Michael reaction of indoles with alpha, beta unsaturated carbonyl compounds by using environmental benign reagent DIB

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Abstract

The Michael addition reaction represents a pivotal strategy for carbon–carbon bond formation in organic synthesis. In this study, we report a green and efficient protocol for the Michael reaction of indoles with α,β-unsaturated carbonyl compounds utilizing the environmentally benign reagent 1,3-dibromo-5,5-dimethylhydantoin (DIB).

This method offers a mild, solvent-free and metal-free approach, promoting high yields and regioselectivity under ambient conditions. The use of DIB not only facilitates the reaction but also aligns with principles of green chemistry by minimizing hazardous waste and energy consumption. This protocol demonstrates broad substrate scope and operational simplicity, rendering it an attractive alternative for sustainable synthesis in heterocyclic chemistry.

Keywords: Michael addition, indoles, α,β-unsaturated carbonyl compounds, 1,3-dibromo-5,5-dimethylhydantoin (DIB), green chemistry, environmentally benign reagent, solvent-free synthesis, regioselectivity, sustainable synthesis, heterocyclic compounds.

Introduction

Indole moiety is a recurring structural motif in a number of natural products having important biological activities.[1,2] Among them 3-aminoindole derivatives are important class of compounds owing to the emergence in polycyclic structures and carbolines[3] and some of them are used as CNS drugs.[4] Synthetic derivatives of 3-aminoindoles represent attractive pharmacological targets such as HIV inhibitors[5] and antagonists of different receptors[6-9] (Figure 1). Furthermore, these derivatives show anti-bacterial, anti-malarial, anti-plasmoidal, anti-muscarinic and anti-fungal activities.[10] Since there exists an equilibrium between amine and imine functionalities, these substrates are useful for electrochemical research.[11]

However, the development of methods for these entities is not straightforward since the two fragments to be coupled are nucleophilic in nature. Although, indoles readily undergo electrophilic substitution on position-3; the nucleophlic substitution, which involves either replacement of hydrogen or halogen, is less common.[12,13] In order to employ such substitutions on indole moiety, the presence of leaving groups such as hydroxyl, methoxy and phenylsulfonyl are necessary on nitrogen atom.[14] Koutentis and his co-workers[23] introduced a method for the synthesis of 3-aminoindoles-2-carbonitriles from neutral 1,2,3-dithiazoles.

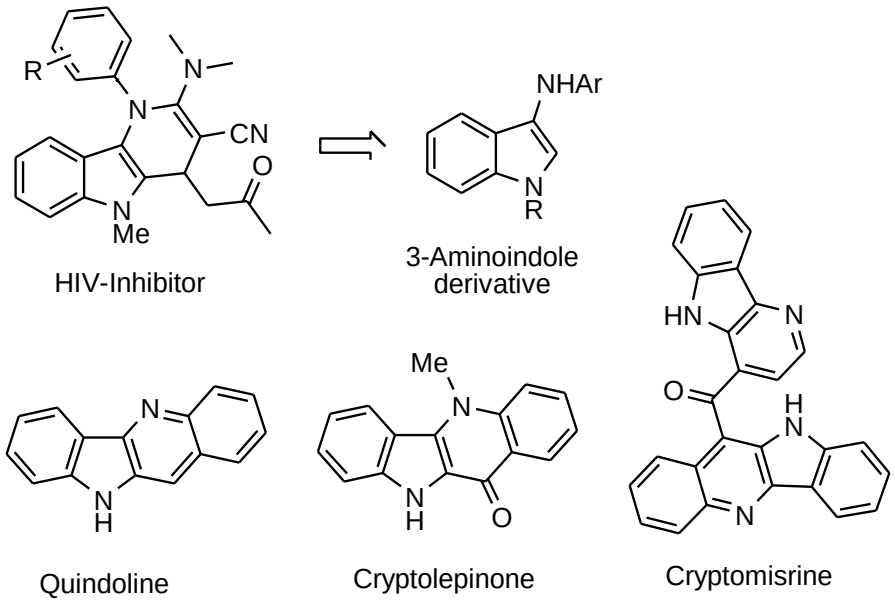


Figure 1: HIV-inhibitors and δ-carbolines having 3-aminoindole core.

The common approach to 3-aminoindole derivatives is either nitrosylation or nitration on indole moiety and reduction followed by derivatization of the amine functionality. Zinc-salt mediated synthesis of 3-aminoindole derivatives *via* hydroamination reaction was reported. A simple and straight forward method for the synthesis of prefunctionlized 3-aminoindoles would be of enormous value for the study of their chemistry and biology.

Material and Methods

General Procedure: A solution of *p*-aminophenol (1.2 equiv.) in tetrahydrofuran (3 mL) was added drop-wise to a solution of indole (1, 1 mmol), iodine (1.5 mmol) and potassium carbonate (3 mmol) in tetrahydrofuran (5 mL) at room temperature under aerobic conditions. The reaction mixture was stirred at the same temperature for 6 hours (including addition time). After which the solvent was removed under reduced pressure, the crude reaction mixture was loaded directly on silica gel column (100-200 mesh). The product was eluted by using ethyl acetate in hexanes (3:7).

2-Hydroxy-5-(1*H*-indol-3-ylamino)benzonitrile:
Yield: 0.201 g (80%) as yellow solid.
MP: 164-165 ^{o}C.
IR (KBr) ν_{max}: 3324, 3050, 2218, 966, 834 cm^{-1}.
^{1}H NMR (DMSO-d_6, 500 MHz): δ 7.93 (d, *J* = 2.0 Hz, 1H), 7.83 (d, *J* = 4.5 Hz, 1H), 7.73 (dt, *J* = 2.0, 9.0 Hz, 2H), 7.52 (dt, *J* = 1.5, 8.5 Hz, 1H), 7.33 (d, *J* = 8.5 Hz, 1H), 7.02 (d, *J* = 8.5 Hz, 1H),6.98 (d, *J* = 7.5 Hz, 1H), 5.68 (d, *J* = 5.0 Hz, 1H) ppm.

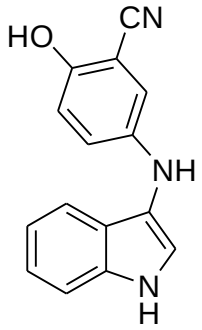
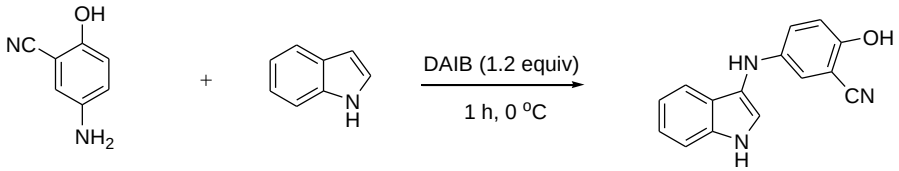


Figure 2: Structure of 2-Hydroxy-5-(1*H*-indol-3-ylamino) benzonitrile

^{13}C NMR (DMSO-d_6, 125 MHz): δ 164.3 (*C*), 156.6 (*C*), 145.1 (*C*), 135.7 (*C*), 135.0 (*C*H), 131.7 (*C*H), 129.6 (*C*H), 123.3 (*C*H), 119.8 (*C*H), 119.4 (*C*), 118.1 (*C*), 117.7 (*C*H), 111.7 (*C*H), 104.8 (*C*), 81.7 (*C*H) ppm.

HRMS (ES+): *m/z*calcd for $C_{15}H_{11}N_3O$ [M+Na]$^{+}$: 272.0800, found 272.0803.

Table 1
Optimization studies of aminoindoles.



1d **37** **44d**

Entry	Solvent	Base	Temp. (0 ^{o}C)	44d Yield (%)^{b}
1	THF	-	0	32
2	THF	$KHCO_3$	0	81
3	THF	Et_3N	0	-
4	THF	Pyridine	0	36
5	THF	$KHCO_3$	RT	64
6	THF	$KHCO_3$	50	42
7	CH_2Cl_2	$KHCO_3$	0	68
8	CH_2Cl_2	-	0	30
9	CH_2Cl_2	Et_3N	0	-
10	CH_3CN	$KHCO_3$	0	72

Methyl 5-(1*H*-indol-3-ylamino)-2-hydroxybenzoate:
Yield: 0.225 g (78%) as yellow solid.
MP: 162-163 ^{o}C.
IR (KBr) ν_{max}: 3425, 2257, 1732, 967 cm^{-1}.

^{1}H NMR (DMSO-d_6, 500 MHz): δ 7.98 (d, *J* = 2.0 Hz, 1H), 7.86 (dd, *J* = 2.5, 8.5 Hz, 1H), 7.78 (d, *J* = 4.5 Hz, 1H), 7.75 (d, *J* = 7.5 Hz, 1H), 7.51 (dt, *J* = 2.0, 8.5 Hz, 1H), 7.26 (d, *J* = 8.0 Hz, 1H), 7.11 (d, *J* = 8.0 Hz, 1H), 6.98 (d, *J* = 7.5 Hz, 1H), 5.65 (d, *J* = 4.5 Hz, 1H), 3.92 (s, 3H) ppm.

