Supporting Information

for

Hydroquinone–pyrrole dyads with varied linkers

Hao Huang[1], Christoffer Karlsson[1], Maria Strømme[1], Martin Sjödin[1] and Adolf Gogoll*[,2]

Address: [1] Nanotechnology and Functional Materials, Department of Engineering Sciences, The Ångström Laboratory, Uppsala University, Box 534, SE-751 21 Uppsala, Sweden and [2] Department of Chemistry - BMC, Biomedical Centre, Uppsala University, Box 576, SE-751 23 Uppsala, Sweden

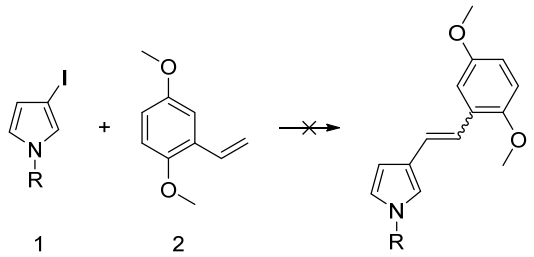
Email: Adolf Gogoll - adolf.gogoll@kemi.uu.se

*Corresponding author

Optimization of experimental conditions, computated electron distributions, UV–vis, IR, and NMR spectral data

Contents

Optimization attempts for Heck reaction: Synthesis of 4c.



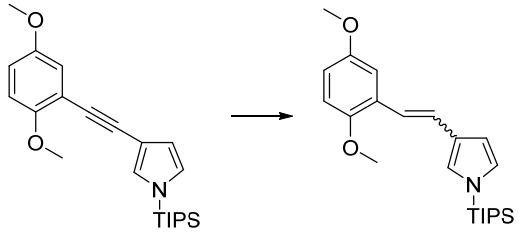
1 2

Trial	R	Solvent	Temperature	Catalyst	Base	additives	time
1	TIPS	DMF	150	$Pd(OAc)_2$	K_2CO_3	TBAB	overnight
2	TIPS	DMF	80	$Pd(OAc)_2$	KOAc	TBAB	overnight
3	TIPS	DMF	150	$PdCl_2$	KOAc	MeOH	overnight
4	TIPS	MeCN	80	$Pd(OAc)_2$	Et_3N	PPh_3	overnight
5	TIPS	Toluene	150	$Pd(PPh_3)_4$	Et_3N		20 mins
6	TIPS	Dioxane	150	$Pd_2(dba)_3$	$CsCO_3$	$P(^tBu)_3$	2 h
7	Tosyl	DMF	120	$Pd(PPh_3)_2Cl_2$	Et_3N		1 h
8	Boc	DMF	120	$Pd(PPh_3)_2Cl_2$	Et_3N		1 h

Procedure:

To a solution of **1** (50 mg, 0.14 mmol), **2** (1.2 eq.), base (2 eq.) and additives (for TBAB 1.5 eq. respectly, for PPh3 and $P(^tBu)_3$, 0.1 eq respectly, MeOH was added as co-solvent)in the dry solvent in a heavy-wall Smith process vial, palladium catalyst (0.05 eq.)was added, the vial was sealed and then heat it up in oil bath at the indicated temperature (according to the description of reaction vial provider, this vial sealed can withstand pressures beyond 30 bar in a wide range of conditions). No product was formed in any of the trials.

Optimization attempts for hydrogenation of 4d.



Trial	Condition	Yield	**E:Z** ratio
1[a]	Lindlar catalyst, quinoline, benzene, RT, H_2 (1 atm), overnight	No reaction	n. a.
2[b]	$HSiEt_3$, $Pd(PPh_3)_2Cl_2$, dppf, Cu_2SO_4, Toluene/H_2O, 100 ^oC, H_2 (1 atm), overnight	34 %	E:Z =3:1
3[c]	$Pd(OAc)_2$, KOH, DMF, 145 ^oC, H_2 (1 atm), 3 h	25 %[d]	Z only

[a] To a benzene solution (2 ml) of Lindlar catalyst (33 mg, 5 % Pd/C loading) suspended in a 10 ml round-bottom flask, fresh distilled quinoline (2 ul) was added. The resulting solution was degassed by switching between vacuum and Ar gas for 5 times, and then connected with a hydrogen reservoir. Bubbling H_2 gas for 5 mins and then the starting material (60 mg, 0.16 mmol) in 2 ml benzene was added. The reaction mixture was stirred overnight.

[b] Luo, F.; Pan, C.; Wang, W.; Ye, Z.; Cheng, J., *Tetrahedron* **2010,** *66* (6), 1399-1403.

[c] J. Li, R. Hua, T. Liu, *J. Org. Chem.* **2010**, *75*, 2966-2970.

[d] Deprotection occurred during reaction, the yield was calculated referring to deprotected product.

Table S 1. Wavelength (λ , nm) and extinction coefficient (ε , $cm^{-1}M^{-1}$) in UV-vis spectra of compounds **3a** – **3d** and **1**, measured for MeCN solutions, and calculated wavelengths (λ , nm) with corresponding oscillator strength(*f*).

Compound	Experimental		Calculation	
	λ	ε	λ	*f*
3a	221	16830	229	0.07
	290	5060	272	0.114
3b	224	11080	229	0.07
	290	3580	272	0.11
trans-**3c**	222	7030	230	0.11
	298	4510	295	0.2
	336	4450	337	0.82
cis-**3c**	230	14860	240	0.09
	297	8150	288	0.11
	325	7220	314	0.29
3d	217	37560	228	0.14
	252	12940	248	0.08
	273	14540	263	0.1
	288	20640	287	0.19
	322	18260	328	0.66
1	214	27090	237	0.09
	265	9590	251	0.08
	270	8970	264	0.1
	308	7840	297	0.3

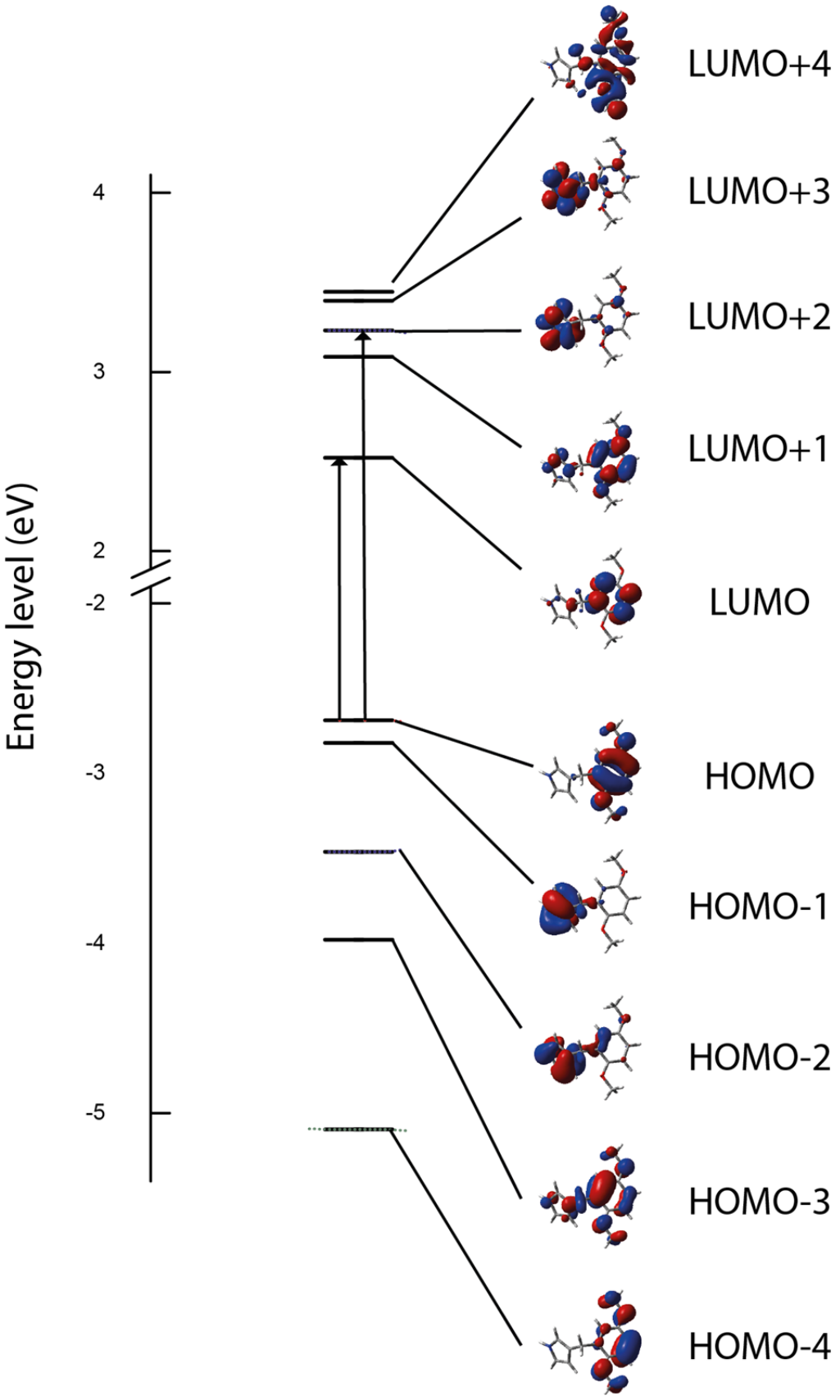


Figure S 1. Energy diagram of 3a with MOs, transitions indicated by calculations marked by arrows.

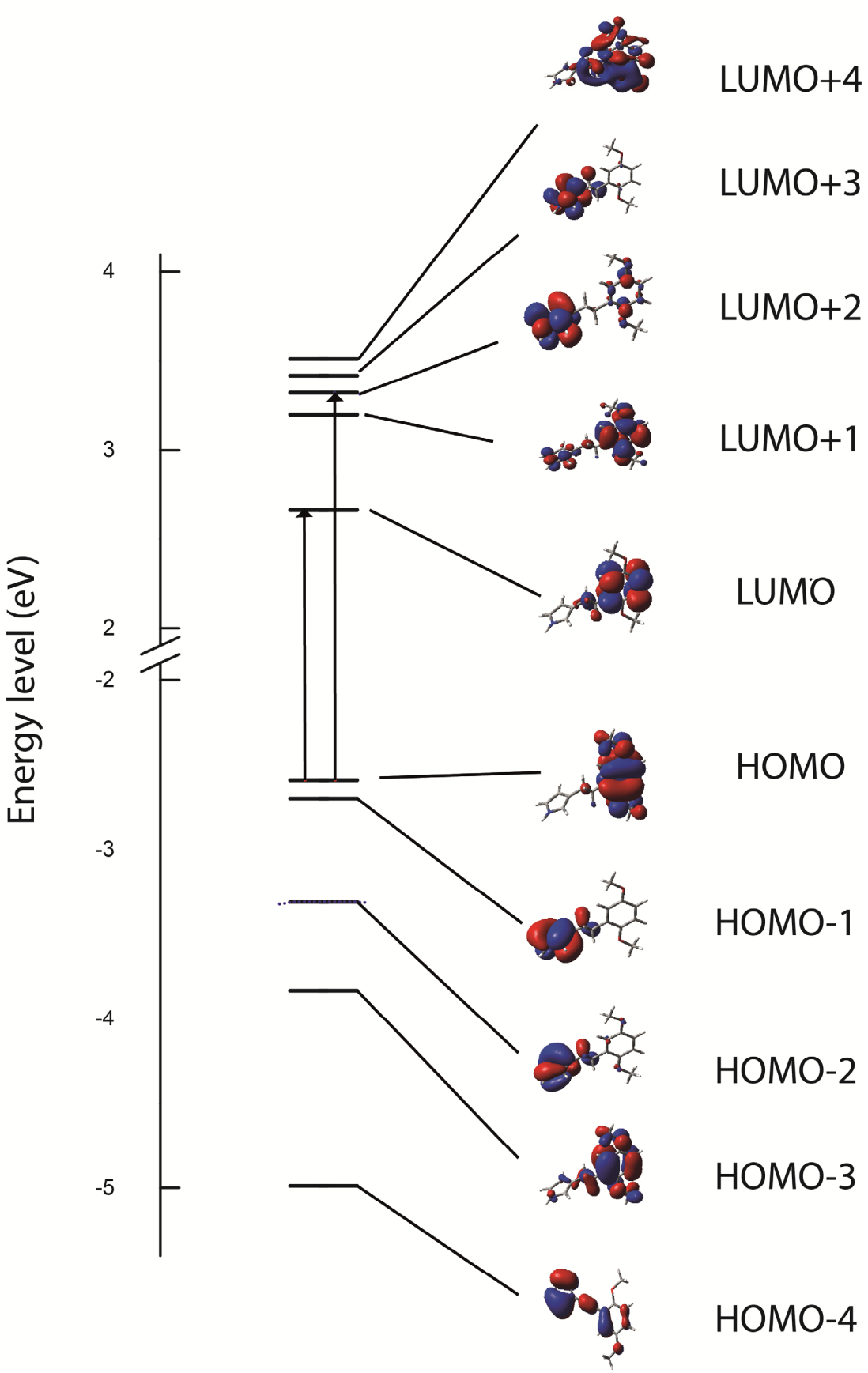


Figure S 2. Energy diagram of **3b** with MOs**,** transitions indicated by calculations marked by arrows.

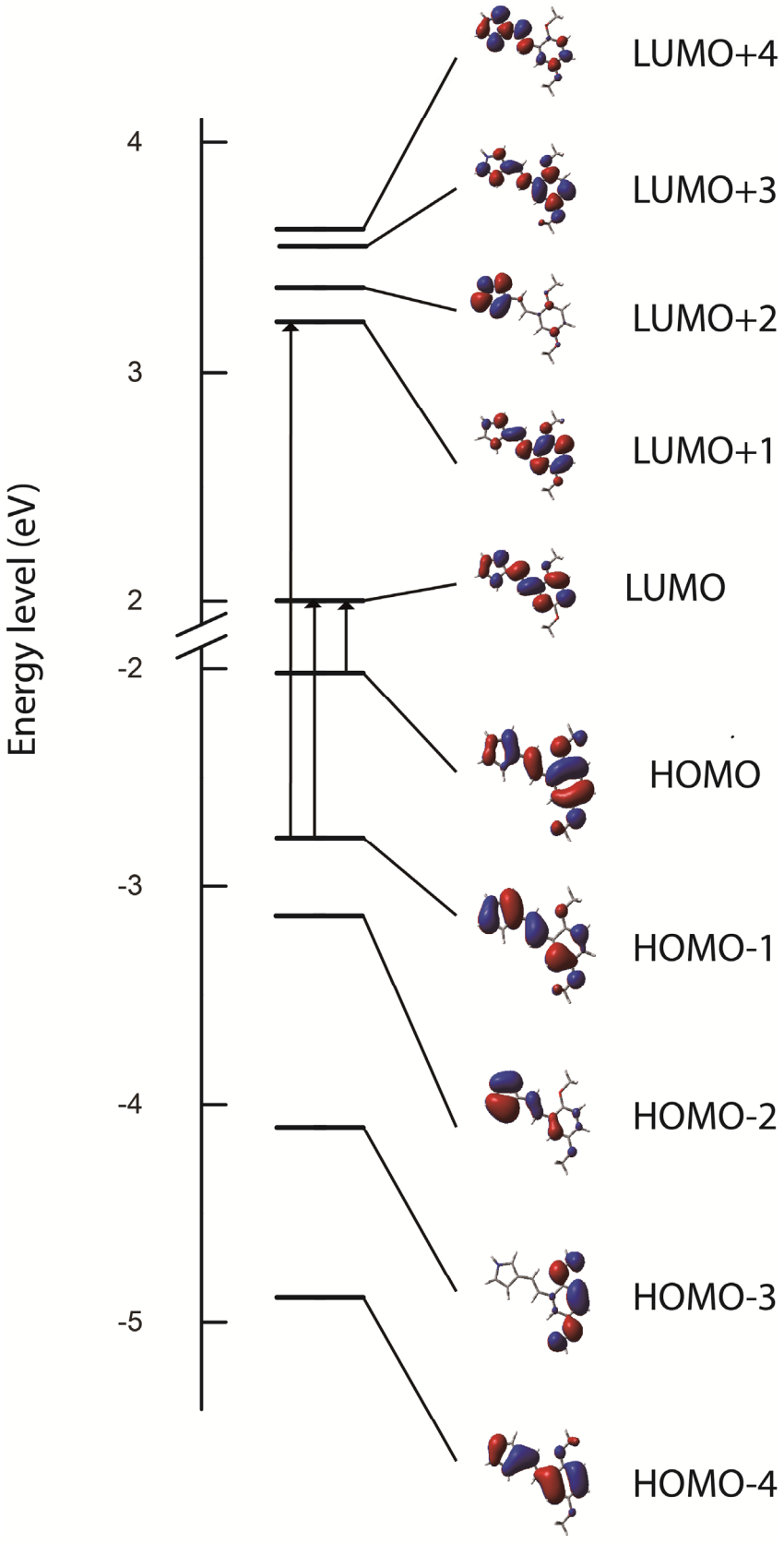


Figure S 3. Energy diagram of *trans*-**3c** with MOs**,** transitions indicated by calculations marked by arrows.

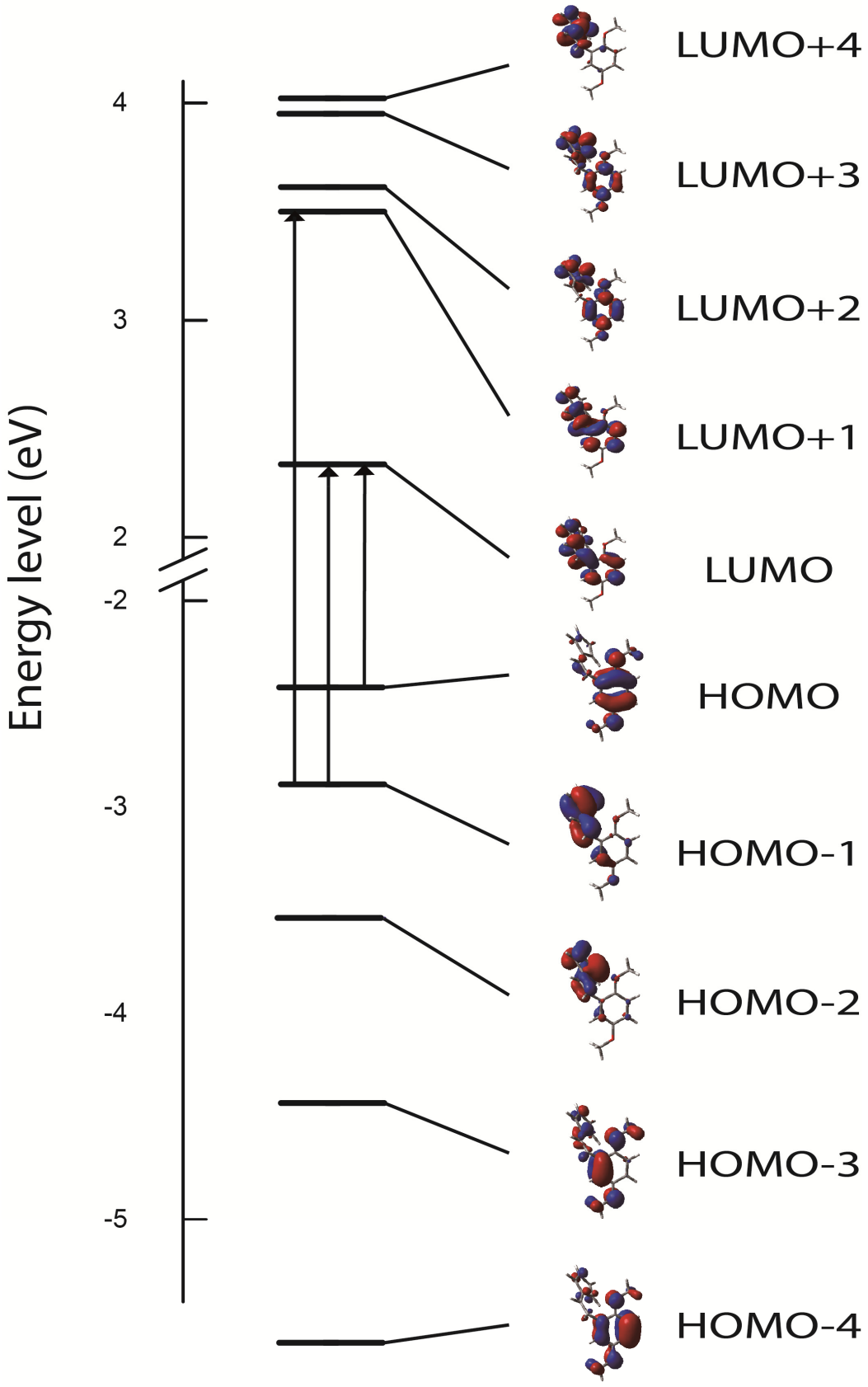


Figure S 4. Energy diagram of *cis*-**3c** with MOs**,** transitions indicated by calculations marked by arrows.

