

Synthesis and biological evaluation of (S)-2-(substituted arylmethyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-*a*]indole-3-carboxamide analogs and their synergistic effect against PTEN-deficient MDA-MB-468 cells

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Tel.: +82-51-510-2816 (Y.-S.J.); +82-51-663-4889 (J.-H.K.);

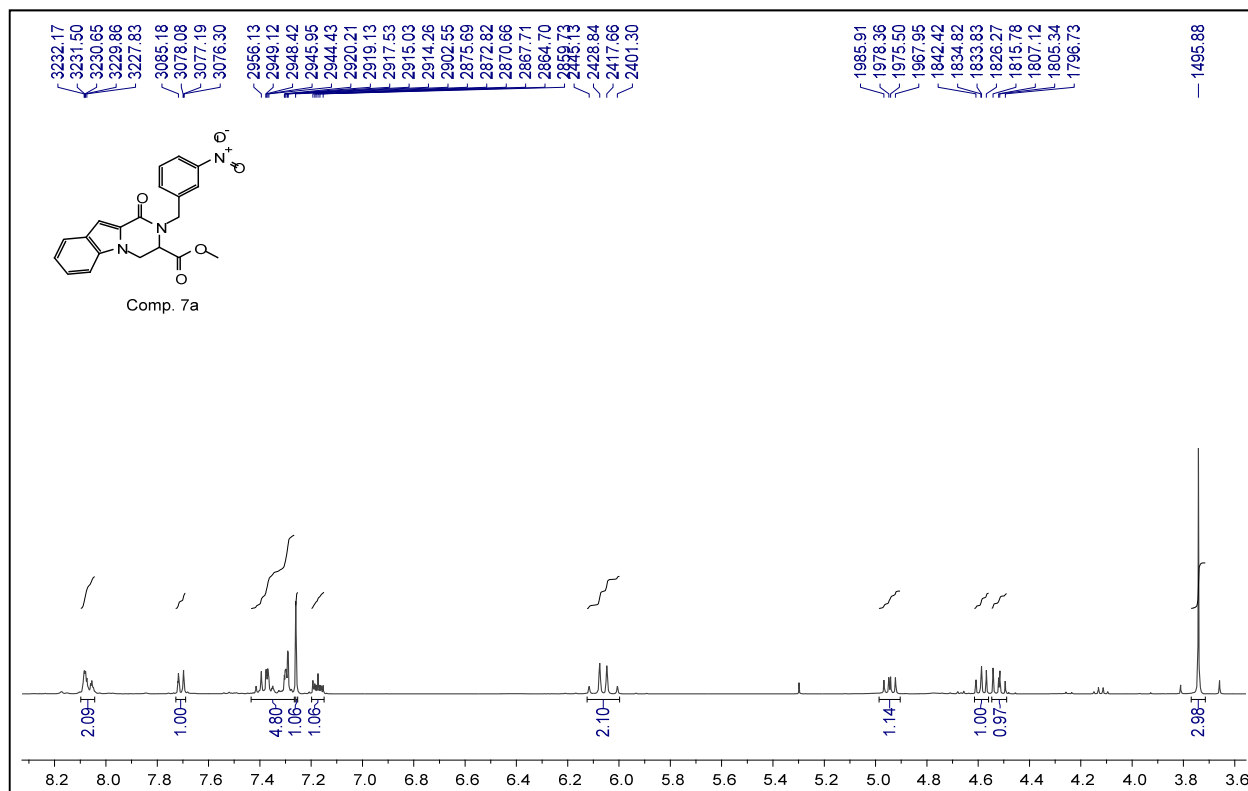
† These authors contributed equally to this work.

Supplementary Materials

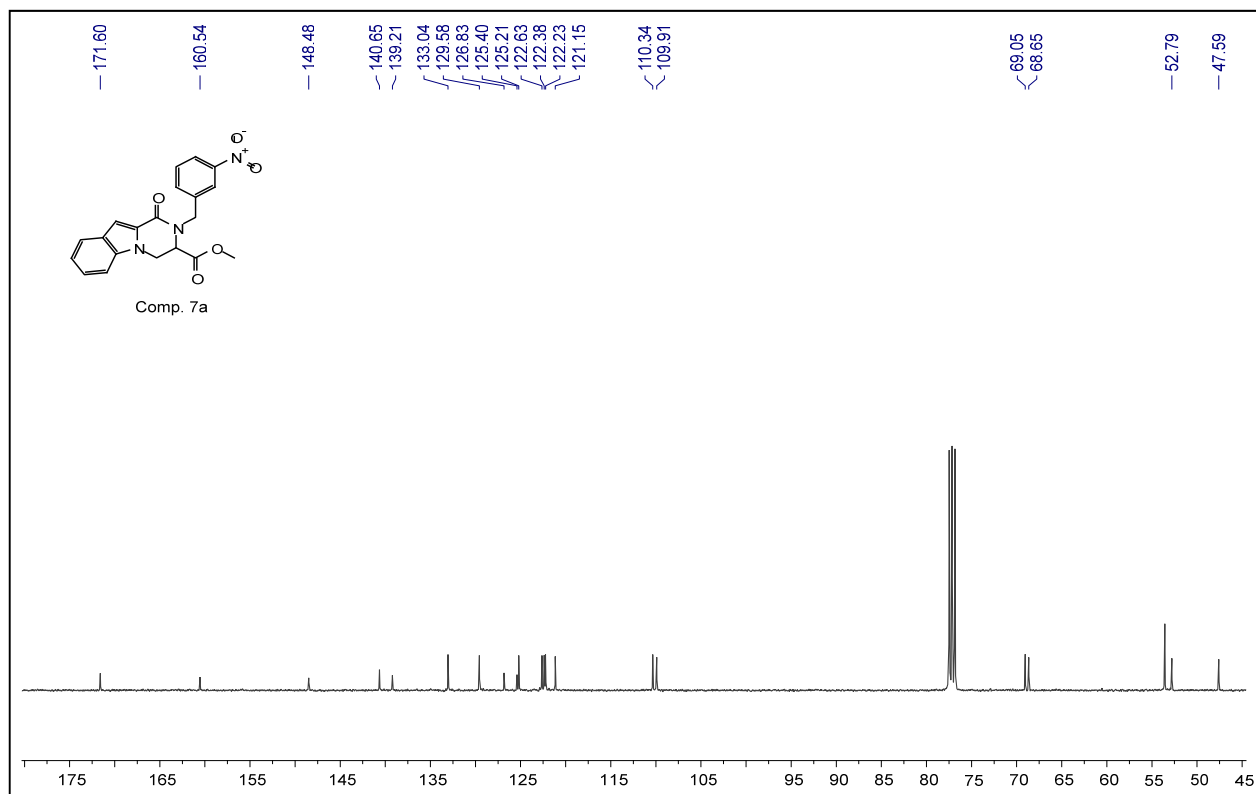
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1. ^1H and ^{13}C NMR spectra

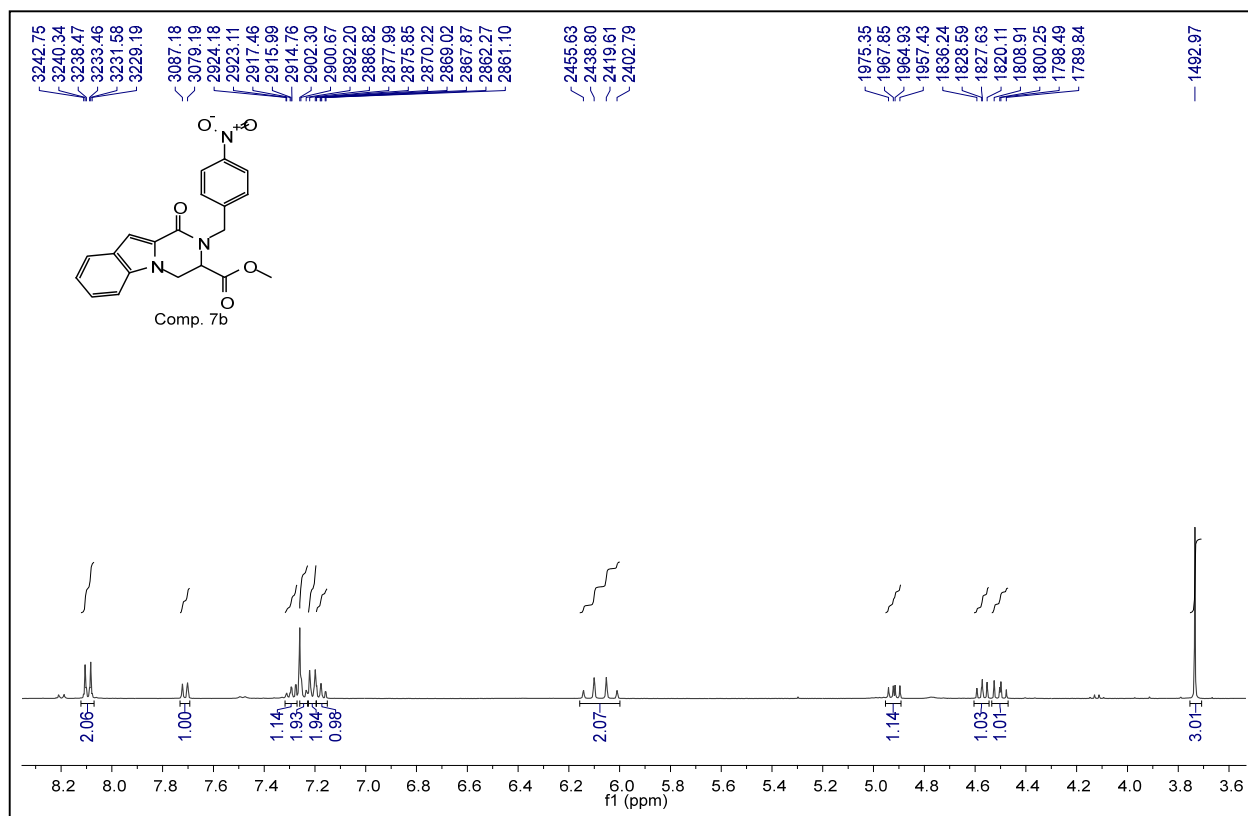
¹H NMR: Methyl (*S*)-2-(3-nitrobenzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-*a*]indole-3-carboxylate (7a)



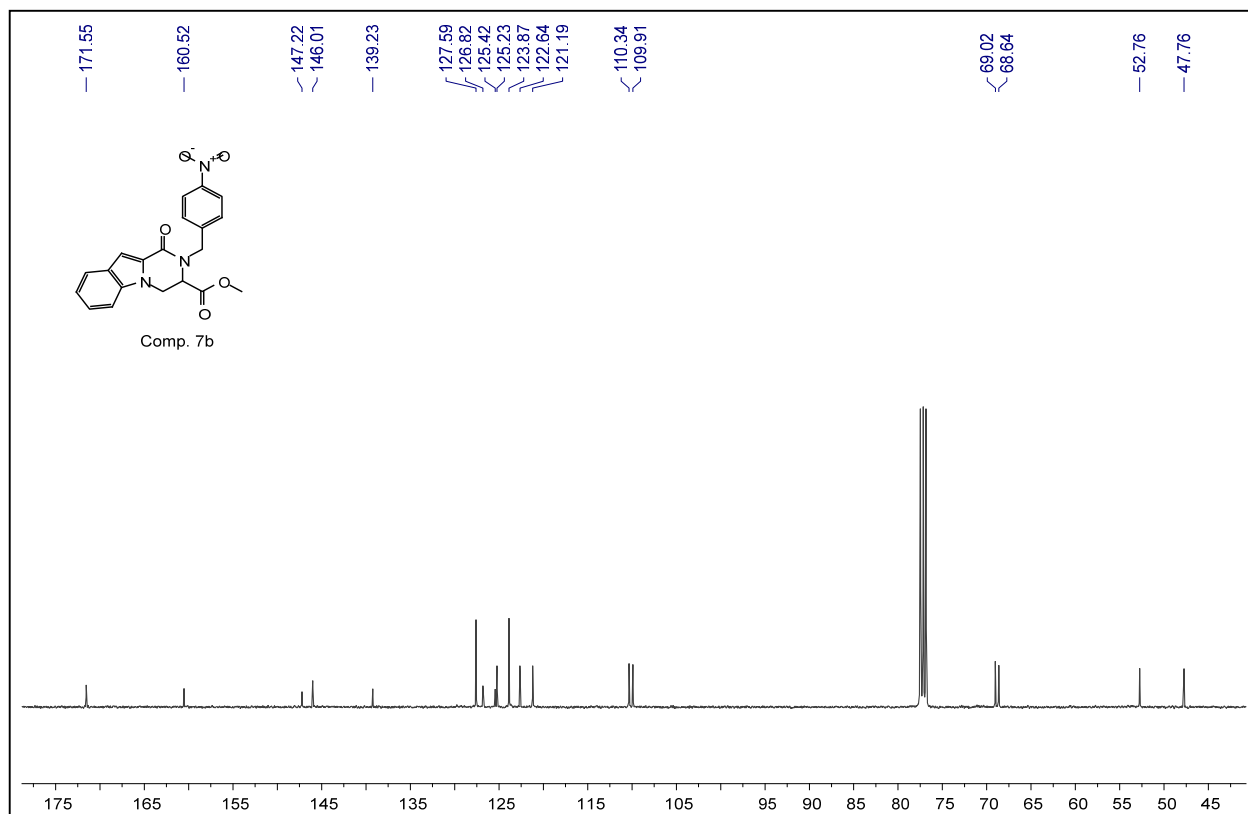
¹³C NMR: Methyl (*S*)-2-(3-nitrobenzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-*a*]indole-3-carboxylate (7a)



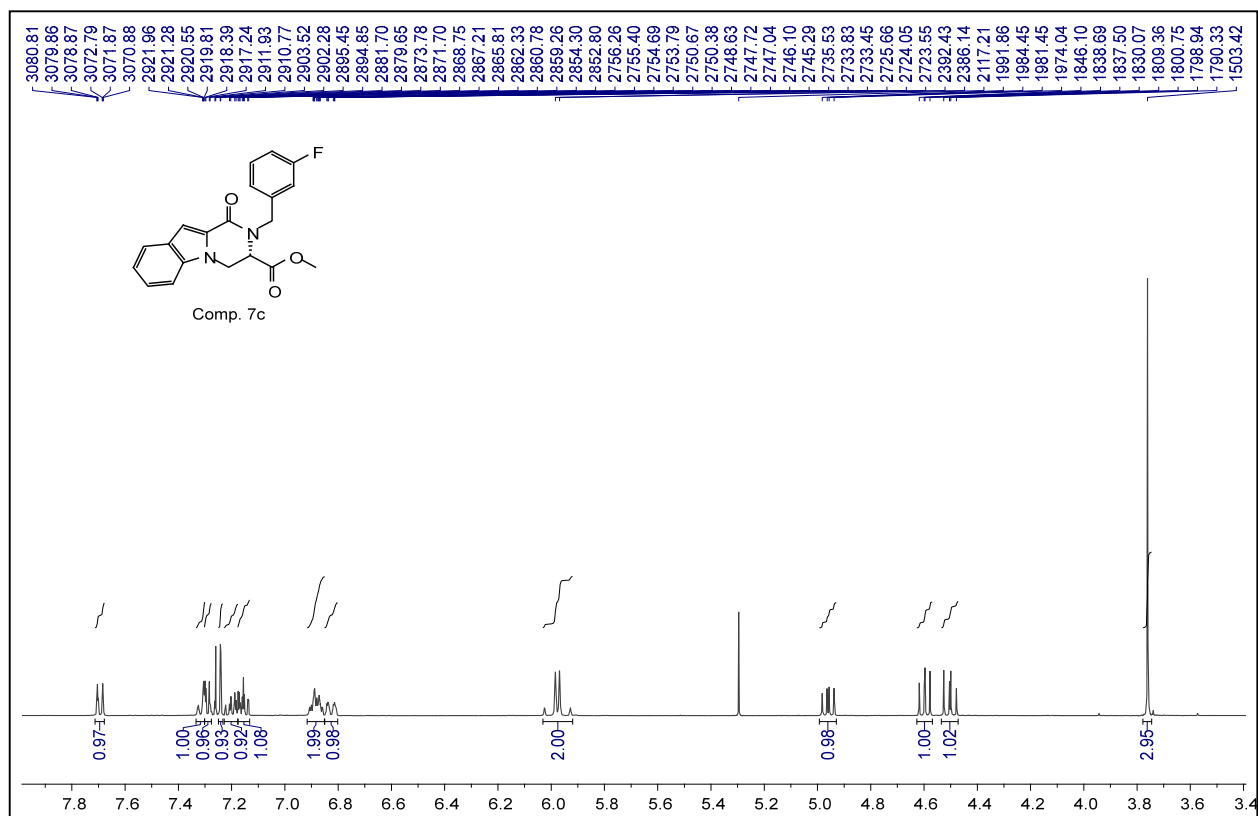
¹H NMR: Methyl (*S*)-2-(4-nitrobenzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-*a*]indole-3-carboxylate (7b)



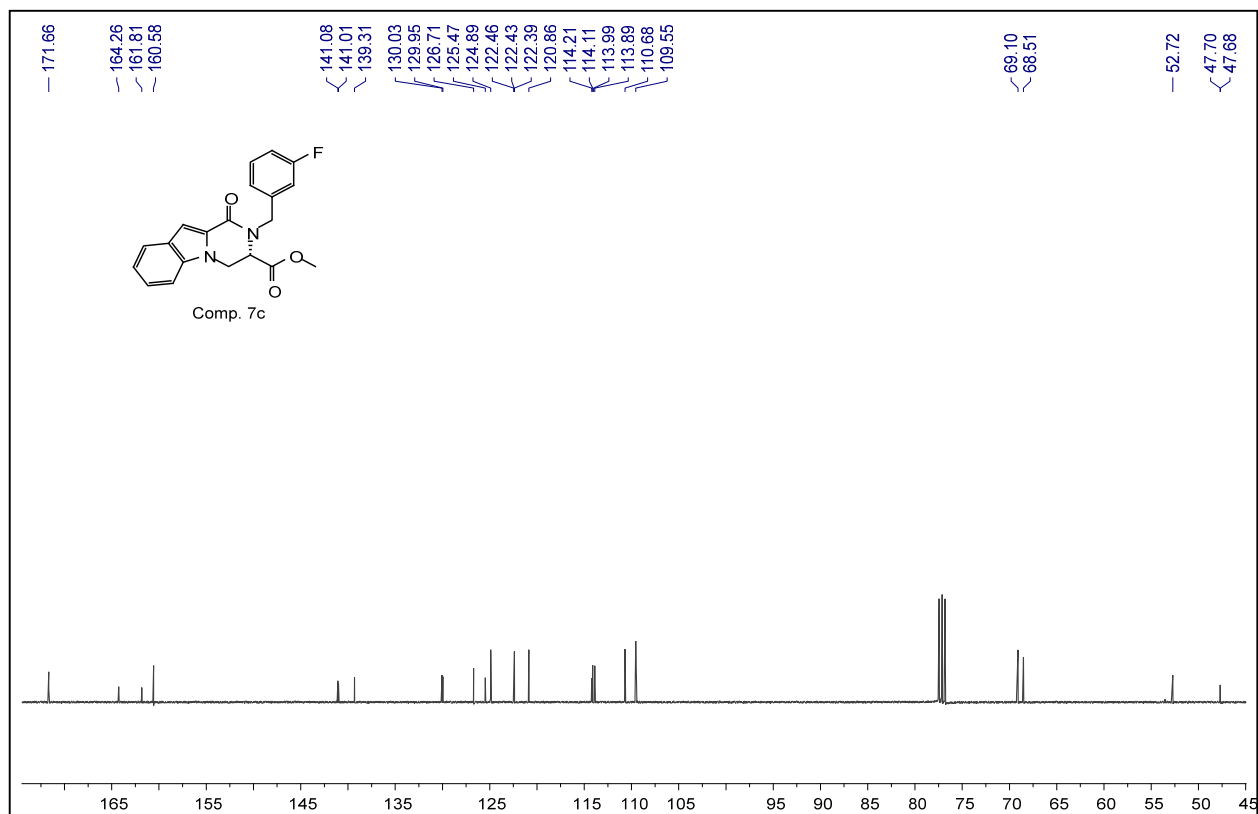
¹³C NMR: Methyl (*S*)-2-(4-nitrobenzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-*a*]indole-3-carboxylate (**7b**)



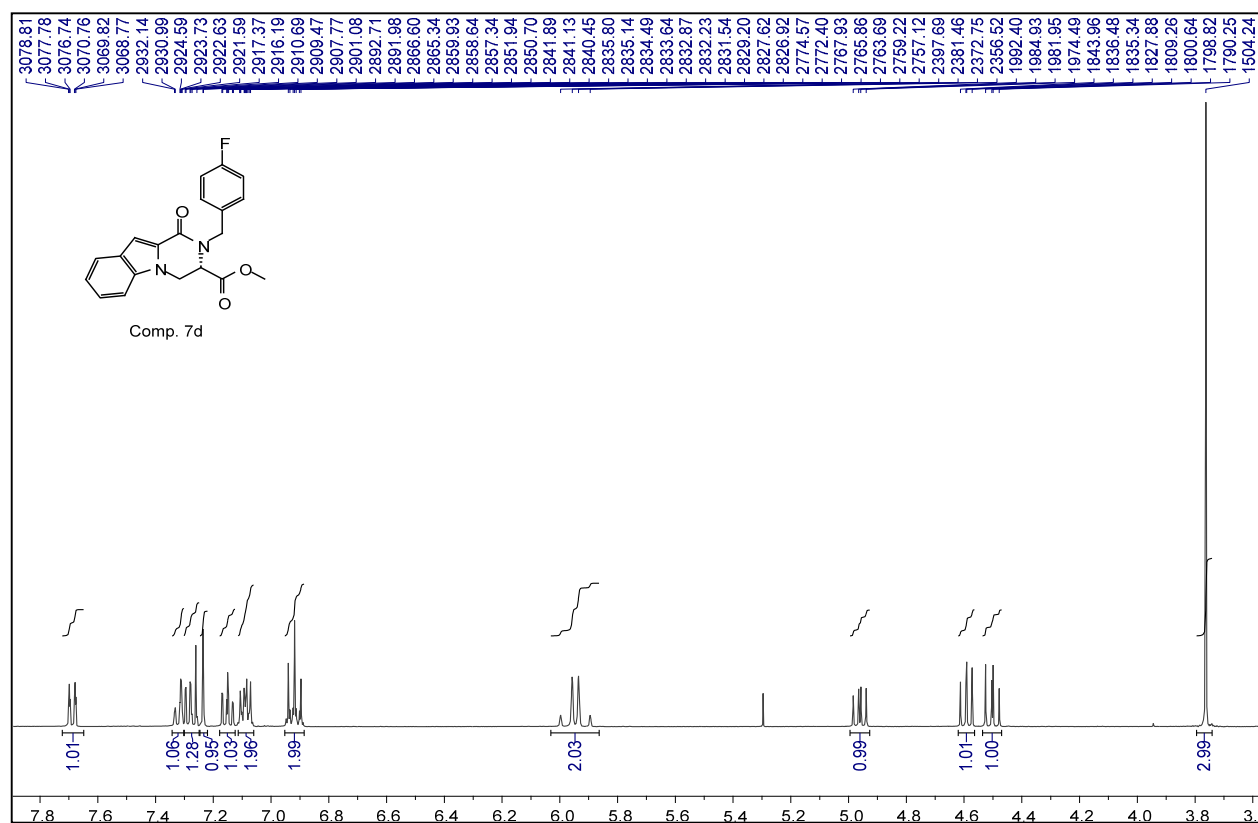
¹H NMR: Methyl (*S*)-2-(3-fluorobenzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-*a*]indole-3-carboxylate (7c)



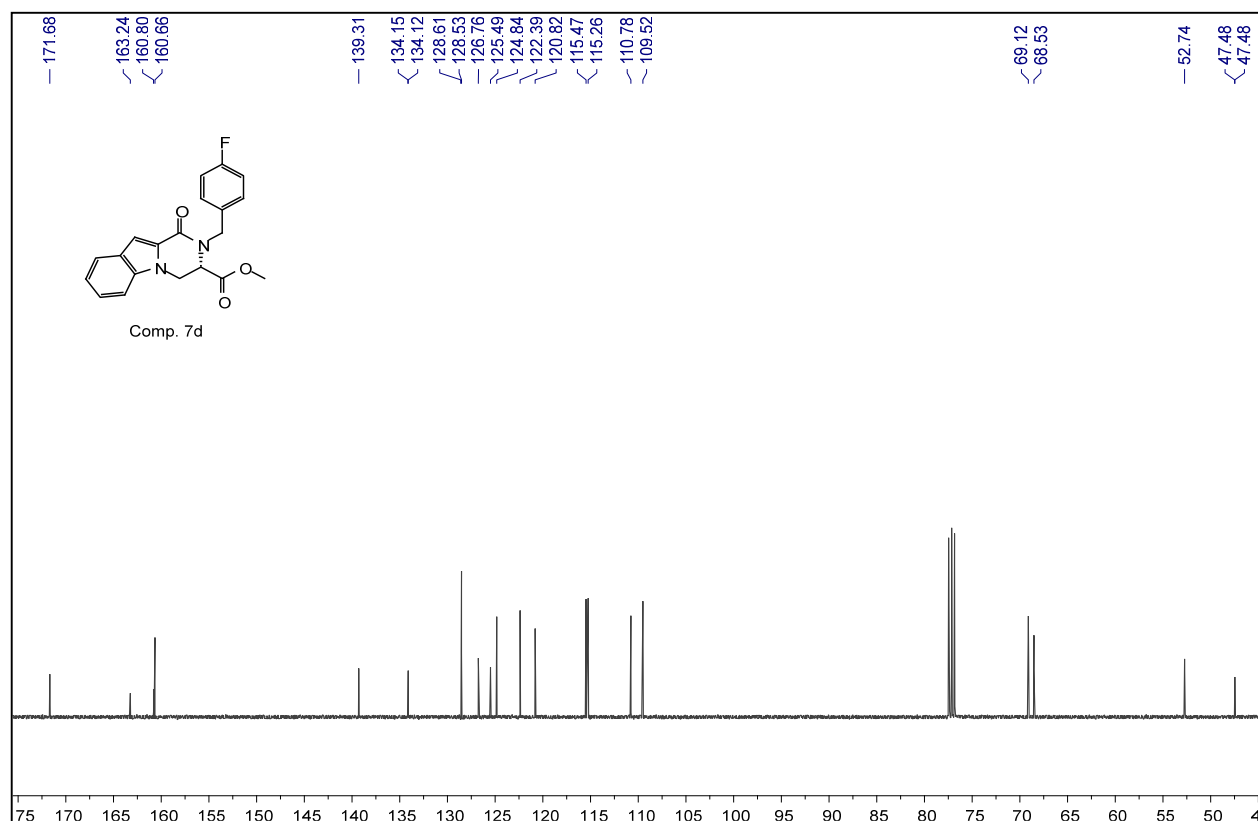
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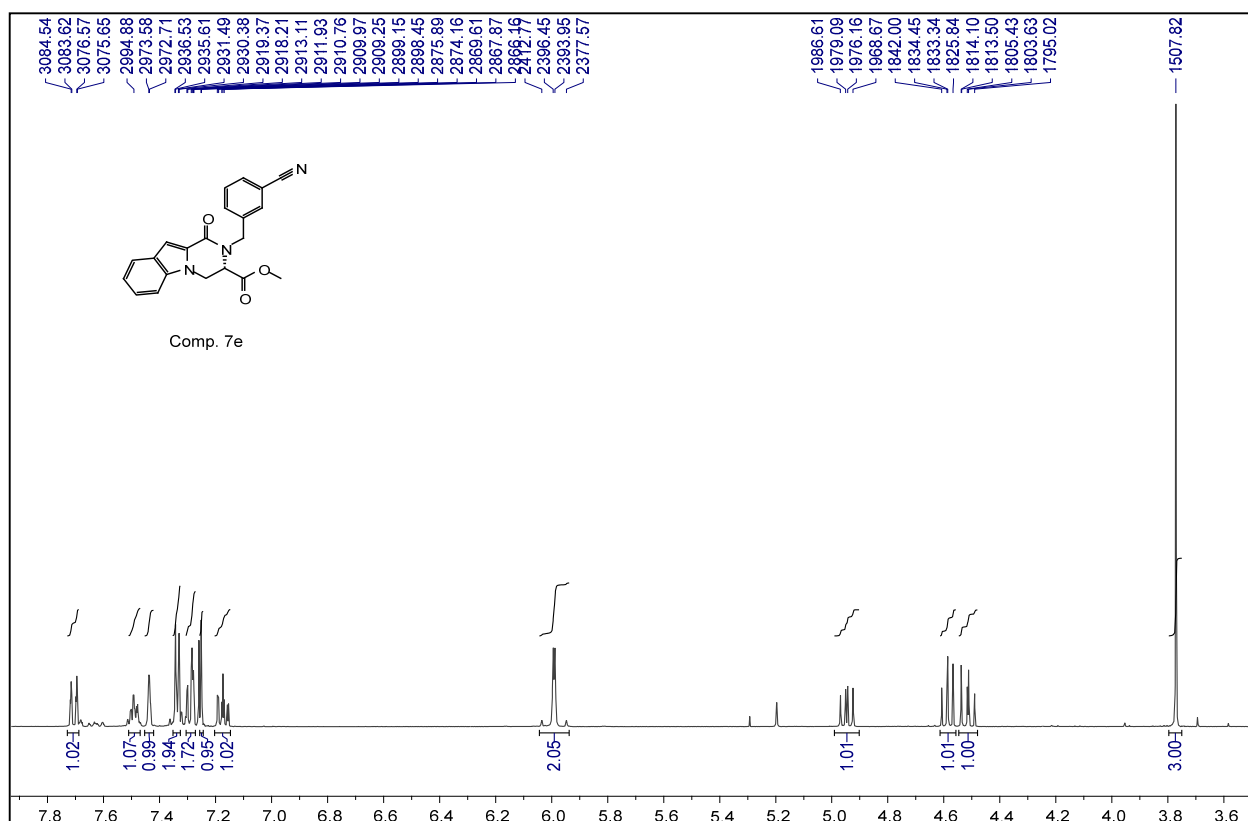
¹H NMR: Methyl (*S*)-2-(4-fluorobenzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-*a*]indole-3-carboxylate (7d)



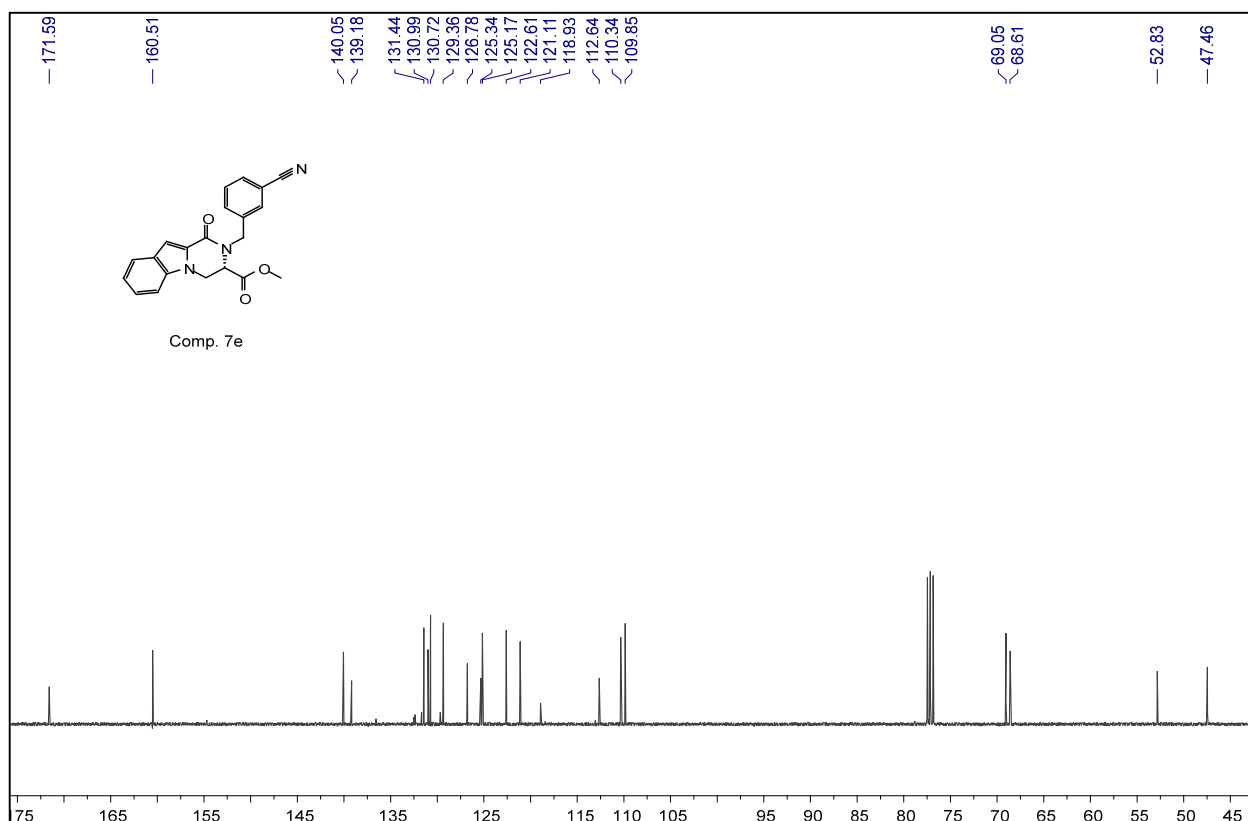
¹³C NMR: Methyl (*S*)-2-(4-fluorobenzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-*a*]indole-3-carboxylate (7d)



