

SUPPORTING INFORMATION

Combinatorial Synthesis of Nicotine Analogs Using an Ugi-4CR/Cyclization-Reduction Strategy

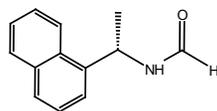
Luis A. Polindara-García and Alfredo Vazquez*

*Departamento de Química Orgánica, Facultad de Química, Universidad Nacional
Autónoma de México, Ciudad Universitaria, 04510, México D.F., México*

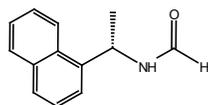
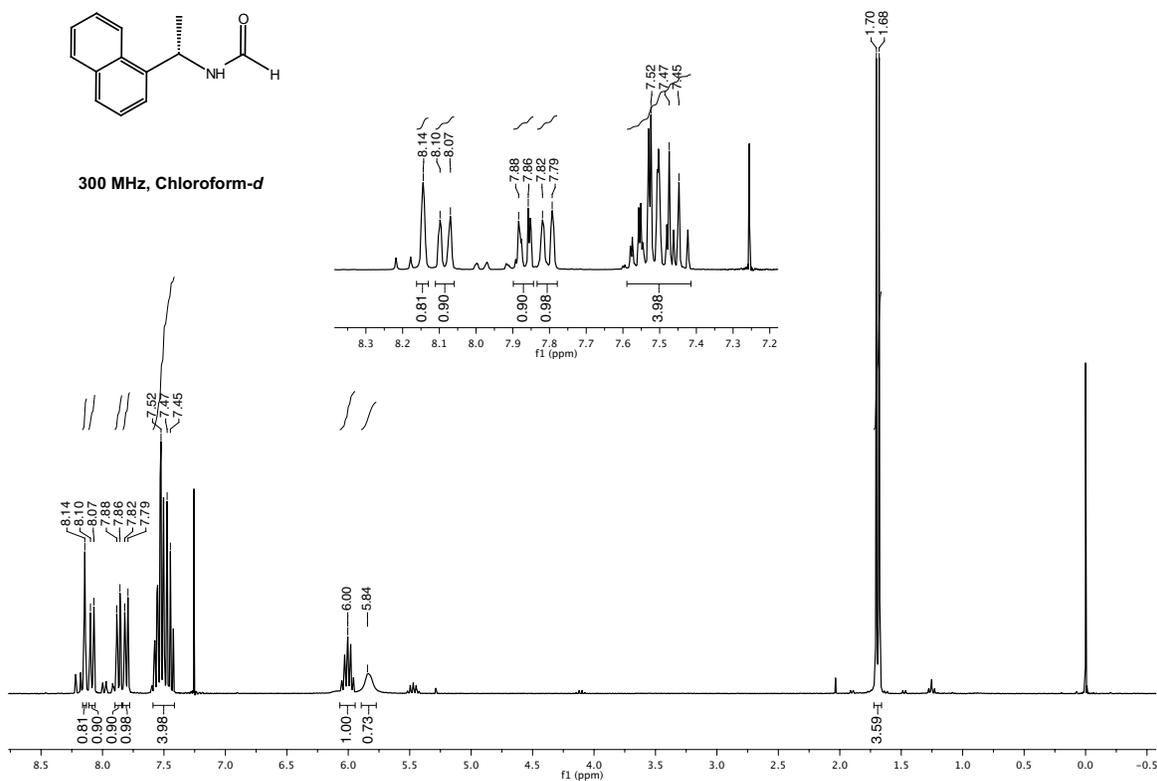
Starting Materials spectra	S2-S5
Ugi adducts spectra	S6-S30
Nicotine analogs spectra	S31-S56

STARTING MATERIALS SPECTRA

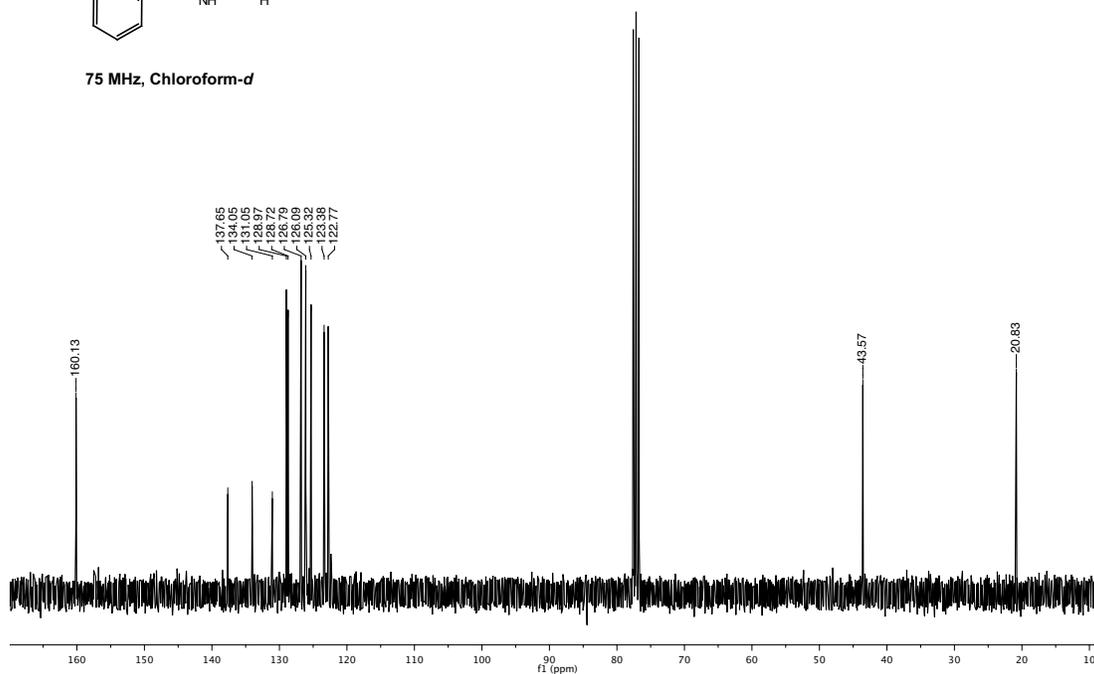
(S)-N-(1-(naphthalen-1-yl)ethyl)formamide



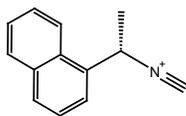
300 MHz, Chloroform-*d*



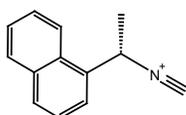
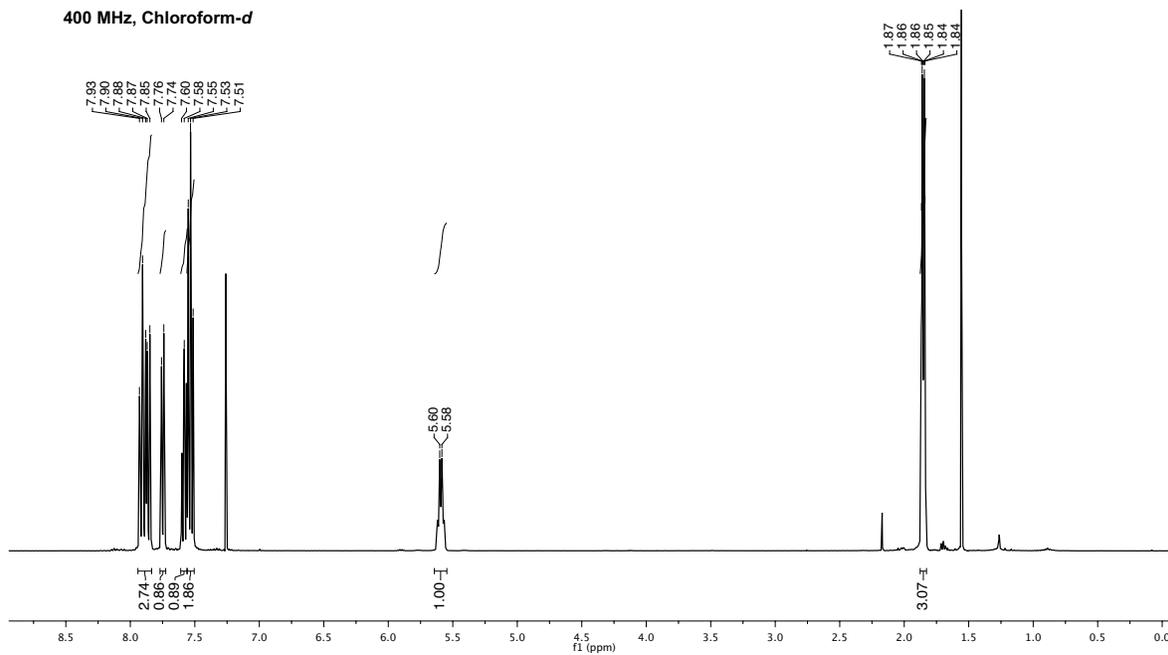
75 MHz, Chloroform-*d*



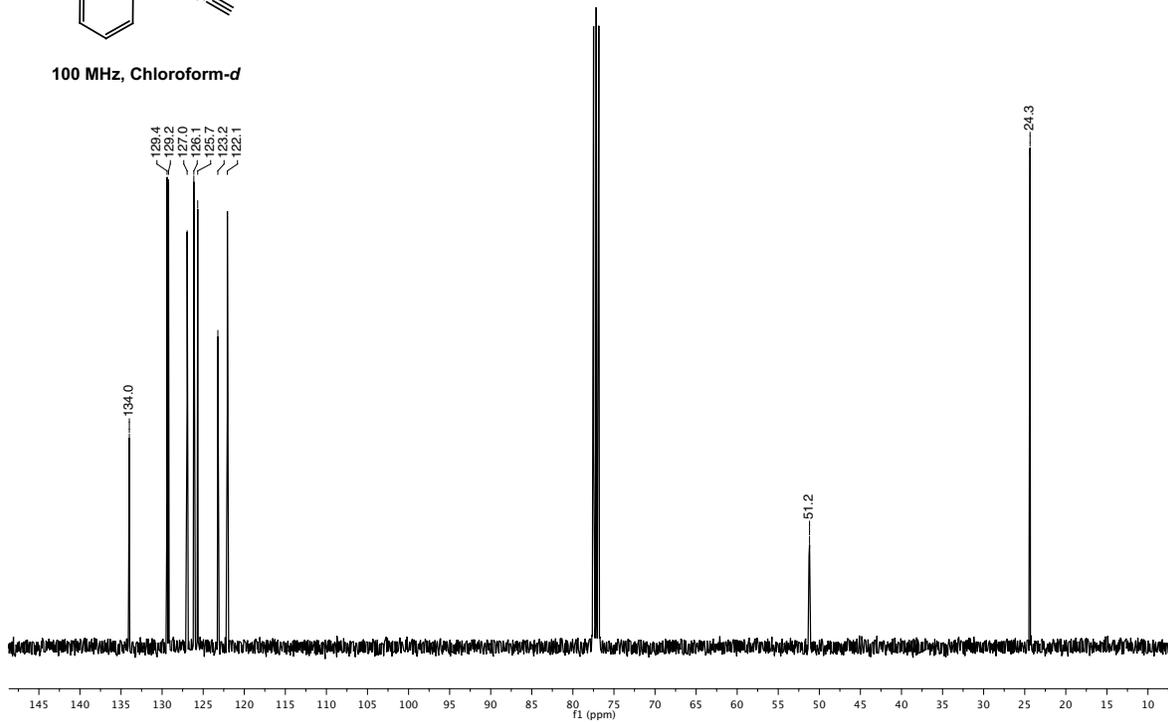
(S)-1-(1-isocyanoethyl)naphthalene



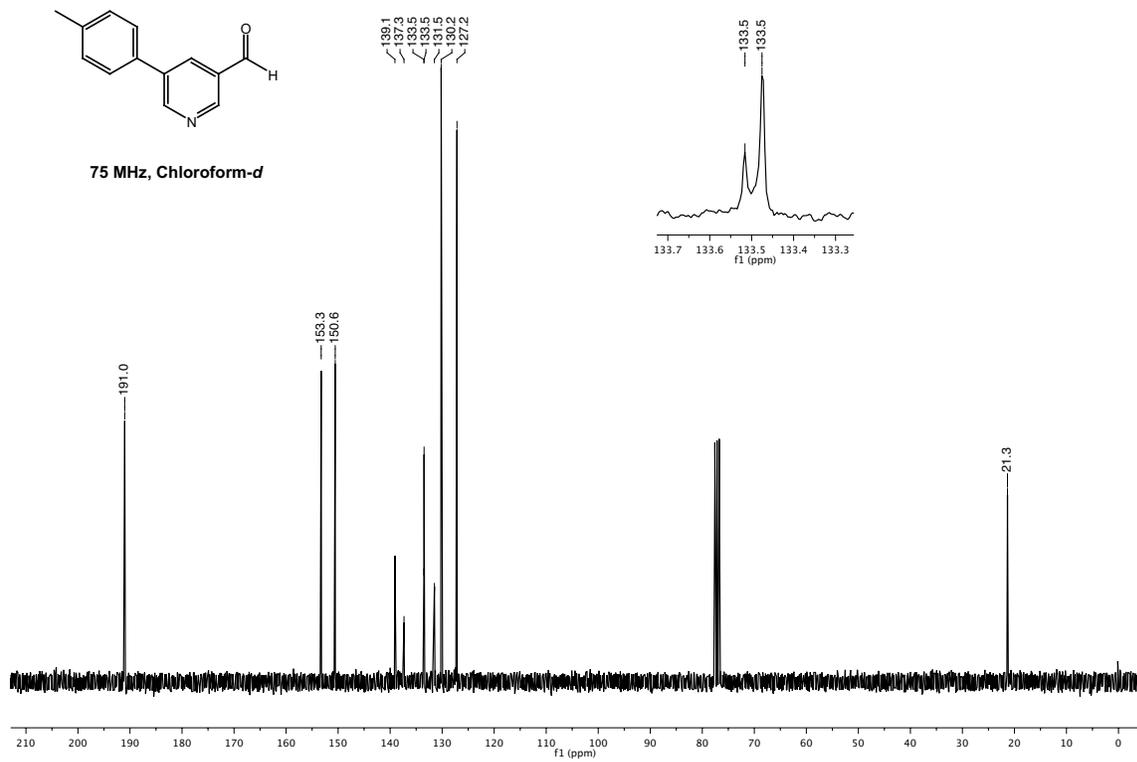
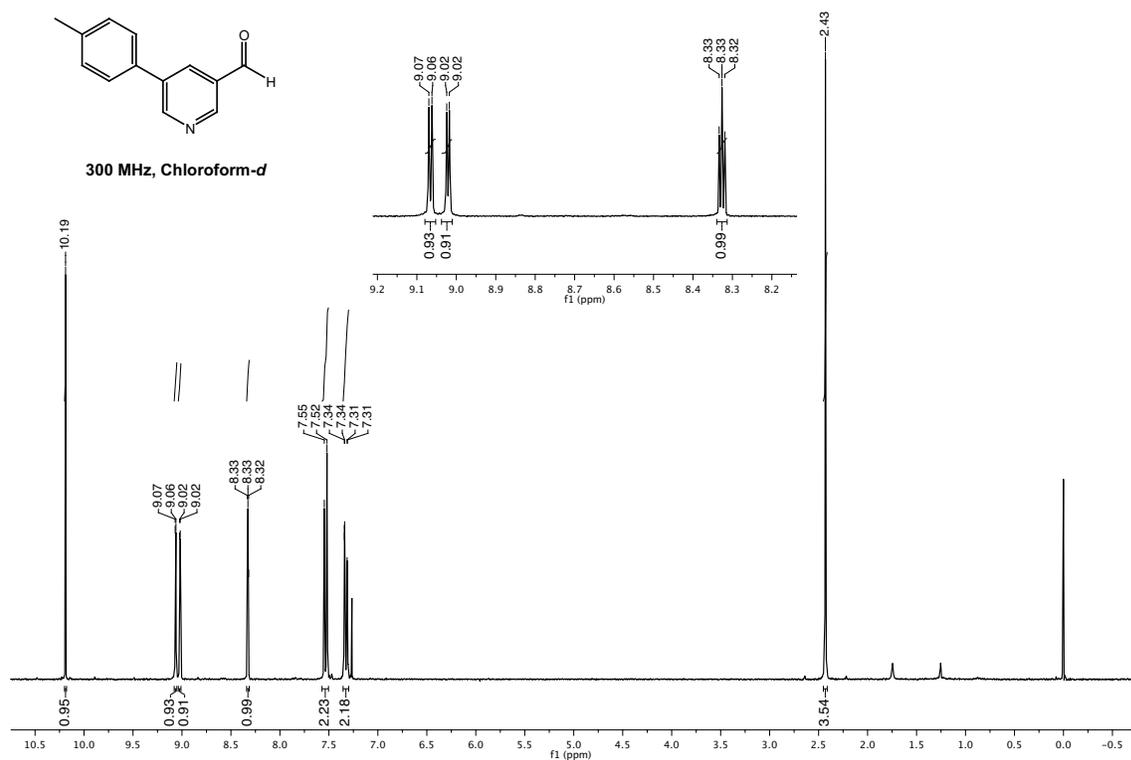
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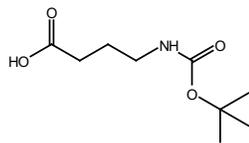
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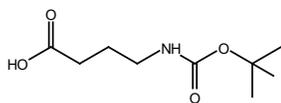
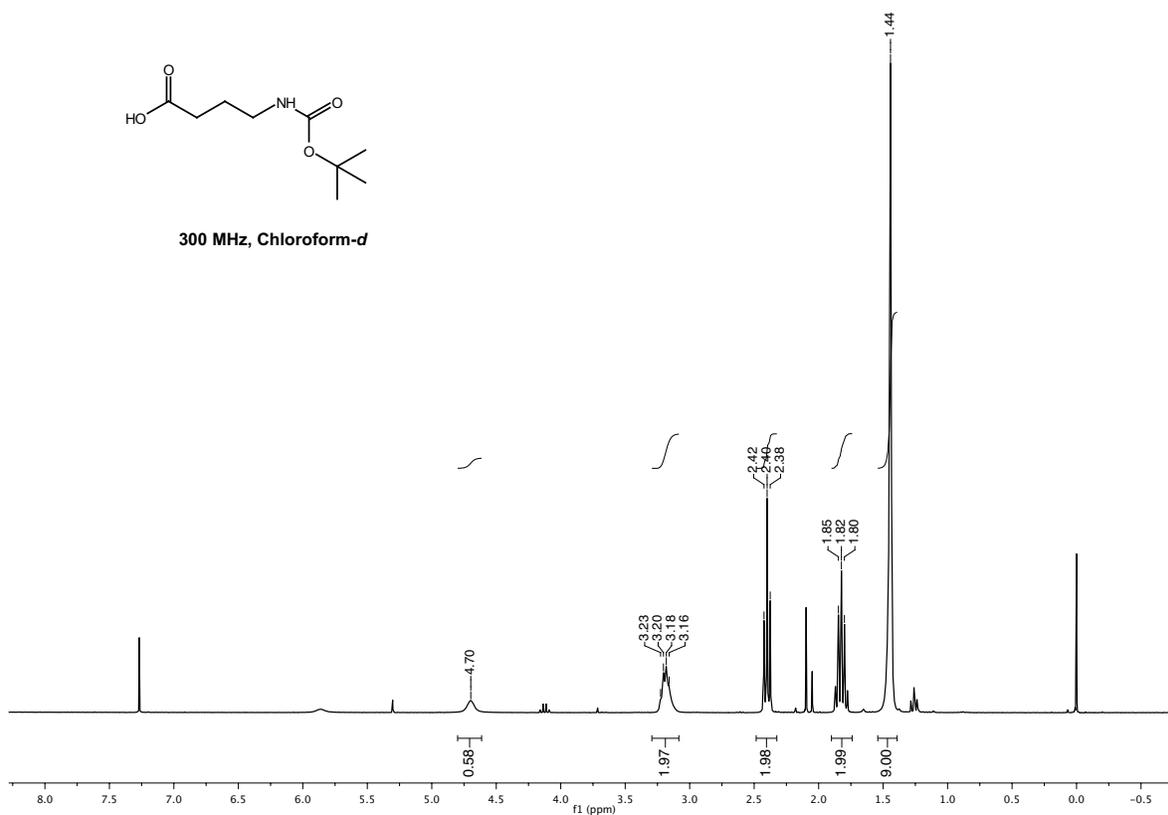
5-(*p*-tolyl)nicotinaldehyde 11k.



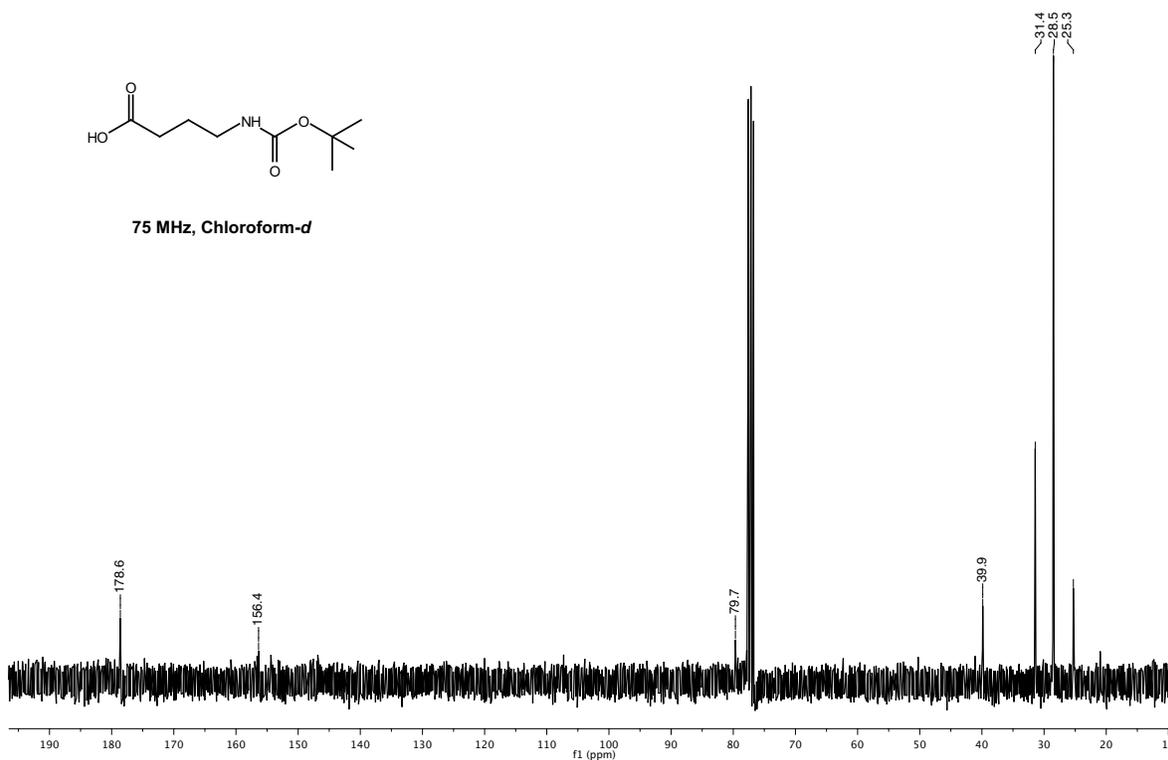
4-((*tert*-butoxycarbonyl)amino)butanoic acid 12t.



300 MHz, Chloroform-*d*

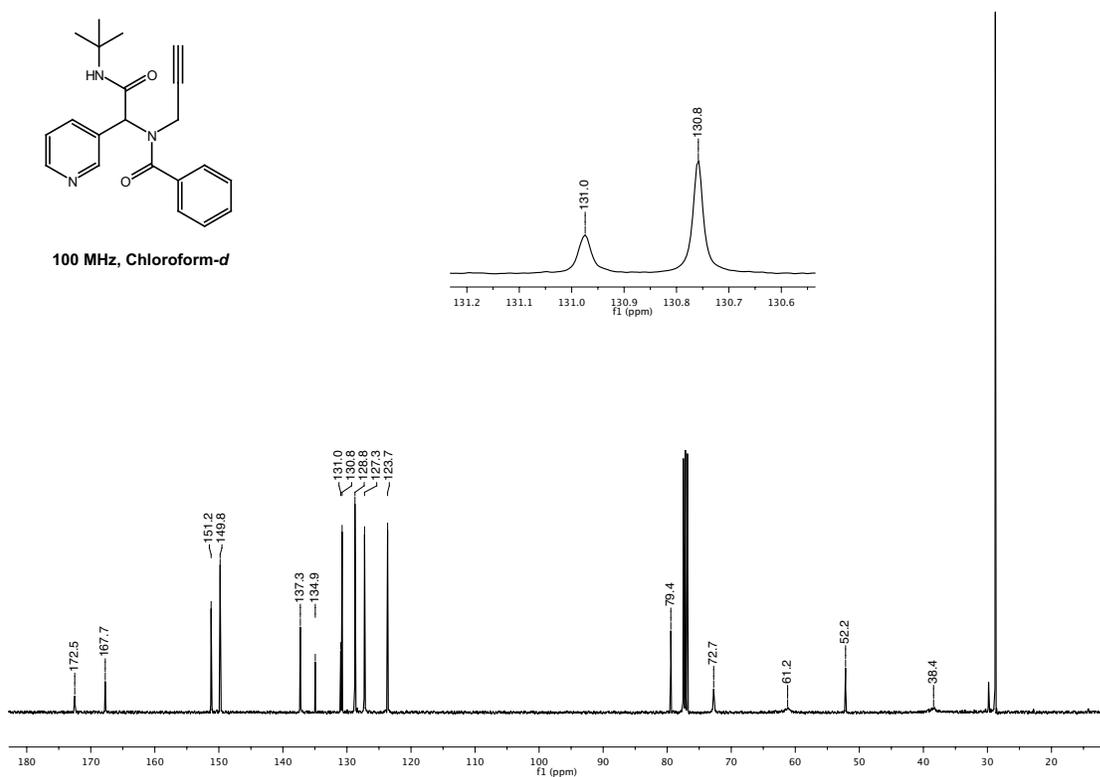
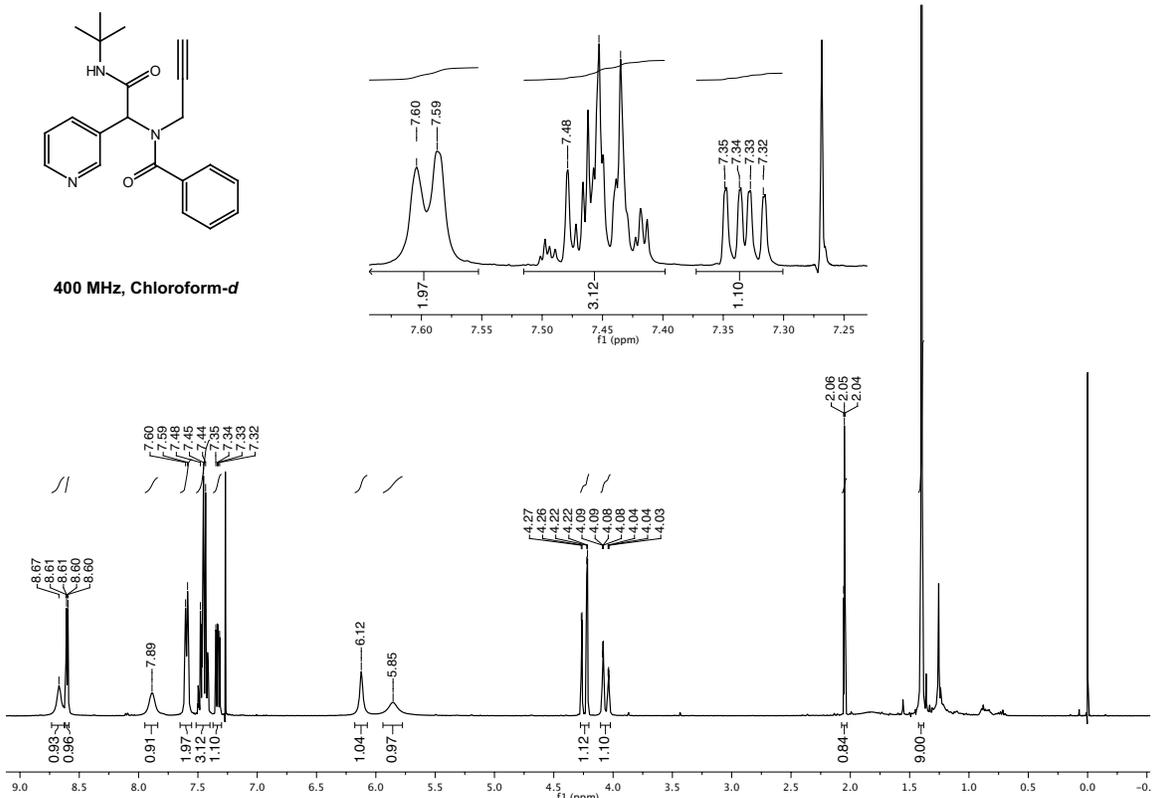


75 MHz, Chloroform-*d*

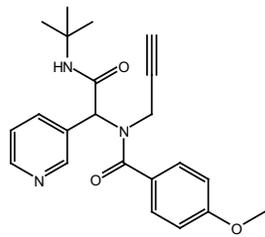


UGI ADDUCTS SPECTRA

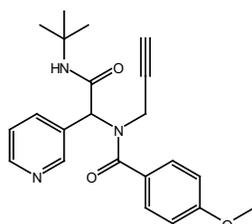
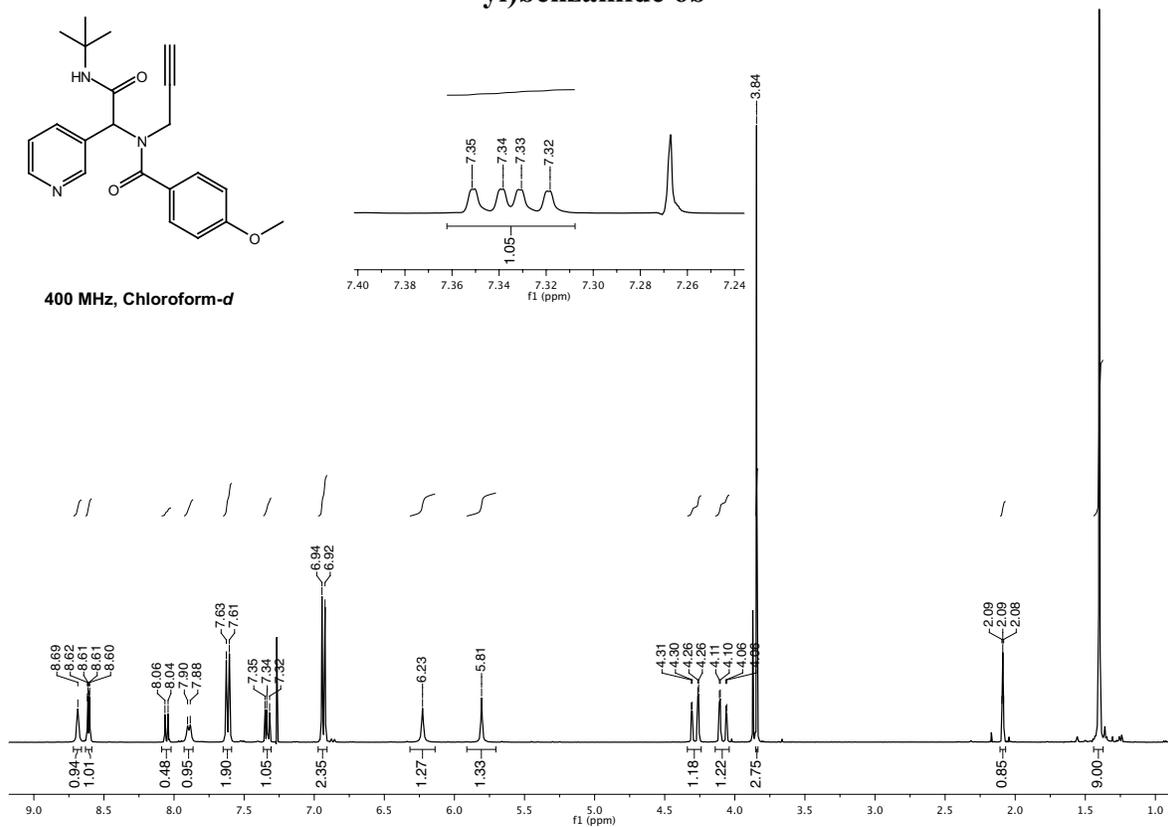
N-(2-(*tert*-butylamino)-2-oxo-1-(pyridin-3-yl)ethyl)-*N*-(prop-2-yn-1-yl)benzamide 6a



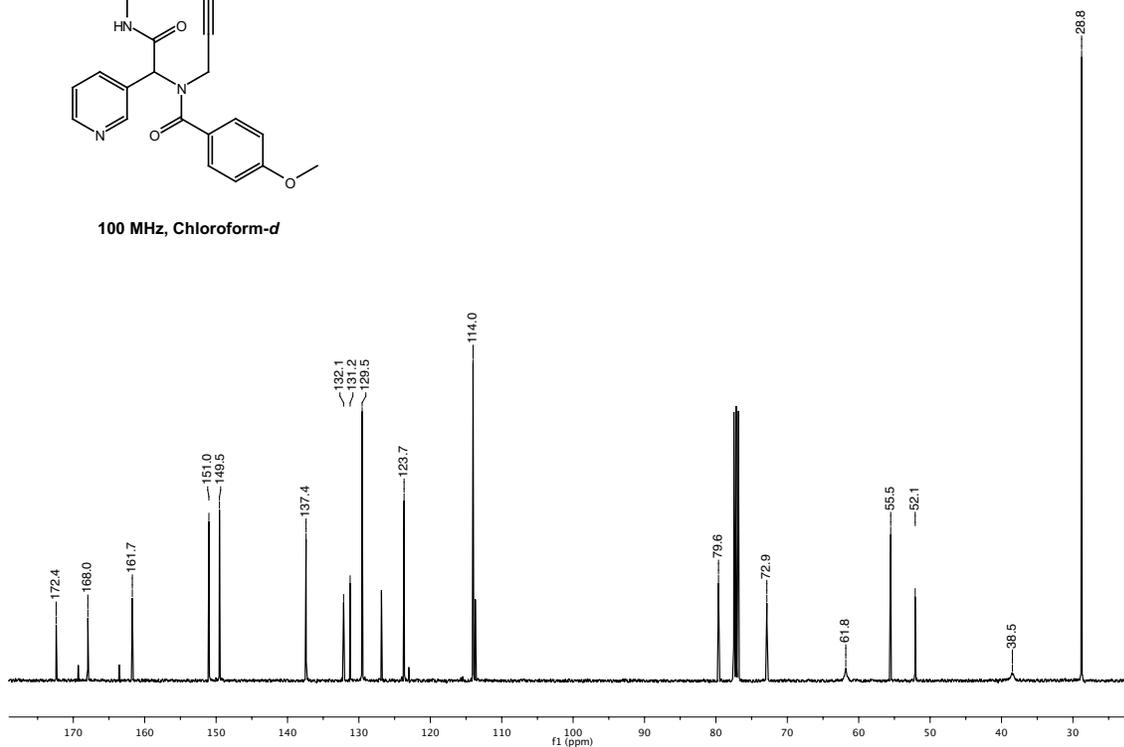
***N*-(2-(*tert*-butylamino)-2-oxo-1-(pyridin-3-yl)ethyl)-4-methoxy-*N*-(prop-2-yn-1-yl)benzamide 6b**