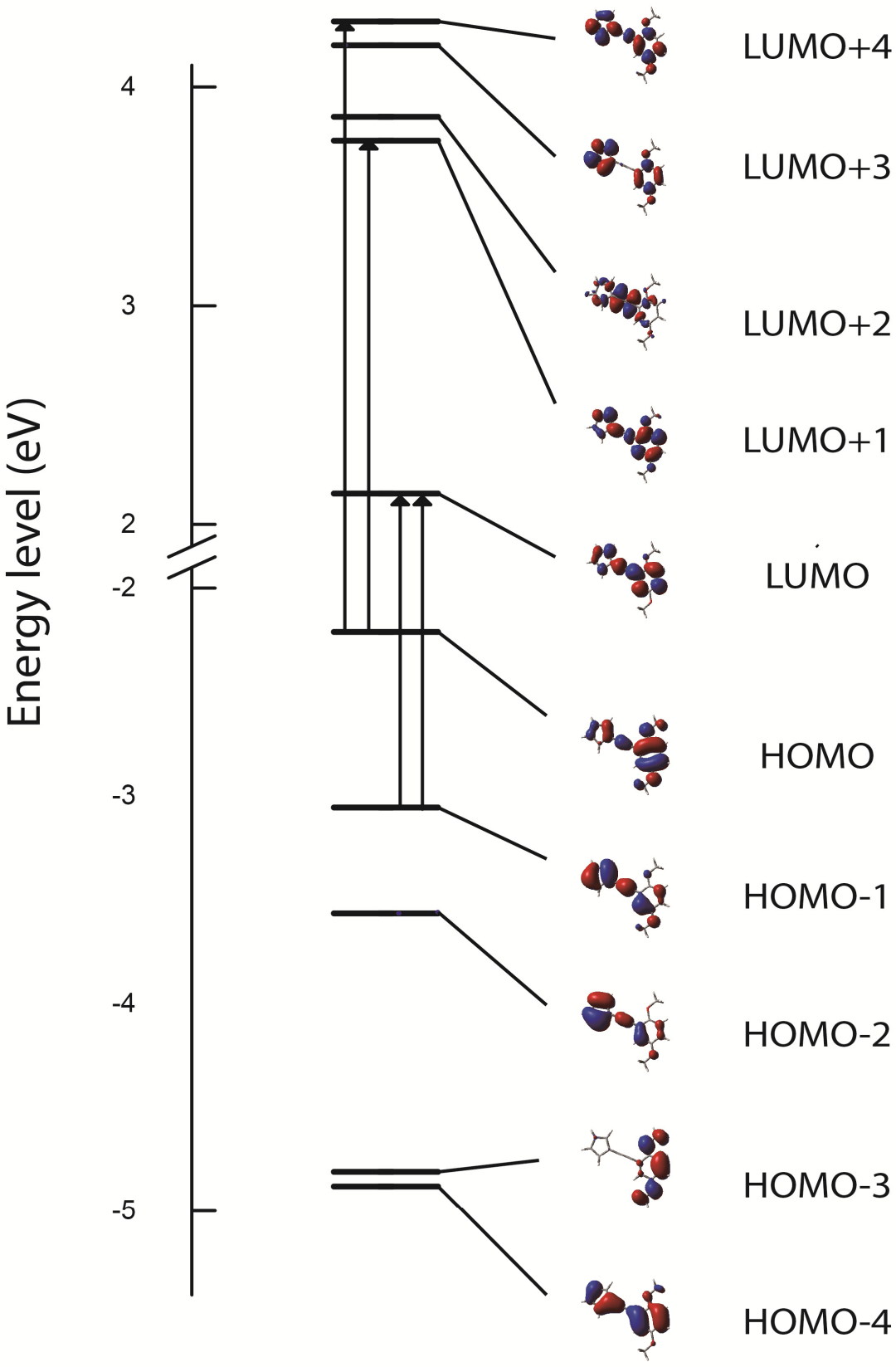


Figure S 5. Energy diagram of **3d** with MOs**,** transitions indicated by calculations marked by arrows.

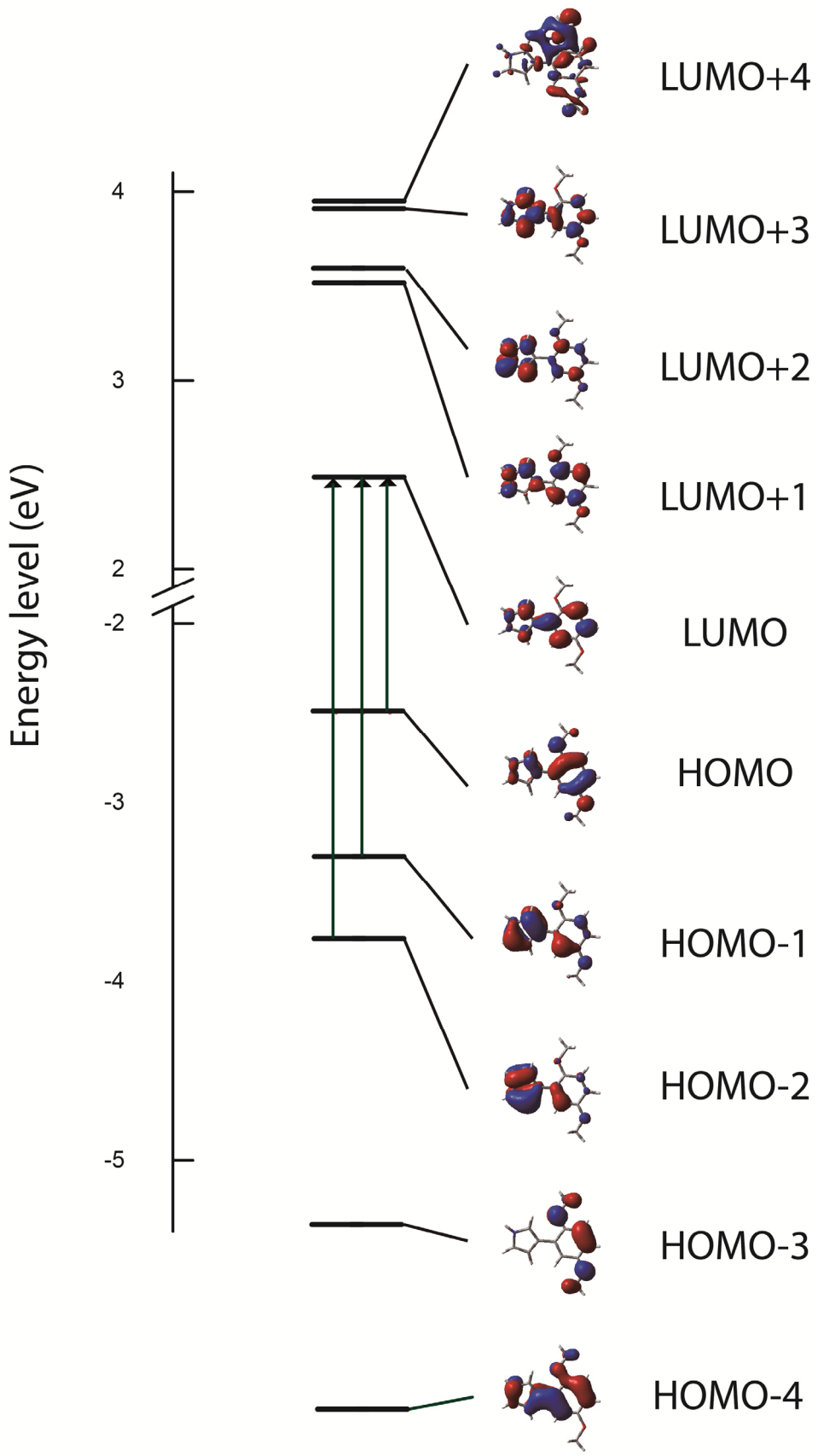


Figure S 6. Energy diagram of **1** with MOs**,** transitions indicated by calculations marked by arrows.

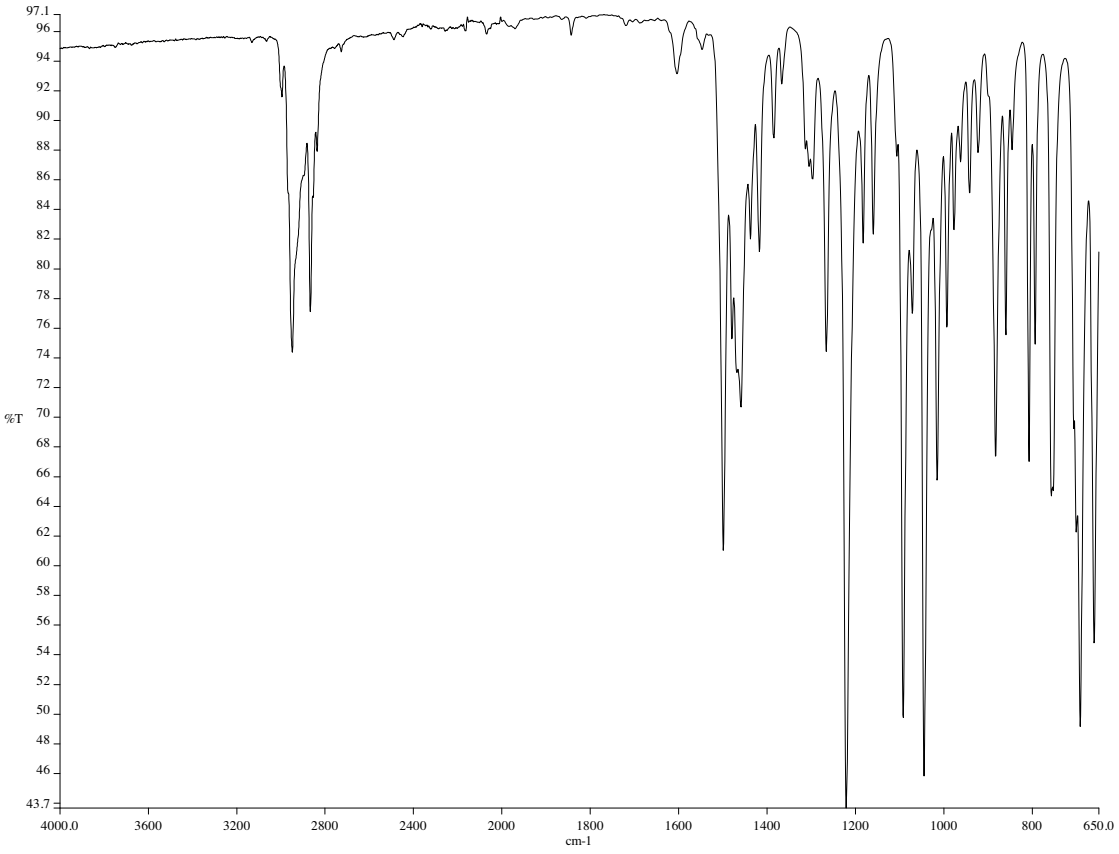


Figure S 7. IR spectrum of **4a**.

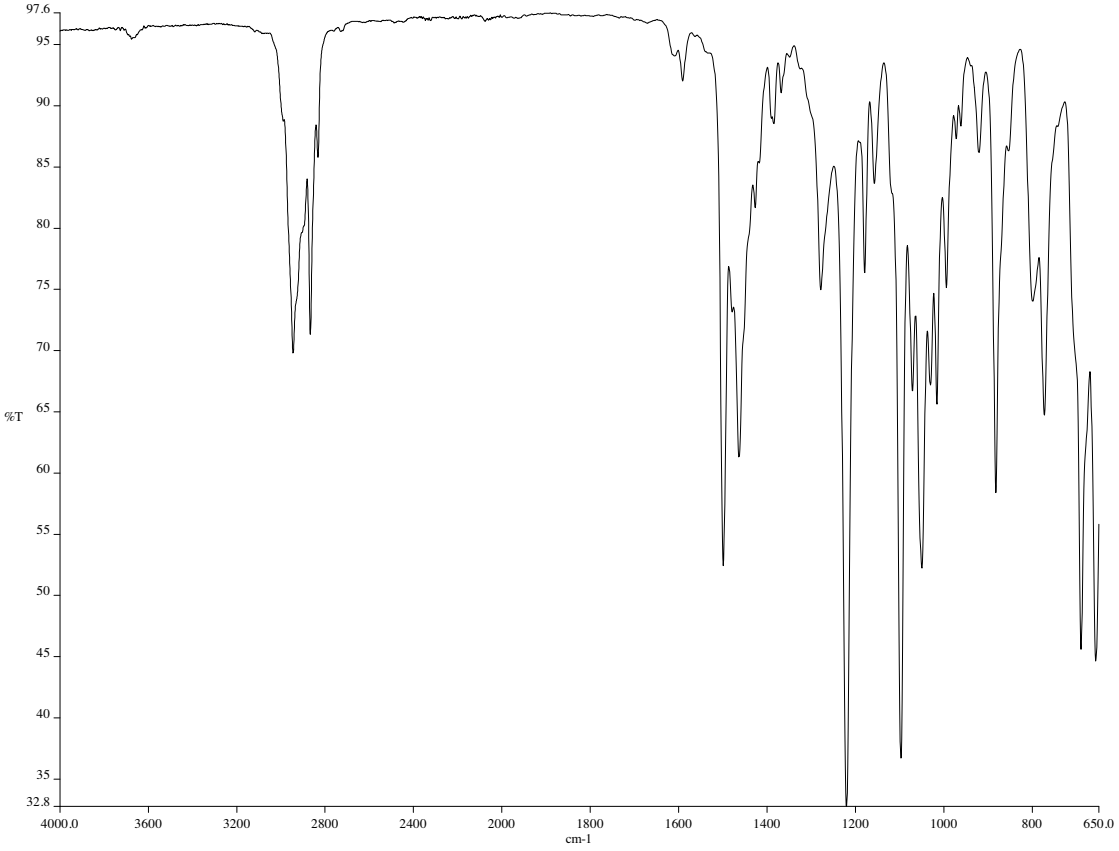


Figure S 8. IR spectrum of **4b**.