^{13}C NMR (DMSO-d_6, 125 MHz): δ 165.1 (*C*=O), 163.6 (*C*), 156.3 (*C*), 145.3 (*C*), 135.2 (*C*), 134.7 (*C*H), 128.7 (*C*H), 126.8 (*C*), 123.8 (*C*), 123.2 (*C*H), 119.7 (*C*), 119.6 (*C*H), 111.6 (*C*H), 99.0 (*C*), 81.8 (*C*H), 51.6 (O*C*H$_3$) ppm.

HRMS (ES+): *m/z*calcd for $C_{16}H_{14}N_2O_3$ $[M+Na]^+$: 305.0902, found 305.0912.

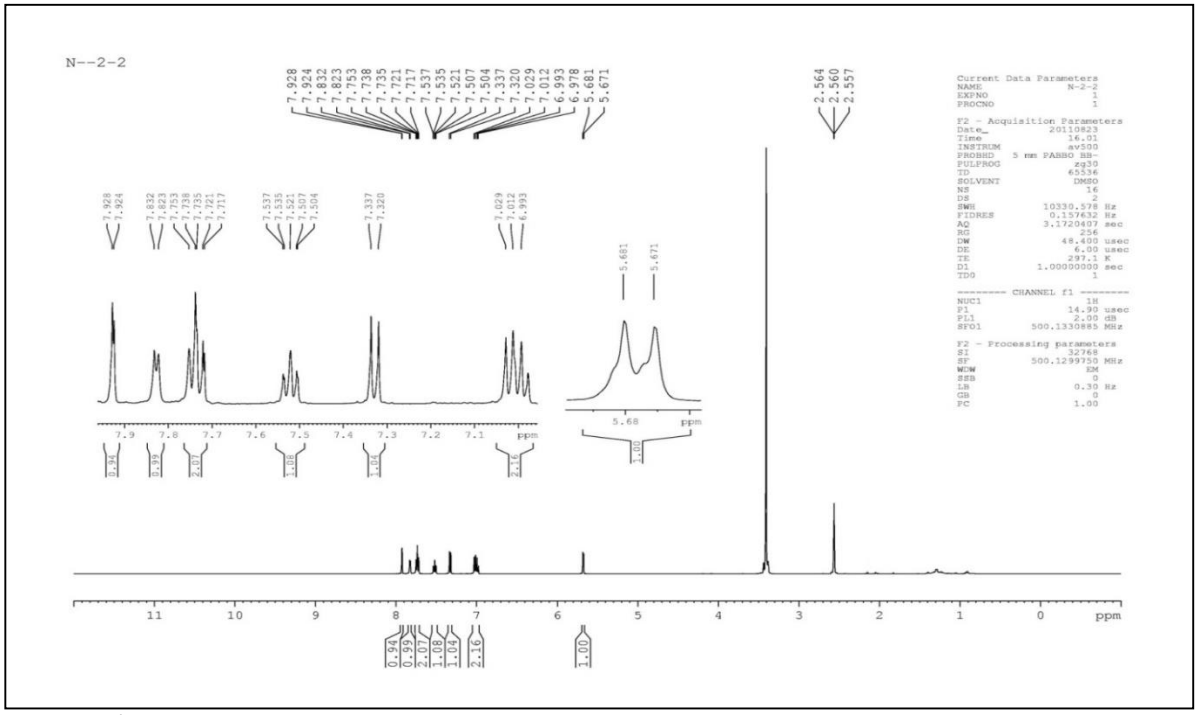


Figure 3: ^{1}H NMR (500 MHz, DMSO-d_6) Spectrum of -Hydroxy-5-(1*H*-indol-3-ylamino) benzonitrile

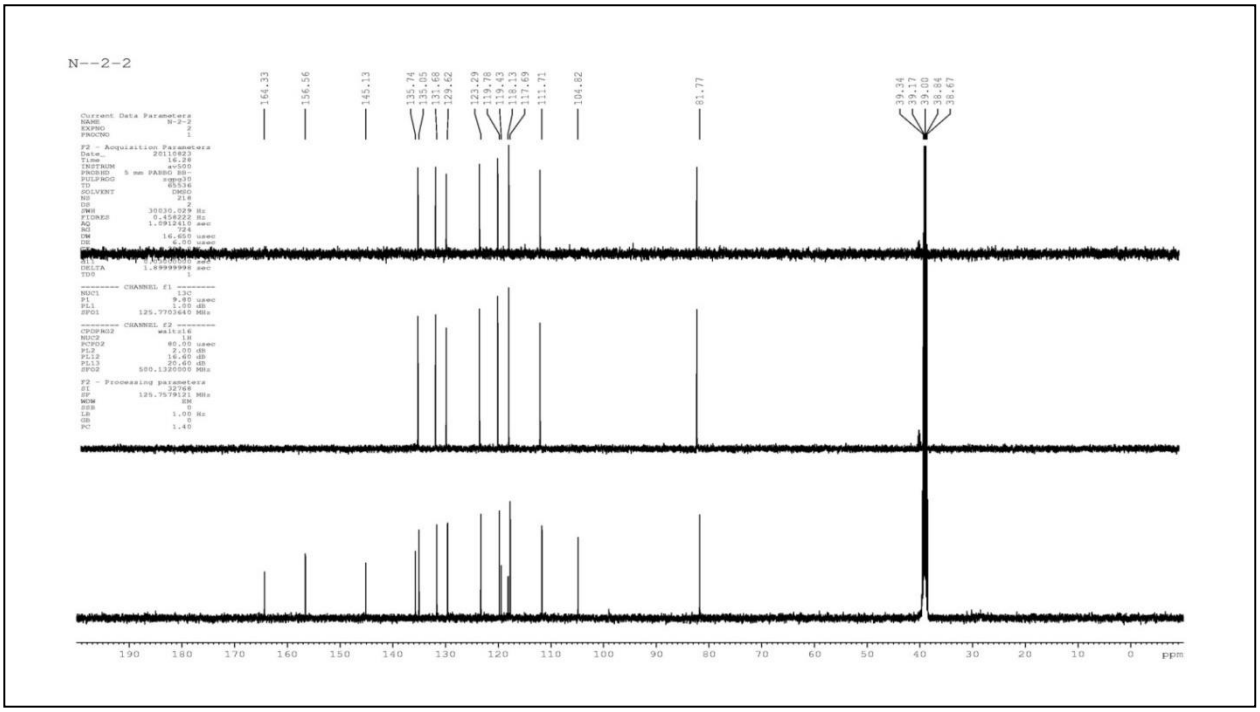


Figure 4: ^{13}C DEPT (125 MHz, DMSO-d_6) Spectra of -Hydroxy-5-(1*H*-indol-3-ylamino) benzonitrile

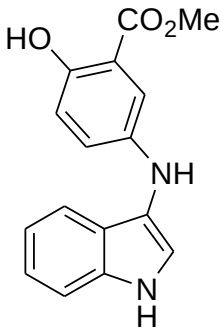


Figure 5: Methyl 5-(1*H*-indol-3-ylamino)-2-hydroxybenzoate

Methyl 5-(5-methoxy-1*H*-indol-3-ylamino)-2-hydroxy benzoate:
Yield: 0.246 g (80%) as yellow solid.
MP: 182-183 ^{o}C.
IR (KBr) ν_{max}: 3468, 2257, 1741, 932 cm^{-1}.

^{1}H NMR (DMSO-d_6, 500 MHz): δ 7.93 (d, *J* = 2.0 Hz, 1H), 7.82 (dd, *J* = 2.0, 8.0 Hz, 1H), 7.40 (d, *J* = 5.0 Hz, 1H), 7.22 (s, 1H), 7.21 (d, *J* = 11.5 Hz, 1H), 7.12 (dd, *J* = 2.5, 8.5 Hz, 1H), 6.96 (d, *J* = 8.5 Hz, 1H), 5.59 (d, *J* = 5.0 Hz, 1H), 3.89 (s, 3H), 3.52 (s, 3H) ppm.

^{13}C NMR (DMSO-d_6, 125 MHz): δ 165.2 (*C*=O), 163.8 (*C*), 153.3 (*C*), 151.1 (*C*), 145.4 (*C*), 135.1 (*C*), 128.7 (*C*H), 126.9 (*C*H), 123.8 (*C*H), 123.3 (*C*), 120.2 (*C*), 116.5 (*C*H), 113.1 (*C*H), 105.2 (*C*H), 82.4 (*C*H), 55.1 (O*C*H$_3$), 51.6 (O*C*H$_3$) ppm.

1-(5-(5-Methoxy-1*H*-indol-3-ylamino)-2-hydroxyphenyl) ethanone:
Yield: 0.239 g (81%) as yellow solid.
MP: 168-169 ^{o}C.
IR (KBr) ν_{max}: 3394, 2253, 1703, 958 cm^{-1}.

^{1}H NMR (DMSO-d_6, 500 MHz): δ 8.01 (d, *J* = 2.0 Hz, 1H), 7.87 (d, *J* = 2.0 Hz, 1H), 7.85 (d, *J* = 2.5 Hz, 1H), 7.42 (d, *J* = 6.5 Hz, 1H), 7.24 (d, *J* = 1.0 Hz, 1H), 7.23 (d, *J* = 4.5 Hz, 1H), 7.16 (d, *J* = 2.5 Hz, 1H), 7.14 (d, *J* = 2.5 Hz, 1H), 6.98 (d, *J* = 9.0 Hz, 1H), 5.61 (d, *J* = 5.5 Hz, 1H), 3.82 (s, 3H), 2.64 (s, 3H) ppm.