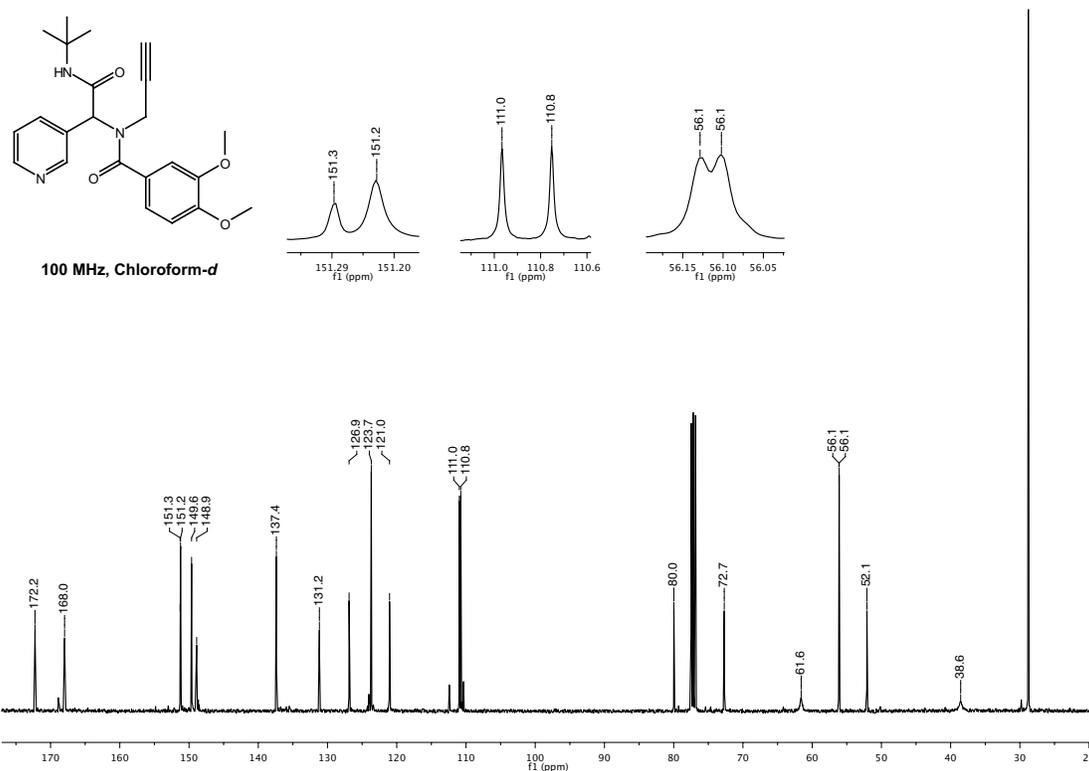
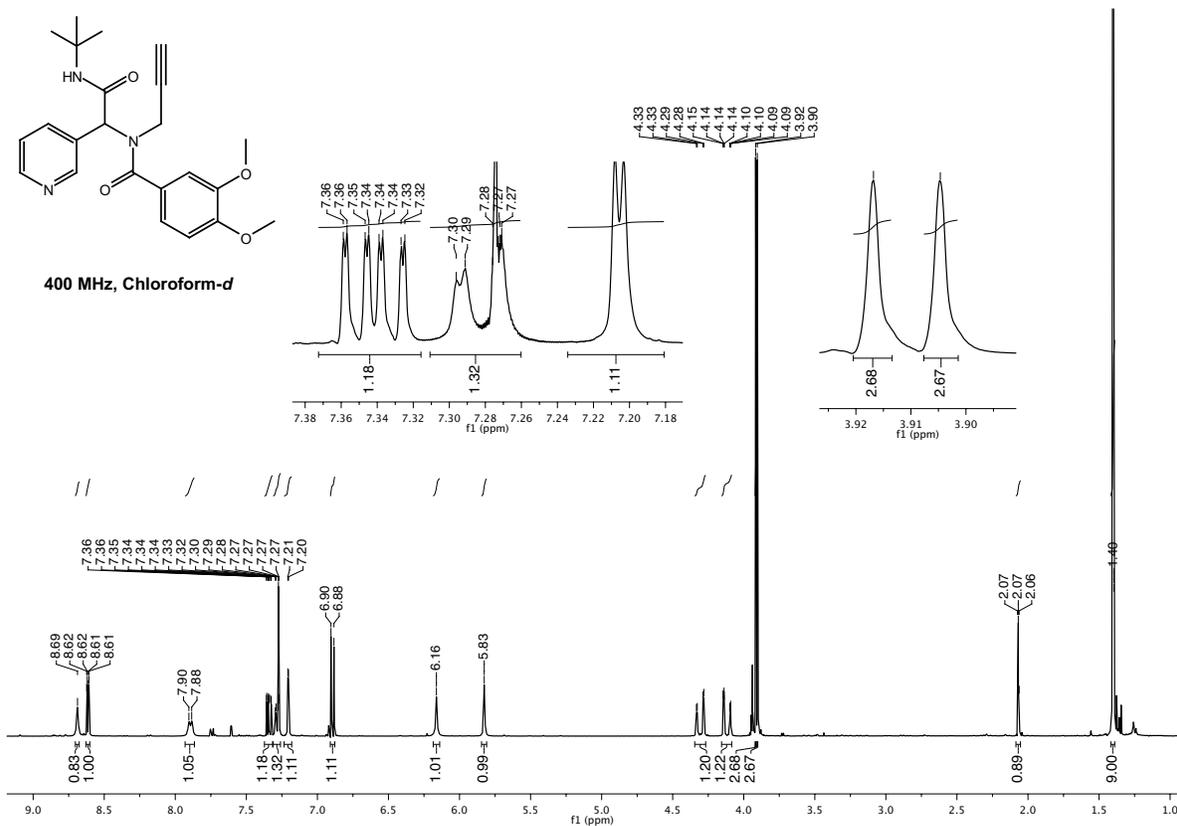
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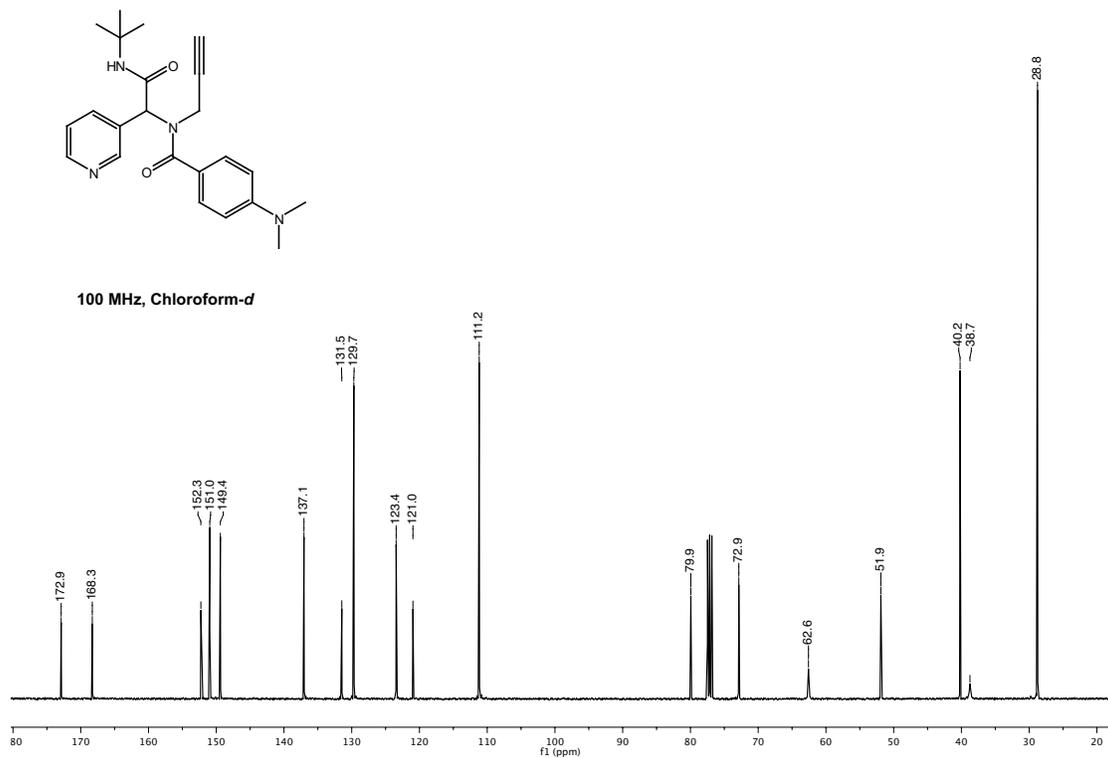
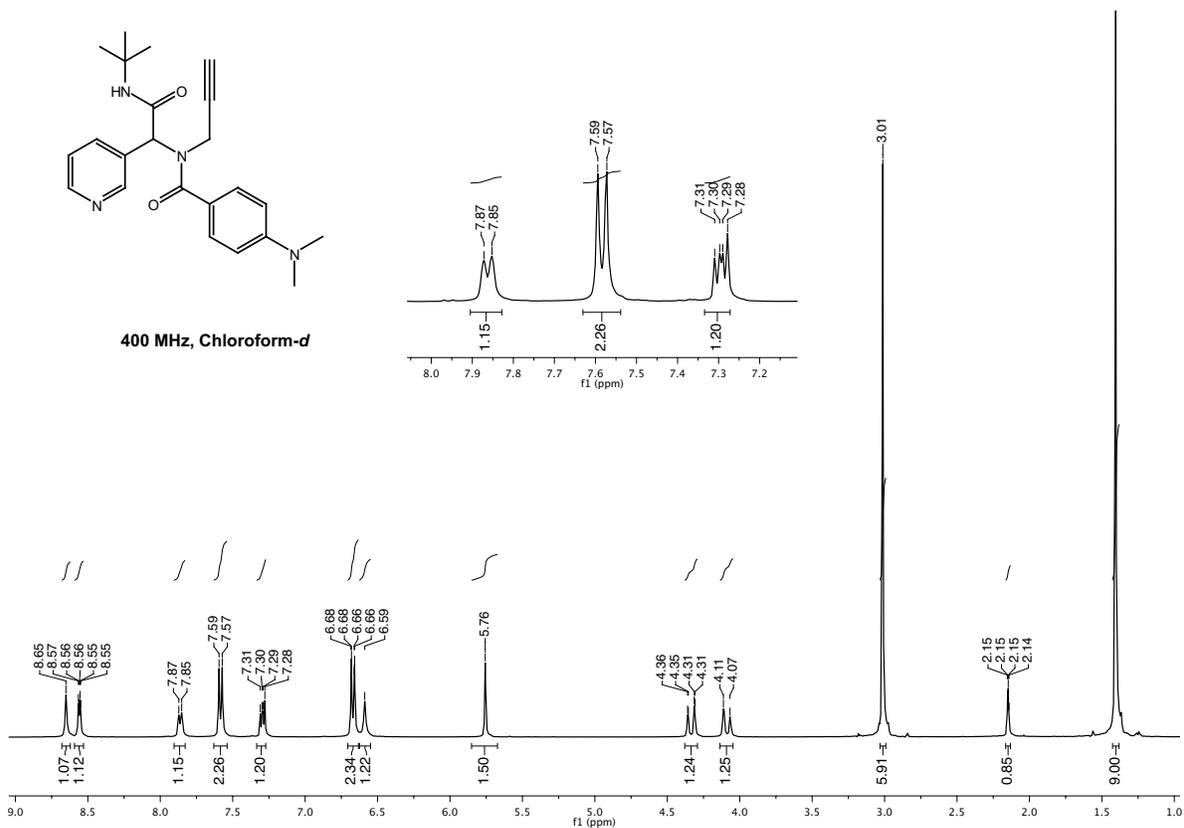
100 MHz, Chloroform-*d*



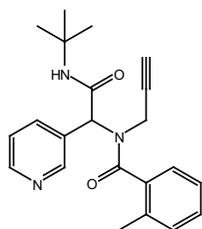
***N*-(2-(*tert*-butylamino)-2-oxo-1-(pyridin-3-yl)ethyl)-3,4-dimethoxy-*N*-(prop-2-yn-1-yl)benzamide 6c**



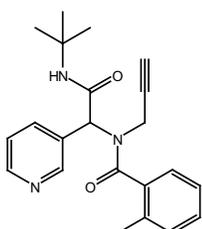
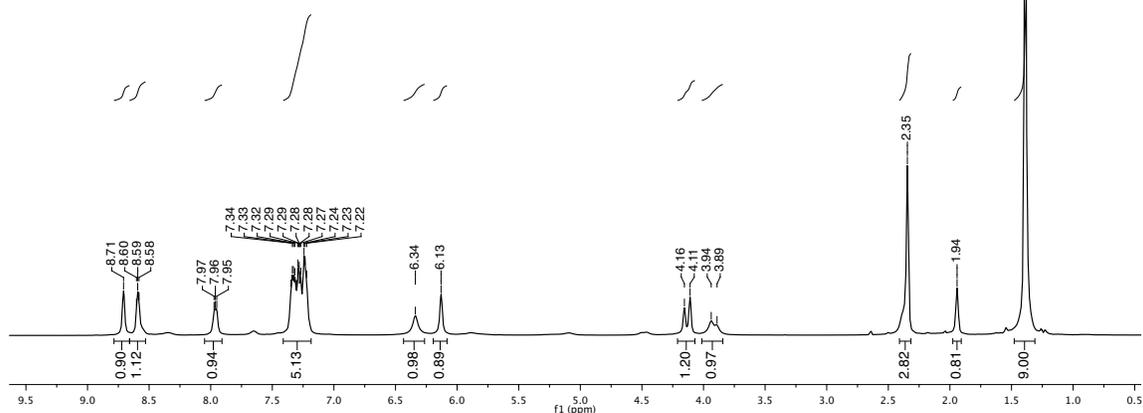
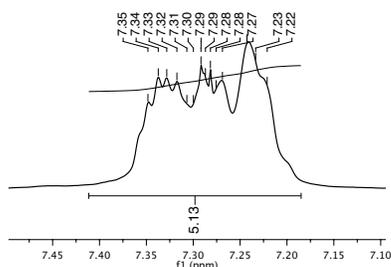
***N*-(2-(*tert*-butylamino)-2-oxo-1-(pyridin-3-yl)ethyl)-4-(dimethylamino)-*N*-(prop-2-yn-1-yl)benzamide 6d**



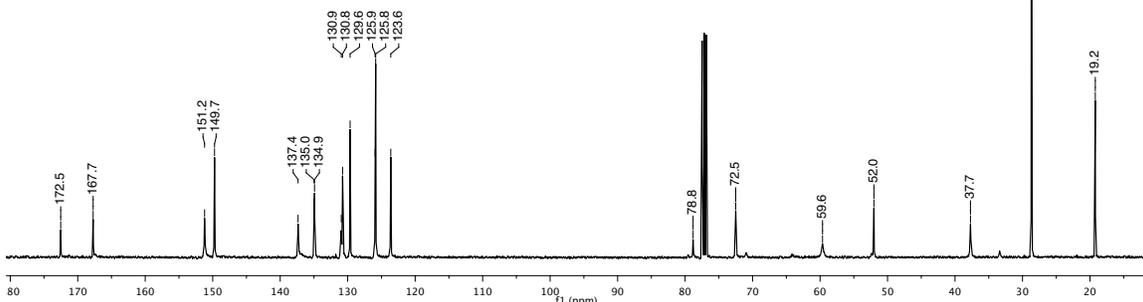
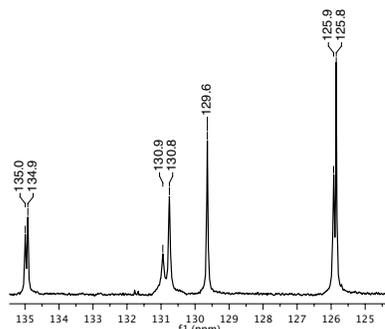
***N*-(2-(*tert*-butylamino)-2-oxo-1-(pyridin-3-yl)ethyl)-2-methyl-*N*-(prop-2-yn-1-yl)benzamide 6e**



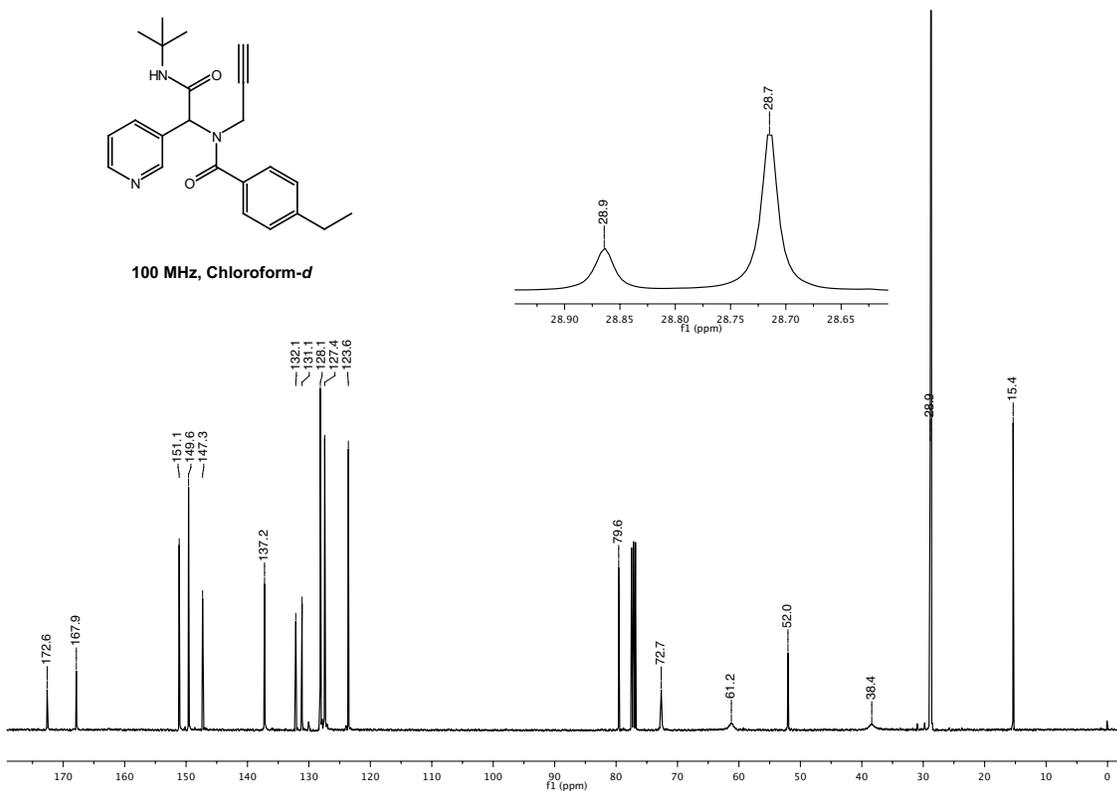
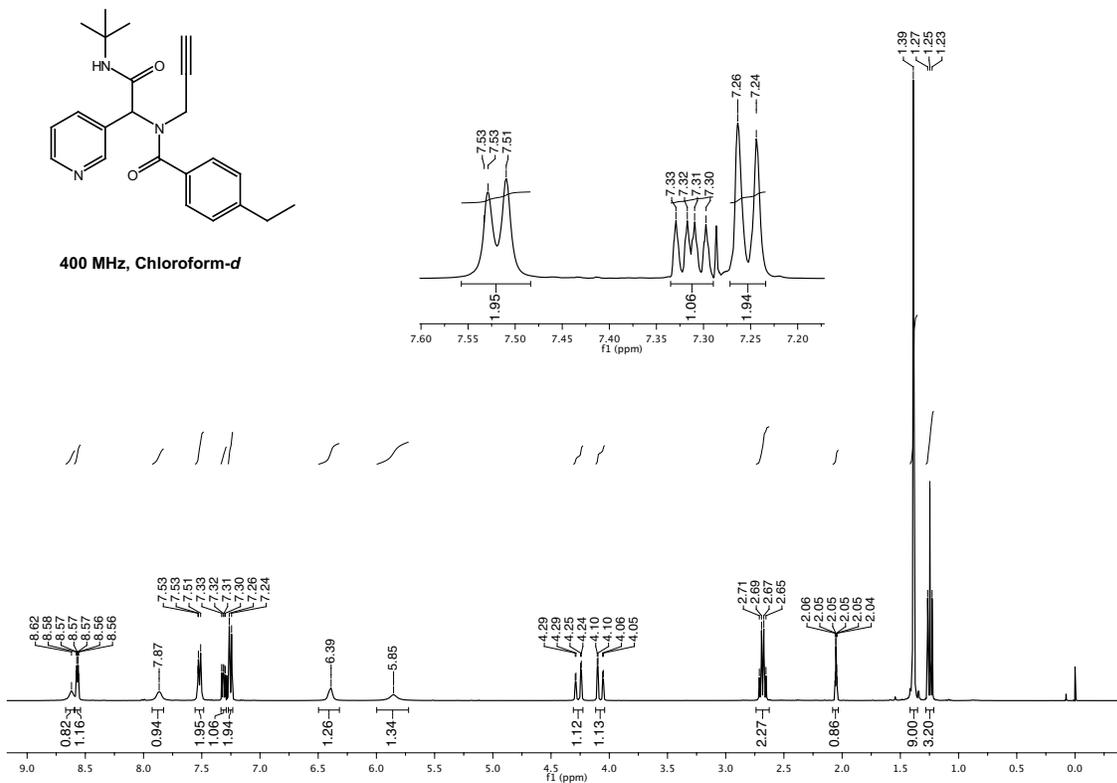
400 MHz, Chloroform-*d*



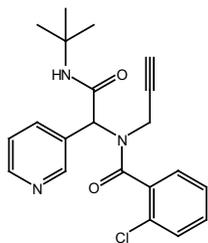
100 MHz, Chloroform-*d*



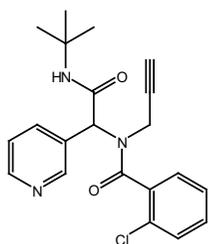
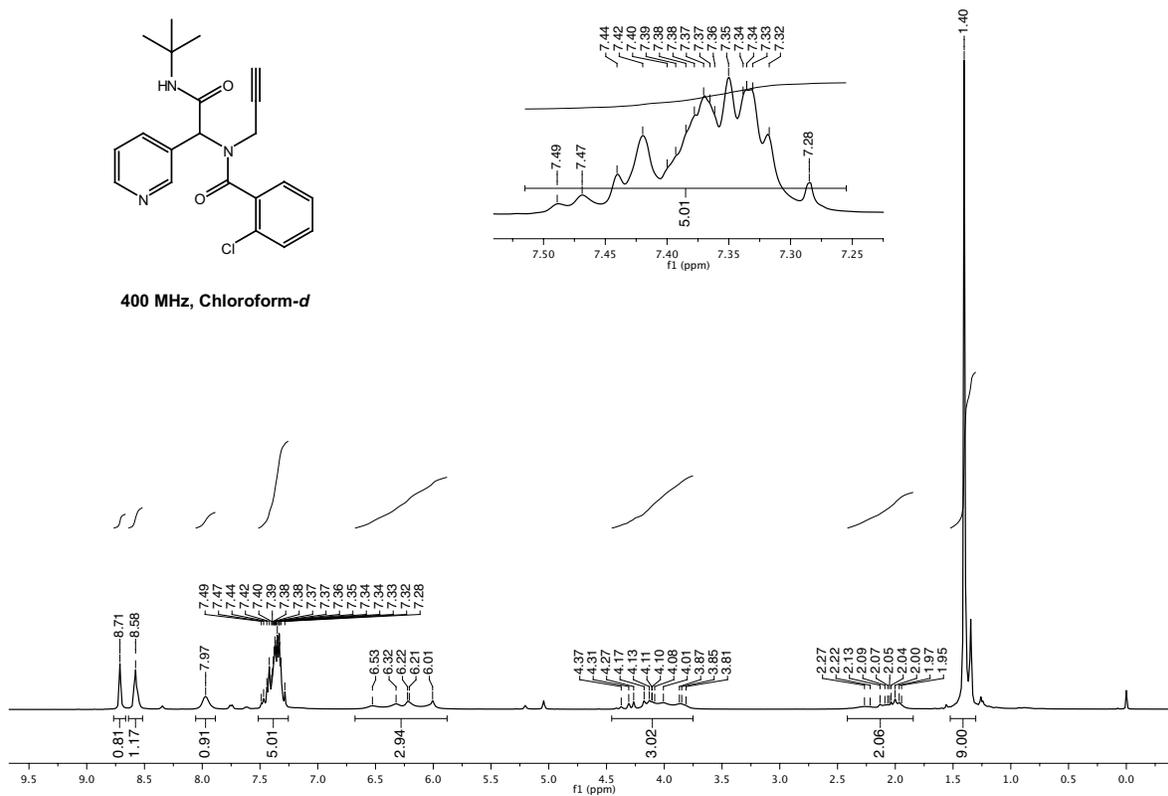
***N*-(2-(*tert*-butylamino)-2-oxo-1-(pyridin-3-yl)ethyl)-4-ethyl-*N*-(prop-2-yn-1-yl)benzamide 6f**



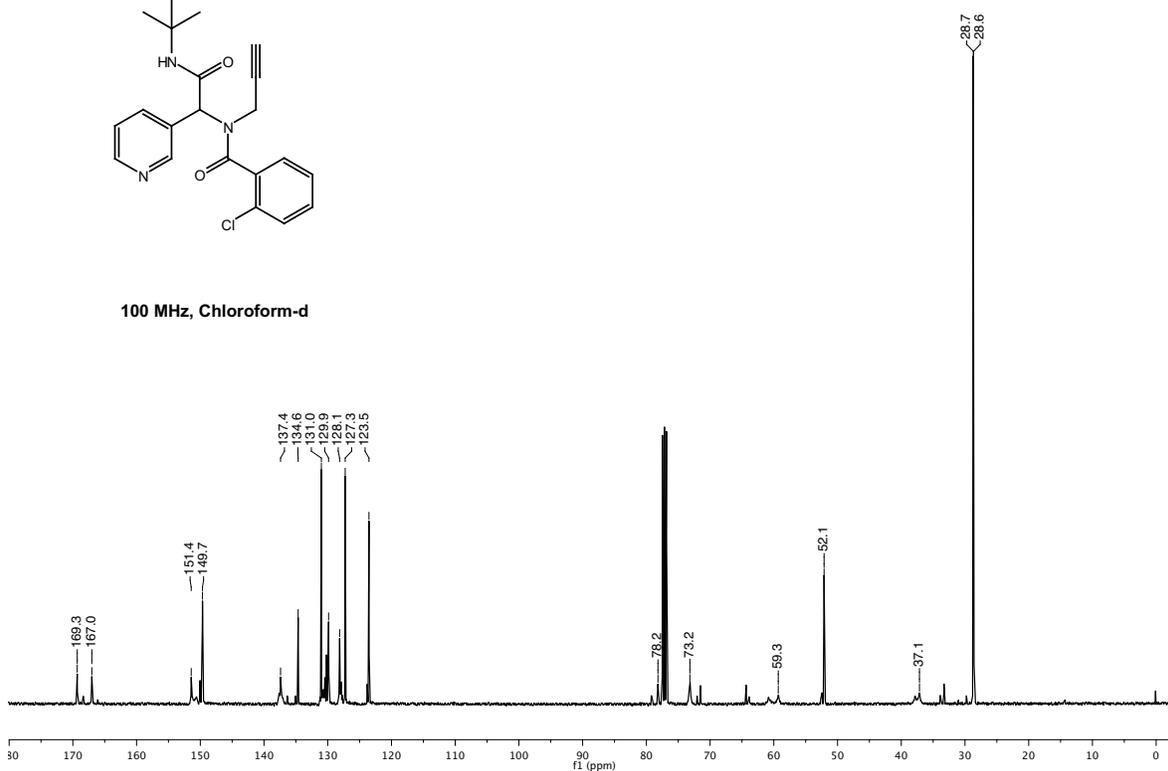
***N*-(2-(*tert*-butylamino)-2-oxo-1-(pyridin-3-yl)ethyl)-2-chloro-*N*-(prop-2-yn-1-yl)benzamide 6g**



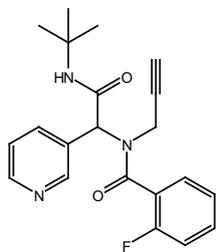
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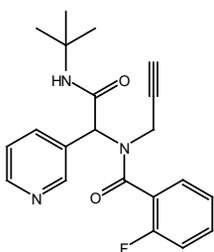
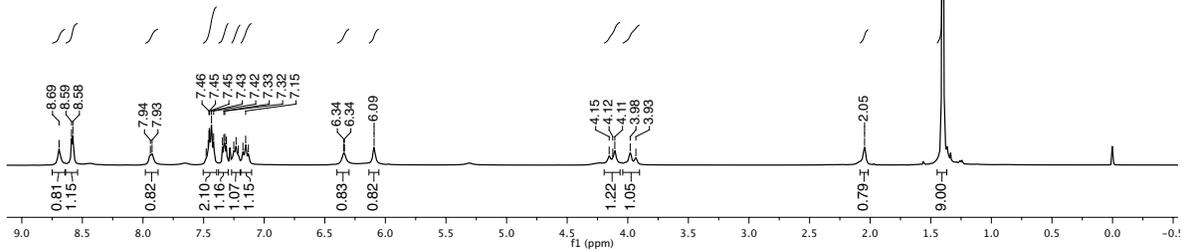
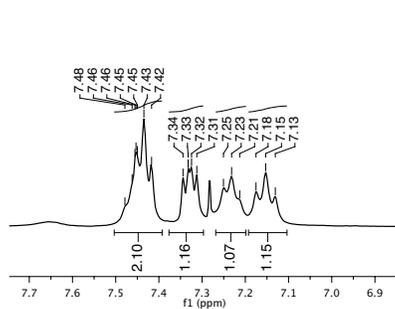
100 MHz, Chloroform-*d*



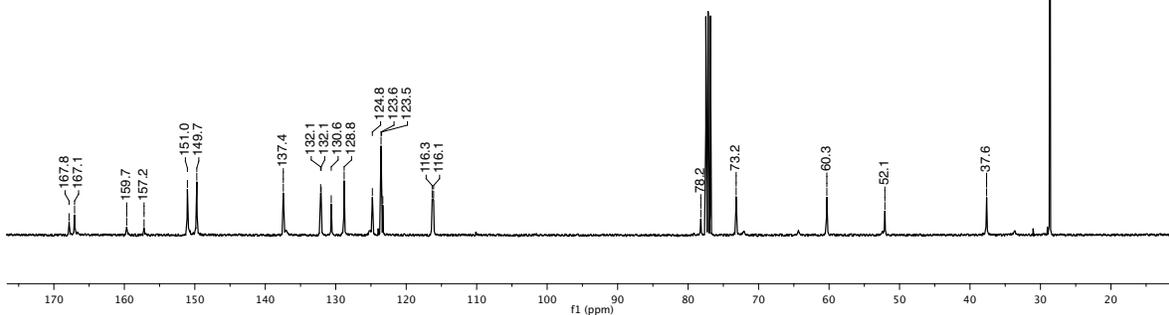
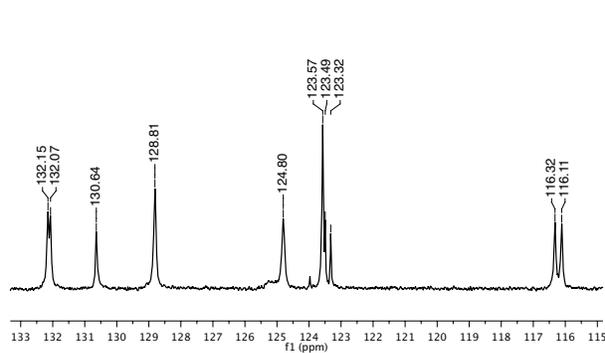
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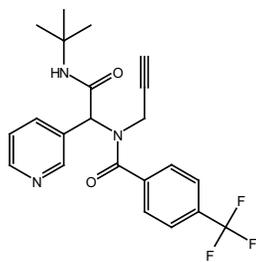
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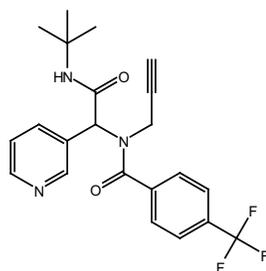
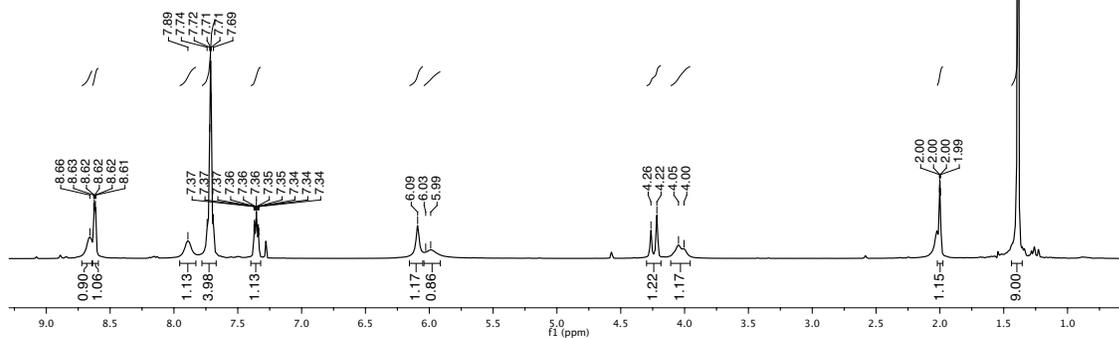
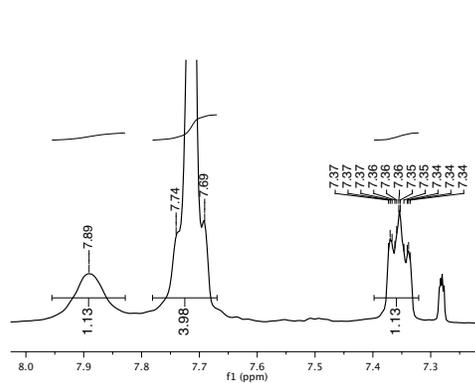
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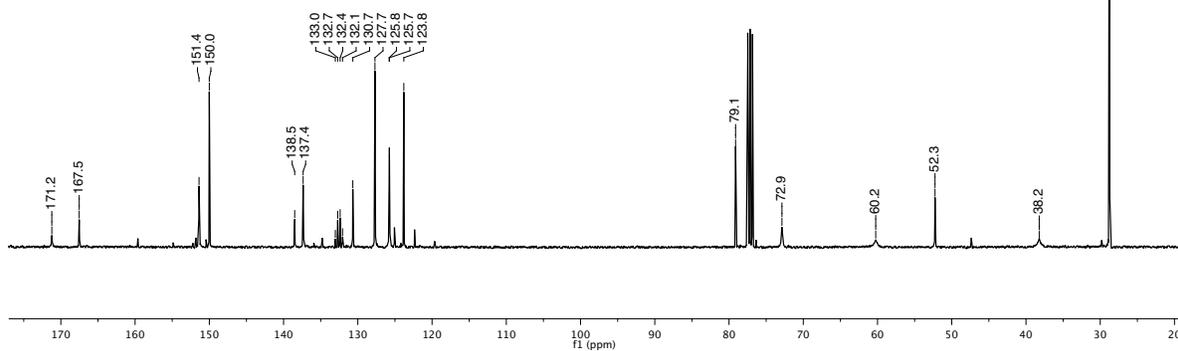
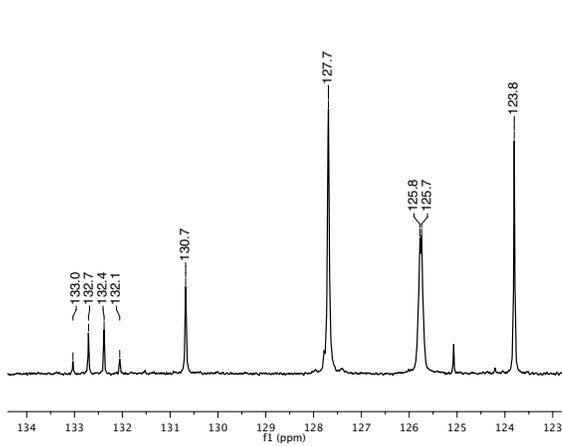
N*-(2-(*tert*-butylamino)-2-oxo-1-(pyridin-3-yl)ethyl)-*N*-(prop-2-yn-1-yl)-4-(trifluoromethyl)benzamide **6i*