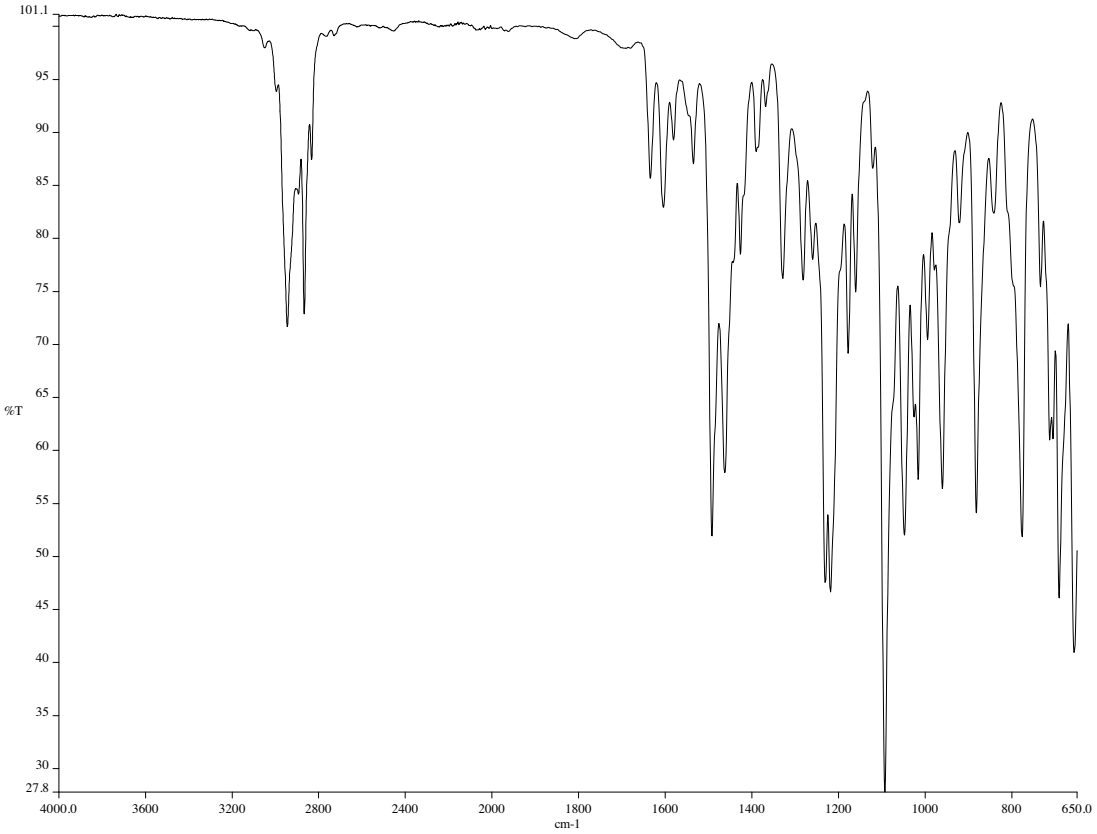


Figure S 9. IR spectrum of *trans*-**4c.**

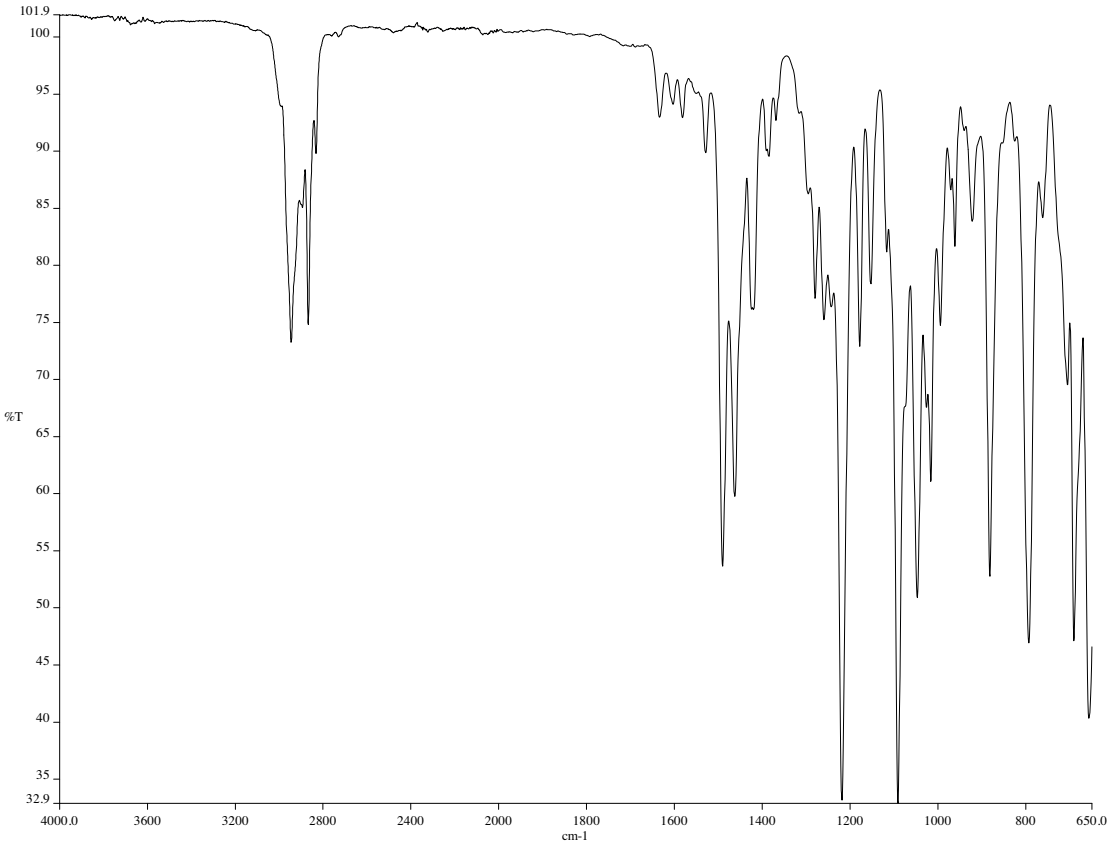


Figure S 10. IR spectrum of *cis*-**4c.**

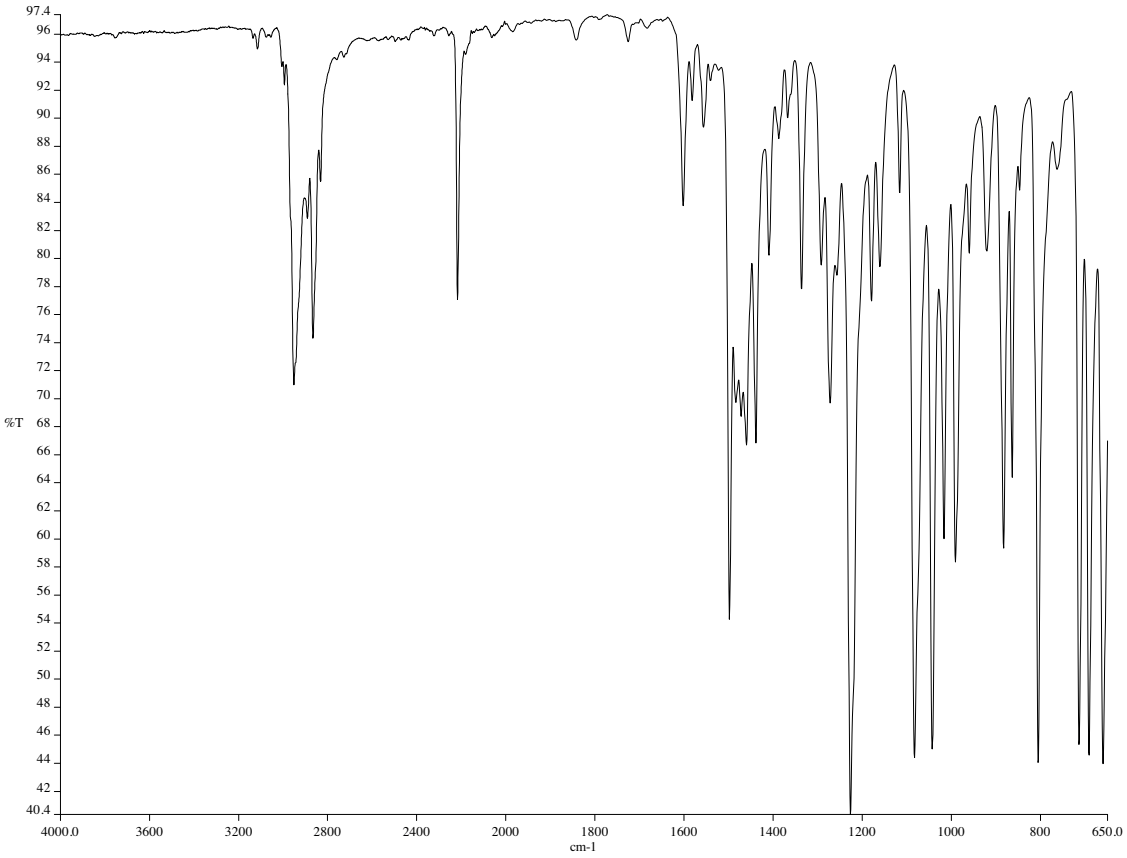


Figure S 11. IR spectrum of **4d.**

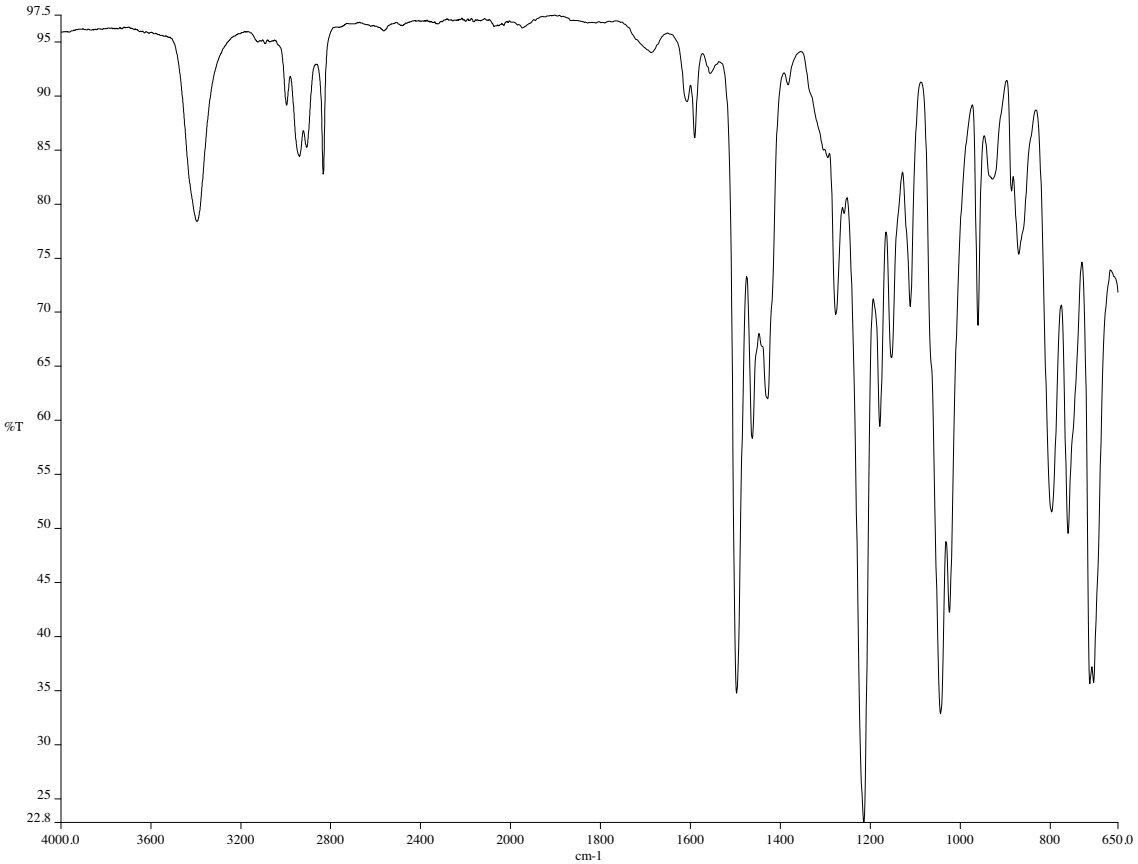


Figure S 12. IR spectrum of **3a.**

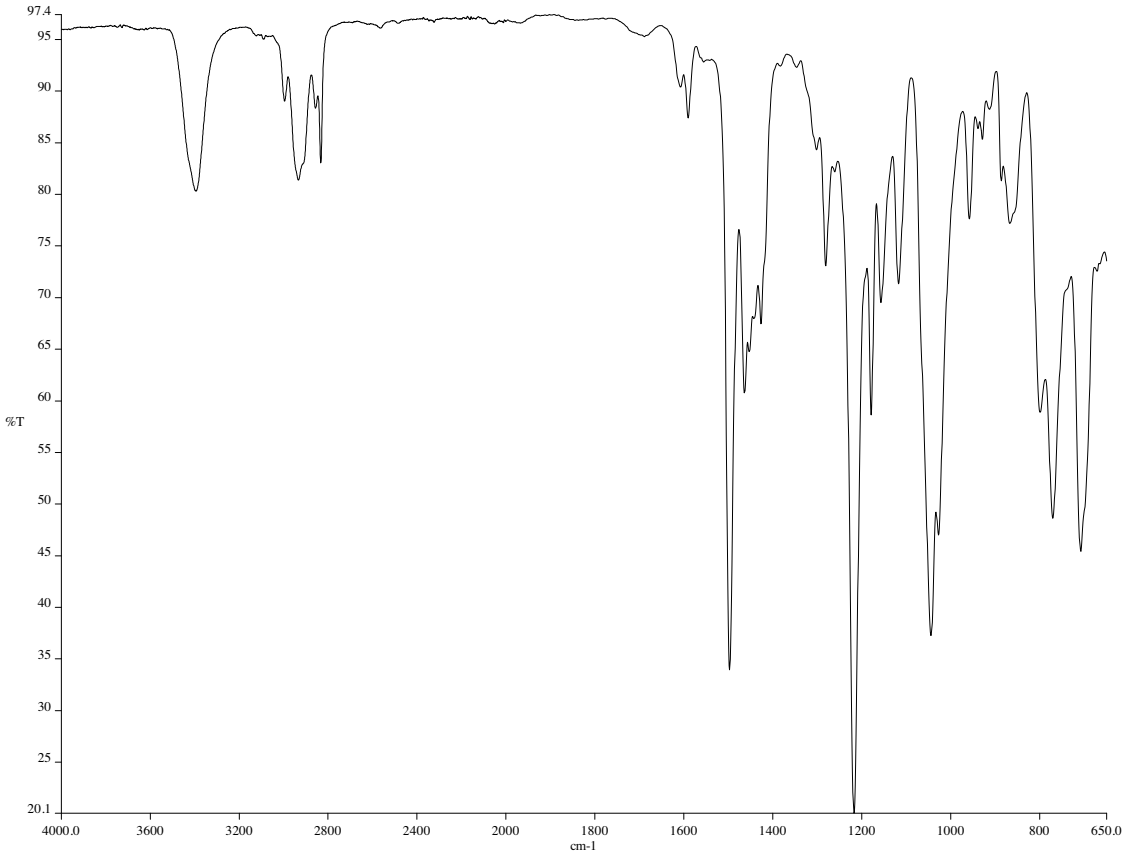


Figure S 13. IR spectrum of **3b.**

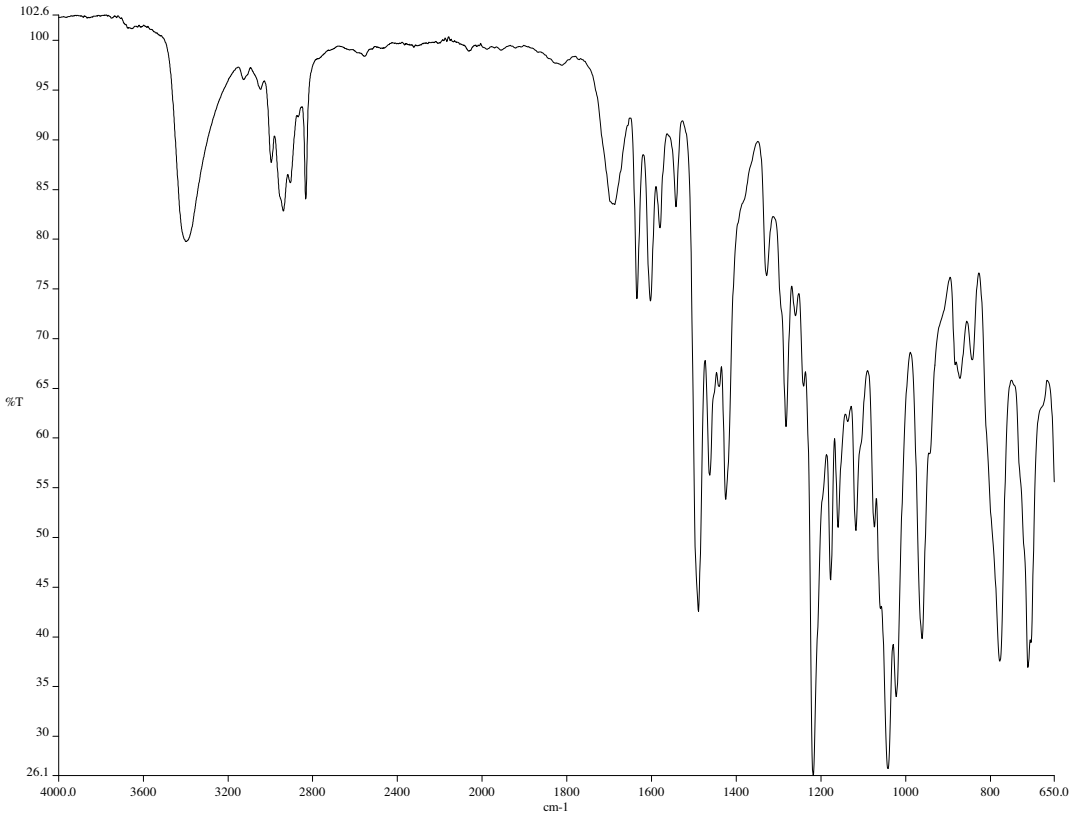


Figure S 14. IR spectrum of *trans*-**3c.**

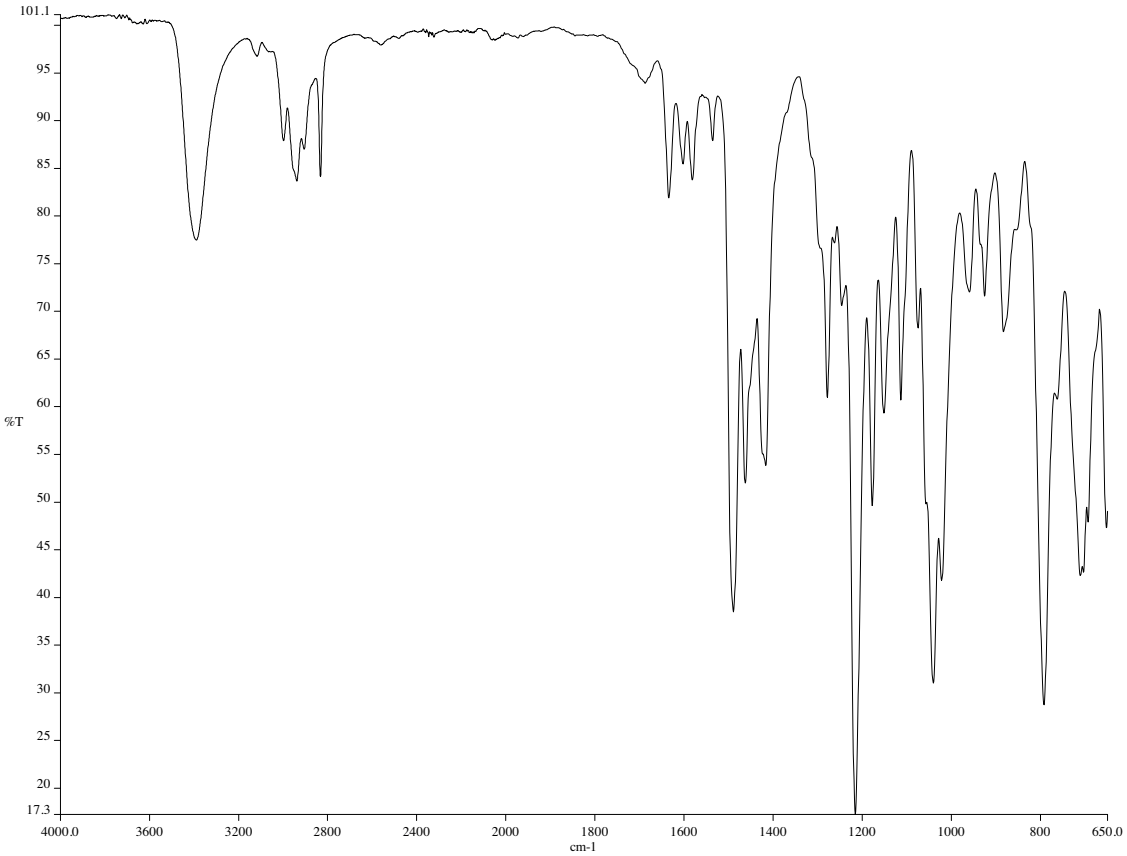


Figure S 15. IR spectrum of *cis*-**3c.**

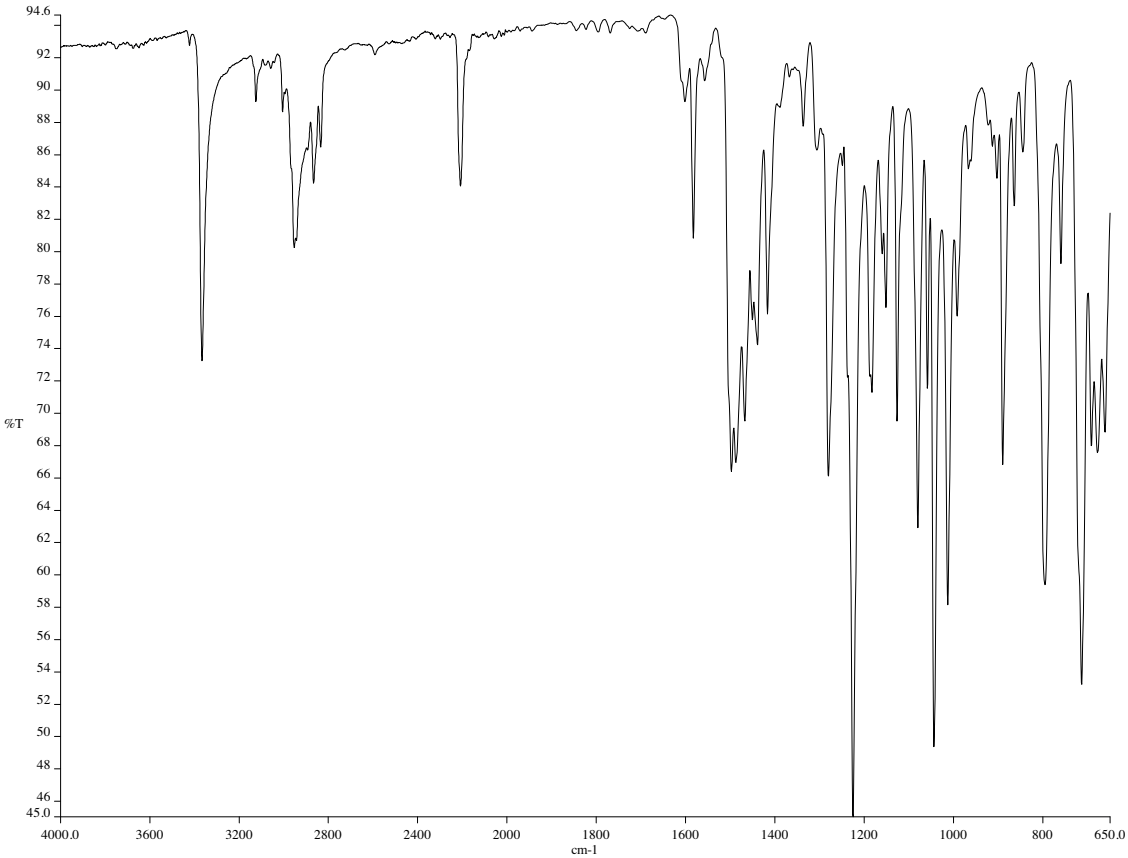


Figure S 16. IR spectrum of **3d.**

NMR spectra

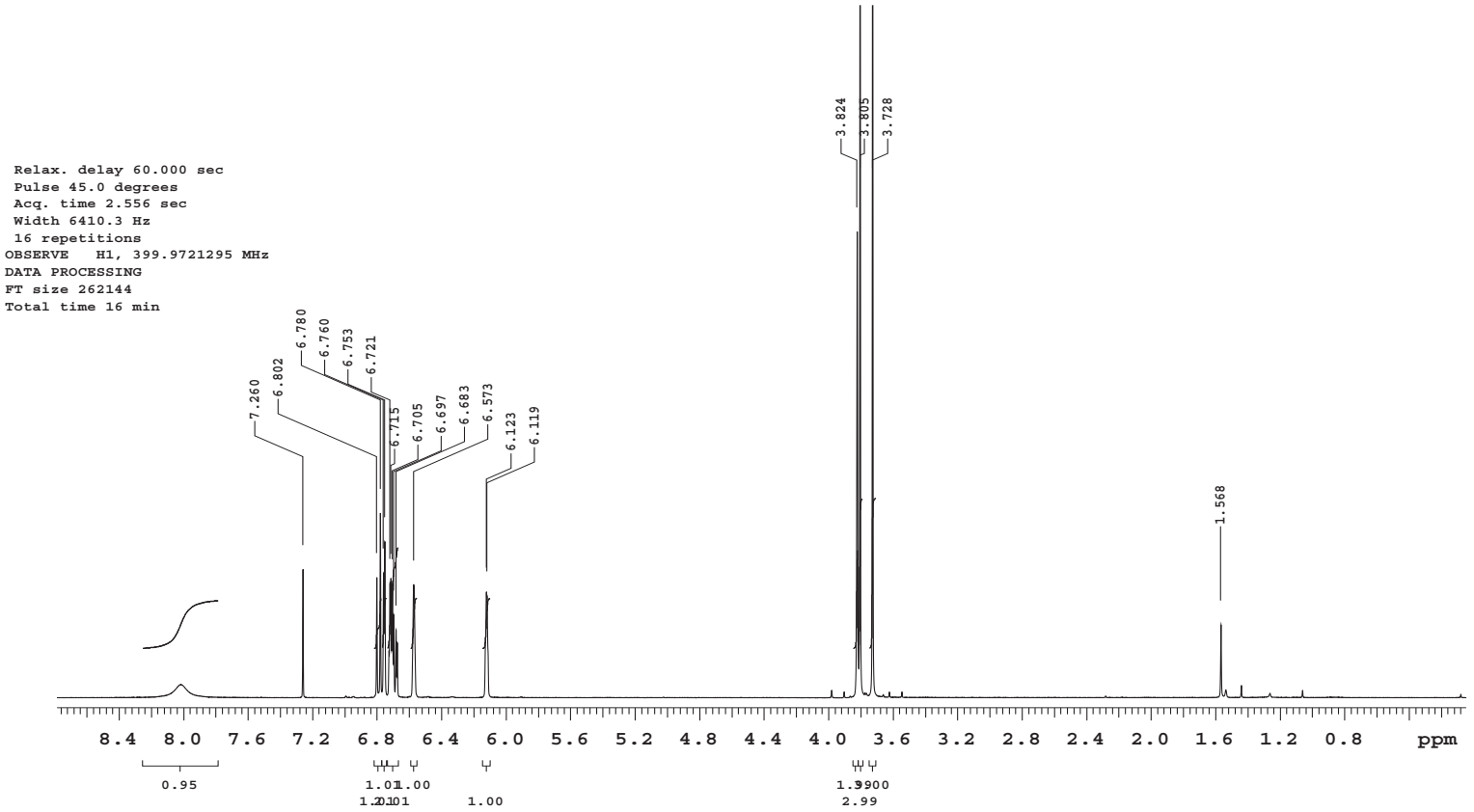


Figure S 17. ^{1}H NMR spectrum (400 MHz, $CDCl_3$ solution) of **3a**.

