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Halogen···halogen interactions in diiodo-xylenes†

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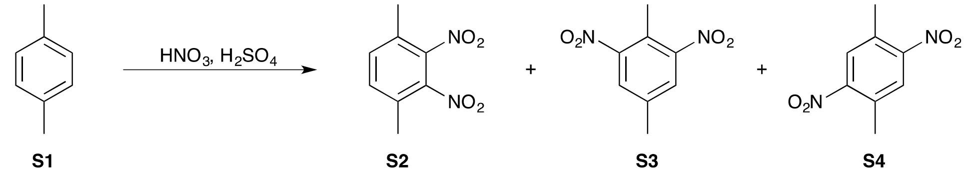
Table of Contents — Page

General Information

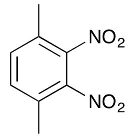
Commercially available reagents *p*-xylene and *m*-xylene were purchased and used as received. All reactions were performed in air unless otherwise specified. TLC analysis was performed on glass backed plates (60Å) and flash chromatography was performed on ultra-pure flash silica (230-400 mesh size). NMR spectra were recorded using a Varian Inova 300 MHz (^{1}H: 299.838 MHz, ^{13}C: 75.402 MHz) or Varian Unity 400 MHz spectrometer (^{1}H: 399.945 MHz, ^{13}C: 100.577 MHz) with $CDCl_3$ referenced at 7.26 ppm (^{1}H) or 77.16 ppm (^{13}C). X-ray diffraction data sets for compounds **1-4** were collected on a Bruker AXS P4/SMART 1000 diffractometer. IR spectra were recorded using KBr discs on a Nicolet Nexus 470 FTIR spectrometer. High resolution mass spectra were recorded on a Bruker Daltonics spectrometer using Electrospray Ionization (ESI). Melting points were determined using a DigiMelt melting point apparatus.

Experimental Data

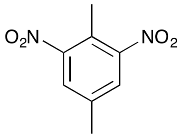


Scheme S1. Synthesis of dinitro-*p*-xylene isomers **S2, S3, S4**.

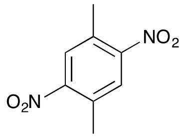
2,3-dinitro-*p*-xylene (S2); 2,6-dinitro-*p*-xylene (S3); 2,6-dinitro-*p*-xylene (S4)



S2

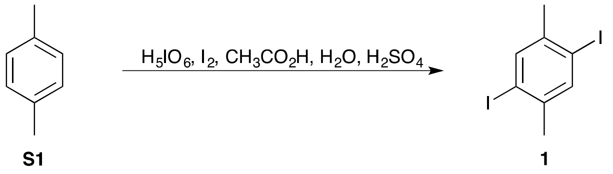


S3



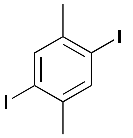
S4

p-Xylene **S1** (11.5 mL, 93.3 mmol) was added to a cooled solution of H_2SO_4 and kept at 0 °C for 1 minute. A 1:1 solution of H_2SO_4 (12 mL) and HNO_3 (12 mL) at 0 °C was added slowly to the *p*-xylene solution then heated to 80 °C for 30 minutes. The solution was dumped on ice then extracted with DCM (3 x 10 mL). The organic layer was washed with H_2O (3 x 10 mL) and $NaHCO_3$ (5 mL) then dried over $MgSO_4$. The solvent was removed by reduced pressure and all three isomers were obtained in a 2:2:1 (S2:S3:S4) ratio with an 80% overall yield. The 2,3-dinitro-p-xylene **S2** was obtained pure from the mixture of isomers using flash column chromatography (2:1 hexane:ethyl acetate; SiO_2) in a yield of 32% (5.86g). The 2,6-dinitro-p-xylene **S3** was then separated from 2,5-dinitro-p-xylene **S4** by sequential recrystallizations in propanol (2.00 g, 11%). The ^{1}H and ^{13}C NMR spectra of **S2** and **S3** agreed with literature reports.[1] The 2,5-dinitro-p-xylene **S4** was not isolated pure from this reaction.



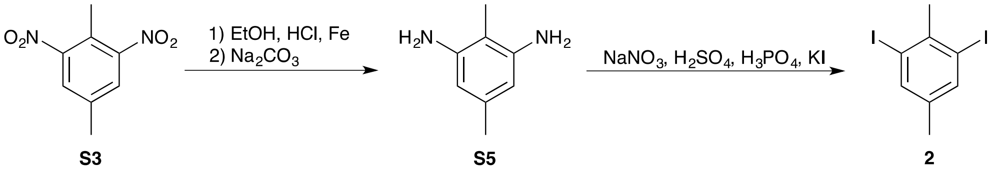
Scheme S2. Synthesis of 2,5-diiodo-*p*-xylene (**1**).

2,5-diiodo-*p*-xylene (1)



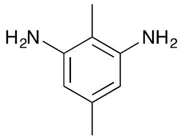
1

A mixture of *p*-xylene **S1** (0.656 g, 6.18 mmol), periodic acid (0.564 g, 2.47 mmol), iodine (1.26 g, 4.96 mmol), acetic acid (3 mL), water (0.6 mL), and concentrated H_2SO_4 (0.10 mL) were stirred at 70 °C for 4 h. The reaction mixture was poured into a saturated $NaHSO_3$ solution. The pink solid was filtered then washed with H_2O (3 x 10 mL) and methanol (3 x 10 mL). The filtrate was left overnight to crystallize and white crystals formed were collected (645 mg, 29%). mp 103-104 °C; R_f 0.67 (hexane); IR (film, KBr) vmax/cm^{-1} 2974 (CH_3), 2942 (CH_3), 2911 (CH_3), 1435 (CC), 1040 (CH), 741 (CH); δH(400 MHz, $CDCl_3$) 2.34 (6H, s), 7.65 (2H, s); δC(100 MHz, $CDCl_3$) 27.0, 100.8, 139.4, 140.8; HRMS (ESI+) for $C_8H_8I_2$ $[M]^+$: calcd. 357.8710, found 357.8720.



Scheme S3. Synthesis of 2,6-diiodo-*p*-xylene (**2**).

