Synthesis and organocatalytic asymmetric nitro-aldol initiated cascade reactions of 2-acylbenzonitriles leading to 3,3-disubstituted isoindolinones

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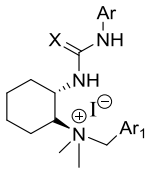
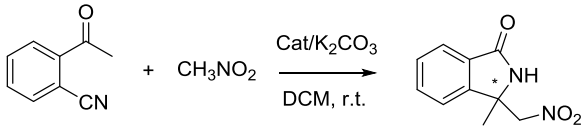
Screening with $MeNO_2$



C1: X=O, Ar=Ar_1=3,5-$(CF_3)C_6H_3$
C2: X=O, Ar=3-$NO_2C_6H_4$, Ar_1=3,5-$(CF_3)C_6H_3$
C3: X=O, Ar=4-$NO_2C_6H_4$, Ar_1=3,5-$(CF_3)C_6H_3$
C4: X=O, Ar=Et, Ar_1=3,5-$(CF_3)C_6H_3$
C5: X=O, Ar=Ar_1=3-$NO_2C_6H_4$
C6: X=O, Ar=Ar_1=Ph
C7: X=S, Ar=Ar_1=3,5-$(CF_3)C_6H_3$

Figure S1

Table S1



Entry	Catalyst (10 mol%)	Time (days)	Yield (%)	e.e.
1	**C1**	3d	99	41
2	**C2**	3d	95	39
3	**C3**	3d	93	38
4	**C4**	7d	15	20
5	**C5**	3d	95	40
6	**C6**	7d	99	7
7	**C7**	7d	50	39

Table S2

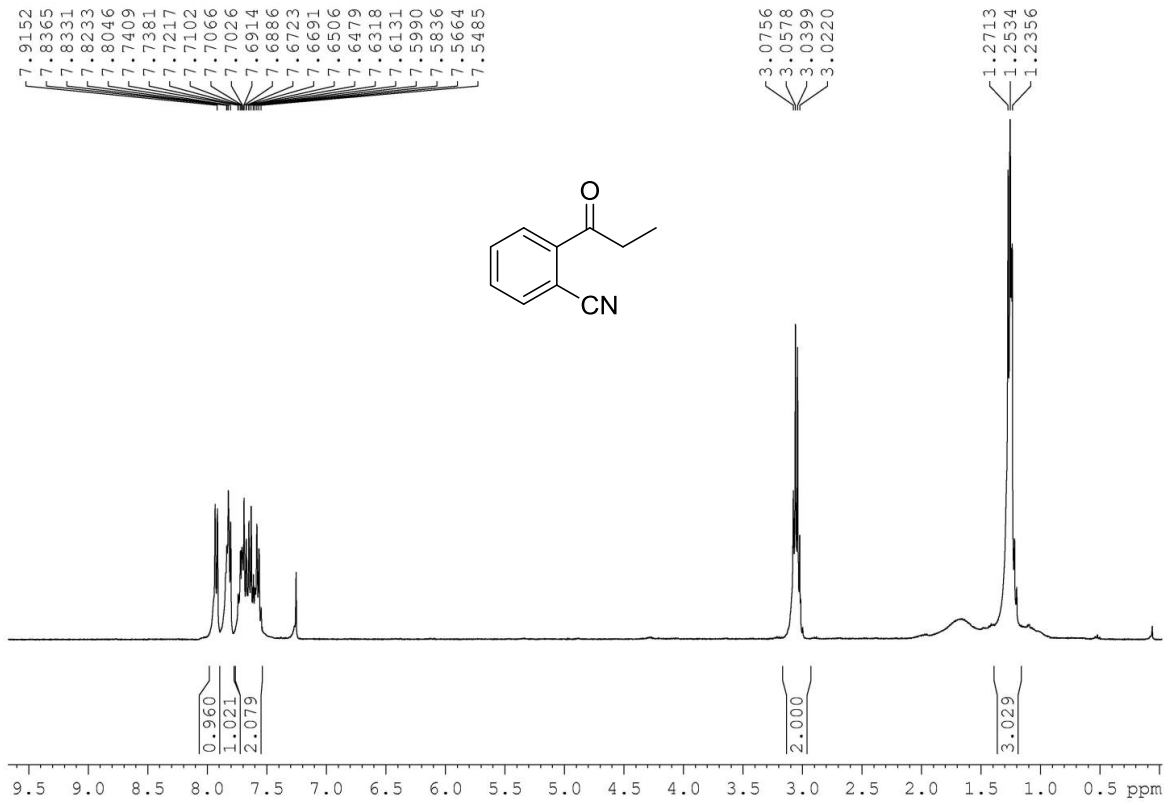
Entry	[ketone] [M]	Base (1 eq)	Cat (eq)	T (°C)	Time (days)	Yield (%)[b]	e.r. (%)[c]
1	0.061	K_2CO_3	0.1	r.t.	3d	99	41
2	0.18	K_2CO_3	0.1	r.t.	1d	20	30
3	0.092	K_2CO_3	0.1	r.t.	2d	99	33
4	0.061	K_3PO_4	0.1	r.t.	3d	25	45
5	0.061	K_3PO_4	0.1	5	7d	25	37
6	0.061	K_3PO_4	0.1	35	2d	18	35
7	0.061	K_3PO_4	0.2	r.t.	2d	25	44
8	0.061	K_3PO_4	0.05	r.t.	7d	25	41

Table S3

Entry[a]	Solvent	Base (1 eq)	Time (days)	Yield (%)[b]	e.e. (%)[c]
1	DCM	K_2CO_3	3d	99	41
2	DCM	K_2CO_3 (aq.50%)	7d	20	30
3	DCM	Cs_2CO_3	3d	99	33
4	DCM	KOH	7d	25	38
5	DCM	LiOH	7d	18	35
6	DCM	K_3PO_4	3d	99	45
7	DCM	No base	7d	--	
8	Toluene	K_3PO_4	1d	99	18
9	THF	K_3PO_4	3d	99	14
10	$CHCl_3$	K_3PO_4	3d	99	45
11	$CHCl_3$	K_3PO_4 (5 eq)	2d	99	42
12	$CHCl_3$	K_3PO_4 (0.2 eq)	6d	99	43

[a] All the experiments were performed at [ketone]=0.061M, 0.1 eq of the catalyst and with 1 eq of the inorganic base.
[b] Yields refer to chromatographically pure compounds [c] Enantiomeric excesses were determined by HPLC on chiral stationary phase column.