^{13}C NMR (DMSO-d_6, 125 MHz): δ 196.0 (*C*=O), 163.7 (*C*), 153.3 (*C*), 151.0 (*C*), 145.4 (*C*), 135.0 (*C*), 131.6 (*C*), 127.9 (*C*H), 126.3 (*C*H), 123.3 (*C*H), 120.3 (*C*), 116.4 (*C*H), 113.2 (*C*H), 105.2 (*C*H), 82.4 (*C*H), 55.1 (*C*H), 26.2 (*C*H) ppm.

HRMS (ES+): *m/z*calcd for $C_{17}H_{16}N_2O_3$ $[M+Na]^+$: 319.1059, found 319.1052.

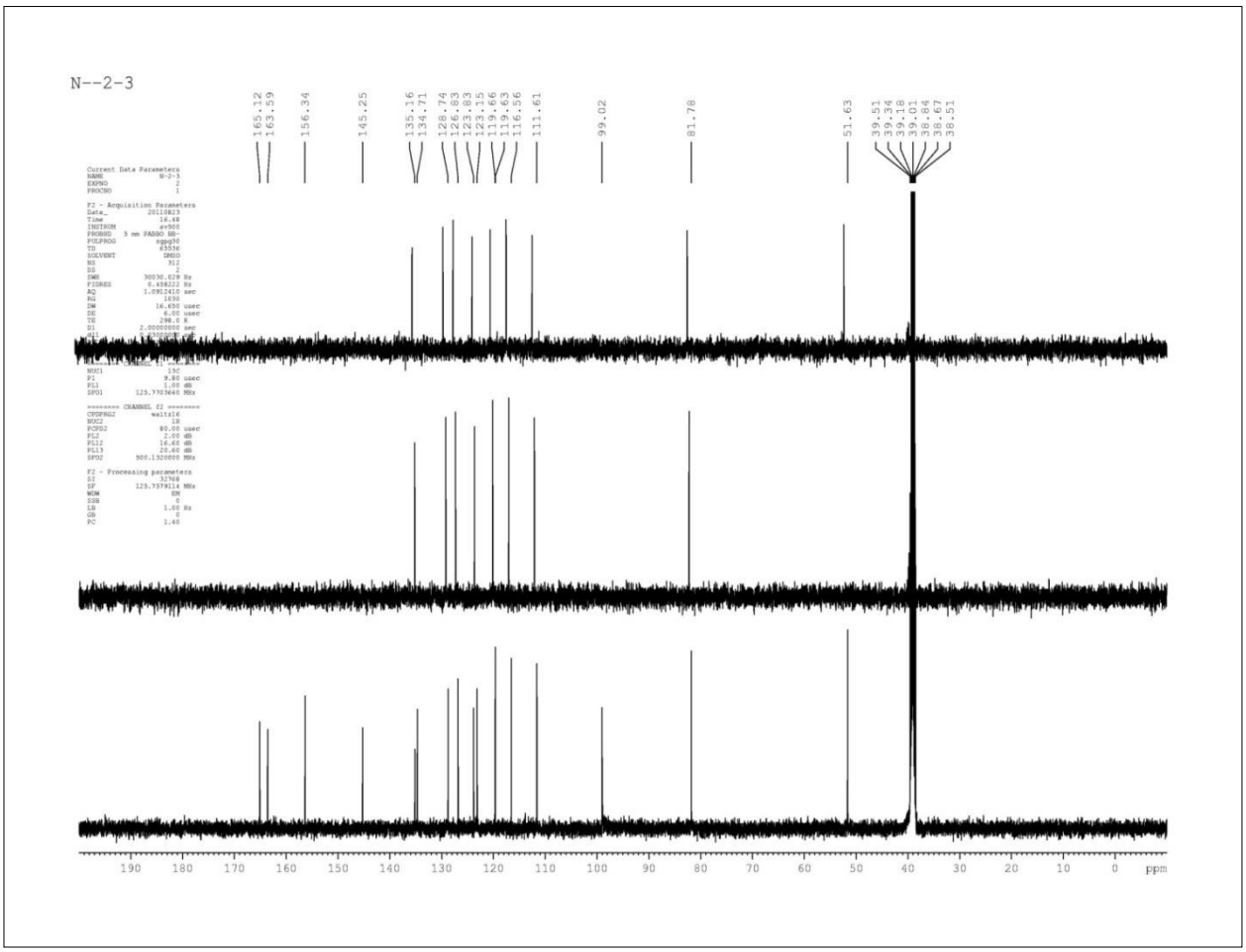


Figure 6: ^{13}C DEPT (125 MHz, DMSO-d_6) Spectra of Methyl 5-(1*H*-indol-3-ylamino)-2-hydroxybenzoate

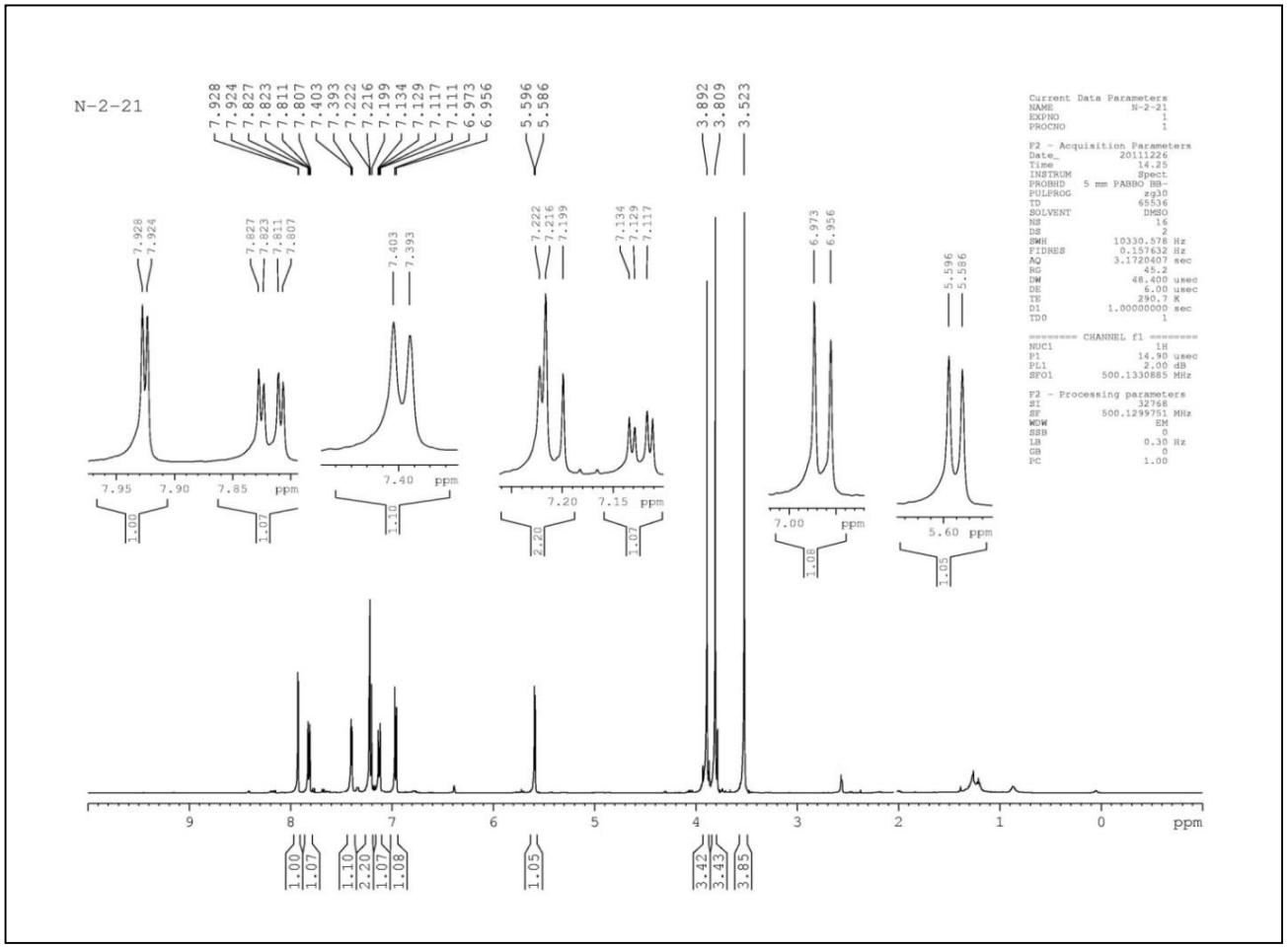


Figure 7: ^{1}H NMR (500 MHz, DMSO-d_6) Spectrum of Methyl 5-(1*H*-indol-3-ylamino)-2-hydroxybenzoate

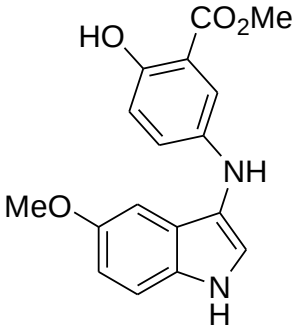


Figure 8: Methyl 5-(5-methoxy-1*H*-indol-3-ylamino)-2-hydroxybenzoate

2-Hydroxy-5-(5-methyl-1*H*-indol-3-ylamino) benzonitrile:
Yield: 0.205 g (78%) as yellow solid.
MP: 174-175 ^{o}C.
IR (KBr) ν_{max}: 3324, 3452, 2272, 1642, 938 cm^{-1}.