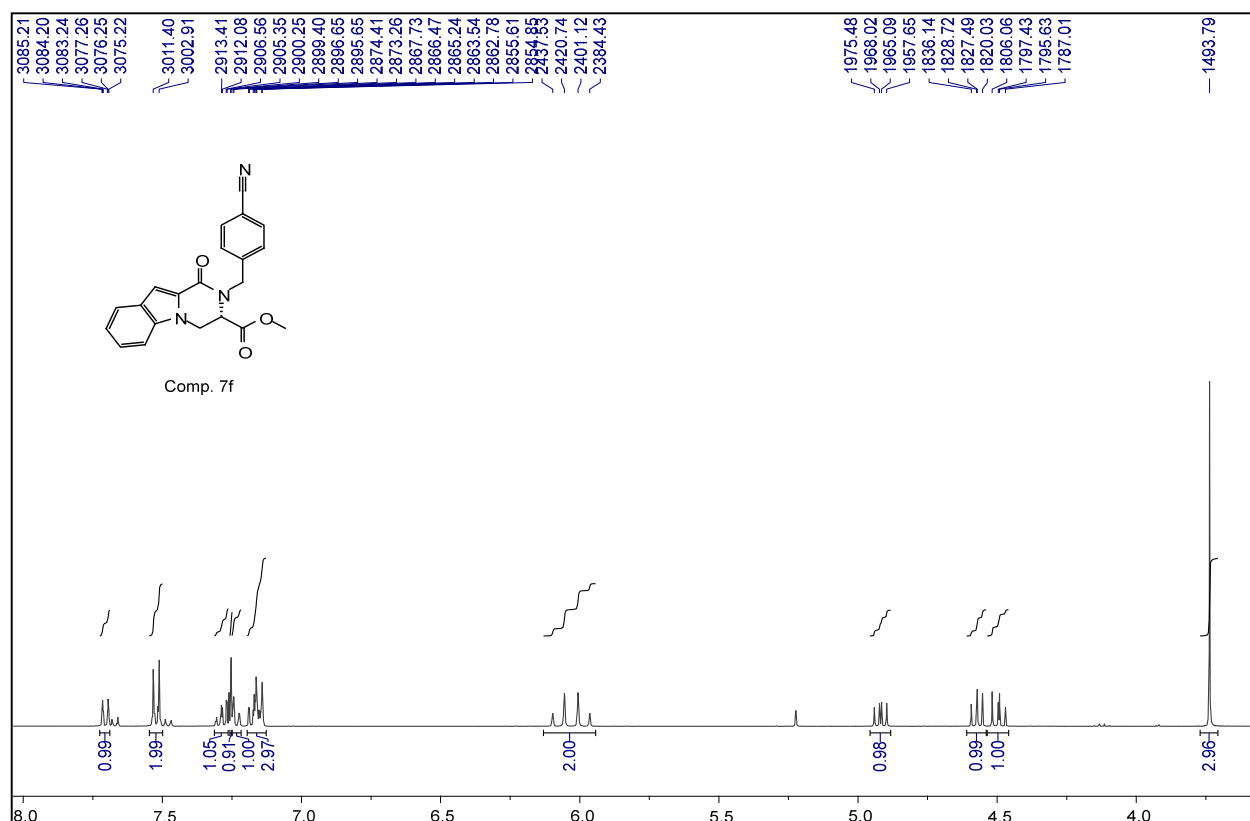
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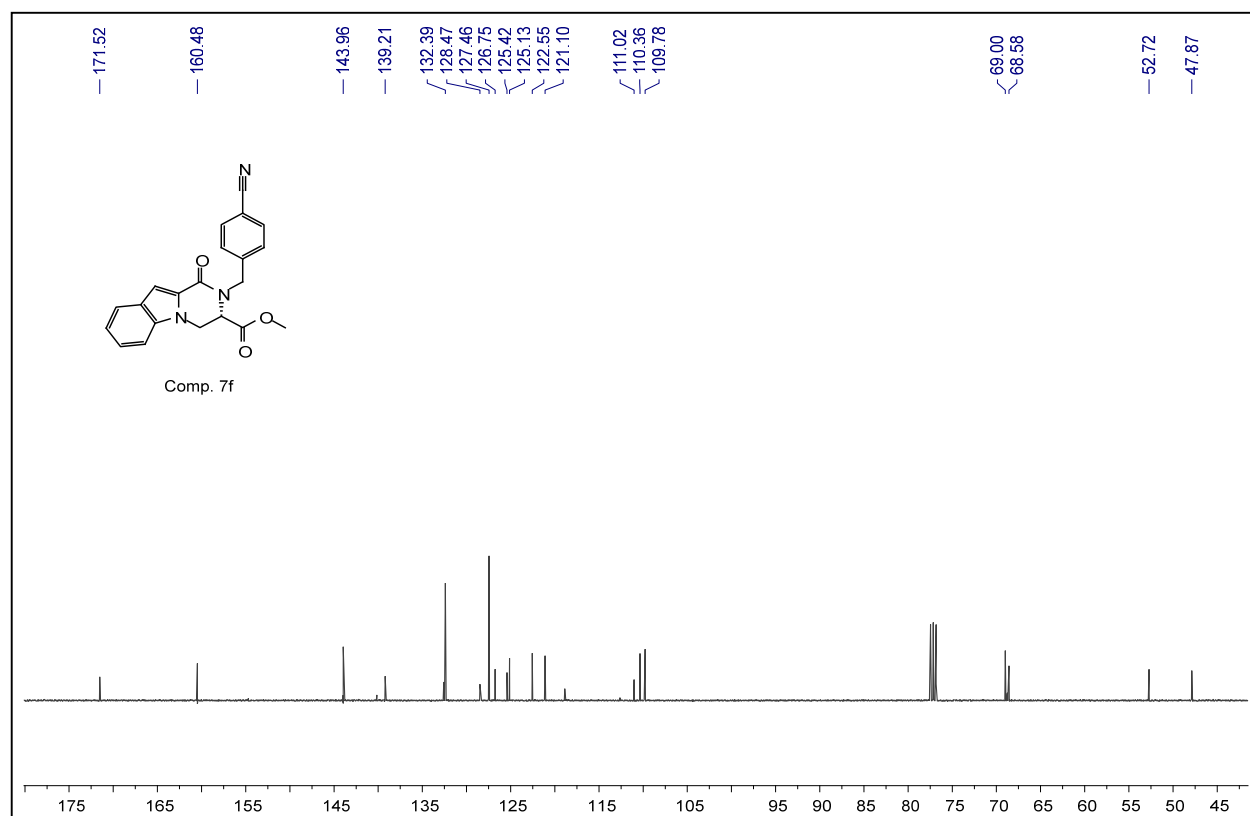
¹³C NMR: Methyl (*S*)-2-(3-cyanobenzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-*a*]indole-3-carboxylate (7e)



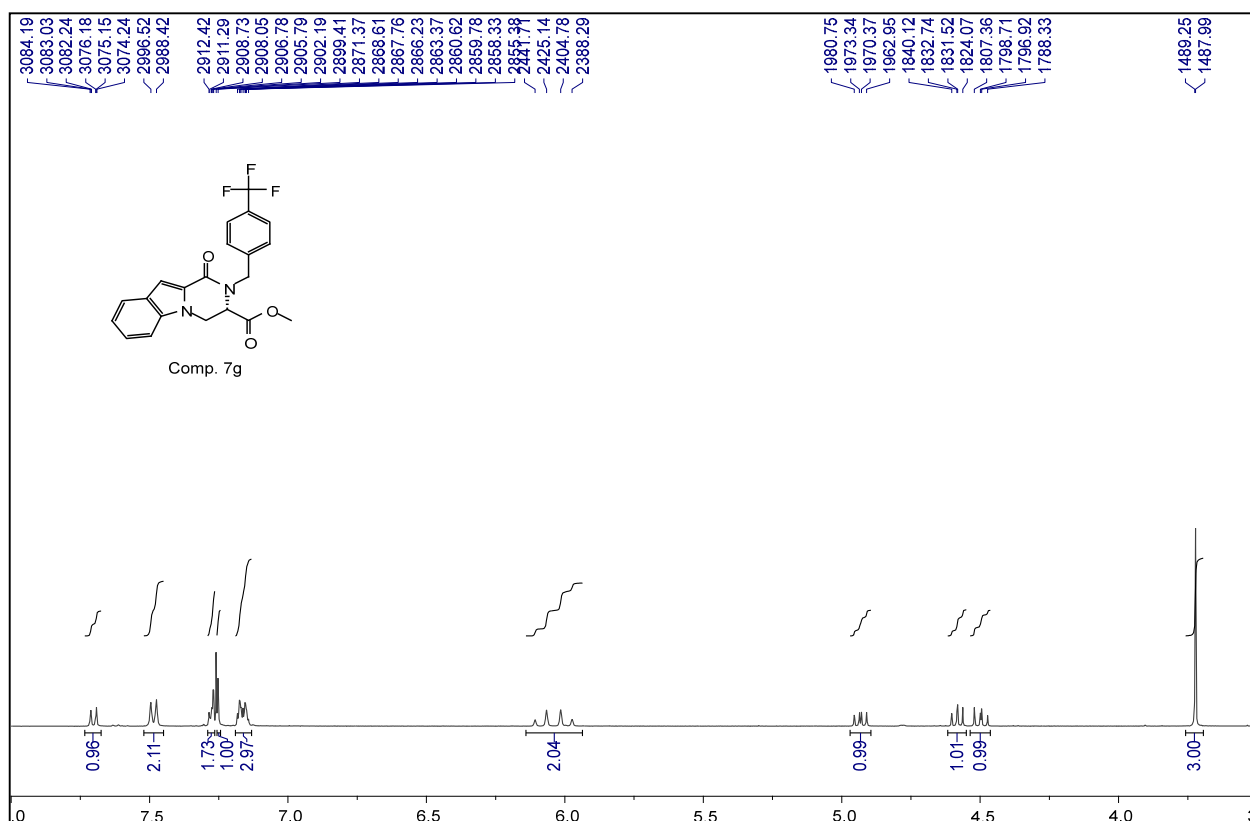
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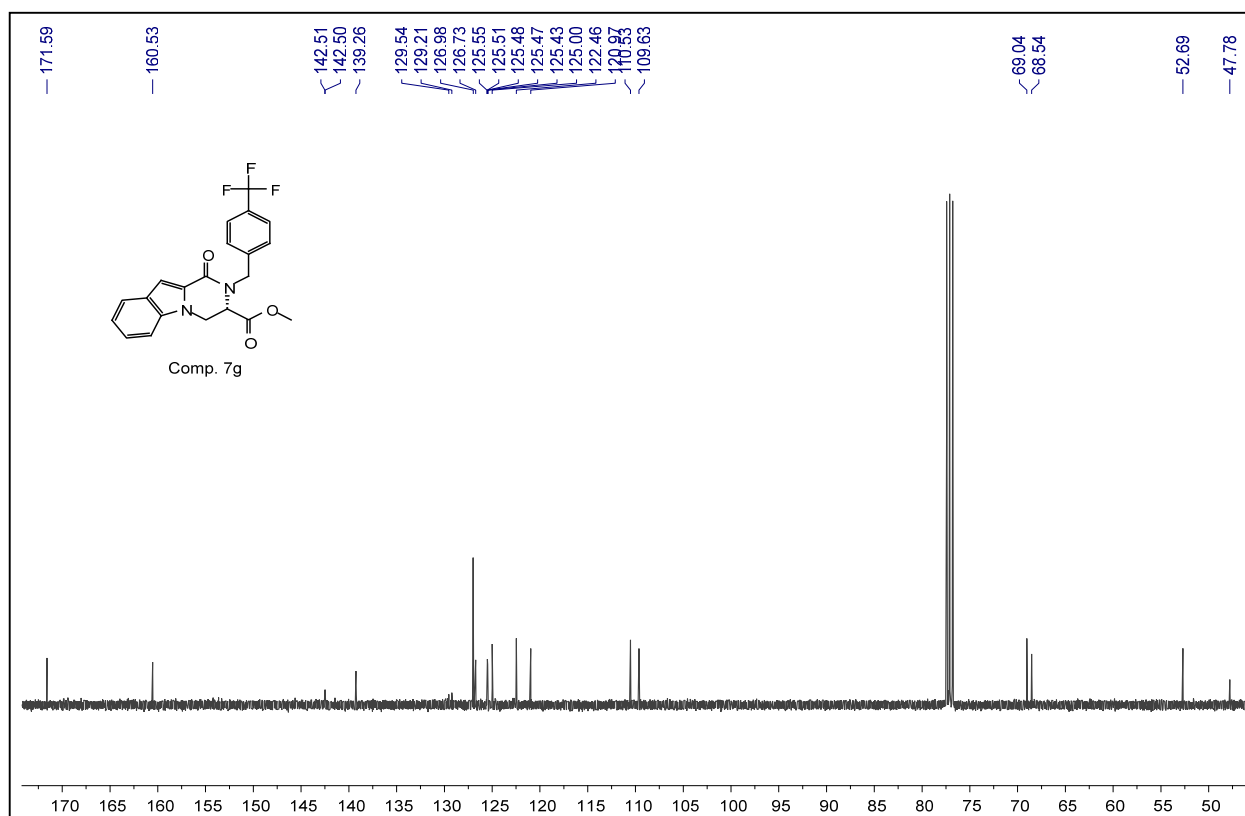
¹³C NMR: Methyl (*S*)-2-(4-cyanobenzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-*a*]indole-3-carboxylate (7f)



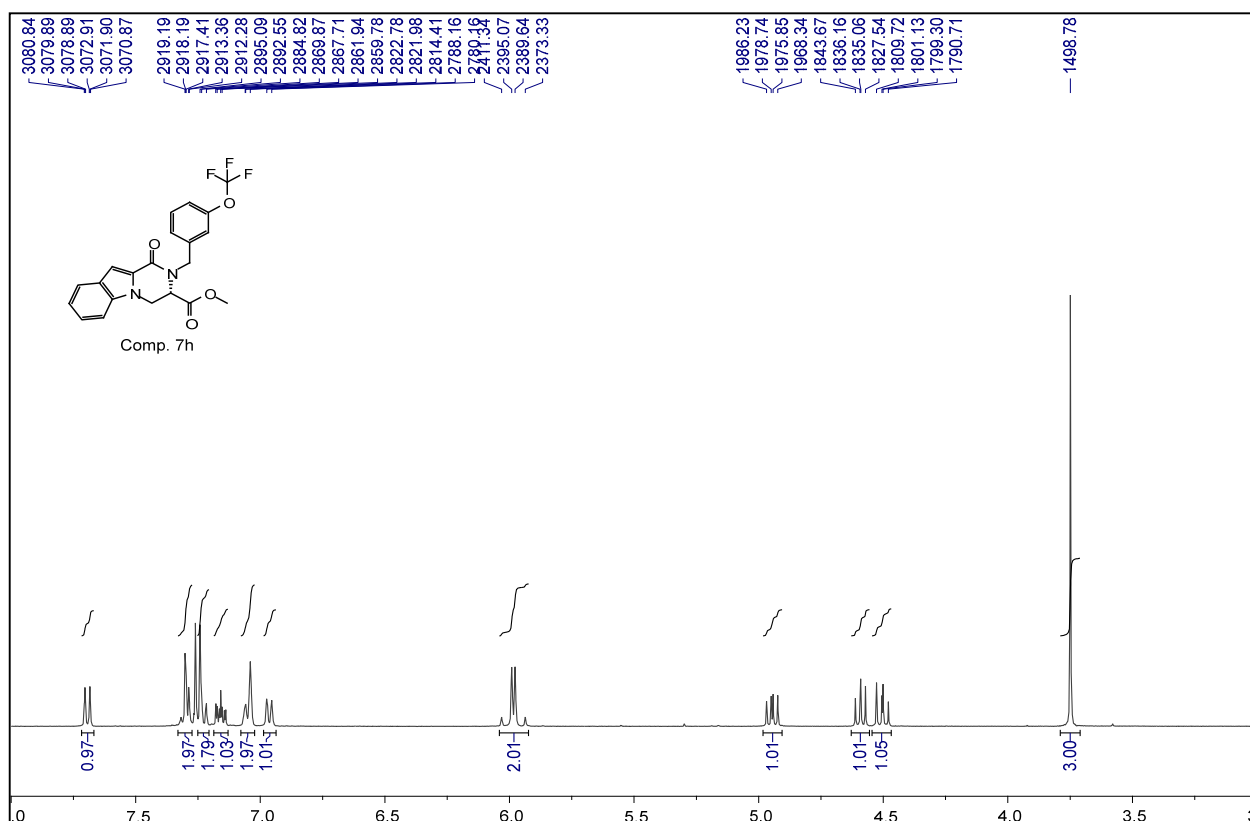
¹H NMR: Methyl (*S*)-2-(4-(trifluoromethyl)benzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-*a*]indole-3-carboxylate (7g)



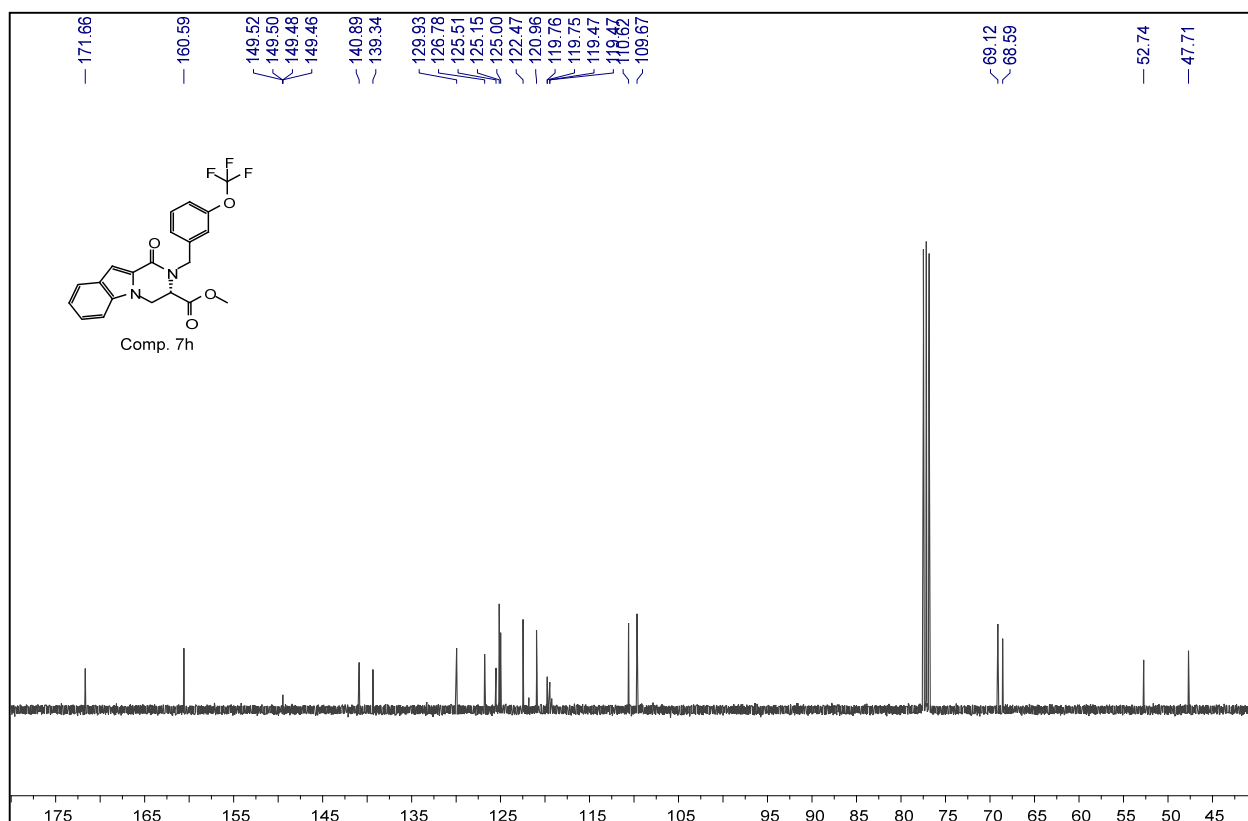
¹³C NMR: Methyl (*S*)-2-(4-(trifluoromethyl)benzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-*a*]indole-3-carboxylate (7g)



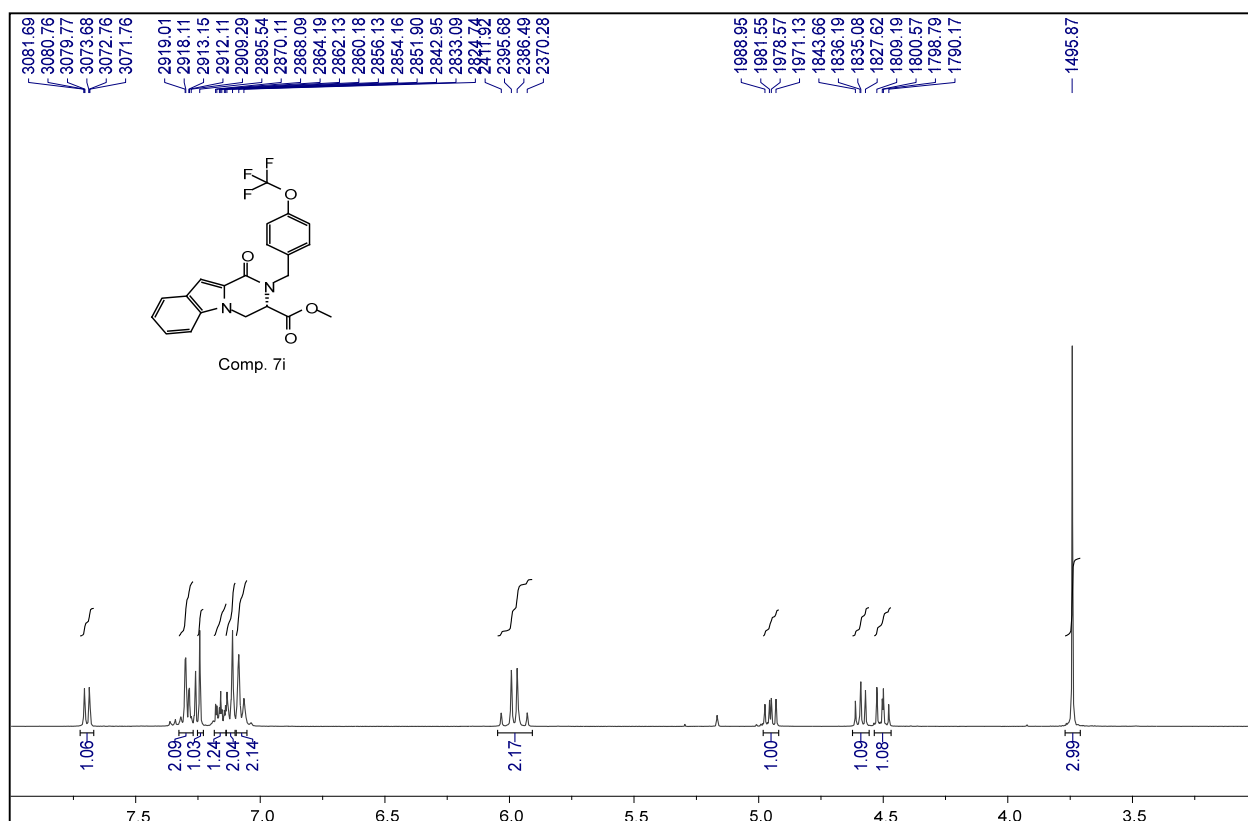
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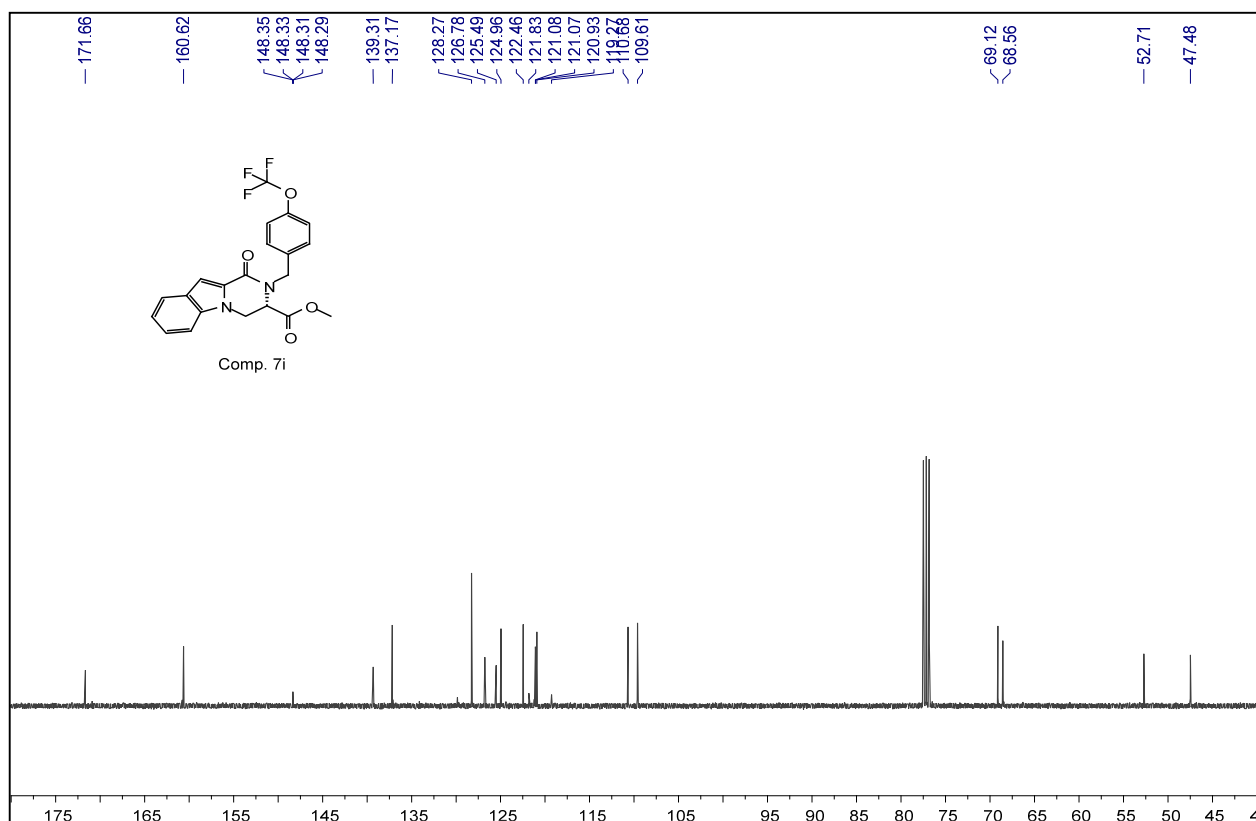
¹³C NMR: Methyl (*S*)-2-(3-(trifluoromethoxy)benzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-*a*]indole-3-carboxylate (7h)



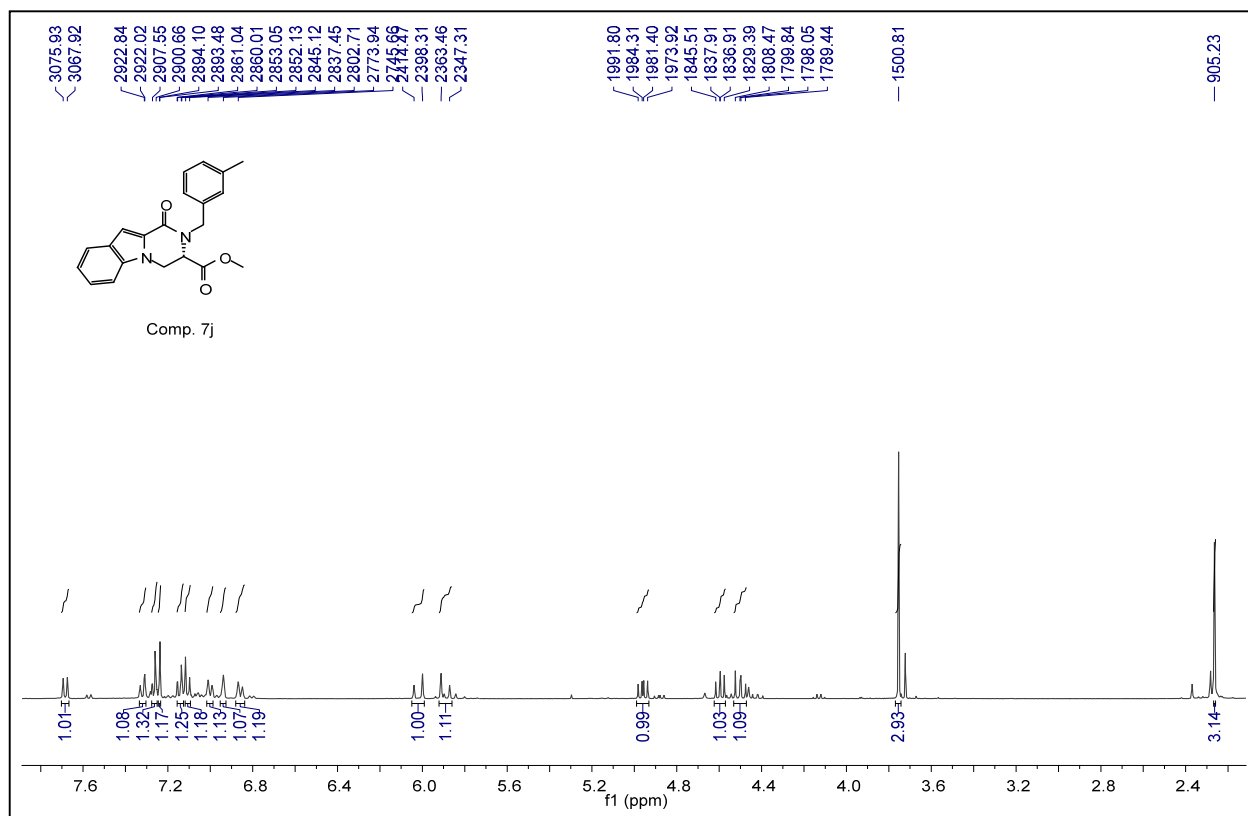
¹H NMR: Methyl (*S*)-2-(4-(trifluoromethoxy)benzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-*a*]indole-3-carboxylate (7i)