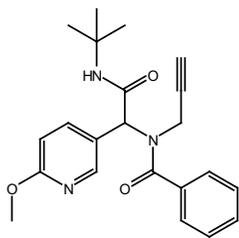
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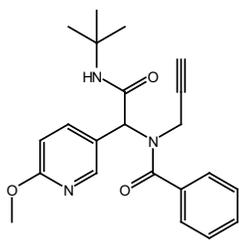
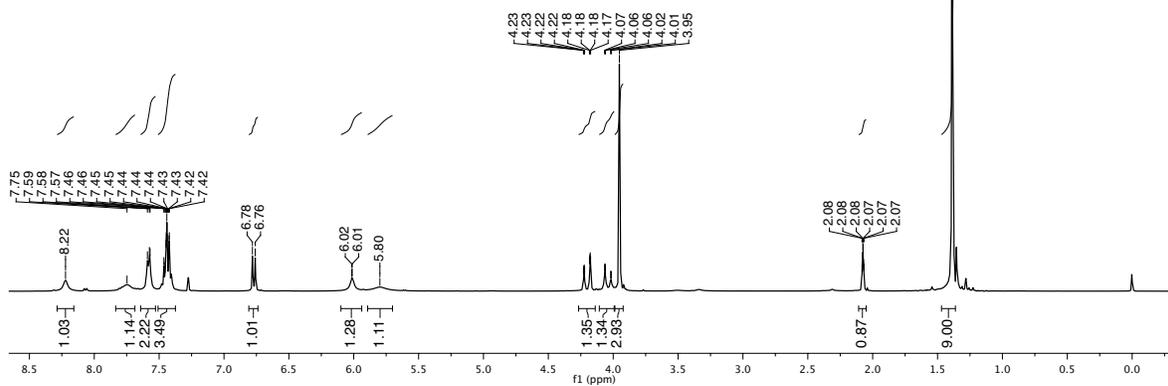
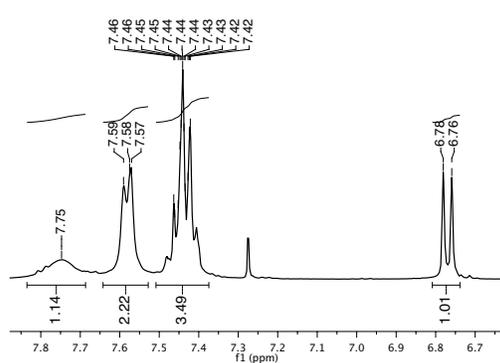
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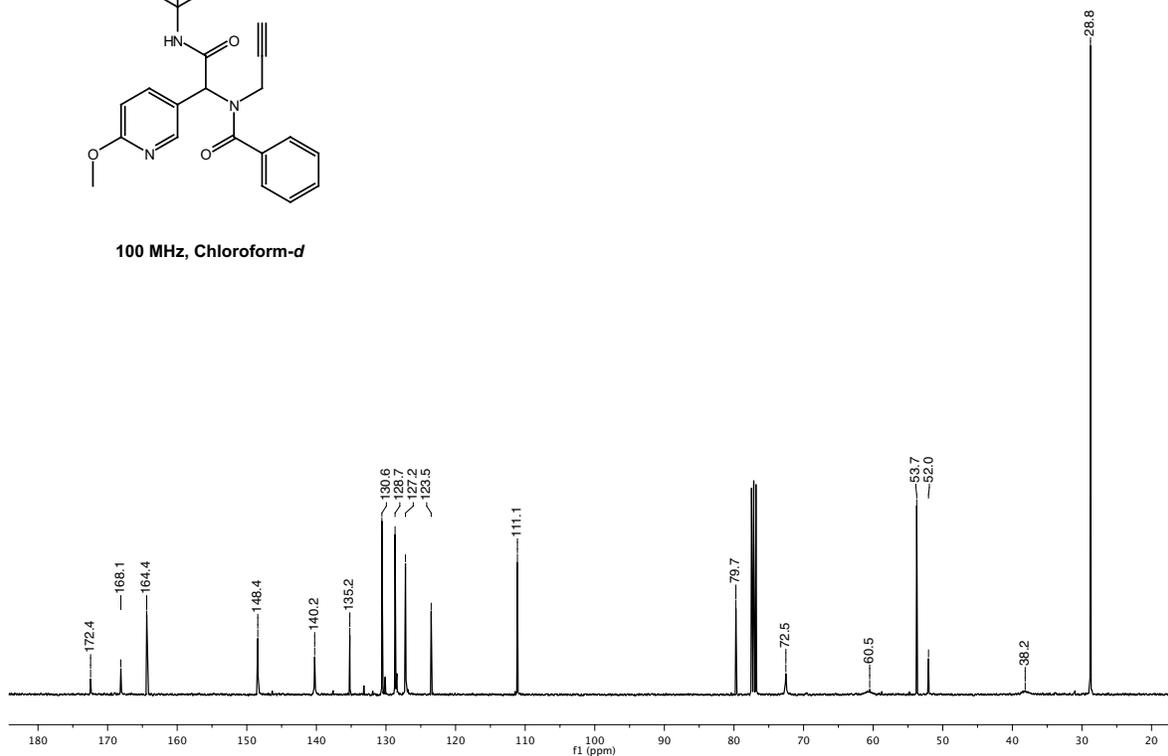
***N*-(2-(*tert*-butylamino)-1-(6-methoxypyridin-3-yl)-2-oxoethyl)-*N*-(prop-2-yn-1-yl)benzamide 6j**



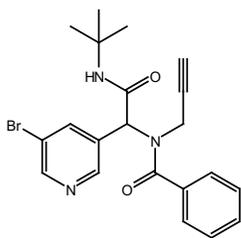
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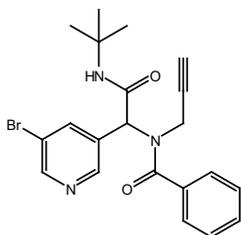
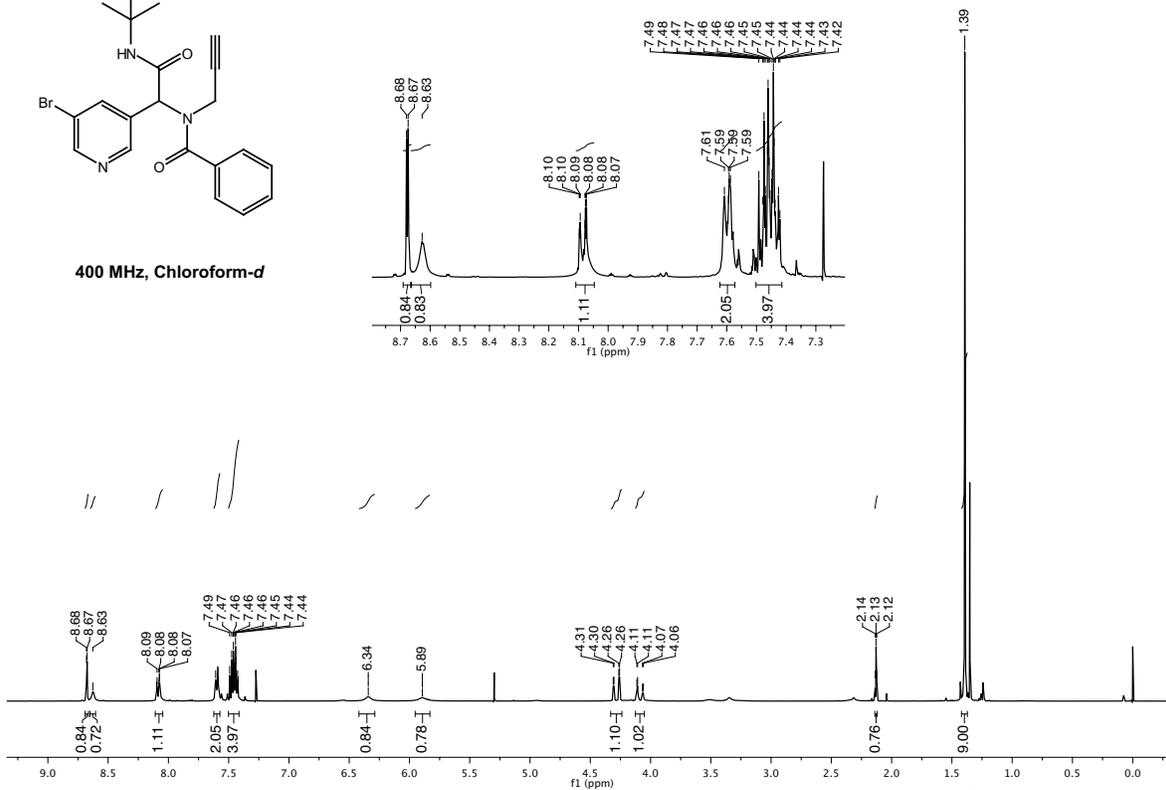
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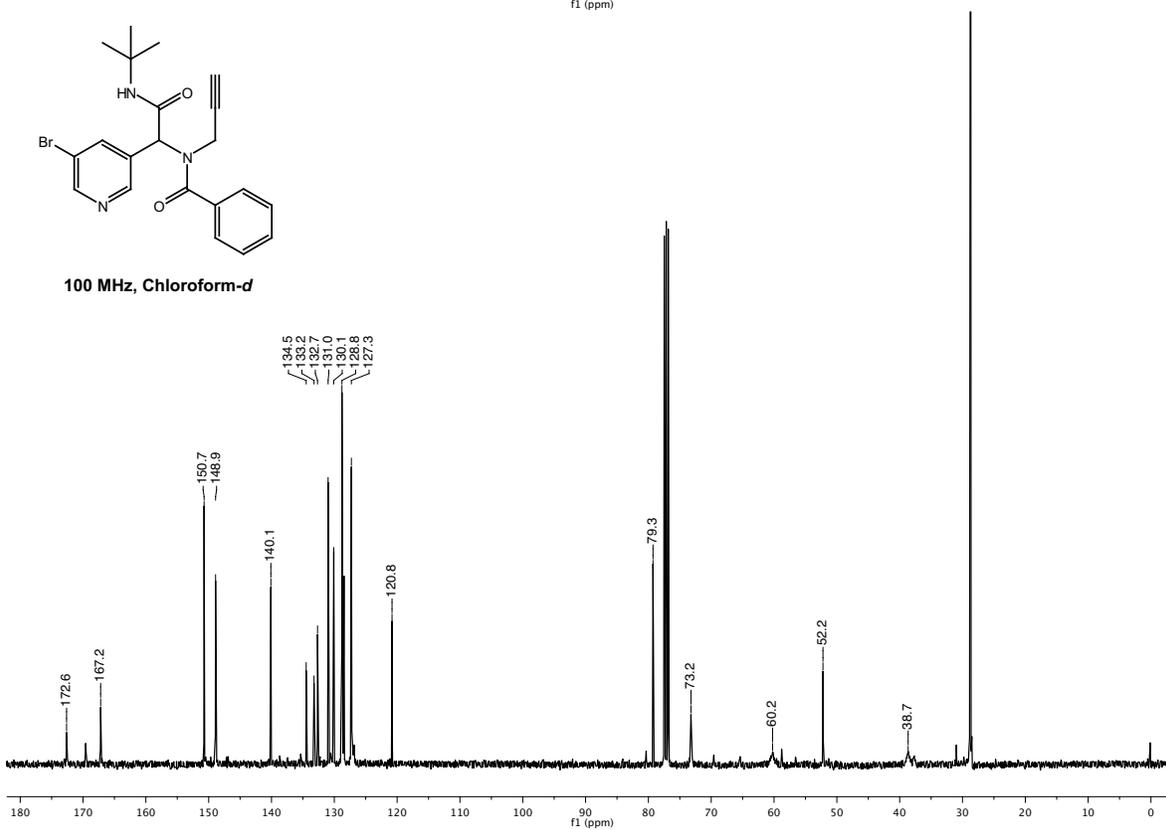
***N*-(1-(5-bromopyridin-3-yl)-2-(*tert*-butylamino)-2-oxoethyl)-*N*-(prop-2-yn-1-yl)benzamide 6l**



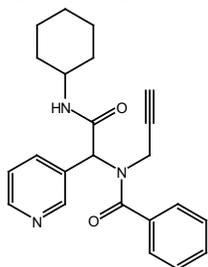
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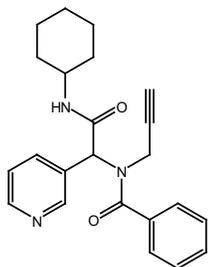
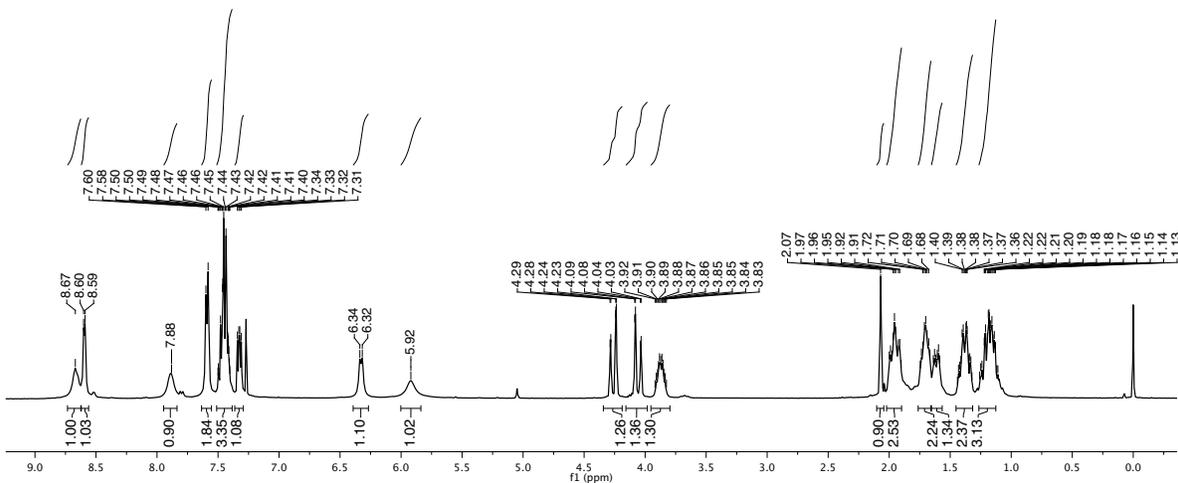
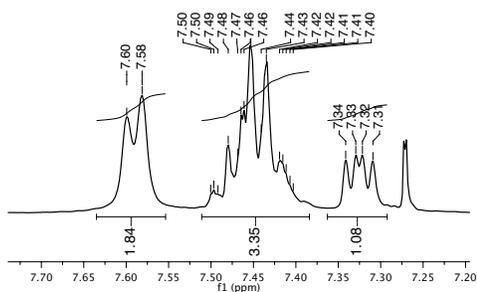
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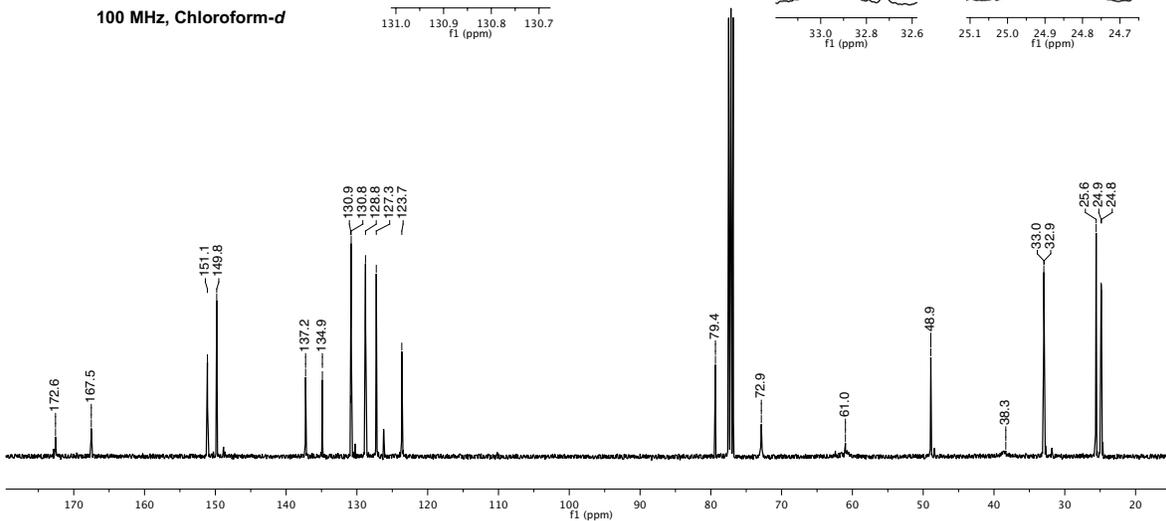
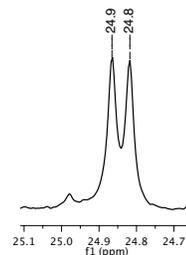
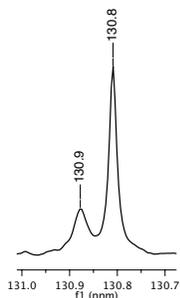
***N*-(2-(cyclohexylamino)-2-oxo-1-(pyridin-3-yl)ethyl)-*N*-(prop-2-yn-1-yl)benzamide 6m**



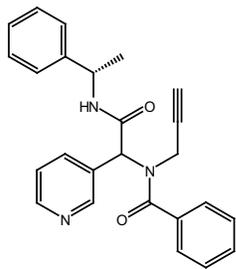
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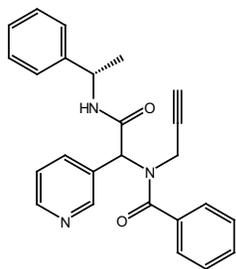
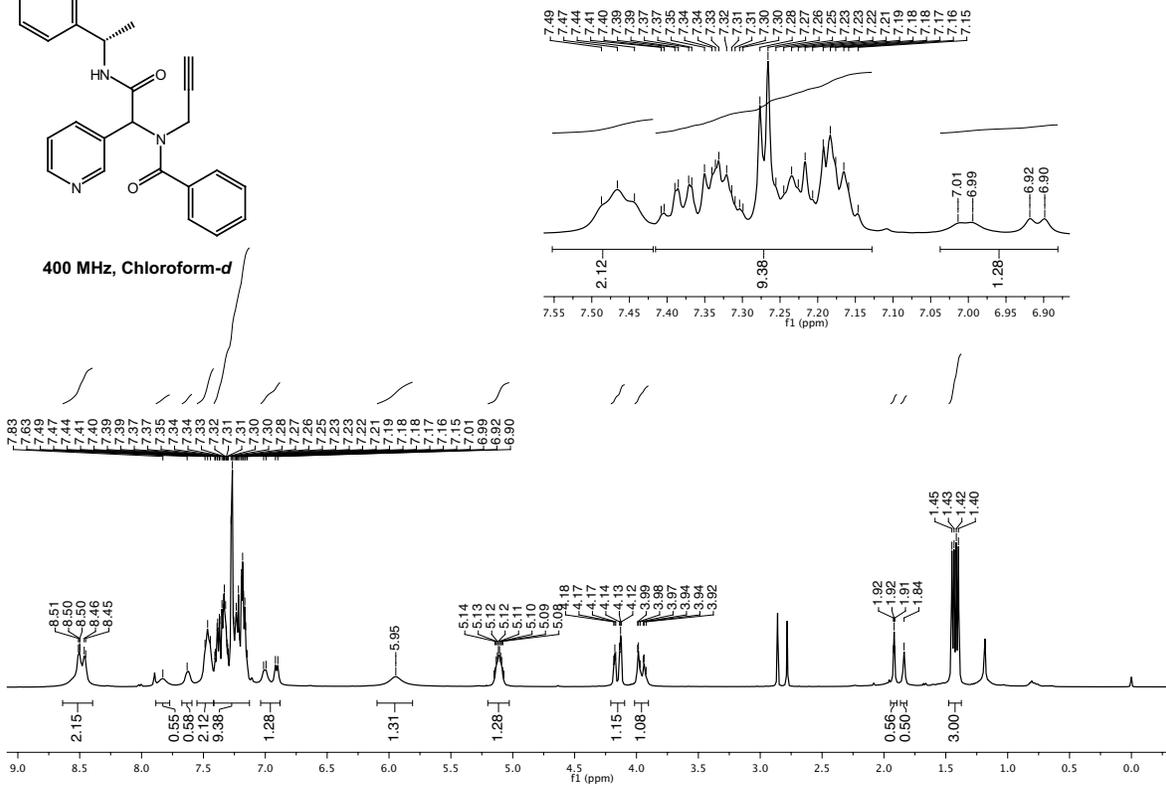
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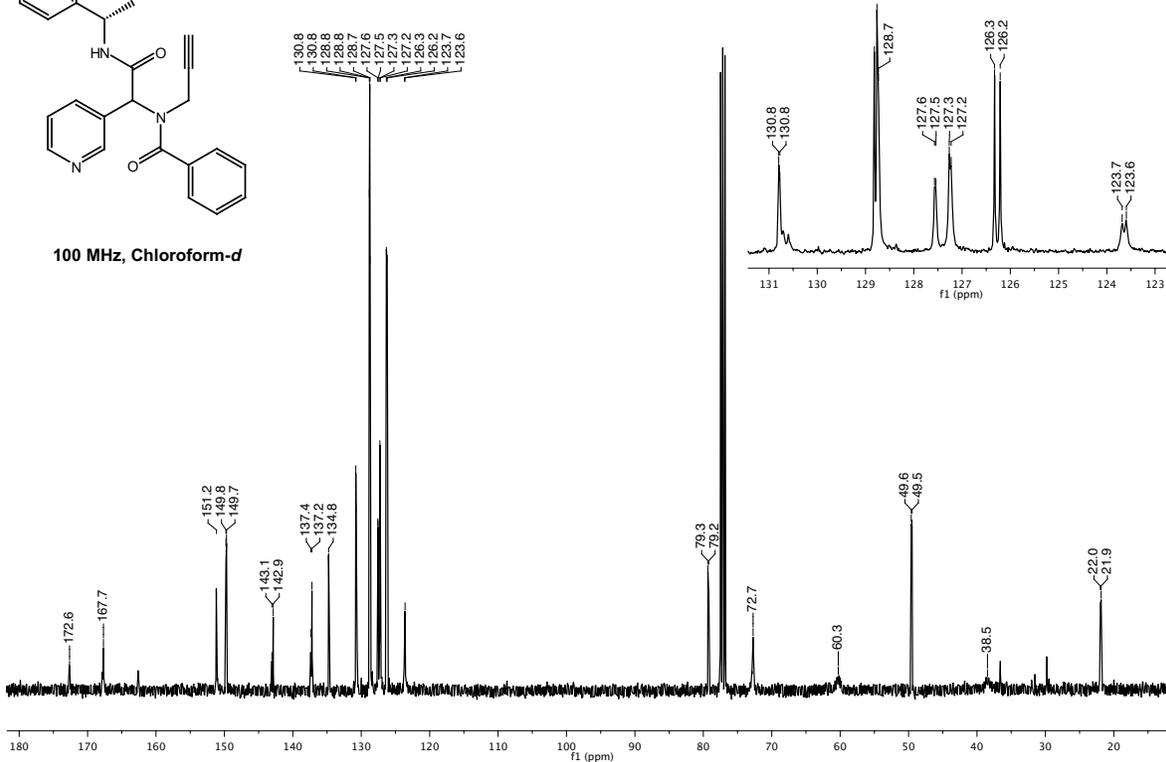
***N*-(2-oxo-2-(((*S*)-1-phenylethyl)amino)-1-(pyridin-3-yl)ethyl)-*N*-(prop-2-yn-1-yl)benzamide 6n**



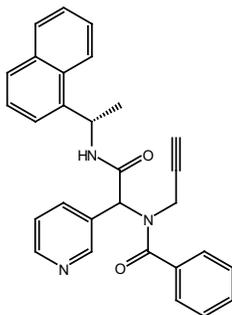
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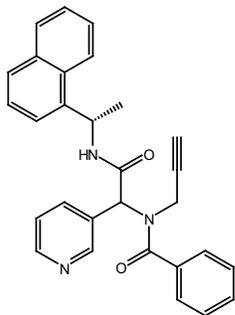
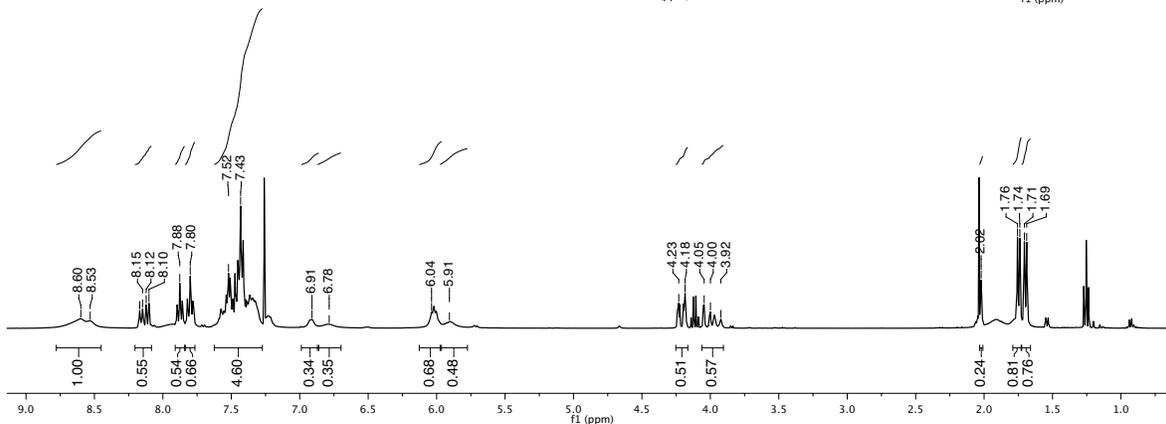
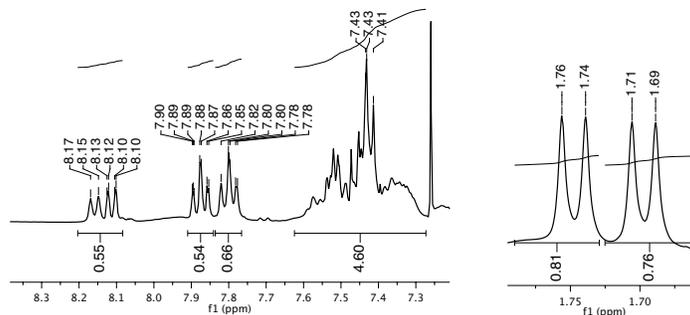
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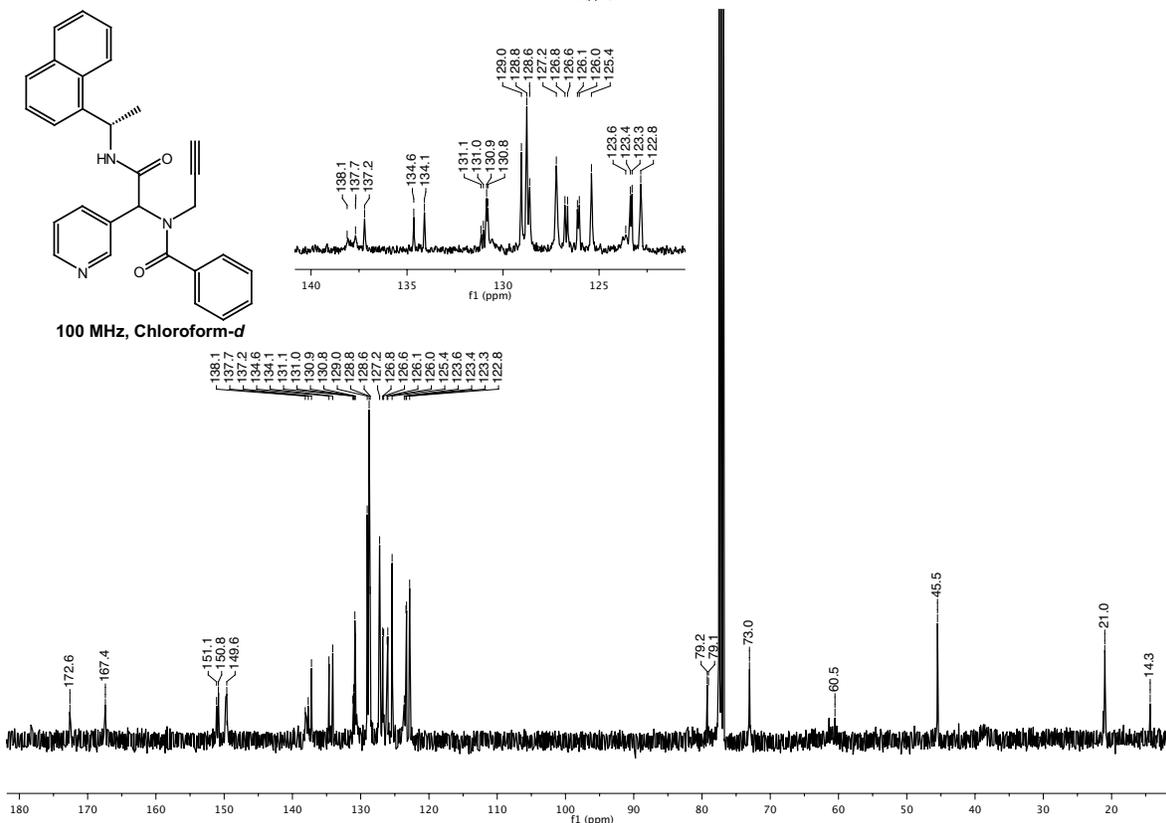
***N*-(2-(((*S*)-1-(naphthalen-1-yl)ethyl)amino)-2-oxo-1-(pyridin-3-yl)ethyl)-*N*-(prop-2-yn-1-yl)benzamide 6n'**



