

Supporting Information

Development of a regioselective N-methylation of (benz)imidazoles providing the more sterically hindered isomer

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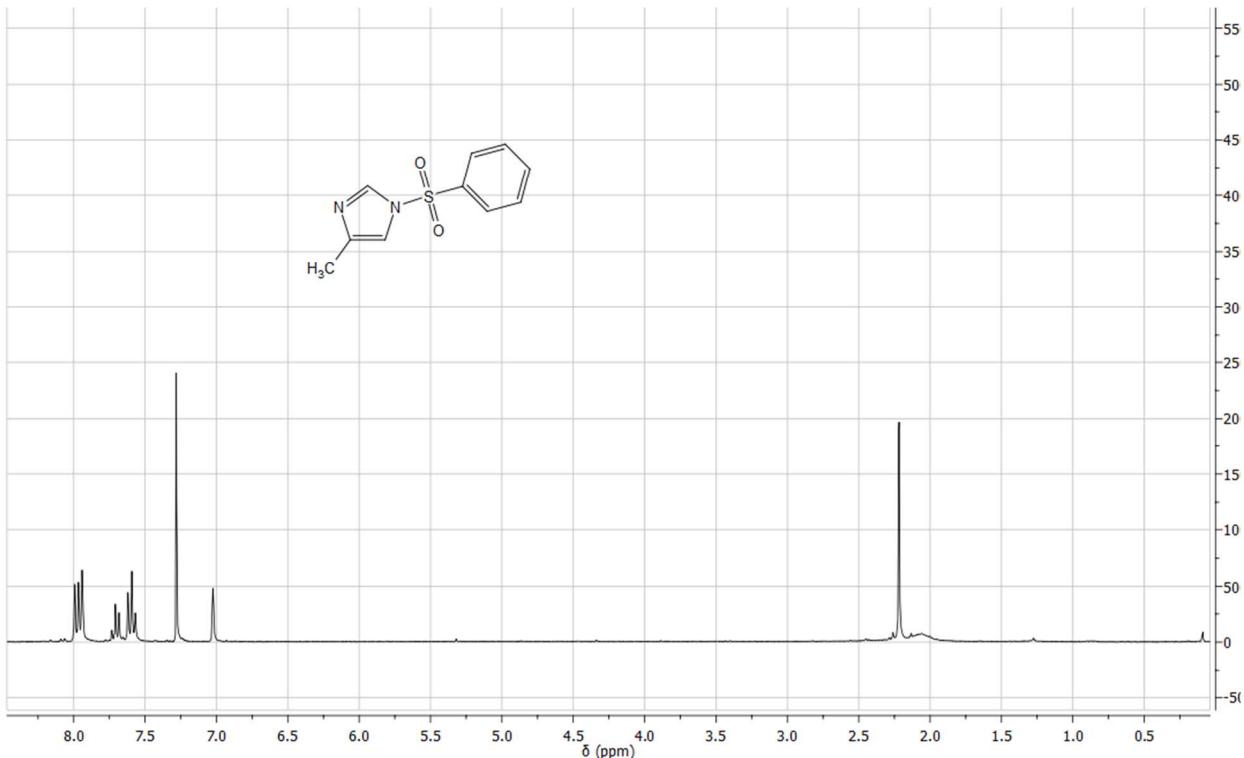
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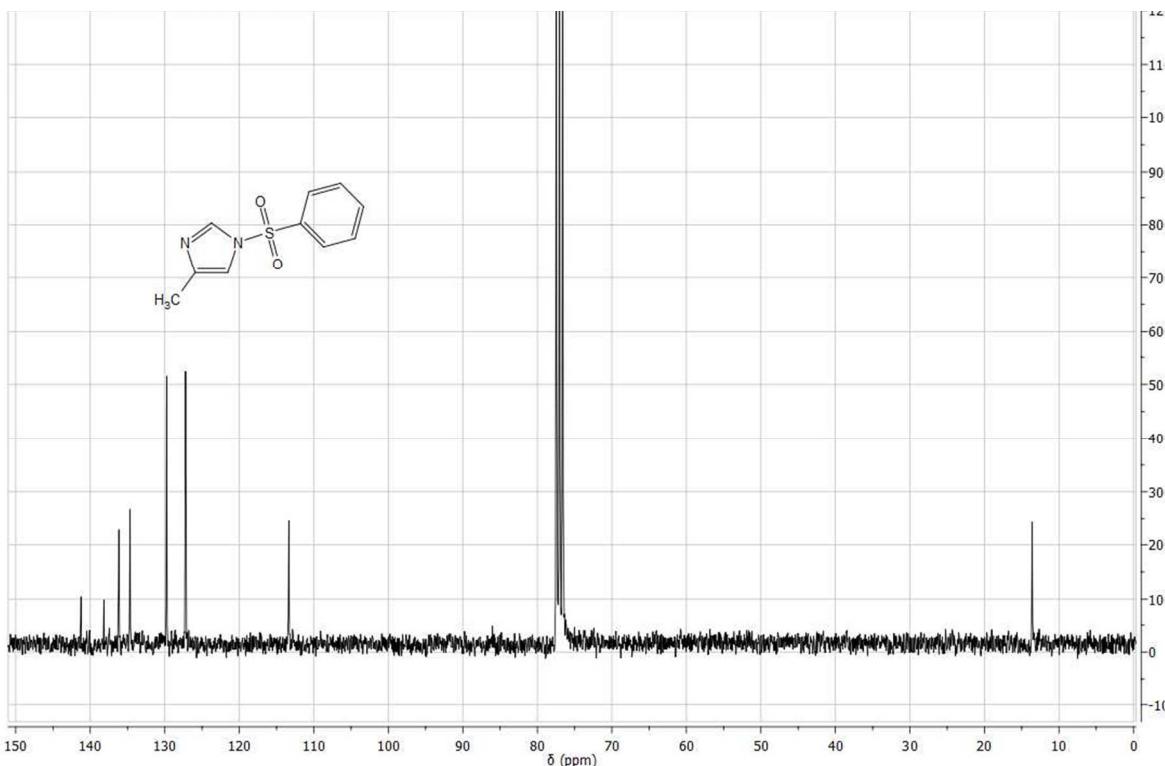
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¹H and ¹³C NMR spectra

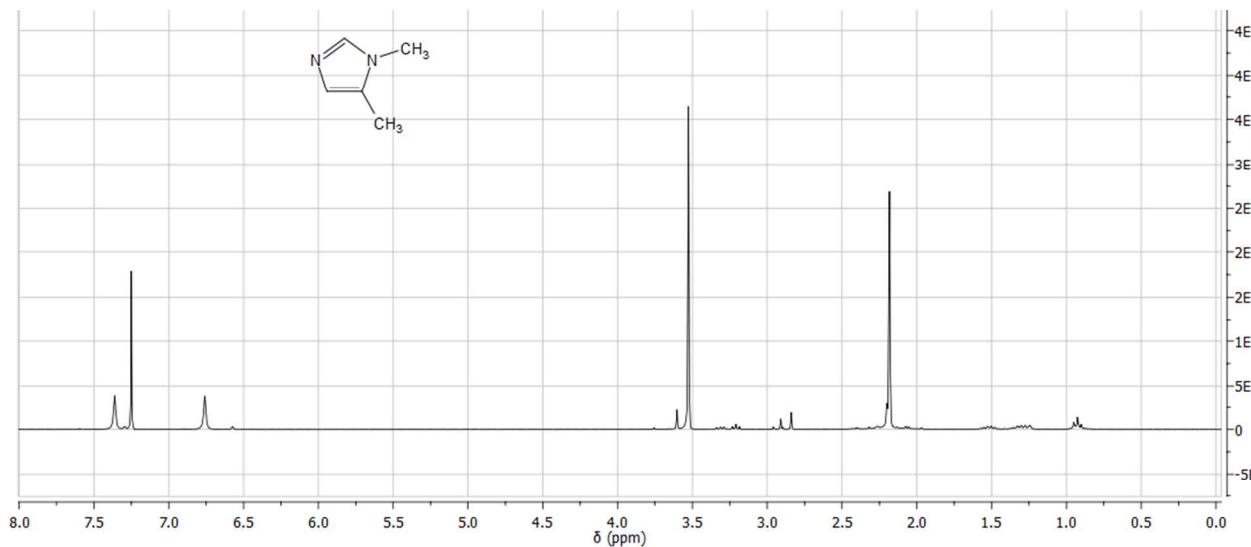
Compound **1d** (¹H NMR, CDCl₃, 300 MHz):



