Electronic Supplementary Information

Organocatalytic Asymmetric Povarov Reactions with 2- and 3-Vinylindoles

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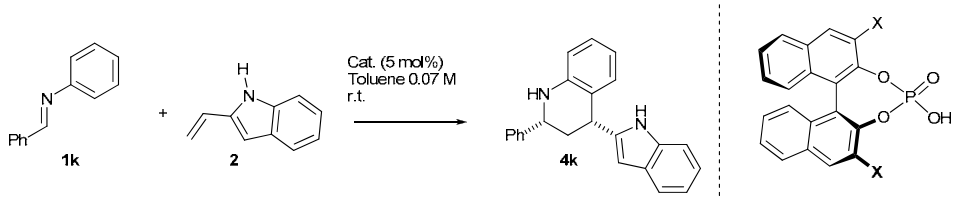
Representative results from the screening of different catalysts and reaction conditions for the catalytic enantioselective Povarov reaction with vinylindoles.

Table S1. Representative results from the screening of catalysts in the catalytic enantioselective Povarov reaction between *N*-phenyl imine **1k** and 2-vinylindole **2**.[a]

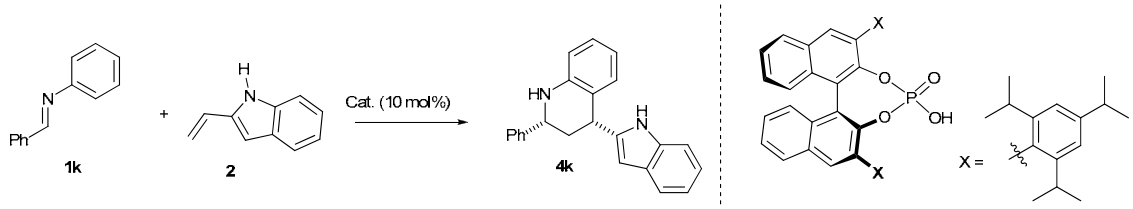


Entry	X	t (h)	Conversion[b] (%)	Ee[c] (%)
1	H	24	90	26
2	$SiPh_3$	72	85	38
3	C_6H_5	72	80	54
4	4-PhC_6H_4	24	78	75
5	9-anthryl	72	88	66
6	4-$NO_2C_6H_4$	62	27	16
7[d]	3,5-$(CF_3)_2C_6H_3$	3	95	20
8	2,4,6-$(i\text{-}Pr)_3C_6H_2$	62	>95	86
9	[e]	24	10	60

[a] Conditions: imine **1k** (0.05 mmol), 2-vinylindole **2** (0.055 mmol, 1.1 equiv.), catalyst (0.0025 mmol), toluene (0.25 mL). [b] Determined by ^{1}H NMR spectroscopy on the crude mixture. The diastereomeric ratio was always found >9:1 in favour of the *cis*-isomer. [c] Determined by chiral stationary phase HPLC analysis. [d] 0.2 M reaction. [e] (*R*)-VAPOL derived phosphoric acid was used as the catalyst.

As shown in Table S1, among the catalysts tested, the 2,4,6-tris-*i*-propylphenyl derivative (*S*)-TRIP gave the best results in terms of enantioinduction (entry 8), giving also full conversion of the starting imine, and was thus selected for further optimisation studies.

Table S2. Representative results from the screening of solvents and reaction conditions in the catalytic enantioselective Povarov reaction between *N*-phenyl imine **1k** and 2-vinylindole **2**.[a]



Entry	Solvent	Conc. (M)	T (°C)	Additives	t (h)	Conversion[b] (%)	Ee[c] (%)
1[d]	Toluene	0.07	25	-	62	>95	86
2	Toluene	0.07	25	-	20	>95	87
3	Anh. toluene	0.07	25	-	25	>95	89
4	CH_3CN	0.07	25	-	20	>95	23
5	Et_2O	0.07	25	-	94	95	87
6	Xilenes	0.07	25	-	10	90	86
7	$C_6H_5CF_3$	0.07	25	-	20	>95	79
8	Toluene	0.07	25	H_2O[e]	20	95	85
9	Anh. toluene	0.07	25	3Å MS	70	94	87
10	Anh. toluene	0.07	25	4Å MS	20	>95	81
11	Anh. toluene	0.07	25	5Å MS	25	>95	88
12	Anh. toluene	0.07	25	$CaSO_4$	20	90	90
13	Anh. toluene	0.05	25	-	20	>95	90
14	Anh. toluene	0.05	45	-	1.5	>95	90
15	Anh. toluene	0.05	45	$CaSO_4$	1.5	>95	90
16	Anh. toluene	0.05	45	3Å MS	3	>95	91
17[f]	Anh. toluene	0.05	45	3Å MS	3	>95	98
18	Anh. MTBE	0.05	45	3Å MS	22	>95	81
19	Anh. AcOEt	0.05	45	3Å MS	24	>95	70
20	Anh. *i*-Pr_2O	0.05	45	3Å MS	25	>95	78
21	Anh. Et_2O	0.05	reflux	3Å MS	4	>95	73

[a] Conditions: imine **1k** (0.05 mmol), 2-vinylindole **2** (0.055 mmol, 1.1 equiv.), catalyst (*S*)-TRIP (0.005 mmol), solvent. [b] Determined by ^{1}H NMR spectroscopy on the crude mixture. The diastereomeric ratio was always found >9:1 in favour of the *cis*-isomer. [c] Determined by chiral stationary phase HPLC analysis. [d] 5 mol% catalyst was used. [e] 2 μL of H_2O. [f] *N*-*p*-methoxyphenyl imine **1a** was used.

From the data shown in Table S2, it is possible to draw the following conclusions:

-an increase in catalyst loading from 5 mol% to 10 mol% shortens considerably the reaction time (entries 1,2).

-toluene seems to be the best solvent for this reaction (entries 2,4-7).

-it is necessary to perform the reaction under dry conditions, and using an anhydrous solvent (entries 2,3,8).

-molecular sieves and other desiccants give different effects, but with the exception of 4 Å MS do not influence the enantioselectivity observed (entries 9-12).

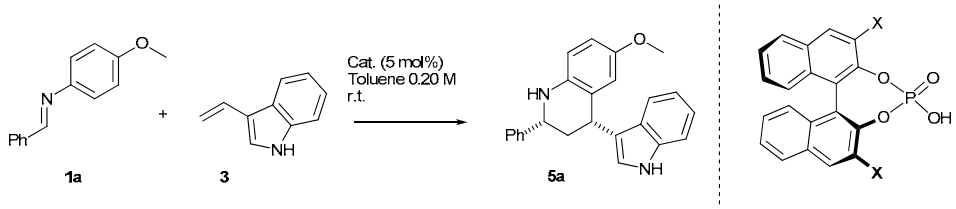
-a dilution of the reaction mixture improves slightly the enantioselectivity (entries 3 and 13).

-performing the reaction at 45 °C shortens dramatically the reaction time, without compromising the enantioselectivty (entries 14-17), with the best result being observed in the presence of 3 Å MS. The enantioselectivity is even higher when the *N*-4-methoxyphenyl imine **1a** is used (entry 17).

-ethereal solvents, which are the optimal reaction media in the 3-vinylindole **3** case (vide infra), tested under these conditions, give worse results than toluene (entries 18-21). If coordination of the solvent to the catalyst is beneficial for 3-vinylindole, in the case of its 2-vinyl counterpart slows down the reaction and decreases the enantioselectivity, probably caused by catalyst inactivation.

The conditions described in entries 16 and 17 were then used to investigate the scope of the reaction.

Table S3. Representative results from the screening of catalysts in the catalytic enantioselective Povarov reaction between *N*-4-methoxyphenyl imine **1a** and 3-vinylindole **3**.[a]

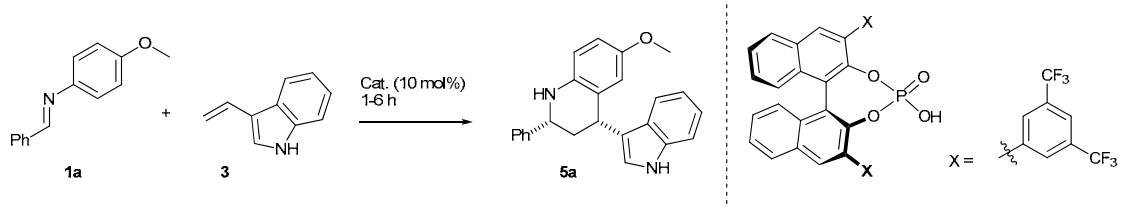


Entry	X	t (h)	Conversion[b] (%)	Ee[c] (%)
1	H	24	45	23
2	$SiPh_3$	18	50	58
3	C_6H_5	24	53	43
4	4-PhC_6H_4	24	50	51
5	9-anthryl	24	60	58
6	4-$NO_2C_6H_4$	19	35	56
7	3,5-$(CF_3)_2C_6H_3$	3	80	81
8	2,4,6-$(i\text{-}Pr)_3C_6H_2$	6	15	82
9	[d]	24	47	<10

[a] Conditions: imine **1a** (0.05 mmol), 3-vinylindole **3** (0.055 mmol, 1.1 equiv.), catalyst (0.0025 mmol), toluene (0.25 mL). [b] Determined by ^{1}H NMR spectroscopy on the crude mixture. The diastereomeric ratio was always found >9:1 in favour of the *cis*-isomer. [c] Determined by chiral stationary phase HPLC analysis. [d] (*R*)-VAPOL derived phosphoric acid was used as the catalyst.

As shown in Table S3, among the different catalysts tested the 3,5-bis(trifluoromethyl)phenyl and the 2,4,6-tris-*iso*-propylphenyl ((*S*)-TRIP) derivatives gave the best results in terms of enantioinduction (entries 7,8). These two catalysts were thus selected for further optimization studies. The very low conversion observed with the (*S*)-TRIP catalyst, as well as with many of the others, was not due to a slow reaction, but to extensive decomposition of the acid-sensitive 3-vinylindole **3** under the reaction conditions.

Table S4. Representative results from the screening of reaction conditions in the enantioselective Povarov reaction between *N*-4-methoxyphenyl imine **1a** and 3-vinylindole **3** catalysed by *(S)*-3,3′-bis(3,5-bis(trifluoromethyl)-1,1′-binaphthyl-2,2′-diyl hydrogenphosphate.[a]



Entry	Solvent	Conc. (M)	Additives	T (°C)	Conversion[b] (%)	Ee[c] (%)
1	toluene	0.2	-	25	80	81
2	toluene	0.07	-	25	68	80
3	CH_2Cl_2	0.07	-	25	51	75
4	CCl_4	0.2	-	25	45	79
5	toluene	0.2	-	0	80	78
6	toluene	0.2	-	45	80	82
7	Anh. toluene	0.2	-	25	86	86
8	Anh. toluene	0.05	-	25	57	80
9	Anh. toluene	0.2	3Å MS[d]	25	60	78
10	Anh. toluene	0.2	4Å MS[d]	25	60	75
11	Anh. toluene	0.2	5Å MS[d]	25	>80	88
12	Anh. toluene	0.2	$CaSO_4$[d]	25	70	87
13	Anh. toluene	0.2	Pyridine[e]	25	70	84

[a] Conditions: imine **1a** (0.05 mmol), 3-vinylindole **3** (0.055 mmol, 1.1 equiv.), catalyst (0.005 mmol), solvent, 1-6 h. [b] Determined by ^{1}H NMR spectroscopy on the crude mixture. The diastereomeric ratio was always found >9:1 in favour of the *cis*-isomer. [c] Determined by chiral stationary phase HPLC analysis. [d] Activated by heating under vacuum. [e] 10 mol%.

From the data shown in Table S4, it is possible to draw the following conclusions:

-toluene seems to be the best solvent for this reaction (entries 1-4).

-the use of anhydrous solvent leads to a considerable improvement in terms of conversion and ee (compare entries 1 and 7).

-a lowering of reaction temperature does not give any beneficial effect (entry 5), whereas the reaction at 45 °C (entry 6) gives very similar results to the reaction at r.t.

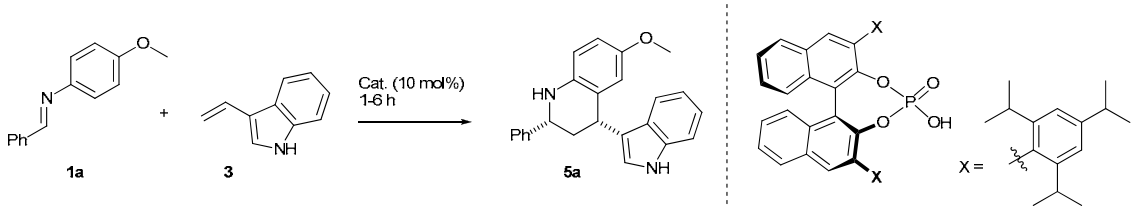
-optimal concentration is 0.2 M (entries 7,8).

-use of drying agents such as molecular sieves has different effects depending on pore size: whereas 3Å and 4Å MS lower the ee observed, 5Å MS give a small positive effect. Also the use of $CaSO_4$ as desiccant leads to a small improvement in terms of ee.

-a basic additive such s pyridine,[1] employed to lower catalyst acidity thus preventing the decomposition of 3-vinylindole, did not give the expected result, leading instead to a lowering of conversion and ee values presumably due to catalyst inactivation (entry 13).

[1] J. Itoh, K. Fuchibe and T. Akiyama, *Angew. Chem. Int. Ed.*, 2006, **45**, 4796.

Table S5. Representative results from the first screening of reaction conditions in the enantioselective Povarov reaction between *N*-4-methoxyphenyl imine **1a** and 3-vinylindole **3** catalysed by (*S*)-TRIP.[a]

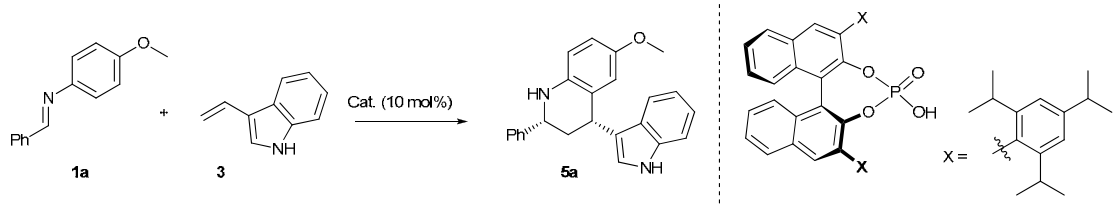


Entry	Solvent	Conc. (M)	Additives	T (°C)	Conversion[b] (%)	Ee[c] (%)
1	toluene	0.2	-	25	15	82
2	toluene	0.2	-	45	12	n.d.
3	toluene	0.05	-	45	20	88
4	Anh. Toluene	0.05	3Å MS[d]	45	14	85
5	Anh. toluene	0.05	5Å MS[d]	45	<10	n.d.
6	Anh. toluene	0.05	$CaSO_4$[d]	45	<10	n.d.
7	Anh. toluene	0.05	Pyridine[e]	45	16	n.d.
8[f]	Anh. toluene	0.05	-	45	55	89

[a] Conditions: imine **1a** (0.05 mmol), 3-vinylindole **3** (0.055 mmol, 1.1 equiv.), (*S*)-TRIP (0.005 mmol), solvent, 1-6 h. [b] Determined by ^{1}H NMR spectroscopy on the crude mixture. The diastereomeric ratio was always found >9:1 in favour of the *cis*-isomer. [c] Determined by chiral stationary phase HPLC analysis. N.d. = not determined. [d] Activated by heating under vacuum. [e] 10 mol%. [f] Slow addition (syringe pump, ca. 1 h) of 3-vinylindole **3** dissolved in toluene, final concentration 0.05 M.

As already mentioned and shown in Table S5, entry 1, the (*S*)-TRIP catalyst gave a very low conversions due to extensive decomposition of 3-vinylindole **3**. However, it was possible to increase the ee observed to a satisfactory 88% value decreasing the concentration of the reaction solution and performing the reaction at 45 °C (entry 3). Acidic additives were tested as desiccants but gave even worse conversions fastening the decomposition of the olefin (enties 4-6). A basic additive such as pyridine was tested hoping that it would lower the acidity of the system. However, as already observed in the case of the bis-(3,5-bis(trifluoromethyl)phenyl) derived catalyst, it did not give any significant improvement (entry 7). Finally, it was found that the slow addition of a 3-vinylindole solution, which avoids a long time coexistence of the acid sensitive olefin with the catalyst, could considerably increase the conversion without compromising the ee observed (entry 8).

Table S6. Representative results from the second screening of reaction conditions in the enantioselective Povarov reaction between *N*-4-methoxyphenyl imine **1a** and 3-vinylindole **3** catalysed by (*S*)-TRIP.[a]



Entry	Solvent	T (°C)	t (h)	Slow addition[b]	Conversion[c] (%)	Ee[d] (%)
1	MTBE	45	1	-	30	91
2	THF	45	4	-	58	97
3	*i*-Pr_2O	45	0.5	-	42	84
4	Et_2O	45	0.5	-	43	92
5	AcOEt	45	1	-	55	95
6	Anh. THF	45	4	2.5 h	78	94
7	Anh. AcOEt	45	2.5	2.5 h	92	87
8	Anh. dioxane	45	65	2.5 h	65	93
9	Anh. acetone	45	2.5	2.5 h	<10	n.d.
10	Anh. THF	60	3	2.5 h	73	94
11	Anh. THF	45	13	12 h	87	92

[a] Conditions: imine **1a** (0.05 mmol), 3-vinylindole **3** (0.055 mmol, 1.1 equiv.), (*S*)-TRIP (0.005 mmol), solvent (1.0 mL). [b] Slow addition (syringe pump) of 3-vinylindole **3** dissolved in the solvent, final concentration 0.05 M. [c] Determined by ^{1}H NMR spectroscopy on the crude mixture. The diastereomeric ration was always found >9:1 in favour of the *cis*-isomer. [d] Determined by chiral stationary phase HPLC analysis. N.d. = not determined.

Among the different solvents tested, THF and AcOEt proved to be the best both in terms of conversion and enantioselectivity (entries 1-5). It is worth noting that using these more coordinating solvents it was possible to reach considerable higher conversions with respect to the reactions performed in toluene (Table S5), especially considering that these reactions were run adding the olefin all at once. Apparently, coordination of the acid by the solvent slowed down the decomposition of 3-vinylindole **3**. Slow addition over 5 h was then tested using the best solvents THF and AcOEt, with the former furnishing better levels of enantioselectivity, though accompanied by a lower conversion (entries 6,7). Other coordinating solvents such as dioxane and acetone were tested at this stage, the former giving results slightly worse than THF, the latter not furnishing the product at all, due to a parasitic reaction pathway involving the solvent itself reacting with the imine **1a** (entries 8,9). In order to improve the conversion in THF, the temperature was varied to 60 °C (entry 10), not giving however the desired result. Finally, slowing further the rate of the addition of vinylindole, it was possible to reach a satisfactory level of conversion also in THF, without compromising the enantioselectivity (entry 11). Using a slightly higher excess of olefin (1.5 equiv. instead of 1.1 equiv. used during the optimization studies), these latter conditions were taken to investigate the scope of the reaction.

Experimental Details

General Methods. ^{1}H, ^{13}C NMR spectra were recorded on a Varian AS 400 or 600 spectrometer. Chemical shifts (δ) are reported in ppm relative to residual solvent signals for ^{1}H and ^{13}C NMR (^{1}H NMR: 7.26 ppm for $CDCl_3$, 2.50 ppm for DMSO-d_6, 2.05 ppm for acetone-d_6; ^{13}C NMR: 77.0 ppm for $CDCl_3$, 39.5 ppm for DMSO-d_6, 29.8 ppm for acetone-d_6) or using an external reference for ^{19}F NMR (C_6F_6, -163.0 ppm). ^{13}C NMR spectra were acquired with ^{1}H broad band decoupled mode. Mass spectra were recorded on a micromass LCT spectrometer using electrospray (ES) ionisation techniques. Optical rotations were measured on a Perkin-Elmer 241 polarimeter. The enantiomeric excess (ee) of the products was determined by chiral stationary phase HPLC (Daicel Chiralpak AD-H, Chiralcel OJ-H, Chiralcel OD), using a UV detector operating at 254 nm. Relative configuration was determined as 2,4-*cis* for compounds **4a**,**4j** and **5j** as shown below. We assumed a similar reaction pathway leading mainly to 2,4-*cis* cycloadducts in the other cases.

Materials. Analytical grade solvents and commercially available reagents were used as received, unless otherwise stated. Chromatographic purifications were performed using 70-230 mesh silica. Racemic samples were prepared using *rac*-1,1'-binaphthyl-2,2'-diyl hydrogenphosphate or 1,2-bis(3,5-bistrifluoromethylphenyl)thiourea[2] as the catalyst, in CH_2Cl_2 or toluene or THF at room temperature for 24-60 h. THF was distilled from Na/benzophenone before use. Toluene and EtOAc were dried over activated 4 Å molecular sieves. 2-Vinyl-1*H*-indole **2**[3] and 3-vinyl-1*H*-indole **3**[4] were prepared through Wittig reactions as described in the literature. *(S)*-3,3′-Bis(2,4,6-tri-*iso*-propylphenyl)-1,1′-binaphthyl-2,2′-diyl hydrogenphosphate ((*S*)-TRIP catalyst) was prepared following literature procedures.[5] N-4-methoxyphenyl imines **1a-h** were obtained refluxing an equimolar mixture of 4-methoxyaniline and the appropriate aldehyde in EtOH for a few hours, and collected by filtration. Imines **1k-n** were obtained stirring for 48-60 h benzaldehyde and the appropriate aniline derivative in CH_2Cl_2 in the presence of activated 4 Å molecular sieves.

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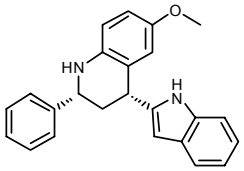
[2] P. R. Schreiner and A. Wittkopp, *Org. Lett.* 2002, **4**, 217.
[3] J. Waser, B. Gaspar, H. Nambu and E. M. Carreira, *J. Am. Chem. Soc.*, 2006, **128**, 11693.
[4] M. S. Scott, A. C. Lucas, C. A. Luckhurst, J. C. Prodger and D. J. Dixon, *Org. Biomol. Chem.*, 2006, **4**, 1313.
[5] Preparation of the 3,3'-dibromo derivative: (*a*) P. Wipf and J. K. Jung, *J. Org. Chem.*, 2000, **65**, 6319. $Ni(PPh_3)_2Cl_2$ coupling and ether cleavage: (*b*) X. Teng, D. R. Cefalo, R. R. Schrock and A. H. Hoveyda, *J. Am. Chem. Soc.*, 2002, **124**, 10779. Phosphoric acid formation: (*c*) W. J. Liu, X. H. Chen and L. Z. Gong, *Org. Lett.*, 2008, **10**, 5357.

General procedure for the organocatalytic, enantioselective Povarov reaction of aldimines 1a-n with 2-vinyl-1*H*-indole 2.

To a flame dried Schlenk tube equipped with a magnetic stirring bar, 3 Å spherical-shaped molecular sieves (200 mg) were added under a nitrogen atmosphere. The molecular sieves were then thermally activated under vacuum for 10 minutes and then allowed to cool to r.t.. The aldimine **1** (0.10 mmol) was then added under a nitrogen atmosphere, followed by anhydrous toluene (2.0 mL) and the catalyst (*S*)-TRIP (7.5 mg, 0.010 mmol). After heating to 45 °C, 2-vinylindole **2** (17.2 mg, 0.12 mmol) was added in one portion. The mixture was then stirred at the same temperature under a nitrogen atmosphere. After 3 h, the reaction mixture was filtered through a plug of silica gel, and the plug washed with EtOAc (4x). After concentration of the solvents, the residue was analyzed by ^{1}H NMR spectroscopy to determine the diastereomeric ratio of the cycloadducts **4**. Finally, the residue was purified by chromatography on silica gel (*n*-hexane/EtOAc mixtures).

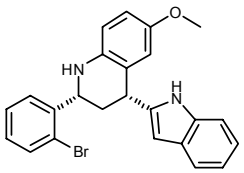
(2*R*,4*R*)-4-(1*H*-Indol-2-yl)-6-methoxy-2-phenyl-1,2,3,4-tetrahydroquinoline (4a).



Following the general procedure, the title compound was obtained as an orange solid in 92% yield and as a single diastereoisomer, after chromatography on silica gel (*n*-hexane/EtOAc 80:20). ^{1}H NMR of the crude mixture showed the presence of a single diastereoisomer. The ee of the product was determined by HPLC using a Chiralcel OD column (*n*-hexane/*i*-PrOH 80:20, flow-rate 1.0 mL/min, t_{maj} = 19.8 min, t_{min} = 15.9 min, 98% ee). $[\alpha]_D^{20}$ = +114 (c = 0.37 in CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.89 (br s, 1H), 7.60-7.55 (m, 1H), 7.49-7.44 (m, 2H), 7.41-7.35 (m, 2H), 7.35-7.28 (m, 1H), 7.26-7.22 (m, 1H), 7.16-7.07 (m, 2H), 6.72-6.67 (m, 1H), 6.59 (d, *J* = 8.4 Hz, 1H), 6.51-6.46 (m, 2H), 4.62 (dd, *J* = 12.1, 6.1 Hz, 1H), 4.55 (dd, *J* = 11.1, 2.6 Hz, 1H), 3.93 (br s, 1H), 3.59 (s, 3H), 2.41 (ddd, *J* = 13.2, 6.2, 2.7 Hz, 1H), 2.31 (br q, *J* = 11.7 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 152.5, 143.4, 140.9, 139.3, 136.3, 128.7, 128.4, 127.8, 126.6, 123.3, 121.4, 120.0, 119.6, 115.9, 114.6, 114.2, 110.7, 101.8, 57.3, 55.8, 40.4, 38.5; ESI-MS: 377 [M^+ + Na].

The relative and absolute configuration of the title compound were determined as 2*R*,4*R* (vide infra).

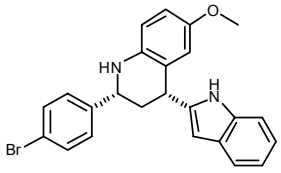
(2*R,4*R**)-2-(2-Bromophenyl)-4-(1*H*-indol-2-yl)-6-methoxy-1,2,3,4-tetrahydroquinoline (4b).**



Following the general procedure, the title compound was obtained as a white solid in 98% yield and as a mixture of two diastereoisomers after chromatography on silica gel (*n*-hexane/EtOAc 85:15). ^{1}H NMR analysis of the crude mixture showed a 95:5 diastereomeric ratio. The ee of the major diastereoisomer was determined by HPLC using a Chiralpak ADH column (*n*-hexane/*i*-PrOH 80:20, flow-rate 0.75 mL/min; major diastereoisomer: t_{maj} = 19.1 min, t_{min} = 16.6 min, ee_{maj} = 96%; minor diastereoisomer: not separated, t = 19.3 min). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.93 (br s, 1H$_{min}$), 7.87 (br s, 1H$_{maj}$), 7.69 (dd, *J* = 7.9, 1.6 Hz, 1H$_{maj}$), 7.62 (dd, *J* = 7.5, 1.7 Hz, 1H$_{min}$), 7.57 (br d, *J* = 8.0 Hz, 2H$_{maj}$), 7.53 (br d, *J* = 8.0, 2H$_{min}$), 7.39-7.20 (m, 2H$_{maj}$, 2H$_{min}$), 7.19-7.05 (m, 3H$_{maj}$, 3H$_{min}$), 6.80 (br dd *J* = 8.8, 2.8 Hz, 1H$_{min}$), 6.72 (br dd *J* = 8.6, 2.8 Hz, 1H$_{maj}$), 6.68-6.59 (m,

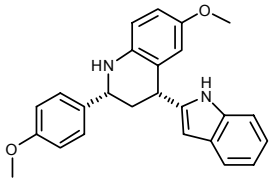
$1H_{maj}$, $2H_{min}$), 6.53-6.48 (m, $2H_{maj}$), 6.33-6.32 (m, $1H_{min}$), 4.97 (dd, J = 11.0, 2.2 Hz, $1H_{maj}$), 4.83 (br dd, J = 9.1, 3.3 Hz, $1H_{min}$), 4.64 (dd, J = 12.4, 5.7 Hz, $1H_{maj}$), 4.26 (br t, J = 4.6 Hz, $1H_{min}$), 3.90 (br s, $1H_{maj}$, $1H_{min}$), 3.71 (s, $3H_{min}$), 3.60 (s, $3H_{maj}$), 2.61-2.44 (m, $1H_{maj}$, $1H_{min}$), 2.27-2.08 (m, $1H_{maj}$, $1H_{min}$); ^{13}C NMR ($CDCl_3$, 100 MHz) [signals of the major diastereoisomer] δ 152.6, 141.9, 140.8, 139.3, 136.2, 132.9, 129.0, 128.4, 127.9, 127.6, 123.5, 123.1, 121.4, 120.0, 119.6, 116.2, 114.6, 114.2, 110.6, 101.8, 55.8, 55.7, 38.8, 38.5; ESI-MS: 455 [M^+ + Na].

(2*R,4*R**)-2-(4-Bromophenyl)-4-(1*H*-indol-2-yl)-6-methoxy-1,2,3,4-tetrahydroquinoline (4c).**



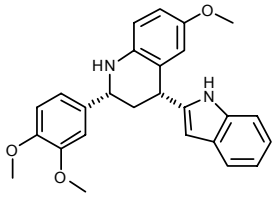
Following the general procedure, the title compound was obtained as a white solid in 66% yield and as a single diastereoisomer, after dissolving the crude mixture in acetone, filtration through a plug of silica to remove the catalyst and the molecular sieves, evaporation of the acetone and collection of the solid product, (suspended in toluene), by Buchner filtration. The ee of the product was determined by HPLC using a Chiralpak ADH column (*n*-hexane/*i*-PrOH 90:10, flow-rate 0.75 mL/min, t_{maj} = 45.3 min, t_{min} = 41.9 min, ee >99%). $[\alpha]_D^{20}$ = +135 (c = 0.36 in THF); ^1H NMR (DMSO-d_6, 400 MHz) δ 10.98 (br s, 1H), 7.57 (br d, J = 8.1 Hz, 2H), 7.45 (br d, J = 8.6 Hz, 3H), 7.26 (d, J = 8.0 Hz, 1H), 7.04-6.89 (m, 2H), 6.67-6.58 (m, 2H), 6.33 (br d, J = 1.3 Hz, 1H), 6.18 (br s, 1H), 5.77 (s, 1H), 4.57-4.46 (m, 2H), 3.47 (s, 3H), 2.36-2.12 (m, 2H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 150.9, 143.9, 141.6, 139.6, 136.4, 131.2, 128.9, 127.8, 123.3, 120.3, 120.0, 119.3, 118.6, 115.3, 114.1, 112.8, 110.9, 99.9, 55.33, 55.3, 37.7; ESI-MS: 455 [M^+ + Na].

(2*R,4*R**)-4-(1*H*-Indol-2-yl)-6-methoxy-2-(4-methoxyphenyl)-1,2,3,4-tetrahydroquinoline (4d).**



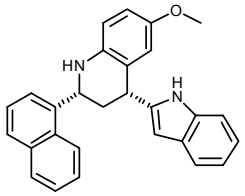
Following the general procedure (4 h reaction time) the title compound was obtained as a pale yellow solid in 88% yield and as a single diastereoisomer after chromatography on silica gel (*n*-hexane/EtOAc 75:25). ^1H NMR analysis of the crude mixture showed a 90:10 diastereomeric ratio. The ee of the product was determined by HPLC using a Chiralpak ADH column (*n*-hexane/*i*-PrOH 80:20, flow-rate 0.75 mL/min, t_{maj} = 25.1 min, t_{min} = 26.9 min, ee = 97%). $[\alpha]_D^{20}$ = +125 (c = 0.41 in AcOEt); ^1H NMR (DMSO-d_6, 400 MHz) δ 10.98 (br s, 1H), 7.45 (br d, J = 8.0 Hz, 1H), 7.43-7.38 (m, 2H), 7.27 (br dd, J = 7.9, 0.9 Hz, 1H), 7.03-6.98 (m, 1H), 6.97-6.91 (m, 3H), 6.66-6.56 (m, 2H), 6.34 (br d, J = 1.4 Hz, 1H), 6.18 (br d, J = 2.4 Hz, 1H), 5.65 (br s, 1H), 4.56-4.42 (m, 2H), 3.75 (s, 3H), 3.47 (s, 3H), 2.30 (q, J = 12.4 Hz, 1H), 2.14 (ddd, J = 12.4, 5.1, 2.7 Hz, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 158.5, 150.7, 141.8, 139.9, 136.4, 127.8, 127.7, 123.2, 120.3, 119.3, 118.6, 115.2, 114.2, 113.7, 112.7, 110.9, 99.8, 55.4, 55.3, 55.1, 44.5, 37.9; the ^{13}C NMR signal at 44.5 ppm, not observable in the ^{13}C NMR spectrum due to the overlap with the DMSO-d_6 signals, was detected by means of a ^{13}C DEPT experiment (mult = 1.5). ESI-MS: 407 [M^+ + Na].

(2*R,4*R**)-2-(3,4-Dimethoxyphenyl)-4-(1*H*-indol-2-yl)-6-methoxy-1,2,3,4-tetrahydroquinoline (4e).**



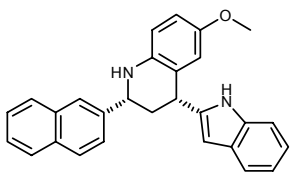
Following the general procedure (20 h reaction time) the title compound was obtained as a pale yellow solid in 96% yield and as a single diastereoisomer after chromatography on silica gel (*n*-hexane/EtOAc 60:40). ^{1}H NMR analysis of the crude mixture showed the presence of a single diastereoisomer. The ee of the product was determined by HPLC using a Chiralpak ADH column (*n*-hexane/*i*-PrOH 80:20, flow-rate 0.75 mL/min, t_{maj} = 27.2 min, t_{min} = 55.0 min, ee = 92%). $[\alpha]_D^{20}$ = +86 (c = 0.41 in CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.89 (br s, 1H), 7.57 (br d, *J* = 7.5 Hz, 1H), 7.24 (br d, *J* = 8.0 Hz, 1H), 7.16-7.06 (m, 2H), 7.04-6.94 (m, 2H), 6.85 (br d, *J* = 8.2 Hz, 1H), 6.69 (br dd, *J* = 8.6, 2.9 Hz, 1H), 6.59 (br d, *J* = 8.6 Hz, 1H), 6.48-6.45 (m, 2H), 4.61 (dd, *J* = 12.1, 5.8 Hz, 1H), 4.49 (dd, *J* = 11.1, 2.4 Hz, 1H), 3.89 (s, 3H), 3.89 (br s, 1H), 3.88 (s, 3H), 3.59 (s, 3H), 2.38 (ddd, *J* = 13.1, 6.0, 2.5 Hz, 1H), 2.28 (q, *J* = 11.9 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 152.4, 149.2, 148.6, 141.0, 139.5, 136.2, 136.1, 128.4, 123.1, 121.4, 120.0, 119.6, 118.8, 115.8, 114.6, 114.2, 111.1, 110.6, 109.5, 101.7, 57.0, 55.9, 55.8, 55.7, 40.6, 38.6; ESI-MS: 437 [M^+ + Na].

(2*R,4*R**)-4-(1*H*-Indol-2-yl)-6-methoxy-2-(naphthalen-1-yl)-1,2,3,4-tetrahydroquinoline (4f).**



Following the general procedure, the title compound was obtained as a pale yellow solid in 97% yield and a single diastereoisomer, after chromatography on silica gel (*n*-hexane/EtOAc 85:15). ^{1}H NMR analysis of the crude mixture showed the presence of a single diastereoisomer. The ee of the product was determined by HPLC using a Chiralpak ADH column (*n*-hexane/*i*-PrOH 80:20, flow-rate 0.75 mL/min, t_{maj} = 25.2 min, t_{min} = 21.6 min, ee = 95%). $[\alpha]_D^{20}$ = +243 (c = 0.37 in acetone); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.20 (d, *J* = 8.3 Hz, 1H), 7.95-7.75 (m, 4H), 7.60-7.47 (m, 4H), 7.24-7.18 (m, 1H), 7.16-7.04 (m, 2H), 6.73 (ddd, *J* = 8.7, 2.9, 0.7 Hz, 1H), 6.63 (br d, *J* = 8.7 Hz, 1H), 6.53 (br dd, *J* = 2.8, 1.0 Hz, 1H), 6.51 (br dd, *J* = 2.1, 0.7 Hz, 1H), 5.37 (br dd, *J* = 11.2, 2.0 Hz, 1H), 4.75 (br dd, *J* = 12.2, 5.8 Hz, 1H), 3.99 (br s, 1H), 3.61 (s, 3H), 2.62 (ddd, *J* = 13.1, 5.9, 2.3 Hz, 1H), 2.43 (q, *J* = 12.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 152.5, 140.9, 139.7, 138.7, 136.2, 133.9, 130.7, 129.1, 128.3, 128.1, 126.3, 125.7, 123.4, 123.2, 122.5, 121.4, 120.0, 119.6, 116.1, 114.7, 114.2, 110.6, 101.8, 55.8, 52.8, 39.2, 38.7; ESI-MS: 427 [M^+ + Na].

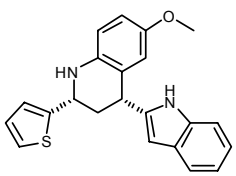
(2*R,4*R**)-4-(1*H*-Indol-2-yl)-6-methoxy-2-(naphthalen-2-yl)-1,2,3,4-tetrahydroquinoline (4g).**



Following the general procedure, the title compound was obtained as an orange solid in 96% yield and as a single diastereoisomer after chromatography on silica gel (*n*-hexane/EtOAc 80:20). ^{1}H NMR analysis of the crude mixture showed the presence of a single diastereoisomer. The ee of the product was determined by HPLC using a Chiralpak ADH column (*n*-hexane/*i*-PrOH 80:20, flow-rate 0.75 mL/min, t_{maj} = 35.5 min, t_{min} = 26.9 min, ee = 92%). $[\alpha]_D^{20}$ = +135 (c = 0.415 in acetone); ^{1}H NMR (acetone-d_6, 400 MHz) δ 10.07 (br s, 1H), 7.98 (br s, 1H), 7.92-7.86 (m, 3H), 7.66 (dd, *J* = 8.5, 1.7 Hz, 1H), 7.54-7.44 (m, 3H), 7.35-7.31 (m, 1H),

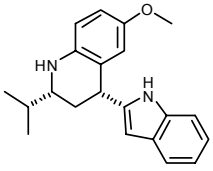
7.08-6.94 (m, 2H), 6.73 (d, *J* = 8.7 Hz, 1H), 6.65 (br ddd, *J* = 8.6, 2.9, 0.8 Hz, 1H), 6.45 (br dd, *J* = 2.1, 0.5 Hz, 1H), 6.40 (br dd, *J* = 2.8, 0.9 Hz, 1H), 5.08 (br s, 1H), 4.75 (dd, *J* = 10.8, 3.2 Hz, 1H), 4.66 (dd, *J* = 12.0, 6.0 Hz, 1H), 3.53 (s, 3H), 2.53-2.37 (m, 2H); ^{13}C NMR (acetone-d_6, 100 MHz) δ 152.9, 143.0, 142.7, 140.8, 137.8, 134.5, 134.0, 129.5, 128.9, 128.6, 128.5, 126.9, 126.5, 126.03, 126.0, 124.6, 121.6, 120.5, 119.8, 116.5, 115.3, 114.0, 111.7, 101.5, 57.9, 55.8, 40.7, 39.4; ESI-MS: 427 [M^+ + Na].

(2*R,4*R**)-4-(1*H*-Indol-2-yl)-6-methoxy-2-(thiophen-2-yl)-1,2,3,4-tetrahydroquinoline (4h).**



Following the general procedure, (6 h reaction time), the title compound was obtained as a pale yellow solid in 91% yield and as a single diastereoisomer after chromatography on silica gel (*n*-hexane/EtOAc 80:20). ^{1}H NMR analysis of the crude mixture showed a 95:5 diastereomeric ratio. The ee of the product was determined by HPLC using a Chiralpak ADH column (*n*-hexane/*i*-PrOH 80:20, flow-rate 0.75 mL/min, t_{maj} = 22.3 min, t_{min} = 24.2 min, ee >99%). $[\alpha]_D^{20}$ = +140 (c = 0.235 in acetone); ^{1}H NMR (acetone-d_6, 400 MHz) δ 10.07 (br s, 1H), 7.52-7.49 (m, 1H), 7.35-7.31 (m, 2H), 7.14-7.11 (m, 1H), 7.07-7.01 (m, 1H), 7.01-6.95 (m, 2H), 6.69 (br d, *J* = 8.7 Hz, 1H), 6.65-6.61 (m, 1H), 6.43 (br dd, *J* = 2.1, 0.7 Hz, 1H), 6.35 (br dd, *J* = 2.8, 1.1 Hz, 1H), 5.11 (br s, 1H), 4.95-4.89 (m, 1H), 4.62 (br t, *J* = 9.1 Hz, 1H), 3.51 (s, 3H), 2.44-2.37 (m, 2H); ^{13}C NMR (acetone-d_6, 100 MHz) δ 153.1, 149.5, 142.4, 140.2, 137.9, 129.4, 127.3, 124.8, 124.6, 124.5, 121.6, 120.5, 119.8, 116.7, 115.2, 114.0, 111.7, 101.6, 55.7, 53.6, 42.0, 39.2; ESI-MS: 383 [M^+ + Na].