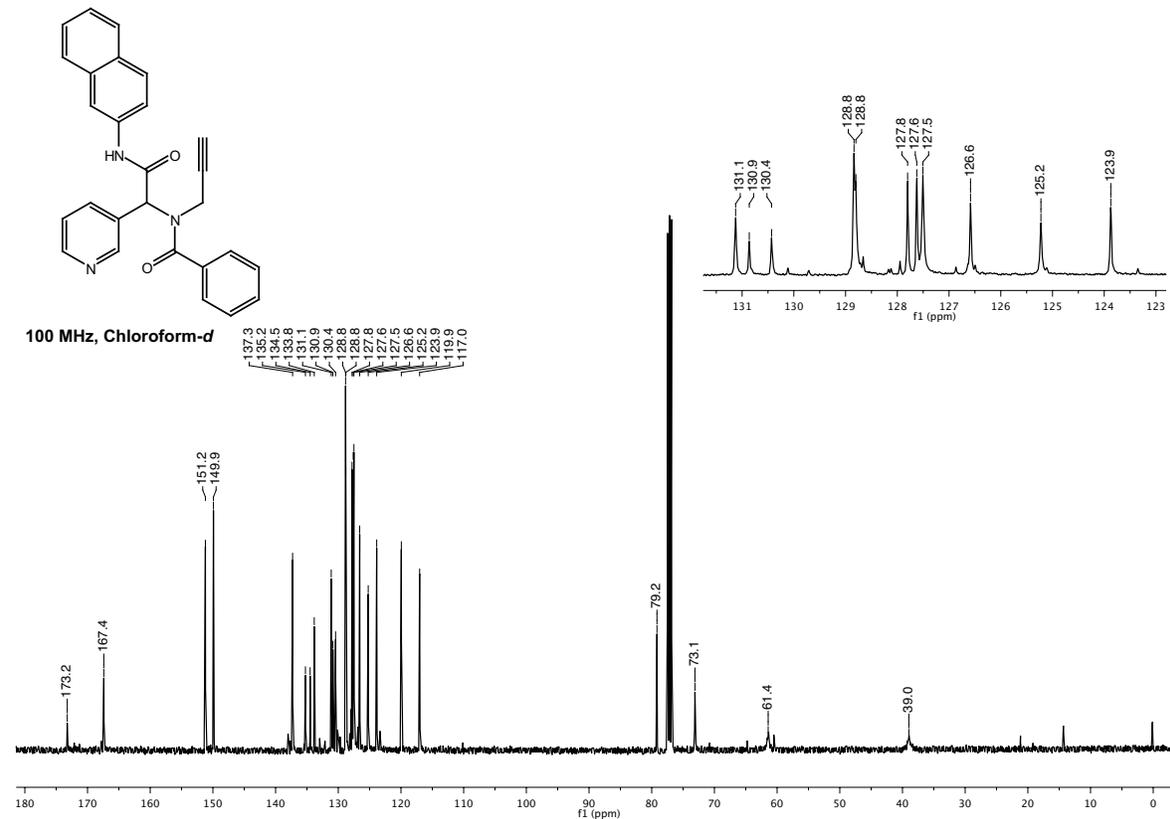
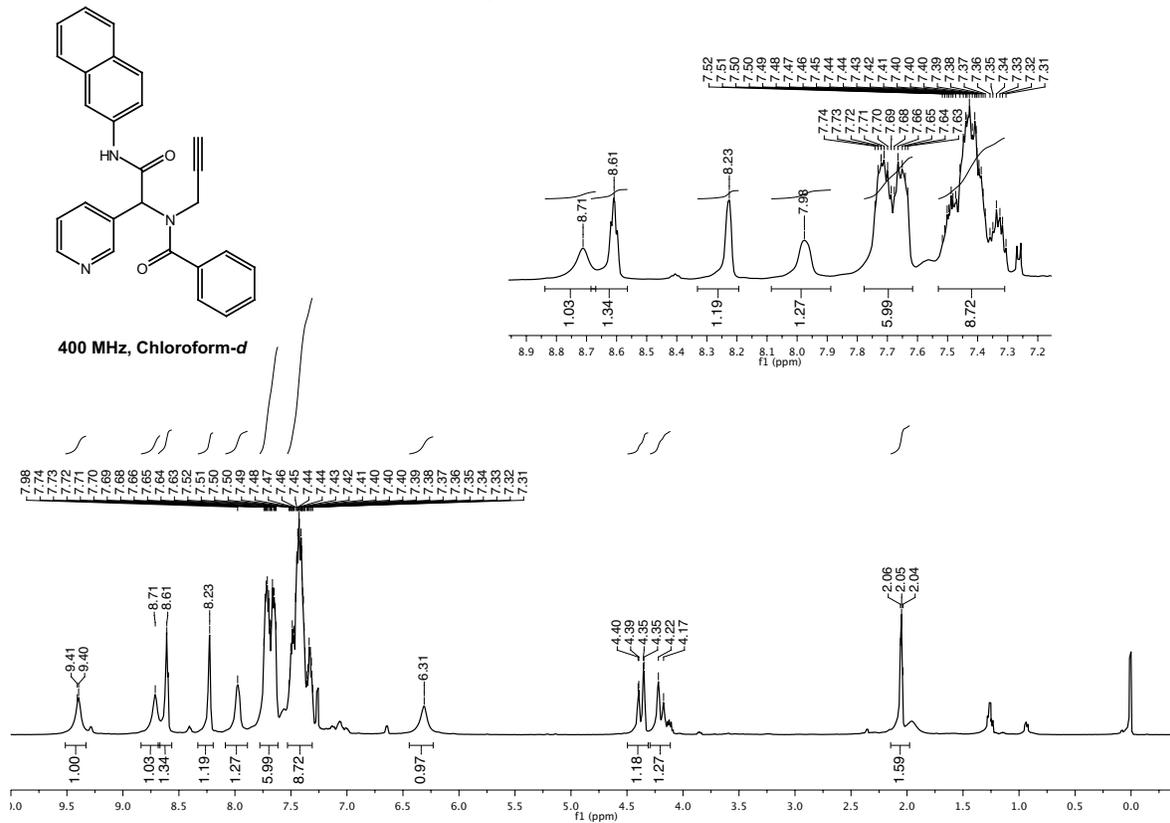
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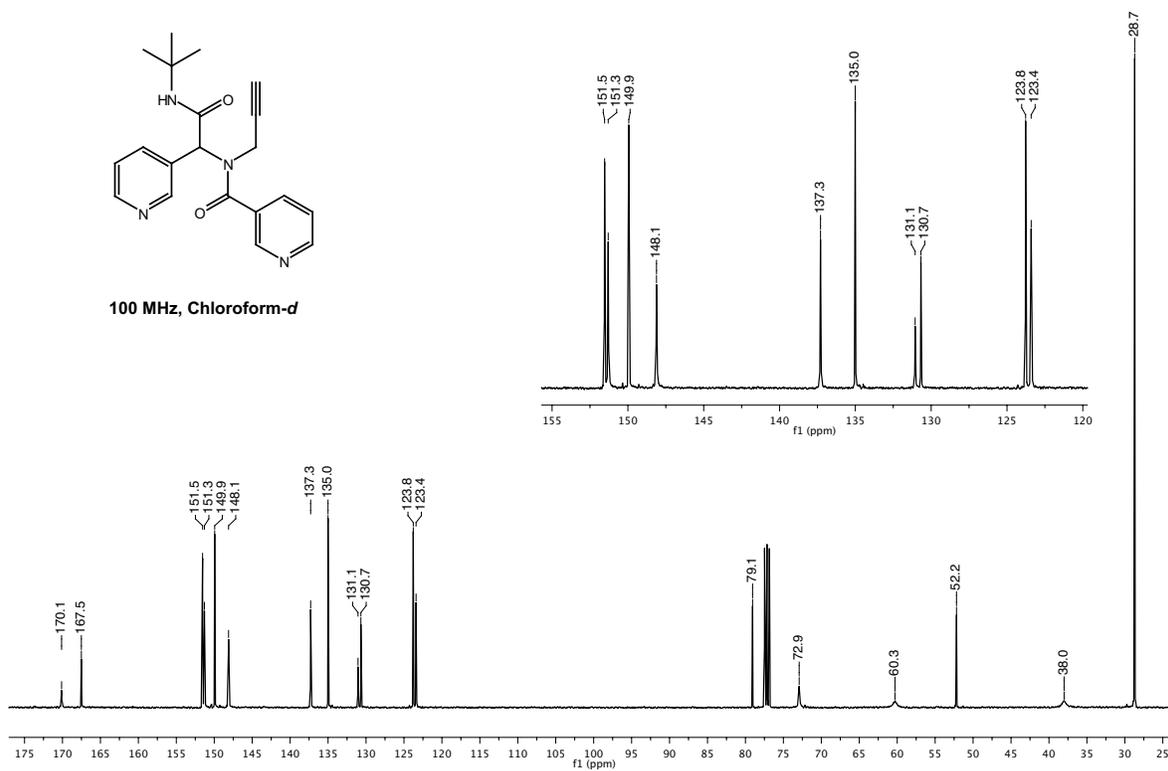
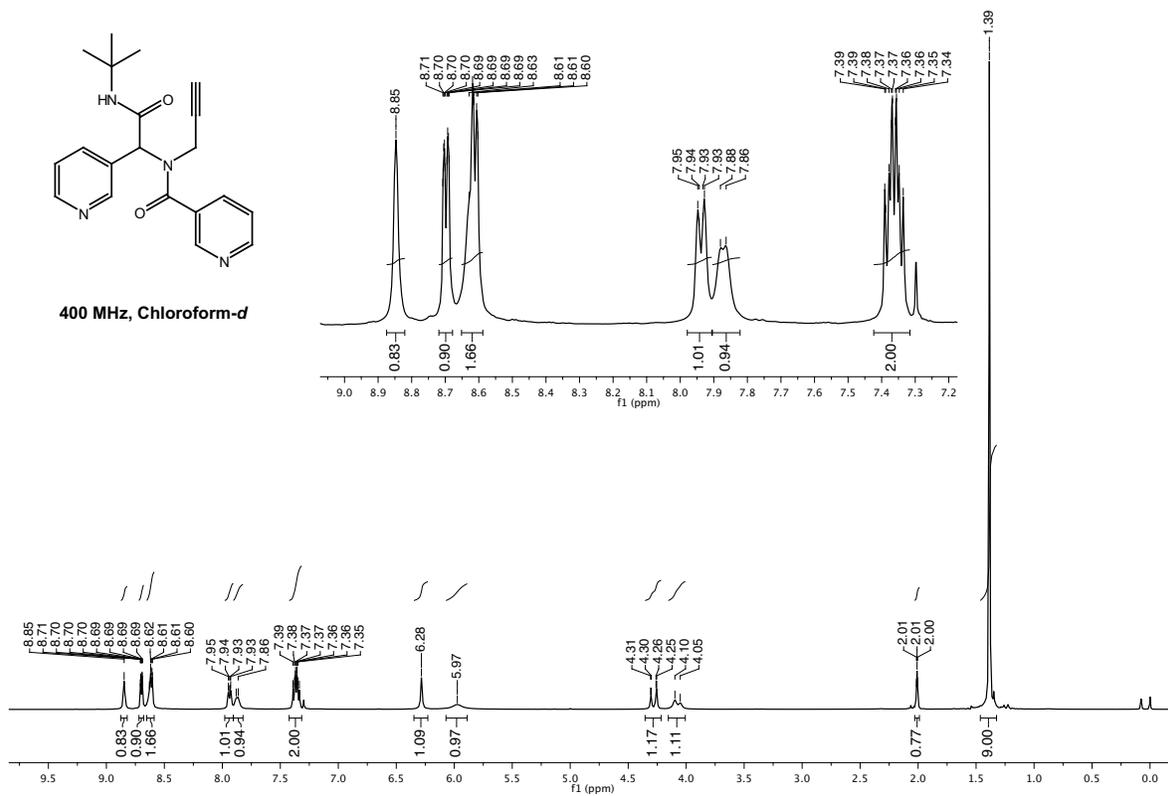
100 MHz, Chloroform-*d*



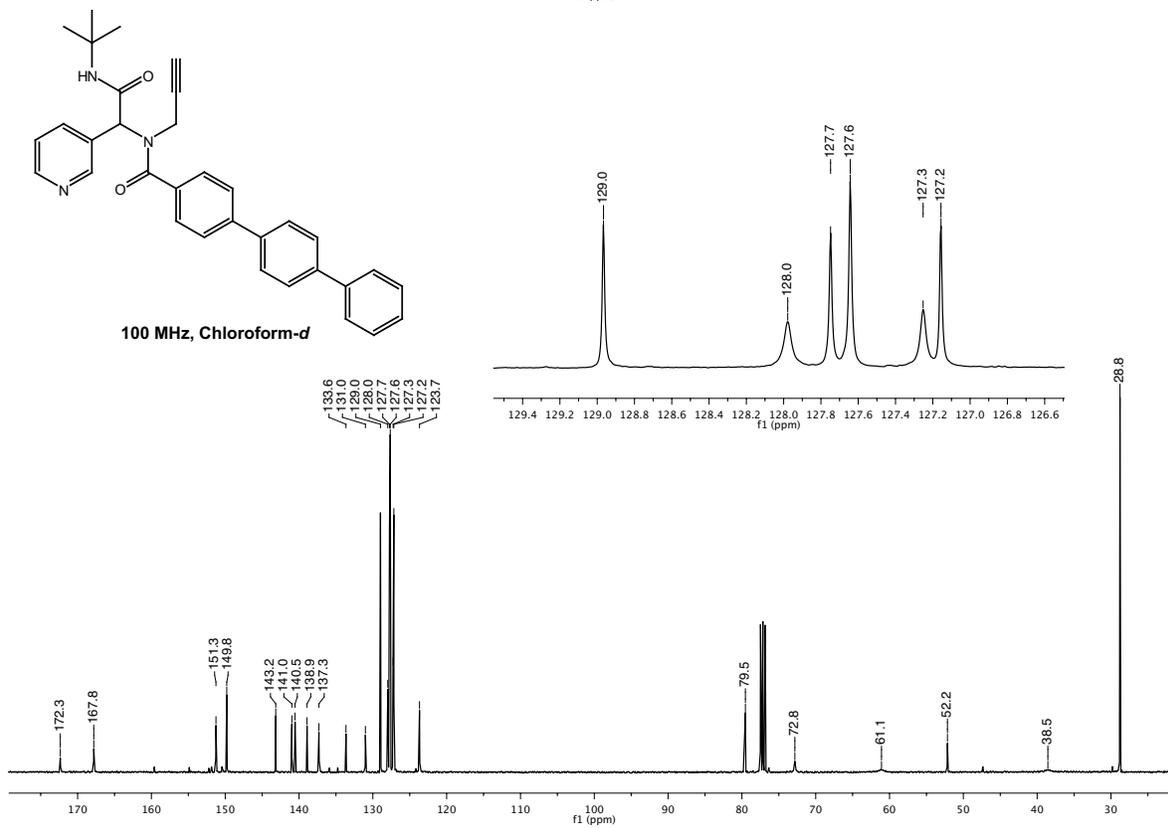
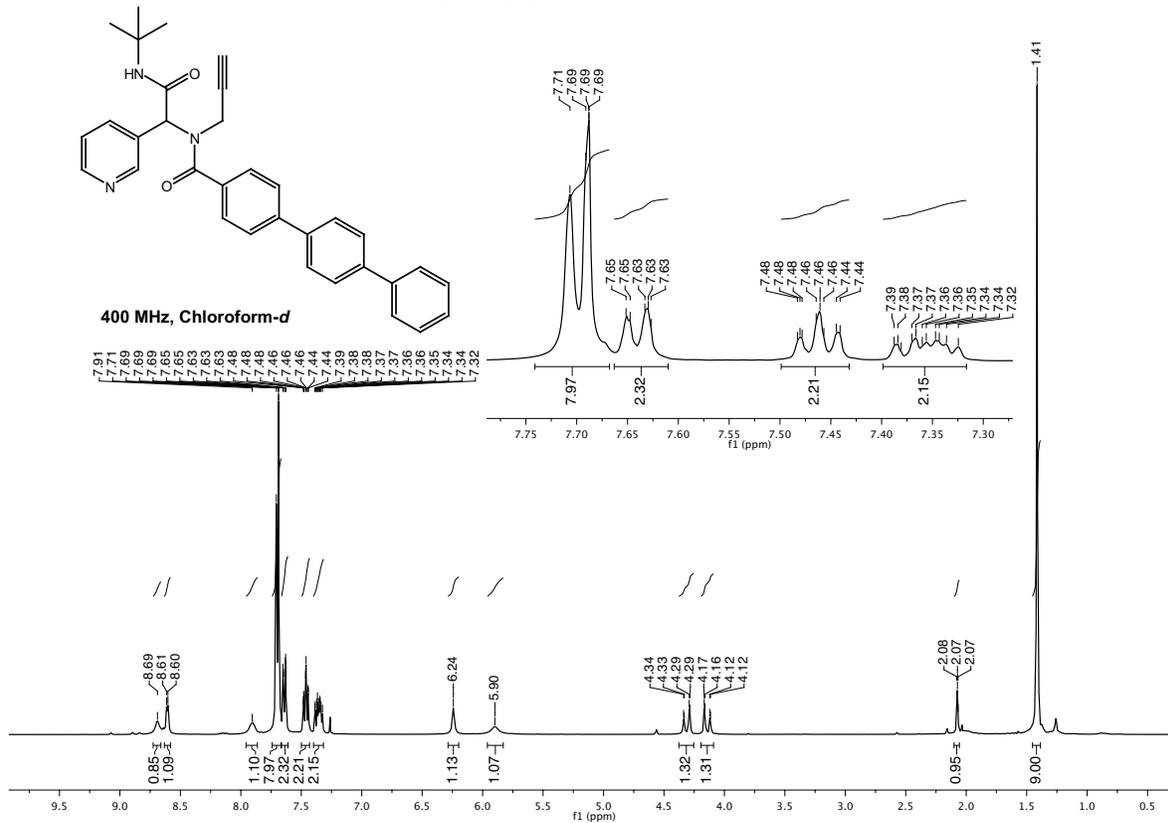
***N*-(2-(naphthalen-2-ylamino)-2-oxo-1-(pyridin-3-yl)ethyl)-*N*-(prop-2-yn-1-yl)benzamide 60**



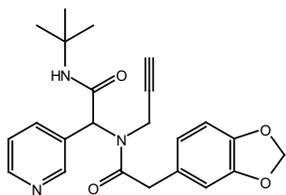
***N*-(2-(*tert*-butylamino)-2-oxo-1-(pyridin-3-yl)ethyl)-*N*-(prop-2-yn-1-yl)nicotinamide 6p**



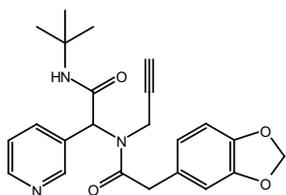
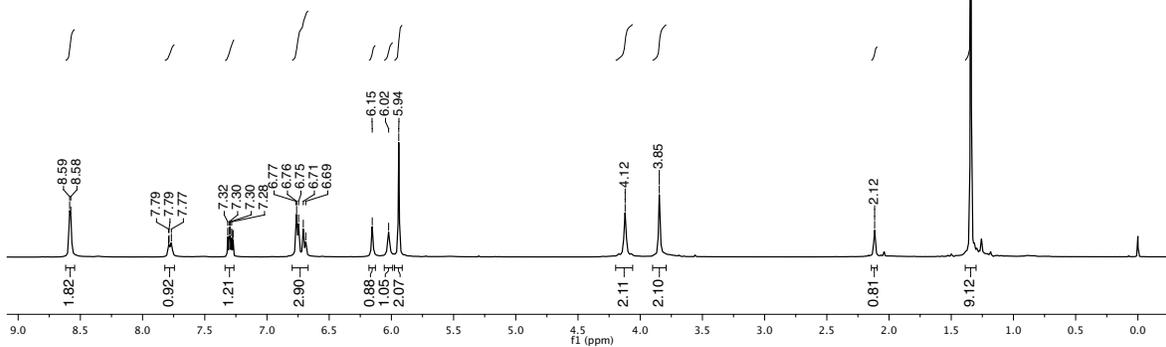
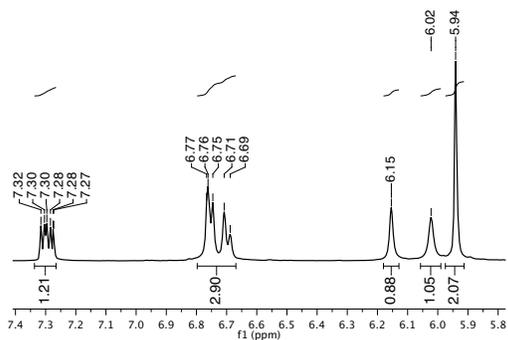
***N*-(2-(*tert*-butylamino)-2-oxo-1-(pyridin-3-yl)ethyl)-*N*-(prop-2-yn-1-yl)-[1,1':4',1''-terphenyl]-4-carboxamide 6r**



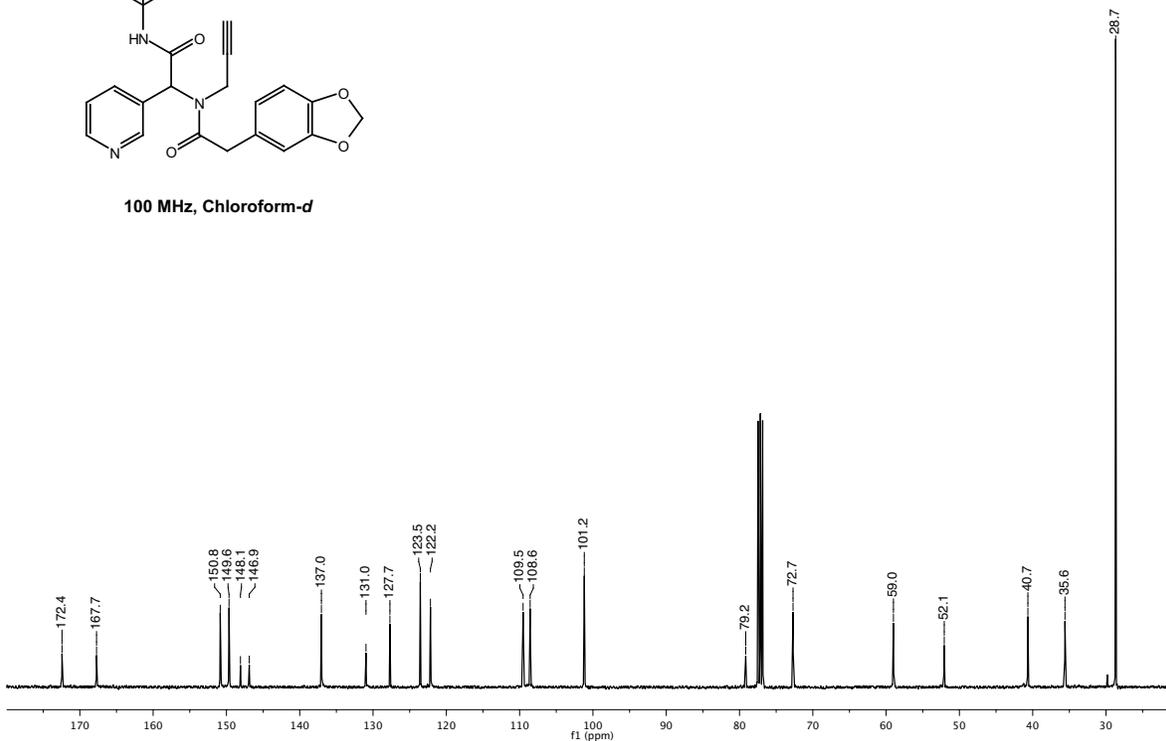
2-(benzo[d][1,3]dioxol-5-yl)-N-(2-(*tert*-butylamino)-2-oxo-1-(pyridin-3-yl)ethyl)-N-(prop-2-yn-1-yl)acetamide 6s



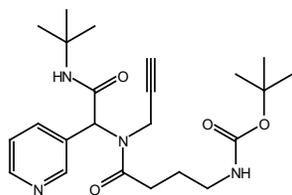
400 MHz, Chloroform-*d*



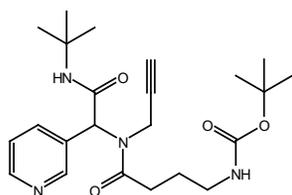
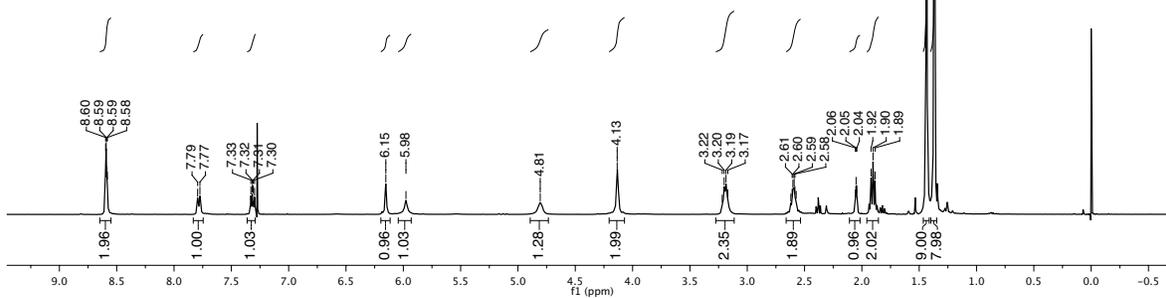
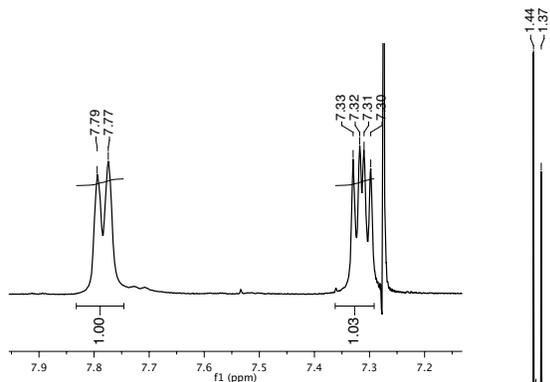
100 MHz, Chloroform-*d*



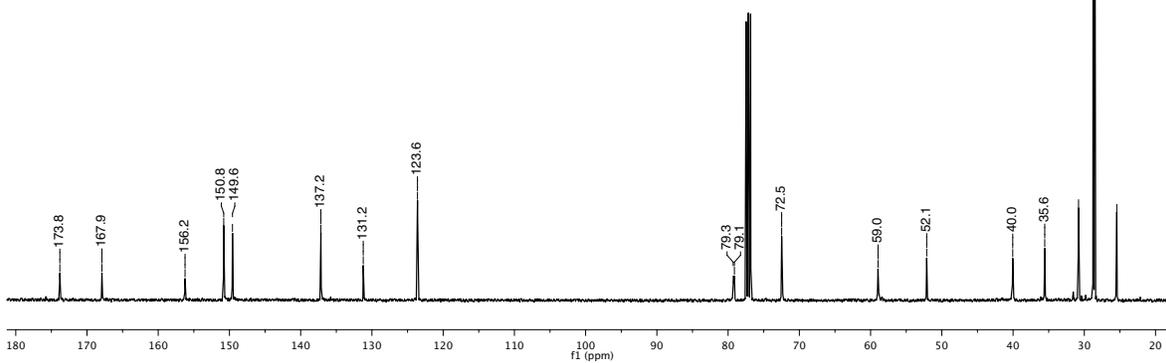
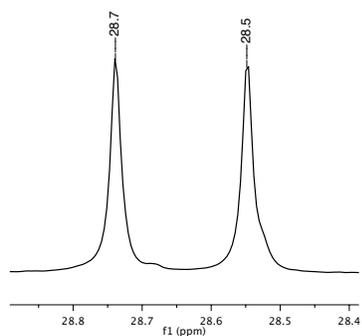
***tert*-butyl (4-((2-((*tert*-butylamino)-2-oxo-1-(pyridin-3-yl)ethyl)(prop-2-yn-1-yl)amino)-4-oxobutyl)carbamate 6t**



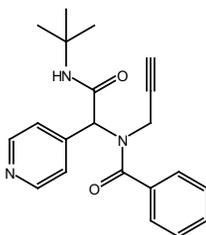
400 MHz, Chloroform-*d*



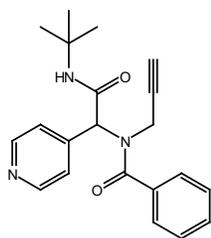
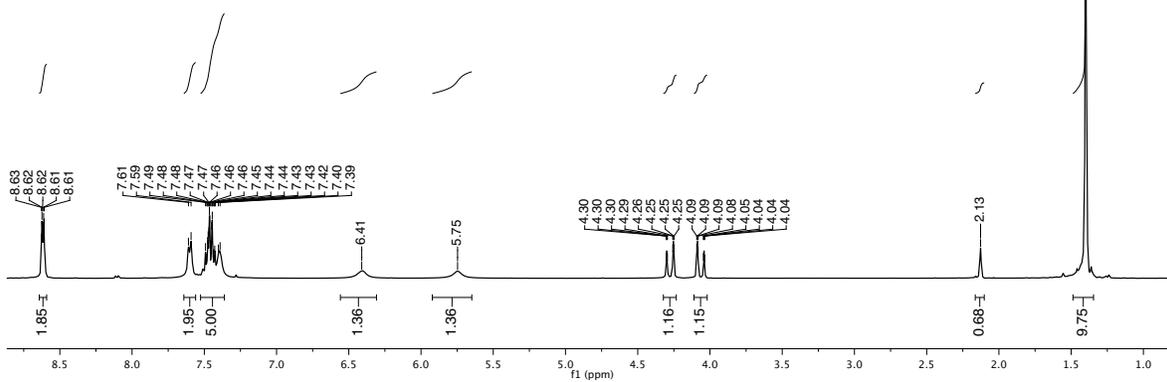
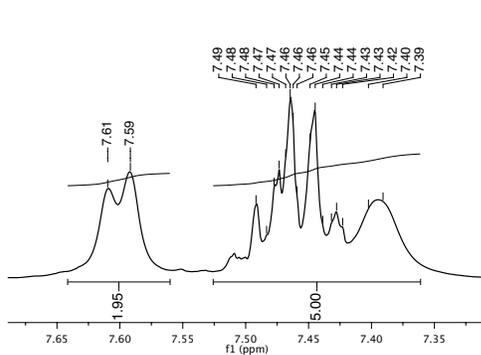
100 MHz, Chloroform-*d*



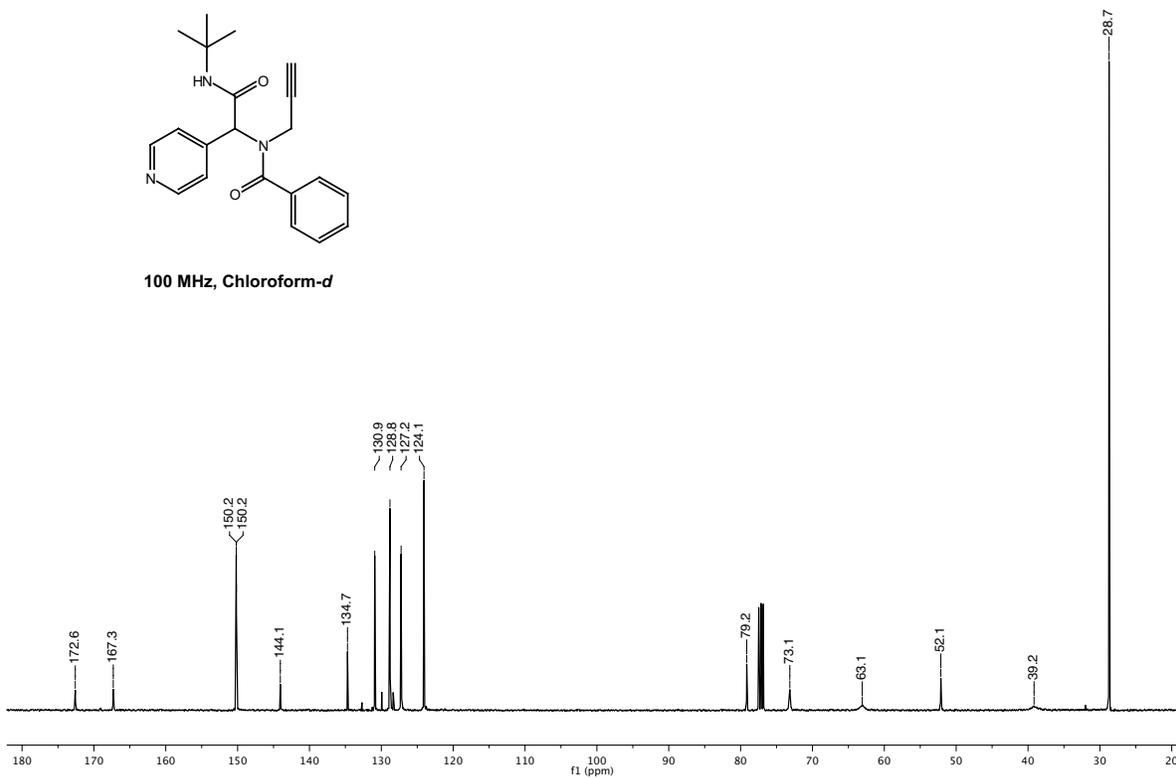
***N*-2-(*tert*-butylamino)-2-oxo-1-(pyridin-4-yl)ethyl)-*N*-(prop-2-yn-1-yl)benzamide 6v**



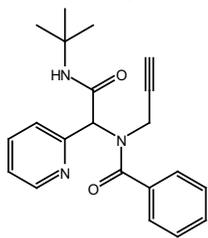
400 MHz, Chloroform-*d*



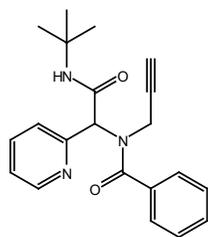
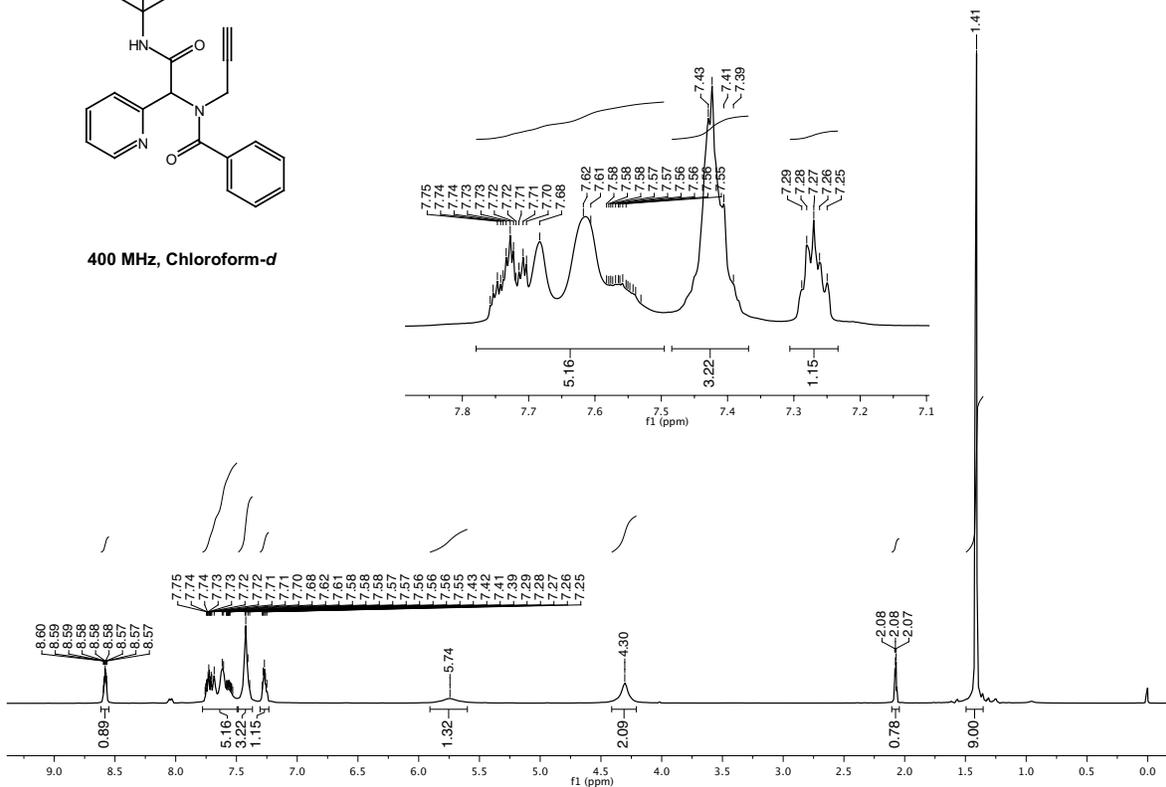
100 MHz, Chloroform-*d*