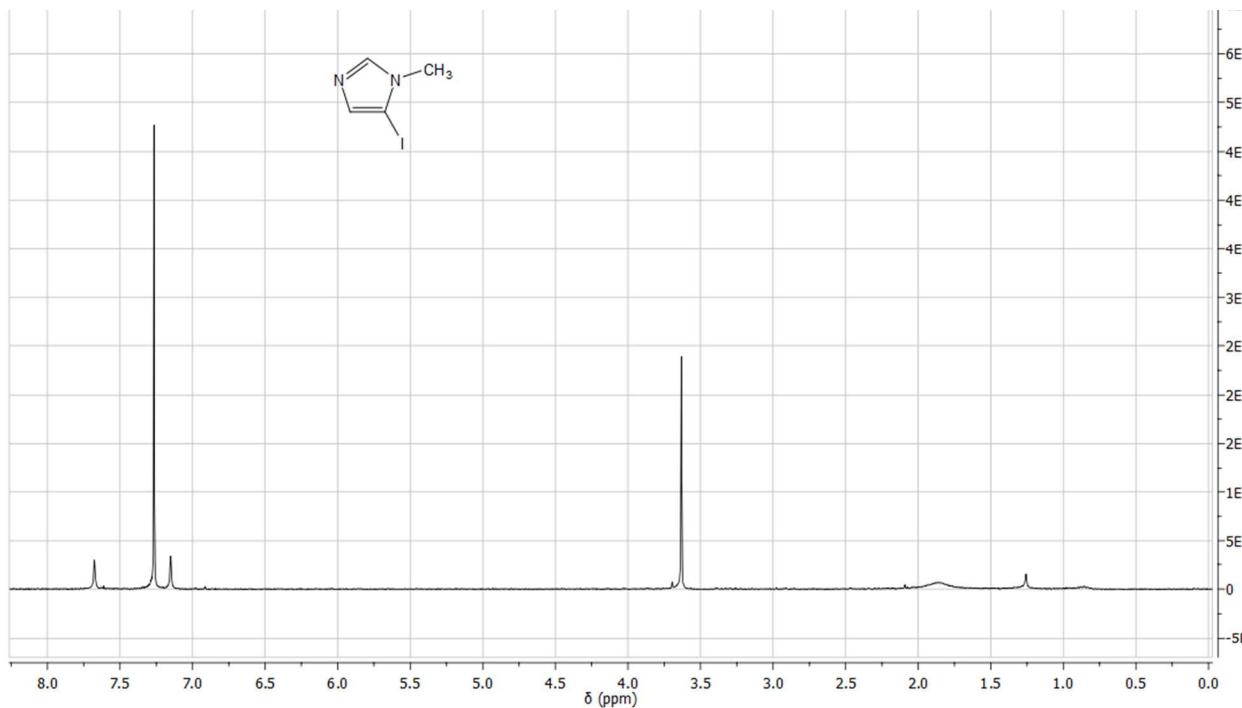
Compound **1d** (¹³C NMR, CDCl₃, 125 MHz):



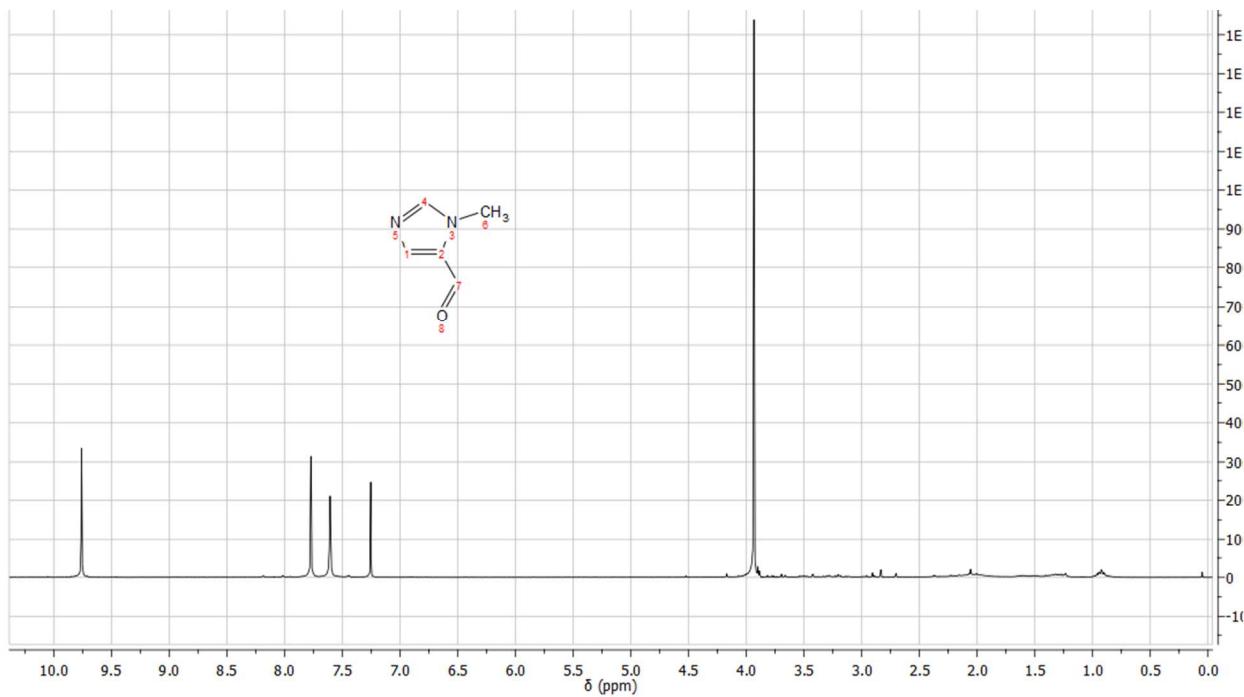
Compound 4 (^1H NMR, CDCl_3 , 300 MHz):



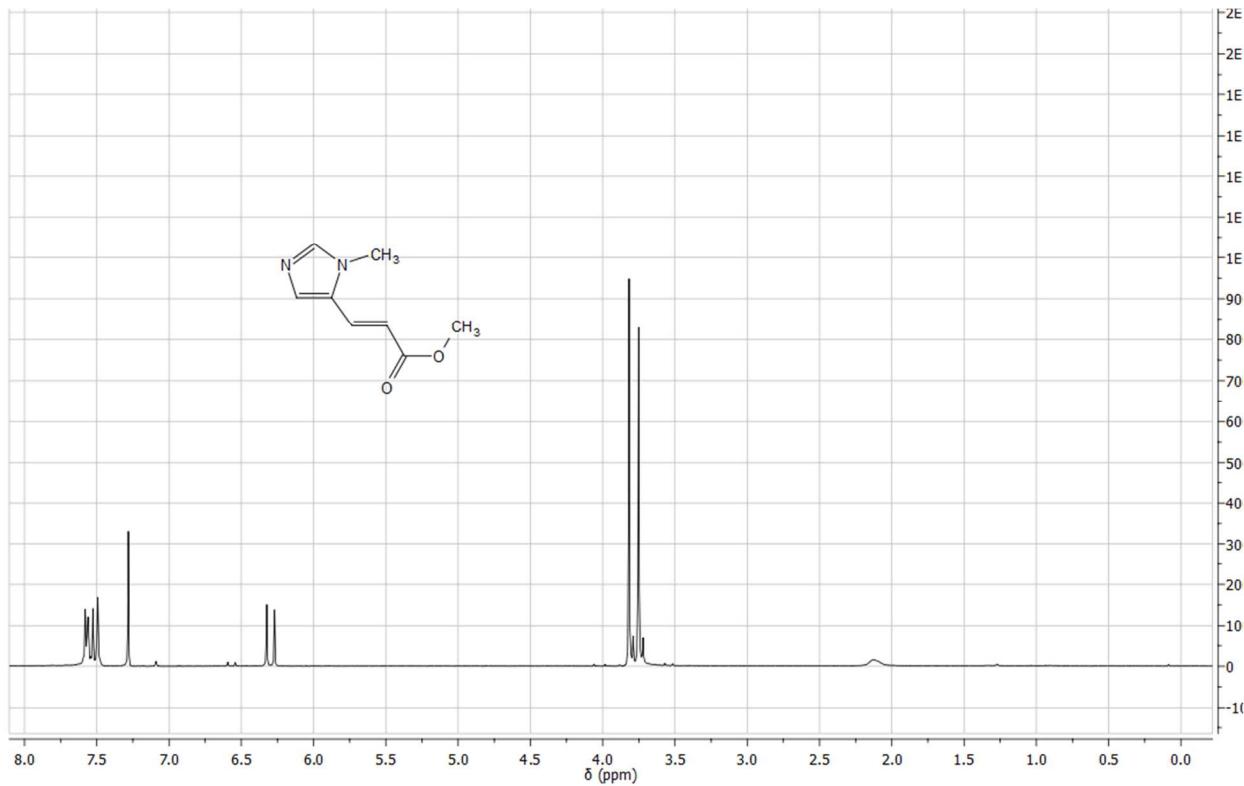
Compound 5 (^1H NMR, CDCl_3 , 300 MHz):



