.2 mmol sacle.
[b] Isolated yield.
[c] Besides **4i**, **5i** was obtained in 37% yield.
[d] The relative configuration is undetermined.

Based on the previous results, this transformation could be hypothesized following two routes which were depicted in Scheme 6: (1) Friedel-Crafts cyclization (Hypothesis 1, Scheme 6) [16, 18]; (2) the oxidative addition and reduction elimination pathways (Hypothesis 2, Scheme 6) [19]. The formation of **2** and **4** is in accordance with the mechanism of Friedel-Crafts cyclization [16, 18] (Scheme 6), therefore, the Friedel-Crafts type mechanism was proposed (Hypothesis 1, Scheme 6). Apart from this mechanism, it is also possible the transformation proceeded through oxidative addition and reduction elimination pathways. At the present stage, we cannot distinguish between these two mechanisms, but we think that oxidative addition and reduction elimination mechanism is less likely. For Hypothesis 2 (Scheme 6), the reactions would afford the products via Pd-catalyzed seven-member-cyclic intermediates which were less stable in principle and unfavorable to the transformation.



Scheme 6. The plausible mechanisms for the transformation of **1** and **3**.

It is interesting to see the reactions of **1j**–**1n** and **3k**, the former gave two regioisomers **2j**–**2n**, of which the sterically less hindered products **2j-1**–**2n-1** were the major products due to the steric effect (Figure 1, structures I and II). However, for the latter, the sterically hindered **4k-1** was the major product (Table 2, entry 10). This difference was possibly due to the favorable interaction formed between the substituent bromine and the palladium at the transition state (Figure 1, structure III and IV). Moreover, the oxygen (air) had a slightly influence on the transformation (Table 1, entries 6 and 15; Scheme 5).

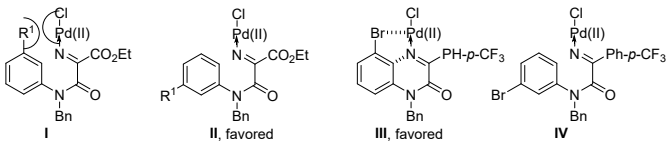


Figure 1. Tentative explanation for the regioselectivity of **2j**–**2n** and **4k**.

Conclusion

In conclusion, we have developed a novel Pd(II)-promoted N-Cl cleavage/*N*-arylation route to synthesis quinoxalin-2(1*H*)-ones via cyclization process. The reaction proceeds with good functional group compatibility and broad substrate scope. Meanwhile, the present protocol also provides a method to not only construct C-N bond efficiently but also to synthesize the quinoxalin-2(1*H*)-ones in good to excellent yields under oxidant and ligand-free conditions.

Supplementary Material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.tetlet.2020.XXXXXX.

Acknowledgments

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References

[1] (a) R. Liu, Z. Huang, M. G. Murray, X. Guo, G. Liu, *J. Med. Chem.* **2011**, *54*, 5747–5768; (b) L. Zhang, R. Qiu, X. Xue, Y. Pan, C. Xu, H. Li, L. Xu, *Adv. Synth. Catal.* **2015**, *357*, 3529–3537; (c) M. Imanishi, M. Sonoda, H. Miyazato, K. Sugimoto, M. Akagawa, S. Tanimori, *ACS Omega* **2017**, *2*, 1875−1885;
[2] (a) S. A. Galal, S. H. M. Khairat, F. A. F. Ragab, A. S. Abdelsamie, M. M. Ali, S. M. Soliman, J. Mortier, G. Wolber, H. El Diwani, *Eur. J. Med. Chem.* **2014**, *86*, 122–132; (b) A. M. S. E. Newahie, N. S. M. Ismail, D. A. A. E. Ella, K. A. M. Abouzid, Arch. Pharm. *Chem. Life Sci*. **2016**, *349*, 309–326;
[3] Y.-M. Huang, N. S. Alharbi, B. Sun, C. S. Shantharam, K. P. Rakesh, H.-L. Qin, *Eur. J. Med. Chem.* **2019**, *181*, 111566;
[4] Y. Deng, T. Wu, S.-Q. Zhai, C.-H. Li, *Eur. J. Med. Chem.* **2019**, *183*, 111711;
[5] D. A. E. Issa, N. S. Habib, A. E. Abdel, A. E. Abdel Wahab, *MedChemComm*, **2015**, *6*, 202–211;
[6] M. Weïwer, J. Spoonamore, J. Wei, B. Guichard, N. T. Ross, K. Masson, W. Silkworth, S. Dandapani, M. Palmer, C. A. Scherer, A. M. Stern, S. L. Schreiber, B. Munoz, *ACS Med. Chem. Lett.* **2012**, *3*, 1034–1038;
[7] For recent examples, see: (a) W. Wei, L. Wang, P. Bao, Y. Shao, H. Yue, D. Yang, X. Yang, X. Zhao, H. Wang, *Org. Lett.* **2018**, *20*, 7125−7130; (b) S. Toonchue, L. Sumunnee, K. Phomphrai, S. Yotphan, *Org. Chem. Front.* **2018**, *5*, 1928–1932; (c) L. Wang, Y. Zhang, F. Li, X. Hao, H.-Y. Zhang, J. Zhao, *Adv. Synth. Catal.* **2018**, *360*, 3969–3977; (d) J. Xu, H. Yang, H. Cai, H. Bao, W. Li, P. Zhang, *Org. Lett.* **2019**, *21*, 4698−4702; (e) F. Lian, K. Xu, W. Meng, H. Zhang, Z. Tana, C. Zeng, *Chem. Commun.* **2019**, *55*, 14685–14688; (f) L. Wang, H. Liu, F. Li, J. Zhao, H.-Y. Zhang, Y. Zhang, *Adv. Synth. Catal.* **2019**, *361*, 2354–2359; (g) Z. Wei, S. Qi, Y. Xu, H. Liu, J. Wu, H. Li, C. Xia, G. Duan, *Adv. Synth. Catal.* **2019**, *361*, 5490–5498; (h) Q. Ke, G. Yan, J. Yu, X. Wu, *Org. Biomol. Chem.* **2019**, *17*, 5863–5881;
[8] (a) G. A. Eller, B. Datterl, W. Holzer, *J. Heterocycl. Chem.* **2007**, *44*, 1139–1143; (b) J. Gris, R. Glisoni, L. Fabian, B. Fernández, A. G. Moglioni, *Tetrahedron Lett.* **2008**, *49*, 1053–1056; (c) S. Gräßle, S. Vanderheiden, P. Hodapp, B. Bulat, M. Nieger, N. Jung, S. Bräse, *Org. Lett.* **2016**, *18*, 3598–3601;
[9] (a) S. Balalaie, M. Bararjanian, S. Hosseinzadeh, F. Rominger, H. Reza Bijanzadeh, E. Wolf, *Tetrahedron* **2011**, *67*, 7294–7300; (b) Z. Xu, G. Martinez-Ariza, A. P. Cappelli, S. A. Roberts, C. Hulme, *J. Org. Chem.*

2016, *72*, 3548–3557;
[10] For selective examples, see: (a) D. Chen, W. Bao, *Adv. Synth. Catal.* **2010**, *352*, 955–960; (b) X. Luo, E. Chenard, P. Martens, Y.-X. Cheng, M. J. Tomaszewski, *Org. Lett.* **2010**, *12*, 3574–3577; (c) V. A. Vaillard, R. A. Rossi, S. E. Martín, *Org. Biomol. Chem.* **2011**, *9*, 4927–4935; (d) J. Areephong, B. Huo, I. I. Mbaezue, K. E. O. Ylijoki, *Tetrahedron Lett.* **2016**, *57*, 3124–3126;
[11] A. Gogoi, P. Sau, W. Ali, S. Guin, B. K. Patel, *Eur. J. Org. Chem.* **2016**, 1449–1453;
[12] S. Sankararaman, A. Chandrasekhar, *Org. Biomol. Chem.* **2020**, *18*, 1612–1622;
[13] G. Bencivenni, T. Lanza, R. Leardini, M. Minozzi, D. Nanni, P. Spagnolo, G. Zanardi, *J. Org. Chem.* **2008**, *73*, 4721–4724;
[14] Z.-S. Li, W.-X. Wang, J.-D. Yang, Y.-W. Wu, W. Zhang, *Org. Lett.* **2013**, *15*, 3820–3823;
[15] (a) R.-L. Guo, X.-Q. Zhu, X.-L. Zhang, Y.-Q. Wang, *Chem. Commun.* **2020**, *56*, 8976–8979; (b) D. Li, T. Yang, H. Su, W. Yu, *Adv. Synth. Catal.* **2015**, *357*, 2529–2539; (c) D. Li, H. Ma, W. Yu, *Adv. Synth. Catal.* **2015**, *357*, 3696–3702;
[16] (a) D. Li, H. Ma, W. Yu, *Tetrahedron* **2016**, *72*, 846–852; (b) D. Li, W. Yu, *Adv. Synth. Catal.* **2013**, *355*, 3708–3714;
[17] (a) X. Luo, E. Chenard, P. Martens, Y.-X. Cheng, M. J. Tomaszewski, *Org. Lett.* **2010**, *12*, 3574–3577; (b) Y. Kobayashi, M. Kuroda, N. Toba, H. Ma, D. Li, W. Yu, *Org. Lett.* **2016**, *18*, 868−871; (d) H. Ma, X. Zhang, L. Chen, W. Yu, *J. Org. Chem.* **2017**, *82*, 11841−11847;
[18] (a) M. Bandini, A. Melloni, A. Umani-Ronchi, *Angew. Chem. Int. Ed.* **2004**, *43*, 550–556; (b) M. Yokota, D. Fujita, J. Ichikawa, *Org. Lett.* **2007**, *9*, 4639–4642; (c) T. Nemoto, Y. Ishige, M. Yoshida, Y. Kohno, M. Kanematsu, Y. Hamada, *Org. Lett.* **2010**, *12*, 5020–5023; (d) D. N. Mai, B. R. Rosen, J. P. Wolfe, *Org. Lett.* **2011**, *13*, 2932–2935; (e) Y. Suzuki, T. Nemoto, K. Kakugawa, A. Hamajima, Y. Hamada, *Org. Lett.* **2012**, *14*, 2350–2353; (d) M. Yoshida, T. Nemoto, Z. Zhao, Y. Ishige, Y. Hamada, *Tetrahedron: Asymmetry* **2012**, *23*, 859–866;
[19] (a) X. Chen, K. M. Engle, D.-H. Wang, J.-Q. Yu, *Angew. Chem. Int. Ed.* **2009**, *48*, 5094–5115; (b) H. Jiang, W. Wu, B. Nie, Y. Zhang, J. Zhang, *Org. Chem. Front*. **2020**, doi: 10.1039/D0QO00510J; (c) Y. Liu, A. M. Kaiser, B. A. Arndtsen, *Chem. Sci.* **2020**, *11*, 8610–8616; (d) K. Yang, M. Song, H. Liu, H. Ge, *Chem. Sci.* **2020**, doi: 10.1039/D0SC03052J.

Ligand-free Pd(II)-catalyzed Cyclization of α-Chloroimino-*N*-arylamides to Synthesis of Quinoxalin-2(1*H*)-ones

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Supporting Imformation

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General methods

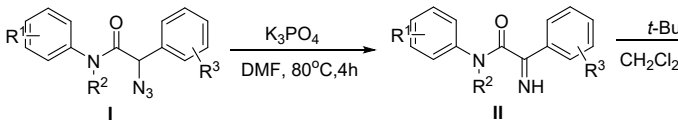
The ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AM-400 MHz spectrometer with $CDCl_3$. The chemical shifts in ^{1}H NMR and ^{13}C NMR spectra were determined with $Si(CH_3)_4$ as the internal standard (δ = 0.00, 77.00 ppm). The high resolution mass spectra (HRMS) were measured on a Bruker micrOTOF QII by ESI. The EI-MS spectra were measured on an HP 5988A spectrometer by direct inlet at 70 eV. Melting points were measured on an XT-4 melting point apparatus and were uncorrected. Flash column chromatography was carried out on silica gel (200-

Aldrich. 1,2-Dichloroethane (DCE) was distilled over P_2O_5 under argon atmosphere before use.

General procedure for the synthesis of 3

The ethyl 3-arylamino-2-chloroimino-3-oxopropanoate were prepared according to the previous literature methods.[1]

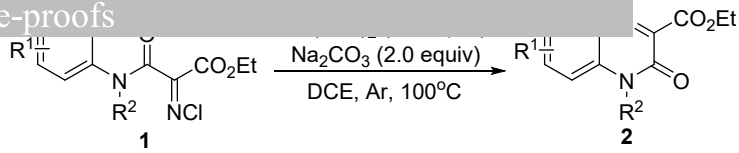
Preparation of compound **3**[1,2]



I II 3

To a DMF solution of the starting materials **I** (8 mmol), which was prepared according to the previous reported methods [1], was added K_3PO_4 (5.10 g, 24 mmol) at room temperature. The mixture was heated at 80 °C for 4hrs. After the reaction was completed, the reaction mixture was diluted with water (20 mL), extracted with EtOAc (20 mL × 4). The combined organic layers were then washed with brine (30 mL × 6), and then dried over Na_2SO_4. The organic solvents were then removed with a rotary evaporator to afford the crude 2-Imino-*N*,2-diarylacetamide **II** without further purification for the next step. The product **II** was dissolved in freshly distilled CH_2Cl_2 (2 mL) and stirred in an ice-water bath for 10 min. *t*-BuOCl (0.57 mL, 5.0 mmol) was added dropwise into the thus prepared solution, and the reaction mixture was stirred for 30 min at room temperature. Upon completion, the solvent was removed under reduced pressure, and the residual was treated with flash column chromatography on silica gel (using ethyl acetate/petroleum ether as the eluent) to afford pure 2-chloromino-*N*,2-diarylacetamides **3**.

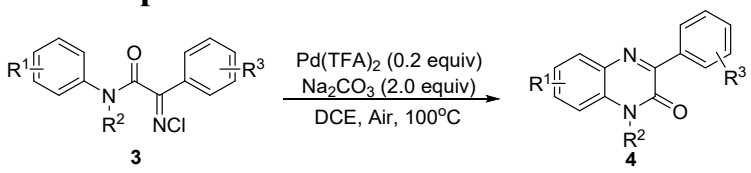
General procedure for the reactions of 1



1 2

To a 35 mL tube equipped with a magnetic stirring bar were added **1** (0.5 mmol, 1.0 equiv.), palladium trifluroacatate ($Pd(TFA)_2$, 35 mg, 0.2 equiv.), Na_2CO_3 (108 mg, 2.0 equiv.), and 1,2-dichloroethane (DCE, 5 mL). The tube was sealed and stirred in an oil bath at 100 °C under an argon atmosphere. After the reaction was completed as indicated by TLC, the reaction mixture was poured into a saturated aqueous NH_4Cl solution (15 mL), and was extracted with ethyl acetate (3×10 mL). The combined organic layers were washed with brine (30 mL) and dried with anhydrous Na_2SO_4. The solvent was removed under reduced pressure, and the residual was treated with silica gel chromatography to give product.

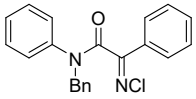
General procedure for the reactions of 3



3 4

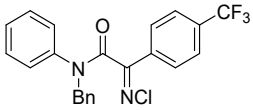
To a 35 mL tube equipped with a magnetic stirring bar, compounds **3** (0.5 mmol), $Pd(TFA)_2$ (35 mg, 0.2 equiv.) and Na_2CO_3 (108 mg, 2.0 equiv.) was added followed by DCE (5 ml). The mixture was heated in an oil bath at 100 °C under air atmosphere. After the reaction was completed, the reaction mixture was poured into a saturated aqueous NH_4Cl solution (15 mL) and extracted with ethyl acetate (3×10 mL). The combined organic phases were washed with brine, dried over Na_2SO_4, filtered and concentrated. The product **4** was purified using silica chromatography.

Spectroscopic data for the substrate 3



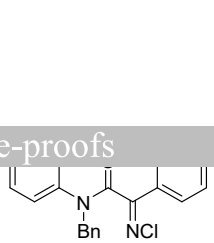
_N_-benzyl-2-(chloroimino)-_N_,2-diphenylacetamide (3a)

Pale yellow oil; R_f = 0.37 (petroleum ether : EtOAc = 10 : 1); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.48-7.44 (m, 1.5H), 7.41-7.36 (m, 1H), 7.31-7.14 (m, 9H), 7.06 (t, *J* = 7.6 Hz, 1.5H), 6.85 (t, *J* = 7.6 Hz, 1.5H), 6.80 (t, *J* = 7.6 Hz, 0.5H), 5.13 (d, *J* = 14.0 Hz, 0.7H), 4.99-4.94 (m, 1.2H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 174.5, 174.2, 163.8, 163.4, 139.7, 138.3, 136.0, 133.1, 132.0, 131.6, 130.6, 129.24, 129.19, 129.13, 129.06, 129.01, 128.97, 128.9, 128.6, 128.5, 128.3, 128.2, 128.0, 127.9, 127.8, 127.7, 127.52, 127.46, 127.4, 126.8, 53.1, 52.3; HRMS (ESI): calcd. for $C_{21}H_{17}ClN_2O$ + H = 349.1102, found: 349.1100.



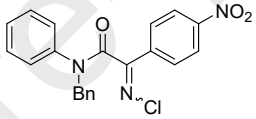
_N_-benzyl-2-(chloroimino)-_N_-phenyl-2-(4-(trifluoromethyl)phenyl)acetamide (3b)

Yellow oil; R_f = 0.26 (petroleum ether : EtOAc = 10 : 1); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.60-7.57 (m, 4H), 7.30-7.23 (m, 5H), 7.21-7.19 (m, 1H), 7.12-7.08 (m, 2H), 6.84 (d, *J* = 7.6 Hz, 2H), 5.13 (d, *J* = 14.0 Hz, 0.9H), 5.01-4.95 (m, 1.1H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 173.5, 162.8, 138.1, 136.3, 135.8, 135.7, 133.6, 133.2, 132.9, 132.6, 129.3, 129.13, 129.08, 128.7, 128.6, 128.0, 127.8, 127.2, 125.71, 125.68, 125.64, 125.60, 125.20, 125.17, 124.9, 122.2, 53.3, 52.5; HRMS (ESI): calcd. for $C_{22}H_{16}ClF_3N_2O$ + H = 417.0976, found: 417.0975.



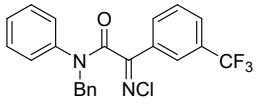
_N_-benzyl-2-(chloroimino)-2-(4-chlorophenyl)-_N_-phenylacetamide (3c)

Yellow oil; R_f = 0.31 (petroleum ether : EtOAc = 10 : 1); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.41-7.38 (m, 1.5H), 7.28-7.13 (m, 9H), 7.09 (t, *J* = 7.6 Hz, 1.5H), 6.85 (t, *J* = 7.6 Hz, 1.5H), 6.81-6.79 (m, 0.5H), 5.11 (d, *J* = 14.0 Hz, 0.7H), 5.00-4.94 (m, 1.3H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 173.4, 173.2, 163.4, 163.0, 139.6, 138.2, 137.8, 136.9, 135.8, 131.5, 130.2, 129.4, 129.3, 129.14, 129.12, 129.00, 128.96, 128.9, 128.8, 128.7, 128.6, 128.51, 128.49, 128.43, 128.36, 128.0, 127.9, 127.8, 127.7, 127.3, 53.1, 52.4; HRMS (ESI): calcd. for $C_{21}H_{16}Cl_2N_2O$ + H = 383.0712, found: 383.0710.



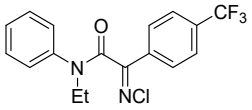
_N_-benzyl-2-(chloroimino)-2-(4-nitrophenyl)-_N_-phenylacetamide (3d)

Pale yellow oil; R_f = 0.35 (petroleum ether : EtOAc = 10 : 1); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 8.18-8.14 (m, 2H), 7.62 (d, *J* = 8.8 Hz, 1.6H), 7.34-7.18 (m, 7H), 7.11 (t, *J* = 8.0 Hz, 1.5H), 6.84 (d, *J* = 7.6 Hz, 2H), 5.16-4.96 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 172.9, 162.7, 162.4, 149.2, 148.5, 139.3, 138.4, 137.8, 137.7, 135.54, 135.51, 129.44, 129.38, 129.2, 129.1, 129.0, 128.8, 128.7, 128.61, 128.56, 128.5, 128.4, 128.1, 127.9, 127.7, 123.9, 123.8, 123.4, 53.2, 52.5; HRMS (ESI): calcd. for $C_{21}H_{16}ClN_3O_3$ + Na = 416.0772, found: 416.0769.



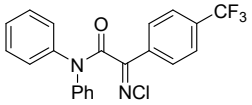
_N_-benzyl-2-(chloroimino)-_N_-phenyl-2-(3-(trifluoromethyl)phenyl)acetamide (3e)

Yellow oil; R_f = 0.31 (petroleum ether : EtOAc = 10 : 1); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.66-7.64 (m, 2.4H), 7.47-7.38 (m, 1.4H), 7.31-7.17 (m, 7H), 7.07 (d, *J* = 8.0 Hz, 1.4H), 6.83-6.78 (m, 1.9H), 5.07 (d, *J* = 13.6 Hz, 1.5H), 4.95 (s, 0.5H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 173.4, 173.2, 163.2, 162.8, 139.4, 138.1, 135.8, 133.9, 132.8, 131.7, 131.4, 131.0, 130.8, 130.7, 130.5, 130.4, 129.8, 129.6, 129.45, 129.36, 129.28, 129.27, 129.2, 129.1, 129.04, 128.96, 128.8, 128.7, 128.65, 128.62, 128.58, 128.5, 128.4, 128.2, 128.0, 127.9, 127.80, 127.76, 127.4, 127.20, 127.16, 124.7, 124.45, 124.4, 123.9, 123.82, 123.79, 123.75, 122.0, 119.3, 53.3, 53.1, 52.4; HRMS (ESI): calcd. for $C_{22}H_{16}ClF_3N_2O$ + H = 417.0976, found: 417.0975.



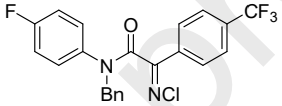
2-(Chloroimino)-*N*-ethyl-*N*-phenyl-2-(4-(trifluoromethyl)phenyl)acetamide (3f)

Yellow oil; R_f = 0.38 (petroleum ether : EtOAc = 10 : 1); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.60-7.58 (m, 3.2H), 7.38-7.35 (m, 1H), 7.27-7.25 (m, 1.4H), 7.22-7.18 (m, 1.4H), 7.05-7.00 (m, 2H), 4.02-3.81 (m, 2H), 1.25 (td, *J* = 7.2, 2.8 Hz, 2.1H), 1.16 (td, *J* = 7.2, 2.8 Hz, 0.9H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 173.7, 173.6, 162.7, 162.3, 139.6, 138.3, 136.4, 135.6, 133.2, 132.9, 129.6, 129.4, 129.30, 129.26, 129.1, 128.6, 128.6, 127.8, 127.6, 127.4, 127.2, 125.71, 125.68, 125.64, 125.60, 125.2, 125.1, 124.9, 112.2, 45.6, 44.5, 43.6, 13.8, 12.9, 12.6; HRMS (ESI): calcd. for $C_{17}H_{14}ClF_3N_2O$ + H = 355.0820, found: 355.0825.



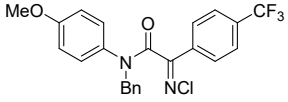
2-(Chloroimino)-*N*,*N*-diphenyl-2-(4-(trifluoromethyl)phenyl)acetamide (3g)

Yellow oil; R_f = 0.49 (petroleum ether : EtOAc = 10 : 1); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.73-7.69 (m, 1.5H), 7.63 (d, *J* = 8.4 Hz, 2H), 7.45-7.38 (m, 3.5H), 7.35-7.34 (m, 1H), 7.30-7.18 (m, 4H), 7.13-7.08 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 173.4, 173.2, 162.8, 162.5, 140.4, 139.0, 136.5, 135.3, 133.4, 133.1, 129.7, 129.6, 129.4, 129.3, 129.2, 128.6, 128.3, 128.1, 128.0, 127.3, 125.9, 125.84, 125.80, 125.77, 125.6, 125.3, 125.2, 124.9, 122.2; HRMS (ESI): calcd. for $C_{21}H_{14}ClF_3N_2O$ + H = 403.0820, found: 403.0823.