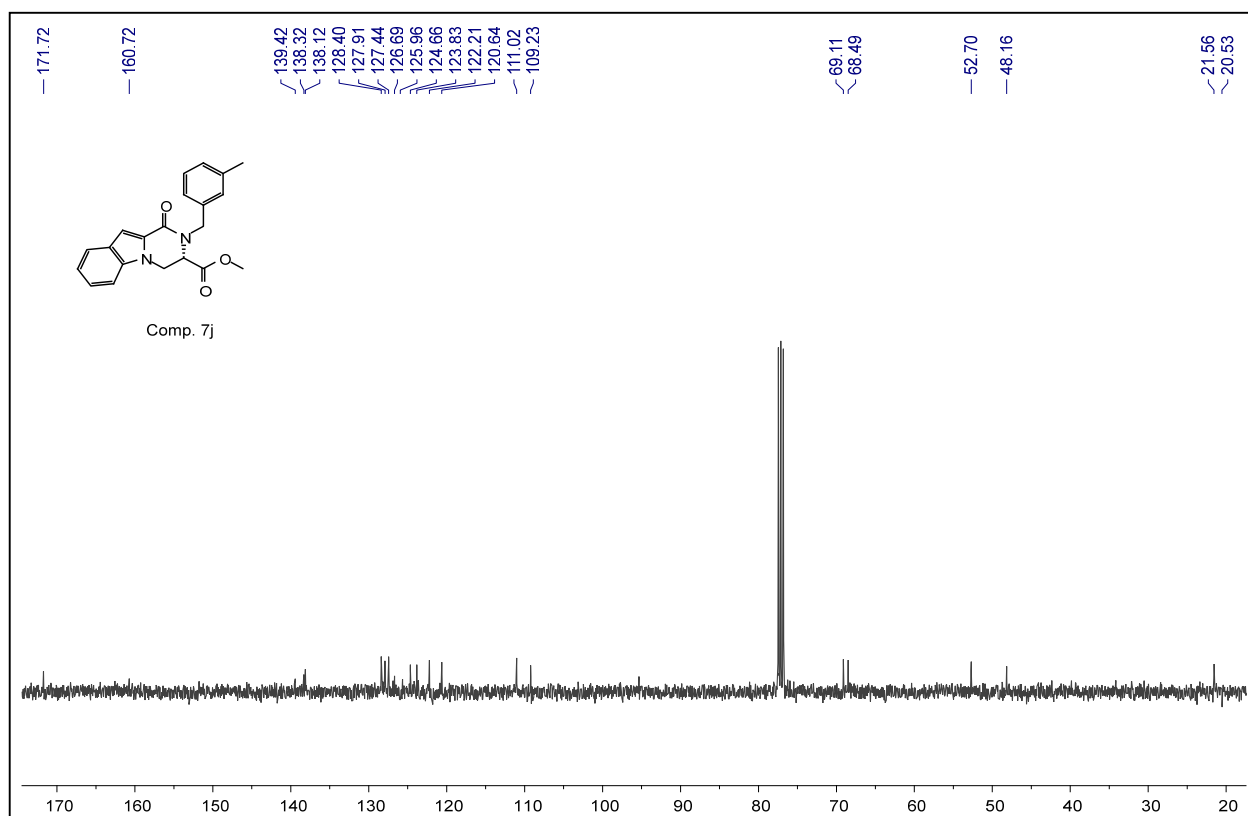
¹³C NMR: Methyl (*S*)-2-(4-(trifluoromethoxy)benzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-*a*]indole-3-carboxylate (7i)



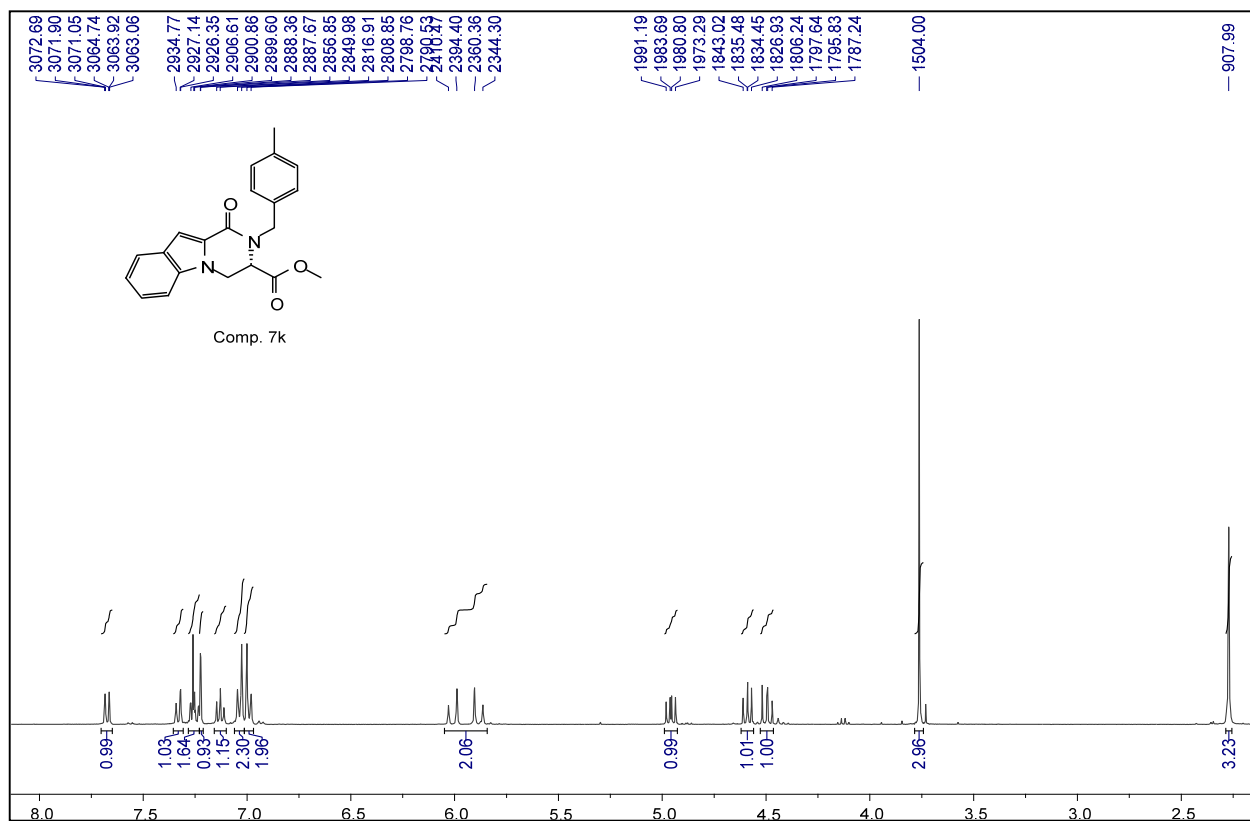
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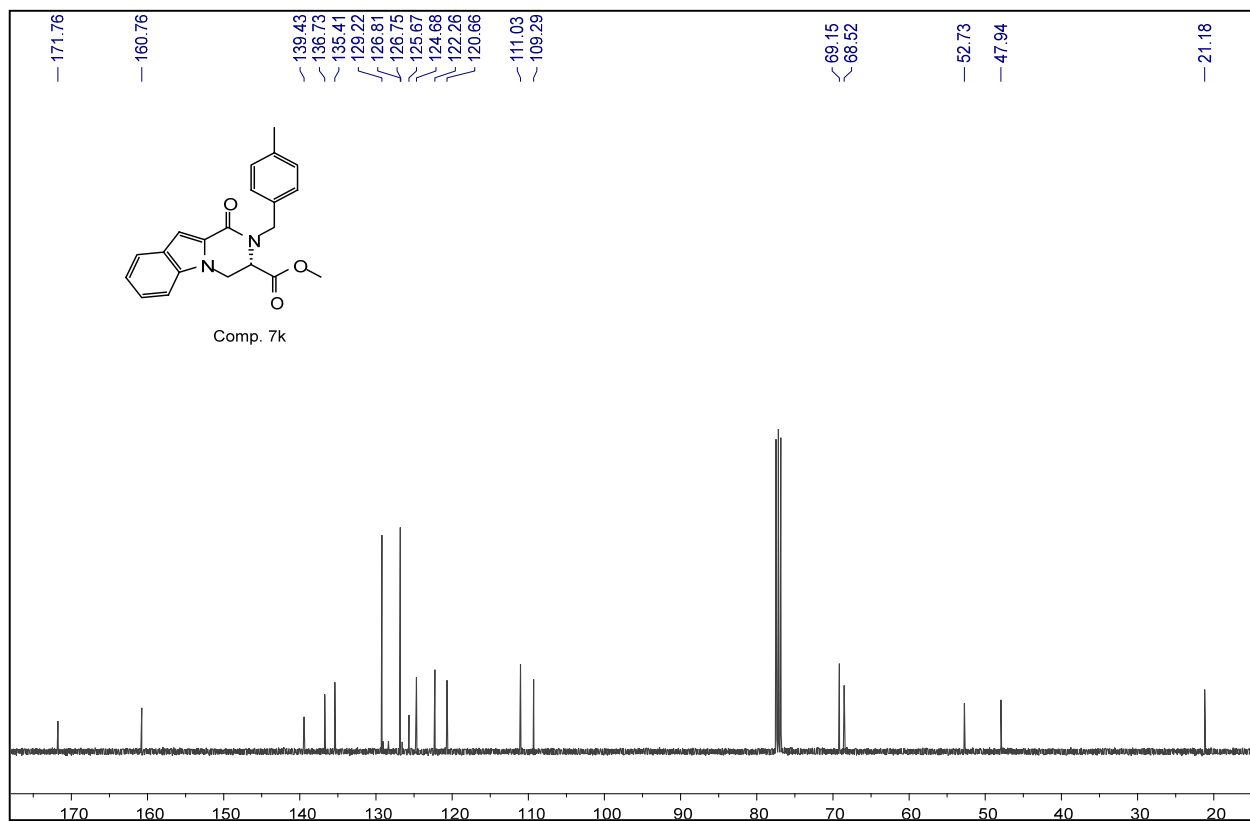
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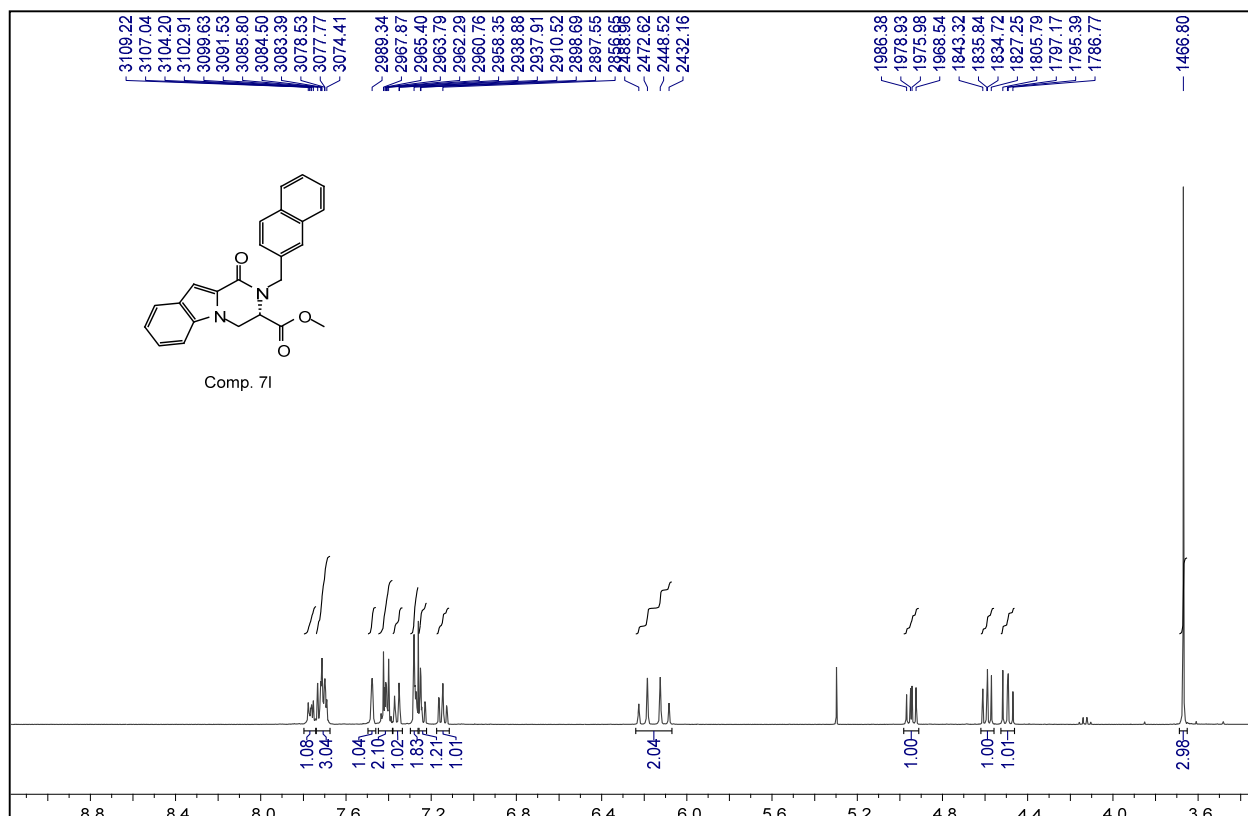
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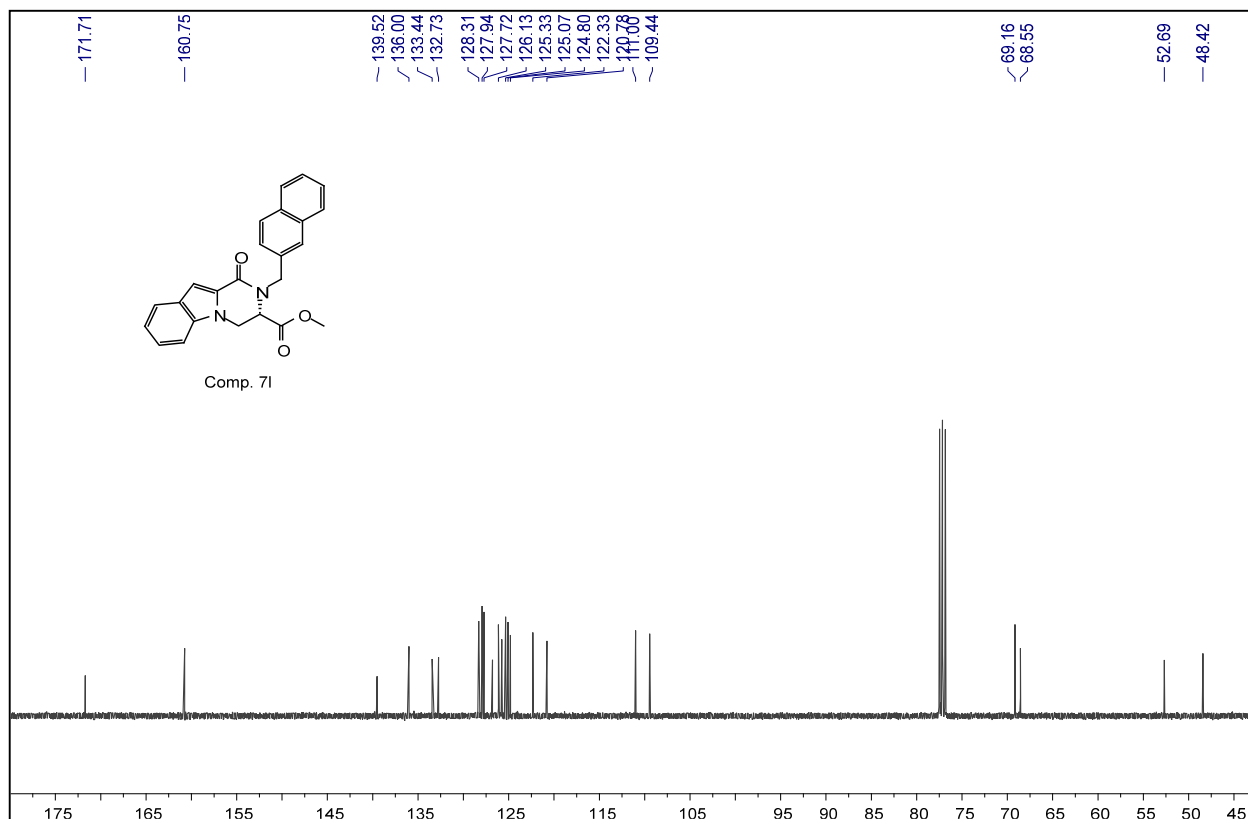
¹³C NMR: Methyl (*S*)-2-(4-methylbenzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-*a*]indole-3-carboxylate (7k)



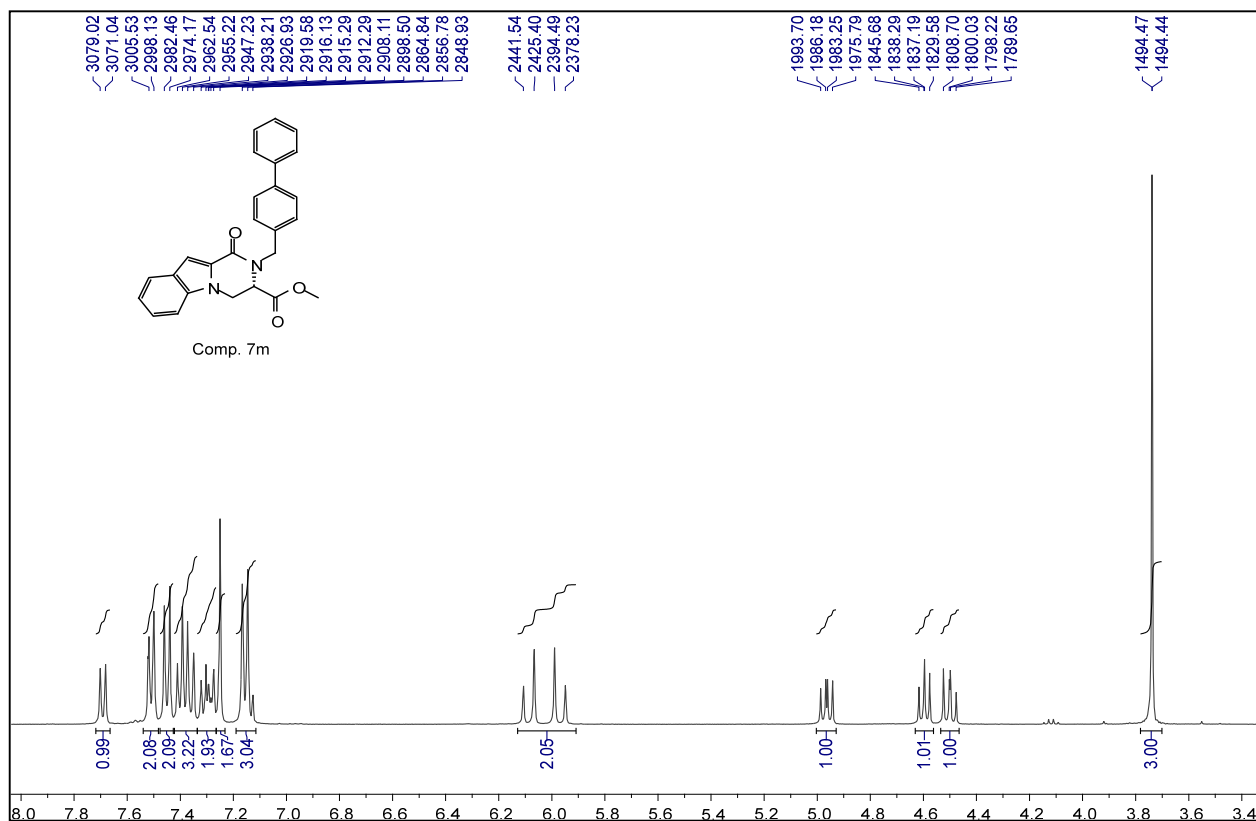
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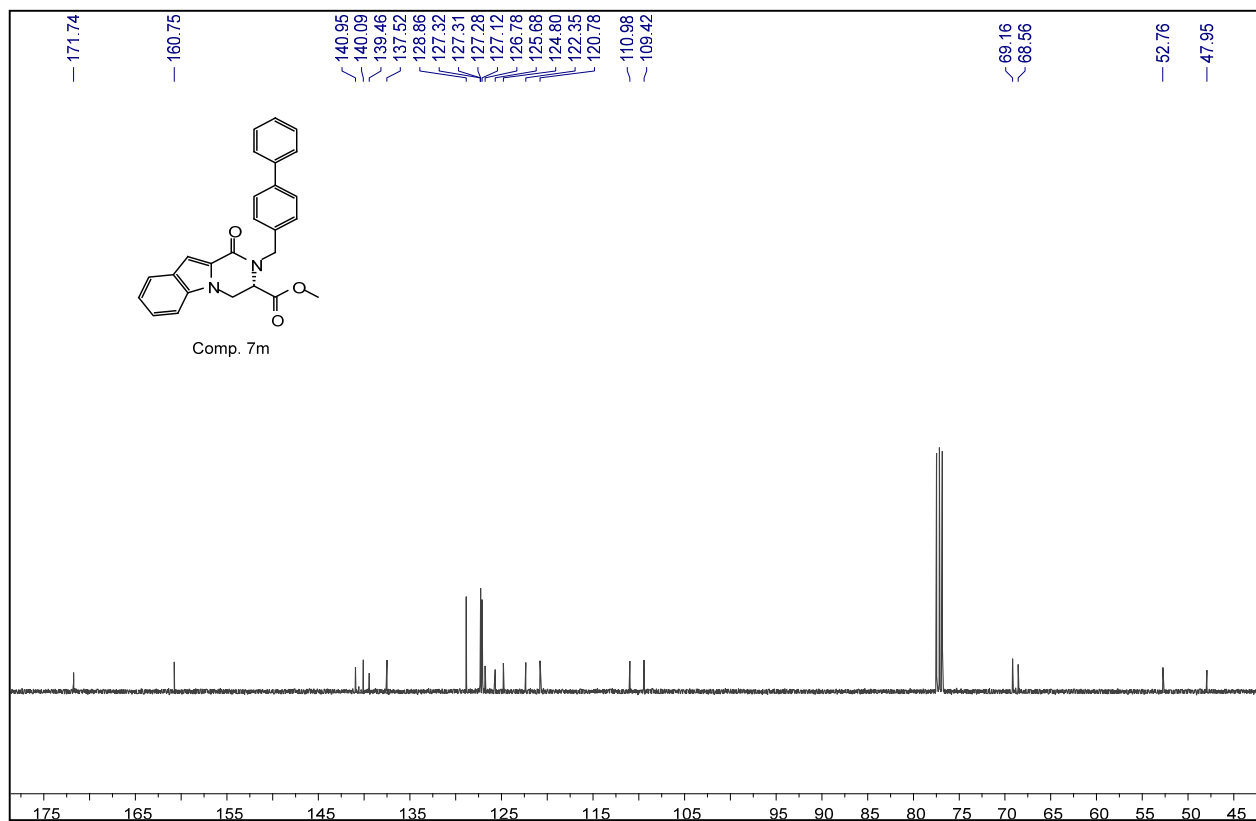
¹³C NMR: Methyl (*S*)-2-(naphthalen-2-ylmethyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-*a*]indole-3-carboxylate (71)



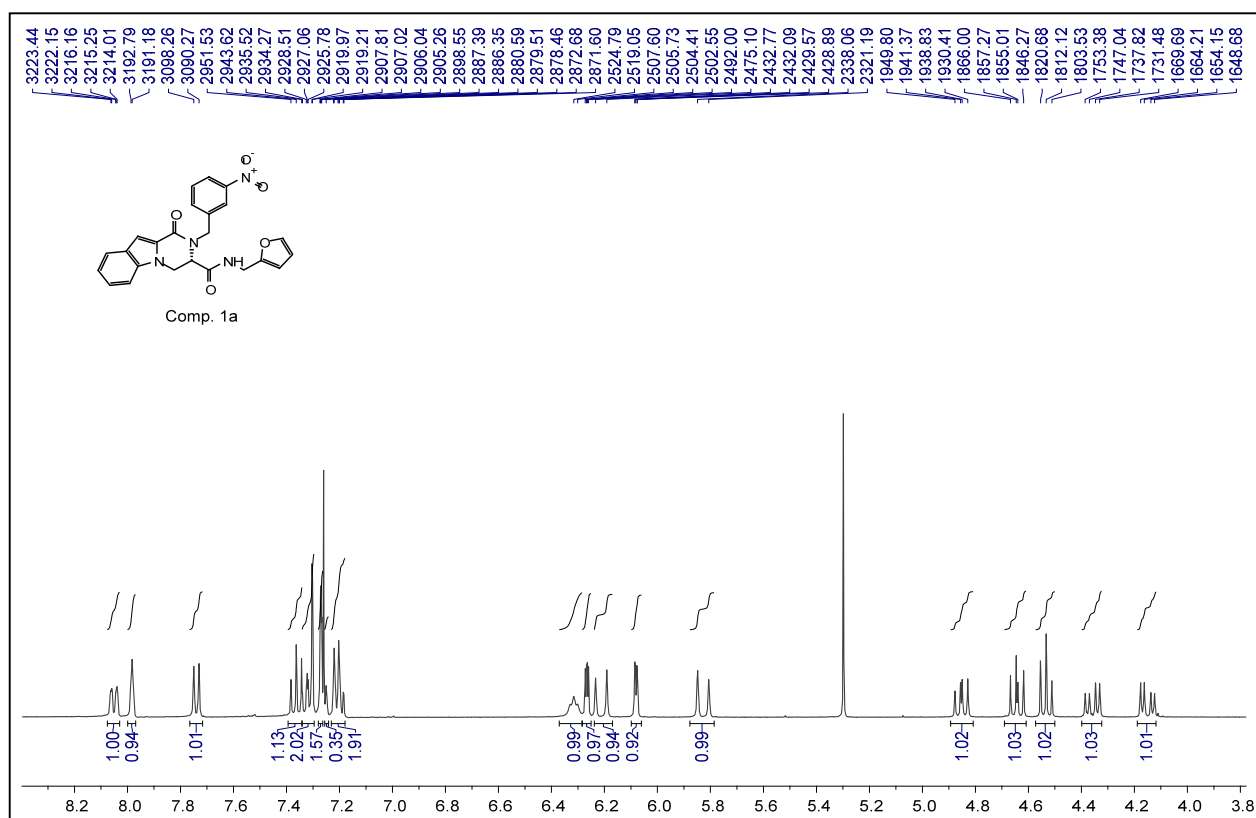
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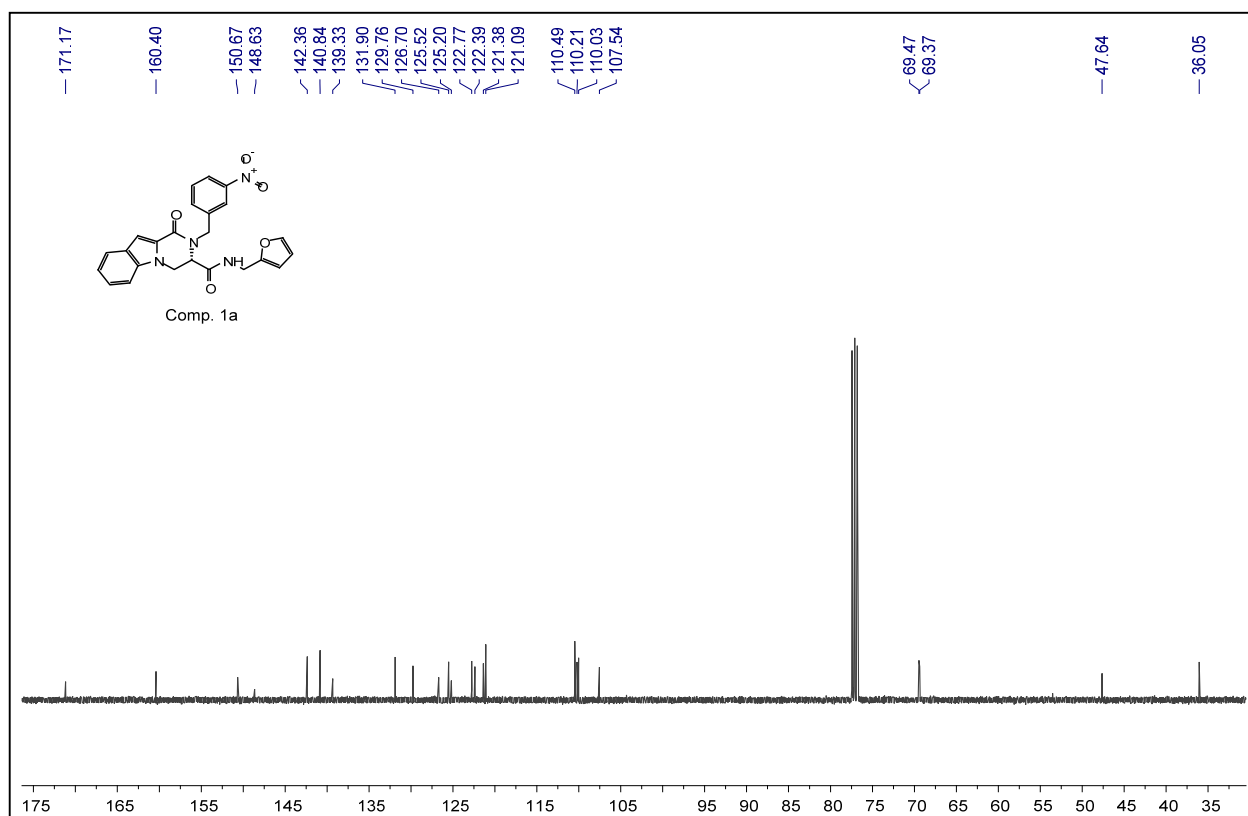
¹³C NMR: Methyl (*S*)-2-([1,1'-biphenyl]-4-ylmethyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-*a*]indole-3-carboxylate (7m)



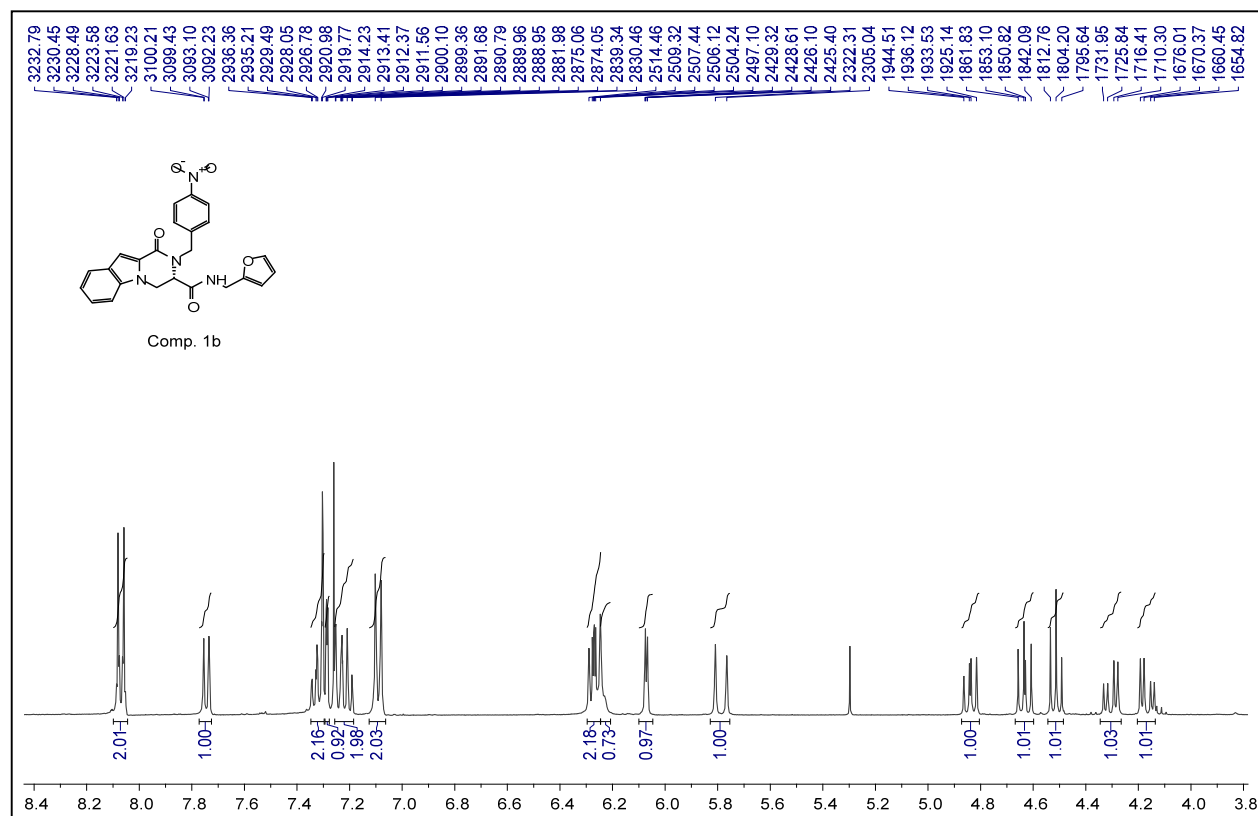
¹H NMR: (S)-N-(Furan-2-ylmethyl)-2-(3-nitrobenzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-a]indole-3-carboxamide (1a)