^{1}HNMR and ^{13}CNMR spectra of compounds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7.6914
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7.5664
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3.0399
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1.2534
1.2356
O
CN
0.960
1.021
2.079
2.000
3.029
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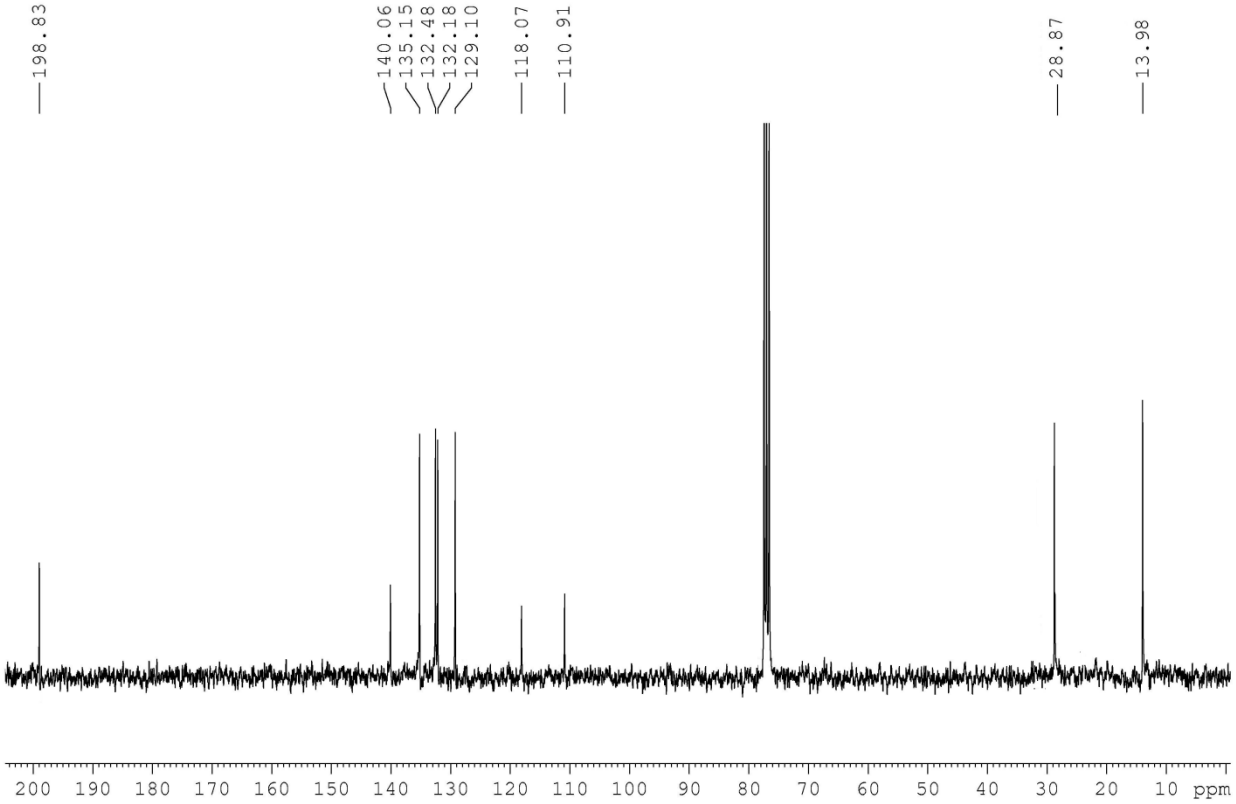
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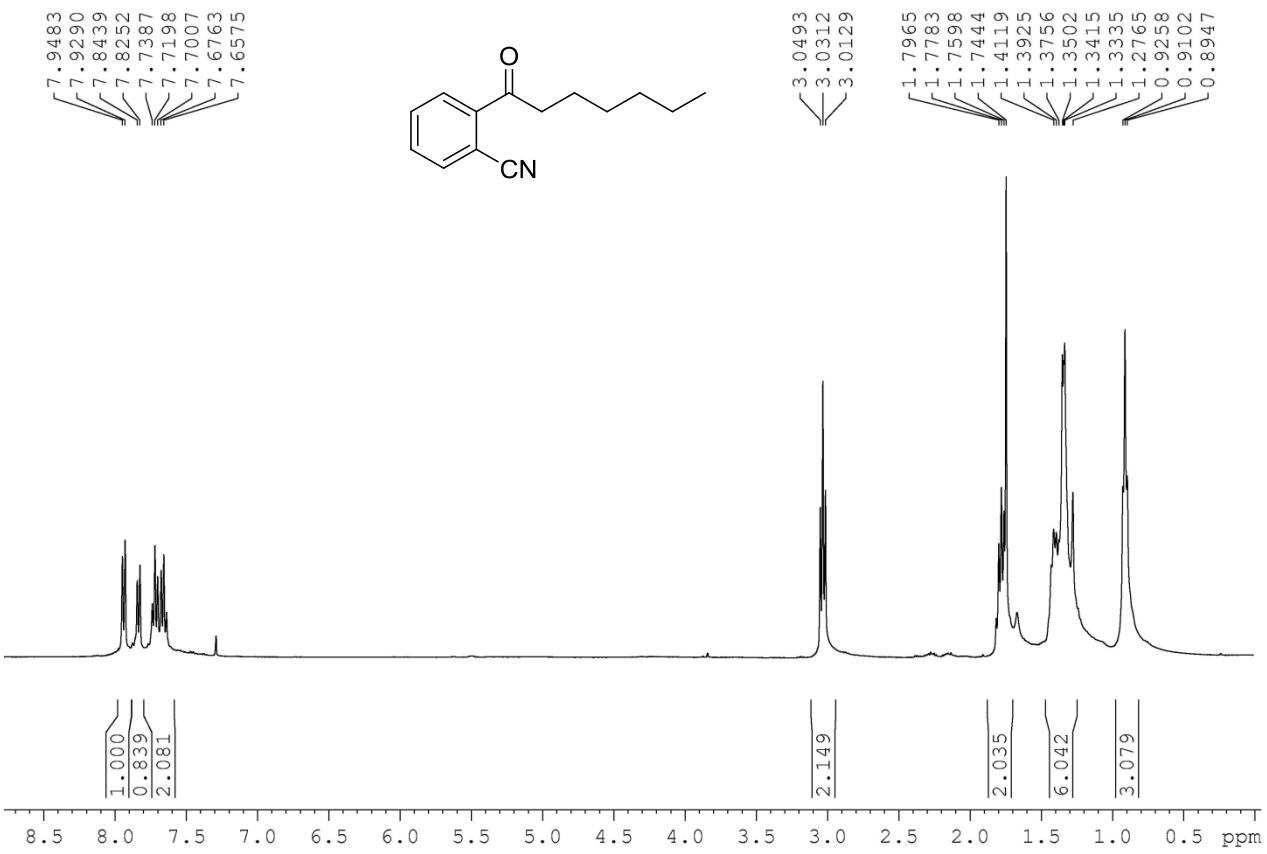