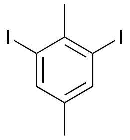
2,6-diamino-*p*-xylene (S5)



S5

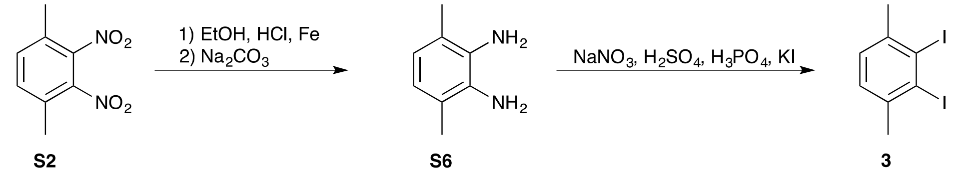
To a stirred solution of *m*-nitroxylene **S3** (1.185 g, 6.041 mmol) in ethanol (21 mL), was added concentrated HCl (1.8 mL) and Fe powder (2.699 g, 48.33 mmol). The mixture was refluxed for 6 hours then Na_2CO_3 (0.932 g, 8.79 mmol) was added and reflux continued for 30 minutes. Ammonia was added to the mixture to obtain a pH of approx. 10 then cooled to room temperature. The mixture was extracted with ethyl acetate (10 mL) and the organic layer washed with H_2O (3 x 10mL) then dried over $MgSO_4$. The solvent was removed by reduced pressure and a brown solid was obtained (301 mg, 36%). The ^1H and ^{13}C NMR spectra agreed with literature reports.[3]

2,6-diiodo-*p*-xylene (2)



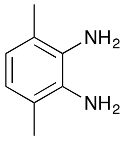
2

Diaminoxylene **S5** (200 mg, 1.47 mmol) and $NaNO_2$ (304 mg, 4.41 mmol) were added to concentrated H_2SO_4 (3.6 mL and 3.0 mL, respectively) in separate flasks. The first solution of **S5** and H_2SO_4 was added to the latter at 0 °C. H_3PO_4 (3.6 mL) was added while the temperature was kept between 0 °C and – 10 °C. The mixture was poured onto a mixture of ice and KI (1.22 g, 7.35 mmol) and allowed to stir overnight. The mixture was extracted with chloroform (3 x 10mL). The organic layer was washed with H_2O (3 x 10 mL), sodium bisulphite (5 mL), then dried over $MgSO_4$. The solvent was removed by reduced pressure and a yellow solid was obtained. The crude product was purified using flash chromatography (hexane; SiO_2) which afforded a white solid (190 mg, 25%). mp 70 – 71 °C; R_f 0.69 (hexane); IR (film, KBr) vmax/cm^{-1} 3050 (CH), 2914 (CH_3), 2854 (CH_3), 1444 (CC), 1041 (CH), 845 (CH), 705 (CH); δH(300 MHz, $CDCl_3$) 2.21 (3H, s), 2.70 (3H, s), 7.65 (2H, s); δC(100 MHz, $CDCl_3$) 19.7, 34.5, 99.1, 139.3, 139.9, 140.3; HRMS (ESI+) for $C_8H_8I_2$ $[M]^+$: calcd. 357.8710, found 357.8708.



Scheme S4. Synthesis of 2,3-diiodo-*p*-xylene (**3**).

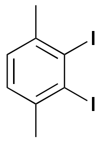
2,3-diamino-*p*-xylene (S6)



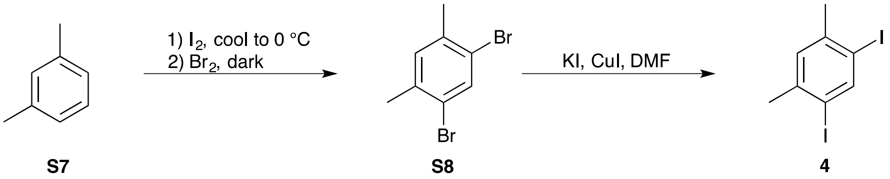
S6

To a stirred solution of *o*-nitroxylene **S2** (3.81 g, 19.4 mmol) in ethanol (50 mL) was added concentrated HCl (6 mL) and Fe powder (7.700 g, 137.9 mmol). The mixture was refluxed for 6 hours then Na_2CO_3 (2.450 g, 23.11 mmol) was added and reflux continued for 30 minutes. Ammonia was added to the mixture to obtain a pH of approx. 10 then cooled to room temperature. The mixture was extracted with ethyl acetate (10 mL) and the organic layer washed with H_2O (3 x 10mL) then dried over $MgSO_4$. The solvent was removed by reduced pressure and a brown solid was obtained (2.17 g, 82%). The ^1H and ^{13}C NMR spectra agreed with literature reports.[2]

2,3-diiodo-*p*-xylene (3)

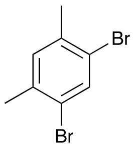

3

Diaminoxylene **S6** (0.250 g, 1.84 mmol) and $NaNO_2$ (2.07 g, 30.0 mmol) were added to concentrated H_2SO_4 (4.5 mL and 3.7 mL, respectively) in separate flasks. The first solution of **S6** and H_2SO_4 was added to the latter at 0 °C. H_3PO_4 (4.5 mL) was added while the temperature was kept between 0 °C and – 10 °C. The mixture was poured unto a mixture of ice and KI (1.52 g, 9.18 mmol) and allowed to stir overnight. The mixture was extracted with chloroform (3 x 10mL). The organic layer was washed with H_2O (3 x 10 mL), sodium bisulphite (5 mL), then dried over $MgSO_4$. The solvent was removed by reduced pressure and a yellow solid was obtained. The crude product was purified using flash chromatography (hexane; SiO_2) and a colorless liquid was obtained which solidified in the fridge (85 mg, 13%). mp 20 °C; R_f: 0.65 (hexane); IR (film, KBr) vmax/cm^{-1} 3038 (CH), 2967 (CH_3), 2915 (CH_3), 2851 (CH_3), 1445 (CC), 1053 (CH), 803 (CH); δH(300 MHz, $CDCl_3$) 2.58 (6H, s), 7.14 (2H, s); δC(100 MHz, $CDCl_3$) 33.0, 116.4, 129.1, 141.8; HRMS (ESI+) for $C_8H_8I_2$ $[M]^+$: calcd. 357.8710, found 357.8694.



Scheme S5. Synthesis of 2,4-diiodo-*m*-xylene (**4**).

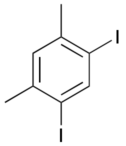
2,4-dibromo-*m*-xylene (S8)



S8

Compound **S8** was prepared from m-xylene **S7,** according to a literature procedure. The ^{1}H and ^{13}C NMR spectra agreed with literature reports.[4]

2,4-diiodo-*m*-xylene (4)



4

Dibromoxylene **S8** (3.10 g, 11.8 mmol) was dissolved in 120 mL anhydrous DMF then KI (24.3 g, 147 mmol) and CuI (22.4 g, 118 mmol) were added. The solution was refluxed for 72 hours and filtered. Saturated NH_4Cl (10 mL) was added and the mixture was extracted repeatedly with ether (3 x 10 mL), dried over $MgSO_4$ and concentrated under reduced pressure to give a crude yellow solid. The compound was purified by column chromatography (hexane; SiO_2) followed by a recrystallization (chloroform) to give a white solid (2.19 g, 52%). mp 71 – 72 °C; R_f 0.64 (hexane); δH(300 MHz, $CDCl_3$) 2.34 (6H, s) 7.11 (1H, s) 8.18 (1H, s); δC(100 MHz, $CDCl_3$) 27.5, 97.9, 130.9, 141.6, 147.3; IR (film, KBr) vmax/cm^{-1} 2977 (CH_3), 2951 (CH_3), 2916 (CH_3), 1456 (CC), 1024 (CH), 866 (CH); HRMS (ESI+) for $C_8H_8I_2$ $[M]^+$: calcd. 357.8710, found 357.8697.

