

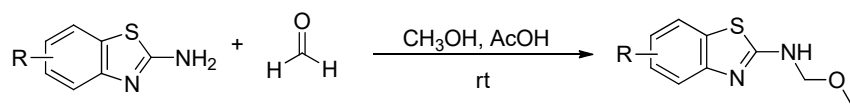
Synthesis, isolation, identification and characterization of a drug-excipient interaction degradation impurity in pramipexole by HPLC, LC/MS and NMR

1. Supplementary Tables:

Table S1: Unit composition of pramipexole dihydrochloride extended-release tablets.

#.	ingredients	Reference	Qty/Tablet (mg)						
			0.375	0.75	1.5	2.25	3.0	3.75	4.5
Dry Mixing									
1.	Pramipexole dihydrochloride monohydrate	USP	0.375	0.75	1.5	2.25	3.0	3.75	4.5
2.	Mannitol	USPNF/Ph. Eur.	12.025	11.65	10.9	10.15	9.4	11.75	14.1
3.	Hypromellose	USPNF/Ph. Eur.	126	126	126	126	126	157.5	189
4.	Pregelatinized Starch	USPNF/Ph. Eur.	129.2	129.2	129.2	129.2	129.2	161.5	193.8
5.	Carbomer homopolymer	USPNF/Ph. Eur.	10	10	10	10	10	12.5	15
6.	Colloidal Silicon Dioxide	USPNF/Ph. Eur.	1	1	1	1	1	1.25	1.5
Lubrication									
7.	Magnesium Stearate	USPNF/Ph. Eur.	1.4	1.4	1.4	1.4	1.4	1.75	2.1
Un-coated Tablet Weight			280	280	280	280	280	350	420

2. Supplementary Figures:



R = -H, 4-OCH₃, 4-Cl, 6-CH₃, 6-OCH₃, 6-OCH₂CH₃, 6-F, 6-Cl, 6-Br or 6-NO₂

Figure S1: Synthesis of *N*-(methoxymethyl)benzothiazole reported by Z. Ji et al. / Bioorg. Med. Chem. Lett. 25 (2015) 4065–4068

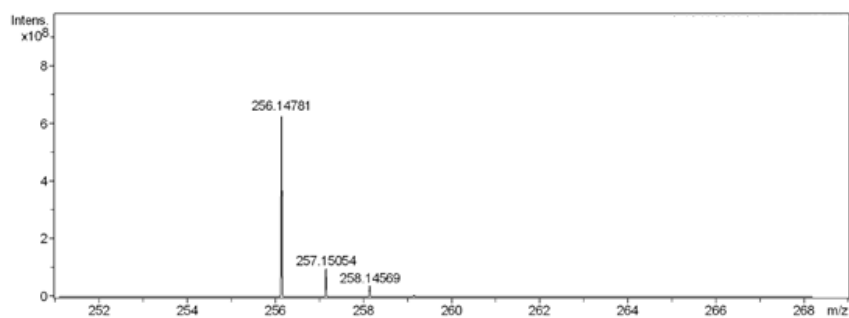


Figure S2: High-Resolution MS spectrum of the synthesized impurity.