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1.7783
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1.3756
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1.000
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2.035
6.042
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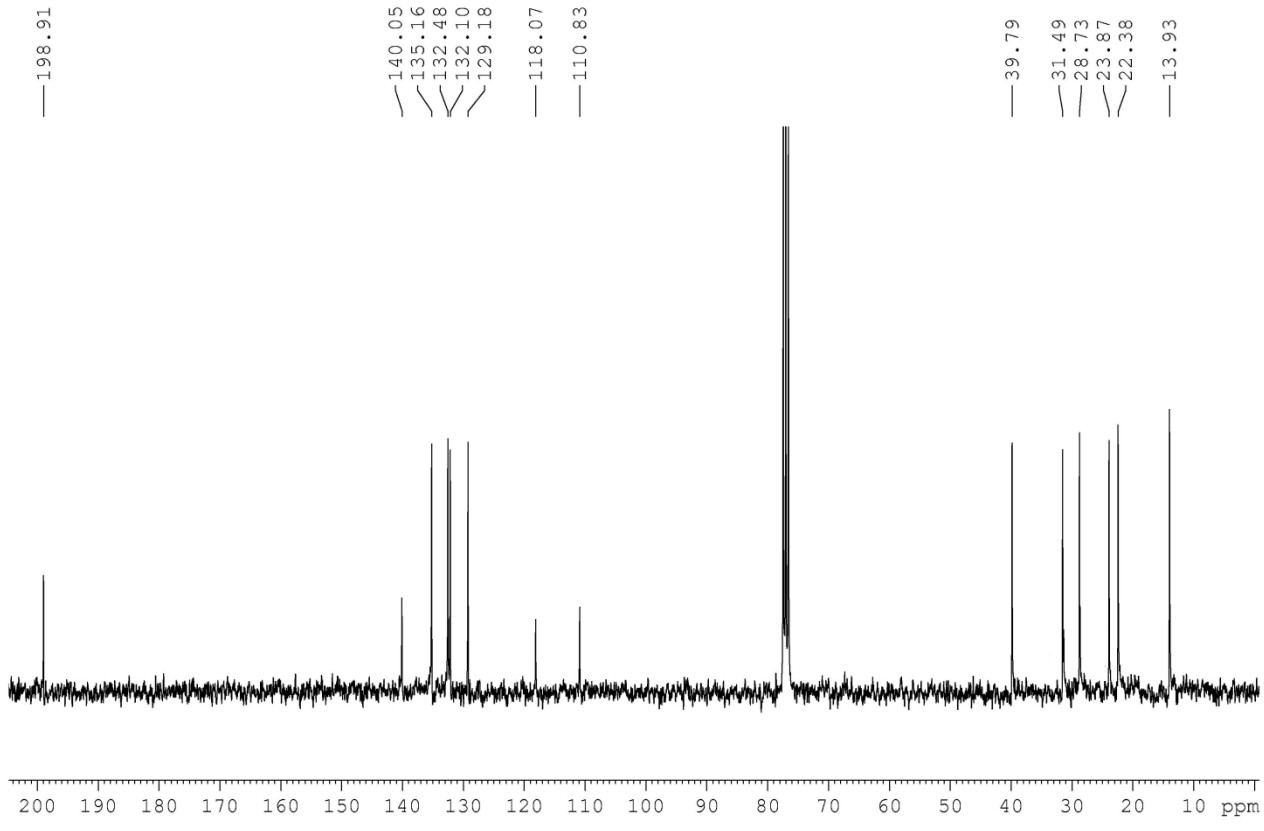
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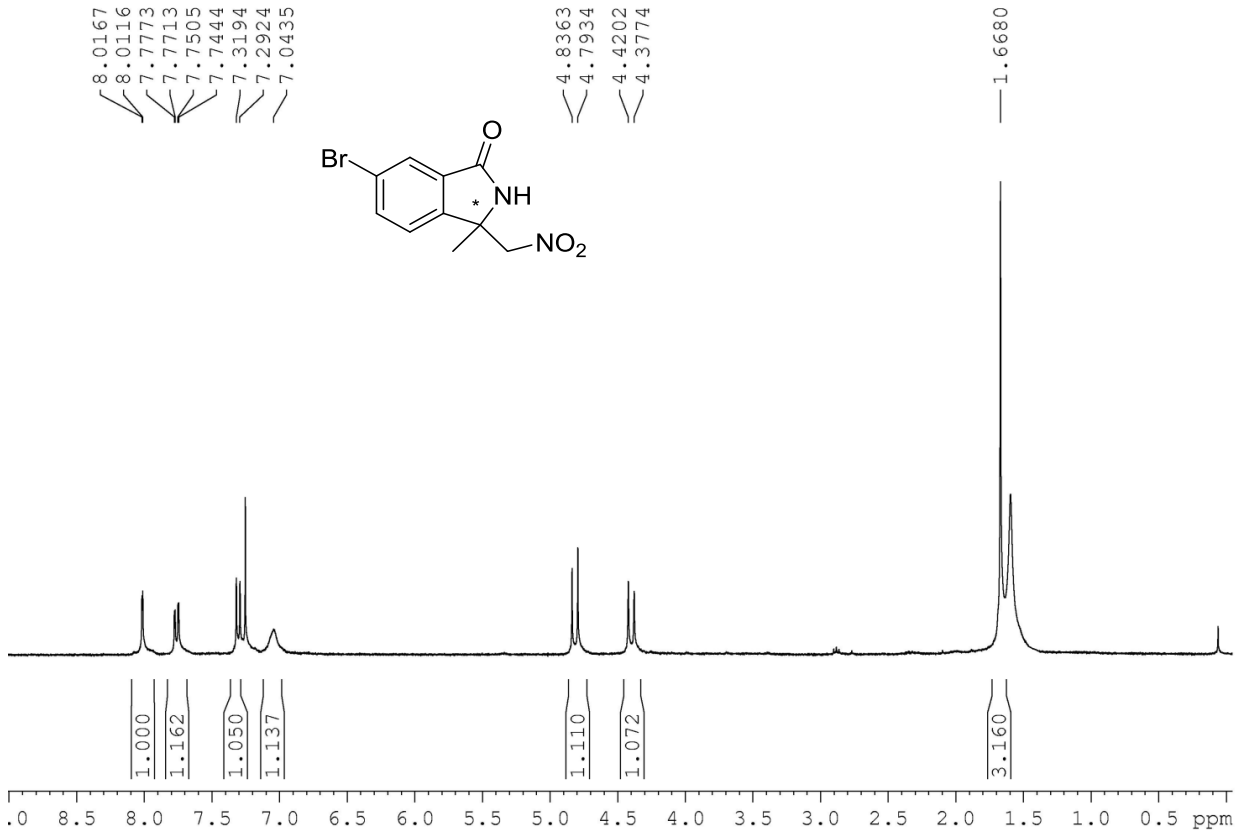
