

## Electronic Supporting Information

# Facile access to amides and hydroxamic acids directly from nitroarenes

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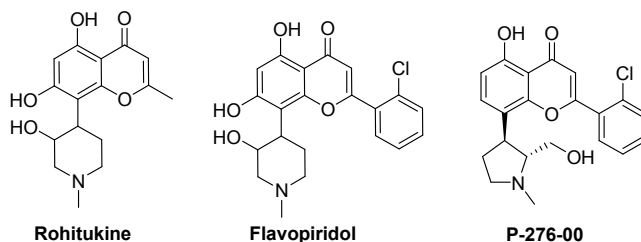
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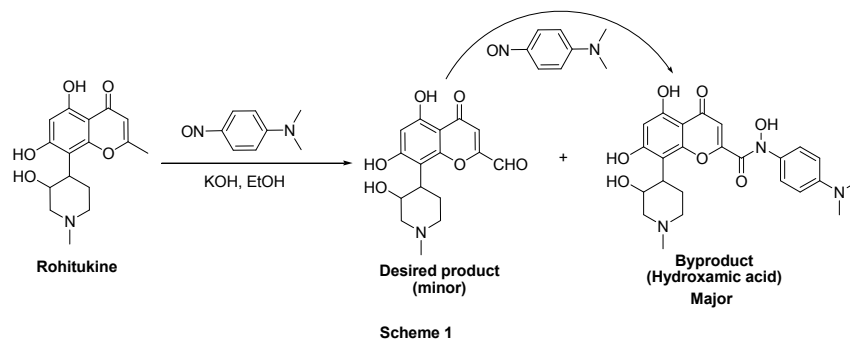
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## Section S1. Observations from investigation on rohitukine

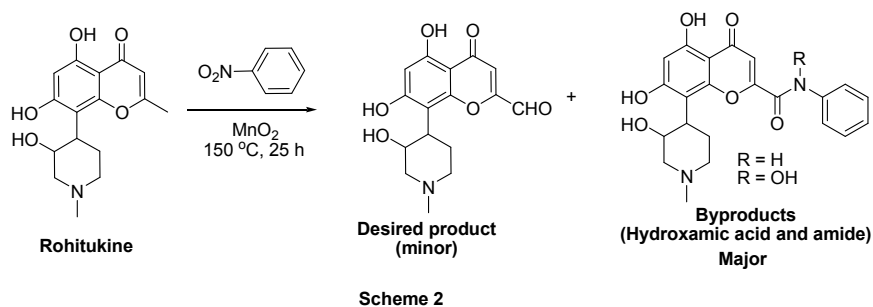
Rohitukine is a chromone alkaloid isolated from barks of *Dysoxylum binectariferum*. This natural product led to the discovery of two anticancer clinical candidates viz. flavopiridol and P-276-00.



During our efforts on medicinal chemistry of rohitukine,<sup>1</sup> present synthetic method was discovered. One of the targeted modification was conversion of allylic methyl group into –CHO functionality, for which we used *N,N*-dimethylnitrosoanilin<sup>2</sup> which produced hydroxamic acid as a major product along with traces of desired 2-formyl product (Scheme 1).



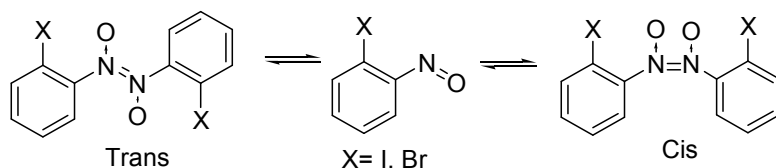
Then, in order to get desired formyl product in good yield, we attempted to generate *in situ* ‘nitroso’ from nitrobenzene and Mn-oxide.<sup>3</sup> However, again the desired formyl product was obtained only in traces and hydroxamic acid and amide products (revealed by LCMS) were the major side products (Scheme 2).



These results led to assumption that the 2-formyl product must have been formed, however it undergoes further reaction with N,N-dimethylnitrosoanilin to produce corresponding hydroxamic acid. This unexpected result was then implemented to establish a facile methodology for synthesis amides and hydroxamic acid from benzaldehydes and nitroarenes in presence of MnO<sub>2</sub>.

## Section S2. Monomer-dimer equilibrium of nitroso compounds

Dimerized product was observed as main product (Table 2, entries 13, 14) in case of 2-bromo-nitrobenzene and 2-iodo-nitrobenzene. These nitroarenes failed to give desired product in significant amount because the corresponding nitroso favoured dimerization.

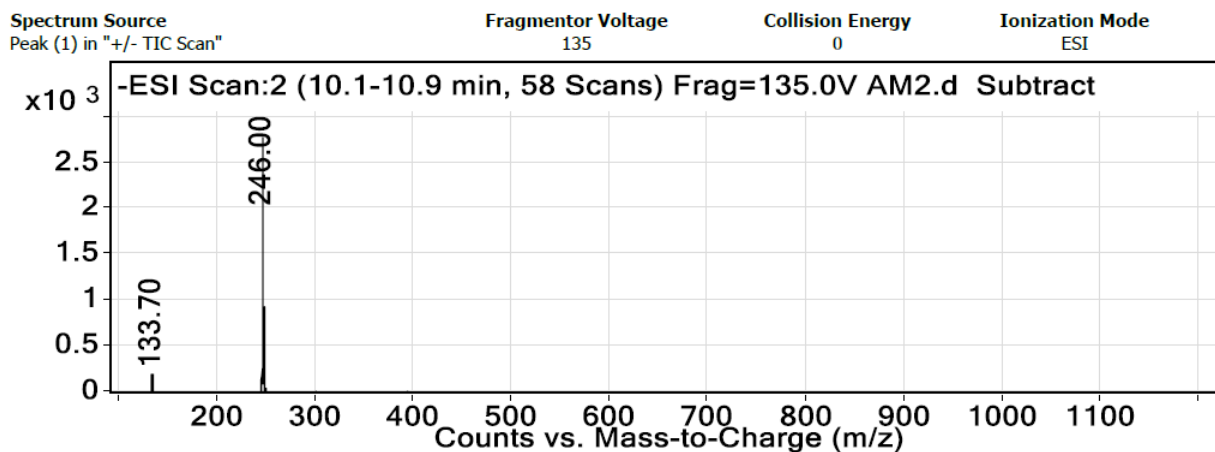
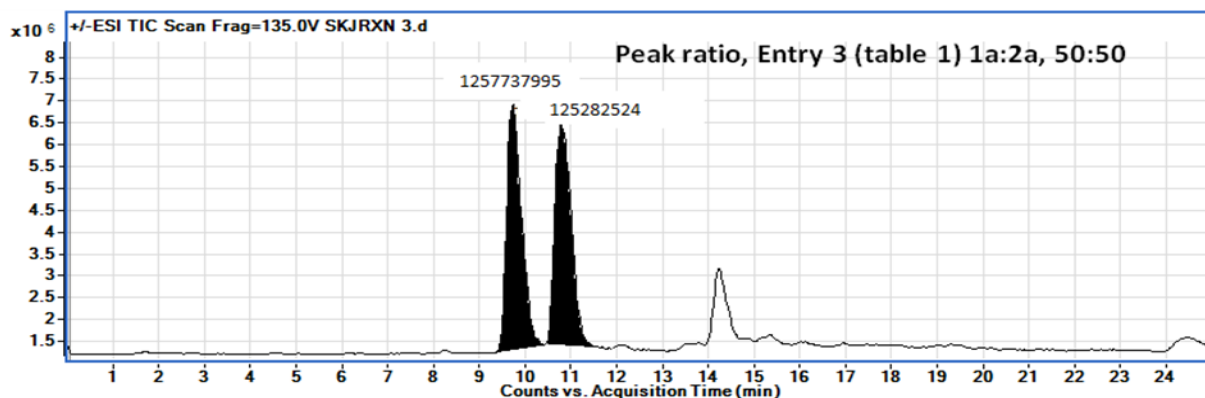


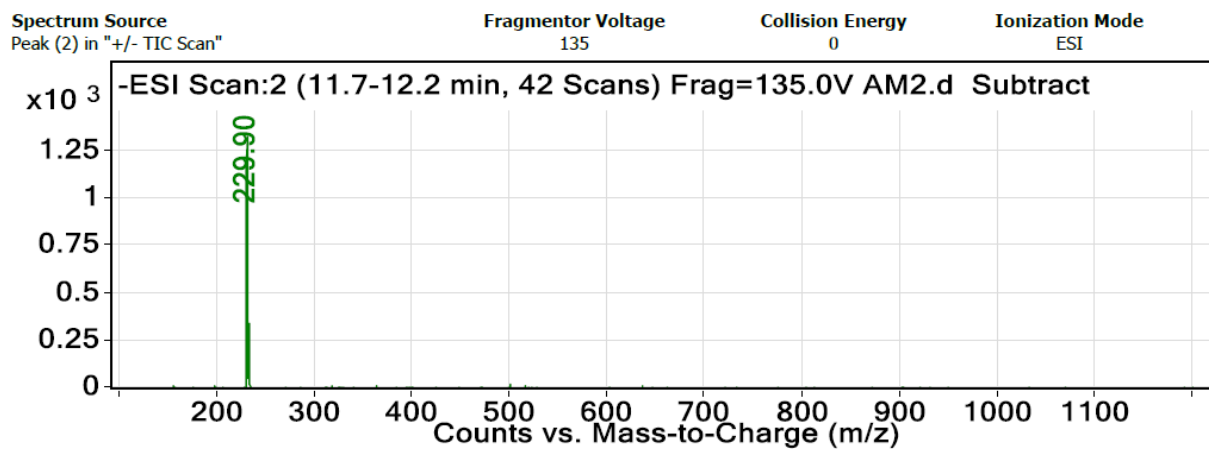
Nitroso compounds are usually reactive intermediate and stabilized either by dimerization or resonance: noteworthy feature of nitroso compounds is their tendency to get stabilized by dimerization to azodioxy dimer, as a consequence of their low HOMO-LUMO energy gap and thus promotes high reactivity at low excitation energy.<sup>4</sup> It was observed that o-iodo-nitrobenzene (**4m**) and o-bromo-nitrobenzene (**4n**) were failed to give desired amide in significant yield (yield: 7-8%; Table 2). The major product was characteristic colorless crystalline, organic solvent insoluble dimeric azodioxy compound which displayed characteristic IR spectrum. It is again important to discuss that yield of product in these cases depends on the equilibrium between monomer and dimer of nitroso. A controlled equilibrium can be translated to product yield. It is known from previous work that unhindered aromatics favor monomer formation, while o-substituted and hindered aromatics favor dimer formation. Low temperature with UV  $\lambda_{\text{max}}$  254-350 nm favor monomer while high temperature and visible wavelength favors dimer.<sup>5</sup> Monomer-dimer interchange depends on the availability of electrons on the N of nitroso, to form dimeric bond and would therefore decrease with increasing electronegativity of the R<sub>2</sub> (here Ph or substituted Ph). If R<sub>2</sub> is sufficient electron-donating, it favours dimerization and if the R<sub>2</sub> is electron-deficient or electron-withdrawing, it favors monomer and gets stabilized by resonance.

