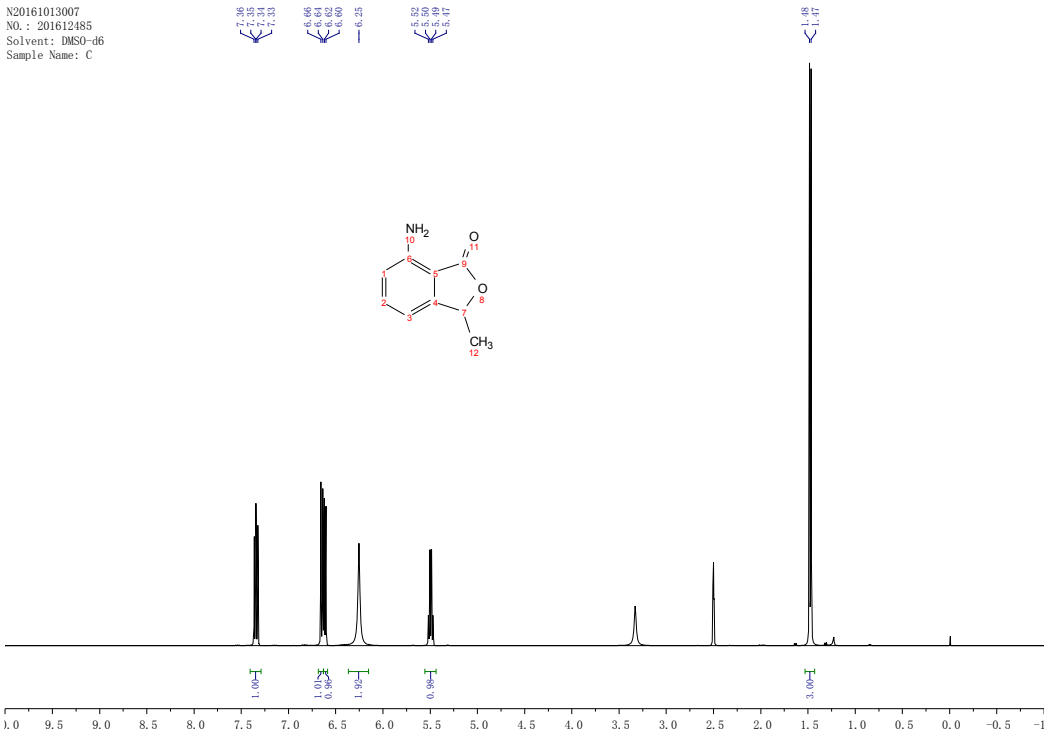
Supporting Information for Concise Synthesis of Key Intermediates of Pyriftalid and Paquinimod via Hydrogenation Method

Zhong Li[1], Bing Li[2], An-Jiang Yang[1], Fu-Li Zhang*[1]

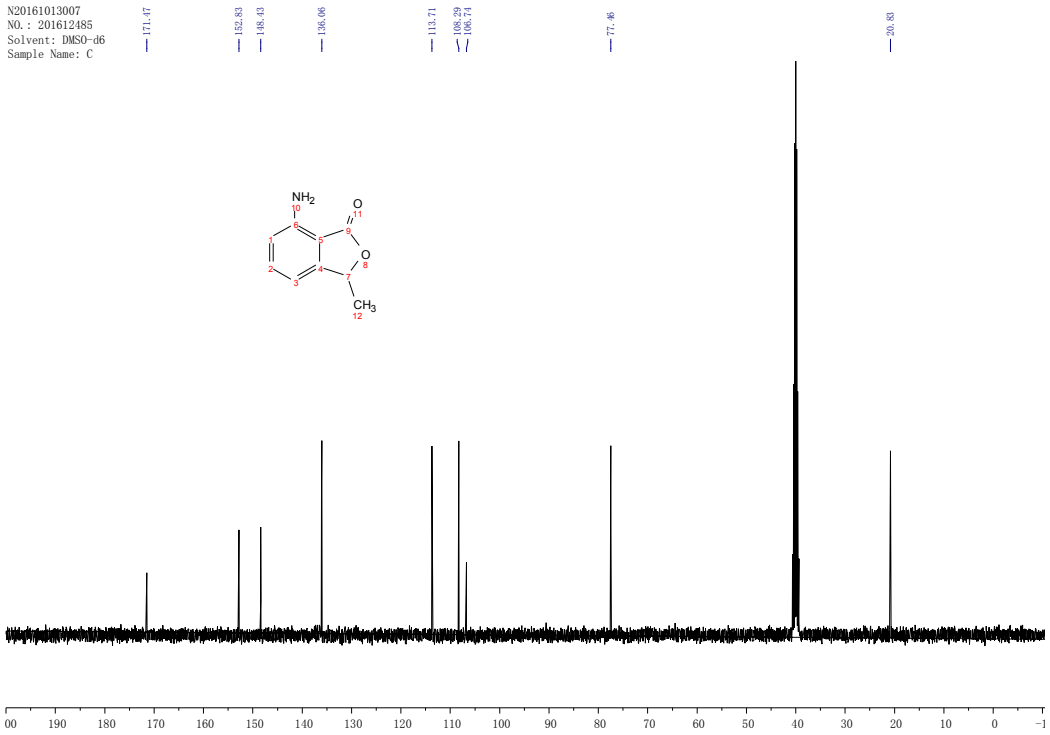
[1]Shanghai Institute of Pharmaceutical Industry, China State Institute of Pharmacetical Industry, 285 Gebaini Road, Pudong, Shanghai 201203, China and [2]Zhejiang University of Technology, 18 Chaowang Road, Xiacheng, Hangzhou 310014, China.

