Supplementary Data

Efficient synthesis of *t*-butyl 3-alkyl-*N*-hydroxy-oxindole-3-carboxylates from di-*t*-butyl 2-nitrophenyl-malonates

Yu-suke Yamai, Kyoji Ishida, Itaru Natsutani, Shinichi Uesato, Yasuo Nagaoka, and Takaaki Sumiyoshi *

Department of Life Science and Biotechnology, Faculty of Chemistry, Materials and Bioengineering, Kansai University, Yamate-cho 3-3-35, Suita, Osaka, 564-8680, Japan

Tel: +81-6-6368-1773
Fax: +81-6-6388-8690
E-mail: t-sumiyo@kansai-u.ac.jp

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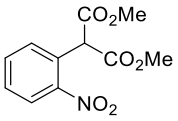
1. Additional experimental section

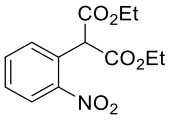
General procedure for preparation of di-alkyl 2-(2-nitrophenyl)malonate (Table 1)

1-Fluoro-2-nitrobenzene was dissolved in DMSO (2.0 M). Di-alkyl malonate (1.1 eq.) and K_2CO_3 (2.2 eq.) were added to the reaction mixture. The resultant mixture was stirred at 110 ºC. After 2 hours, the reaction mixture was diluted with 1N HCl aq. and extracted with EtOAc/*n*-hexane = 2/1. The combined organic phases were washed with 1N HCl aq. and brine, dried over Na_2SO_4, filtered, and the filtrate was concentrated *in vacuo*. Crystallization of the residue from *n*-hexane afforded target compound.



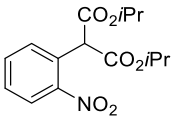
Dimethyl 2-(2-nitrophenyl)malonate[1]

Yield: 74% as a brownish solid; ^{1}H NMR ($CDCl_3$) δ: 8.08 (1H, dd, *J* = 7.6, 1.4 Hz), 7.67 (1H, td, *J* = 7.6, 1.4 Hz), 7.54 (1H, td, *J* = 7.6, 1.4 Hz), 7.52 (1H, td, *J* = 7.6, 1.4 Hz), 5.34 (1H, s), 3.81 (6H, s); ^{13}C NMR ($CDCl_3$) δ: 167.6, 148.7, 133.6, 131.3, 129.3, 127.9, 126.2, 54.0, 53.1; HRMS (ESI): *m/z* calcd. for $C_{11}H_{12}NO_6$: 254.0659 $[M+H]^+$; found: 254.0660.



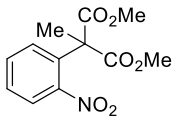
Diethyl 2-(2-nitrophenyl)malonate[2]

Yield: 95% as a yellow solid; ^{1}H NMR ($CDCl_3$) δ: 8.07 (1H, d, *J* = 7.9 Hz), 7.65 (1H, t, *J* = 7.9 Hz), 7.53 (1H, d, *J* = 7.9 Hz), 7.52 (1H, t, *J* = 7.9 Hz), 5.29 (1H, s), 4.27 (4H, q, *J* = 7.3 Hz), 1.29 (6H, t, *J* = 7.3 Hz); ^{13}C NMR ($CDCl_3$) δ: 167.2, 148.8, 133.5, 131.2, 129.2, 128.2, 125.2, 62.2, 54.5, 13.9; HRMS (ESI): *m/z* calcd. for $C_{13}H_{16}NO_6$: 282.0972 $[M+H]^+$; found: 282.0971.



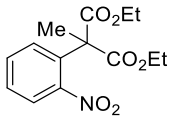
Diisopropyl 2-(2-nitrophenyl)malonate[3]

Yield: 95% as a yellow solid; ^{1}H NMR ($CDCl_3$) δ: 8.07 (1H, dd, *J* = 8.5, 1.6 Hz), 7.65 (1H, td, *J* = 8.5, 1.6 Hz), 7.52 (1H, td, *J* = 8.5, 1.6 Hz), 7.51 (1H, dd, *J* = 8.5, 1.6 Hz), 5.21 (1H, s), 5.13 (2H, sep, *J* = 6.4 Hz), 1.29 (6H, d, *J* = 6.4 Hz), 1.27 (6H, d, *J* = 6.4 Hz); ^{13}C NMR ($CDCl_3$) δ: 166.8, 148.9, 133.4, 131.2, 129.1, 128.5, 125.2, 70.0, 54.9, 21.6, 21.5; HRMS (ESI): *m/z* calcd. for $C_{15}H_{20}NO_6$: 310.1291 $[M+H]^+$; found: 310.1286.



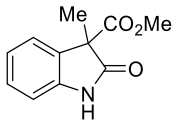
Dimethyl 2-methyl-2-(2-nitrophenyl)malonate (3a)[1]

See preparation of di-alkyl 2-methyl-2-(2-nitrophenyl)malonate derivatives in experimental section. Yield: quant. as a yellow solid; ^{1}H NMR ($CDCl_3$) δ: 8.04 (1H, dd, *J* = 8.3, 1.4 Hz), 7.61 (1H, td, *J* = 8.3, 1.4 Hz), 7.49 (1H, td, *J* = 8.3, 1.4 Hz), 7.32 (1H, dd, *J* = 8.3, 1.4 Hz), 3.75 (6H, s), 2.01 (3H, s); ^{13}C NMR ($CDCl_3$) δ: 170.1, 148.6, 134.2, 133.3, 129.1, 128.7, 126.0, 59.3, 53.1, 23.5; HRMS (ESI): *m/z* calcd. for $C_{12}H_{14}NO_6$: 268.0816 $[M+H]^+$; found: 268.0811.



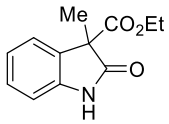
Diethyl 2-methyl-2-(2-nitrophenyl)malonate (3b)[4]

See preparation of di-alkyl 2- methyl -2-(2-nitrophenyl)malonate derivatives in experimental section. Yield: quant. as a yellow solid; ^{1}H NMR ($CDCl_3$) δ: 8.03 (1H, dd, *J* = 8.3, 1.4 Hz), 7.60 (1H, td, *J* = 8.3, 1.4 Hz), 7.48 (1H, td, *J* = 8.3, 1.4 Hz), 7.33 (1H, dd, *J* = 8.3, 1.4 Hz), 4.29–4.15 (4H, m), 2.01 (3H, s), 1.23 (6H, t, *J* = 7.1 Hz); ^{13}C NMR ($CDCl_3$) δ: 169.7, 148.8, 134.6, 133.2, 129.3, 128.5, 125.9, 62.3, 59.6, 23.6, 13.8; HRMS (ESI): *m/z* calcd. for $C_{14}H_{18}NO_6$: 296.1134 $[M+H]^+$; found: 296.1130.



Methyl 3-methyl-oxindole-3-carboxylate (2a)[1]

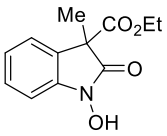
See general procedure for tandem reduction-lactamization reaction of di-alkyl 2-methyl-2-(2-nitrophenyl)malonate in experimental section. Yield: 52% as a pale yellow solid; ^{1}H NMR (DMSO-d_6) δ: 10.68 (1H, s), 7.23 (1H, t, *J* = 7.3 Hz), 7.19 (1H, d, *J* = 7.3 Hz), 6.97 (1H, t, *J* = 7.3 Hz), 6.88 (1H, d, *J* = 7.3 Hz), 3.56 (3H, s), 1.49 (3H, s); ^{13}C NMR ($CDCl_3$) δ: 177.7, 170.1, 140.8, 130.6, 129.1, 123.4, 122.9, 110.3, 55.4, 53.1, 20.2; HRMS (ESI): *m/z* calcd. for $C_{11}H_{12}NO_3$: 206.0812 $[M+H]^+$; found: 206.0813.



Ethyl 3-methyl-oxindole-3-carboxylate (2b)[4]

See general procedure for tandem reduction-lactamization reaction of di-alkyl 2-methyl-2-(2-nitrophenyl)malonate in experimental section. Yield: 50% as a pale yellow solid; ^{1}H NMR (DMSO-d_6) δ: 10.65 (1H, s), 7.23 (1H, t, *J* = 7.6 Hz), 7.18 (1H, d, *J* = 7.6 Hz), 6.97 (1H, t, *J* =

7.6 Hz), 6.88 (1H, d, *J* = 7.6 Hz), 4.07 (1H, dq, *J* = 11.6, 7.0 Hz), 4.01 (1H, dq, *J* = 11.6, 7.0 Hz), 1.48 (3H, s), 1.04 (3H, t, *J* = 7.0 Hz); ^{13}C NMR ($CDCl_3$) δ: 177.5, 169.6, 140.7, 130.7, 128.9, 123.3, 122.8, 110.1, 62.0, 55.5, 20.1, 13.9; HRMS (ESI): *m/z* calcd. for $C_{12}H_{14}NO_3$: 220.0974 $[M+H]^+$; found: 220.0968.



Ethyl 1-hydroxy-3-methyl-oxindole-3-carboxylate (1b)[4]

See general procedure for tandem reduction-lactamization reaction of di-alkyl 2-methyl-2-(2-nitrophenyl)malonate in experimental section. Yield: 45% as a pale yellow solid; ^{1}H NMR (DMSO-d_6) δ: 11.07 (1H, s), 7.34 (1H, t, *J* = 7.9 Hz), 7.26 (1H, d, *J* = 7.9 Hz), 7.06 (1H, t, *J* = 7.9 Hz), 6.98 (1H, d, *J* = 7.9 Hz), 4.08 (1H, dq, *J* = 12.8, 7.0 Hz), 4.04 (1H, dq, *J* = 12.8, 7.0 Hz), 1.52 (3H, s), 1.05 (3H, t, *J* = 7.0 Hz); ^{13}C NMR ($CDCl_3$) δ: 171.6, 168.8, 141.0, 129.3, 126.5, 123.9, 122.7, 109.0, 62.2, 54.0, 19.7, 13.8; HRMS (ESI): *m/z* calcd. for $C_{12}H_{14}NO_4$: 236.0923 $[M+H]^+$; found: 236.0918.

2. References

[1] B. Nammalwar, R. A. Bunce, and J. T. Hiett, *Org. Prep. Proced. Int.*, 2015, **47**, 338.

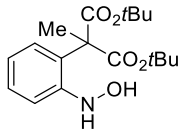
[2] X.-P. Yin, X.-P. Zeng, Y.-L. Liu, F.-M. Liao, J.-S. Yu, F. Zhou, and J. Zhou, *Angew. Chem. Int. Ed.*, 2014, **53**, 13740.

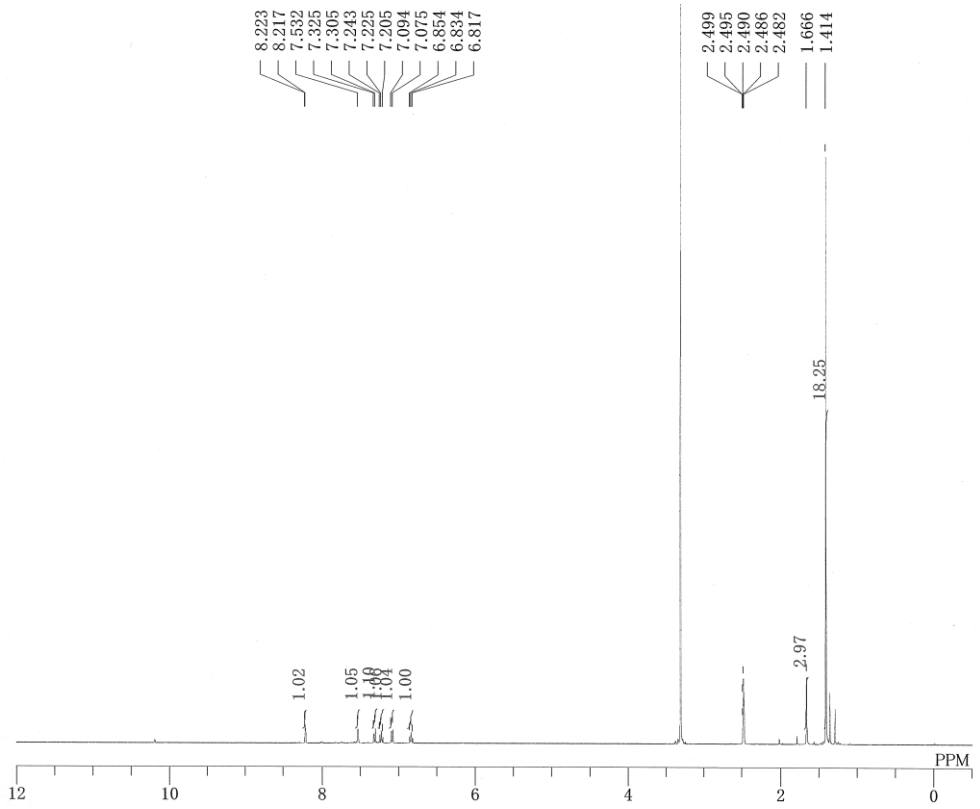
[3] E. E. Maciver, S. Thompson, M. D. Smith, *Angew. Chem. Int. Ed.*, 2009 **48**, 9979.