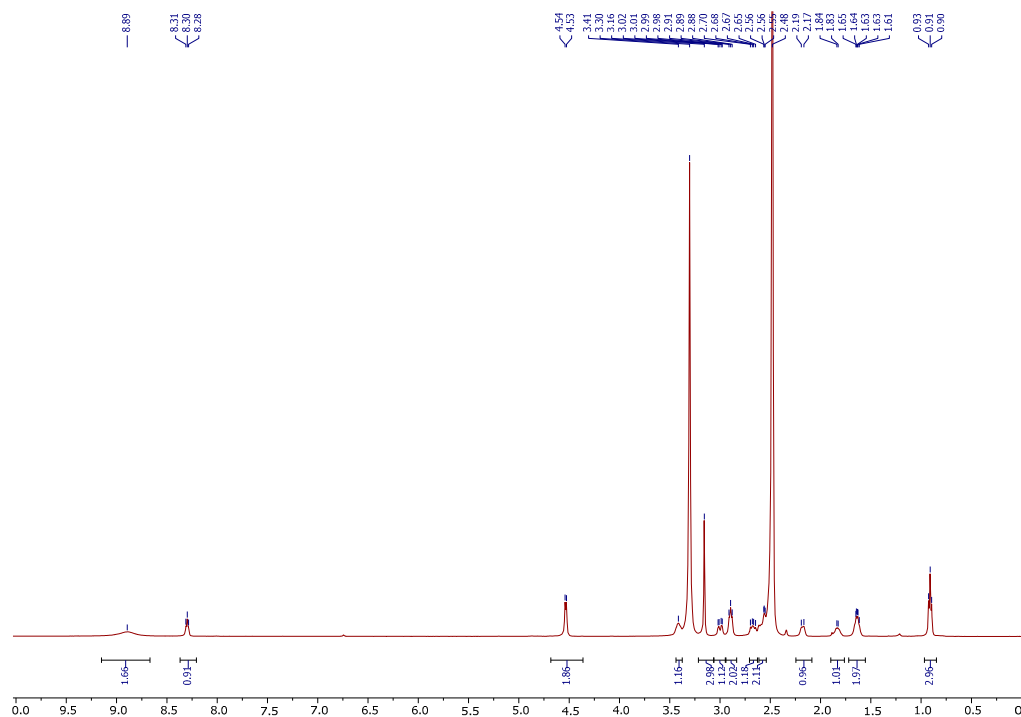


Figure S3: ^1H -NMR spectrum (in $\text{DMSO}-d_6$) of the synthesized impurity.

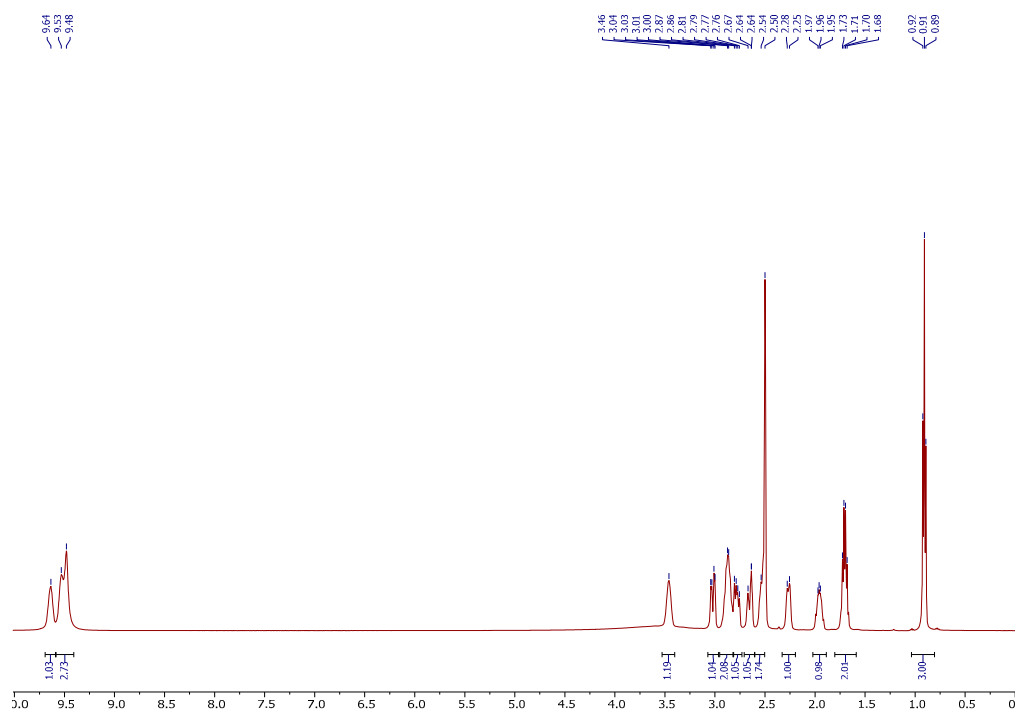


Figure S4: ^1H -NMR spectrum (in $\text{DMSO}-d_6$) of the pramipexole API.