(2*R,4*R**)-4-(1*H*-Indol-2-yl)-2-*iso*propyl-6-methoxy-1,2,3,4-tetrahydroquinoline (4i).**



Following the general procedure but forming the imine in situ mixing an equimolar (0.10 mmol) amount of 2-propionaldehyde and 4-methoxyaniline before adding the catalyst, the title compound was obtained as a white solid in 98% yield and as a single diastereoisomer, after chromatography on silica gel (*n*-hexane/EtOAc 90:10). ^{1}H NMR analysis of the crude mixture showed the presence of a single diastereoisomer. The ee of the product was determined by HPLC using a Chiralpak ADH column (*n*-hexane/*i*-PrOH 80:20, flow-rate 0.75 mL/min, t_{maj} = 12.5 min, t_{min} = 15.3 min, 96% ee). $[\alpha]_D^{20}$ = +32 (c = 0.58 in CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.89 (br s, 1H), 7.60-7.57 (m, 1H), 7.25-7.23 (m, 1H), 7.16-7.07 (m, 2H), 6.66 (ddd, *J* = 8.7, 3.0, 1.0 Hz, 1H), 6.58 (br d, *J* = 8.7 Hz, 1H), 6.49 (dd, *J* = 2.1, 0.7 Hz, 1H), 6.40 (dd, *J* = 2.8, 0.9 Hz, 1H), 4.42 (dd, *J* = 12.5, 5.9 Hz, 1H), 3.70 (br s, 1H), 3.57 (s, 3H), 3.24 (ddd, *J* = 11.2, 5.4, 2.2 Hz, 1H), 2.23 (ddd, *J* = 12.8, 5.8, 2.3 Hz, 1H), 1.92 (q, *J* = 12.2 Hz, 1H), 1.75 (oct, *J* = 6.6 Hz, 1H), 1.03 (d, *J* = 7.0 Hz, 3H), 1.00 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 152.2, 141.6, 139.5, 136.2, 128.3, 123.7, 121.3, 119.9, 119.6, 115.8, 114.5, 114.0, 110.7, 101.5, 57.8, 55.8, 38.2, 34.3, 32.7, 18.3, 18.0; ESI-MS: 343 [M^+ + Na].

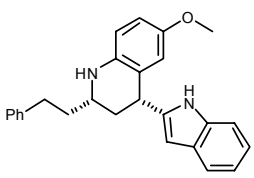
The relative configuration of the title compound was determined as 2,4-*cis* by NOESY1D NMR experiments as follows:

-Irradiation at the *iso*-propyl CH_3 (1.00 ppm) caused an enhancement of the signals at 1.75 ppm (*iso*-propyl CH), 1.92 and 2.23 ppm (H_{3a} and H_{3b}) and 3.24 ppm (H_2), whereas no NOE effect could be observed on the signal at 4.42 ppm (H_4).

-Irradiation at the *iso*-propyl CH (1.75 ppm) caused an enhancement of the signals at 1.00 and 1.03 ppm (*iso*-propyl CH_3), 1.92 and 2.23 ppm (H_{3a} and H_{3b}) and 3.24 ppm (H_2), whereas no NOE effect could be observed on the signal at 4.42 ppm (H_4).

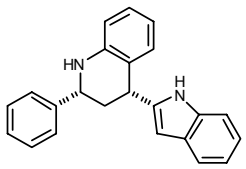
-Irradiation at H_4 (4.42 ppm) caused an enhancement of some aromatic signals, plus of the signals at 3.24 ppm (H_2), 2.23 and 1.92 ppm (H_{3a} and H_{3b}), whereas no NOE effect could be observed on the signal at 1.75 ppm (*iso*-propyl CH), nor at 1.00 and 1.03 ppm (*iso*-propyl CH_3).

(2*S,4*R**)-4-(1*H*-Indol-2-yl)-6-methoxy-2-phenethyl-1,2,3,4-tetrahydroquinoline (4j).**



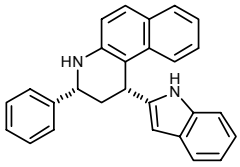
Following the general procedure, but forming the imine in situ mixing an equimolar (0.10 mmol) amount of phenethyl aldehyde and *p*-methoxyaniline before adding the catalyst, the title compound was obtained as a white solid in 95% yield and as a single diastereoisomer, after chromatography on silica gel (*n*-hexane/EtOAc 80:20). ^{1}H NMR analysis of the crude mixture showed the presence of a single diastereoisomer. The ee of the product was determined by HPLC using a Chiralpak ADH column (*n*-hexane/*i*-PrOH 80:20, flow-rate 0.75 mL/min, t_{maj} = 17.3 min, t_{min} = 18.0 min, >99% ee). $[\alpha]_D^{20}$ = +34 (c = 0.70 in CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.89 (br s, 1H), 7.61-7.58 (m, 1H), 7.36-7.29 (m, 2H), 7.26-7.21 (m, 4H), 7.17-7.09 (m, 2H), 6.67 (ddd, *J* = 8.6, 2.9, 0.6 Hz, 1H), 6.55 (d, *J* = 8.5 Hz, 1H), 6.49 (br d, *J* = 1.6 Hz, 1H), 6.42 (dd, *J* = 2.8, 0.9 Hz, 1H), 4.43 (dd, *J* = 12.2, 5.9 Hz, 1H), 3.58 (s, 3H), 3.57 (br s, 1H), 3.45 (ddt, J_d = 10.9, 2.2 Hz, J_t = 6.2 Hz 1H), 2.81-2.71 (m, 2H), 2.33 (ddd, *J* = 13.0, 5.8, 2.3 Hz, 1H), 1.98 (q, *J* = 12.1 Hz, 1H), 1.88 (q, *J* = 7.9 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 152.4, 141.5, 141.4, 138.9, 136.2, 128.5, 128.3, 126.1, 123.8, 121.3, 119.9, 119.6, 115.9, 114.6, 114.0, 110.7, 101.6, 55.7, 51.9, 38.2, 38.0, 37.7, 31.9; ESI-MS: 405 [M^+ + Na].

(2*R,4*R**)-4-(1*H*-Indol-2-yl)-2-phenyl-1,2,3,4-tetrahydroquinoline (4k).**



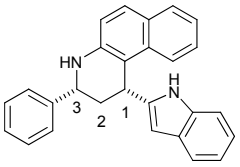
Following the general procedure, the title compound was obtained as a white solid in 93% yield and as a single diastereoisomer, after chromatography on silica gel (*n*-hexane/EtOAc 90:10). ^{1}H NMR analysis of the crude mixture showed a 95:5 diastereomeric ratio. The ee of the product was determined by HPLC using a Chiralpak ADH column (*n*-hexane/*i*-PrOH 90:10, flow-rate 0.75 mL/min, t_{maj} = 25.8 min, t_{min} = 23.2 min, 90% ee). $[\alpha]_D^{20}$ = +95 (c = 0.80 in CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.90 (br s, 1H), 7.58 (br d, *J* = 7.6 Hz, 1H), 7.52-7.44 (m, 2H), 7.43-7.29 (m, 3H), 7.29-7.22 (m, 1H), 7.17-6.98 (m, 3H), 6.85 (br d, *J* = 7.6 Hz, 1H), 6.69-6.58 (m, 2H), 6.51 (br d, *J* = 1.6 Hz, 1H), 4.67-4.59 (m, 2H), 4.22 (br s, 1H), 2.48-2.27 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 145.5, 143.6, 141.3, 136.5, 129.5, 129.0, 128.6, 128.2, 128.1, 126.8, 122.2, 121.6, 120.2, 119.9, 118.2, 114.8, 110.9, 102.1, 57.2, 40.5, 38.5; ESI-MS: 347 [M^+ + Na].

(1*R,3*R**)-1-(1*H*-Indol-2-yl)-3-phenyl-1,2,3,4-tetrahydrobenzo[*f*]quinoline (4l).**

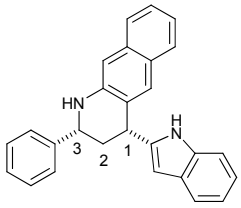


Following the general procedure, the title compound was obtained as a white solid in 98% yield, and as a single regio- and diastereoisomer after chromatography on silica gel (*n*-hexane/EtOAc 80:20). ^{1}H NMR analysis of the crude mixture showed the presence of a single regio- and diastereoisomer. The ee of the product was determined by HPLC using a Chiralpak ADH column (*n*-hexane/*i*-PrOH 80:20, flow-rate 0.75 mL/min, t_{maj} = 29.4 min, t_{min} = 13.8 min, ee >99%). $[\alpha]_D^{20}$ = +303 (c = 0.395 in THF); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.75-7.60 (m, 3H), 7.54-7.49 (m, 1H), 7.45 (br s, 1H), 7.43-7.38 (m, 2H), 7.35-7.12 (m, 5H), 7.06-6.98 (m, 3H), 6.95 (br d, *J* = 8.9 Hz, 1H), 6.41 (br d, *J* = 1.9 Hz, 1H), 5.05 (br t, *J* = 8.5 Hz, 1H), 4.50 (br dd, *J* = 10.1, 2.8 Hz, 1H), 4.26 (br s, 1H), 2.73 (ddd, *J* = 13.5, 7.7, 2.7 Hz, 1H), 2.52-2.41 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 144.7, 143.3, 142.8, 135.5, 133.4, 129.1, 128.8, 128.6, 128.5, 128.3, 127.6, 126.8, 126.6, 122.9, 122.2, 120.7, 119.6, 119.4, 118.5, 111.5, 110.6, 99.5, 55.0, 42.6, 34.8; ESI-MS: 397 [M^+ + Na].

The structure of the obtained regioisomer was assigned by NMR experiments as follows. A gHSQC experiment showed a correlation between the ^{1}H NMR signal of indolic H_3 (δ 6.41 ppm) and the ^{13}C NMR signal at 99.5 ppm, and between ^{1}H NMR signals of aliphatic CH's at 4.50 and 5.05 ppm with the ^{13}C NMR signals at 55.0 and 34.8 ppm, respectively. A gHMBC experiment showed a correlation between the H_3 signal of the indolic residue at 6.41 ppm with the 34.8 ppm ^{13}C NMR signal assignable to the tetrahydroquinolinic C_1 because it is the only aliphatic carbon that could present a correlation with that proton. Considering the previous observations deriving from the gHSQC experiment it was thus possible to assign the 5.05 ppm ^{1}H NMR signal to the tetrahydroquinolinic H_1, the 4.50 ppm ^{1}H NMR signal to H_3 of the same system and the 55.0 ppm ^{13}C NMR signal to C_3. The regioisomeric structure was determined at this point by the long range correlations of tetrahydroquinolinic C_1 (34.8 ppm) observable in the gHMBC spectrum; this carbon presented correlations with the aliphatic protons of the tetrahydroquinolinic ring and the indolic H_3 but not with other aromatic ones. The obtained regioisomer is thus presenting unambiguously the 1,2,3,4-tetrahydrobenzo[*f*]quinolinic system showed below, as the other possible 1,2,3,4-tetrahydrobenzo[*g*]quinolinic regioisomer should have presented a correlation of that carbon with an aromatic proton of the benzo[*g*]quinoline system.

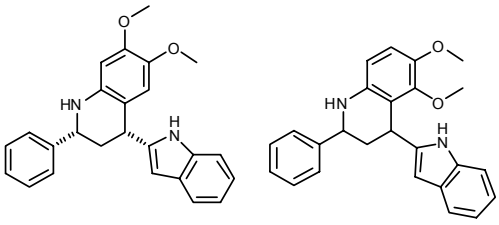


1,2,3,4-tetrahydrobenzo[f]quinoline



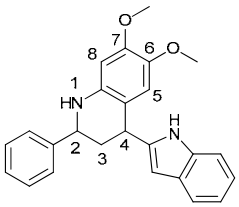
1,2,3,4-tetrahydrobenzo[g]quinoline

(2*R,4*R**)-4-(1*H*-Indol-2-yl)-6,7-dimethoxy-2-phenyl-1,2,3,4-tetrahydroquinoline and 4-(1*H*-indol-2-yl)-5,6-dimethoxy-2-phenyl-1,2,3,4-tetrahydroquinoline (4m).**

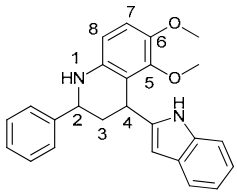


Following the general procedure, the title compound was obtained as a white solid in 95% overall yield and as single regioisomers, after chromatography on silica gel. The regioisomeric ratio (58:42 in favour of the 5,6-dimethoxy isomer), was determined by ^{1}H NMR analysis of the crude reaction mixture. The 5,6-dimethoxy regioisomer was obtained as a mixture of two diastereoisomers (d.r. = 58:42 determined by ^{1}H NMR analysis of the crude reaction mixture); the 6,7-dimethoxy isomer was obtained as a single diastereoisomer. Analytical data of the 6,7-dimethoxy regioisomer: the ee of this product was determined by HPLC using a Chiralpak ADH column (*n*-hexane/*i*-PrOH 80:20, flow-rate 0.75 mL/min, t_{maj} = 36.5 min, t_{min} = 32.2 min, ee = 90%). $[\alpha]_D^{20}$ = +108 (c = 0.355 in THF); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.91 (br s, 1H), 7.56 (br dd, *J* = 7.6, 0.6 Hz, 1H), 7.44 (br d, *J* = 7.3 Hz, 2H), 7.41-7.21 (m, 4H), 7.16-7.05 (m, 2H), 6.48 (br d, *J* = 1.9 Hz, 1H), 6.41 (br s, 1H), 6.24 (br s, 1H), 4.63-4.49 (m, 2H), 3.86 (br s, 1H), 3.82 (s, 3H), 3.57 (s, 3H), 2.39 (ddd, *J* = 13.3, 5.9, 2.6 Hz, 1H), 2.35-2.19 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 149.1, 143.3, 142.0, 141.4, 139.7, 136.2, 128.7, 128.4, 127.8, 126.6, 121.3, 119.9, 119.5, 113.3, 113.0, 110.6, 101.6, 99.5, 57.3, 56.7, 55.8, 40.8, 37.9; ESI-MS: 407 [M^+ + Na].

The structure of this regioisomer was determined by the analysis of its ^{1}H NMR spectrum. The spectrum showed two broad singlets at 6.41 and 6.24 ppm which could be assigned to the aromatic protons of the 1,2,3,4-tetrahydroquinolinic system. This system fits well with the signals given by two aromatic protons disposed in *para* position. For this reason, the structure of this regioisomer was assigned as the 6,7-dimethoxy structure showed in the figure below on the left.

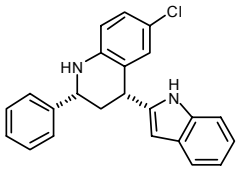


6,7-dimethoxy-1,2,3,4-tetrahydroquinoline



5,6-dimethoxy-1,2,3,4-tetrahydroquinoline

(2*R,4*R**)-6-Chloro-4-(1*H*-indol-2-yl)-2-phenyl-1,2,3,4-tetrahydroquinoline (4n).**



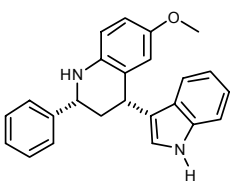
Following the general procedure, the title compound was obtained as a white solid in 82% yield and as a mixture of two diastereoisomers, after chromatography on silica gel (*n*-hexane/EtOAc 90:10). ^{1}H NMR analysis of the crude mixture showed a 95:5 diastereomeric ratio. The ee of the major diastereoisomer was determined by HPLC using a Chiralpak ADH column (*n*-hexane/*i*-PrOH 80:20, flow-rate 0.75 mL/min, major diastereomer: t_{maj} = 13.7 min, t_{min} = 12.5 min, 93% ee; minor diastereoisomer: not separated, t = 14.9 min). ^{1}H NMR (DMSO-d_6, 400 MHz) δ 11.24 (br s, 1H$_{min}$), 11.04 (br s, 1H$_{maj}$), 7.51-7.43 (m, 3H$_{maj}$), 7.42-6.34 (m, 2H$_{maj}$, 1H$_{min}$), 7.34-7.24 (m, 2H$_{maj}$, 5H$_{min}$), 7.04-6.97 (m, 1H$_{maj}$, 2H$_{min}$), 6.97-6.90 (m, 2H$_{maj}$), 6.86 (br s, 1H$_{min}$), 6.80 (br d, *J* =

2.5 Hz, $1H_{min}$), 6.72 (br s, $1H_{min}$), 6.71 (br d, J = 2.5 Hz, $1H_{min}$), 6.67 (d, J = 8.6 Hz, $1H_{maj}$), 6.63-6.62 (m, $1H_{min}$), 6.52-6.50 (m, $1H_{min}$), 6.43 (br d, J = 2.3 Hz, $1H_{maj}$), 6.38-6.34 (m, $2H_{maj}$), 4.59 (dd, J = 11.2, 2.6 Hz, $1H_{maj}$), 4.50 (dd, J = 12.2, 4.7 Hz, $1H_{maj}$), 4.37-4.30 (m, $1H_{min}$), 4.12-4.07 (m, $1H_{min}$), 2.32 (q, J = 12.0 Hz, $1H_{maj}$, $2H_{min}$), 2.21-2.13 (m, $1H_{maj}$); ^{13}C NMR (DMSO-d_6, 100 MHz) [signals of the major diastereoisomer] δ 145.2, 144.6, 141.4, 137.1, 129.1, 128.5, 128.1, 127.8, 127.4, 127.3, 124.6, 121.2, 120.1, 119.6, 119.4, 116.2, 111.7, 110.9, 56.3, 38.6, 38.0; ESI-MS: 359 [M^+ + Na].

General procedure for the organocatalytic, enantioselective Povarov reaction of aldimines 1 with 3-vinyl-1*H*-indole 3.

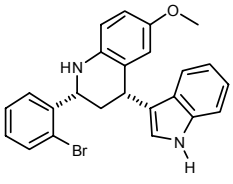
To a flame dried Schlenk tube equipped with a magnetic stirring bar, were sequentially added, under a nitrogen atmosphere, the aldimine **1** (0.10 mmol), anhydrous THF (1.0 mL) and the catalyst (*S*)-TRIP (7.5 mg, 0.010 mmol). After heating to 45 °C, a solution of 3-vinylindole **3** (21.4 mg, 0.15 mmol in 1.0 mL of anhydrous THF) was added via a syringe pump over 12 h. The reaction was stirred for an additional 1 h at the same temperature, then filtered through a plug of silica gel, and the plug washed with EtOAc (4x). After concentration of the solvents, the residue was analyzed by ^{1}H NMR spectroscopy to determine the diastereomeric ratio of the cycloadducts **5**. Finally, the residue was purified by chromatography on silica gel (*n*-hexane/EtOAc mixtures).

(2*R,4*S**)-4-(1*H*-Indol-3-yl)-6-methoxy-2-phenyl-1,2,3,4-tetrahydroquinoline (5a).**



Following the general procedure, the title compound was obtained as a white solid in 87% yield and as a mixture of two diastereoisomers, after chromatography on silica gel (*n*-hexane/EtOAc 80:20). ^{1}H NMR analysis of the crude mixture showed a 97:3 diastereomeric ratio. The ee of the the two diastereoisomers was determined by HPLC using a Chiralpak ADH column (*n*-hexane/*i*-PrOH 80:20, flow-rate 0.75 mL/min, major diastereoisomer: t_{maj} = 34.6 min, t_{min} = 21.1 min, ee_{maj} = 92%; minor diastereoisomer: t_{maj} = 16.3 min, t_{min} = 43.7 min, ee_{min} = 11%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.18 (br s, $1H_{min}$), 8.01 (br s, $1H_{maj}$), 7.64-7.61 (m, $1H_{min}$), 7.53-7.39 (m, $3H_{maj}$, $1H_{min}$), 7.39-7.21 (m, $4H_{maj}$, $7H_{min}$), 7.21-7.13 (m, $1H_{maj}$), 7.13-6.97 (m, $2H_{maj}$, $1H_{min}$), 6.86-6.53 (m, $3H_{maj}$, $2H_{min}$), 6.49-6.38 (m, $1H_{min}$), 4.65 (dd, *J* = 12.1, 6.0 Hz, $1H_{maj}$), 4.60 (dd, *J* = 11.0, 2.7 Hz, $1H_{maj}$), 4.52-4.45 (m, $1H_{min}$), 4.34-4.22 (m, $1H_{min}$), 3.99 (br s, $1H_{maj}$, $1H_{min}$), 3.68 (s, $3H_{min}$), 3.55 (s, $3H_{maj}$), 2.50-2.17 (m, $2H_{maj}$, $2H_{min}$); ^{13}C NMR ($CDCl_3$, 100 MHz) [signals of the major diasteroisomer] δ 152.2, 144.1, 139.6, 136.6, 128.6, 127.6, 126.2, 121.97, 121.90, 119.7, 119.4, 119.2, 115.4, 115.0, 113.0, 111.1, 57.8, 55.7, 40.4, 36.0; ESI-MS: 377 [M^+ + Na].

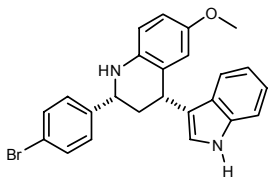
(2*R,4*S**)-2-(2-Bromophenyl)-4-(1*H*-indol-3-yl)-6-methoxy-1,2,3,4-tetrahydroquinoline (5b).**



Following the general procedure, the title compound was obtained as a pale yellow solid in 96% yield and as a single diastereoisomer after chromatography on silica gel (*n*-hexane/EtOAc 80:20). ^{1}H NMR of the crude mixture showed the presence of a single diastereoisomer. The ee of the product was determined by HPLC using a Chiralcel OD column (*n*-hexane/*i*-PrOH 90:10, flow-rate 1.0 mL/min, t_{maj} = 23.9 min, t_{min} = 18.2 min, ee = 90%); $[\alpha]_D^{20}$ = +167 (c = 0.385 in THF); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.02 (br s, 1H), 7.73 (br dd, *J* = 7.8, 1.7 Hz, 1H), 7.55 (br dd, *J* = 8.0, 1.2 Hz, 1H), 7.47 (br d, *J* = 7.8 Hz, 1H), 7.38-7.29 (m, 2H), 7.21-7.10 (m, 2H), 7.10-6.99 (m, 2H), 6.71-6.57 (m, 3H), 5.03 (dd, *J* = 11.4, 2.4 Hz, 1H), 4.69 (dd, *J* = 12.4, 5.8 Hz, 1H), 3.96 (br s, 1H), 3.56 (s, 3H), 2.50 (ddd, *J* = 13.1, 5.6, 2.4 Hz, 1H), 2.31-2.20 (m, 1H); ^{13}C NMR ($CDCl_3$, 100

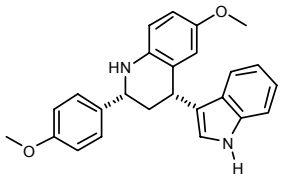
MHz) δ 152.4, 142.6, 139.1, 136.6, 132.8, 128.8, 127.9, 127.8, 126.6, 126.4, 123.1, 122.1, 121.9, 119.7, 119.3, 119.2, 115.7, 115.0, 113.1, 111.1, 56.2, 55.7, 38.8, 35.9; ESI-MS: 455 [M^+ + Na].

(2*R,4*S**)-2-(4-Bromophenyl)-4-(1*H*-indol-3-yl)-6-methoxy-1,2,3,4-tetrahydroquinoline (5c).**



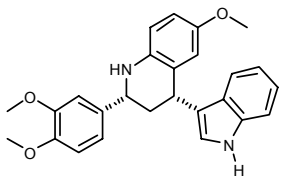
Following the general procedure, the title compound was obtained as a pale yellow solid in 86% yield and as a mixture of diastereoisomers after chromatography on silica gel (*n*-hexane/EtOAc 80:20). ^{1}H NMR analysis of the crude mixture showed a 96:4 diastereomeric ratio. The ee of the two diastereoisomers was determined by HPLC using a Chiralpak ADH column (*n*-hexane/*i*-PrOH 80:20, flow-rate 0.75 mL/min, major diastereoisomer: t_{maj} = 27.3 min, t_{min} = 25.1 min, ee_{maj} = 93%; minor diastereoisomer: t_{maj} = 63.5 min, t_{min} = 18.9 min, ee_{min} = 1%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.01 (br s, 1H$_{maj}$, 1H$_{min}$), 7.83-7.78 (m, 1H$_{min}$), 7.64-7.59 (m, 2H$_{min}$), 7.53-7.31 (m, 6H$_{maj}$), 7.25-7.09 (m, 1H$_{maj}$, 6H$_{min}$), 7.09-6.97 (m, 2H$_{maj}$, 1H$_{min}$), 6.78-6.75 (m, 1H$_{min}$), 6.73 (br dd, *J* = 8.6, 2.9 Hz, 1H$_{min}$), 6.65 (br ddd, *J* = 8.6, 2.8, 0.50 Hz, 1H$_{maj}$), 6.58 (d, *J* = 8.5 Hz, 1H$_{maj}$), 6.54 (br dd, *J* = 2.8, 0.96 Hz, 1H$_{maj}$), 4.63 (dd, *J* = 11.9, 6.1 Hz, 1H$_{maj}$), 4.56 (dd, *J* = 10.9, 3.0 Hz, 1H$_{maj}$), 4.48-4.43 (m, 1H$_{min}$), 4.26 (br dd, *J* = 10.2, 3.0 Hz, 1H$_{min}$), 3.88 (br s, 1H$_{maj}$, 1H$_{min}$), 3.68 (s, 3H$_{min}$), 3.55 (s, 3H$_{maj}$), 2.45-2.25 (m, 2H$_{maj}$, 2H$_{min}$); ^{13}C NMR ($CDCl_3$, 100 MHz) [signals of the major diasteroisomer] δ 160.4, 152.3, 143.2, 138.9, 136.6, 131.6, 128.4, 126.6, 126.1, 122.0, 121.2, 119.7, 119.3, 119.2, 115.4, 115.0, 113.0, 111.2, 57.2, 55.7, 40.8, 35.9; ESI-MS: 455 [M^+ + Na].

(2*R,4*S**)-4-(1*H*-Indol-3-yl)-6-methoxy-2-(4-methoxyphenyl)-1,2,3,4-tetrahydroquinoline (5d).**



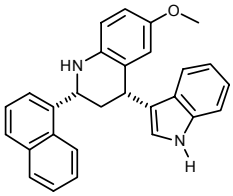
Following the general procedure, the title compound was obtained as an orange oil in 57% yield and as a mixture of two diastereoisomers after chromatography on silica gel (*n*-hexane/EtOAc 75:25). ^{1}H NMR analysis of the crude mixture showed a 95:5 diastereomeric ratio. The ee of the major diastereoisomer was determined by HPLC using a Chiralpak ADH column (*n*-hexane/*i*-PrOH 80:20, flow-rate 0.75 mL/min, major diastereoisomer: t_{maj} = 42.9 min, t_{min} = 33.5 min, ee_{maj} = 84%; minor diastereoisomer: not separated, t = 25.2 min). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.02 (br s, 1H$_{maj}$), 7.99 (br s, 1H$_{min}$), 7.63 (br d, *J* = 7.7 Hz, 1H$_{min}$), 7.47 (br d, *J* = 7.9 Hz, 1H$_{min}$), 7.43-7.32 (m, 3H$_{maj}$), 7.25-7.20 (m, 3H$_{min}$), 7.20-7.13 (m, 1H$_{maj}$), 7.13-7.09 (m, 1H$_{maj}$), 7.09-6.98 (m, 2H$_{maj}$), 6.96-6.86 (m, 2H$_{maj}$), 6.85-6.79 (m, 3H$_{min}$), 6.79-6.71 (m, 3H$_{min}$), 6.70-6.61 (m, 1H$_{maj}$, 1H$_{min}$), 6.61-6.53 (m, 2H$_{maj}$), 4.64 (dd, *J* = 12.0, 5.8 Hz, 1H$_{maj}$), 4.55 (dd, *J* = 11.2, 2.8 Hz, 1H$_{maj}$), 4.50-4.46 (m, 1H$_{min}$), 4.24 (br dd, *J* = 10.4, 2.9 Hz, 1H$_{min}$), 3.96 (br s, 1H$_{maj}$, 1H$_{min}$), 3.81 (s, 3H$_{maj}$), 3.78 (s, 3H$_{min}$), 3.75 (s, 3H$_{min}$), 3.55 (s, 3H$_{maj}$), 2.47-2.26 (m, 2H$_{maj}$, 2H$_{min}$); ^{13}C NMR ($CDCl_3$, 100 MHz) [signals of the major diasteroisomer] δ 159.0, 152.1, 139.3, 136.5, 136.2, 127.8, 126.7, 126.1, 121.9, 121.8, 119.7, 119.5, 119.2, 115.2, 115.0, 113.9, 113.0, 111.1, 57.2, 55.7, 55.3, 40.7, 36.0; ESI-MS: 407 [M^+ + Na].

(2*R,4*S**)-2-(3,4-Dimethoxyphenyl)-4-(1*H*-indol-3-yl)-6-methoxy-1,2,3,4-tetrahydroquinoline (5e).**



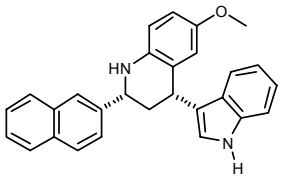
Following the general procedure, using 3.0 eq of 3-vinylindole, the title compound was obtained as a yellow oil in 86% yield and as a mixture of two diastereoisomers after chromatography on silica gel (*n*-hexane/EtOAc 70:30). ^{1}H NMR analysis of the crude mixture showed a 95:5 diastereomeric ratio. The ee of the major diastereoisomer was determined by HPLC using a Chiralpak ADH column (*n*-hexane/*i*-PrOH 80:20, flow-rate 0.75 mL/min, major diastereoisomer: t_{maj} = 80.1 min, t_{min} = 67.7 min, ee_{maj} = 91%; minor diastereoisomer: not separated, t = 36.6 min). ^{1}H NMR (acetone-d_6, 400 MHz) δ 10.06 (br s, 1H$_{maj}$, 1H$_{min}$), 8.01 (br d, *J* = 8.4 Hz, 1H$_{min}$), 7.81 (br s, 1H$_{min}$), 7.61-7.52 (m, 2H$_{min}$), 7.51-7.43 (m, 2H$_{min}$), 7.39 (br dd, *J* = 7.7, 1.2 Hz, 2H$_{maj}$), 7.33-7.29 (m, 1H$_{min}$), 7.26 (d, *J* = 2.4 Hz, 1H$_{maj}$), 7.22-7.17 (m, 1H$_{min}$), 7.12 (d, *J* = 2.0 Hz, 1H$_{maj}$), 7.10-6.99 (m, 2H$_{maj}$), 6.97-6.88 (m, 2H$_{maj}$), 6.82 (d, *J* = 8.2 Hz, 1H$_{min}$), 6.76 (br dd, *J* = 8.3, 2.2 Hz, 1H$_{min}$), 6.74-6.65 (m, 1H$_{maj}$, 1H$_{min}$), 6.59 (br ddd, *J* = 8.6, 2.9, 0.7 Hz, 1H$_{maj}$), 6.44 (br dd, *J* = 2.9, 1.0 Hz, 1H$_{maj}$), 4.89 (br s, 1H$_{min}$), 4.79 (br s, 1H$_{maj}$), 4.62 (dd, *J* = 12.1, 5.7 Hz, 1H$_{maj}$), 4.55 (br dd, *J* = 10.8, 2.3 Hz, 1H$_{maj}$), 4.43-4.38 (m, 1H$_{min}$), 4.31-4.25 (m, 1H$_{min}$), 3.80 (s, 3H$_{maj}$), 3.78 (s, 3H$_{maj}$), 3.75 (s, 3H$_{min}$), 3.73 (s, 3H$_{min}$), 3.60 (s, 3H$_{min}$), 3.46 (s, 3H$_{maj}$), 2.60 (br s, 1H$_{min}$), 2.45-2.34 (m, 1H$_{maj}$), 2.29 (br s, 1H$_{min}$), 2.25 (ddd, *J* = 12.9, 5.8, 2.7 Hz, 1H$_{maj}$); ^{13}C NMR (acetone-d_6, 100 MHz) [signals of the major diasteroisomer] δ 152.0, 149.8, 149.0, 140.3, 137.9, 137.5, 127.0, 126.1, 123.0, 121.4, 119.8, 118.9, 118.8, 118.6, 115.4, 115.0, 112.5, 112.1, 111.7, 110.8, 57.4, 55.5, 55.4, 55.0, 41.4, 36.5; ESI-MS: 437 [M^+ + Na].

(2*R,4*S**)-4-(1*H*-Indol-3-yl)-6-methoxy-2-(naphthalen-1-yl)-1,2,3,4-tetrahydroquinoline (5f).**



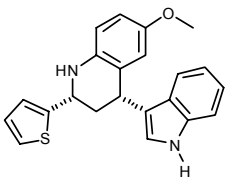
Following the general procedure, the title compound was obtained as an orange oil in 84% yield and as a single diastereoisomer after chromatography on silica gel (*n*-hexane/EtOAc 80:20). ^{1}H NMR of the crude mixture showed the presence of a single diastereoisomer. The ee of the product was determined by HPLC using a Chiralpak ADH column (*n*-hexane/*i*-PrOH 80:20, flow-rate 0.75 mL/min, t_{maj} = 29.1 min, t_{min} = 19.4 min, ee = 87%); $[\alpha]_D^{20}$ = +176 (c = 0.455 in THF); ^{1}H NMR (acetone-d_6, 400 MHz) δ 10.04 (br s, 1H), 8.38 (d, *J* = 8.5 Hz, 1H), 7.94-7.88 (m, 2H), 7.82 (br d, *J* = 8.4 Hz, 1H), 7.60-7.47 (m, 3H), 7.43 (br d, *J* = 8.1 Hz, 1H), 7.40-7.37 (m, 1H), 7.30 (d, *J* = 2.4 Hz, 1H), 7.08-7.03 (m, 1H), 6.97-6.90 (m, 1H), 6.79 (d, *J* = 8.6 Hz, 1H), 6.64 (br ddd, *J* = 8.7, 2.9, 0.9 Hz, 1H), 6.50 (br dd, *J* = 3.0, 0.9 Hz, 1H), 5.47 (br t, *J* = 6.7 Hz, 1H), 4.97 (br s, 1H), 4.83 (br t, *J* = 8.8 Hz, 1H), 3.49 (s, 3H), 2.56-2.47 (m, 2H); ^{13}C NMR (acetone-d_6, 100 MHz) δ 152.9, 141.3, 141.1, 138.1, 134.9, 131.9, 129.7, 128.3, 127.6, 127.2, 126.8, 126.6, 126.3, 124.1, 123.9, 123.7, 122.0, 120.4, 119.5, 119.3, 116.4, 115.8, 113.2, 112.3, 55.6, 55.0, 40.9, 37.1; ESI-MS: 427 [M^+ + Na].

(2*R,4*S**)-4-(1*H*-Indol-3-yl)-6-methoxy-2-(naphthalen-2-yl)-1,2,3,4-tetrahydroquinoline (5g).**



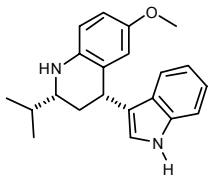
Following the general procedure, the title compound was obtained as an orange oil in 53% yield and as a mixture of two diastereoisomers after chromatography on silica gel (*n*-hexane/EtOAc 75:25). ^{1}H NMR analysis of the crude mixture showed a 98:2 diastereomeric ratio. The ee of the two diastereoisomers was determined by HPLC using a Chiralpak ADH column (*n*-hexane/*i*-PrOH 80:20, flow-rate 0.75 mL/min, major diastereoisomer: t_{maj} = 48.7 min, t_{min} = 32.6 min, ee_{maj} = 90%; minor diastereoisomer: t_{maj} = 24.4 min, t_{min} = 73.0 min, ee_{min} = 7%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.00 (br s, 1H$_{maj}$, 1H$_{min}$), 7.93 (br s, 1H$_{maj}$), 7.87-7.73 (m, 3H$_{maj}$, 4H$_{min}$), 7.72-7.55 (m, 1H$_{maj}$, 2H$_{min}$), 7.54-7.39 (m, 3H$_{maj}$, 3H$_{min}$), 7.36 (br dt, *J* = 8.1, 0.8 Hz, 1H$_{maj}$), 7.22-7.13 (m, 1H$_{maj}$, 1H$_{min}$), 7.13-7.02 (m, 2H$_{maj}$, 1H$_{min}$), 7.00-6.97 (m, 1H$_{min}$), 6.78-6.70 (m, 1H$_{min}$), 6.70-6.59 (m, 2H$_{maj}$, 2H$_{min}$), 6.57 (br dd, *J* = 2.7, 0.7 Hz, 1H$_{maj}$), 4.77 (dd, *J* = 11.0, 2.8 Hz, 1H$_{maj}$), 4.70 (dd, *J* = 12.1, 5.9 Hz, 1H$_{maj}$), 4.54-4.49 (m, 1H$_{min}$), 4.49-4.44 (m, 1H$_{min}$), 4.00 (br s, 1H$_{maj}$, 1H$_{min}$), 3.69 (s, 3H$_{min}$), 3.56 (s, 3H$_{maj}$), 2.51 (q, *J* = 11.5 Hz, 1H$_{maj}$), 2.46-2.33 (m, 1H$_{maj}$, 2H$_{min}$); ^{13}C NMR ($CDCl_3$, 100 MHz) [signals of the major diasteroisomer] δ 152.3, 143.5, 141.5, 139.1, 136.5, 133.4, 133.0, 128.3, 127.8, 127.6, 126.7, 126.1, 125.7, 125.2, 125.0, 122.0, 121.9, 119.7, 119.4, 119.3, 115.4, 115.0, 113.0, 111.1, 57.9, 55.7, 40.6, 36.1; ESI-MS: 427 [M^+ + Na].

(2*R,4*S**)-4-(1*H*-Indol-3-yl)-6-methoxy-2-(thiophen-2-yl)-1,2,3,4-tetrahydroquinoline (5h).**



Following the general procedure, using 3.0 eq of 3-vinylindole, the title compound was obtained as an orange oil in 63% yield and as a mixture of two diastereoisomers after chromatography on silica gel (*n*-hexane/EtOAc 80:20). ^{1}H NMR analysis of the crude mixture showed a 90:10 diastereomeric ratio. The ee of the two diastereoisomers was determined by HPLC using a Chiralpak ADH column (*n*-hexane/*i*-PrOH 80:20, flow-rate 0.75 mL/min, major diastereoisomer: t_{maj} = 46.2 min, t_{min} = 25.3 min, ee_{maj} = 97%; minor diastereoisomer: t_{maj} = 20.1 min, t_{min} = 67.2 min, ee_{min} = 12%). ^{1}H NMR (acetone-d_6, 400 MHz) δ 10.06 (br s, 1H$_{maj}$, 1H$_{min}$), 7.59-7.53 (m, 2H$_{min}$), 7.43-7.25 (m, 4H$_{maj}$, 1H$_{min}$), 7.16-6.84 (m, 4H$_{maj}$, 5H$_{min}$), 6.77-6.64 (m, 1H$_{maj}$, 2H$_{min}$), 6.63-6.55 (m, 1H$_{maj}$, 1H$_{min}$), 6.43 (br d, *J* = 2.6 Hz, 1H$_{maj}$), 5.18 (br s, 1H$_{min}$), 5.05 (br s, 1H$_{maj}$), 4.95 (br dd, *J* = 10.9, 2.4 Hz, 1H$_{maj}$), 4.71-4.59 (m, 1H$_{maj}$, 1H$_{min}$), 4.44 (br t, *J* = 4.8 Hz, 1H$_{min}$), 3.60 (s, 3H$_{min}$), 3.47 (s, 3H$_{maj}$), 2.52-2.29 (m, 2H$_{maj}$, 2H$_{min}$); ^{13}C NMR (acetone-d_6, 100 MHz) [signals of the major diasteroisomer] δ 152.4, 149.3, 139.6, 137.5, 126.8, 126.5, 126.2, 123.9, 123.6, 123.1, 121.4, 119.7, 118.7, 118.5, 115.7, 114.9, 112.5, 111.7, 54.9, 53.4, 42.5, 36.1; ESI-MS: 383 [M^+ + Na].

(2*R,4*R**)-4-(1*H*-Indol-3-yl)-6-methoxy-2-(2-methyl)ethyl-1,2,3,4-tetrahydroquinoline (5i).**



Following the general procedure, but using anhydrous EtOAc as the solvent and forming the imine in situ mixing an equimolar (0.10 mmol) amount of 2-propionaldehyde and 4-methoxyaniline before adding the catalyst, and adding the solution of 3-vinylindole **3** all at once, the title compound was obtained after 3 h as a

pale pink solid in 90% yield after chromatography on silica gel (*n*-hexane/EtOAc 80:20).The ^{1}H NMR analysis of the crude mixture showed a 98:2 diastereomeric ratio. The ee was determined by HPLC using a Chiralpak ADH column (*n*-hexane/*i*-PrOH 90:10, flow-rate 0,75 mL/min, t_{maj} = 35.4 min, t_{min} = 24.2 min, ee = 73%). ^{1}H NMR ($CDCl_3$, 400 MHz) [signals of the major diastereoisomer] δ 8.05 (br s , 1H), 7.42 (d, *J* = 8.0 Hz, 1H), 7.36 (d, *J* = 8.1 Hz, 1H), 7.20-7.14 (m, 1H), 7.07-7.00 (m, 2H), 6.58 (br s, 2H), 6.65-6.49 (m, 1H), 4.45 (dd, *J* = 12.2, 5.4, 1H), 3.53 (s, 3H), 3.28 (ddd, *J* = 11.2, 5.4, 2.3 Hz, 1H), 2.19 (ddd, *J* = 12.2, 5.4, 2.3 Hz), 2.03 (q, *J* = 12.2 Hz, 1H), 1.81-1.72 (m, 1H), 1.02 (d, *J* = 6.8 Hz, 3H), 0.99 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) [signals of the major diastereoisomer] δ 151.9, 139.4, 136.6, 126.7, 126.6, 122.0, 121.9, 119.9, 119.8, 119.2, 115.2, 115.0, 112.9, 111.1, 58.3, 55.7, 35.7, 34.5, 32.9, 18.5, 18.2; ESI-MS: 343 [M^+ + Na].