**Section S3. LCMS analysis of reaction mixture (for entry 3, 12, 13 and 14 of Table 1) to determine ratio of compound 1a and 2a**

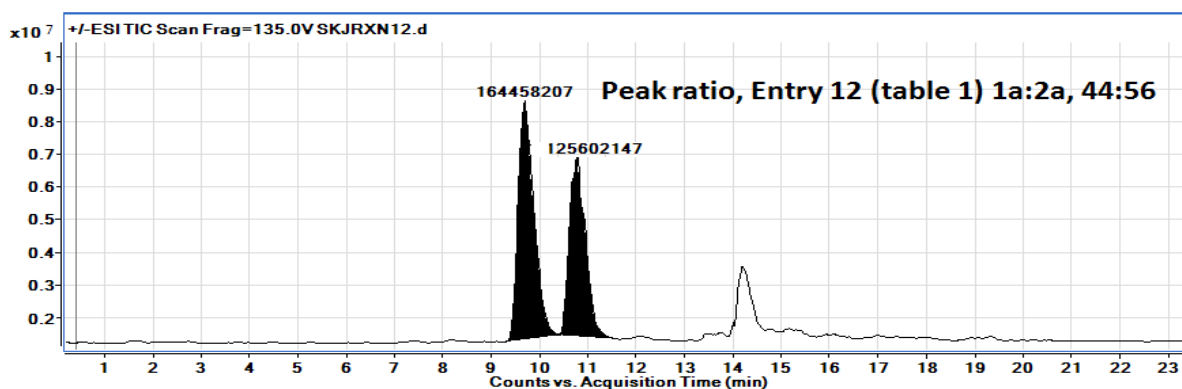
Reaction was carried out using condition mentioned in entries 3, 12, 13 and 14 of Table 1. The LCMS analysis was done after the time point which is mentioned in Table 1.

**Method:** Chromolith column (50 mm x 4.6 mm, RP-18), Mobile phase: Acetonitrile/water (1% acetic acid), gradient elution over 25 min (0 min: 0/100, 15 min: 50/50, 20 min: 50/50, 22 min: 0/100, 25 min: 0/100), flow rate: 0.5 ml/min.



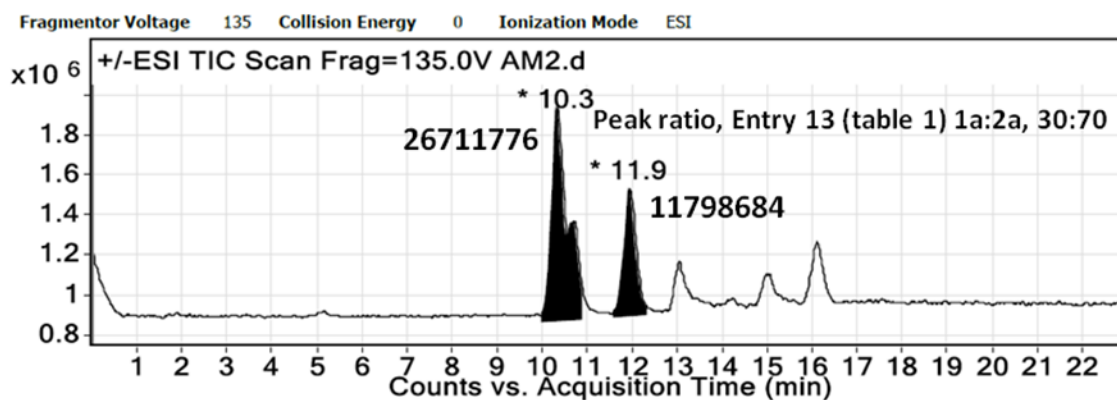


(a). LCMS analysis for reaction performed as per entry no 3 (LCMS spectra and MS spectras are shown)

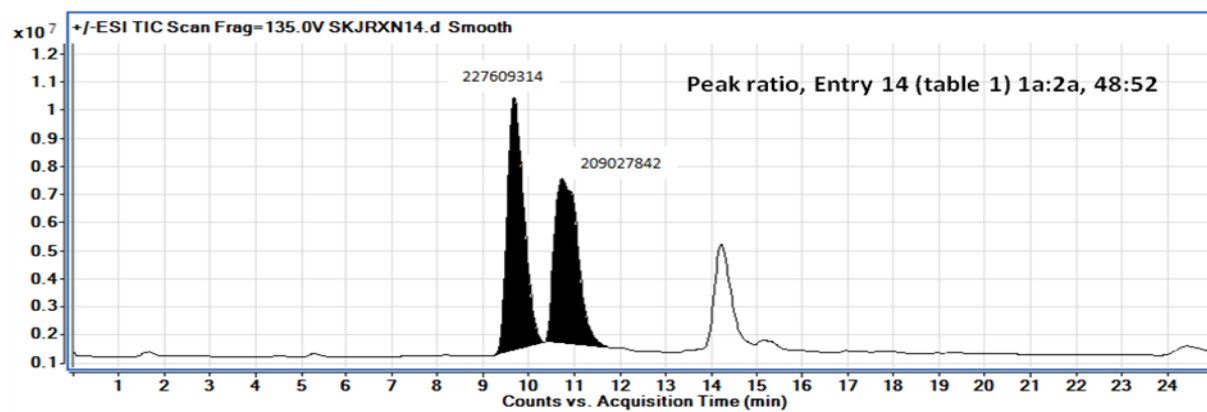


(b) LCMS analysis for reaction performed as per entry no 12.

### User Chromatograms



(c) LCMS analysis for reaction performed as per entry no 13.

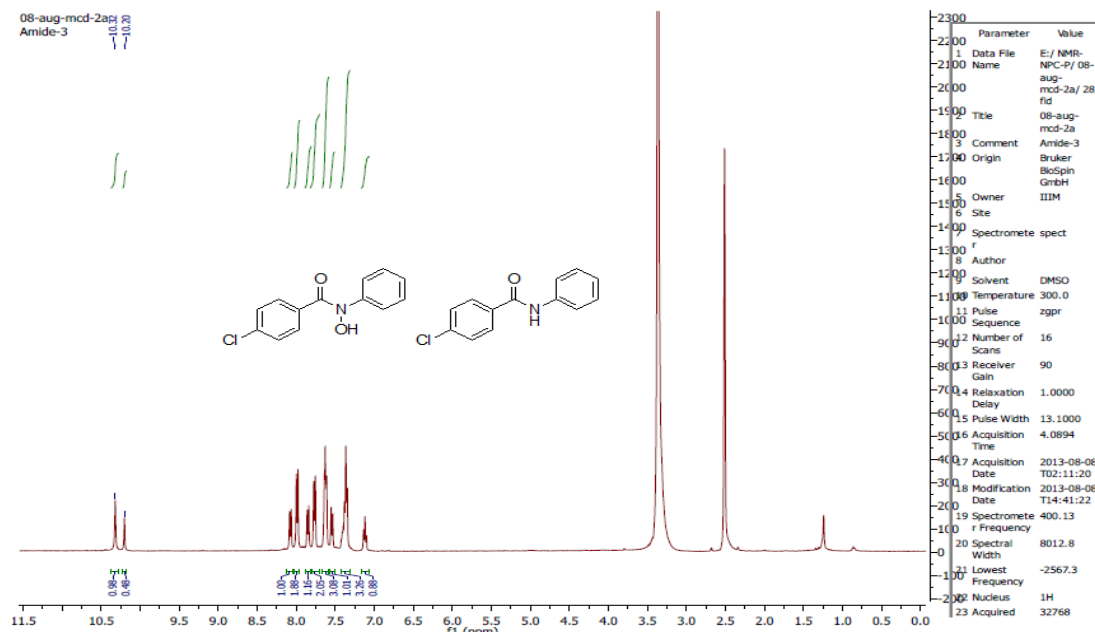


(d) LCMS analysis for reaction performed as per entry no 14.

