Electronic Supplementary Material (ESI) for Chemical Communications.

Supporting Information

Palladium Catalysed Cross-Dehydrogenative-Coupling (CDC) of 1,3,5-Trialkoxybenzenes with Simple Arenes

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Contents

1.1 General Experimental Details

Nuclear Magnetic Resonance (NMR) spectra were recorded on a 500, 400 or 300 MHz Bruker NMR spectrometers in $CDCl_3$ at 300 K (unless stated otherwise). For proton NMR, samples were prepared using ca. 10 mg of compound dissolved in 1.0 mL of $CDCl_3$ and for carbon NMR using *ca.* 20 mg of compound dissolved in 1.0 mL of $CDCl_3$. All spectra were referenced to the residual solvent peak $CHCl_3$ (δ = 7.26 ppm) for ^1H NMR and the $CDCl_3$ solvent peak (δ = 77.0 ppm) for $^{13}C\{^1H\}$ NMR. NMR Chemical shifts (δ) are reported in ppm; coupling constants (*J*) are reported in Hz; splitting patterns are assigned s = singlet, d = doublet, t = triplet, q = quartet, br = broad signal and app = the apparent multiplicity. Where possible, when mixtures of isomers were isolated, the ^1H NMR spectrum was used to assign the substitution patterns and the ratio of isomers using comparison to literature data and authentic compounds. When purified compounds had inseparable residual starting material present, ^1H NMR spectrum was used to calculate the quantity and mass of the product and is quoted in the characterisation data. High resolution mass spectrometry (HRMS) was measured using electrospray ionization or electron impact ionisation (EI) using a 0.5-1.0 $mMoldm^{-3}$ solution of compound in acetonitrile. Solvents, unless otherwise stated, were purchased in reagent grade or anhydrous quality and used as received. Reagents were either purchased directly from commercial suppliers or prepared according to literature procedures. All reactions were carried out in glass microwave vials equipped with aluminium crimpcaps or a round bottomed flask and sealed with a glass stopper and heated in oil baths with a thermocouple temperature control. Flash column chromatography was performed manually on silica gel eluting with hexane/ethyl acetate under pressurised air flow. 1,3,5-trialkoxyarenes were synthesized from 1,3,5-trifluorobenzene and the respective alcohol according to the procedure described by Jalalian and Olofsson[1] or from phlouroglucinol or 3,5-dimethoxyphenol and alkylhalides using literature protocols.[2]

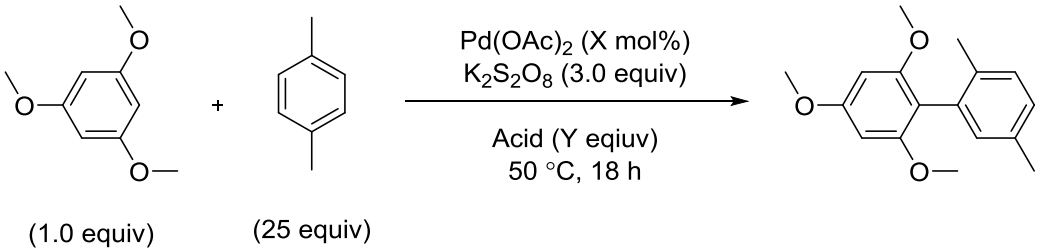
1.2 General Procedure for the Arylation of 1,3,5-Trialkoxyarenes

To a 10 ml microwave vial, or round bottomed flask, equipped with a magnetic stirrer bar was palladium(II) acetate (5.6 mg, 25 µmol, 10 mol%), 1,3,5-trialkoxyarene (0.25 mmol, 1.0 equiv), potassium peroxodisulfate (203 mg, 0.75 mmol, 3.0 equiv) and arene (6.25 mmol, 25 equiv). The reaction vessel was then briefly flushed with N_2 and trifluoroacetic acid (955 µL, 12.5 mmol, 50 equiv) was then added under N_2 flow and sealed. The reaction mixture was then heated with stirring to 50 ^oC in an oil bath for 18 hours. After the allotted reaction time the reaction was then allowed to cool to room temperature, diluted with CH_2Cl_2 (10 mL), filtered through cotton wool and adsorbed onto silica gel *in vacuo*. The sample was then dry loaded onto a silica gel column and purified eluting with hexane/ethyl acetate (100:0 to 95:5). The fractions containing the arylated product were then concentrated *in vacuo* to yield the pure product.