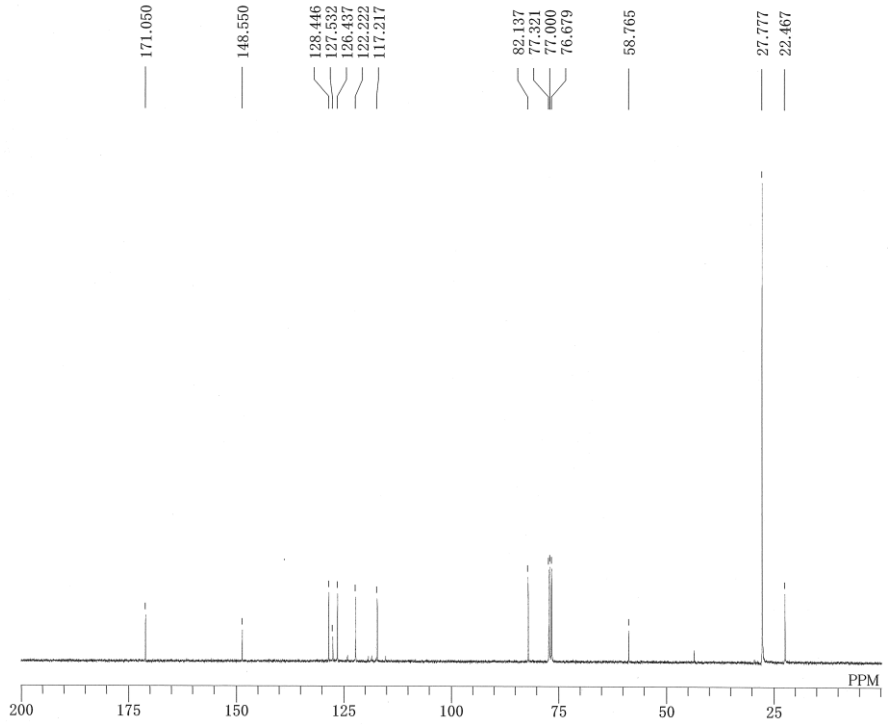
[4] R. M. Acheson, R. J. Prince, and G. Procter, *J. Chem. Soc.*, *Perkin Trans. 1*, 1979, 595.

3. ^{1}H NMR and ^{13}C NMR spectra of the compounds

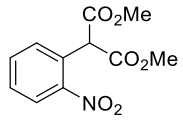
Di-*t*-butyl 2-(2-(hydroxyamino)phenyl)-2-methylmalonate (4)

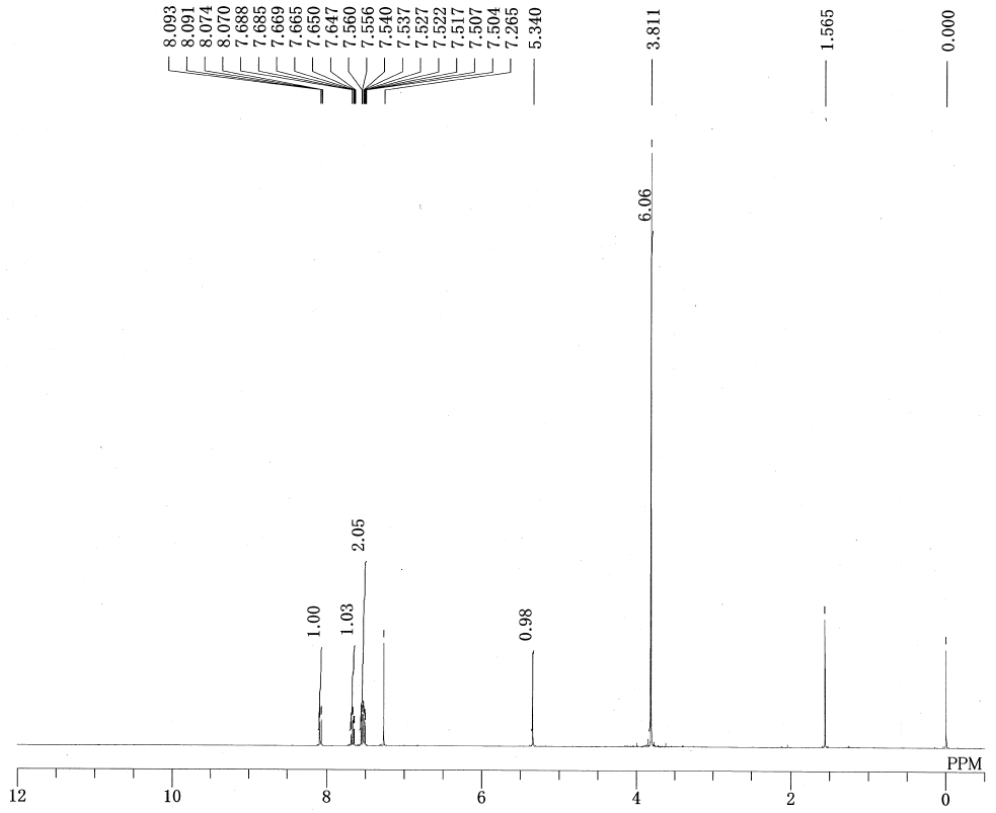


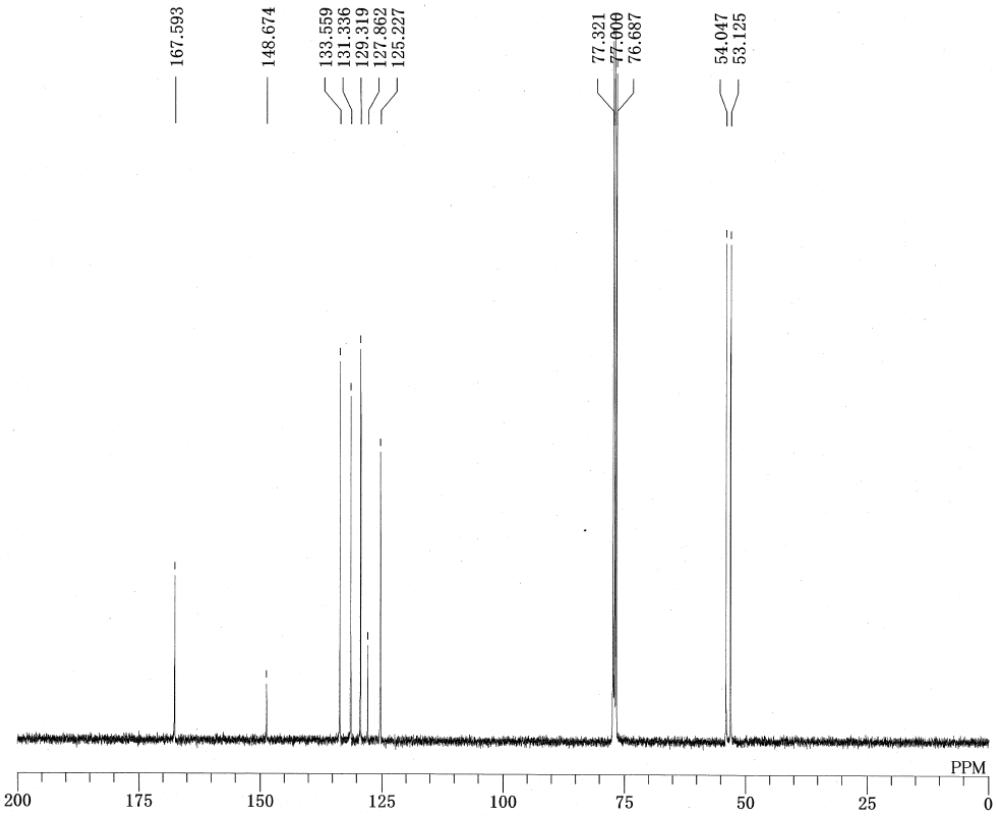




Dimethyl 2-(2-nitrophenyl)malonate







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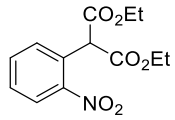
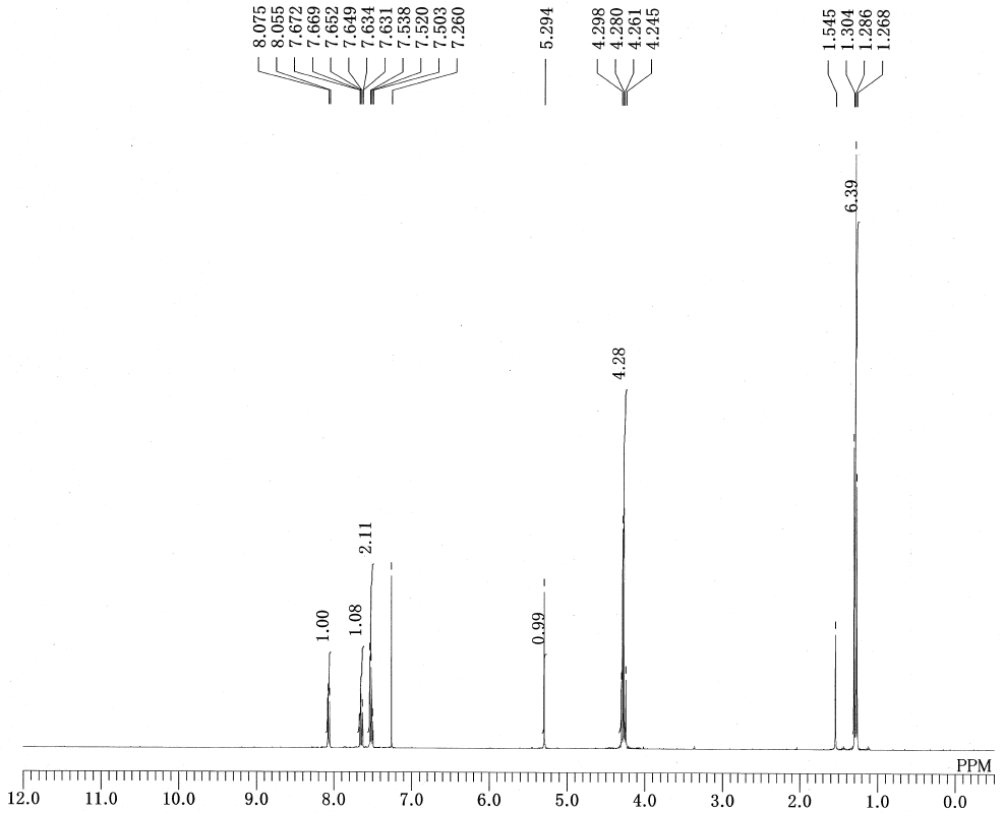
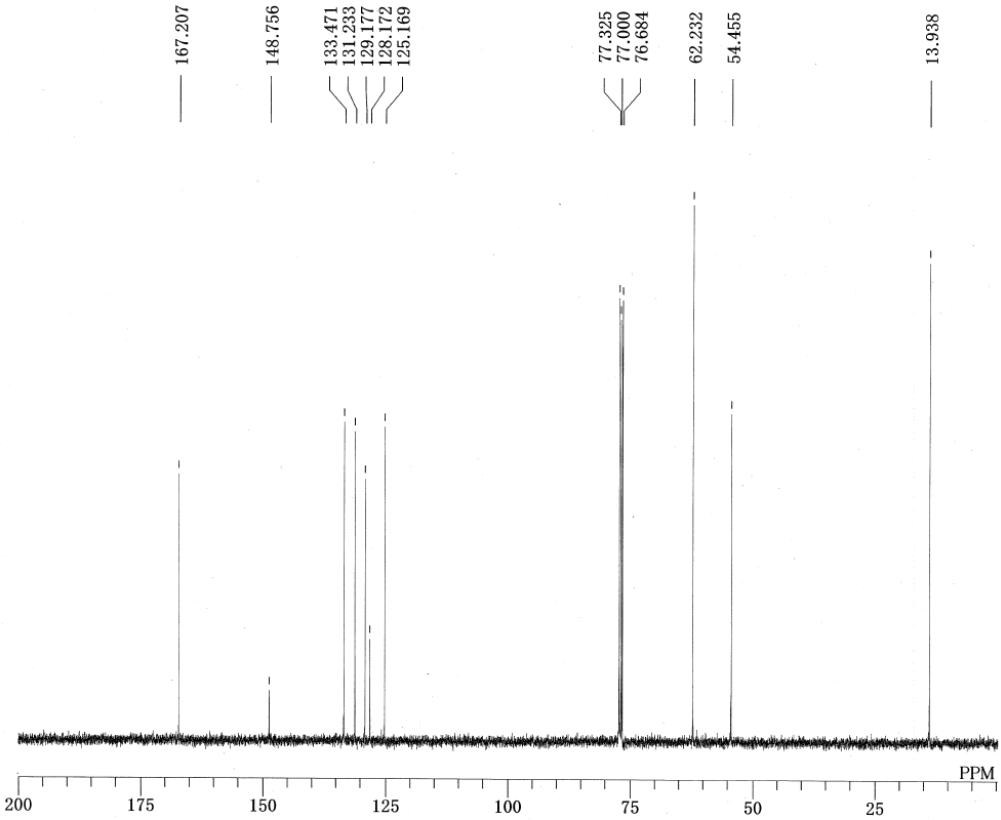
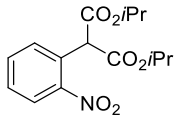
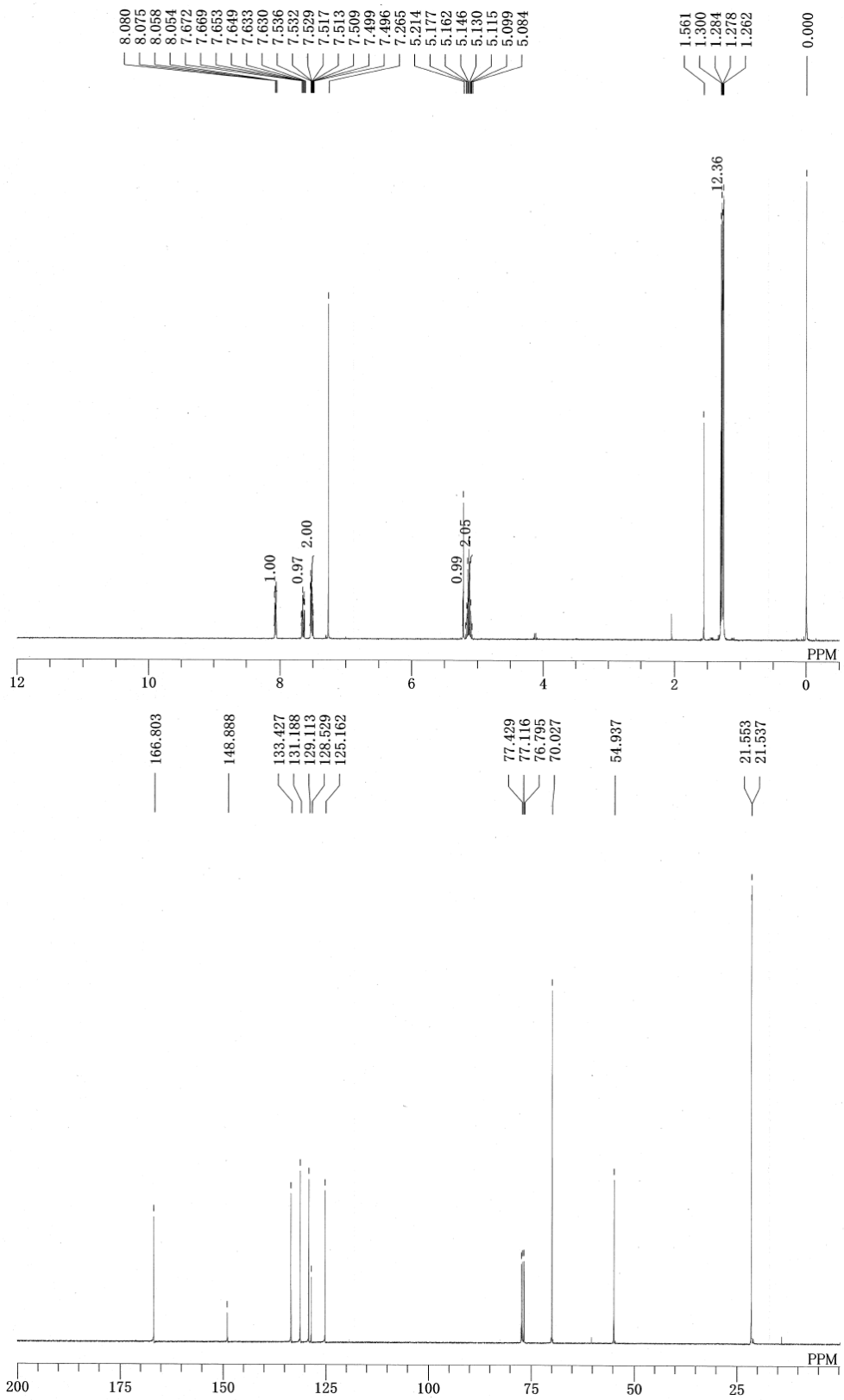