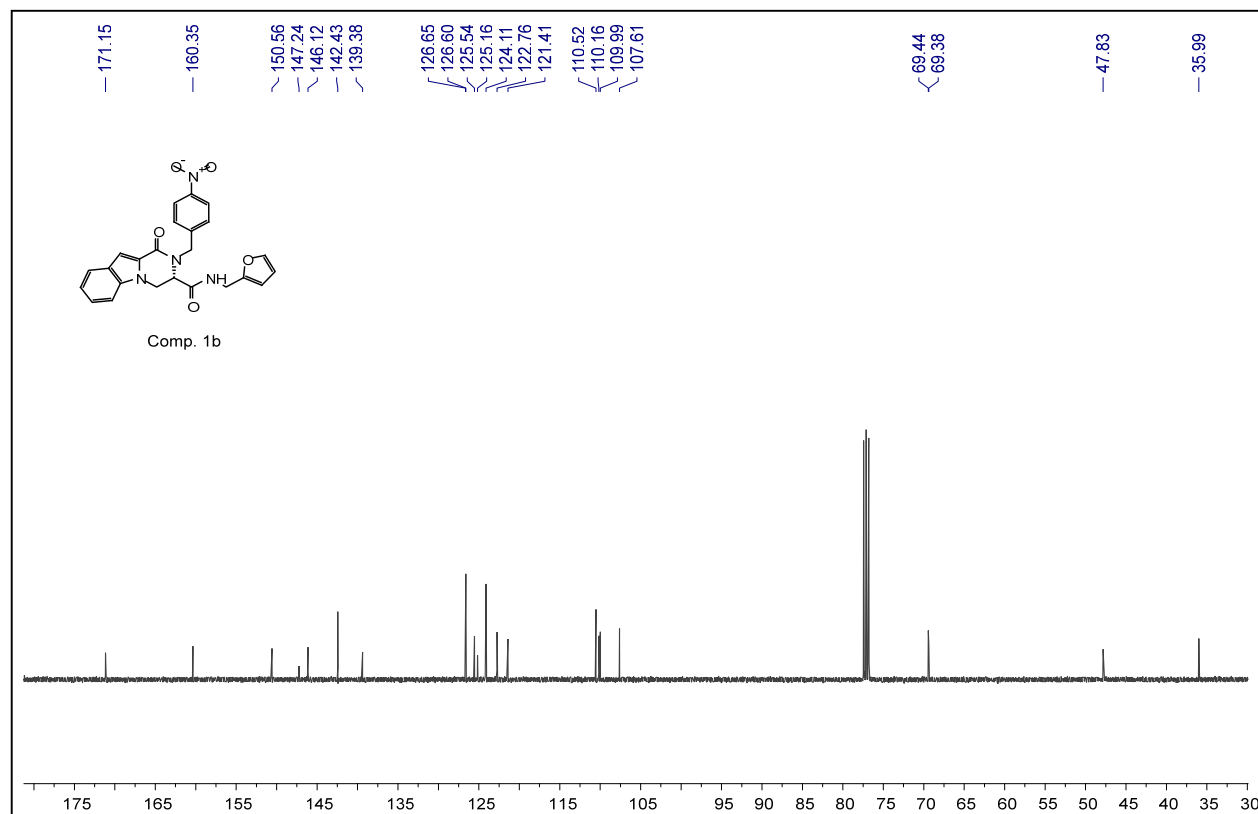
¹³C NMR: (S)-N-(Furan-2-ylmethyl)-2-(3-nitrobenzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-a]indole-3-carboxamide (1a)



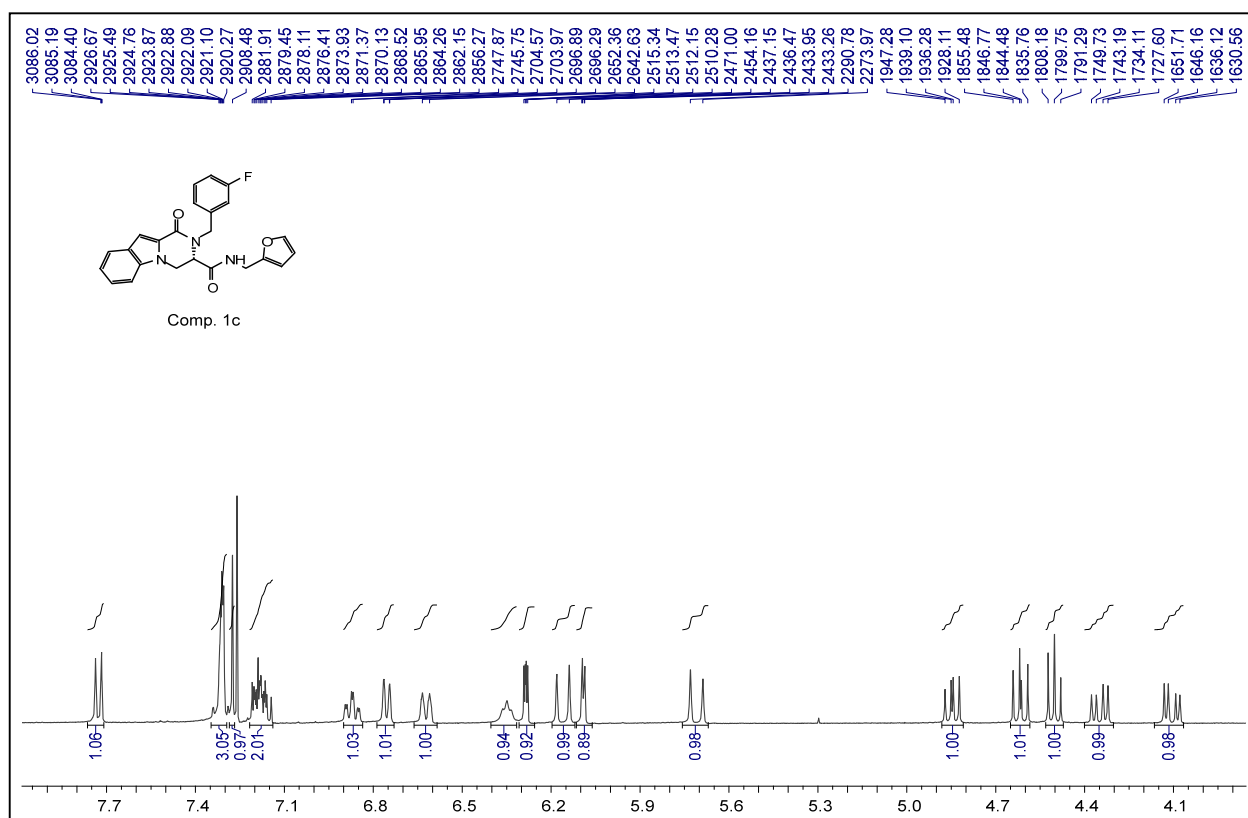
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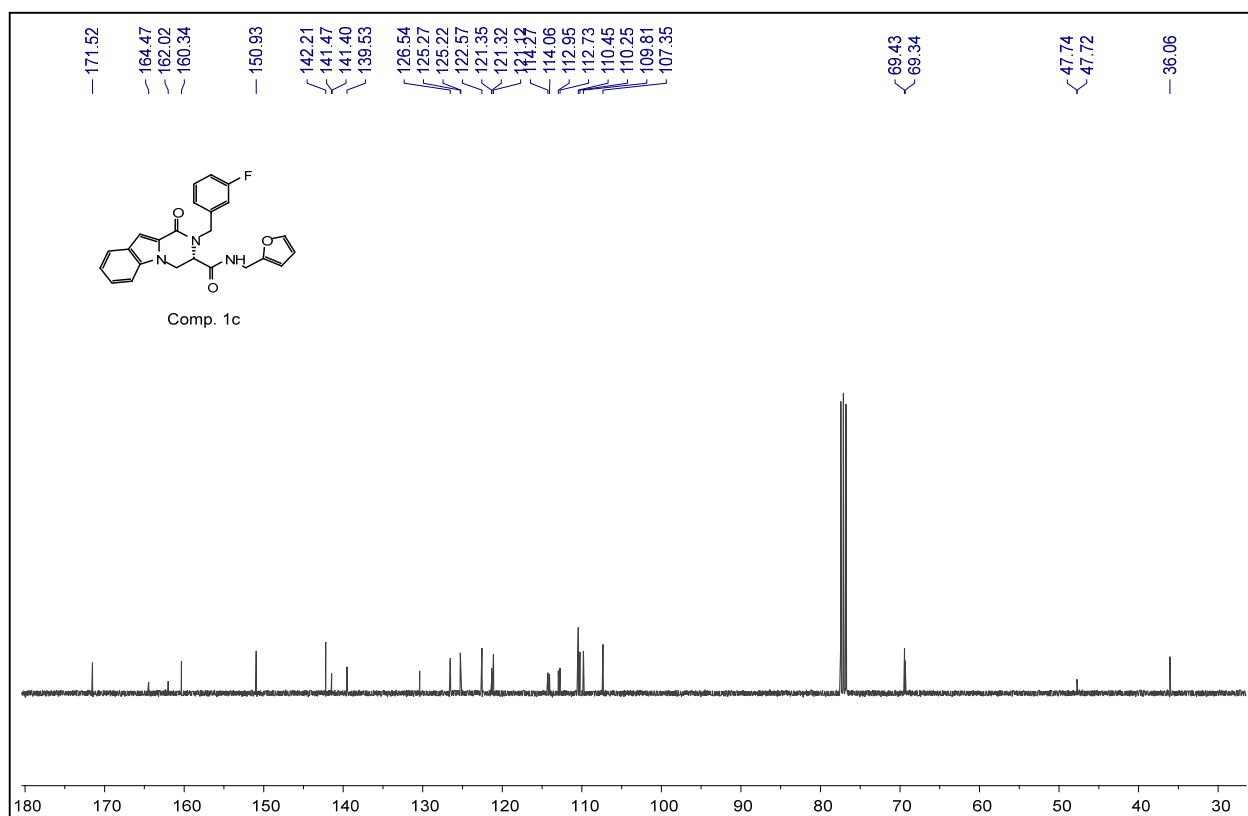
¹³C NMR: (S)-N-(Furan-2-ylmethyl)-2-(4-nitrobenzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-a]indole-3-carboxamide (1b)



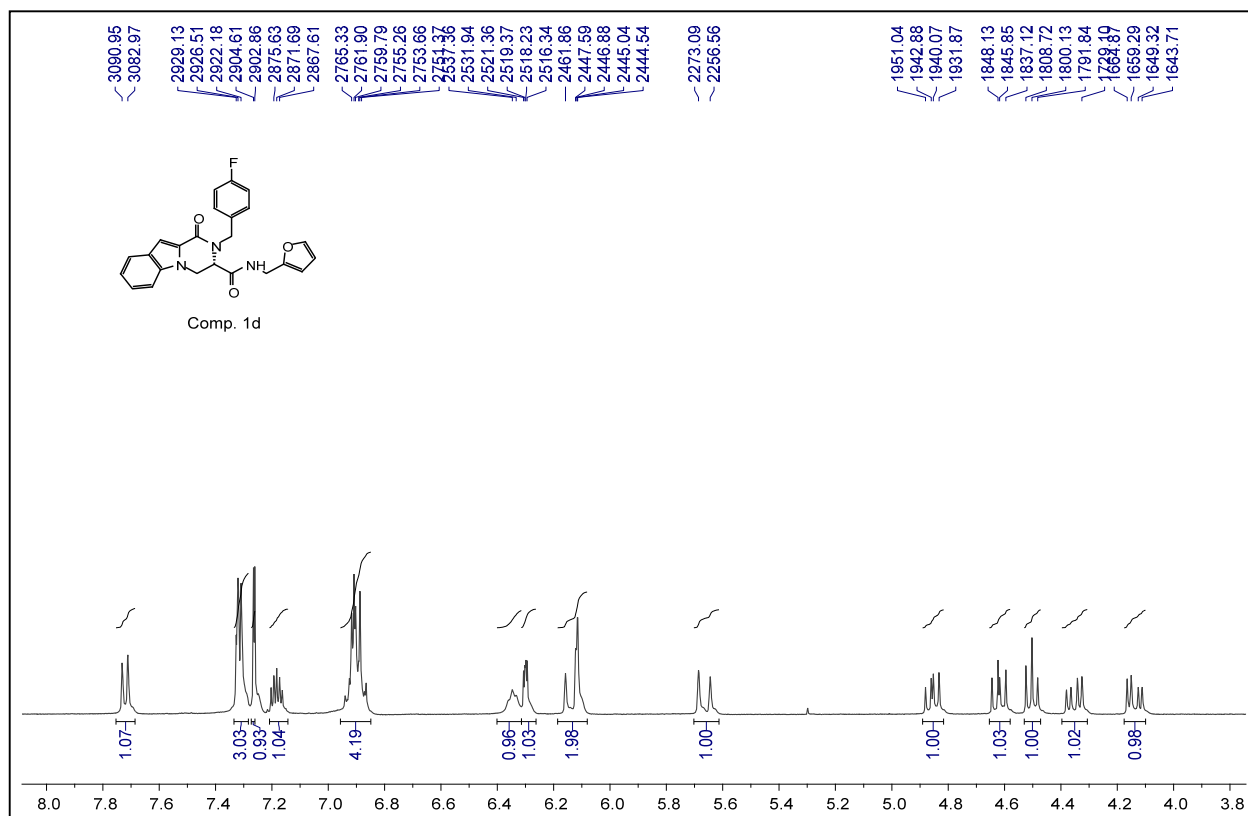
¹H NMR: (S)-N-(Furan-2-ylmethyl)-2-(3-fluorobenzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-a]indole-3-carboxamide (1c)



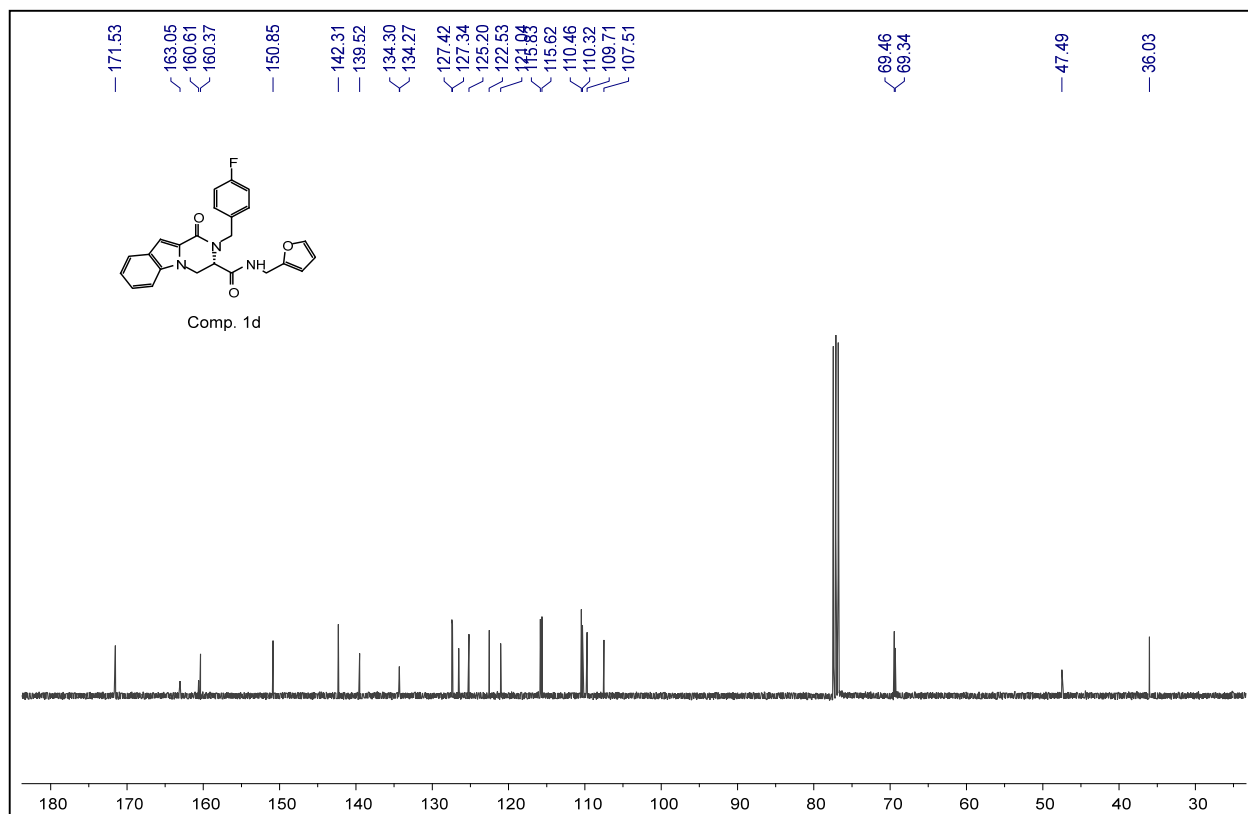
¹³C NMR: (S)-N-(Furan-2-ylmethyl)-2-(3-fluorobenzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-a]indole-3-carboxamide (1c)



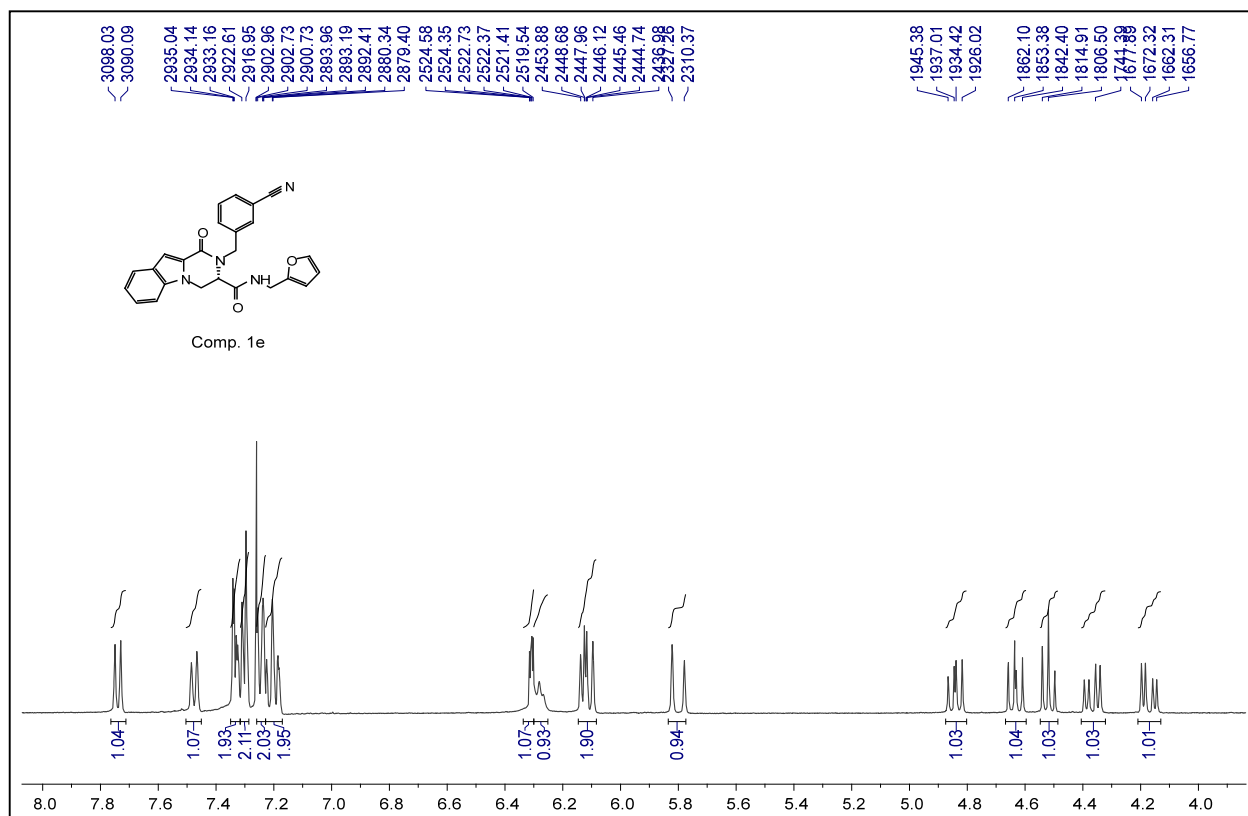
¹H NMR: (S)-N-(Furan-2-ylmethyl)-2-(4-fluorobenzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-a]indole-3-carboxamide (1d)



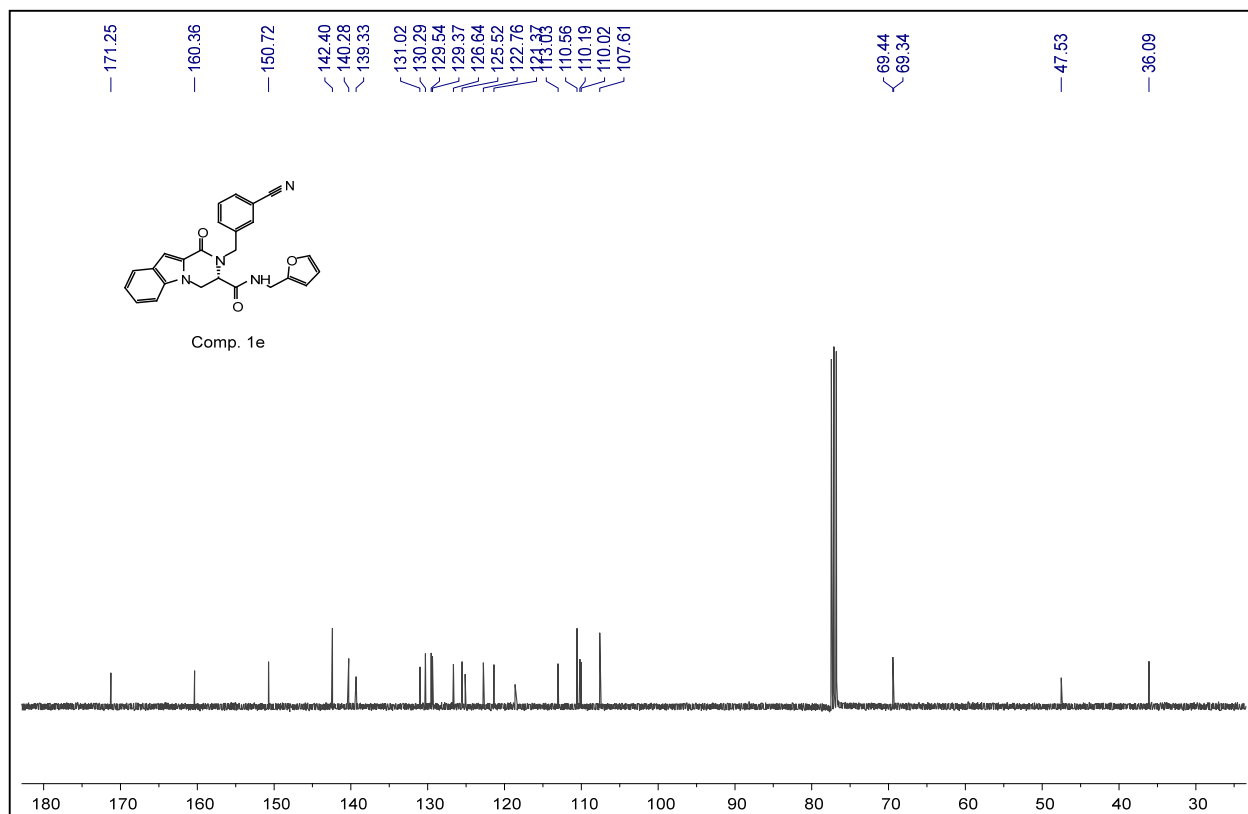
¹³C NMR: (S)-N-(Furan-2-ylmethyl)-2-(4-fluorobenzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-a]indole-3-carboxamide (1d)



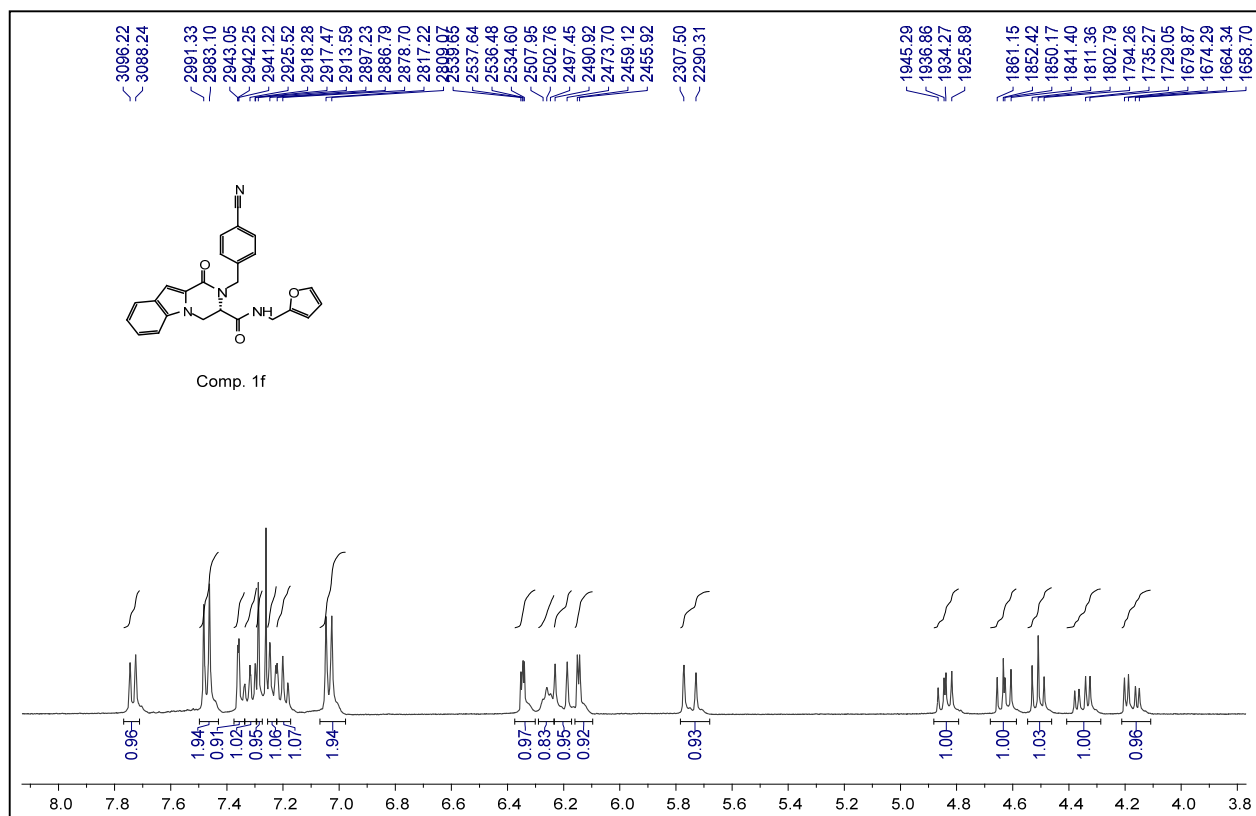
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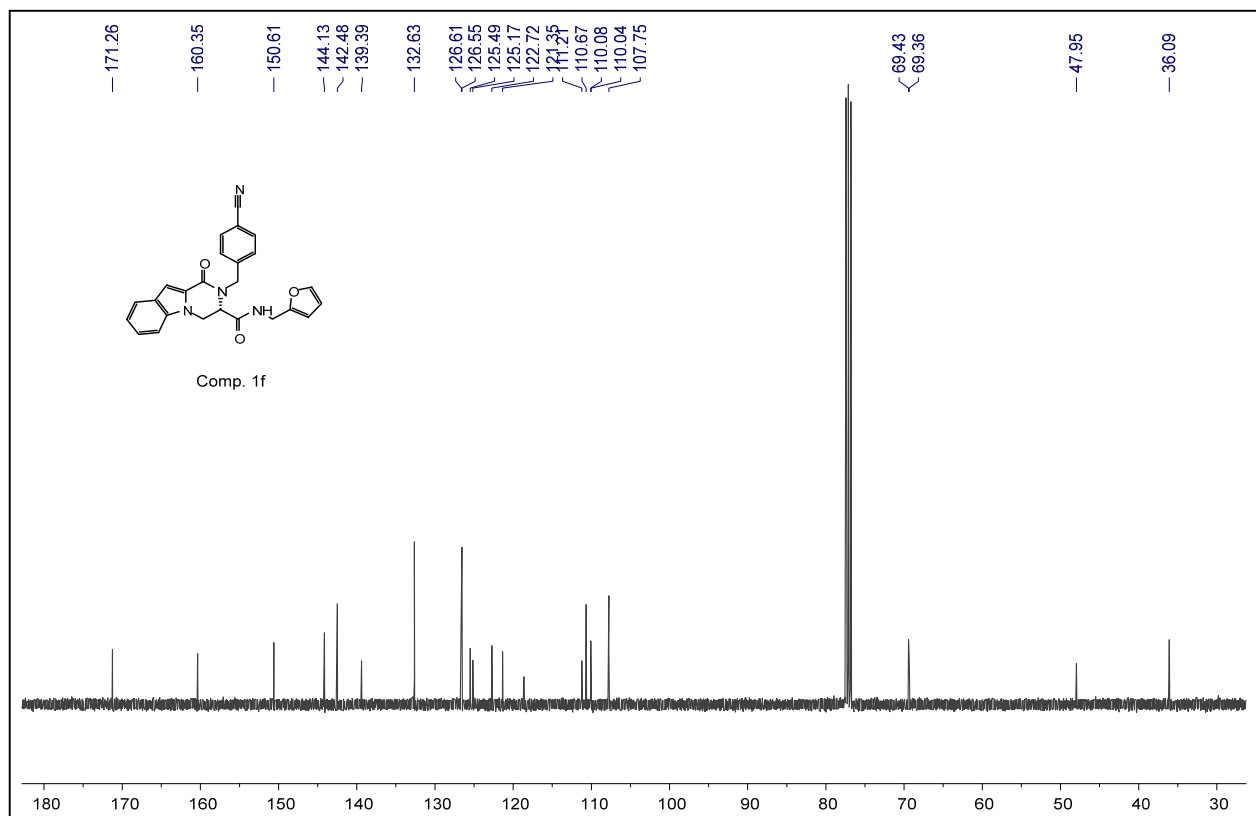
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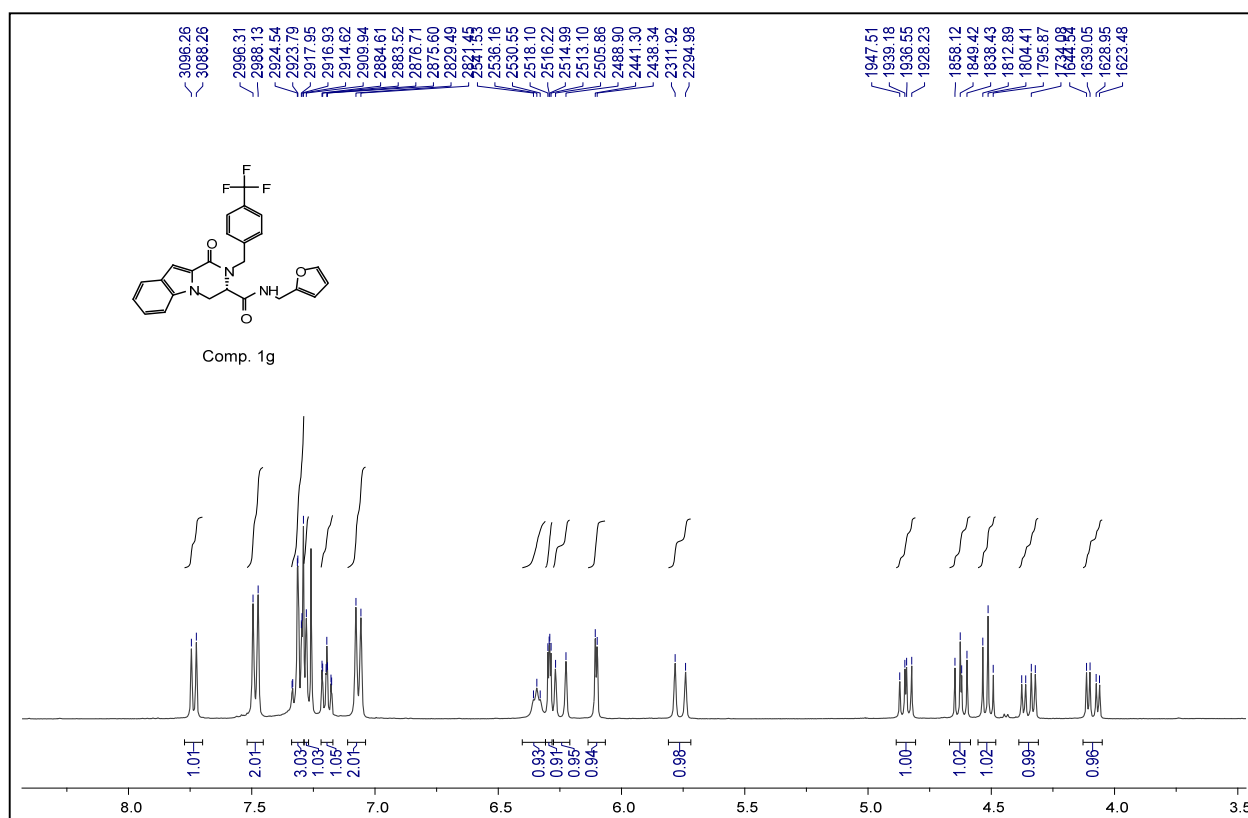
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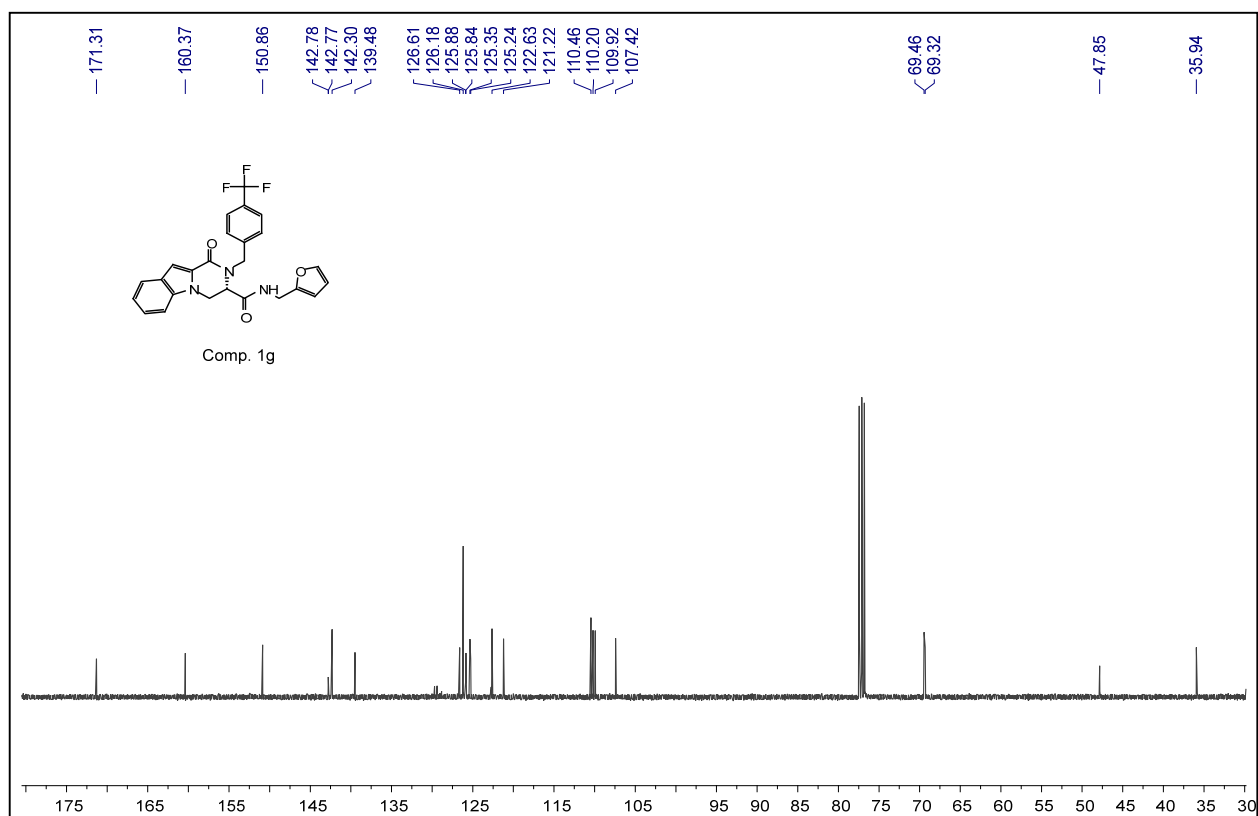
¹³C NMR: (S)-N-(Furan-2-ylmethyl)-2-(4-cyanobenzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-a]indole-3-carboxamide (1f)