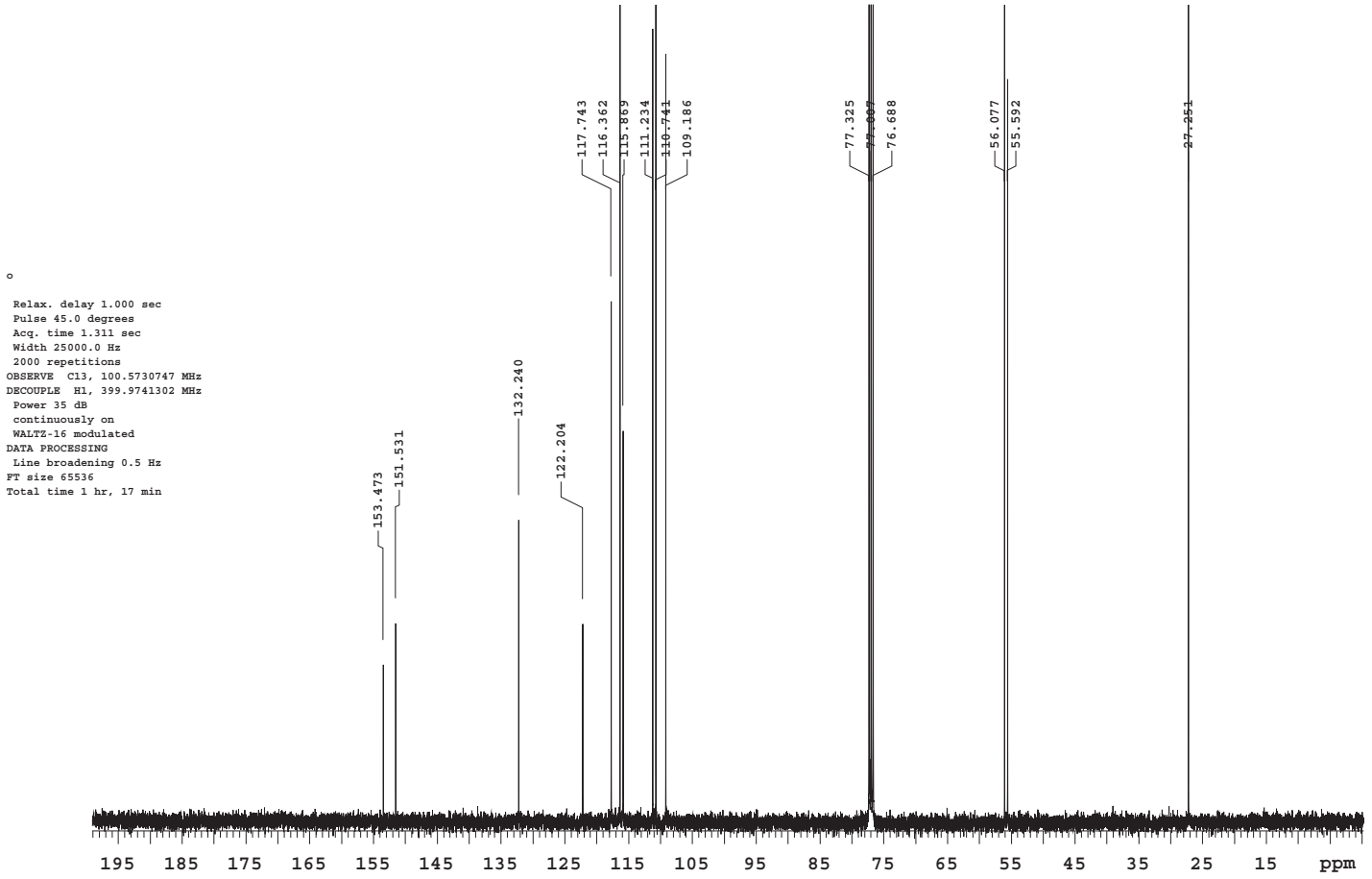


Figure S 18. ^{13}C NMR spectrum (100.6 MHz, $CDCl_3$ solution) of **3a**.

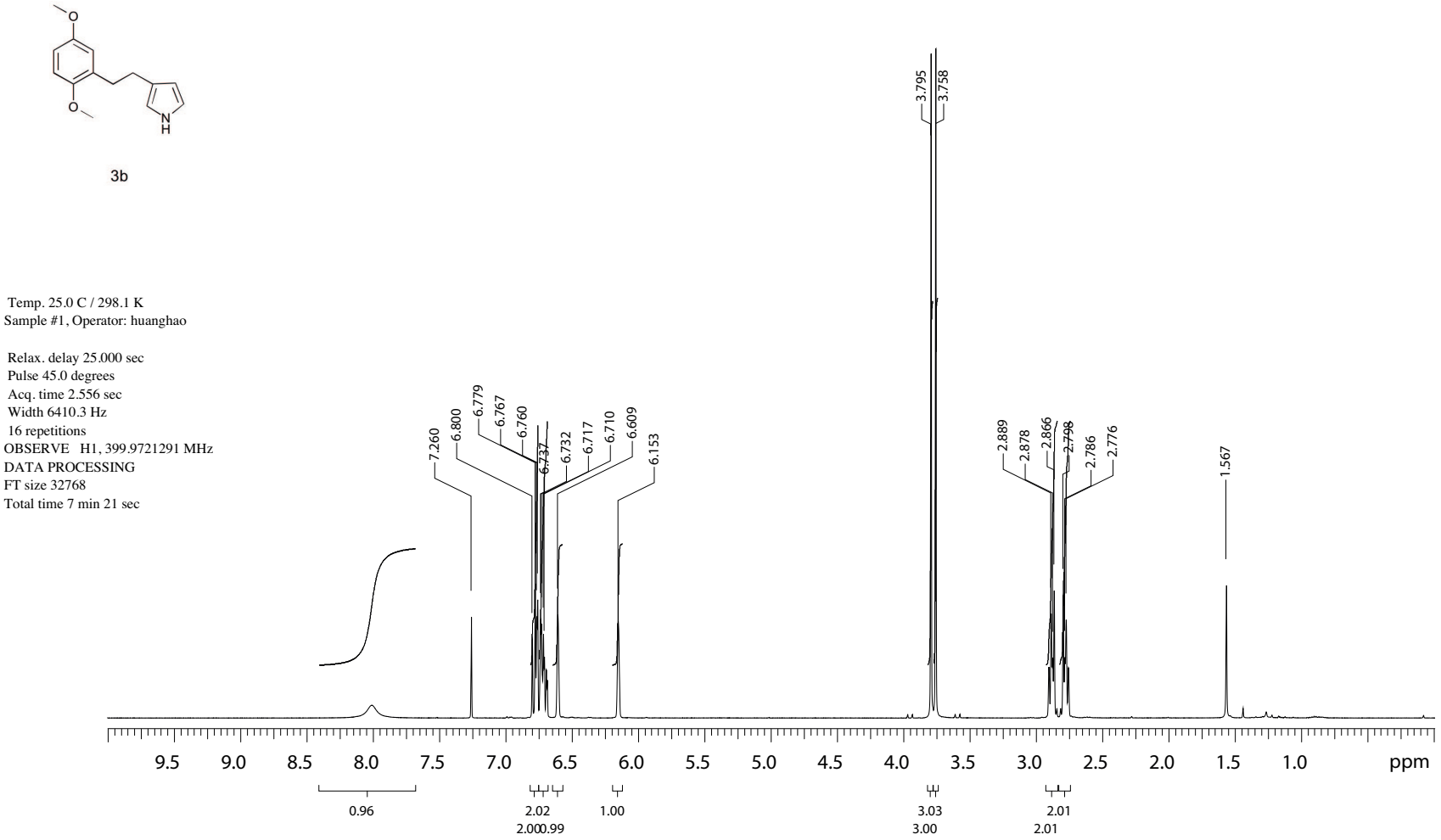


Figure S 19. ^{1}H NMR spectrum (400 MHz, $CDCl_3$ solution) of **3b**.

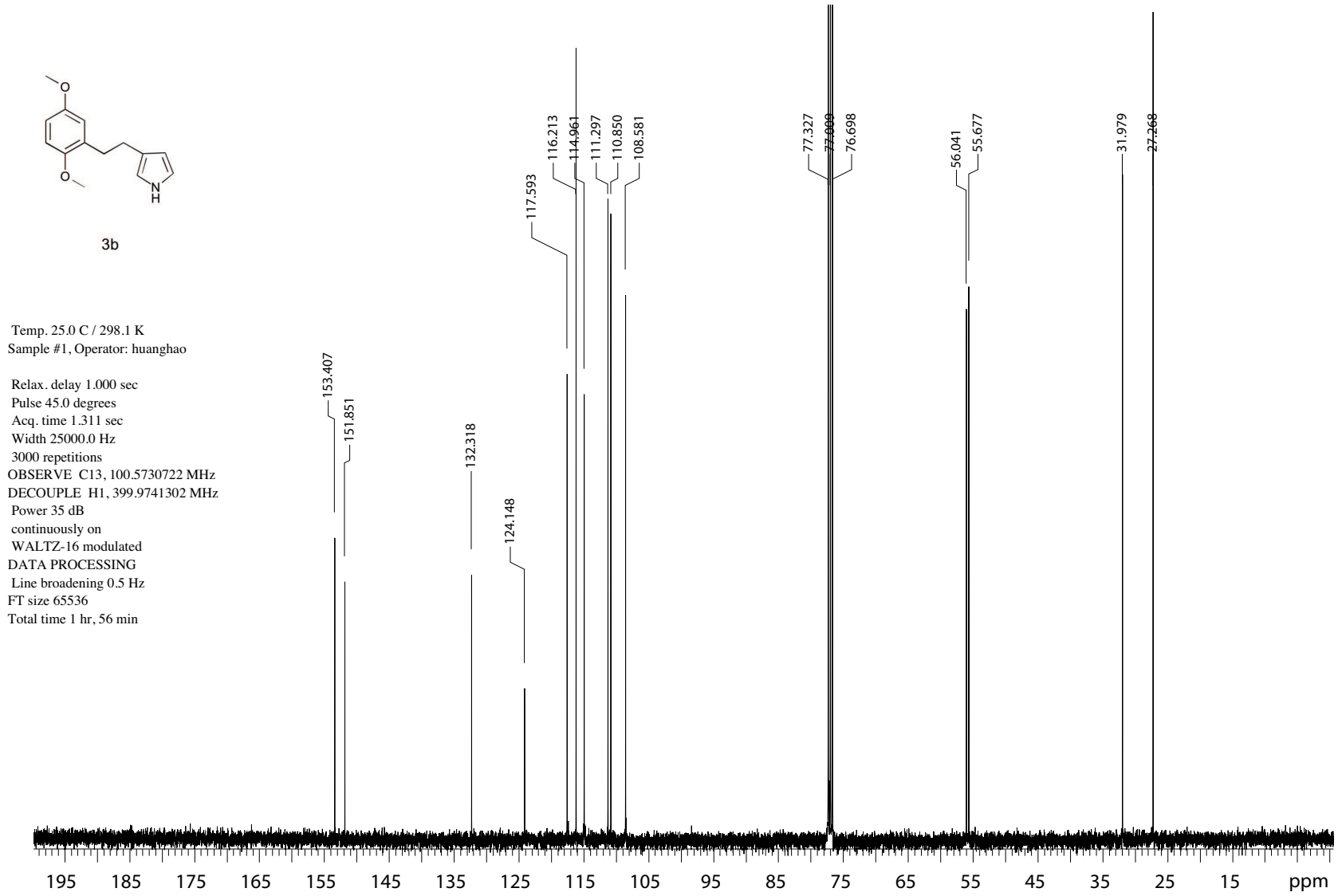


Figure S 20. ^{13}C NMR spectrum (100.6 MHz, $CDCl_3$ solution) of **3b**.

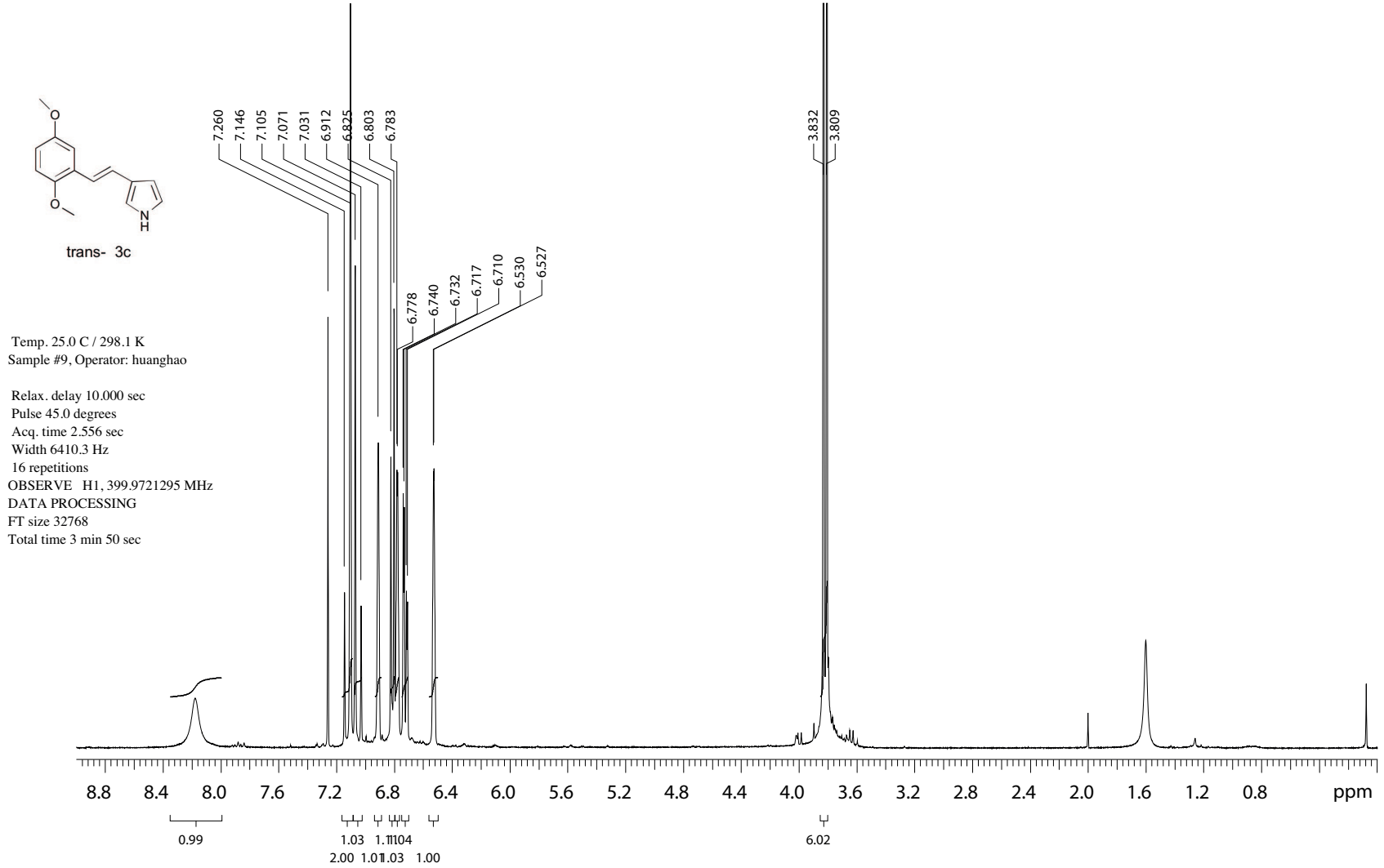


Figure S 21. ^{1}H NMR spectrum (400 MHz, $CDCl_3$ solution) of *trans*-**3c**.

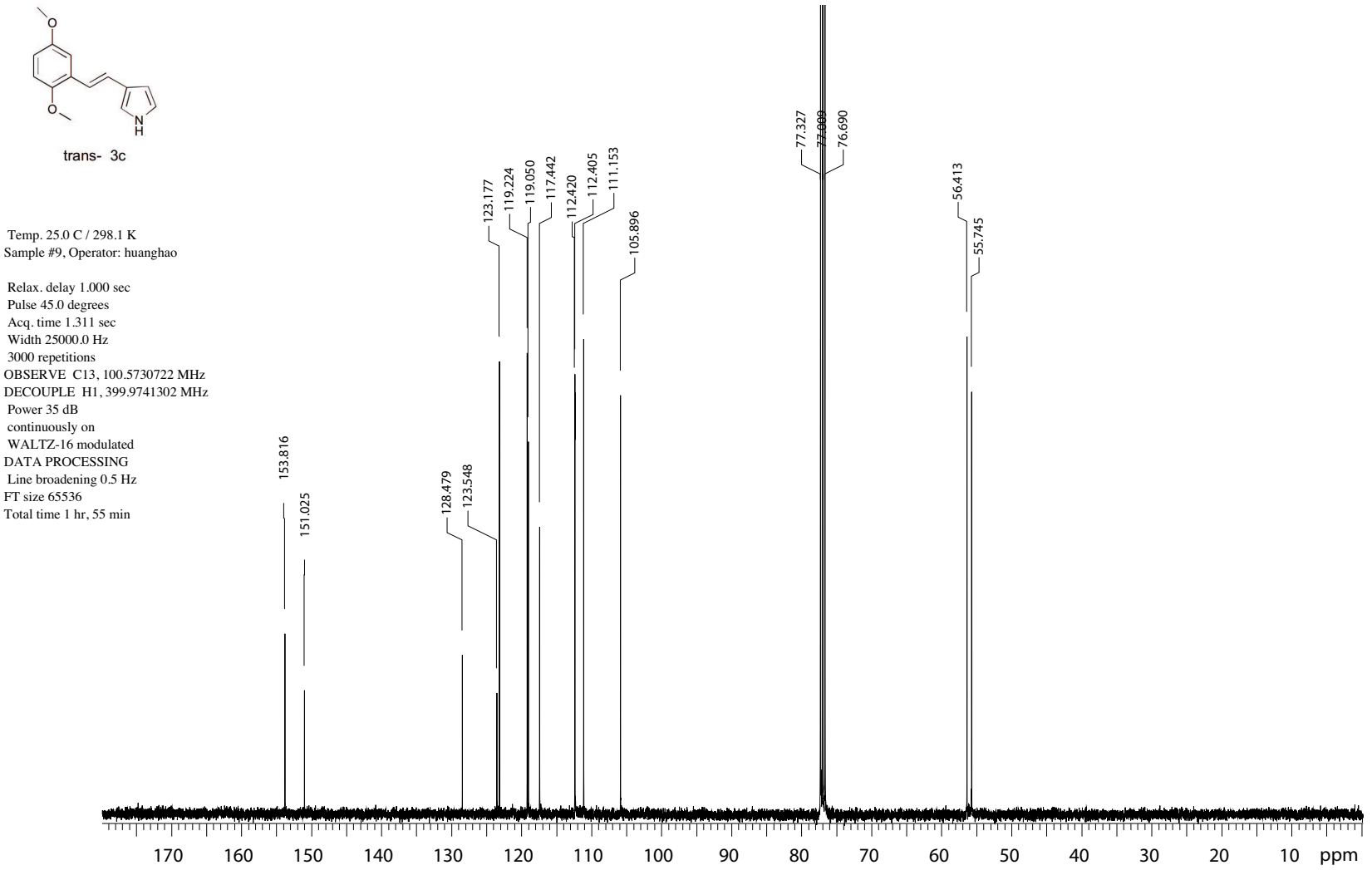


Figure S 22. ^{13}C NMR spectrum (100.6 MHz, $CDCl_3$ solution) of *trans*-**3c**.

