Supporting Information

Discovery of 7-azanorbornane-based dual agonists for the delta and kappa opioid receptors through an *in situ* screening protocol

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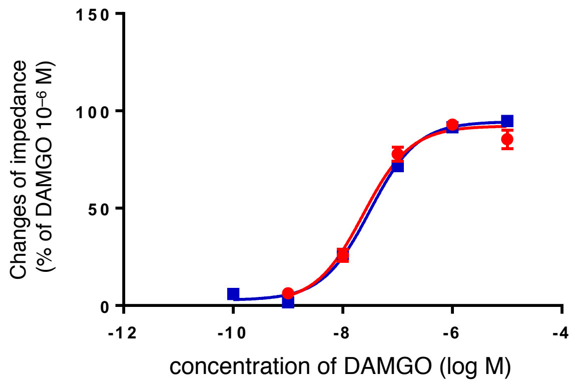


Figure S1. Concentration-dependent effect of DAMGO on the MOR-expressing cells in the presence (red line) and absence (blue line) of the click catalysts (copper sulfate: 1 mol%, sodium ascorbate: 5 mol%).

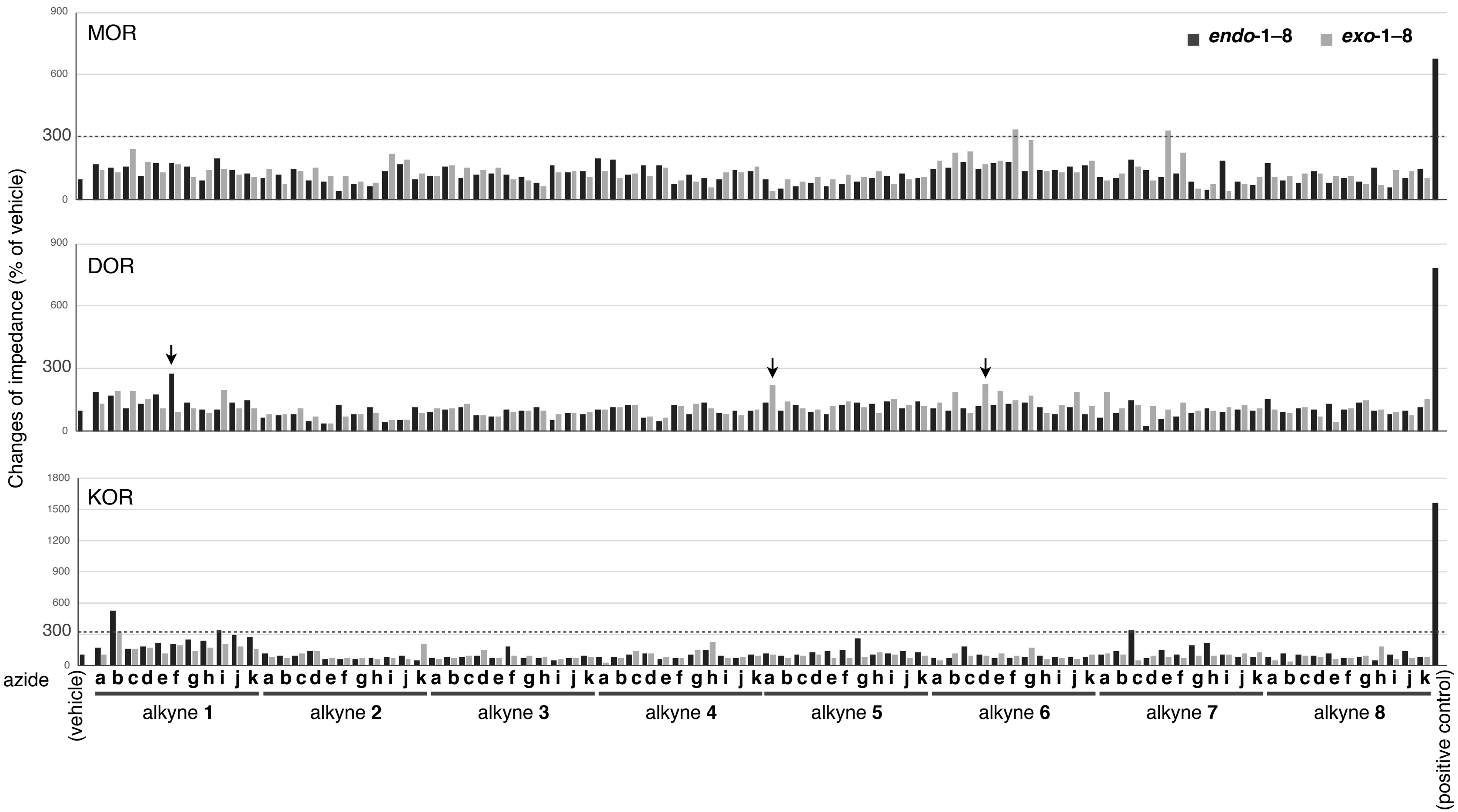


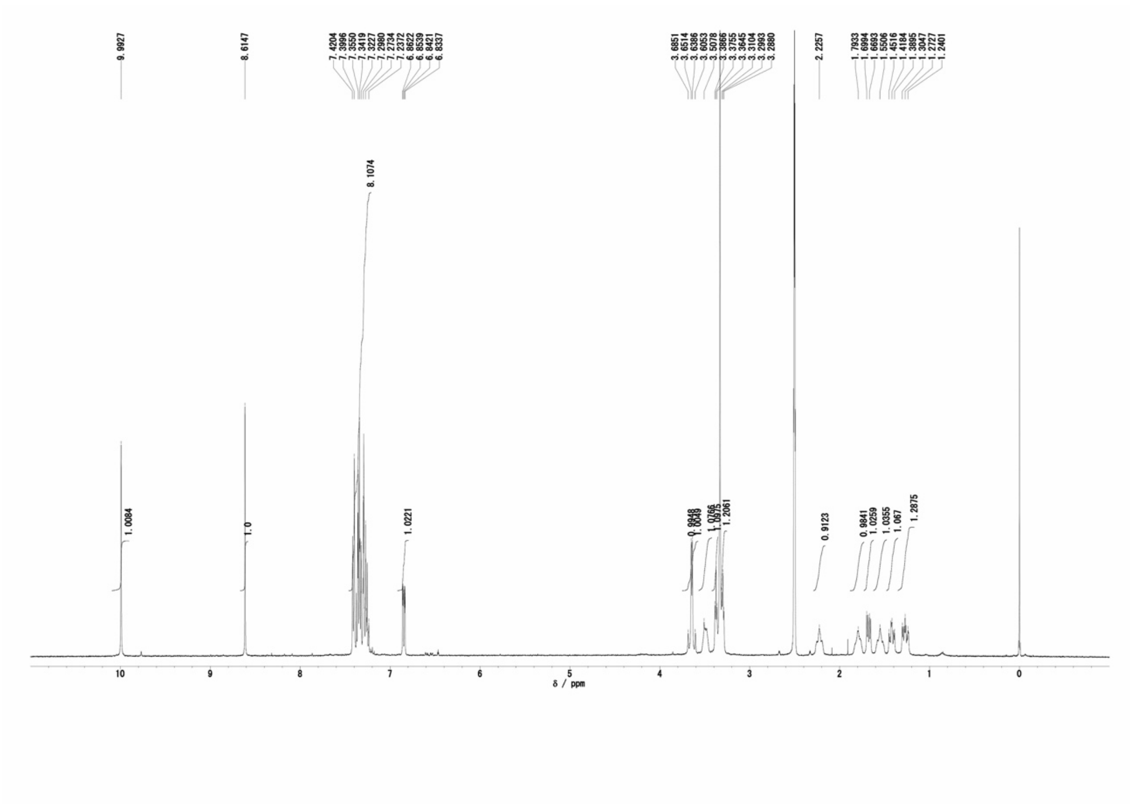
Figure S2. The results of the first screening assays (n = 2 × 1). The concentrations of the triazoles should be 10 μM, assuming that the