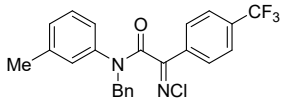
***N*-benzyl-2-(chloroimino)-*N*-(4-fluorophenyl)-2-(4-(trifluoromethyl)phenyl)acetamide (3h)**

Yellow oil; R_f = 0.40 (petroleum ether : EtOAc = 10 : 1); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.63-7.60 (m, 3.5H), 7.36-7.26 (m, 5H), 7.18-7.16 (m, 0.5H), 6.95-6.91 (m, 0.5H), 6.83-6.76 (m, 3.5H), 5.07 (d, *J* = 14.4 Hz, 0.8H), 4.98-4.92 (m, 1.2H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 173.4, 173.1, 163.9, 163.2, 162.8, 161.4, 160.9, 136.1, 135.52, 135.48, 135.3, 134.00, 133.97, 133.5, 133.2, 132.8, 131.2, 131.1, 129.9, 129.8, 129.2, 128.8, 128.73, 128.69, 128.6, 128.2, 128.0, 127.9, 127.2, 125.9, 125.8, 125.7, 125.4, 125.3, 124.8, 122.1, 116.4, 116.3, 116.2, 116.0, 53.4, 52.6; HRMS (ESI): calcd. for $C_{22}H_{15}ClF_4N_2O$ + NH_4 = 452.1147, found: 452.1154.



***N*-benzyl-2-(chloroimino)-*N*-(4-methoxyphenyl)-2-(4-(trifluoromethyl)phenyl)acetamide (3i)**

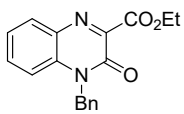
Yellow oil; R_f = 0.32 (petroleum ether : EtOAc = 10 : 1); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.61-7.56 (m, 3.5H), 7.32-7.17 (m, 5.5H), 6.73 (dd, *J* = 8.0, 3.2 Hz, 2.6H), 6.57 (dd, *J* = 8.0, 3.2 Hz, 1.4H), 5.06 (d, *J* = 14.0 Hz, 0.7H), 4.96-4.90 (m, 1.3H), 3.77 (s, 0.9H), 3.68 (s, 2.1H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 173.7, 173.6, 163.4, 163.1, 160.0, 159.4, 140.6, 136.3, 135.8, 135.6, 133.2, 132.9, 131.9, 130.5, 130.4, 129.2, 129.1, 128.8, 128.6, 128.5, 128.4, 128.0, 127.8, 127.2, 125.7, 125.65, 125.61, 125.57, 125.2, 125.1, 124.9, 122.2, 114.3, 114.1, 55.4, 55.2, 53.4, 52.6; HRMS (ESI): calcd. for $C_{23}H_{18}ClF_3N_2O_2$ + H = 447.1082, found: 447.1079.



***N*-benzyl-2-(chloroimino)-*N*-(m-tolyl)-2-(4-(trifluoromethyl)phenyl)acetamide(3j)**

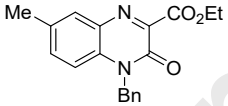
Yellow oil; R_f = 0.31 (petroleum ether : EtOAc = 10 : 1); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.59-7.53 (m, 3.4H), 7.31-7.18 (m, 5.5H), 7.14-7.08 (m, 0.7H), 7.02-6.95 (m, 1.4H), 6.63-6.59 (m, 2H), 5.10 (d, *J* = 14.0 Hz, 0.7H), 4.98-4.93 (m, 1.3H), 2.20 (s, 0.9H), 2.06 (s, 2.1H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 173.6, 173.4, 163.2, 162.9, 139.5, 139.4, 139.2, 138.0, 136.6, 135.9, 135.8, 135.6, 133.2, 132.8, 130.0, 129.5, 129.3, 129.0, 128.8, 128.7, 128.6, 128.5, 128.4, 128.0, 127.9, 127.8, 127.2, 126.1, 125.62, 125.59, 125.55, 125.51, 125.14, 125.10, 125.07, 124.9, 124.8, 122.2, 53.2, 52.4, 20.9, 20.8; HRMS (ESI): calcd. for $C_{23}H_{18}ClF_3N_2O$ + H = 431.1133, found: 431.1132.

Spectroscopic data for the products 2 and 4



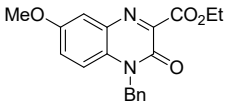
Ethyl 4-benzyl-3-oxo-3,4-dihydroquinoxaline-2-carboxylate[1] (2a)

Yellow solid; mp 94-95 °C; yield: 133 mg (86%); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.92 (d, *J* = 8.0 Hz, 1H), 7.52-7.48 (m, 1H), 7.34-7.24 (m, 7H), 5.48 (s, 2H), 4.52 (q, *J* = 7.2 Hz, 2H), 1.44 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 163.6, 152.5, 149.0, 134.5, 133.2, 132.2, 131.9, 131.0, 128.7, 127.6, 126.8, 124.0, 114.5, 62.3, 45.8, 13.9; EI-MS m/z (rel. int., %): 308 (M^+, 49), 234 (30), 207 (73), 206 (76), 91 (100).



Ethyl 4-benzyl-7-methyl-3-oxo-3,4-dihydroquinoxaline-2-carboxylate[1] (2b)

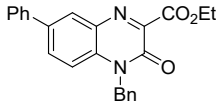
White solid; mp 117-118 °C; yield: 160 mg (99%); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.71 (s, 1H), 7.33-7.18 (m, 7H), 5.46 (s, 2H), 4.51 (q, *J* = 7.2 Hz, 2H), 2.38 (s, 3H), 1.44 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 163.7, 152.4, 148.8, 134.6, 134.0, 133.6, 131.9, 131.0, 130.6, 128.7, 127.6, 126.8, 114.3, 62.2, 45.7, 20.3, 14.0; EI-MS m/z (rel. int., %): 322 (M^+, 48), 248 (27), 221 (67), 220 (62), 91 (100).



Ethyl 4-benzyl-7-methoxy-3-oxo-3,4-dihydroquinoxaline-2-carboxylate[1] (2c)

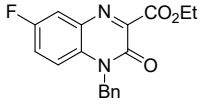
Pale yellow solid; mp 124-125 °C; yield: 82 mg (48%); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.38 (d, *J* = 2.8 Hz, 1H), 7.31-7.21 (m, 6H), 7.14 (dd, *J* = 9.2, 2.8 Hz, 1H), 5.48 (s, 2H), 4.52 (q, *J* = 7.2 Hz, 2H), 3.82 (s, 3H), 1.46 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 163.7, 156.1, 152.2, 149.2, 134.7, 132.8, 128.8, 127.7, 127.6, 126.8, 122.0, 115.5, 111.9, 62.4, 55.6, 45.9, 14.0;

EI-MS m/z (rel. int., %): 338 (M^+, 36), 237 (46), 236 (35), 233 (22), 91 (100).



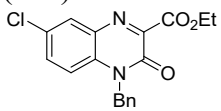
Ethyl 4-benzyl-3-oxo-7-phenyl-3,4-dihydroquinoxaline-2-carboxylate[1] (2d)

Yellow oil; R_f = 0.56 (petroleum ether : EtOAc = 3 : 1); yield: 93 mg (49%); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 8.16 (s, 1H), 7.75-7.73 (m, 1H), 7.57-7.55 (m, 2H), 7.42 (t, *J* = 7.2 Hz, 2H), 7.36-7.25 (m, 7H), 5.50 (s, 2H), 4.53 (q, *J* = 7.2 Hz, 2H), 1.46 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 163.6, 152.4, 149.3, 138.4, 137.1, 134.6, 132.4, 132.3, 131.1, 128.93, 128.87, 127.80, 127.77, 126.9, 126.6, 115.0, 62.4, 45.9, 14.0; EI-MS m/z (rel. int., %): 384 (M^+, 40), 283 (46), 282 (42), 91 (100).



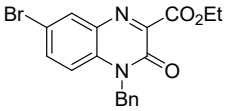
Ethyl 4-benzyl-7-fluoro-3-oxo-3,4-dihydroquinoxaline-2-carboxylate[1] (2e)

White solid; mp 123-124 °C; yield: 121 mg (74%); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.62-7.60 (m, 1H), 7.32-7.23 (m, 7H), 5.49 (s, 2H), 4.52 (q, *J* = 7.2 Hz, 2H), 1.45 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 163.4, 159.7, 157.3, 152.2, 150.5, 134.3, 132.6, 132.5, 129.93, 129.91, 128.9, 127.9, 126.8, 120.3, 120.1, 116.3, 116.1, 116.0, 115.9, 62.5, 46.1, 14.0; EI-MS m/z (rel. int., %): 326 (M^+, 33), 252 (16), 225 (48), 224 (52), 91 (100).



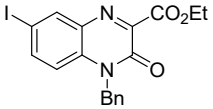
Ethyl 4-benzyl-7-chloro-3-oxo-3,4-dihydroquinoxaline-2-carboxylate[1] (2f)

White solid; mp 154-155 °C; yield: 137 mg (80%); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.92 (d, *J* = 2.4 Hz, 1H), 7.46 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.34-7.23 (m, 6H), 5.48 (s, 2H), 4.52 (q, *J* = 7.2 Hz, 2H), 1.46 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 163.4, 152.3, 150.4, 134.3, 132.6, 132.3, 132.0, 130.3, 129.6, 129.0, 128.0, 126.9, 115.8, 62.6, 46.1, 14.1; EI-MS m/z (rel. int., %): 344 (M^+ + 2, 19), 342 (M^+, 60), 242 (29), 240 (80), 91 (100).



Ethyl 4-benzyl-7-bromo-3-oxo-3,4-dihydroquinoxaline-2-carboxylate[1] (2g)

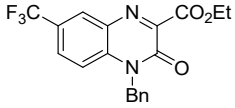
White solid; mp 165-166 °C; yield: 164 mg (85%); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 8.04 (d, *J* = 2.4 Hz, 1H), 7.56 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.32-7.18 (m, 6H), 5.46 (s, 2H), 4.51 (q, *J* = 7.2 Hz, 2H), 1.45 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 163.2, 152.1, 150.2, 134.9, 134.2, 133.2, 132.7, 132.3, 128.9, 127.9, 126.8, 116.6, 116.1, 62.5, 46.0, 14.0; EI-MS m/z (rel. int., %): 388 (M^+ + 2, 13), 386 (M^+, 13), 287 (17), 286 (22), 285 (20), 284 (21), 91 (100).



Ethyl 4-benzyl-7-iodo-3-oxo-3,4-dihydroquinoxaline-2-carboxylate[1] (2h)

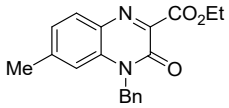
White solid; mp 163-164 °C; yield: 140 mg (65%); ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): 8.25 (d, *J* = 2.0 Hz, 1H), 7.74 (dd, *J* = 8.8, 2.0 Hz, 1H), 7.32-7.22 (m, 5H), 7.05 (d, *J* = 9.2 Hz, 1H), 5.45 (s, 2H), 4.51 (q, *J* = 7.2 Hz, 2H), 1.45 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 163.2, 152.2, 149.9, 140.6, 139.5, 134.2, 133.02, 132.98, 129.0, 127.9, 126.8, 116.3, 86.7, 62.6, 45.9, 14.0; EI-MS

m/z (rel. int., %): 454 (M^+, 25), 353 (21), 352 (24), 91 (100).



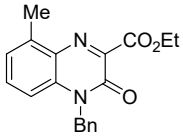
Ethyl 4-benzyl-3-oxo-7-(trifluoromethyl)-3,4-dihydroquinoxaline-2-carboxylate (2i)

White solid; mp 120-121 °C; yield: 140 mg (74%); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 8.21 (d, *J* = 0.8 Hz, 1H), 7.73 (dd, *J* = 8.8, 2.0 Hz, 1H), 7.44 (d, *J* = 9.2 Hz, 1H), 7.33-7.24 (m, 5H), 5.51 (s, 2H), 4.53 (q, *J* = 7.2 Hz, 2H), 1.46 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 163.0, 152.4, 150.6, 135.6, 134.0, 131.4, 129.0, 128.6, 128.53, 128.49, 128.43, 128.40, 128.36, 128.0, 127.3, 126.9, 126.8, 126.6, 126.2, 125.9, 124.6, 121.9, 119.2, 115.5, 62.6, 46.1, 14.0; EI-MS m/z (rel. int., %): 376 (M^+, 29), 302 (19), 275 (50), 274 (62), 91 (100).



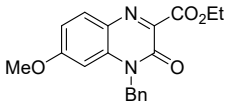
Ethyl 4-benzyl-6-methyl-3-oxo-3,4-dihydroquinoxaline-2-carboxylate[1] (2j-1)

White solid; mp 116-117 °C; yield: 72 mg (45%); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.81 (d, *J* = 8.0 Hz, 1H), 7.33-7.25 (m, 5H), 7.15 (d, *J* = 8.4 Hz, 1H), 7.10 (s, 1H), 5.48 (s, 2H), 4.52 (q, *J* = 7.2 Hz, 2H), 2.41 (s, 3H), 1.45 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 163.8, 152.7, 147.5, 143.7, 134.7, 133.4, 130.9, 130.3, 128.9, 127.7, 126.9, 125.6, 114.5, 62.3, 45.8, 22.2, 14.1; EI-MS m/z (rel. int., %): 322 (M^+, 51), 248 (36), 221 (74), 220 (62), 91 (100).



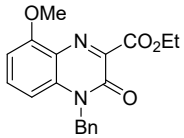
Ethyl 4-benzyl-8-methyl-3-oxo-3,4-dihydroquinoxaline-2-carboxylate[1] (2j-2)

White solid; mp 119-120 °C; yield: 72 mg (45%); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.37 (t, *J* = 8.0 Hz, 1H), 7.30-7.22 (m, 5H), 7.17 (d, *J* = 7.2 Hz, 1H), 7.11 (d, *J* = 8.8 Hz, 1H), 5.48 (s, 2H), 4.51 (q, *J* = 7.2 Hz, 2H), 2.67 (s, 3H), 1.45 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 164.2, 152.5, 147.5, 140.3, 134.8, 133.5, 132.0, 130.9, 128.8, 127.6, 126.8, 125.3, 112.4, 62.2, 45.9, 17.5, 14.0; EI-MS m/z (rel. int., %): 322 (M^+, 44), 248 (40), 221 (61), 220 (53), 91 (100).



Ethyl 4-benzyl-6-methoxy-3-oxo-3,4-dihydroquinoxaline-2-carboxylate (2k-1)

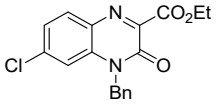
White solid; mp 128-129 °C; yield: 82 mg (49%); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.84 (t, *J* = 8.5 Hz, 1H), 7.33-7.24 (m, 5H), 6.90 (dd, *J* = 9.0, 2.0 Hz, 1H), 6.69 (d, *J* = 2.4 Hz, 1H), 5.47 (s, 2H), 4.51 (q, *J* = 7.2 Hz, 2H), 3.78 (s, 3H), 1.45 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 163.8, 162.9, 152.9, 144.6, 135.3, 134.6, 132.7, 128.8, 127.8, 126.9, 112.0, 98.4, 62.2, 55.6, 46.0, 14.0; EI-MS m/z (rel. int., %): 338 (M^+, 44), 292 (32), 249 (33), 237 (53), 91 (100).



Ethyl 4-benzyl-8-methoxy-3-oxo-3,4-dihydroquinoxaline-2-carboxylate (2k-2)

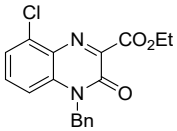
White solid; mp 134-135 °C; yield: 77 mg (46%); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.44 (t, *J* = 8.4 Hz, 1H), 7.32-7.23 (m, 5H), 6.86 (d, *J* = 8.8 Hz, 1H), 6.78 (d, *J* = 8.0 Hz, 1H), 5.47 (s, 2H), 4.49 (q, *J* = 7.2 Hz, 2H), 4.00 (s, 3H), 1.44 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 163.6, 157.0, 152.7, 146.5, 134.9, 134.7, 133.4, 128.8,

127.7, 126.8, 122.8, 100.6, 105.5, 62.2, 56.5, 46.2, 14.0; EI-MS m/z (rel. int., %): 338 (M^+, 49), 237 (44), 233 (22), 91 (100).



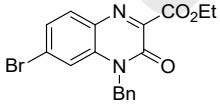
Ethyl 4-benzyl-6-chloro-3-oxo-3,4-dihydroquinoxaline-2-carboxylate[1] (2l-1)

White solid; mp 124-125 °C; yield: 86 mg (51%); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.86 (d, J = 8.8 Hz, 1H), 7.36-7.26 (m, 7H), 5.45 (s, 2H), 4.52 (q, J = 7.2 Hz, 2H), 1.45 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 163.4, 152.4, 148.9, 138.6, 134.3, 134.1, 132.3, 130.6, 129.1, 128.1, 127.0, 124.7, 114.6, 62.6, 46.1, 14.1; EI-MS m/z (rel. int., %): 344 (M^+ + 2, 10), 342 (M^+, 28), 241 (47), 240 (39), 91 (100).



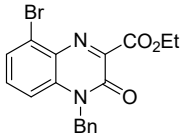
Ethyl 4-benzyl-8-chloro-3-oxo-3,4-dihydroquinoxaline-2-carboxylate[1] (2l-2)

White solid; mp 134-135 °C; yield: 63 mg (37%); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.42-7.40 (m, 2H), 7.34-7.19 (m, 6H), 5.49 (s, 2H), 4.53 (q, J = 7.2 Hz, 2H), 1.46 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 163.4, 152.3, 149.5, 136.1, 134.9, 134.3, 132.2, 129.04, 129.02, 128.0, 126.8, 125.1, 113.5, 62.6, 46.4, 14.0; EI-MS m/z (rel. int., %): 344 (M^+ + 2, 10), 342 (M^+, 28), 243 (14), 241 (44), 91 (100).



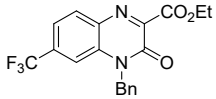
Ethyl 4-benzyl-6-bromo-3-oxo-3,4-dihydroquinoxaline-2-carboxylate (2m-1)

White solid; mp 140-141 °C; yield: 89 mg (46%); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.77 (d, J = 8.4 Hz, 1H), 7.48 (s, 1H), 7.43 (d, J = 8.8 Hz, 1H), 7.35-7.26 (m, 5H), 5.44 (s, 2H), 4.50 (q, J = 7.2 Hz, 2H), 1.45 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 163.3, 152.2, 149.1, 134.3, 134.1, 132.3, 130.8, 129.0, 128.0, 127.5, 126.94, 126.90, 117.6, 62.6, 46.0, 14.0; EI-MS m/z (rel. int., %): 388 (M^+ + 2, 15), 386 (M^+, 15), 287 (22), 286 (23), 285 (25), 284 (22), 91 (100).



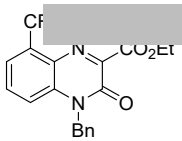
Ethyl 4-benzyl-8-bromo-3-oxo-3,4-dihydroquinoxaline-2-carboxylate (2m-2)

White solid; mp 132-133 °C; yield: 69 mg (36%); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.60 (d, J = 7.6 Hz, 1H), 7.35-7.21 (m, 7H), 5.48 (s, 2H), 4.52 (q, J = 7.2 Hz, 2H), 1.45 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 163.3, 152.3, 149.6, 134.7, 134.3, 132.4, 129.9, 129.0, 128.4, 127.9, 126.9, 126.8, 114.3, 62.5, 46.3, 14.0; EI-MS m/z (rel. int., %): 388 (M^+ + 2, 15), 386 (M^+, 15), 287 (21), 286 (23), 285 (24), 284 (21), 91 (100).



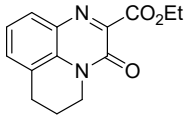
Ethyl 4-benzyl-3-oxo-6-(trifluoromethyl)-3,4-dihydroquinoxaline-2-carboxylate (2n-1)

White solid; mp 114-115 °C; yield: 120 mg (64%); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 8.05 (d, J = 8.4 Hz, 1H), 7.61 (s, 1H), 7.57 (d, J = 8.4 Hz, 1H), 7.36-7.27 (m, 5H), 5.52 (s, 2H), 4.54 (q, J = 7.2 Hz, 2H), 1.46 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 163.2, 152.3, 151.6, 134.0, 133.9, 133.7, 133.6, 133.3, 133.2, 132.9, 132.0, 129.1, 128.2, 127.1, 124.4, 121.7, 120.6, 120.5, 120.6, 120.5, 112.13, 112.09, 112.05, 112.01, 62.8, 46.2, 14.0; EI-MS m/z (rel. int., %): 376 (M^+, 27), 302 (17), 275 (50), 274 (59), 91 (100).



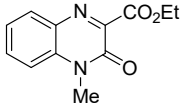
Ethyl 4-benzyl-3-oxo-8-(trifluoromethyl)-3,4-dihydroquinoxaline-2-carboxylate (2n-2)

White solid; mp 170-171 °C; yield: 27 mg (14%); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.66 (d, *J* = 7.6 Hz, 1H), 7.58 (t, *J* = 8.0 Hz, 1H), 7.51 (d, *J* = 8.4 Hz, 1H), 7.35-7.23 (m, 5H), 5.52 (s, 2H), 4.52 (q, *J* = 7.2 Hz, 2H), 1.45 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 163.3, 152.1, 150.1, 134.2, 131.4, 130.1, 129.8, 129.14, 129.07, 128.1, 126.8, 124.3, 122.13, 122.08, 122.05, 121.97, 121.5, 118.7, 62.6, 46.3, 14.0; EI-MS m/z (rel. int., %): 376 (M^+, 30), 275 (35), 274 (41), 193 (18), 91 (100).



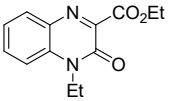
Ethyl 3-oxo-3,5,6,7-tetrahydropyrido[*1,2,3-de*]quinoxaline-2-carboxylate (2o)

White solid; mp 167-168 °C; yield: 70 mg (54%); ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): 7.77 (d, *J* = 8.0 Hz, 1H), 7.40 (d, *J* = 7.2 Hz, 1H), 7.30-7.26 (m, 1H), 4.51 (q, *J* = 7.2 Hz, 2H), 4.16 (t, *J* = 5.0 Hz, 2H), 3.00 (t, *J* = 6.0 Hz, 2H), 2.15 (t, *J* = 6.0 Hz, 2H), 1.44 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 163.8, 151.8, 148.4, 131.6, 131.3, 130.5, 128.7, 124.7, 123.6, 62.3, 41.8, 26.3, 20.0, 14.0; EI-MS m/z (rel. int., %): 258 (M^+, 57), 186 (100), 185 (32), 158 (67), 157 (74).



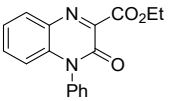
Ethyl 4-methyl-3-oxo-3,4-dihydroquinoxaline-2-carboxylate (2p)

White solid; mp 53-54 °C; yield: 100 mg (86%); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.91 (d, *J* = 8.0 Hz, 1H), 7.65 (t, *J* = 7.6 Hz, 1H), 7.40-7.34 (m, 2H), 4.51 (q, *J* = 7.2 Hz, 2H), 3.71 (s, 3H), 1.45 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 163.6, 152.3, 148.8, 133.8, 132.7, 131.6, 130.8, 123.9, 113.7, 62.2, 28.9, 13.9; EI-MS m/z (rel. int., %): 232 (M^+, 59), 160 (100), 159 (40), 132 (45), 131 (58).



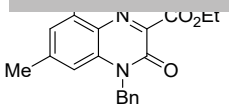
Ethyl 4-ethyl-3-oxo-3,4-dihydroquinoxaline-2-carboxylate (2q)

White solid; mp 74-75 °C; yield: 104 mg (85%); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.93 (d, *J* = 8.0 Hz, 1H), 7.69-7.65 (m, 1H), 7.41-7.35 (m, 2H), 4.52 (q, *J* = 7.2 Hz, 2H), 4.35 (q, *J* = 7.2 Hz, 2H), 1.46 (t, *J* = 7.2 Hz, 3H), 1.40 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 163.6, 151.8, 148.8, 132.8, 132.2, 131.9, 131.1, 123.7, 113.5, 62.1, 37.3, 13.9, 12.1; EI-MS m/z (rel. int., %): 246 (M^+, 87), 174 (74), 172 (70), 146 (96), 145 (75), 118 (100).



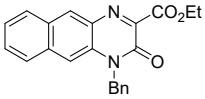
Ethyl 3-oxo-4-phenyl-3,4-dihydroquinoxaline-2-carboxylate (2r)

White solid; mp 151-152 °C; yield: 142 mg (96%); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.97 (d, *J* = 8.0 Hz, 1H), 7.63-7.53 (m, 3H), 7.44 (t, *J* = 7.6 Hz, 1H), 7.35 (t, *J* = 7.6 Hz, 1H), 7.30 (d, *J* = 7.6 Hz, 2H), 6.73 (d, *J* = 8.4 Hz, 1H), 4.50 (q, *J* = 7.2 Hz, 2H), 1.43 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 163.5, 152.0, 149.6, 134.8, 134.7, 131.9, 131.6, 130.5, 130.1, 129.5, 127.9, 124.1, 115.5, 62.2, 13.9; EI-MS m/z (rel. int., %): 294 (M^+, 32), 222 (34), 194 (28), 193 (100), 192 (20).