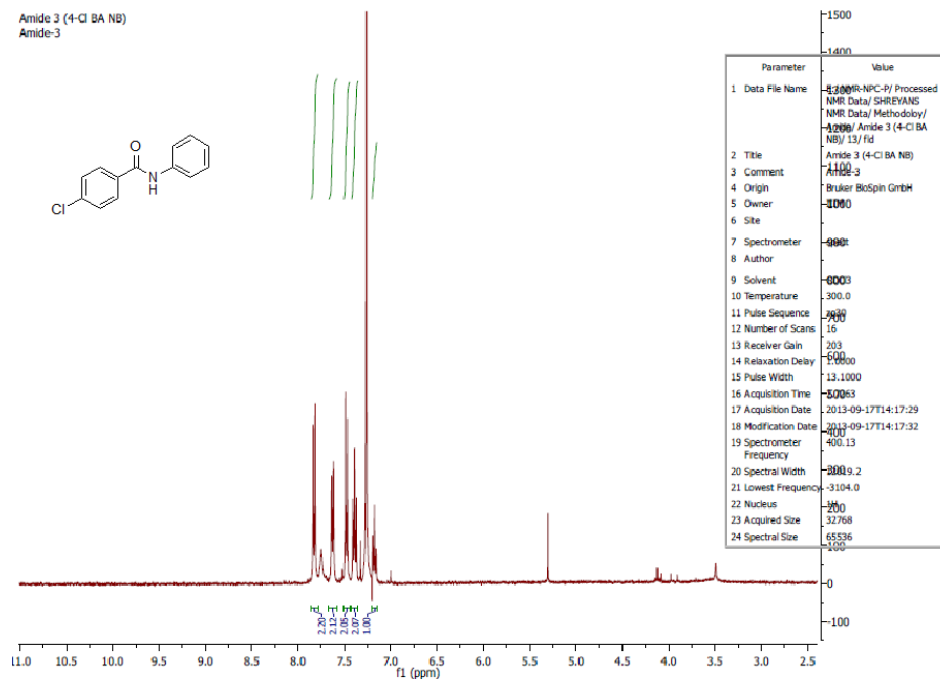


## Section S4. NMR data scans

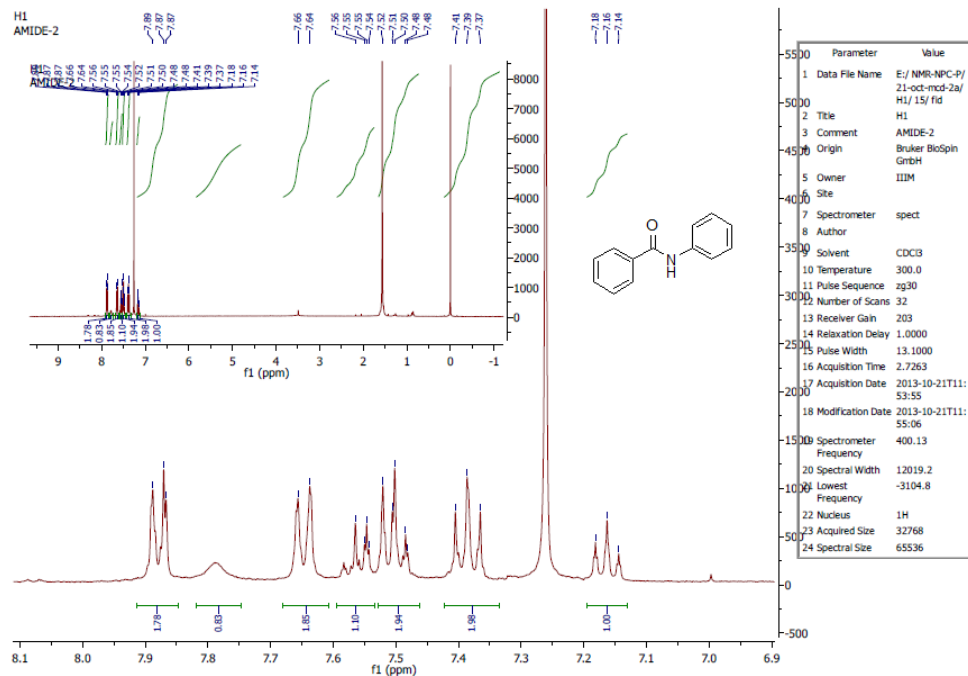
### S4a. <sup>1</sup>H NMR of mixture of **1a** and **2a** (obtained from entry 3 of Table 1) in CDCl<sub>3</sub>



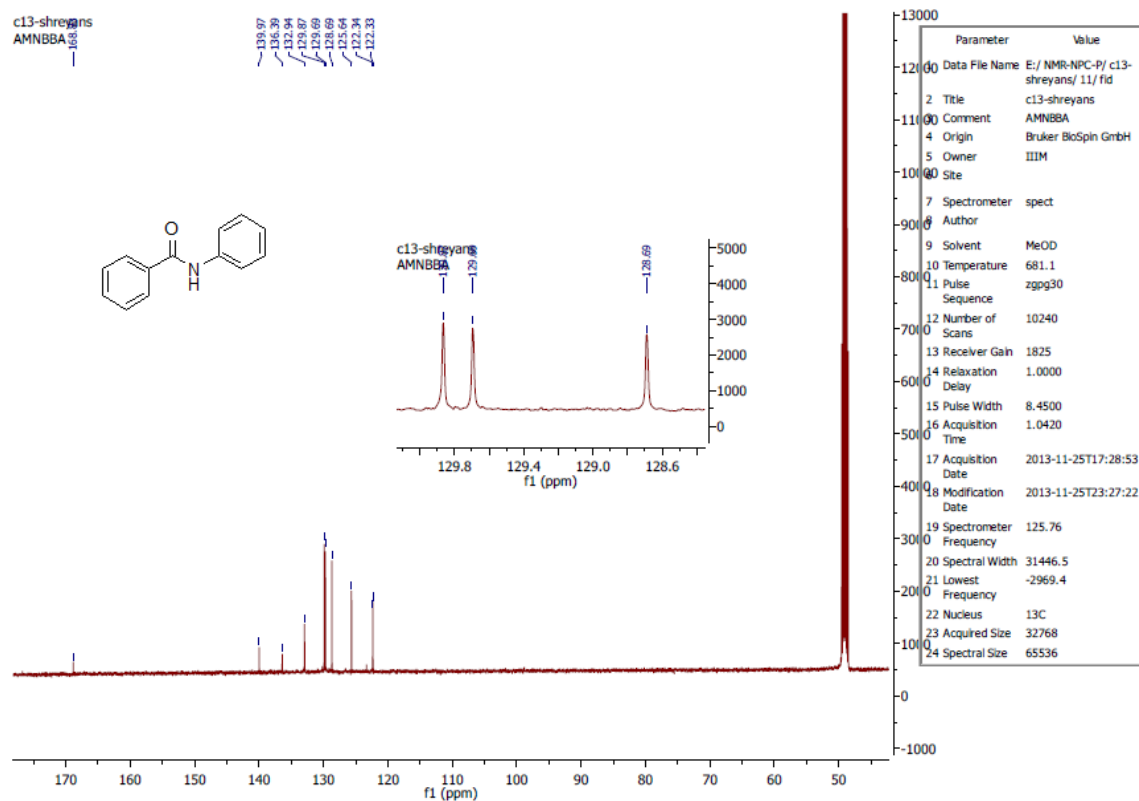
### S4b. <sup>1</sup>H NMR of 4-chloro-N-phenylbenzamide **1a**



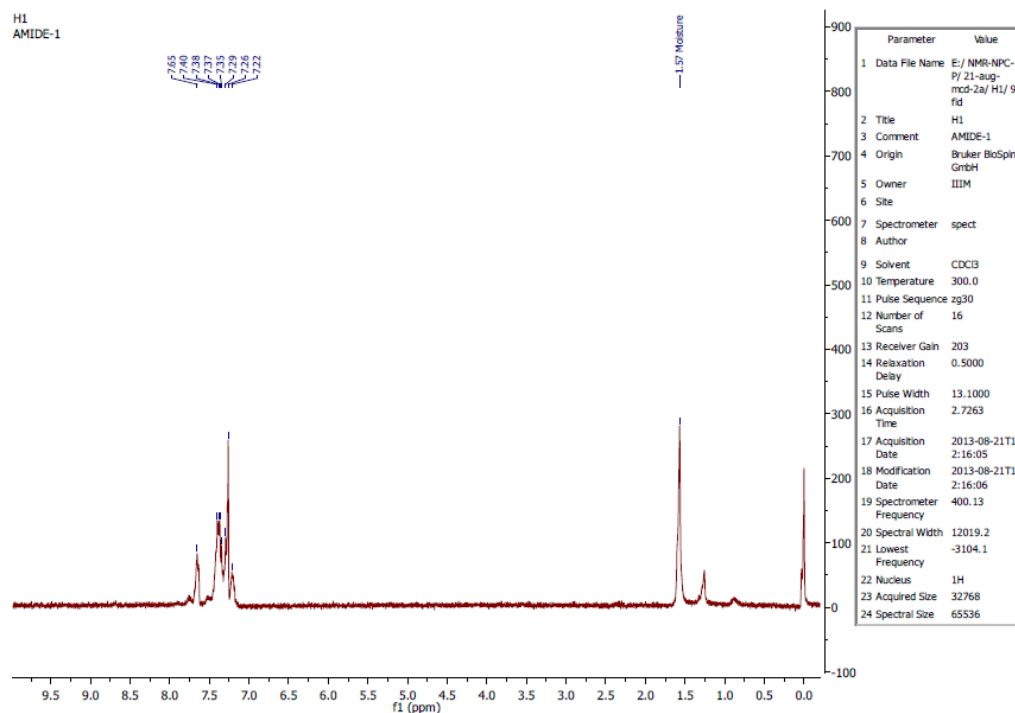
### S4c. <sup>1</sup>H NMR spectrum of N-phenylbenzamide (**1b**)



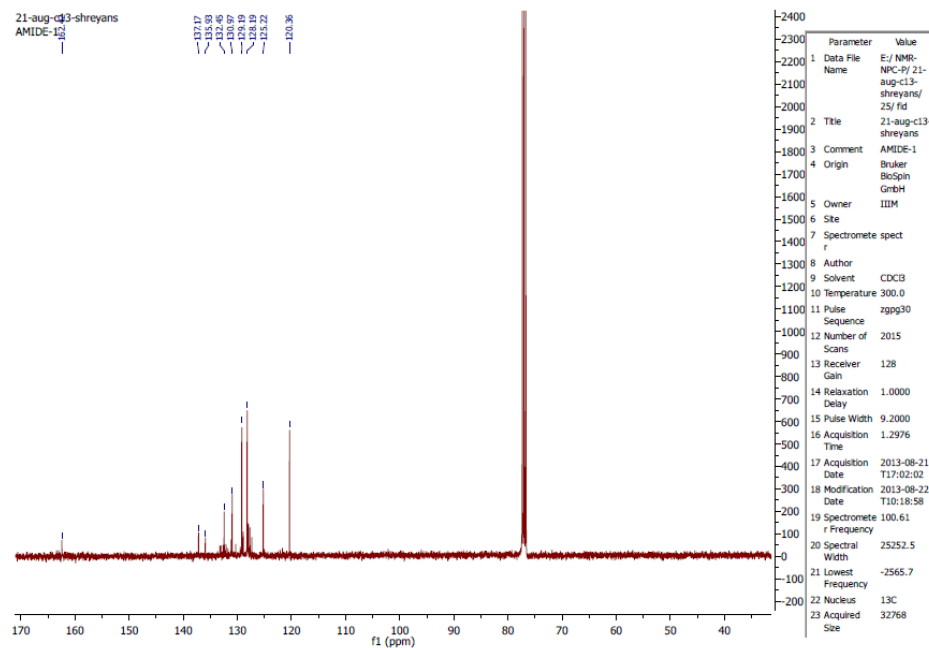
#### S4.d. <sup>13</sup>C NMR spectrum of N-phenylbenzamide (**1b**)