Email: zhangfuli1@sinopharm.com

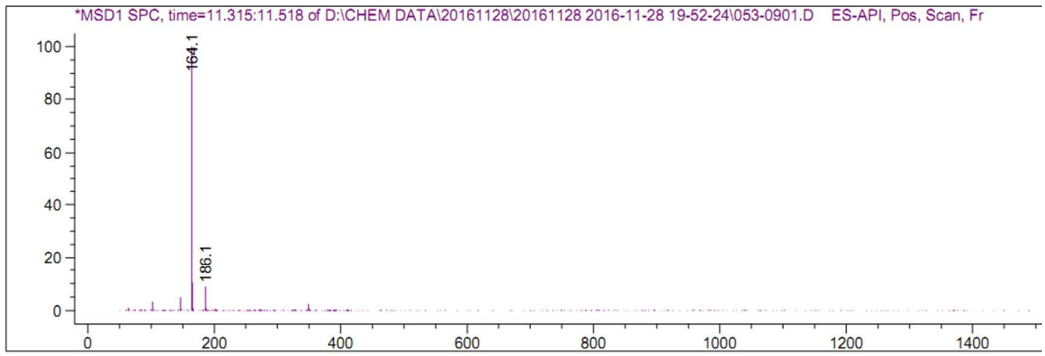
Table of Contents



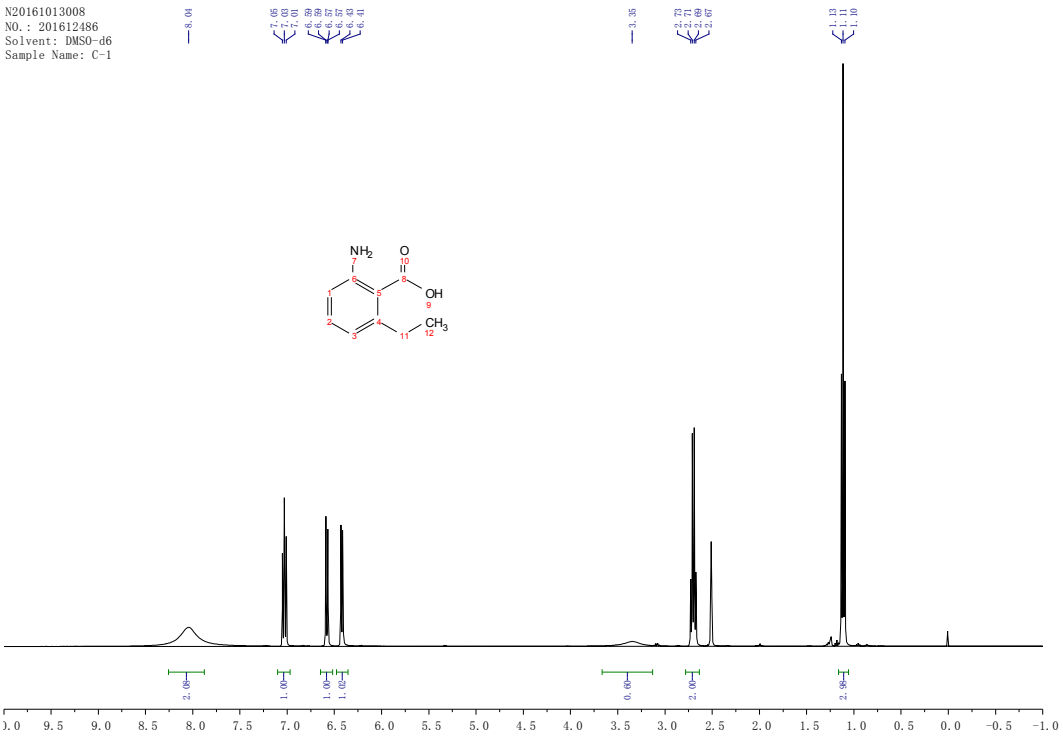
^{1}H NMR spectrum of compound **1**



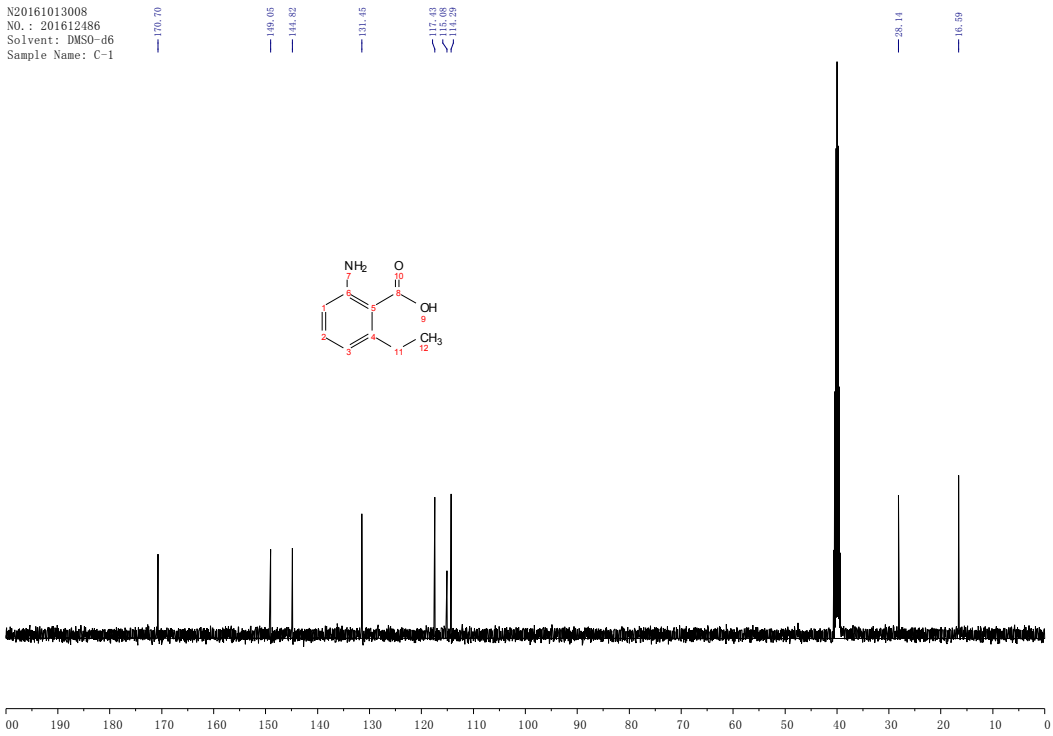
^{13}C NMR spectrum of compound **1**



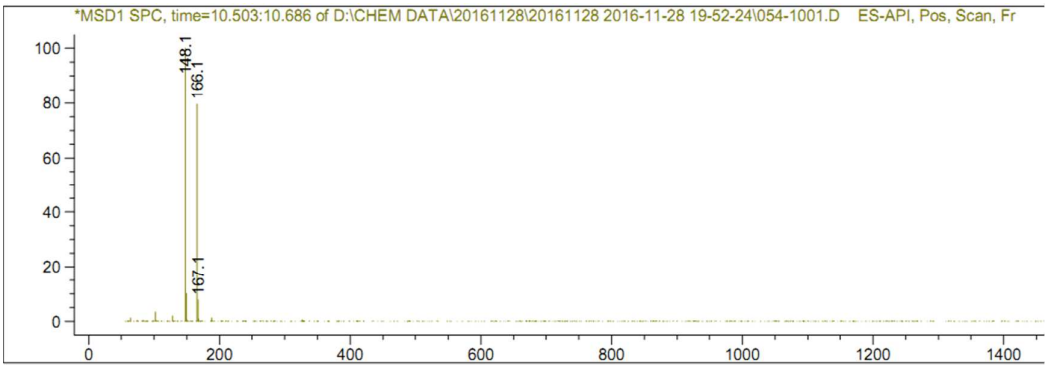
MS spectrum of compound **1**



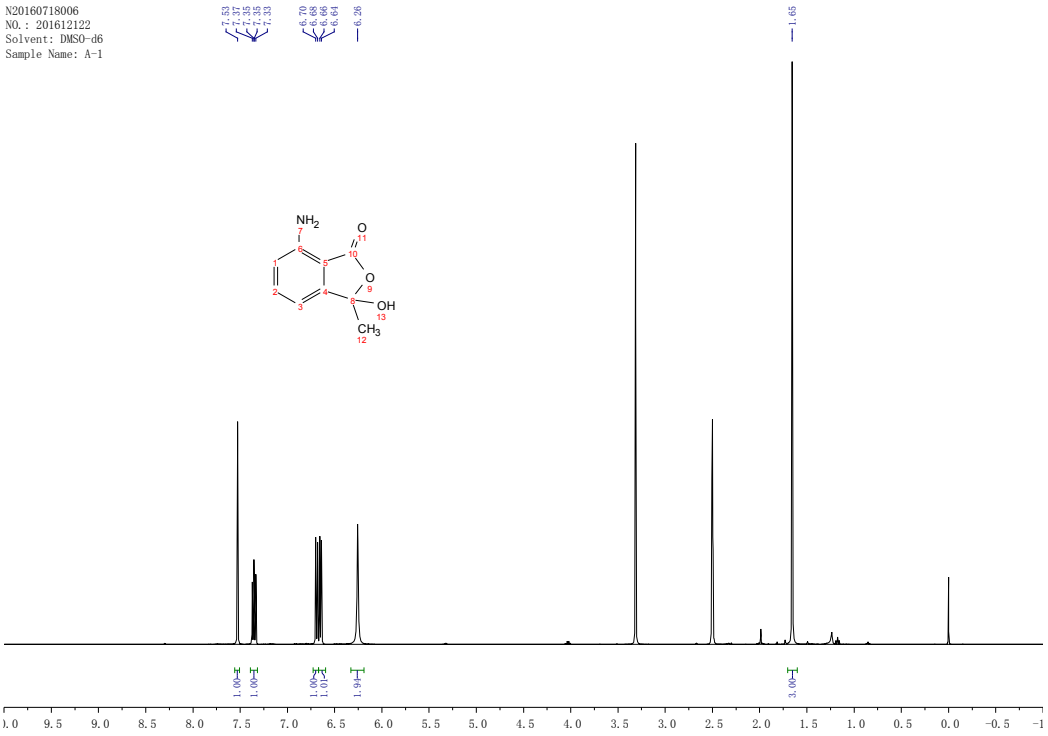
^{1}H NMR spectrum of compound **2**