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4.4202
4.3774
1.6680
Br
O
NH
*
NO2
1.000
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1.050
1.137
1.110
1.072
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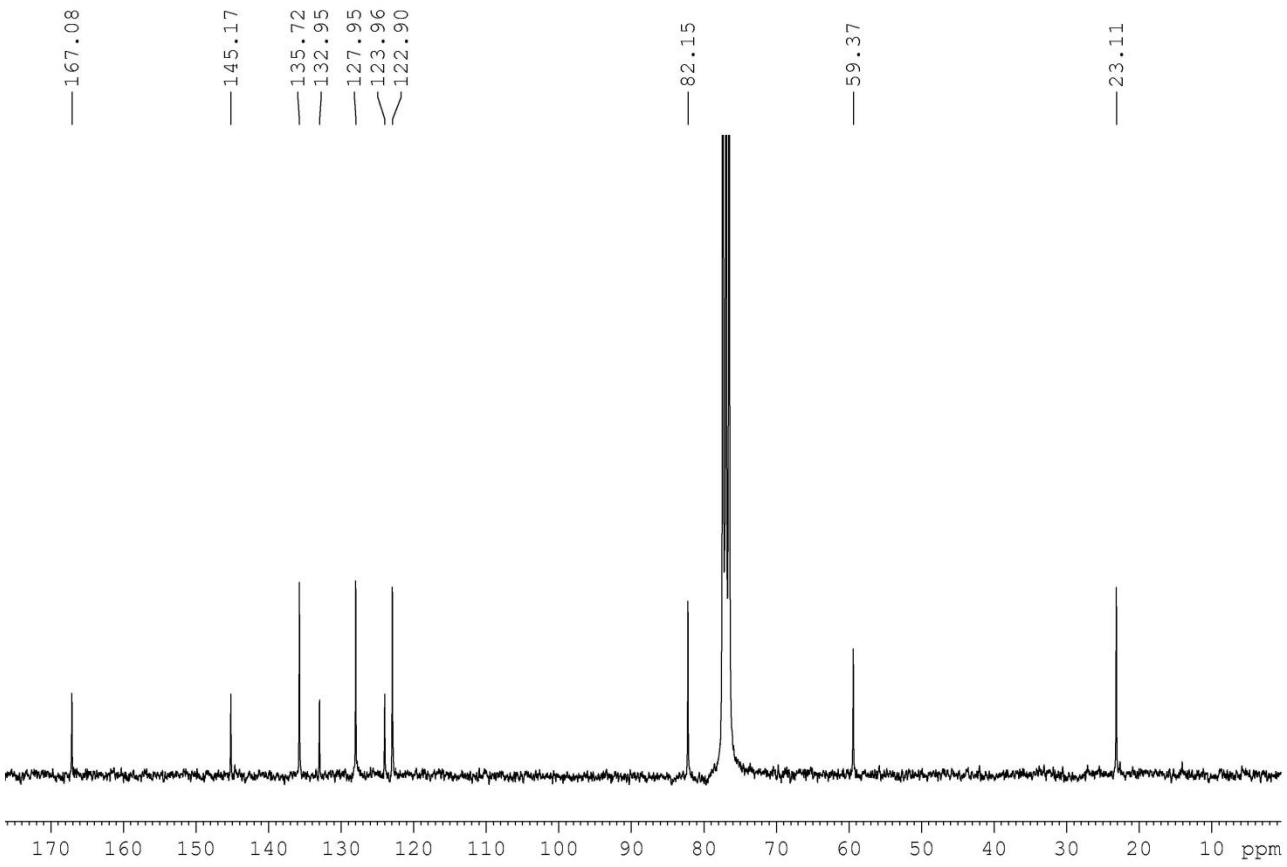
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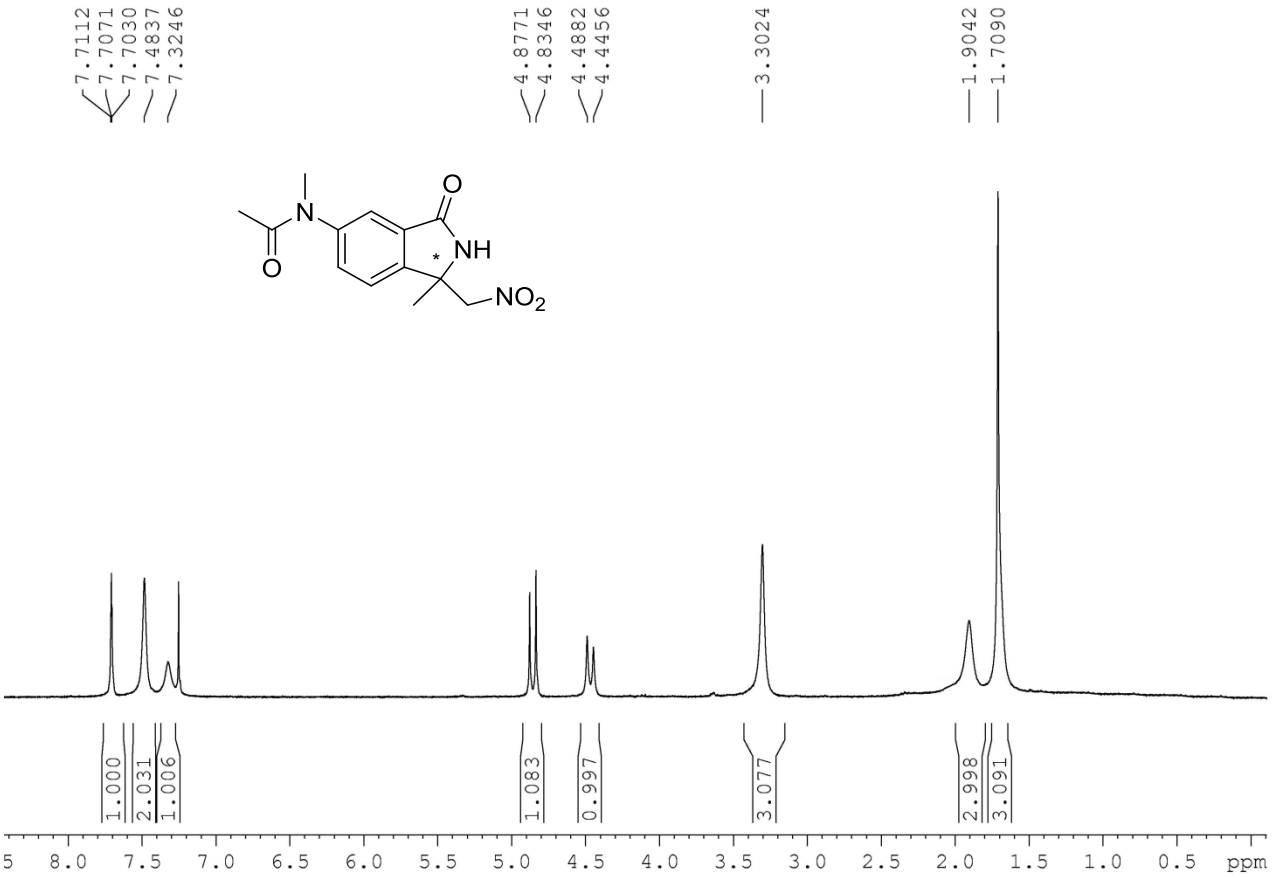
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1.7090
O
N
O
NH
*
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1.083