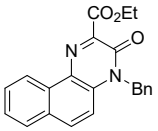
Ethyl 4-benzyl-6,8-dimethyl-3-oxo-3,4-dihydroquinoxaline-2-carboxylate (2t)

White solid; mp 136-137 °C yield: 142 mg (84%); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.31-7.23 (m, 5H), 7.00 (s, 1H), 6.91 (s, 1H), 5.46 (s, 2H), 4.50 (q, *J* = 7.2 Hz, 2H), 2.62 (s, 3H), 2.34 (s, 3H), 1.45 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 164.3, 152.7, 146.0, 143.2, 139.9, 134.9, 133.6, 129.2, 128.8, 127.6, 126.8, 112.4, 62.1, 45.8, 22.2, 17.3, 14.0; EI-MS m/z (rel. int., %): 336 (M^+, 49), 262 (55), 235 (63), 234 (46), 91 (100).



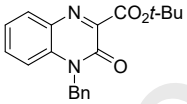
Ethyl 4-benzyl-3-oxo-3,4-dihydrobenzo[*g*]quinoxaline-2-carboxylate (2u-1)

Yellow oil; R_f = 0.50 (petroleum ether : EtOAc = 3 : 1); yield: 23 mg (13%); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 8.48 (s, 1H), 7.90 (d, *J* = 8.4 Hz, 1H), 7.78 (d, *J* = 8.4 Hz, 1H), 7.60 (s, 1H), 7.55 (t, *J* = 7,6 Hz, 1H), 7.47 (d, *J* = 9.2 Hz, 1H), 7.34-7.26 (m, 5H), 5.57 (s, 2H), 4.55 (q, *J* = 7.2 Hz, 2H), 1.48 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 163.7, 152.6, 149.8, 134.8, 134.6, 131.3, 130.9, 129.7, 129.0, 128.87, 128.76, 127.8, 127.4, 127.0, 125.8, 111.3, 62.6, 46.0, 14.2; HRMS (ESI): calcd. for $C_{22}H_{18}N_2O_3$ + Na = 381.1210, found: 381.1205.



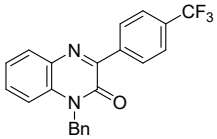
Ethyl 4-benzyl-3-oxo-3,4-dihydrobenzo[*f*]quinoxaline-2-carboxylate (2u-2)

Pale yellow solid; mp 129-130 °C; yield: 55 mg (30%); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 8.93 (d, *J* = 8.8 Hz, 1H), 7.90 (d, *J* = 9.2 Hz, 1H), 7.78 (d, *J* = 8.0 Hz, 1H), 7.69 (t, *J* = 7,6 Hz, 1H), 7.55 (t, *J* = 7,6 Hz, 1H), 7.37 (d, *J* = 9.2 Hz, 1H), 7.32-7.24 (m, 5H), 5.60 (s, 2H), 4.57 (q, *J* = 7.2 Hz, 2H), 1.50 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 164.2, 153.1, 146.1, 134.8, 134.1, 132.1, 131.2, 129.7, 129.0, 128.6, 127.8, 127.6, 127.2, 126.9, 126.7, 123.3, 113.8, 62.3, 46.3, 14.2; EI-MS m/z (rel. int., %): 358 (M^+, 28), 284 (32), 257 (32), 256 (23), 91 (100).



***Tert*-butyl 4-benzyl-3-oxo-3,4-dihydroquinoxaline-2-carboxylate (2v)**

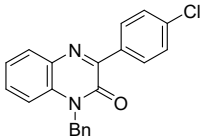
White solid; mp 106-107 °C; yield: 96 mg (57%); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.93 (d, *J* = 8.0 Hz, 1H), 7.49 (t, *J* = 8.0 Hz, 1H), 7.35-7.25 (m, 7H), 5.50 (s, 2H), 1.68 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 163.4, 152.7, 150.4, 134.7, 133.3, 132.2, 131.9, 131.1, 129.0, 127.8, 126.9, 124.0, 114.6, 84.2, 45.9, 28.1; HRMS (ESI): calcd. for $C_{20}H_{20}N_2O_3$ + Na = 359.1366, found: 359.1361.



1-Benzyl-3-(4-(trifluoromethyl)phenyl)quinoxalin-2(1H)-one (4b)

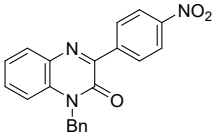
Yellow oil; R_f = 0.21 (petroleum ether : EtOAc = 20 : 1); yield: 106 mg (56%); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 8.52 (d, *J* = 8.4 Hz, 2H), 7.96 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.73 (d, *J* = 8.4 Hz, 2H), 7.48 (td, *J* = 8.0, 1.2 Hz, 1H), 7.37-7.26 (m, 7H), 5.57 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 154.6, 152.6, 139.2, 135.1, 133.2, 132.9, 132.3, 132.0,

131.7, 131.4, 131.0, 130.8, 130.0, 128.1, 127.8, 126.9, 125.4, 124.98, 124.95, 124.91, 124.87, 124.0, 122.7, 120.0, 114.4, 46.2; HRMS (ESI): calcd. for $C_{22}H_{15}F_3N_2O$ + H = 381.1209, found: 381.1210.



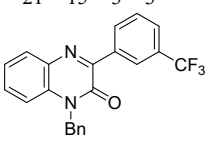
1-Benzyl-3-(4-chlorophenyl)quinoxalin-2(1H)-one (4c)

Yellow oil; R_f = 0.30 (petroleum ether : EtOAc = 10 : 1); yield: 82 mg (47%); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 8.40 (d, *J* = 8.8 Hz, 2H), 7.93 (d, *J* = 7.6 Hz, 1H), 7.46-7.43 (m, 3H), 7.34-7.25 (m, 7H), 5.55 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 154.6, 152.6, 136.6, 135.2, 134.4, 133.2, 132.7, 131.1, 130.6, 130.5, 128.9, 128.3, 127.7, 126.9, 123.9, 114.4, 46.1; HRMS (ESI): calcd. for $C_{21}H_{15}ClN_2O$ + H = 347.0946, found: 347.0945.



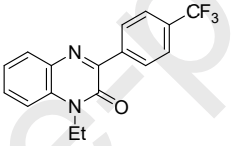
1-Benzyl-3-(4-nitrophenyl)quinoxalin-2(1H)-one (4d)

Yellow solid; mp 183-184 °C; yield: 71 mg (39%); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 8.64 (d, *J* = 8.8 Hz, 2H), 8.34 (d, *J* = 8.4 Hz, 2H), 8.00 (d, *J* = 8.0 Hz, 1H), 7.53 (t, *J* = 8.0 Hz, 1H), 7.51-7.34 (m, 7H), 5.60 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 154.6, 151.6, 148.7, 141.8, 135.0, 133.2, 133.0, 131.6, 131.1, 130.7, 129.1, 127.9, 126.9, 124.3, 123.2, 114.6, 46.3; HRMS (ESI): calcd. for $C_{21}H_{15}N_3O_3$ + H = 358.1186, found: 358.1181.



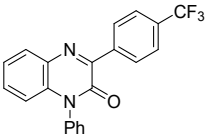
1-Benzyl-3-(3-(trifluoromethyl)phenyl)quinoxalin-2(1H)-one (4e)

White solid; mp 145-146 °C; yield: 95 mg (50%); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 8.78 (s, 1H), 8.65 (d, *J* = 8.0 Hz, 1H), 7.96 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.59 (t, *J* = 8.0 Hz, 1H), 7.45 (td, *J* = 8.4, 1.2 Hz, 1H), 7.34-7.25 (m, 7H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 154.6, 152.2, 136.6, 135.1, 133.1, 132.9, 132.8, 130.9, 130.74, 130.67, 130.4, 128.9, 128.5, 127.7, 126.85, 126.79, 126.62, 126.58, 126.54, 125.49, 124.0, 122.8, 114.4, 46.1; HRMS (ESI): calcd. for $C_{22}H_{15}F_3N_2O$ + H = 381.1209, found: 381.1212.



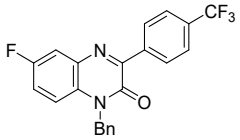
1-Ethyl-3-(4-(trifluoromethyl)phenyl)quinoxalin-2(1H)-one (4f)

Yellow solid; mp 93-94 °C; yield: 88 mg (56%); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 8.48 (d, *J* = 8.0 Hz, 2H), 7.94 (d, *J* = 8.0 Hz, 1H), 7.71 (d, *J* = 8.4 Hz, 2H), 7.60-7.56 (m, 1H), 7.36 (t, *J* = 8.0 Hz, 2H), 4.37 (q, *J* = 7.2 Hz, 2H), 1.41 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 153.9, 152.3, 139.2, 133.2, 132.4, 131.8, 131.4, 130.9, 129.9, 128.1, 125.4, 124.84, 124.81, 124.77, 124.73, 123.7, 122.7, 113.4, 37.6, 12.3; HRMS (ESI): calcd. for $C_{17}H_{13}F_3N_2O$ + H = 319.1053, found: 319.1051.



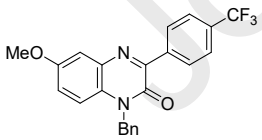
1-Phenyl-3-(4-(trifluoromethyl)phenyl)quinoxalin-2(1H)-one (4g)

White solid; mp 103-104 °C; yield: 86 mg (47%); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 8.56 (d, J = 8.0 Hz, 2H), 8.00-7.98 (m, 1H), 7.71 (d, J = 8.4 Hz, 2H), 7.66-7.62 (m, 2H), 7.59-7.55 (m, 1H), 7.40-7.33 (m, 4H), 6.72-6.70 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 154.3, 152.8, 139.0, 135.9, 134.3, 132.8, 132.0, 131.7, 130.6, 130.4, 130.3, 130.0, 129.7, 129.5, 129.2, 128.2, 125.6, 125.4, 124.92, 124.88, 124.84, 124.81, 124.1, 122.7, 115.4; HRMS (ESI): calcd. for $C_{21}H_{13}F_3N_2O$ + H = 367.1053, found: 367.1052.



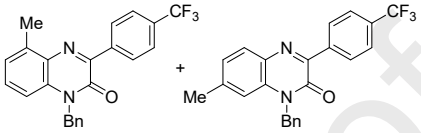
1-Benzyl-6-fluoro-3-(4-(trifluoromethyl)phenyl)quinoxalin-2(1H)-one (4h)

White solid; mp 138-139 °C; yield: 116 mg (59%); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 8.52 (d, J = 8.4 Hz, 2H), 7.72 (d, J = 8.4 Hz, 2H), 7.63 (dd, J = 8.4, 2.8 Hz, 1H), 7.34-7.20 (m, 7H), 5.53 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 160.0, 157.5, 154.2, 153.7, 138.8, 134.8, 133.8, 133.6, 132.3, 132.0, 131.6, 130.1, 129.49, 129.47, 129.0, 128.0, 127.9, 126.8, 125.3, 125.0, 124.93, 124.90, 124.86, 122.6, 118.9, 118.7, 116.0, 115.8, 115.65, 115.56, 46.4; HRMS (ESI): calcd. for $C_{22}H_{14}F_4N_2O$ + H = 399.1115, found: 399.1120.



1-Benzyl-6-methoxy-3-(4-(trifluoromethyl)phenyl)quinoxalin-2(1H)-one (4i)

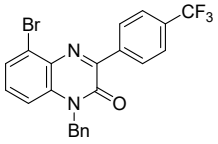
Yellow solid; mp 121-122 °C; yield: 64 mg (31%); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 8.52 (d, J = 8.4 Hz, 2H), 7.72 (d, J = 8.4 Hz, 2H), 7.40 (d, J = 2.8 Hz, 1H), 7.32-7.19 (m, 6H), 7.09 (dd, J = 9.2, 2.8 Hz, 1H), 5.53 (s, 2H), 3.86 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 156.2, 154.2, 152.8, 139.3, 135.2, 134.0, 131.9, 131.6, 130.0, 128.9, 128.7, 127.7, 127.1, 126.9, 125.4, 124.9, 124.85, 124.81, 122.7, 120.5, 115.3, 111.8, 55.7, 46.2; HRMS (ESI): calcd. for $C_{23}H_{17}F_3N_2O_2$ + H = 411.1315, found: 411.1313.



1-Benzyl-5-methyl-3-(4-(trifluoromethyl)phenyl)quinoxalin-2(1H)-one (4j-1)

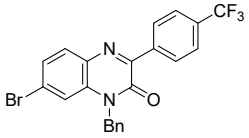
1-Benzyl-7-methyl-3-(4-(trifluoromethyl)phenyl)quinoxalin-2(1H)-one (4j-2)

White solid; mp 144-145 °C; yield: 127 mg (64%); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 8.62 (d, J = 8.4 Hz, 1H), 8.51 (d, J = 8.4 Hz, 1H), 7.80 (d, J = 8.0 Hz, 0.5H), 7.70 (d, J = 8.0 Hz, 1H), 7.69 (d, J = 8.0 Hz, 1H), 7.34-7.20 (m, 5.5H), 7.17-7.07 (m, 2H), 5.51-5.50 (m, 2H), 2.73 (s, 1.6H), 2.40 (s, 1.4H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 154.6, 154.4, 151.0, 150.0, 142.0, 139.6, 139.3, 135.3, 135.2, 133.0, 132.8, 131.71, 131.66, 131.4, 131.3, 130.8, 130.5, 129.9, 129.8, 128.9, 128.8, 127.7, 127.6, 126.9, 126.8, 125.45, 125.39, 125.1, 124.81, 124.78, 124.7, 122.8, 114.3, 112.3, 46.2, 46.0, 22.1, 17.5; HRMS (ESI): calcd. for $C_{23}H_{17}F_3N_2O$ + H = 395.1366, found: 395.1367



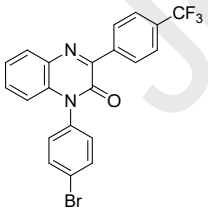
1-Benzyl-5-bromo-3-(4-(trifluoromethyl)phenyl)quinoxalin-2(1H)-one (4k-1)

Yellow solid; mp 165-164 °C; yield: 72 mg (32%); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 8.69 (d, J = 8.0 Hz, 2H), 7.75 (d, J = 8.4 Hz, 2H), 7.62 (dd, J = 7.6, 1.6 Hz, 1H), 7.34-7.23 (m, 7H), 5.56 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 154.3, 152.2, 138.8, 134.8, 134.2, 132.4, 132.1, 131.8, 131.2, 130.7, 130.6, 130.4, 129.6, 129.1, 128.84, 128.76, 128.1, 127.9, 126.81, 126.77, 125.9, 125.4, 125.09, 125.05, 125.02, 124.98, 122.7, 120.0, 114.1, 46.5; HRMS (ESI): calcd. for $C_{22}H_{14}BrF_3N_2O$ + H = 459.0314, found: 459.0318.



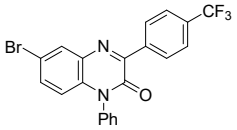
1-Benzyl-7-bromo-3-(4-(trifluoromethyl)phenyl)quinoxalin-2(1H)-one (4k-2)

Yellow solid; mp 181-182 °C; yield: 56 mg (25%); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 8.51 (d, J = 8.4 Hz, 2H), 7.79 (d, J = 8.8 Hz, 1H), 7.73 (d, J = 8.4 Hz, 2H), 7.47 (d, J = 2.0 Hz, 1H), 7.45 (dd, J = 8.4, 2.0 Hz, 1H), 7.35-7.28 (m, 5H), 5.50 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 154.3, 152.6, 138.8, 134.6, 133.8, 132.2, 132.00, 131.95, 130.0, 129.1, 128.0, 127.4, 127.0, 125.4, 125.3. 125.04, 125.00, 124.96, 124.92, 122.6, 117.4, 46.3; HRMS (ESI): calcd. for $C_{22}H_{14}BrF_3N_2O$ + H = 459.0314, found: 459.0317.



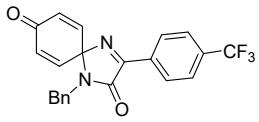
1-(4-Bromophenyl)-3-(4-(trifluoromethyl)phenyl)quinoxalin-2(1H)-one (4l-1)

Pale yellow solid; mp 174-175 °C; yield: 69 mg (31%); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 8.53 (d, J = 8.4 Hz, 2H), 8.01-7.99 (m, 1H), 7.77 (d, J = 8.8 Hz, 2H), 7.71 (d, J = 8.4 Hz, 2H), 7.44-7.36 (m, 2H), 7.25-7.22 (m, 2H), 6.72 (dd, J = 8.0, 1.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 154.1, 152.8, 138.8, 134.8, 134.0, 133.7, 132.8, 132.3, 132.2, 131.8, 131.5, 130.8, 130.5, 130.1, 130.0, 128.1, 127.0, 125.4, 125.0, 124.91, 124.88, 124.4, 123.7, 122.7, 115.2; HRMS (ESI): calcd. for $C_{21}H_{12}BrF_3N_2O$ + H = 445.0158, found: 445.0166.



6-Bromo-1-phenyl-3-(4-(trifluoromethyl)phenyl)quinoxalin-2(1H)-one (4l-2)

Yellow oil; R_f = 0.34 (petroleum ether : EtOAc = 10 : 1); yield: 41 mg (19%); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 8.55 (d, J = 8.4 Hz, 2H), 8.15 (d, J = 2.0 Hz, 1H), 7.72 (d, J = 8.4 Hz, 2H), 7.65 (t, J = 7.6 Hz, 2H), 7.59 (t, J = 7.6 Hz, 1H), 7.47 (dd, J = 8.8, 2.0 Hz, 1H), 7.32 (d, J = 7.2 Hz, 2H), 6.59 (d, J = 9.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 154.0, 153.9, 138.5, 135.5, 133.6, 133.42, 133.36, 132.6, 132.4, 132.1, 130.5, 130.1, 129.8, 128.1, 125.3, 125.0, 124.94, 124.90, 122.6, 116.9, 116.7; HRMS (ESI): calcd. for $C_{21}H_{12}BrF_3N_2O$ + H = 445.0158, found: 445.0157.



1-Benzyl-3-(4-(trifluoromethyl)phenyl)-1,4-diazaspiro[4.5]deca-3,6,9-triene-2,8-dione (5h)

Pale brown solid; mp 182-183; yield: 75 mg (37%); ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 8.65 (d, J = 8.4 Hz, 2H), 7.76 (d, J = 8.0 Hz, 2H), 7.30-7.23 (m, 5H), 6.36 (d, J = 10.0 Hz, 2H), 6.07 (d, J = 9.6 Hz, 2H), 4.61 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, δ

ppm): 165.8, 164.7, 163.1, 142.6, 135.7, 134.2, 133.8, 132.9, 132.0, 129.0, 128.8, 128.7, 128.4, 128.3, 127.7, 125.60, 125.56, 125.52, 125.49, 125.0, 122.2, 80.5, 45.1; HRMS (ESI): calcd. for $C_{22}H_{15}F_3N_2O_2$ + H = 397.1155, found: 397.1159.

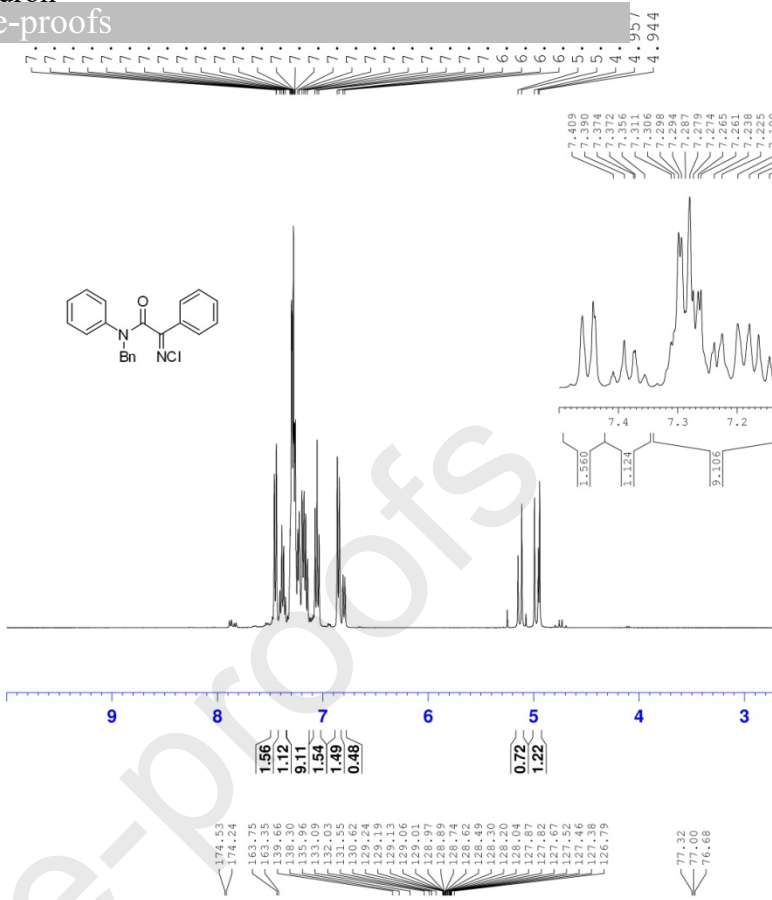
References

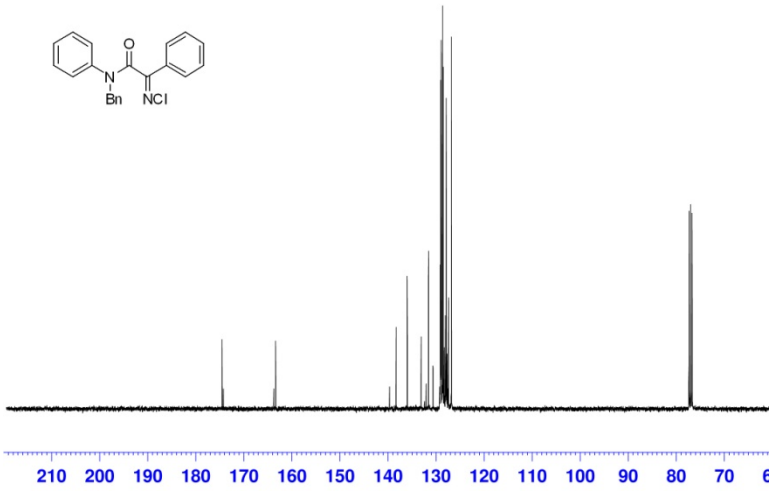
[1] D. Li, T. Yang, H. Su, W. Yu, *Adv. Synth. Catal.* **2015**, *357*, 3696–3702;

[2] R. Reck, J. C. Jochims, *Chem. Ber.* **1982**, *115*, 1494–1508.