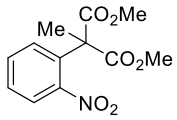


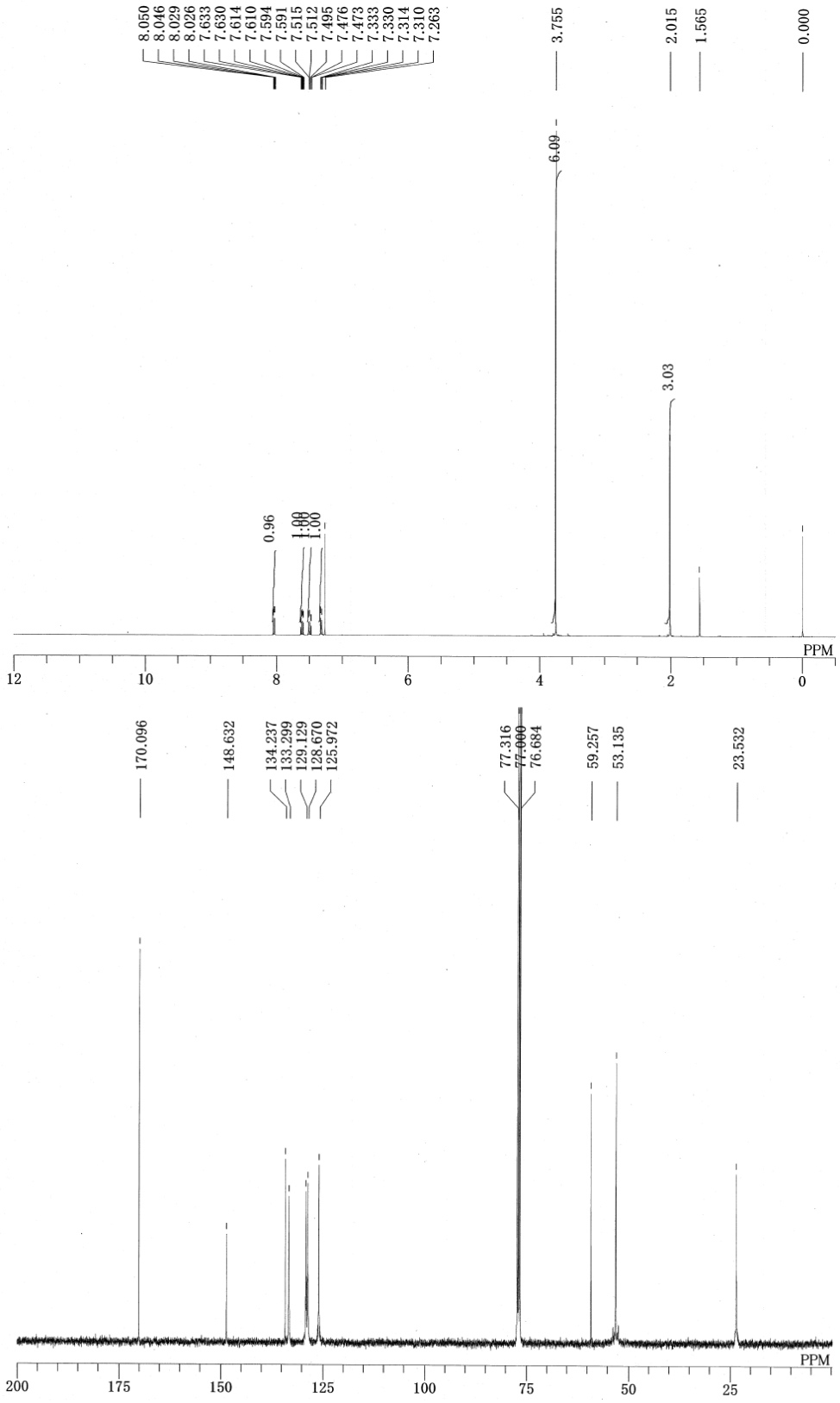
Diisopropyl 2-(2-nitrophenyl)malonate



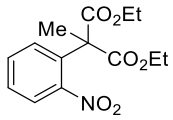


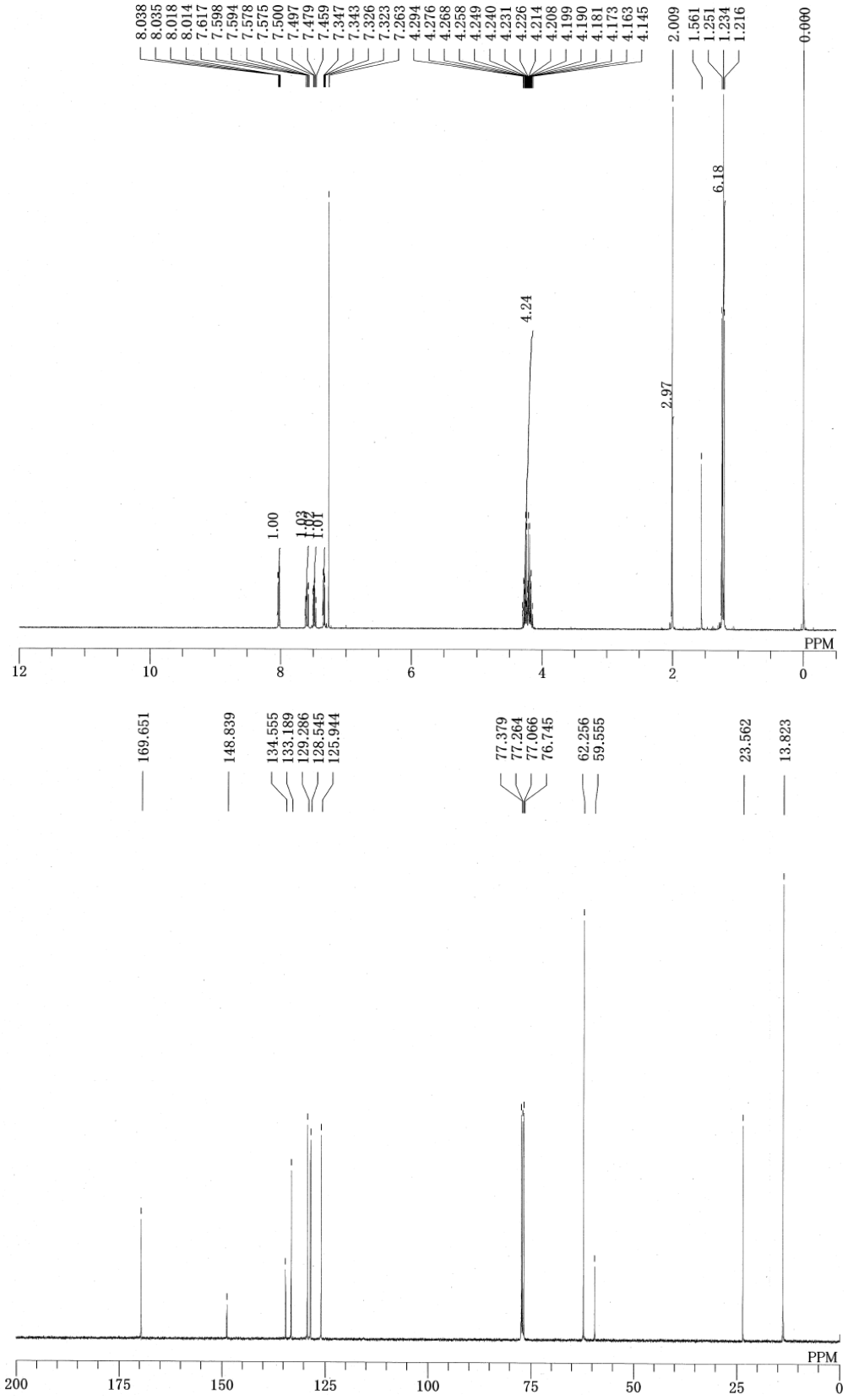
Dimethyl 2-methyl-2-(2-nitrophenyl)malonate (3a)