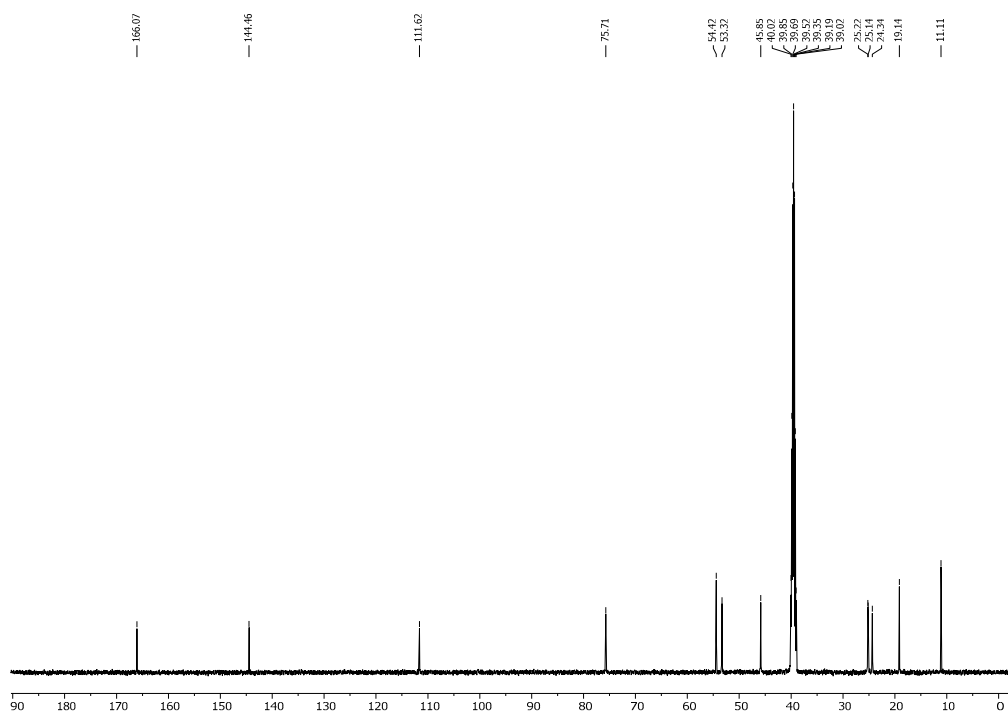


Figure S5: ^{13}C NMR spectrum (in $\text{DMSO-}d_6$) of the synthesized impurity.