^{1}H and ^{13}C NMR Spectra

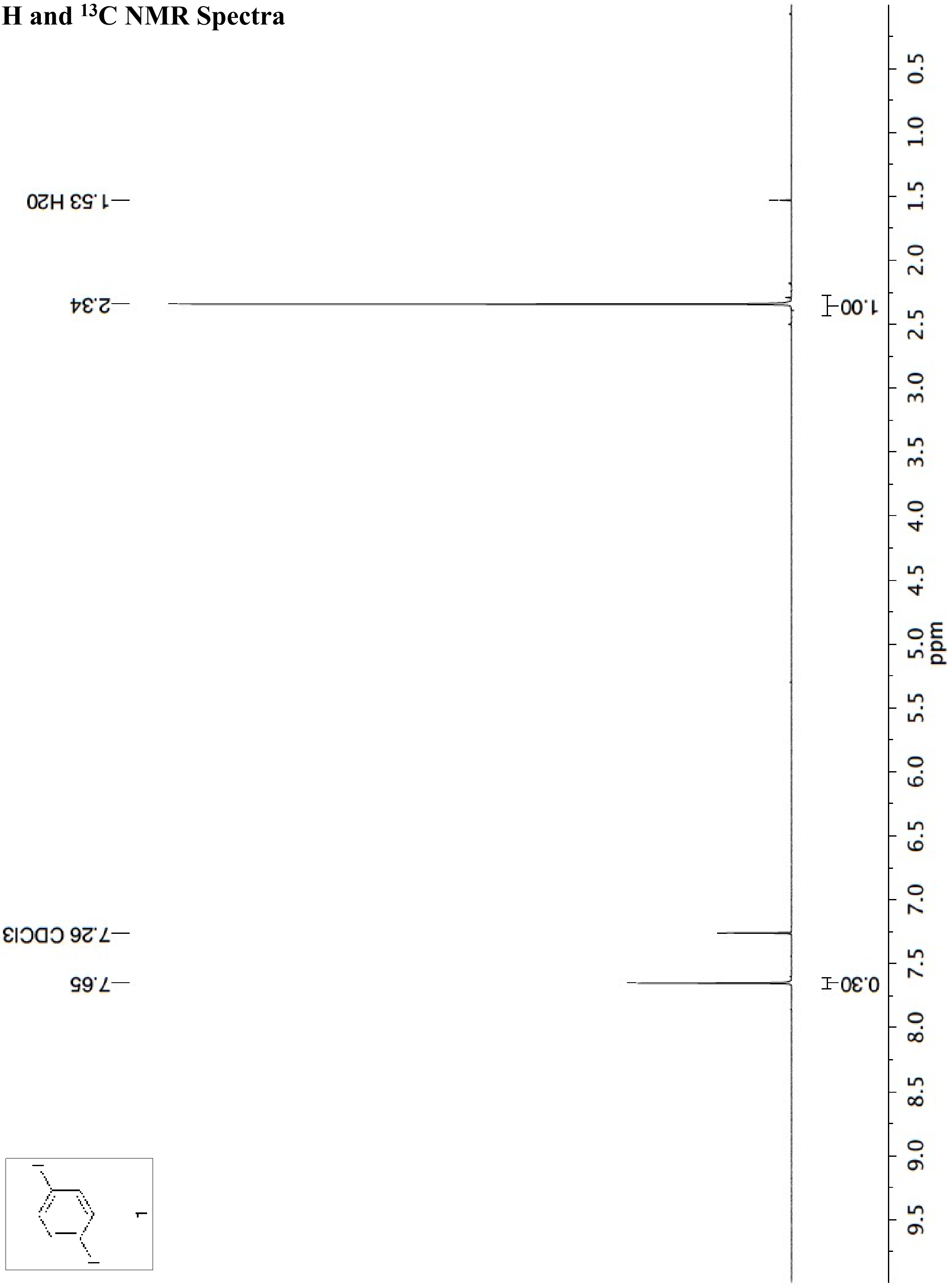


Figure S1. ^{1}H NMR spectrum in $CDCl_3$ of 2,5-diiodo-*p*-xylene (**1**).