reaction yield was 100%. The positive controls are DAMGO (for MOR), SNC80 (for DOR), and (–)-U-50,488H (for KOR), and they were treated at a concentration of 10 μM.

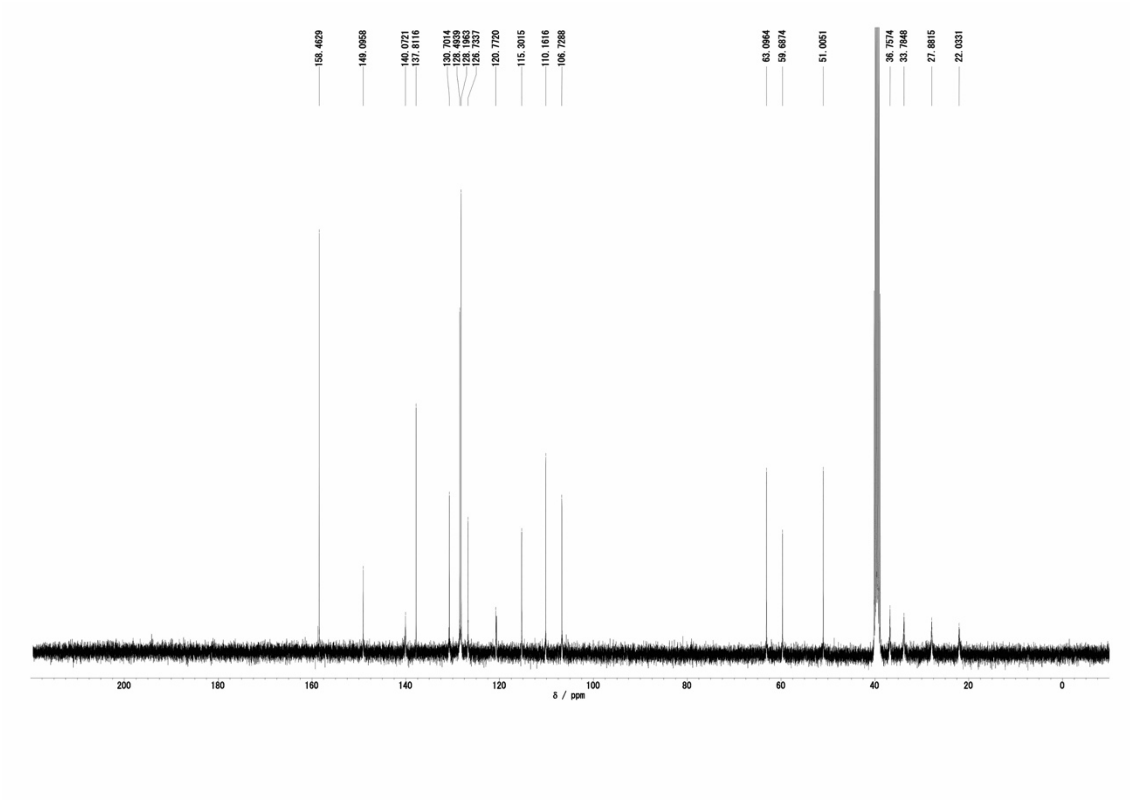
Table S1. The E_{max} and $logEC_{50}$ values of the agonistic activities. N.D. = not determined

	DOR		KOR	
	E_{max} (%)	$logEC_{50}$	E_{max} (%)	$logEC_{50}$
positive control	100	−8.46	100	−8.45
***exo*-7e**	90.9	−5.96	84.7	−5.75
***endo*-1b**	60.1	−5.42	82.9	−5.83
***endo*-1i**	N.D.	N.D.	N.D.	N.D.
***endo*-7c**	71.0	−6.36	79.2	−5.40
***endo*-1**	N.D.	N.D.	72.4	−6.75
***exo*-1**	N.D.	N.D.	N.D.	N.D.
***exo*-5**	N.D.	N.D.	N.D.	N.D.
***endo*-7**	N.D.	N.D.	N.D.	N.D.