^{1}H NMR (DMSO-d_6, 500 MHz): δ 7.91 (s, 1H), 7.72 (d, *J* = 8.0 Hz, 1H), 7.64 (d, *J* = 4.5 Hz, 1H), 7.56 (s, 1H), 7.35 (d, *J* = 8.0 Hz, 1H), 7.32 (d, *J* = 8.5 Hz, 1H), 6.94 (d, *J* = 8.5 Hz, 1H), 5.64 (d, *J* = 5.0 Hz, 1H), 2.34 (s, 3H) ppm.

^{13}C NMR (DMSO-d_6, 125 MHz): δ 164.4 (*C*), 154.7 (*C*), 145.3 (*C*), 136.1 (*C*), 135.8 (*C*), 131.6 (*C*H), 129.6 (*C*H), 128.9 (*C*), 123.0 (*C*H), 119.6 (*C*), 118.1 (*C*), 117.7 (*C*H), 111.7 (*C*H), 104.8 (*C*H), 82.0 (*C*H), 19.8 (*C*H$_3$) ppm.
HRMS (ES+): *m/z*calcd for $C_{16}H_{13}N_3O$ [M+Na]$^{+}$: 286.0956, found 286.0952.

1-(5-(5-Methyl-1*H*-indol-3-ylamino)-2-hydroxyphenyl) ethanone:
Yield: 0.218 g (78%) as yellow solid.
MP: 138-139 ^{o}C.
IR (KBr) ν_{max}: 3456, 1700, 1234,987 cm^{-1}.

^{1}H NMR (DMSO-d_6, 500 MHz): δ 8.07 (d, *J* = 2.0 Hz, 1H), 7.87 (d, *J* = 2.5 Hz, 1H), 7.85 (d, *J* = 2.5 Hz, 1H), 7.73 (d, *J* = 7.5 Hz, 1H), 7.70 (s, 1H), 7.49 (dt, *J* = 1.0, 8.5 Hz, 1H),

7.21 (d, *J* = 8.5 Hz, 1H), 6.98-6.94 (m, 2H), 2.64 (s, 3H), 1.39 (s, 3H) ppm.

^{13}C NMR (DMSO-d_6, 125 MHz): δ 196.0 (*C*=O), 164.8 (*C*), 154.8 (*C*), 145.3 (*C*), 134.7 (*C*H), 133.5 (*C*), 131.4 (*C*), 128.0 (*C*H), 126.5 (*C*H), 123.4 (*C*H), 119.6 (*C*H), 119.1 (*C*), 116.4 (*C*H), 111.6 (*C*H), 87.3 (*C*), 26.1 (CH_3), 18.3 (CH_3) ppm.
HRMS (ES+): *m/z*calcd for $C_{17}H_{16}N_2O_2$ $[M+Na]^+$: 303.1109, found 303.1116.

2-Hydroxy-5-(1-methyl-1*H*-indol-3-ylamino) benzonitrile:
Yield: 0.189 g (72%) as yellow solid.
MP: 142-143 ^oC.
IR (KBr) ν_{max}: 3324, 3468, 2224, 1654, 895 cm^{-1}.

^{1}H NMR (DMSO-d_6, 500 MHz): δ 7.96 (d, *J* = 2.0 Hz, 1H), 7.77 (d, *J* = 6.5 Hz, 1H), 7.75 (dd, *J* = 2.0, 8.0 Hz, 1H), 7.61 (dt, *J* = 1.5, 8.5 Hz, 1H), 7.37 (d, *J* = 8.0 Hz, 1H), 7.13 (d, *J* = 8.5 Hz, 1H), 7.04 (t, *J* = 7.0 Hz, 1H), 5.43 (s, 1H), 3.15 (s, 3H) ppm.

^{13}C NMR (DMSO-d_6, 125 MHz): δ 162.5 (*C*), 156.8 (*C*), 145.0 (*C*), 135.5 (*C*), 135.3 (*C*H), 131.9 (*C*H), 129.9 (*C*H), 123.1 (*C*H), 119.8 (*C*H), 119.4 (*C*), 118.1 (*C*), 117.8 (*C*H), 109.6 (*C*H), 105.1 (*C*), 86.6 (*C*H), 32.7 (CH_3) ppm.

HRMS (ES+): *m/z*calcd for $C_{16}H_{13}N_3O$ $[M+Na]^+$: 286.0956, found 286.0959.

Results and Discussion

In an early experiment, when 2-hydroxy-5-aminobenzonitrile 1a was treated with indole (3) in the presence of DIB in THF, 3-aminosubstituted indole 2a was obtained in 32% yield. The formation of 2a in low yield was the result of the decomposition of the product in the reaction medium due to the presence of acetic acid which was released from DAIB. Consequently, the reaction was carried out in basic conditions. In order to obtain the optimal conditions, we carried out the reaction of aminophenol 1a with indole (3) in the presence of DAIB (1.2 equiv) under different conditions. The results are shown in table 4. Of the tested solvents, THF was found to be effective. Among the bases used, $KHCO_3$ increased the efficiency of the reaction (Table 7, entry 2).

Addition of triethylamine to the solution of 1a in DCM rendered the solution to red colour immediately. The reaction in the presence of pyridine gave the product in low yield (Table 7, entry 4). It was also noticed that the product was obtained in low yield when the reaction was performed at 50 ^oC. This may be attributed to the decomposition of highly reactive *p*-quinone monoimine species at this temperature.

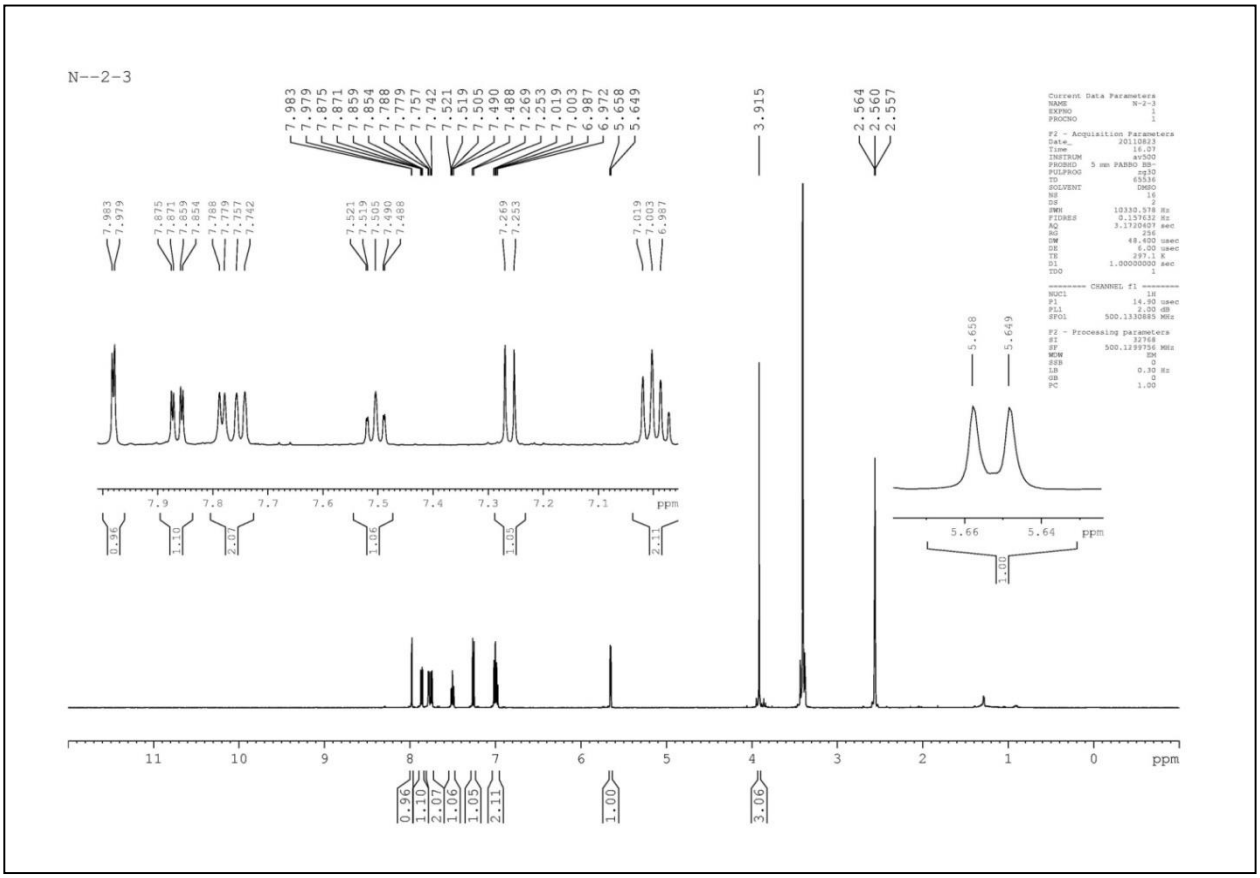


Figure 9: ^{1}H NMR (500 MHz, DMSO-d_6) Spectrum Methyl 5-(5-methoxy-1*H*-indol-3-ylamino)-2-hydroxybenzoate