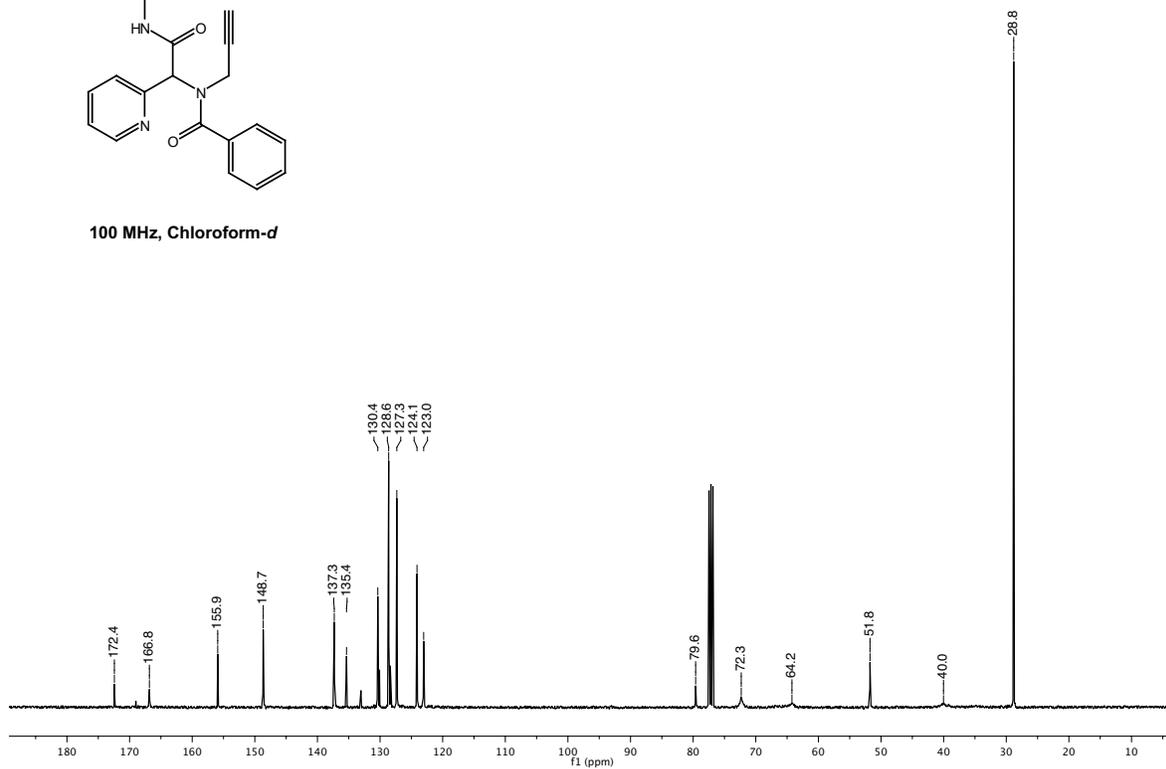
***N*-(2-(*tert*-butylamino)-2-oxo-1-(pyridin-2-yl)ethyl)-*N*-(prop-2-yn-1-yl)benzamide 6w**



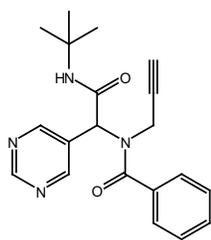
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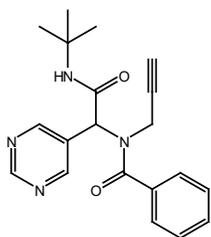
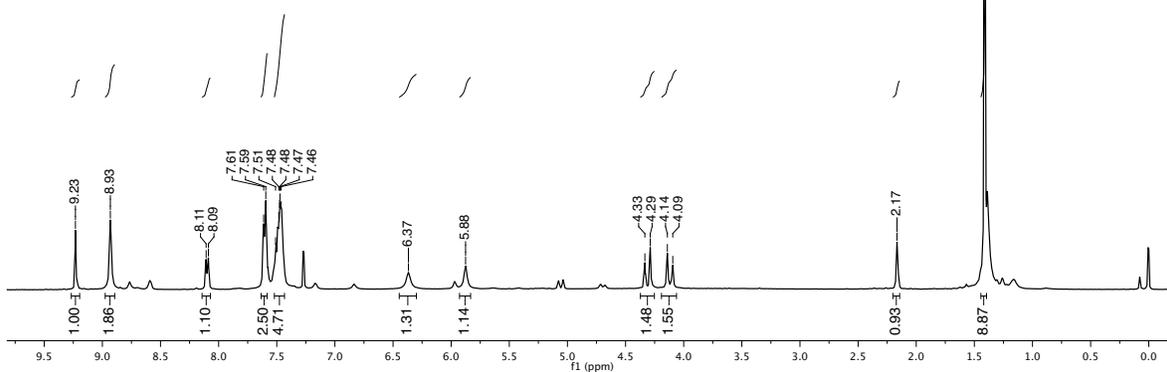
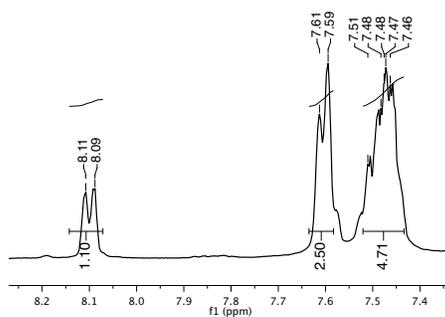
100 MHz, Chloroform-*d*



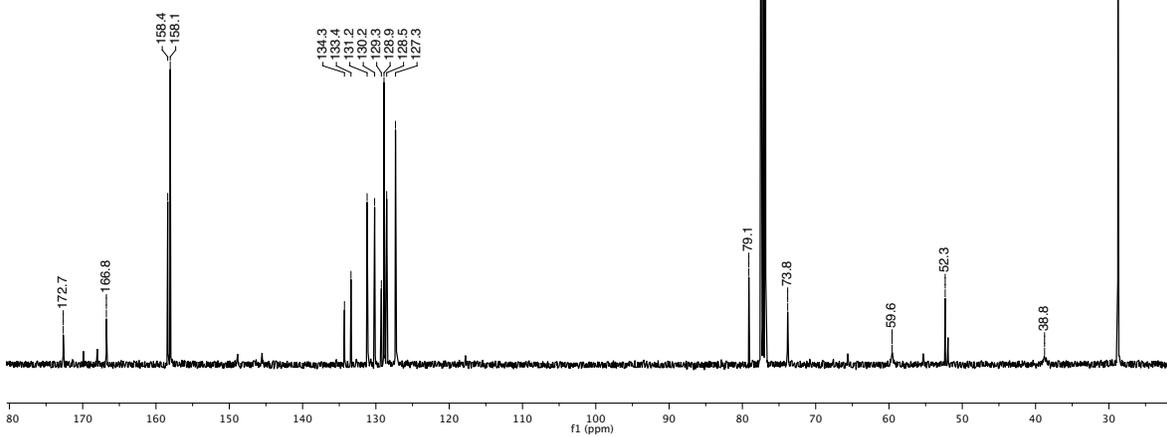
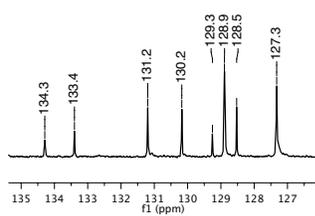
***N*-(2-(*tert*-butylamino)-2-oxo-1-(pyrimidin-5-yl)ethyl)-*N*-(prop-2-yn-1-yl)benzamide 6x**



400 MHz, Chloroform-*d*

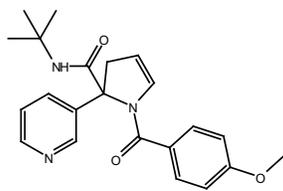


100 MHz, Chloroform-*d*

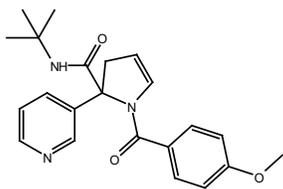
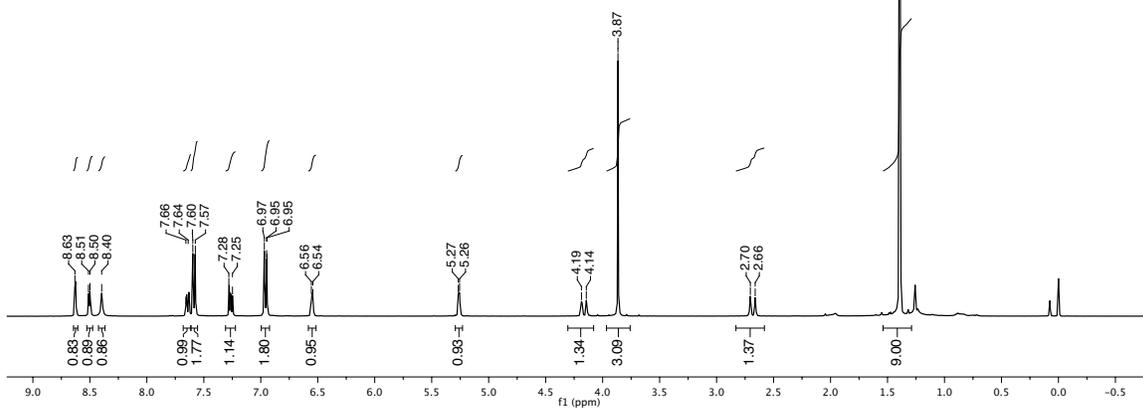
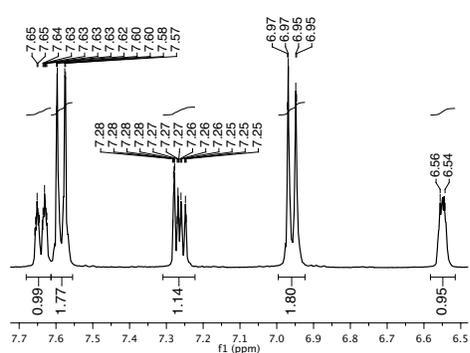


NICOTINE ANALOGS SPECTRA

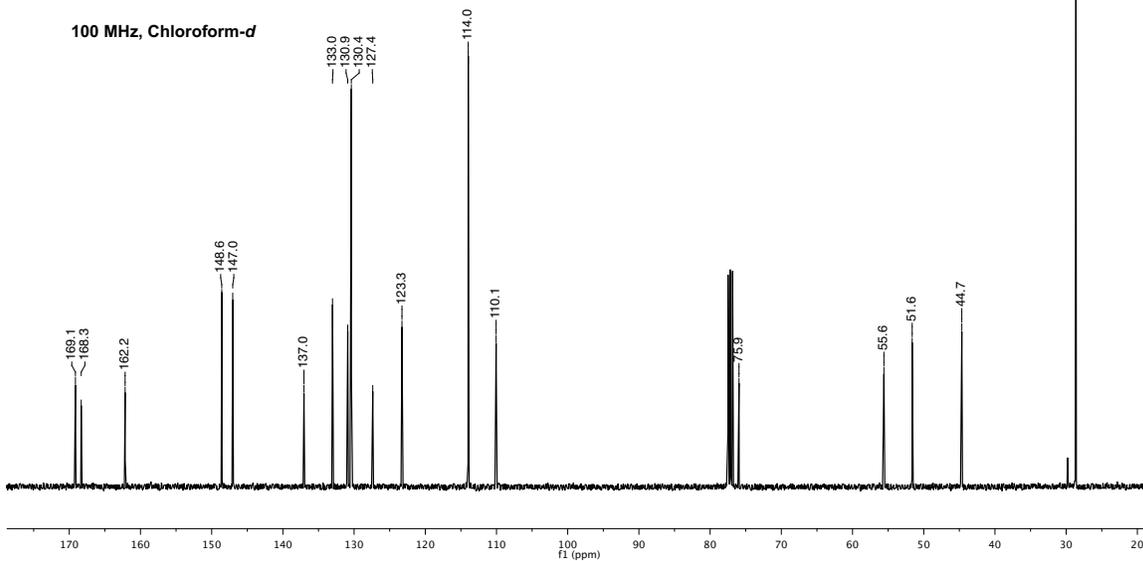
N-(*tert*-butyl)-1-(4-methoxybenzoyl)-2-(pyridin-3-yl)-2,3-dihydro-1*H*-pyrrole-2-carboxamide **7b**



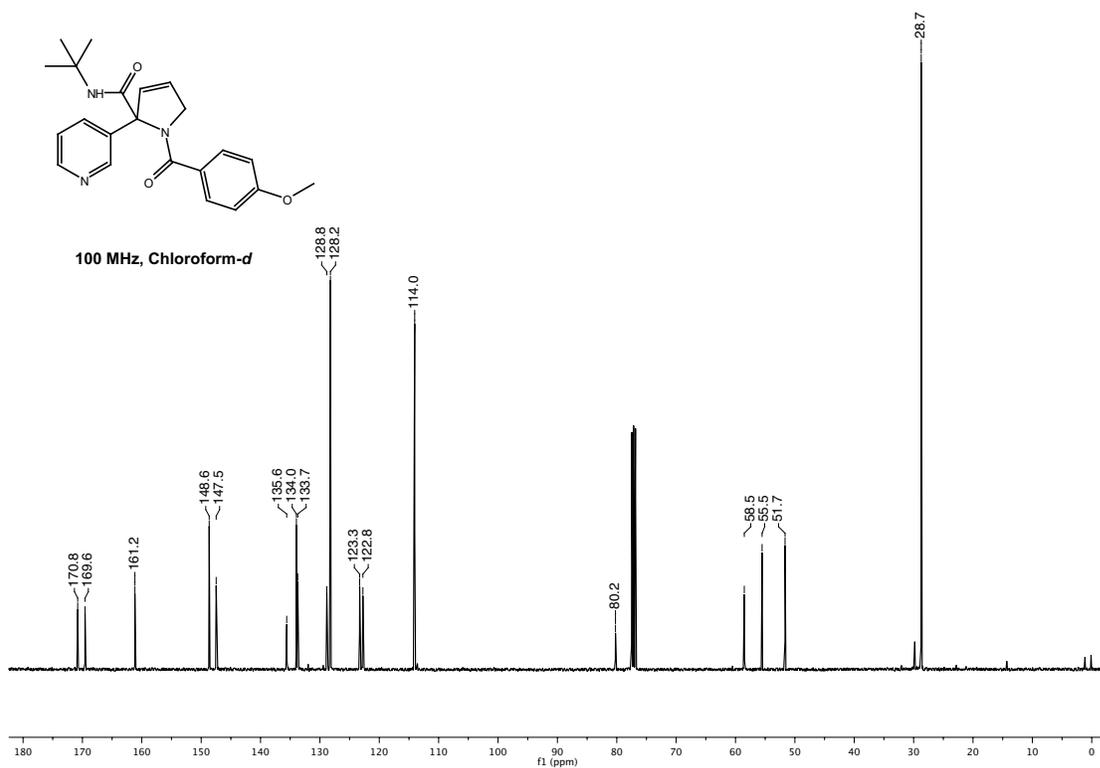
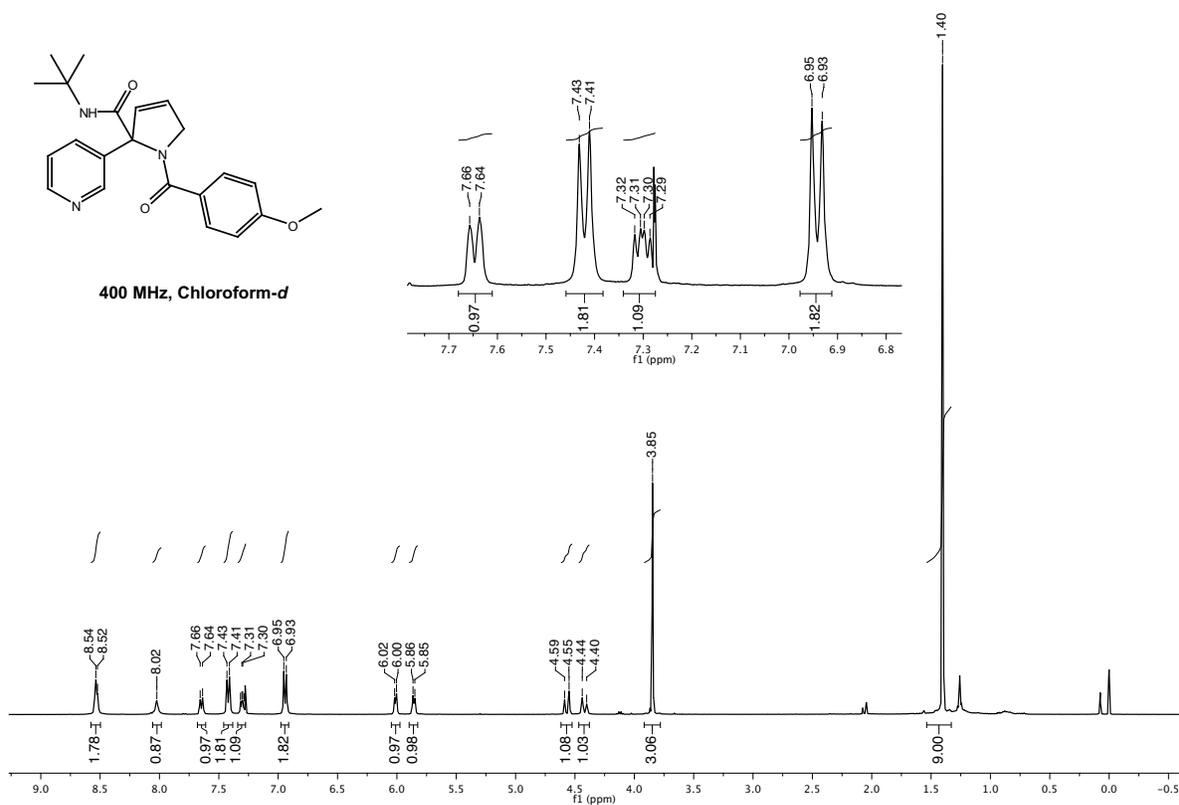
400 MHz, Chloroform-*d*



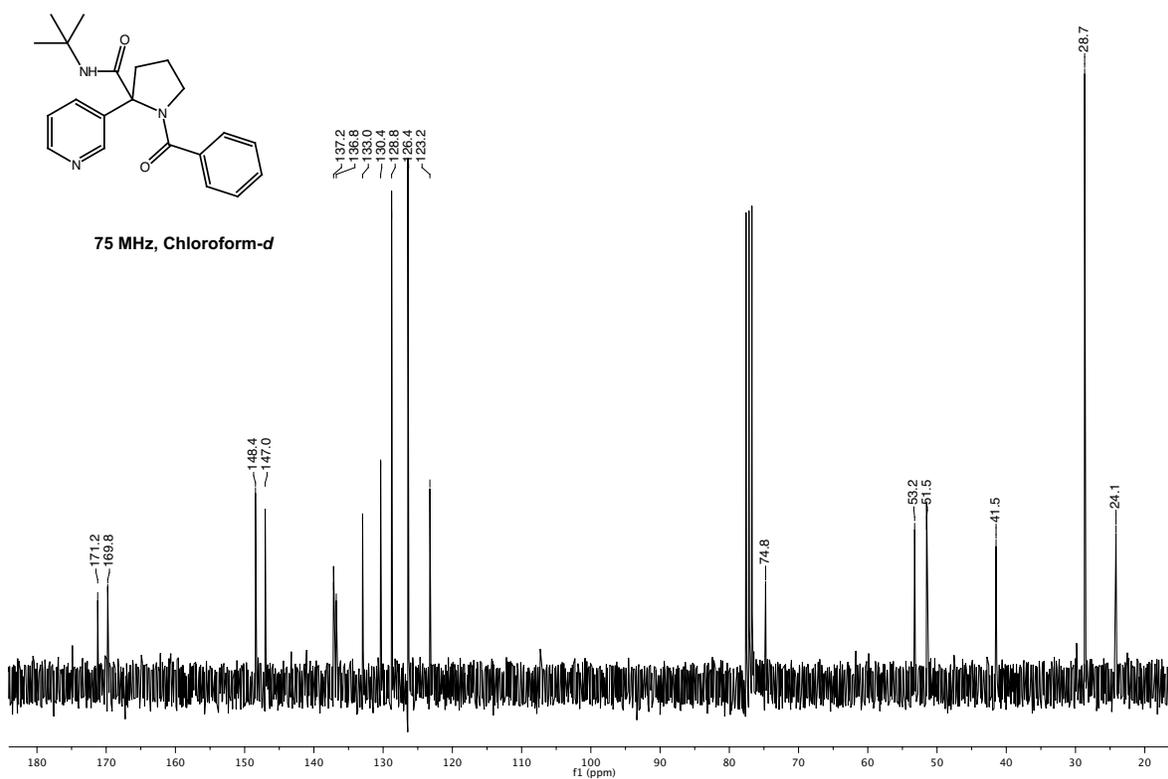
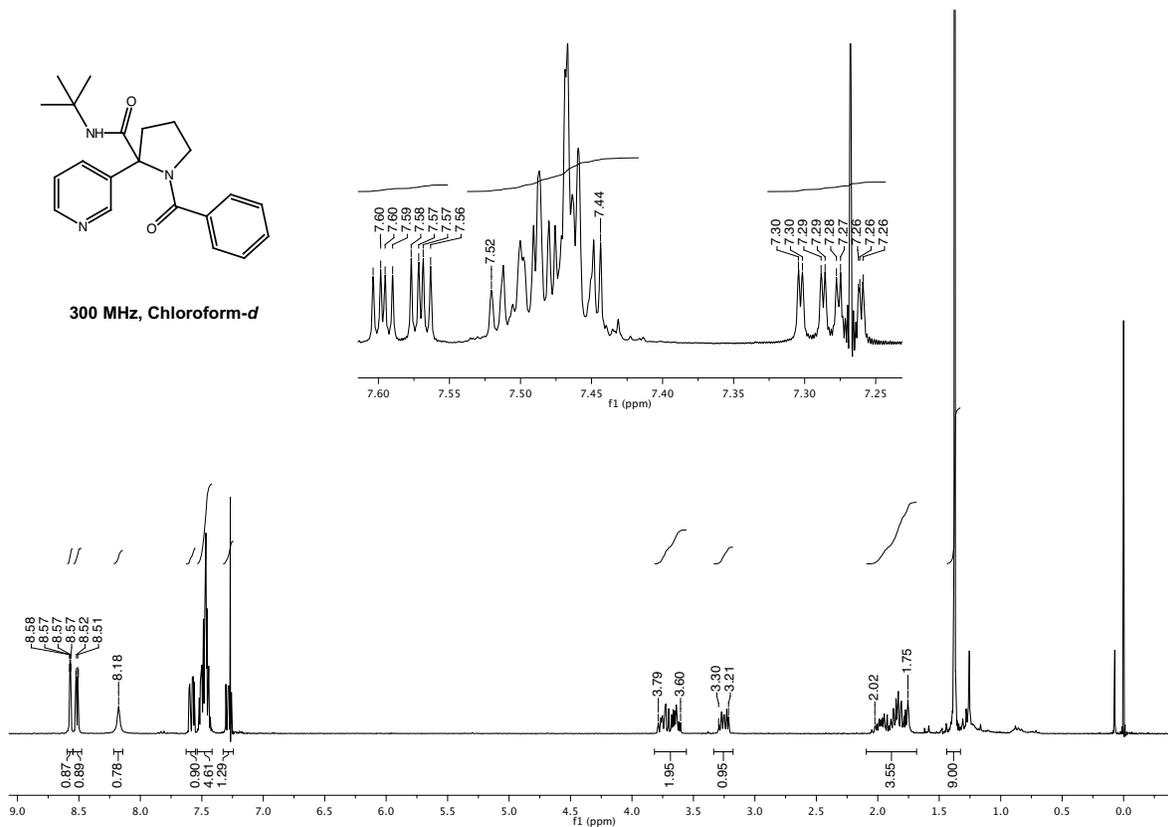
100 MHz, Chloroform-*d*



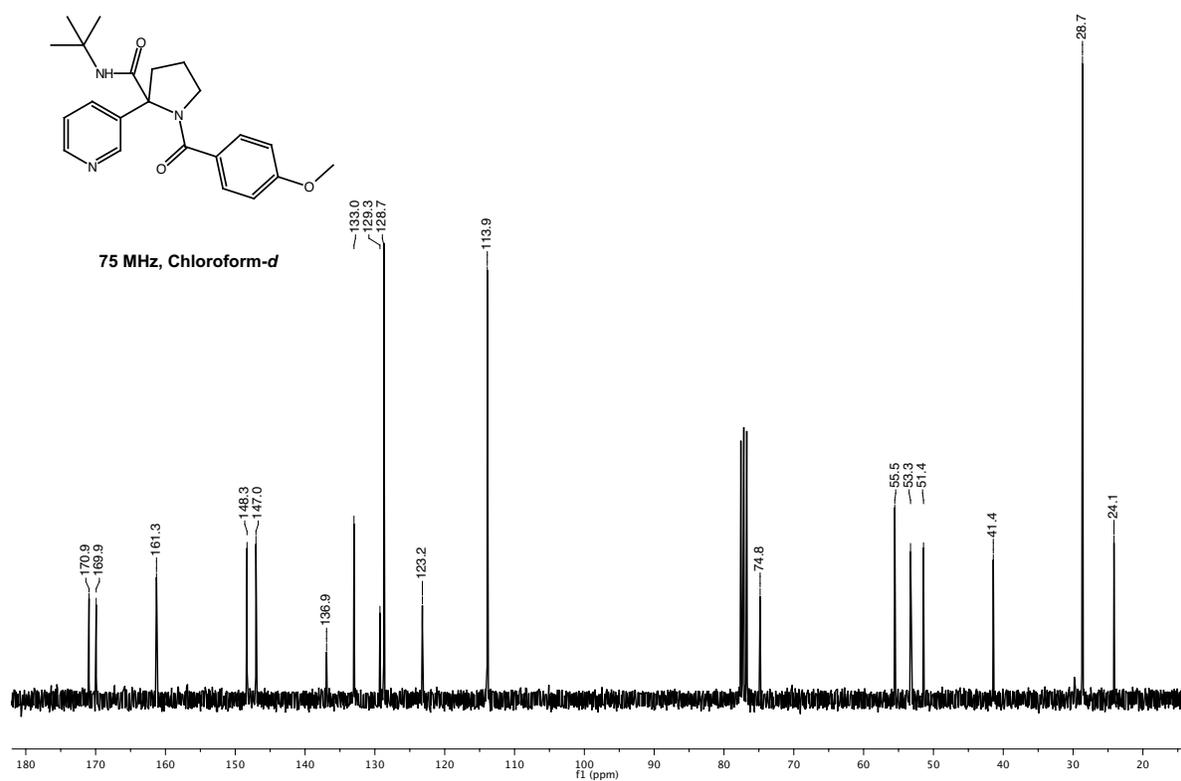
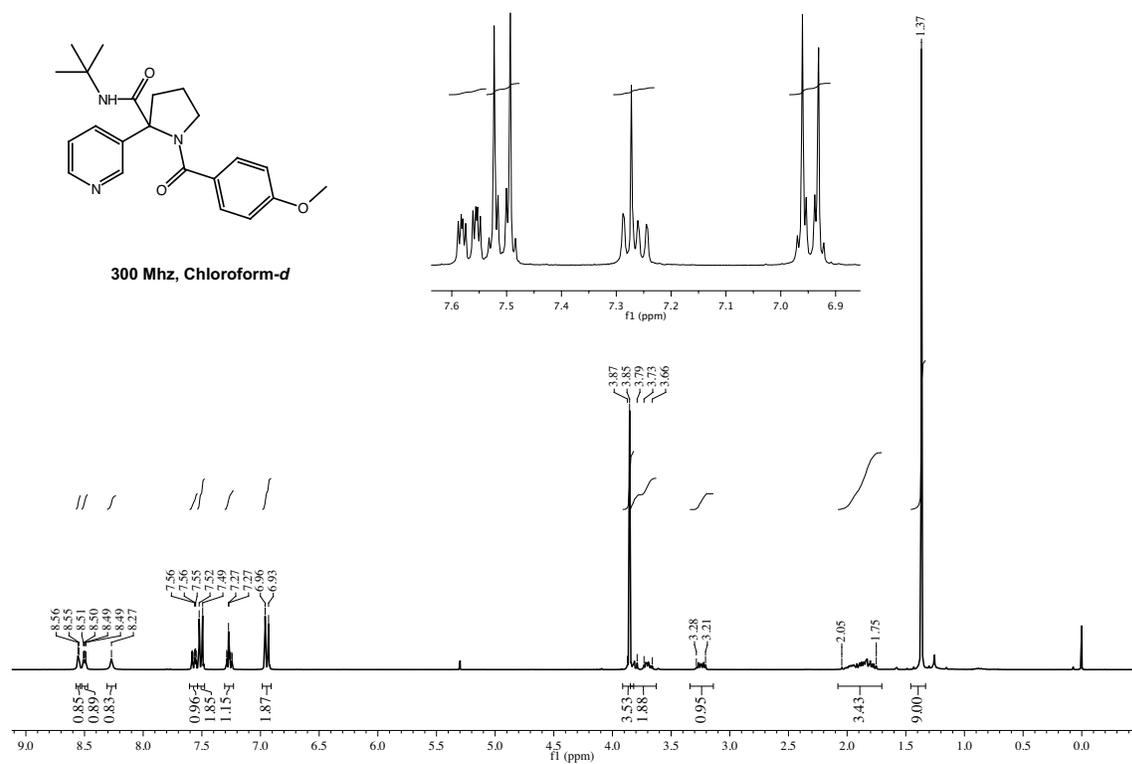
***N*-(*tert*-butyl)-1-(4-methoxybenzoyl)-2-(pyridin-3-yl)-2,5-dihydro-1*H*-pyrrole-2-carboxamide 7b'**



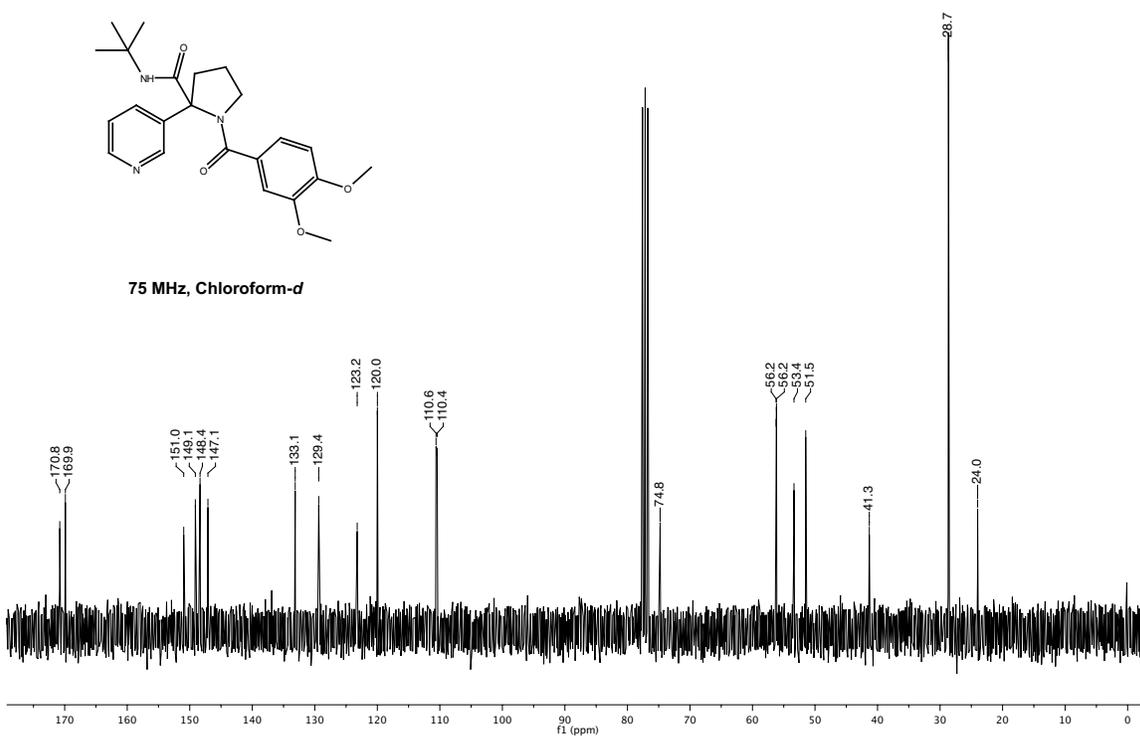
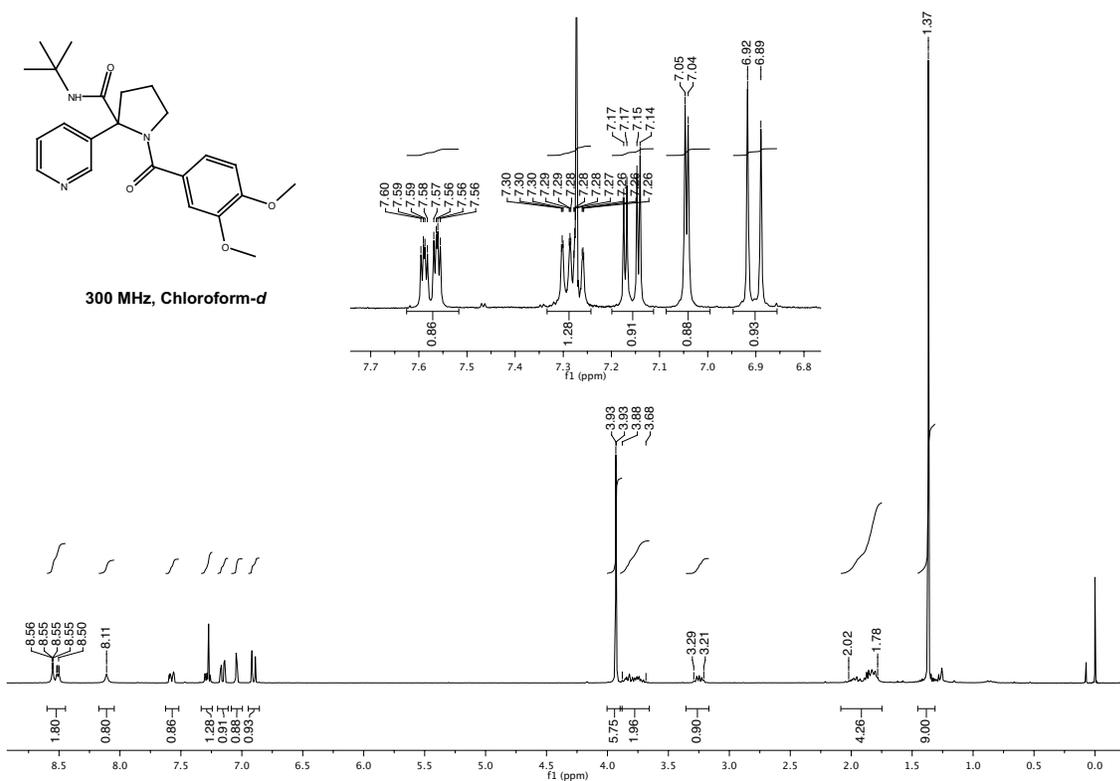
1-benzoyl-N-(tert-butyl)-2-(pyridin-3-yl)pyrrolidine-2-carboxamide 8a