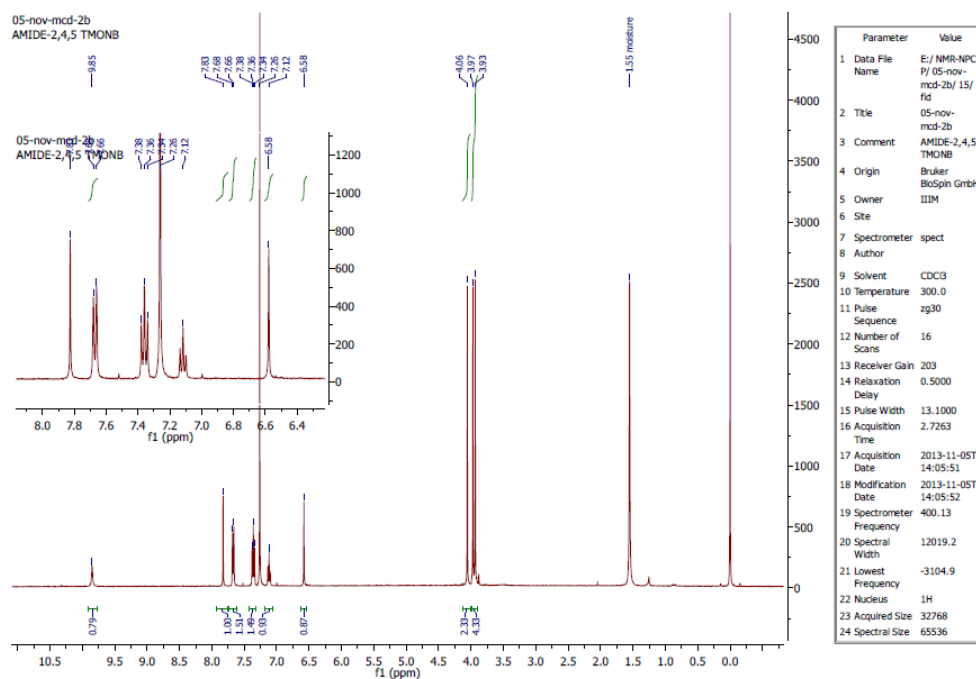
### S4.e. <sup>1</sup>H NMR Spectrum of 2,6-dichloro-N-phenylbenzamide (**1c**)



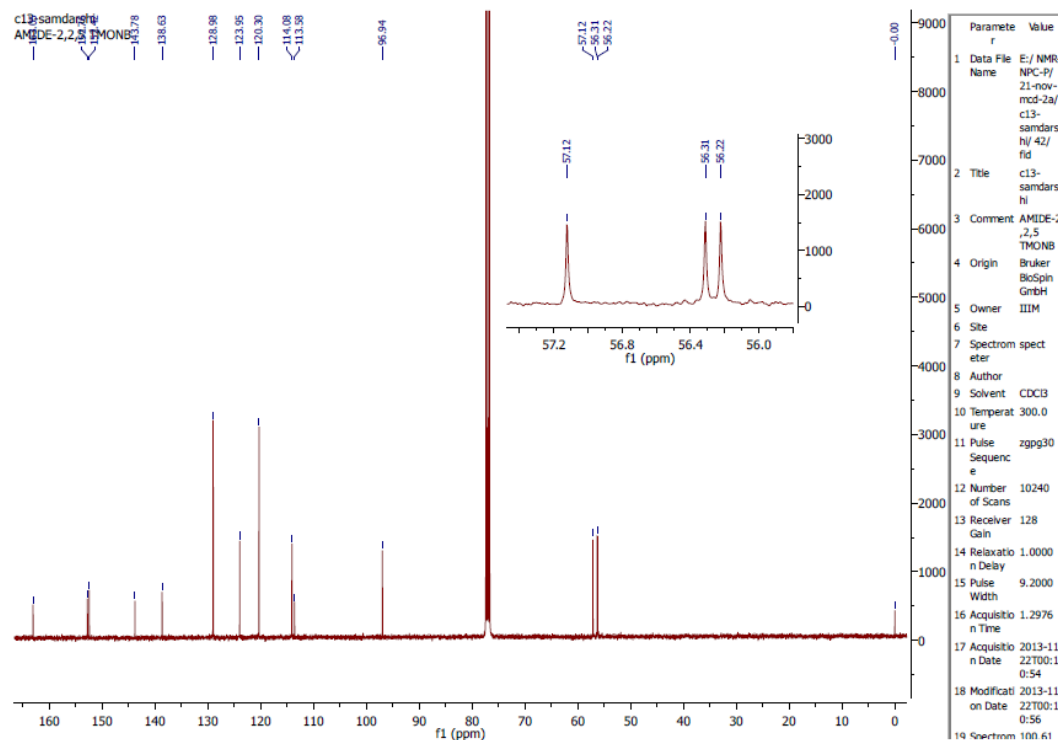
### S4.f. <sup>13</sup>C NMR Spectrum of 2,6-dichloro-N-phenylbenzamide (**1c**)



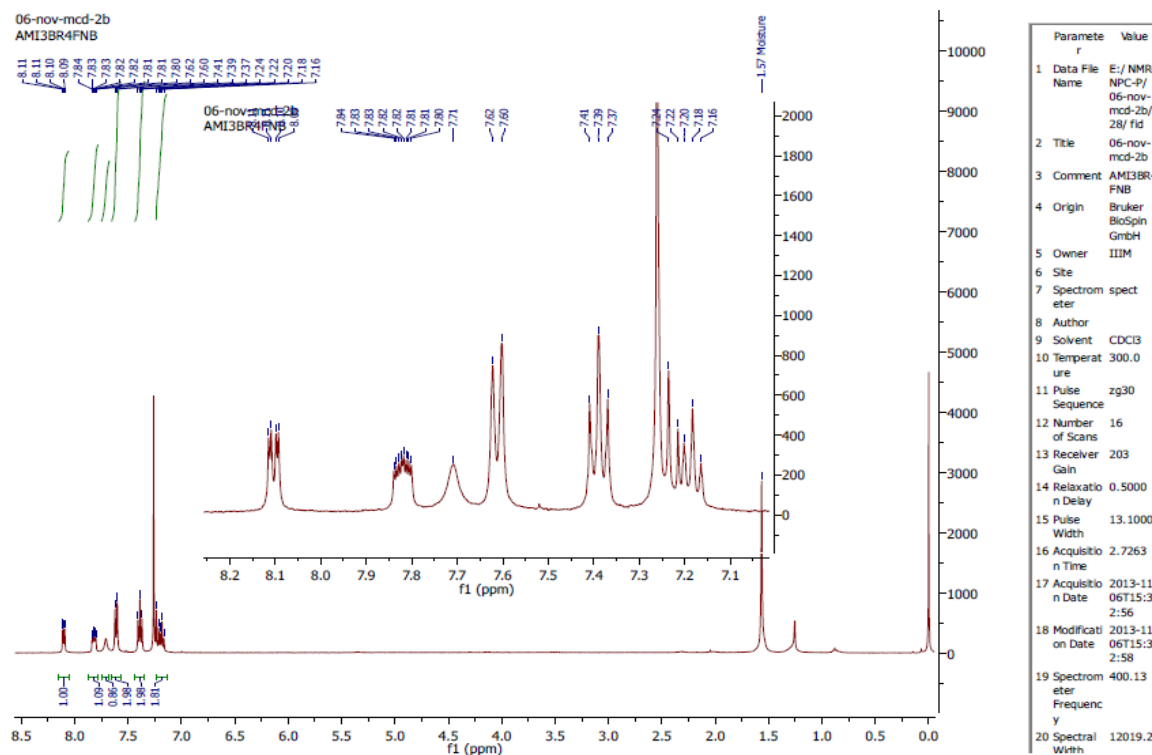
**S4.g.** <sup>1</sup>H NMR Spectrum of 2,4,5-trimethoxy-N-phenylbenzamide (**1d**)



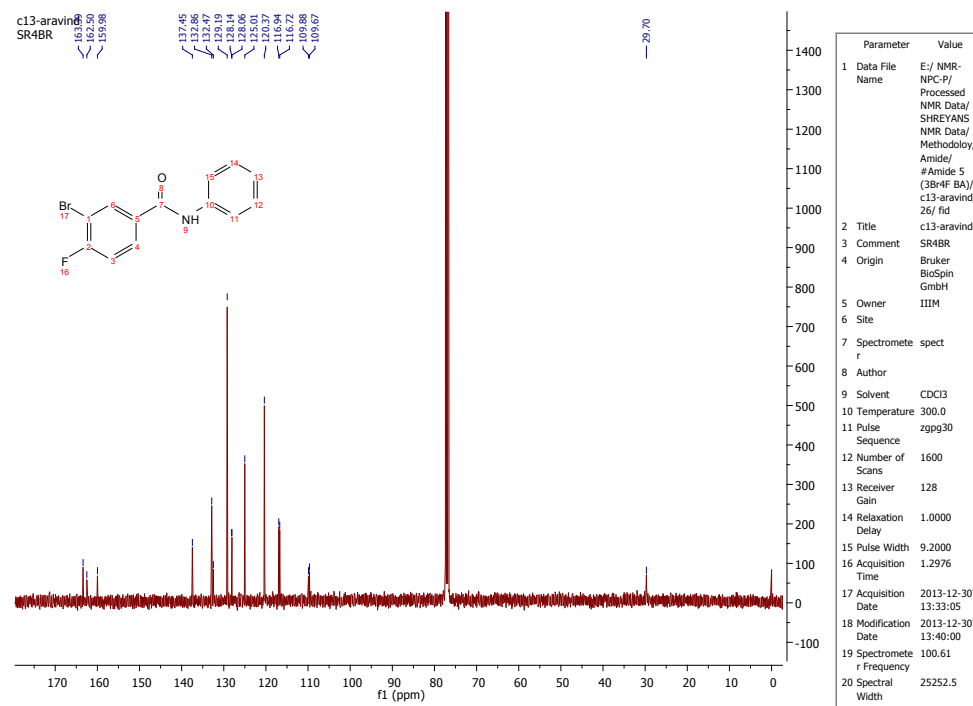
**S4.h.** <sup>13</sup>C NMR Spectrum of 2,4,5-trimethoxy-N-phenylbenzamide (**1d**)