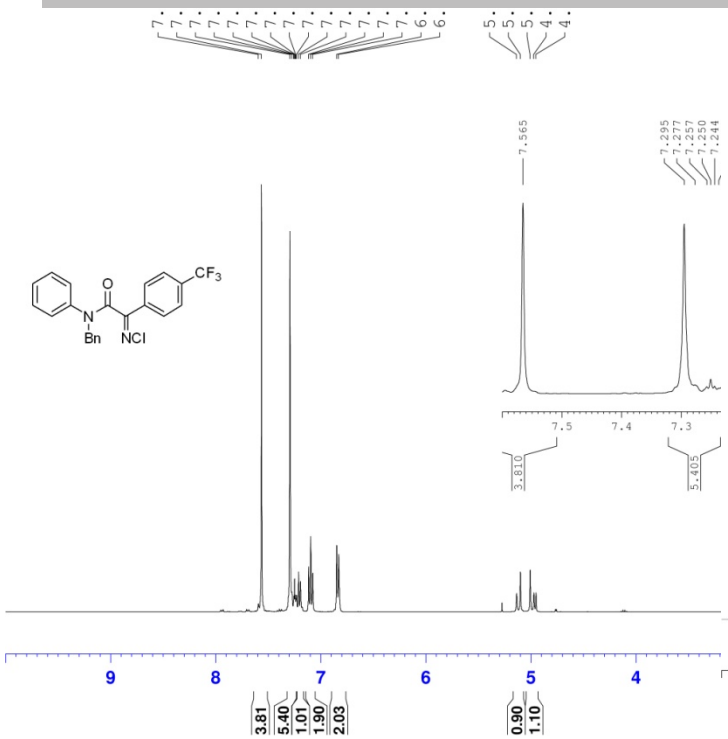
Copies of ^{1}H NMR and ^{13}C NMR spectra of the substrates 3