0.997
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5
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7.5
7.0
6.5
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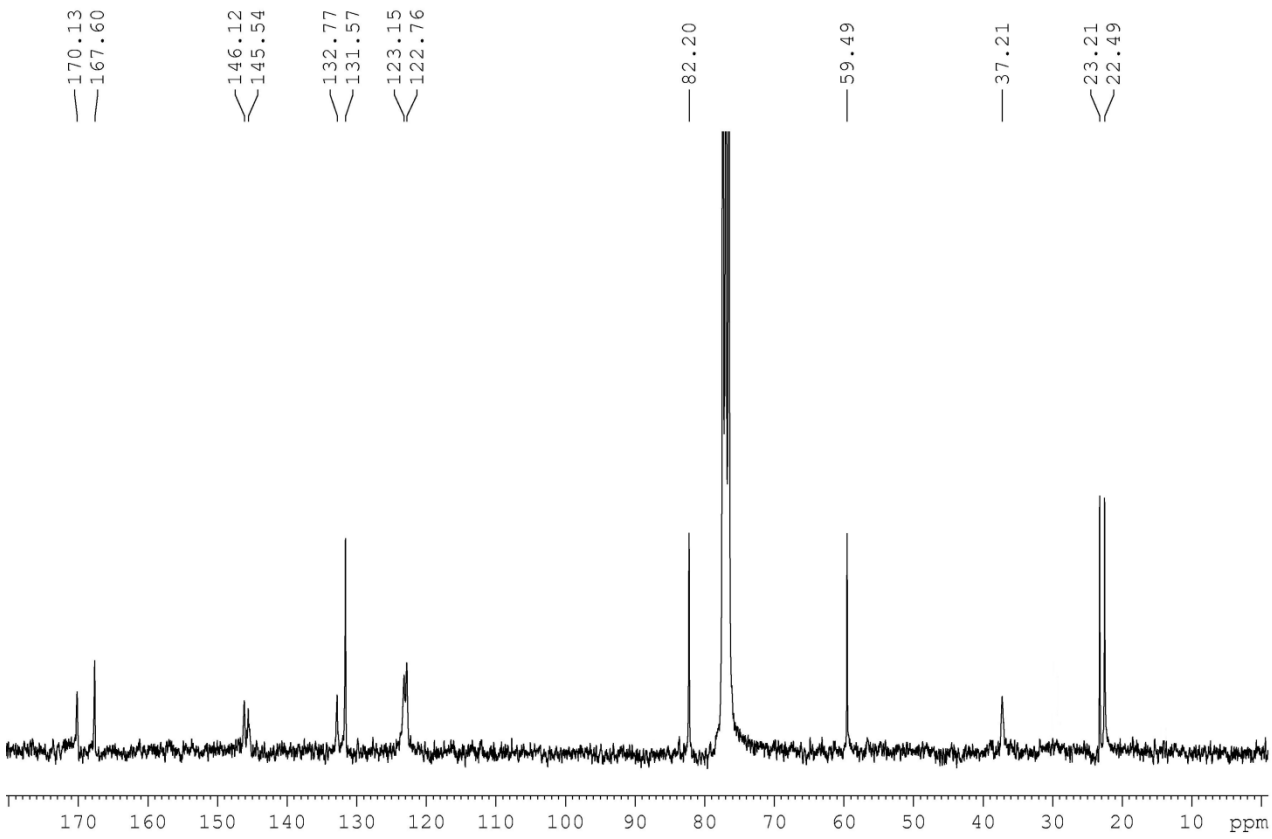
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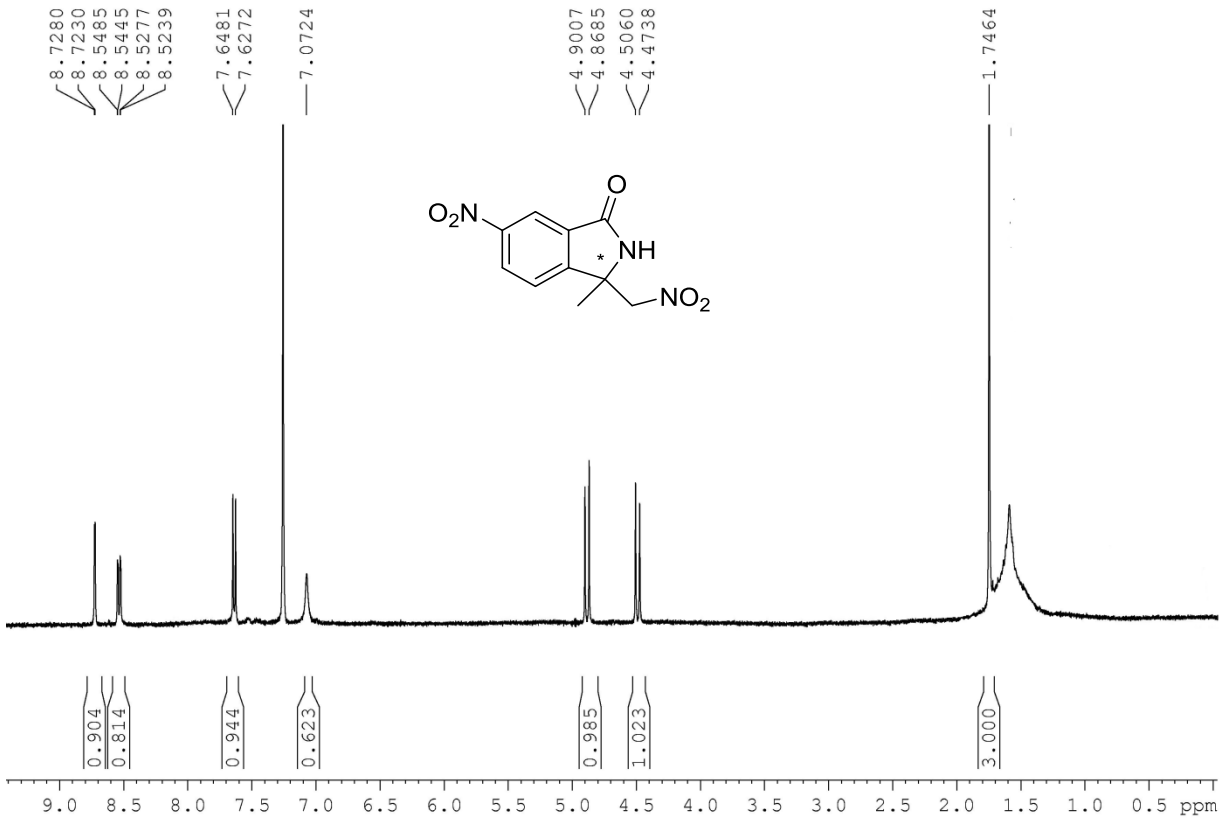
20
10
ppm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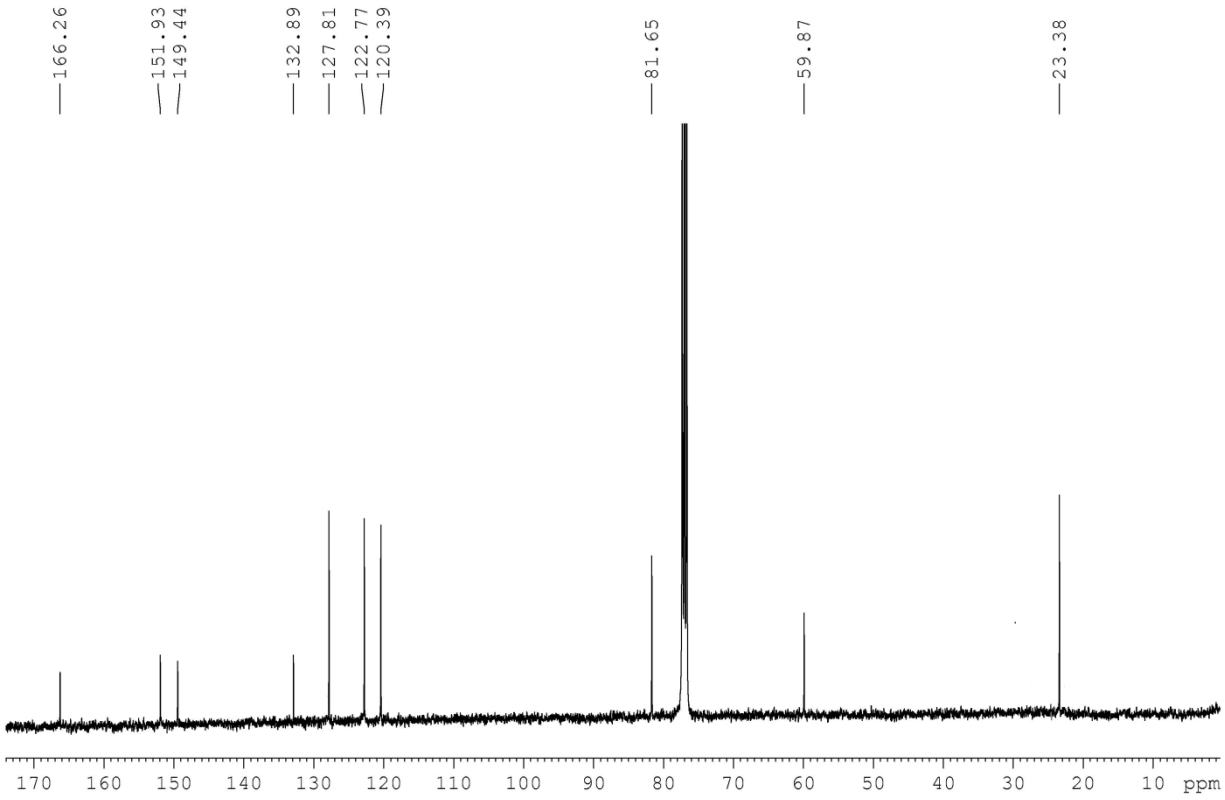
4.5060
4.4738
1.7464
O
O2N
NH
*
NO2
0.904