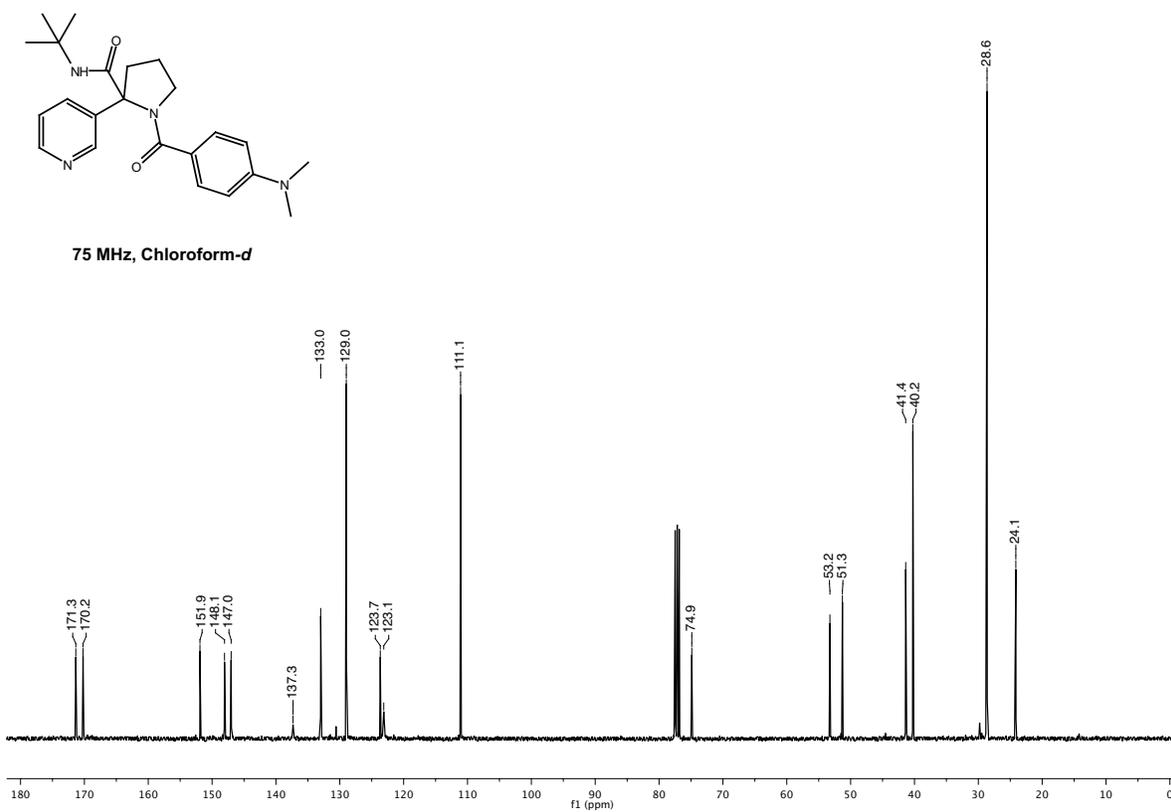
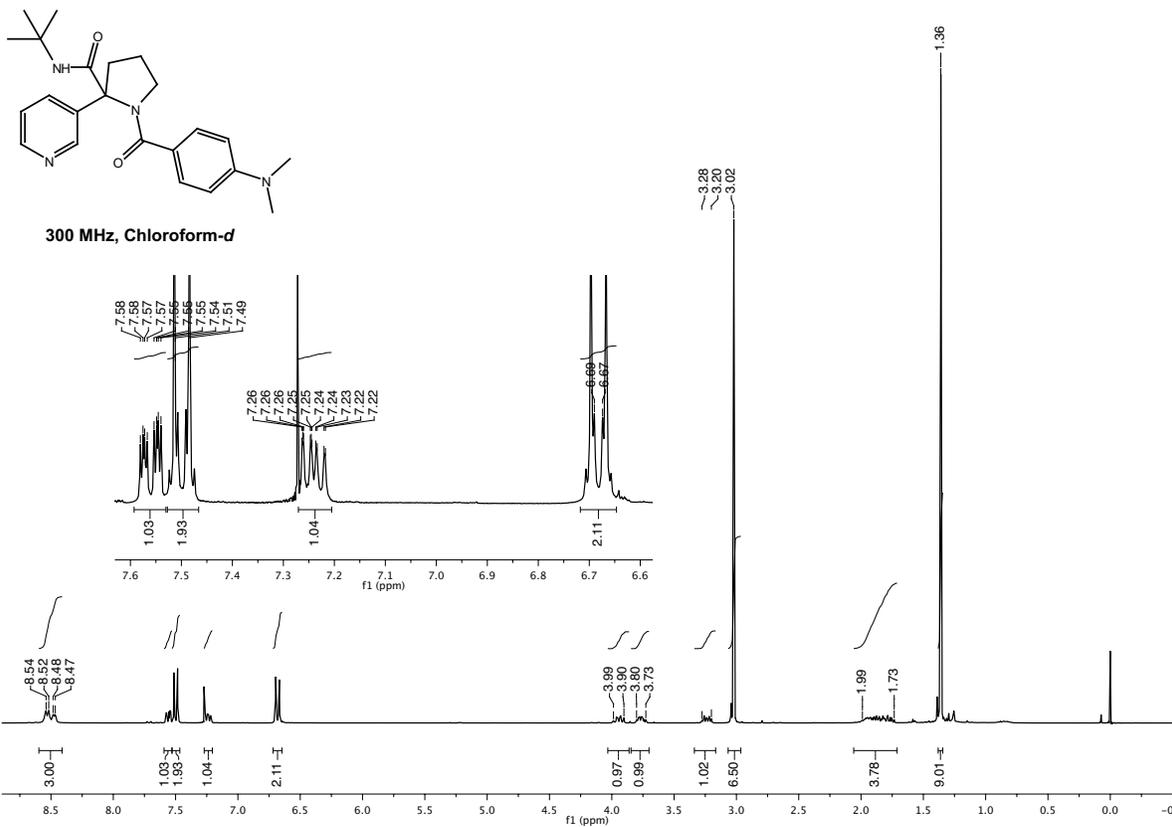
N-(*tert*-butyl)-1-(4-methoxybenzoyl)-2-(pyridin-3-yl)pyrrolidine-2-carboxamide 8b



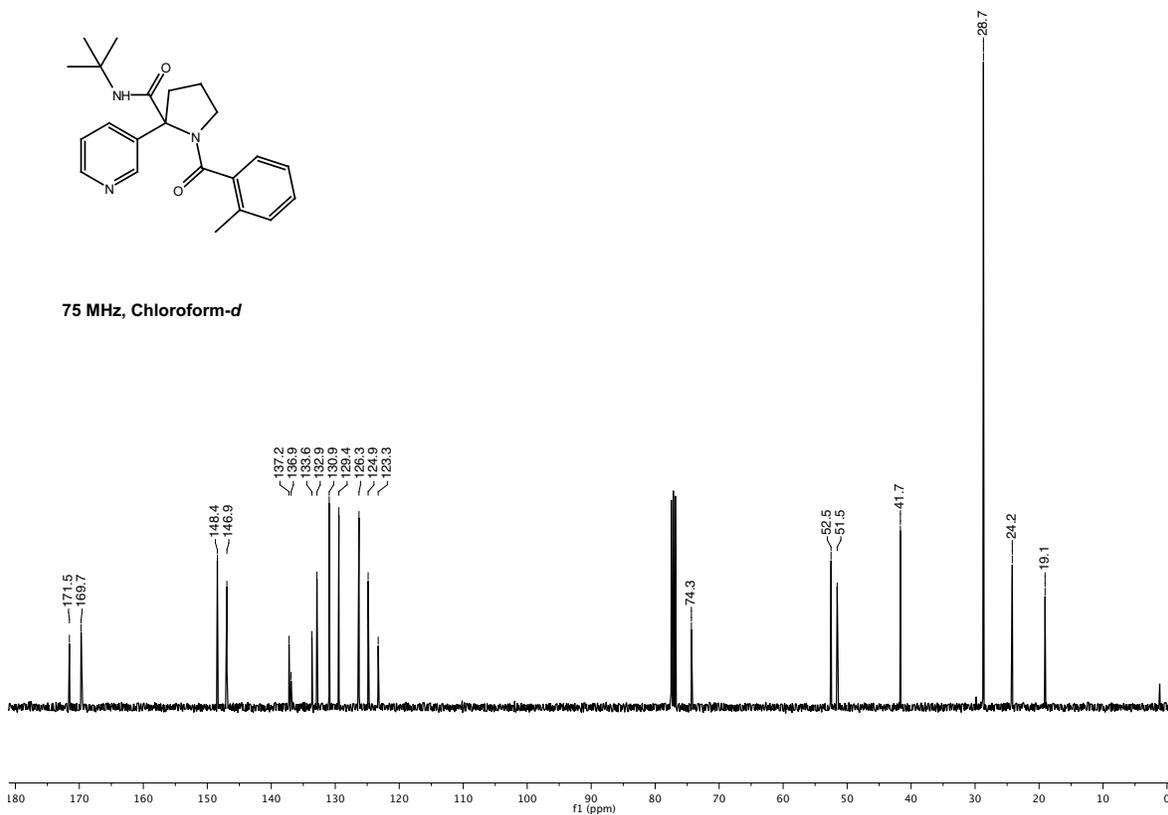
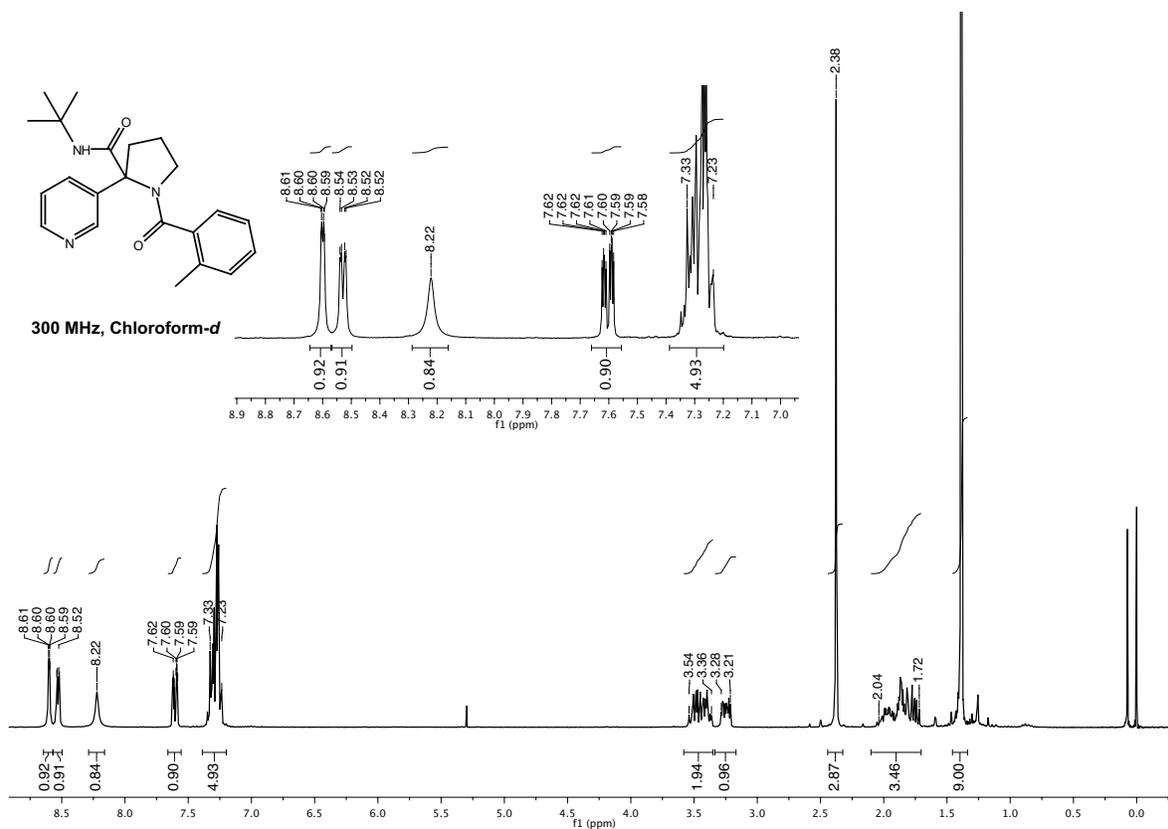
N*-(*tert*-butyl)-1-(3,4-dimethoxybenzoyl)-2-(pyridin-3-yl)pyrrolidine-2-carboxamide **8c*



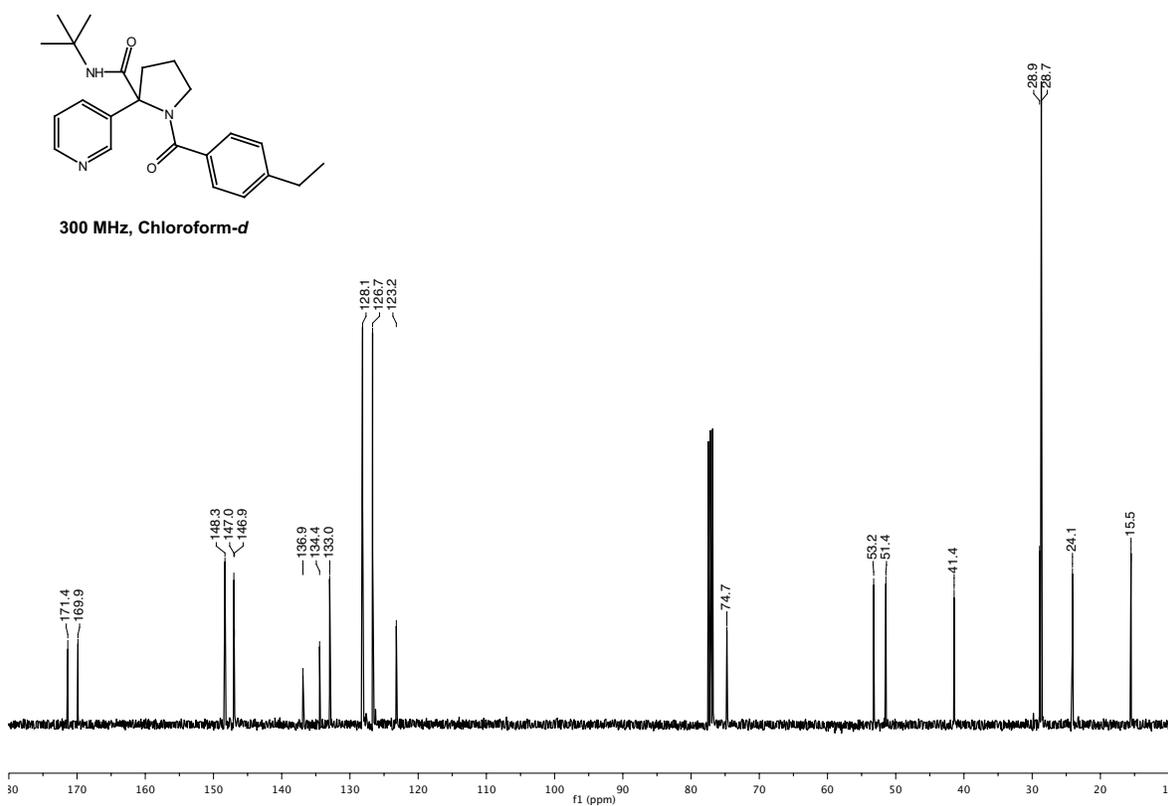
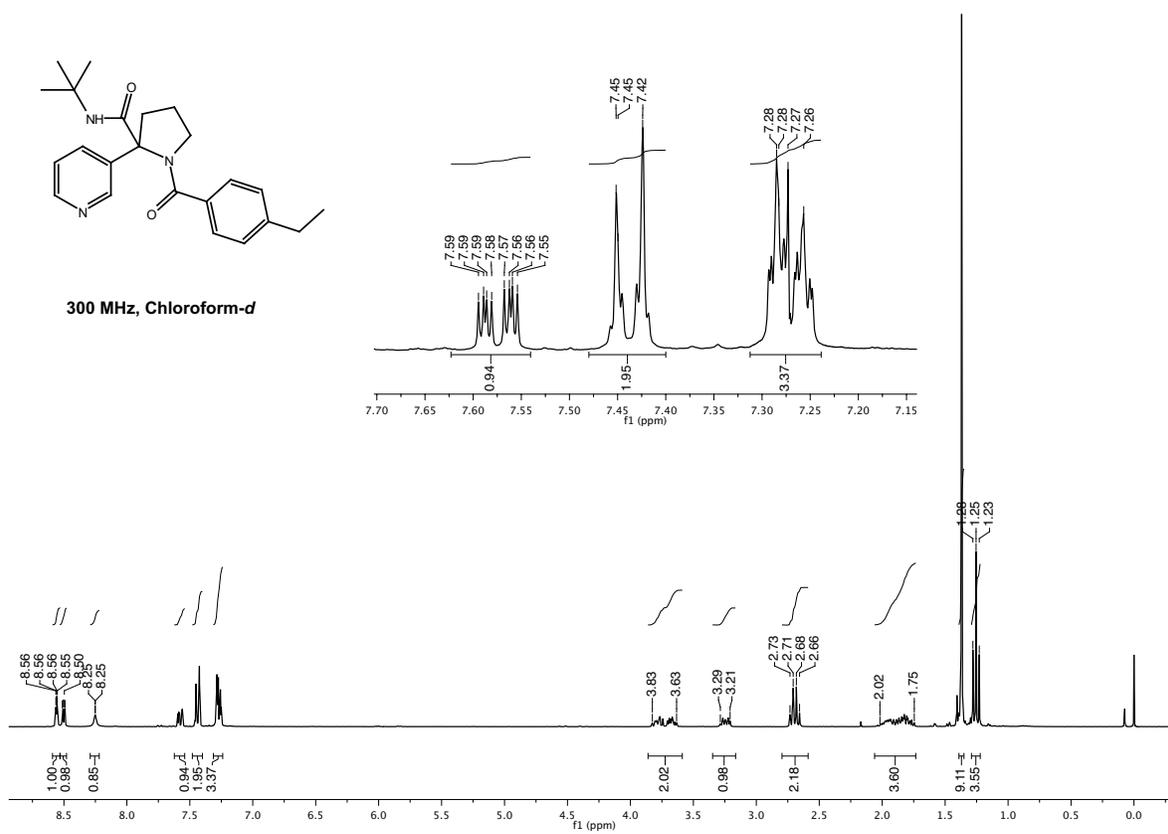
***N*-(*tert*-butyl)-1-(4-(dimethylamino)benzoyl)-2-(pyridin-3-yl)pyrrolidine-2-carboxamide 8d**



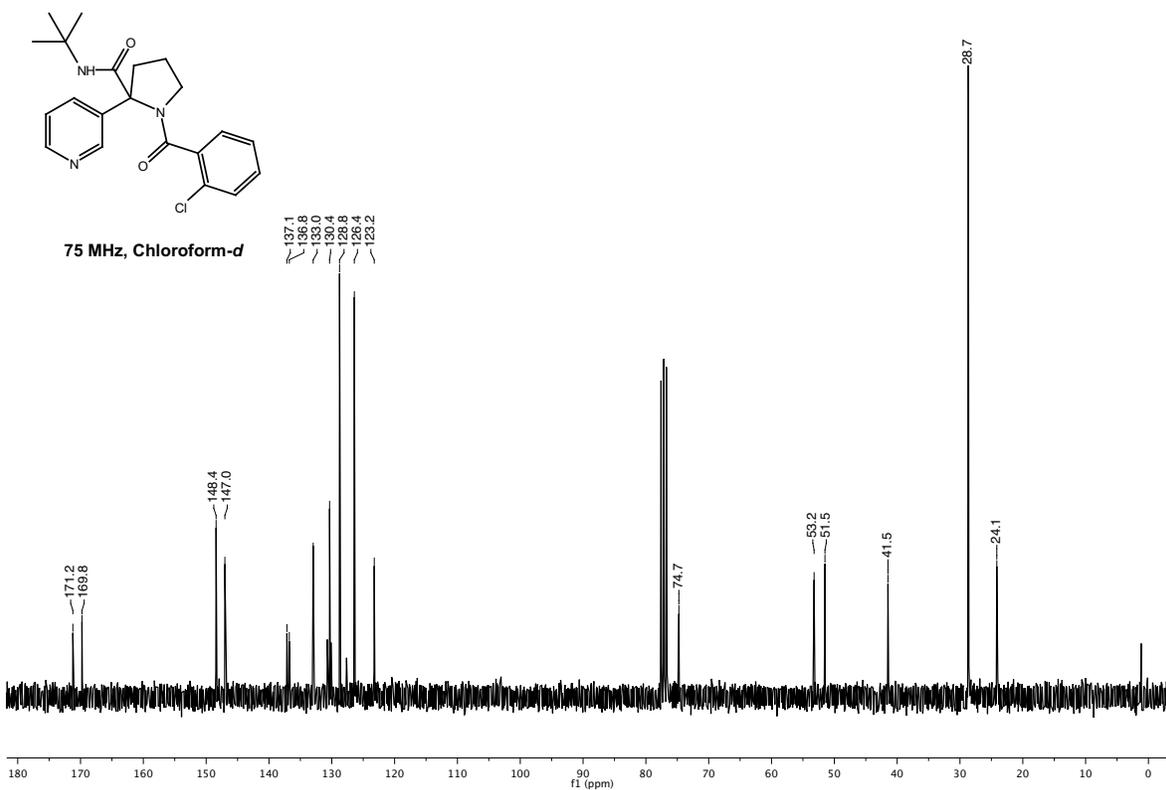
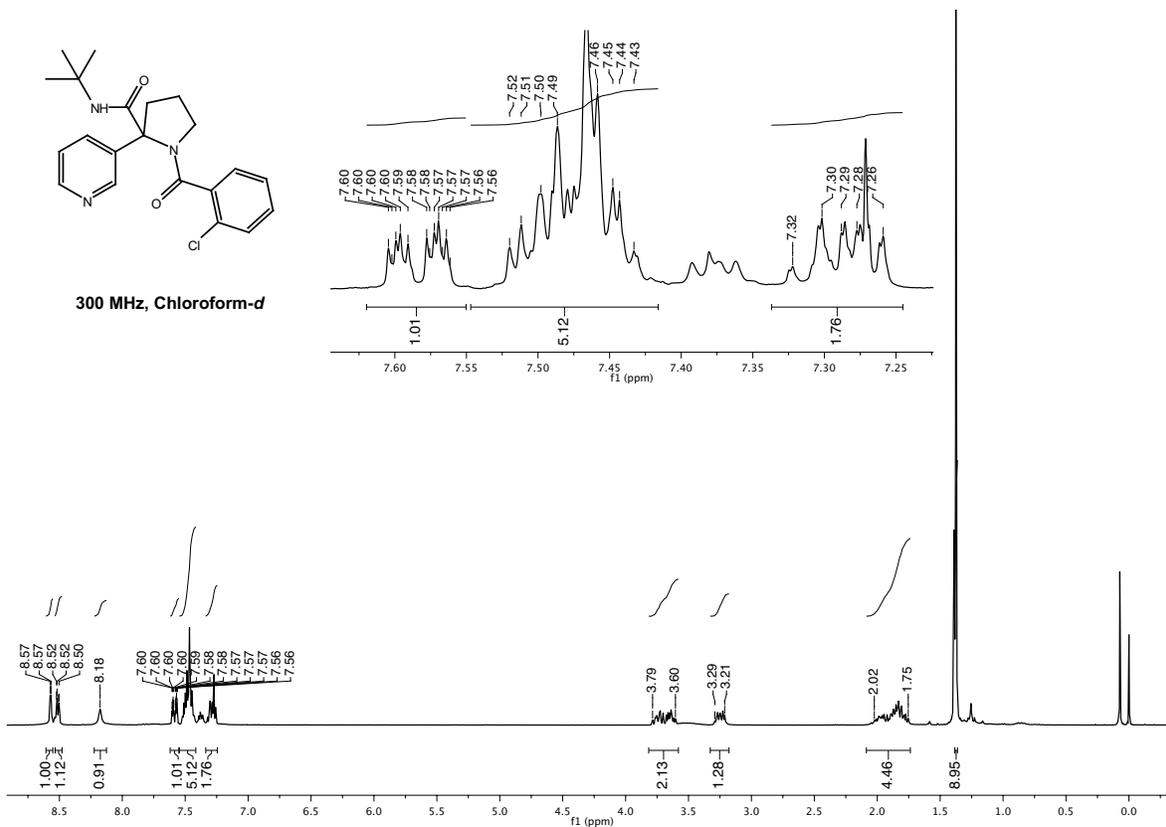
N*-(*tert*-butyl)-1-(2-methylbenzoyl)-2-(pyridin-3-yl)pyrrolidine-2-carboxamide **8e*



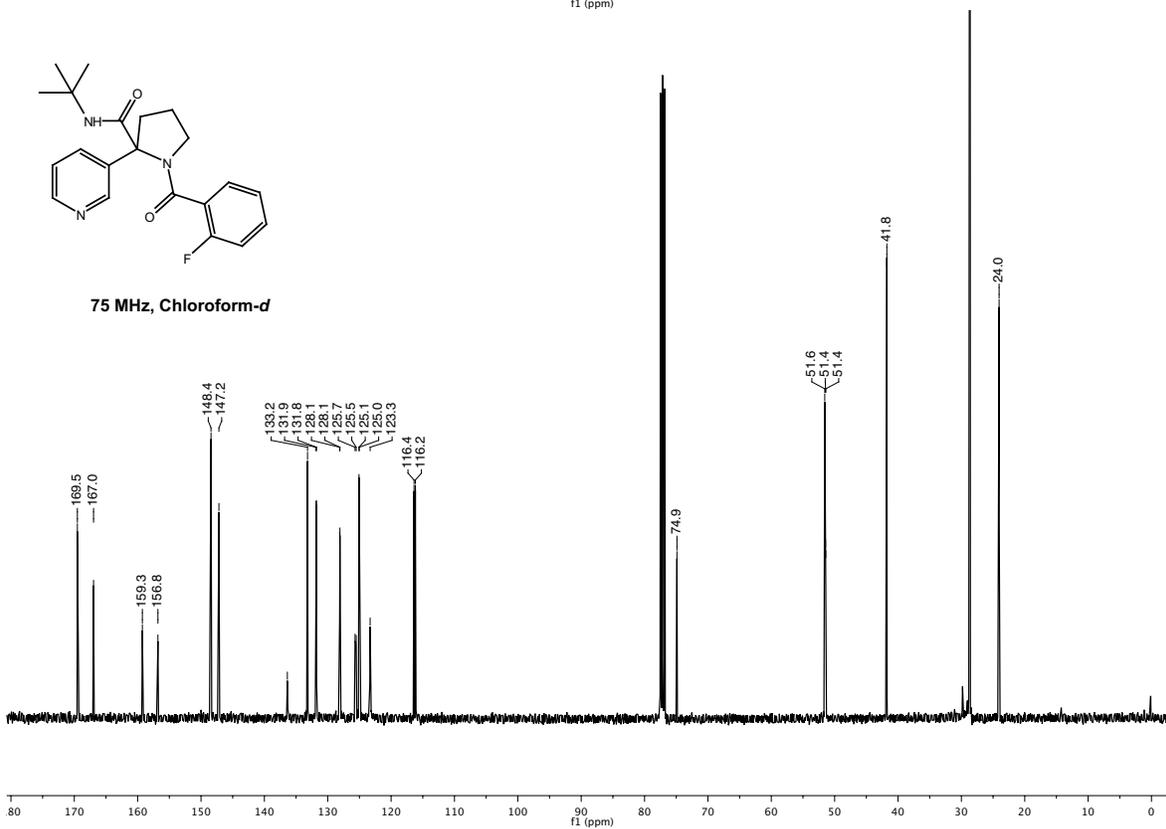
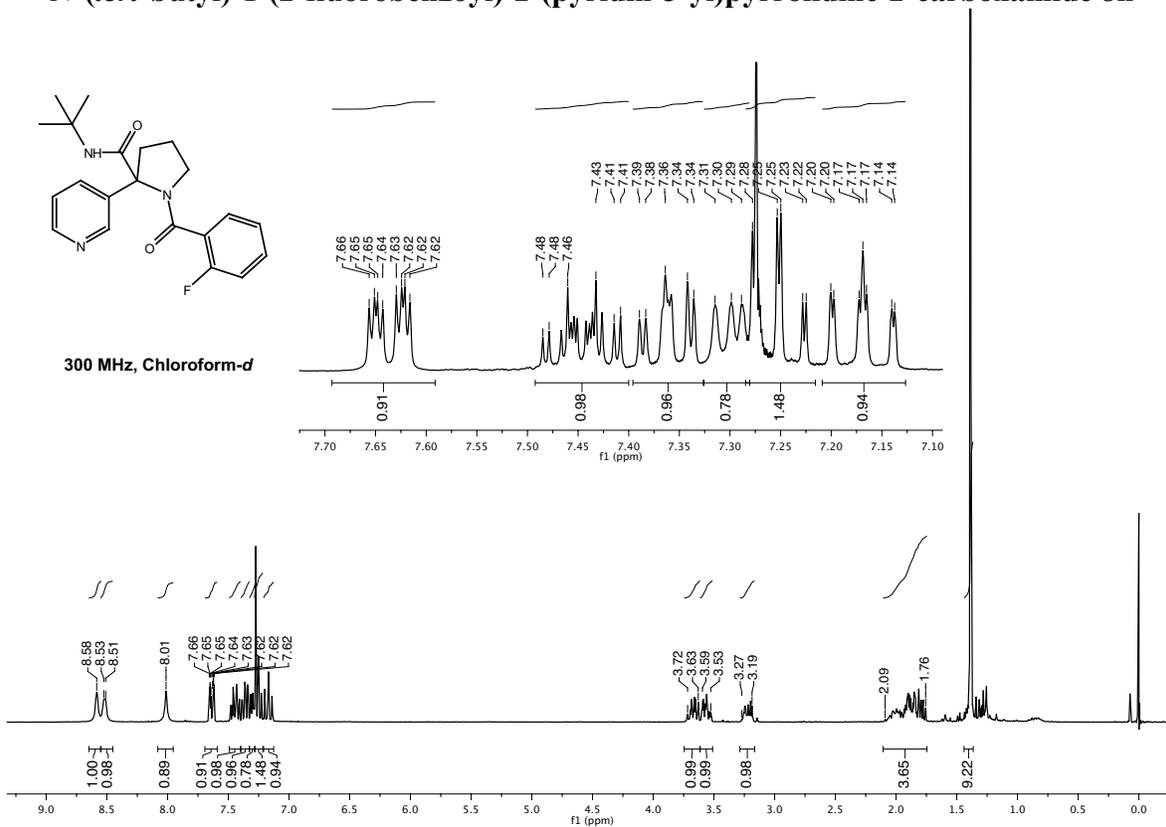
***N*-(*tert*-butyl)-1-(4-ethylbenzoyl)-2-(pyridin-3-yl)pyrrolidine-2-carboxamide 8f**



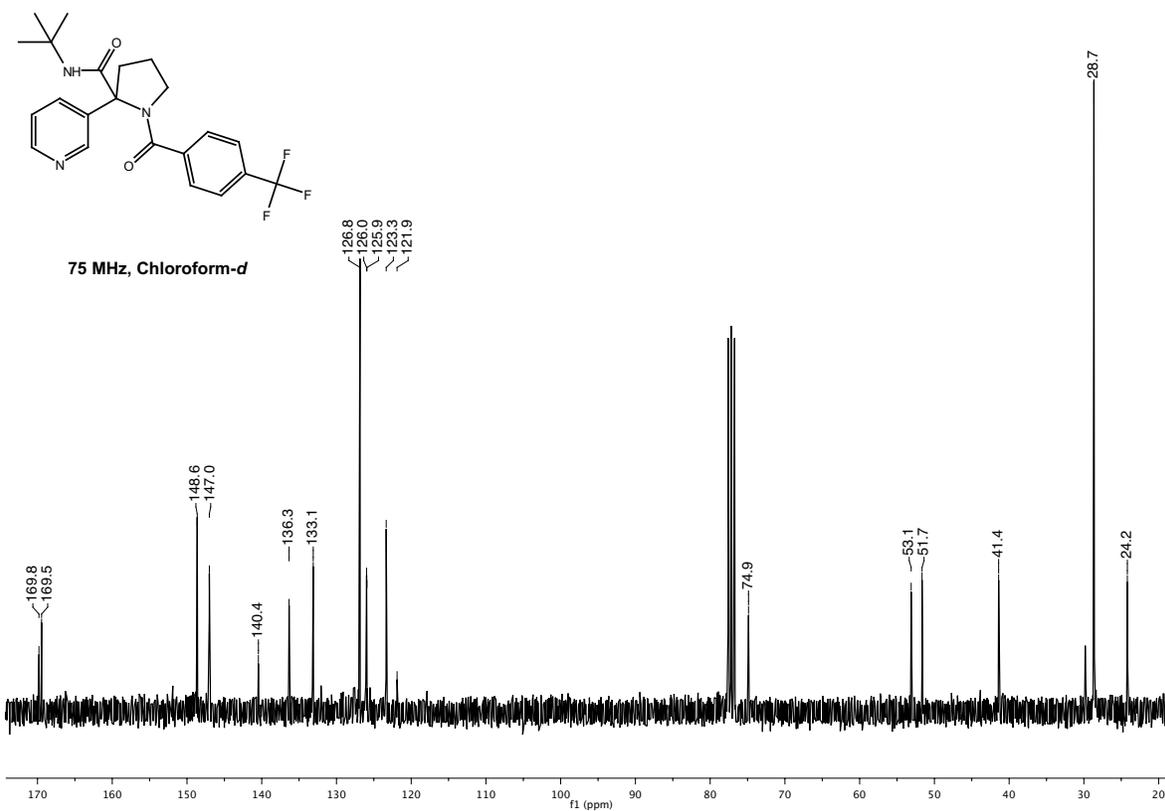
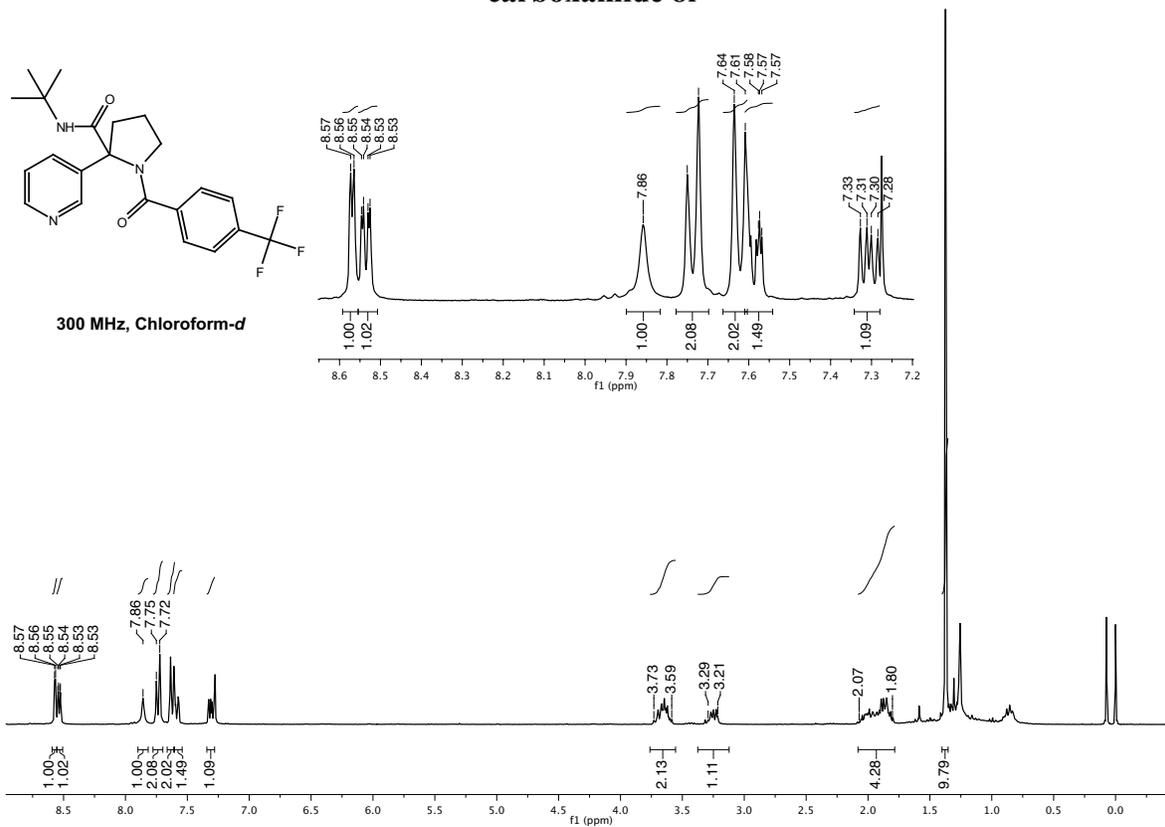
***N*-(*tert*-butyl)-1-(2-chlorobenzoyl)-2-(pyridin-3-yl)pyrrolidine-2-carboxamide 8g**