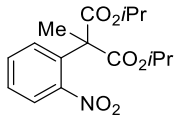


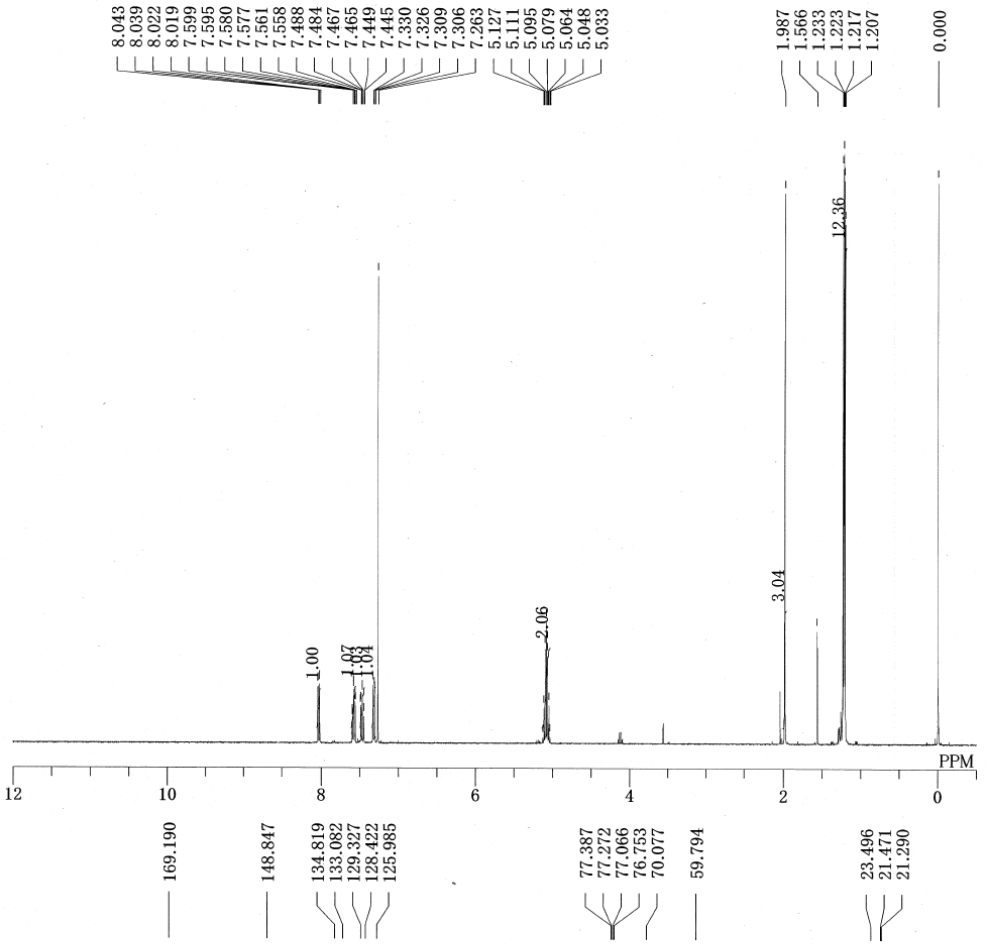
Diethyl 2-methyl-2-(2-nitrophenyl)malonate (3b)

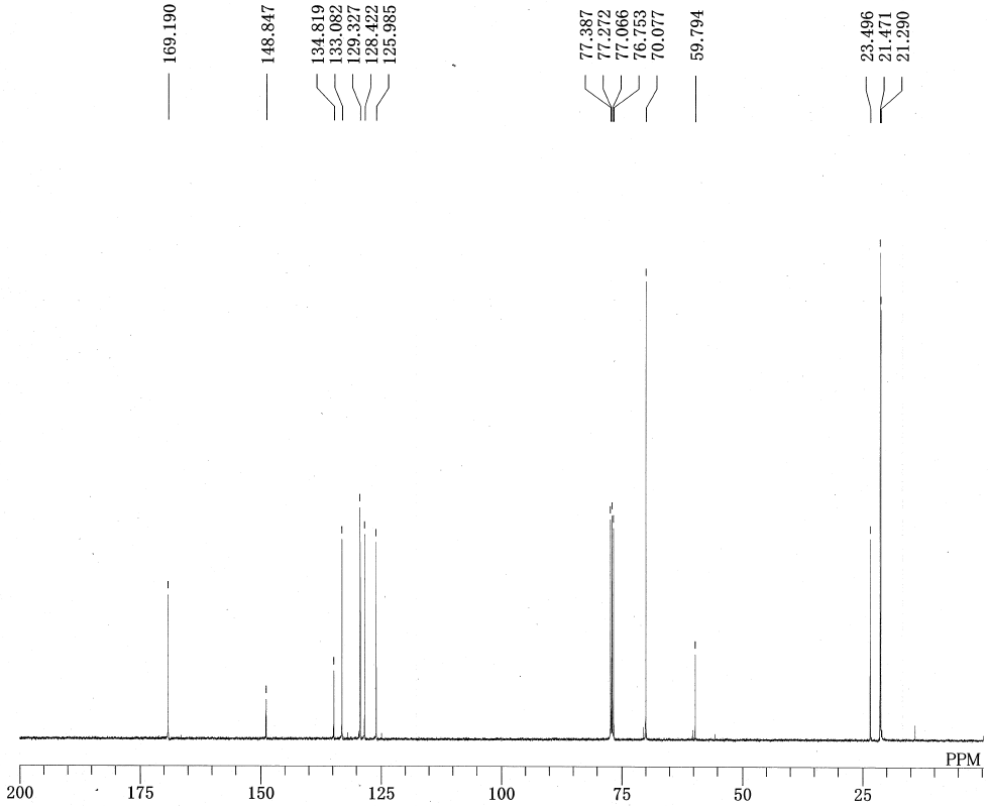




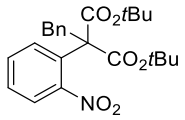
Diisopropyl 2-methyl-2-(2-nitrophenyl)malonate (3c)

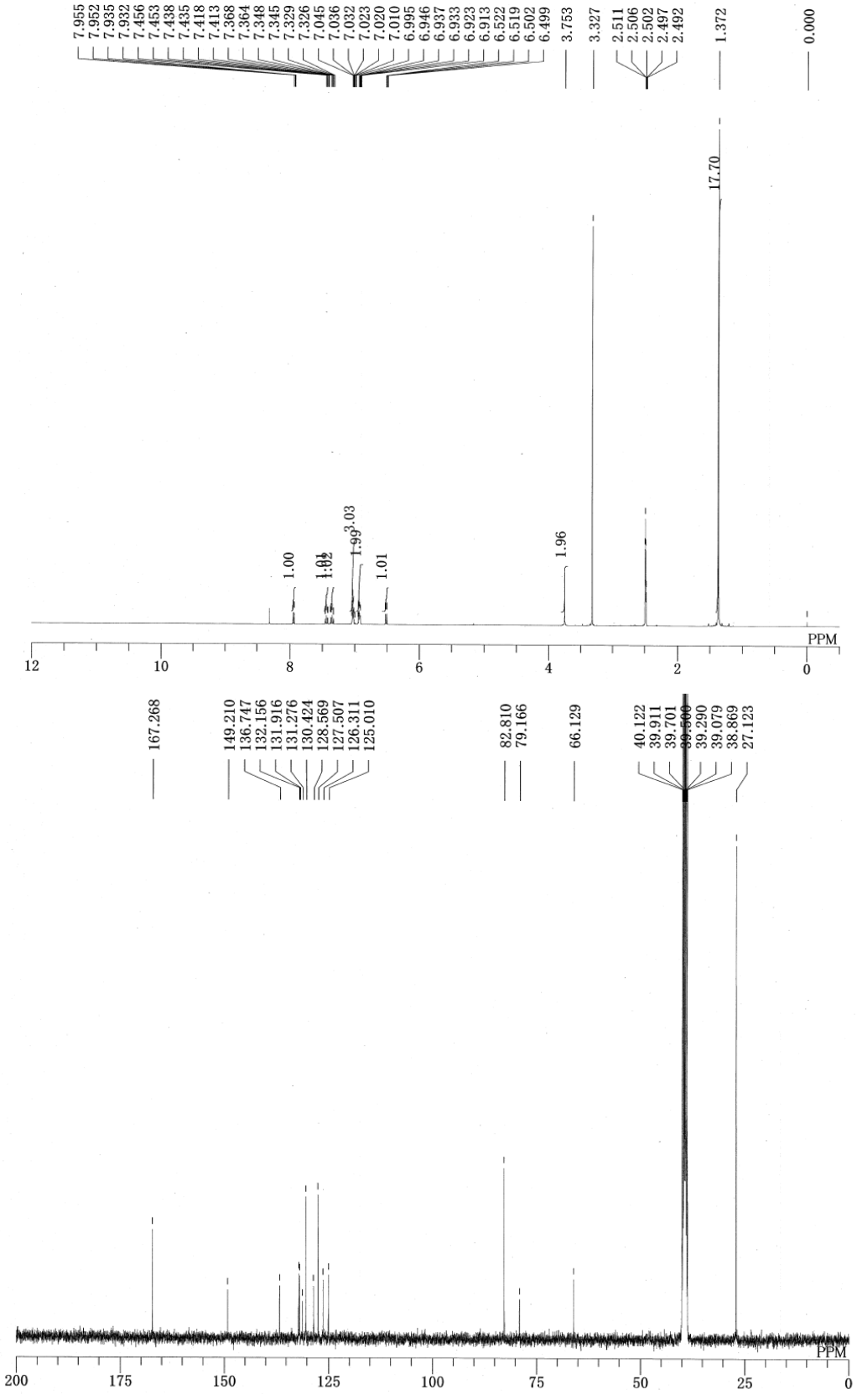




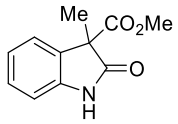


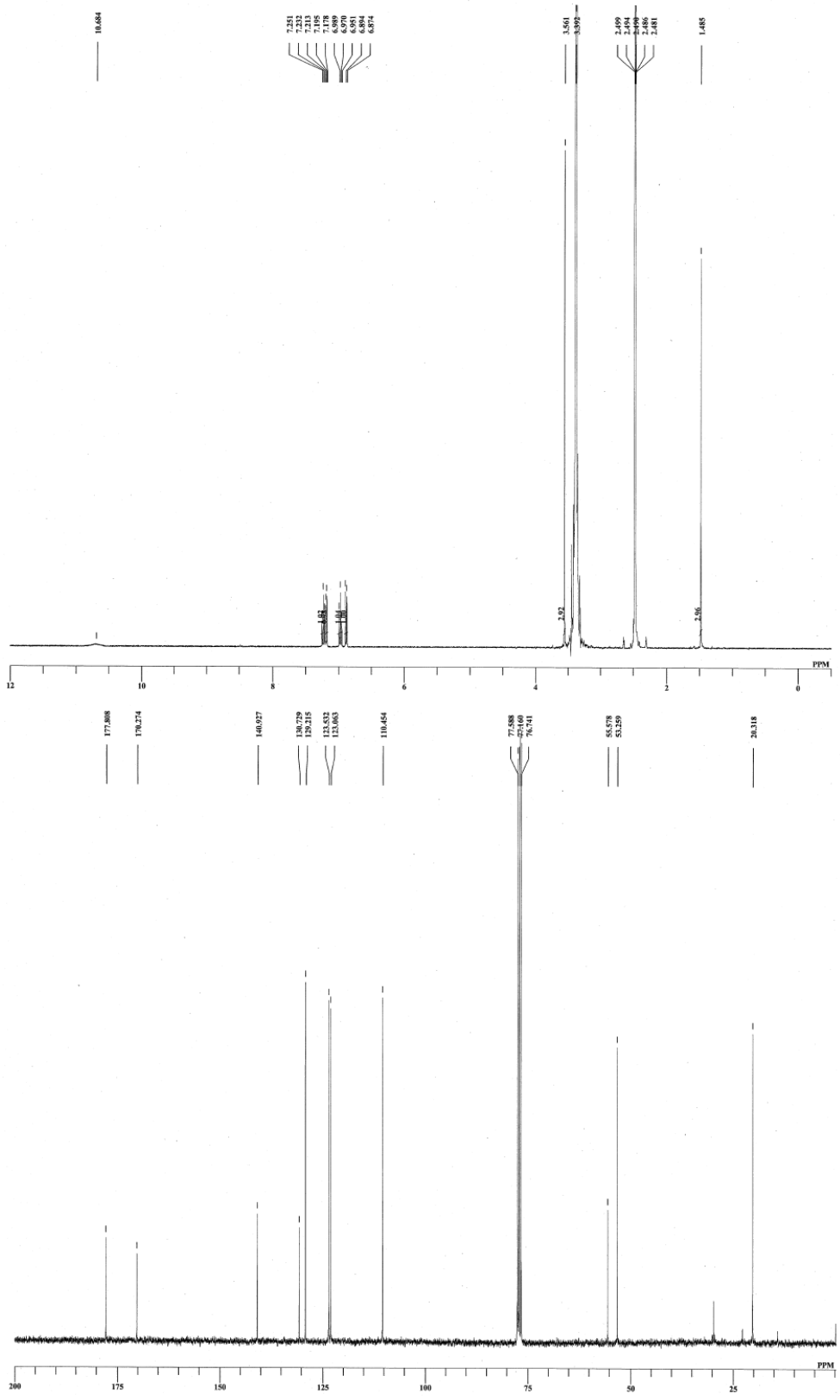
Di-*t*-butyl 2-benzyl-2-(2-nitrophenyl)malonate (3e)