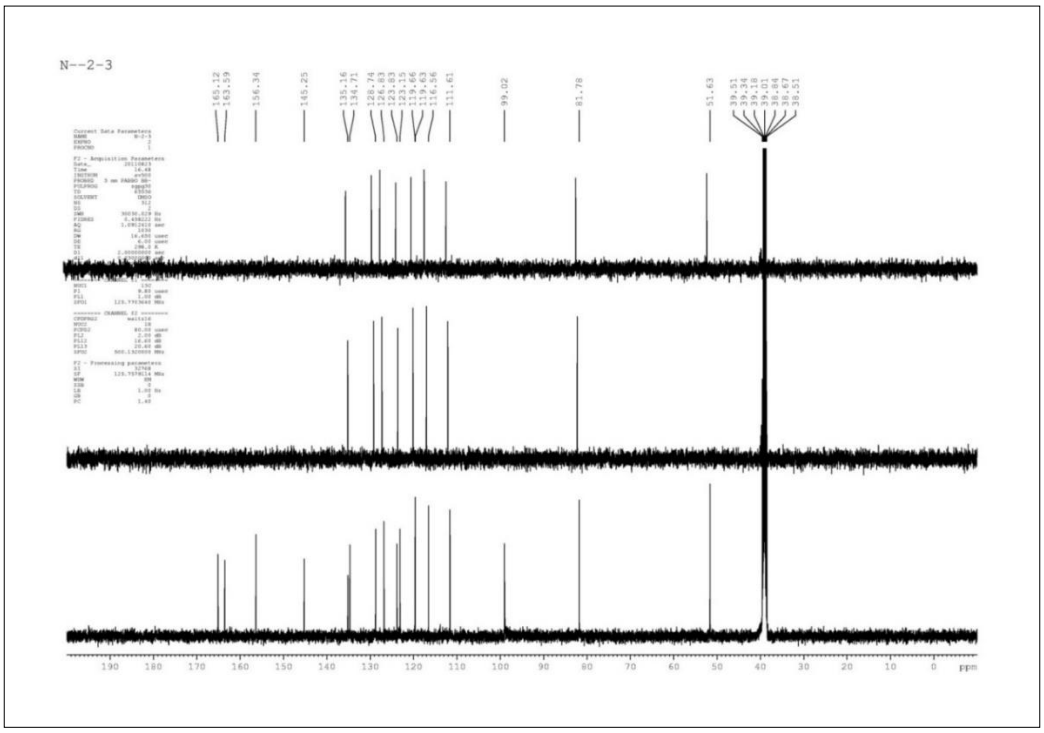


Figure 10: ^{13}C DEPT (125 MHz, DMSO-d_6) Spectra of Methyl 5-(5-methoxy-1*H*-indol-3-ylamino)-2-hydroxybenzoate

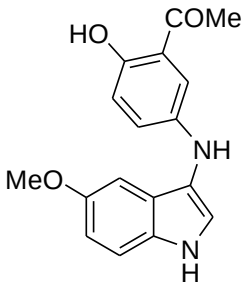


Figure 11: 1-(5-(5-Methoxy-1*H*-indol-3-ylamino)-2-hydroxyphenyl)ethanone

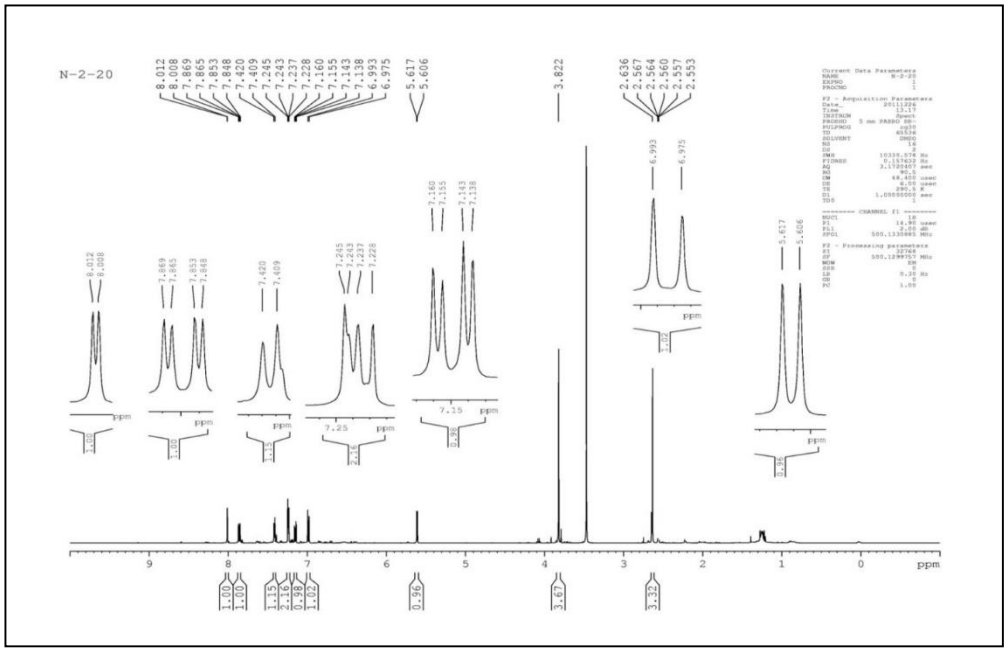


Figure 12: ^{1}H NMR (500 MHz, DMSO-d_6) Spectrum of 1-(5-(5-Methoxy-1*H*-indol-3-ylamino)-2-hydroxyphenyl)ethanone

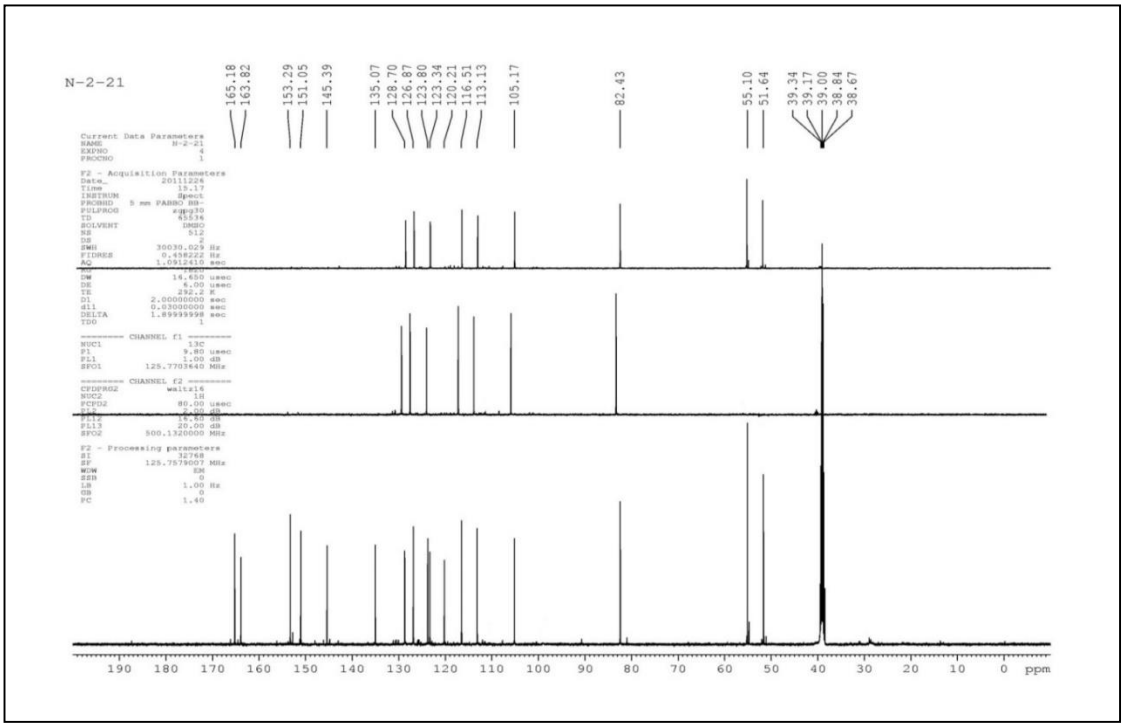


Figure 13: ^{13}C DEPT (125 MHz, DMSO-d_6) Spectra of 1-(5-(5-Methoxy-1*H*-indol-3-ylamino)-2-hydroxyphenyl)ethanone