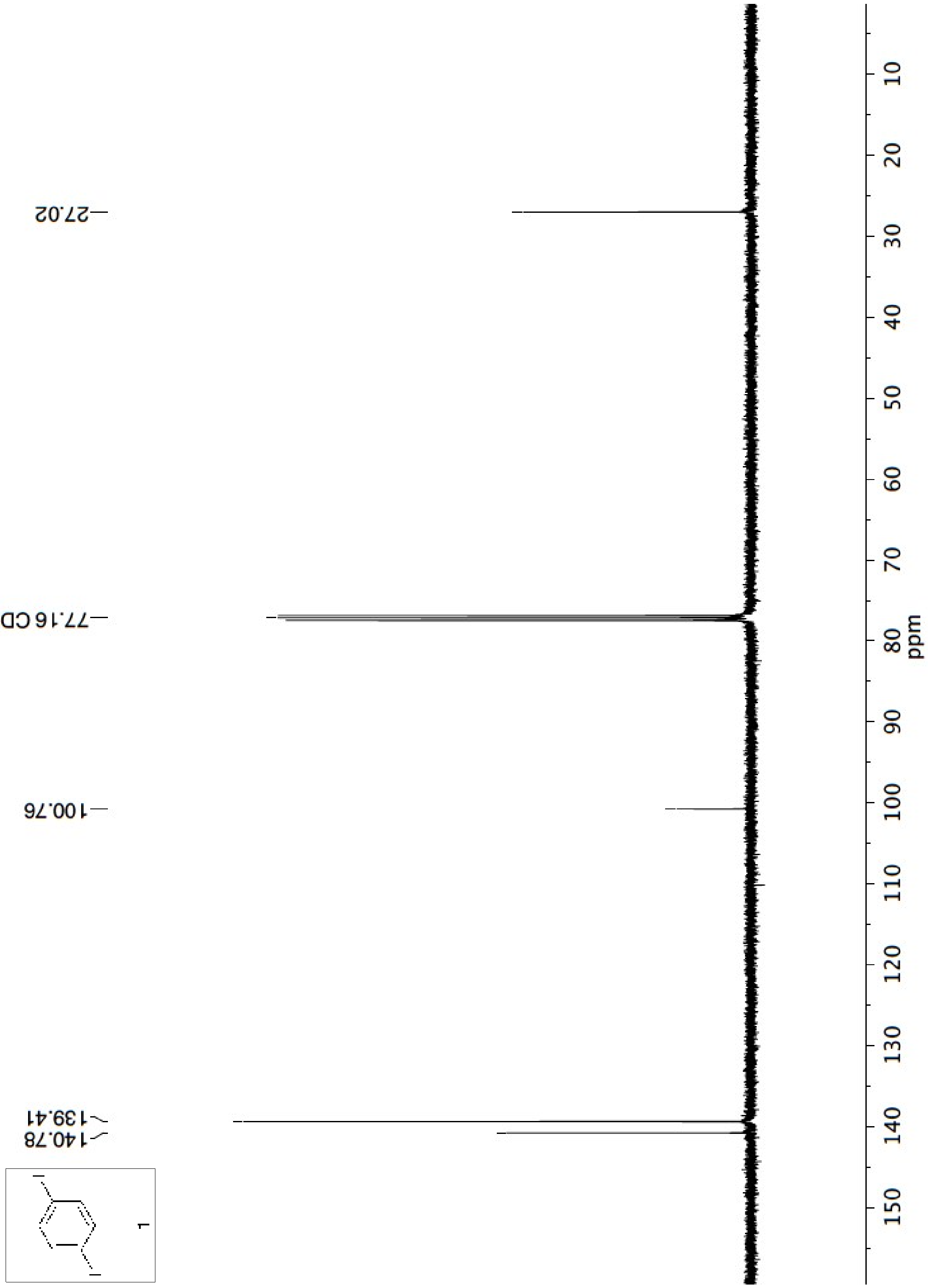


Figure S2. ^{13}C NMR spectrum in $CDCl_3$ of 2,5-diiodo-*p*-xylene (**1**).

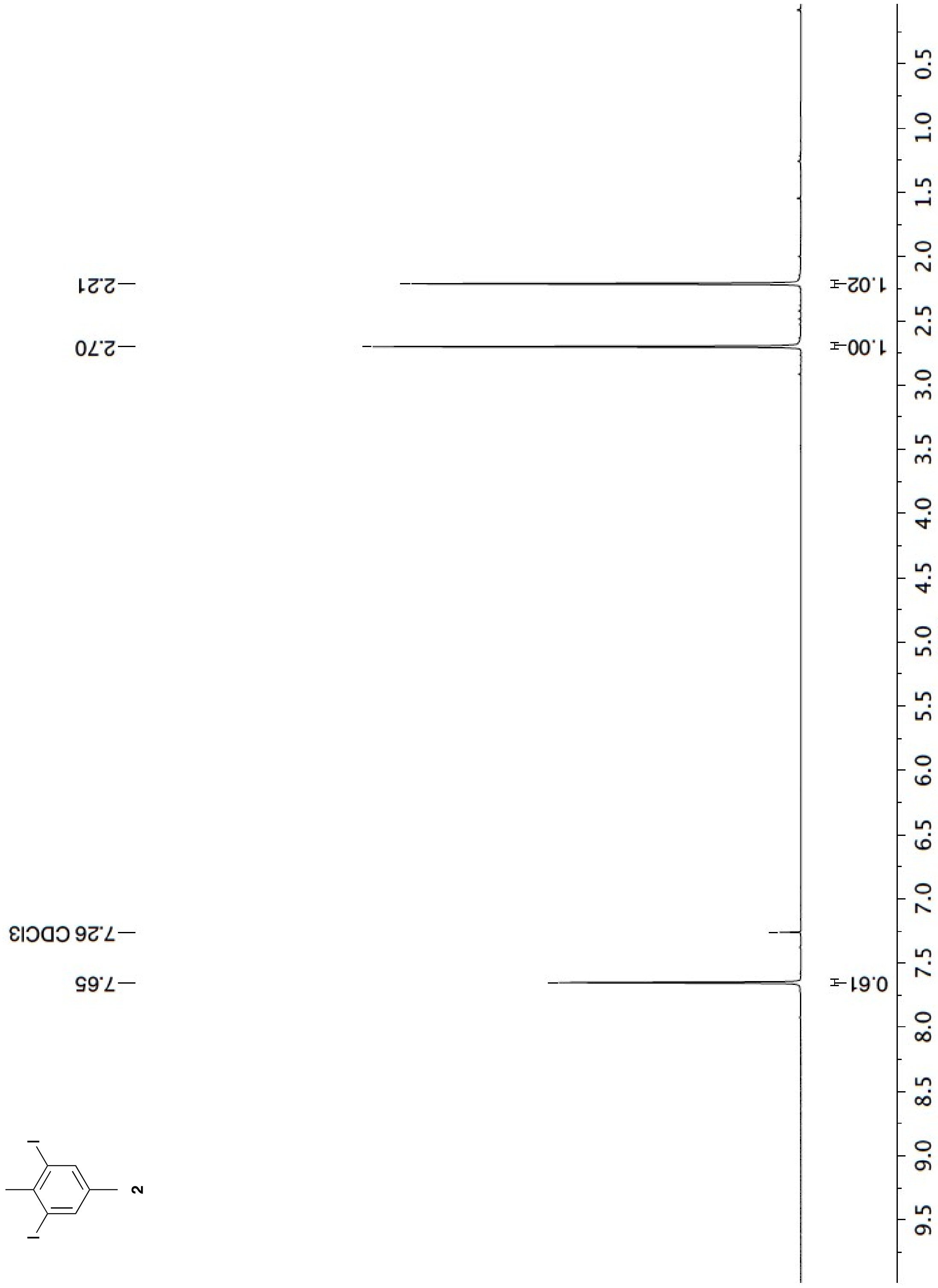


Figure S3. ^{1}H NMR spectrum in $CDCl_3$ of 2,6-diiodo-*p*-xylene (**2**).