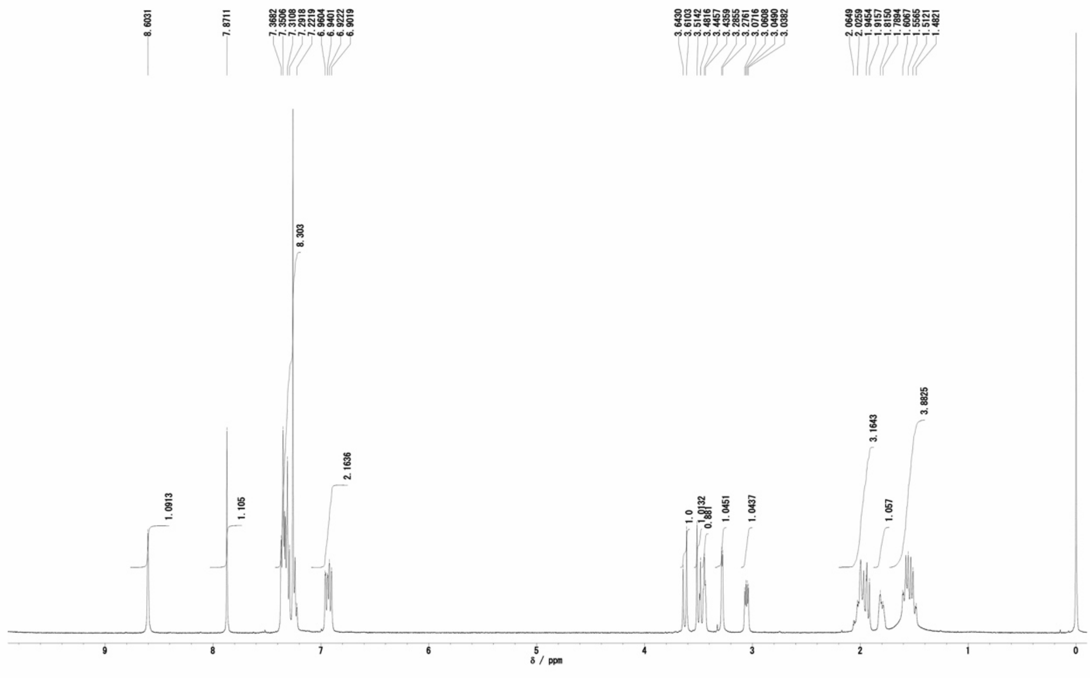
^{1}H and ^{13}C NMR spectra of the triazoles

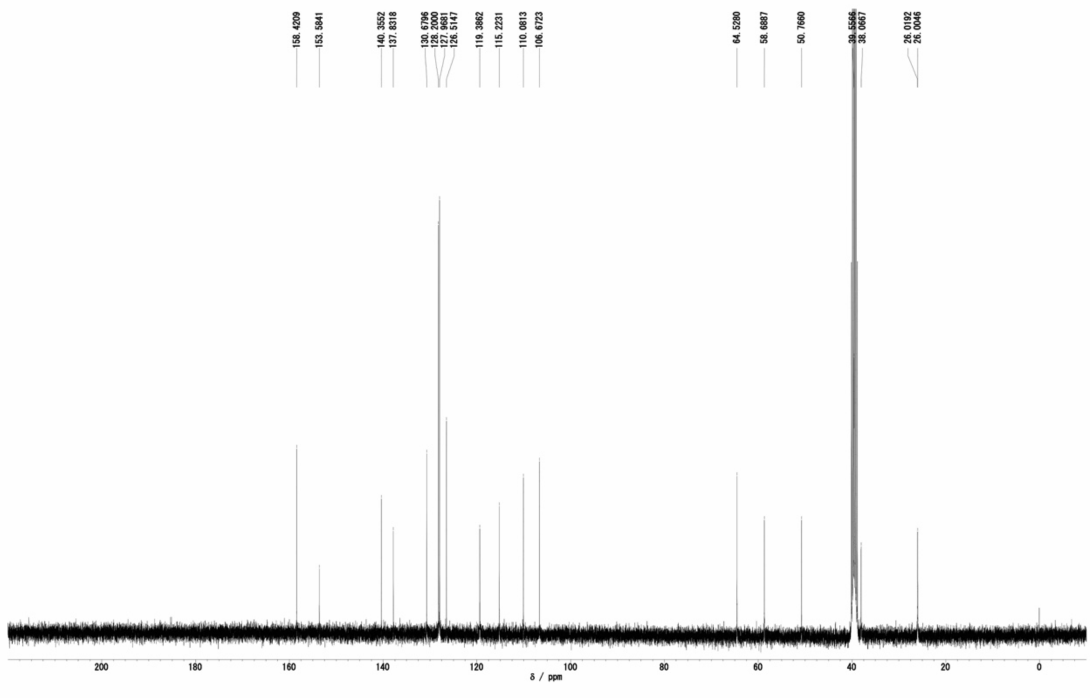
^{1}H (400 MHz, DMSO-d_6) and ^{13}C (100 MHz, CD_3OD) NMR spectra of ***endo*-1b**