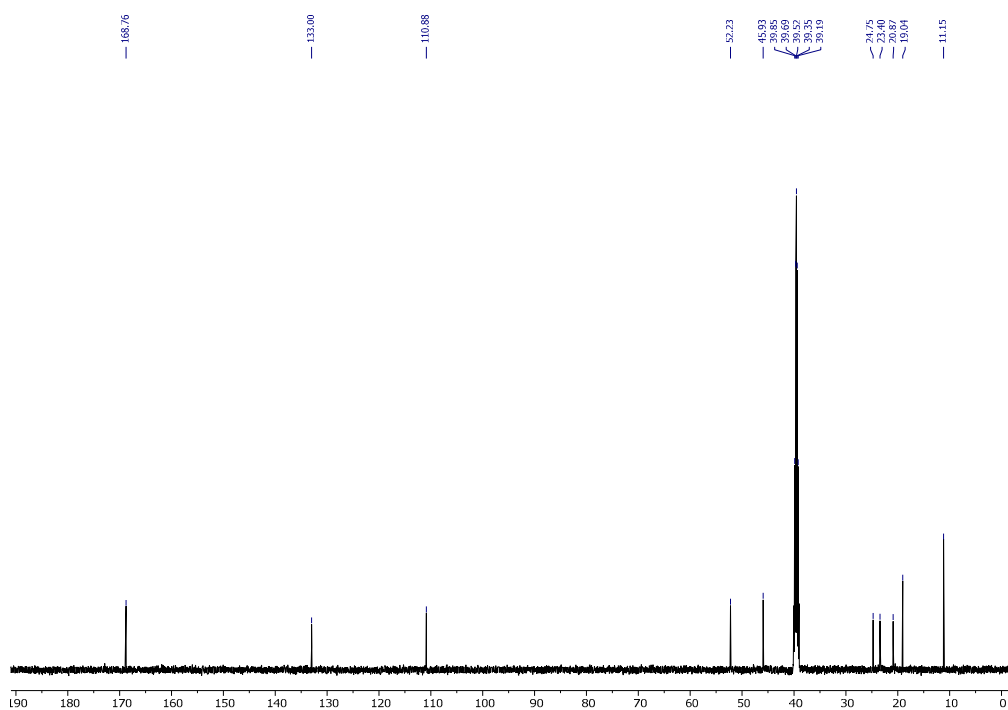


Figure S6: ^{13}C NMR spectrum (in $\text{DMSO-}d_6$) of the pramipexole API.

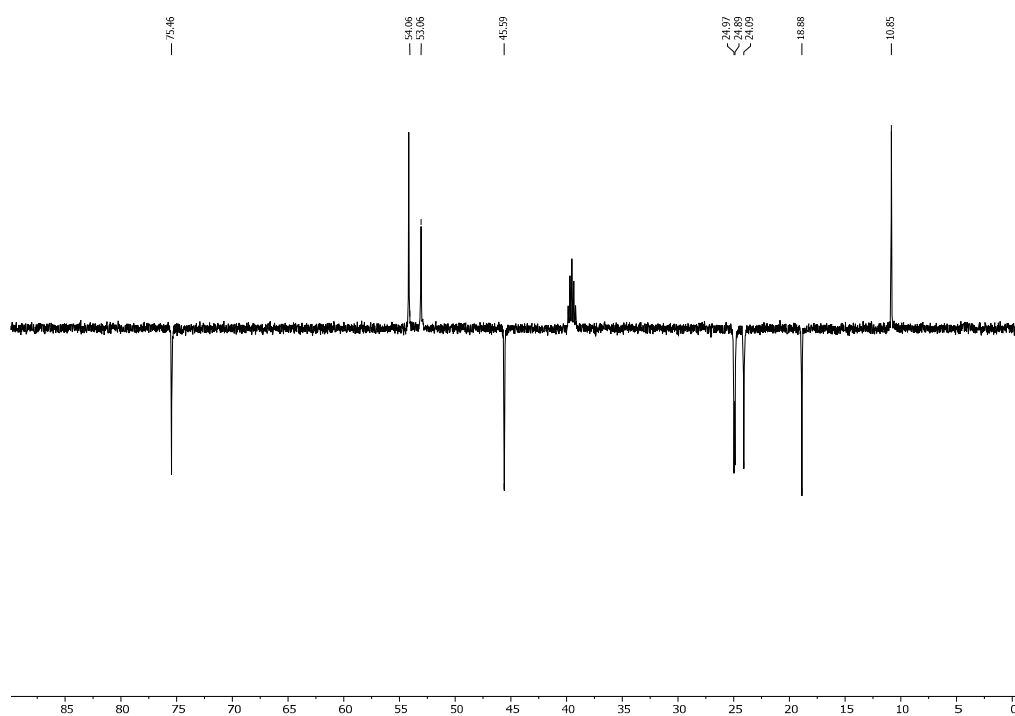


Figure S7: DEPT-135 spectrum of the synthesized impurity.