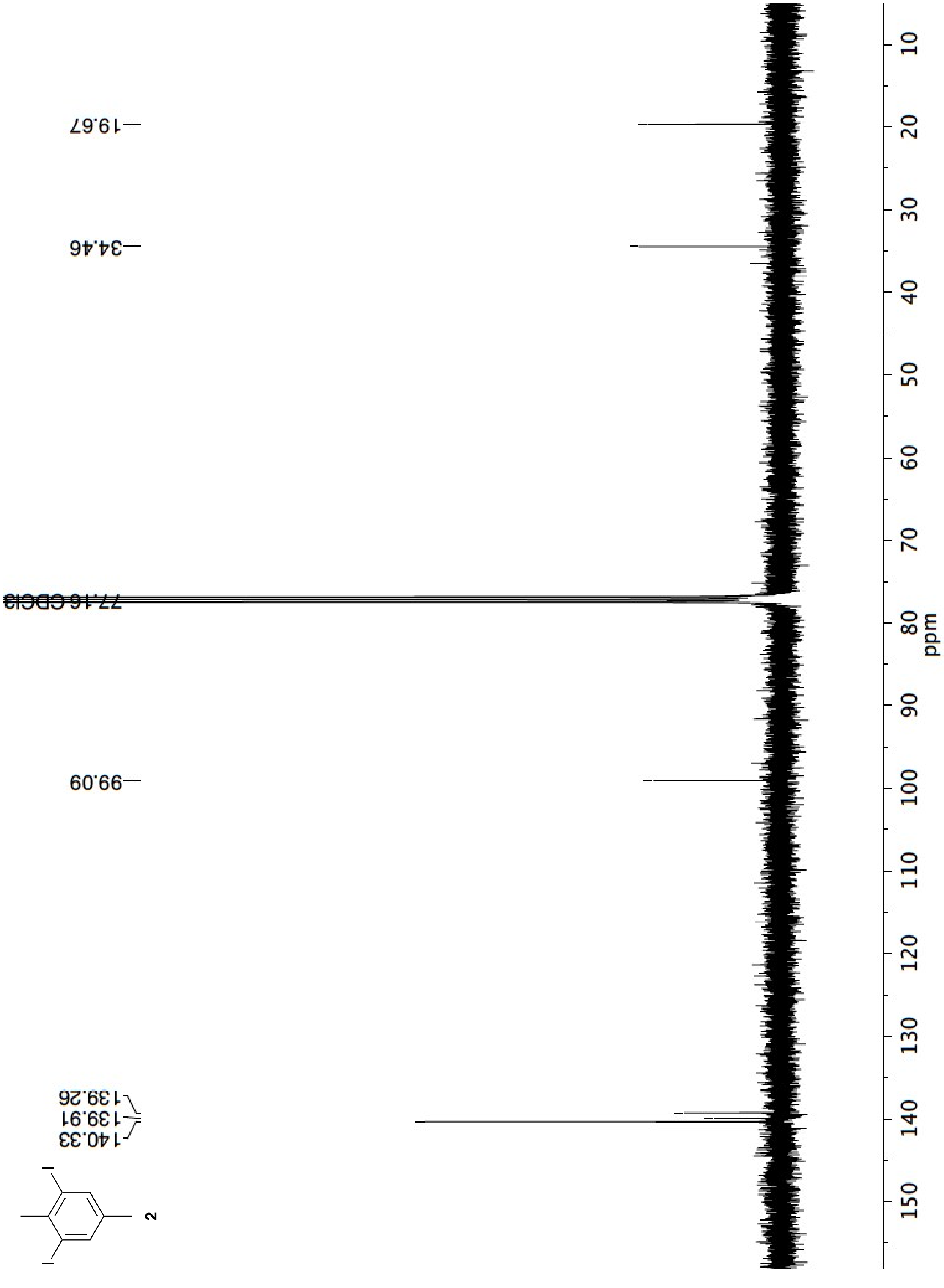


Figure S4. ^{13}C NMR spectrum in $CDCl_3$ of 2,6-diiodo-*p*-xylene (**2**)

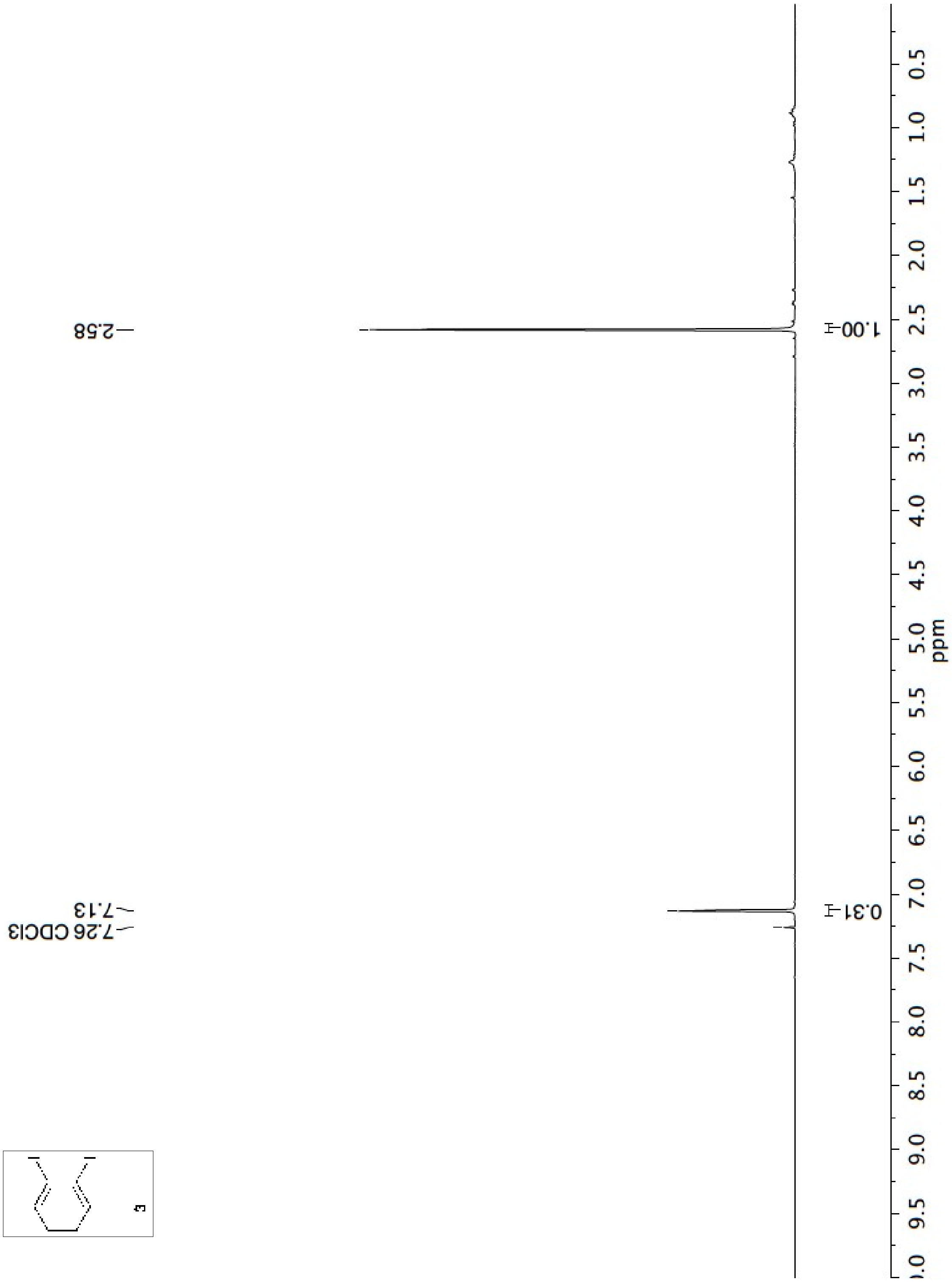


Figure S5. ^{1}H NMR spectrum in $CDCl_3$ of 2,3-diiodo-*p*-xylene (**3**)