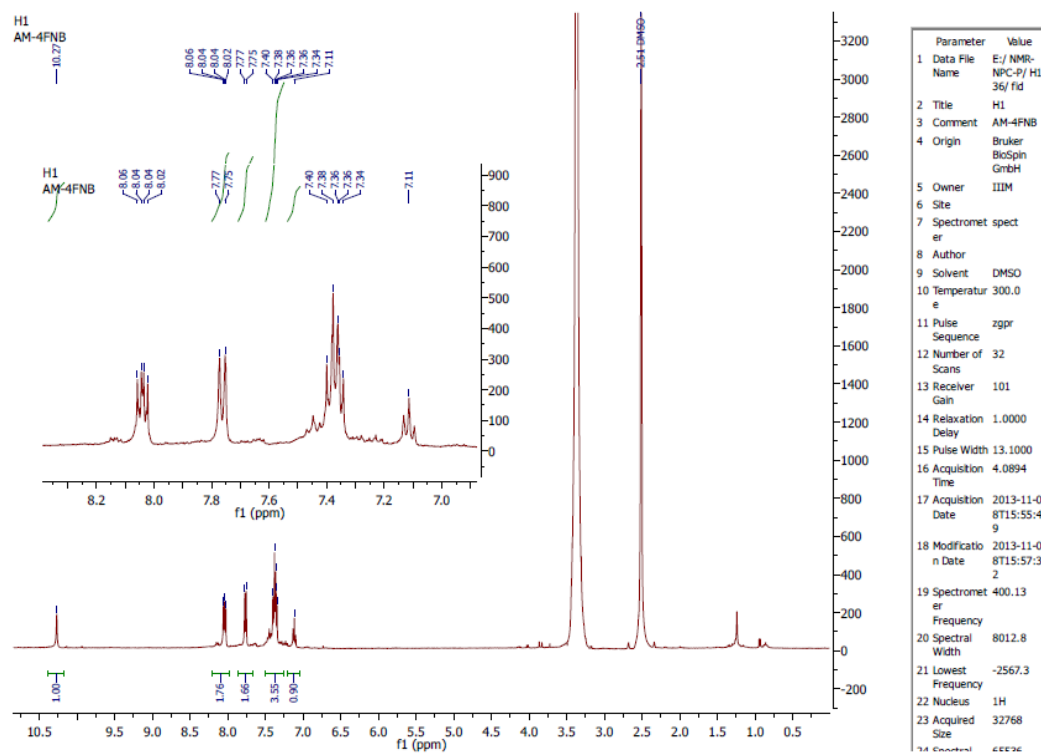
### S4.i. <sup>1</sup>H NMR Spectrum of 3-bromo-4-fluoro-N-phenylbenzamide (1e)



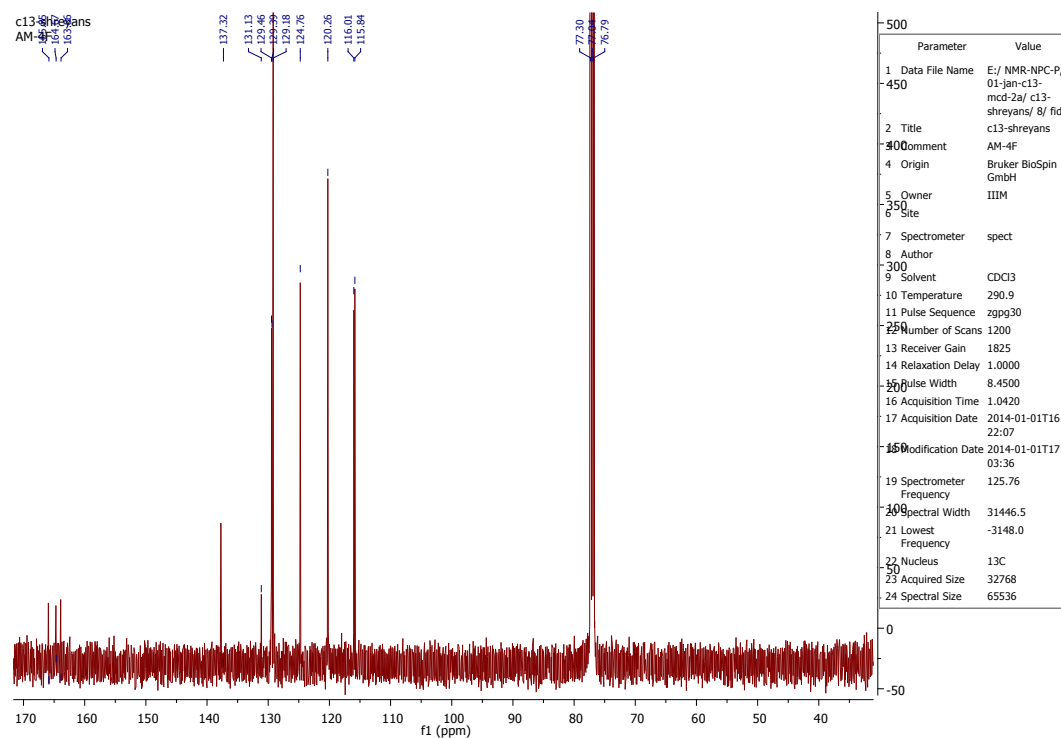
### S4.j. <sup>13</sup>C NMR Spectrum of 3-bromo-4-fluoro-N-phenylbenzamide (1e)



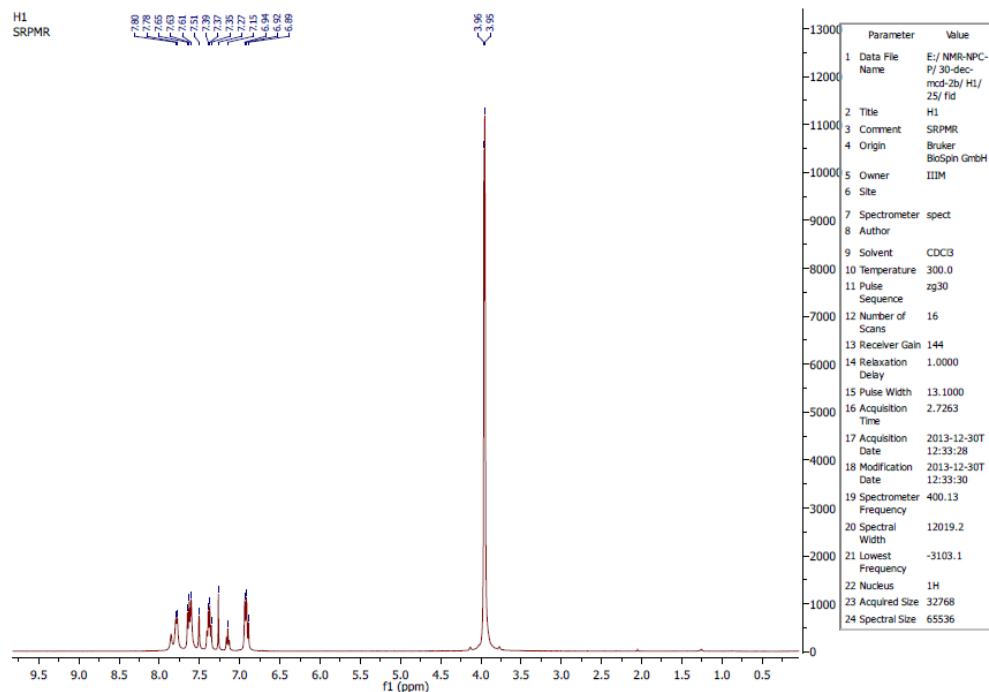
### S4.k. <sup>1</sup>H NMR Spectrum of 4-fluoro-N-phenylbenzamide (**1f**)



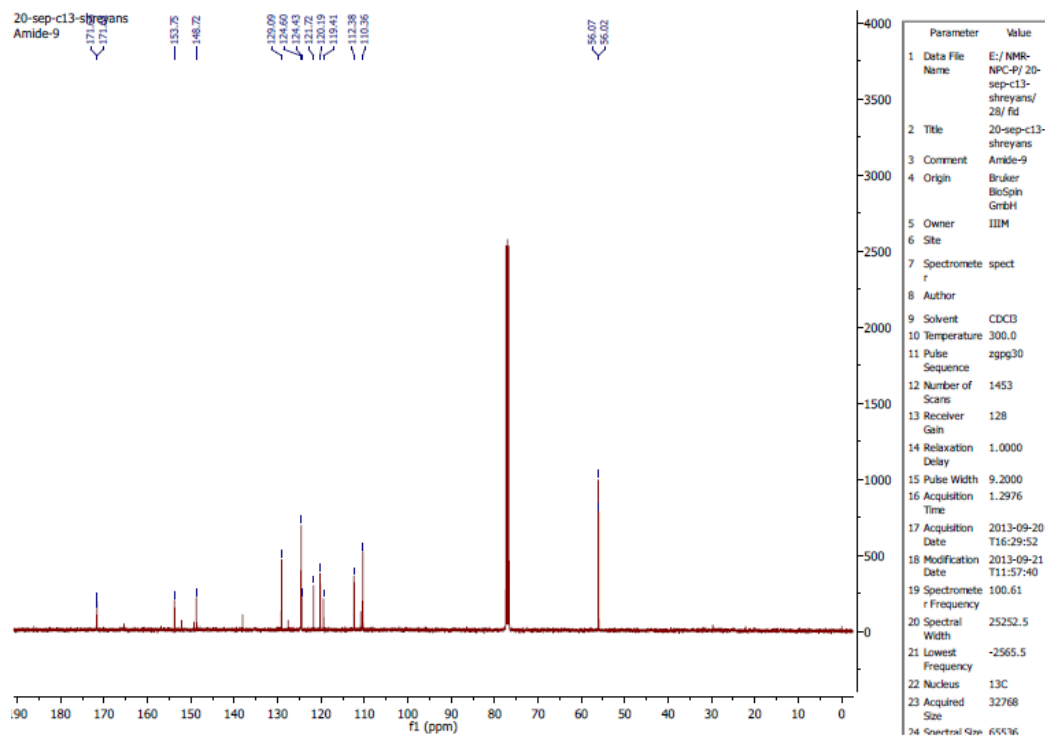
### S4.l. <sup>13</sup>C NMR Spectrum of 4-fluoro-N-phenylbenzamide (**1f**)