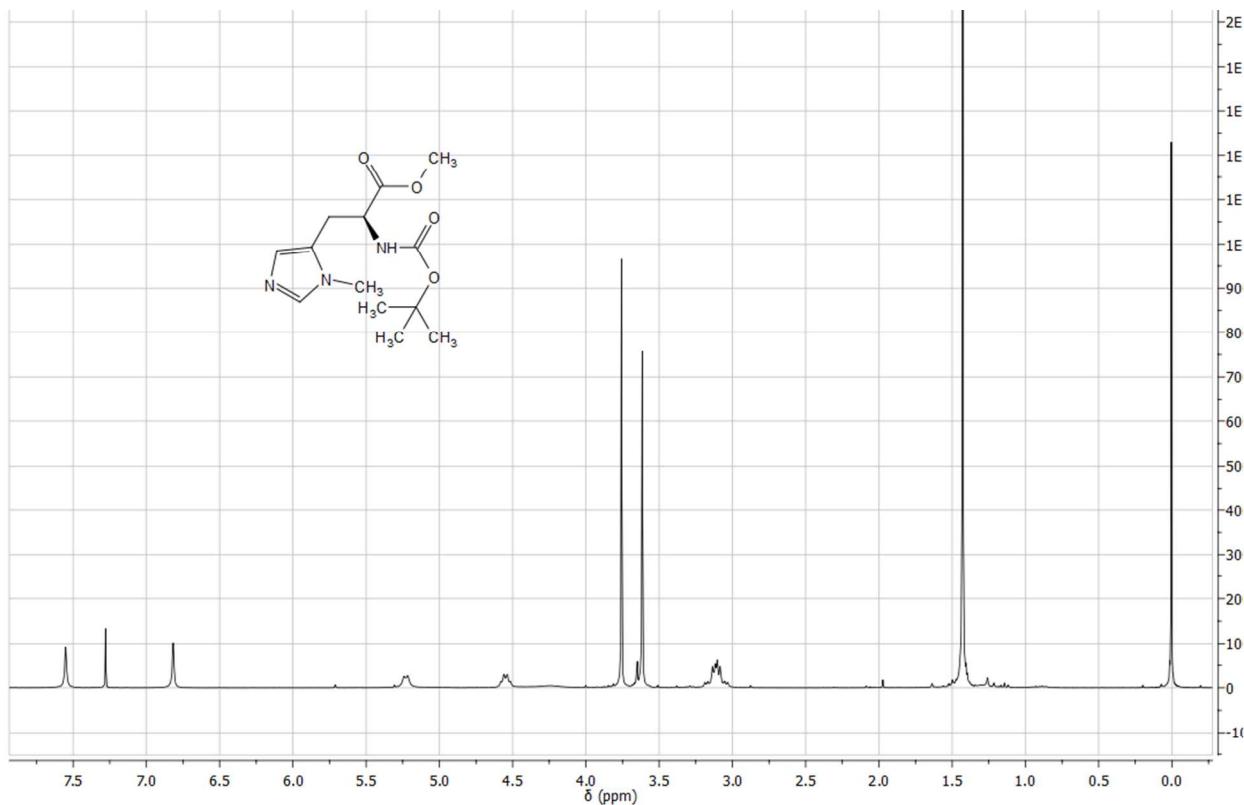
Compound **6** (^1H NMR, CDCl_3 , 300 MHz):



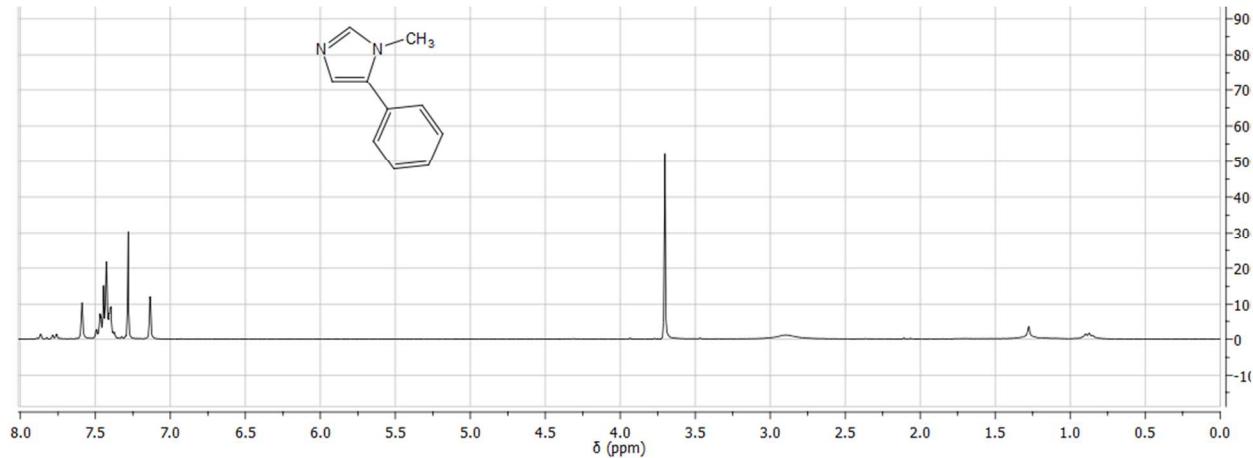
Compound **7** + traces of the other isomer (^1H NMR, CDCl_3 , 300 MHz):



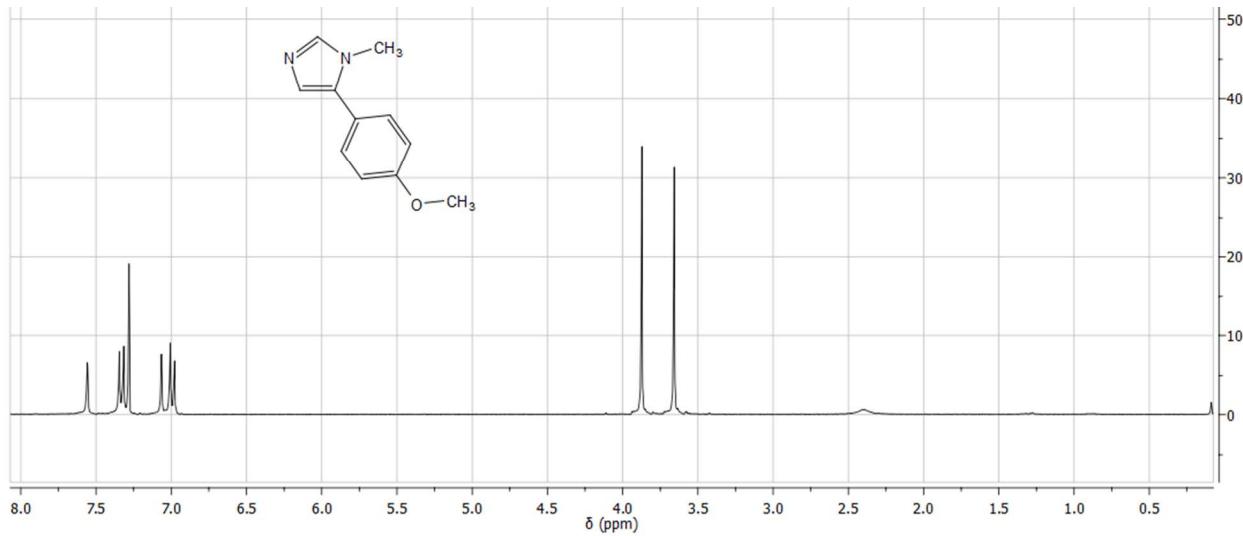
Compound **8** (^1H NMR, CDCl_3 , 300 MHz):