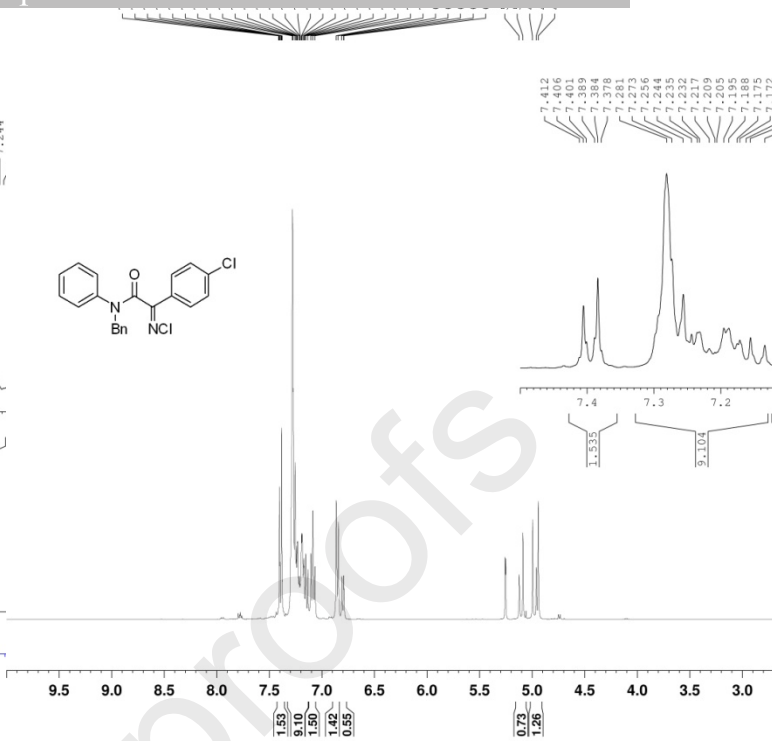
3a

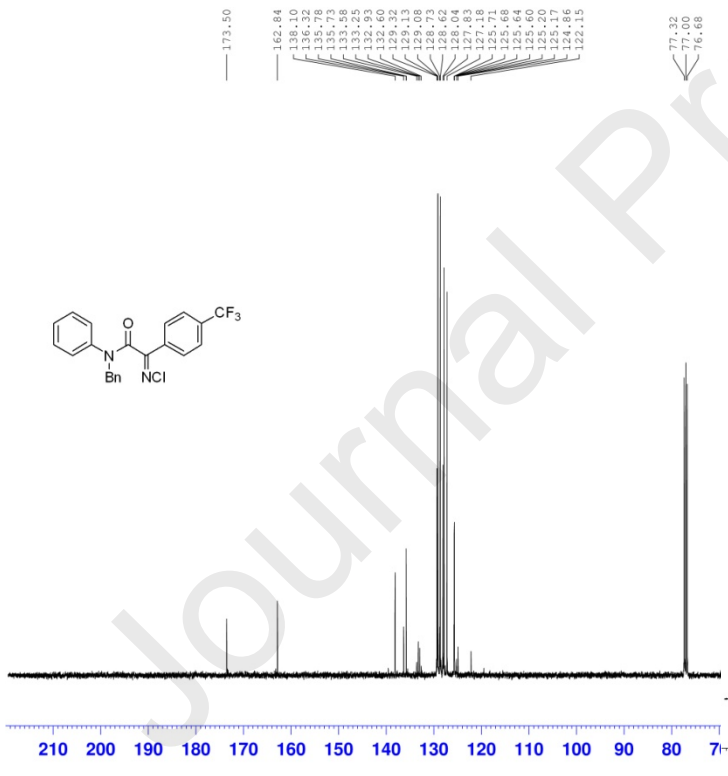


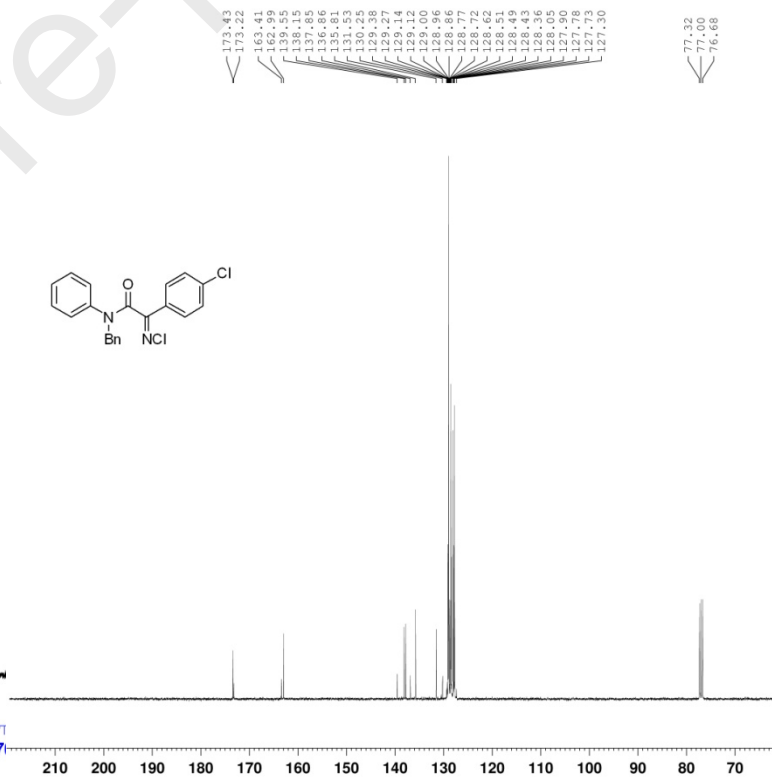


3b



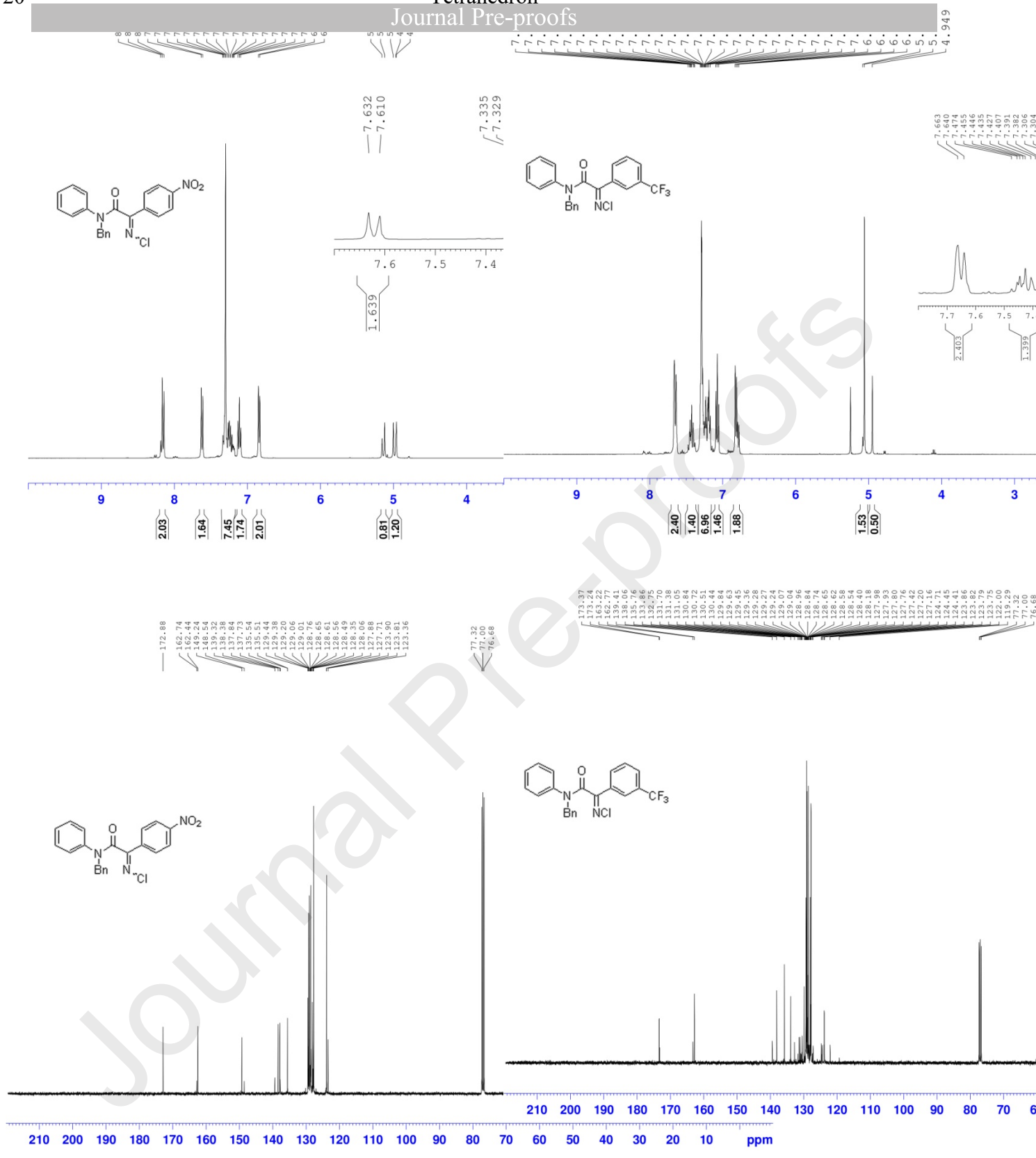




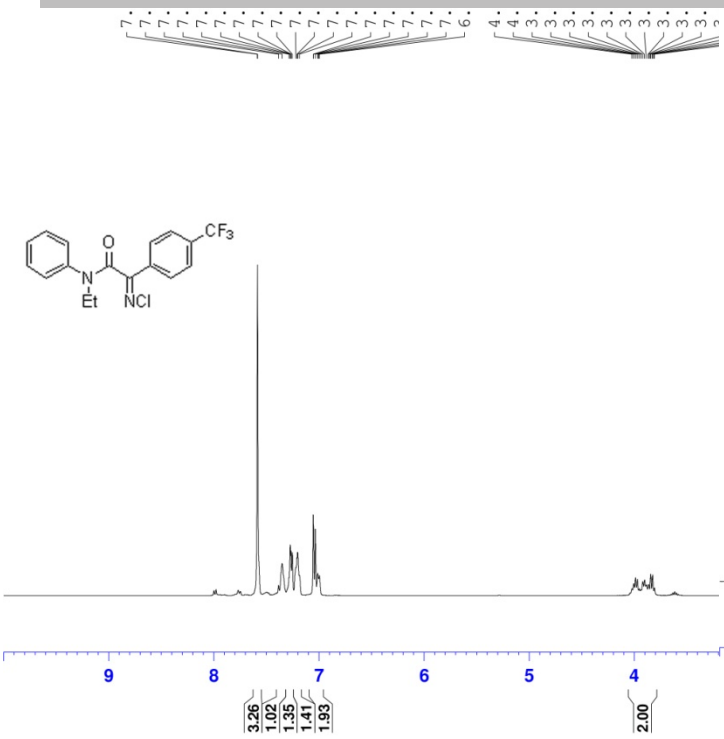


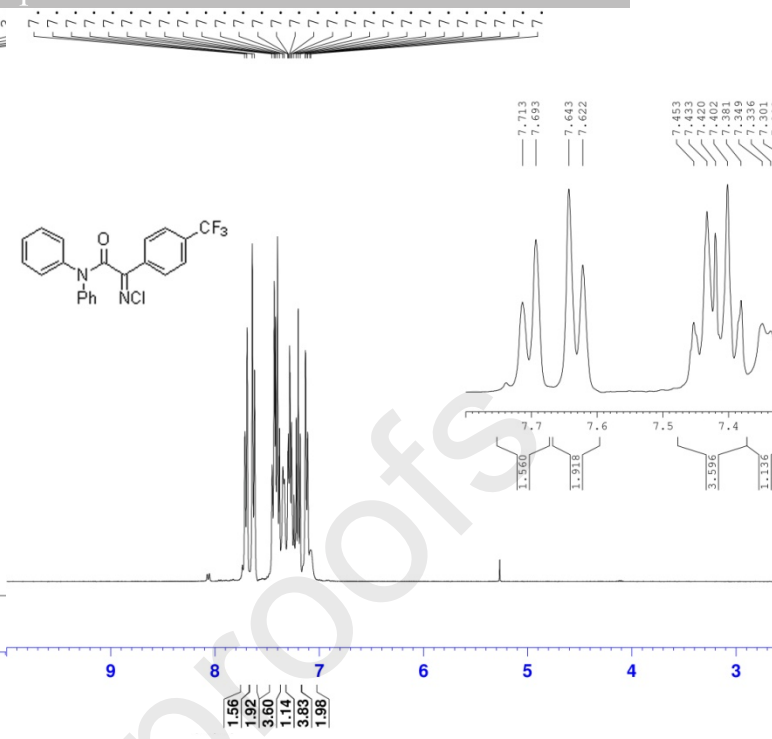
3c

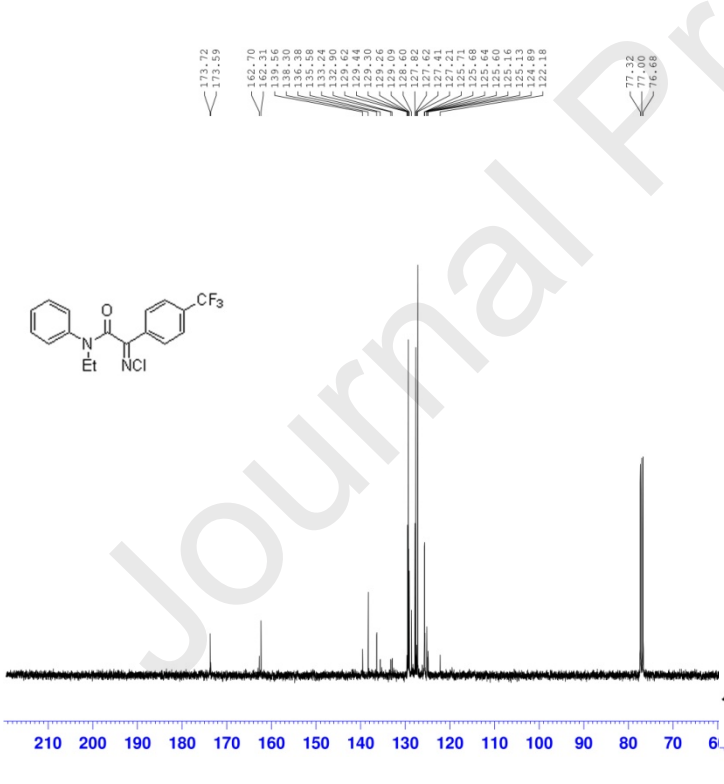
3d

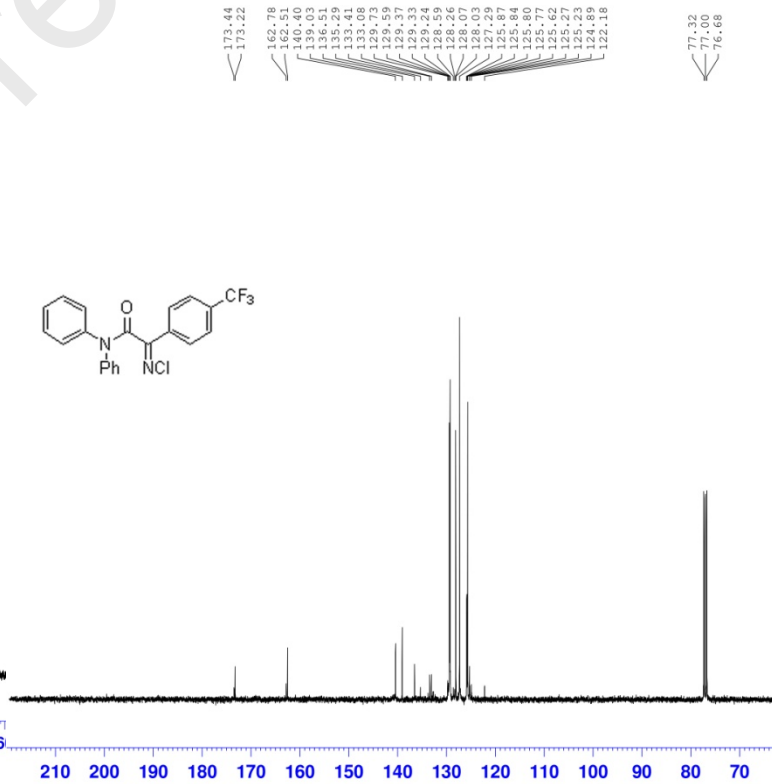


3e **3f**



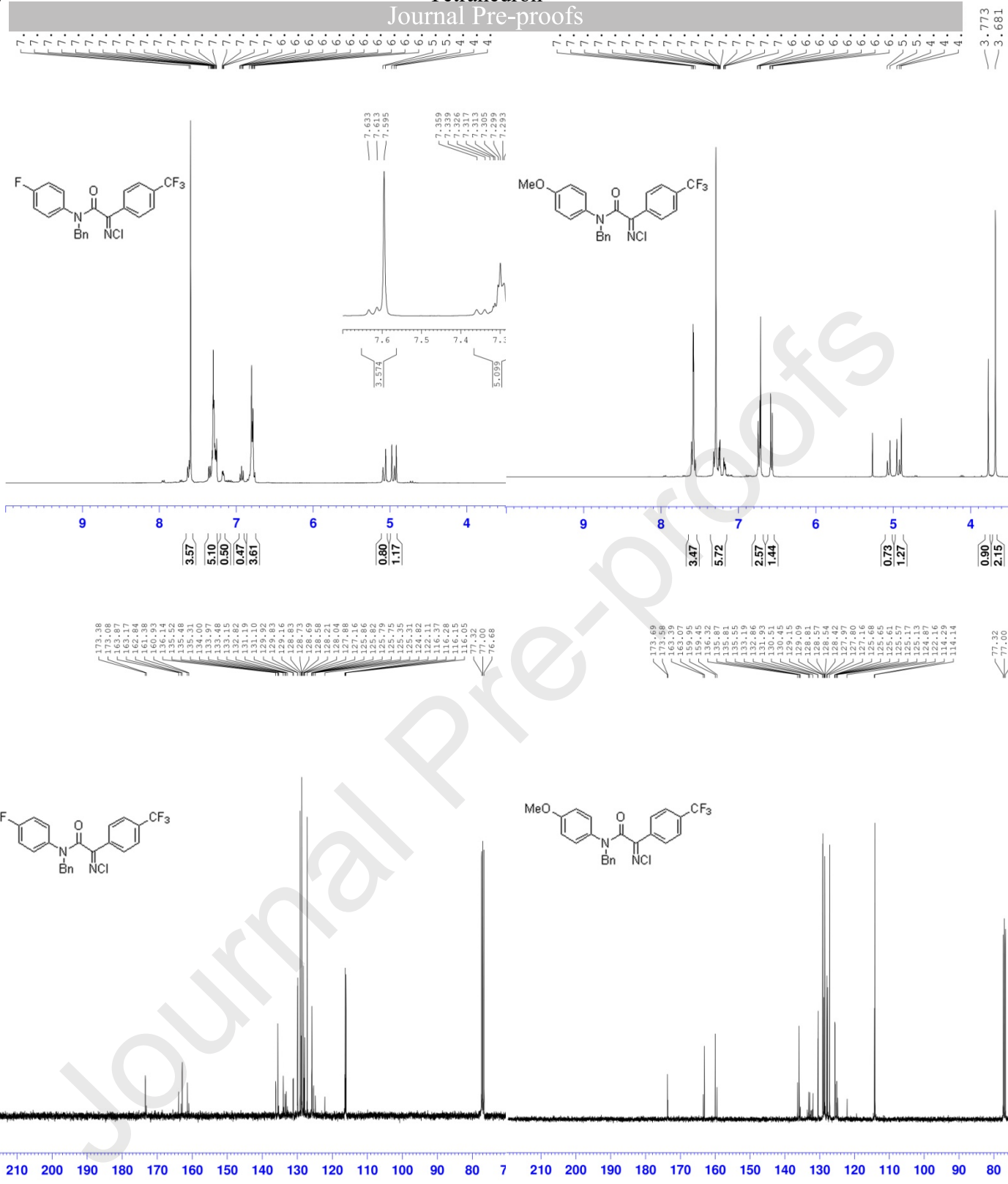




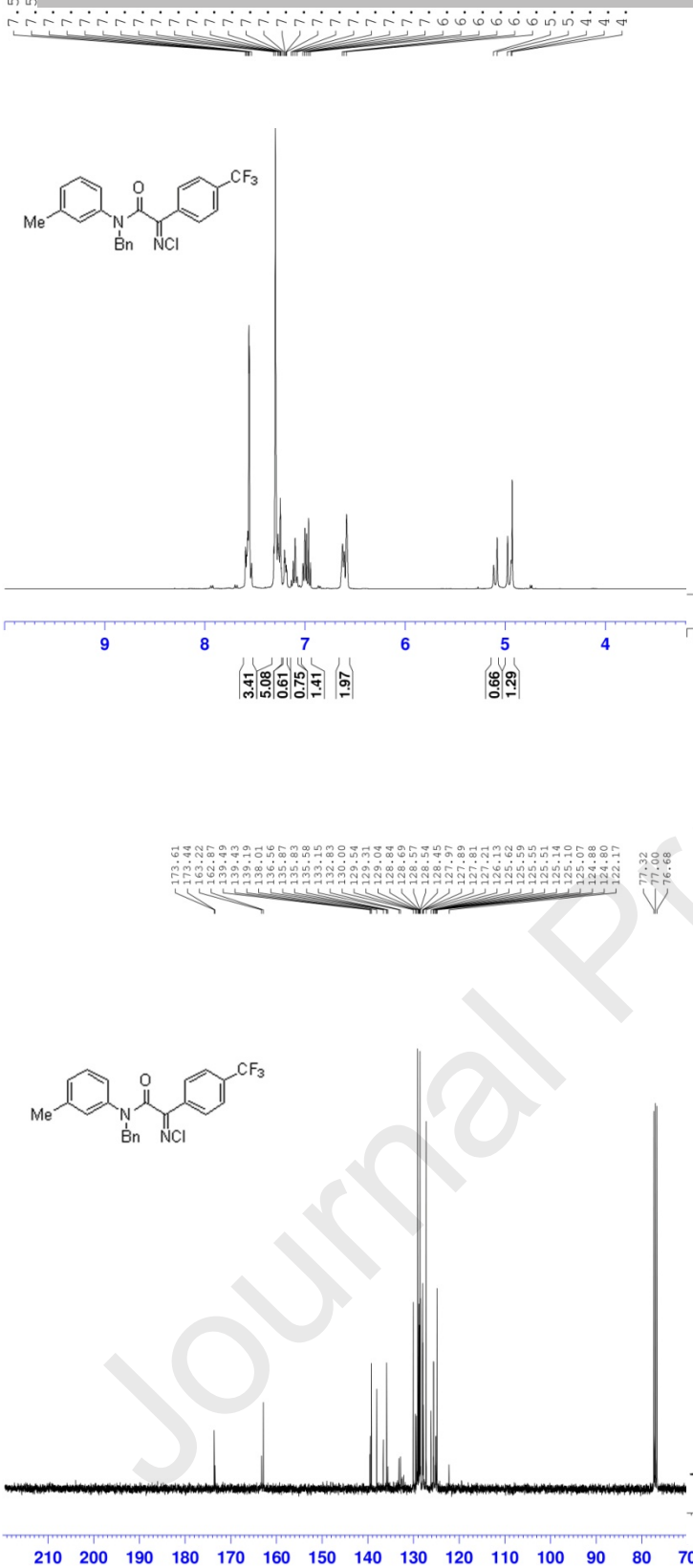


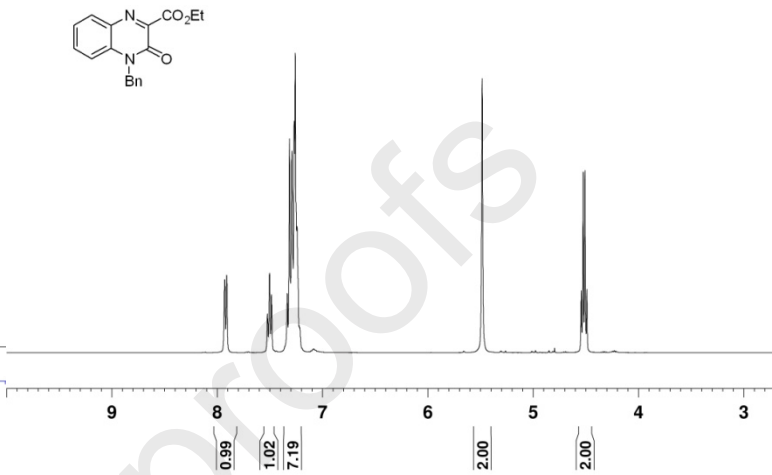
3g

3h

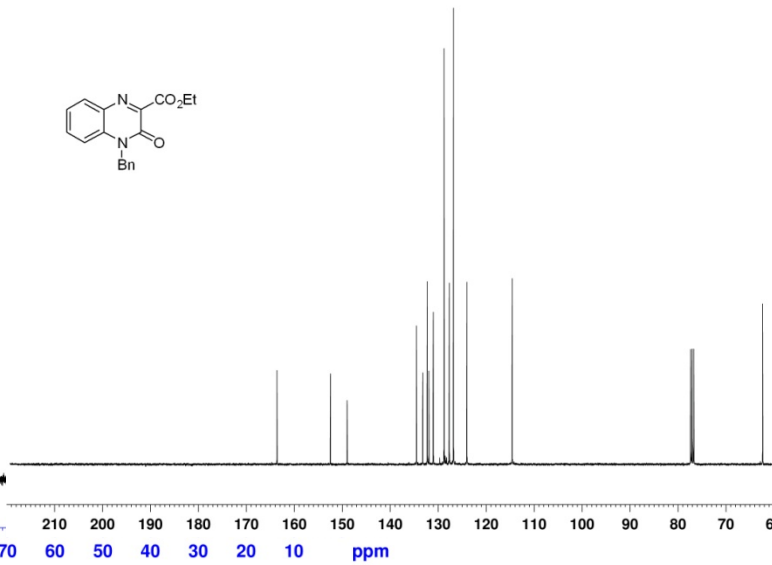


3i **3j**



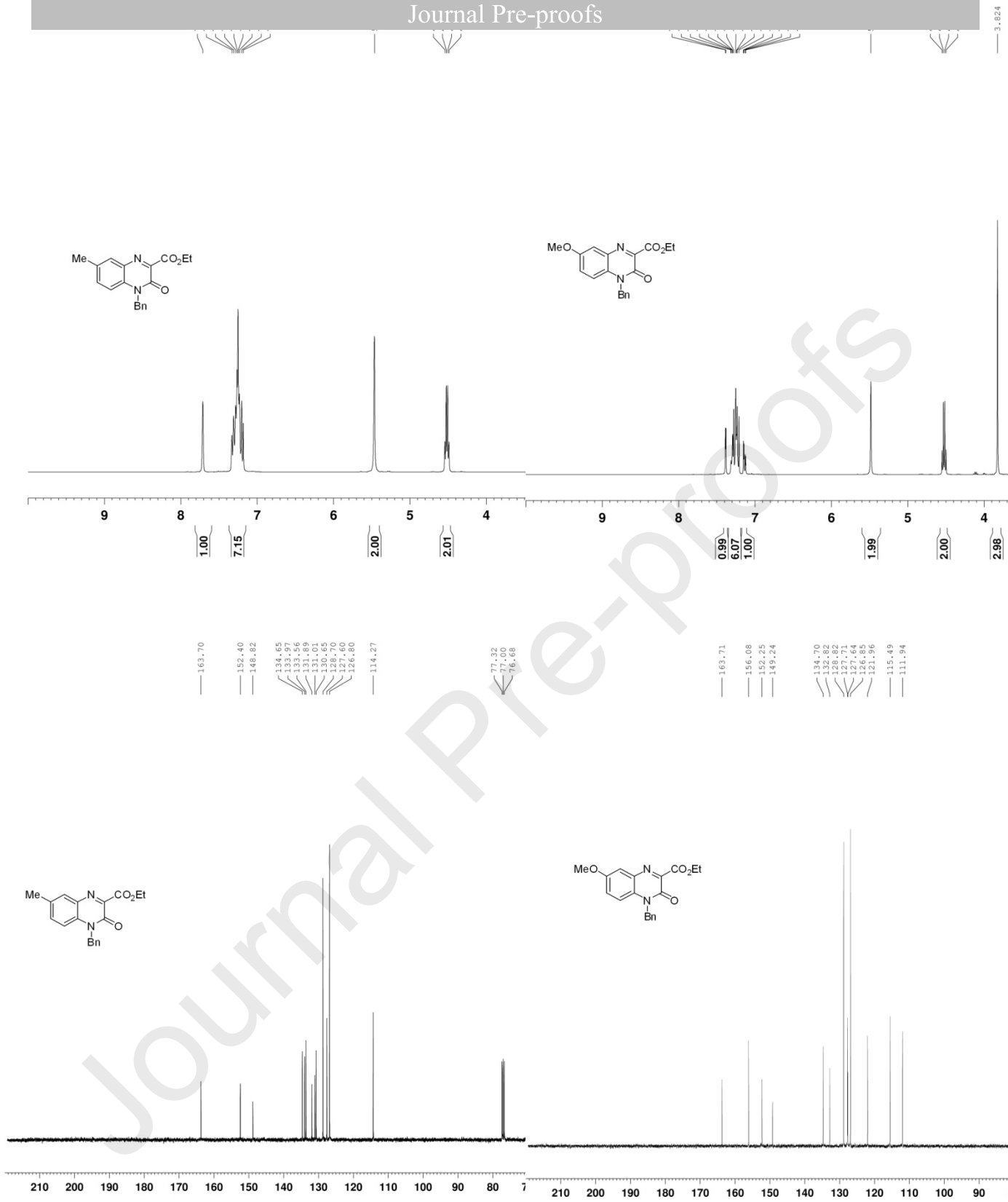


2a

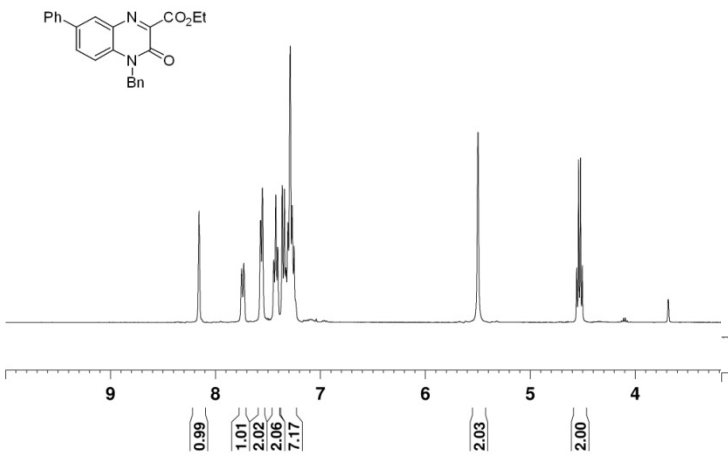


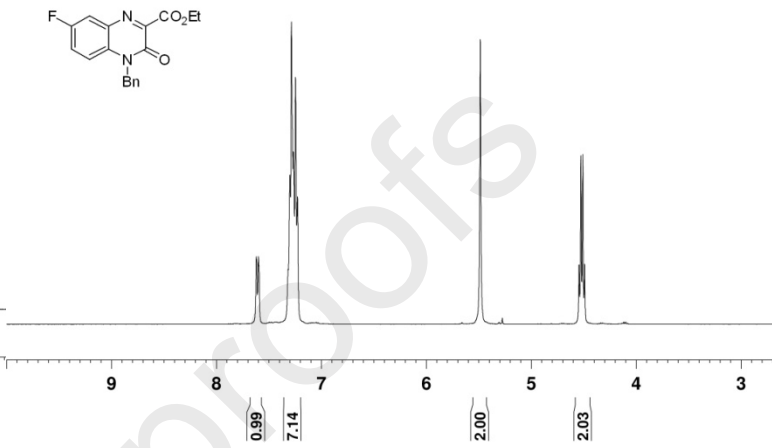
2b

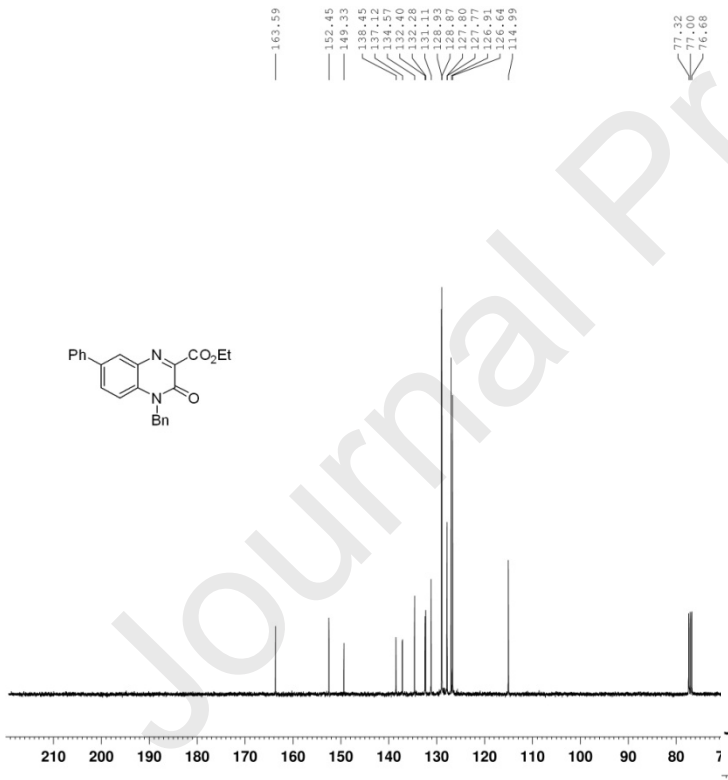
Copies of ^{1}H NMR and ^{13}C NMR spectra of the products