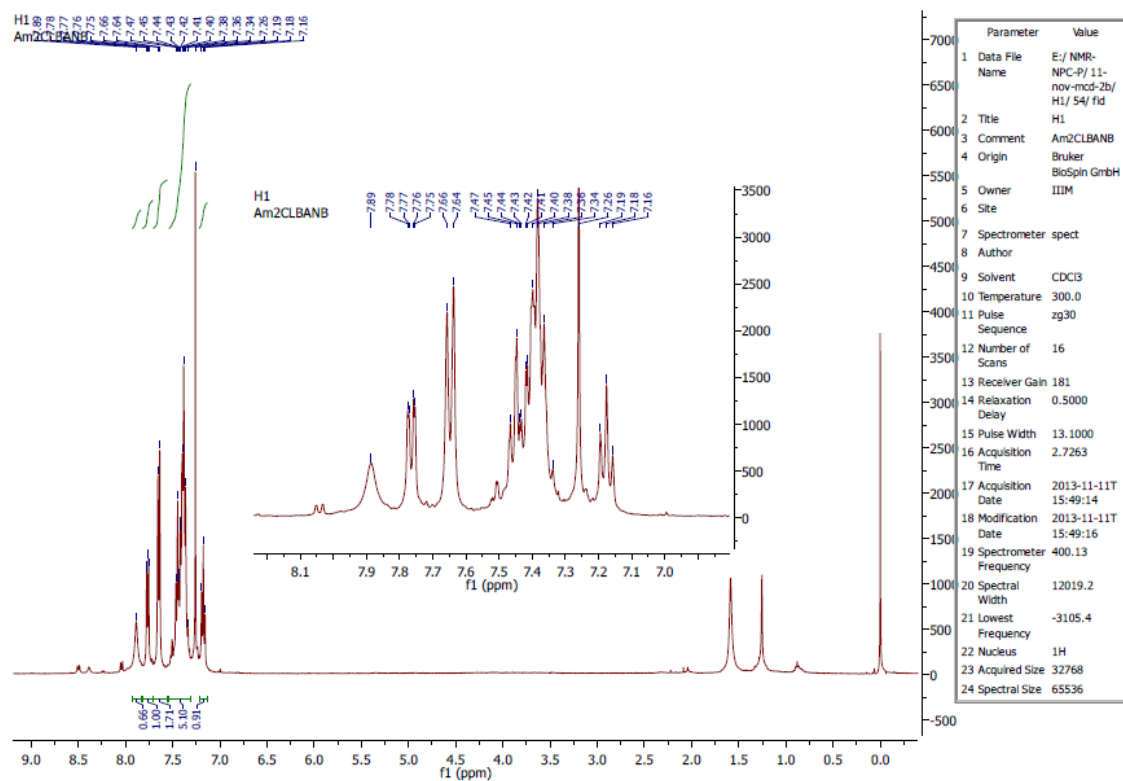
### S4.m. <sup>1</sup>H NMR Spectrum of 3,5-dimethoxy-N-phenylbenzamide (**1g**)



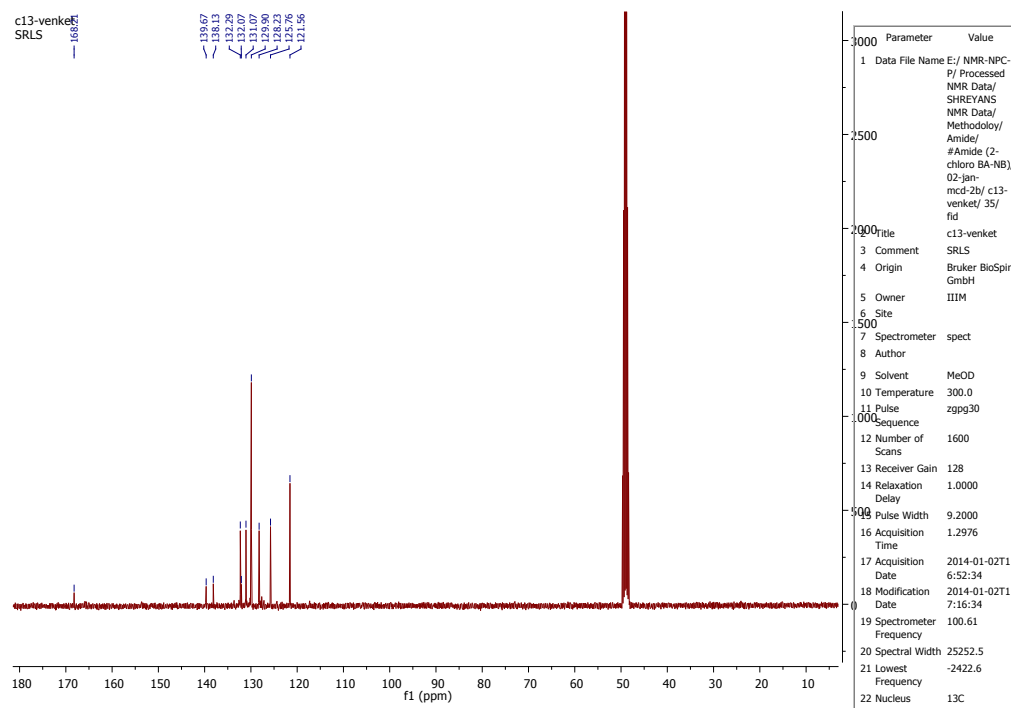
### S4.n. <sup>13</sup>C NMR Spectrum of 3,5-dimethoxy-N-phenylbenzamide (**1g**)