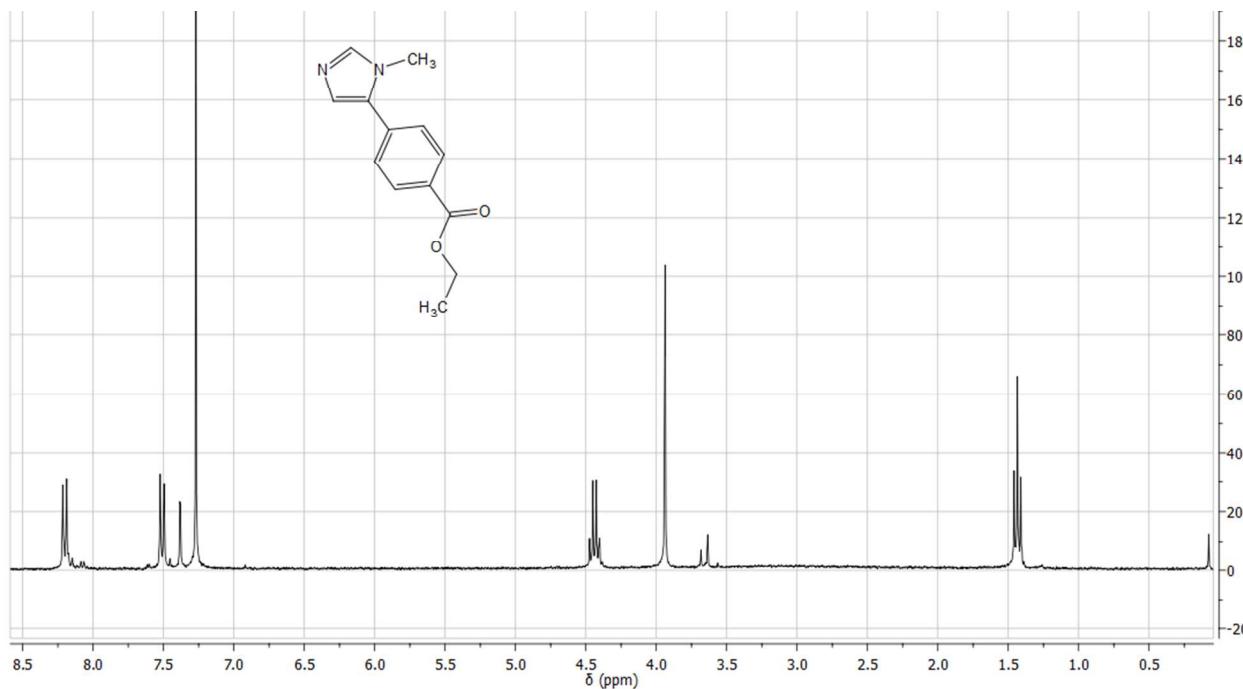
Compound **9** (^1H NMR, CDCl_3 , 300 MHz):



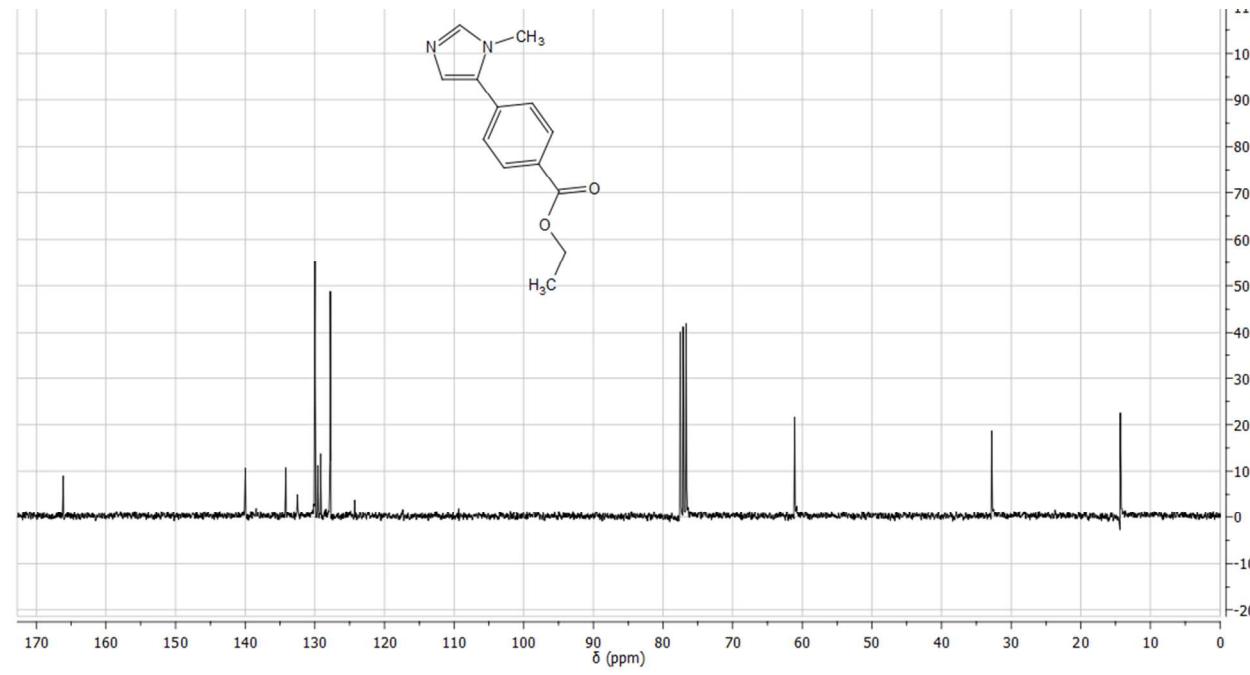
Compound **10** (^1H NMR, CDCl_3 , 300 MHz):



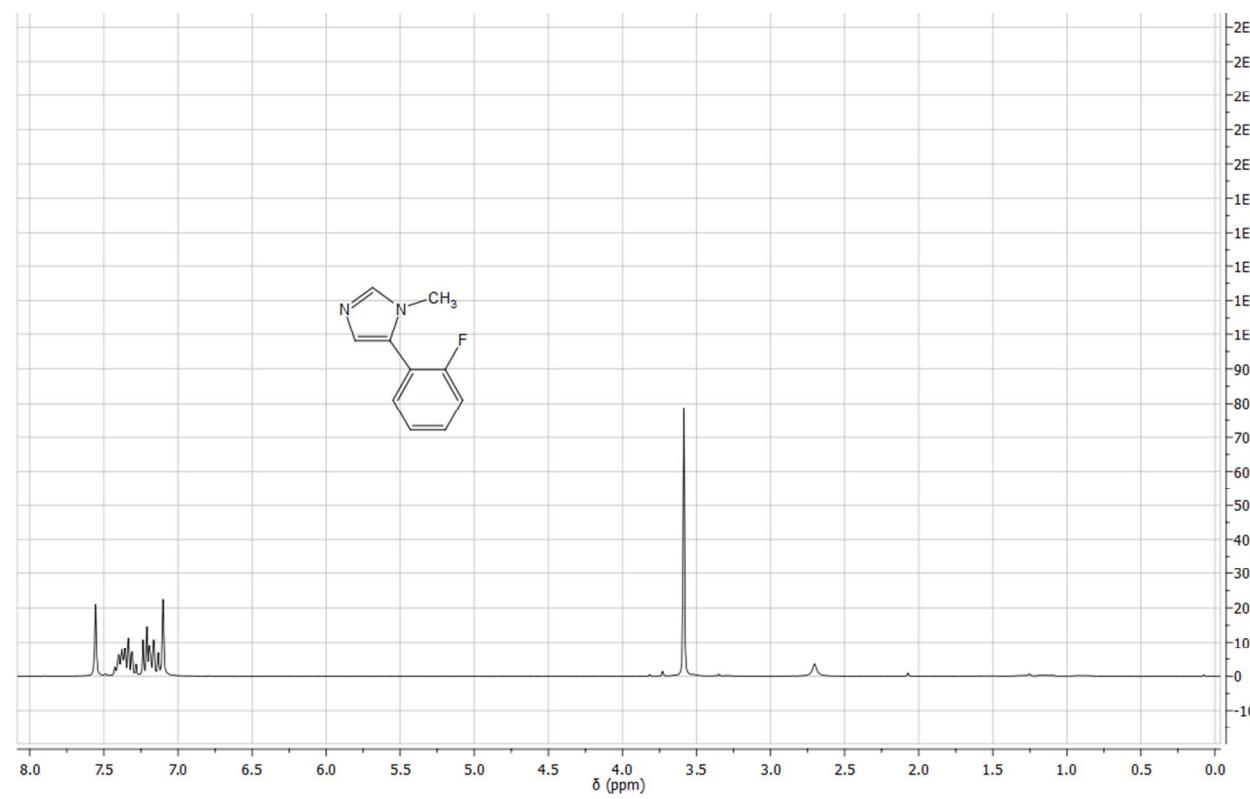
Compound **11** (^1H NMR, CDCl_3 , 300 MHz):