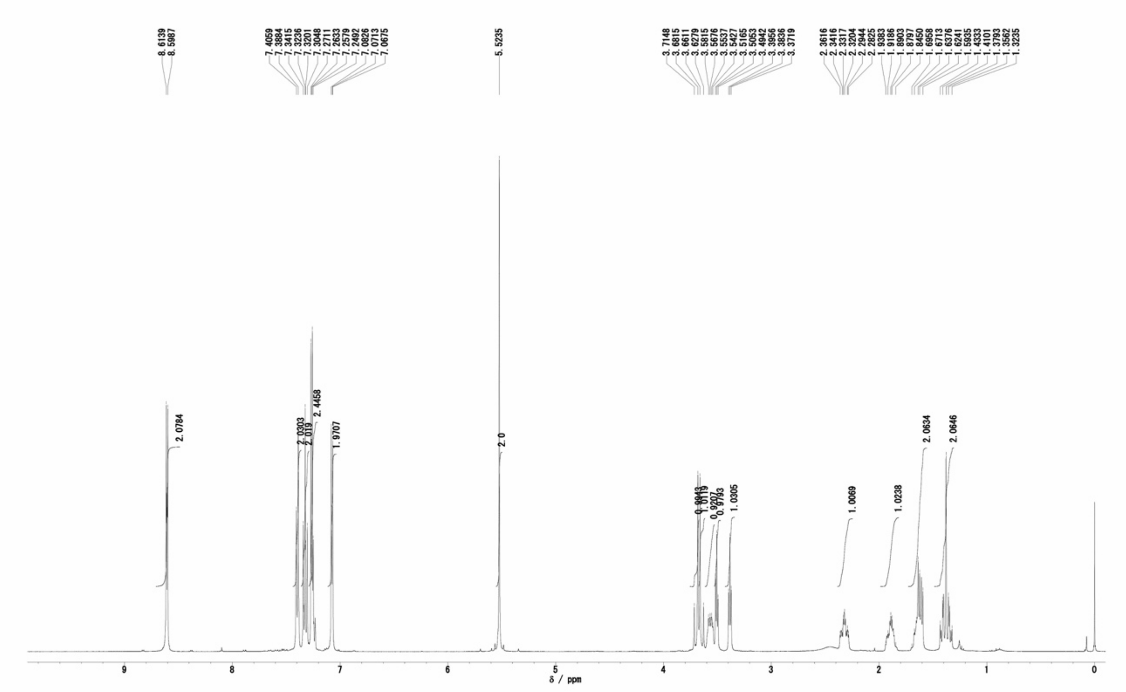


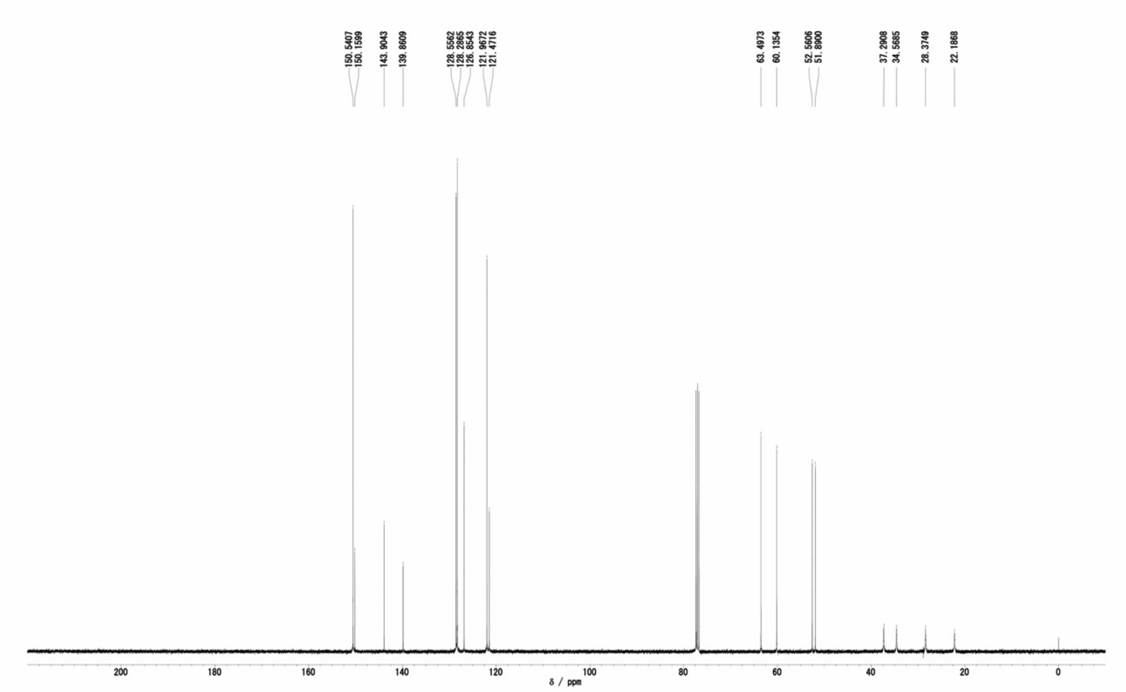
^{1}H (400 MHz, $CDCl_3$) and ^{13}C (100 MHz, DMSO-d_6) NMR spectra of ***exo*-1b**