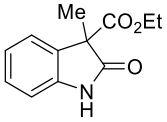


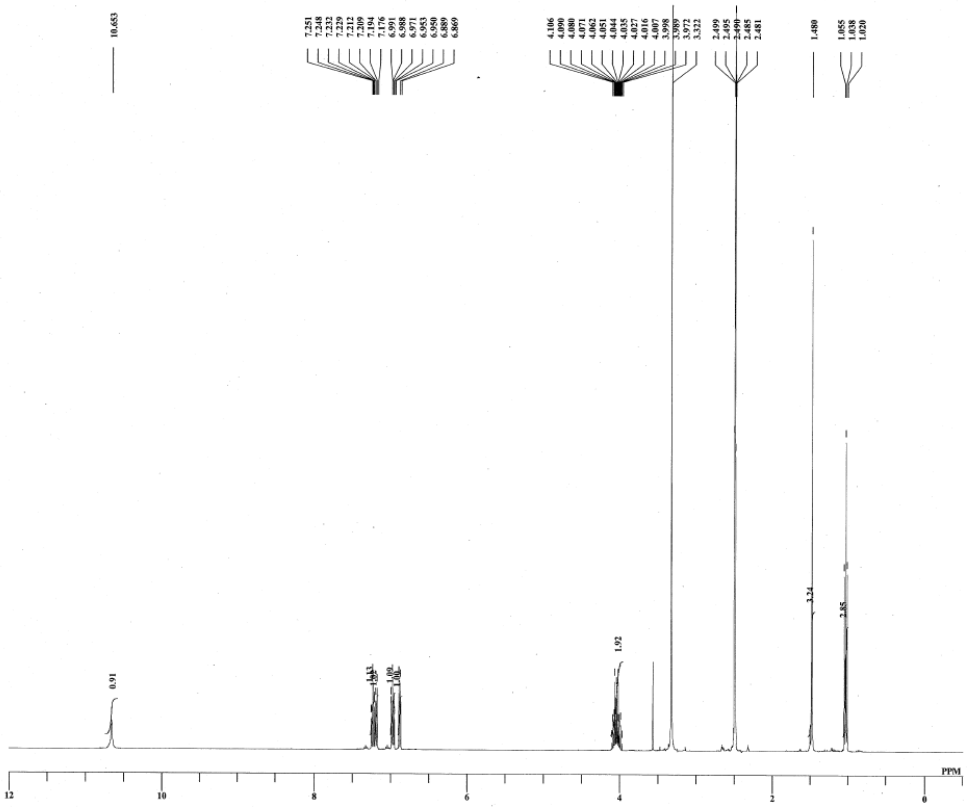
Methyl 3-methyl-oxindole-3-carboxylate (2a)

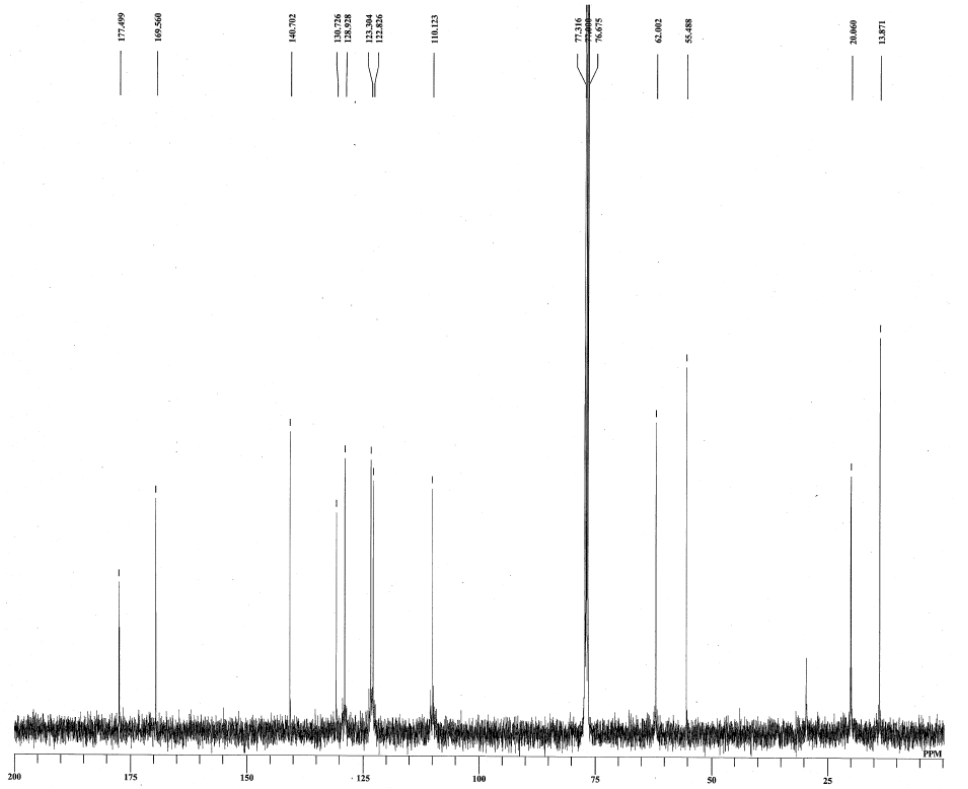




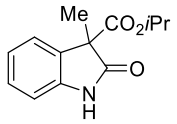
Ethyl 3-methyl-oxindole-3-carboxylate (2b)

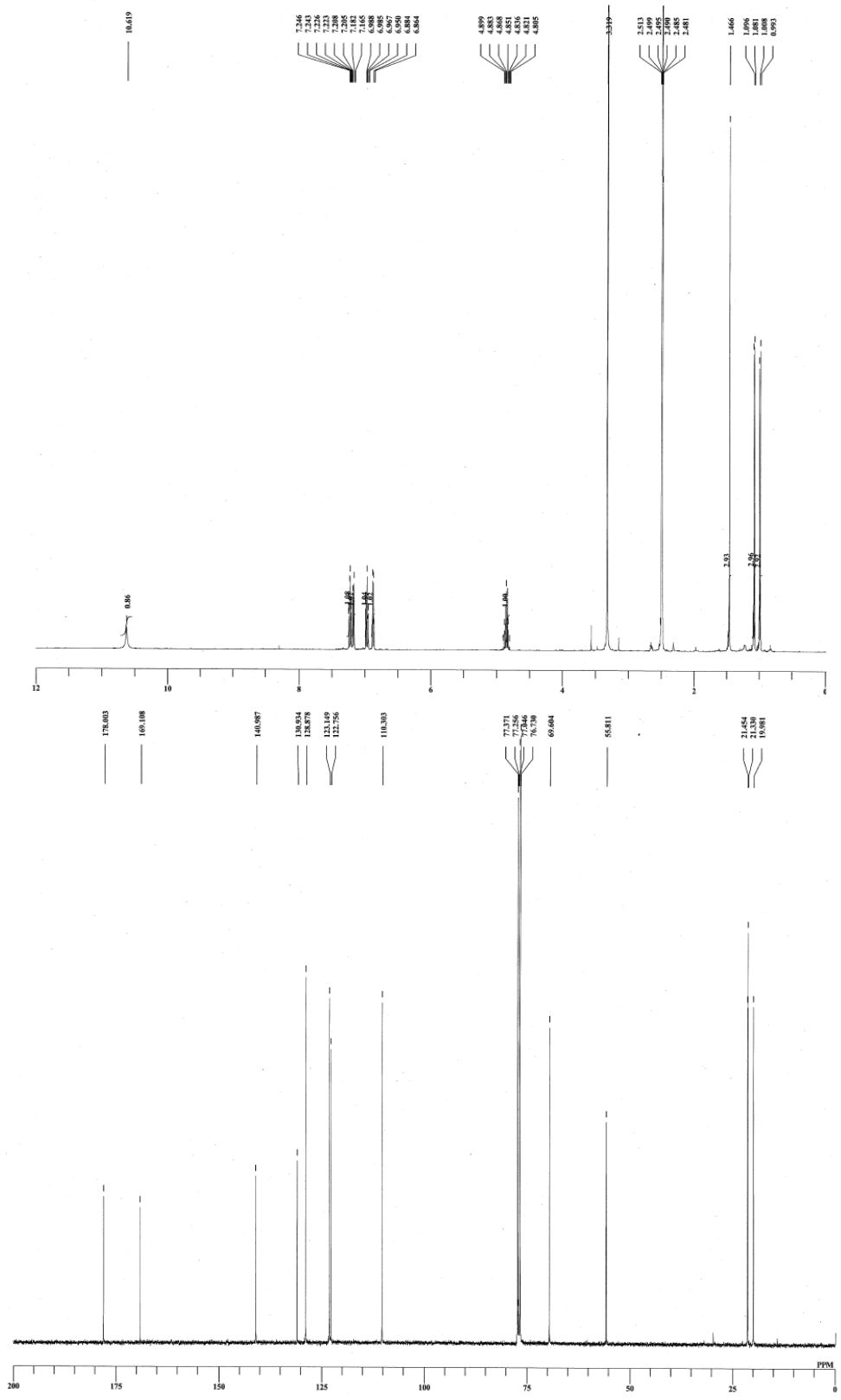




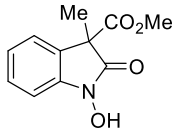


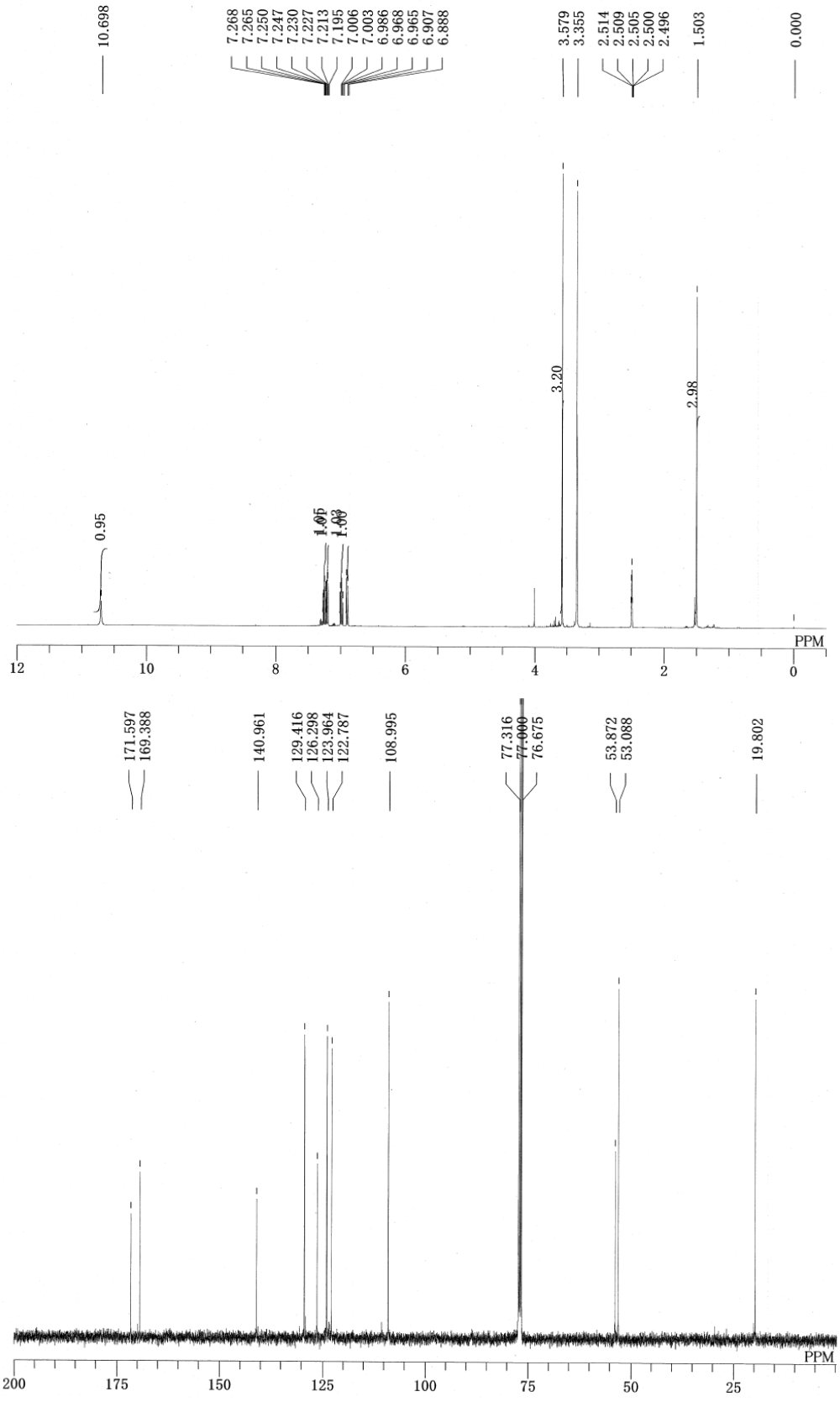
Isopropyl 3-methyl-oxindole-3-carboxylate (2c)