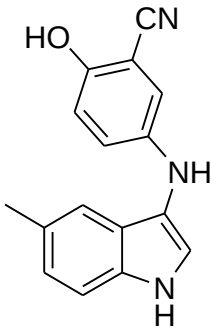


Figure 14: 2-Hydroxy-5-(5-methyl-1*H*-indol-3-ylamino) benzonitrile

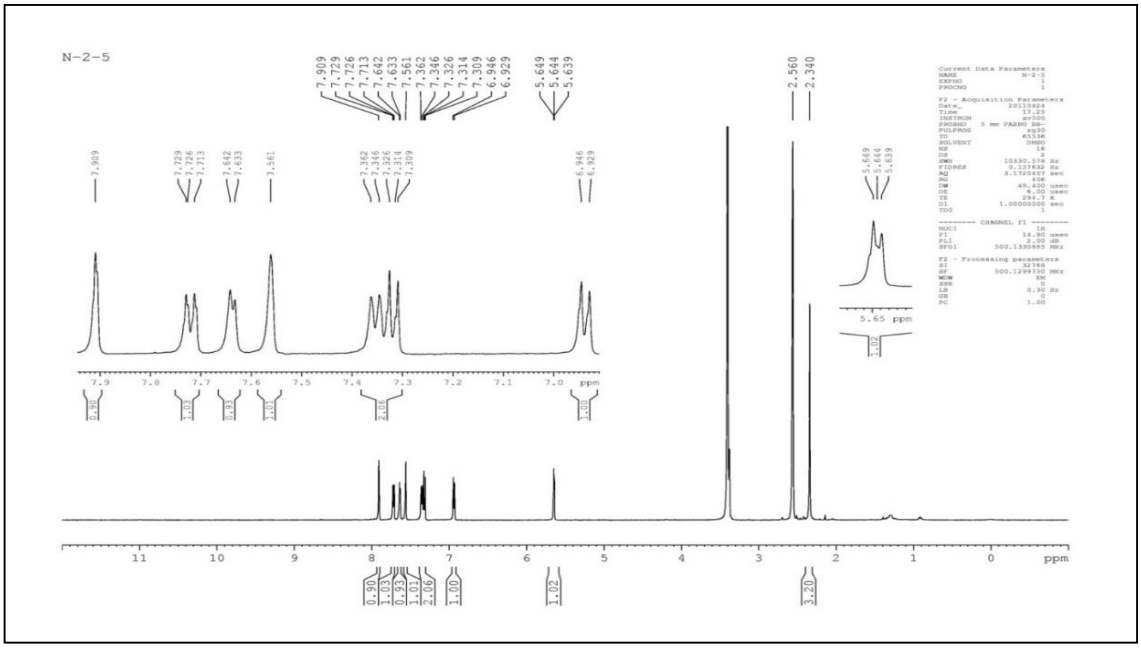


Figure 15: ^{1}H NMR (500 MHz, DMSO-d_6) Spectrum of 2-Hydroxy-5-(5-methyl-1*H*-indol-3-ylamino) benzonitrile

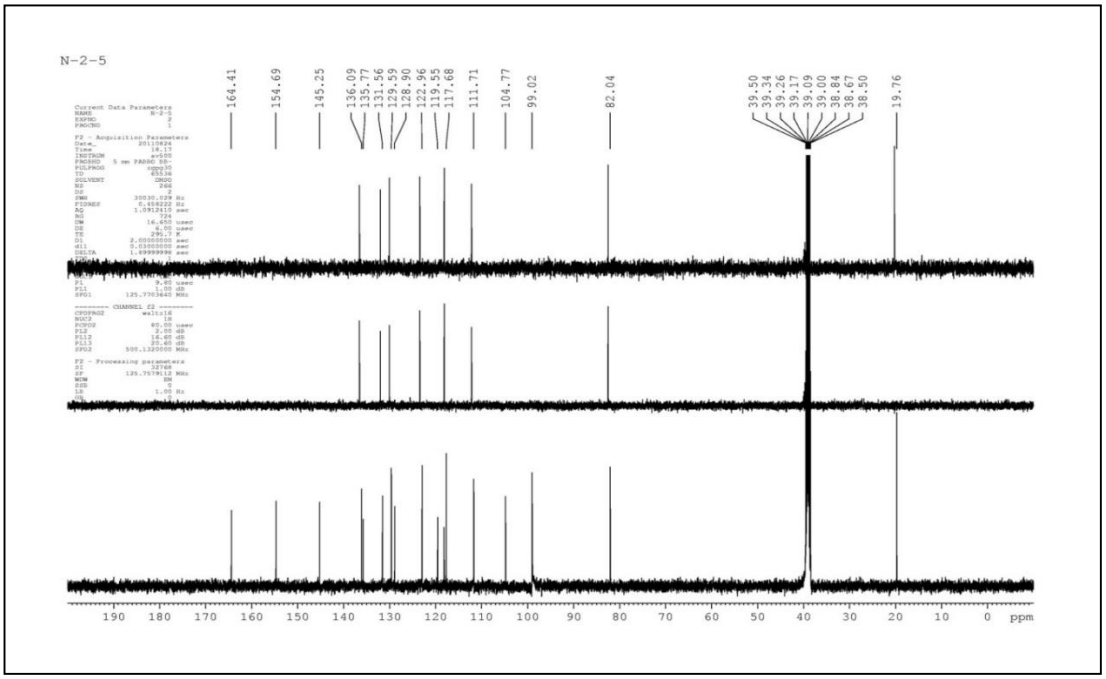


Figure1 16: ^{13}C DEPT (125 MHz, DMSO-d_6) Spectra of 2-Hydroxy-5-(5-methyl-1*H*-indol-3-ylamino) benzonitrile

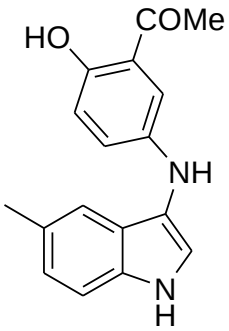


Figure 17: 1-(5-(5-Methyl-1*H*-indol-3-ylamino)-2-hydroxyphenyl) ethanone

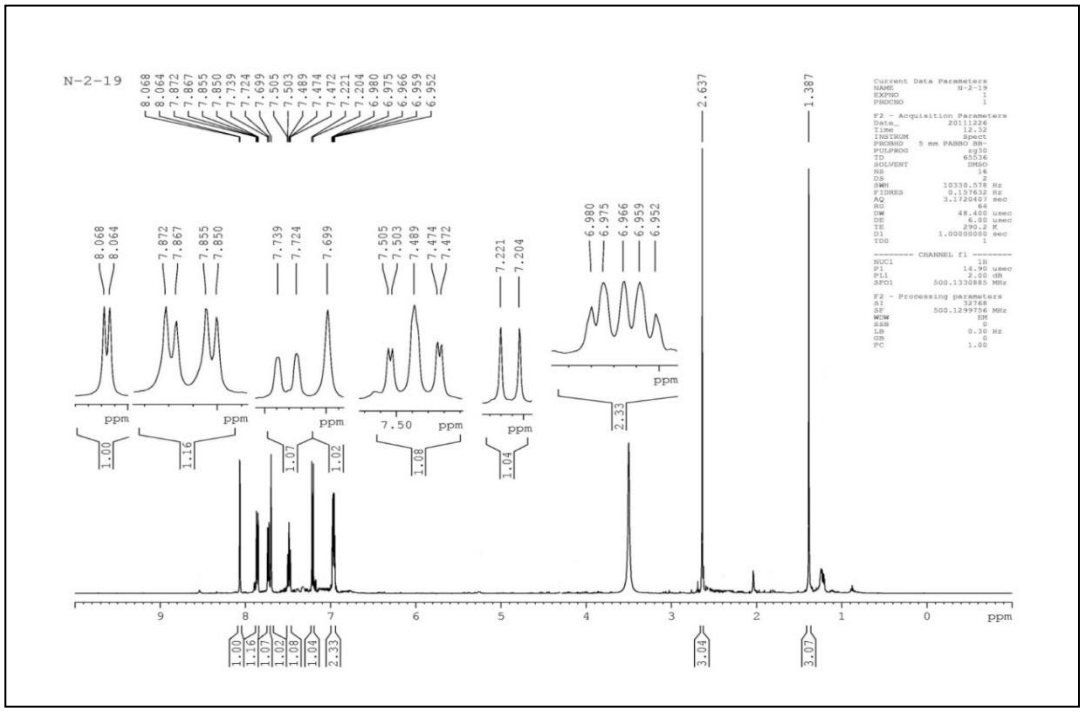


Figure 18: ^{1}H NMR (500 MHz, DMSO-d_6) Spectrum of 2-Hydroxy-5-(5-methyl-1*H*-indol-3-ylamino) benzonitrile