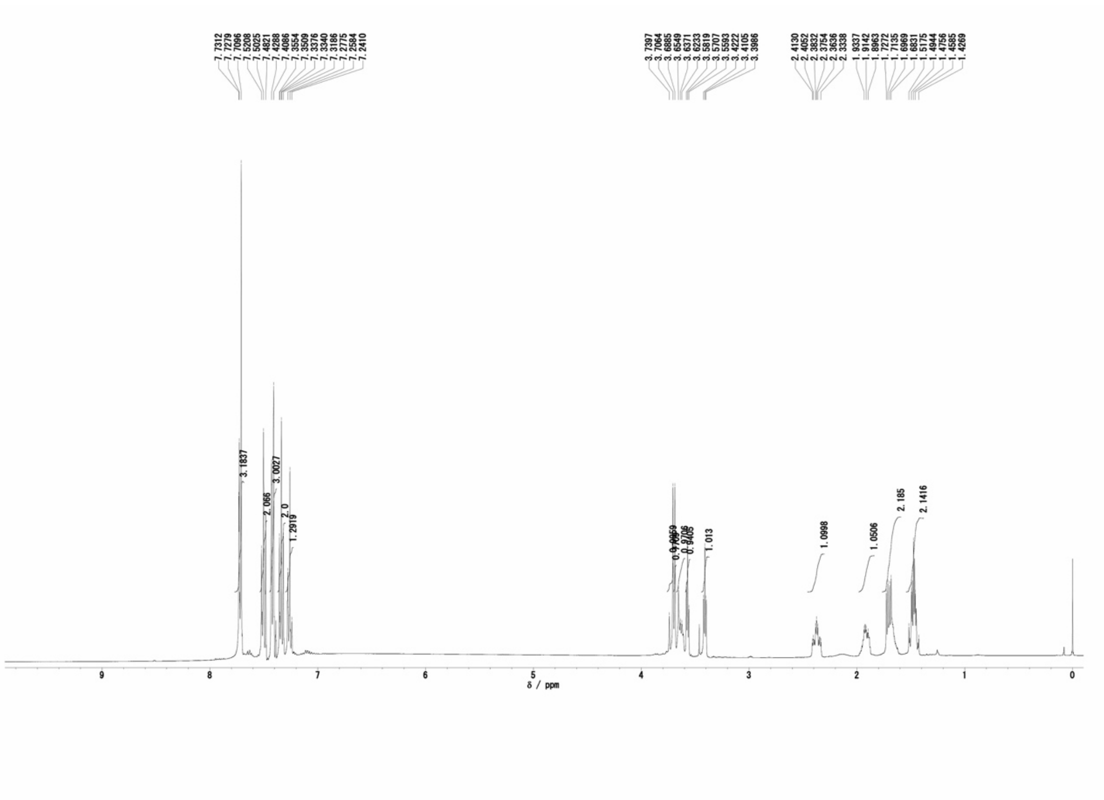


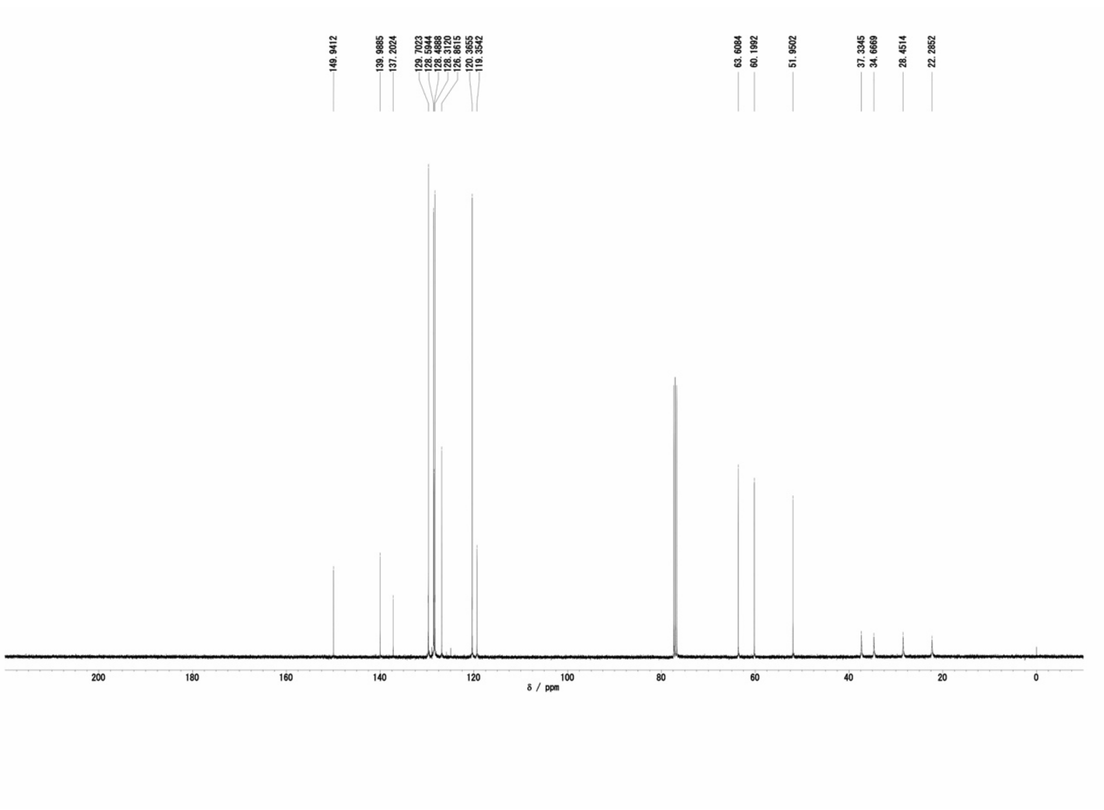
^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectra of ***endo*-1f** ($CDCl_3$)