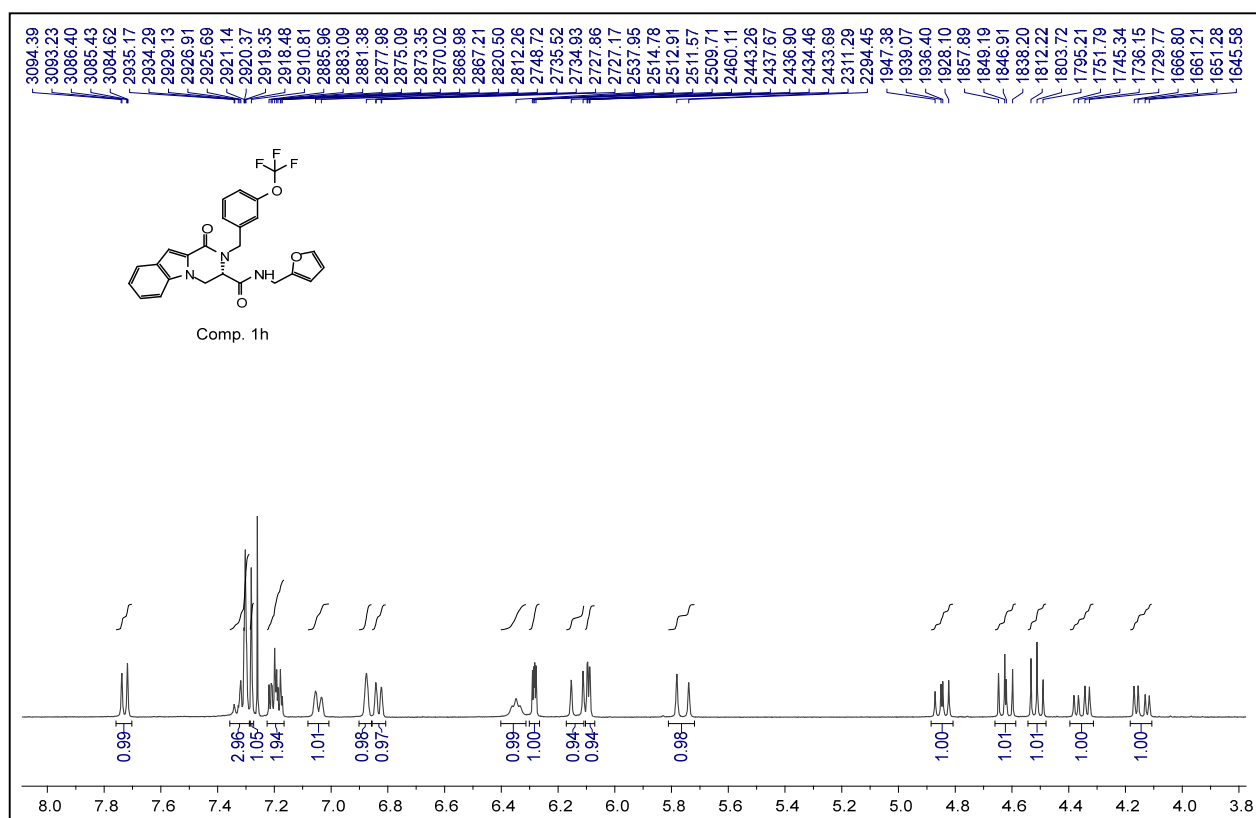
¹H NMR: (*S*)-*N*-(Furan-2-ylmethyl)-2-(4-trifluoromethylbenzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-*a*]indole-3-carboxamide (1g)



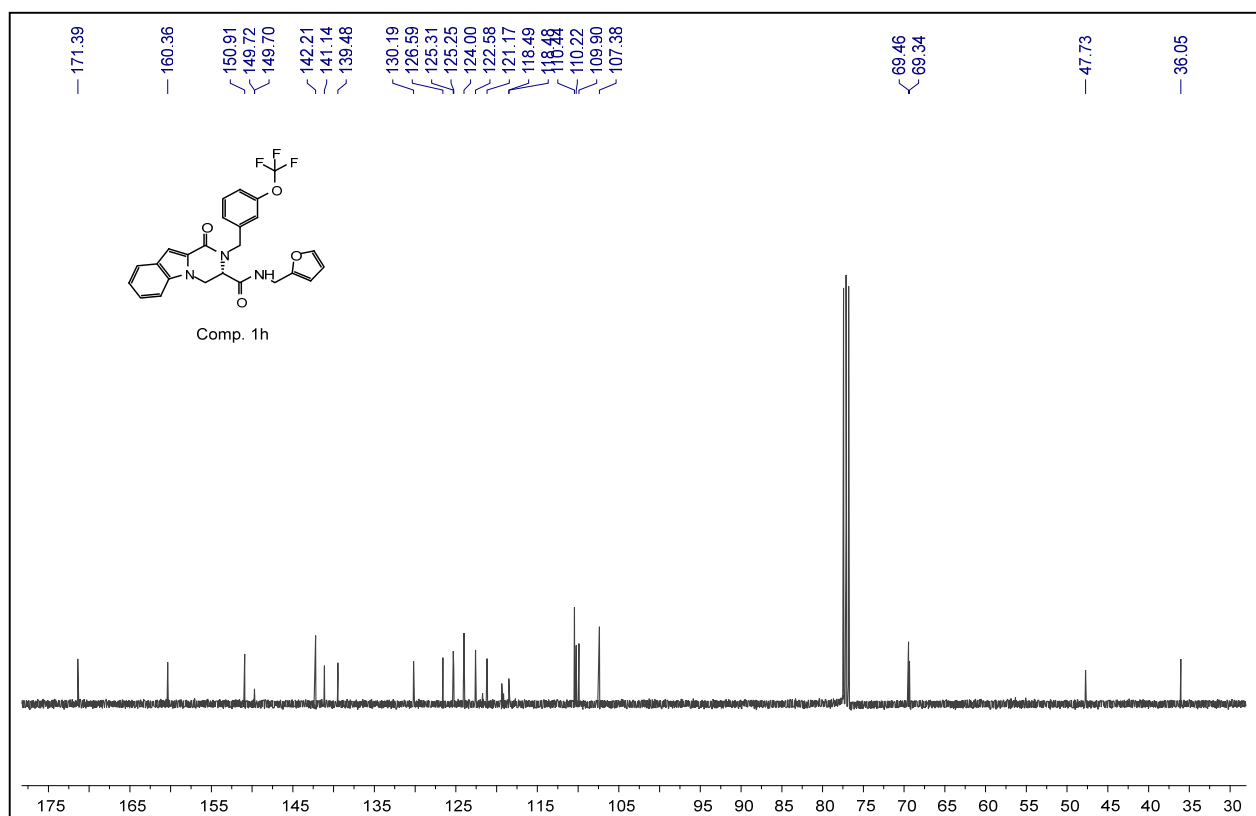
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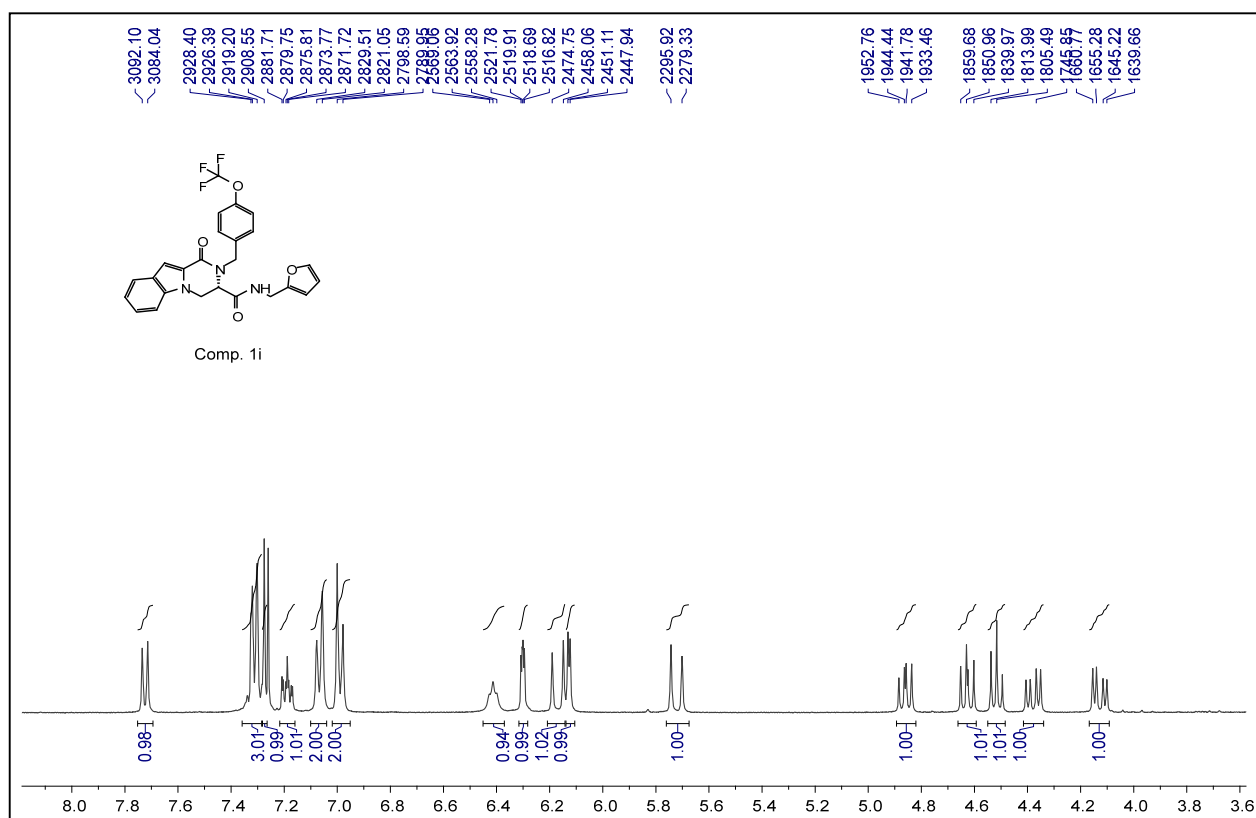
¹H NMR: (*S*)-*N*-(Furan-2-ylmethyl)-2-(3-trifluoromethoxybenzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-*a*]indole-3-carboxamide (1h)



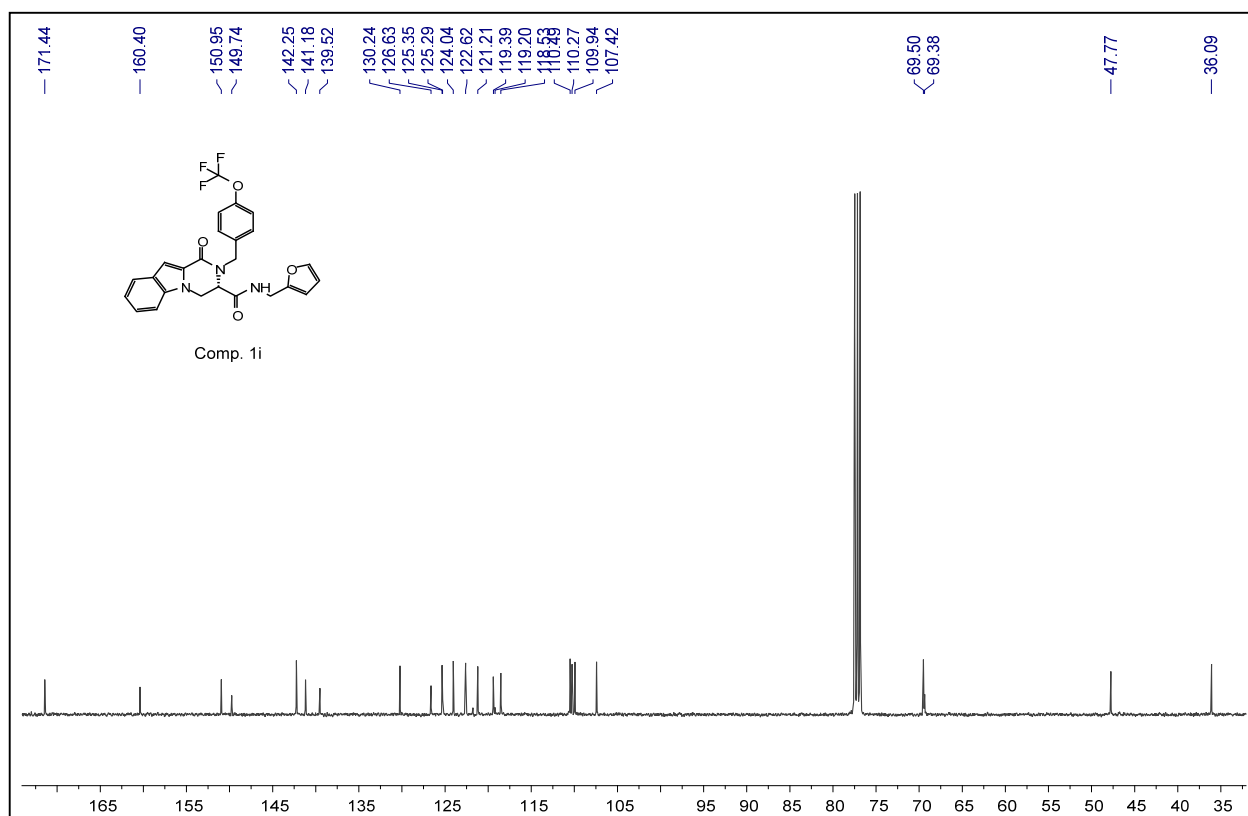
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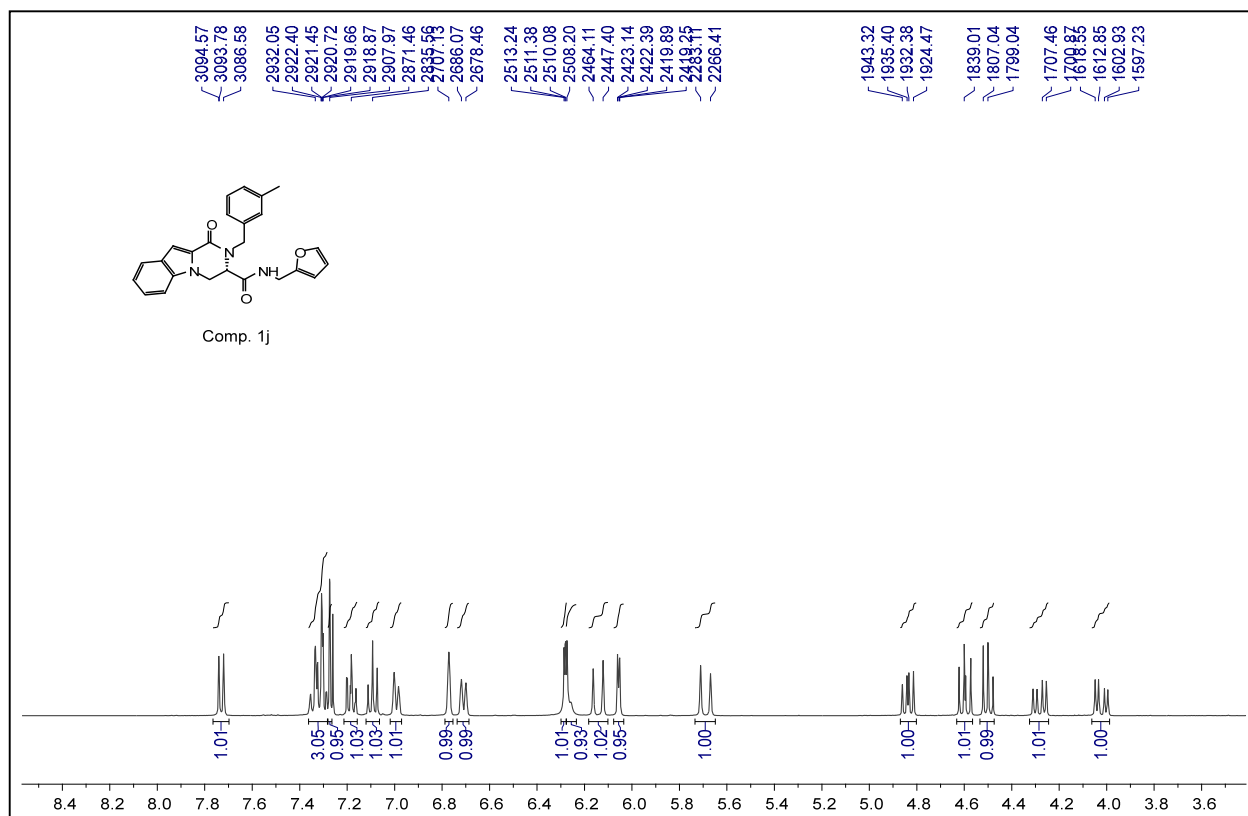
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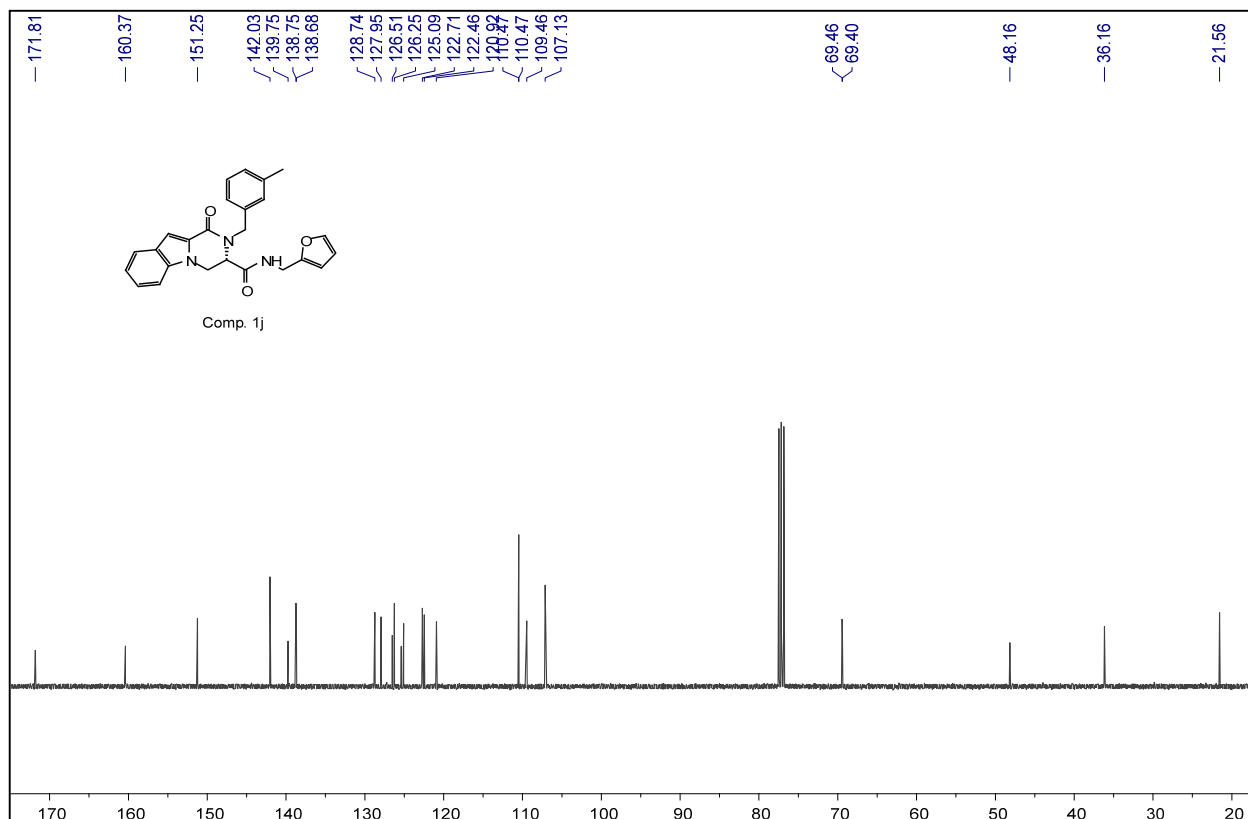
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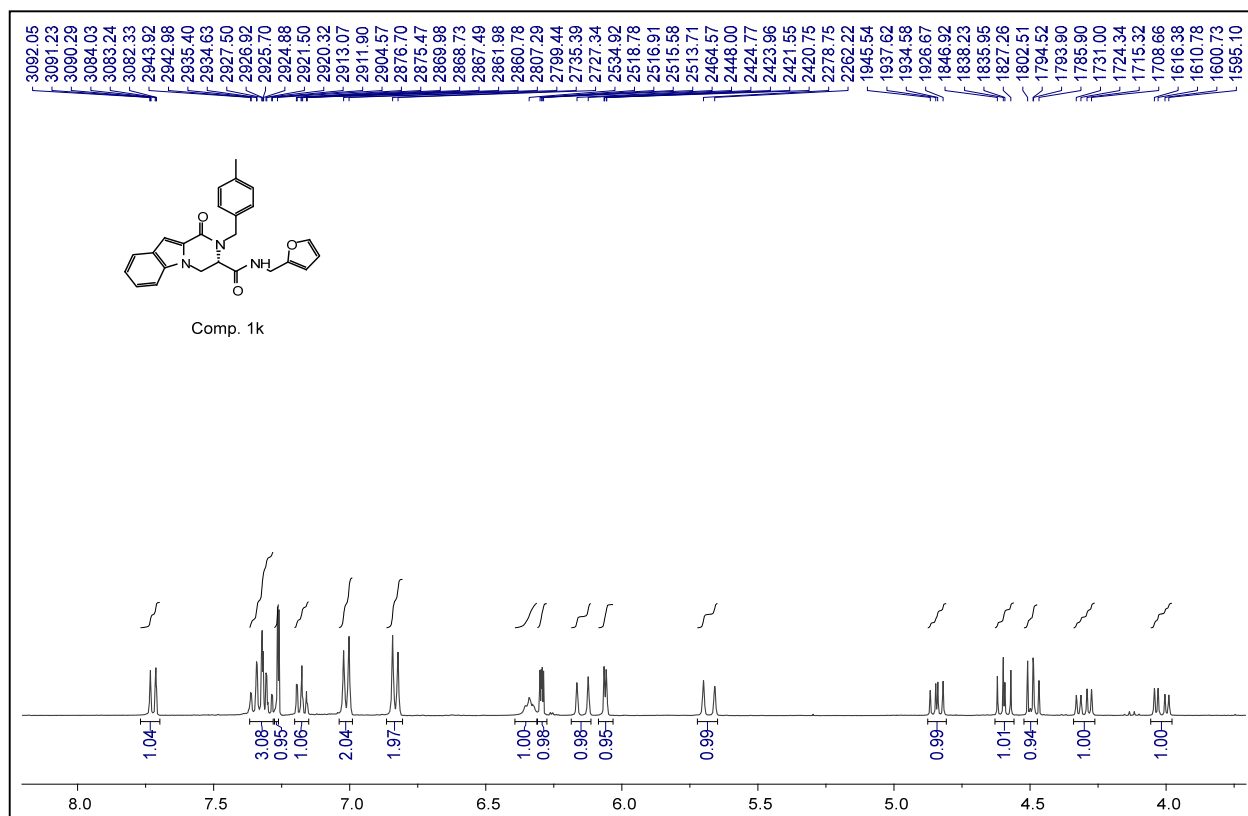
¹H NMR: (*S*)-*N*-(Furan-2-ylmethyl)-2-(3-methylbenzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-*a*]indole-3-carboxamide (1j)



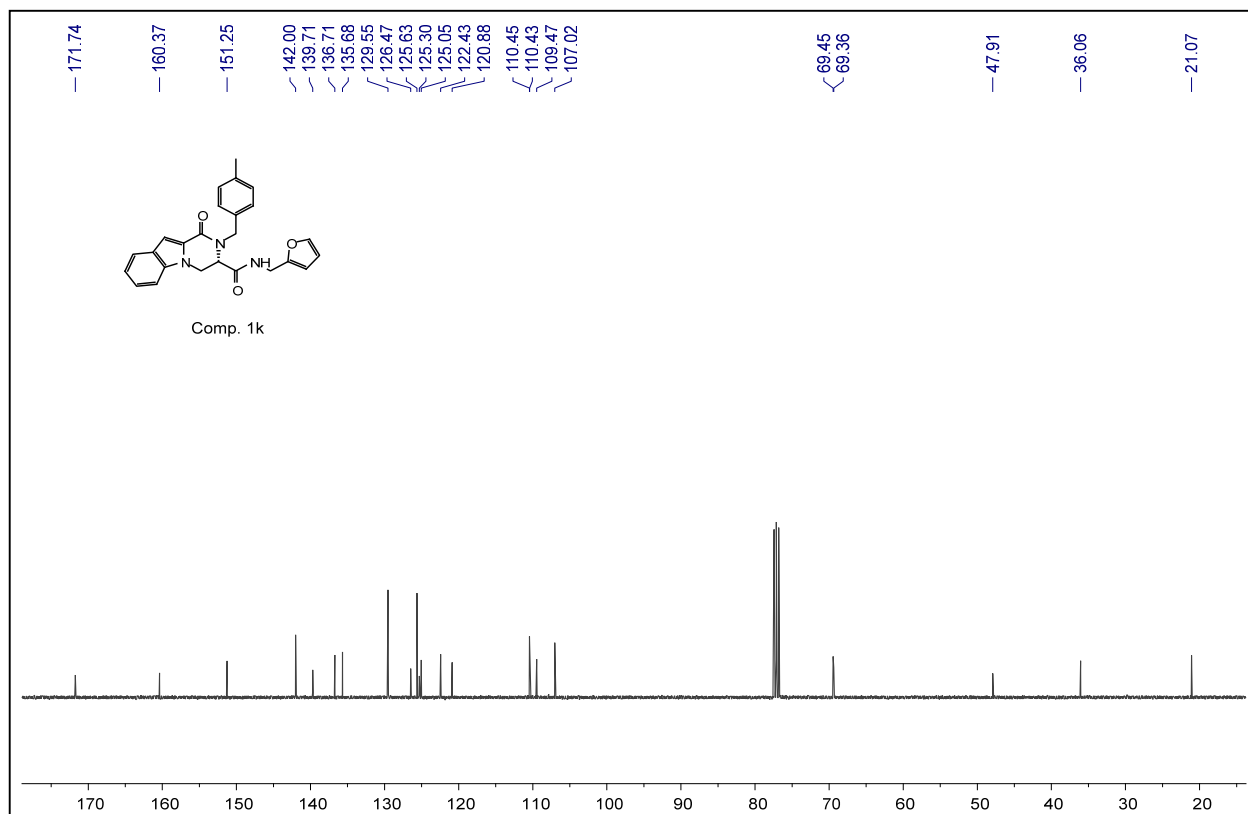
¹³C NMR: (*S*)-*N*-(Furan-2-ylmethyl)-2-(3-methylbenzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-*a*]indole-3-carboxamide (1j)