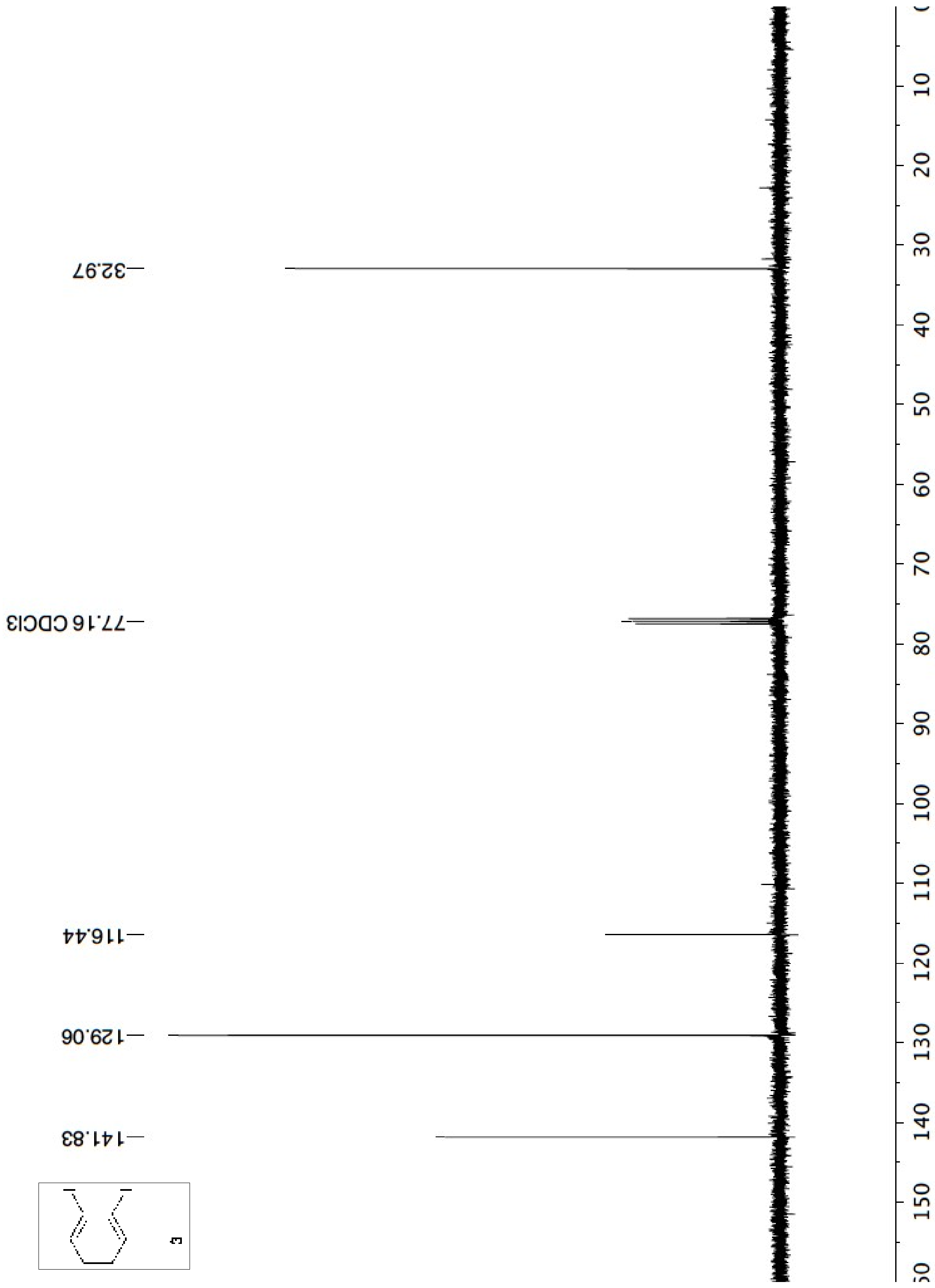


Figure S6. ^{13}C NMR spectrum in $CDCl_3$ of 2,3-diiodo-*p*-xylene (**3**).