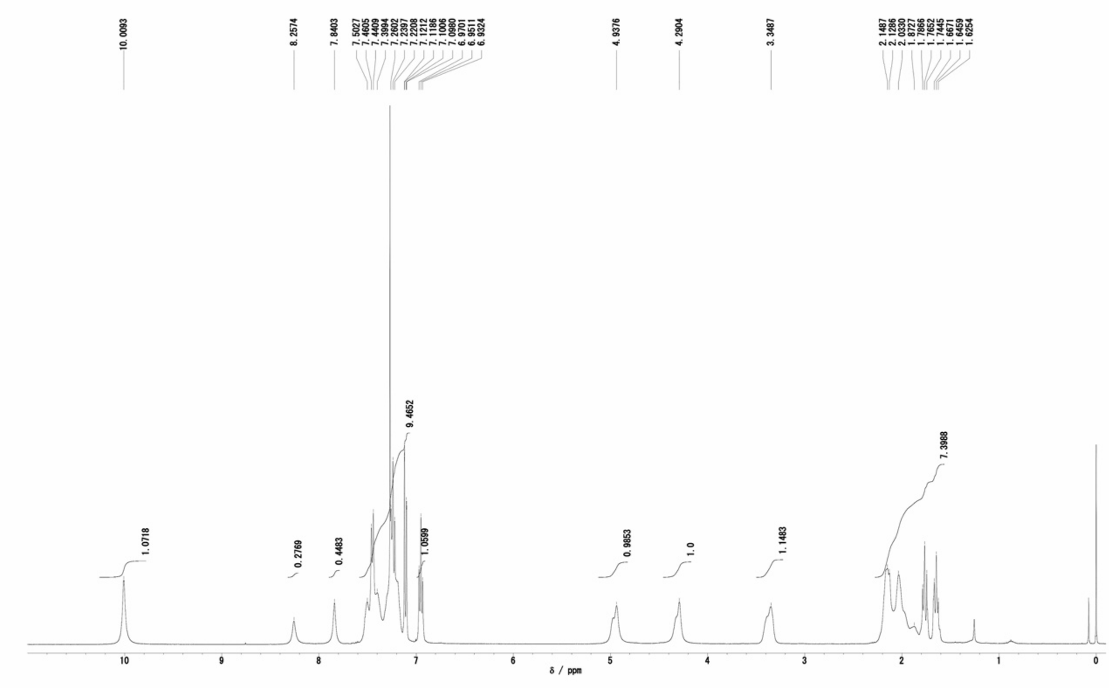


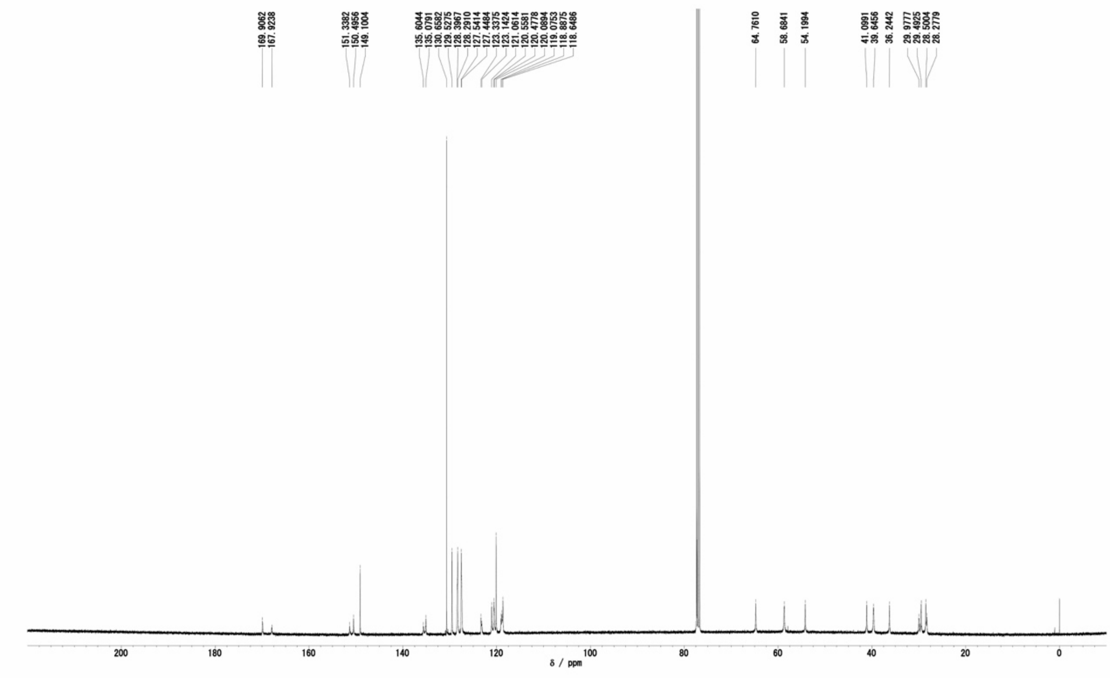
[1]H (400 MHz) and [13]C (100 MHz) NMR spectra of ***endo*-1i** ($CDCl_3$)