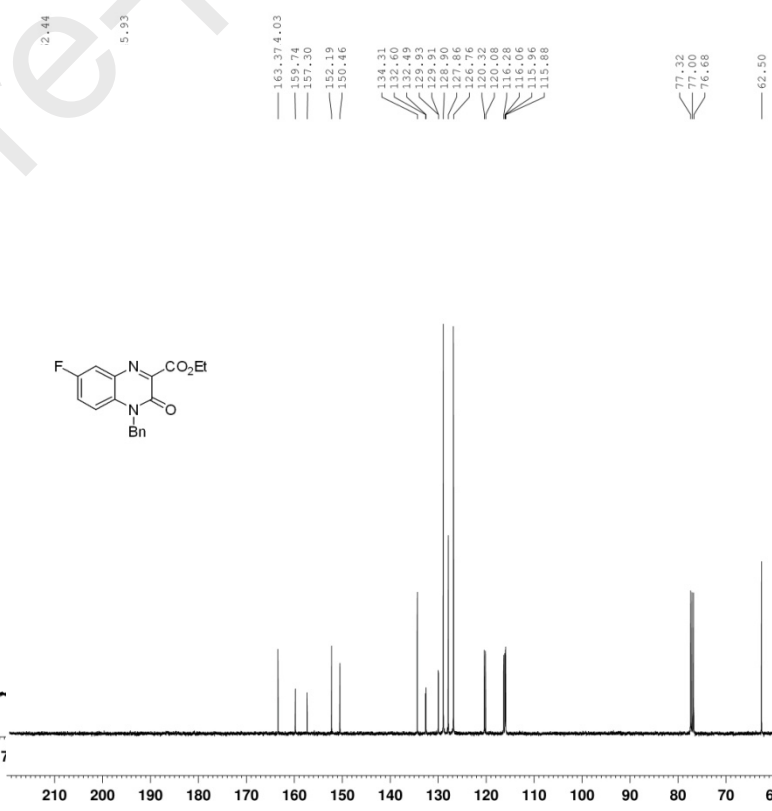


2c **2d**

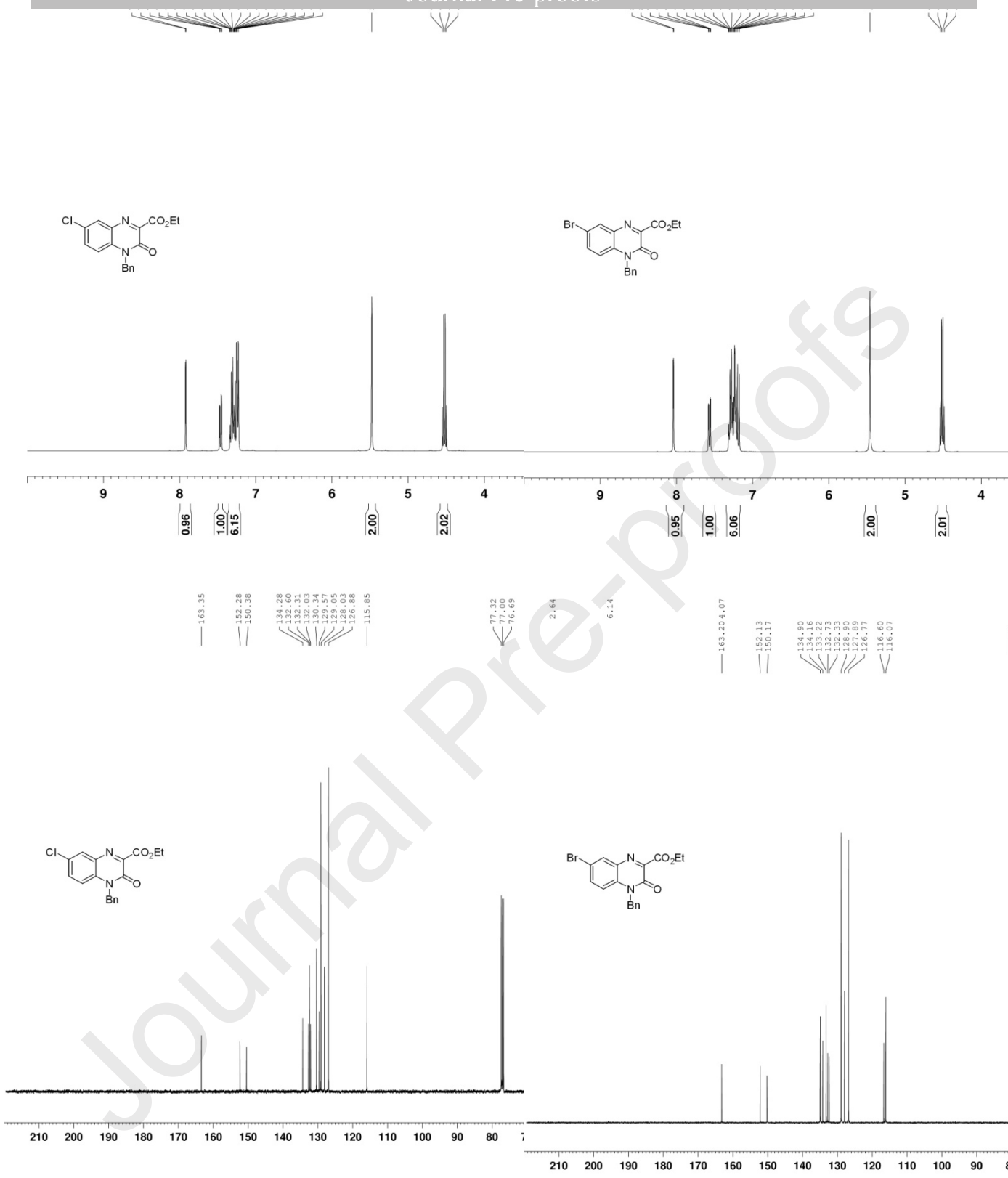




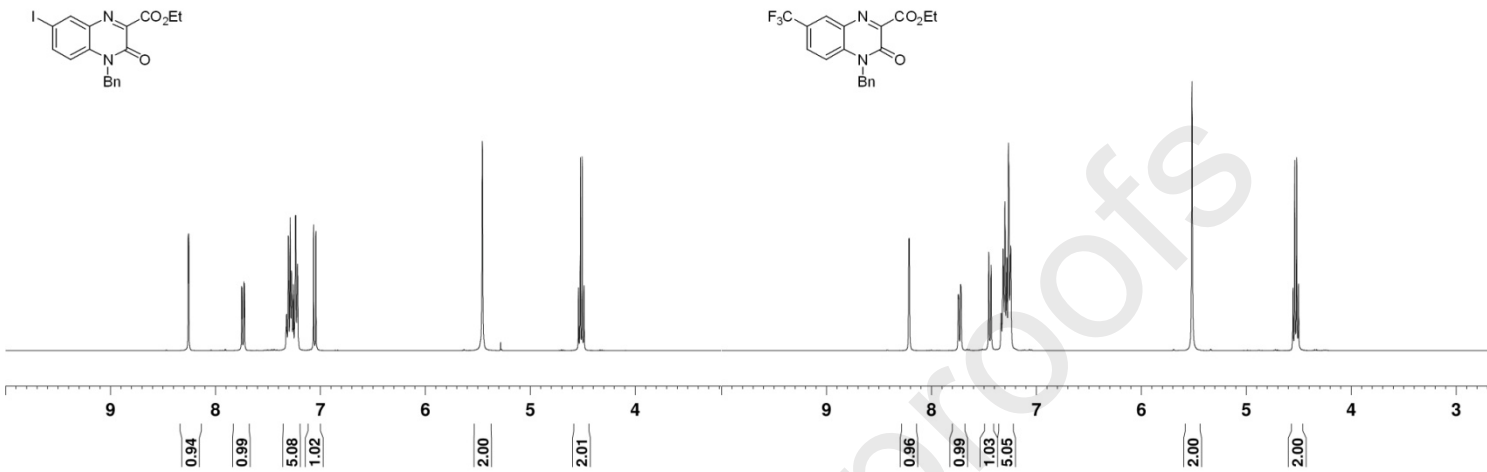


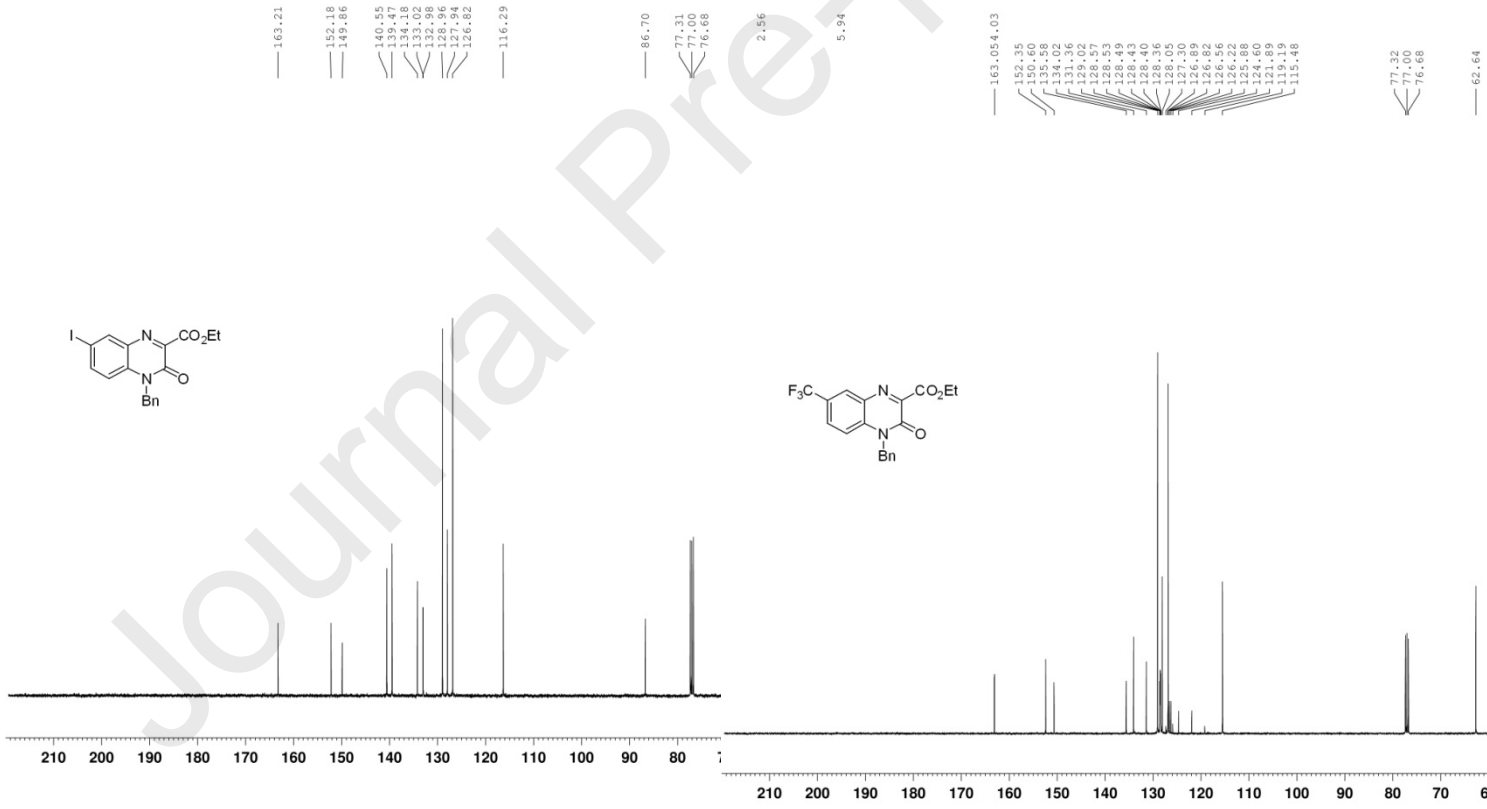


2e **2f**

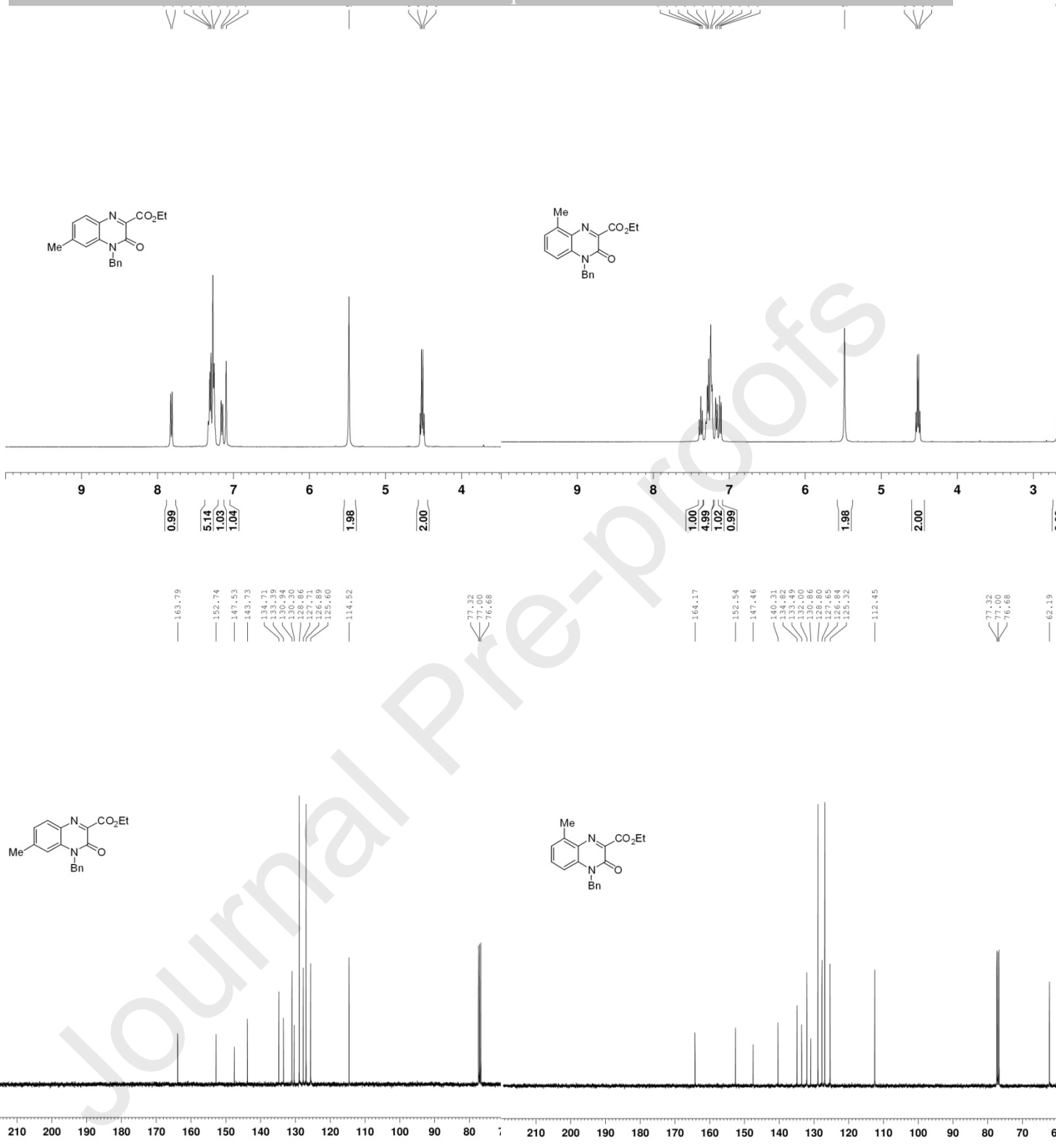


2g **2h**

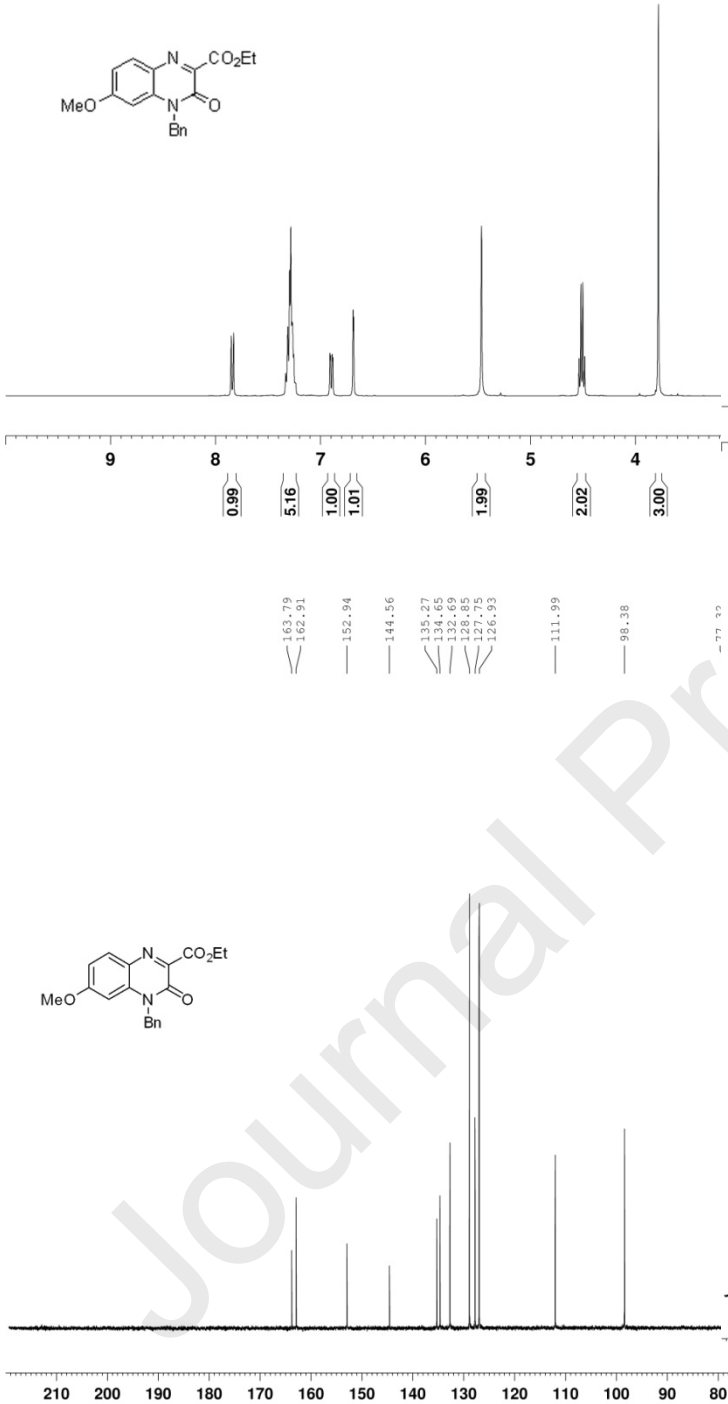




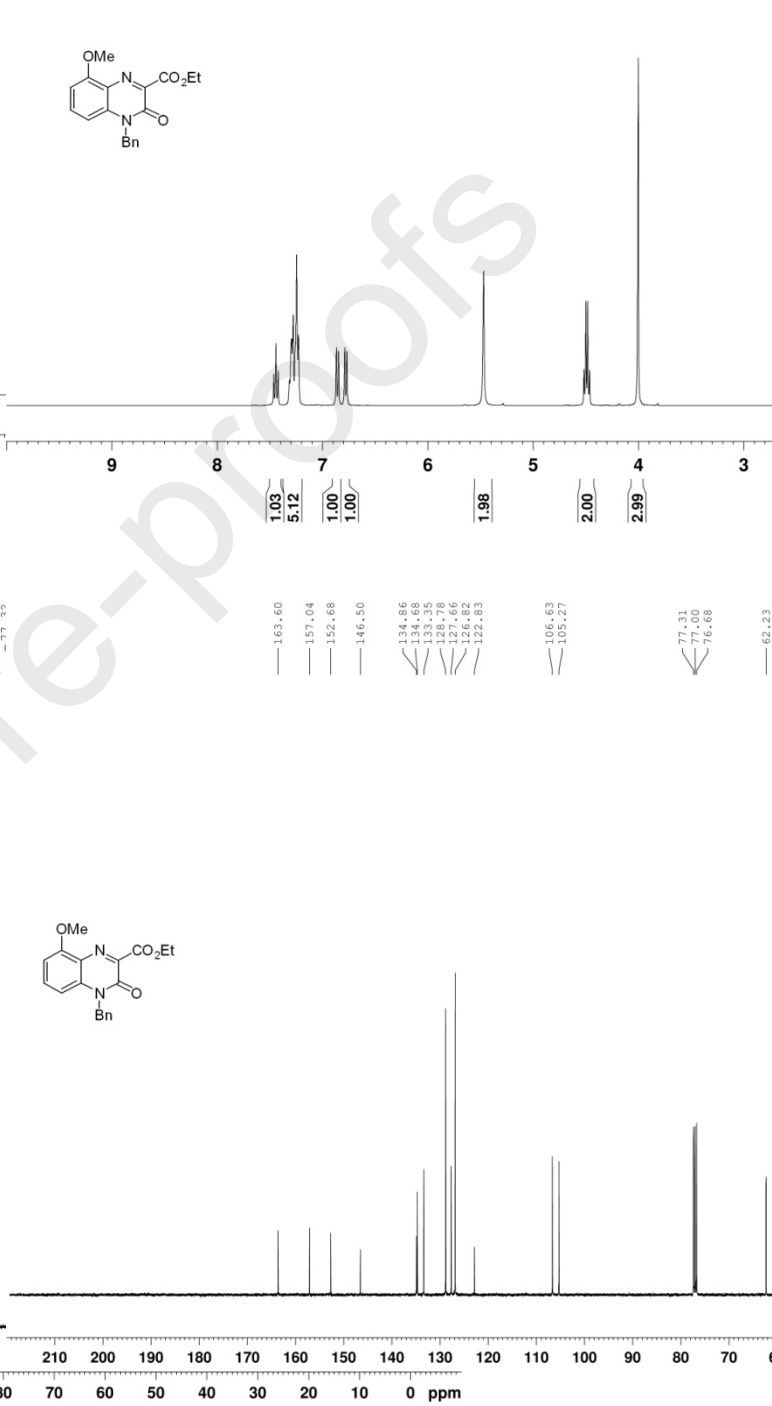
2i **2j-1**



2j-2 **2k-1**



2k-2



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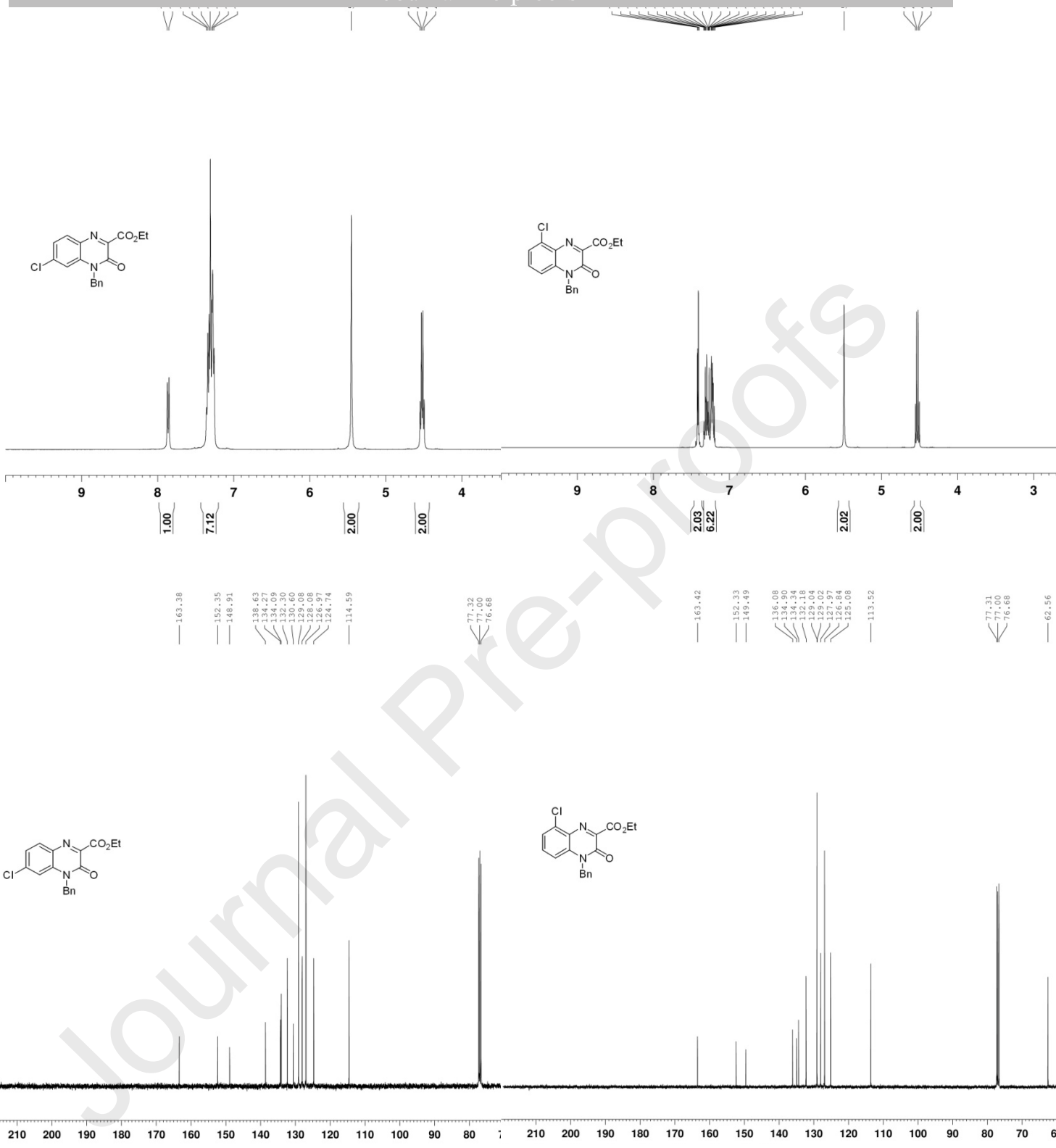

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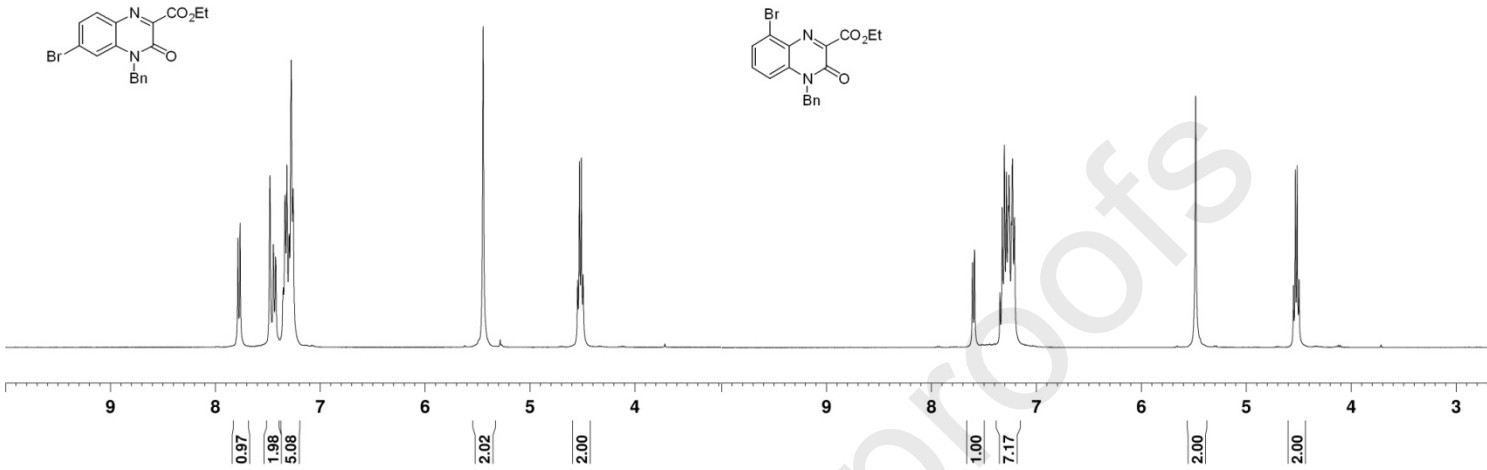
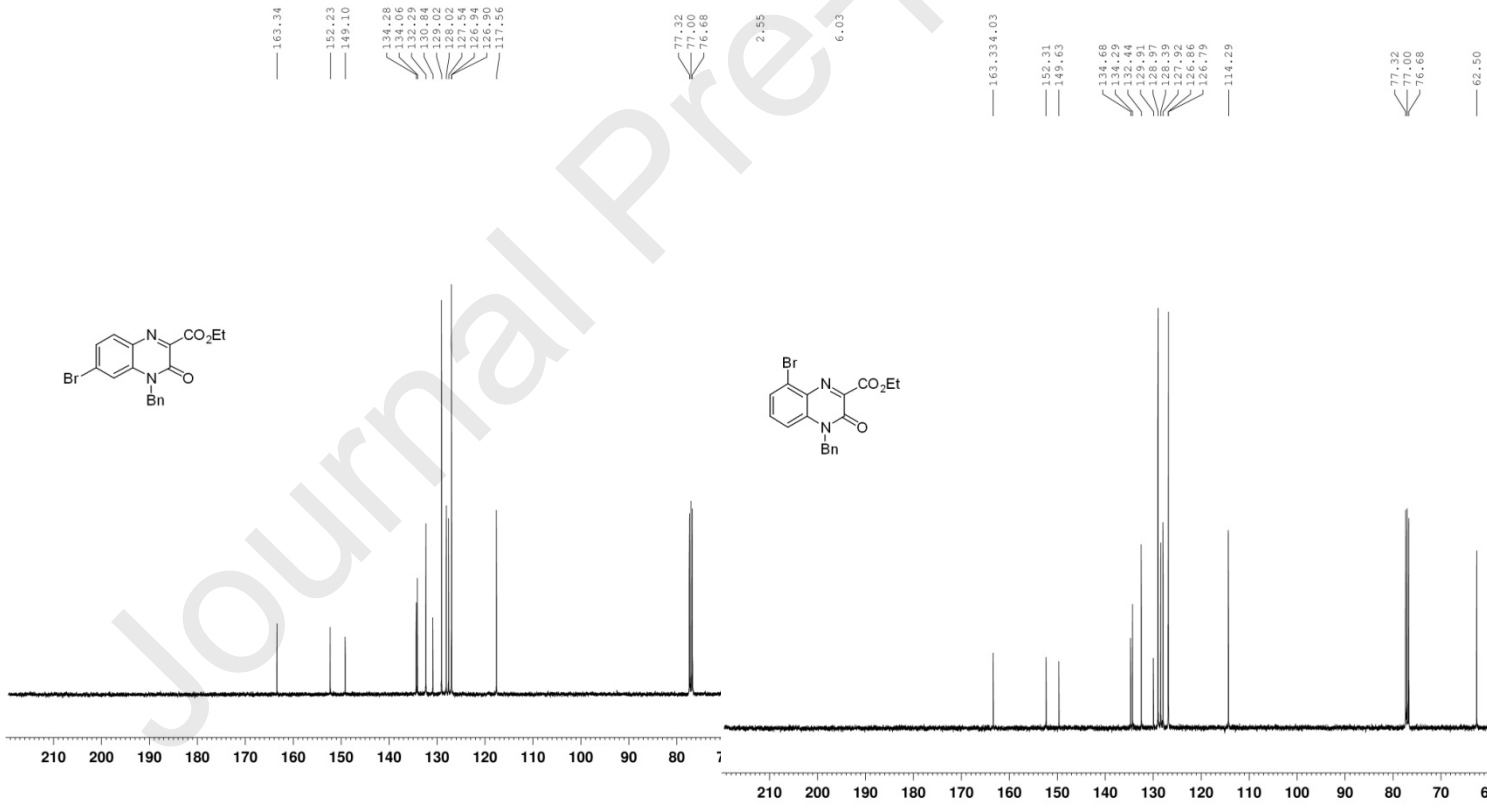
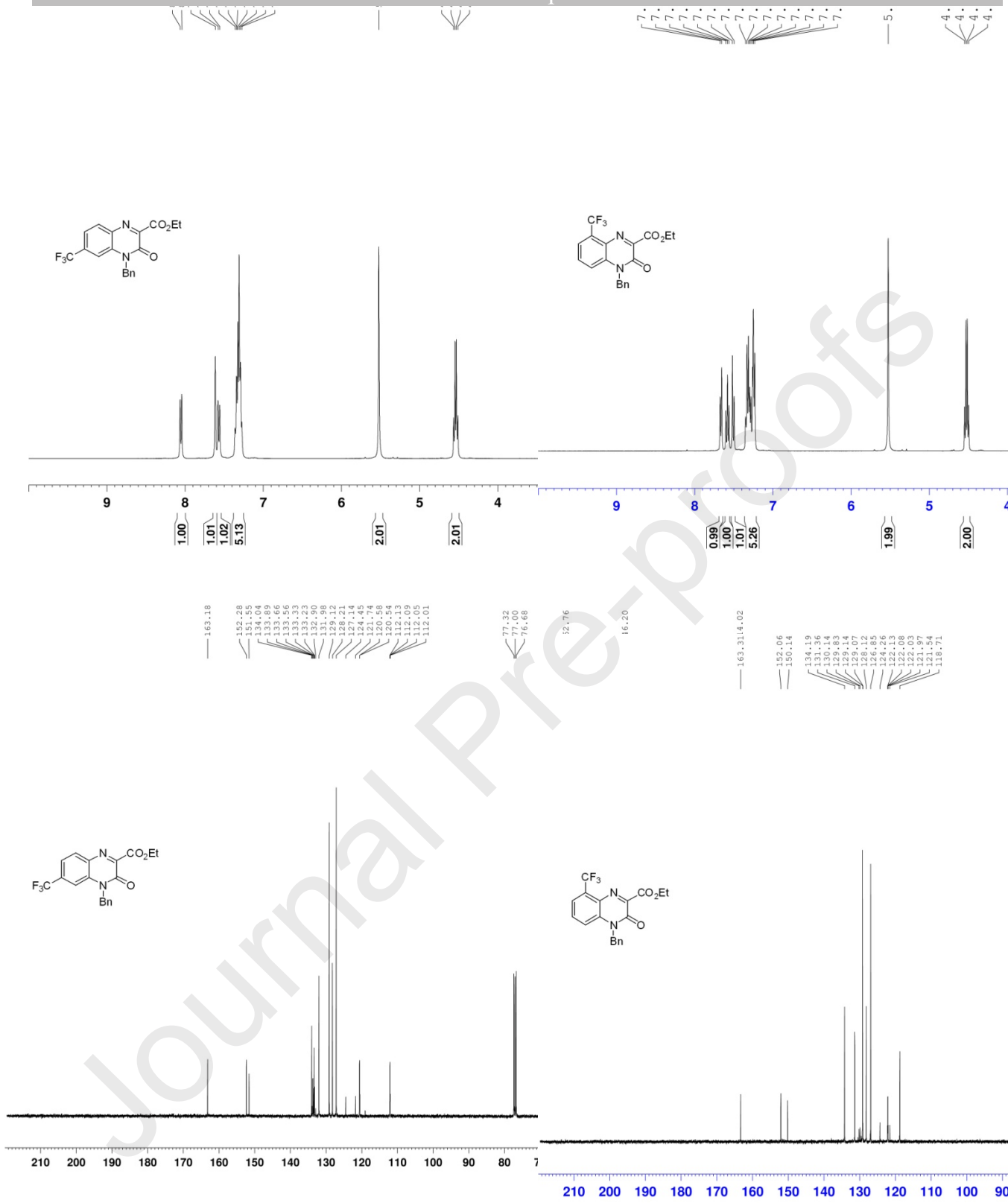