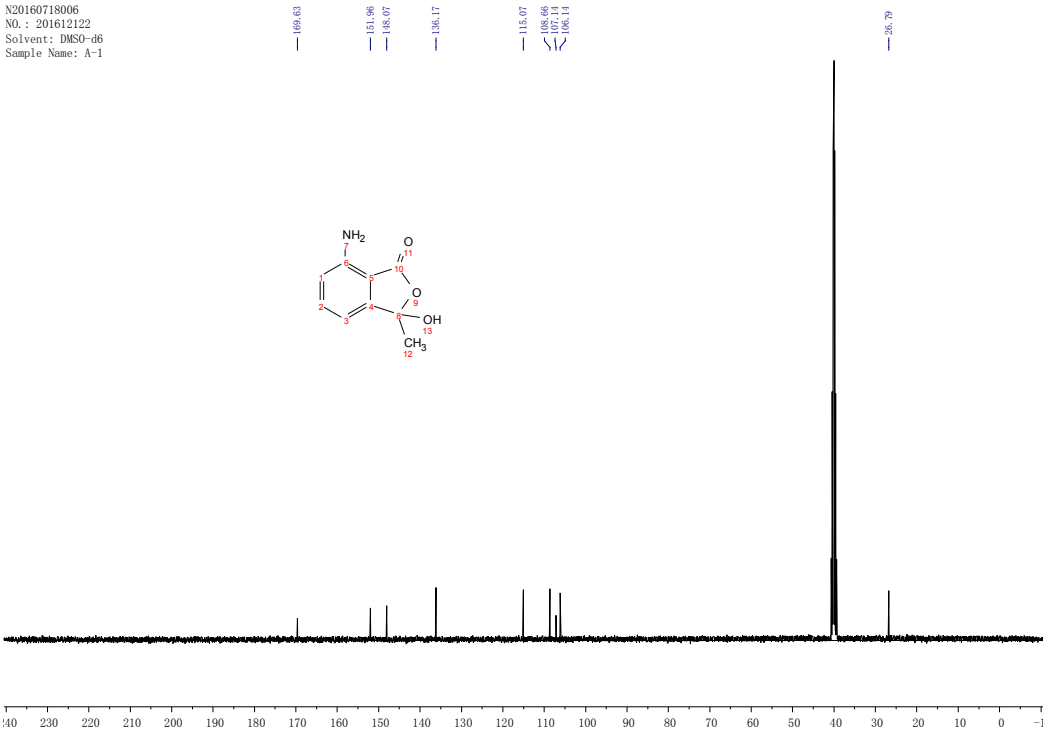
^{13}C NMR spectrum of compound **2**



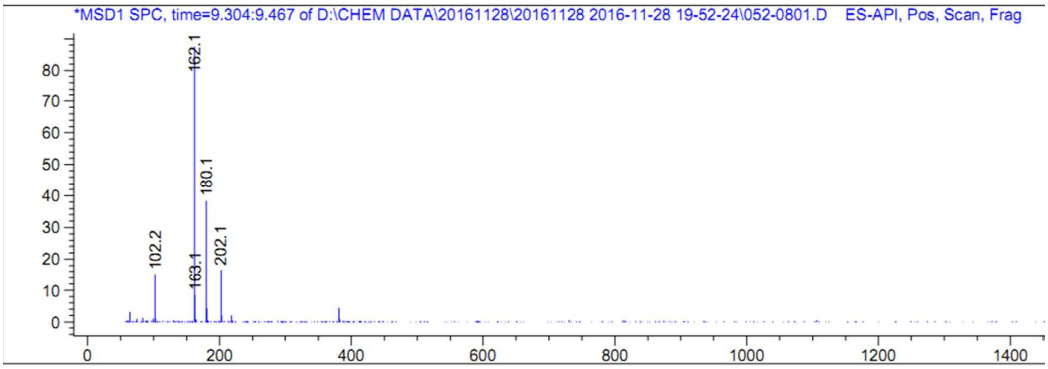
MS spectrum of compound **2**



^{1}H NMR spectrum of compound **4**

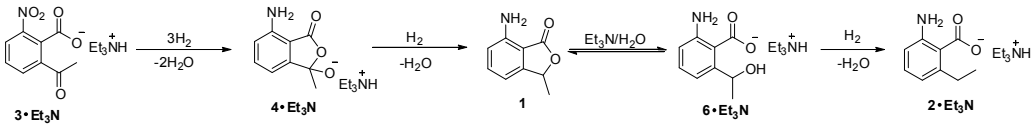


^{13}C NMR spectrum of compound **4**



MS spectrum of compound **4**

Reaction process data about Raney-Ni for Reduction of Triethylammonium salt of **3** to prepare **2**.



[a]Reaction Process detected by HPLC.

[b]Time (h)	HPLC (%)[c]				
	3	**4**	**1**	**6**	**2**
1	26.17	54.90	10.98	1.70	/
2	ND	0.43	71.52	12.69	14.64
4	ND	ND	34.59	1.03	63.85
6	ND	ND	10.84	0.54	87.67
7	ND	ND	6.90	1.19	91.69

[a] Reaction conditions: triethylammonium salt of **3** (6.20 g), Et_3N (4.04 g), Raney-Ni (1.00 g), H_2O (45 mL), 120℃ (Bath temperature)，15-20atm;

[b] The reaction was collected data by hour;

[c] Compositions of reaction mixture were calculated from HPLC area.

As showed in the table above, the nitro reduction intermediates **4** was observed as the main product in 1h; compound **1** was the main product in 2h; as time prolonged, **2** became the main product (4h, 6h, 7h).The nitro reduction is faster compared to the following steps , and the reaction steps proceed mostly by sequence.