2 Reaction Optimisation Studies

2.1 Table 1. Initial Reaction Conditions Assessment

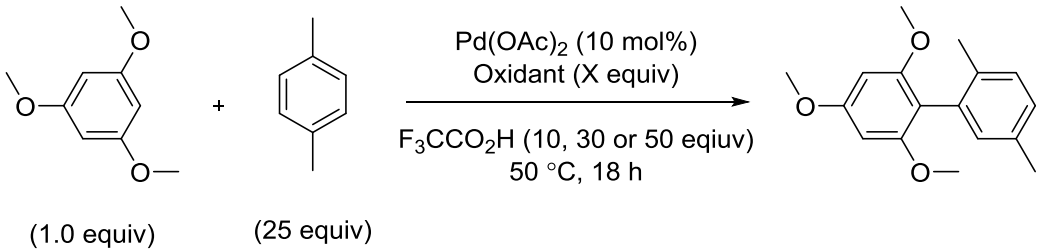
To a 10 ml microwave vial or round bottomed flask equipped with a magnetic stirrer bar was added palladium(II) acetate (5.6 mg, 25 μmol, 10 mol%), 1,3,5-trimethoxybenzene (42.0 mg, 0.25 mmol, 1.0 equiv), potassium peroxodisulfate (203 mg, 0.75 mmol, 3.0 equiv) and *para*-xylene (771 μL, 6.25 mmol, 25 equiv). The reaction vessel was then briefly flushed with N_2 and acid was then added under N_2 flow and sealed. The reaction mixture was then heated with stirring to 50 ^{o}C in an oil bath for 18 hours. After the allotted reaction time the reaction was then allowed to cool to room temperature, diluted with CH_2Cl_2 (10 mL), filtered through cotton wool and adsorbed onto silica gel *in vacuo*. The sample was then dry loaded onto a silica gel column and purified eluting with hexane/ethyl acetate (100:0 to 95:5). The fractions containing the arylated product were then concentrated *in vacuo* to yield the pure product.



Entry	X	Acid	Y	Isolated Yield (%)	Notes
1	10	AcOH	10	0	
2	100	AcOH	10	0	
3	10	AcOH	30	0	
4	10	PivOH	50	0	
5	10	PivOH	100	0	
6	5	F_3CCO_2H	30	56	
7	10	F_3CCO_2H	50	59	
8	100	F_3CCO_2H	10	34	

2.2 Table 2. Acid and Oxidant Assessment

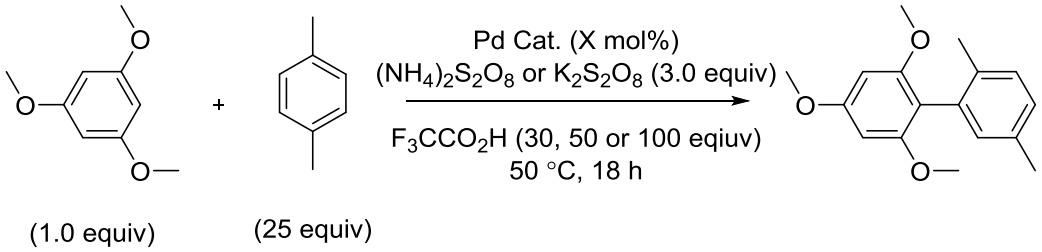
To a 10 ml microwave vial or round bottomed flask equipped with a magnetic stirrer bar was added palladium(II) acetate (5.6 mg, 25 μmol, 10 mol%), 1,3,5-trimethoxybenzene (42.0 mg, 0.25 mmol, 1.0 equiv), oxidant and *para*-xylene (771 μL, 6.25 mmol, 25 equiv). The reaction vessel was then briefly flushed with N_2 and trifluoroacetic acid (191, 573 or 955 μL; 10, 30 or 50 equiv) was then added under N_2 flow and sealed. The reaction mixture was then heated with stirring to 50 °C in an oil bath for 18 hours. After the allotted reaction time the reaction was then allowed to cool to room temperature, diluted with CH_2Cl_2 (10 mL), filtered through cotton wool and adsorbed onto silica gel *in vacuo*. The sample was then dry loaded onto a silica gel column and purified eluting with hexane/ethyl acetate (100:0 to 95:5). The fractions containing the arylated product were then concentrated *in vacuo* to yield the pure product.