2m-2

2n-1



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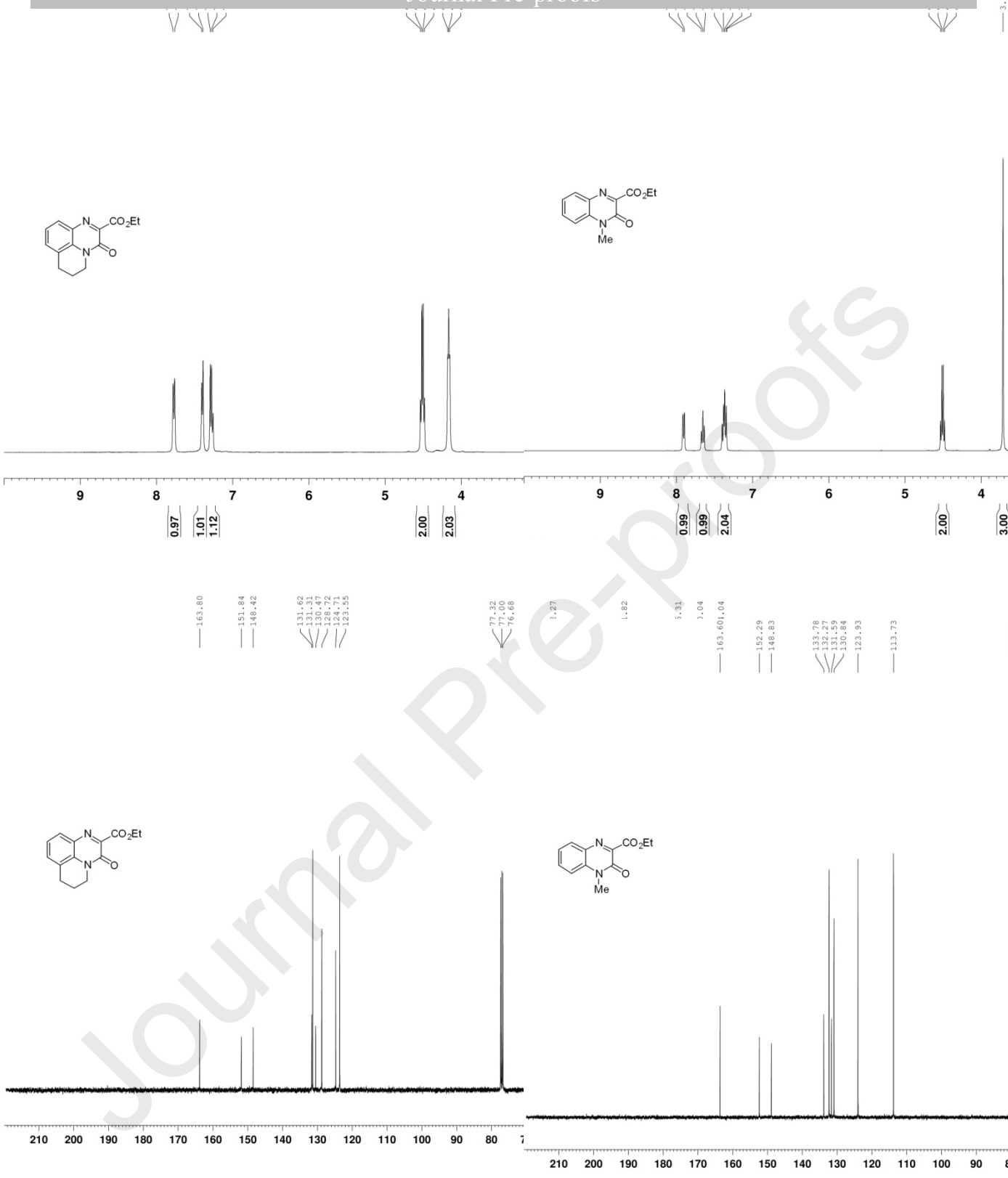
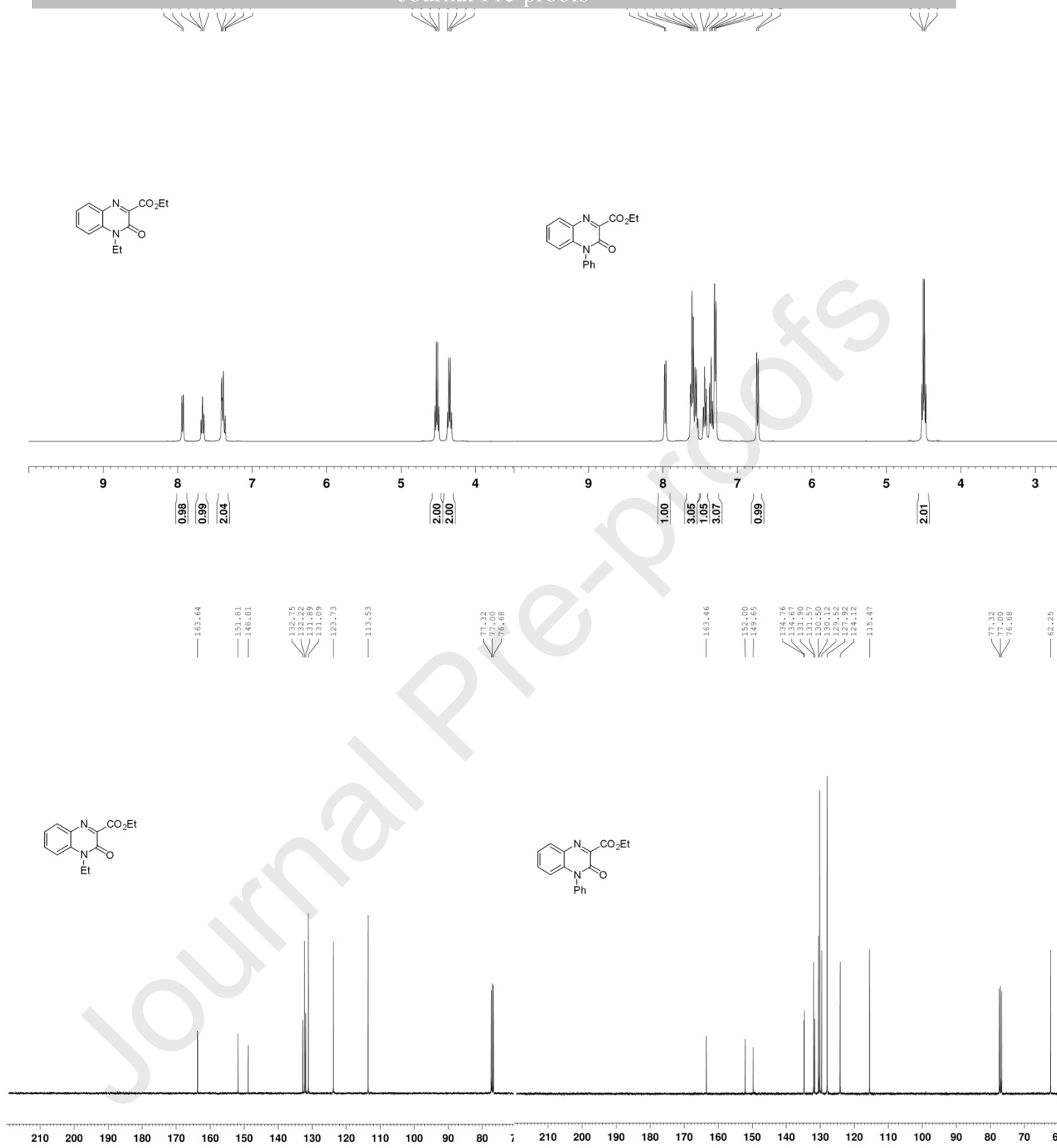
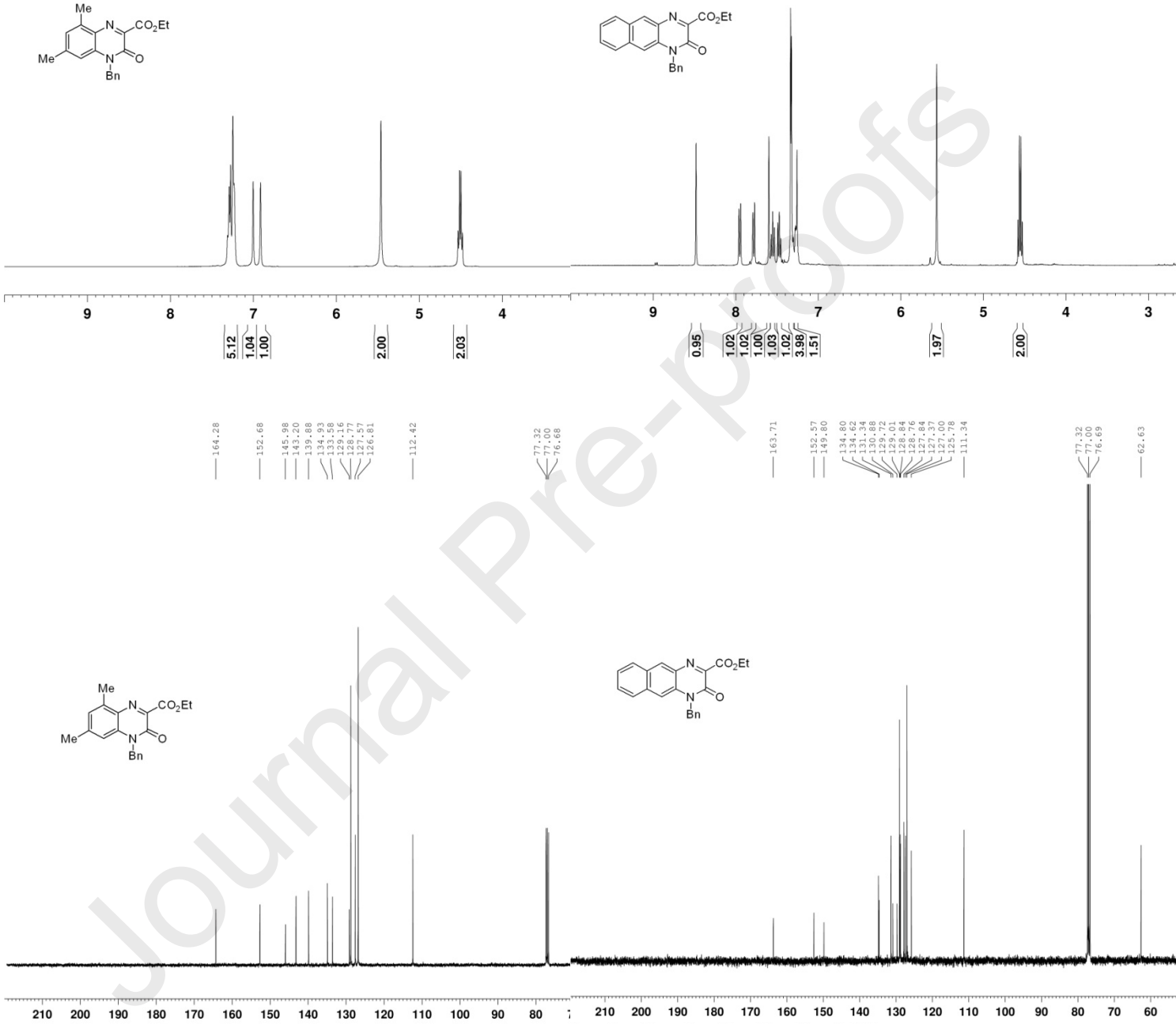


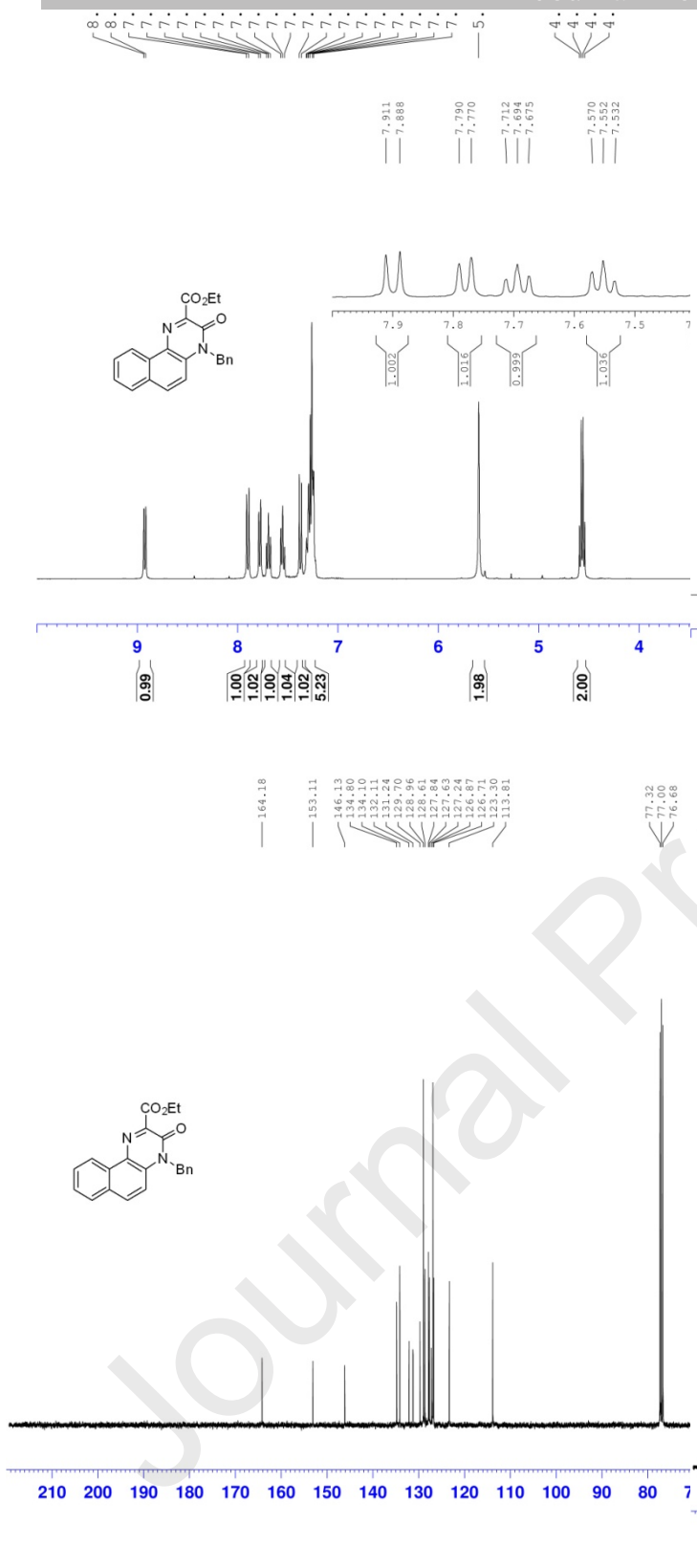
2p **2q**



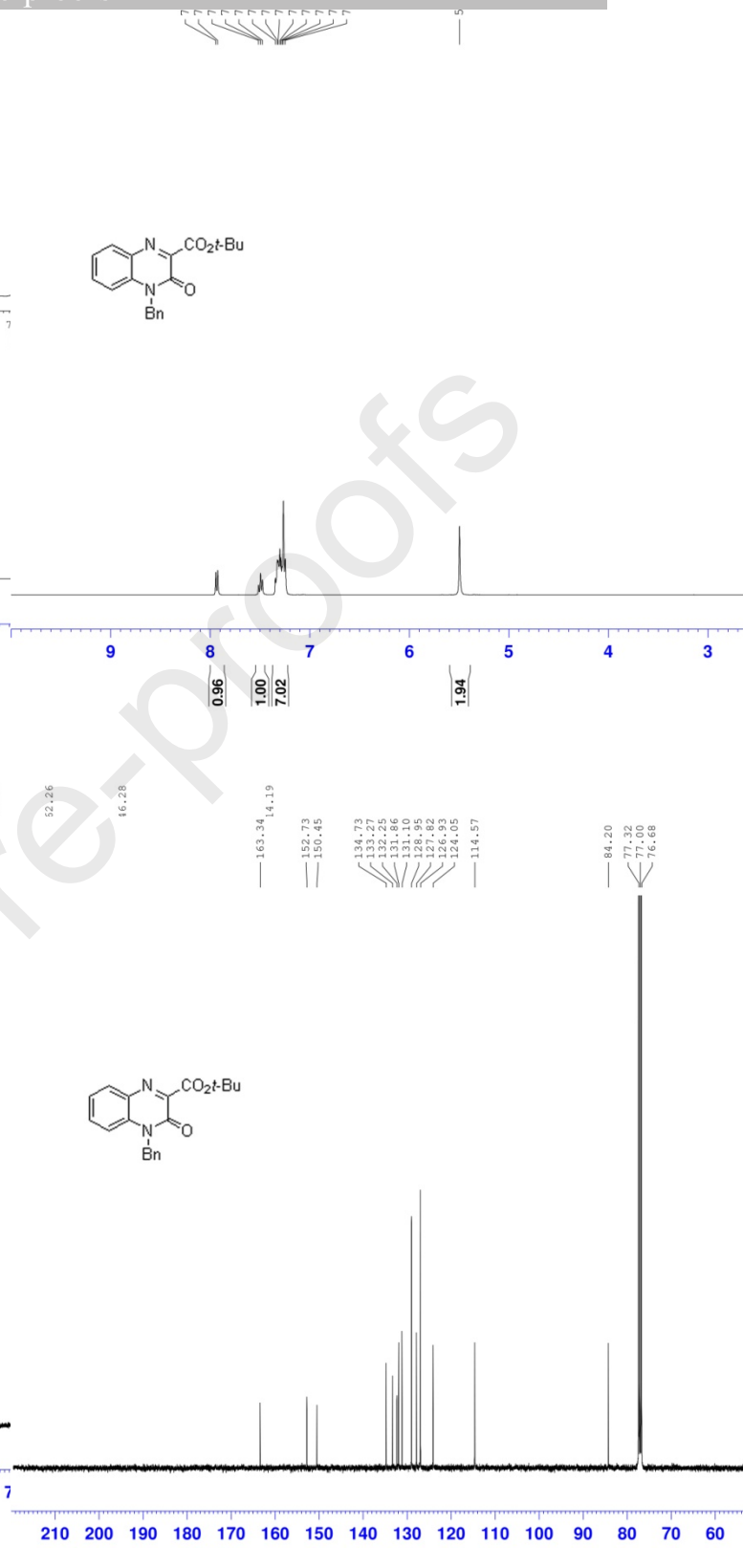
2r **2t**



2u-1 **2u-2**



2v



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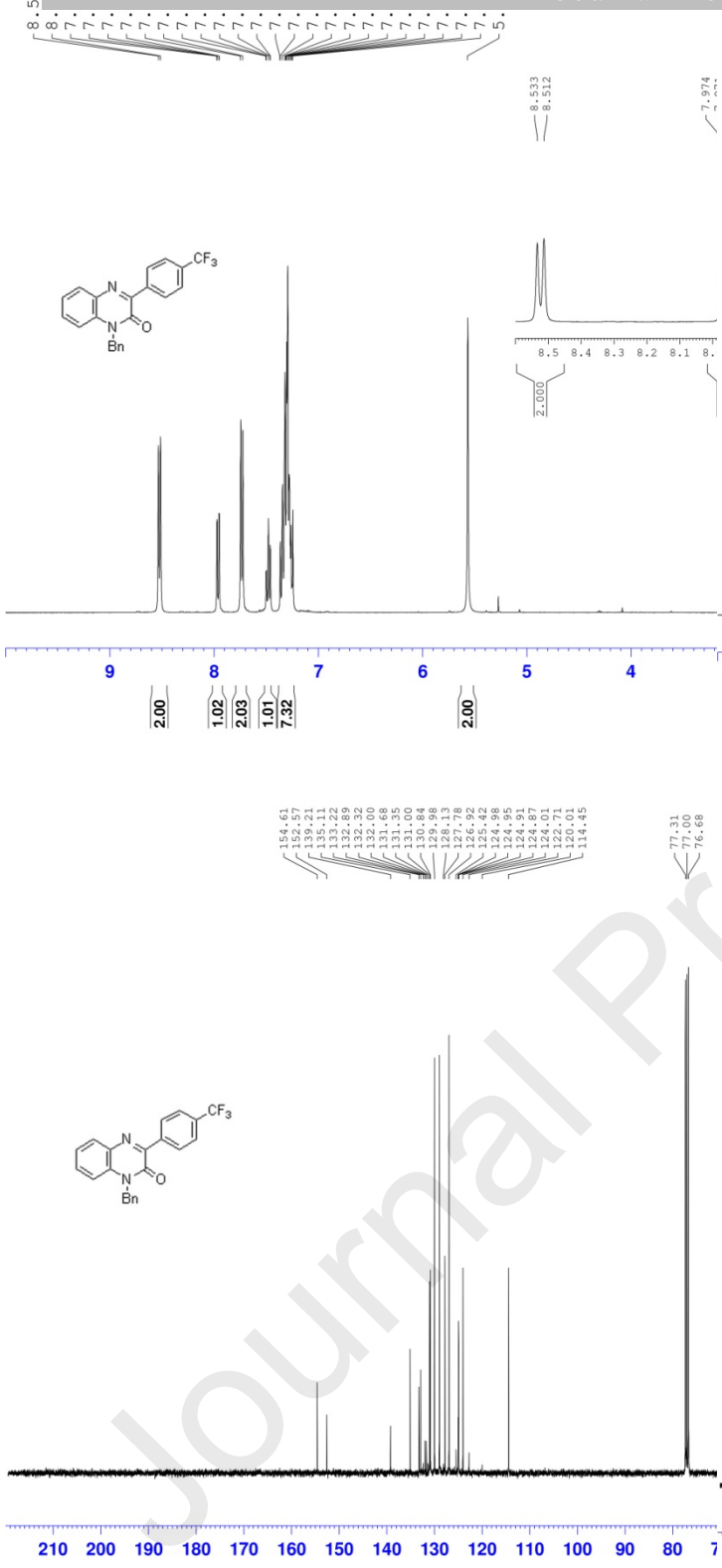

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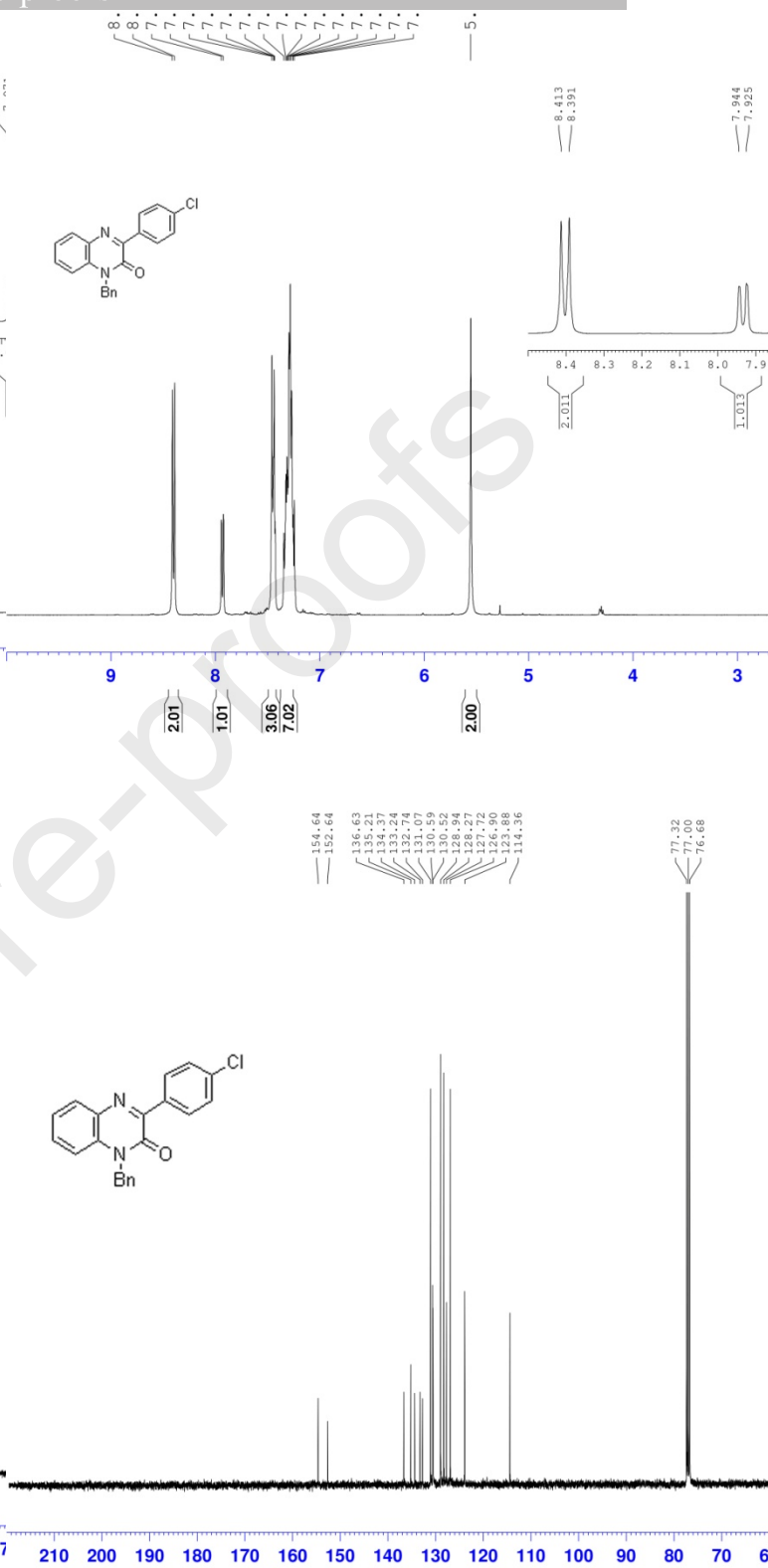

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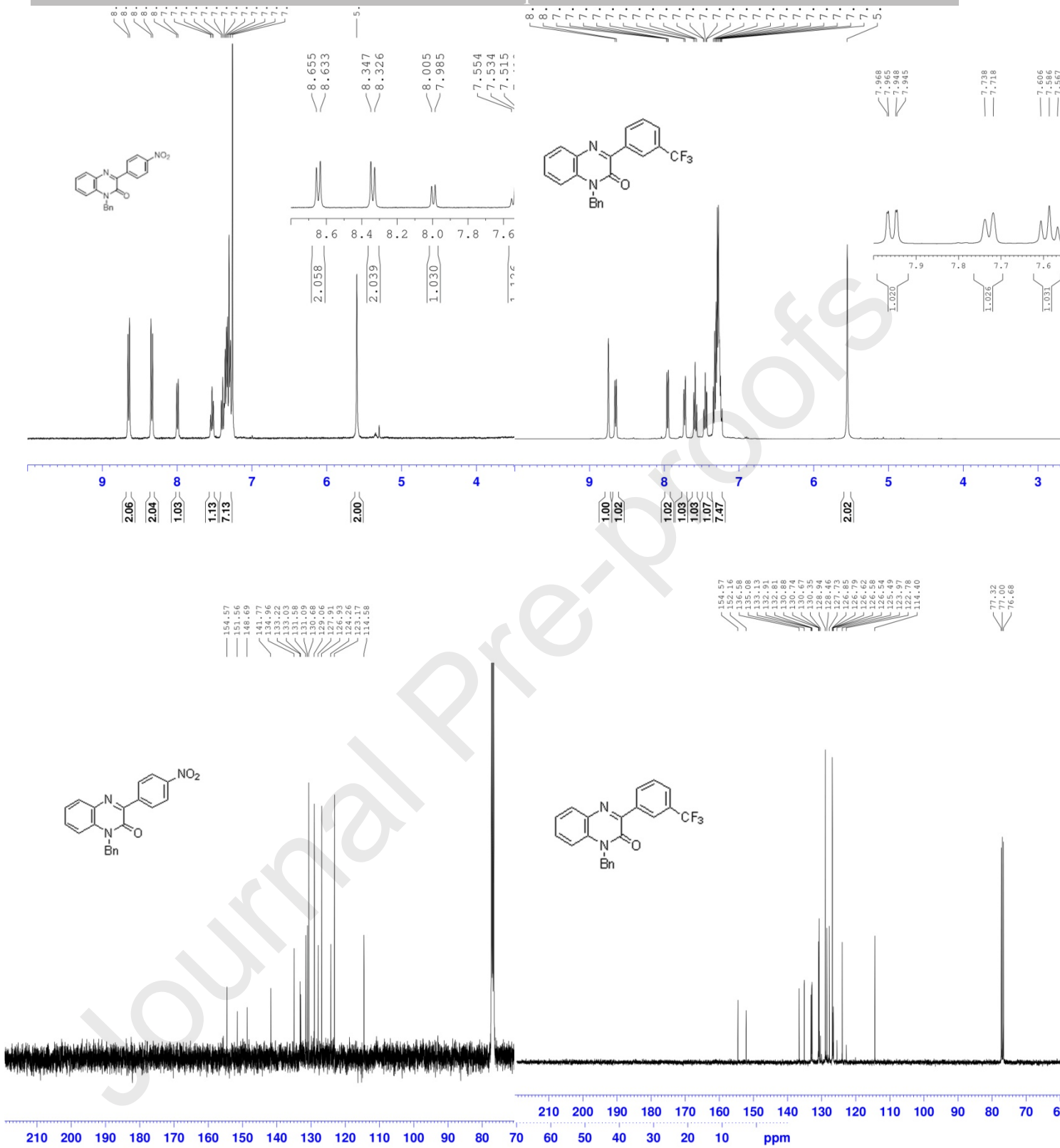