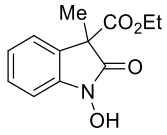


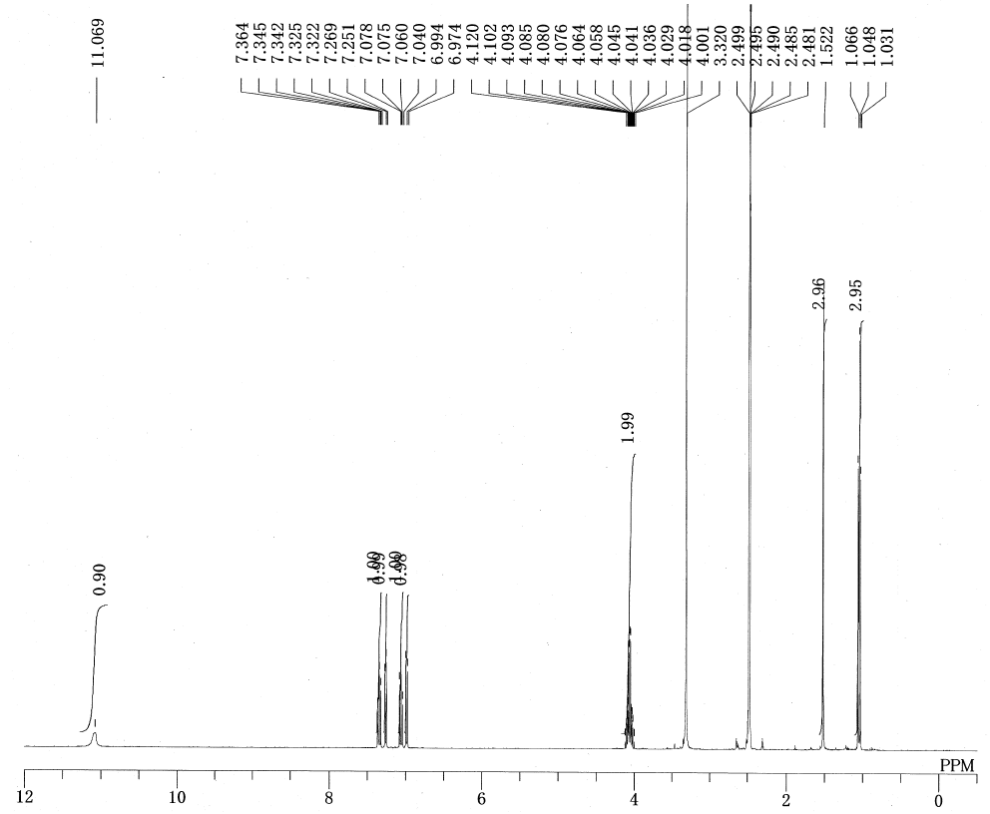
Methyl 1-hydroxy-3-methyl-oxindole-3-carboxylate (1a)

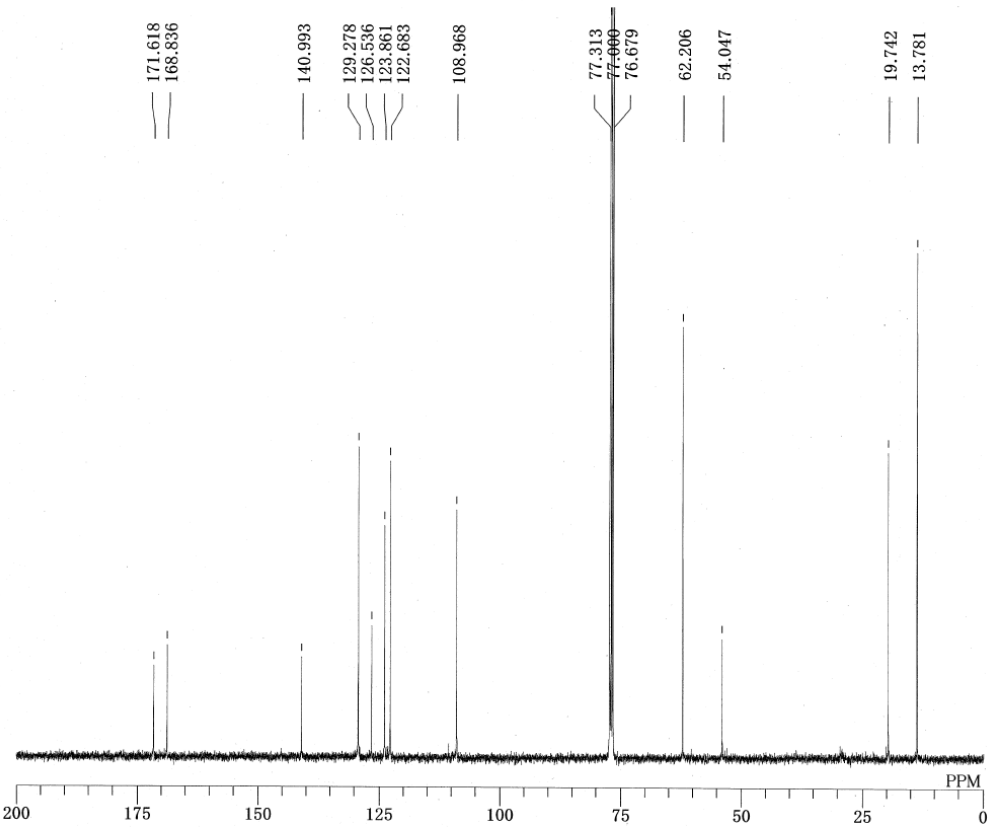




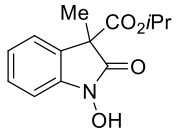
Ethyl 1-hydroxy-3-methyl-oxindole-3-carboxylate (1b)

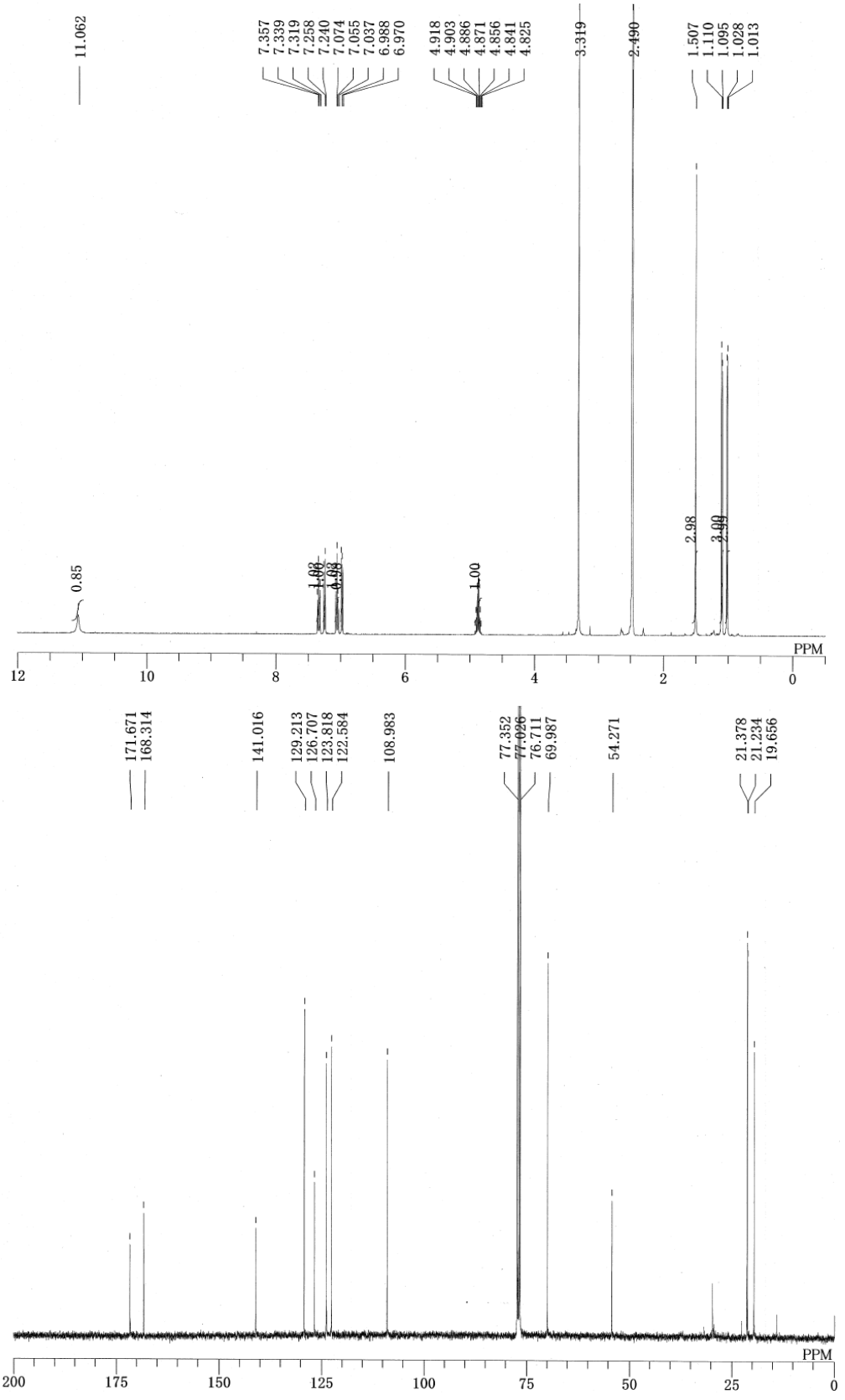




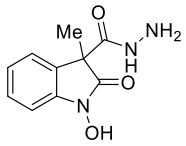


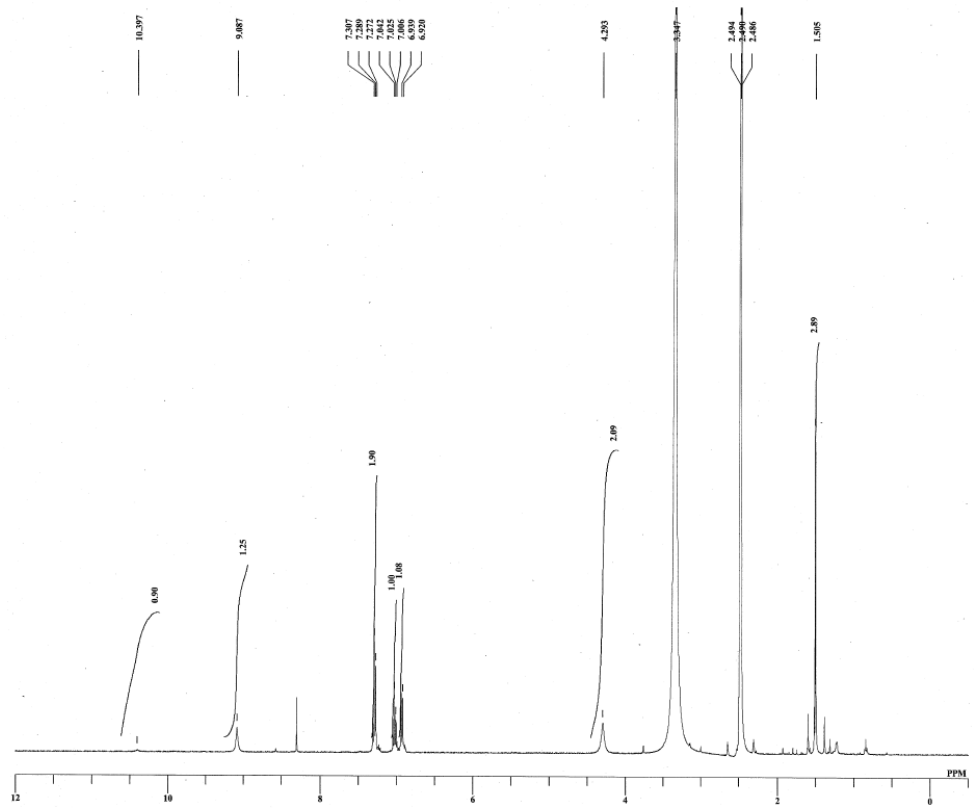
Isopropyl 1-hydroxy-3-methyl-oxindole-3-carboxylate (1c)