0.814
0.944
0.623
0.985
1.023
3.000
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm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81.65
59.87
23.38
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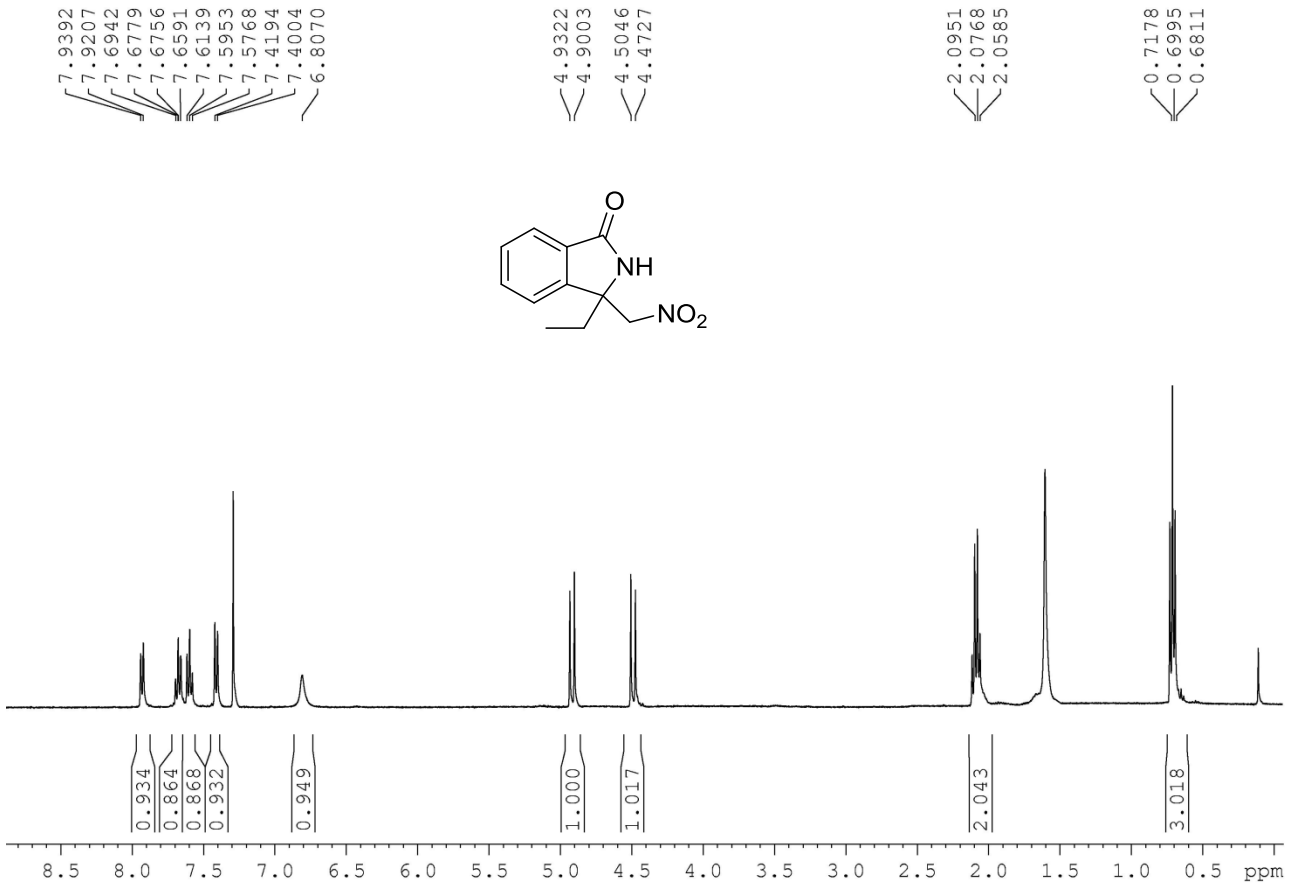
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6.8070
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4.9003
4.5046
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NH
NO2
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0.868