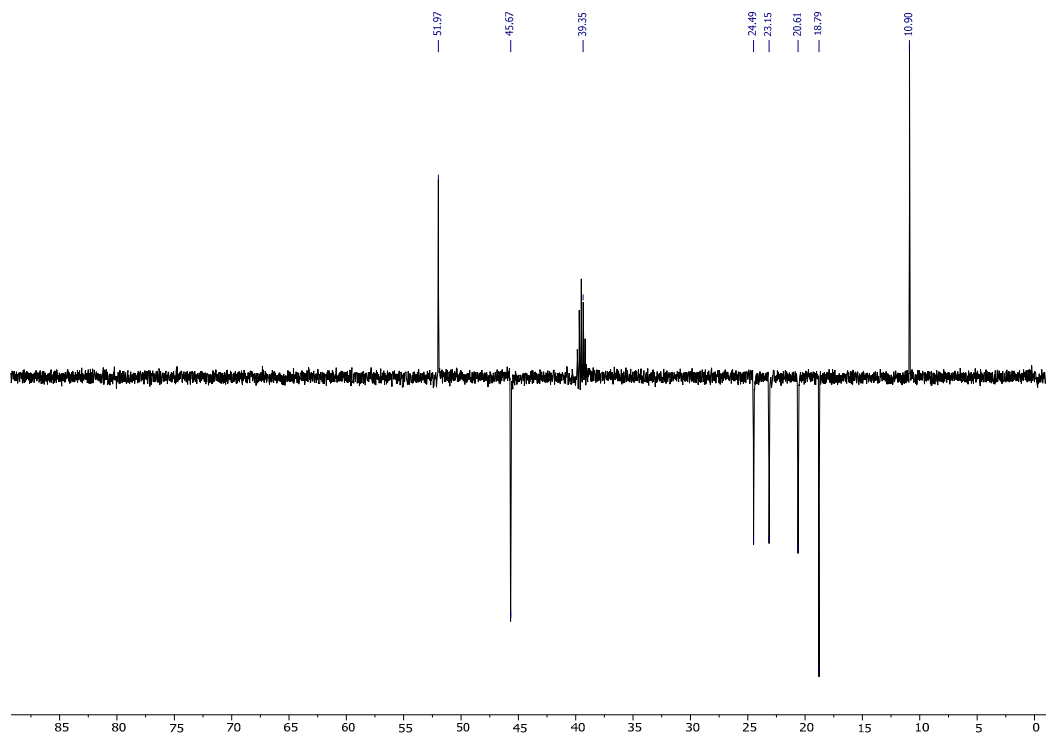


Figure S8: DEPT-135 spectrum of the pramipexole API.