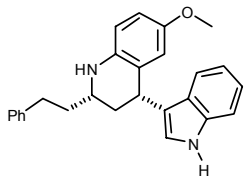
The relative configuration of the title compound was determined as 2,4-*cis* by NOESY1D NMR experiments as follows:

-Irradiation at the *iso*-propyl CH_3 (1.00 ppm) caused an enhancement of the signals at 1.81-1.72 ppm (*iso*-propyl CH), 2.03 and 2.19 ppm (H_{3a} and H_{3b}) and 3.28 ppm (H_2), whereas no NOE effect could be observed on the signal at 4.45 ppm (H_4).

-Irradiation at the *iso*-propyl CH (1.74 ppm) caused an enhancement of the signals at 0.99 and 1.02 ppm (*iso*-propyl CH_3), 2.03 and 2.19 ppm (H_{3a} and H_{3b}) and 3.28 ppm (H_2), whereas no NOE effect could be observed on the signal at 4.45 ppm (H_4).

-Irradiation at H_4 (4.45 ppm) caused an enhancement of some aromatic signals, plus of the signals at 3.28 ppm (H_2), 2.19 and 2.03 ppm (H_{3a} and H_{3b}), whereas no NOE effect could be observed on the signal at 1.74 ppm (*iso*-propyl CH), nor at 0.99 and 1.02 ppm (*iso*-propyl CH_3).

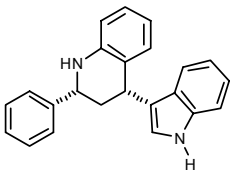
(2*S,4*R**)-4-(1*H*-Indol-3-yl)-6-methoxy-2-(2-phenyl)ethyl-1,2,3,4-tetrahydroquinoline (5j).**



Following the general procedure, but using anhydrous EtOAc as the solvent and forming the imine in situ, to a flame dried Schlenk tube were sequentially added, under a nitrogen atmosphere, 4-methoxyaniline (0.10 mmol), anhydrous EtOAc (1.0 mL) and the catalyst (*S*)-TRIP (7.5 mg, 0.010 mmol). At room temperature a solution of 3-vinylindole **3** (21.4 mg, 0.15 mmol in 0.50 mL of anhydrous EtOAc) and a solution of phenethyl aldehyde (0.020 mL, 0.15 mmol in 0.50 mL of anhydrous EtOAc) were added independently via a syringe pump over 12 h. ^{1}H NMR analysis of the crude mixture showed the presence of a single diastereoisomer The title compound was obtained as a pale yellow oil in 90% yield after chromatography on silica gel (*n*-hexane/EtOAc 80:20). The ee was determined by HPLC using a Chiralpak ADH column (*n*-hexane/*i*-PrOH 90:10, flow-rate 0,75 mL/min, t_{maj} = 50.2 min, t_{min} = 41.9 min, ee = 89%). $[\alpha]_D^{20}$ = -8 (c = 1.15 in $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.05 (br s , 1H), 7.41 (d, *J* = 7.8 Hz, 1H), 7.35 (d, *J* = 8.0 Hz, 1H), 7.32-7.28 (m, 2H), 7.23-7.19 (m, 3H), 7.19-7.15 (m, 1H), 7.05-7.01 (m, 2H), 6.61 (dd, *J* = 8.6, 3.0 Hz 1H), 6.53 (d, *J* = 8.6 Hz, 1H), 6.49 (br d, *J* = 3.0 Hz, 1H), 4.46 (dd, *J* = 12.2, 5.6 Hz, 1H), 3.52 (s, 3H), 3.52-3.43 (m, 1H), 2.81-2.70 (m, 2H), 2.27 (dddd, *J* = 12.6, 6.4, 5.6, 2.4 Hz, 1H), 2.09 (dd, *J* = 12.3, 11.6 Hz, 1H), 1.93-1.82 (m,

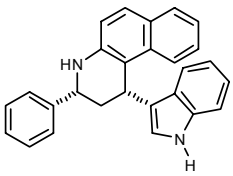
2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 152.1, 141.8, 138.9, 136.6, 128.5, 128.4, 126.6, 126.0, 122.0, 121.9, 119.8, 119.7, 119.2, 115.4, 115.0, 112.9, 111.2, 55.7, 52.3, 38.5, 38.0, 35.5, 32.1, ESI-MS: 405 [M^+ + Na].

(2*R,4*S**)-4-(1*H*-Indol-3-yl)-2-phenyl-1,2,3,4-tetrahydroquinoline (5k).**



Following the general procedure, the title compound was obtained as a white solid in 55% yield and as a mixture of two diastereoisomers after chromatography on silica gel (*n*-hexane/EtOAc 80:20). ^{1}H NMR analysis of the crude mixture showed a 93:7 diastereomeric ratio. The ee of the two diastereoisomers was determined by HPLC using a Chiralpak ADH column (*n*-hexane/*i*-PrOH 80:20, flow-rate 0.75 mL/min, major diastereoisomer: t_{maj} = 21.4 min, t_{min} = 16.2 min, ee_{maj} = 97%; minor diastereoisomer: t_{maj} = 13.3 min, t_{min} = 52.2 min, ee_{min} = 3%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.98 (br s, 1H$_{maj}$), 7.94 (br s, 1H$_{min}$), 7.64-7.41 (m, 3H$_{maj}$, 3H$_{min}$), 7.41-7.31 (m, 3H$_{maj}$, 2H$_{min}$), 7.31-7.25 (m, 1H$_{maj}$, 2H$_{min}$), 7.24-7.13 (m, 1H$_{maj}$, 2H$_{min}$), 7.13-7.06 (m, 1H$_{maj}$, 1H$_{min}$), 7.06-6.96 (m, 2H$_{maj}$), 6.88 (br d, *J* = 7.7 Hz, 1H$_{maj}$), 6.75-6.68 (m, 1H$_{min}$), 6.68-6.62 (m, 1H$_{min}$), 6.60 (br d, *J* = 8.0 Hz, 1H$_{maj}$), 6.58-6.56 (m, 1H$_{min}$), 6.53 (br t, *J* = 7.5 Hz, 1H$_{maj}$), 4.69-4.61 (m, 2H$_{maj}$), 4.48-4.45 (m, 1H$_{min}$), 4.31 (br dd, *J* = 10.2, 3.0 Hz, 1H$_{min}$), 4.20 (br s, 1H$_{maj}$, 1H$_{min}$), 2.45-2.30 (m, 2H$_{maj}$, 2H$_{min}$); ^{13}C NMR ($CDCl_3$, 100 MHz) [signals of the major diasteroisomer] δ 136.5, 129.2, 128.9, 128.6, 128.5, 128.2, 127.7, 127.1, 126.8, 126.7, 122.0, 121.9, 119.8, 119.4, 119.3, 117.8, 114.3, 111.1, 57.6, 40.5, 35.8; ESI-MS: 347 [M^+ + Na].

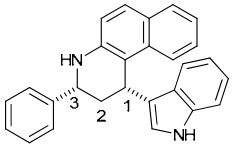
(1*S,3*R**)-1-(1*H*-Indol-3-yl)-3-phenyl-1,2,3,4-tetrahydrobenzo[*f*]quinoline (5l).**



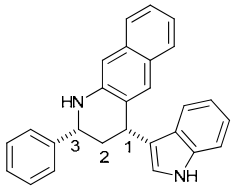
Following the general procedure, the title compound was obtained as an orange solid in 98% yield and as a single regio- and diastereoisomer, after chromatography on silica gel (*n*-hexane/EtOAc 85:15). ^{1}H NMR of the crude mixture showed the presence of a single regio- and diastereo-isomer. The ee of the product was determined by HPLC using a Chiralpak ADH column (*n*-hexane/*i*-PrOH 80:20, flow-rate 0.75 mL/min, t_{maj} = 32.3 min, t_{min} = 21.6 min, ee = 98%). $[\alpha]_D^{20}$ = +220 (c = 0.30 in THF); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.73-7.60 (m, 4H), 7.54 (br dd, *J* = 8.2, 0.9 Hz, 1H), 7.42-7.37 (m, 2H), 7.31-7.18 (m, 4H), 7.18-7.04 (m, 4H), 6.96 (d, *J* = 8.8 Hz, 1H), 6.38 (d, *J* = 2.4 Hz, 1H), 5.09 (t, *J* = 8.5 Hz, 1H), 4.47 (dd, *J* = 10.5, 2.8 Hz, 1H), 4.26 (br s, 1H), 2.88 (ddd, *J* = 13.5, 7.8, 2.7 Hz, 1H), 2.52-2.40 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 136.6, 133.5, 129.1, 128.6, 128.4, 128.3, 127.5, 126.9, 126.5, 125.8, 124.5, 122.1, 122.0, 121.94, 121.91, 119.3, 119.2, 118.8, 111.3, 56.6, 42.8, 32.3; ESI-MS: 397 [M^+ + Na].

The structure of obtained regioisomer was assigned by NMR experiments as follows. A gHSQC experiment showed a correlation between the ^{1}H NMR signal of indolic H_2 (δ 6.38 ppm) and ^{13}C NMR signal of its carbon at 122.1 ppm and between ^{1}H NMR signals of aliphatic CH at 4.47 and 5.09 ppm with the ^{13}C NMR signals at 56.6 and 32.3 ppm, respectively. A gHMBC experiment showed a correlation between the H_2 signal of the indolic residue at 6.38 ppm with the 32.3 ppm ^{13}C NMR signal, thus assignable to the tetrahydroquinolinic C_1 because it was the only aliphatic carbon that could present a correlation with that

proton. Considering the previous observations deriving from the gHSQC experiment it was thus possible to assign the 5.09 ppm ^{1}H NMR signal to the tetrahydroquinolinic H_1, the 4.47 ppm ^{1}H NMR signal to H_3 of the same system and the 56.6 ppm ^{13}C NMR signal to C_3. The regioisomeric structure was determined at this point by the long range correlations of the tetrahydrobenzoquinolinic C_1 observable in the gHMBC spectrum; this carbon presented correlations with the aliphatic protons of the tetrahydroquinolinic ring and the indolic H_2 but not with other aromatic ones. The obtained regioisomer is thus presenting unambiguously the 1,2,3,4-tetrahydrobenzo[*f*]quinolinic system showed below, as the other possible 1,2,3,4-tetrahydrobenzo[*g*]quinolinic regioisomer should have presented a correlation of that carbon with an aromatic proton of the benzo[*g*]quinolinic system.

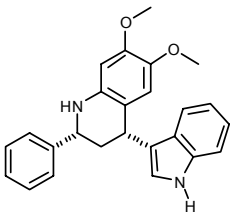


1,2,3,4-tetrahydrobenzo[*f*]quinoline



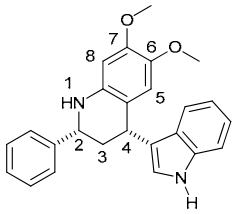
1,2,3,4-tetrahydrobenzo[*g*]quinoline

(2*R,4*S**)-4-(1*H*-Indol-3-yl)-6,7-dimethoxy-2-phenyl-1,2,3,4-tetrahydroquinoline (5m).**

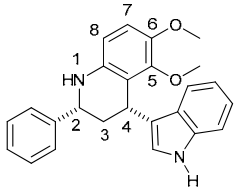


Following the general procedure, the title compound was obtained as a yellow solid in 96% yield and as a single regio- and diastereoisomer after chromatography on silica gel (*n*-hexane/EtOAc 80:20). ^{1}H NMR of the crude mixture showed the presence of a single regio- and diastereo-isomer. The ee of the product was determined by HPLC using a Chiralpak ADH column (*n*-hexane/*i*-PrOH 80:20, flow-rate 0.75 mL/min, t_{maj} = 53.1 min, t_{min} = 26.4 min, ee = 98%). $[\alpha]_D^{20}$ = +64 (c = 0.455 in THF); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.06 (br s, 1H), 7.50-7.45 (m, 3H), 7.39-7.32 (m, 3H), 7.32-7.26 (m, 1H), 7.20-7.13 (m, 1H), 7.09-7.01 (m, 2H), 6.55 (br d, *J* = 0.7 Hz, 1H), 6.24 (s, 1H), 4.69-4.55 (m, 2H), 3.83 (s, 3H), 3.58 (br s, 1H), 3.52 (s, 3H), 2.43-2.32 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.4, 143.9, 141.6, 139.2, 136.5, 128.5, 127.5, 126.6, 121.9, 121.8, 119.7, 119.6, 119.2, 116.0, 113.9, 111.1, 99.3, 57.7, 56.7, 55.8, 41.1, 35.4; ESI-MS: 407 [M^+ + Na].

The structure of the obtained regioisomer was determined by the analysis of its ^{1}H NMR spectrum. The spectrum showed a broad doublet (*J* = 0.7 Hz) at 6.55 ppm which could be assigned to an aromatic proton of the 1,2,3,4-tetrahydroquinolinic system. As this proton shows a characteristic *J* value for two protons disposed in *para* position, the obtained regioisomer could be assigned as the 6,7-dimethoxy structure showed in the figure below on the left.

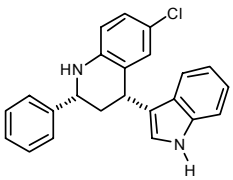


6,7-Dimethoxy-1,2,3,4-tetrahydroquinoline



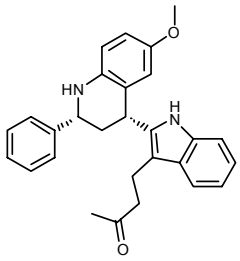
5,6-Dimethoxy-1,2,3,4-tetrahydroquinoline

(2*R,4*S**)-6-Chloro-4-(1*H*-indol-3-yl)-2-phenyl-1,2,3,4-tetrahydroquinoline (5n).**



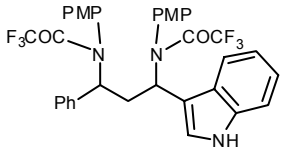
Following the general procedure, the title compound was obtained as a yellow solid in 44% yield and as a mixture of two diastereoisomers after chromatography on silica gel (*n*-hexane/EtOAc 85:15). ^{1}H NMR analysis of the crude mixture showed a 90:10 diastereomeric ratio. The ee of the two diastereoisomers was determined by HPLC using a Chiralpak ADH column (*n*-hexane/*i*-PrOH 80:20, flow-rate 0.75 mL/min, major diastereoisomer: t_{maj} = 18.1 min, t_{min} = 15.7 min, ee_{maj} = 98%; minor diastereoisomer: t_{maj} = 14.7 min, t_{min} = 33.1 min, ee_{min} = 22%). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.03 (br s, $1H_{maj}$, $1H_{min}$), 7.85-7.62 (m, $1H_{min}$), 7.61-7.50 (m, $5H_{min}$), 7.50-7.23 (m, $7H_{maj}$, $5H_{min}$), 7.23-7.14 (m, $1H_{maj}$), 7.14-6.98 (m, $2H_{maj}$, $1H_{min}$), 6.96 (br ddd, *J* = 8.4, 2.4, 0.8 Hz, $1H_{maj}$), 6.85 (br dd, *J* = 2.4, 1.1 Hz, $1H_{maj}$), 6.63-6.55 (m, $1H_{min}$), 6.53 (br d, *J* = 8.5 Hz, $1H_{maj}$), 4.64 (dd, *J* = 11.3, 3.0 Hz, $1H_{maj}$), 4.59 (dd, *J* = 12.2, 5.6 Hz, $1H_{maj}$), 4.44-4.41 (m, $1H_{min}$), 4.31 (br dd, *J* = 10.1, 3.1 Hz, $1H_{min}$), 4.12 (br s, $1H_{maj}$, $1H_{min}$), 2.49-2.27 (m, $2H_{maj}$, $2H_{min}$); ^{13}C NMR ($CDCl_3$, 150 MHz) [signals of the major diasteroisomer] δ 143.6, 143.5, 136.5, 128.7, 127.7, 126.9, 126.5, 126.4, 126.2, 122.1, 122.0, 119.6, 118.5, 115.2, 111.2, 57.4, 40.1, 35.7; ESI-MS: 381 [M^+ + Na].

4-(2-((2*R*,4*R*)-6-Methoxy-2-phenyl-1,2,3,4-tetrahydroquinolin-4-yl)-1*H*-indol-3-yl)butan-2-one (6).



To a flame dried Schlenk tube equipped with a magnetic stirring bar, 3 Å spherical-shaped molecular sieves (200 mg) were added under a nitrogen atmosphere. The molecular sieves were then thermally activated under vacuum for 10 minutes and then allowed to cool to r.t.. Aldimine **1a** (21.1 mg, 0.10 mmol) was then added under a nitrogen atmosphere, followed by anhydrous toluene (2.0 mL) and the catalyst (*S*)-TRIP (7.5 mg, 0.010 mmol). After heating to 45 °C, 2-vinylindole **2** (17.2 mg, 0.12 mmol) was added in one portion. The mixture was then stirred at the same temperature under a nitrogen atmosphere for 3 h, then $Sc(OTf)_3$ (4.9 mg, 0.010 mmol) was added, followed by methyl vinylketone (21 μL, 0.25 mmol). After 40 h stirring at 45 °C, the mixture was directly purified by chromatography on silica gel (*n*-hexane/Et_2O 7:3),giving the title compound in 46% yield as a white solid. The ee of the product was determined by HPLC using a Chiralpak ADH column (*n*-hexane/*i*-PrOH 80:20, flow-rate 0.75 mL/min, t_{maj} = 24.2 min, t_{min} = 27.3 min, 98% ee). $[\alpha]_D^{20}$ = +68 (c = 0.60 in CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.68 (br s, 1H), 7.52 (br d, *J* = 7.7 Hz, 1H), 7.48-7.44 (m, 2H), 7.39-7.34 (m, 2H), 7.32-7.28 (m, 1H), 7.23-7.19 (m, 1H), 7.15-7.06 (m, 2H), 6.68 (dd, *J* = 8.7, 2.8 Hz, 1H), 6.55 (d, *J* = 9.0 Hz, 1H), 6.30 (dd, *J* = 2.8, 0.8 Hz, 1H), 4.77 (dd, *J* = 11.6, 6.0 Hz, 1H), 4.57 (dd, *J* = 10.8, 2.7 Hz, 1H), 3.91 (br s, 1H), 3.59 (s, 3H), 3.11-3.05 (m, 2H), 2.87-2.81 (m, 2H), 2.29 (ddd, *J* = 13.1, 6.3, 2.8 Hz, 1H), 2.25-2.14 (m, 1H), 2.12 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 208.6, 152.4, 143.5, 139.9, 136.8, 135.8, 128.9, 127.9, 127.8, 126.7, 123.2, 121.6, 119.1, 118.1, 115.8, 114.9, 113.8, 112.4, 110.8, 57.3, 55.8, 44.7, 40.0, 35.8, 30.2, 18.3; ESI-MS: 447 [M^+ + Na].

***N*,*N*'-(1-(1*H*-indol-3-yl)-3-phenylpropane-1,3-diyl)bis(2,2,2-trifluoro-*N*-(4-methoxyphenyl)acetamide) (7).**

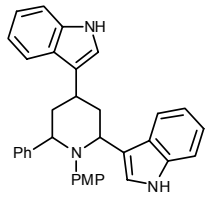


To a flame dried Schlenk tube equipped with a magnetic stirring bar, were sequentially added, under a nitrogen atmosphere, the aldimine **1a** (21.1 mg, 0.10 mmol), 4-methoxyaniline (24.6 mg, 0.20 mmol), anhydrous THF (0.40 mL) and the catalyst (*S*)-TRIP (7.5 mg, 0.010 mmol). After cooling to 0 °C, 3-vinylindole **3** (17.2 mg, 0.12 mmol) was added in one portion. After stirring the reaction mixture for 6 h at 0 °C, CH_2Cl_2 (1.0 mL) was added, followed by Et_2N (41.7 μL, 0.30 mmol) and TFAA (139.1 μL, 1.0 mmol). The mixture was then allowed to warm to r.t. with stirring (ca 20 min), then poured onto sat. $NaHCO_3$, and extracted with Et_2O (3x). The combined organic phases were dried over $MgSO_4$, filtered and evaporated. ^{1}H NMR analysis of the crude showed a 1:1 diastereomeric ratio. The crude product was then purified by chromatography on silica gel. Eluting with *n*-hexane/Et_2O 6:4, the diastereisomer (A) with higher R_f value was obtained as a yellow solid in spectroscopically pure form, whereas the fractions containing the second diastereoisomer (B) with a lower R_f contained an unidentified impurity. Diastereoisomer (B) was then obtained as a white solid in pure form after a second chromatographic purification on silica gel, eluting with CH_2Cl_2. Overall yield: 75%.

Characterisation data of diastereoisomer (A): the ee of this product was determined by HPLC using a Chiralpak ADH column (*n*-hexane/*i*-PrOH 80:20, flow-rate 0.75 mL/min, t_{maj} = 9.7 min, t_{min} = 5.6 min, 92% ee). $[\alpha]_D^{20}$ = -67 (c = 0.60 in CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.16 (br s, 1H), 7.38-7.31 (m, 2H), 7.30-7.01 (m, 10H), 6.92-6.84 (m, 2H), 6.52 (dd, *J* = 9.1, 2.9 Hz, 1H), 6.40 (dd, *J* = 8.9, 2.9 Hz, 1H), 6.14 (dd, *J* = 9.8, 5.9 Hz, 1H), 6.05 (dd, *J* = 9.0, 2.6 Hz, 1H), 6.01 (dd, *J* = 9.8, 5.5 Hz, 1H), 5.89 (dd, *J* = 8.7, 2.4 Hz, 1H), 3.78 (s, 3H), 3.75 (s, 3H), 2.66-2.52 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 159.9, 159.8, 157.0 (q, *J* = 35 Hz), 135.9, 135.1, 132.3, 131.8, 130.9, 130.7, 129.4, 128.8, 128.5, 127.1, 126.9, 124.7, 122.6, 120.3, 118.9, 116.6 (q, *J* = 287 Hz), 113.6, 113.5, 113.4, 113.2, 111.2, 110.9, 58.4, 55.4, 55.3, 50.8, 32.4; ^{19}F NMR ($CDCl_3$, 376 MHz) δ -67.60, -67.66; ESI-MS: 692 [M^+ + Na].

Characterisation data of diastereoisomer (B): the ee of this product was determined by HPLC using a Chiralcel OD column (*n*-hexane/*i*-PrOH 95:5, flow-rate 1.0 mL/min, t_{maj} = 21.5 min, t_{min} = 19.8 min, 93% ee). $[\alpha]_D^{20}$ = +22 (c = 0.55 in CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.10 (br s, 1H), 7.47-7.18 (m, 9H), 7.12-7.01 (m, 3H), 6.94-6.87 (m, 2H), 6.68 (d, *J* = 2.5 Hz, 1H), 6.54 (dd, *J* = 9.0, 3.0 Hz, 1H), 6.42 (dd, *J* = 8.9, 3.0 Hz, 1H), 6.35 (t, *J* = 7.2 Hz, 1H), 6.14 (t, *J* = 7.5 Hz, 1H), 6.05 (dd, *J* = 8.8, 2.6 Hz, 1H), 5.93 (dd, *J* = 8.8, 2.2 Hz, 1H), 3.78 (s, 3H), 3.75 (s, 3H), 2.59 (dt, J_d = 14.1 Hz, J_t = 7.4 Hz, 1H), 2.47 (dt, J_d = 13.8 Hz, J_t = 7.3 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 159.9, 159.8, 157.5 (q, *J* = 35 Hz), 157.2 (q, *J* = 35 Hz), 137.0, 136.0, 132.4, 132.1, 131.7, 131.6, 129.1, 128.7, 128.5, 126.9, 126.8, 126.6, 123.8, 122.8, 120.5, 119.3, 116.5 (q, *J* = 290 Hz), 116.3 (q, *J* = 290 Hz), 113.5, 113.4, 113.1, 113.0, 111.2, 57.7, 55.4, 55.3, 50.7, 32.9; ^{19}F NMR ($CDCl_3$, 376 MHz) δ -67.45, -67.46; ESI-MS: 692 [M^+ + Na].

3,3'-(1-(4-Methoxyphenyl)-6-phenylpiperidine-2,4-diyl)bis(1*H*-indole) (8).



To a flame dried Schlenk tube equipped with a magnetic stirring bar, were sequentially added, under a nitrogen atmosphere, the aldimine **1a** (21.1 mg, 0.10 mmol), anhydrous THF (0.40 mL) and the catalyst (*S*)-TRIP (7.5 mg, 0.010 mmol). After cooling to 0 °C, 3-vinylindole **3** (71.6 mg, 0.50 mmol) was added in one portion. After 14 h stirring the at 0 °C, the mixture was filtered through a short plug of silica, the plug washed several times with EtOAc, and the solvent evaporated. ^{1}H NMR analysis of the crude mixture showed the presence of the three diastereoisomers of the title compound in a 71:19:10 ratio (A:B:C). The residue was then purified by chromatography on silica gel (*n*-hexane/EtOAc 7:3), to give the diastereomeric mixture of the title compound as a pale yellow solid in 68% yield. The ee of the three diastereoisomers was determined by HPLC using a Chiralpak ADH column (*n*-hexane/*i*-PrOH 80:20, flow-rate 0.75 mL/min, diastereoisomer (A): t_{maj} = 19.6 min, t_{min} = 29.6 min, ee_A = 99%; diastereoisomer (B): t_{maj} = 23.7 min, t_{min} = 32.3 min, ee_B = 98%; diastereoisomer (C): t_{maj} = 77.2 min, t_{min} = 48.5 min, ee_B = 60%). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.19-8.06 (m, $2H_A$, $1H_B$), 7.90-7.58 (m, $2H_A$, $3H_B$, $3H_C$), 7.48-7.01 (m, $12H_A$, $12H_B$, $13H_C$), 6.98-6.68 (m, $3H_A$, $3H_B$, $3H_C$), 6.53 (br d, J = 9.0 Hz, $2H_B$), 6.46 (br d, J = 9.0 Hz, $2H_C$), 6.31 (br d, J = 9.0 Hz, $2H_A$), 5.40 (dd, J = 8.6, 3.0 Hz, $1H_B$), 5.24 (br t, J = 4.0 Hz, $1H_B$), 4.73 (dd, J = 11.2, 2.8 Hz, $1H_A$), 4.53 (dd, J = 11.2, 2.9 Hz, $1H_A$, $1H_C$), 4.30 (dd, J = 9.8, 2.4 Hz, $1H_C$), 3.70-3.65 (br m, $1H_A$), 3.58 (s, $3H_B$), 3.48 (s, $3H_A$, $3H_C$), 3.47-3.42 (m, $1H_B$), 3.36-3.29 (m, $1H_B$), 3.35-3.32 (m, $1H_C$), 3.00-2.89 (m, $1H_A$), 2.73 (dt, J_d = 13.4 Hz, J_t = 5.4 Hz, $1H_B$), 2.67-2.37 (m, $3H_A$, $3H_B$, $3H_C$), 2.21 (q, J = 12.4 Hz, $1H_C$); ^{13}C NMR ($CDCl_3$, 100 MHz) [aromatic carbons: signals of the three diastreoisomers; aliphatic carbons: signals of the three diastereoisomers assigned by means of a gHSQC NMR experiment] δ 155.9, 155.1, 152.6, 145.2, 145.1, 144.6, 144.4, 143.7, 143.6, 136.6, 136.5, 136.4, 136.3, 136.2, 128.2, 128.1, 127.8, 127.7, 127.5, 126.5, 126.3, 126.2, 126.1, 122.4, 122.0, 121.8, 121.7, 121.6, 121.5, 121.4, 120.7, 119.9, 119.7, 119.6, 119.5, 119.4, 119.3, 119.1,119.0, 118.9, 118.8, 113.4, 112.7, 112.6, 111.1, 111.0, 110.9, 69.5 (C), 63.6 (A), 63.0 (B), 62.9 (C), 57.6 (A), 55.2 (B), 55.1 (C), 54.9 (A), 51.8 (B), 43.8 (C), 41.4 (C), 39.9 (A), 38.9 (B), 37.6 (A), 36.9 (B), 34.3 (C), 29.4 (A), 27.0 (B); ESI-MS: 520 [M^+ + Na].

Conformational analysis and absolute configuration determination

The presence of the chlorine atom in some compounds like **4n** and **5n** would be suitable for the use of the Bijovet method, based on anomalous X-ray dispersion to unambiguously assign the absolute configuration (AC). However, despite several attempts, single crystals of **4n** and **5n** were not available. Recently, the determination of the absolute configuration of chiral molecules using the chiroptical techniques of optical rotation (OR), electronic circular dichroism (ECD), and vibrational circular dichroism (VCD) has been revolutionized by the development of Time-Dependent Density Functional Theory (TD-DFT) methods for the prediction of these properties. In the present case, theoretical calculation of optical rotations and ECD spectra was carried out by means of the TD-DFT method, since this technique has been successfully employed several times to predict ECD spectra and to assign the AC of organic molecules.[6]

Compound **4a** was selected as representative compound. The relative stereochemistry of the two asymmetric carbons has been determined by means of NMR spectroscopy. Full assignment of the ^{1}H and ^{13}C spectra was achieved by bi-dimensional experiments (HSQC, HMBC and COSY).

A detailed analysis of the ^{1}H spectrum, in particular of the signals corresponding to H-2 and H-4, revealed that both there signals exhibit a large coupling constant (11.9 Hz for H-2 and 10.6 Hz for H-4) with one of the diastereotopic hydrogens of C-3. This indicates that both H-2 and H-4 are in a pseudo-axial position on the tetrahydroquinoline ring, having a trans-diaxial relationship with one of the hydrogens belonging to C-3.

DPFGSE-NOE experiments[7] were acquired in order to confirm the relative stereochemistry. On saturation of the hydrogen in the ortho position of the phenyl ring in position 2 (trace b in Figure S1), NOE enhancement is observable only for H-2. On saturation of H-4 (trace c), a large NOE is observed on H-2, thus confirming the 1-3 diaxial proximity of H-2 and H-4 already deduced from the analysis of the proton spectrum. NMR analysis proves that the relative configuration is therefore 2*R**,4*R**.

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[6] For recent examples of this method to assign the absolute configurations of organic molecules, see: (*a*) C. Diedrich, and S. Grimme, *J. Phys. Chem. A*, 2003, **107**, 2524; (*b*) D. Casarini, L. Lunazzi, M. Mancinelli, A. Mazzanti and C. Rosini, *J. Org. Chem.*, 2007, **72**, 7667; (*c*) A. Goel, F. V. Singh, V. Kumar, M. Reichert, T. A. M. Goulder and G. Bringmann, *J. Org. Chem.*, 2007, **72**, 7765; (*d*) P. J. Stephens, J. J. Pan, F. J. Devlin and J. R. Cheeseman, *J. Nat. Prod.*, 2008, **71**, 285; (*e*) O. Penon, A. Carlone, A. Mazzanti, M. Locatelli, L. Sambri, G. Bartoli and P. Melchiorre, *Chem. Eur. J.*, 2008, **14**, 4788; (*f*) F. Pesciaioli, F. De Vincentiis, P. Galzerano, G. Bencivenni, G. Bartoli, A. Mazzanti, A. and P. Melchiorre, *Angew. Chem. Int. Ed.*, 2008, **47**, 8703; (*g*) R. R. Shaikh, A. Mazzanti, M. Petrini, G. Bartoli and P. Melchiorre, *Angew. Chem. Int. Ed.*, 2008, **47**, 8707. This topic has been also recently reviewed, see G. Bringmann, T. Bruhn, K. Maksimenka and Y.Hemberger, *Eur. J. Org. Chem.*, 2009, 2717-2727.

[7] (*a*) K. Stott, J. Stonehouse, J. Keeler, T.-L. Hwand and A. J. Shaka, *J. Am. Chem. Soc.*, 1995, **117**, 4199; (*b*) K. Stott, J. Keeler, Q. N. Van and A. J. Shaka, *J. Magn. Resonance*, 1997, **125**, 302; (*c*) Q. N. Van, E. M. Smith and A. J. Shaka, *J. Magn. Resonance*, 1999, **141**, 191; (*d*) See also: T. D. W. Claridge, *High Resolution NMR Techniques in Organic Chemistry*; Pergamon: Amsterdam, 1999.

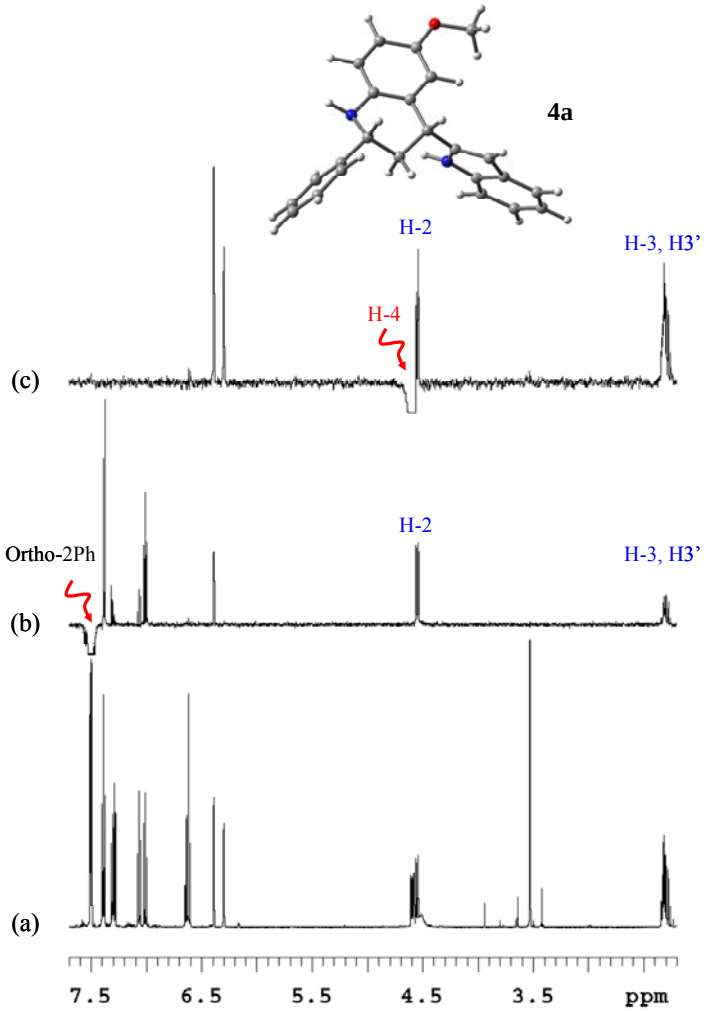

Figure S1: DPFGSE NOE spectra of **4a** (600 MHZ in CD_3CN). Trace a): control spectrum. Trace b): saturation of the ortho hydrogens of the phenyl ring in position 2. Trace c): saturation of H-4.

Absolute configuration

A preliminary conformational search, starting from the relative configuration derived from NMR spectra of **4a** has been carried out using Monte Carlo searching together with the MMFF94 molecular mechanics force field (as implemented in Titan 1.0.5, Wavefunction, Irvine, CA).

All the conformations enclosed in a 5 kcal/mol windows were subsequently subjected to minimization by DFT calculations at the B3LYP/6-31G(d) level.[8] Vibrational analysis was

[8] Gaussian 03, Revision E.01, Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, Jr., J. A.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.;

performed at the same level on each conformation, in order to confirm their stability (no imaginary frequencies observed), and to evaluate the free energy of each conformation by thermochemistry corrections. After DFT minimization, the MMFF structures fall into four stable conformations named A-D in Table S1. All the conformers show the same geometry on the tetrahydroquinoline ring, and they are different because of the orientation of the 2-indolyl ring and of the OMe moiety (Figure S2).

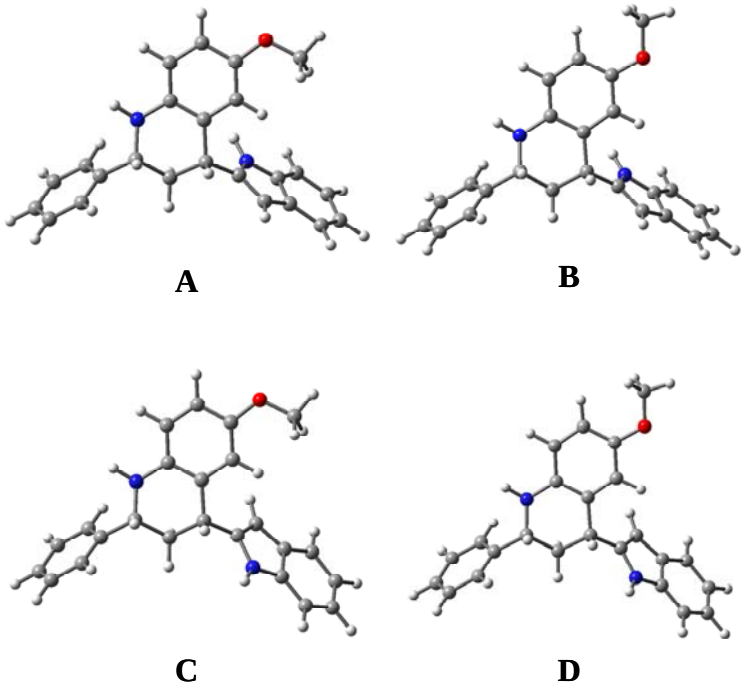

Figure S2. DFT optimized conformation of **4a** (B3LYP/6-31G(d) level)

Table S7: Calculated relative energies (ΔE) and free energies (ΔG) of the conformations of **4a** (in kcal/mol, B3LYP/6-31G(d) level). Populations percentages are calculated on ΔG assuming Boltzmann statistics at T=25°C.

Molecule	Conformer	ΔE	ΔG	Pop % (ΔG)
4a	**A**	0	0	64
	B	0.49	0.42	31
	C	2.04	1.82	3
	D	2.50	2.02	2

Electronic excitation energies and rotational strengths have been calculated for the four conformation of **4a** using TD-DFT at the B3LYP/6-31+G(d,p)//B3LYP/6-31G(d) and supposing 2*R*, 4*R* absolute configuration, with the results given in Figure S3. Rotational strength were calculated in both length and velocity representation. Since the resulting values are very similar,

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Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A.; Gaussian, Inc., Wallingford CT, 2004.

errors due to basis set incompleteness are very small, or negligible.[9]

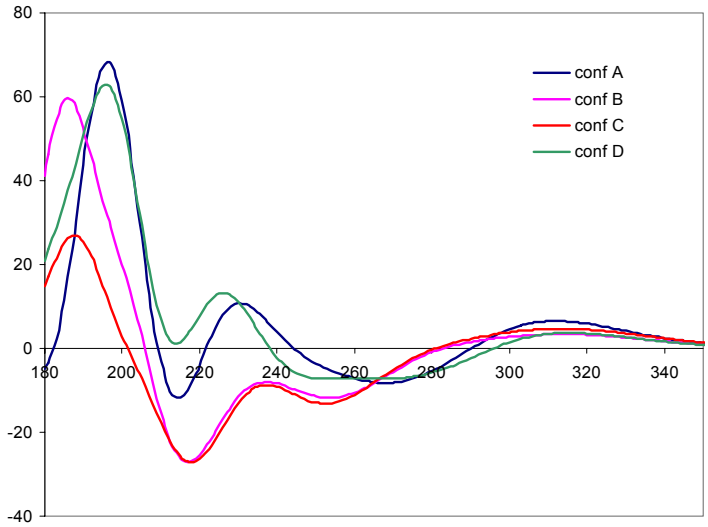


Figure S3. Calculated ECD spectra (TD-DFT-B3LYP/6-31+G(d,p)//B3LYP/6-31G(d) level) for the four conformations of **4a**.

The final simulated ECD spectra was obtained taking into account the 64:31:3:2 population ratios determined assuming Boltzmann statistics from the calculated free energies at the B3LYP/6-31G(d) level (Figure S4).

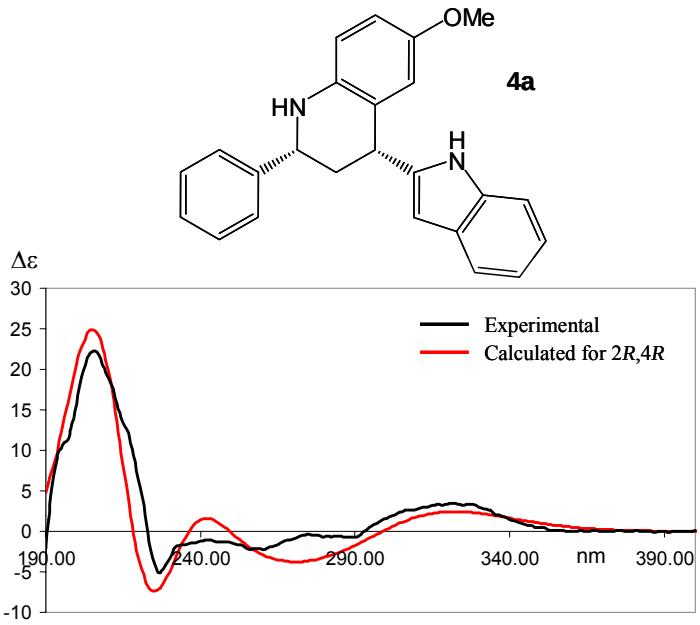


Figure S4. Experimental (black) and calculated ECD spectra (red), weighted on the calculated free energies of the conformations, and blue shifted by 10 nm. Molecular CD (Δε) is expressed in L $mol^{-1}cm^{-1}$. Solvent was acetonitrile. The vertical scale of the final simulated spectrum was scaled in order to obtain the best fit with the experimental trace.