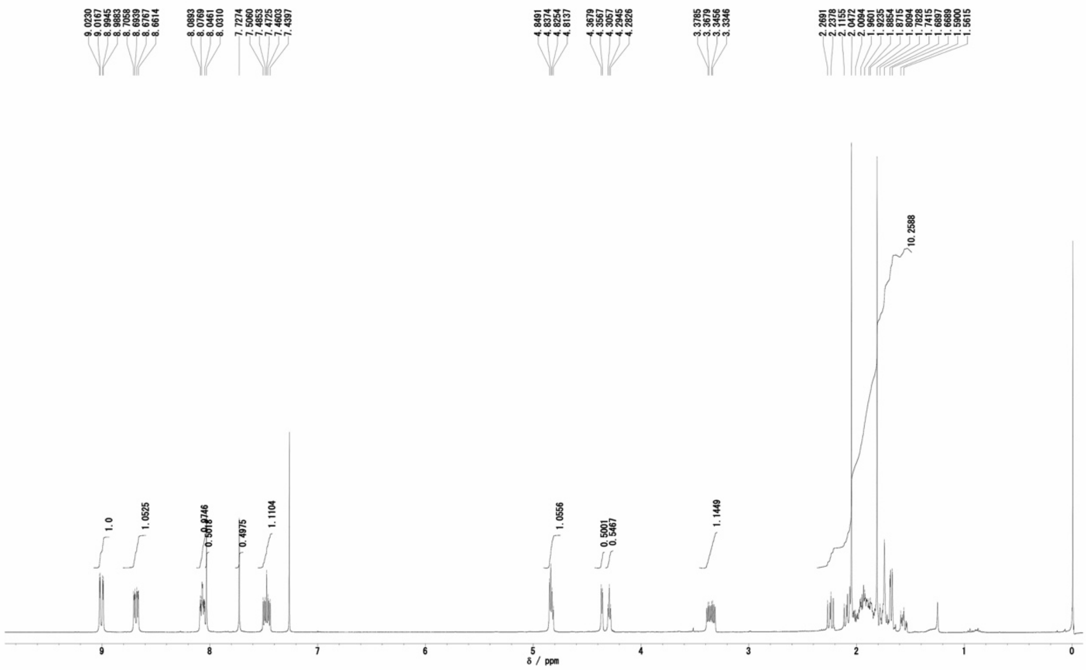


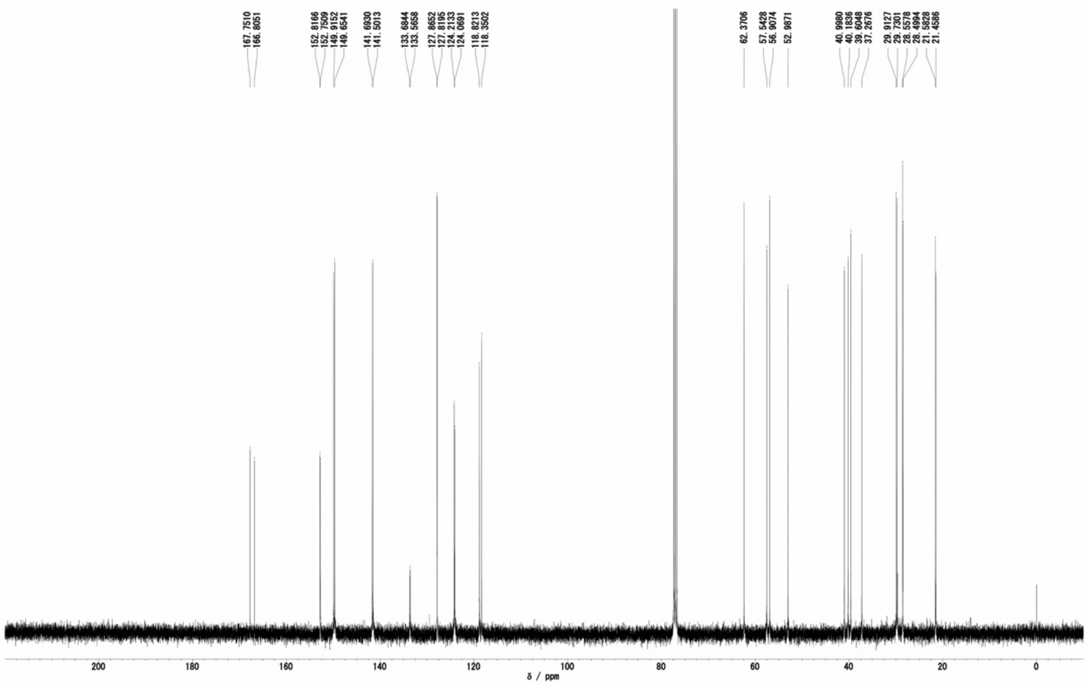
^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectra of ***exo*-5a** ($CDCl_3$)



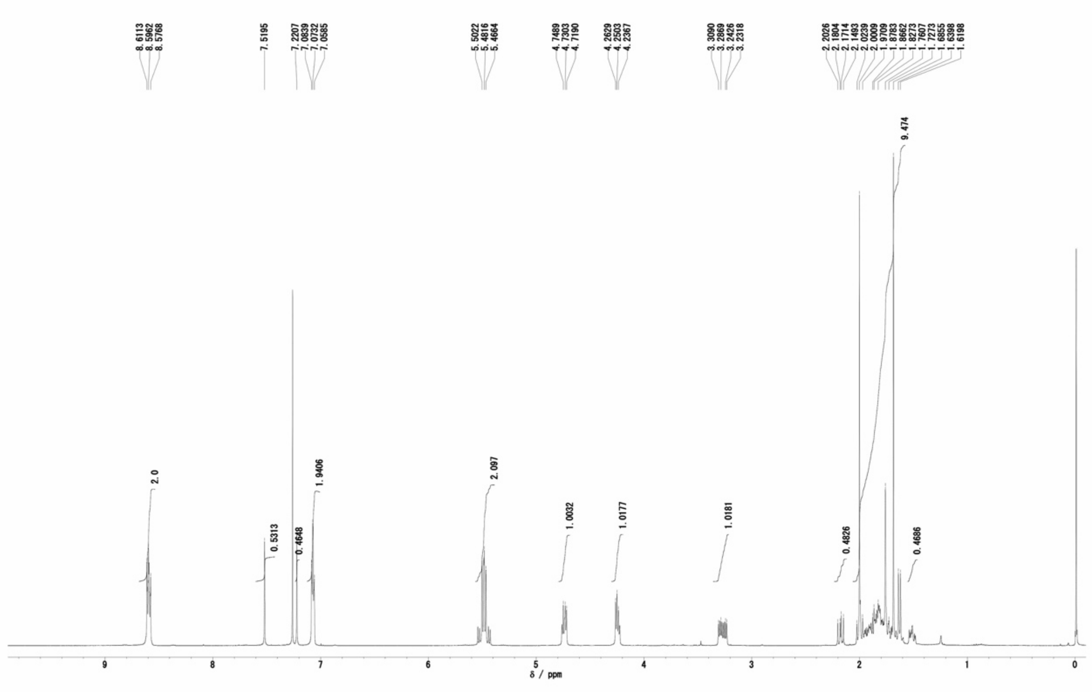


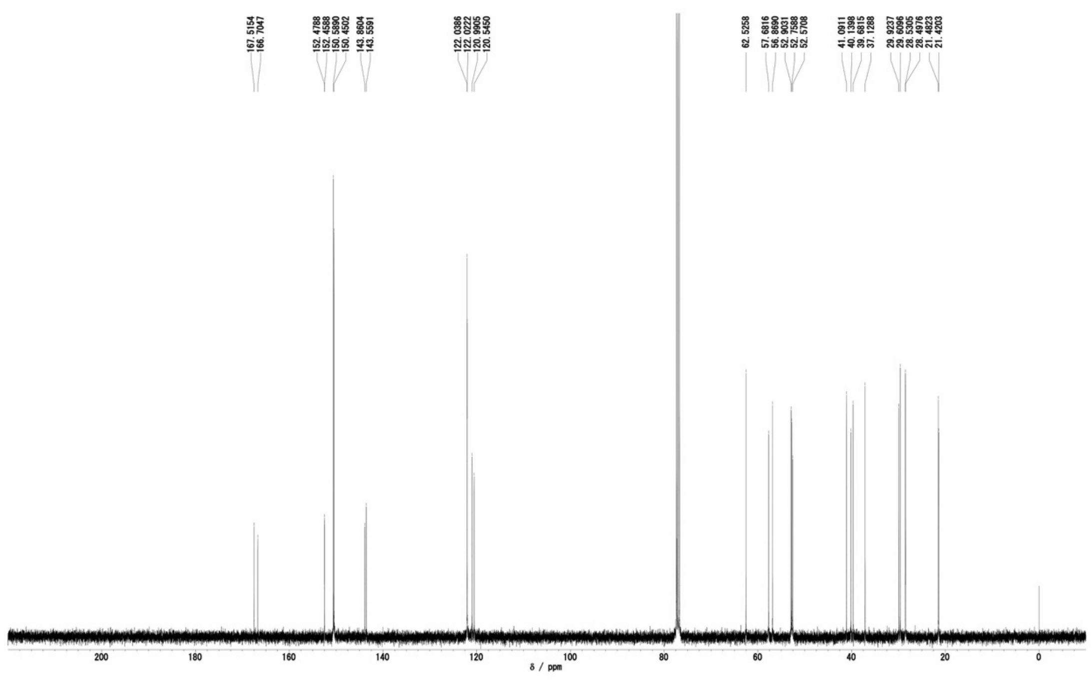
[1]H (400 MHz) and [13]C (100 MHz) NMR spectra of ***exo*-6d** ($CDCl_3$)