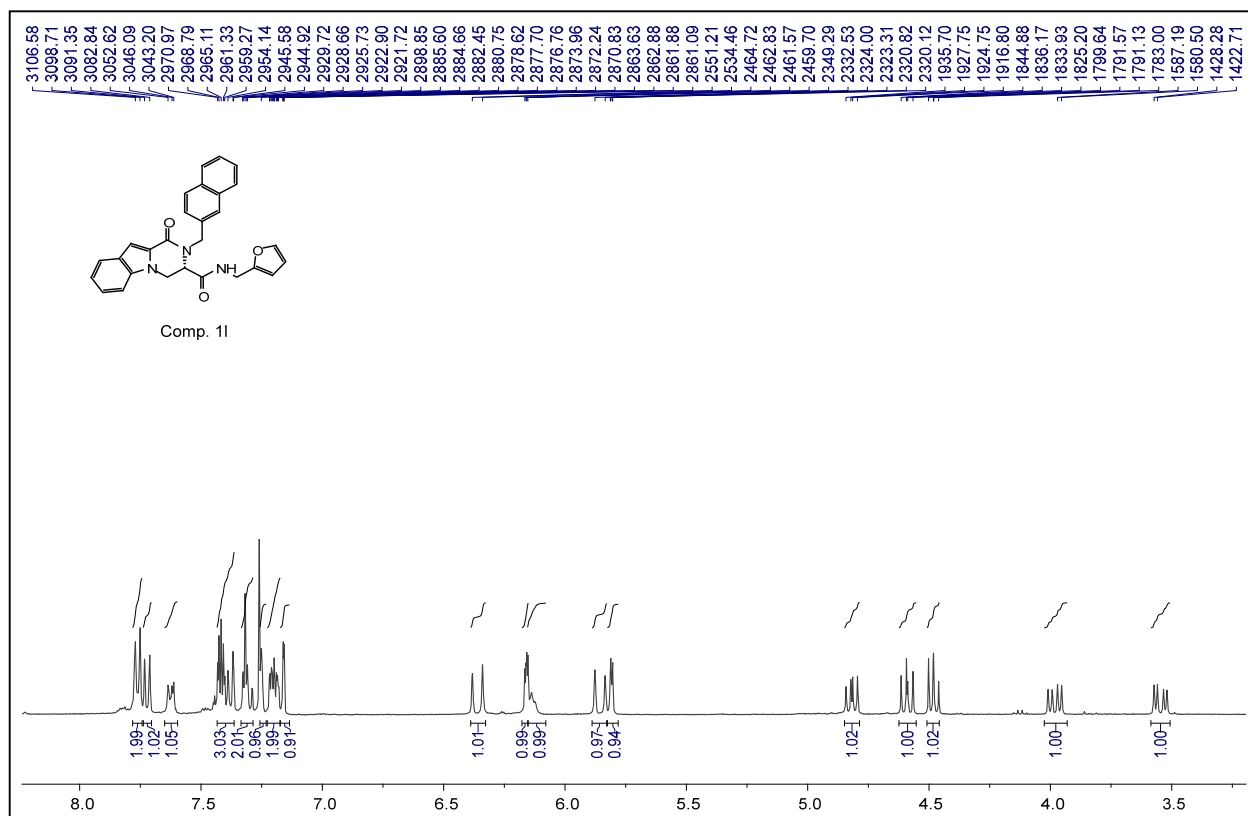
¹H NMR: (S)-N-(Furan-2-ylmethyl)-2-(4-methylbenzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-a]indole-3-carboxamide (1k)



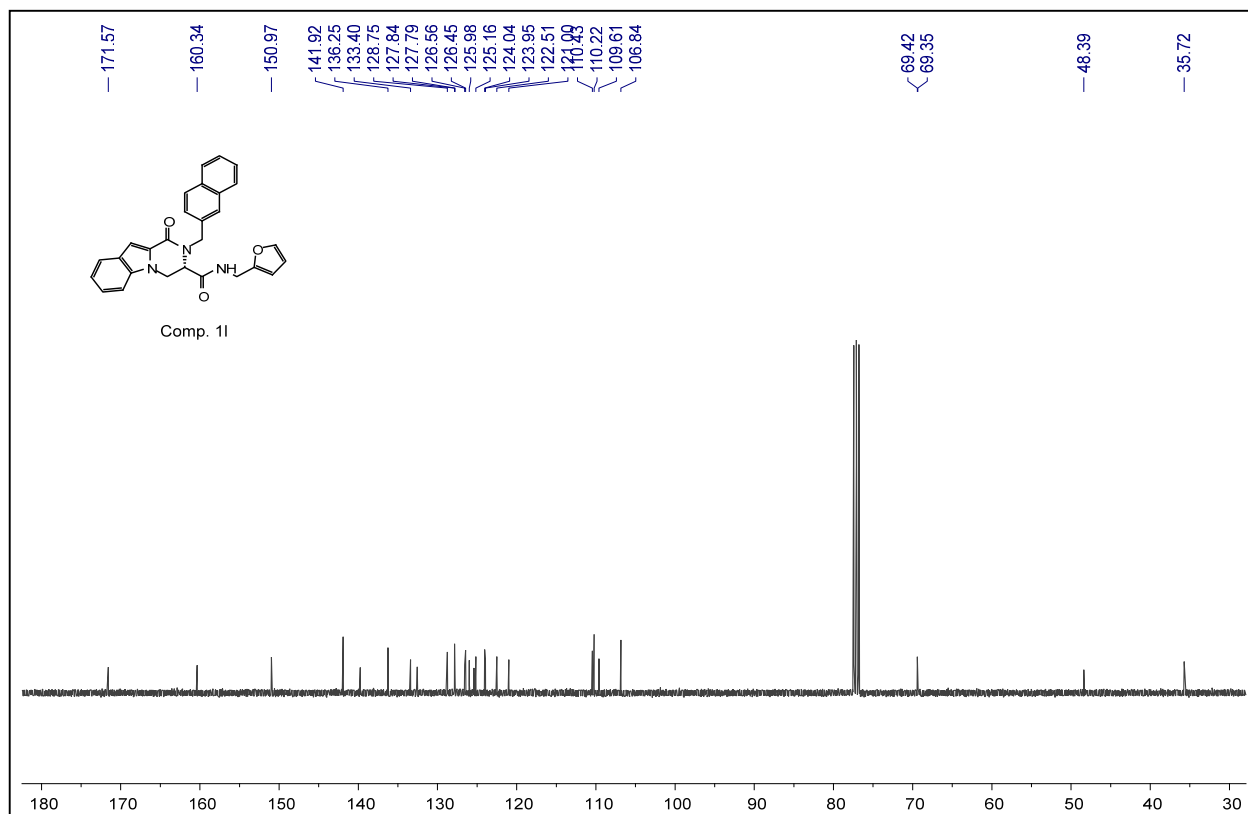
¹³C NMR: (S)-N-(Furan-2-ylmethyl)-2-(4-methylbenzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-a]indole-3-carboxamide (1k)



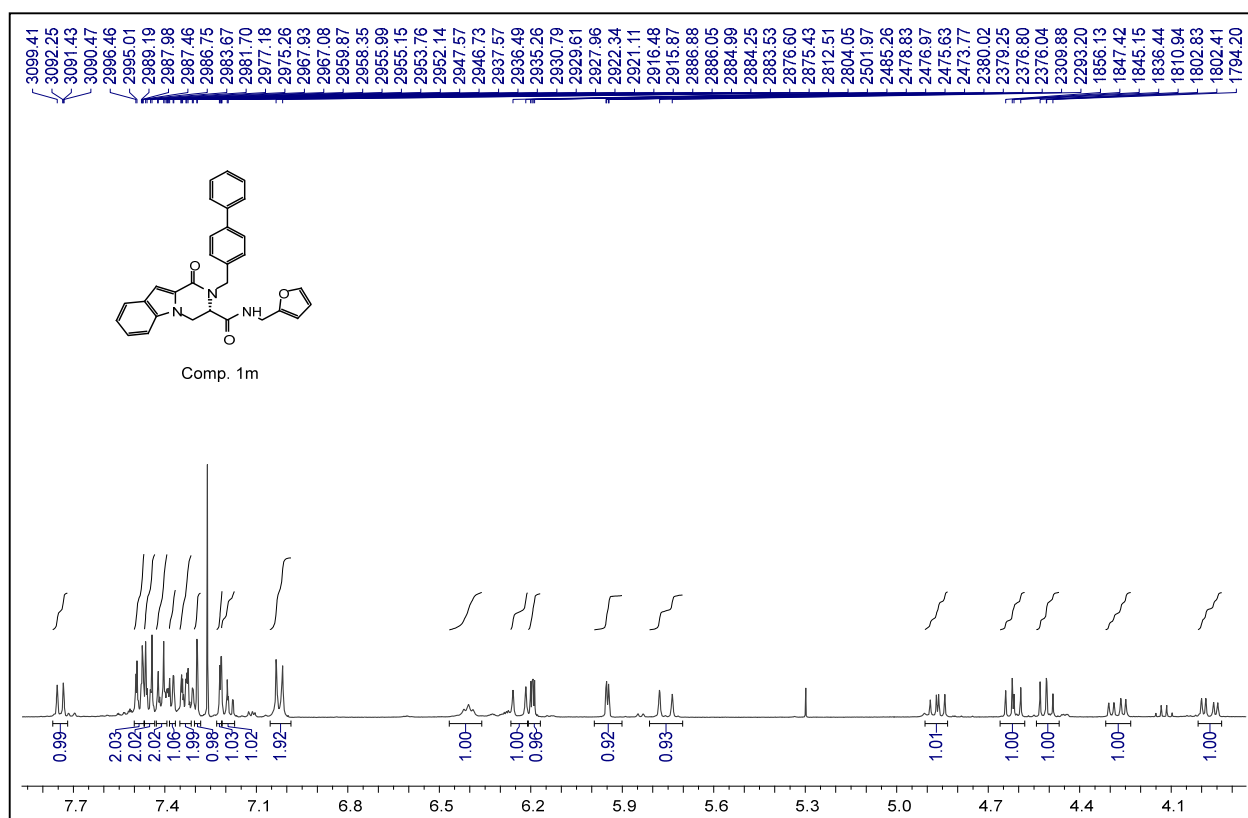
¹H NMR: (S)-N-(Furan-2-ylmethyl)-2-(naphthalen-1-ylmethyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-a]indole-3-carboxamide (11)



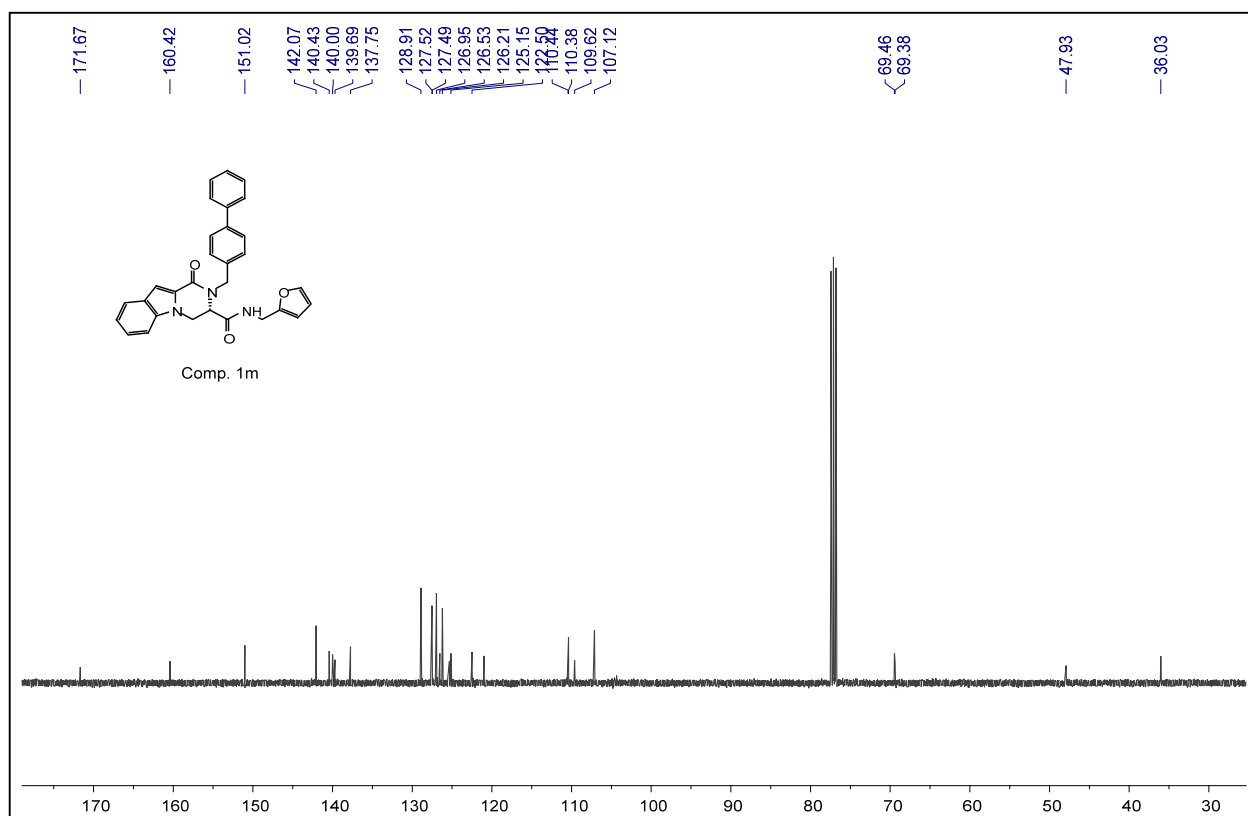
¹³C NMR: (S)-N-(Furan-2-ylmethyl)-2-(naphthalen-1-ylmethyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-a]indole-3-carboxamide (11)



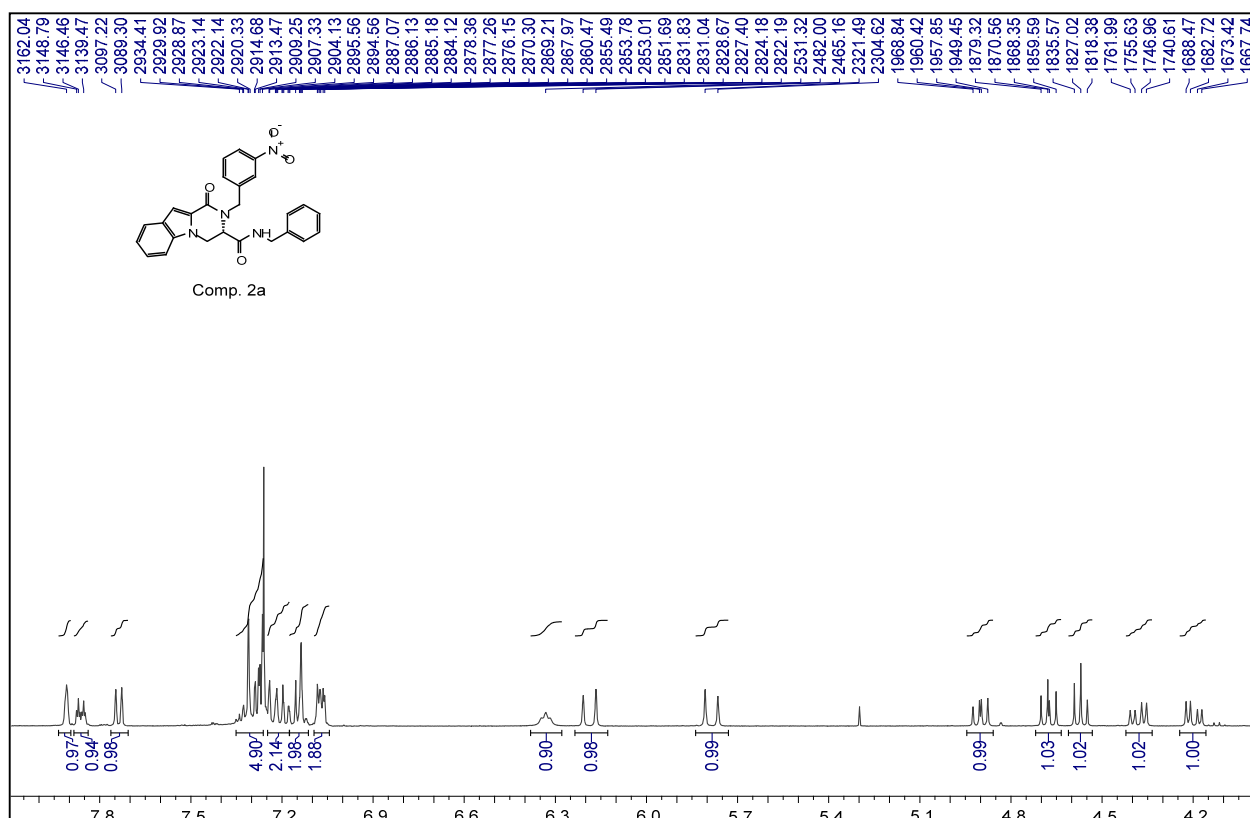
¹H NMR: (*S*)-*N*-(Furan-2-ylmethyl)-2-([1,1'-biphenyl]-4-ylmethyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-*a*]indole-3-carboxamide (1m)



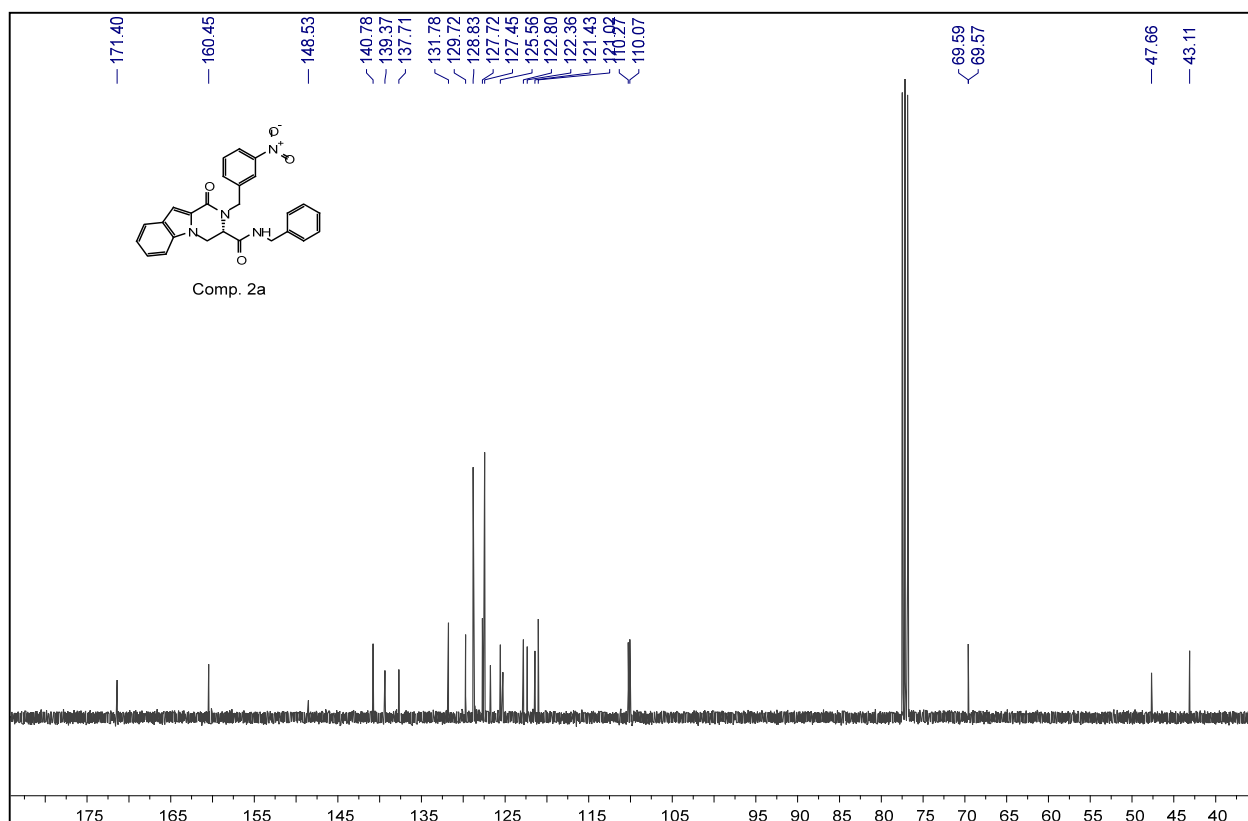
¹³C NMR: (*S*)-*N*-(Furan-2-ylmethyl)-2-([1,1'-biphenyl]-4-ylmethyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-*a*]indole-3-carboxamide (1m)



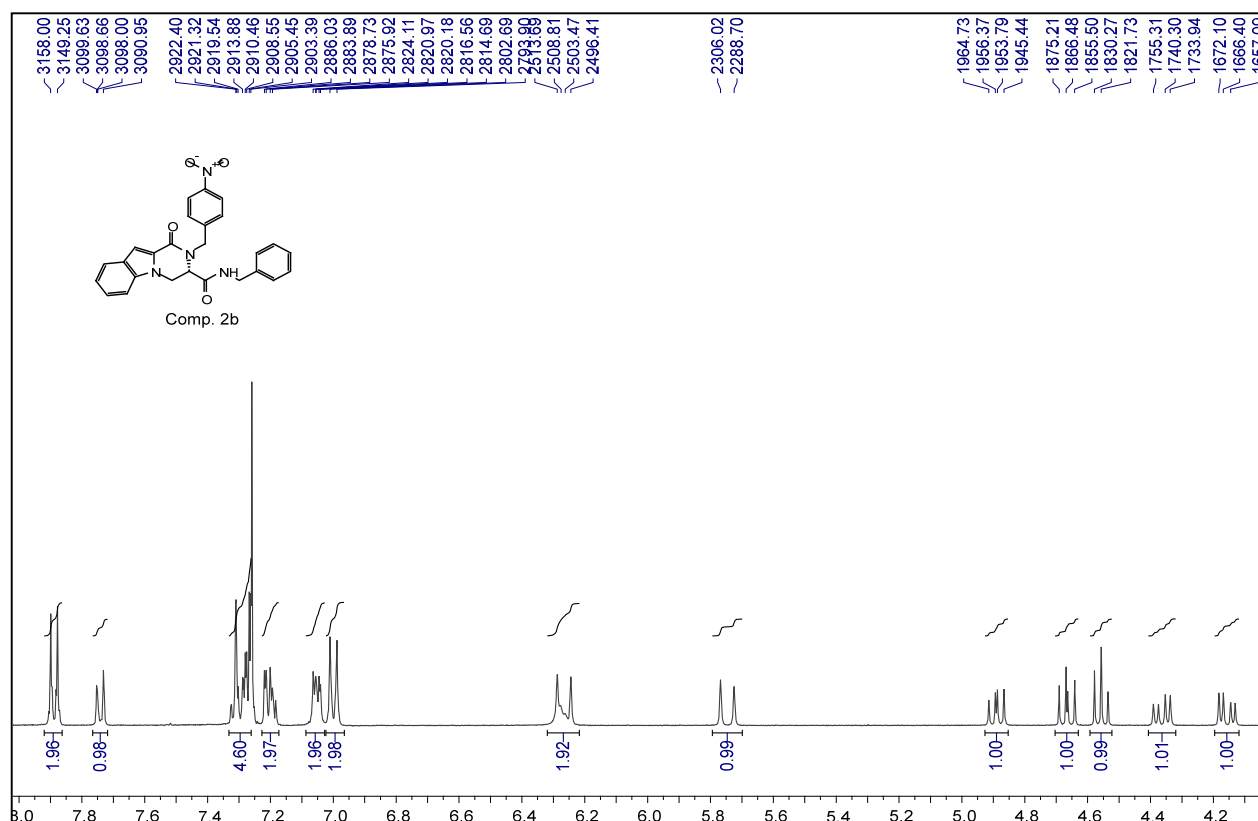
¹H NMR: (S)-N-Benzyl-2-(3-nitrobenzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-a]indole-3-carboxamide (2a)



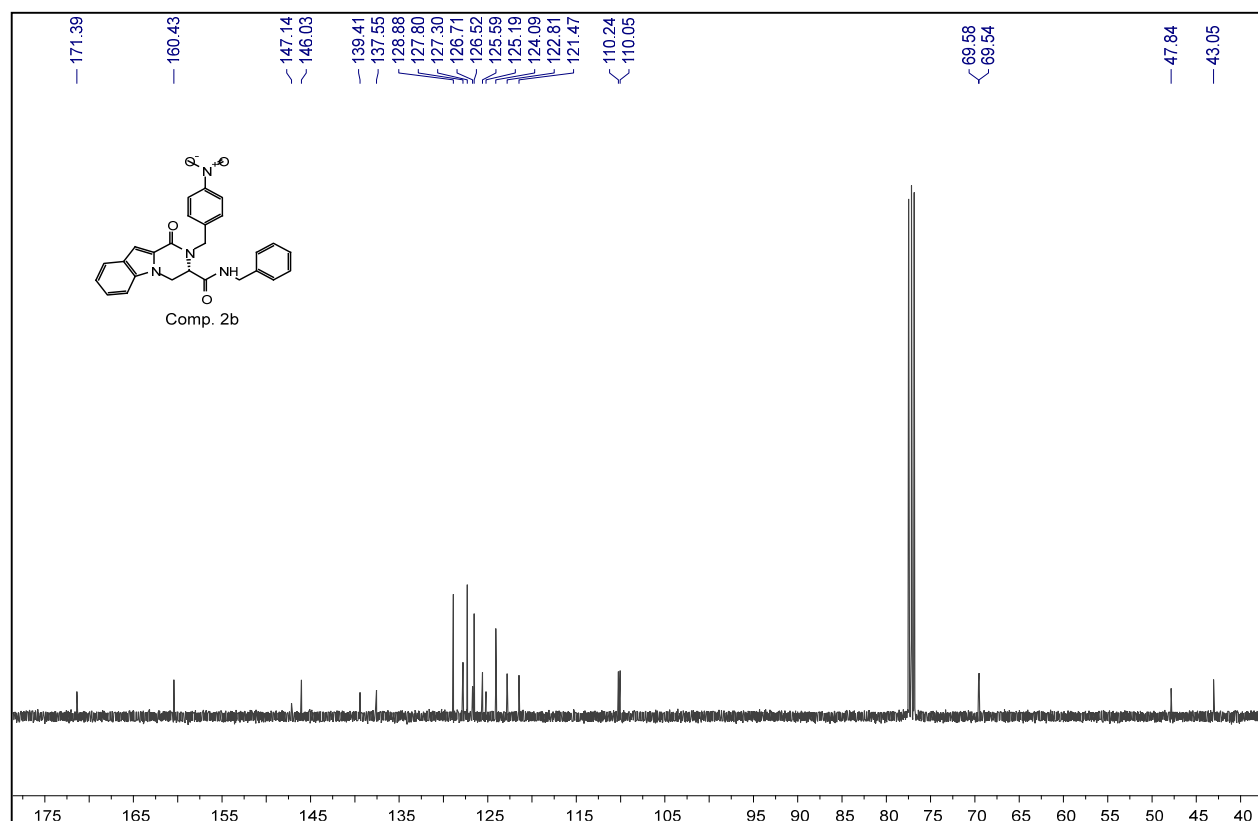
¹³C NMR: (S)-N-Benzyl-2-(3-nitrobenzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-a]indole-3-carboxamide (2a)



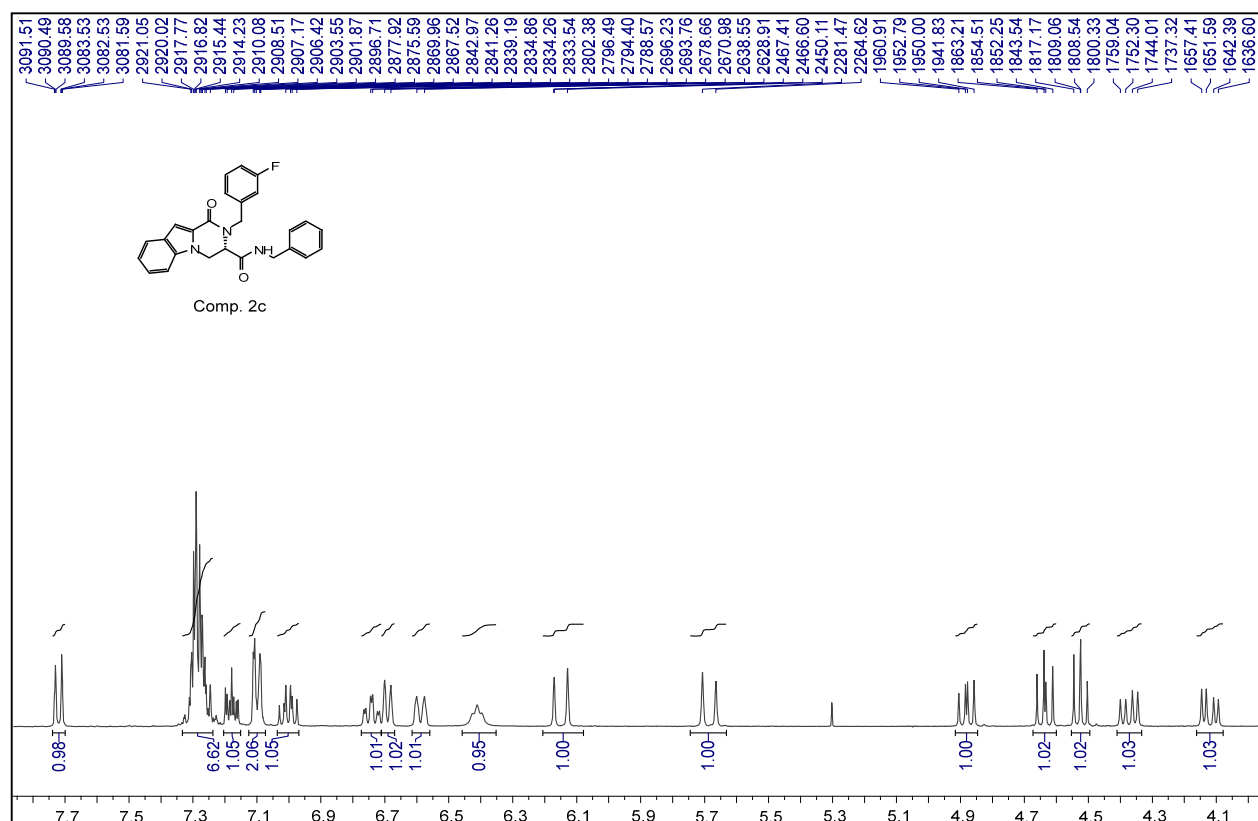
¹H NMR: (S)-N-Benzyl-2-(4-nitrobenzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-a]indole-3-carboxamide (2b)



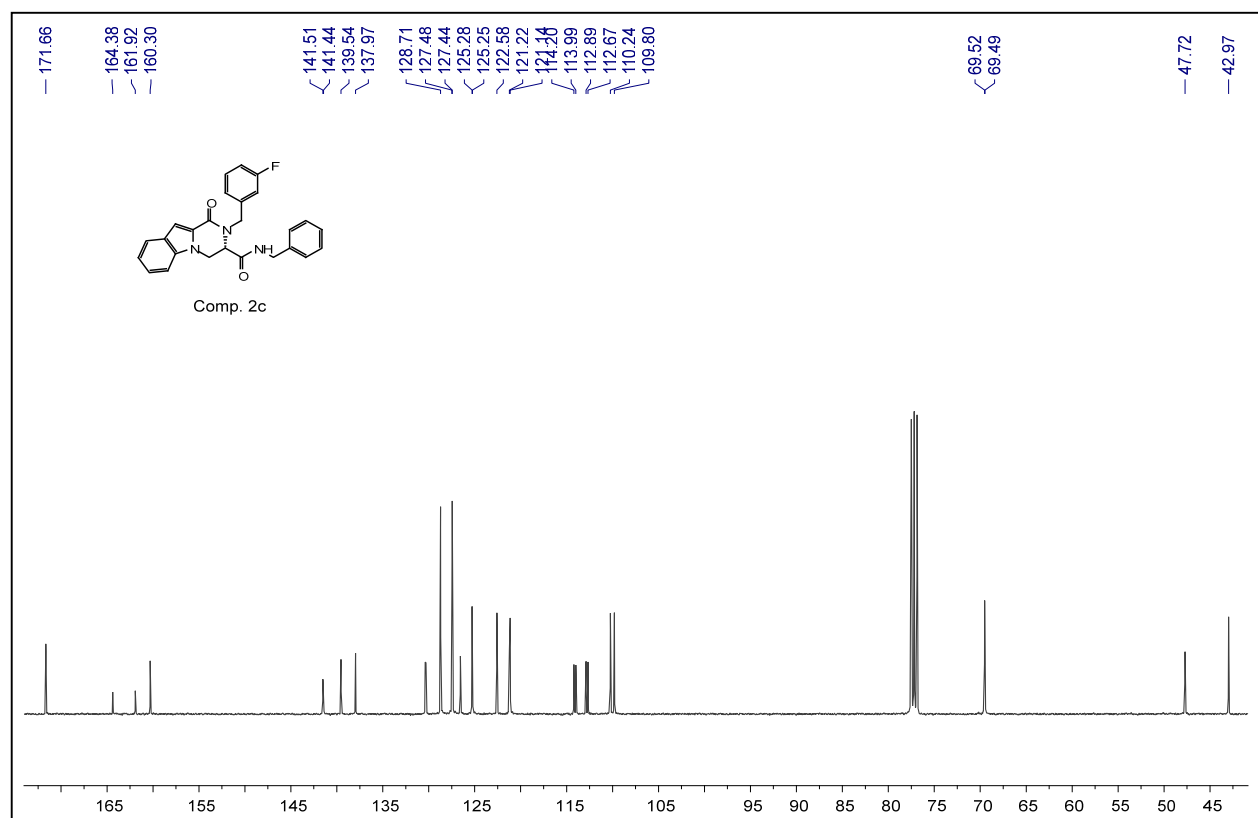
¹³C NMR: (S)-N-Benzyl-2-(4-nitrobenzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-a]indole-3-carboxamide (2b)