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1.017
2.043
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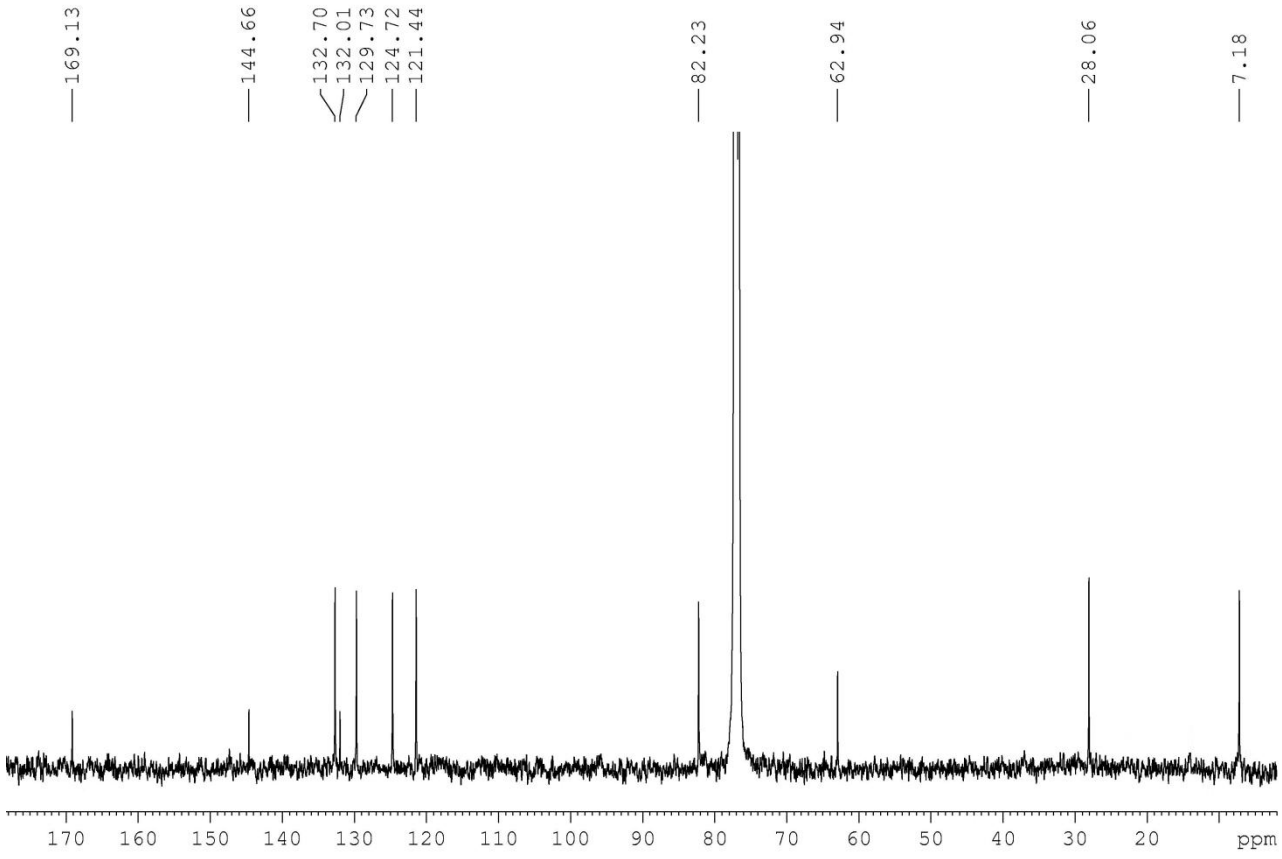
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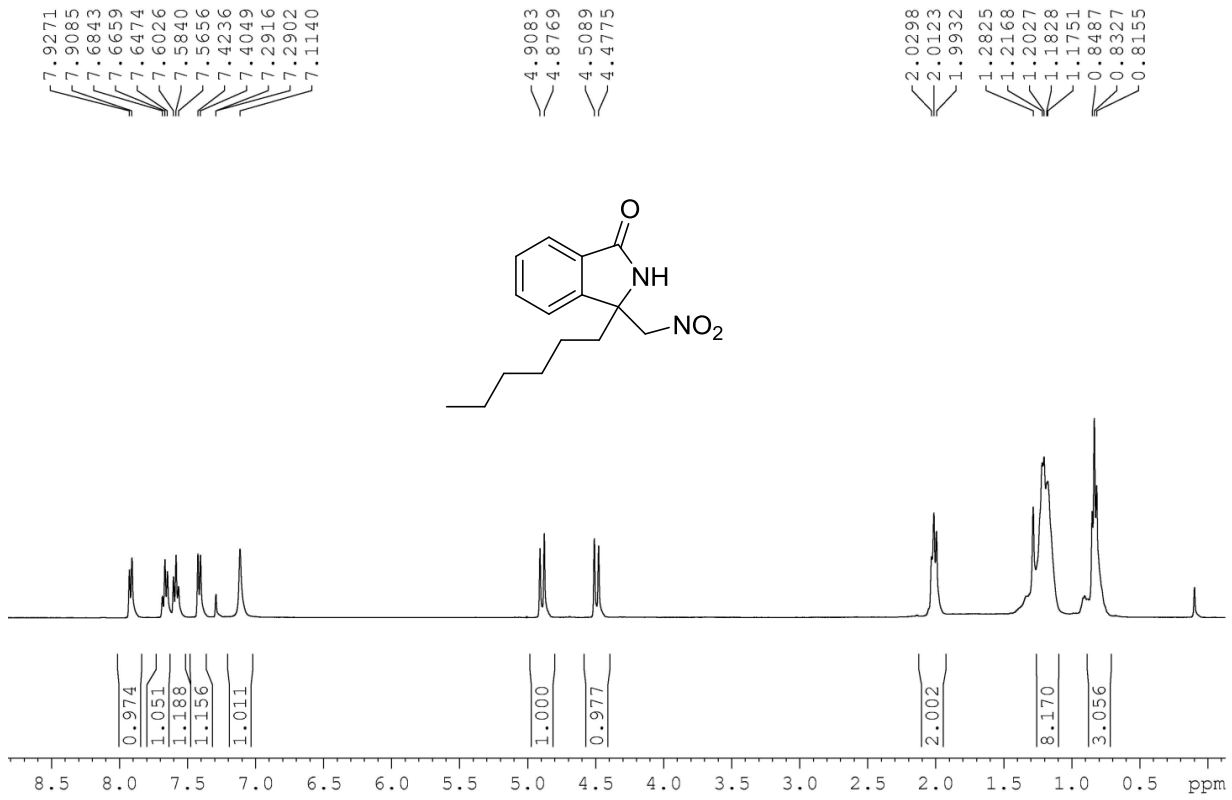
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7.1140
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2.0123
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1.2168