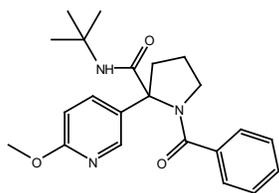
***N*-(*tert*-butyl)-1-(2-fluorobenzoyl)-2-(pyridin-3-yl)pyrrolidine-2-carboxamide 8h**



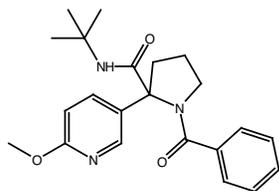
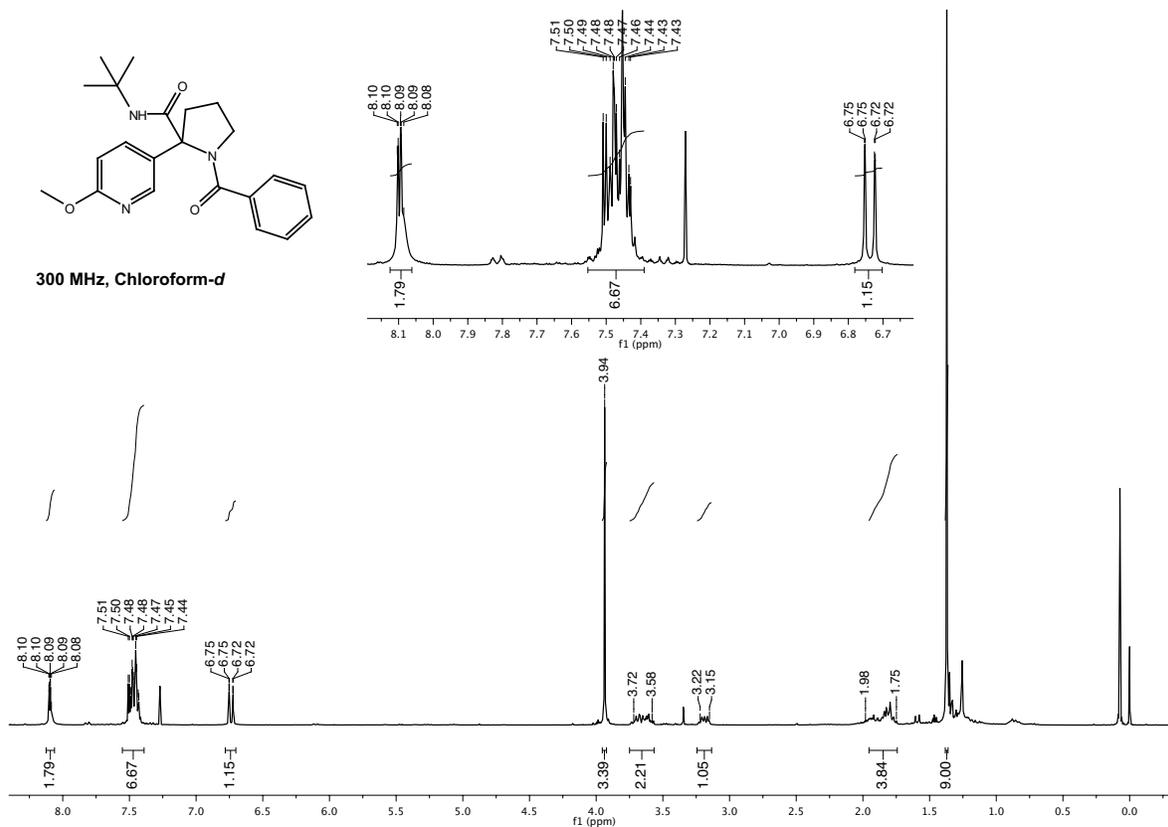
***N*-(*tert*-butyl)-2-(pyridin-3-yl)-1-(4-(trifluoromethyl)benzoyl)pyrrolidine-2-carboxamide 8i**



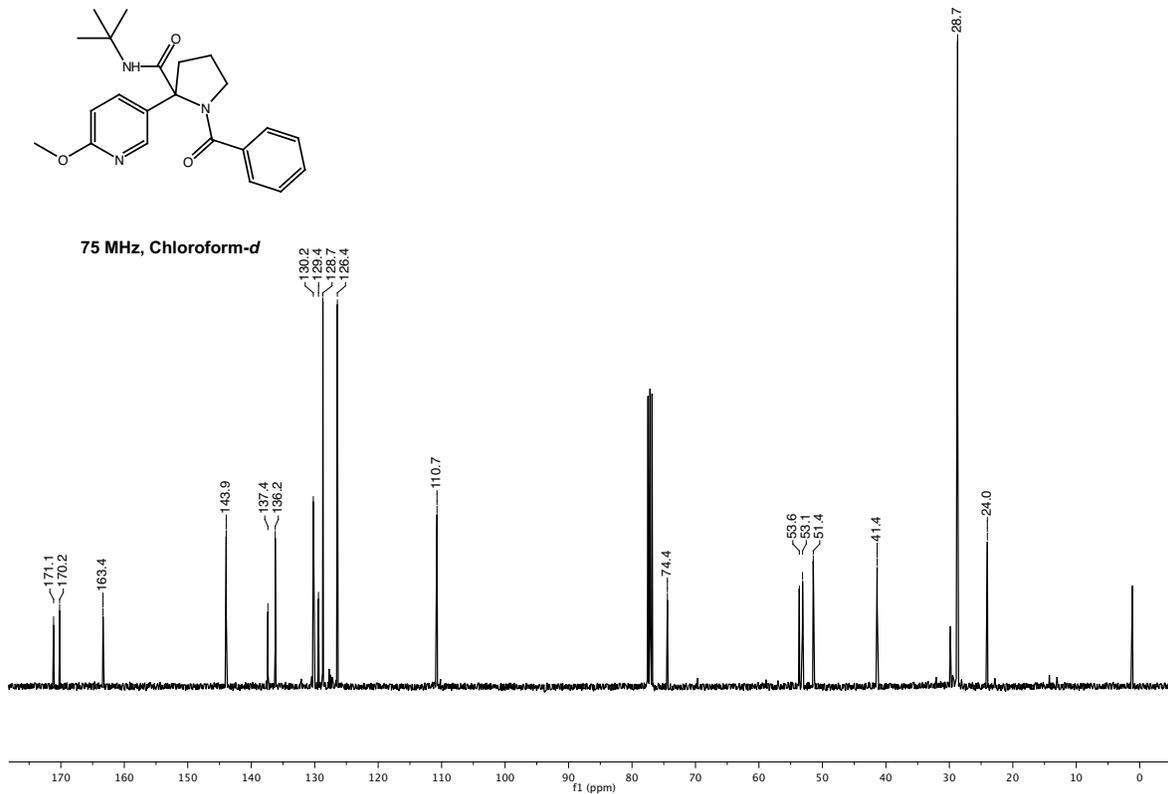
1-benzoyl-N-(tert-butyl)-2-(6-methoxypyridin-3-yl)pyrrolidine-2-carboxamide 8j



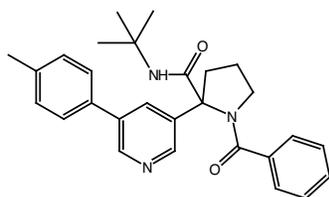
300 MHz, Chloroform-*d*



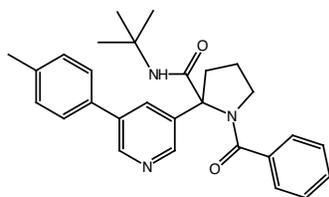
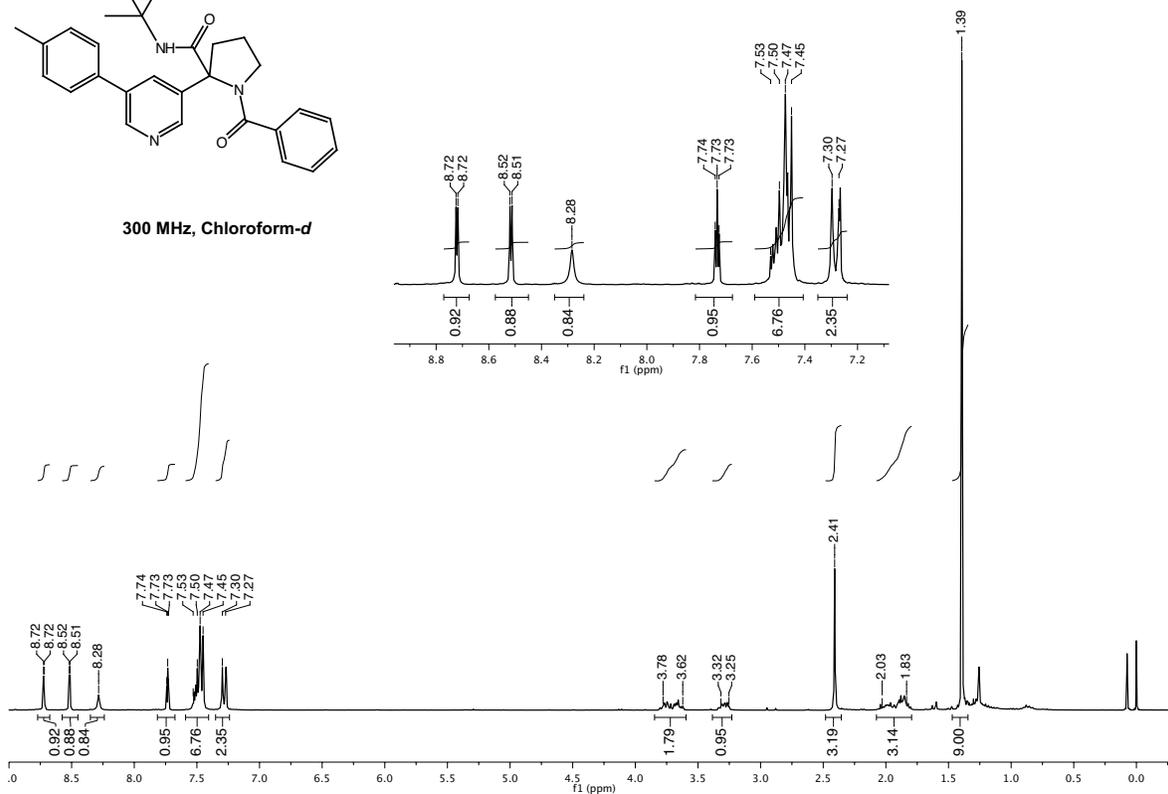
75 MHz, Chloroform-*d*



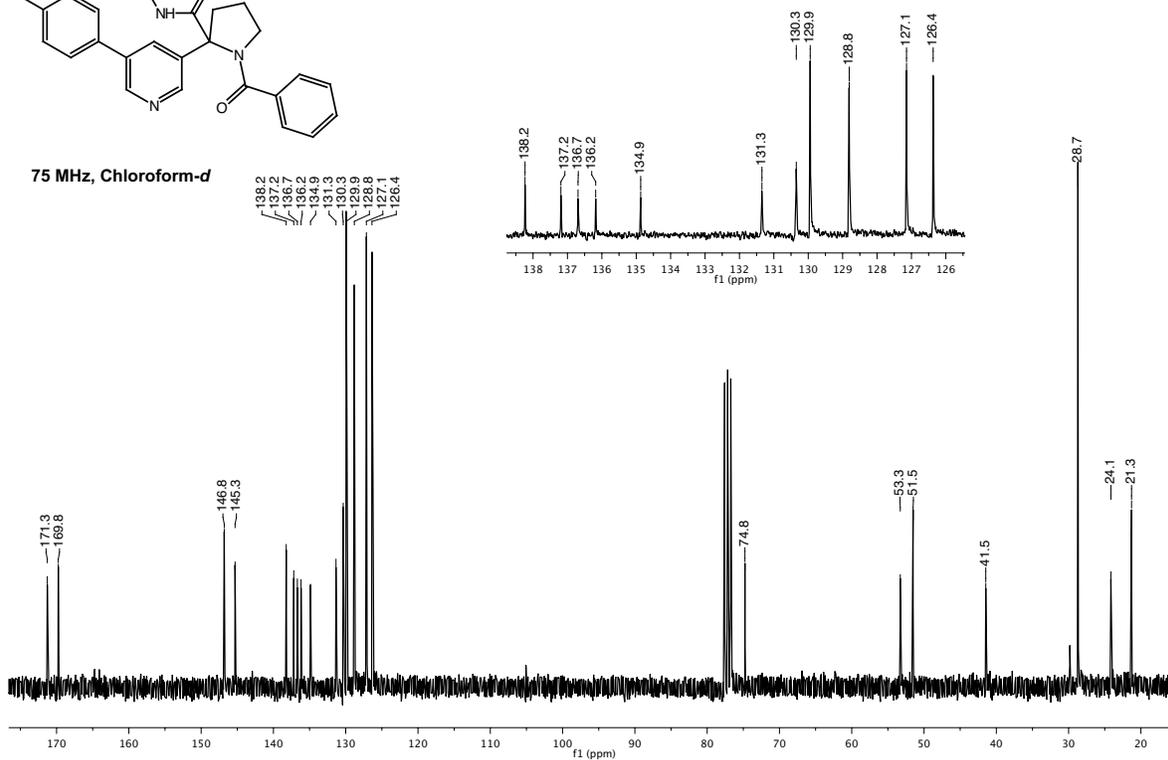
1-benzoyl-N-(tert-butyl)-2-(5-(p-tolyl)pyridin-3-yl)pyrrolidine-2-carboxamide 8k



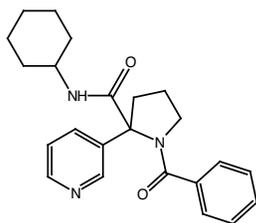
300 MHz, Chloroform-d



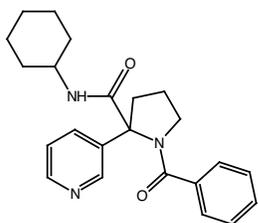
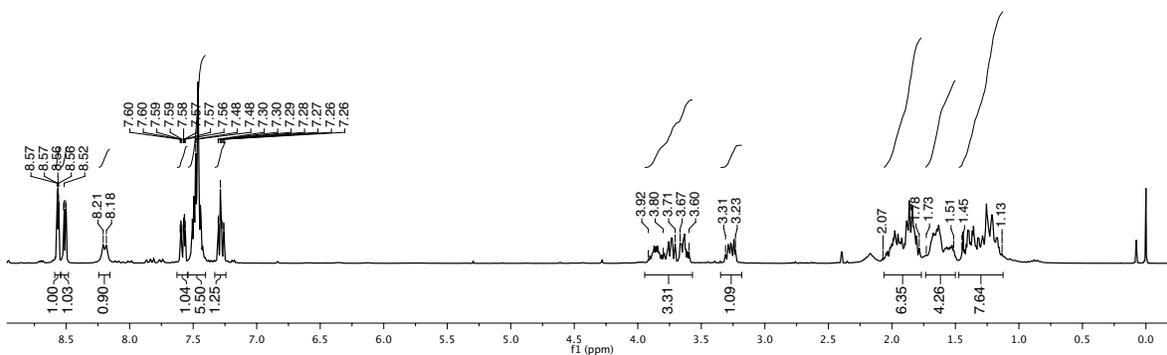
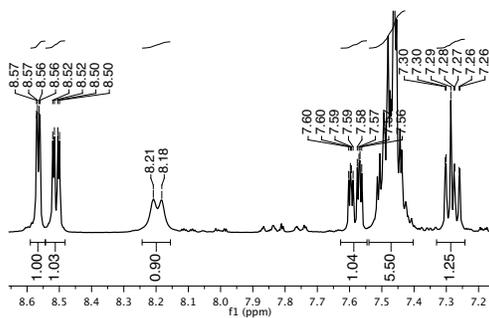
75 MHz, Chloroform-d



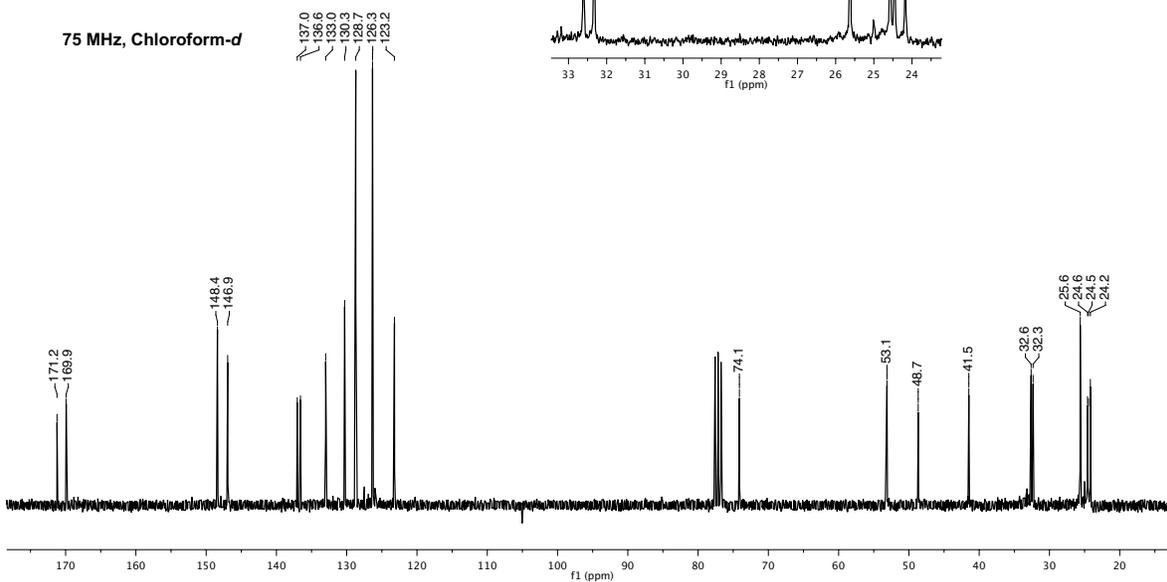
1-benzoyl-N-cyclohexyl-2-(pyridin-3-yl)pyrrolidine-2-carboxamide **8m**



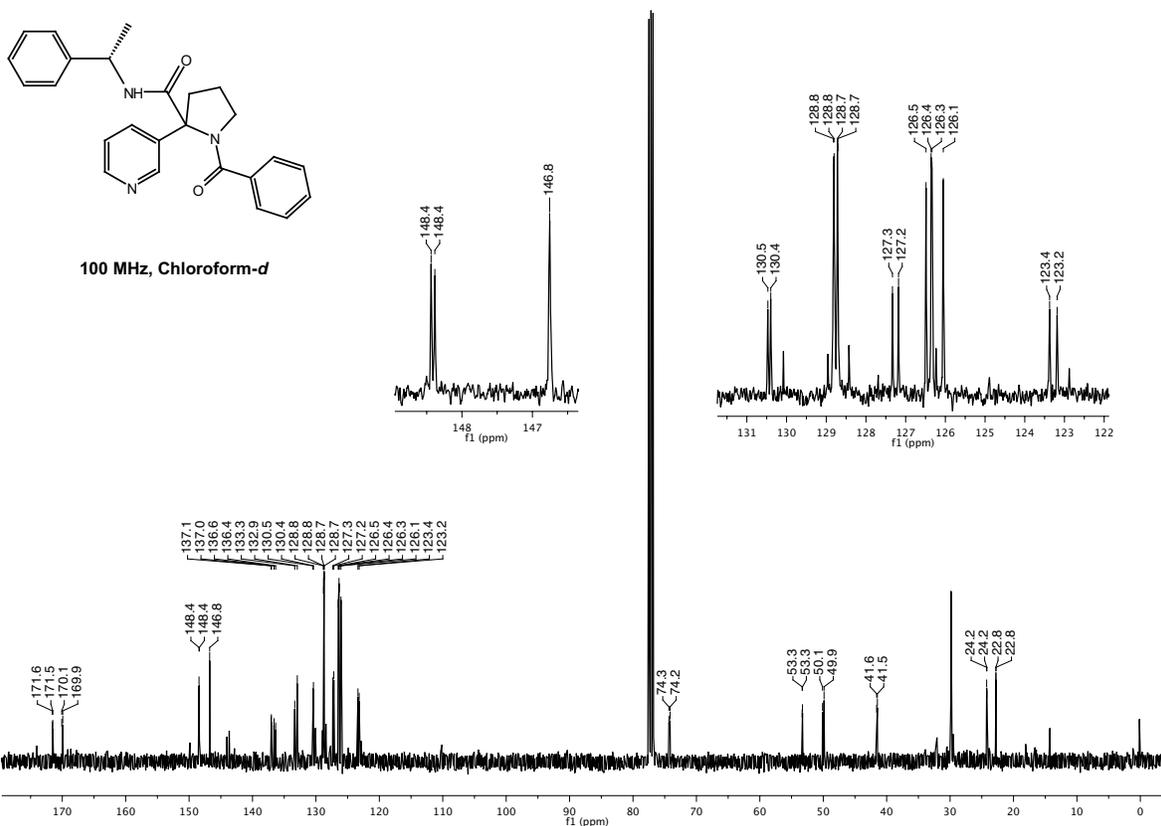
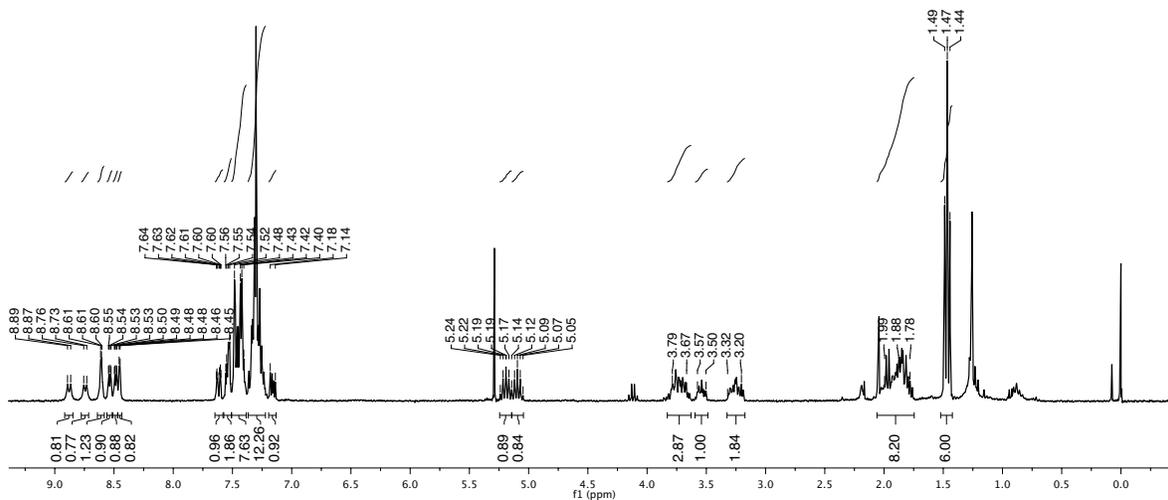
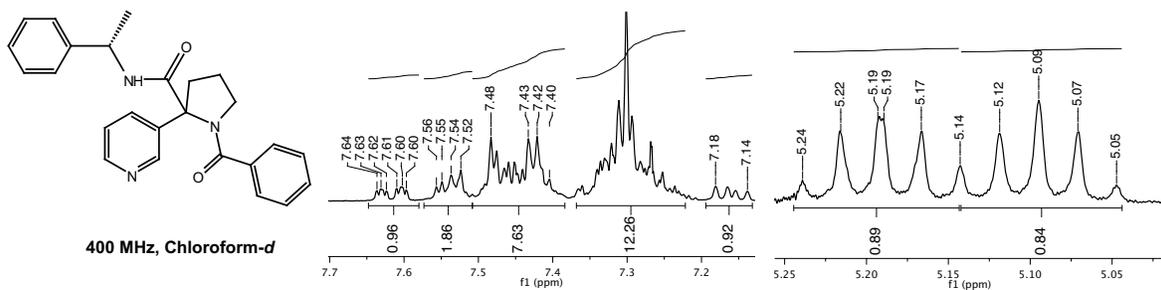
300 MHz, Chloroform-*d*



75 MHz, Chloroform-*d*

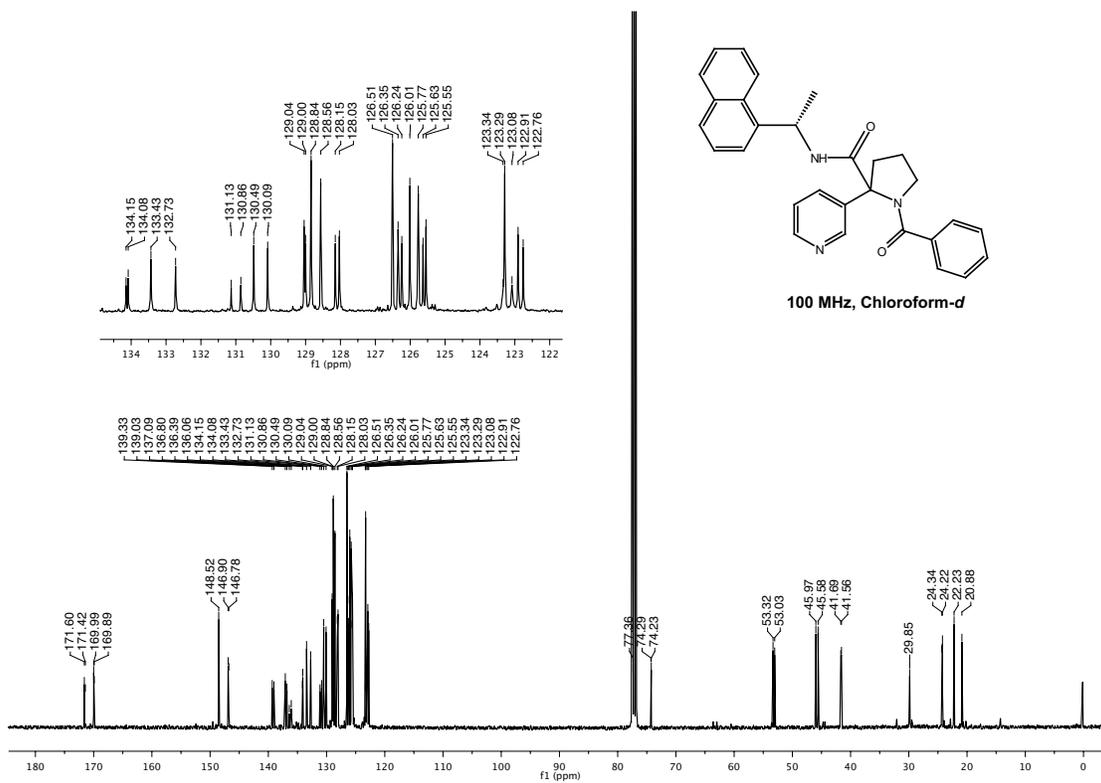
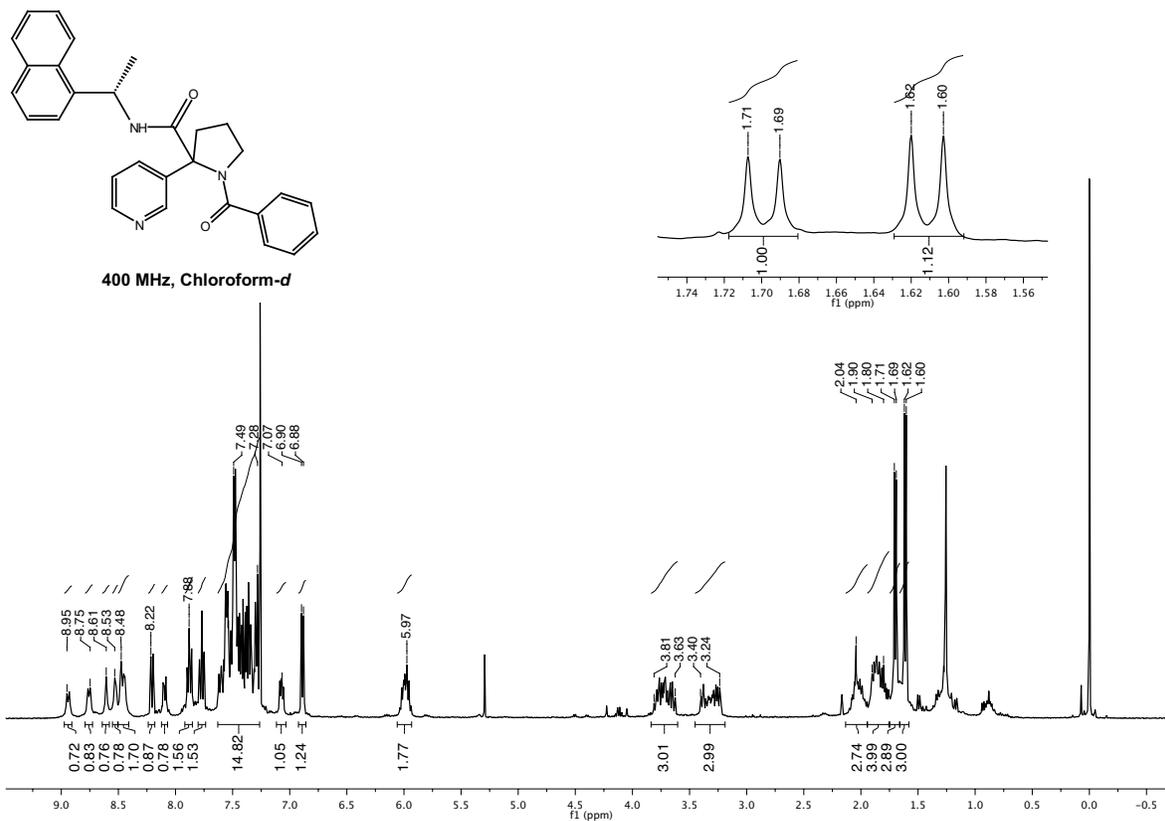