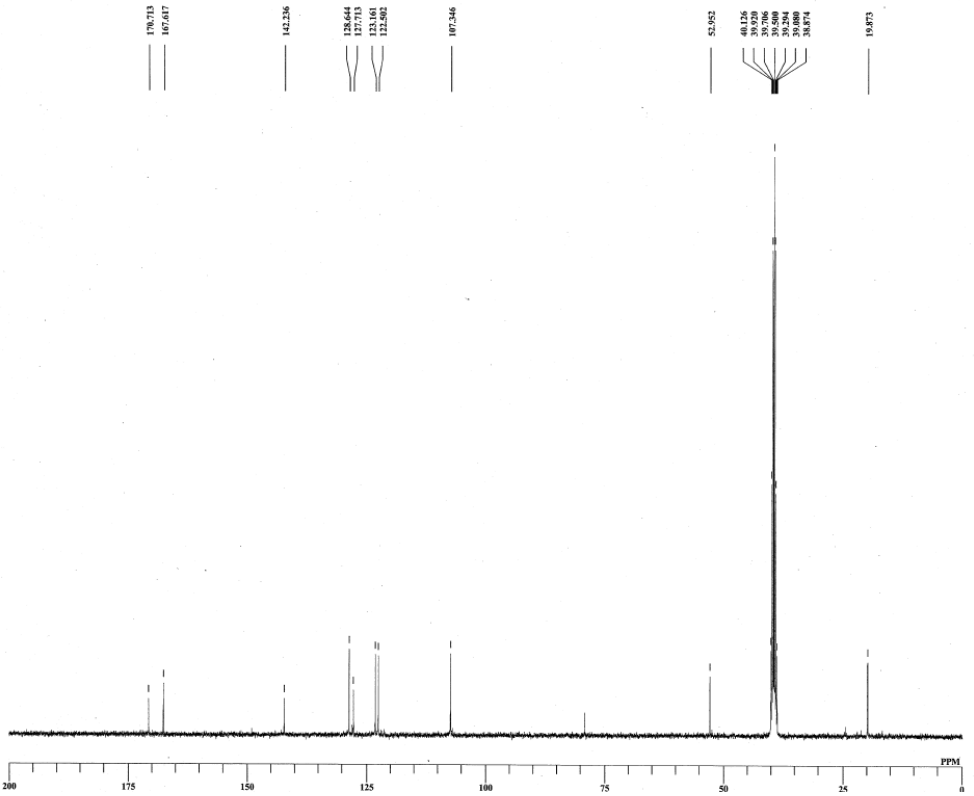




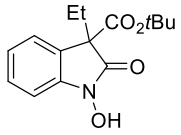
1-Hydroxy-3-methyl-oxindole-3-carbohydrazide (6)

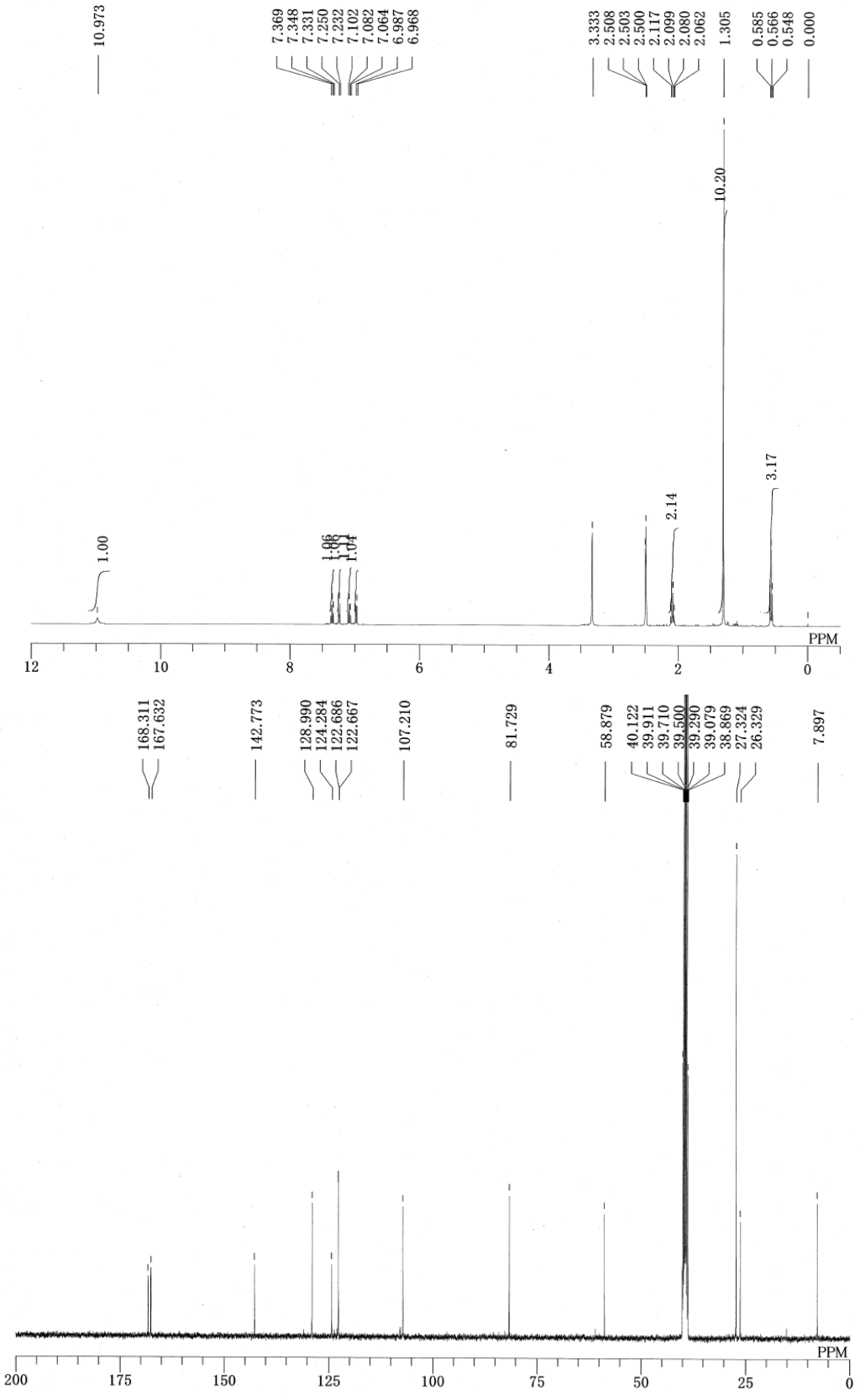




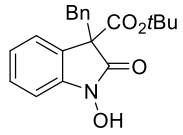


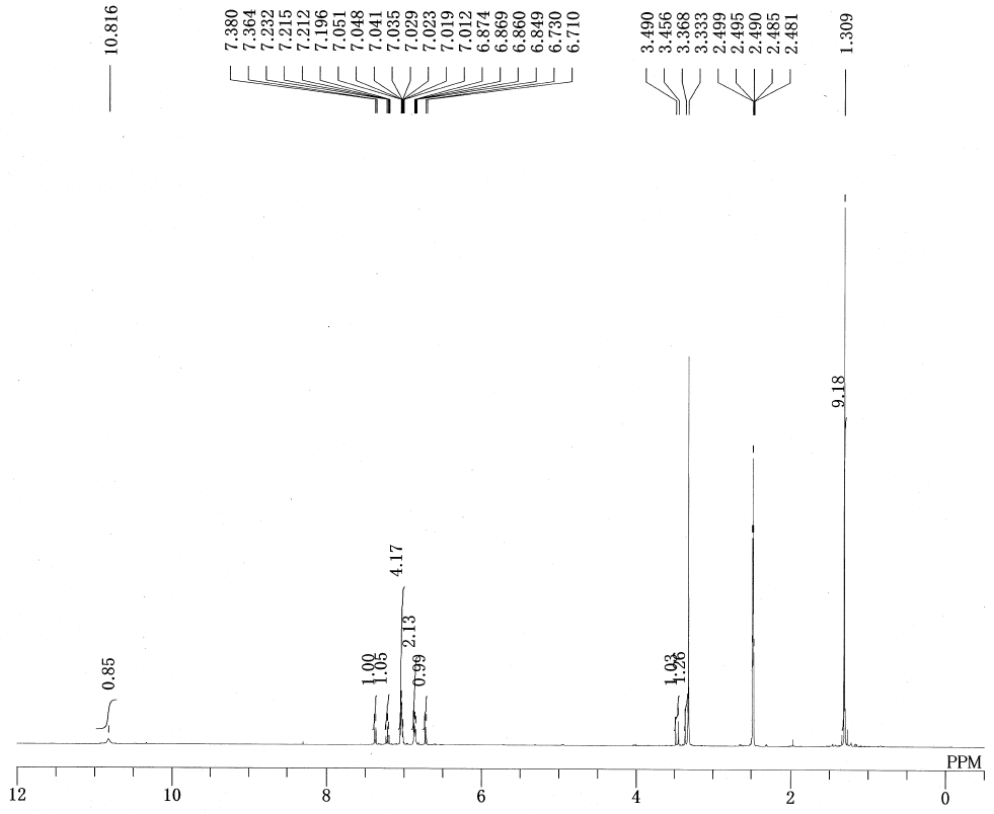
t-Butyl 3-ethyl-1-hydroxy-oxindole-3-carboxylate (1d)

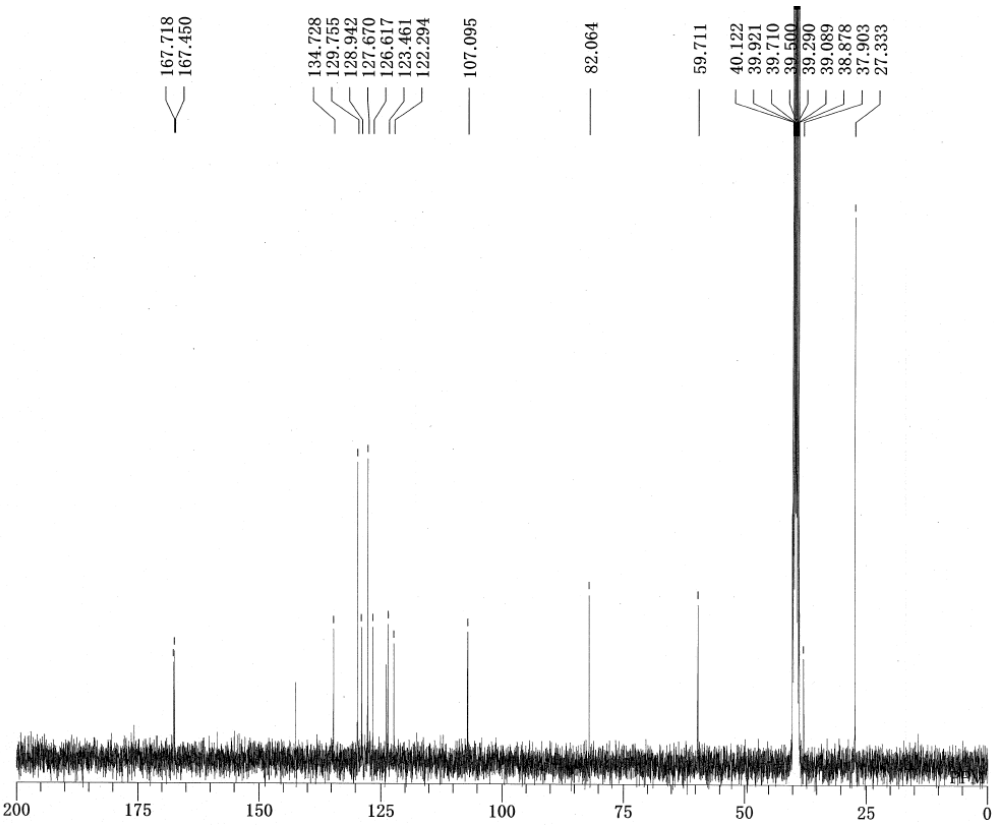




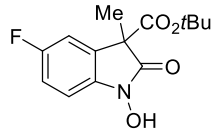
t-Butyl 3-benzyl-1-hydroxy-oxindole-3-carboxylate (1e)