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1.000
0.977
2.002
8.170
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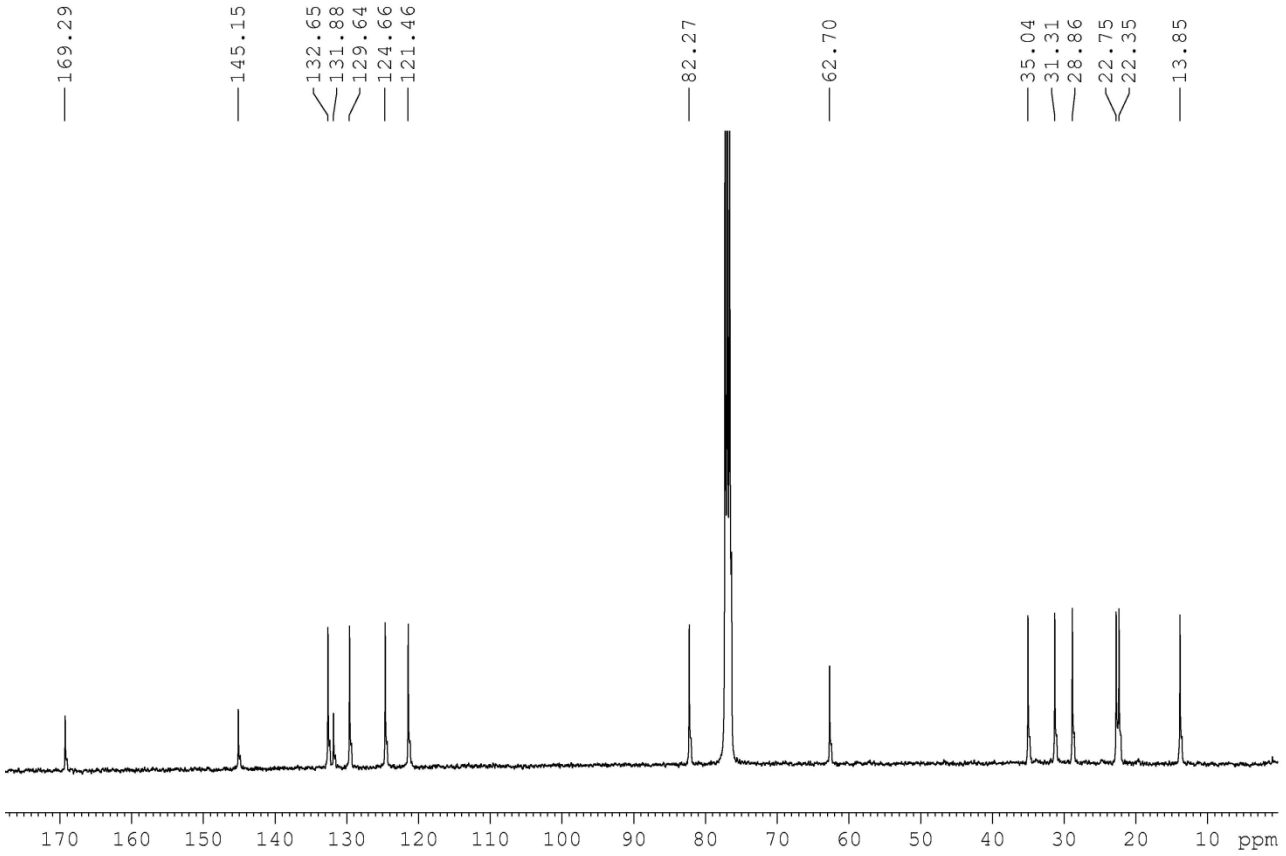
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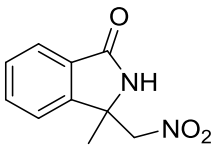
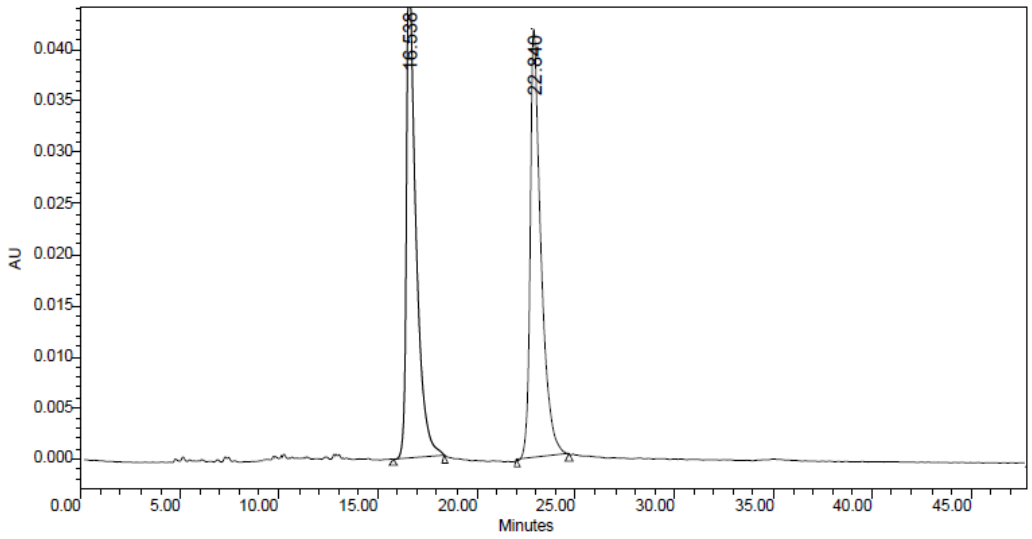
HPLC traces of compound 7a





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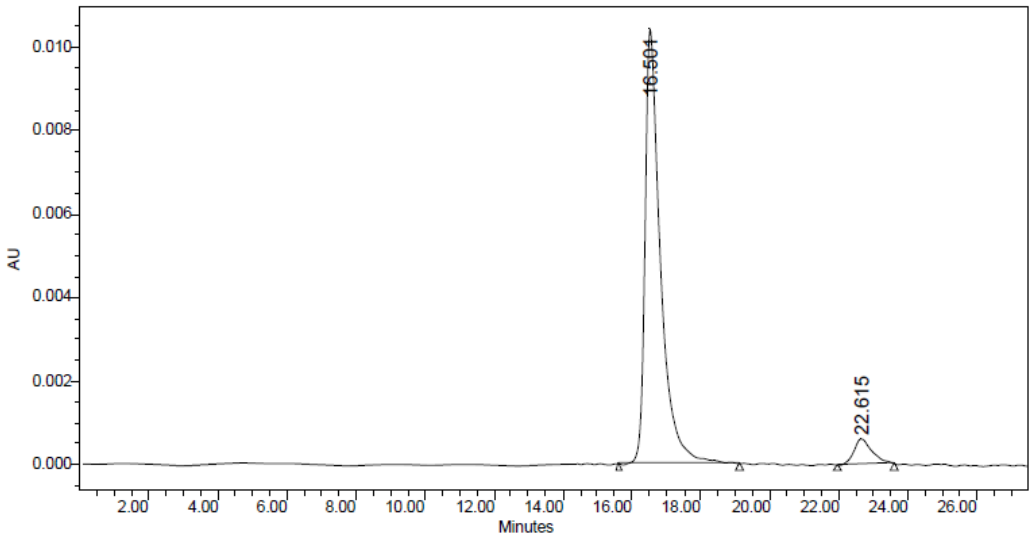

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