### S4.o. <sup>1</sup>H NMR Spectrum of 2-chloro-N-phenylbenzamide (1h)

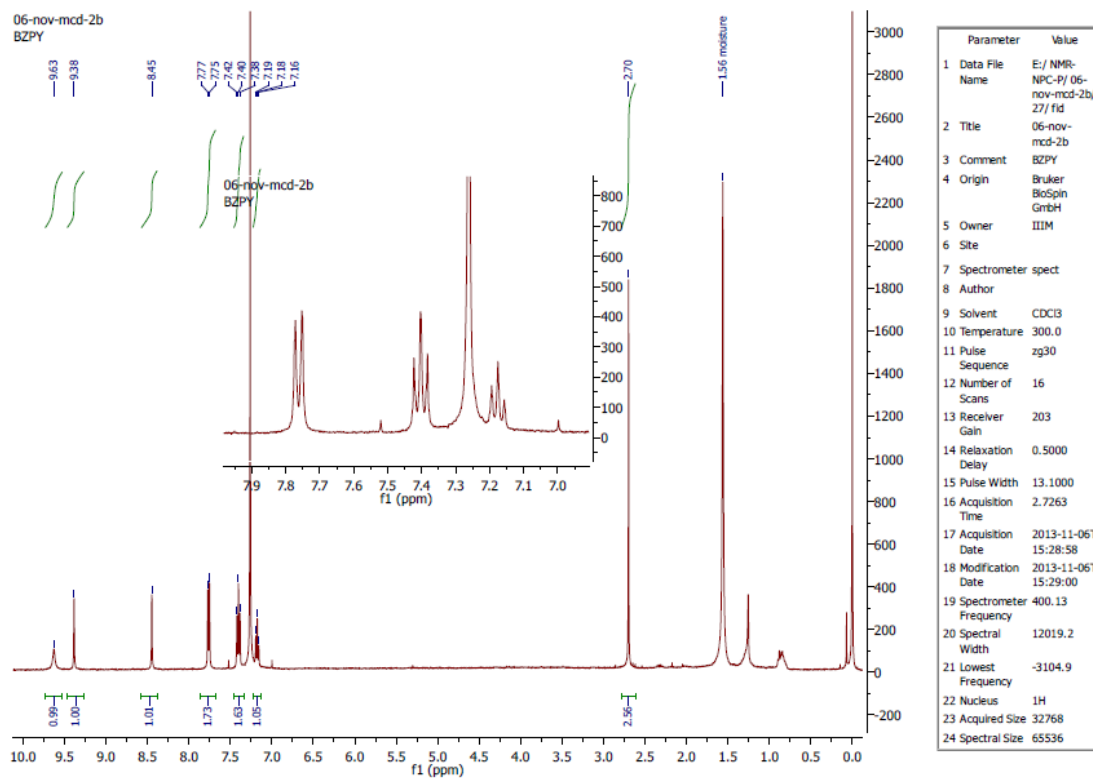


### S4.p. <sup>13</sup>C NMR Spectrum of 2-chloro-N-phenylbenzamide (1h)

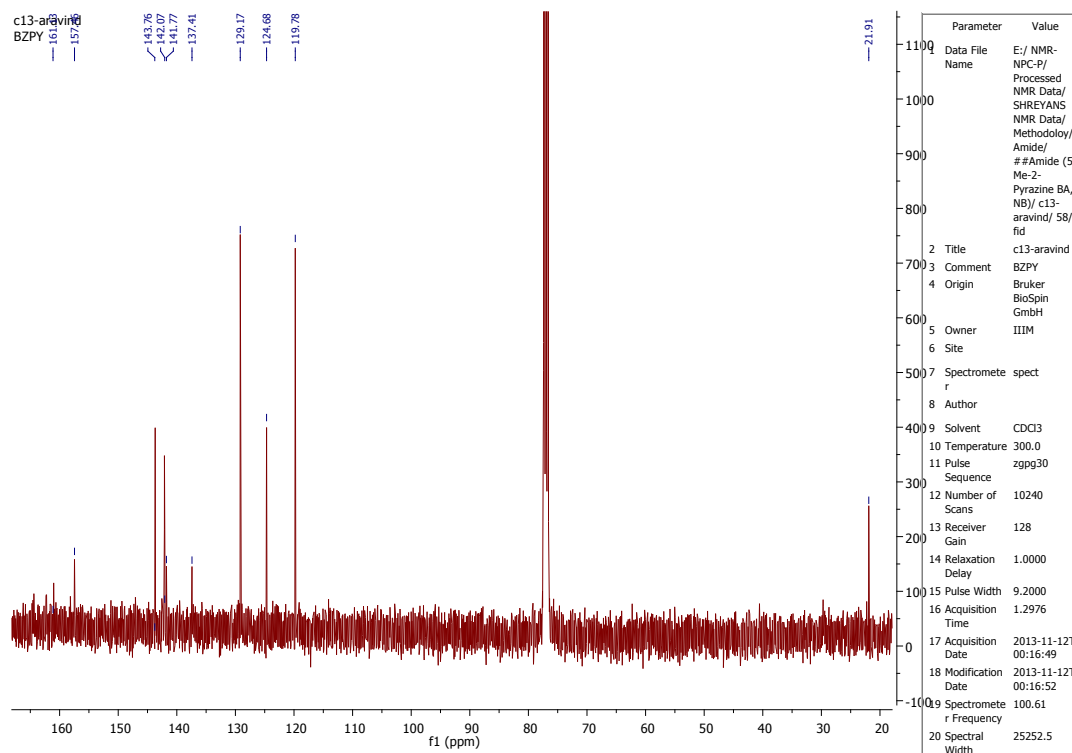




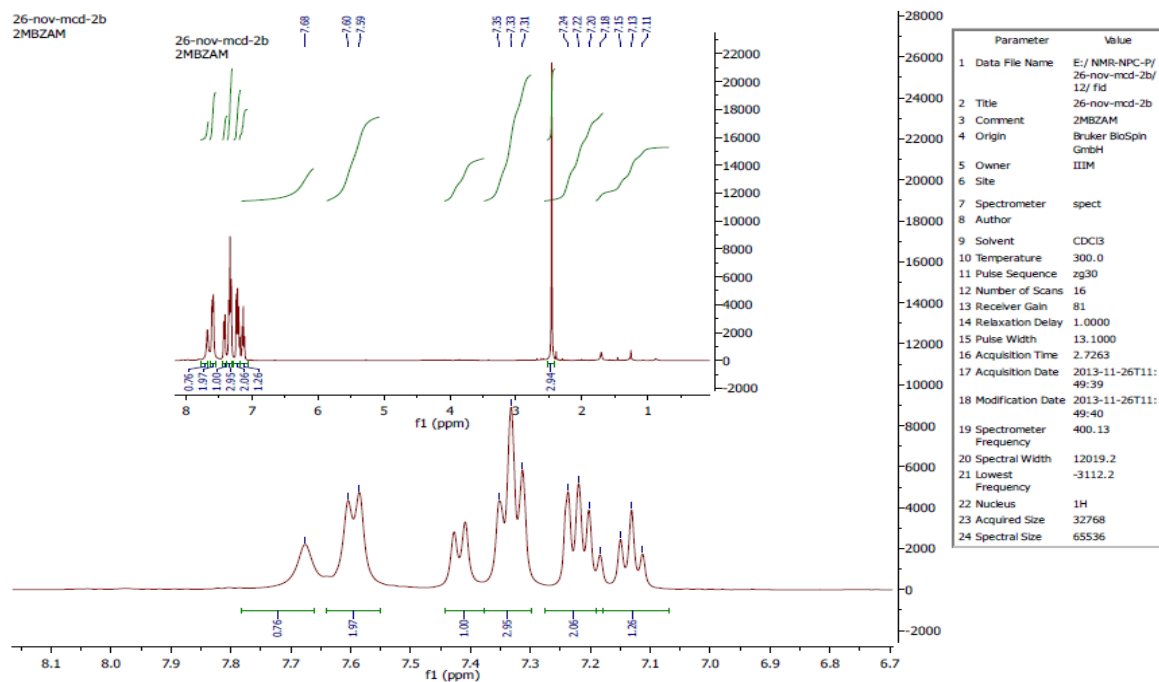
**S4.q.** <sup>1</sup>HNMR Spectrum of 5-methyl-N-phenylpyrazine-2-carboxamide (**1i**)



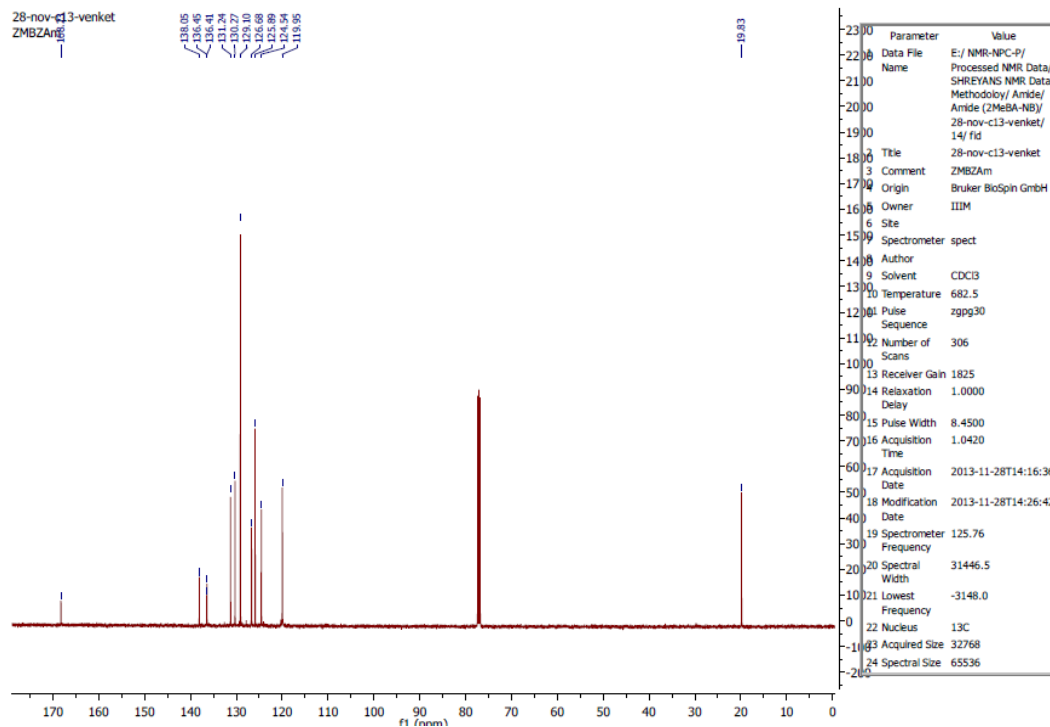
**S4.r.** <sup>13</sup>CNMR Spectrum of 5-methyl-N-phenylpyrazine-2-carboxamide (**1i**)



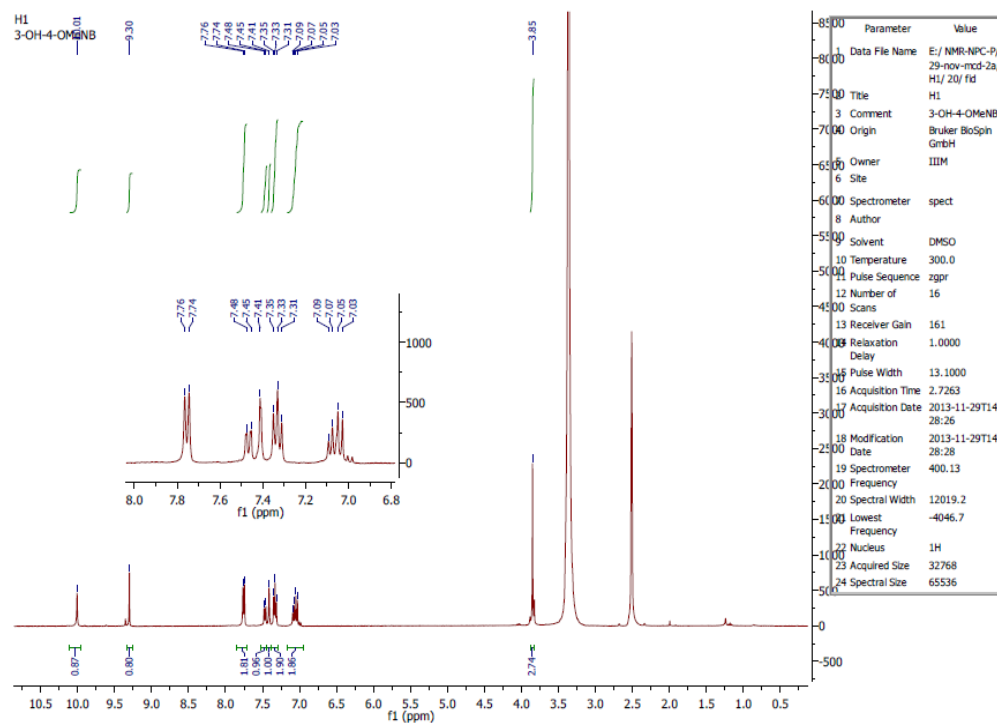
**S4.s.** <sup>1</sup>H NMR Spectrum of 2-methyl-N-phenylbenzamide (**1j**)



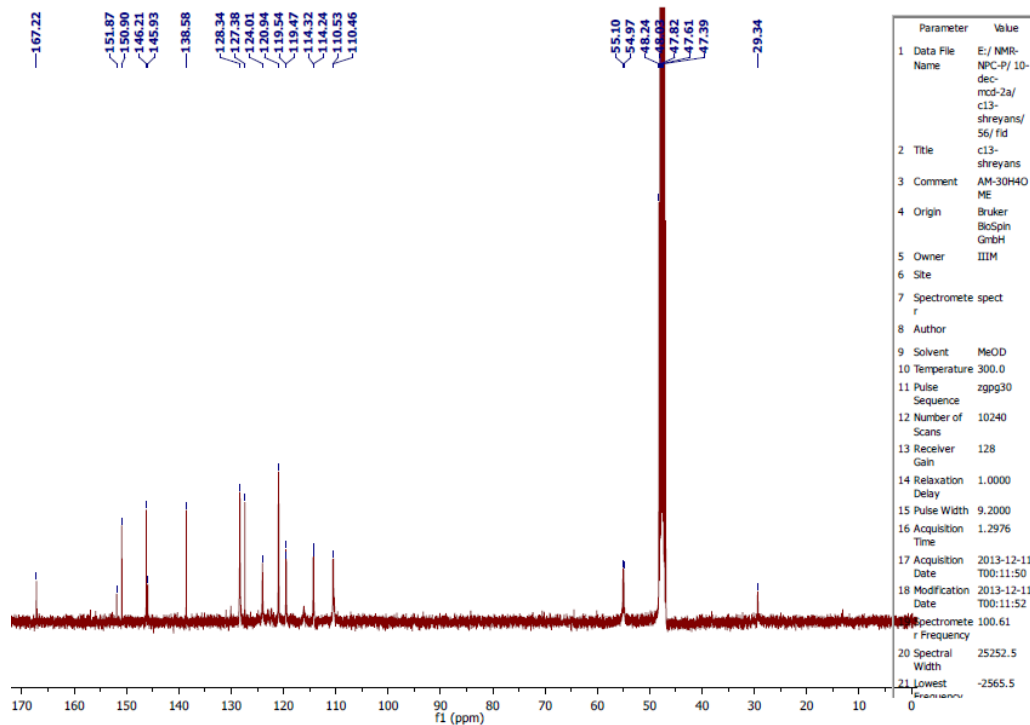
**S4.t.** <sup>13</sup>C NMR Spectrum of 2-methyl-N-phenylbenzamide (**1j**)