Entry	TFA equiv	Oxidant	X	Isolated Yield (%)	Notes
1	30	$K_2S_2O_8$	1.0	48	
2	30	$K_2S_2O_8$	2.0	48	
3	10	$K_2S_2O_8$	3.0	29	
4	30	$K_2S_2O_8$	3.0	59	
5	50	$K_2S_2O_8$	3.0	64	Average of 5 yields
6	100	$K_2S_2O_8$	3.0	67	
7	30	$K_2S_2O_8$	5.0	46	
8	30	$Na_2S_2O_8$	3.0	22	20% RSM
9	10	$Na_2S_2O_8$	3.4	18	
10	30	$(NH_4)_2S_2O_8$	3.0	52	
11	50	$(NH_4)_2S_2O_8$	3.0	60	
12	100	$(NH_4)_2S_2O_8$	3.0	68	
13	30	Oxone	3.0	0	
14	30	$Py.SO_3$	3.0	0	
15	30	$Cu(OAc)_2$	3.0	27	
16	50	$Cu(OAc)_2 + K_2S_2O_8$	3.0 + 3.0	52	

2.3 Table 3. Catalyst and Stoichiometry Assessment

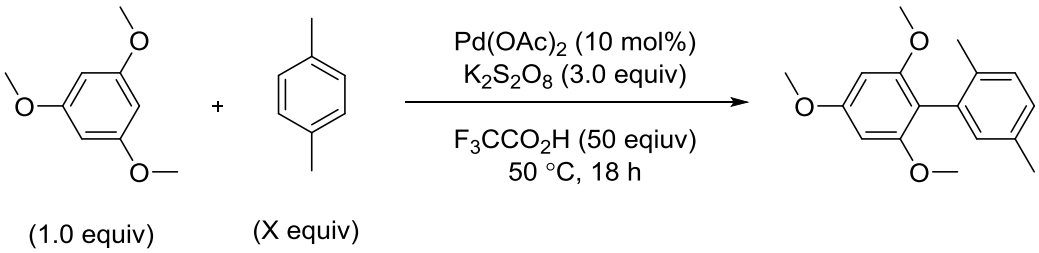
To a 10 ml microwave vial or round bottomed flask equipped with a magnetic stirrer bar was added palladium catalyst, 1,3,5-trimethoxybenzene (42.0 mg, 0.25 mmol, 1.0 equiv), oxidant (0.75 mmol, 3.0 equiv) and *para*-xylene (771 μL, 6.25 mmol, 25 equiv). The reaction vessel was then briefly flushed with N_2 and trifluoroacetic acid (573, 955 or 1910 μL; 30, 50 or 100 equiv) was then added under N_2 flow and sealed. The reaction mixture was then heated with stirring to 50 °C in an oil bath for 18 hours. After the allotted reaction time the reaction was then allowed to cool to room temperature, diluted with CH_2Cl_2 (10 mL), filtered through cotton wool and adsorbed onto silica gel *in vacuo*. The sample was then dry loaded onto a silica gel column and purified eluting with hexane/ethyl acetate (100:0 to 95:5). The fractions containing the arylated product were then concentrated *in vacuo* to yield the pure product.



Entry	Pd Cat.	X	TFA equiv	Oxidant	Isolated Yield (%)	Notes
1	N/A	N/A	50	$K_2S_2O_8$	0	
2	$Pd(OAc)_2$	2	50	$K_2S_2O_8$	25	
3		5	50	$K_2S_2O_8$	58	
4		10	50	$K_2S_2O_8$	64	Average of 5 yields
5		10	100	$K_2S_2O_8$	67	
6		20	50	$K_2S_2O_8$	59	
7	Hermann-Beller Palladacycle	0.5	30	$K_2S_2O_8$	0	
8		1	30	$K_2S_2O_8$	0	
9		2.5	30	$K_2S_2O_8$	28	
10		5	30	$K_2S_2O_8$	60	
11		5	50	$K_2S_2O_8$	67	
12		5	100	$K_2S_2O_8$	64	
13		5	30	$(NH_4)_2S_2O_8$	57	
14		5	50	$(NH_4)_2S_2O_8$	67	
15		5	100	$(NH_4)_2S_2O_8$	65	35 equiv of *para*-xylene used
16	$Pd(O_2CCF_3)_2$	10	100	$K_2S_2O_8$	57	
17	$Pd(acac)_2$	10	100	$K_2S_2O_8$	64	