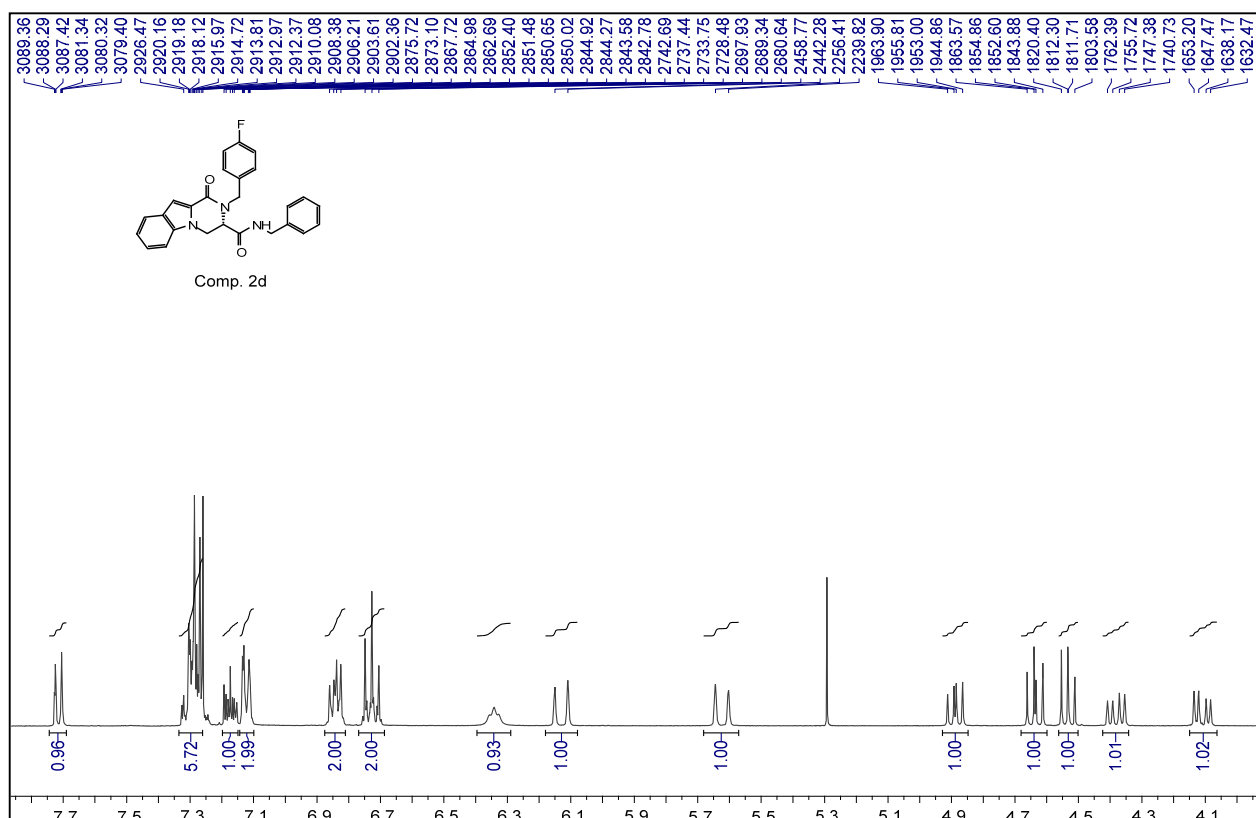
¹H NMR: (*S*)-*N*-Benzyl-2-(3-fluorobenzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-*a*]indole-3-carboxamide (2c)



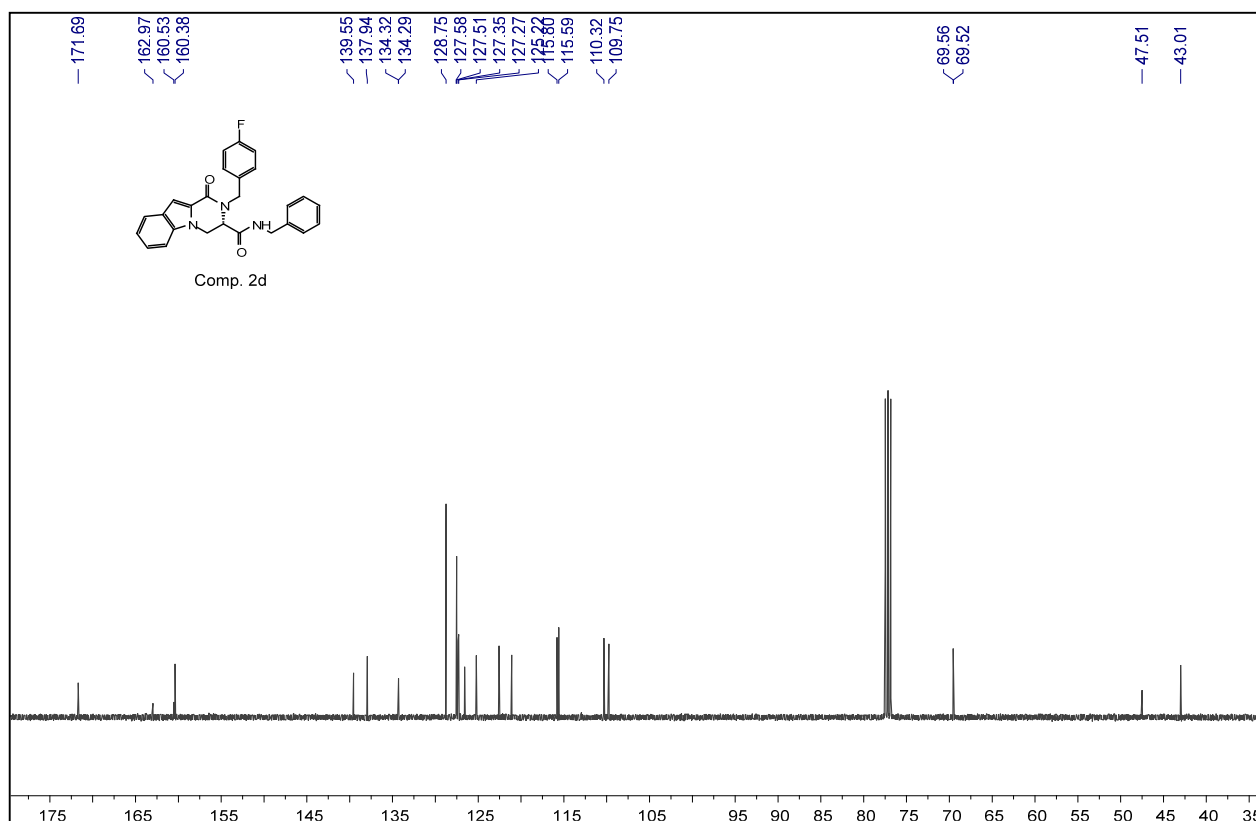
¹³C NMR: (*S*)-*N*-Benzyl-2-(3-fluorobenzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-*a*]indole-3-carboxamide (2c)



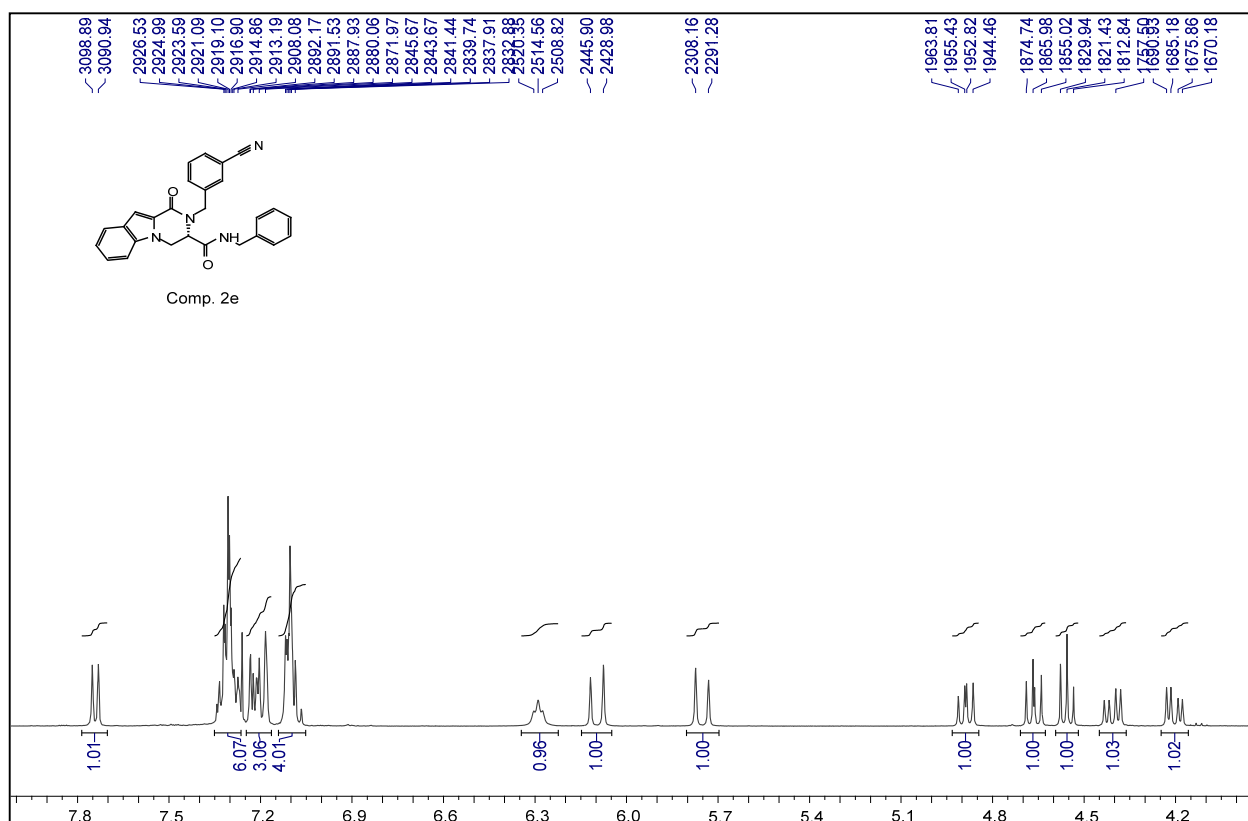
¹H NMR: (S)-N-Benzyl-2-(4-fluorobenzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-a]indole-3-carboxamide (2d)



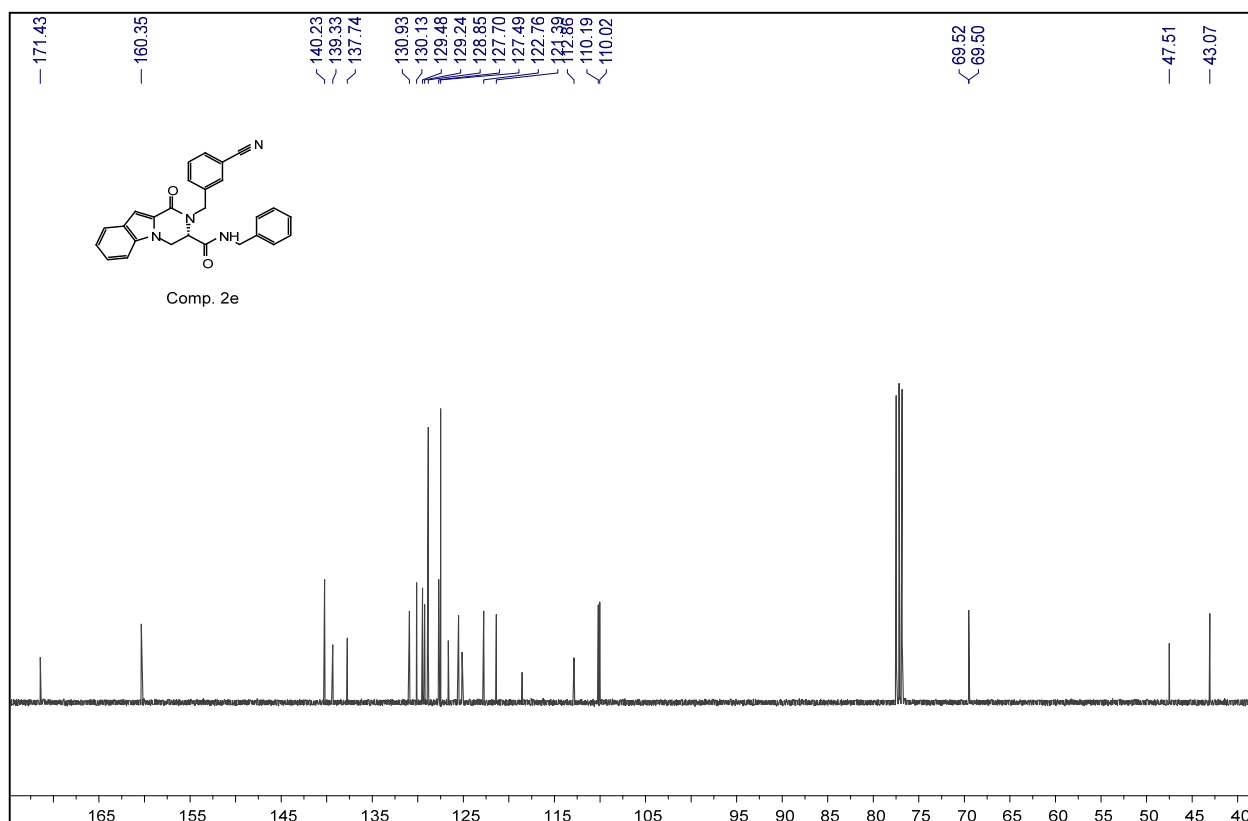
¹³C NMR: (S)-N-Benzyl-2-(4-fluorobenzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-a]indole-3-carboxamide (2d)



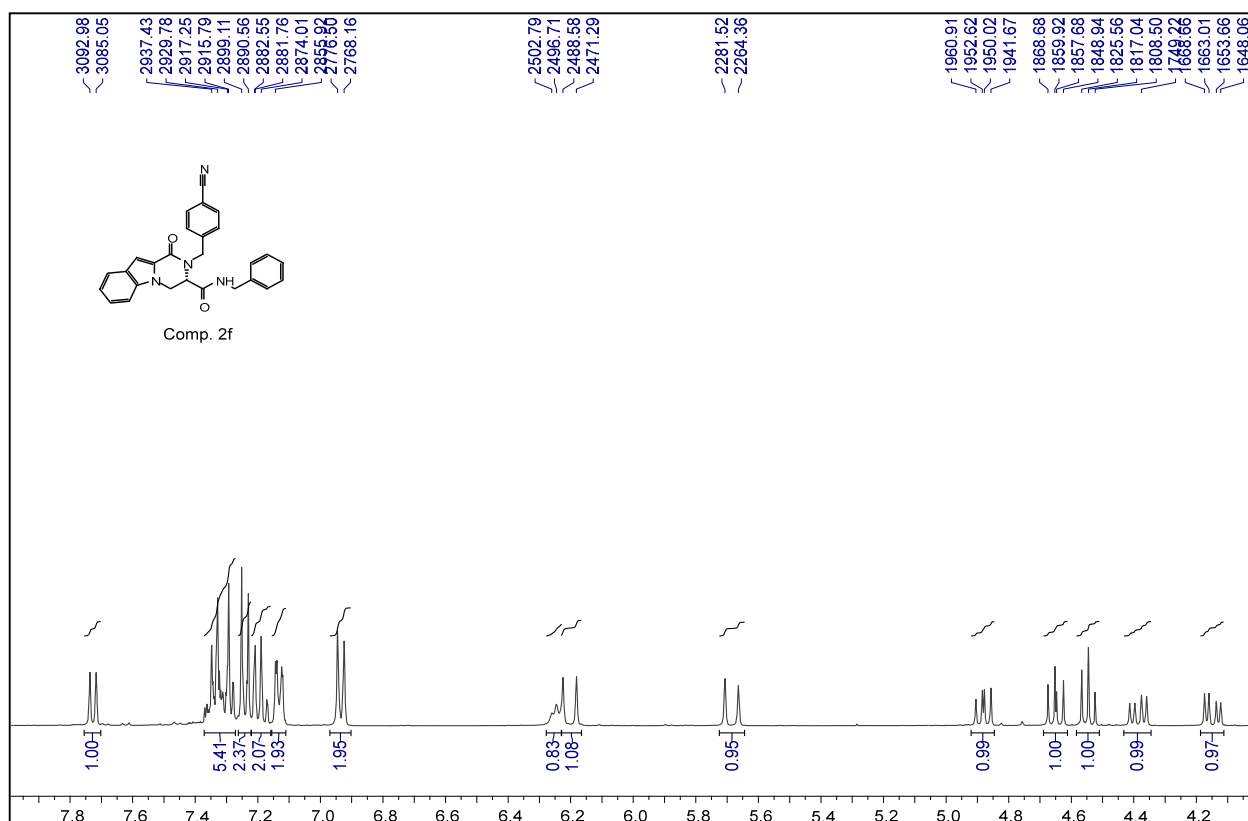
¹H NMR: (S)-N-Benzyl-2-(3-cyanobenzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-*a*]indole-3-carboxamide (2e)



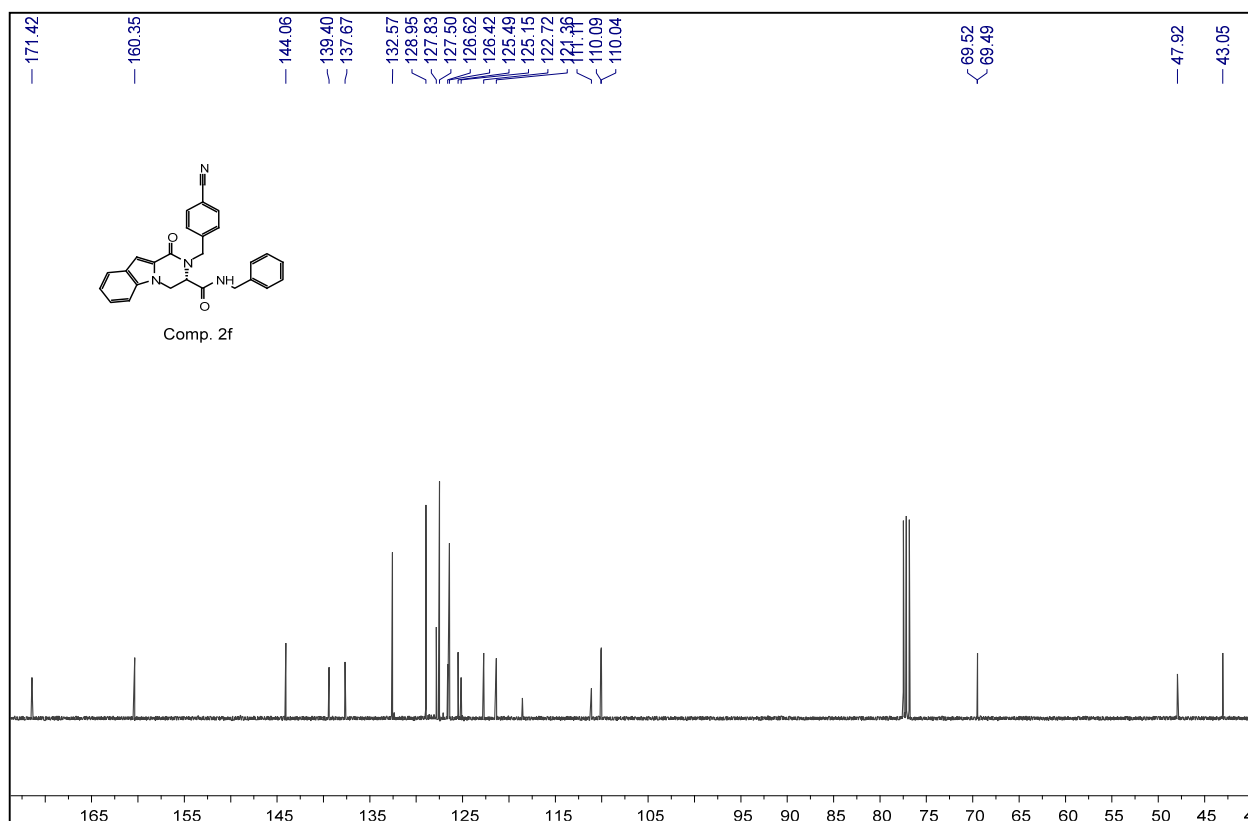
¹³C NMR: (S)-N-Benzyl-2-(3-cyanobenzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-*a*]indole-3-carboxamide (2e)



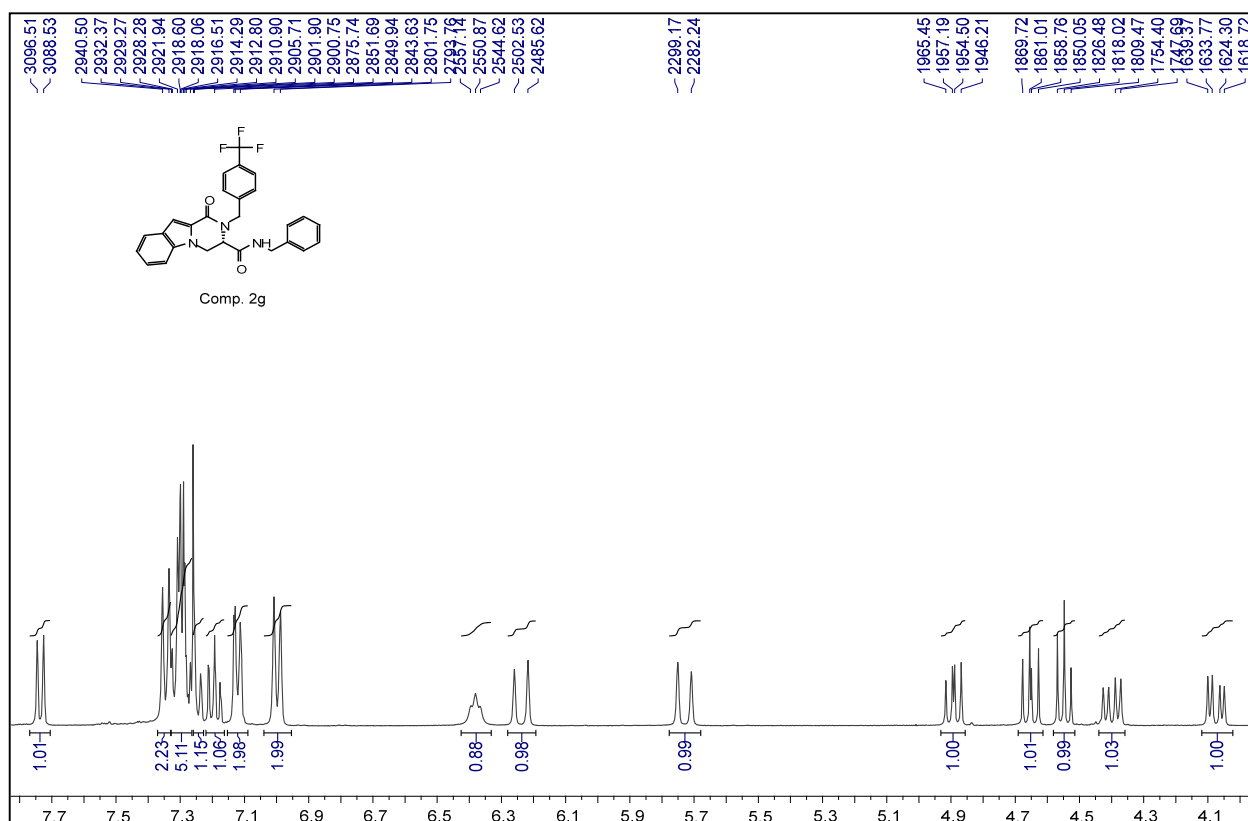
¹H NMR: (S)-N-Benzyl-2-(4-cyanobenzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-a]indole-3-carboxamide (2f)



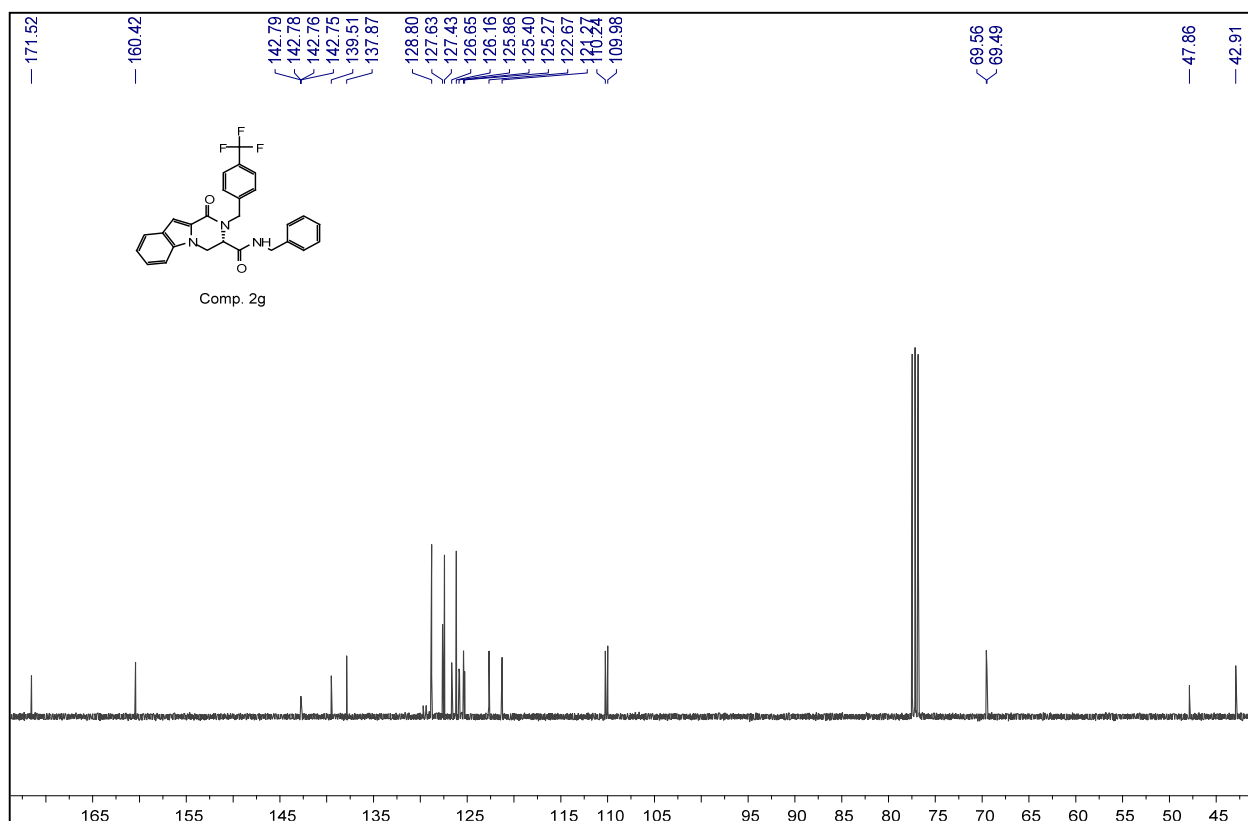
¹³C NMR: (S)-N-Benzyl-2-(4-cyanobenzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-a]indole-3-carboxamide (2f)



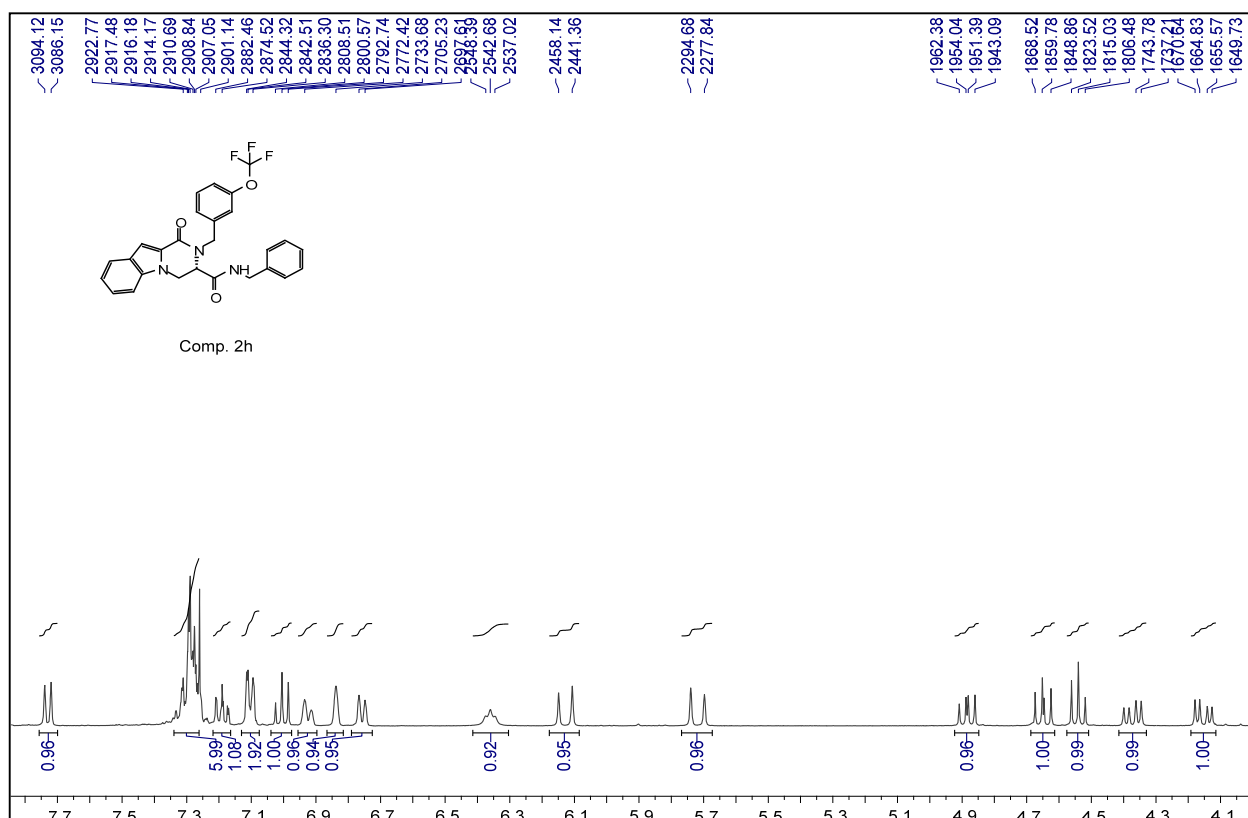
¹H NMR: (S)-N-Benzyl-2-(4-trifluoromethylbenzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-a]indole-3-carboxamide (2g)



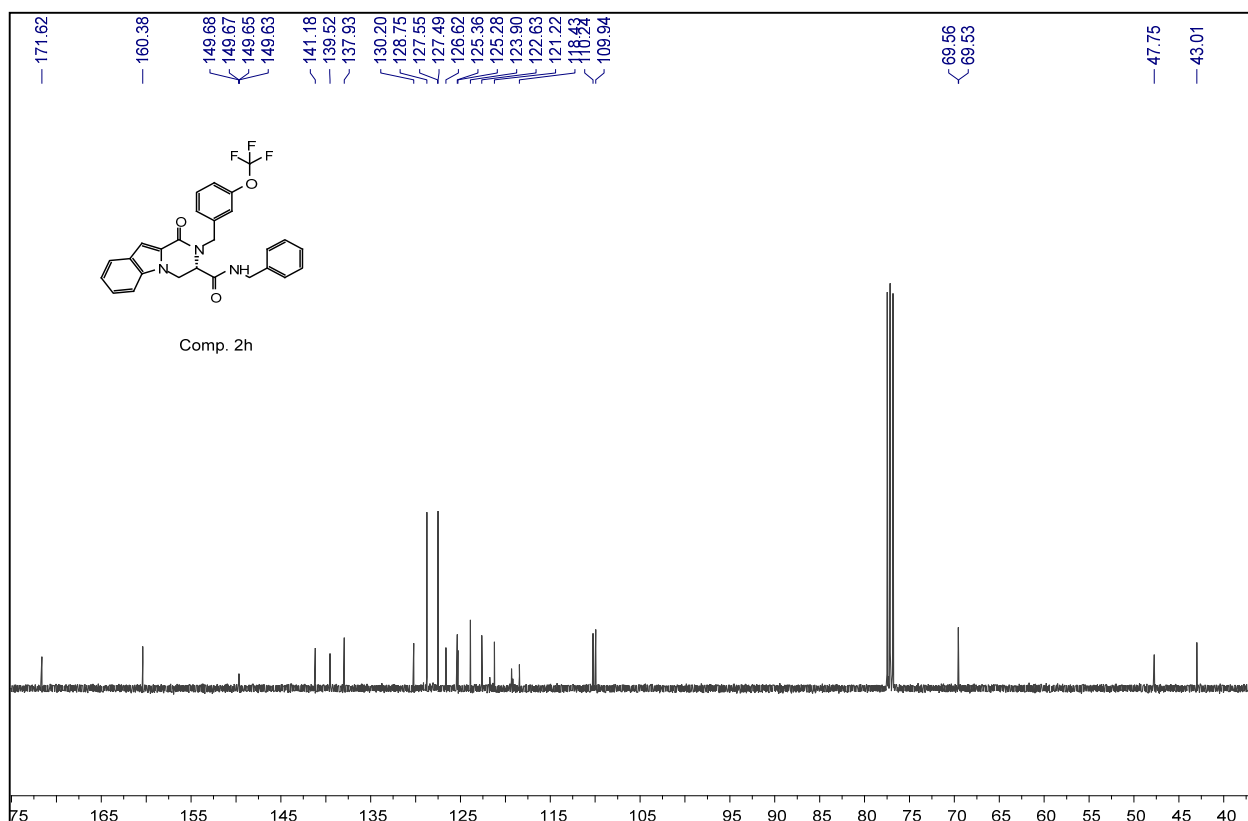
¹³C NMR: (S)-N-Benzyl-2-(4-trifluoromethylbenzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-a]indole-3-carboxamide (2g)