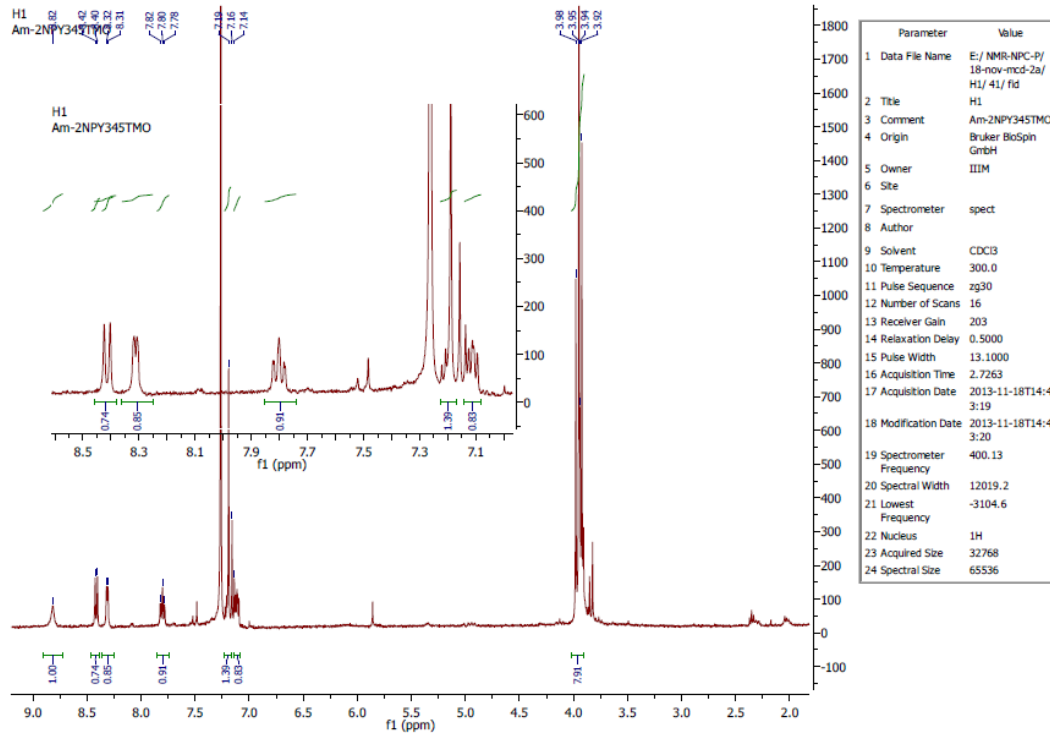
**S4.u.** <sup>1</sup>H NMR Spectrum of 3-hydroxy-4-methoxy-N-phenylbenzamide (**1k**)



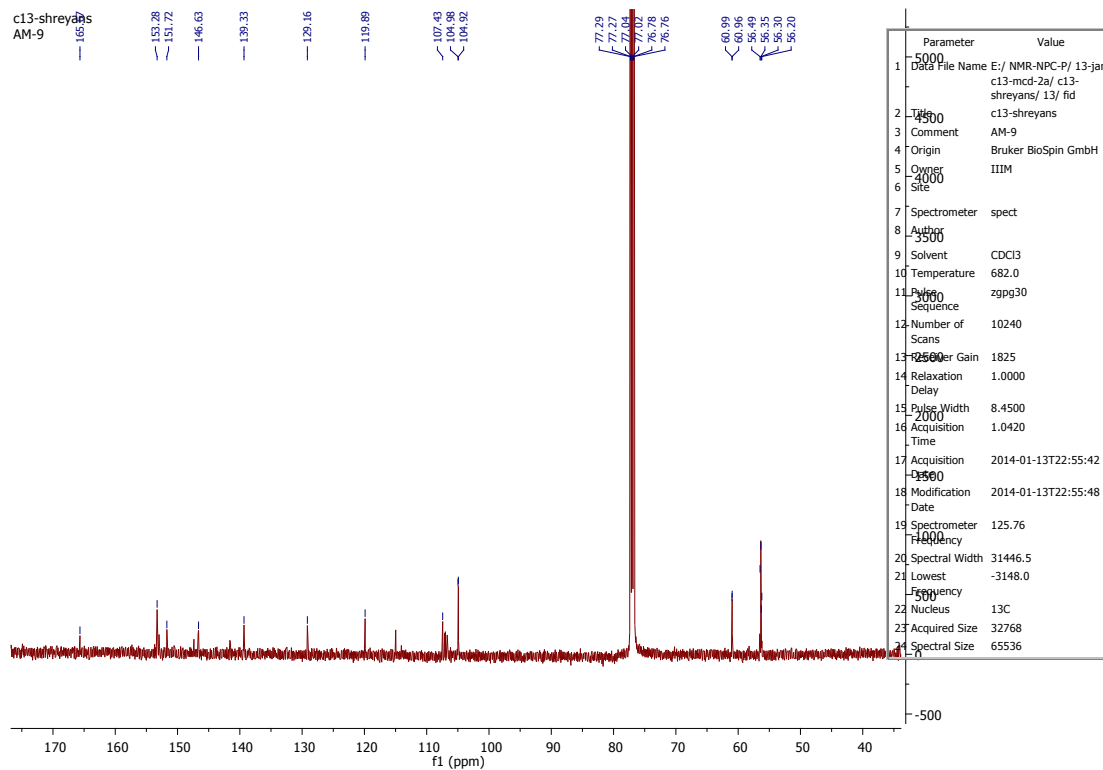
**S4.v.** <sup>13</sup>C NMR Spectrum of 3-hydroxy-4-methoxy-N-phenylbenzamide (**1k**)



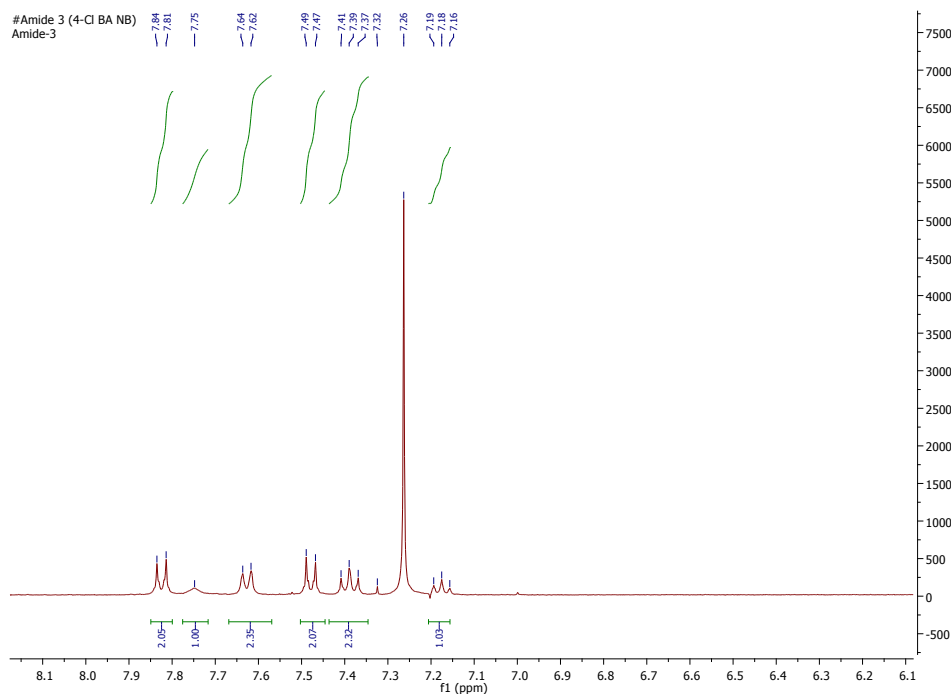
**S4.w.** <sup>1</sup>H NMR Spectrum 2,4,5-trimethoxy-N-(pyridin-2-yl)benzamide (**1l**)



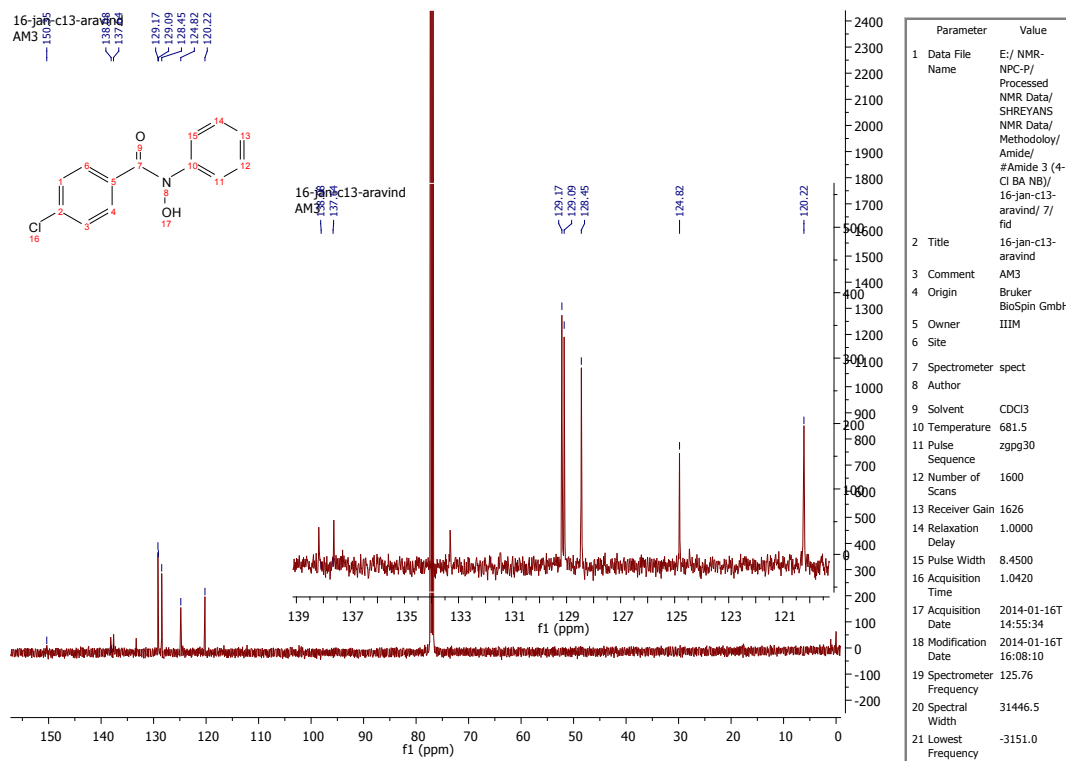
**S4.x.** <sup>13</sup>C-NMR Spectrum of 2,4,5-trimethoxy-N-(pyridin-2-yl)benzamide (**11**)



S4.y. <sup>1</sup>H NMR spectrum of 4-chloro-N-hydroxy-N-phenylbenzamide (**2a**) in CDCl<sub>3</sub>



S4.z. <sup>13</sup>C NMR spectrum of 4-chloro-N-hydroxy-N-phenylbenzamide (**2a**) in CDCl<sub>3</sub>



## Section S5. References associated with ESI

1. (a) S. K. Jain, S. B. Bharate and R. A. Vishwakarma, *Mini-Rev. Med. Chem.*, 2012, **12**, 632-649; (b) S. K. Jain, S. Meena, B. Singh, J. B. Bharate, P. Joshi, V. P. Singh, R. A. Vishwakarma and S. B. Bharate, *RSC Adv.*, 2012, **2**, 8929-8933.
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