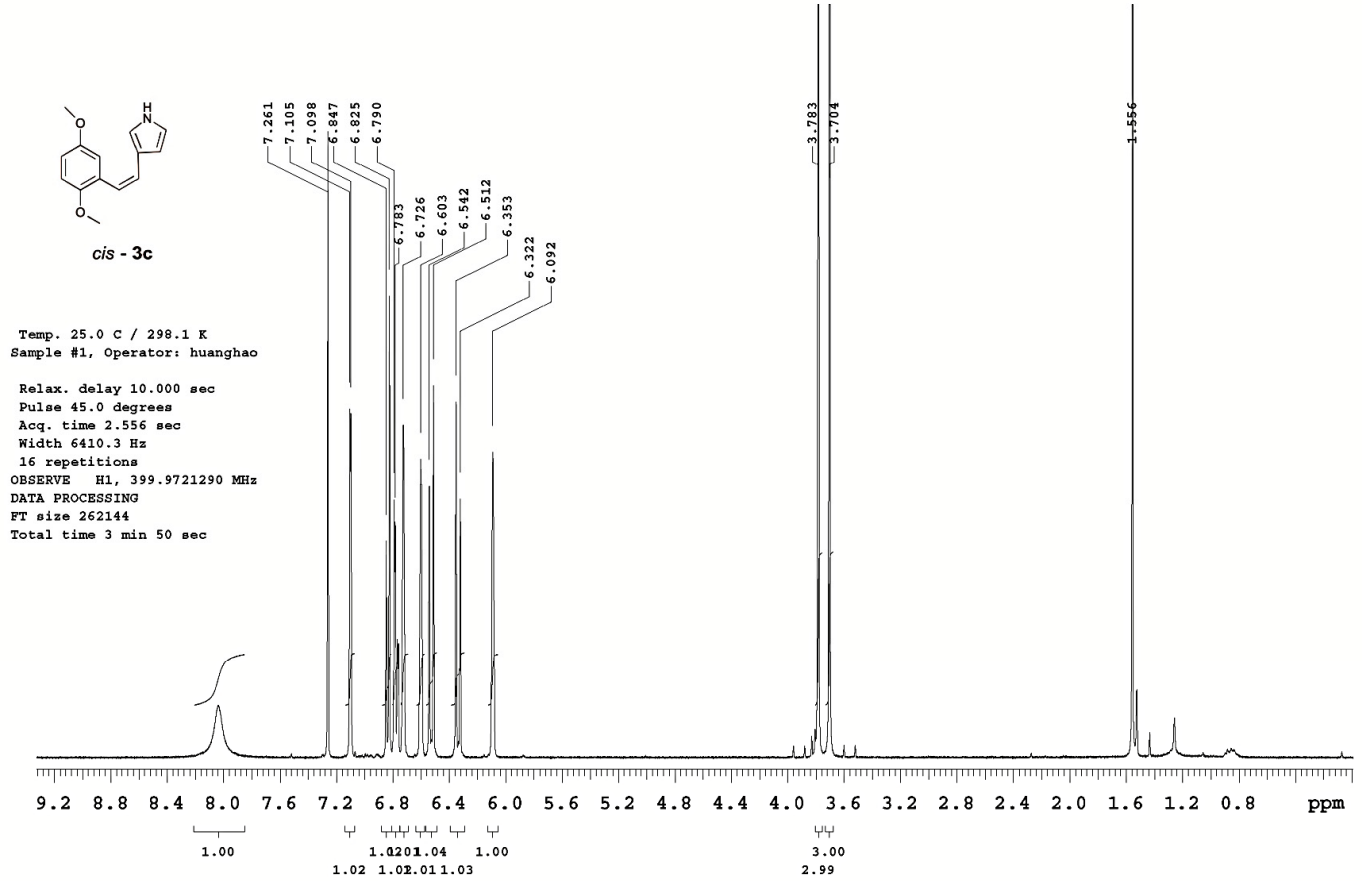


Figure S 23. ^{1}H NMR spectrum (400 MHz, $CDCl_3$ solution) of *cis*-**3c**.

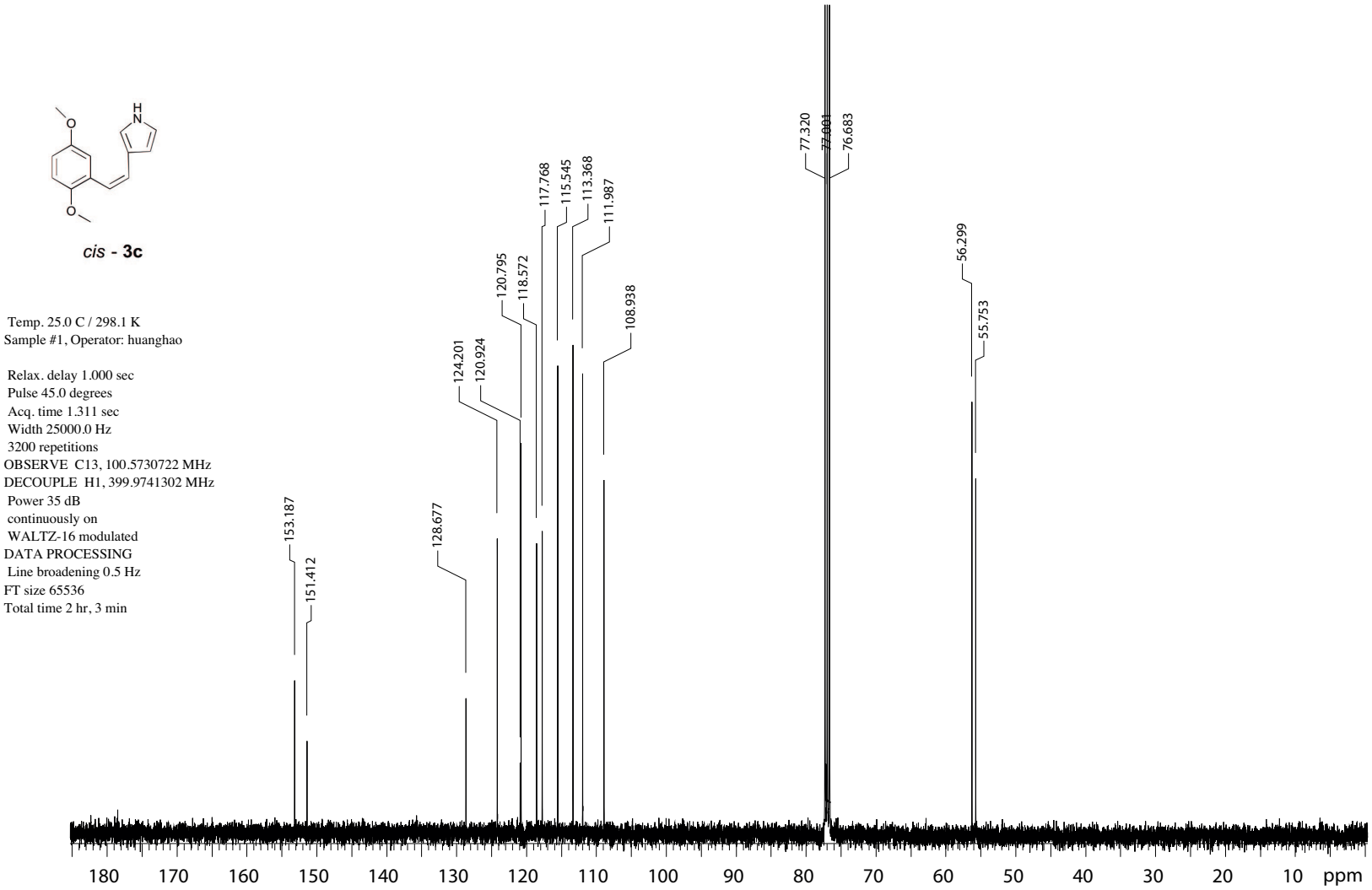


Figure S 24. ^{13}C NMR spectrum (100.6 MHz, $CDCl_3$ solution) of *cis*-**3c**.

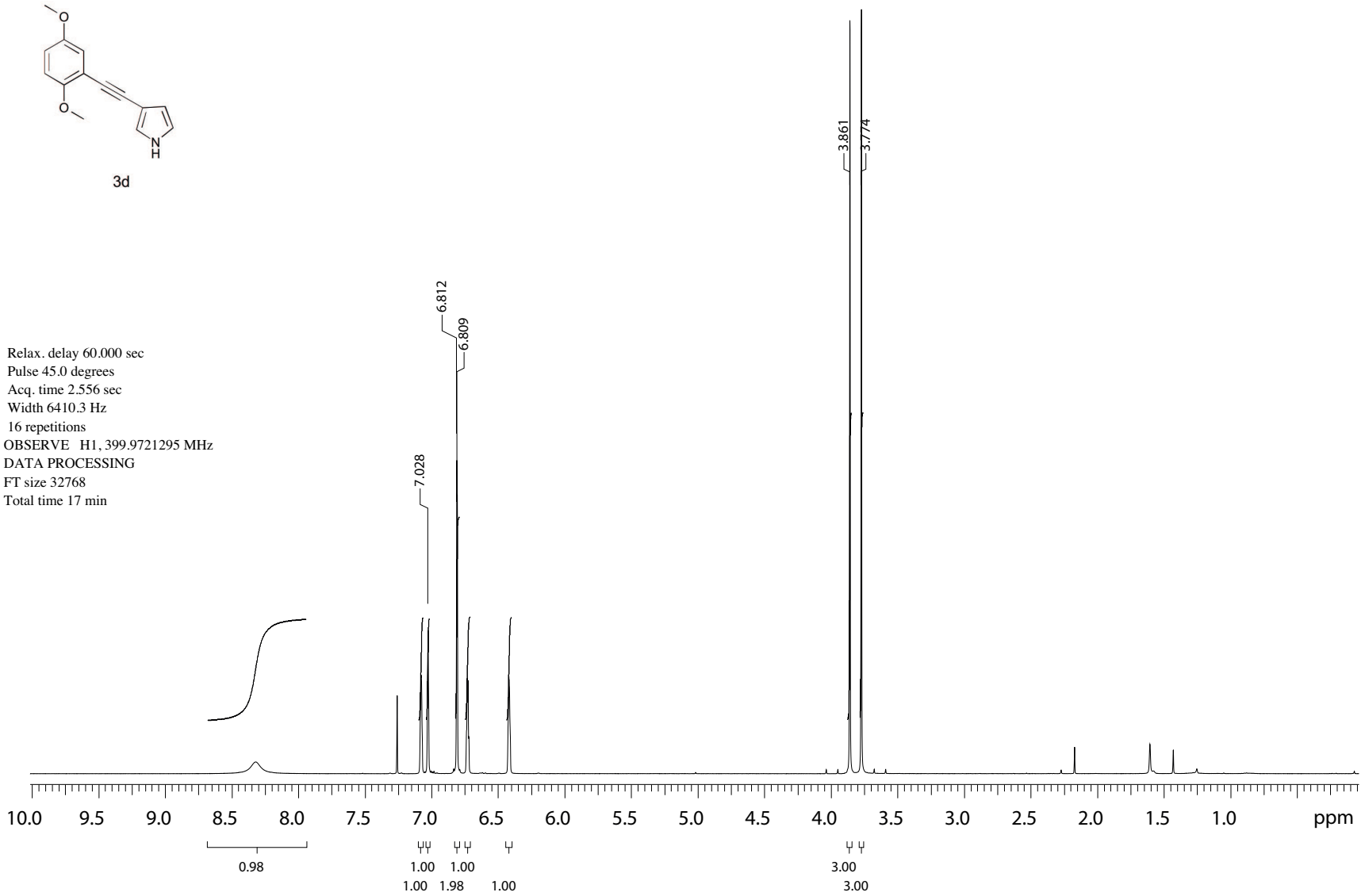


Figure S 25. ^{1}H NMR spectrum (400 MHz, $CDCl_3$ solution) of **3d**.

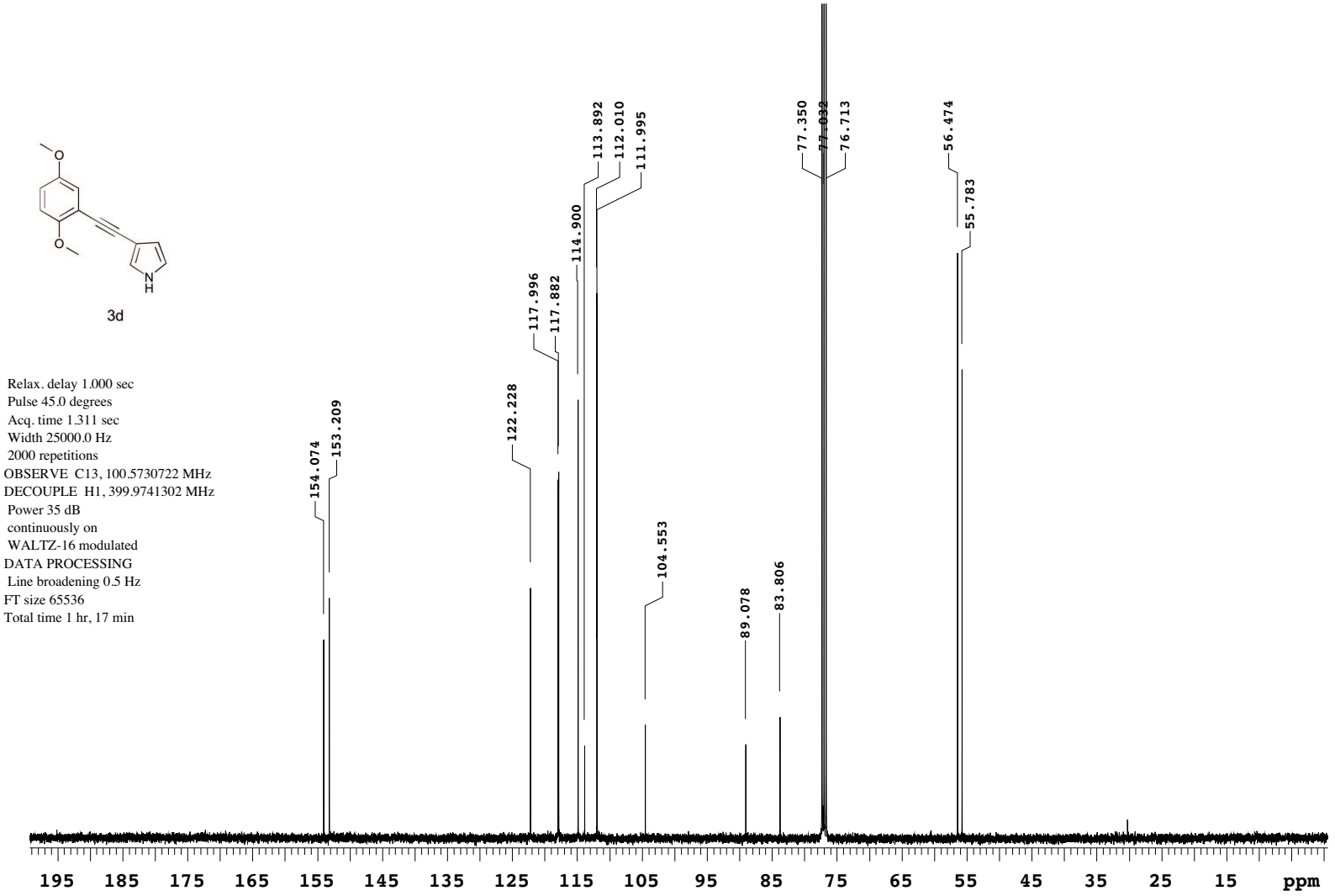


Figure S 26. ^{13}C NMR spectrum (100.6 MHz, $CDCl_3$ solution) of **3d**.

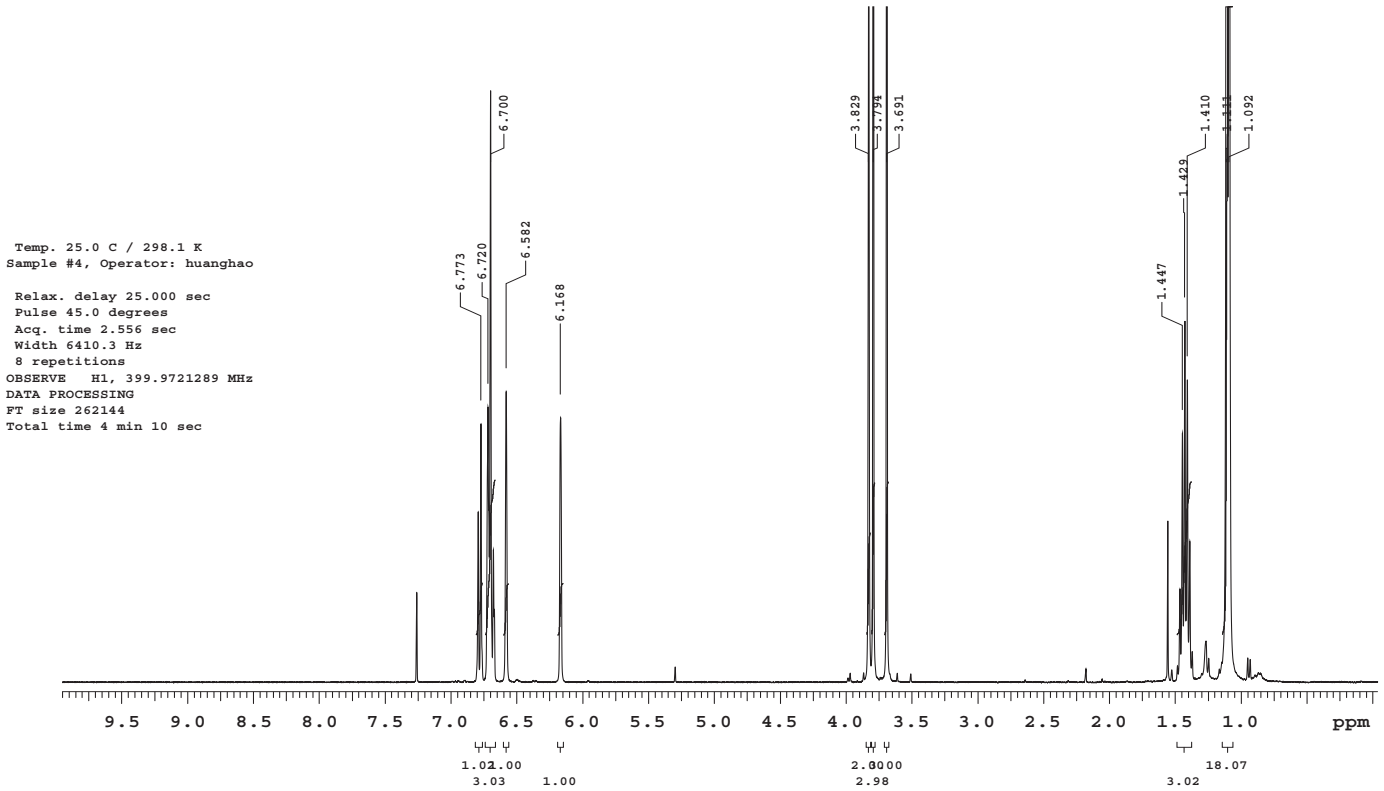


Figure S 27. ^{1}H NMR spectrum (400 MHz, $CDCl_3$ solution) of **4a**.