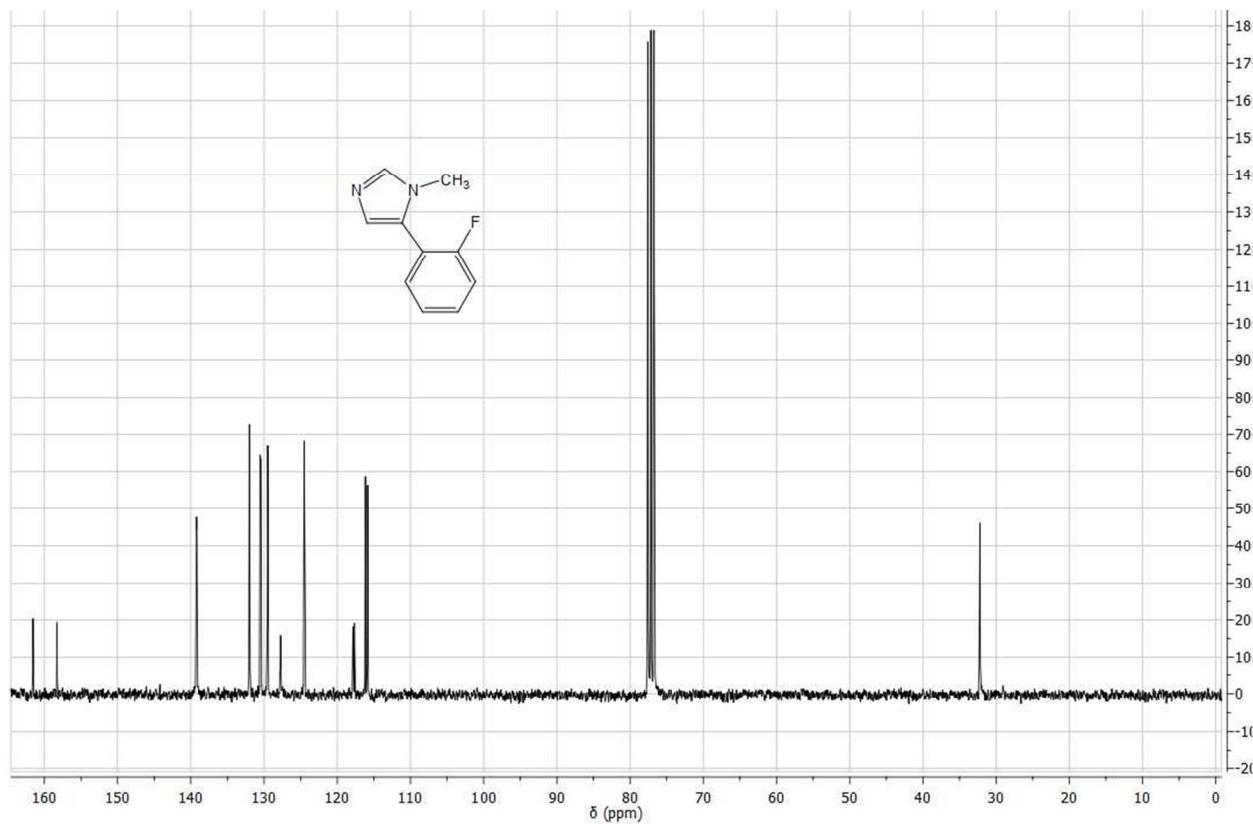
Compound **11** (^{13}C NMR, CDCl_3 , 75 MHz):



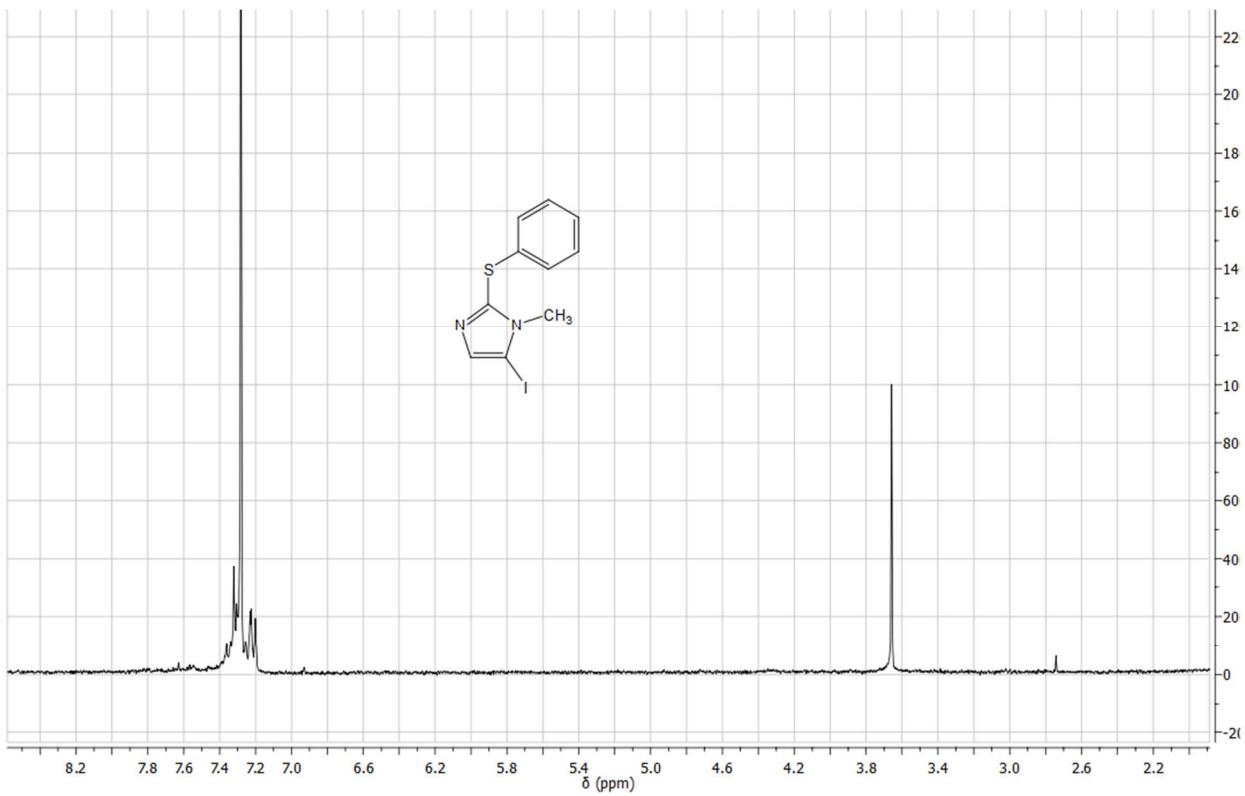
Compound **12** (^1H NMR, CDCl_3 , 300 MHz):