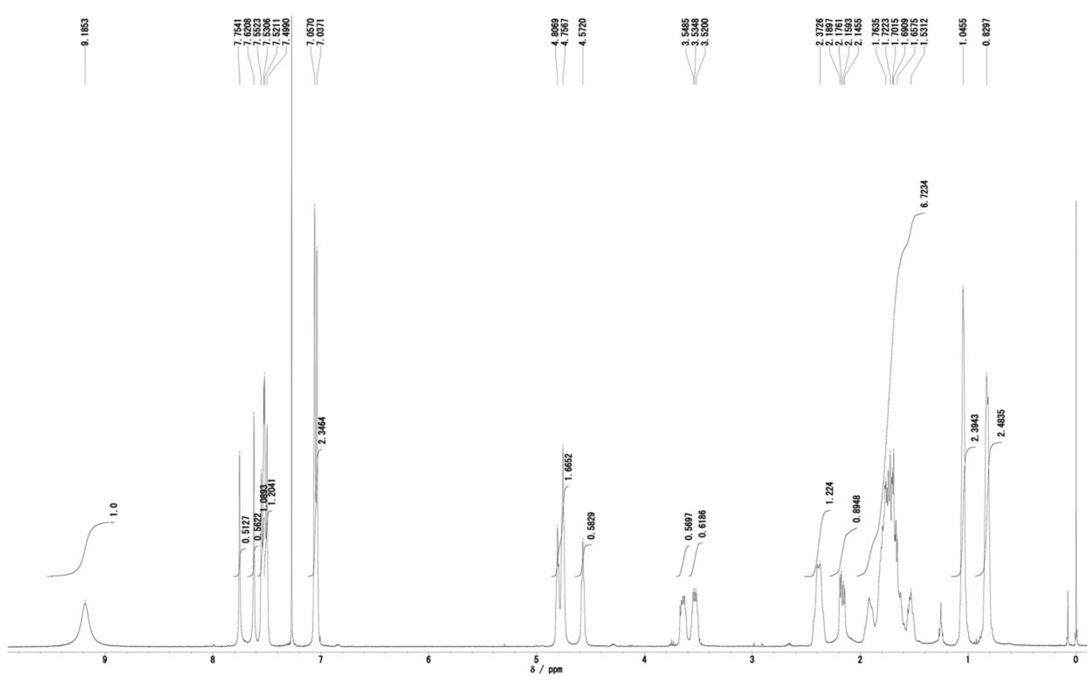


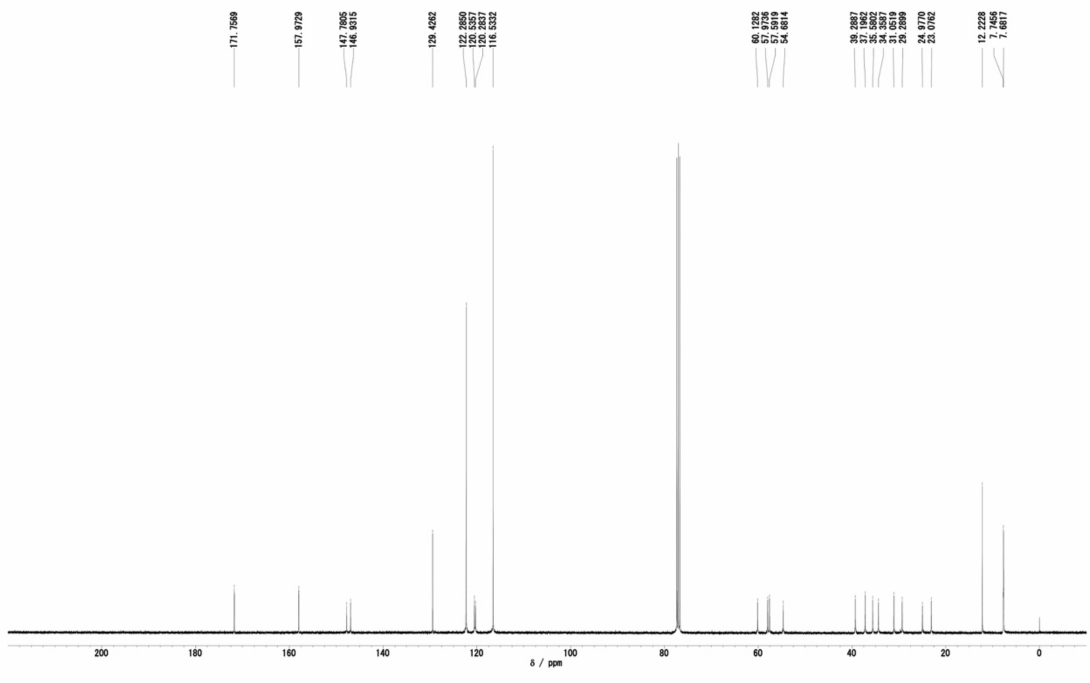
^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectra of ***exo*-6f** ($CDCl_3$)





^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectra of ***endo*-7c** ($CDCl_3$)





^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectra of ***exo*-7e** ($CDCl_3$)