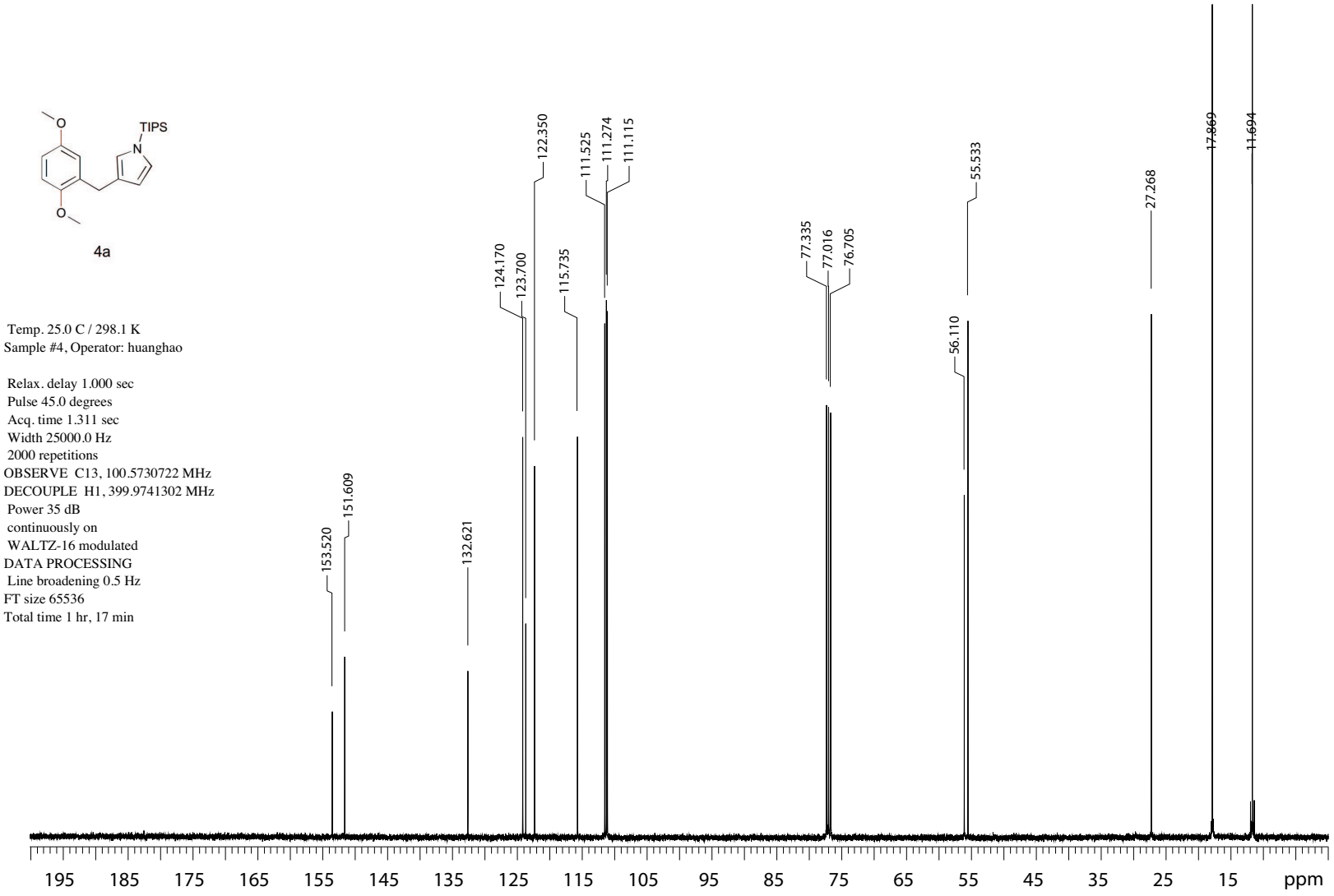


Figure S 28. ^{13}C NMR spectrum (100.6 MHz, $CDCl_3$ solution) of **4a**.

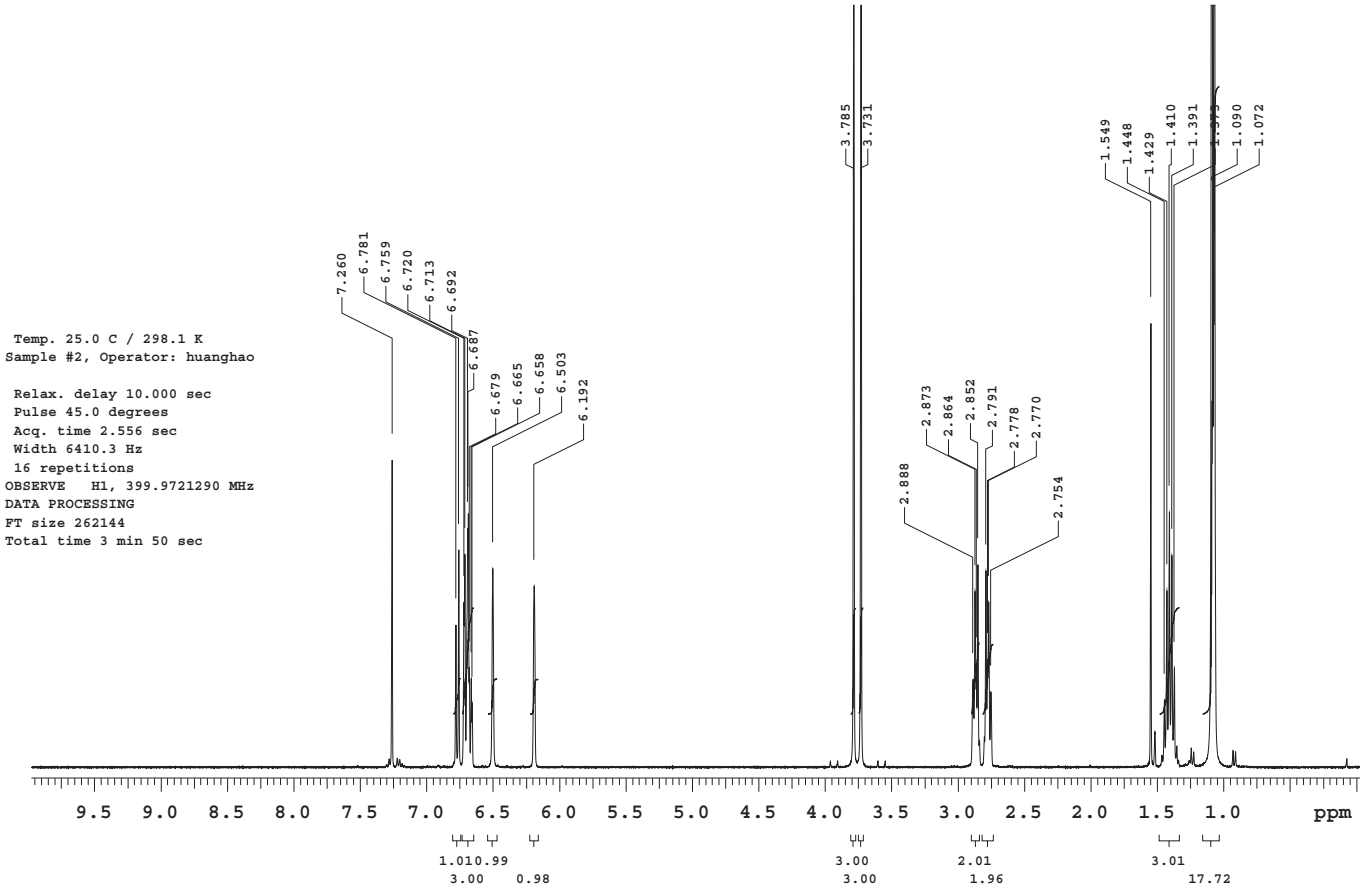


Figure S 29. ^{1}H NMR spectrum (400 MHz, $CDCl_3$ solution) of **4b**.

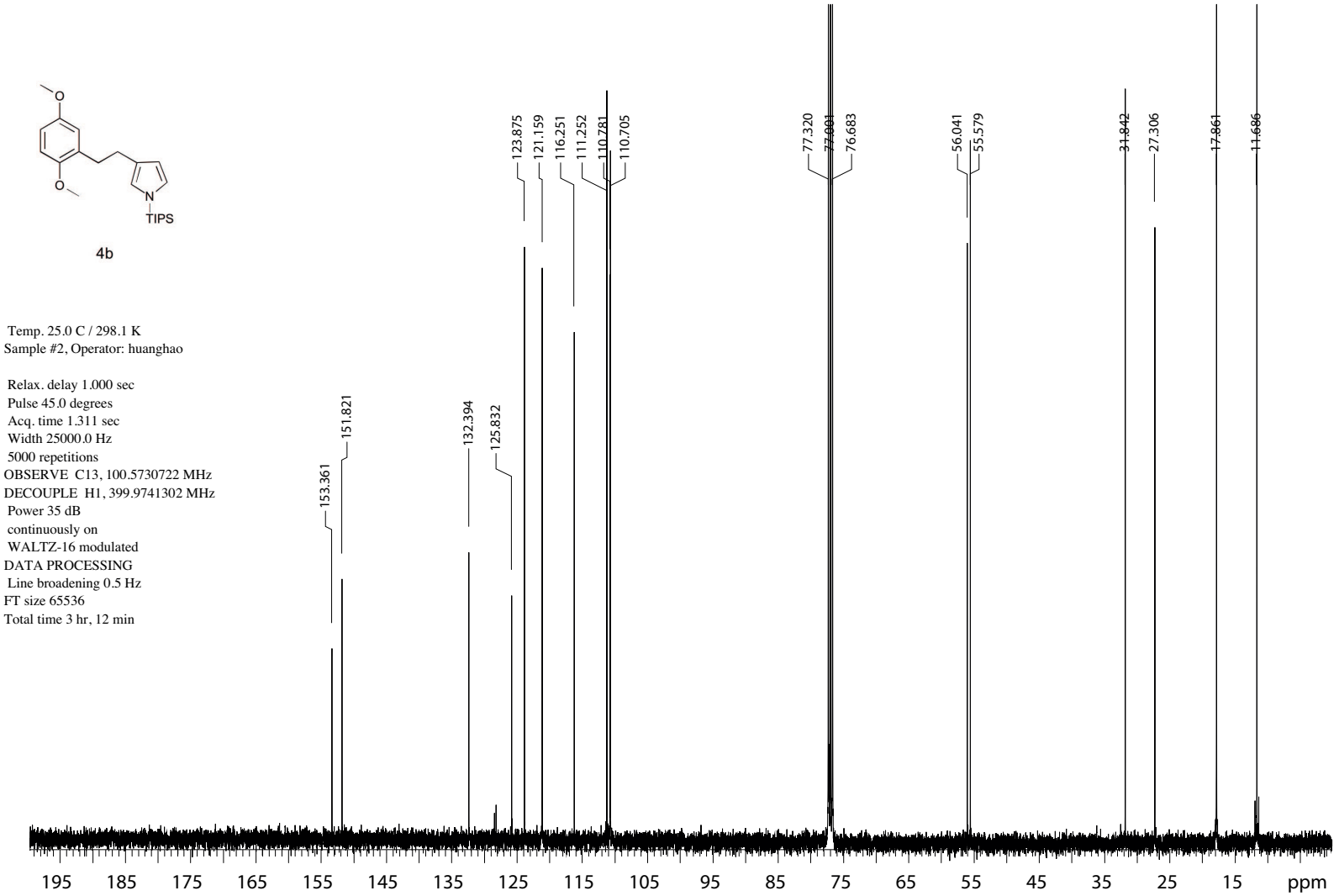


Figure S 30. ^{13}C NMR spectrum (100.6 MHz, $CDCl_3$ solution) of **4b**.

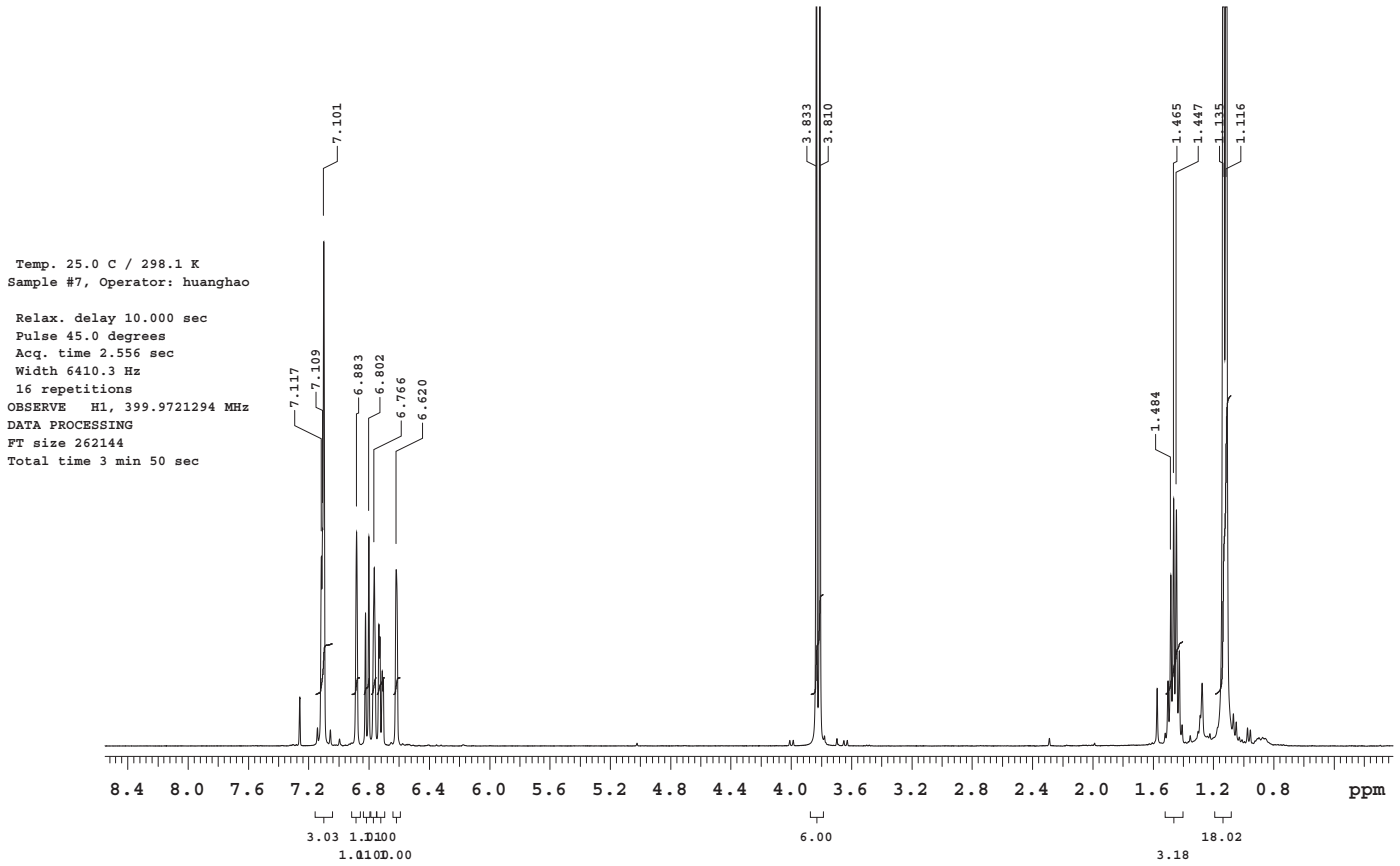


Figure S 31. ^{1}H NMR spectrum (400 MHz, $CDCl_3$ solution) of *trans*-**4c**.

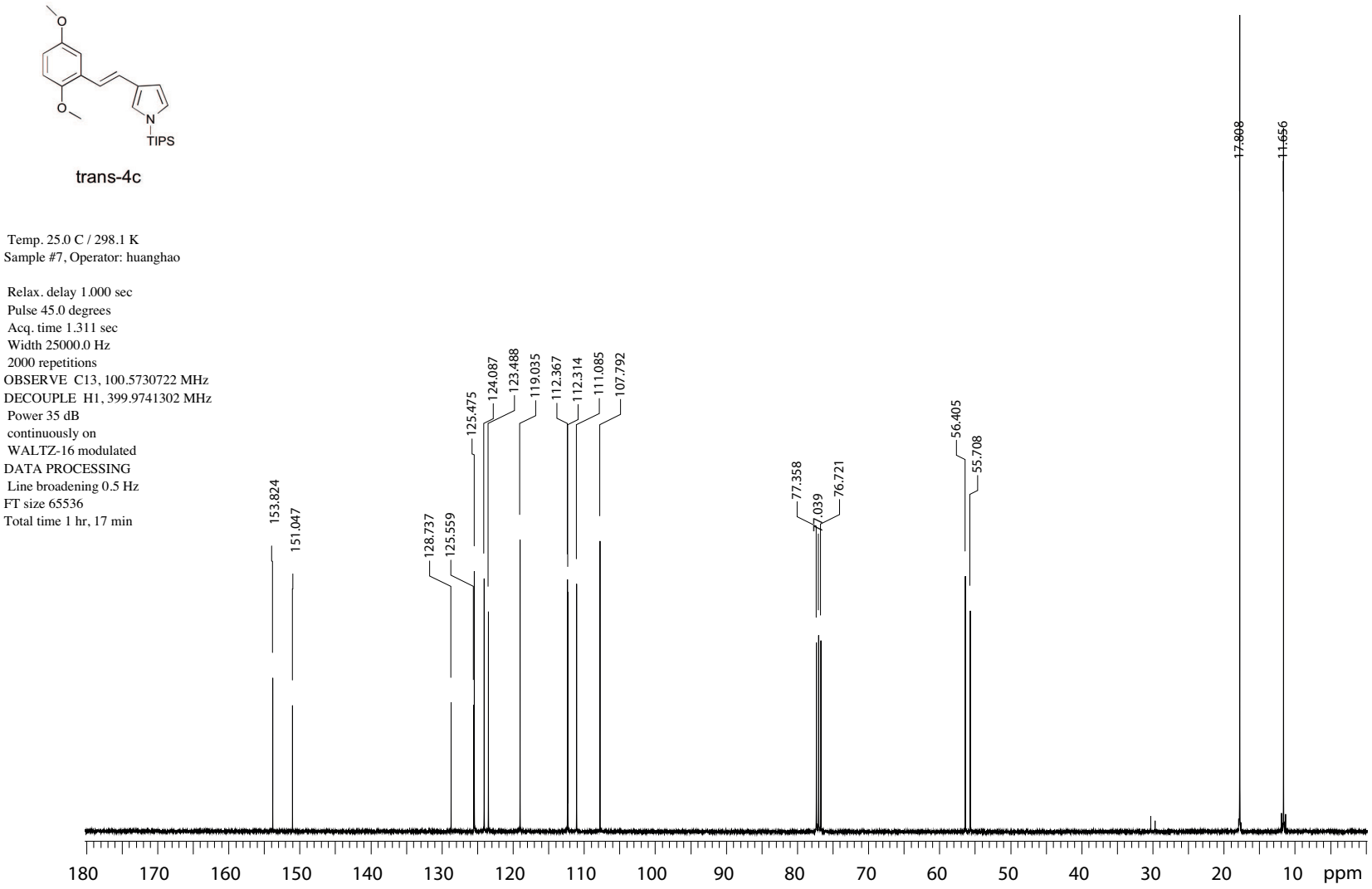


Figure S 32. ^{13}C NMR spectrum (100.6 MHz, $CDCl_3$ solution) of *trans*-**4c**.