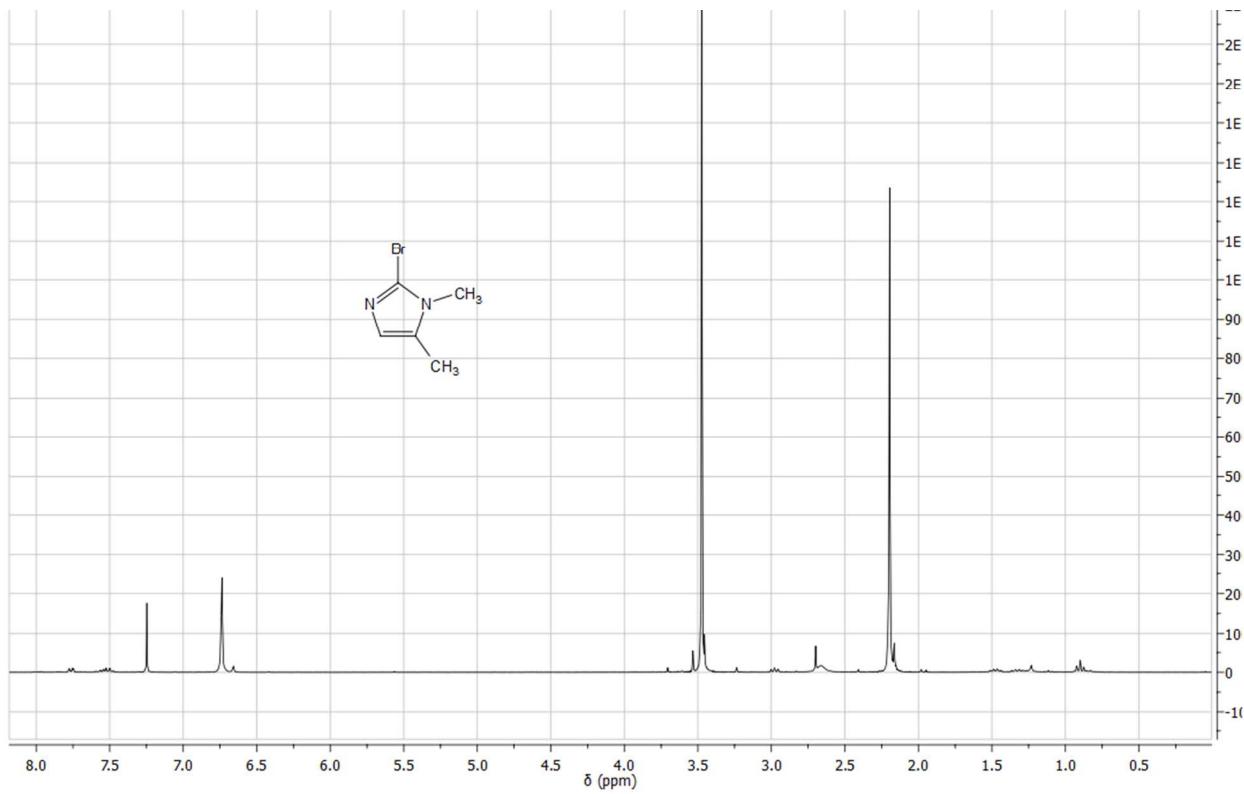
Compound **12** (^{13}C NMR, CDCl_3 , 75 MHz):



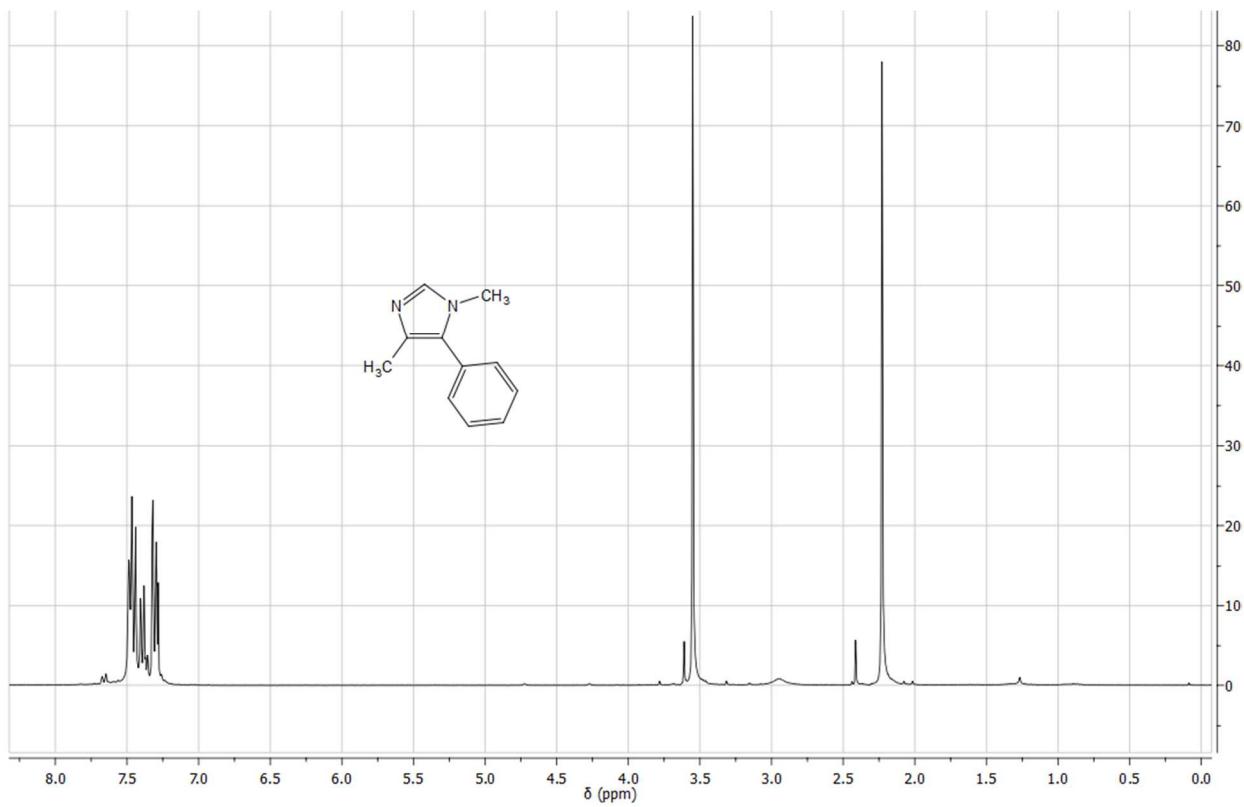
Compound **13** (^1H NMR, CDCl_3 , 300 MHz):



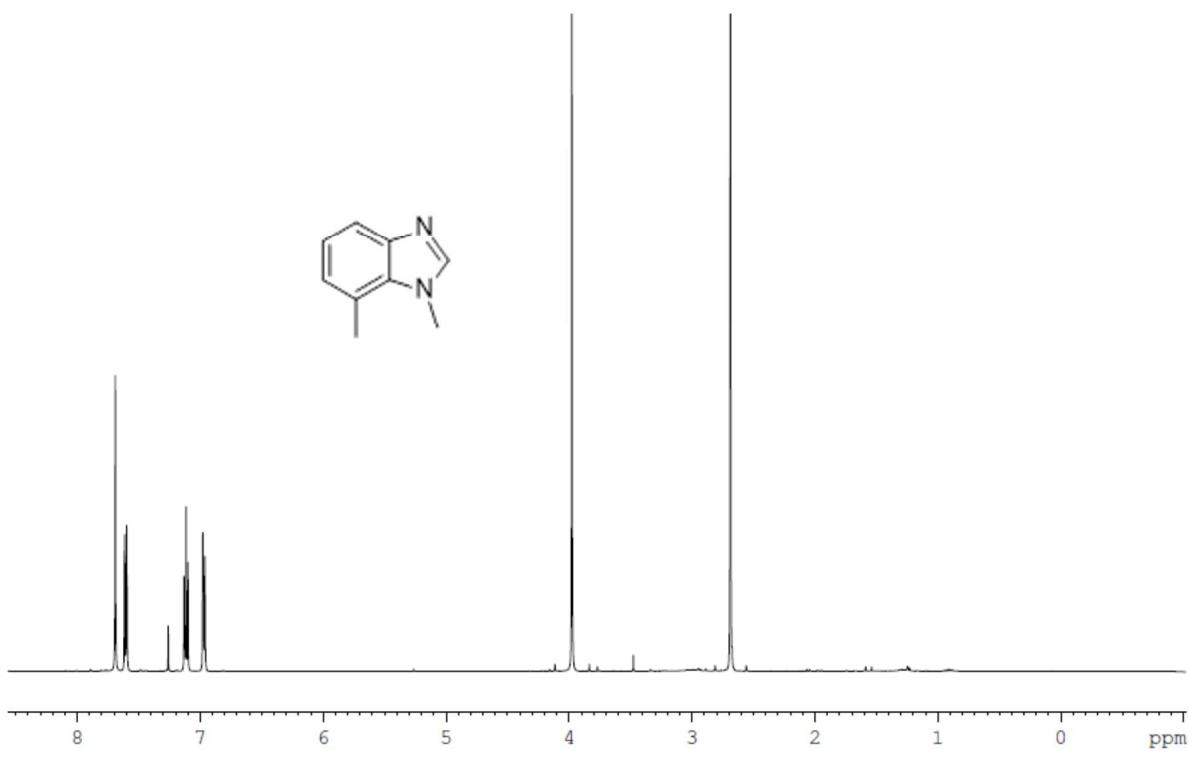
Compound **14** (^1H NMR, CDCl_3 , 300 MHz):