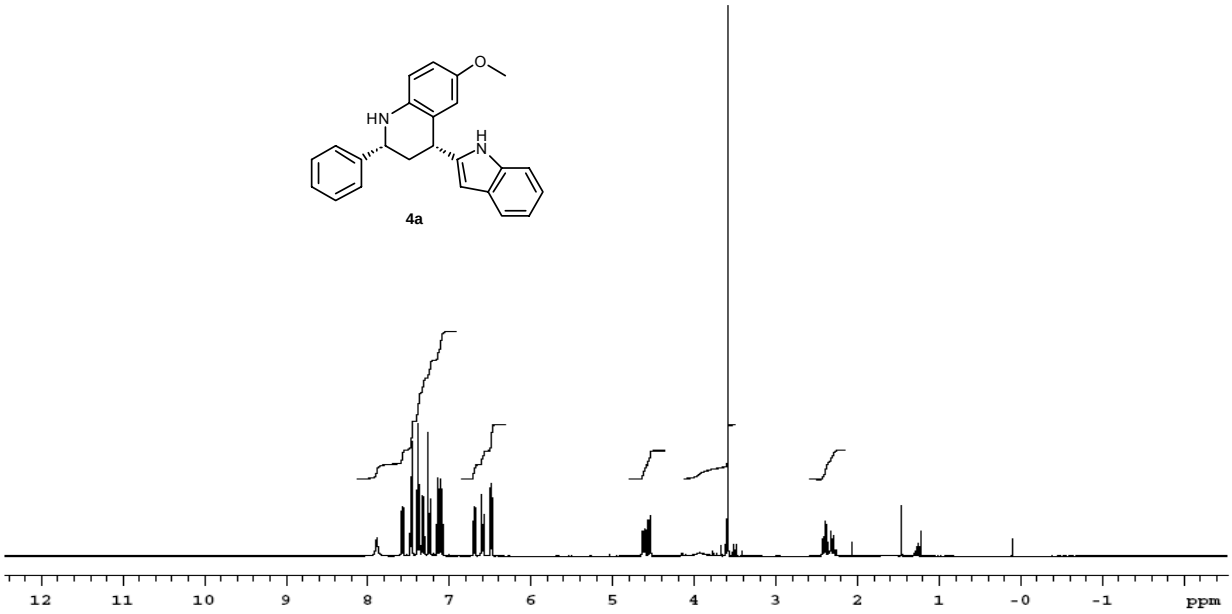
[9] P. J. Stephens, D. M. McCann, F. J. Devlin, J. R. Cheeseman and M. J. Frisch, *J. Am. Chem. Soc.*, 2004, **126**, 7514-7521

The experimental trace (black) is correctly simulated by the calculated one. The CD simulation thus supports the conclusion that the AC of **4a** is 2*R*, 4*R*.

As correctly suggested by some authors,[10] use of more than one chirooptic method is always desirable; in the present case the experimental $[\alpha]_D$ value of **4a** (+114°) is outside of the "uncertainty region",[5b,11] therefore the calculation of the $[\alpha]_D$ could further confirm the assignment made by ECD simulation. Calculation of the optical rotation for each of the four conformers of **4a** was obtained at the B3LYP/6-31+G(d,p)//B3LYP/6-31G(d) level, under the software keyword "polar=optrot". The resulting values (+158, +139, -90 and -45 for conformations A, B, C and D, respectively) were weighted using Boltzmann statistics at +25°C, yielding an average value of +141°, in very good agreement with the experimental value.

[10] (*a*) P. L. Polavarapu, *Chirality*, 2008, **20**, 664; (*b*) P. J. Stephens, J. J. Pan, F. J. Devlin, K. Krohn and T. Kurtn, *J. Org. Chem.*, 2007, **72**, 3521.

[11] (*a*) P. J. Stephens, D. M. McCann, F. J. Devlin and A. B. Smith III, *J. Nat. Prod.*, 2006, **69**, 1055; (*b*) P. J. Stephens, D. M. McCann, J. R. Cheeseman and M. J. Frisch, *Chirality*, 2005, **17**, S52.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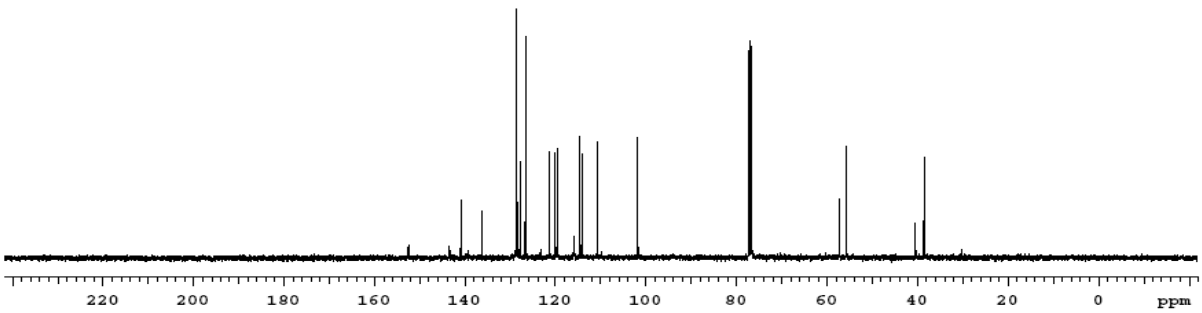
4a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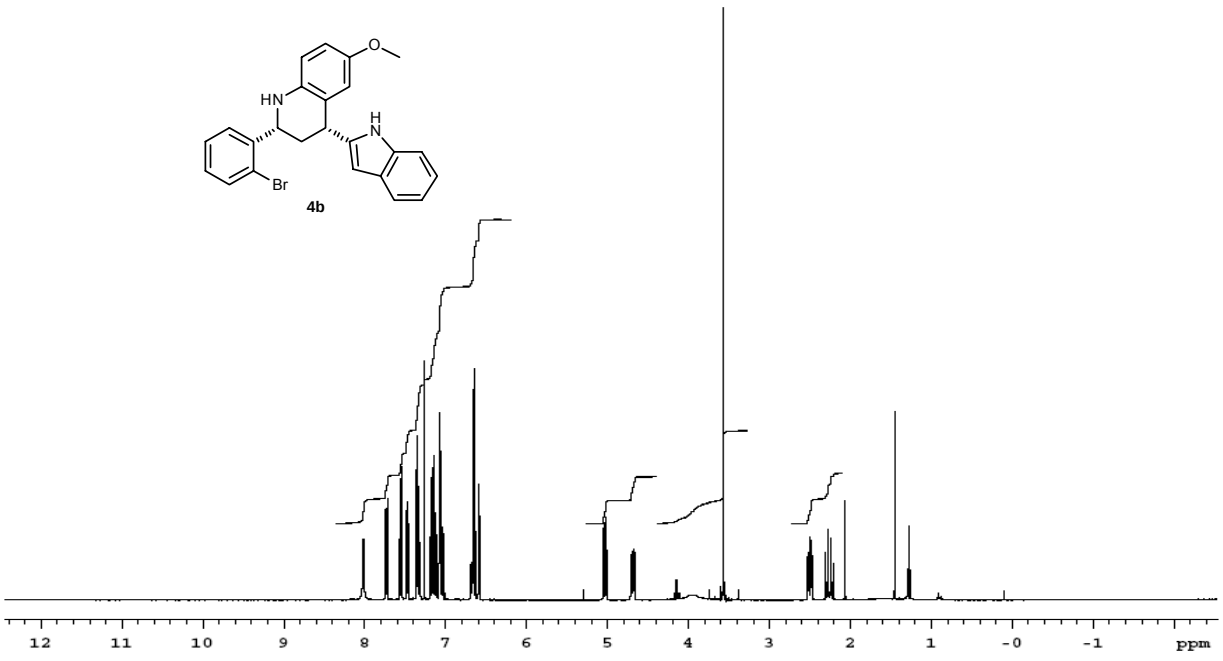
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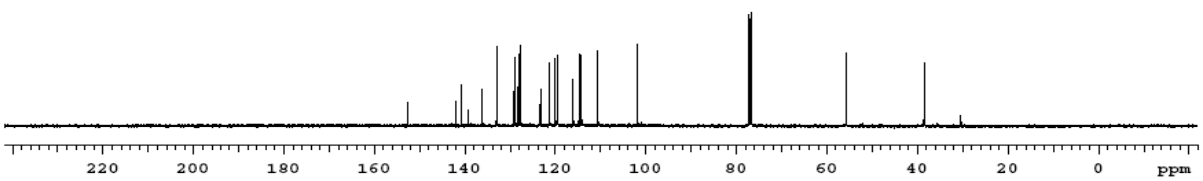
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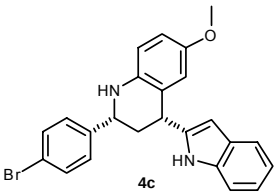
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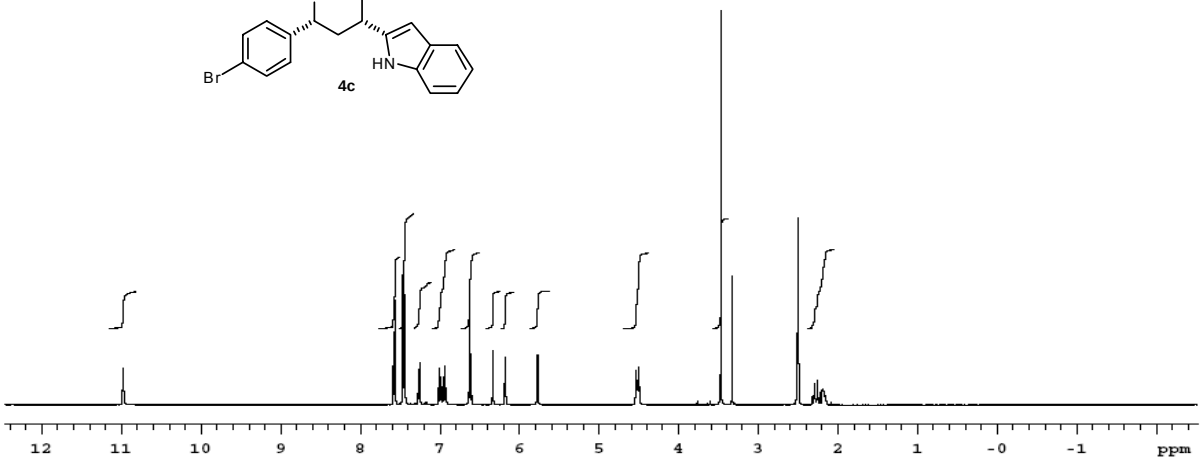
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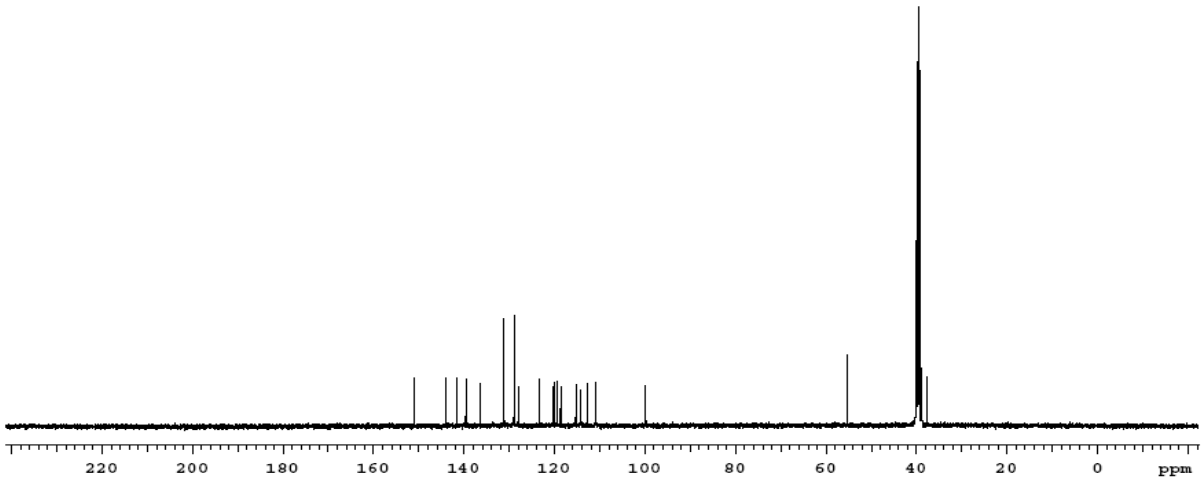
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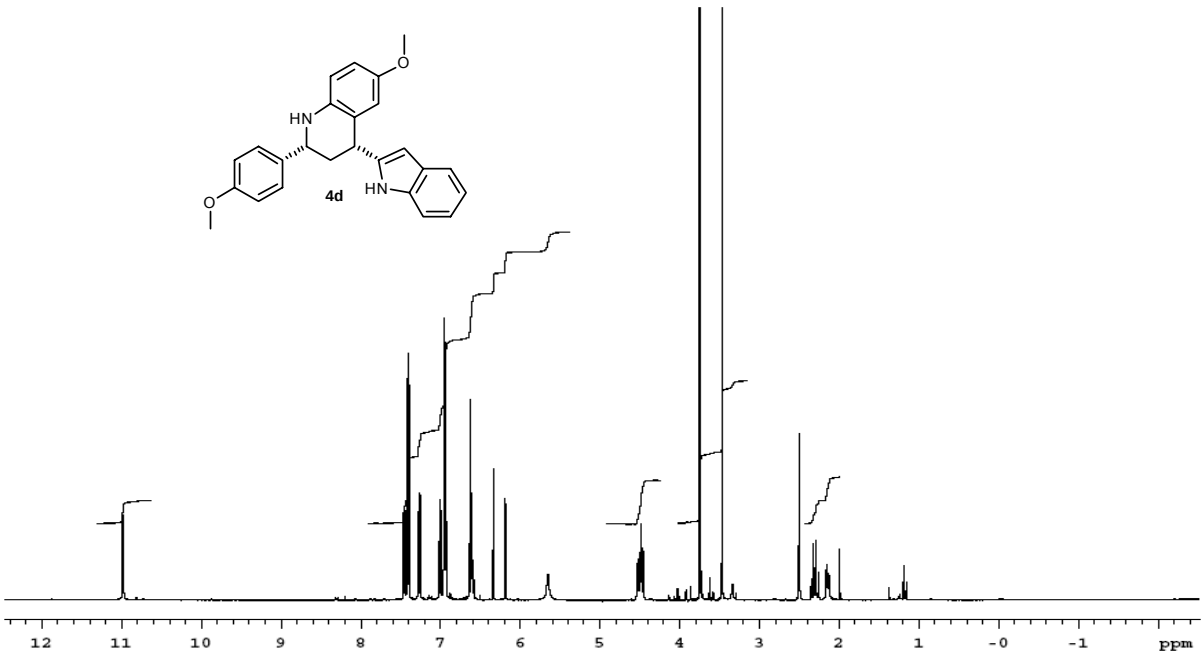
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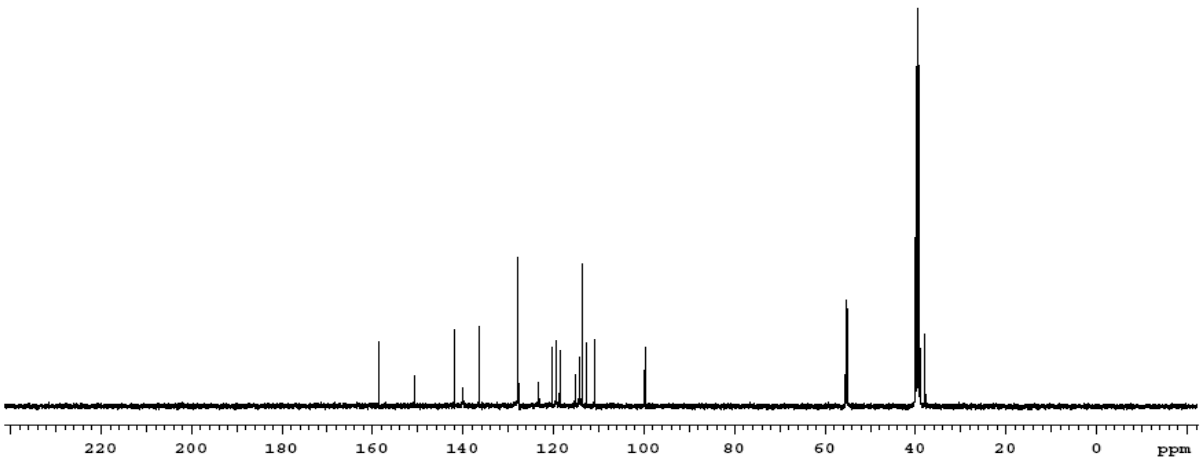
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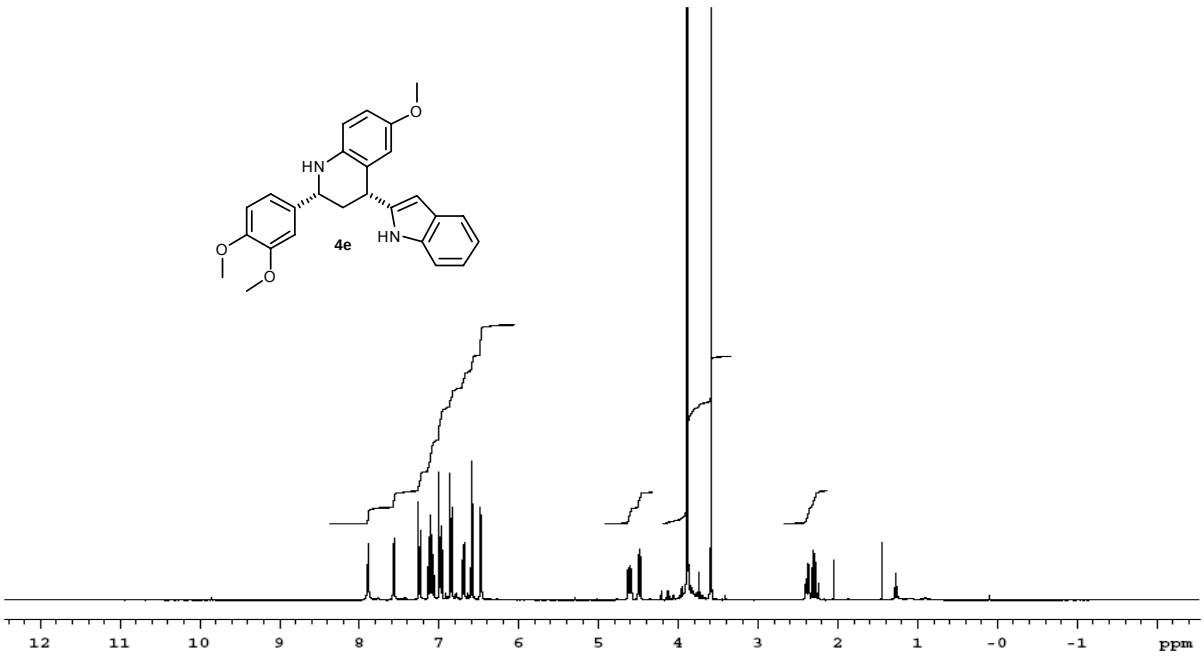
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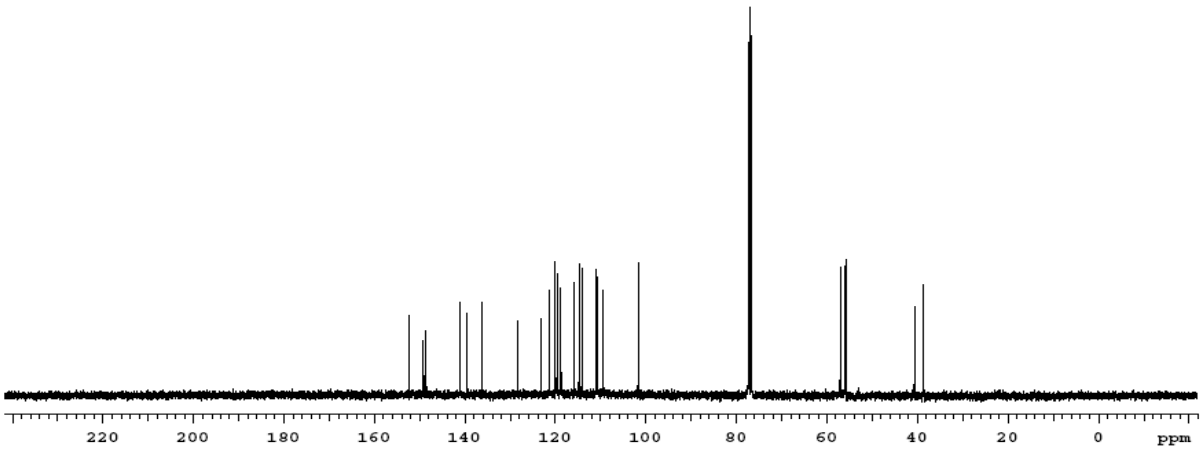
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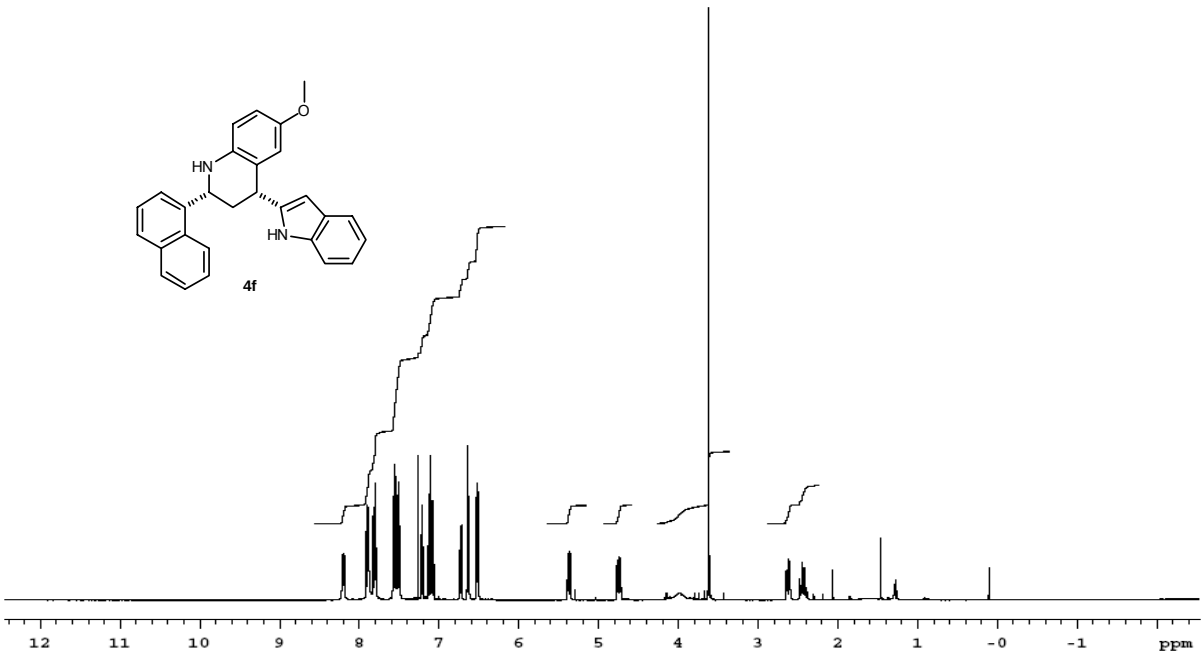
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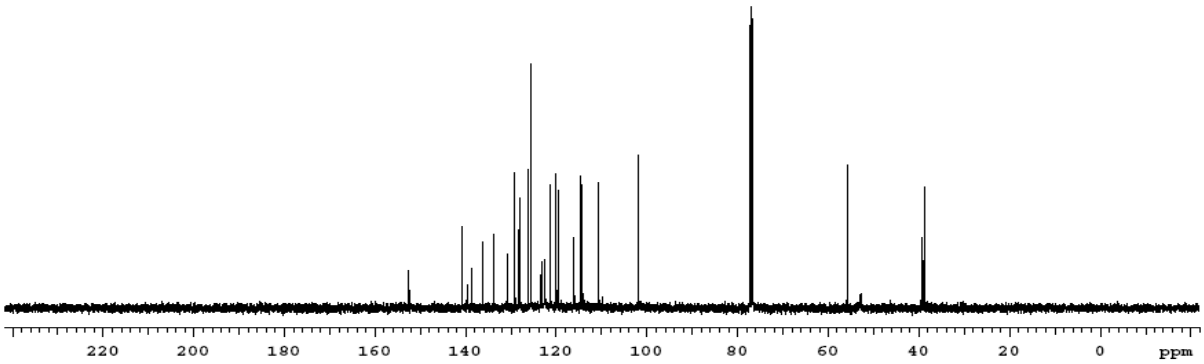
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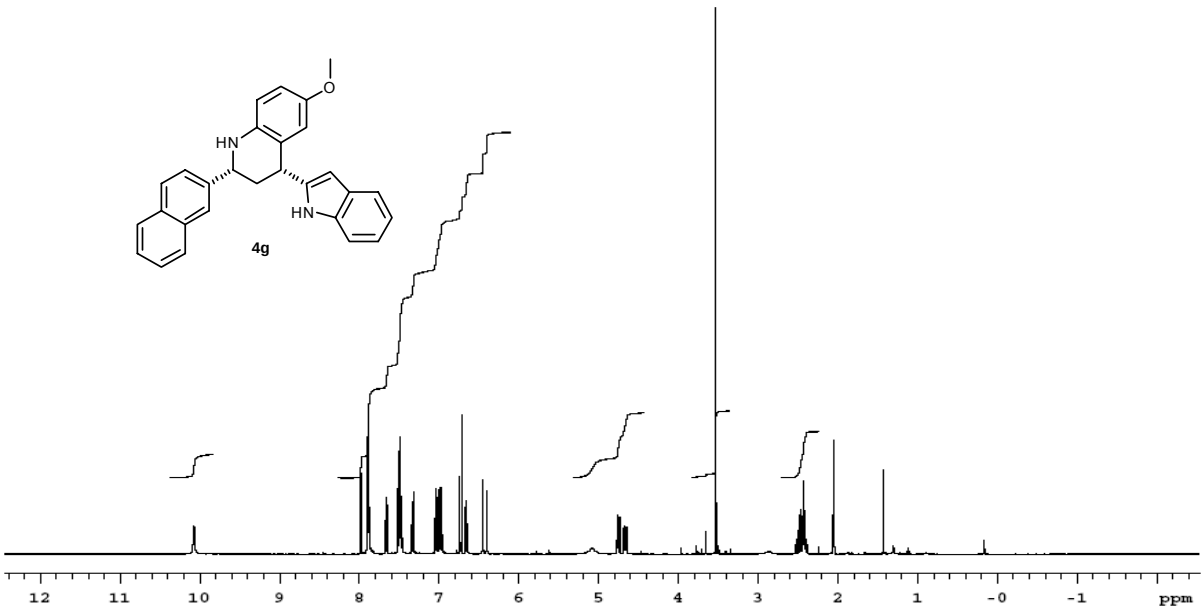
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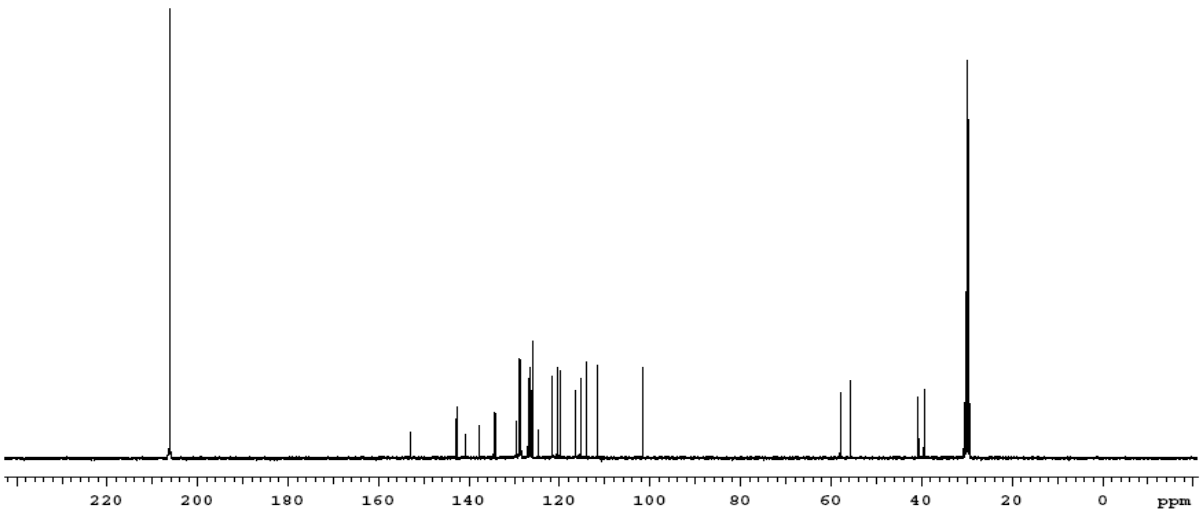
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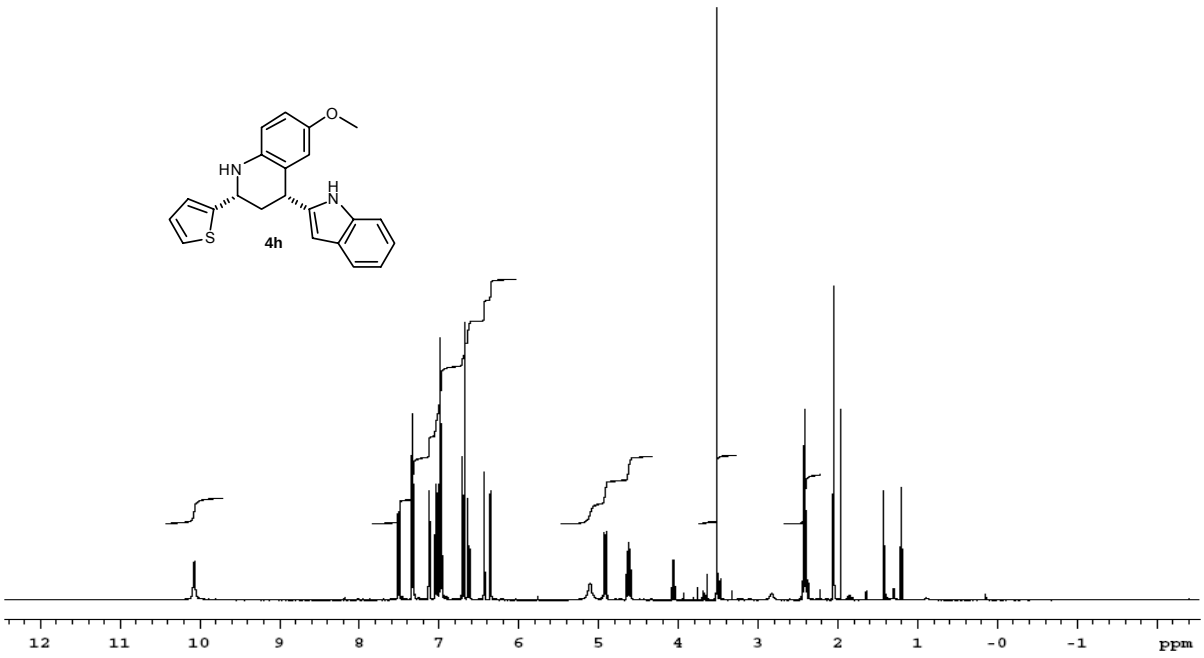
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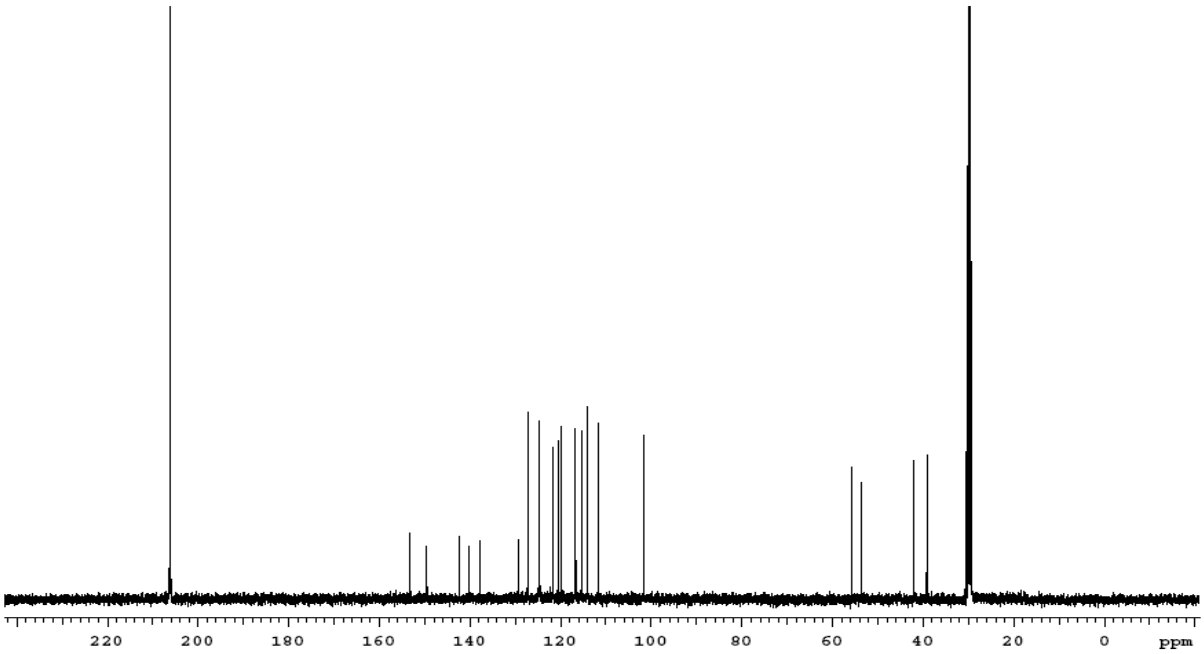
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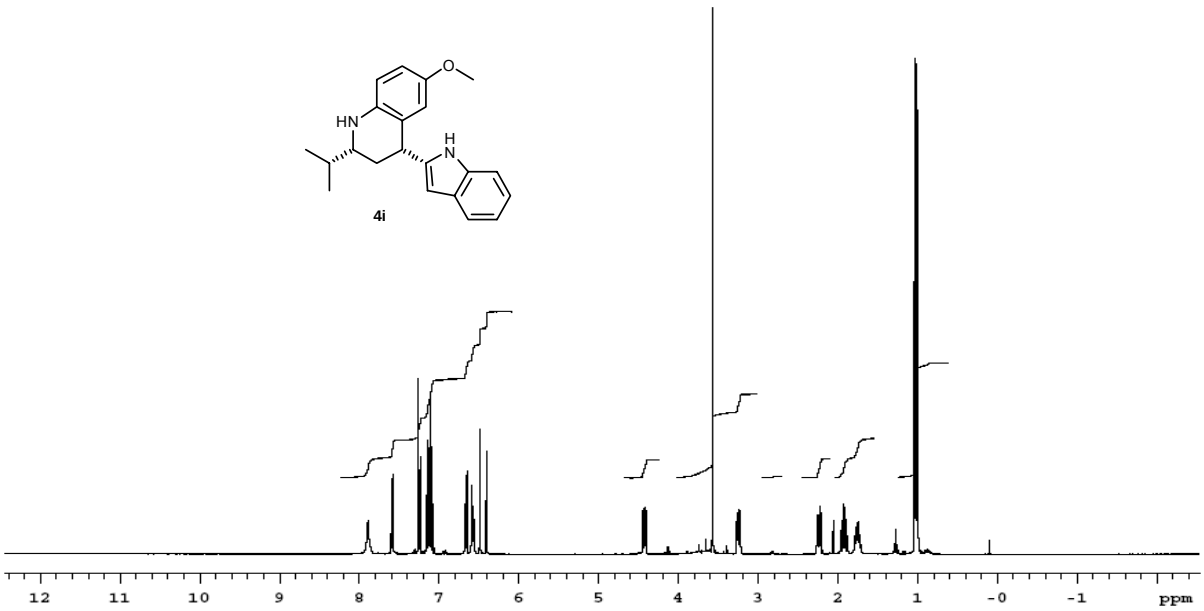
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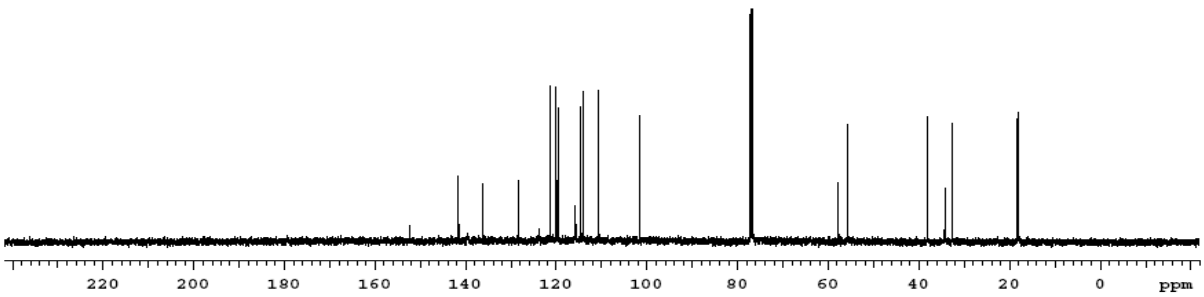
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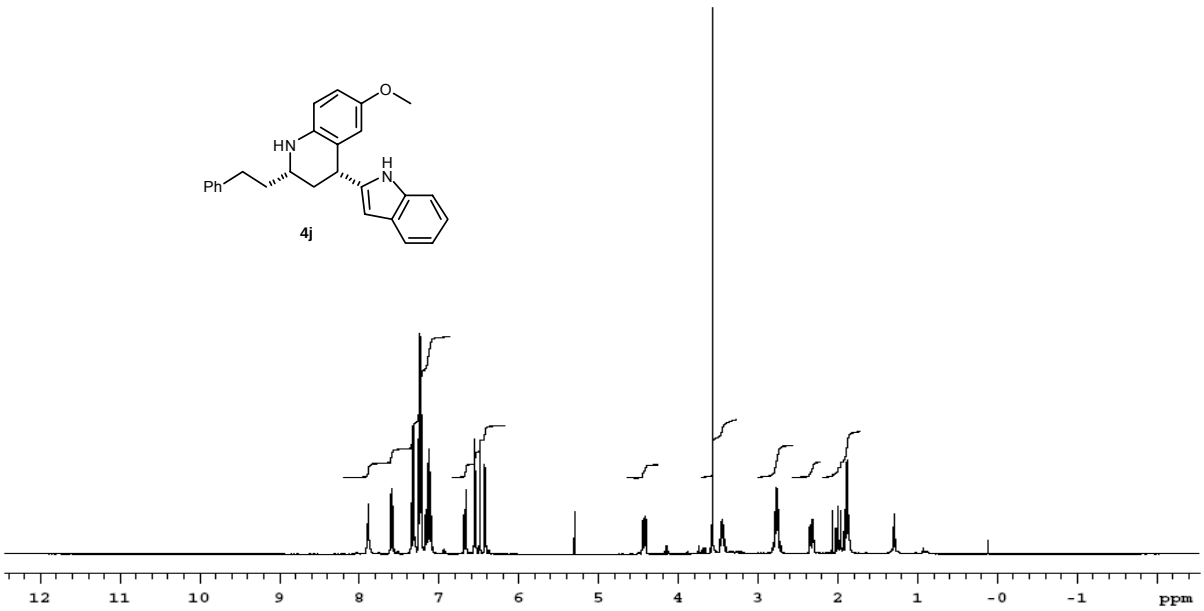
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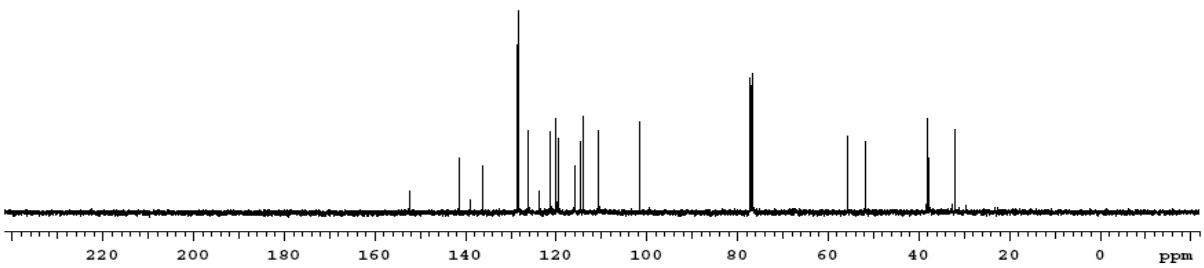
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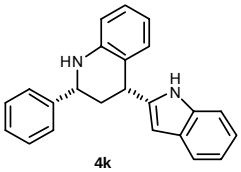
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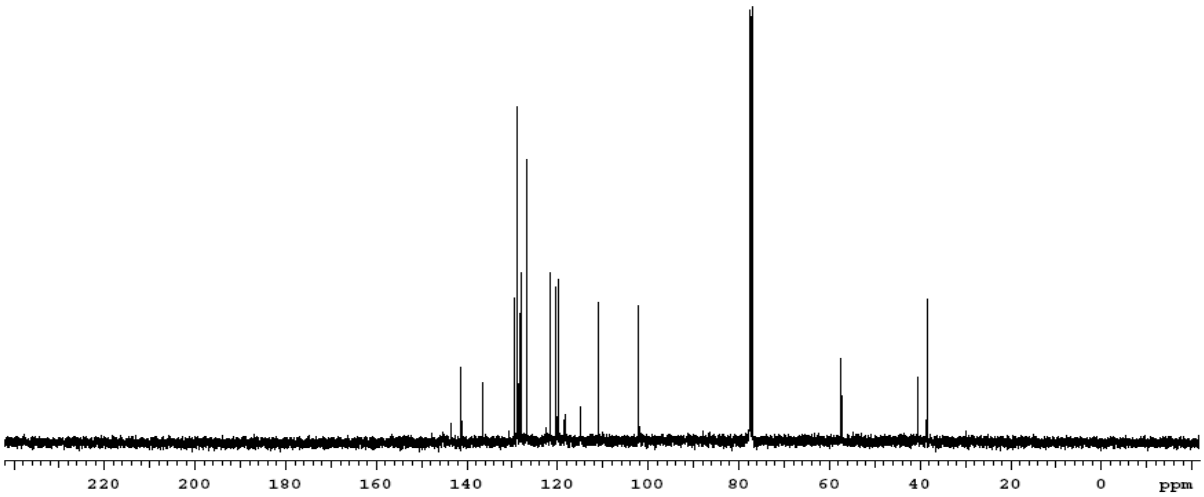
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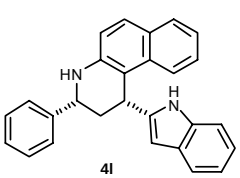
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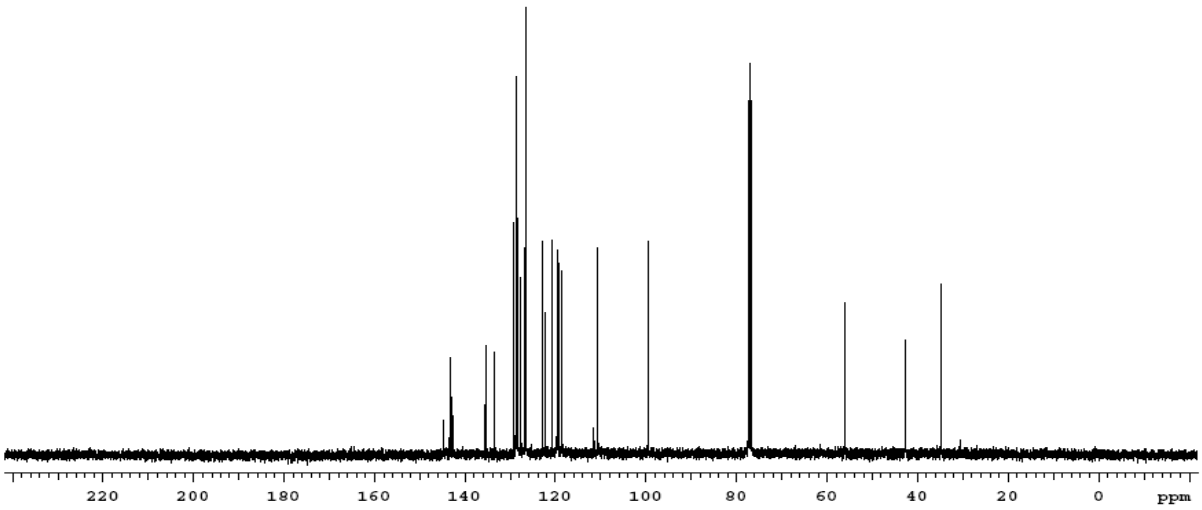
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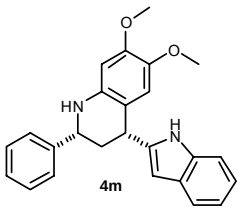
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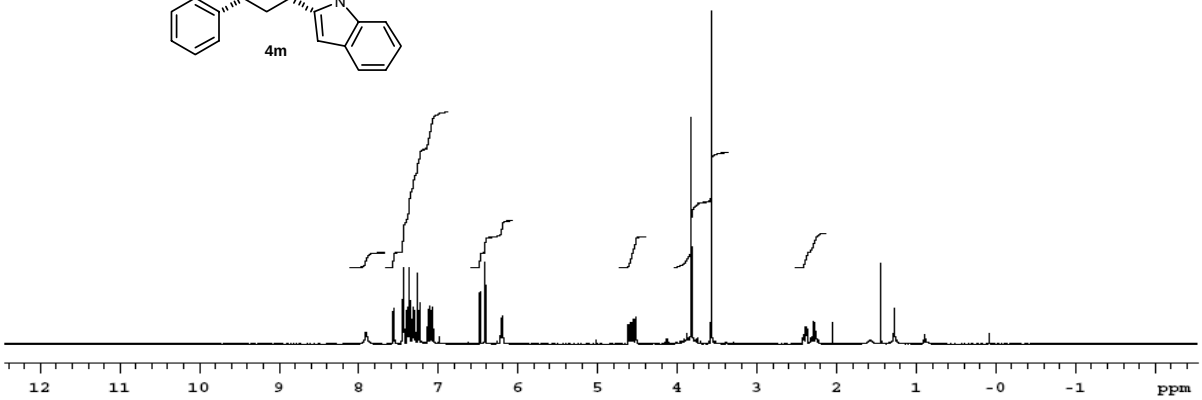
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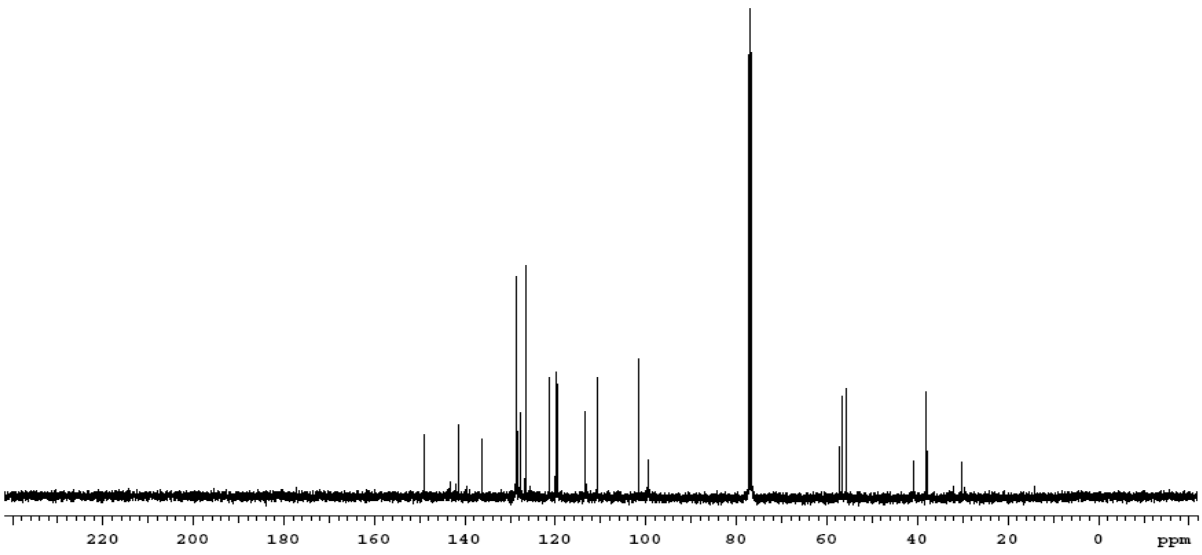
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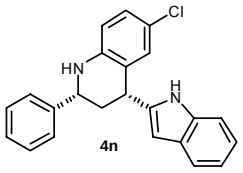
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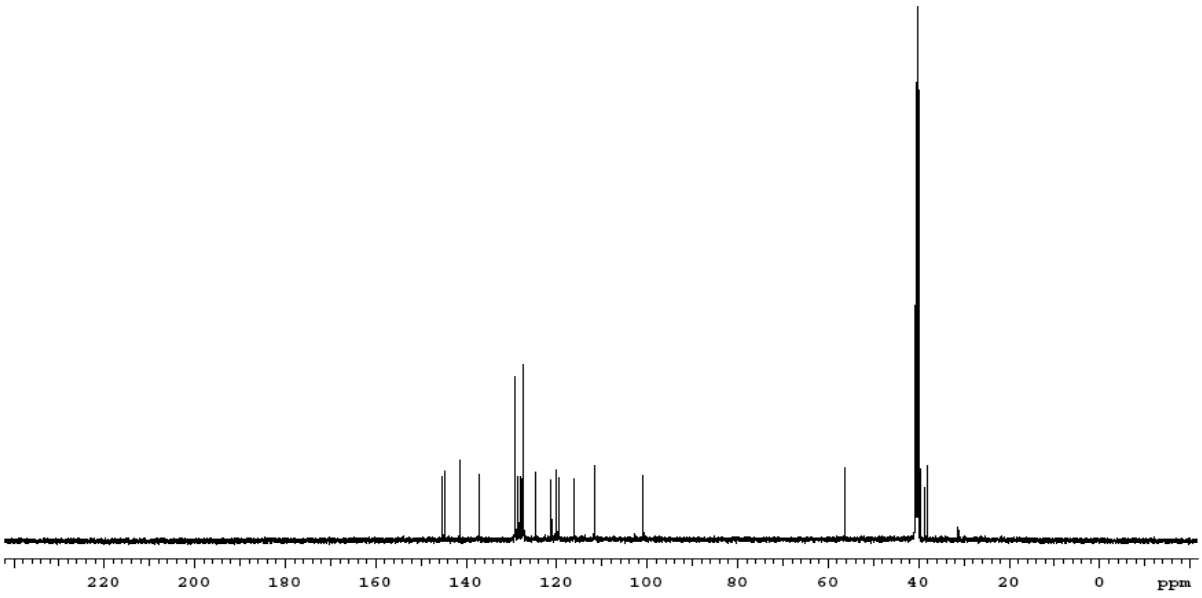
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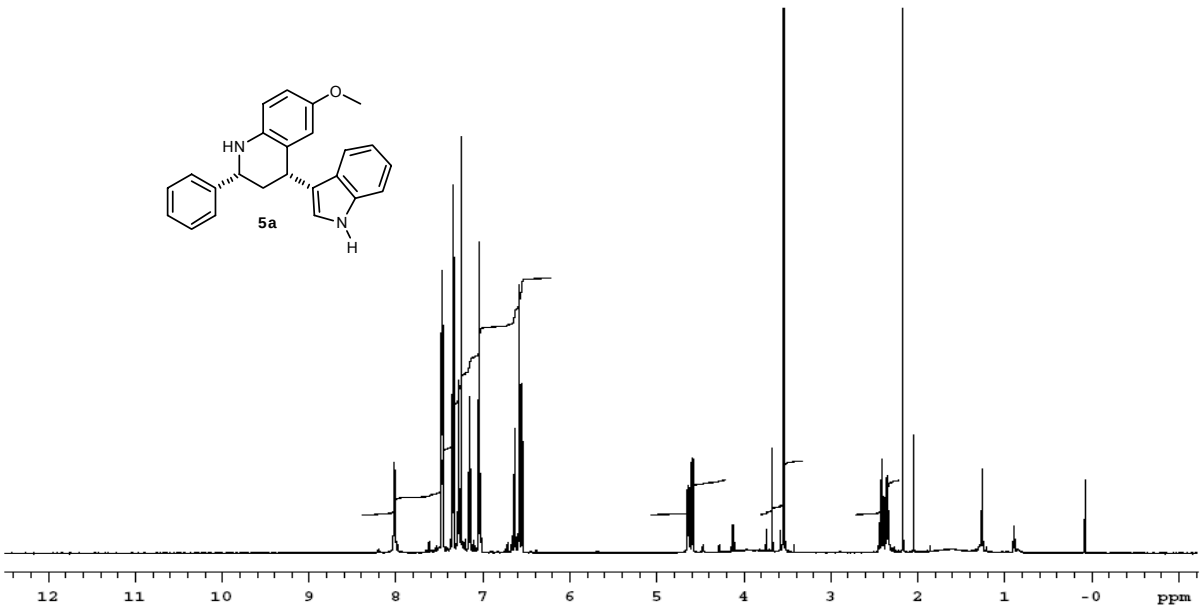
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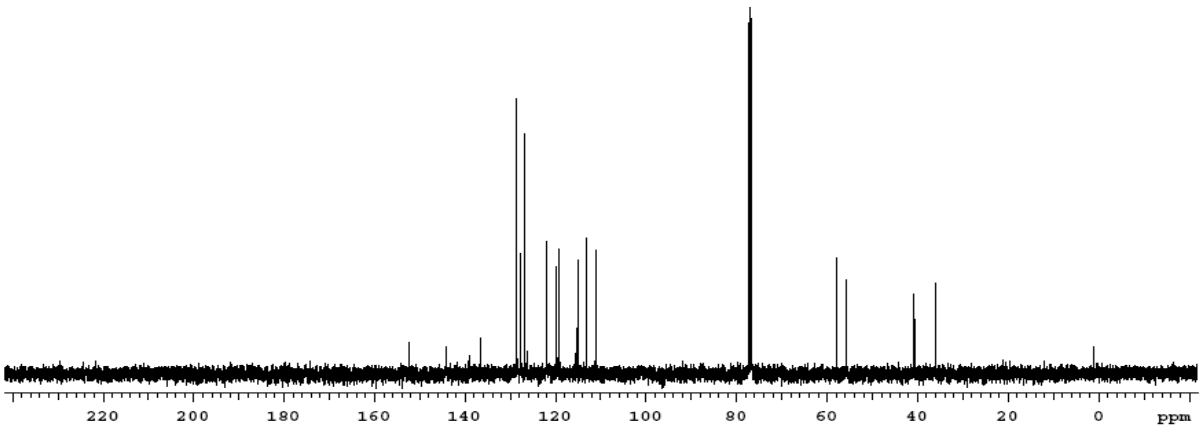
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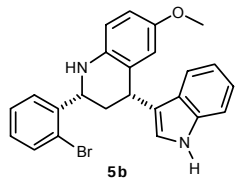
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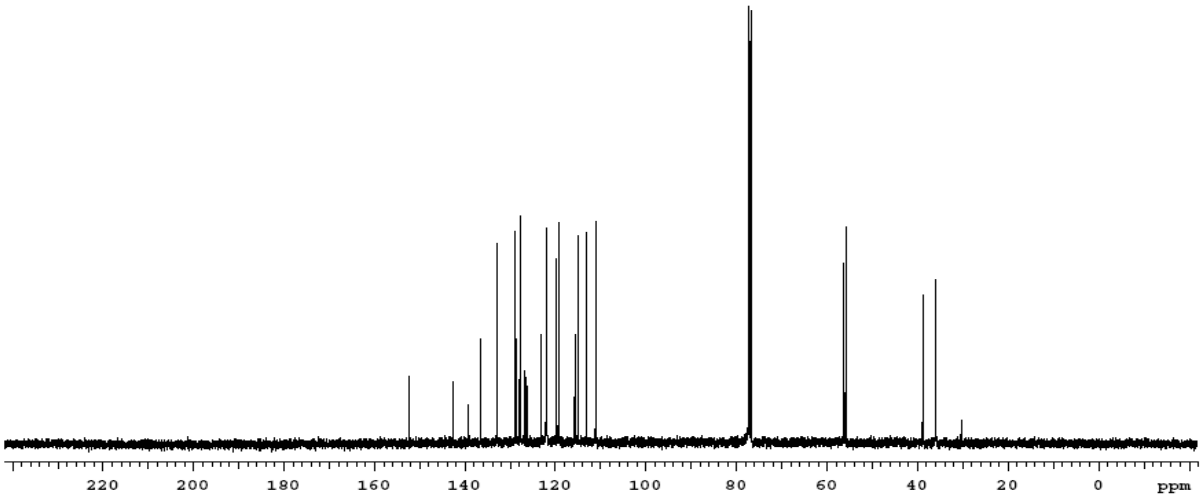
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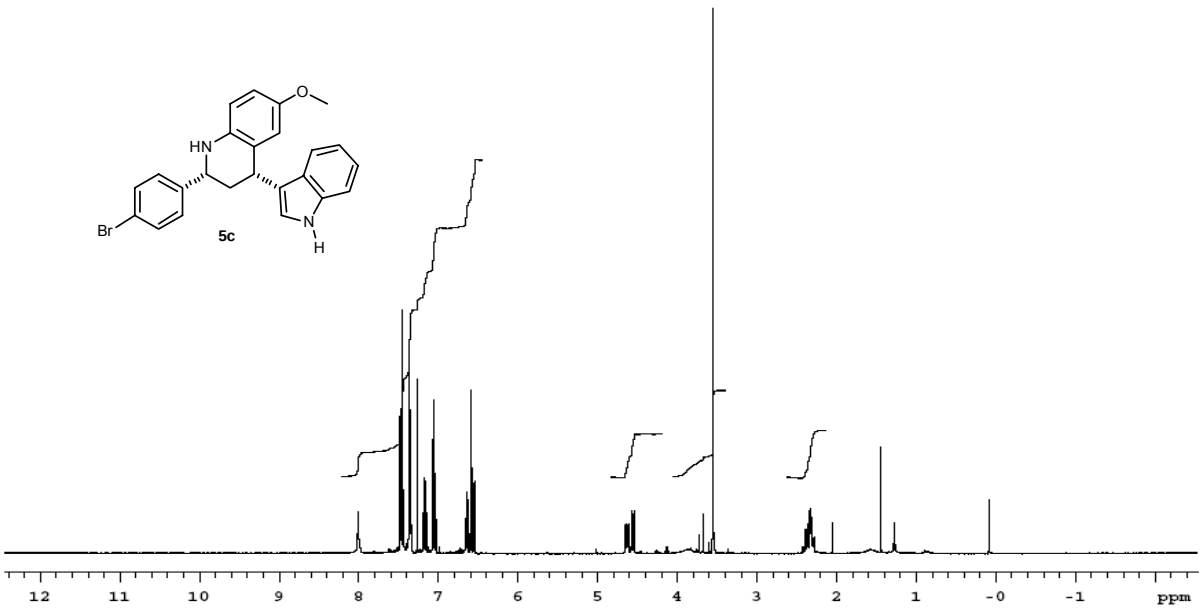
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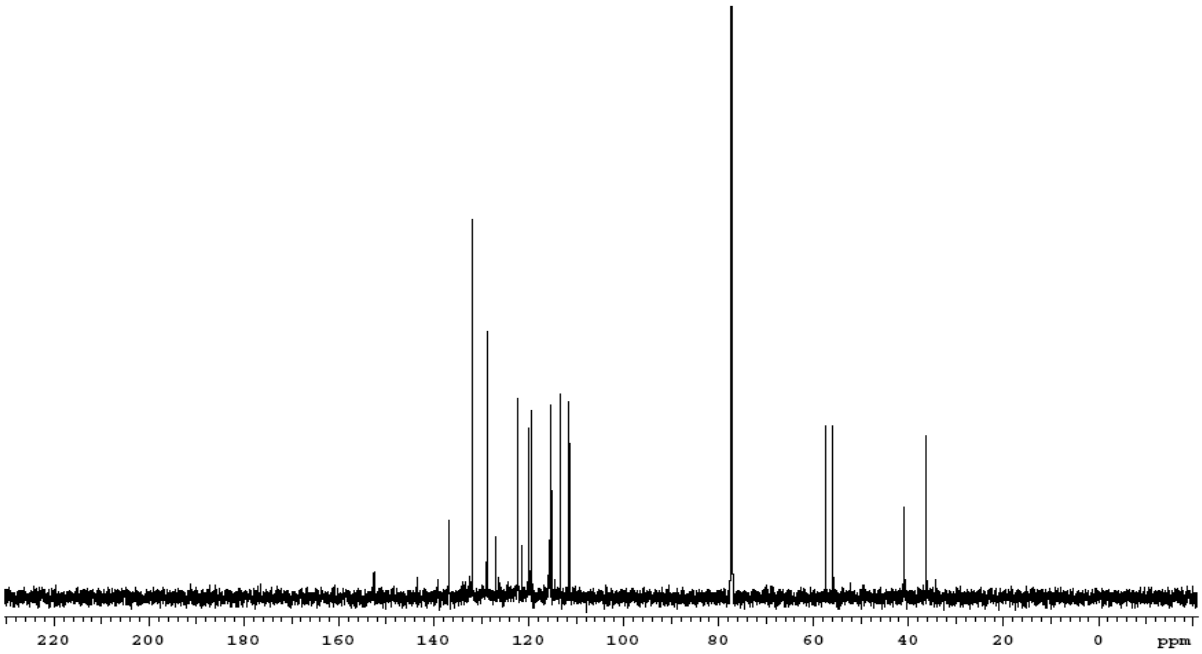
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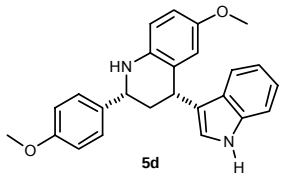
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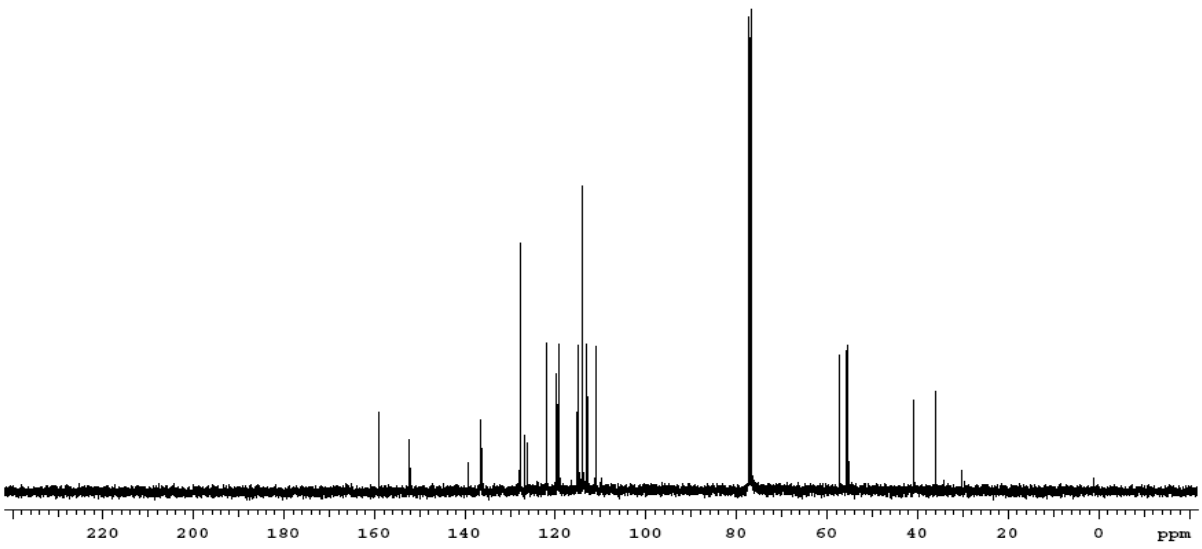
220
200
180
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120
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40
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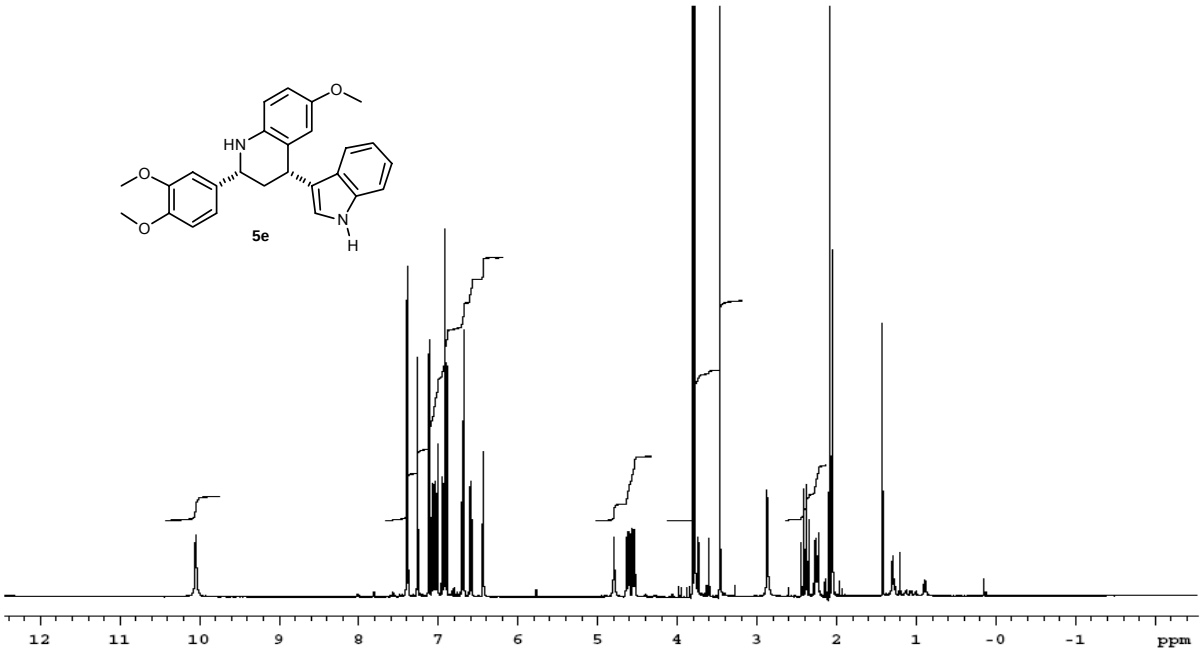
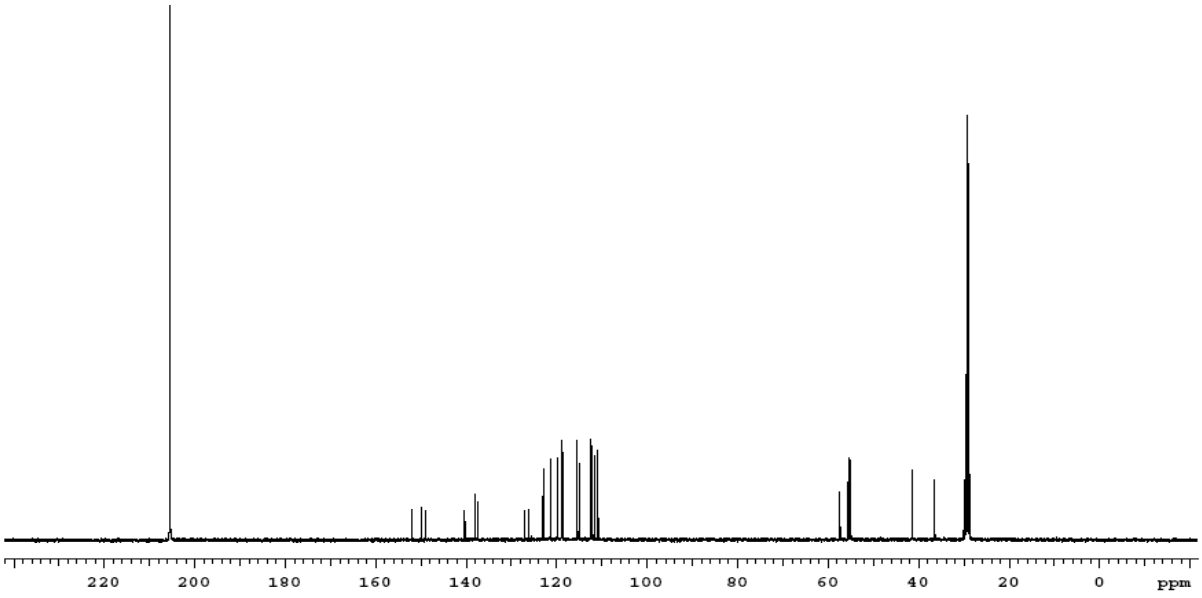
ppm