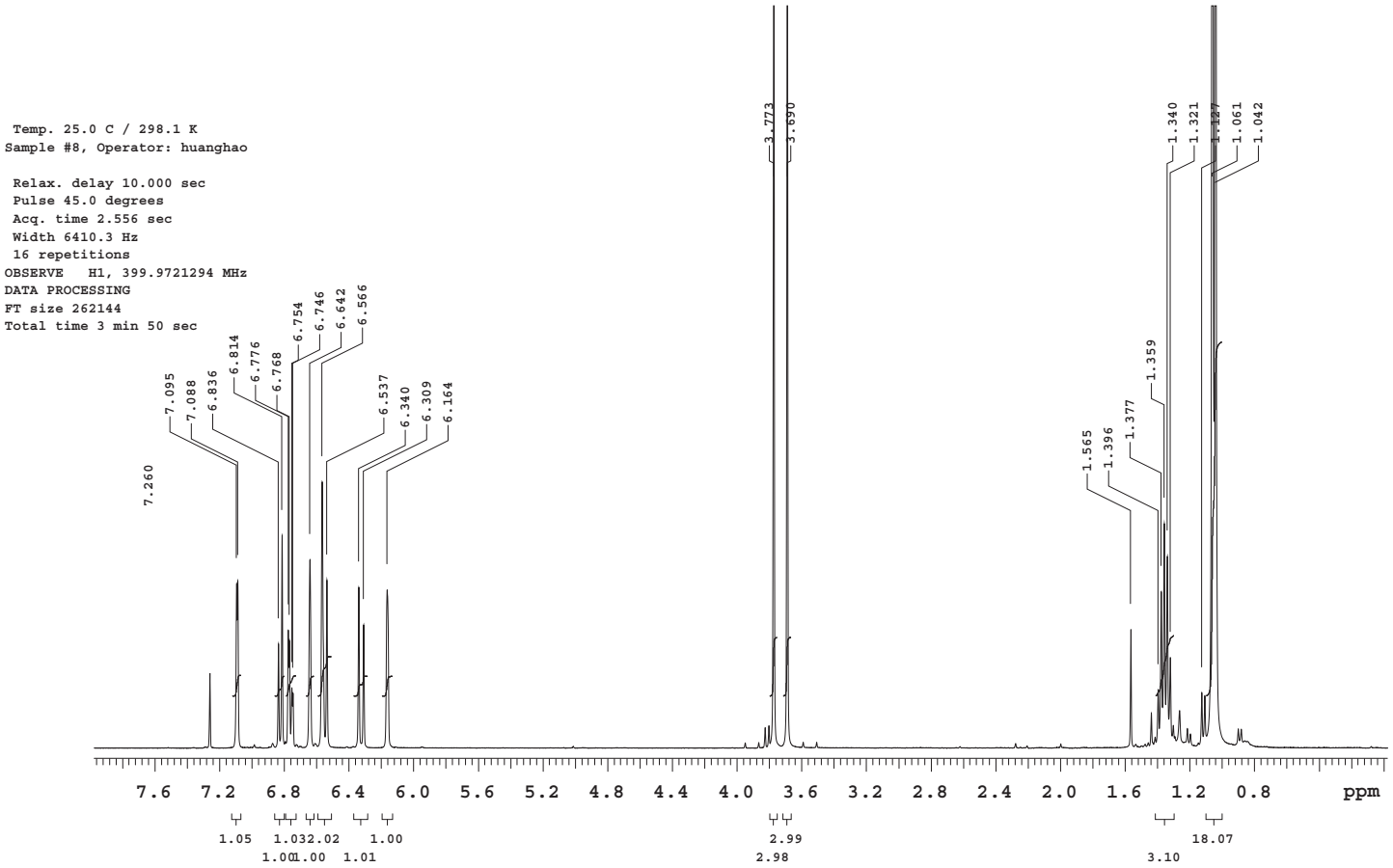


Figure S 33. ^{1}H NMR spectrum (400 MHz, $CDCl_3$ solution) of *cis*-**4c**.

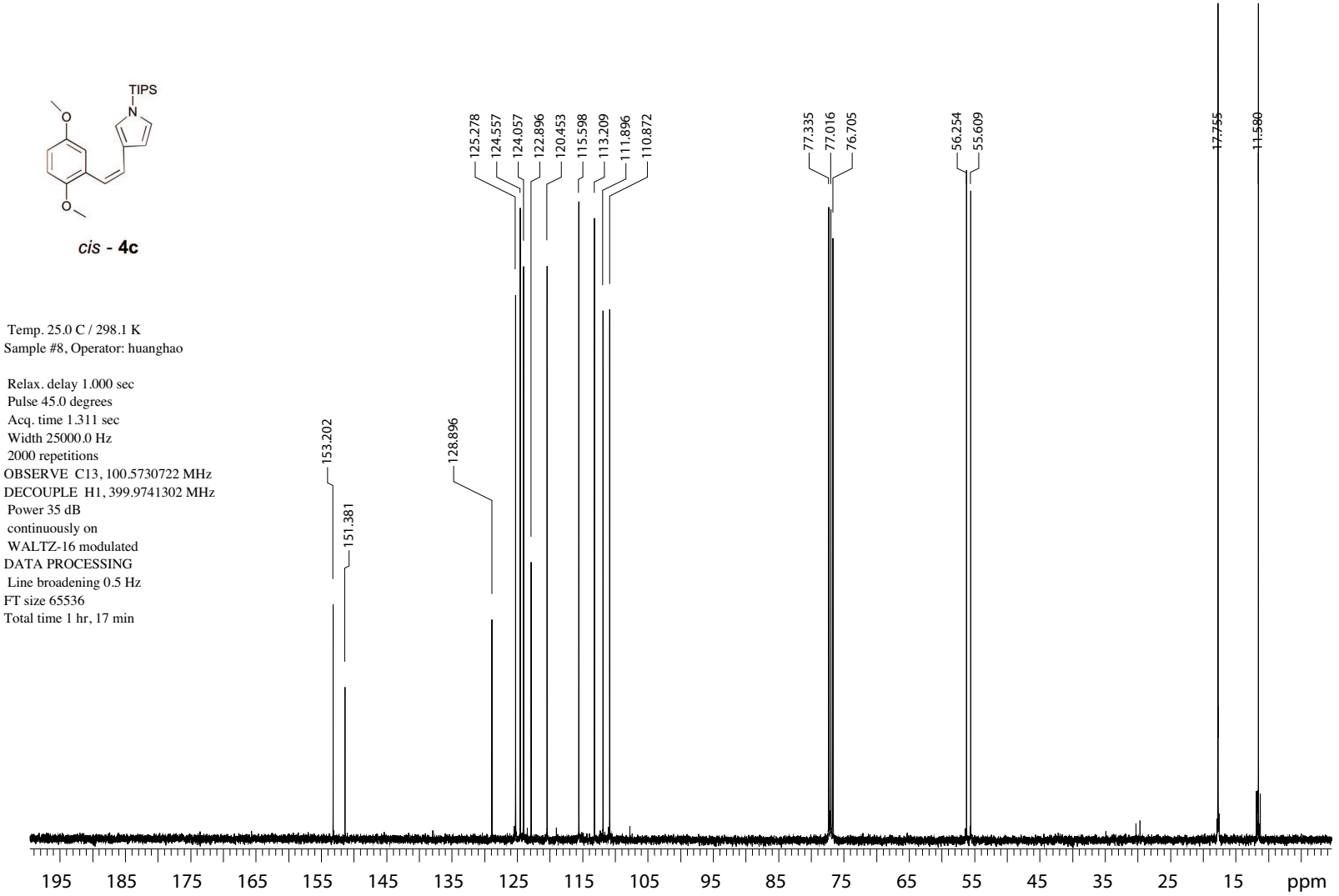


Figure S 34. ^{13}C NMR spectrum (100.6 MHz, $CDCl_3$ solution) of *cis*-**4c**.

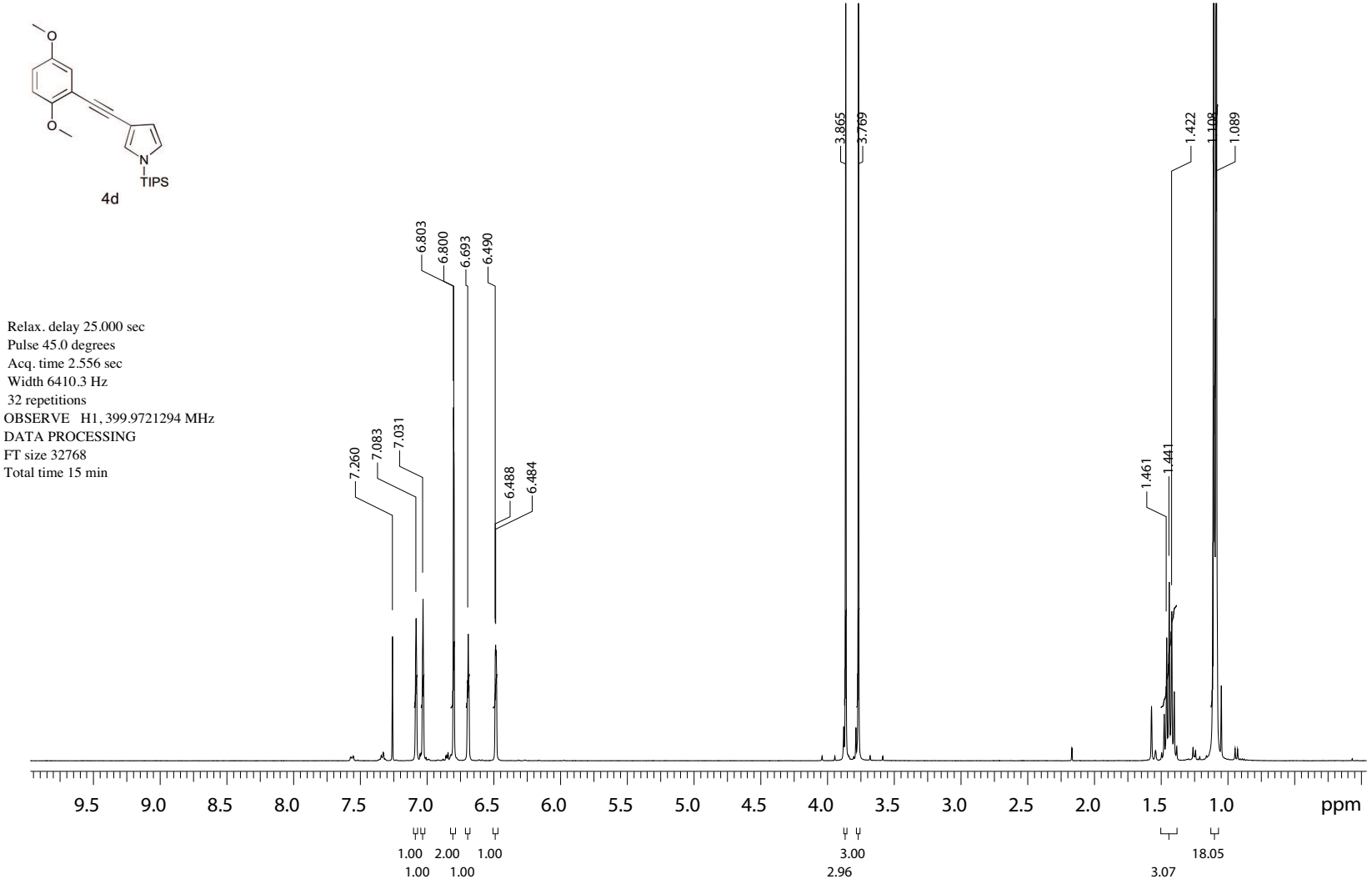


Figure S 35. ^{1}H NMR spectrum (400 MHz, $CDCl_3$ solution) of **4d**.

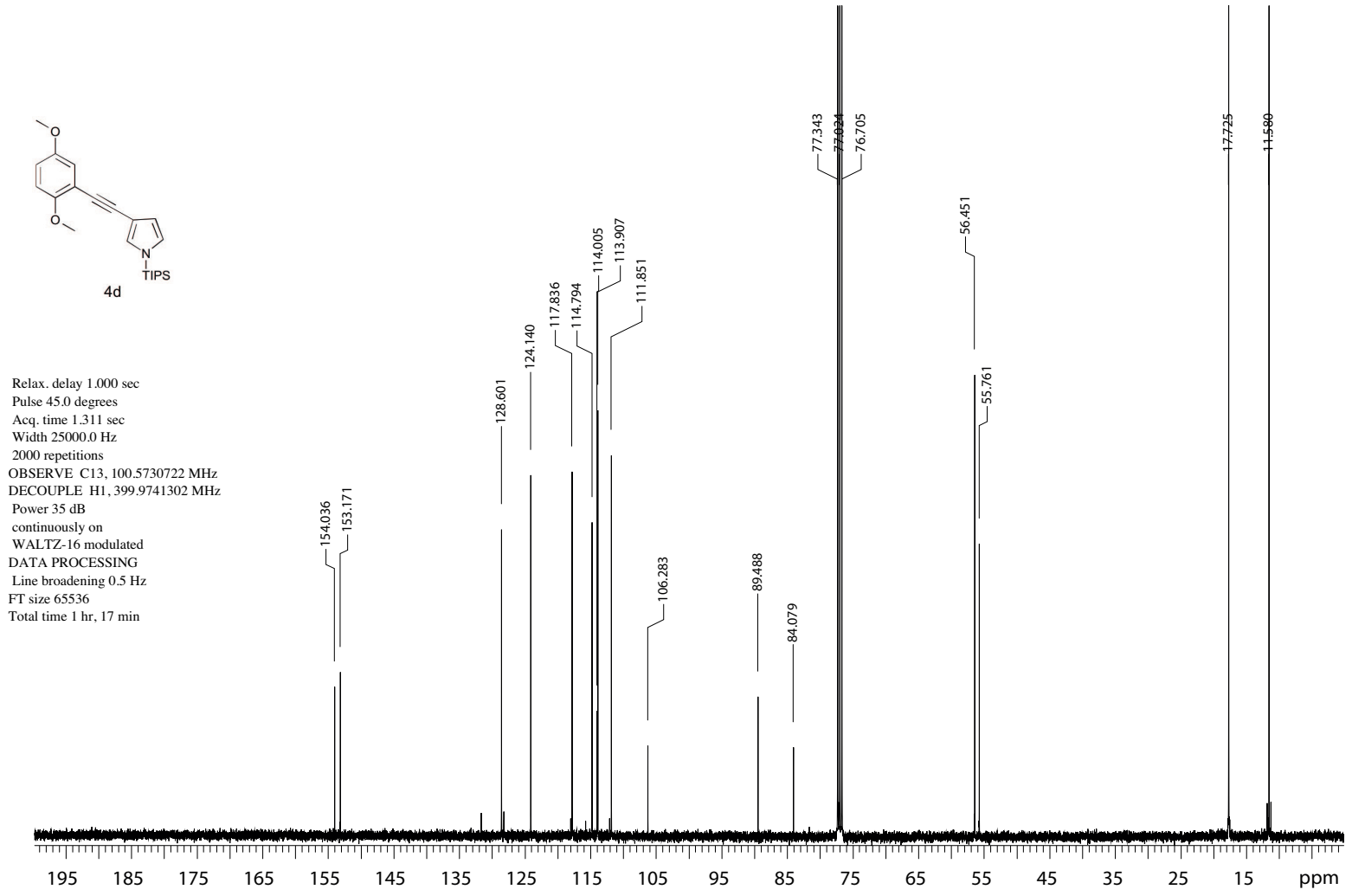


Figure S 36. ^{13}C NMR spectrum (100.6 MHz, $CDCl_3$ solution) of **4d**.

Mass spectra

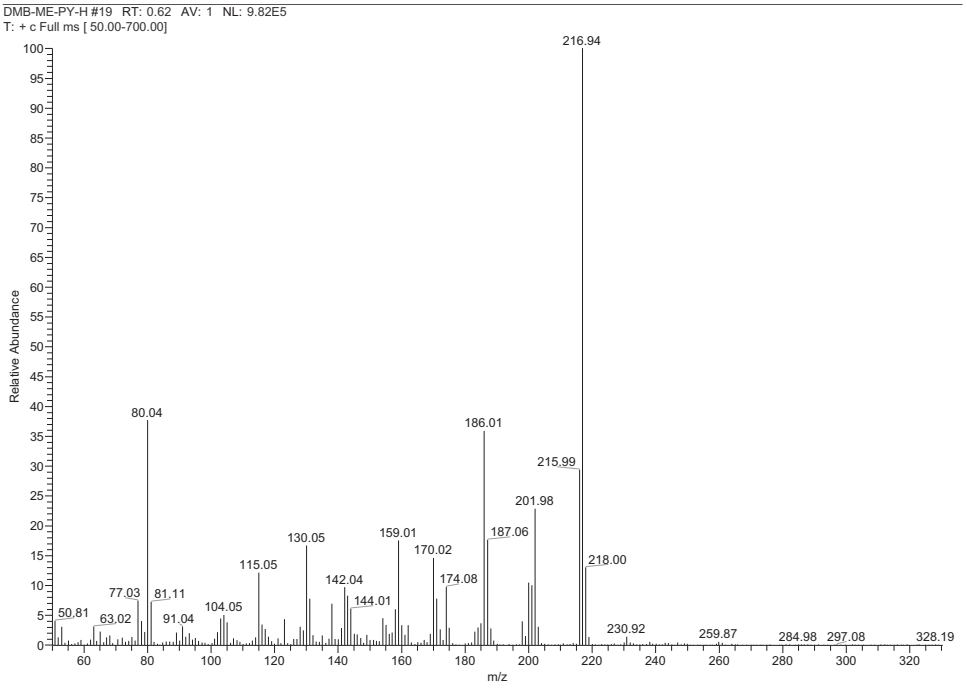


Figure S 37. Mass spectrum of **3a**.

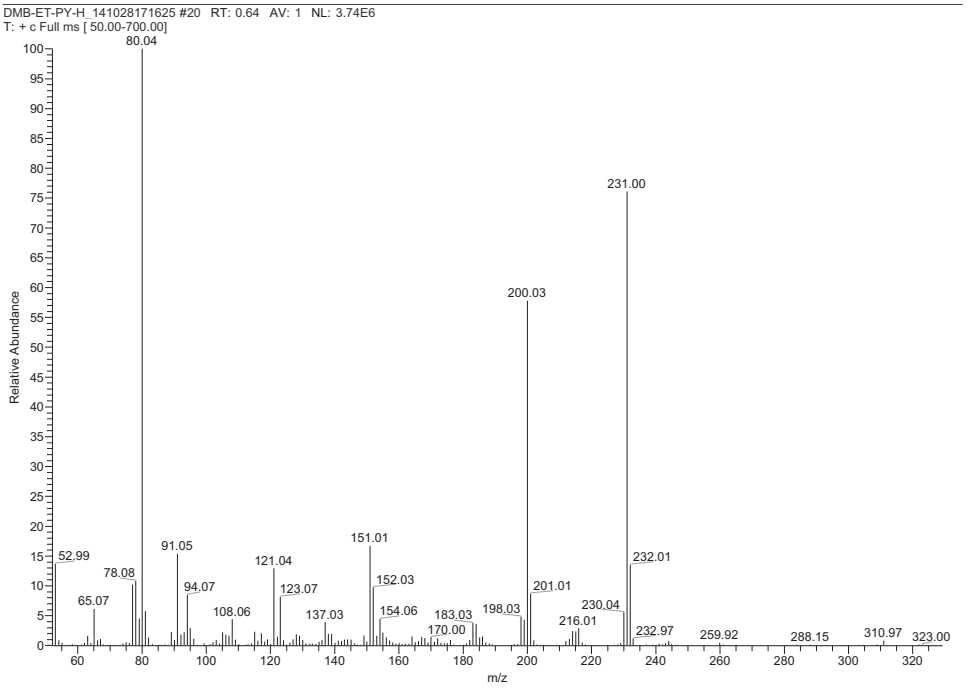


Figure S 38. Mass spectrum of **3b**.

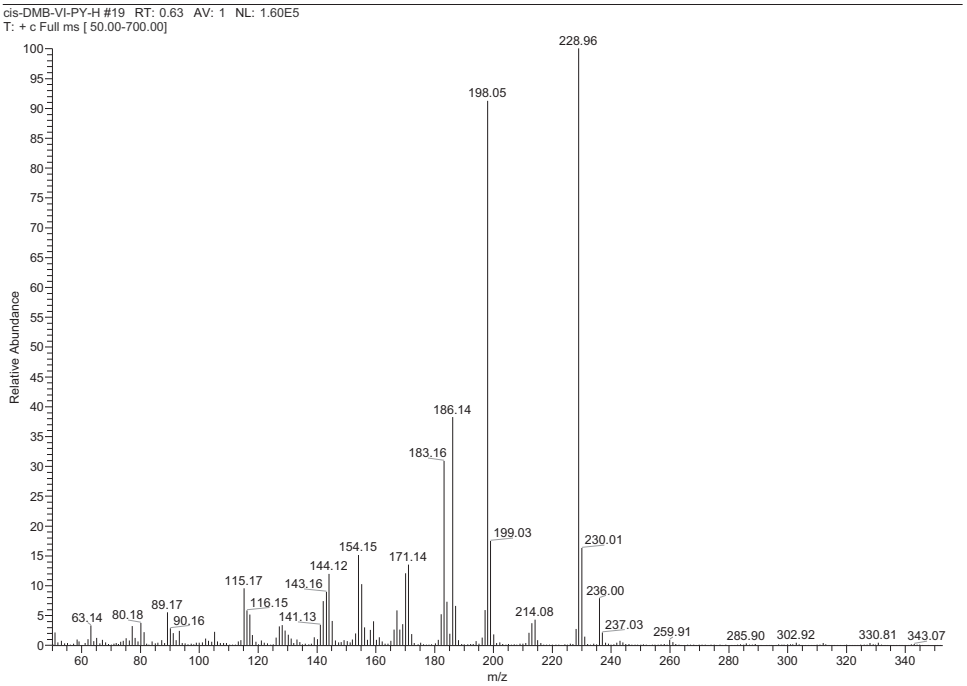


Figure S 39. Mass spectrum of *cis*-**3c**.