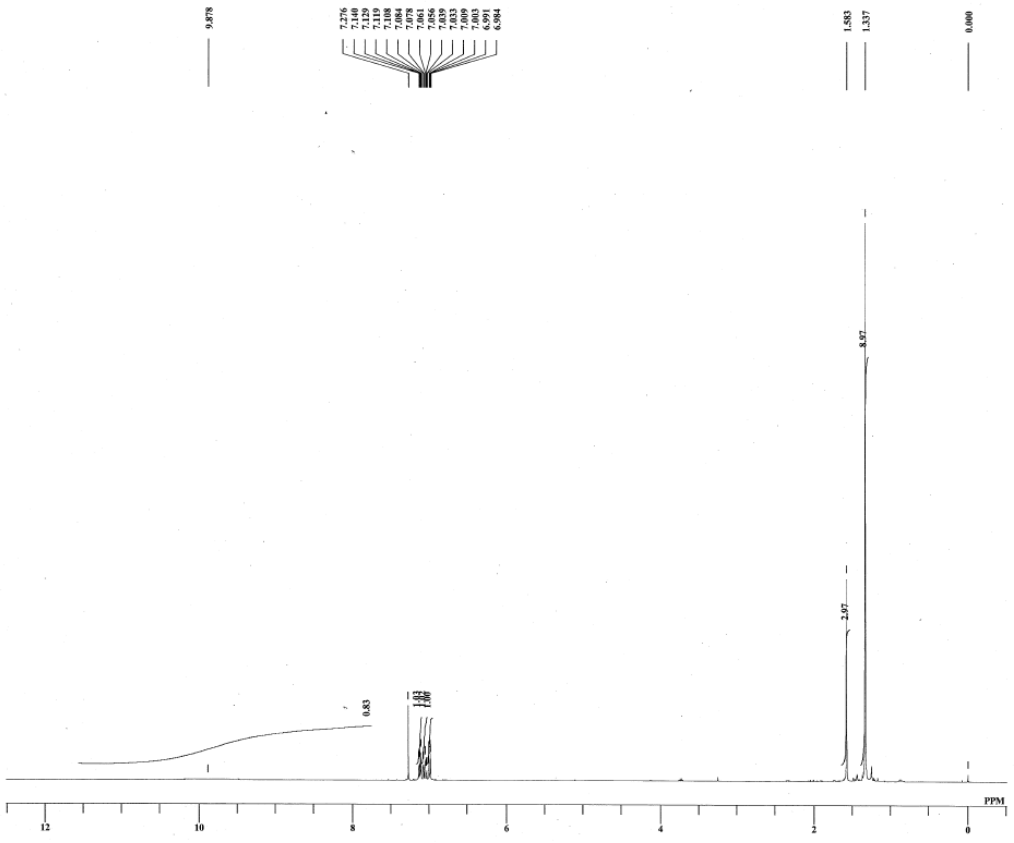


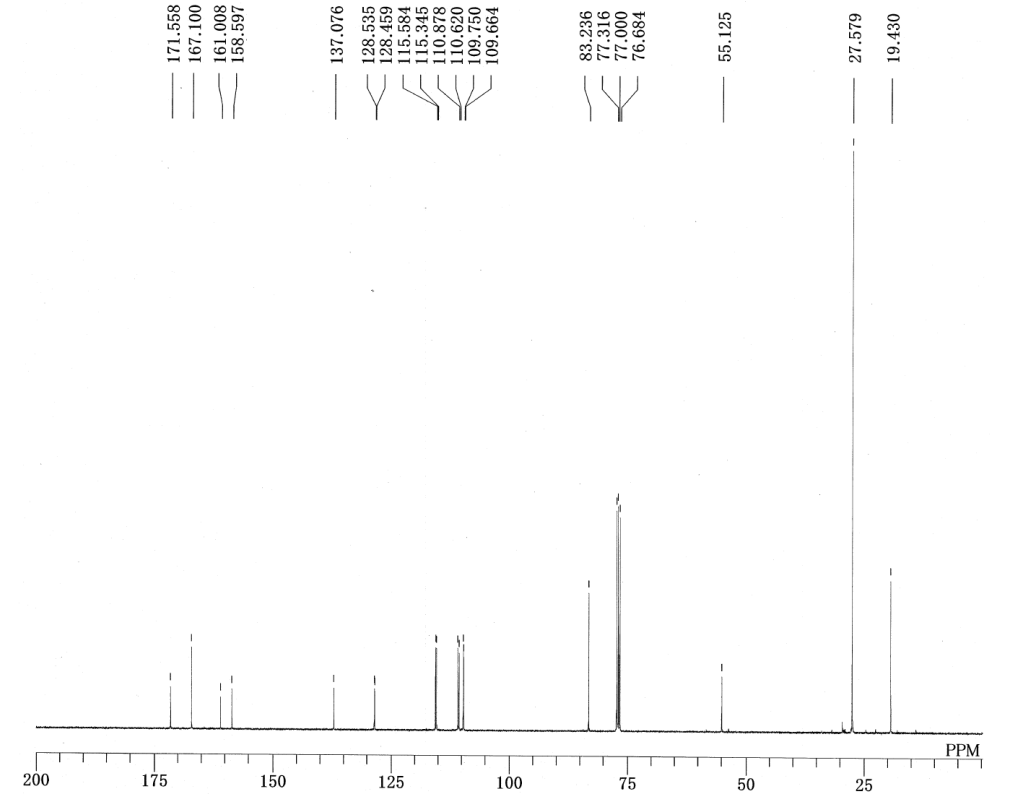




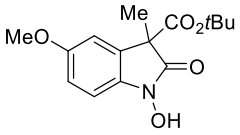
t-Butyl 5-fluoro-1-hydroxy-3-methyl-oxindole-3-carboxylate (1f)

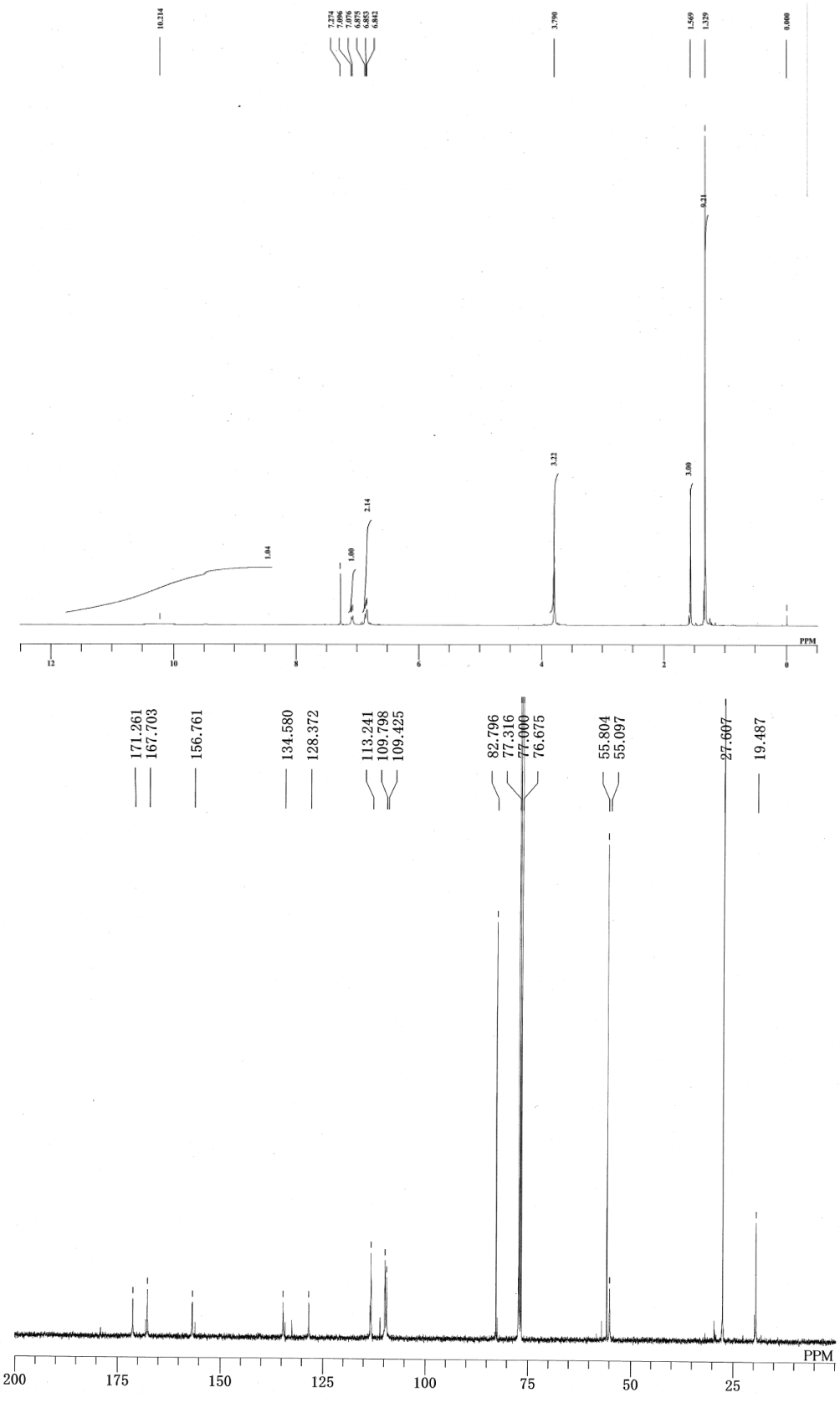




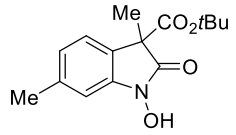


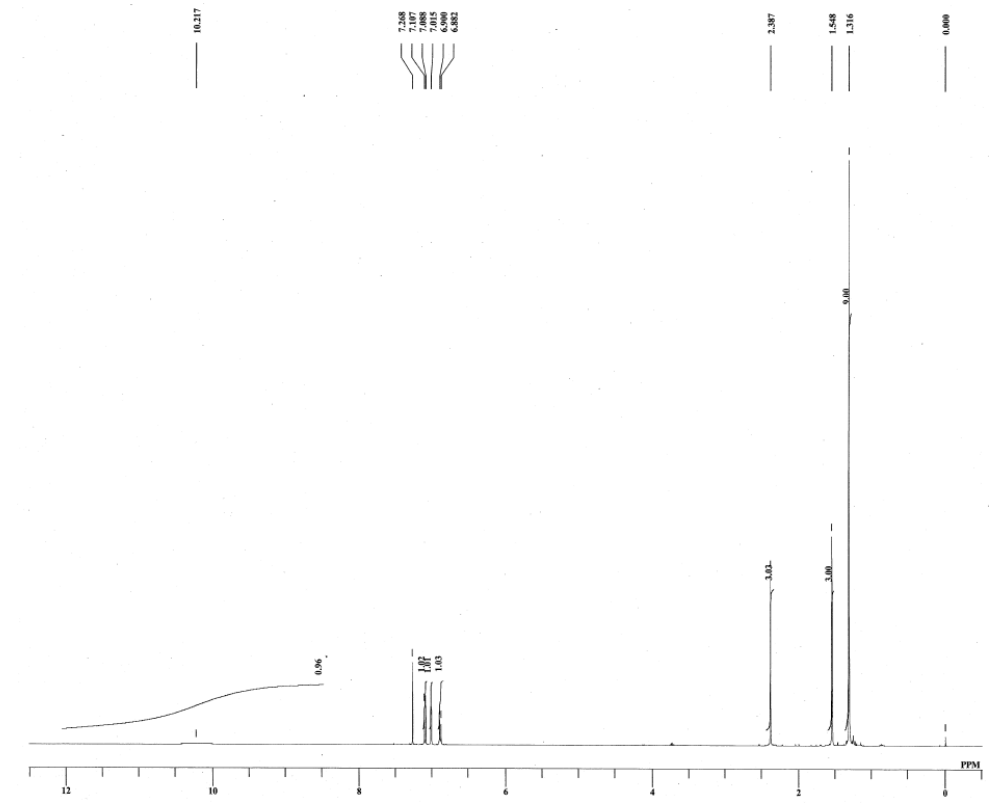
t-Butyl 1-hydroxy-5-methoxy-3-methyl-oxindole-3-carboxylate (1g)

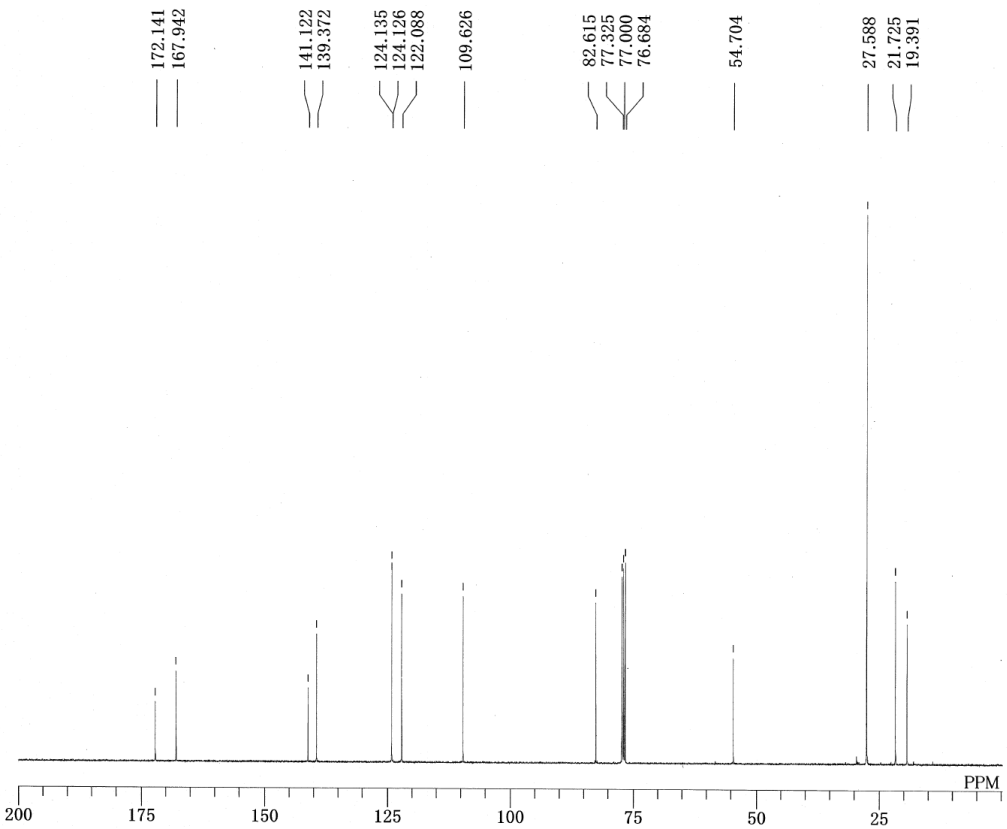




t-Butyl 1-hydroxy-3,6-dimethyl-oxindole-3-carboxylate (1h)







t-Butyl 1-hydroxy-3-methyl-6-(trifluoromethyl)oxindole-3-carboxylate (1i)