HN
O
O
O
N
H
12
11
10
9
8
7
6
5
4
3
2
1
-0
-1
ppm

5e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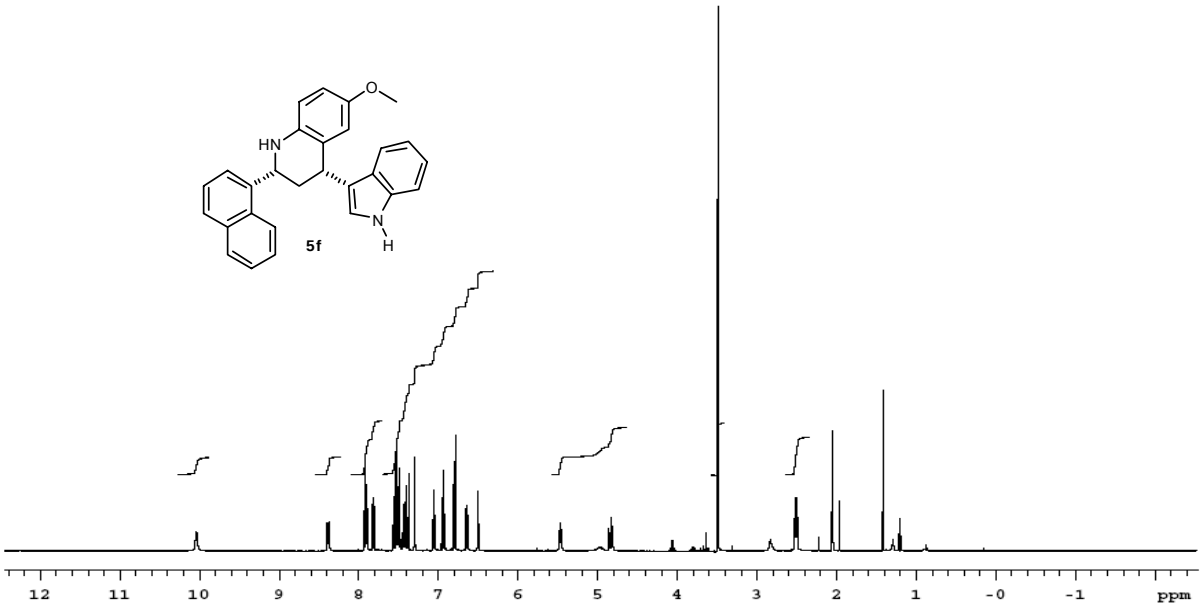
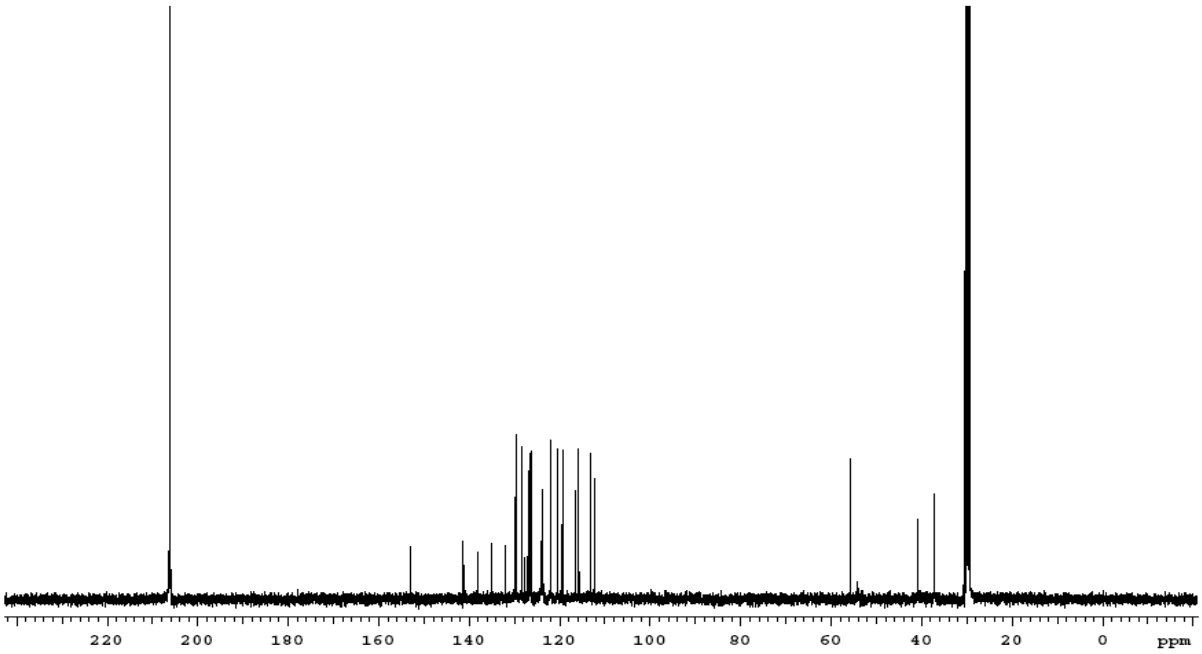
ppm


O
HN
N
H
5f
12
11
10
9
8
7
6
5
4
3
2
1
-0
-1
ppm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200
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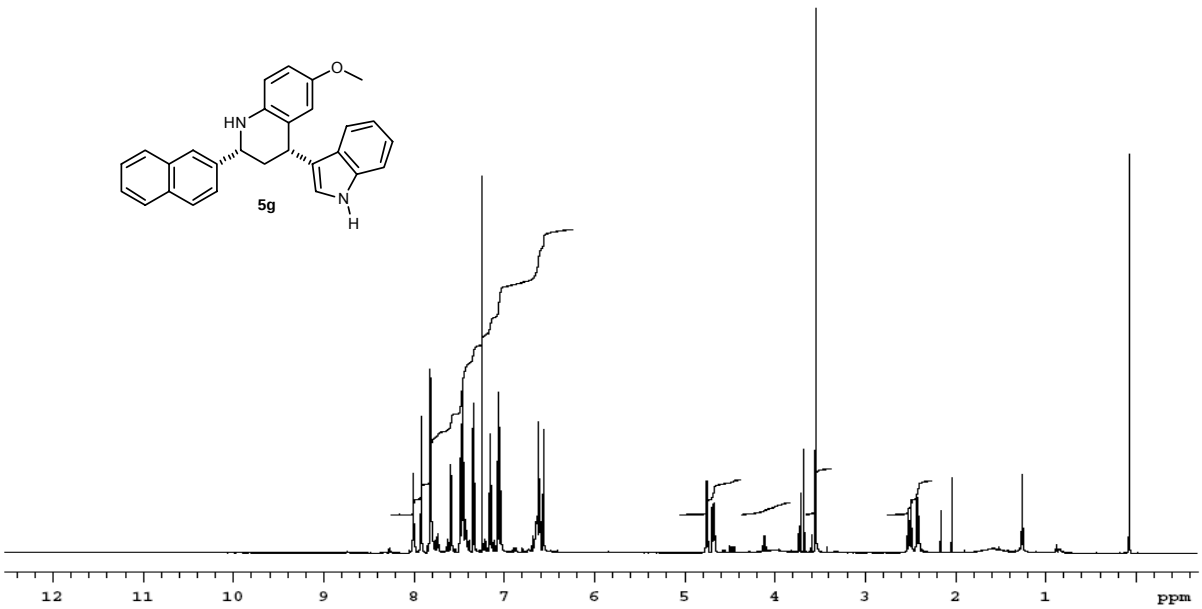
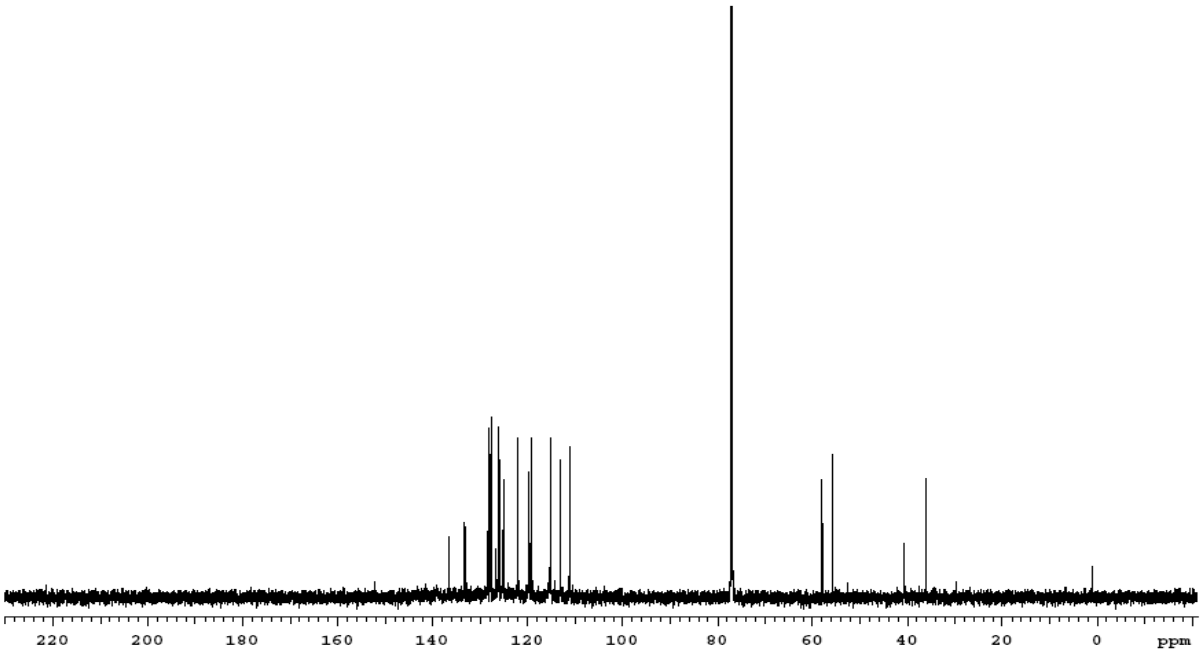
ppm


O
HN
N
H
5g
12
11
10
9
8
7
6
5
4
3
2
1
ppm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200
180
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120
100
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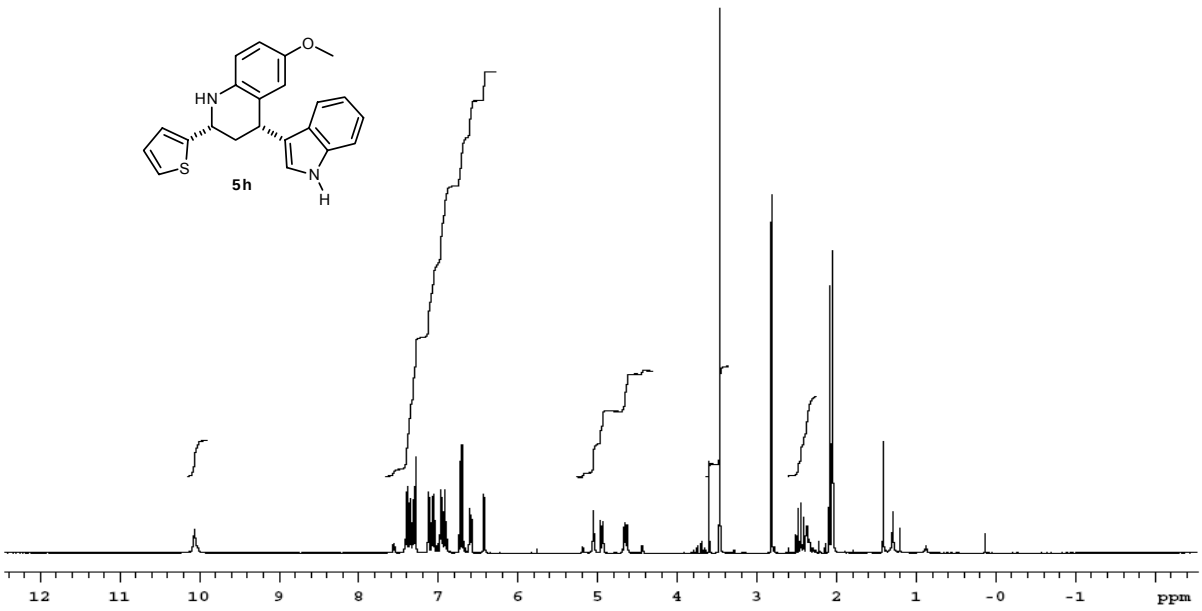
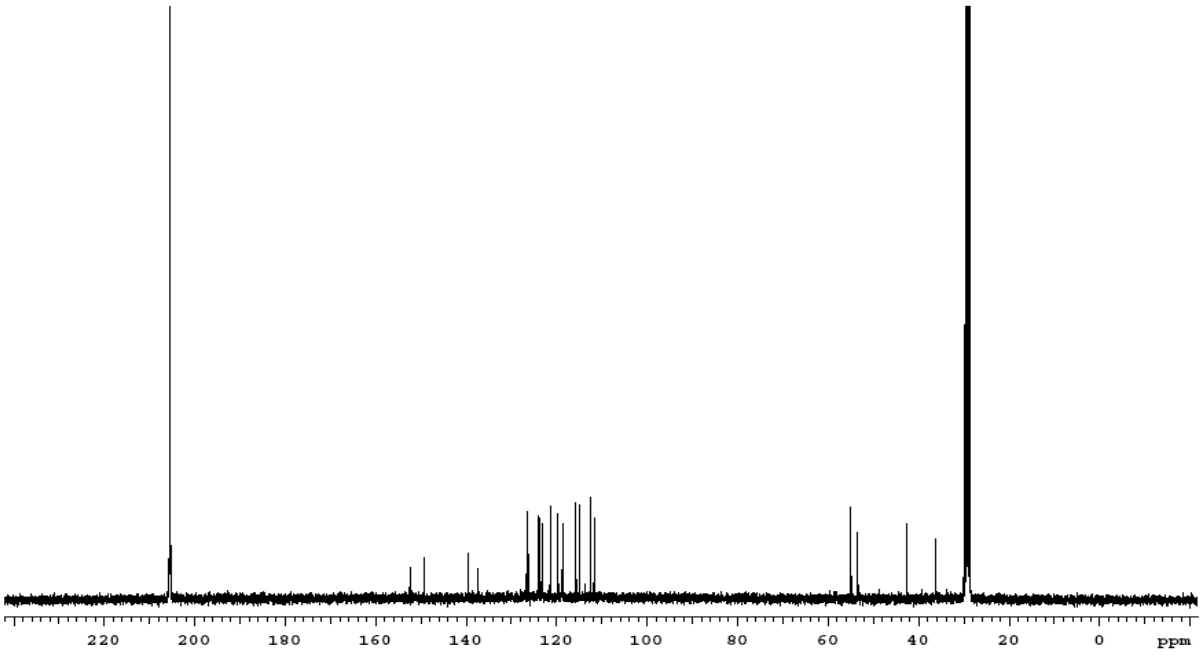
ppm