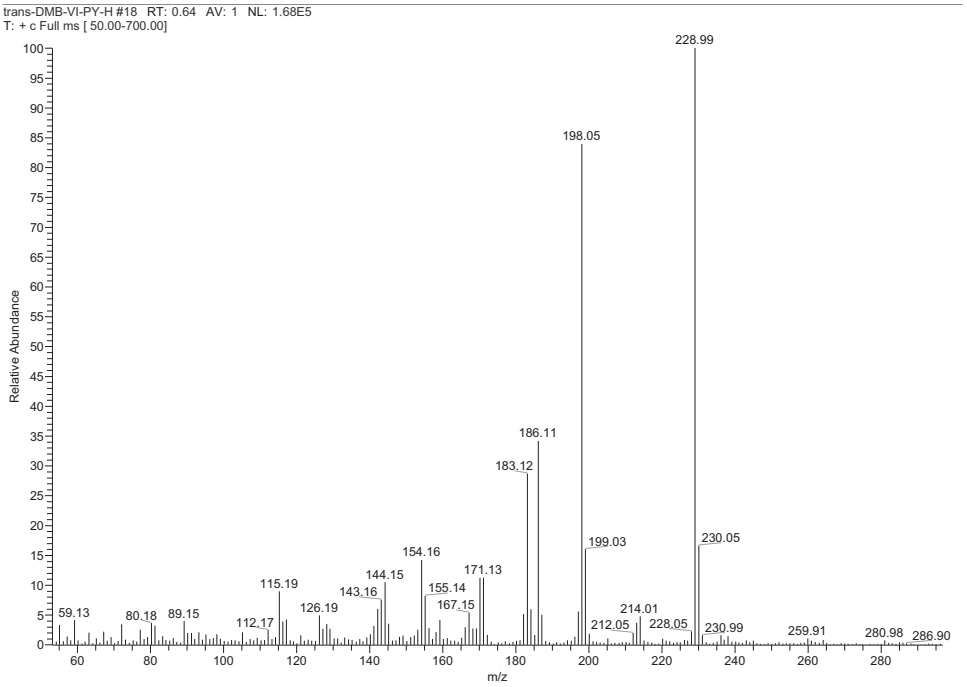


Figure S 40. Mass spectrum of *trans*-**3c**.

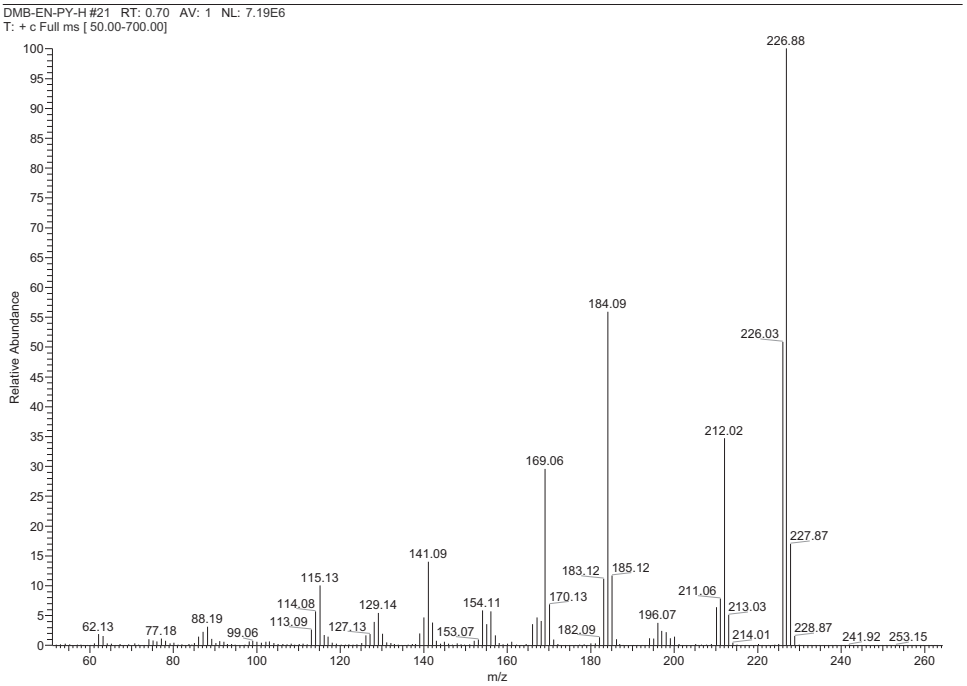


Figure S 41. Mass spectrum of **3d**.

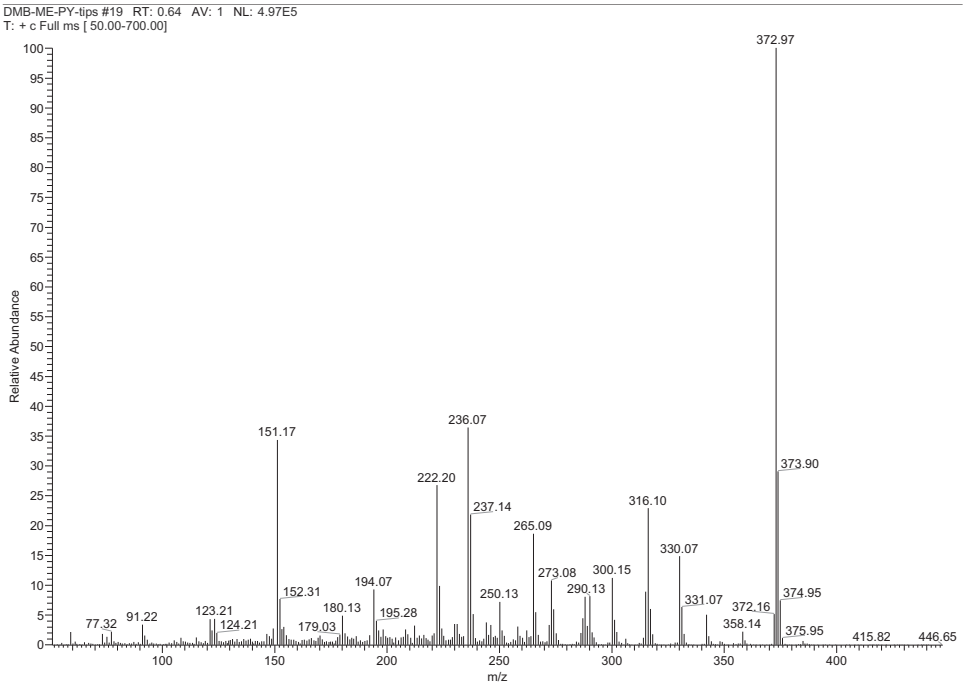


Figure S 42. Mass spectrum of **4a**.

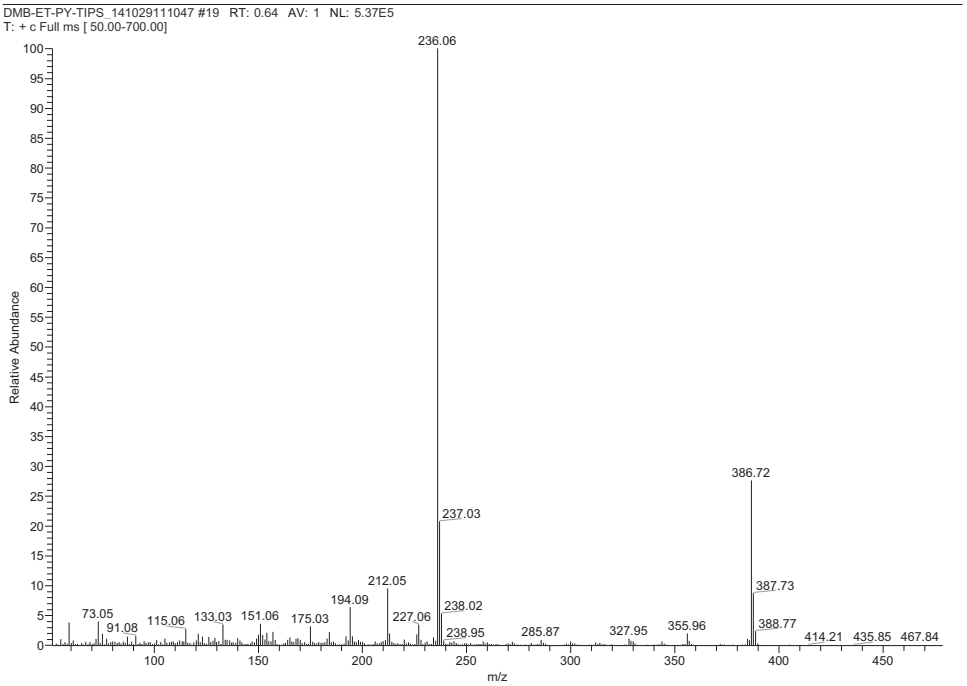


Figure S 43. Mass spectrum of **4b**.

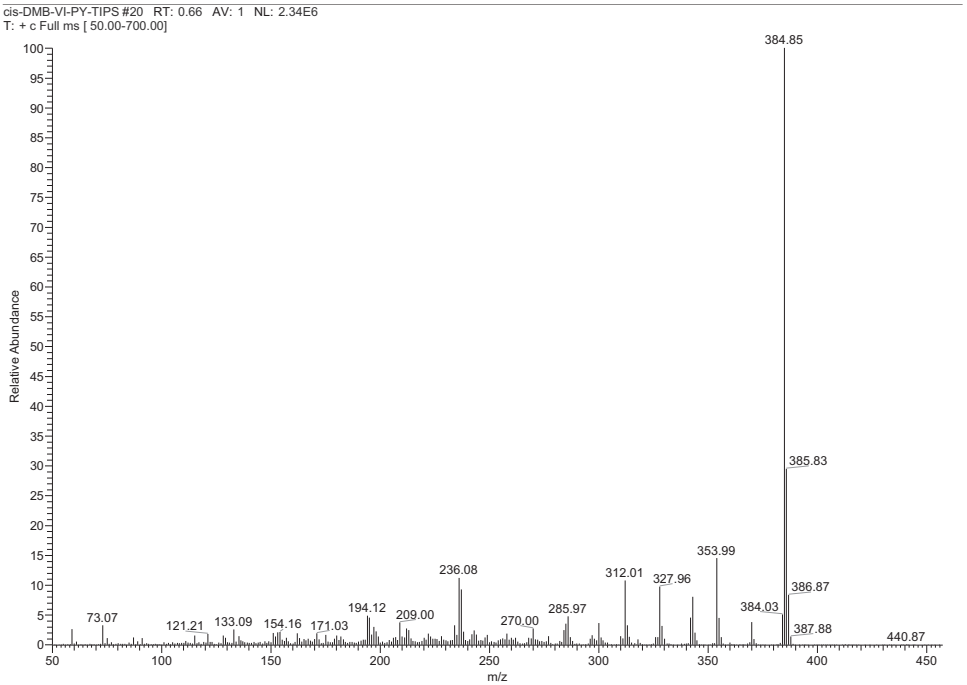


Figure S 44. Mass spectrum of *cis*-**4c**.

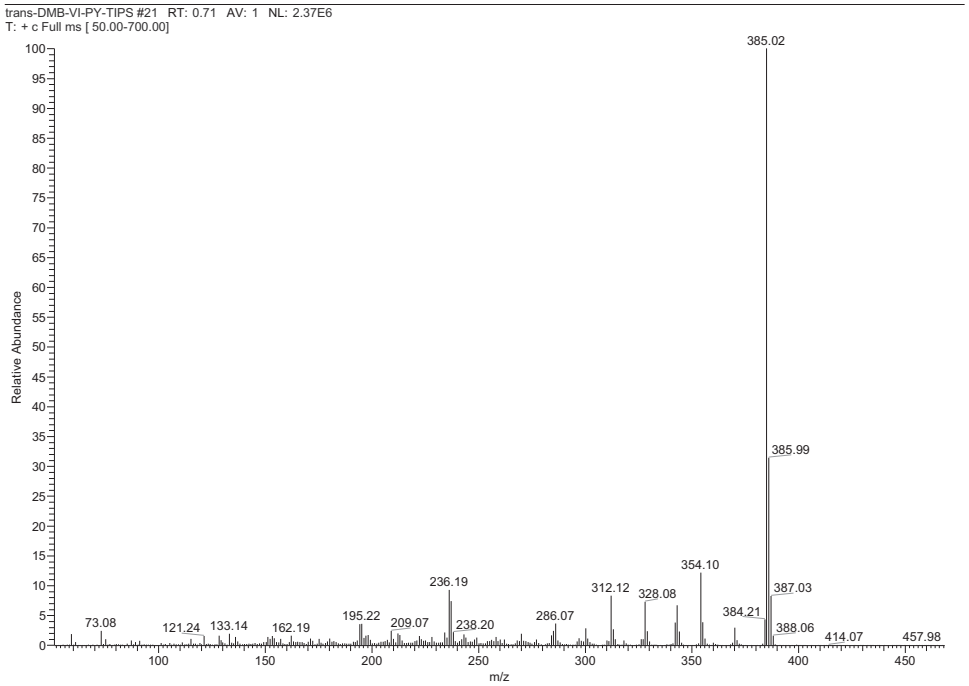


Figure S 45. Mass spectrum of *trans*-**4c**.

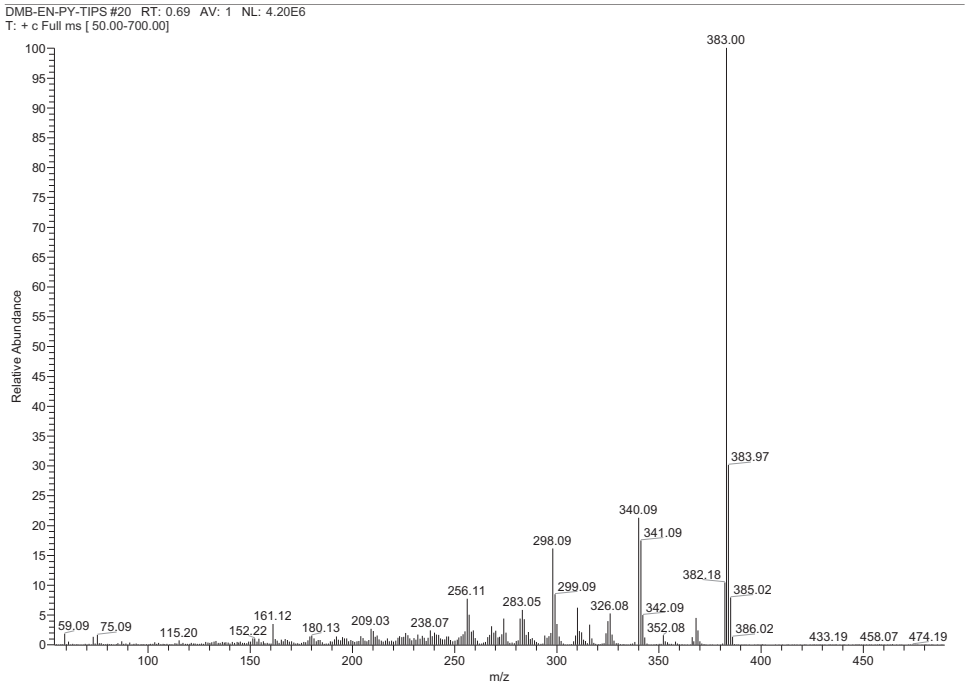


Figure S 46. Mass spectrum of **4d**.

Calculated NMR chemical shifts

Table S 2. Comparison of experimental and calculated ^{1}H chemical shifts for the dyads discussed in the text.

		Py-2	Py-4	Py-5	Ph-3	Ph-4	Ph-6
1	δ_{exp}	7.36	6.62	6.83	6.87	6.70	7.13
	δ_{DFT}	7.30	6.55	6.73	6.75	6.61	7.08
	$Error_{abs}$	0.06	0.07	0.10	0.12	0.09	0.05
3a	δ_{exp}	6.57	6.12	6.72	6.78	6.69	6.76
	δ_{DFT}	6.61	6.20	6.49	6.65	6.66	6.57
	$Error_{abs}$	0.04	0.08	0.23	0.13	0.03	0.19
3b	δ_{exp}	6.63	6.2	6.76	6.84	6.76	6.84
	δ_{DFT}	6.59	5.99	6.68	6.67	6.67	6.62
	$Error_{abs}$	0.04	0.21	0.08	0.17	0.09	0.22
trans-**3c**	δ_{exp}	6.91	6.52	6.78	6.81	6.72	7.10
	δ_{DFT}	6.68	6.52	6.70	6.75	6.62	6.63
	$Error_{abs}$	0.23	0.00	0.08	0.06	0.10	0.47
cis-**3c**	δ_{exp}	6.72	6.09	6.60	6.84	6.78	7.1
	δ_{DFT}	6.68	5.86	6.44	6.64	6.78	6.61
	$Error_{abs}$	0.04	0.23	0.16	0.20	0.00	0.49
3d	δ_{exp}	7.08	6.42	6.73	6.8	6.8	7.03
	δ_{DFT}	7.04	6.32	6.61	6.65	6.75	6.79
	$Error_{abs}$	0.04	0.10	0.12	0.15	0.05	0.24

The average error is 0.13 ppm and the RMS value is 0.17 ppm.

Table S 3. Comparison of experimental and calculated ^{13}C chemical shifts for the dyads discussed in the text.

		Py-2	Py-3	Py-4	Py-5	Ph-1	Ph-2	Ph-3	Ph-4	Ph-5	Ph-6
1	δ_{exp}	118.1	120.2	107.9	117.7	125.6	150.6	112.3	110.6	153.7	114.0
	δ_{DFT}	118.8	121.6	105.4	115.9	125.2	150.1	109.4	112.4	154.4	106.0
	$Error_{abs}$	0.7	1.4	2.4	1.9	0.4	0.5	2.9	1.8	0.6	7.9
3a	δ_{exp}	115.9	122.2	109.2	117.8	132.3	151.5	111.2	110.8	153.5	116.4
	δ_{DFT}	112.8	127.1	107.1	116.5	133.5	150.4	108.9	112.9	153.2	110.0
	$Error_{abs}$	3.1	4.9	2.1	1.3	1.3	1.1	2.3	2.2	0.2	6.4
3b	δ_{exp}	115.0	124.1	108.6	117.6	132.3	151.8	111.3	110.8	153.4	116.2
	δ_{DFT}	111.8	126.4	107.0	116.2	132.2	151.1	108.5	113.8	153.6	110.1
	$Error_{abs}$	3.1	2.3	1.6	1.4	0.1	0.8	2.8	2.9	0.2	6.1
trans **-3c**	δ_{exp}	117.4	123.5	105.9	119.0	128.5	151.0	112.4	112.4	153.8	111.1
	δ_{DFT}	118.3	124.9	102.5	118.2	126.9	152.4	109.8	112.9	153.5	111.4
	$Error_{abs}$	0.8	1.3	3.4	0.8	1.6	1.4	2.6	0.5	0.3	0.2
cis- **3c**	δ_{exp}	118.6	120.9	108.9	117.8	128.7	151.4	112.0	113.4	153.2	115.5
	δ_{DFT}	119.2	124.2	106.5	116.6	129.9	150.7	108.8	114.3	153.1	109.4
	$Error_{abs}$	0.7	3.3	2.4	1.2	1.2	0.7	3.2	1.0	0.1	6.2
3d	δ_{exp}	122.2	104.5	112.0	118.0	113.9	154.1	112.0	114.9	153.2	117.9
	δ_{DFT}	123.0	105.4	111.5	116.8	113.3	154.2	108.9	115.7	153.1	112.3
	$Error_{abs}$	0.8	0.9	0.5	1.2	0.6	0.2	3.1	0.9	0.1	5.5

The average error is 1.9 ppm, and the RMS is 2.6 ppm.

Gaussian 09 was used to perform the DFT calculation at B3LYP level of theory. Structures were optimized in the gas phase with the 6-311+G(d) basis set. NMR chemical shifts were calculated by the GIAO method with 6-311+G(2d,p) at the B3LYP level of theory using the SDM solvent model with chloroform as solvent.[1] NMR chemical shift data were extracted from the computed isotropic shielding constants and the slope and intercept from the linear regression analysis (eq 1):

$$\delta = \frac{A - \sigma}{-B} \qquad \text{(eq. 1)}$$

Here, σ is the isotropic shielding constant, A is the intercept, and B is the slope. The values of intercept and slope were obtained from reference 1.

1. Lodewyk, M. W.; Siebert, M. R.; Tantillo, D. J., *Chem. Rev.* **2012,** *112* (3), 1839-1862.