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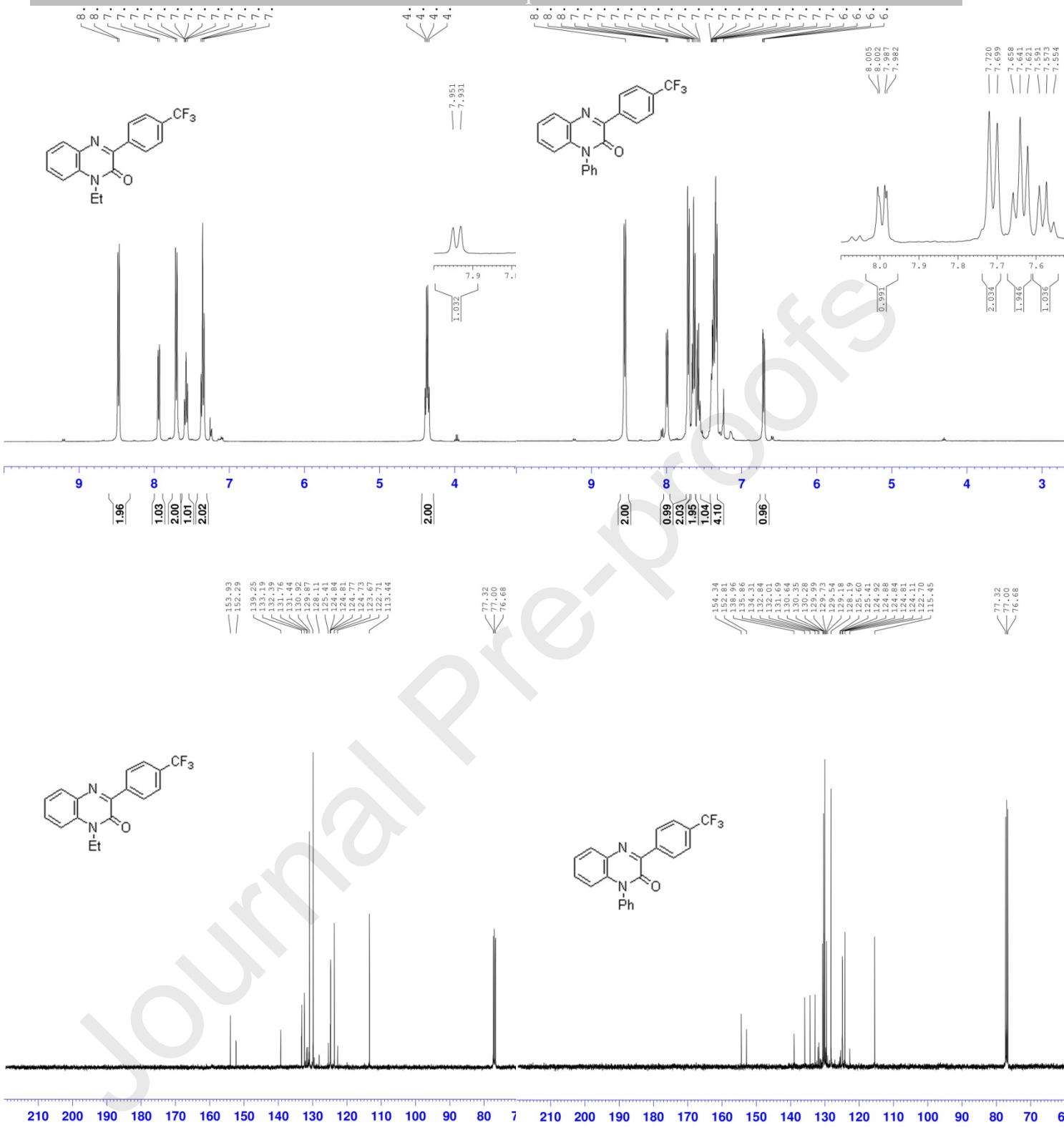
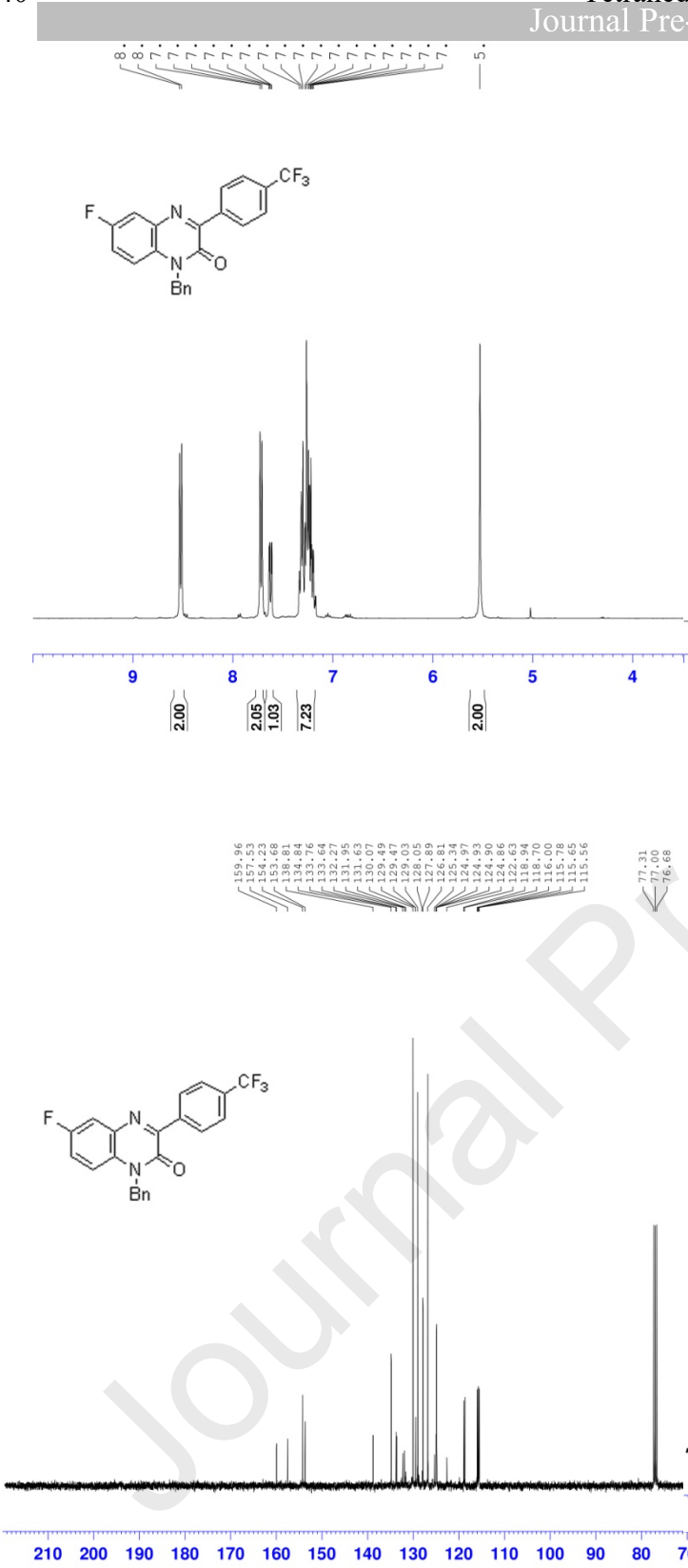
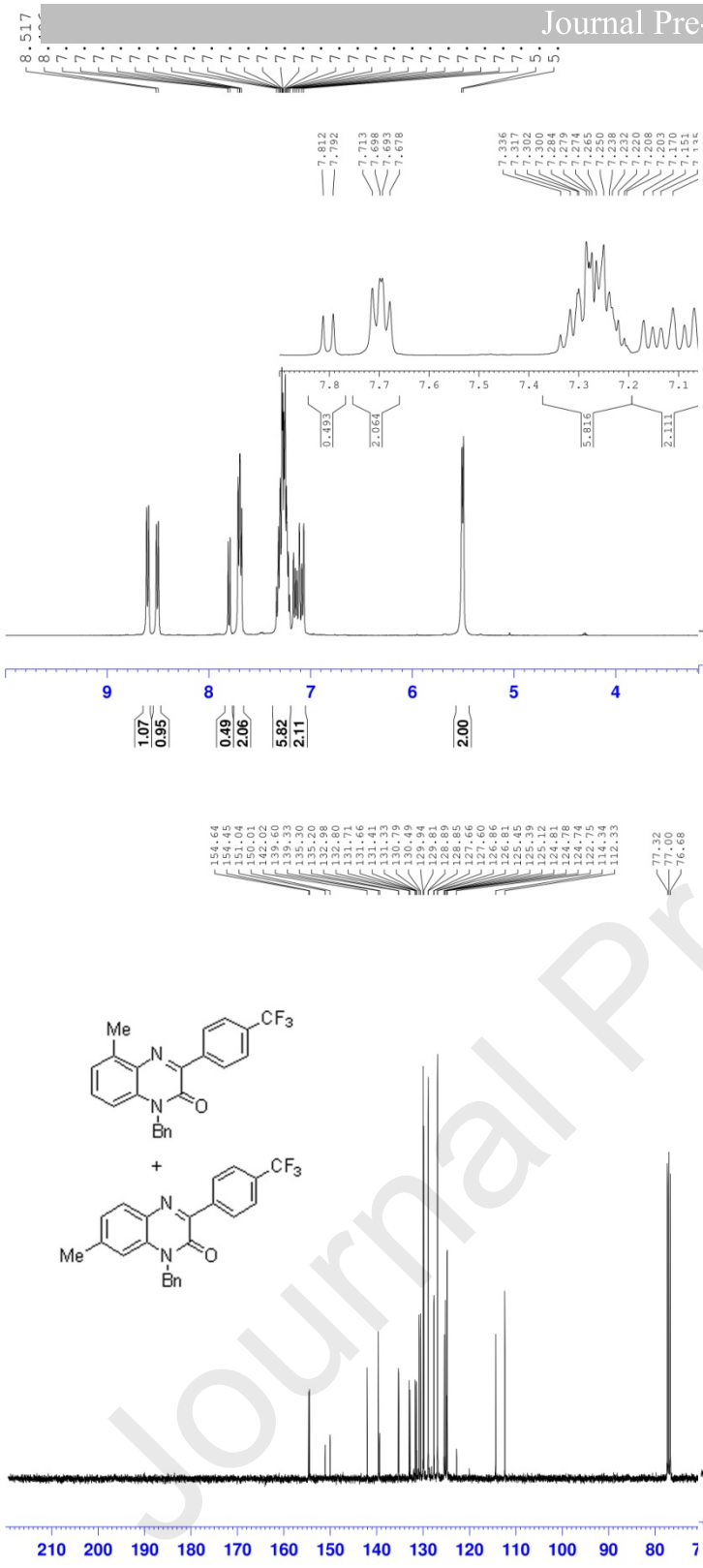


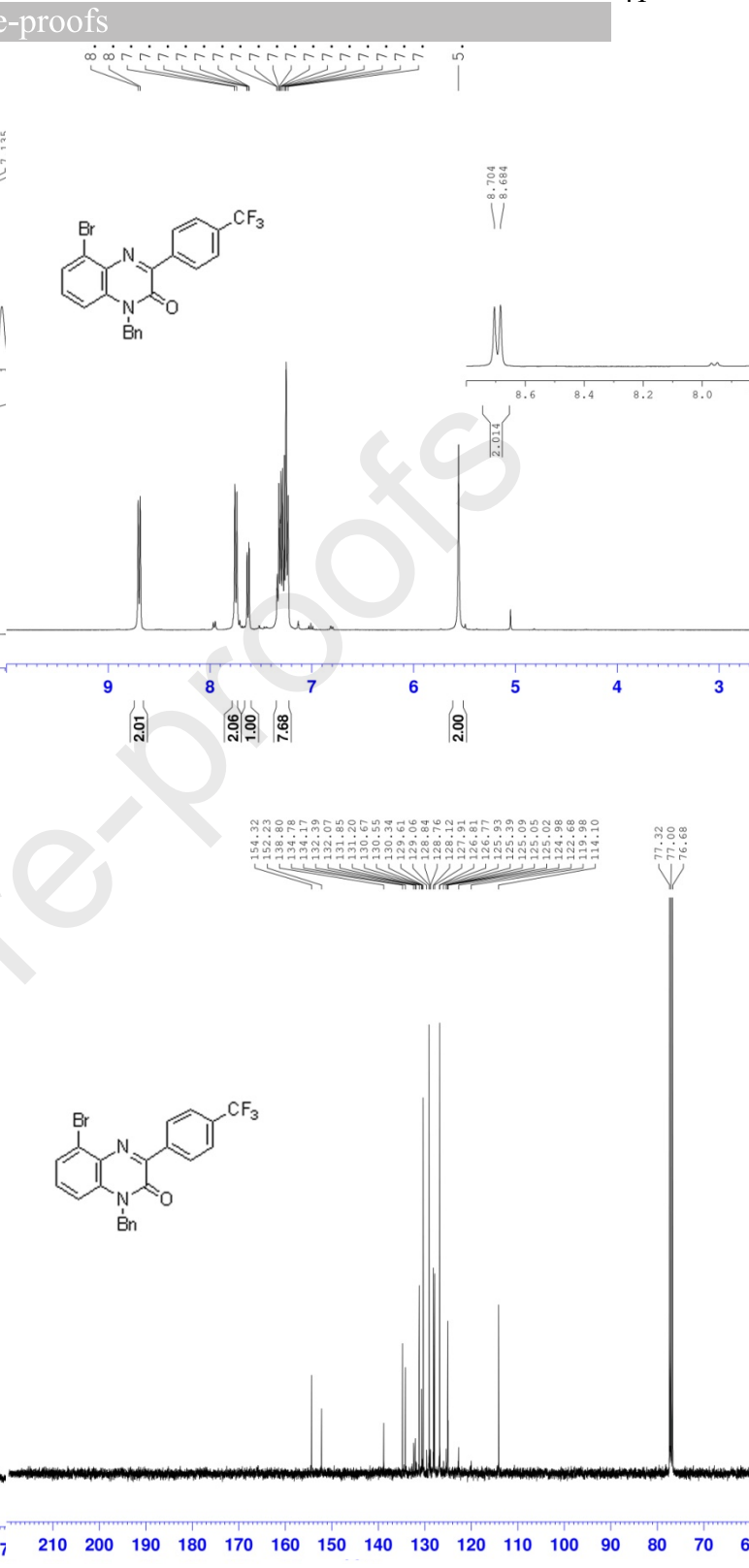
4g **4h**



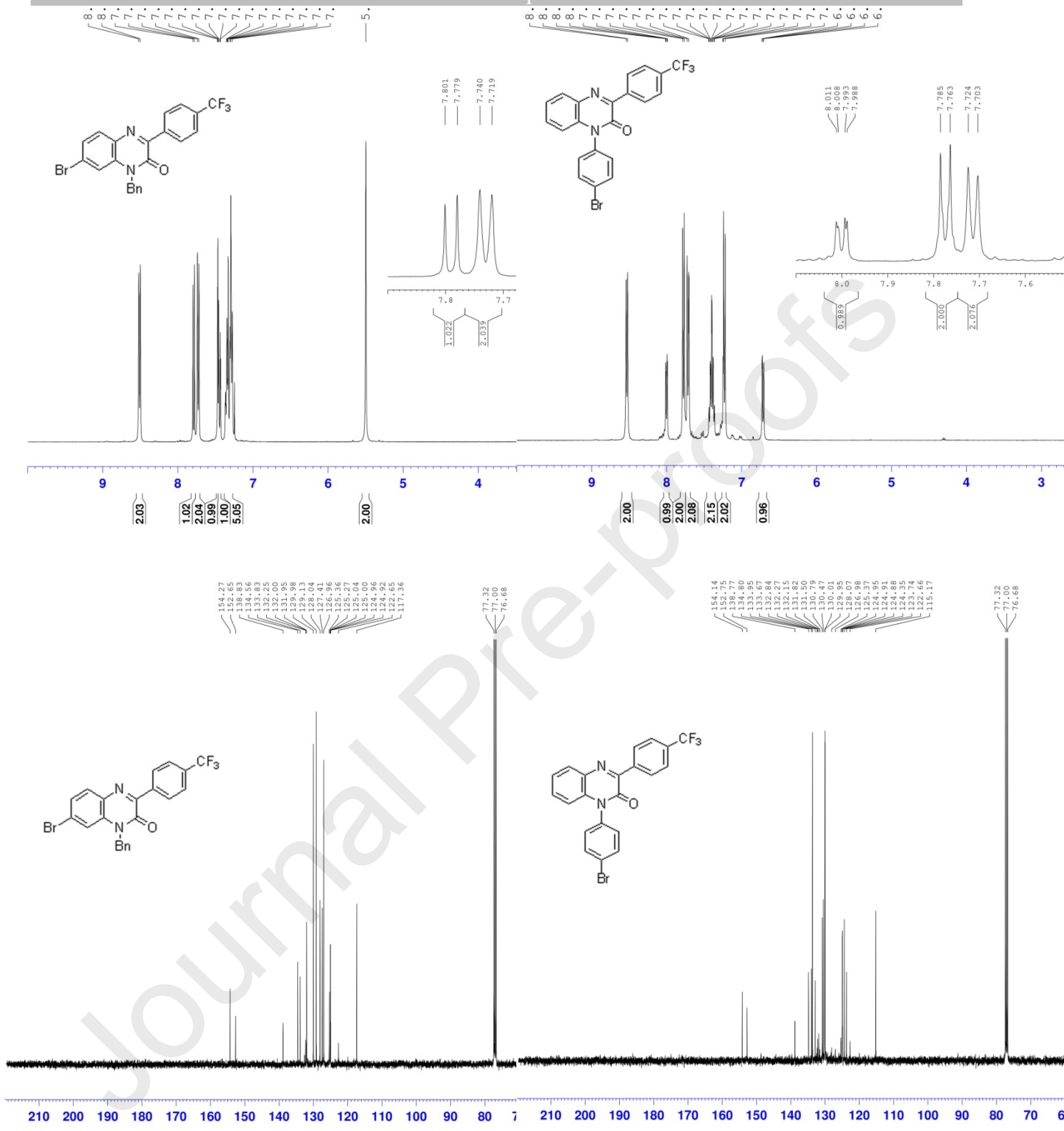
4i **4j-1+4j-2**



4k-1



4k-2



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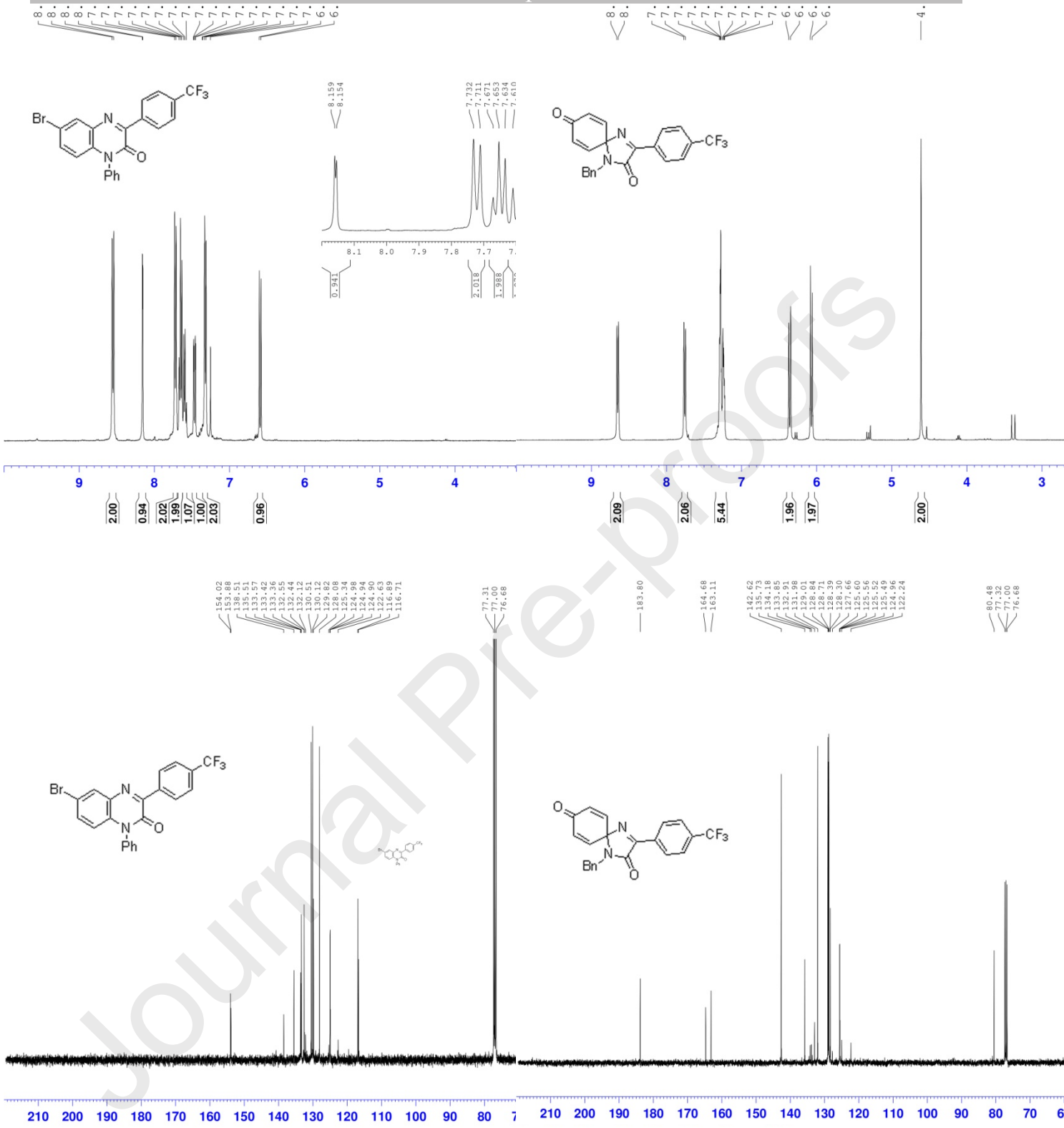
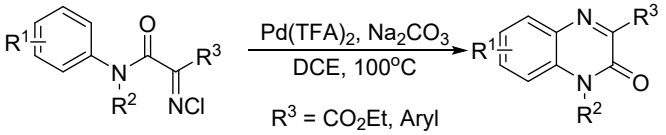


5i

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.



- *wide range of substrates*
- *no ligand*
- *no oxidant*
- *up to 99% yield*

Ligand-free Pd(II)-catalyzed Cyclization of α-Chloroimino-*N*-

arylamides to Synthesis of Quinoxalin-2(1*H*)-ones

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Highlights

- Ligand-free and oxidant-free Pd(II)-catalyzed synthesis of quinoxalin-2(1*H*)-ones.
- Affording quinoxalin-2(1*H*)-ones via tandem N-Cl cleavage and *N*-arylation.
- Cyclization with expanded scope of substrates at C_3 position on the scaffold.
- The oxygen (air) had a slightly influence on the transformation.
- Constructing C-N bonds in moderate to excellent yields.

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