HN
O
S
N
H
5h
12
11
10
9
8
7
6
5
4
3
2
1
-0
-1
ppm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120
100
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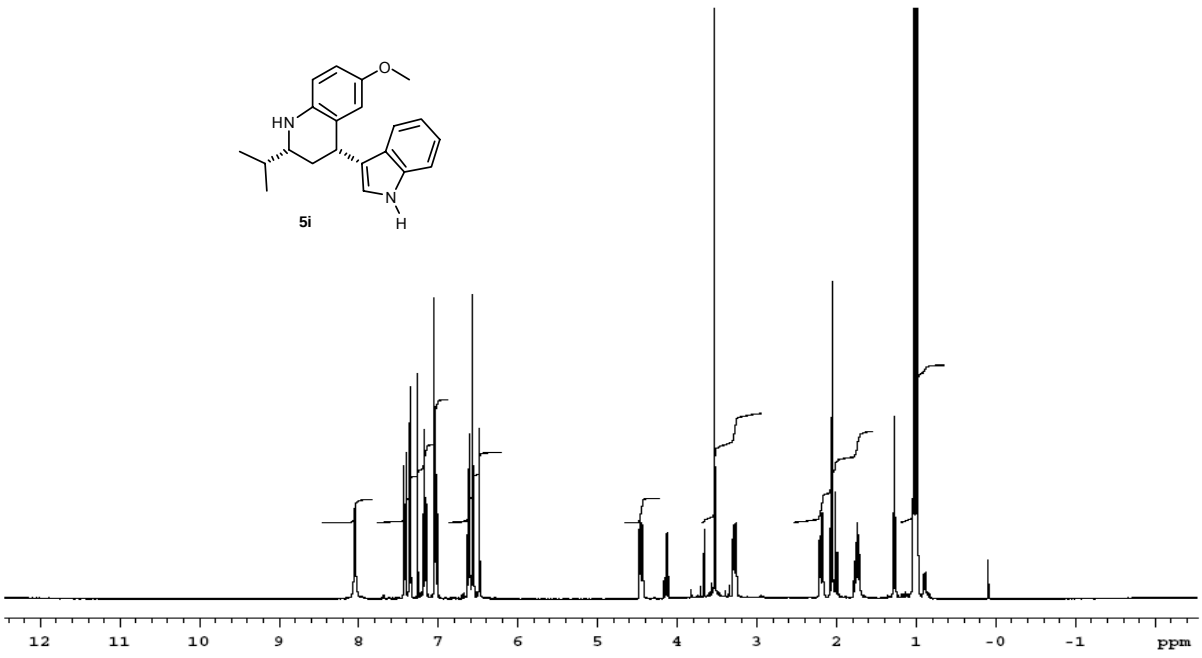
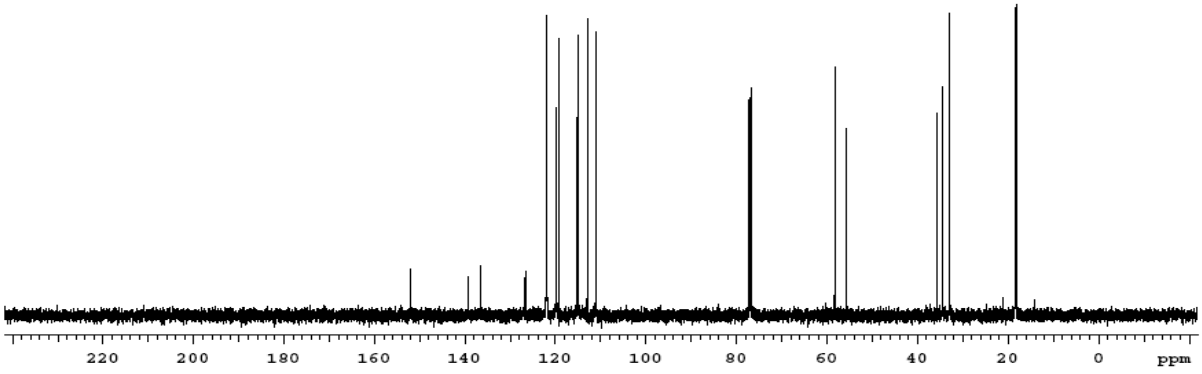

O
HN
N
H
12
11
10
9
8
7
6
5
4
3
2
1
-0
-1
ppm

5i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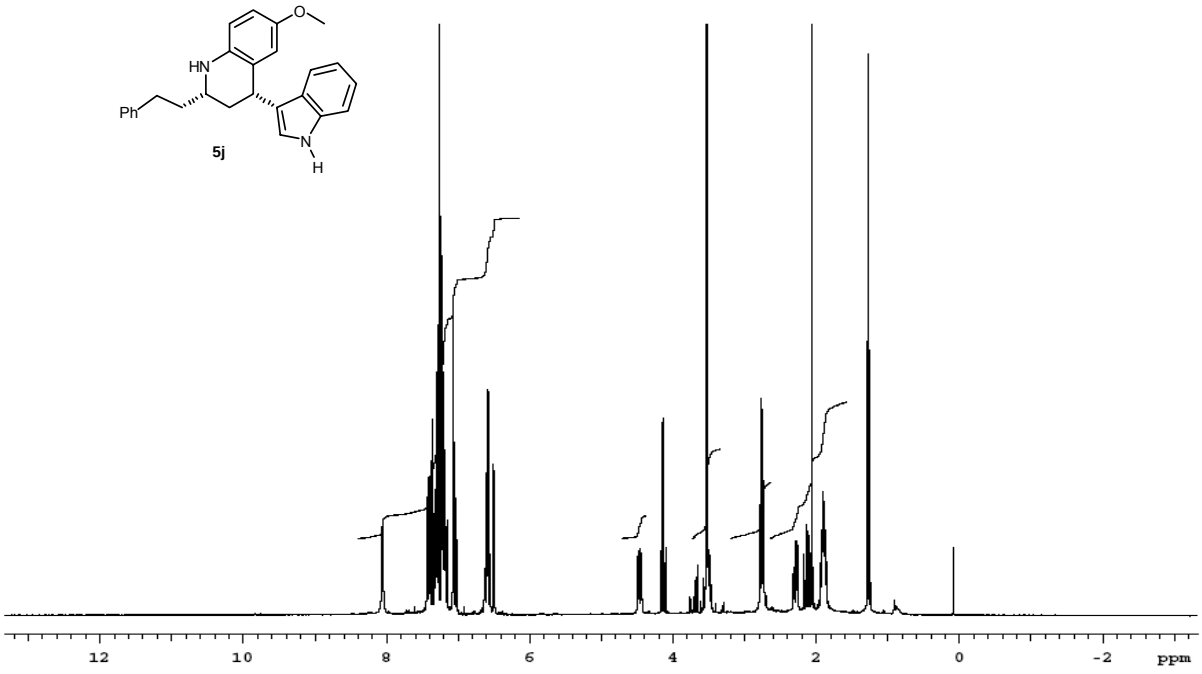
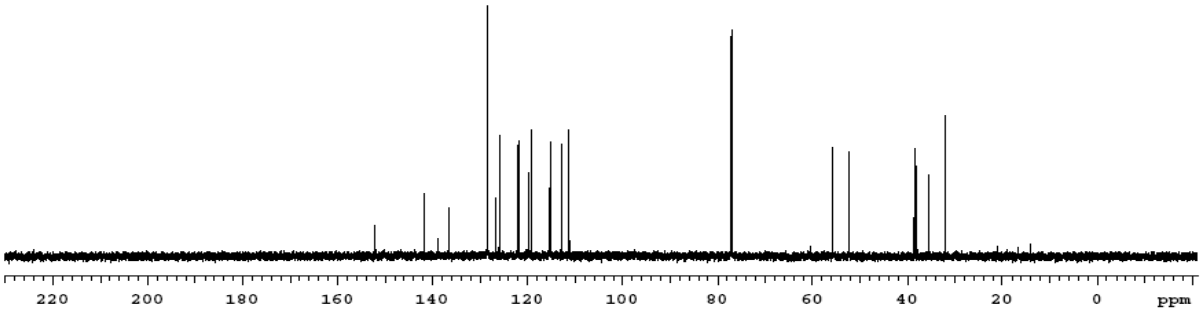
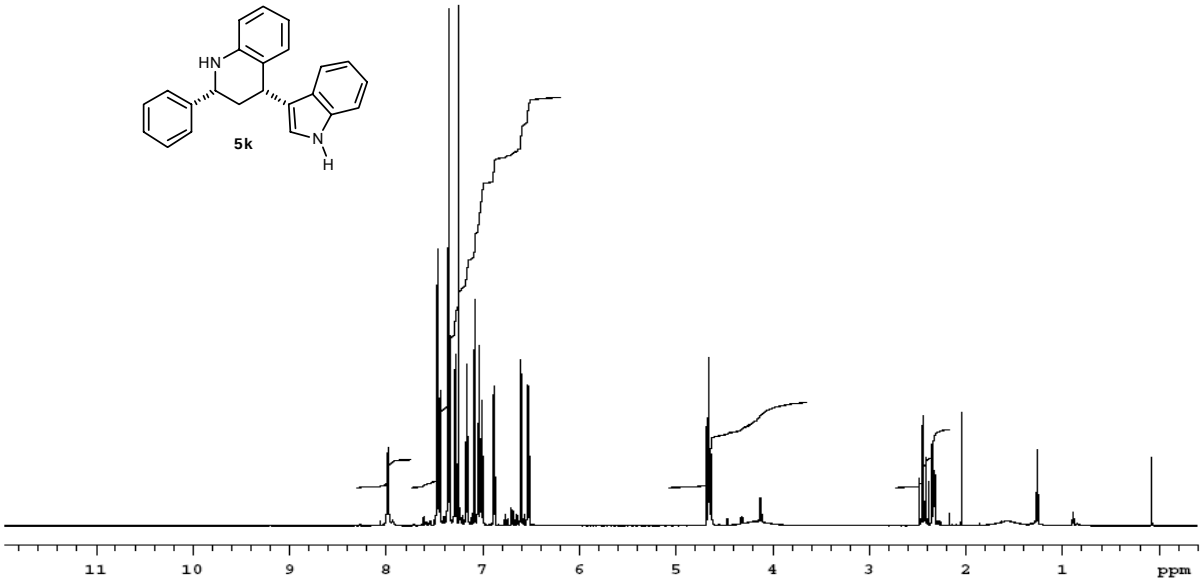
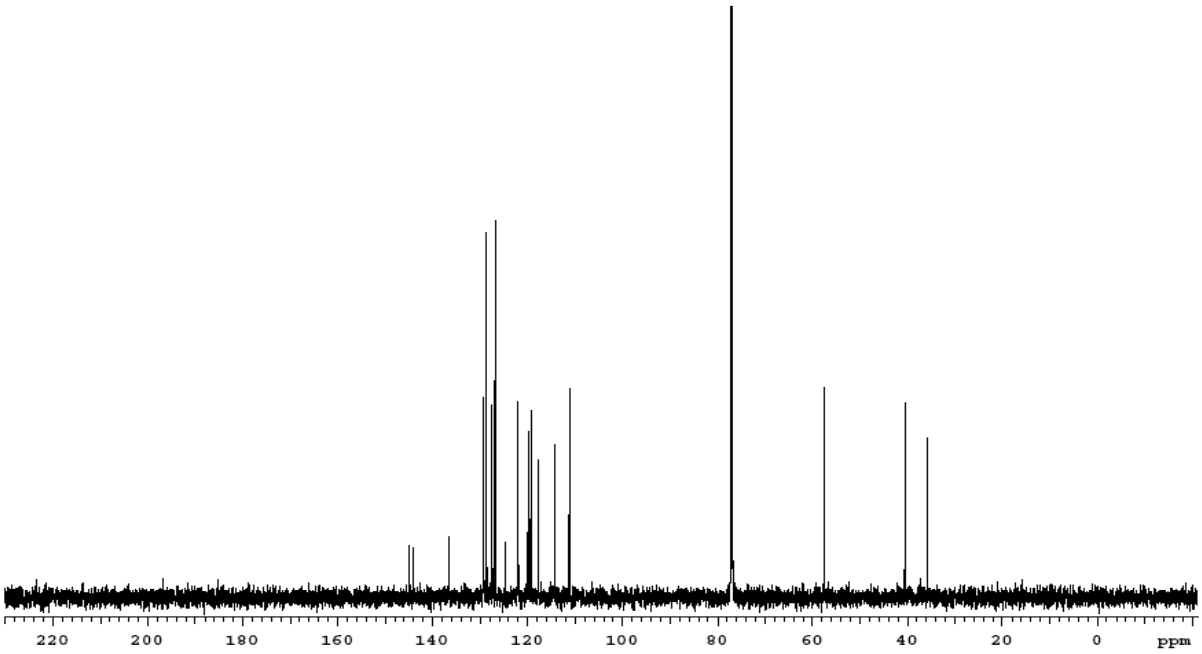
200
180
160
140
120
100
80
60
40
20
0
ppm

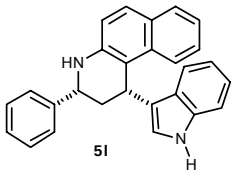

O
HN
Ph
N
H
12
10
8
6
4
2
0
-2
ppm

5j

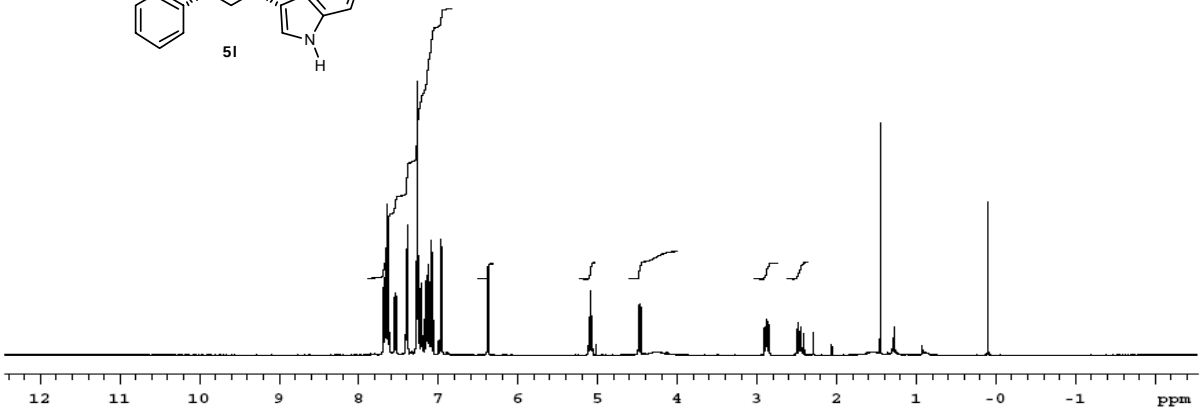

220
200
180
160
140
120
100
80
60
40
20
0
ppm

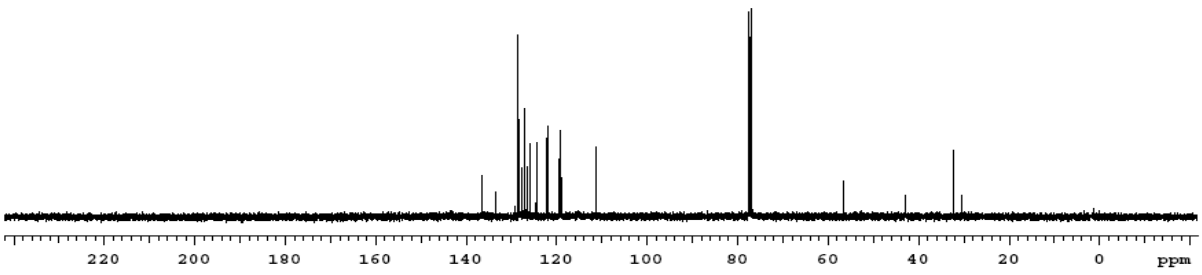

HN
N
H
5k
11
10
9
8
7
6
5
4
3
2
1
ppm

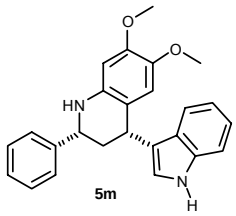

220
200
180
160
140
120
100
80
60
40
20
0
ppm


HN
N
H

5l

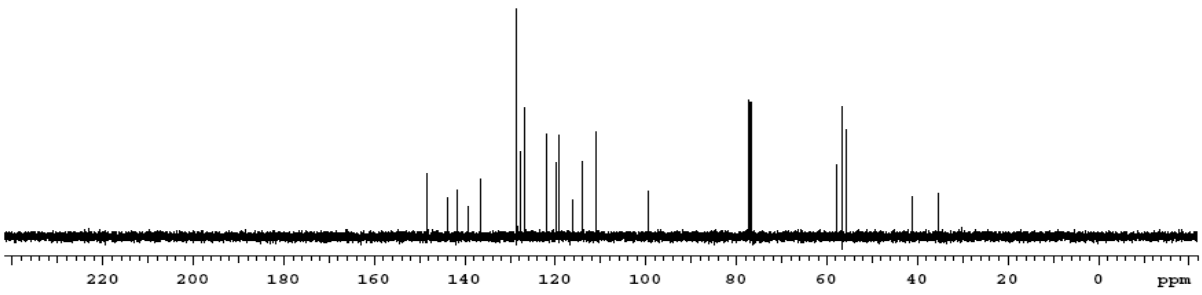

12
11
10
9
8
7
6
5
4
3
2
1
-0
-1
ppm

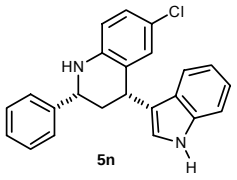

220
200
180
160
140
120
100
80
60
40
20
0
ppm


O
O
HN
N
H

5m

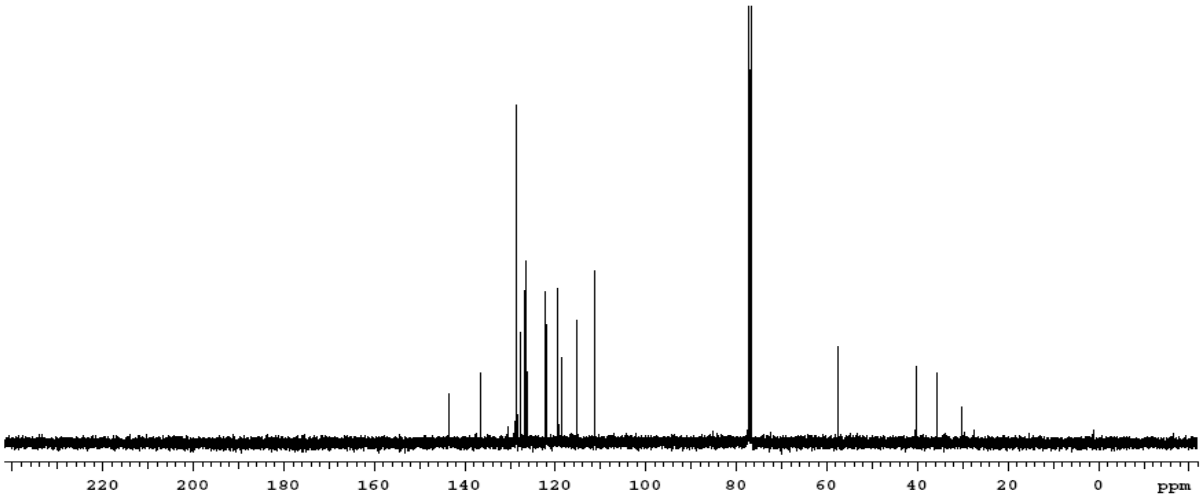
12
11
10
9
8
7
6
5
4
3
2
1
-0
-1
ppm

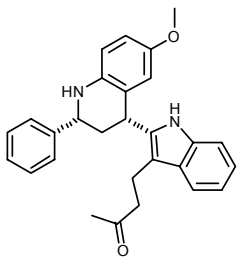

220
200
180
160
140
120
100
80
60
40
20
0
ppm


Cl
HN
N
H

5n

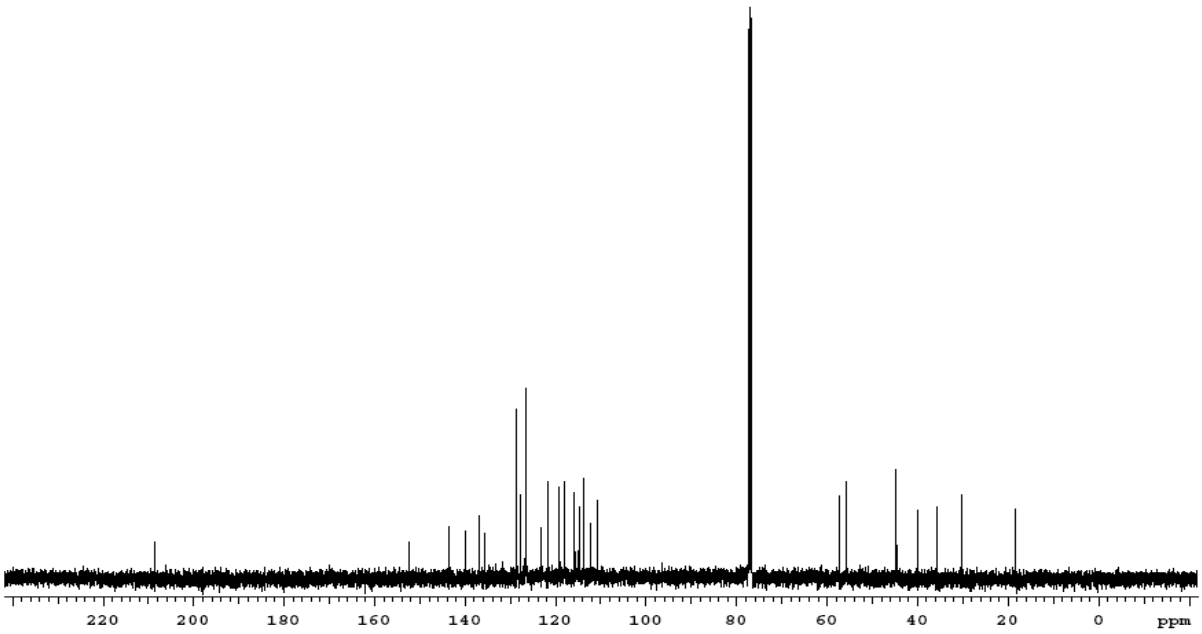
12
11
10
9
8
7
6
5
4
3
2
1
-0
-1
ppm

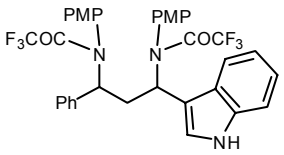

220
200
180
160
140
120
100
80
60
40
20
0
ppm


O
HN
H
N
O

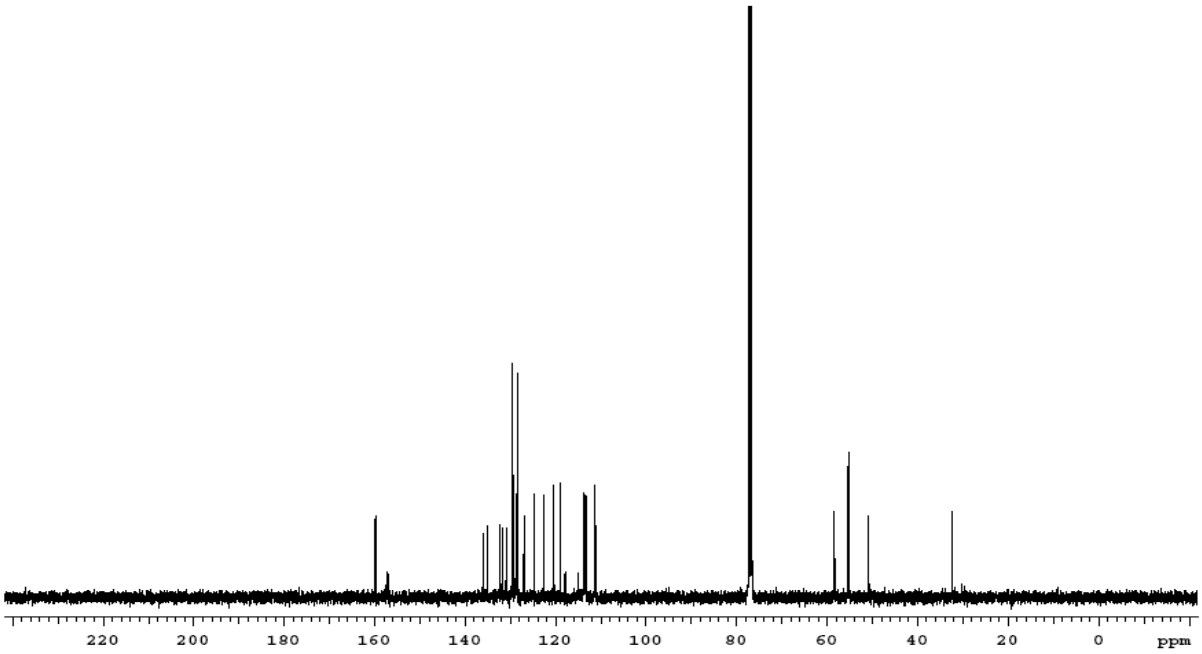
6

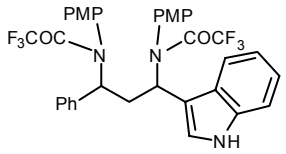
12
11
10
9
8
7
6
5
4
3
2
1
-0
-1
ppm


220
200
180
160
140
120
100
80
60
40
20
0
ppm

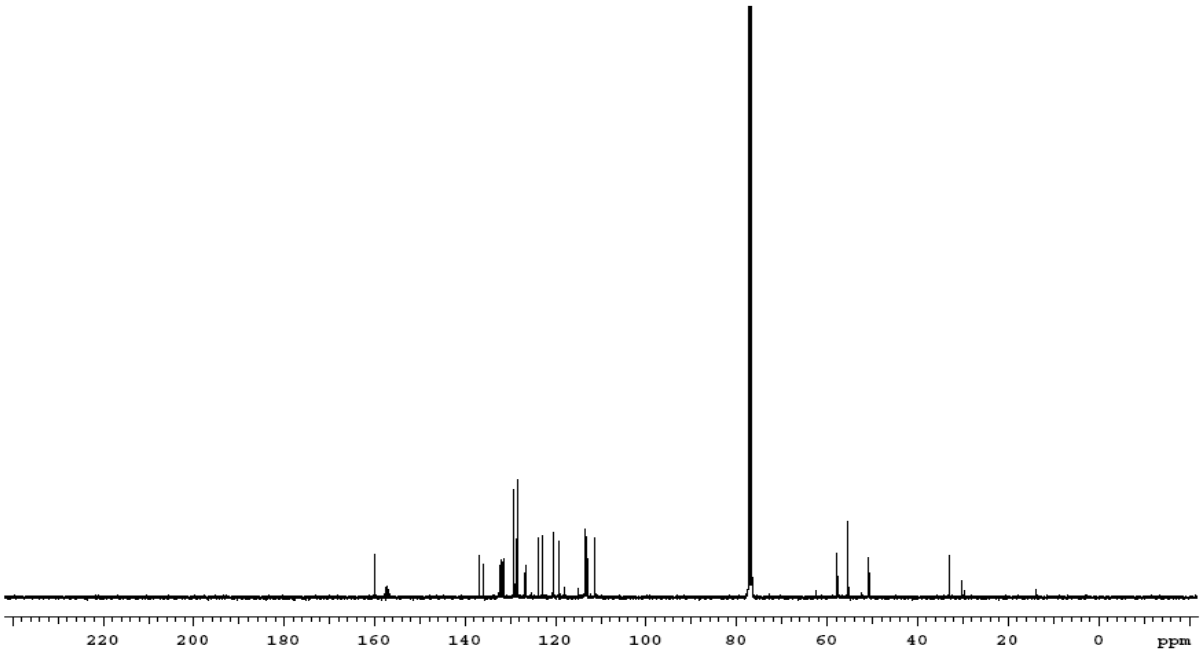


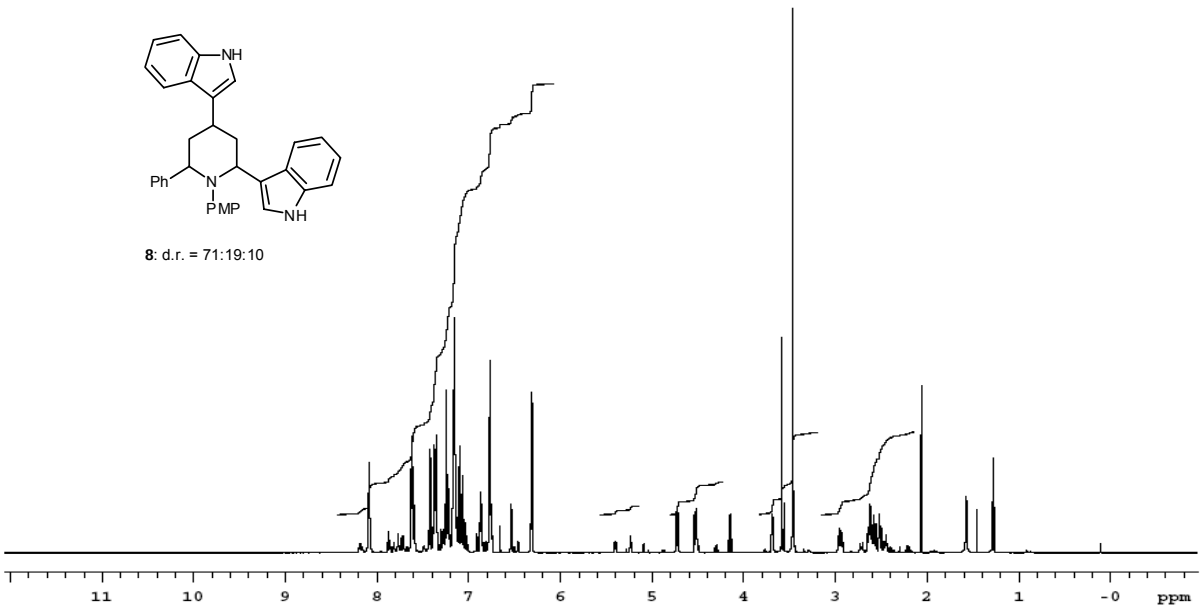
7: diastereoisomer (A)



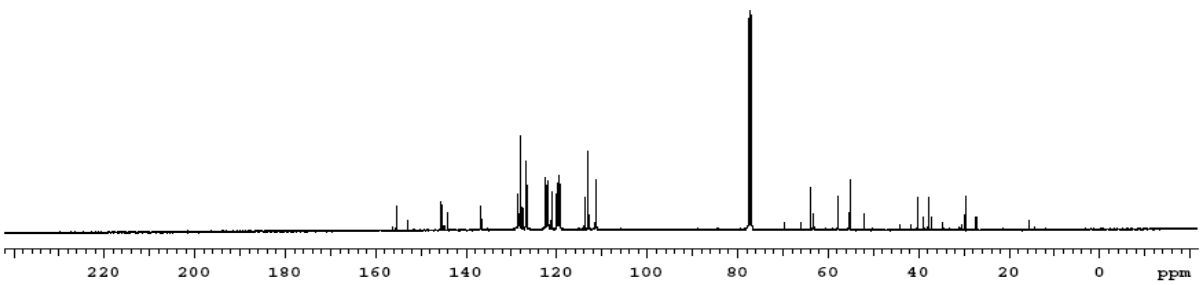


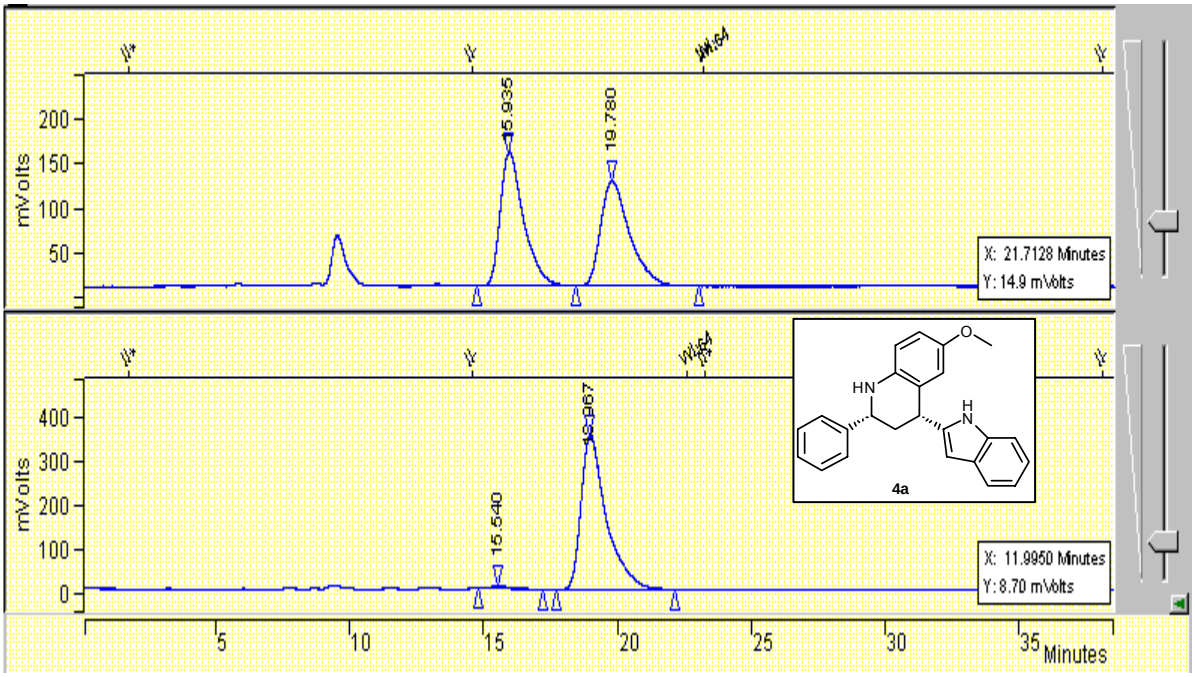
7: diastereoisomer (B)

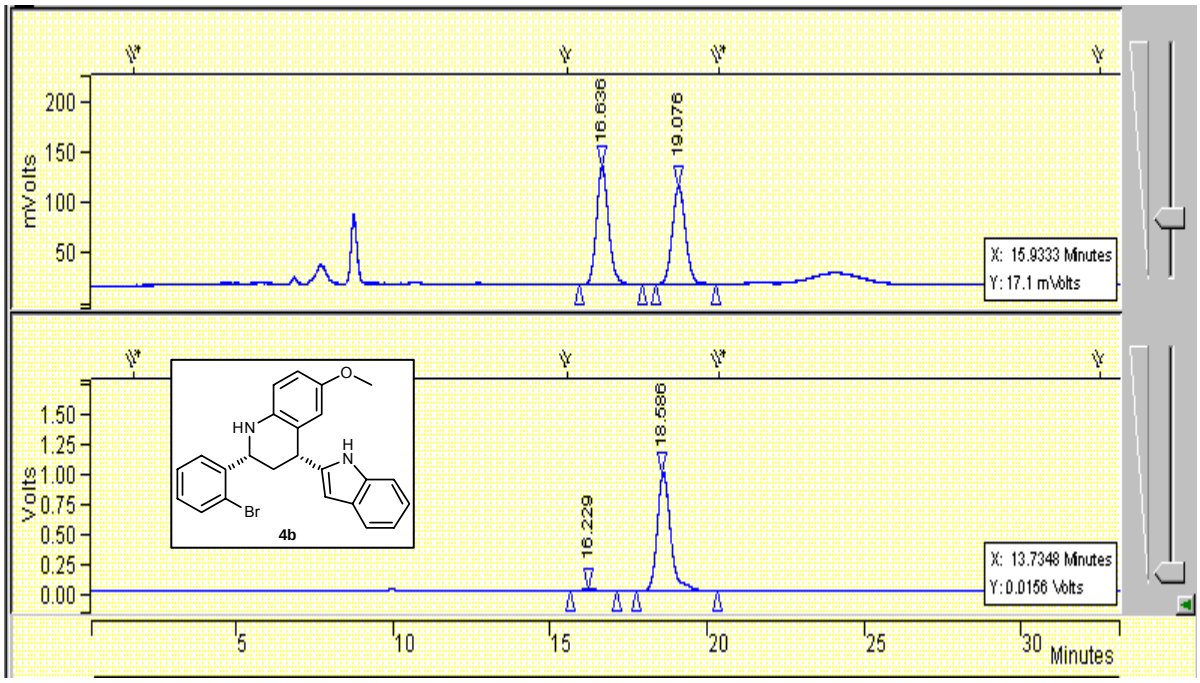


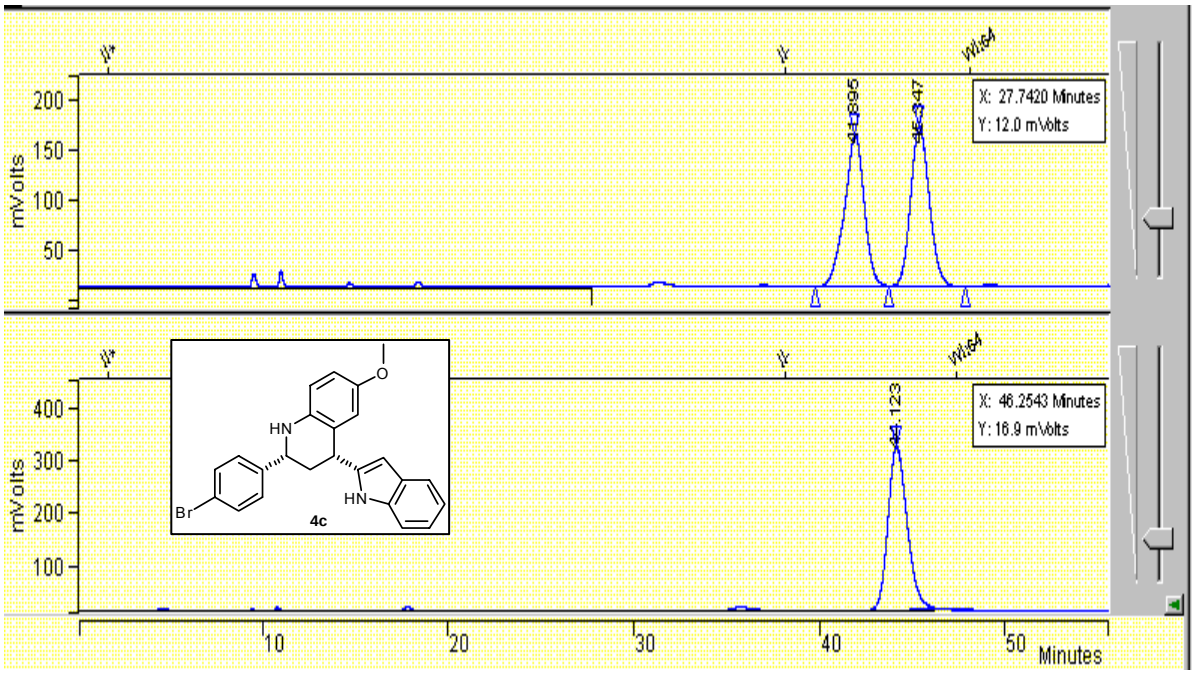

NH
Ph
N
PMP
NH
11
10
9
8
7
6
5
4
3
2
1
-0
ppm

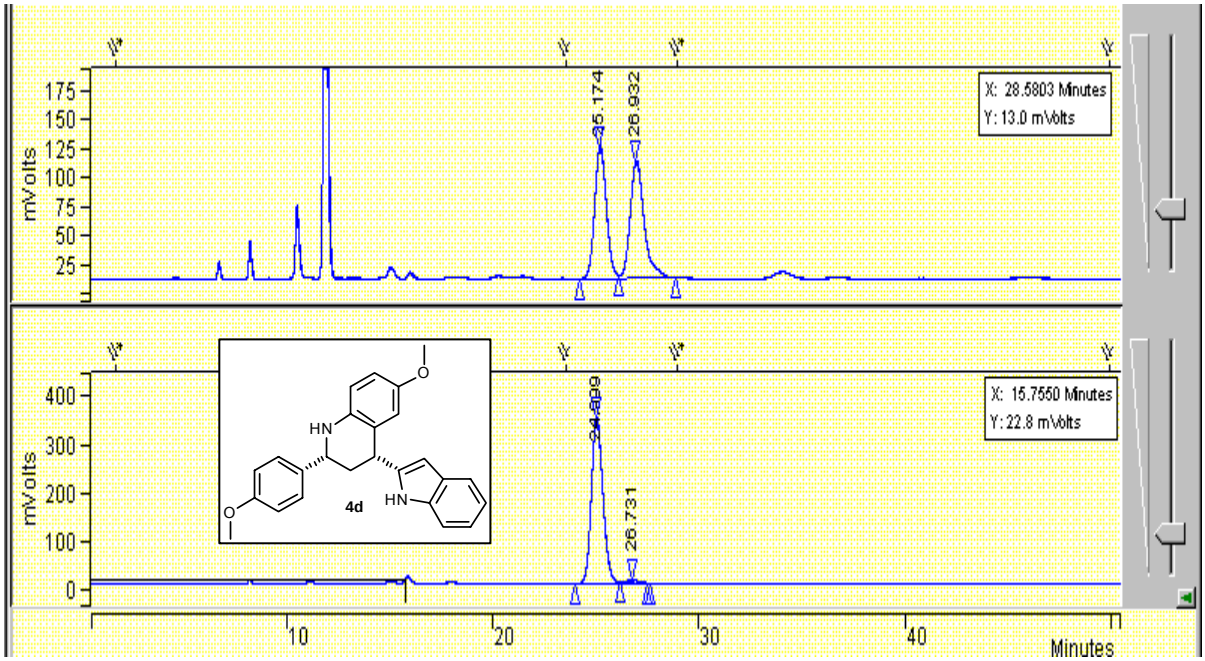
8: d.r. = 71:19:10

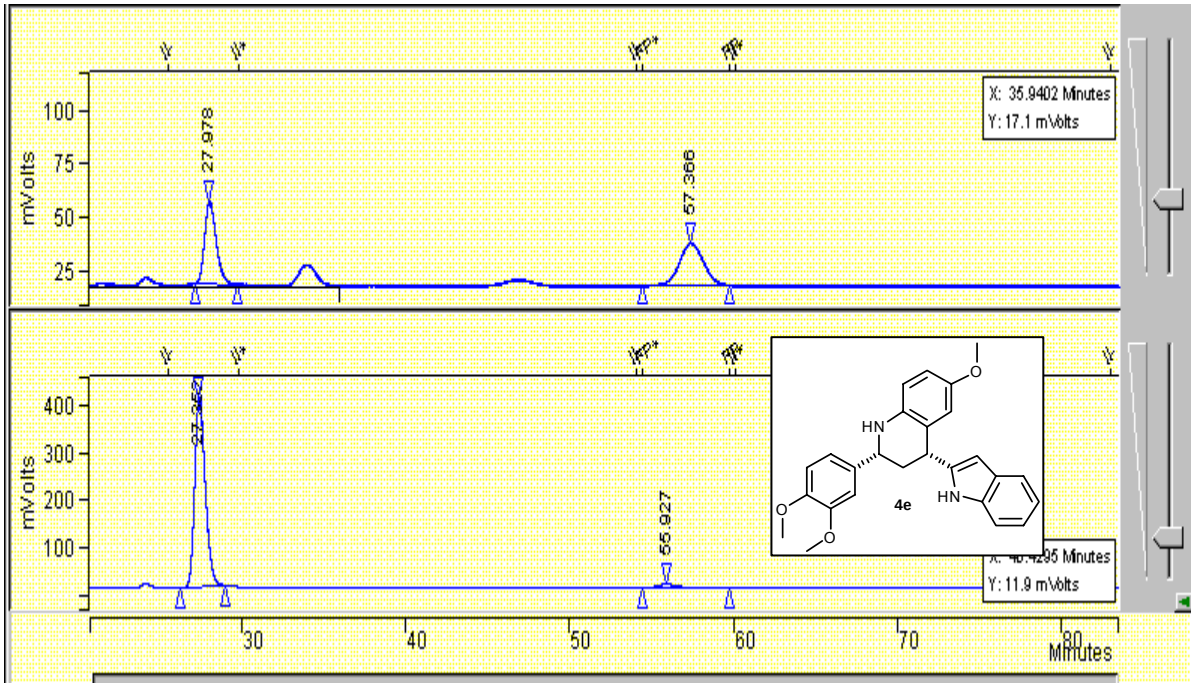

220
200
180
160
140
120
100
80
60
40
20
0
ppm

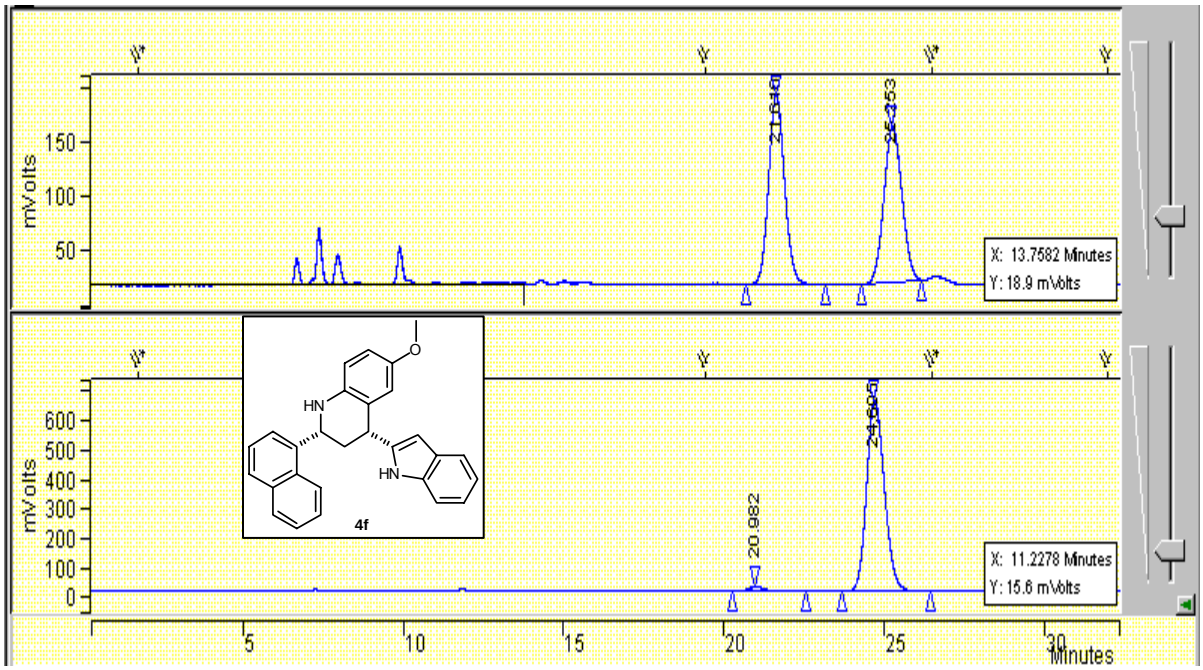

15.935
19.780
X: 21.7128 Minutes
Y: 14.9 mVolts
mVolts
200
150
100
50
15.540
16.967
X: 11.9950 Minutes
Y: 8.70 mVolts
400
300
200
100
0
HN
H
N
O
4a
5
10
15
20
25
30
35
Minutes