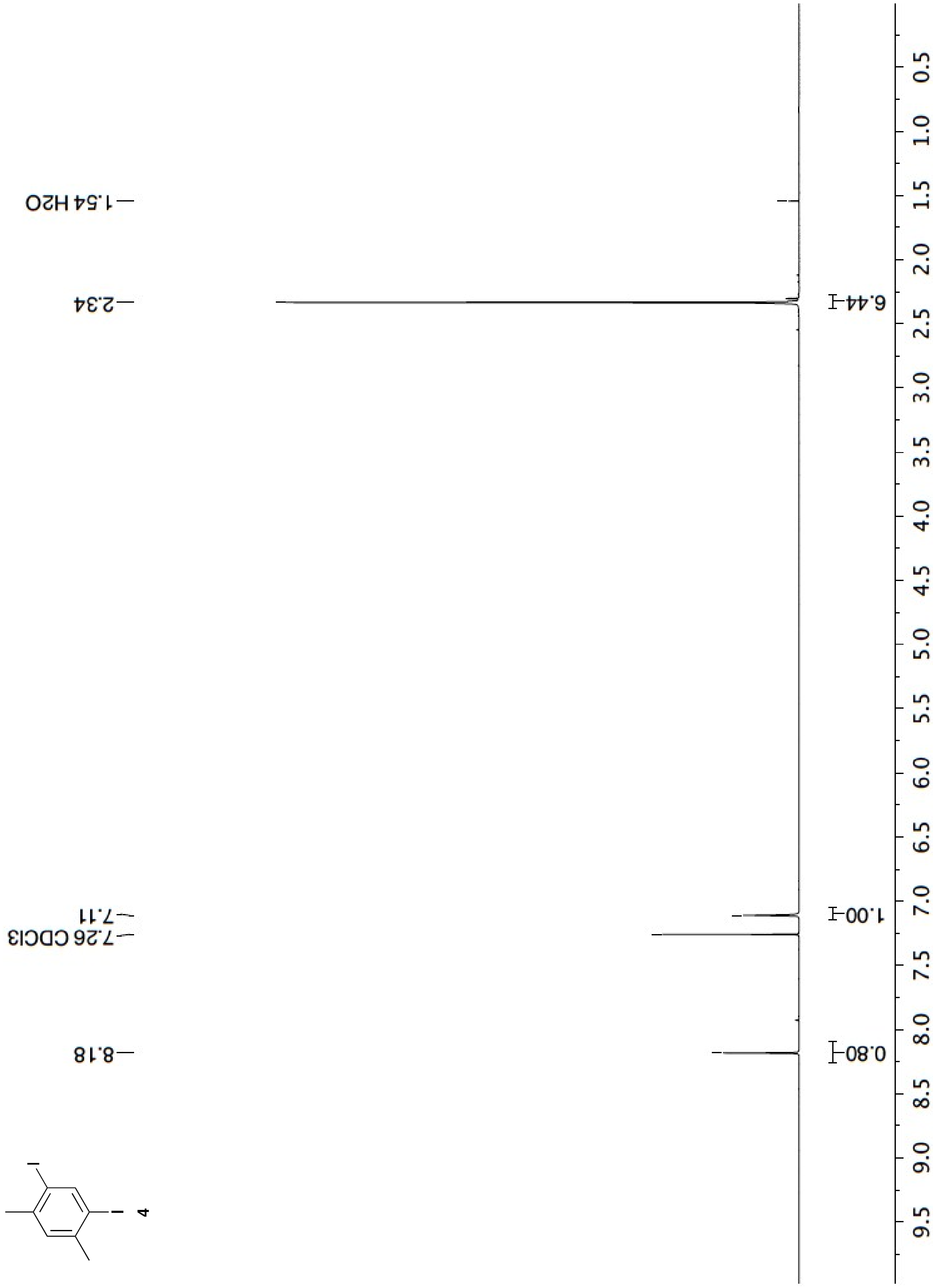


Figure S7. ^{1}H NMR spectrum in $CDCl_3$ of 2,4-diiodo-*m*-xylene (**4**).

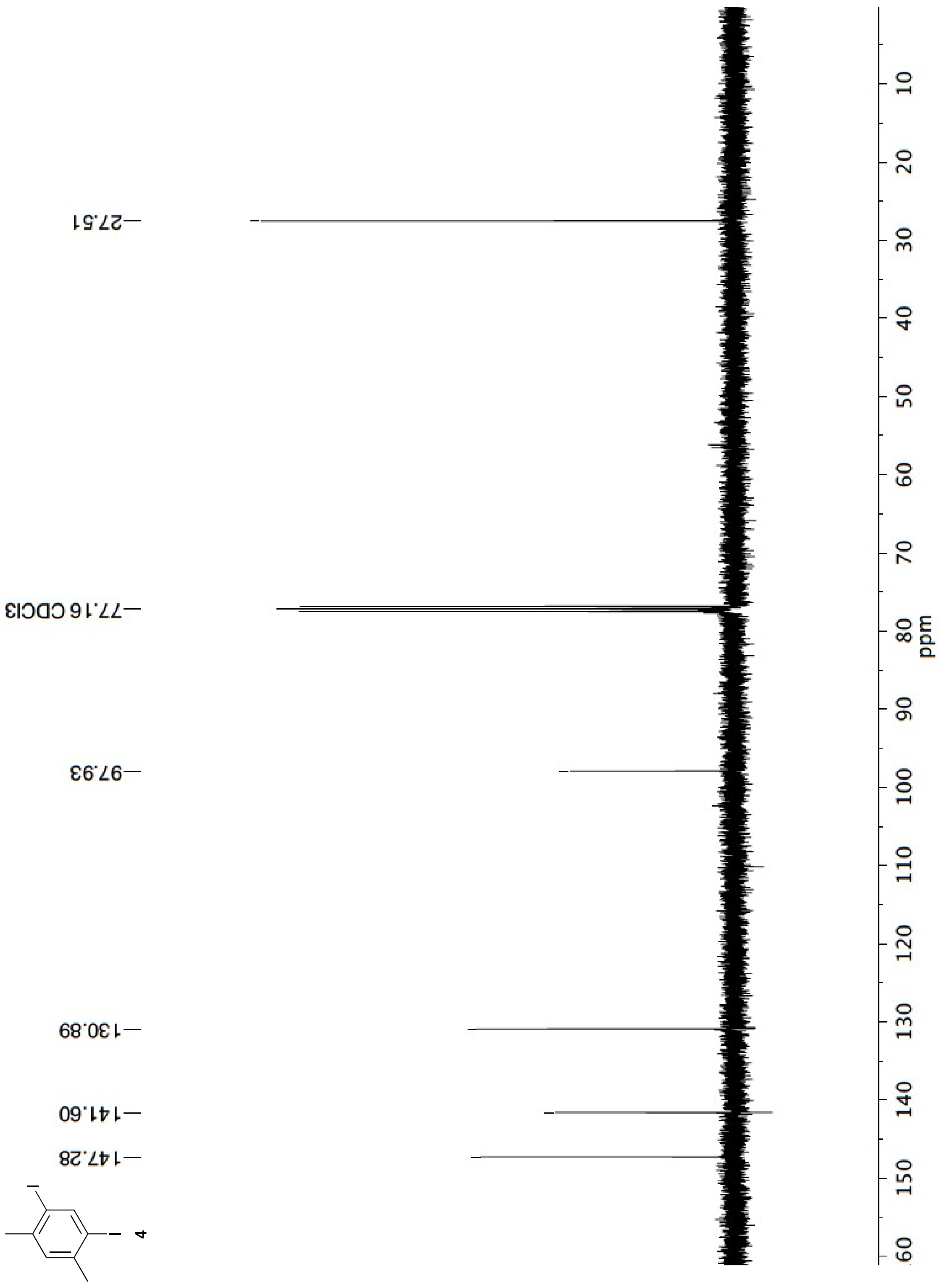


Figure S8. ^{13}C NMR spectrum in CDCl$_3$ of 2,4-diiodo-*m*-xylene (**4**).

Single-Crystal X-ray Diffraction Experiments

The crystal and molecular structures of the prepared samples were determined by single crystal X-ray diffraction. X-ray diffraction data sets for compounds **1-4** were collected on a Bruker AXS P4/SMART 1000 diffractometer. Details of data collection and crystal structure refinement are listed in **Table S1**.