1-benzoyl-N-((S)-1-phenylethyl)-2-(pyridin-3-yl)pyrrolidine-2-carboxamide 8n

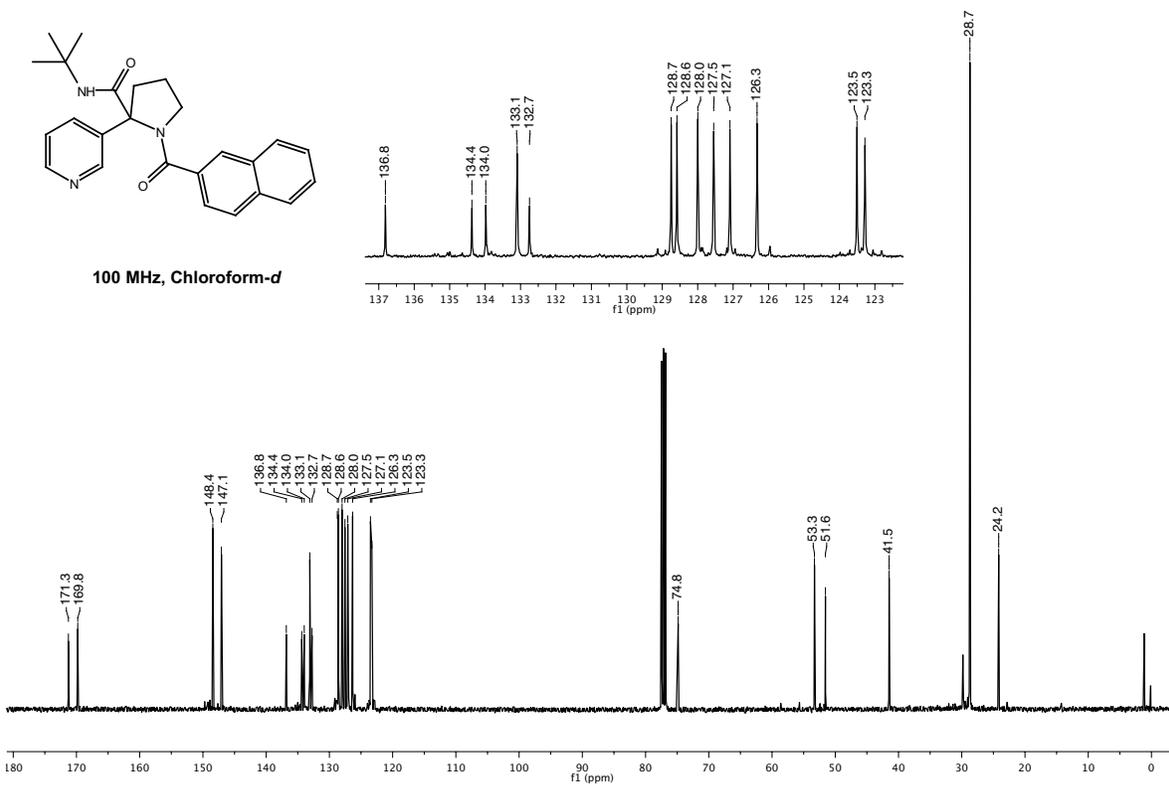
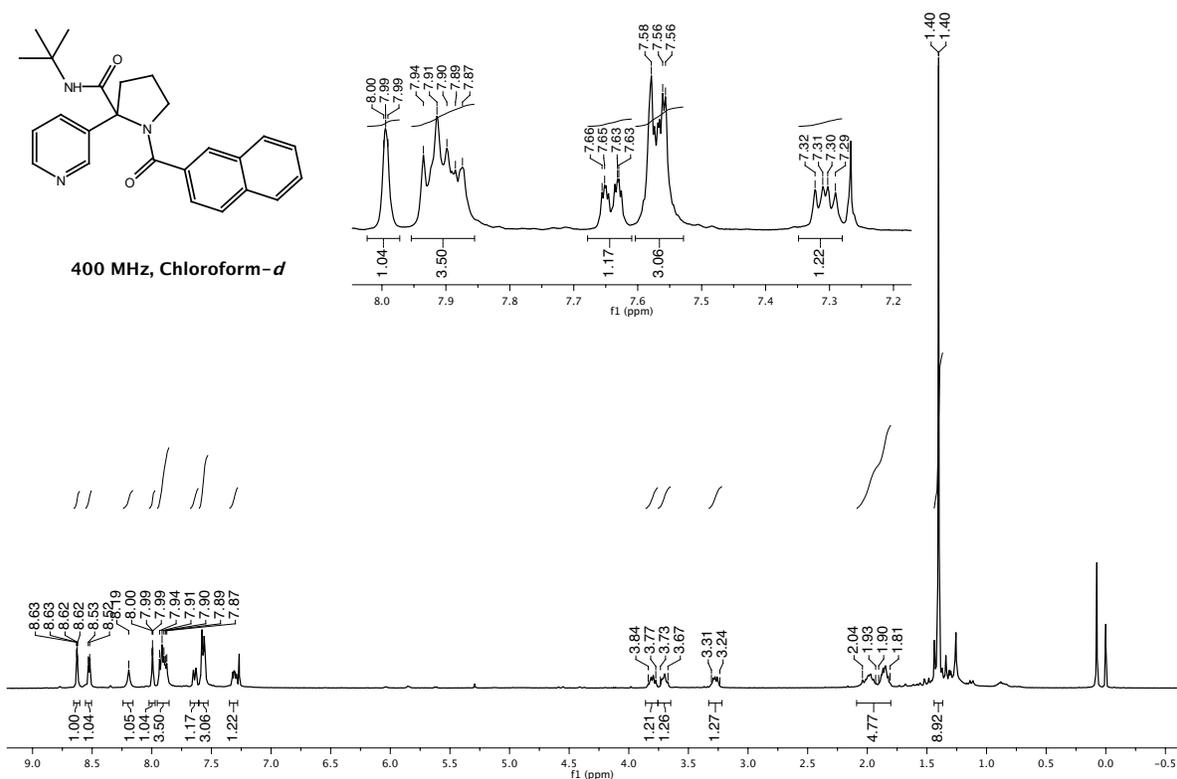


1-benzoyl-N-((S)-1-(naphthalen-1-yl)ethyl)-2-(pyridin-3-yl)pyrrolidine-2-carboxamide

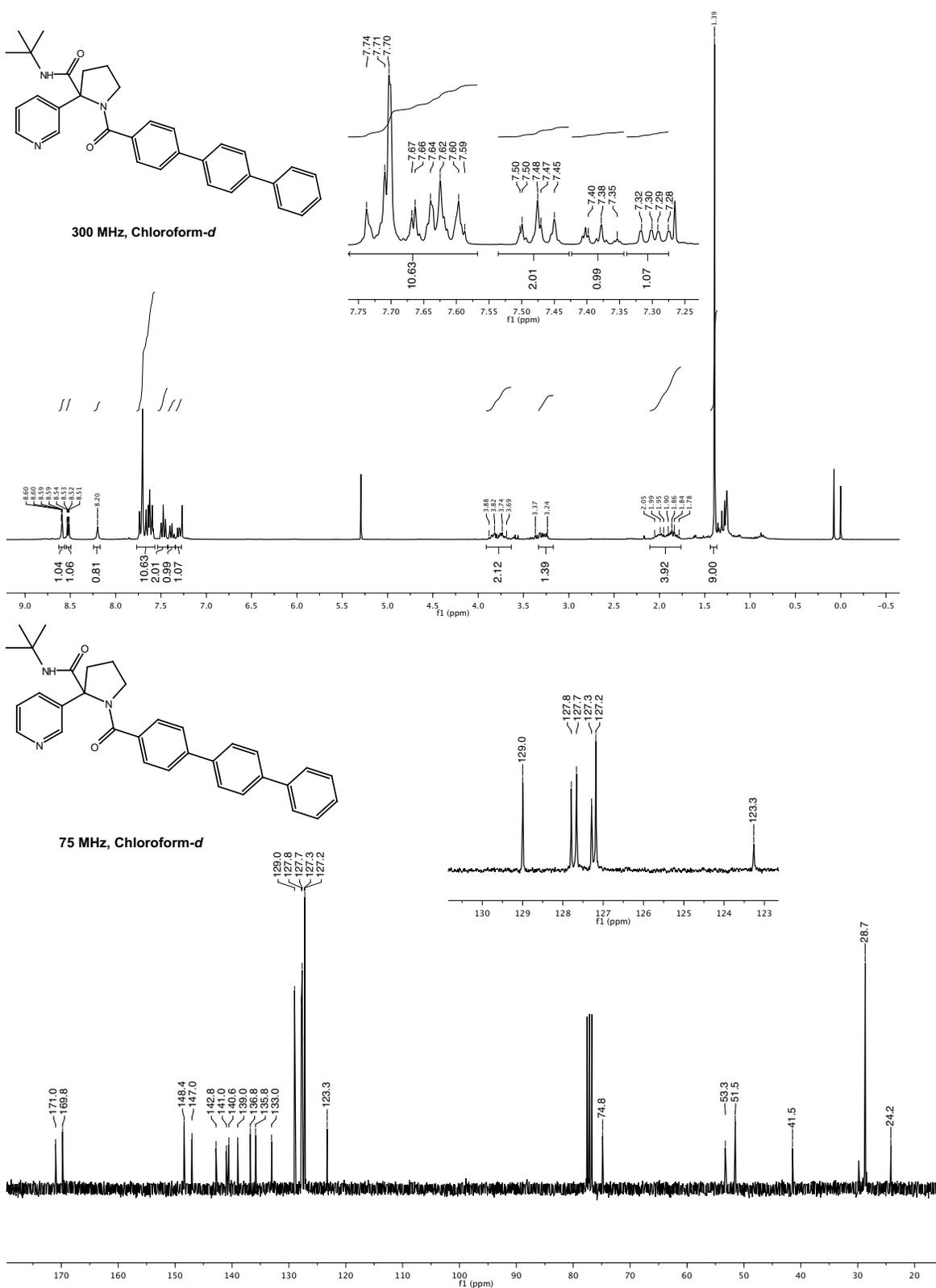
8n'



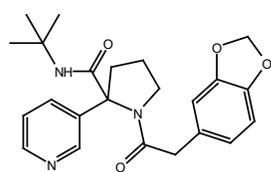
1-(2-naphthoyl)-*N*-(*tert*-butyl)-2-(pyridin-3-yl)pyrrolidine-2-carboxamide 8q



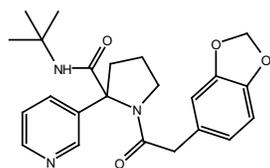
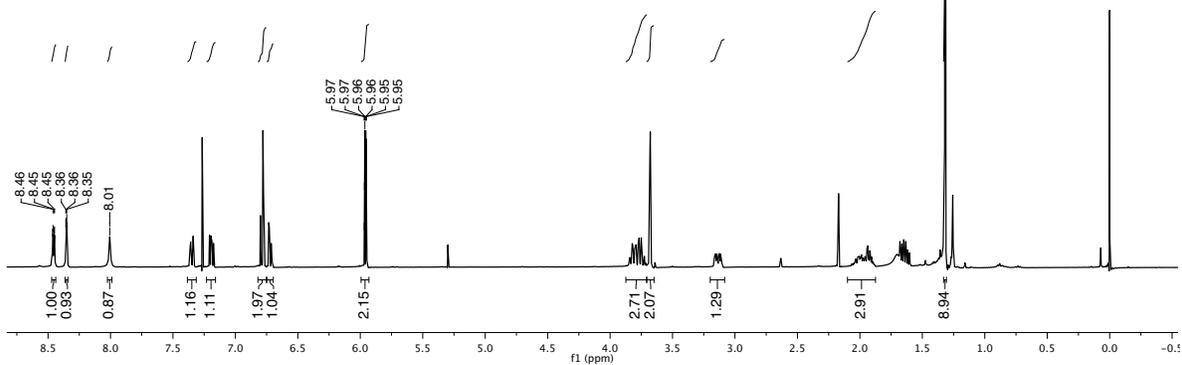
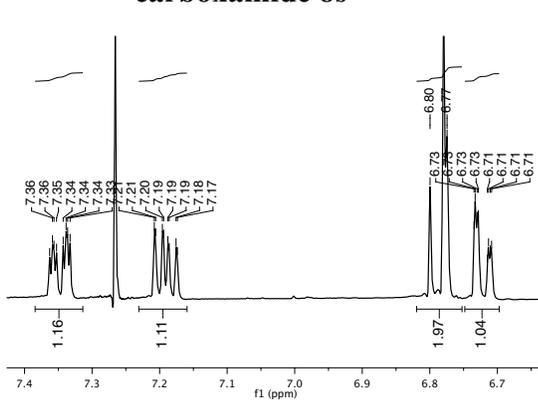
1-([1,1':4,1''-terphenyl]-4-carbonyl)-*N*-(*tert*-butyl)-2-(pyridin-3-yl)pyrrolidine-2-carboxamide 8r



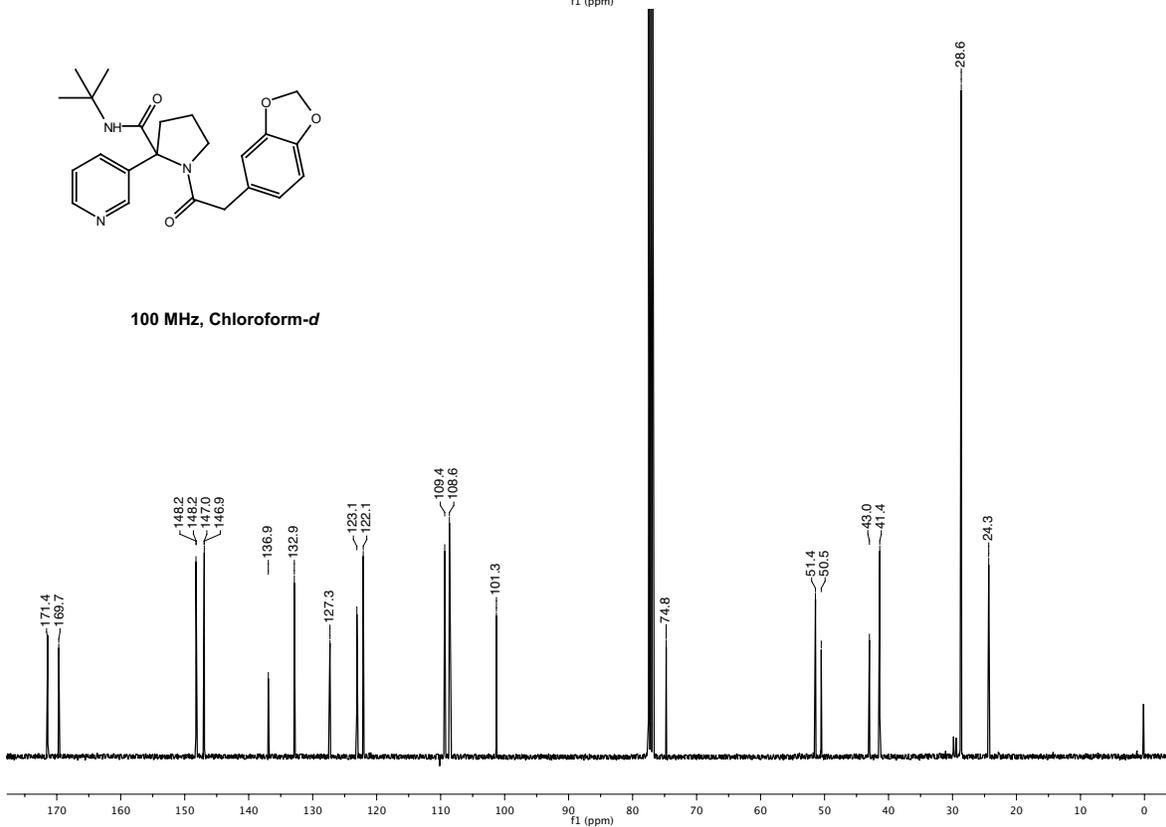
1-(2-(benzo[d][1,3]dioxol-5-yl)acetyl)-*N*-(*tert*-butyl)-2-(pyridin-3-yl)pyrrolidine-2-carboxamide 8s



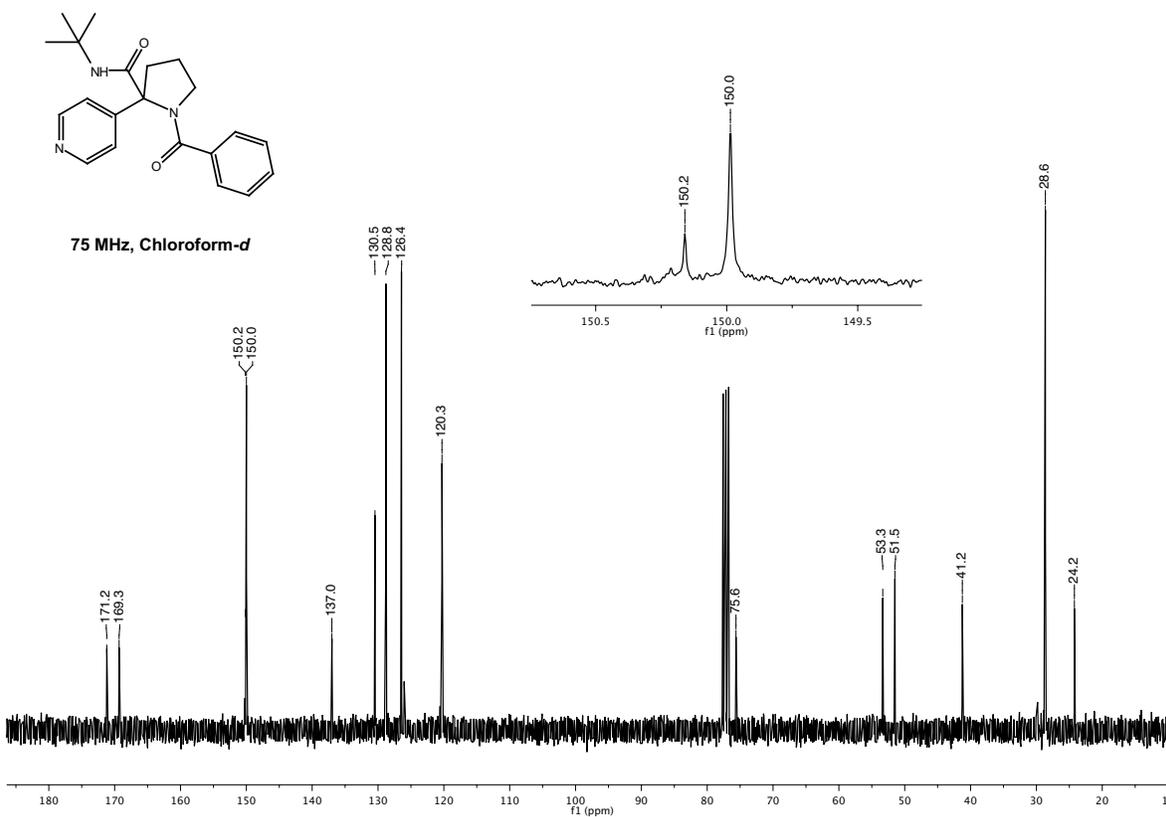
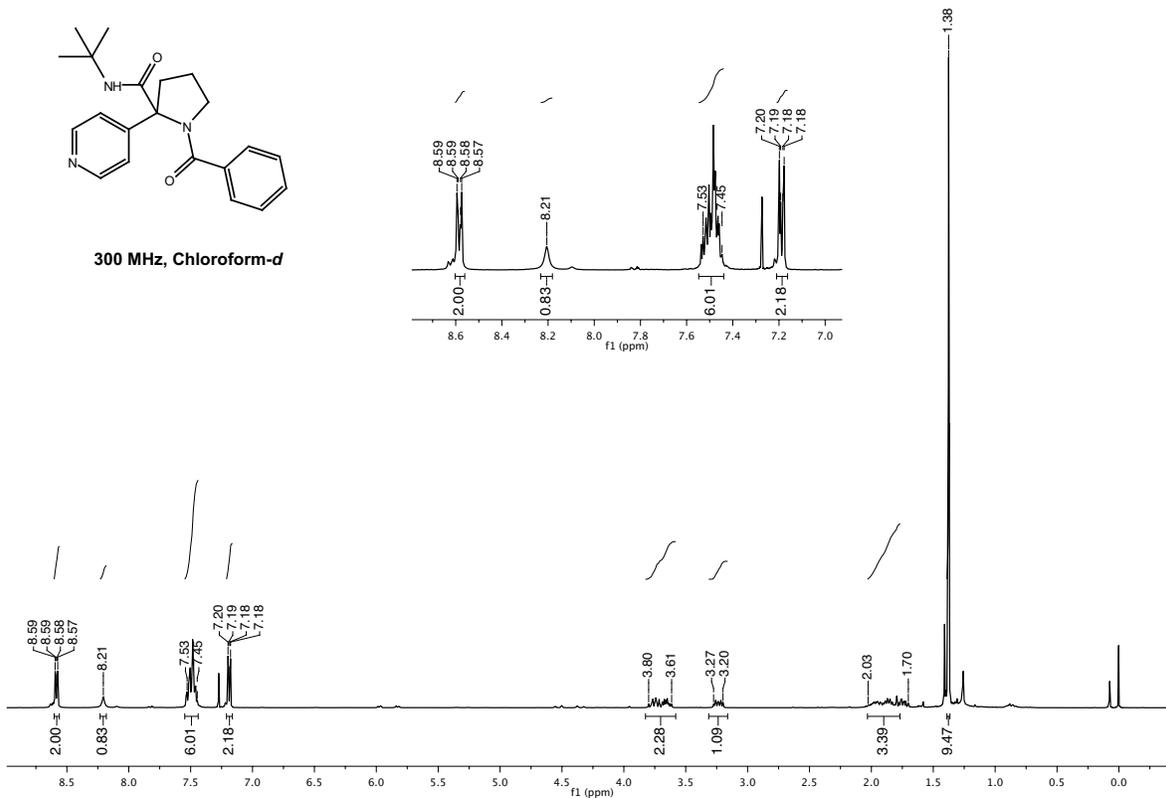
400 MHz, Chloroform-*d*



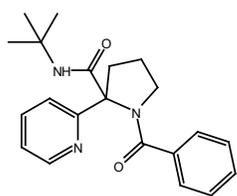
100 MHz, Chloroform-*d*



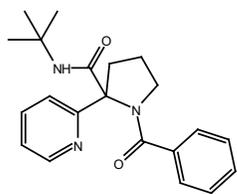
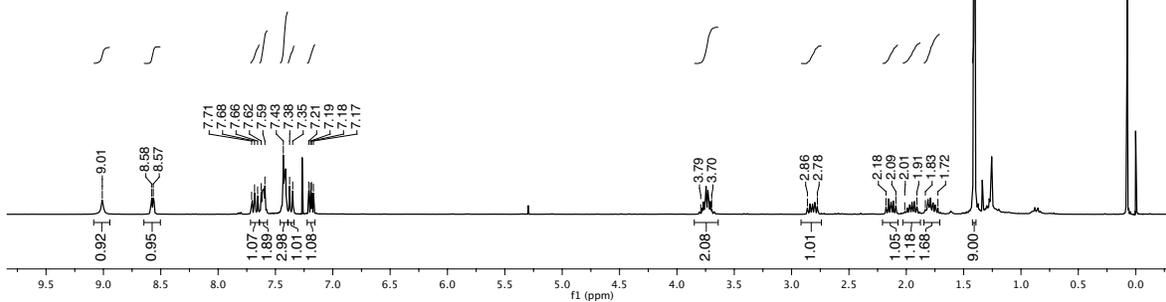
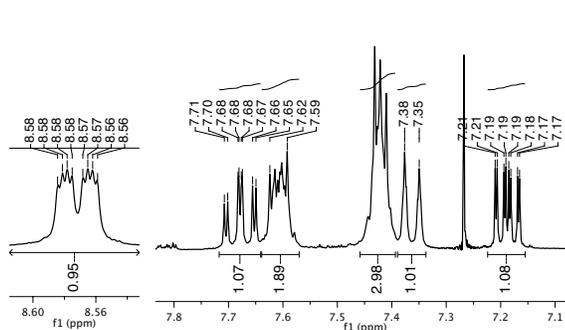
1-benzoyl-N-(tert-butyl)-2-(pyridin-4-yl)pyrrolidine-2-carboxamide **8v**



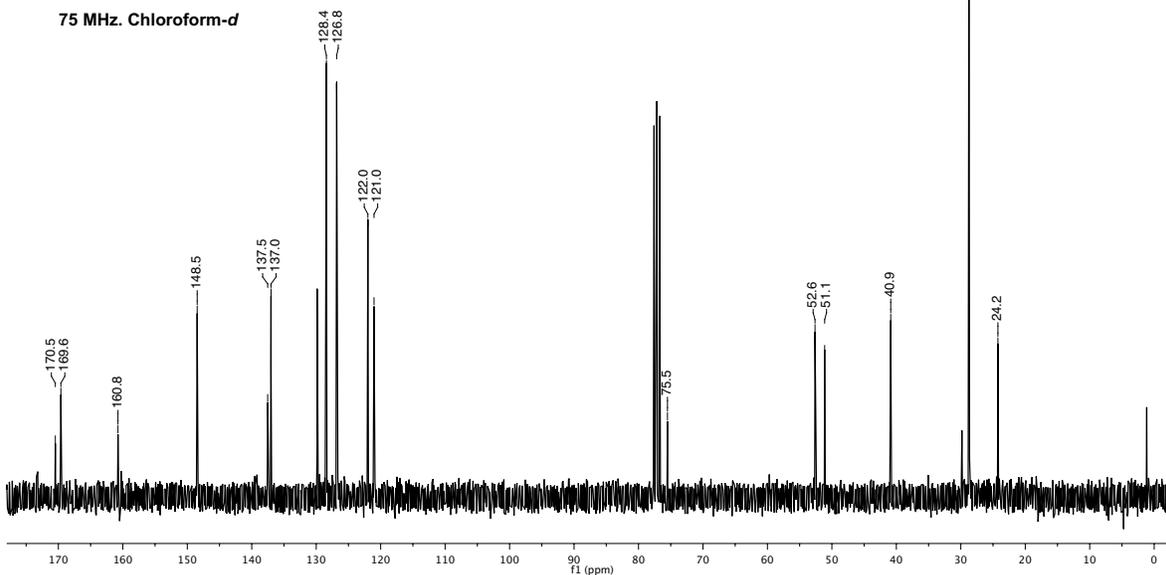
1-benzoyl-N-(tert-butyl)-2-(pyridin-2-yl)pyrrolidine-2-carboxamide 8w



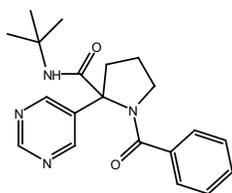
300 MHz, Chloroform-d



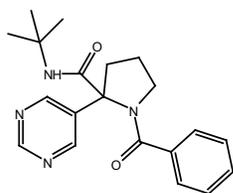
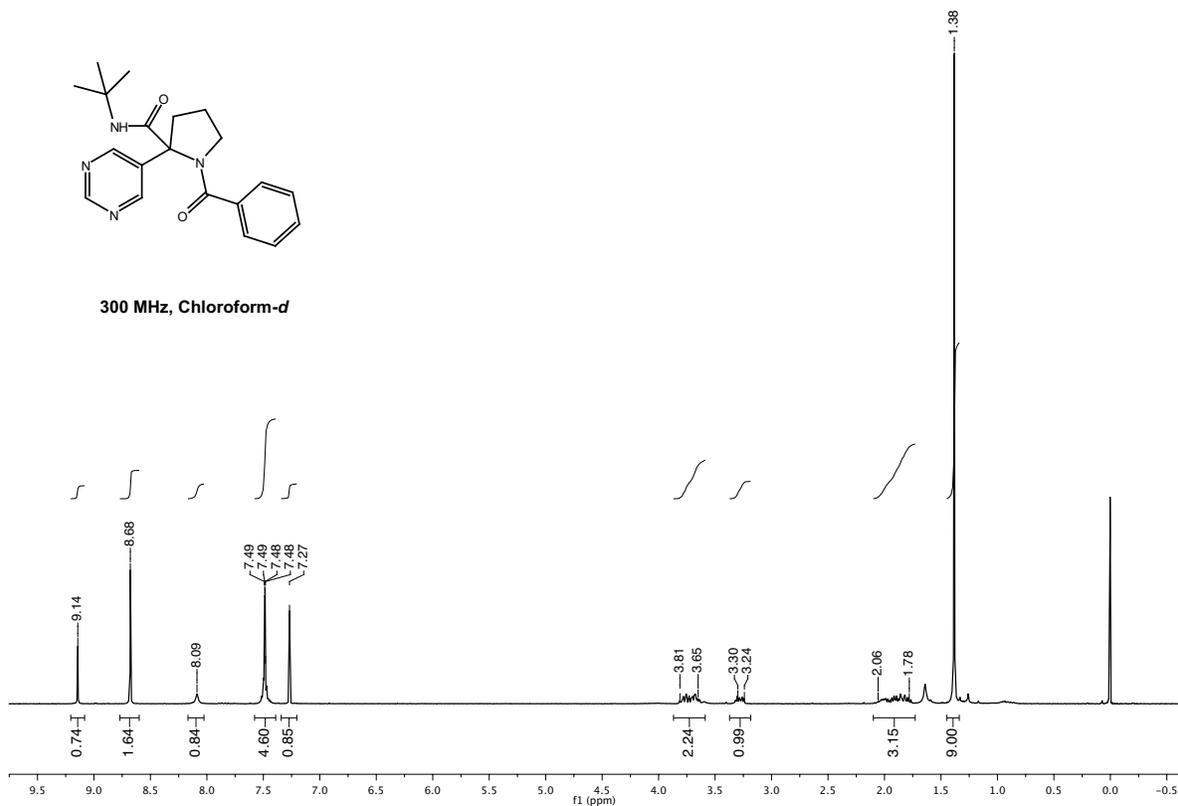
75 MHz, Chloroform-d



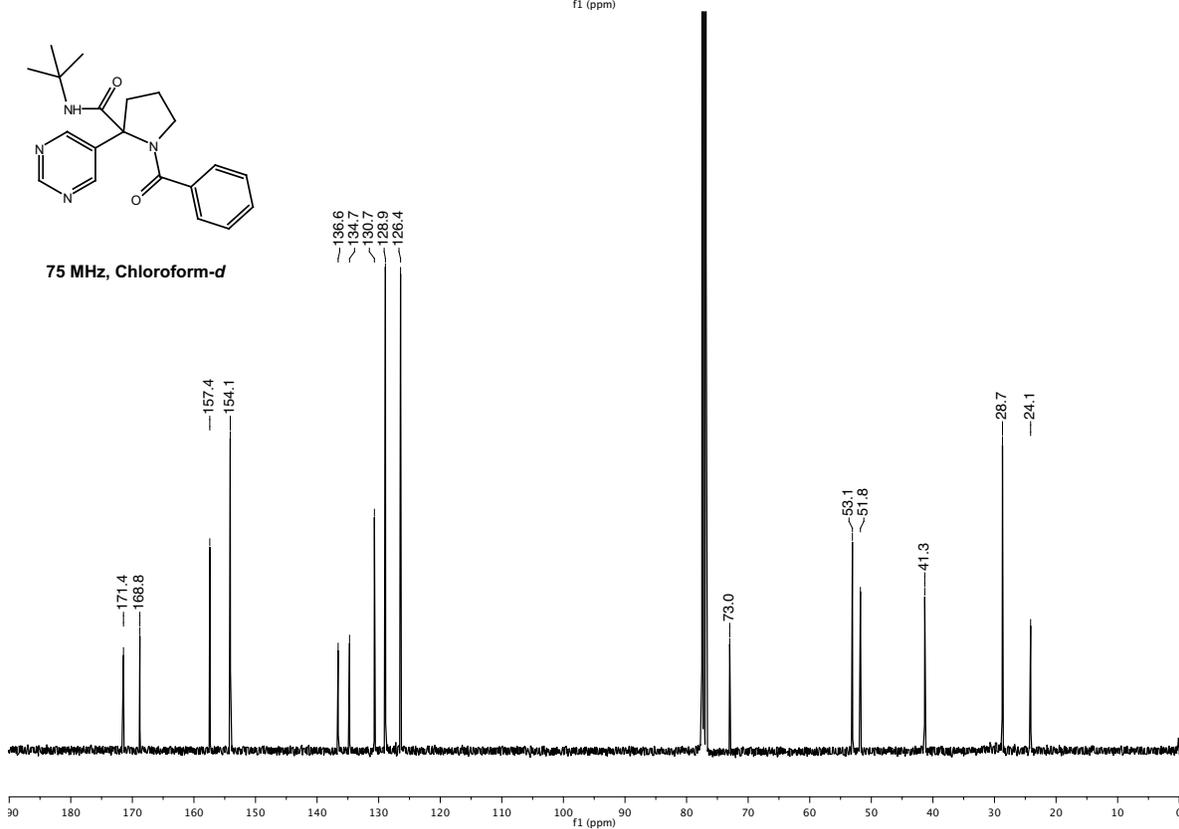
1-benzoyl-N-(*tert*-butyl)-2-(pyrimidin-5-yl)pyrrolidine-2-carboxamide 8x



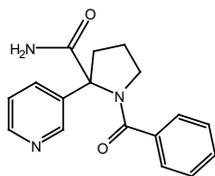
300 MHz, Chloroform-*d*



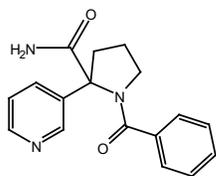
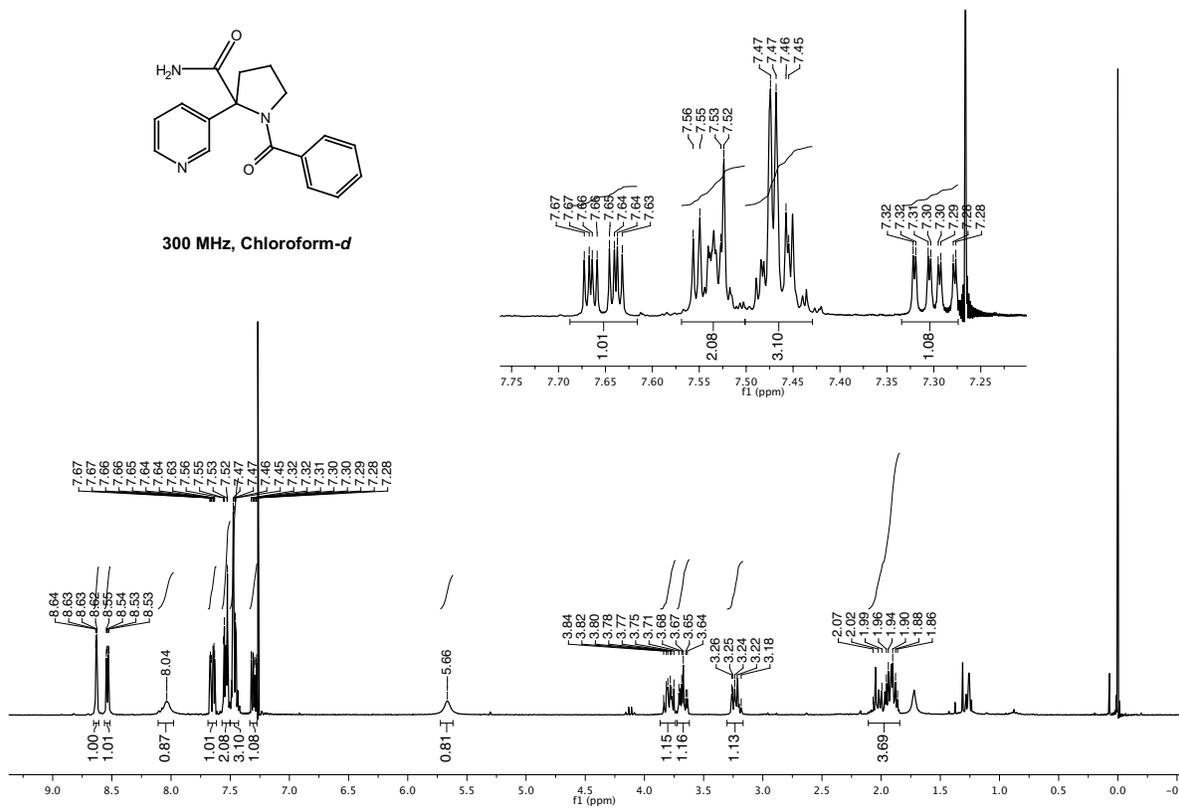
75 MHz, Chloroform-*d*



1-benzoyl-2-(pyridin-3-yl)pyrrolidine-2-carboxamide 13a



300 MHz, Chloroform-*d*



75 MHz, Chloroform-*d*