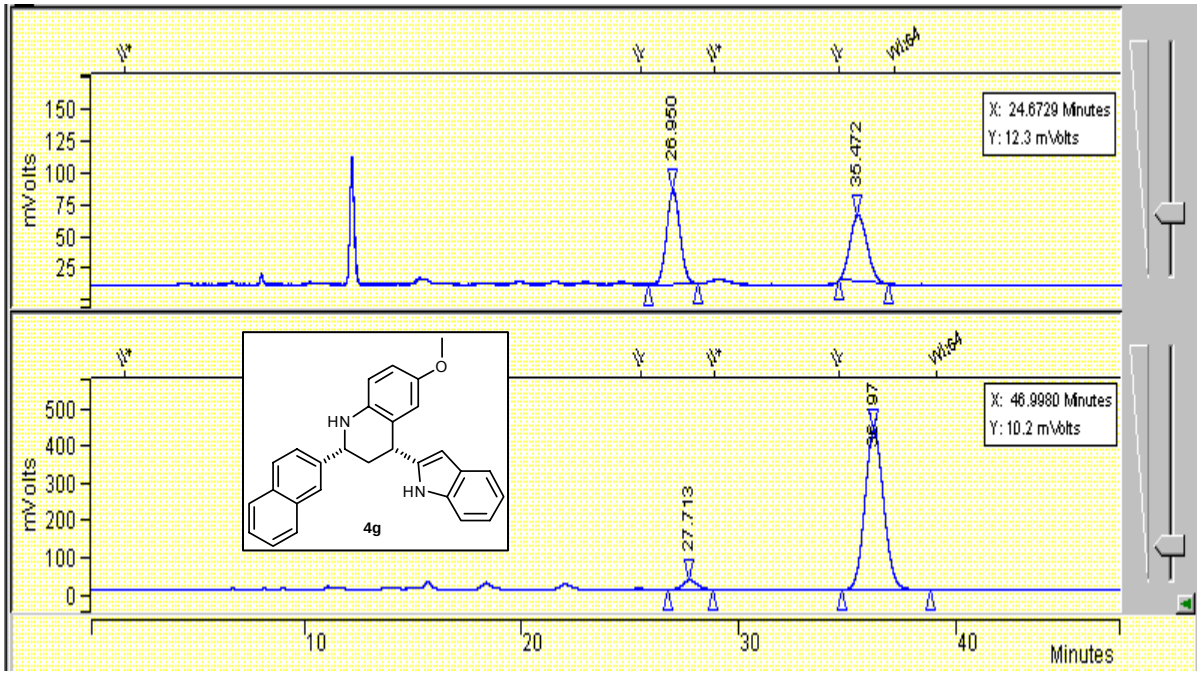

16.636
19.076
X: 15.9333 Minutes
Y: 17.1 mVolts
mVolts
200
150
100
50
16.229
18.586
X: 13.7348 Minutes
Y: 0.0156 Volts
Volts
1.50
1.25
1.00
0.75
0.50
0.25
0.00
HN
H
N
O
Br
4b
5
10
15
20
25
30
Minutes

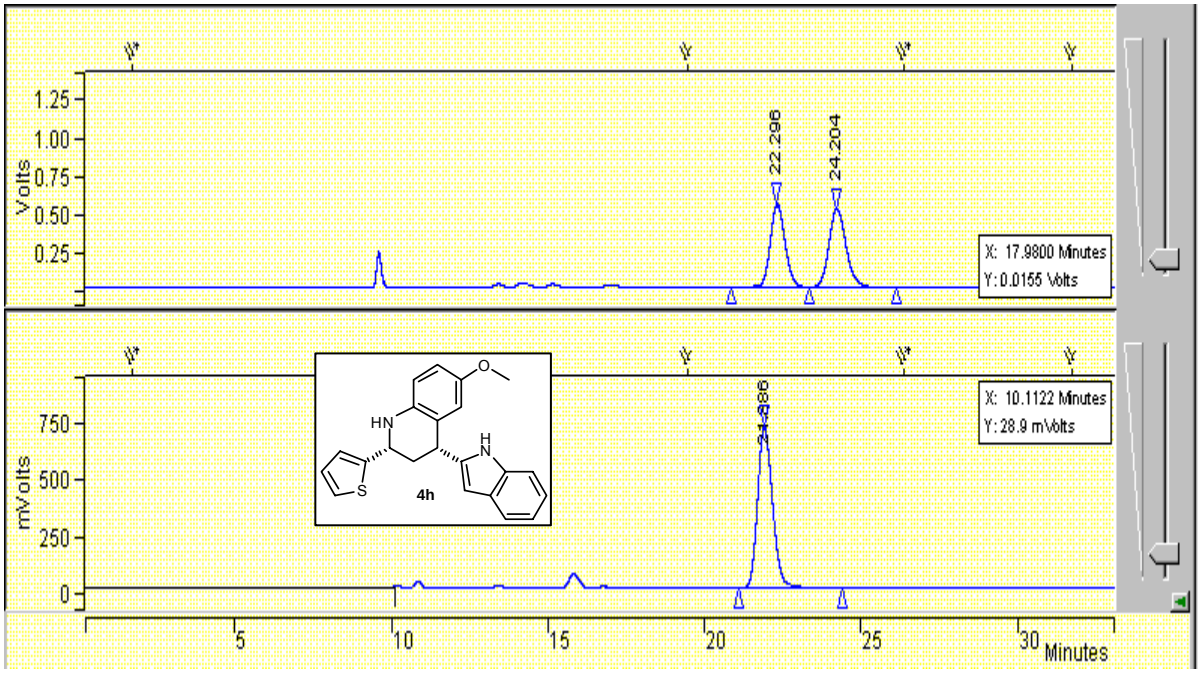

mVolts
200
150
100
50
X: 27.7420 Minutes
Y: 12.0 mVolts
mVolts
400
300
200
100
X: 46.2543 Minutes
Y: 16.9 mVolts
HN
HN
Br
O
4c
10
20
30
40
50
Minutes

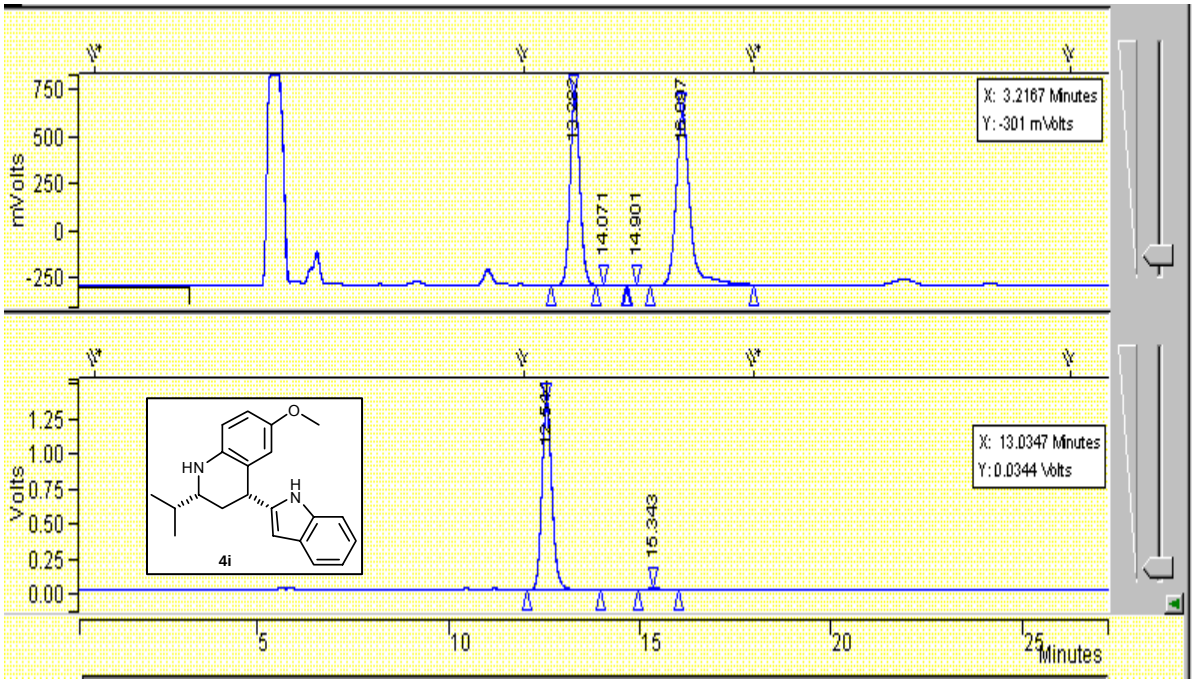

mVolts
175
150
125
100
75
50
25
X: 28.5803 Minutes
Y: 13.0 mVolts
25.174
26.932
mVolts
400
300
200
100
0
X: 15.7550 Minutes
Y: 22.8 mVolts
26.731
HN
HN
O
O
4d
10
20
30
40
Minutes

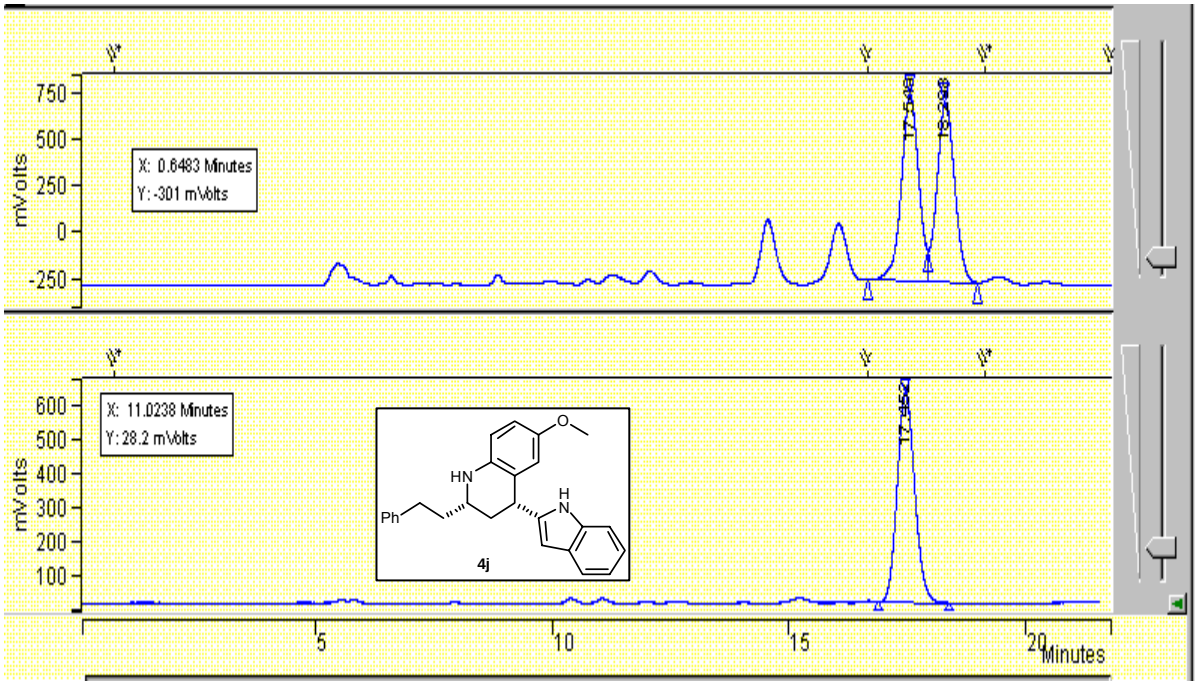

mVolts
100
75
50
25
27.978
57.366
X: 35.9402 Minutes
Y: 17.1 mVolts
mVolts
400
300
200
100
55.927
4e
HN
HN
O
O
O
Y: 11.9 mVolts
30
40
50
60
70
80
Minutes

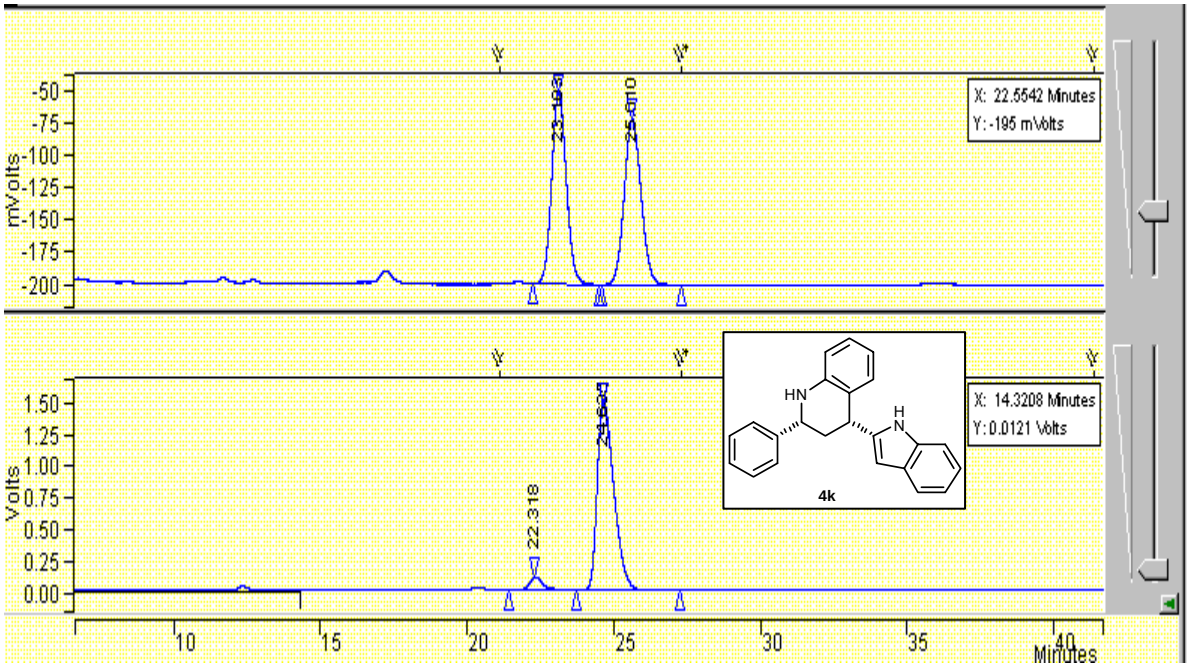

mVolts
150
100
50
X: 13.7582 Minutes
Y: 18.9 mVolts
mVolts
600
500
400
300
200
100
0
20.982
4f
HN
HN
O
X: 11.2278 Minutes
Y: 15.6 mVolts
5
10
15
20
25
30
Minutes

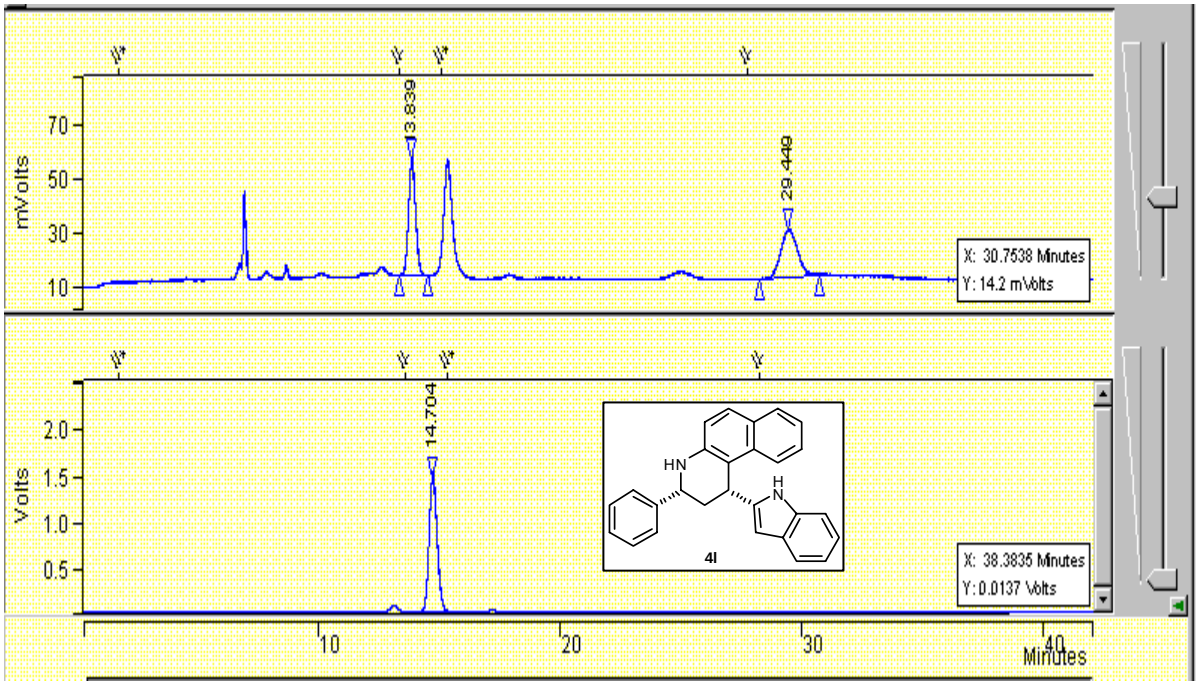

mVolts
150
125
100
75
50
25
26.950
35.472
X: 24.6729 Minutes
Y: 12.3 mVolts
mVolts
500
400
300
200
100
0
27.713
36.197
X: 46.9980 Minutes
Y: 10.2 mVolts
HN
HN
O
4g
10
20
30
40
Minutes

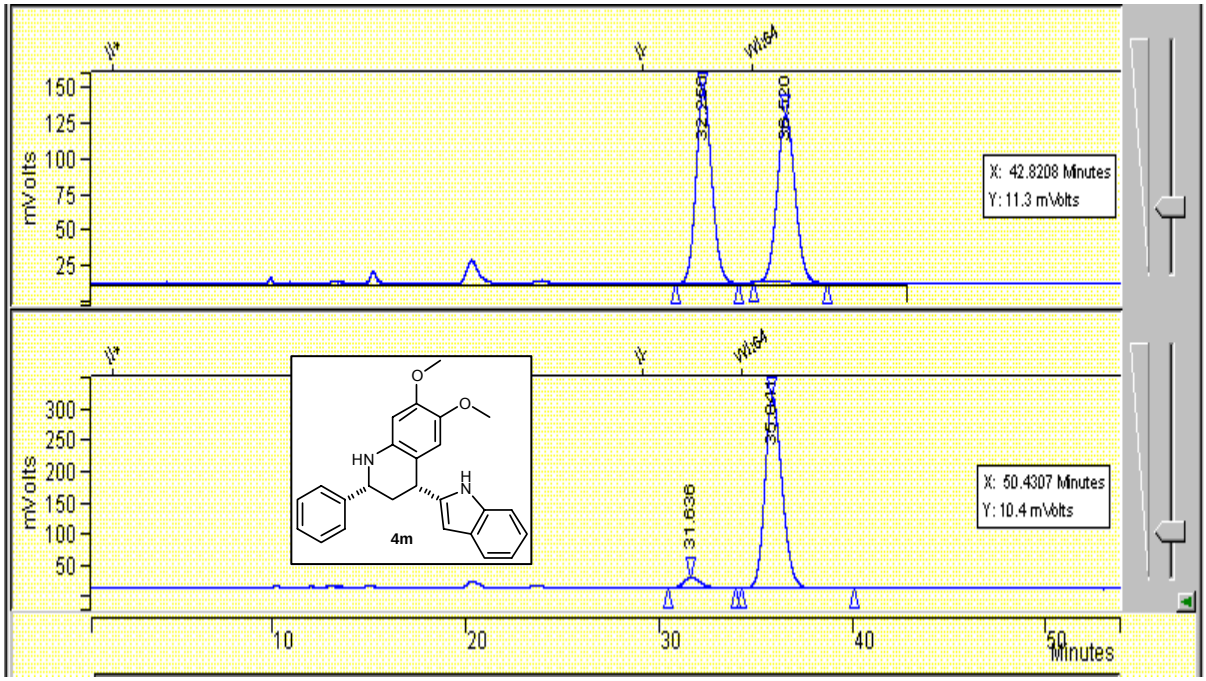

Volts
1.25
1.00
0.75
0.50
0.25
22.296
24.204
X: 17.9800 Minutes
Y: 0.0155 Volts
mVolts
750
500
250
0
24.886
X: 10.1122 Minutes
Y: 28.9 mVolts
HN
H
N
S
O
4h
5
10
15
20
25
30
Minutes

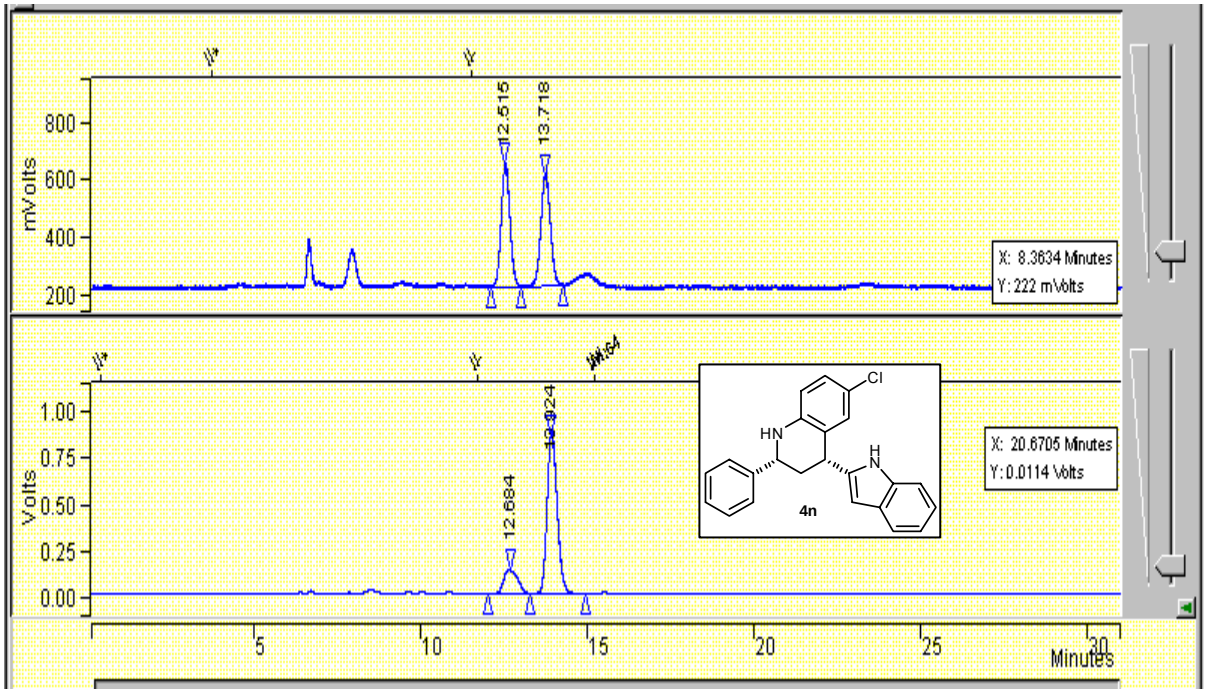

mVolts
750
500
250
0
-250
14.071
14.901
X: 3.2167 Minutes
Y: -301 mVolts
Volts
1.25
1.00
0.75
0.50
0.25
0.00
15.343
X: 13.0347 Minutes
Y: 0.0344 Volts
HN
H
O
4i
5
10
15
20
25
Minutes

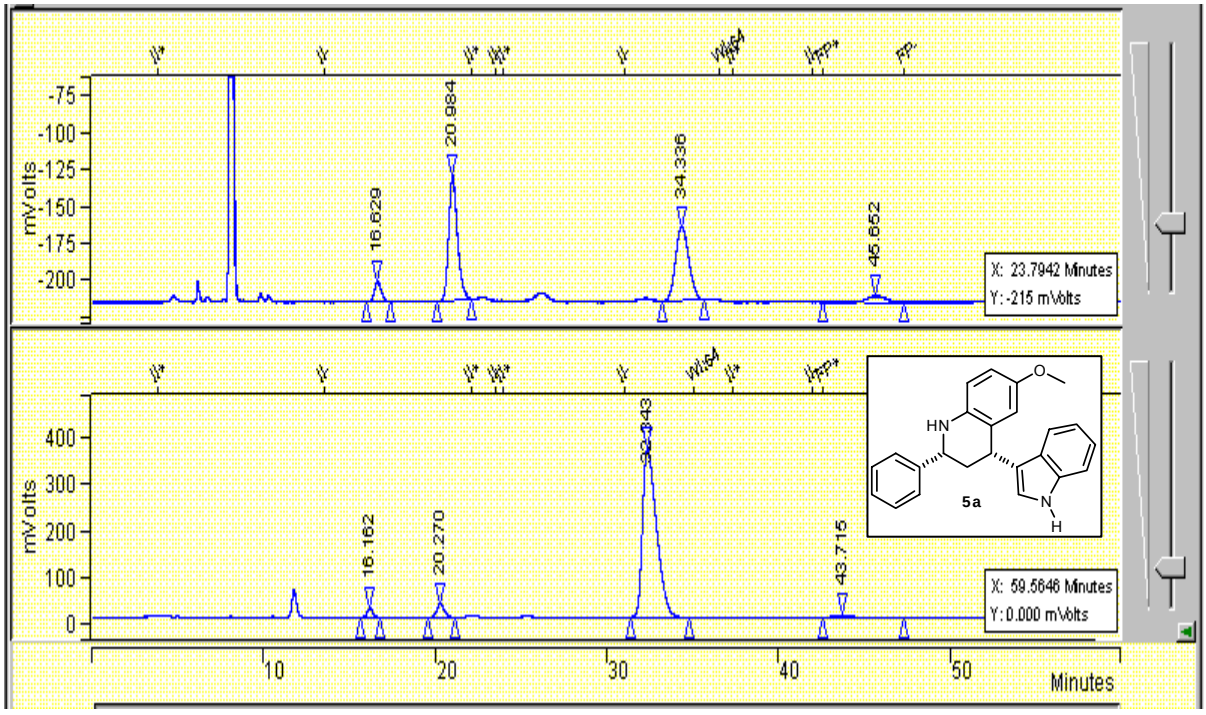

mVolts
750
500
250
0
-250
X: 0.6483 Minutes
Y: -301 mVolts
600
500
400
300
200
100
X: 11.0238 Minutes
Y: 28.2 mVolts
HN
H
O
Ph
4j
5
10
15
20
Minutes

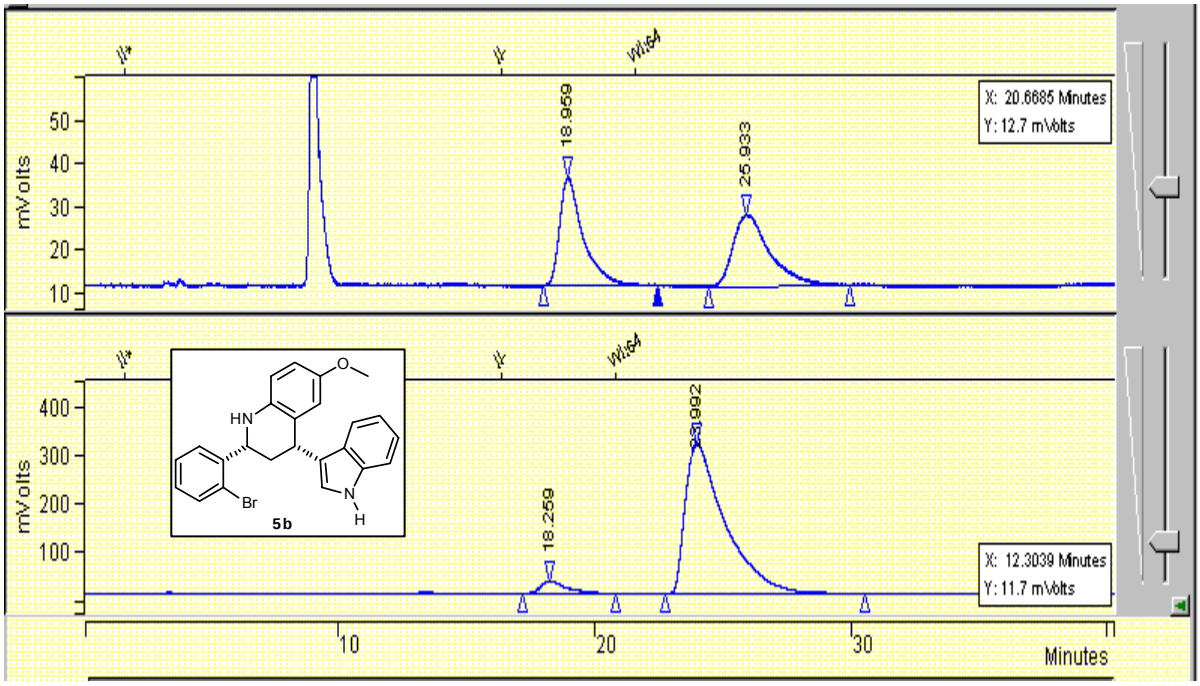

mVolts
-50
-75
-100
-125
-150
-175
-200
X: 22.5542 Minutes
Y: -195 mVolts
Volts
1.50
1.25
1.00
0.75
0.50
0.25
0.00
22.318
X: 14.3208 Minutes
Y: 0.0121 Volts
HN
H
N
4k
10
15
20
25
30
35
40
Minutes

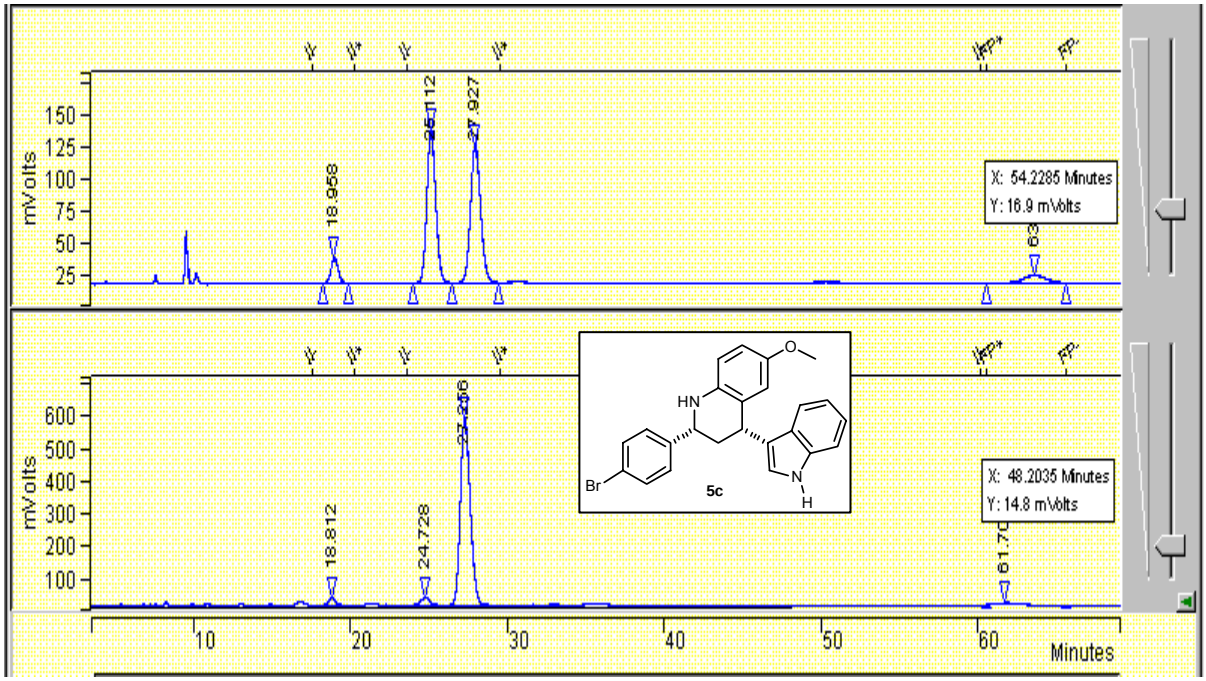

mVolts
70
50
30
10
13.839
29.449
X: 30.7538 Minutes
Y: 14.2 mVolts
Volts
2.0
1.5
1.0
0.5
14.704
HN
H
4l
X: 38.3835 Minutes
Y: 0.0137 Volts
10
20
30
40
Minutes

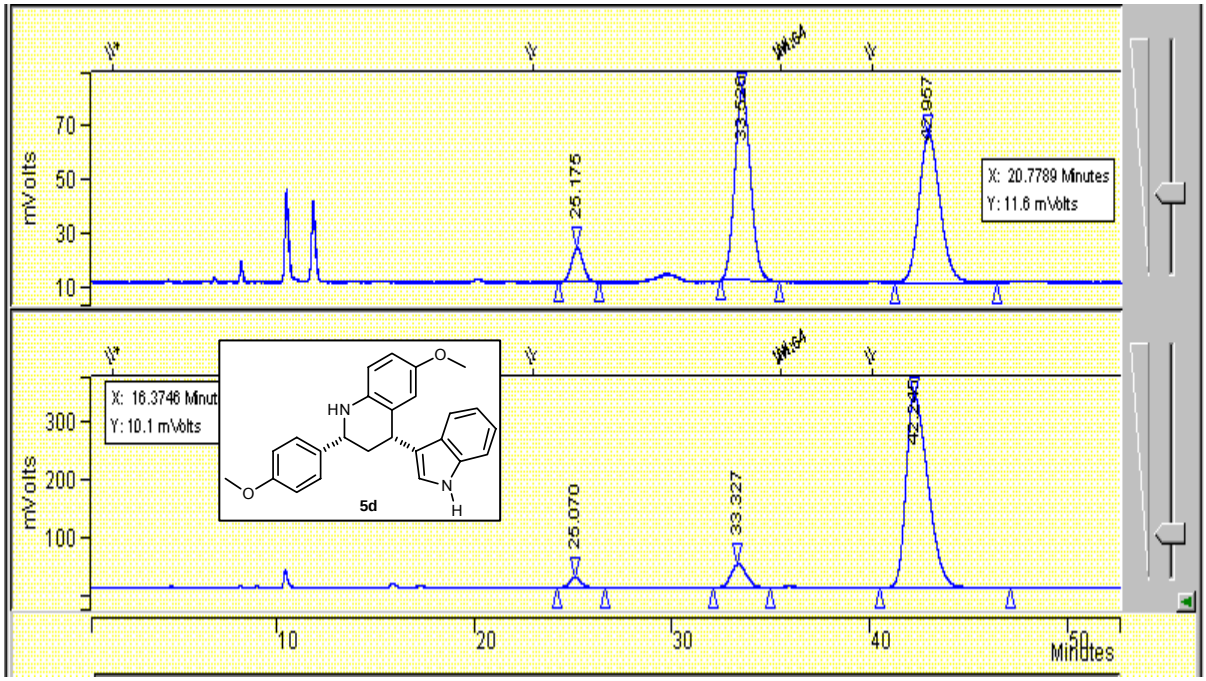

mVolts
X: 42.8208 Minutes
Y: 11.3 mVolts
4m
31.636
X: 50.4307 Minutes
Y: 10.4 mVolts
Minutes

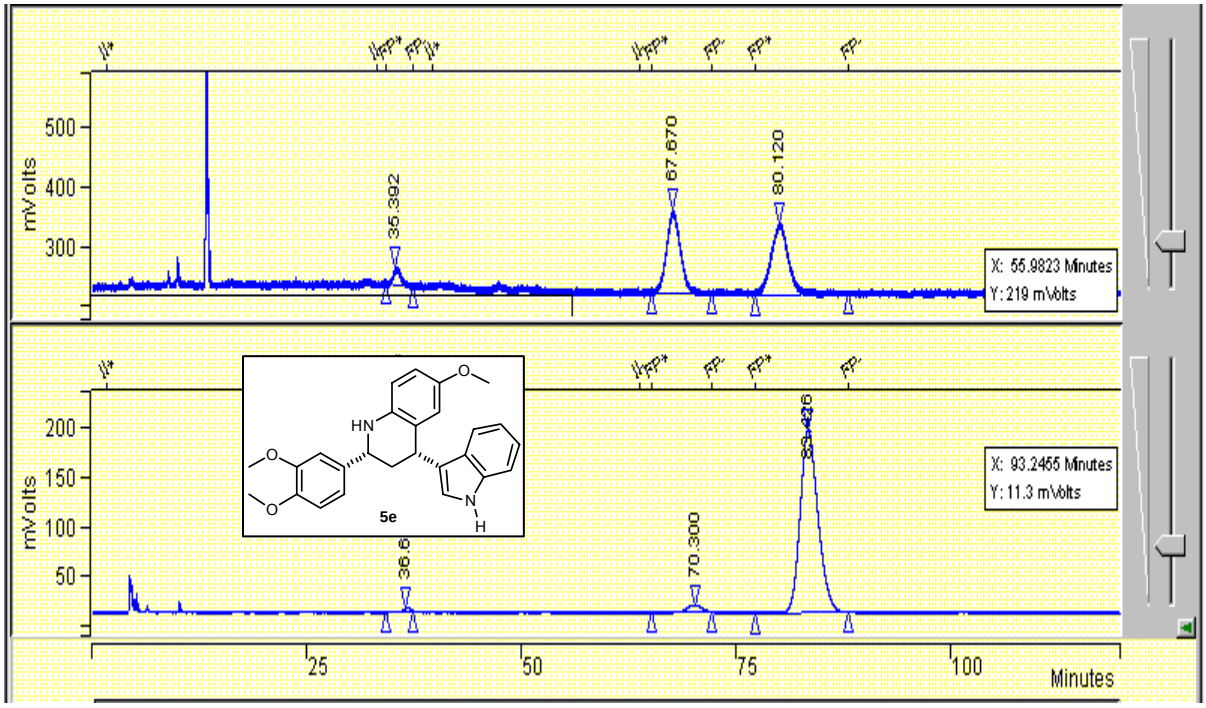

mVolts
12.515
13.718
X: 8.3634 Minutes
Y: 222 mVolts
Volts
12.684
X: 20.6705 Minutes
Y: 0.0114 Volts
4n
Minutes