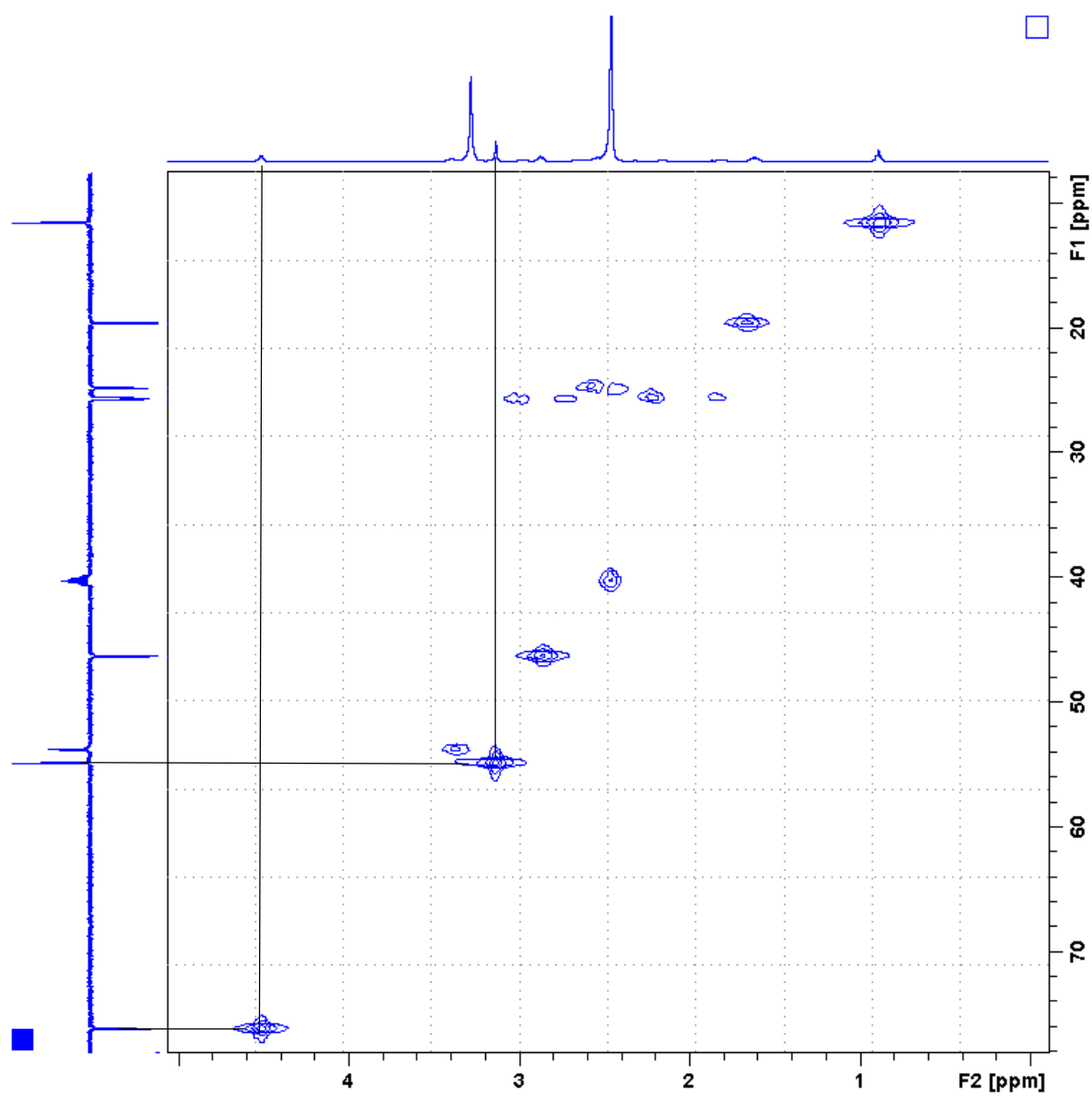


Figure S9: HMQC spectrum of the synthesized impurity.