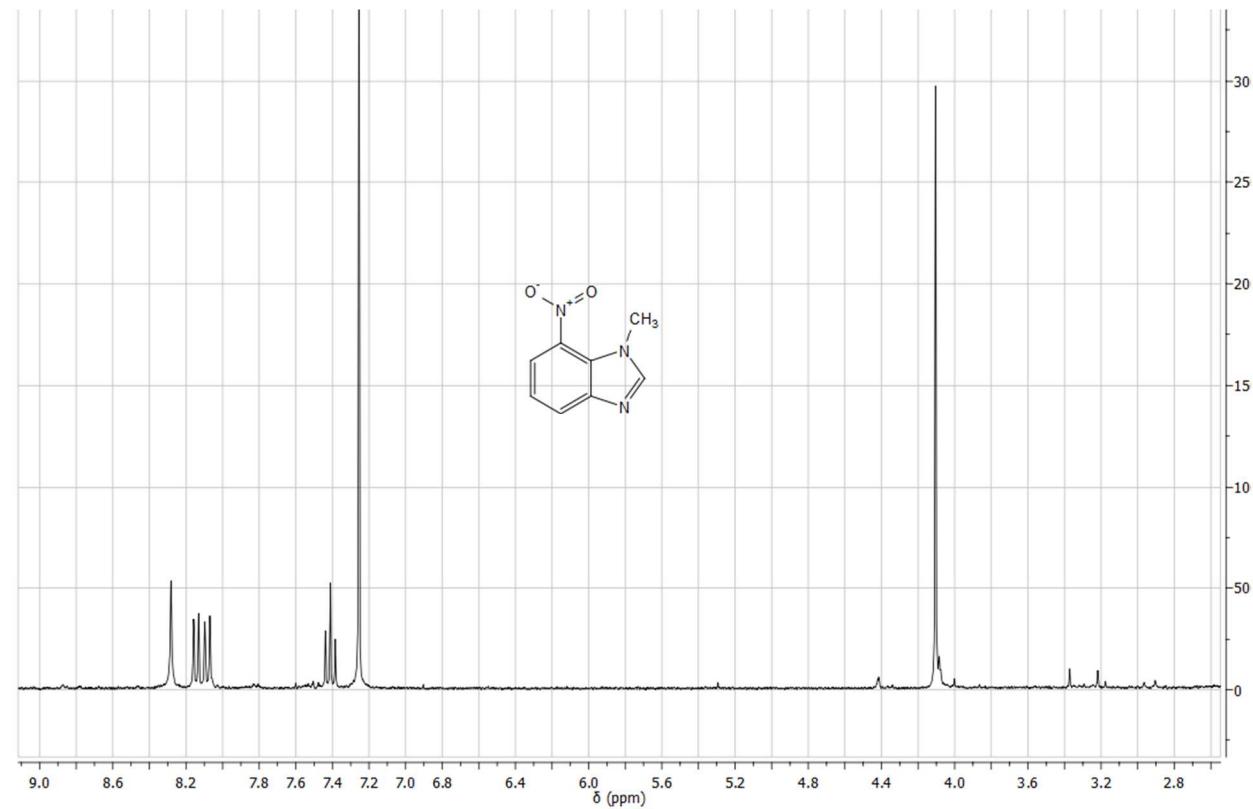
Compound **15** + the other isomer (^1H NMR, CDCl_3 , 300 MHz):



Compound **16** (^1H NMR, CDCl_3 , 500 MHz):



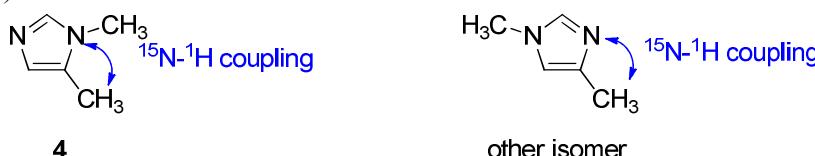
Compound **17** (^1H NMR, CDCl_3 , 300 MHz):



¹H-¹⁵N HMBC

Regiochemistry was determined by ^1H - ^{15}N HMBC for compounds **4**, **15** and **16** whereas for compounds **5-14** and **17** data were compared to the literature (see manuscript for references).

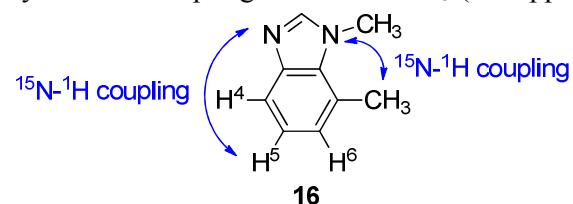
- In the case of **4**, observation of a coupling between N(1) (162.8 ppm) and the ¹H of the methyl group at 2.19 ppm indicates that this latter is in position 5 (and not 4). In the minor isomer (obtained by classical alkylation methods), that is N(3) (at 250.7 ppm) which shows a coupling with the C-CH₃. These attributions are in perfect agreement with reported ¹H NMR data (see Kashima, I.; Harada, Y.; Hosomi, A. *Heterocycles* **1993**, *35*, 433-440).



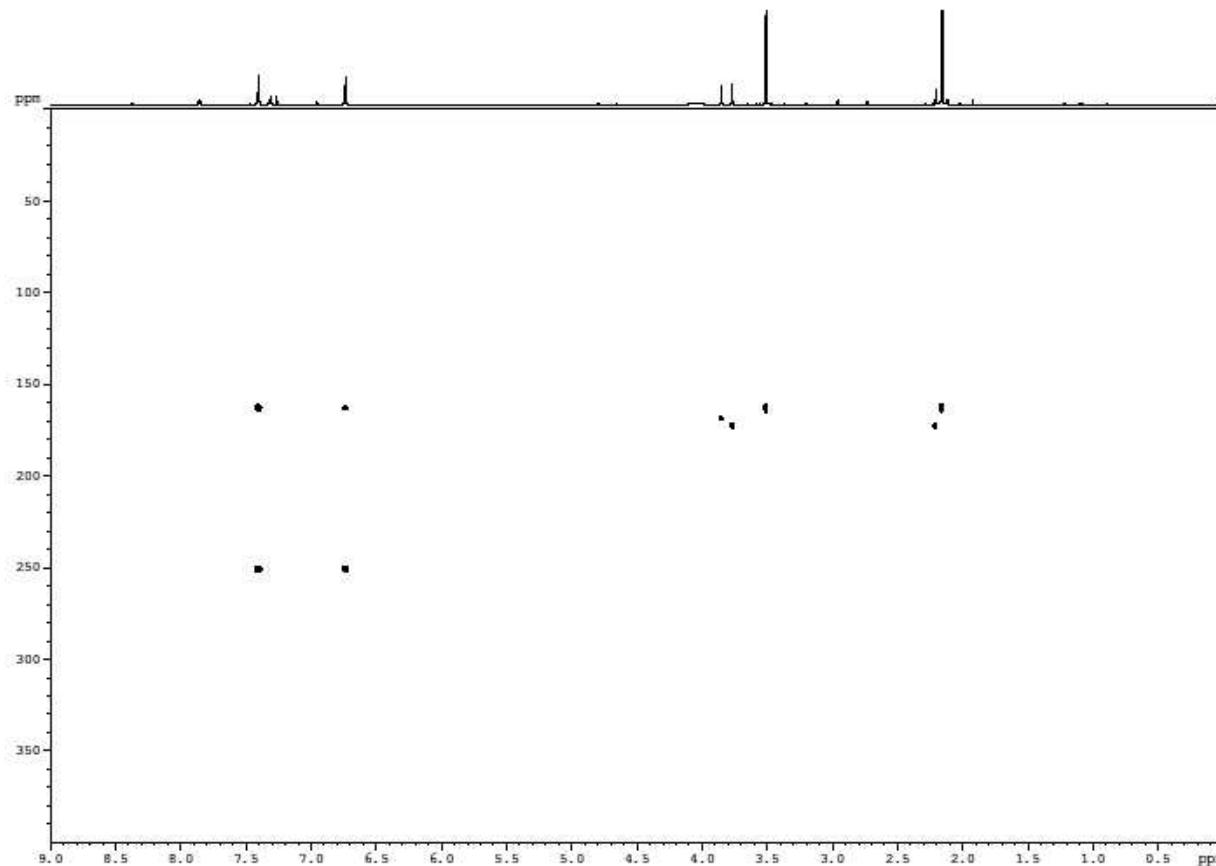
- For **15**, the ^1H - ^{15}N HMBC analysis of the major isomer shows a coupling between N(3) (257.6 ppm) and the C- CH_3 (2.23 ppm) allowing to identify it as 1,4-dimethyl-5-phenyl-1*H*-imidazole. In the minor isomer, that is the N(1) which shows a coupling with C- CH_3 in agreement with the 1,5-dimethyl-4-phenyl-1*H*-imidazole structure.