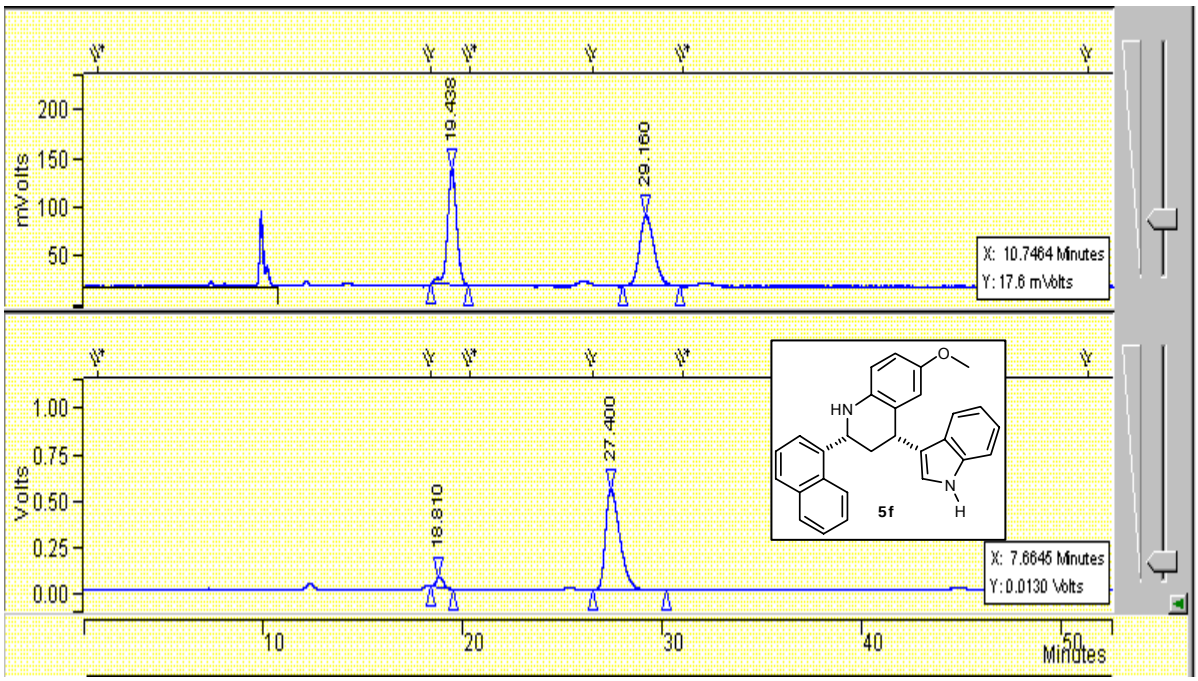

mVolts
-75
-100
-125
-150
-175
-200
16.629
20.984
34.336
46.652
X: 23.7942 Minutes
Y: -215 mVolts
mVolts
400
300
200
100
0
16.162
20.270
30.343
43.715
X: 59.5646 Minutes
Y: 0.000 mVolts
HN
O
N
H
5a
10
20
30
40
50
Minutes

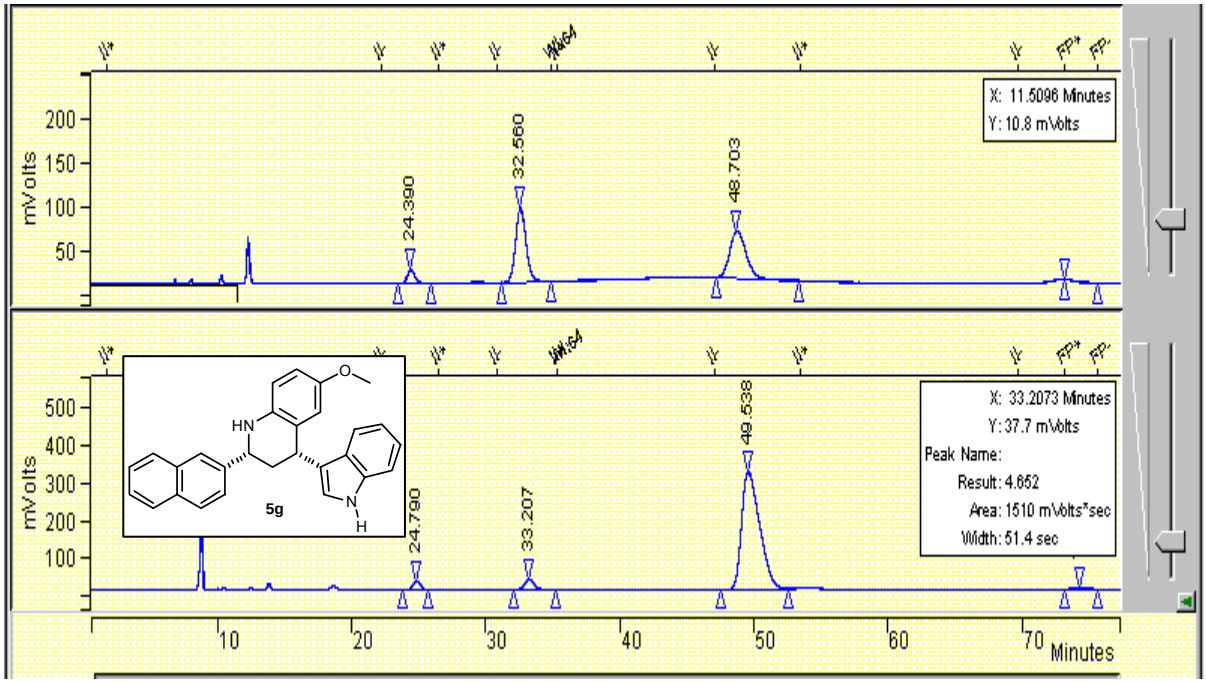

mVolts
50
40
30
20
10
18.959
25.933
X: 20.6685 Minutes
Y: 12.7 mVolts
mVolts
400
300
200
100
18.259
33.992
X: 12.3039 Minutes
Y: 11.7 mVolts
HN
O
N
H
Br
5b
10
20
30
Minutes

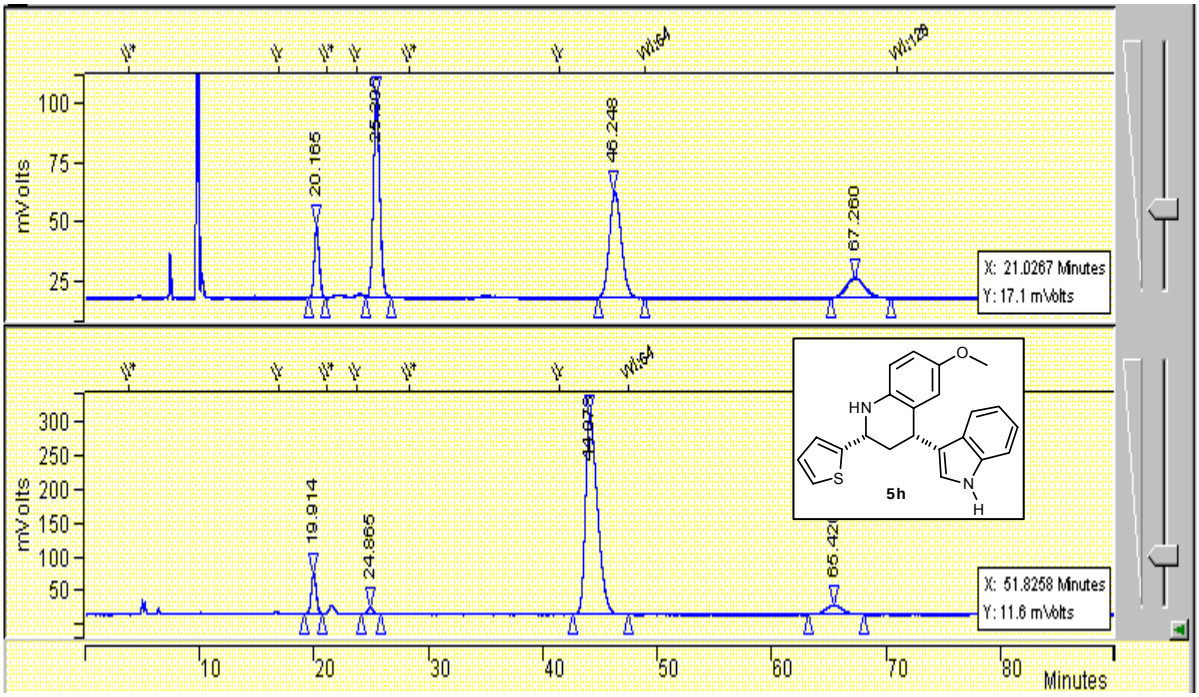

mVolts
150
125
100
75
50
25
18.958
25.112
27.927
X: 54.2285 Minutes
Y: 16.9 mVolts
63
mVolts
600
500
400
300
200
100
18.812
24.728
27.256
X: 48.2035 Minutes
Y: 14.8 mVolts
61.70
HN
O
Br
N
H
5c
10
20
30
40
50
60
Minutes

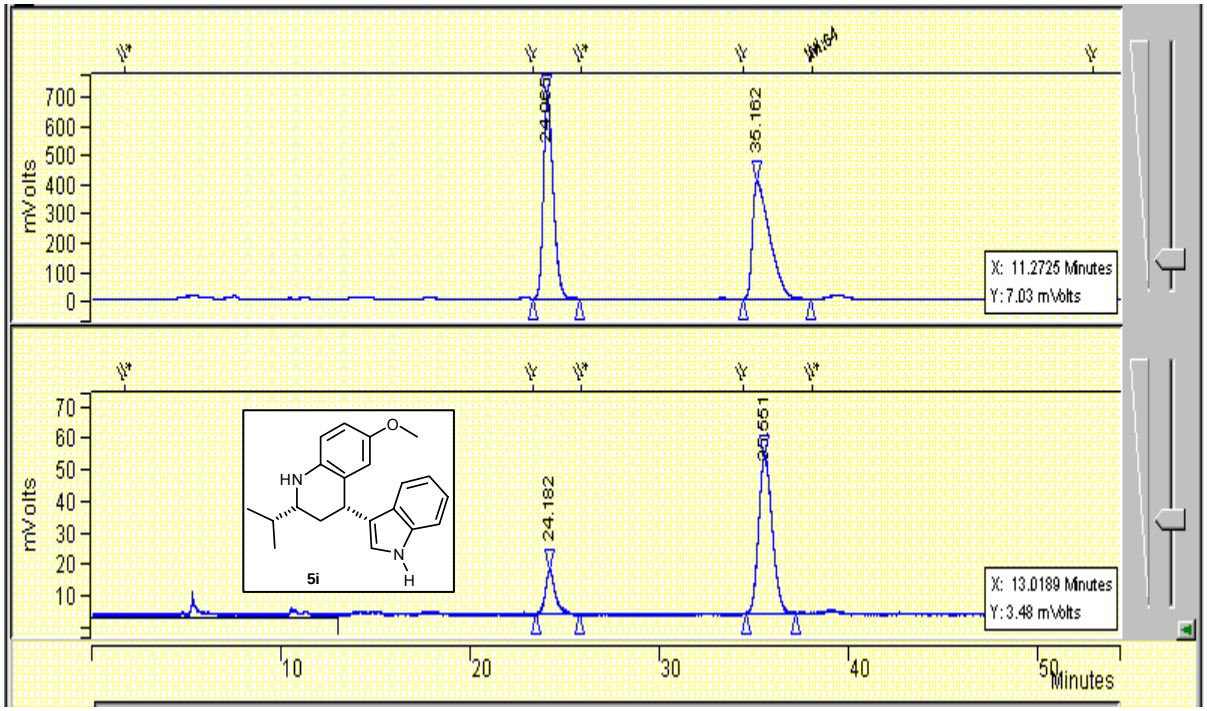

mVolts
70
50
30
10
25.175
33.524
42.957
X: 20.7789 Minutes
Y: 11.6 mVolts
X: 16.3746 Minut
Y: 10.1 mVolts
mVolts
300
200
100
HN
O
O
N
H
5d
25.070
33.327
42.246
10
20
30
40
50
Minutes

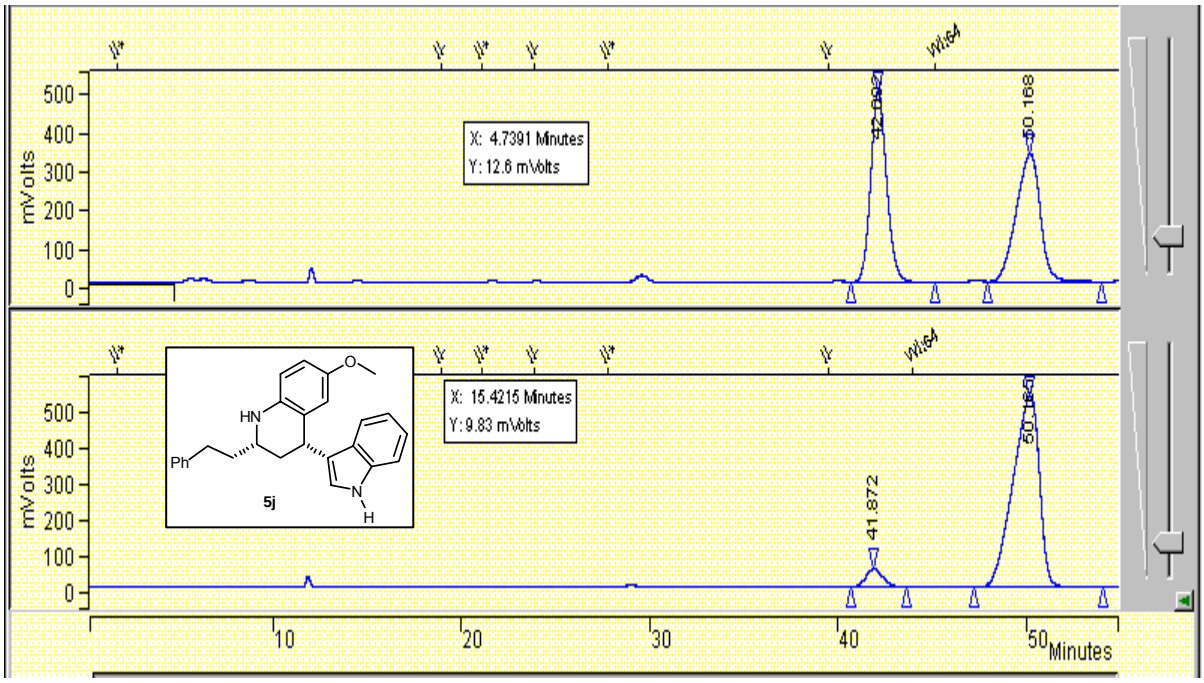

mVolts
500
400
300
35.392
67.670
80.120
X: 55.9823 Minutes
Y: 219 mVolts
mVolts
200
150
100
50
36.6
70.300
83.426
X: 93.2455 Minutes
Y: 11.3 mVolts
HN
O
O
O
N
H
5e
25
50
75
100
Minutes

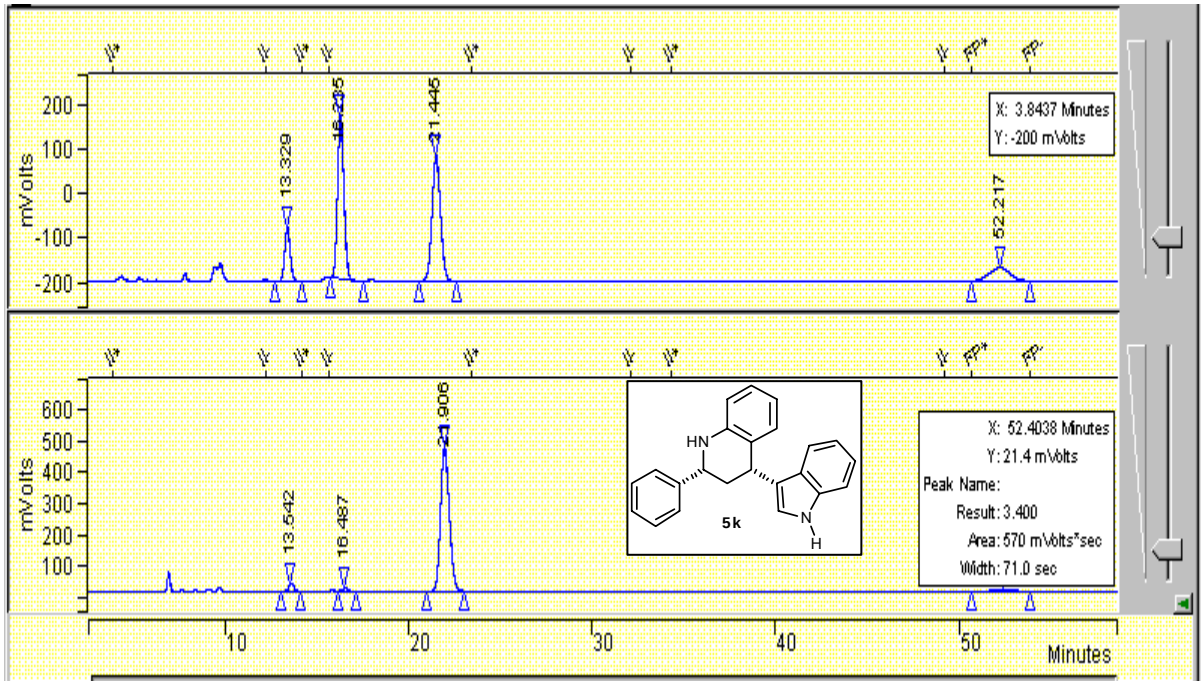

mVolts
200
150
100
50
19.438
29.160
X: 10.7464 Minutes
Y: 17.6 mVolts
Volts
1.00
0.75
0.50
0.25
0.00
18.810
27.400
HN
O
N
H
5f
X: 7.6645 Minutes
Y: 0.0130 Volts
10
20
30
40
50
Minutes

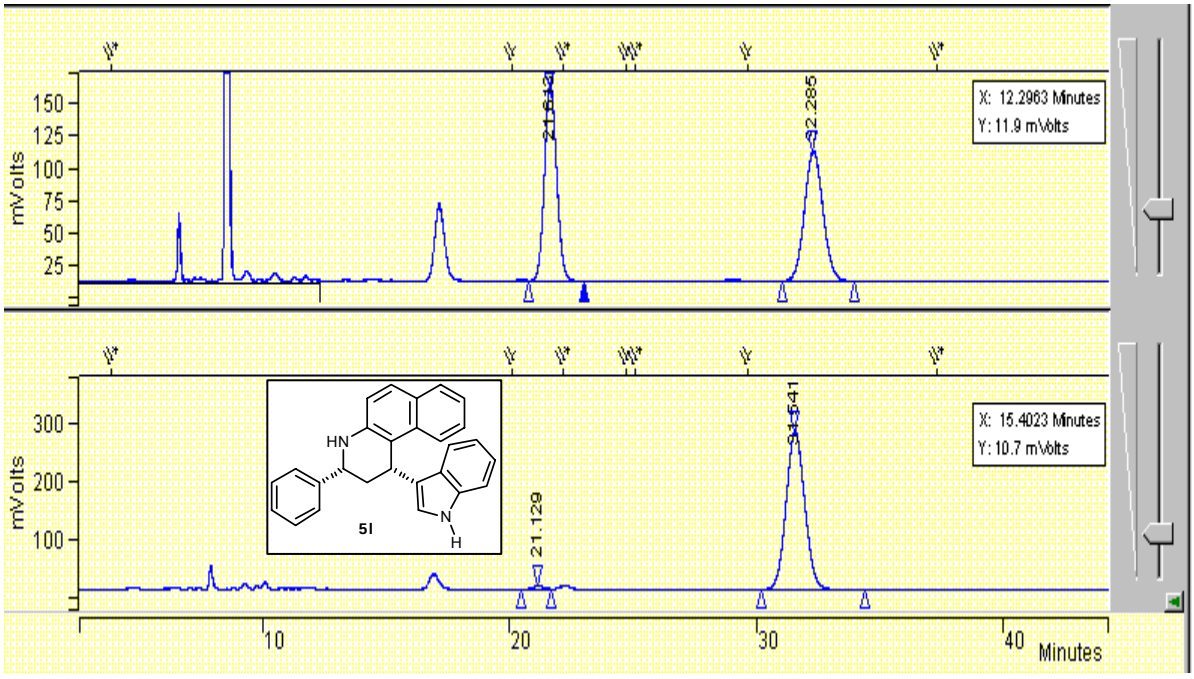

mVolts
200
150
100
50
24.390
32.560
48.703
X: 11.5096 Minutes
Y: 10.8 mVolts
500
400
300
200
100
24.790
33.207
49.538
X: 33.2073 Minutes
Y: 37.7 mVolts
Peak Name:
Result: 4.652
Area: 1510 mVolts*sec
Width: 51.4 sec
HN
O
N
H
5g
10
20
30
40
50
60
70
Minutes

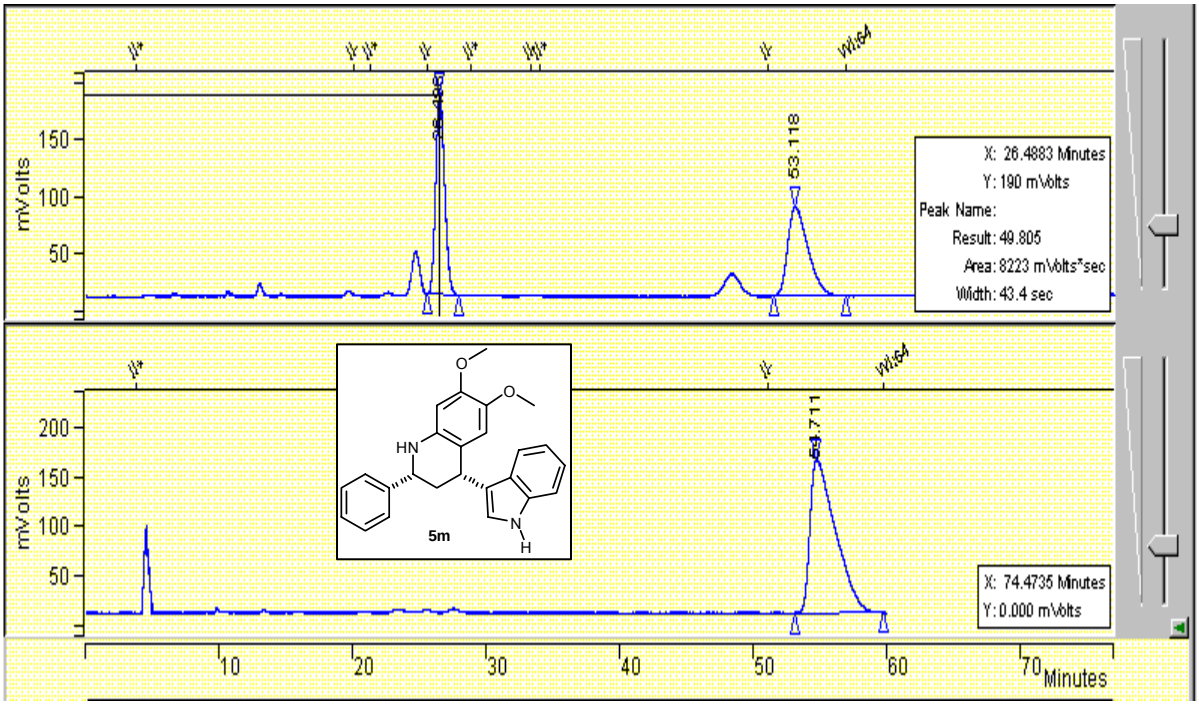

mVolts
100
75
50
25
20.165
46.248
67.260
X: 21.0267 Minutes
Y: 17.1 mVolts
300
250
200
150
100
50
19.914
24.865
65.420
X: 51.8258 Minutes
Y: 11.6 mVolts
HN
O
S
N
H
5h
10
20
30
40
50
60
70
80
Minutes

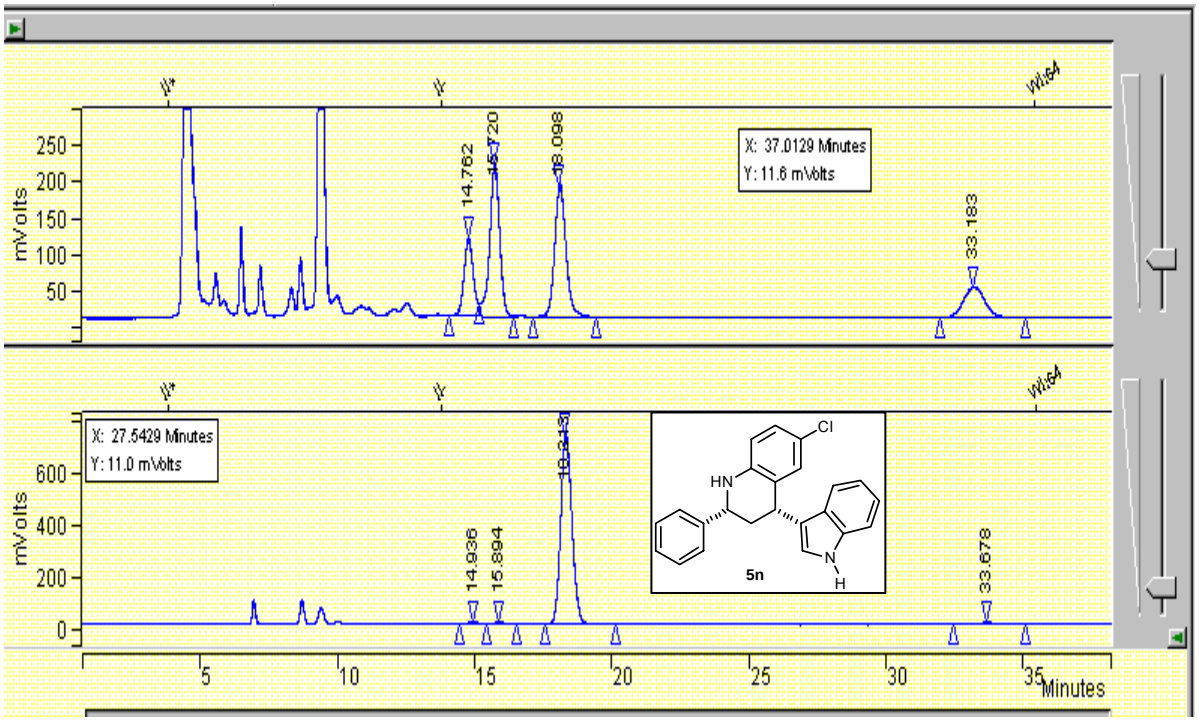

mVolts
700
600
500
400
300
200
100
0
24.065
35.162
X: 11.2725 Minutes
Y: 7.03 mVolts
mVolts
70
60
50
40
30
20
10
HN
O
N
H
5i
24.182
26.551
X: 13.0189 Minutes
Y: 3.48 mVolts
10
20
30
40
50
Minutes

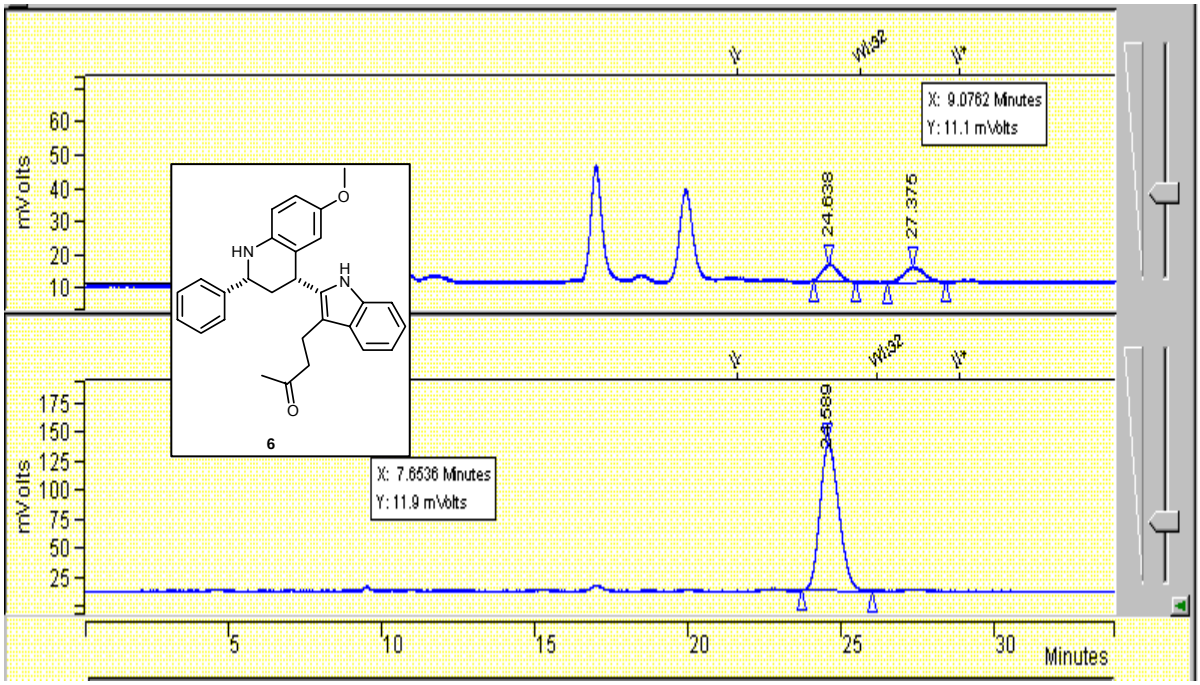

mVolts
500
400
300
200
100
0
X: 4.7391 Minutes
Y: 12.6 mVolts
32.093
50.168
mVolts
500
400
300
200
100
0
HN
O
Ph
N
H
5j
X: 15.4215 Minutes
Y: 9.83 mVolts
41.872
50.164
10
20
30
40
50
Minutes

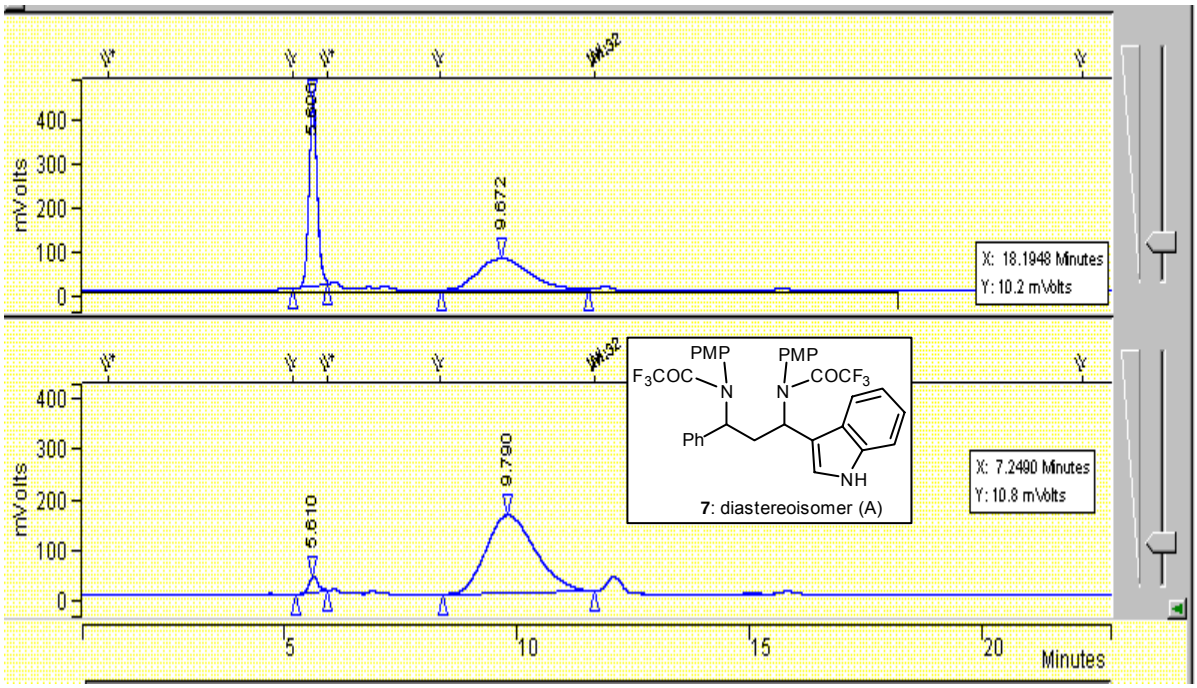

mVolts
200
100
0
-100
-200
13.329
16.235
21.445
52.217
X: 3.8437 Minutes
Y: -200 mVolts
mVolts
600
500
400
300
200
100
13.542
16.487
21.906
HN
N
H
5k
X: 52.4038 Minutes
Y: 21.4 mVolts
Peak Name:
Result: 3.400
Area: 570 mVolts*sec
Width: 71.0 sec
10
20
30
40
50
Minutes

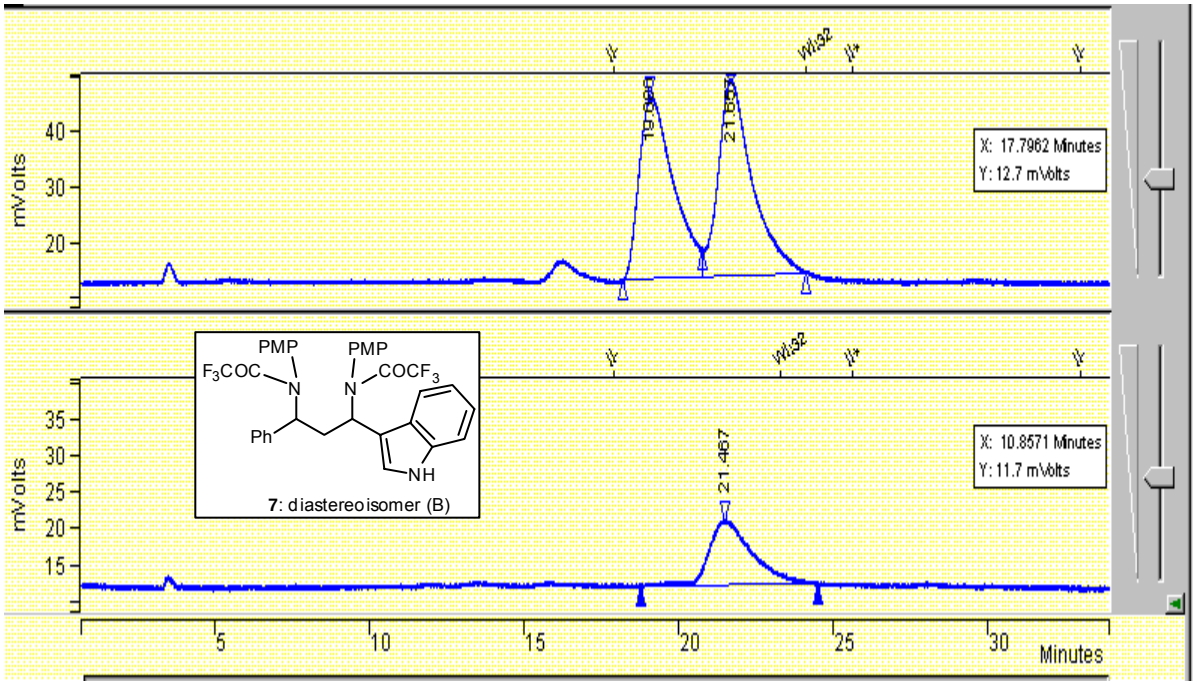

mVolts
150
125
100
75
50
25
21.634
32.285
X: 12.2963 Minutes
Y: 11.9 mVolts
mVolts
300
200
100
HN
N
H
5l
21.129
34.541
X: 15.4023 Minutes
Y: 10.7 mVolts
10
20
30
40
Minutes

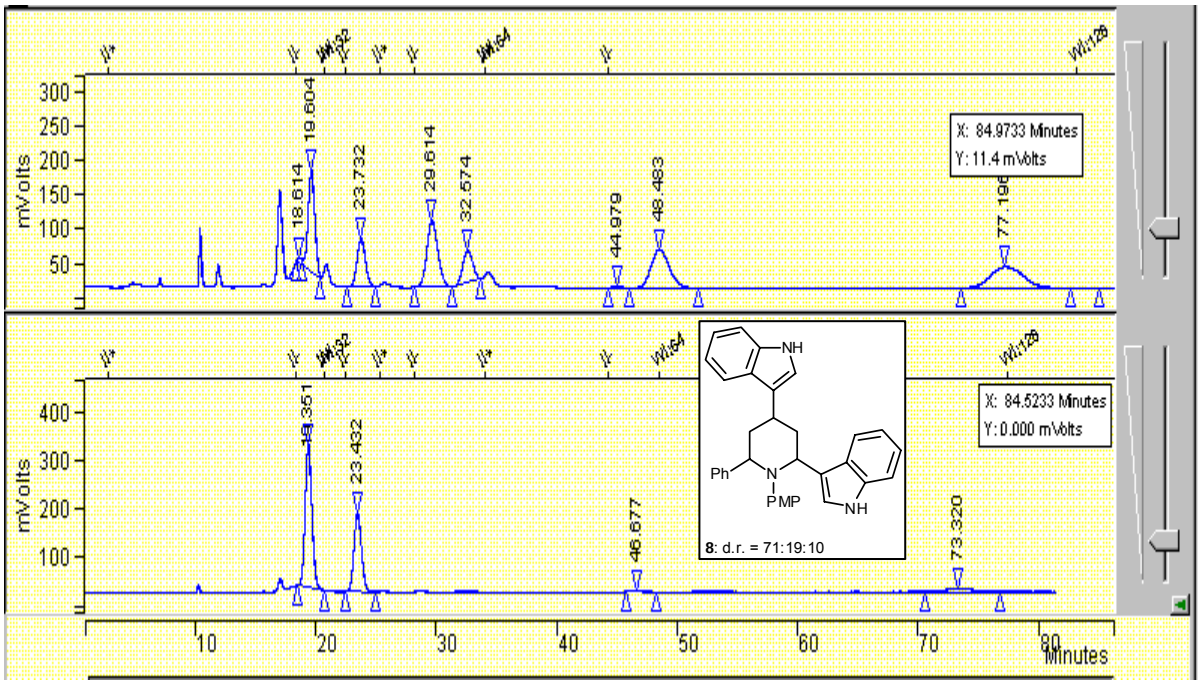

mVolts
150
100
50
26.488
53.118
X: 26.4883 Minutes
Y: 190 mVolts
Peak Name:
Result: 49.805
Area: 8223 mVolts*sec
Width: 43.4 sec
200
150
100
50
54.711
5m
X: 74.4735 Minutes
Y: 0.000 mVolts
10
20
30
40
50
60
70
Minutes


mVolts
250
200
150
100
50
14.762
15.720
18.098
X: 37.0129 Minutes
Y: 11.6 mVolts
33.183
X: 27.5429 Minutes
Y: 11.0 mVolts
600
400
200
0
14.936
15.894
18.343
Cl
HN
5n
33.678
5
10
15
20
25
30
35
Minutes


mVolts
60
50
40
30
20
10
X: 9.0762 Minutes
Y: 11.1 mVolts
24.638
27.375
HN
H
O
O
6
mVolts
175
150
125
100
75
50
25
X: 7.6536 Minutes
Y: 11.9 mVolts
24.589
5
10
15
20
25
30
Minutes


mVolts
400
300
200
100
0
5.606
9.672
X: 18.1948 Minutes
Y: 10.2 mVolts
PMP
F3COC
N
PMP
N
COCF3
Ph
NH
7: diastereoisomer (A)
mVolts
400
300
200
100
0
5.610
9.790
X: 7.2490 Minutes
Y: 10.8 mVolts
5
10
15
20
Minutes


mVolts
40
30
20
19.796
21.855
X: 17.7962 Minutes
Y: 12.7 mVolts
PMP
PMP
F3COC
N
N
COCF3
Ph
NH
7: diastereoisomer (B)
mVolts
35
30
25
20
15
21.467
X: 10.8571 Minutes
Y: 11.7 mVolts
5
10
15
20
25
30
Minutes


mVolts
300
250
200
150
100
50
18.614
19.604
23.732
29.614
32.574
44.979
48.483
77.196
X: 84.9733 Minutes
Y: 11.4 mVolts
mVolts
400
300
200
100
19.351
23.432
46.677
73.320
NH
Ph
N
PMP
NH
8: d.r. = 71:19:10
X: 84.5233 Minutes
Y: 0.000 mVolts
10
20
30
40
50
60
70
80
Minutes