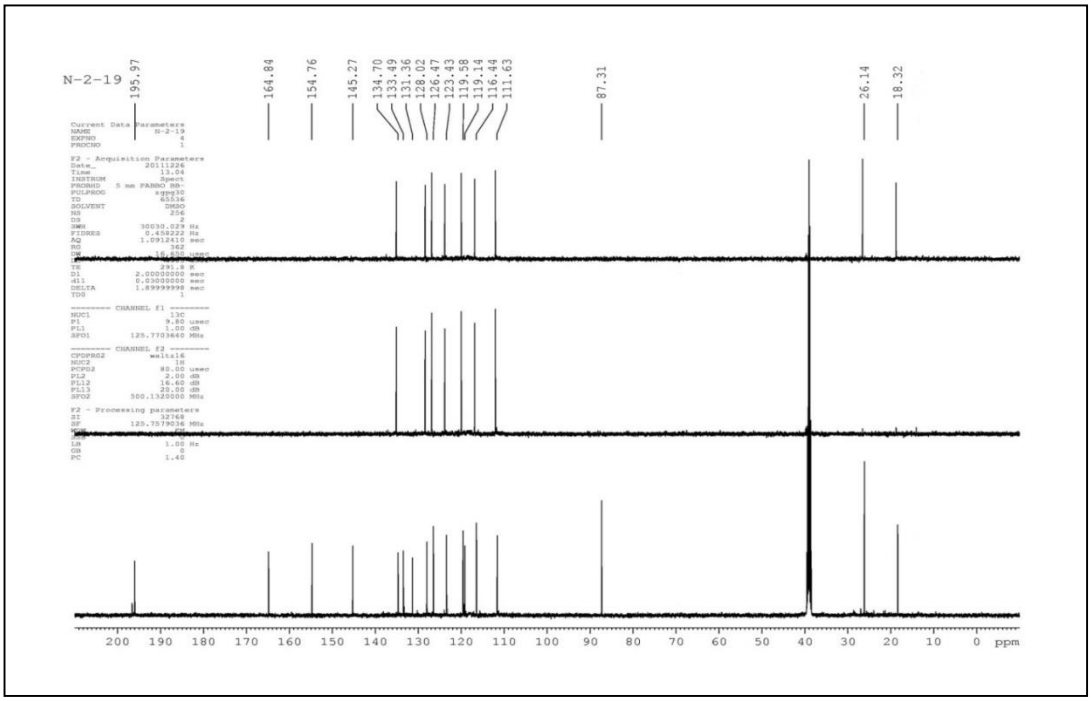


Figure 19: ^{13}C DEPT (125 MHz, DMSO-d_6) Spectra of 2-Hydroxy-5-(5-methyl-1*H*-indol-3-ylamino) benzonitrile

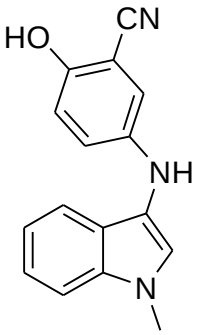


Figure 20: 2-Hydroxy-5-(1-methyl-1*H*-indol-3-ylamino) benzonitrile

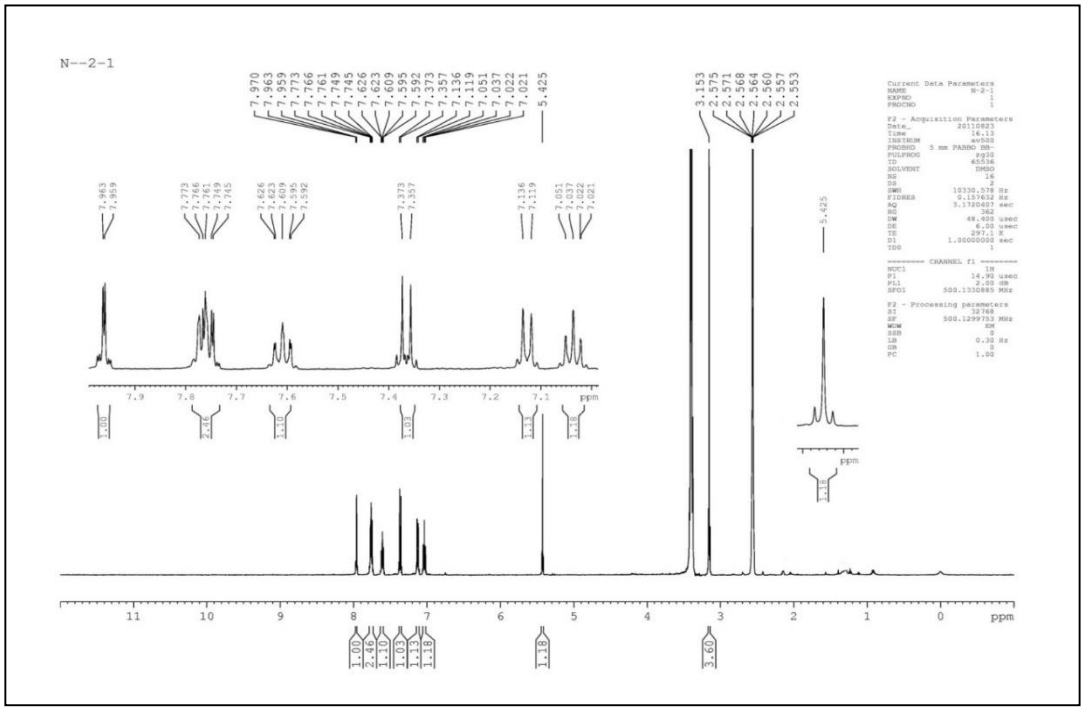


Figure 21: ^{1}H NMR (500 MHz, DMSO-d_6) Spectrum of 2-Hydroxy-5-(1-methyl-1*H*-indol-3-ylamino)benzonitrile

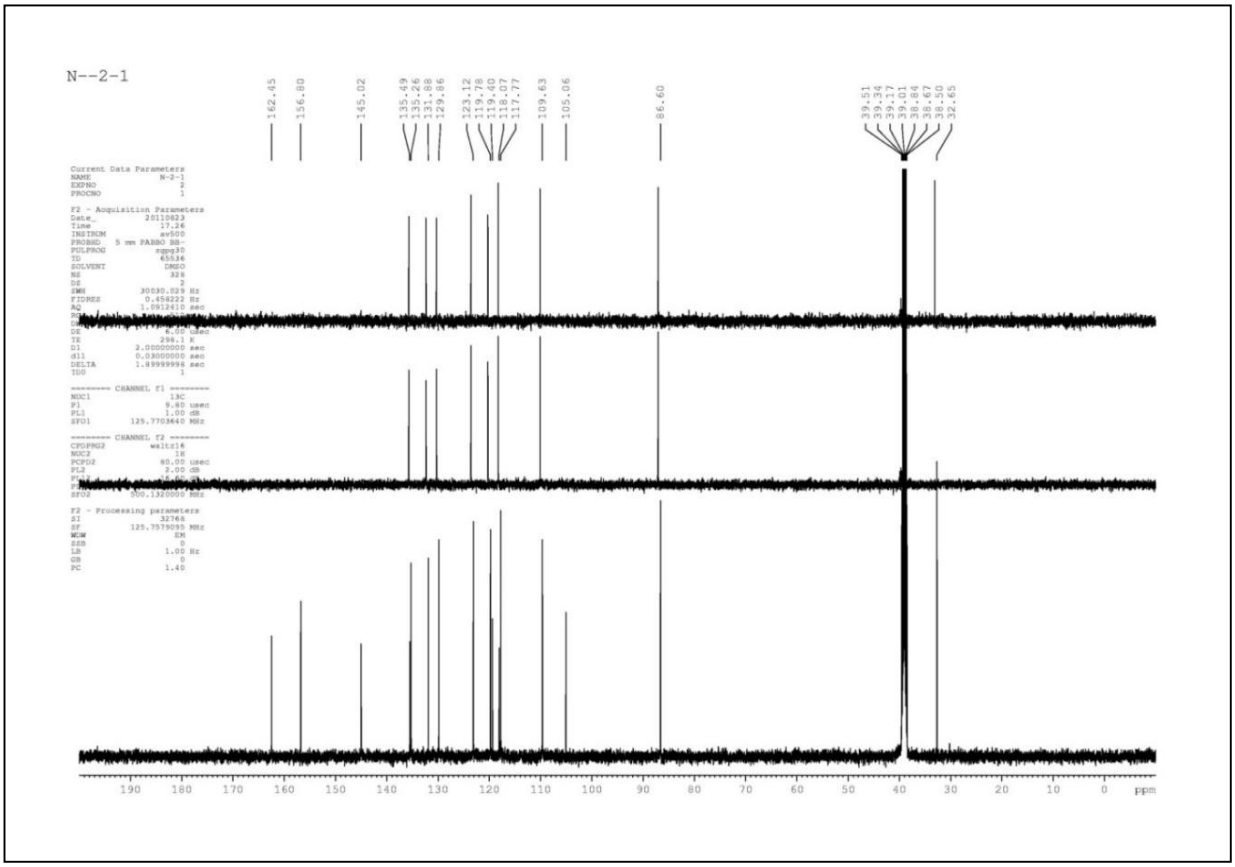


Figure 22: ^{13}C DEPT (125 MHz, DMSO-d_6) Spectra of 2-Hydroxy-5-(1-methyl-1*H*-indol-3-ylamino) benzonitrile

Conclusion

With consistent set of conditions in hand, we extended this strategy for the reactions between differently substituted aminophenols and various indoles. The reactions proceeded smoothly at 0 ^{o}C and reached completion within an hour to furnish the corresponding 3-amino substituted indoles in good yield The procedure worked well with the indoles bearing electron-releasing groups and halogen substituents.