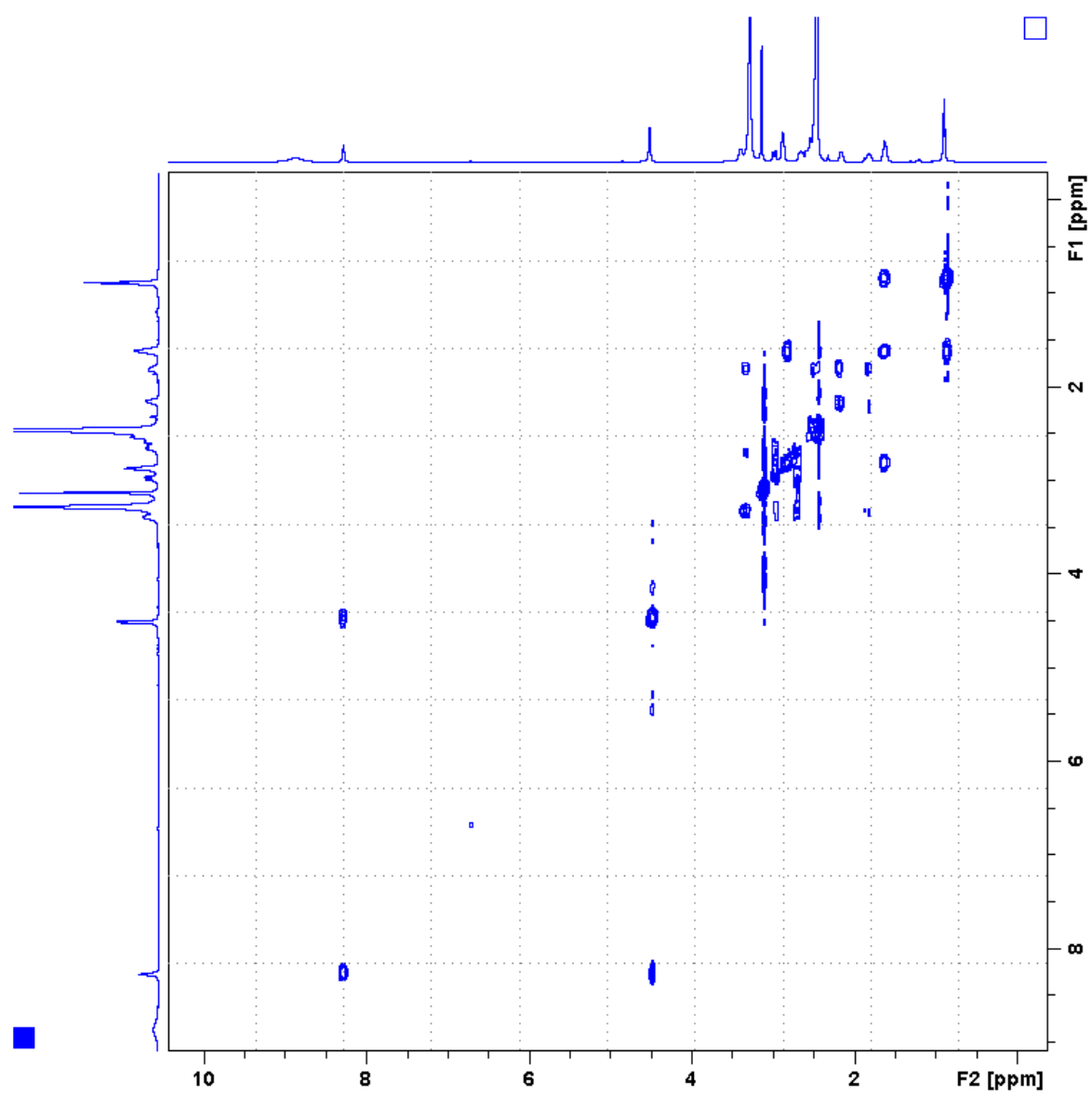


Figure S10: COSY spectrum of the synthesized impurity.