Table S1. Crystallographic Data for Substituted Xylenes **1-4**

	1	**2**	**3**	**4**
molecular formula	$C_8H_8I_2$	$C_8H_8I_2$	$C_8H_8I_2$	$C_8H_8I_2$
formula weight (g mol^{-1})	357.94	357.94	357.94	357.95
crystal system	Monoclinic	Monoclinic	Monoclinic	Orthorhombic
space group	C2/c	$P2_1/c$	$P2_1/n$	$Pca2_1$
a (Å)	9.572(5)	8.107(3)	7.2216(7)	8.8117(9)
b (Å)	8.414(5)	16.238(5)	22.988(2)	7.4263(8)
c (Å)	11.973(6)	14.621(5)	17.6581(19)	14.7072(16)
α (Å)	90	90	90	90
β (Å)	105.341(8)	93.570(4)	101.2350 (10)	90
γ (Å)	90	90	90	90
V (Å^3)	929.9(8)	1920.8(11)	2875.3(5)	962.41(18)
Z	4	8	12	4
ρ_{calcd} (g cm^{-1})	2.557	2.476	2.481	2.470
T (K)	198(1)	173(1)	213(1)	213(1)
μ (mm^{-1})	6.692	6.479	6.493	6.466
F(000)	648	1296	1944	648
R_1, $I > 2\sigma$ (%)	0.0341	0.0267	0.0279	0.0310
R_1, all data (%)	0.0360	0.0310	0.0342	0.0312
ωR_2, $I > 2\sigma$ (%)	0.0954	0.0687	0.0663	0.0846
ωR_2, all data	0.0992	0.0710	0.0707	0.0848
no. of measured reflections	2976	12928	19591	6219
no. of independent reflections	1036	4294	6346	2159
no. of obsd reflections, $I > 2\sigma$ (I)	941	3783	5518	2132

Table S2. Interaction distances and angles for compounds **1 – 4**

	Interaction	Distance (Å)	Angles	Degree (˚)
1	I1···C1π	3.6120(30)	C1-I1···C1π	161.26(8)
2	I4···I3	3.8645(13)	C14-I4···I3	167.83(10) (θ_2)
		-	C10-I3···I4	97.24(10) (θ_1)
	I2···I4	3.8747(11)	C6-I2···I4	174.56(10) (θ_2)
		-	C14-I4···I2	95.46(10) (θ_1)
	I3···I1	3.9018(10)	C10-I3···I1	171.31(10) (θ_2)
		-	C2-I1···I3	96.45(10) (θ_1)
	I1···I2	3.9130(13)	C2-I1···I2	169.32(10) (θ_2)
		-	C6-I2···I1	96.16(10) (θ_1)
	H7c···Cg(2a)[1]	2.96	C7-H7c··· Cg(2a)[1]	164.09
3	I3···I5	3.8956(5)	C10-I3···I5	146.04(10) (θ_2)
		-	C18-I5···I3	81.50(9) (θ_1)
	I6···I1	3.9700(5)	C19-I6···I1	172.31(9) (θ_2)
		-	C2-I1 ···I6	101.48(10) (θ_1)
	I4···I2	3.8780(5)	C11-I4···I2	122.39(9) (θ_2)
		-	C3-I2···I4	152.05(9) (θ_1)
4	I2···I1	3.7927(7)	C6-I2···I1	88.15(15) (θ_1)
		-	C4-I1···I2	166.00(14) (θ_2)
	H7c···Cg(4)[2]	2.85	C7-H7c···Cg[2]	141.06

[1] Cg(2a) is the ring centroid of compound **2,** aryl ring A

[2] Cg(4) is the ring centroid of compound **4**

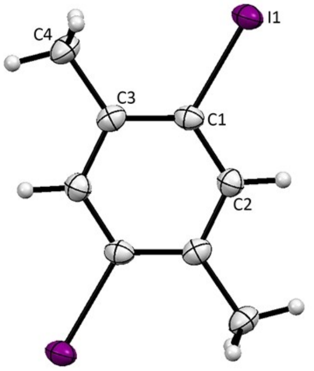


Figure S9. Molecular structure of 2,5-diiodo-*p*-xylene (**1**) showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50 % probability level and H atoms are shown as small spheres of arbitrary radius.

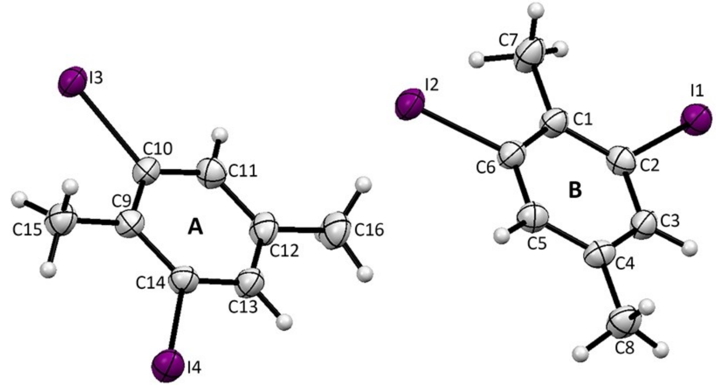


Figure S10. Molecular structure of 2,6-diiodo-*p*-xylene (**2**) showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50 % probability level and H atoms are shown as small spheres of arbitrary radius.

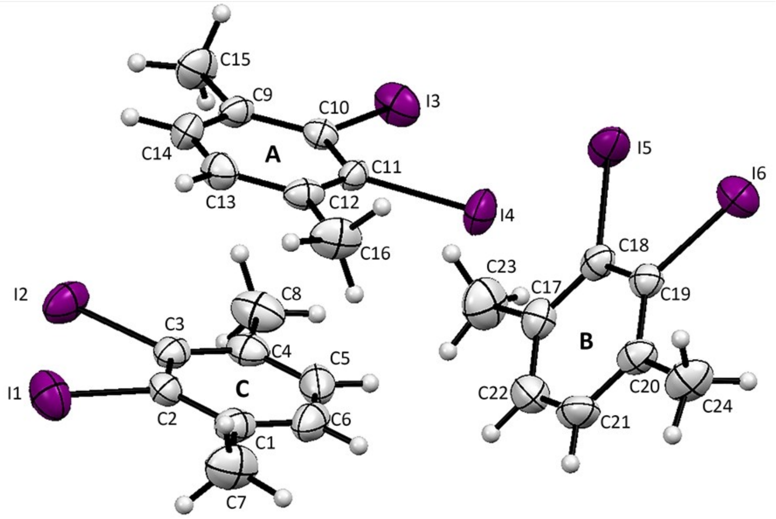


Figure S11. Molecular structure of 2,3-diiodo-*p*-xylene (**3**) showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50 % probability level and H atoms are shown as small spheres of arbitrary radius.

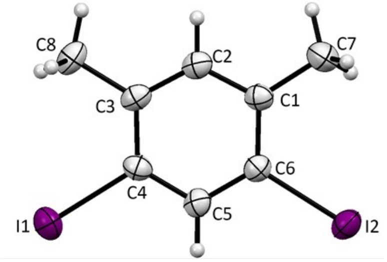


Figure S12. Molecular structure of 2,4-diiodo-*m*-xylene (**4**) showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50 % probability level and H atoms are shown as small spheres of arbitrary radius.

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