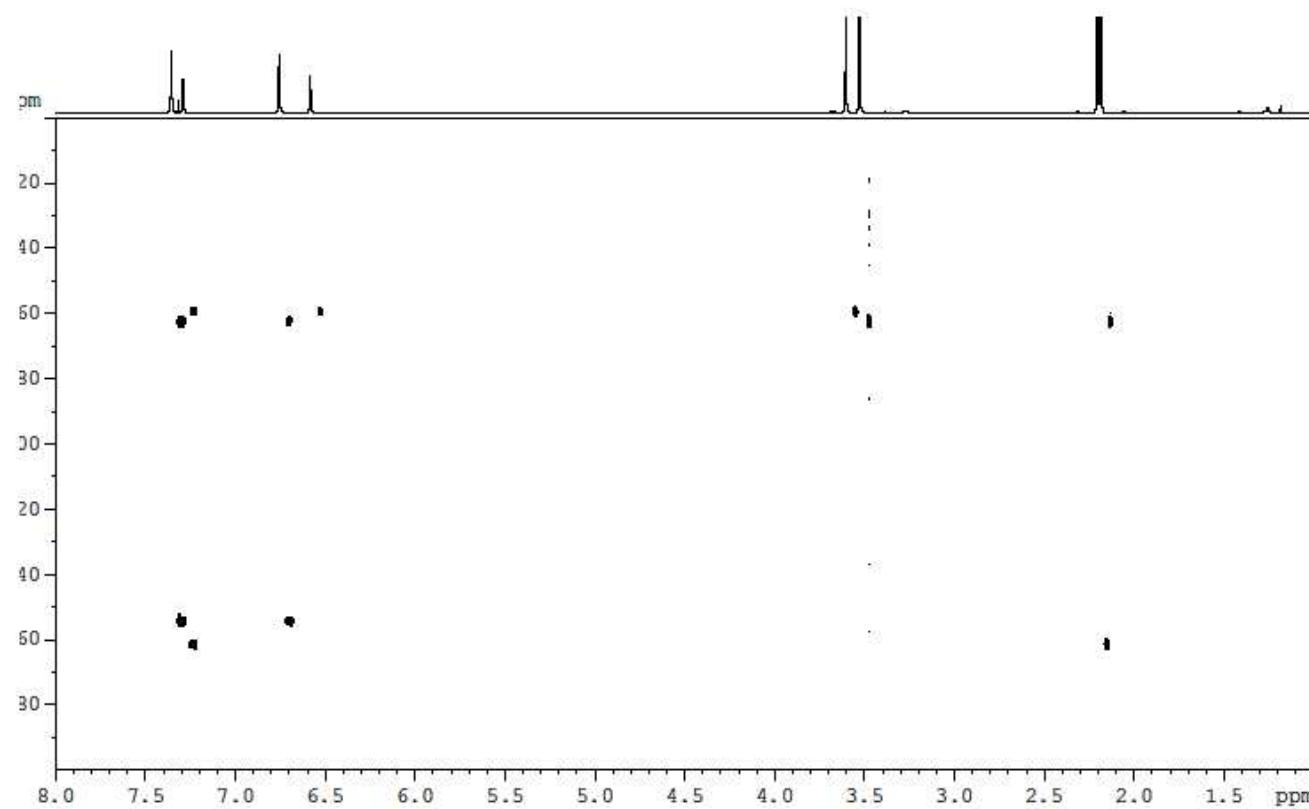
- The ^1H - ^{15}N HMBC analysis of **16** reveals a coupling between H(5) (at 7.15 ppm) and N(3) (at 240.4 ppm) what allows attributing the 1,7-dimethyl-1*H*-benzo[d]imidazole regiochemistry to **16**. A coupling between C-CH₃ (2.74 ppm) and N(1) (144.0 ppm) is also observed.



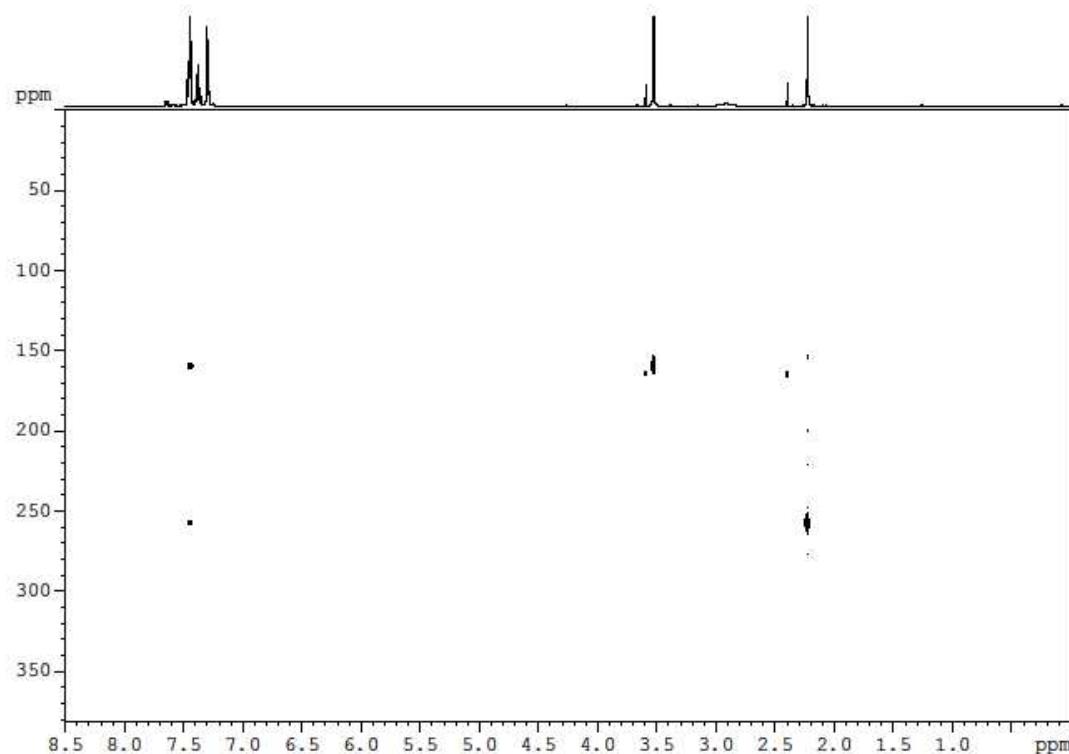
Compound 4 (CDCl₃, 500 MHz)



Compound 4 and the other regioisomer (CDCl₃, 500 MHz)



Compound **15** + traces of the other regioisomer (CDCl₃, 500 MHz)



Compound **16** (CDCl_3 , 500 MHz)