References

1. Arzel E. et al, *J. Med. Chem*., **44**, 949–960 **(2001)**

2. Bandini Marco, Fagioli Matteo, Garavelli Marco and Melloni Alfonso, *The Journal of Organic Chemistry*, **69(22)**, 7511-7518 **(2004)**

3. Barone Mariarita and Catalfo Alfio, *Arabian Journal of Chemistry*, **10**, S3444-S3450 **(2017)**

4. Barraja P., Diana P., Carbone A. and Cirrincione G., *Tetrahedron*, **64**, 11625–11631 **(2008)**

5. Beheshti Saeideh and Morsali Ali, *RSC Advances*, **4(70)**, 37036 **(2014)**

6. Berti C., Creci L., Andruzzi R. and Trazza A., *J. Chem. Soc., Perkin Trans*. I, 607–610 **(1986)**

7. Bissantz C., Grund Schober C., Masciadri R., Ratni H., Rogers-Evans M. and Schnider P., (F. Hoffmann, La Roche AG), WO 2008068184 **(2008)**

8. Breugst Martin and von der Heiden Daniel, Mechanisms in Iodine Catalysis, *Chemistry – A European Journal*, **24(37)**, 9187-9199 **(2018)**

9. Çavdar Hüseyin and Saraçoğlu Nurullah, *The Journal of Organic Chemistry*, **71(2)**, 7793-7799 **(2006)**

10. Chenna Jagadeesh, Mondal Biplab, Pramanik Sourav, Das Dinabandhu and Saha Jaideep, *Angew and te Chemie*, **133(16)**, 8890-8894 **(2021)**

11. Donatoni C. et al, *Tetrahedron*, **70(20)**, 3231-3238 **(2014)**

12. Effland R.C., Klein J.T. and Martin L.L., U.S. Patent 5328920, C07D401/12 **(1994)**

13. Fares Hezam Al-Ostoot et al, *Bioorganic & Medicinal Chemistry Letters*, **33**, 127743 **(2021)**

14. Fares Hezam Al-Ostoot, Stondus Jigmat, Anthal Sumati, Doddenahally Geetha Venkatesh, Yasser Hussein Eissa Mohammed, Mandayam Anandalwar Sridhar, Shaukath Ara Khanum and Rajni Kant, *European Journal of Chemistry*, **10(3)**, 234-238 **(2019)**

15. Görlitzer K., Kramer C., Meyer H., Walter R.D., Jomaa H. and Wiesner J., *Pharmazie*, **59**, 243–250 **(2004)**

16. Gul W. and Hamann M.T., *Life Sci*, **78**, 442–453 **(2005)**

17. Hadi Ameer Mezher, Alfatlawi Wael Rasheed and Hameed Ahmed Shandookh, *Res. J. Biotech*., **19(11)**, 1-6 **(2024)**

18. Hanako Sunaba, Keigo Kamata and Noritaka Mizuno, *Chem Cat Chem*, **6(8)**, 2333-2338 **(2014)**

19. He Qijie, Chau Ming So, Zhaoxiang Bian, Hayashi Tamio and Wang Jung, *An Asian Journal Chem Asian J*., **10(3)**, 540-3 **(2015)**

20. Huo Congde, Kang Lisheng, Xu Xiaolan, Jia Xiaodong, Wang Xicun, Xie Haisheng and Yuan Yong, *Tetrahedron Letters*, **55(4)**, 954-958 **(2014)**

21. Ivan A. Yaremenko, Radulov Peter S., Belyakova Yulia Y., Arina A. Demina, Fomenkov I. Dmitriy, Denis V. Barsukov, Irina R. Subbotina, Fabrice Fleury and Alexander O. Terent'ev, *A European Journal*, **26(21)**, 4734-4751 **(2020)**

22. Kesteleyn B.R.R., Wim V.D.V., Surleraux D.L.N.G., Vendeville S.M.H., Raboisson P.J.M.B., Wigerinck P.T.B.P. and Peeters A.A., EP WO 2005/111044 **(2005)**

23. Koutentis P.A. and Michaelidou S.S., *Tetrahedron*, **66**, 6032–6039 **(2010)**

24. Laxmi Aishwarya, Gupta Jeena and Gupta Pawan, *Res. J. Biotech*., **19(3)**, 58-69 **(2024)**

25. Lee Adam Shih-Yuan, Wu Yu-Chi, Chang Yu-Ting and Wang Bo-Cheng, *Research on Chemical Intermediates*, **40(6)**, 2277-2285 **(2014)**

26. Leo A. Paquette et al, *Organic Letters*, **3(8)**, 1-15 **(2021)**

27. Li Ningbo, Oiu Renhua, Zhang Xiaohong, Yun Chen, Yin Shuang-Feng and Xu Xinhua, *Tetrahedron*, **71(25)**, 4275-4281 **(2015)**

28. Li Wan, Wentong Zhu, Kai Qiao, Xiaoning Sun, Zheng Fang and Kai Guo, *Asian Journal of Organic Chemistry*, **5(7)**, 920-926 **(2016)**

29. Marco Bandini and Astrid Eichholzer, *Angew. Chem. Int. Ed.*, **48**, 9608–9644 **(2009)**

30. M.R. Aiswarya, Chatterjee Rana and Dandela Rambabu, *Current Organic Chemistry*, **29(9)**, 730-748 **(2025)**

31. Margiani P. Fortes, Mariana M. Bassaco, Teodoro S. Kaufman and Claudio C. Silveira, *RSC Adv*., **4(65)**, 34519-34530 **(2014)**

32. Maria Alfonsi, Antonio Arcadi, Massimiliano Aschi, Gabriele Bianchi and Fabio Marinelli, *The Journal of Organic Chemistry*, **70 (6)**, 2265-2273 **(2005)**

33. Michaelidou S.S. and Koutentis P.A., *Tetrahedron*, **66**, 685–688 **(2010)**

34. Michaelidou S.S. and Koutentis P.A., *Tetrahedron*, **65**, 8428–8433 **(2009)**

35. Mistry Bhupendra, Keum Young-Soo and Kim Doo Hwan, *Research on Chemical Intermediates*, **42(4)**, 3241-3256 **(2016)**

36. Mukherjee Ratna and Banik Bimal Krishna, *Letters in Organic Chemistry*, **22(2)**, 87-91 **(2025)**

37. Norgren Anna S., Zhang Suode and Arvidsson Per I., *Organic Letters*, **8(20)**, 4533-4536 **(2006)**

38. Nuno R. Candeias, Luís C. Branco, Pedro M.P. Gois, Carlos A.M. Afonso and Alexandre F., *Chemical Reviews*, **109(6)**, 2703-2802 **(2009)**

39. Oleg V. Bityukov, Vil Vera A., Merkulova Valentina M., Gennady I. Nikishin and Alexander O., *Pure and Applied Chemistry*, **90(1)**, 7-20 **(2018)**

40. Olofsson K., Suna E., Pelcman B., Ozola V., Katkevics M. and Kalvins I., Biolipox AB, WO 2005005415 **(2005)**

41. Pelkey E.T., Barden T.C. and Gribble G.W., *Tetrahedron Lett*., **40**, 7615–7619 **(1999)**

42. Ray N.C., Hynd G., Arienzo R. and Finch H., Argenta Discovery Ltd., WO 2007045867 **(2007)**

43. Renzetti Andrea, Dardennes Emmanuel, Fontana Antonella, Paolo De Maria, Janos Sapi and Gérard Stéphane, *The Journal of Organic Chemistry*, **73(17)**, 6824-6827 **(2008)**

44. Ryabova S.Y., Alekseeva L.M., Lisitsa E.A. and Granik V.G., *Russ. Chem. Bull. Int. Ed.*, **55**, 1248–1254 **(2006)**

45. Salituro F.G. and Baron B.M., Merrell Dow Pharmaceuticals Inc., EP 0483881 **(1992)**

46. Sayyed Zahra Sayyed-Alangi and Zinatossadat Hossaini, *Chemistry of Heterocyclic Compounds*, **51(6)**, 541-544 **(2015)**

47. Shane R. Cochrane and Michael A. Kerr, *Organic Letters*, **24(30)**, 5509-5512 **(2022)**

48. Shanmugam Sakthivel and Rengarajan Balamurugan, *The Journal of Organic Chemistry*, **83(19)**, 12171-12183 **(2018)**

49. Somei M., Kawasaki T., Fukui Y., Yamada F., Kobayashi T., Aoyama H. and Shinmyo D., *Heterocycles*, **34**, 1877–1884 **(1992)**

50. Sundberg R.J., Comprehensive Heterocyclic Chemistry, Katritzky A.R. and Rees C.W., eds., Pergamon, Oxford, 313–376 **(1984**)

51. Toshiyuki Itoh, *Heterocycles*, **92(8)**, 1373 **(2016)**

52. Werner Daniel, Glen B. Deacon, Junk Peter C. and Reiner Anwander, *Dalton Transactions*, **46(19)**, 6265-6277 **(2017)**

53. Xiaochen Sun, Yuan Kun and Yawen Zhang, *Journal of Rare Earths*, **38(8)**, 801-818 **(2020)**

54. Yamada F., Shinmyo D. and Somei M., *Heterocycles*, **38**, 273–276 **(1994)**

55. Yamada K., Kawasaki T., Fujita T. and Somei M., *Heterocycles*, **55**, 1151–1159 **(2001)**

56. Yamada F., Fukui Y., Shin-myo D. and Somei M., *Heterocycles*, **35**, 99–104 **(1993)**

57. Yanlong Gu, Ogawa Chikako and Shū Kobayashi, *Organic Letters*, **9(2)**, 175-178 **(2007)**

58. Zhang Xiaohong, Xu Xinhua, Li Ningbo, Liang Zhiwu and Tang Zilong, *Tetrahedron*, **74(15)**, 1926-1932 **(2018)**

59. Zoë Hearne, Keys Sabrina and Li Chao-Jun, Transition Metal-catalysed Nucleophilic Additions of Terminal Alkynes in Water: Development and Synthetic Utility, 343-403 **(2019)**.

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