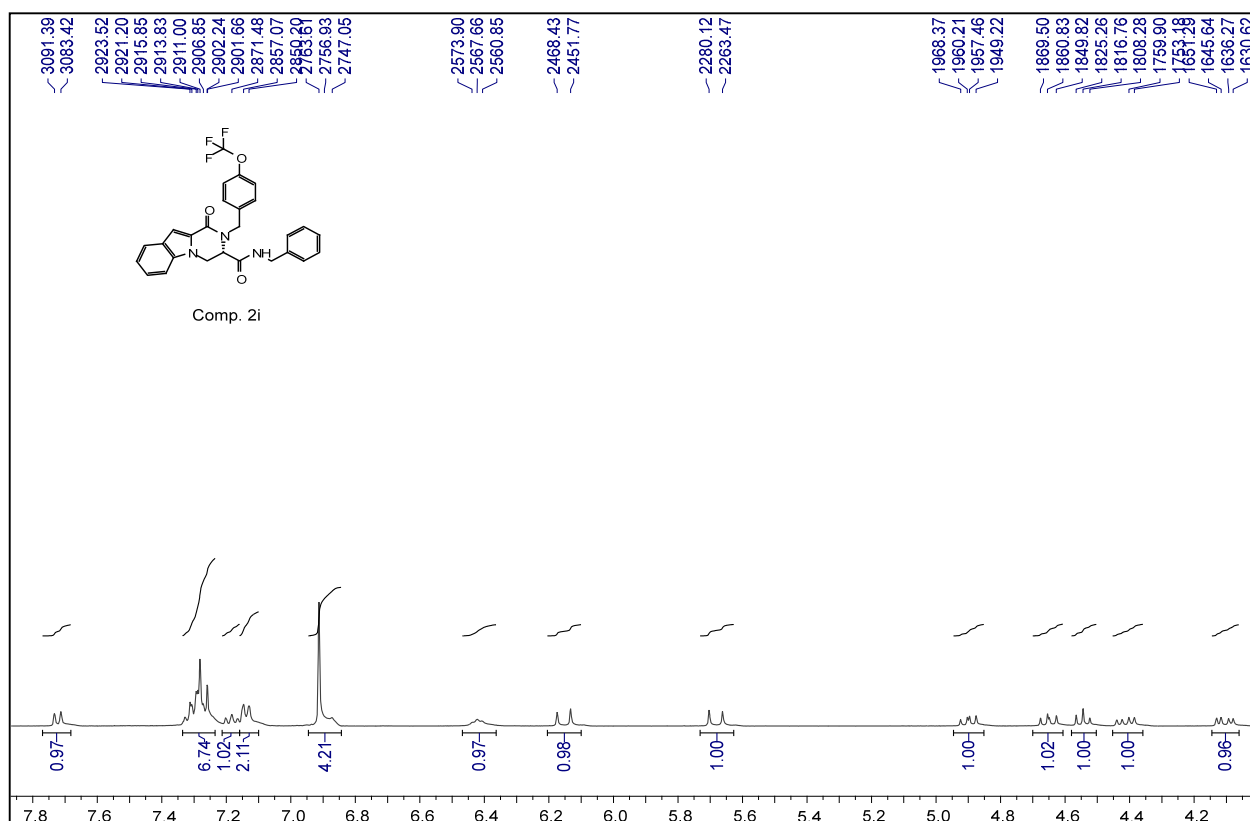
¹H NMR: (S)-N-Benzyl-2-(3-trifluoromethoxybenzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-a]indole-3-carboxamide (2h)



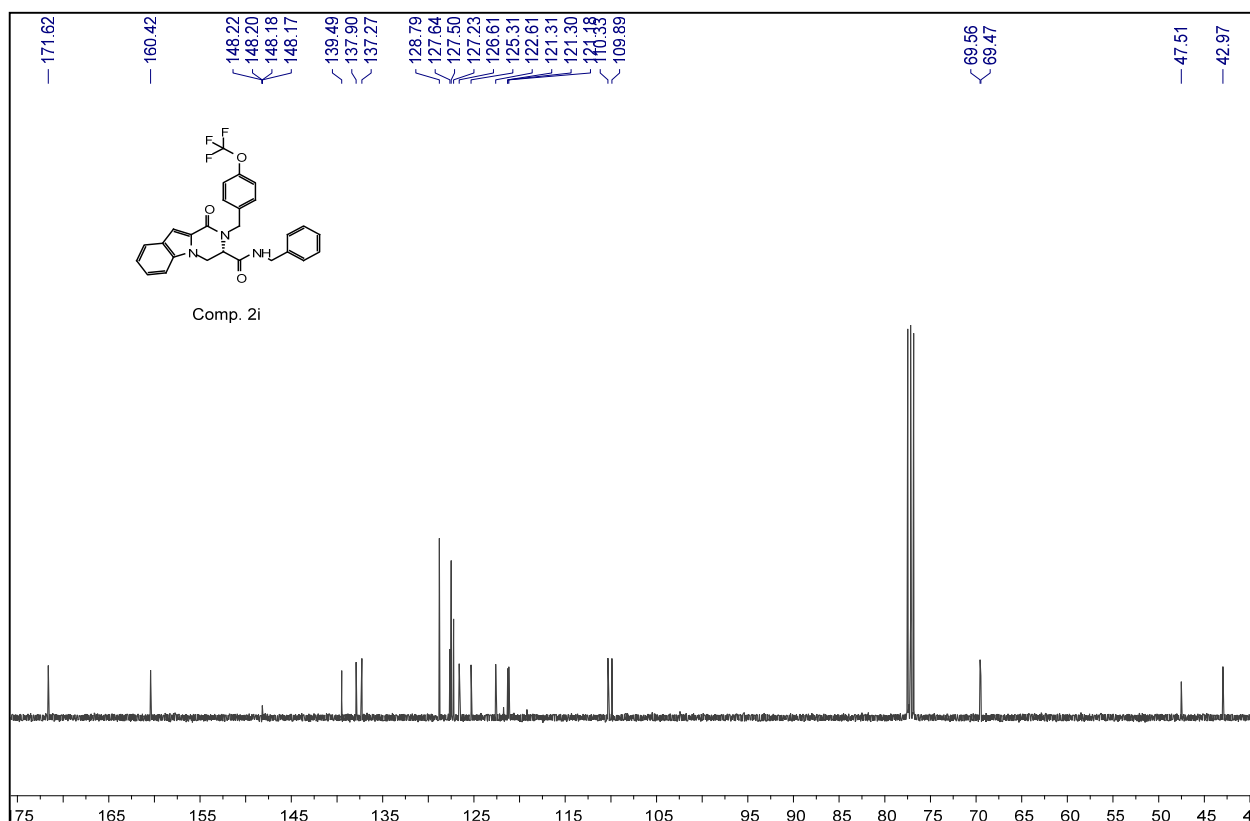
¹³C NMR: (S)-N-Benzyl-2-(3-trifluoromethoxybenzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-a]indole-3-carboxamide (2h)



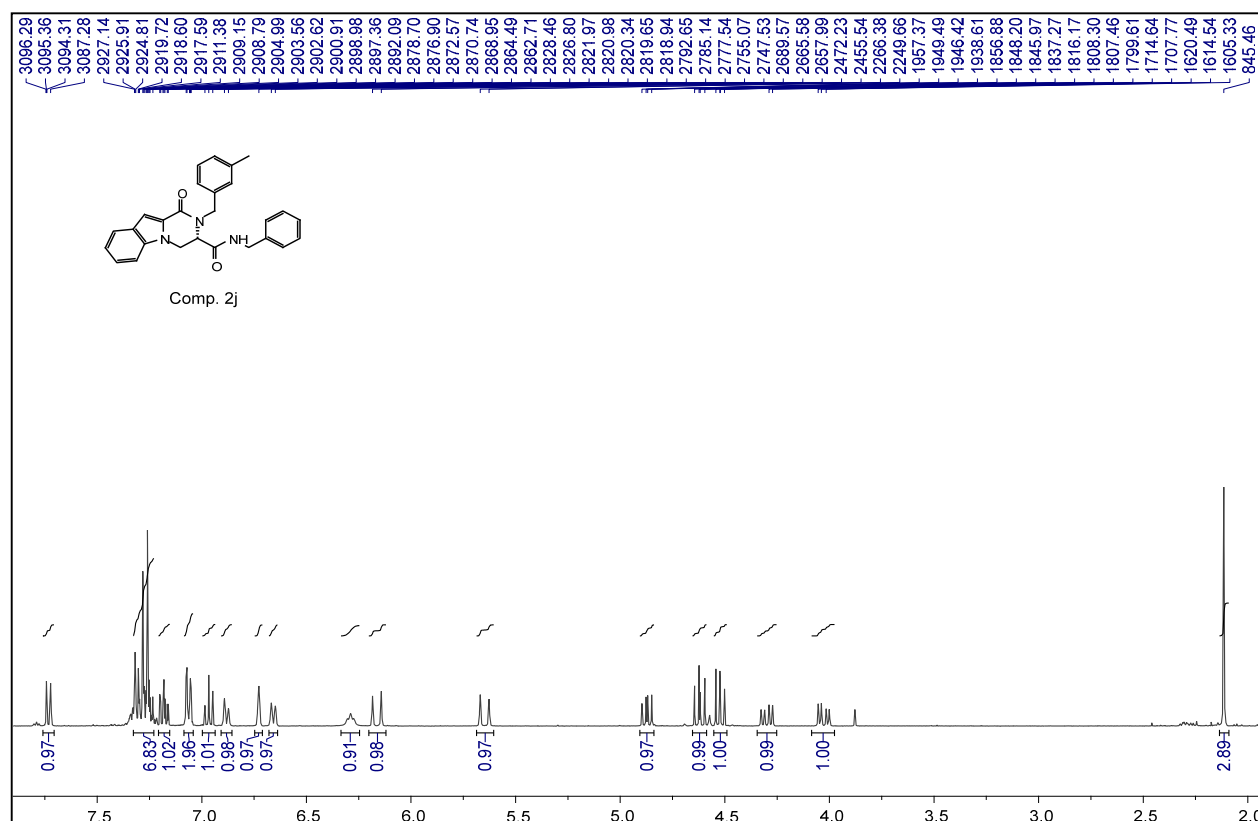
¹H NMR: (S)-N-Benzyl-2-(4-trifluoromethoxybenzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-a]indole-3-carboxamide (2i)



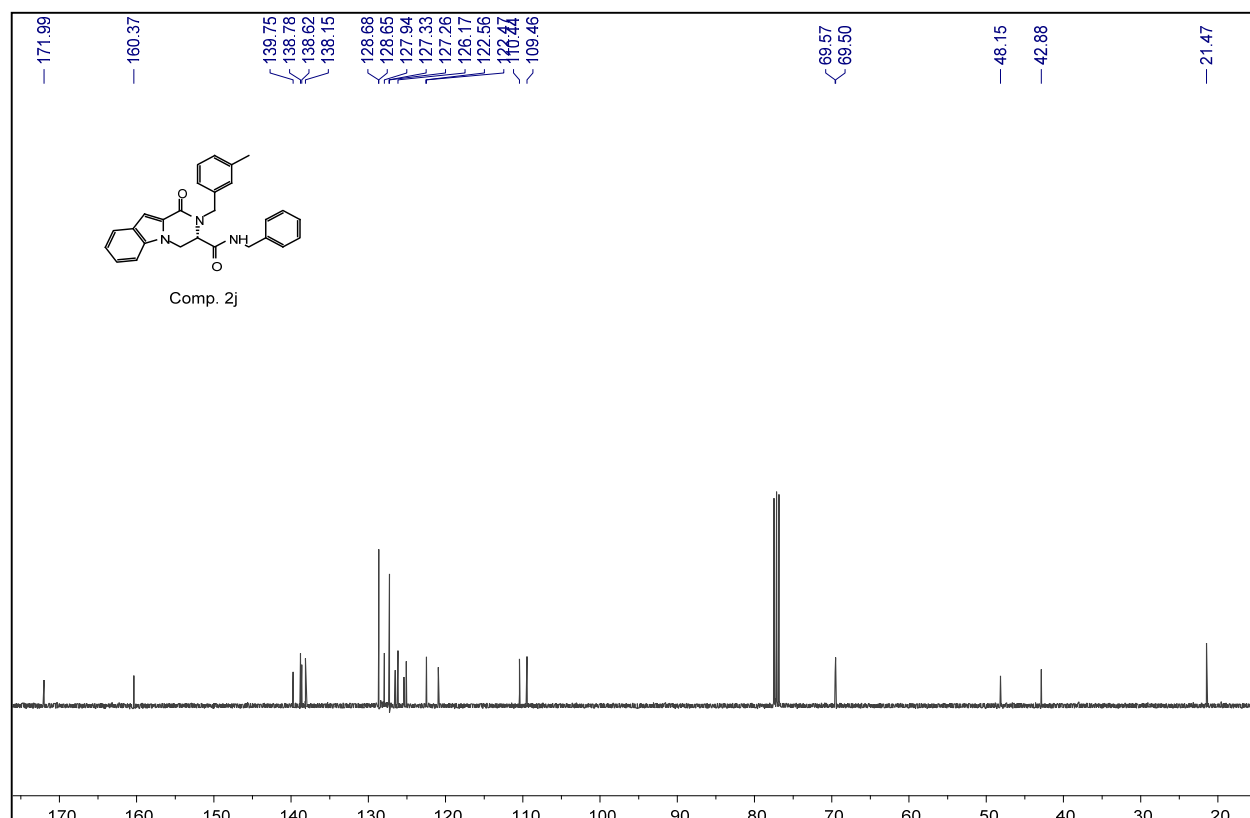
¹³C NMR: (S)-N-Benzyl-2-(4-trifluoromethoxybenzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-a]indole-3-carboxamide (2i)



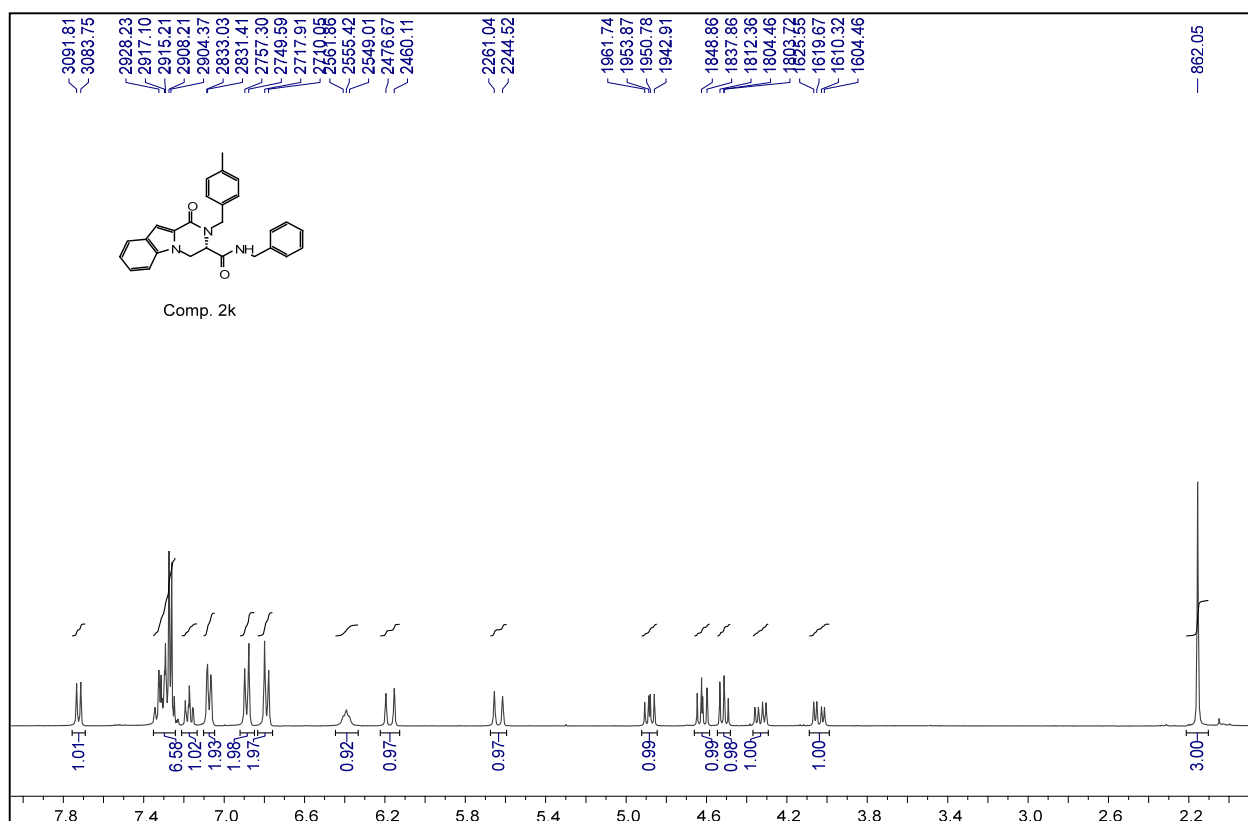
¹H NMR: (S)-N-Benzyl-2-(3-methylbenzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-a]indole-3-carboxamide (2j)



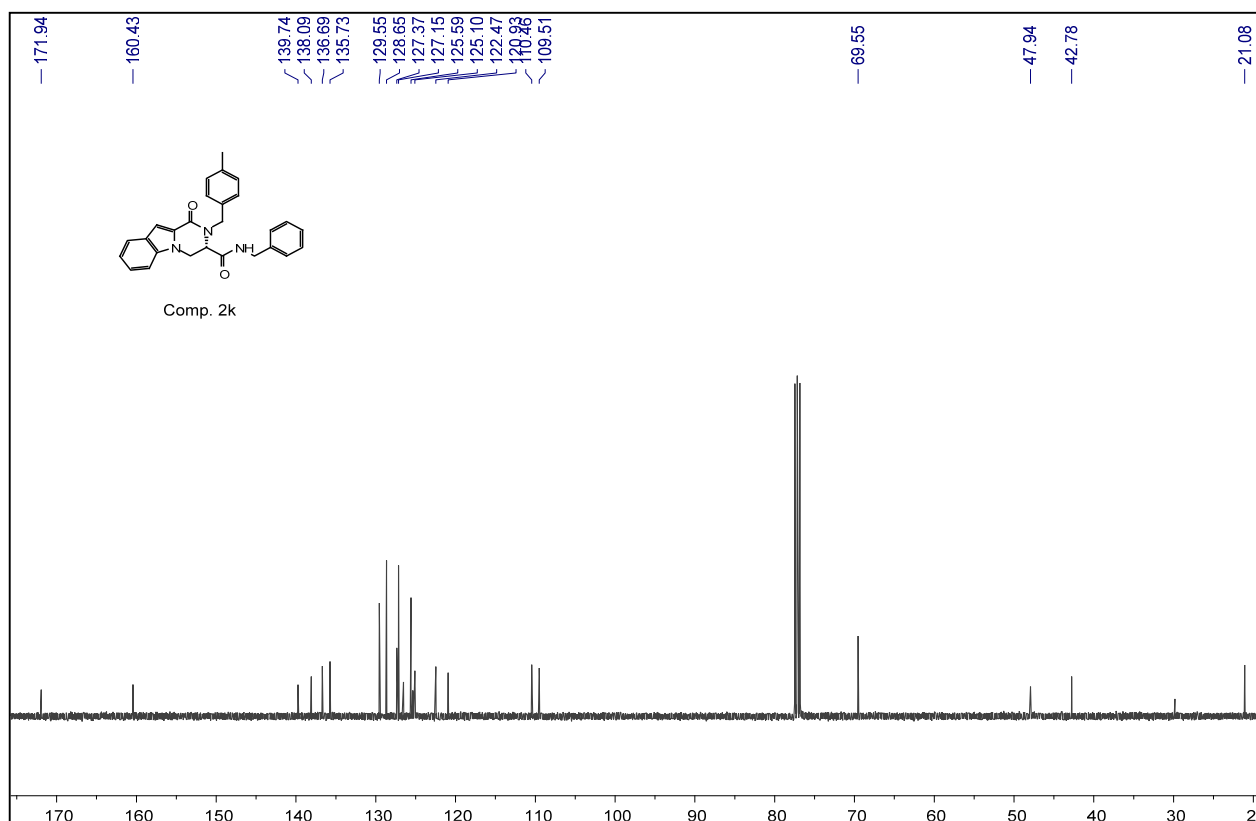
¹³C NMR: (S)-N-Benzyl-2-(3-methylbenzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-a]indole-3-carboxamide (2j)



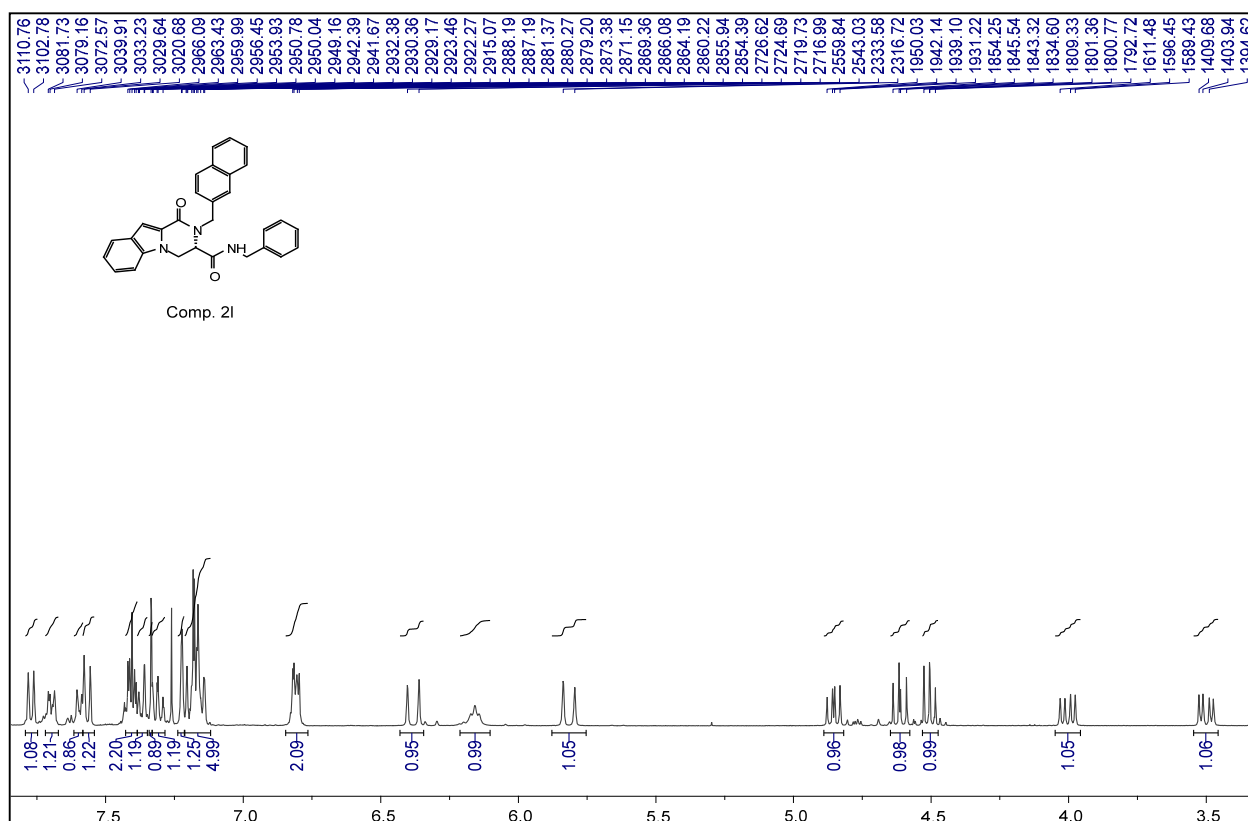
¹H NMR: (S)-N-Benzyl-2-(4-methylbenzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-a]indole-3-carboxamide (2k)



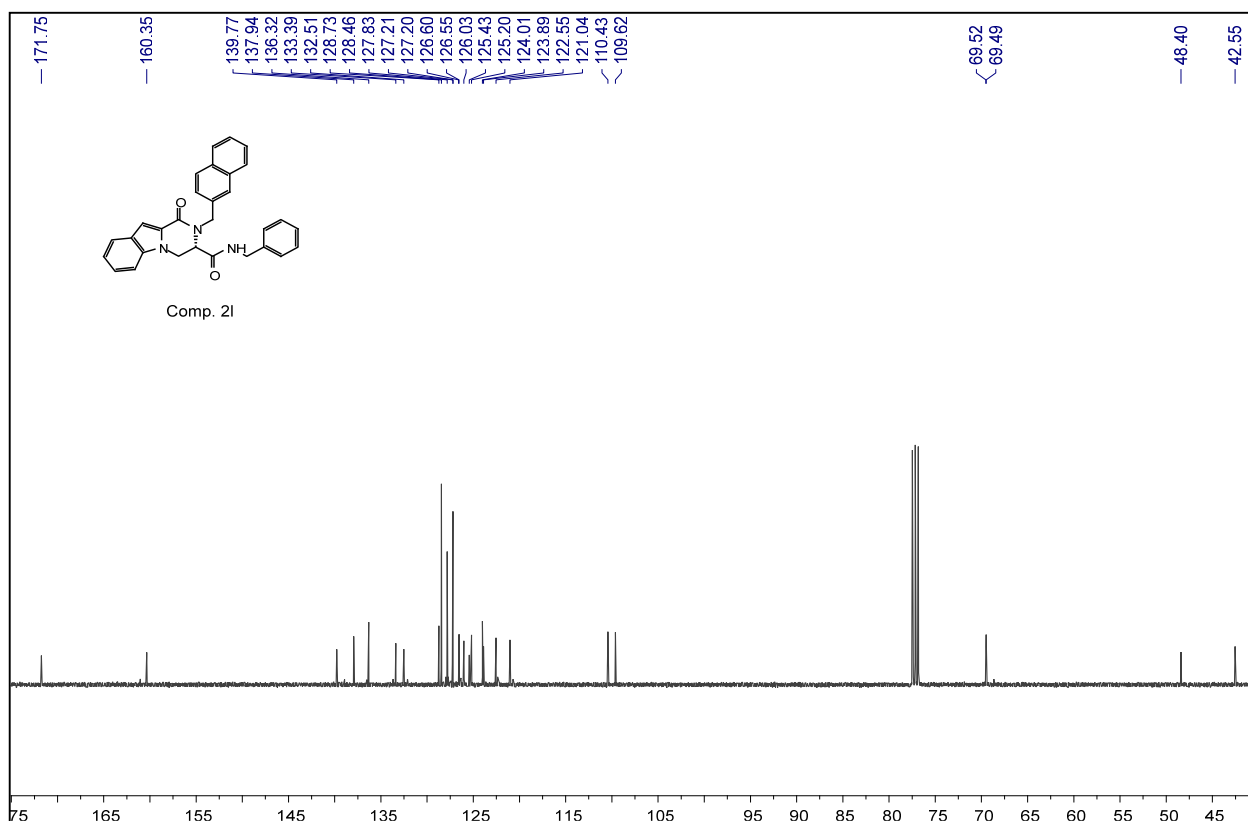
¹³C NMR: (S)-N-Benzyl-2-(4-methylbenzyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-a]indole-3-carboxamide (2k)



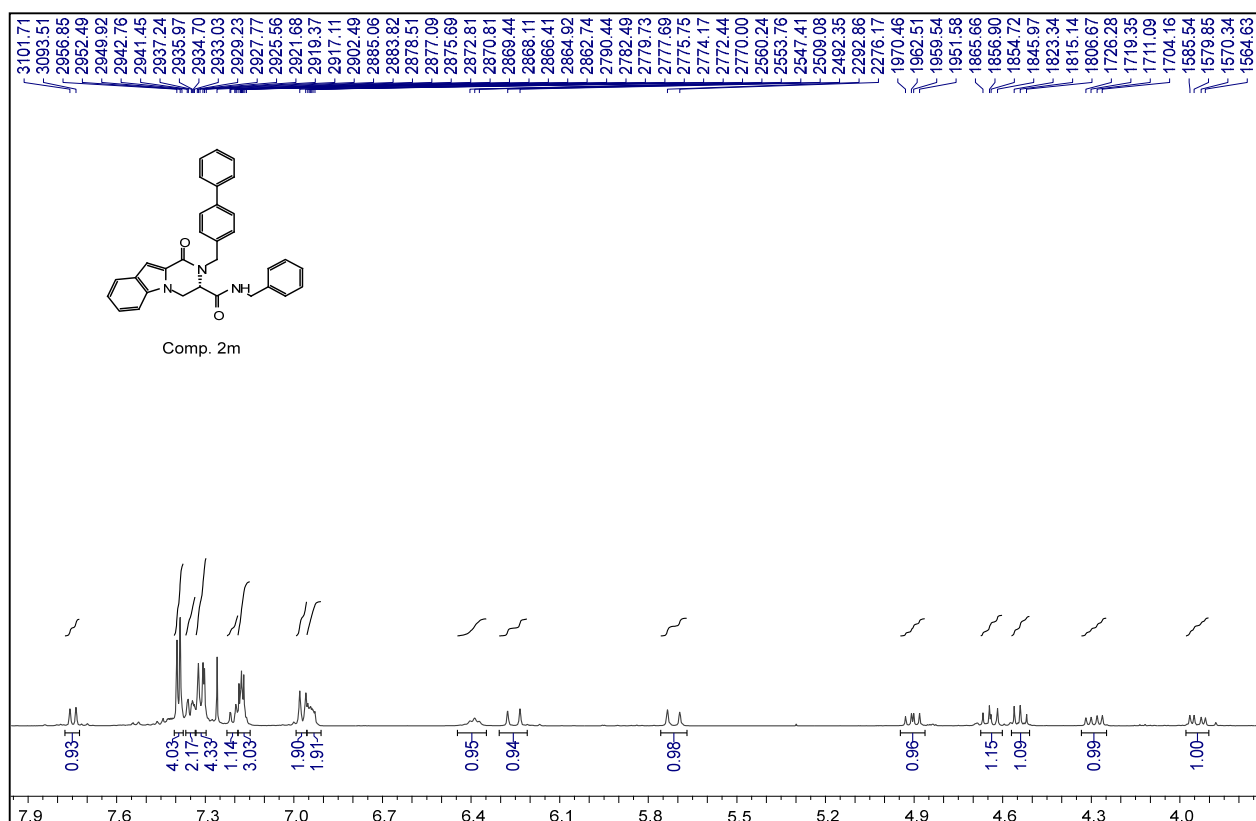
¹H NMR: (S)-N-Benzyl-2-(naphthalen-1-ylmethyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-a]indole-3-carboxamide (2l)



¹³C NMR: (S)-N-Benzyl-2-(naphthalen-1-ylmethyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-a]indole-3-carboxamide (2l)



¹H NMR: (S)-N-Benzyl-2-([1,1'-biphenyl]-4-ylmethyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-a]indole-3-carboxamide (2m)



¹³C NMR: (S)-N-Benzyl-2-([1,1'-biphenyl]-4-ylmethyl)-1-oxo-1,2,3,4-tetrahydropyrazino[1,2-a]indole-3-carboxamide (2m)