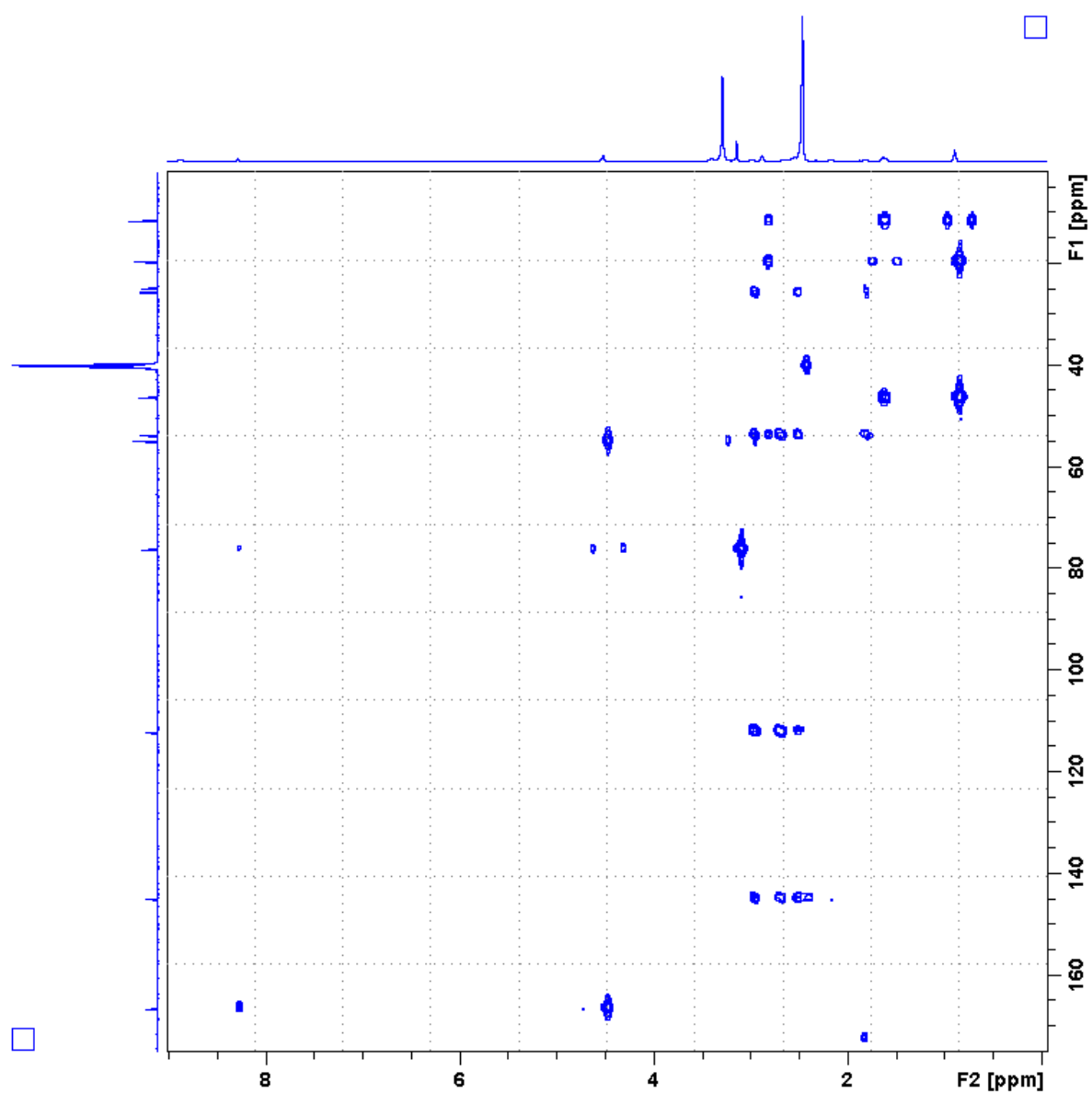


Figure S11: HMBC spectrum of the synthesized impurity.

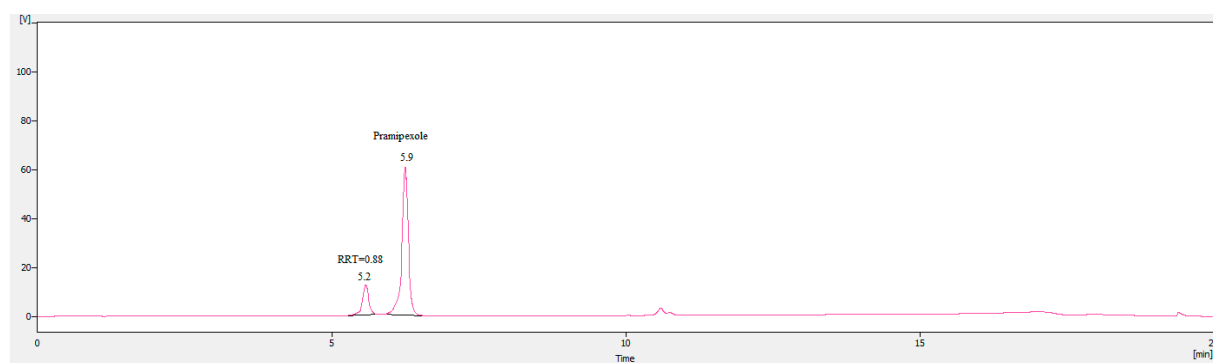


Figure S12: HPLC-UV chromatograms using organic impurity test method in USP monograph of pramipexole corresponding to injection of reaction mixture of HPMC and pramipexole in presence of formaldehyde; temperature: 120°C; time: 2 h.