2.4 Table 4. *para*-Xylene Stoichiometry

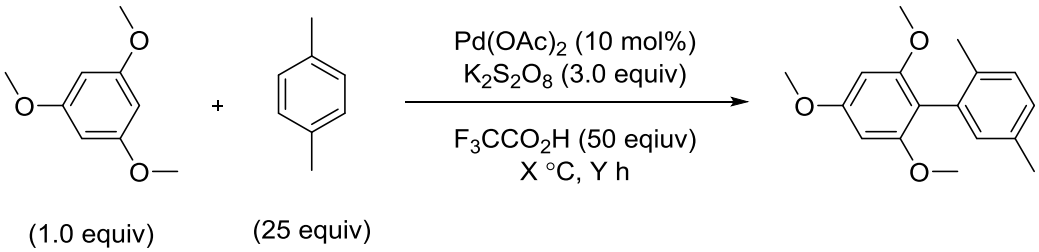
To a 10 ml microwave vial or round bottomed flask equipped with a magnetic stirrer bar was added palladium(II) acetate (5.6 mg, 25 μmol, 10 mol%), 1,3,5-trimethoxybenzene (42.0 mg, 0.25 mmol, 1.0 equiv), potassium peroxodisulfate (203 mg, 0.75 mmol, 3.0 equiv) and *para*-xylene. The reaction vessel was then briefly flushed with N_2 and trifluoroacetic acid (955 μL, 12.5 mmol, 50 equiv) was then added under N_2 flow and sealed. The reaction mixture was then heated with stirring to 50 ^{o}C in an oil bath for 18 hours. After the allotted reaction time the reaction was then allowed to cool to room temperature, diluted with CH_2Cl_2 (10 mL), filtered through cotton wool and adsorbed onto silica gel *in vacuo*. The sample was then dry loaded onto a silica gel column and purified eluting with hexane/ethyl acetate (100:0 to 95:5). The fractions containing the arylated product were then concentrated *in vacuo* to yield the pure product.



Entry	X	Isolated Yield (%)	Notes
1	5	43	
2	10	51	
3	15	53	
4	20	63	
5	25	64	Average of 5 yields
6	30	66	
7	35	61	
8	50	53	

2.5 Table 5. Temperature and Time Assessment

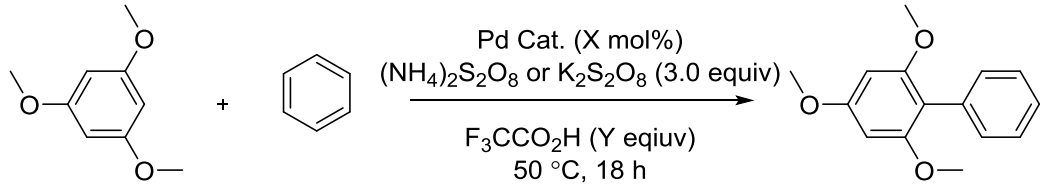
To a 10 ml microwave vial or round bottomed flask equipped with a magnetic stirrer bar was added palladium(II) acetate (5.6 mg, 25 μmol, 10 mol%), 1,3,5-trimethoxybenzene (42.0 mg, 0.25 mmol, 1.0 equiv), potassium peroxodisulfate (203 mg, 0.75 mmol, 3.0 equiv) and *para*-xylene (771 μL, 6.25 mmol, 25 equiv). The reaction vessel was then briefly flushed with N_2 and trifluoroacetic acid (955 μL, 12.5 mmol, 50 equiv) was then added under N_2 flow and sealed. The reaction mixture was then heated with stirring to constant temperature in an oil bath (see table for time and temperature details). After the allotted reaction time the reaction was then allowed to cool to room temperature, diluted with CH_2Cl_2 (10 mL), filtered through cotton wool and adsorbed onto silica gel *in vacuo*. The sample was then dry loaded onto a silica gel column and purified eluting with hexane/ethyl acetate (100:0 to 95:5). The fractions containing the arylated product were then concentrated *in vacuo* to yield the pure product.



Entry	X	Y	Isolated Yield (%)	Notes
1	0	18	33	Yields variable between reactions
2	0	48	43	25% RSM
3	25	18	33	
4	50	1	34	
5	50	2	44	22% RSM
6	50	4	52	33% RSM
7	***50***	***18***	***64***	***Average of 5 yields***
8	50	24	62	
9	75	18	54	
10	100	18	38	

2.6 Table 6. Optimisation of Arylation Using Benzene

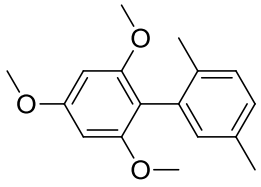
To a 10 ml microwave vial or round bottomed flask equipped with a magnetic stirrer bar was added palladium catalyst, 1,3,5-trimethoxybenzene (42.0 mg, 0.25 mmol, 1.0 equiv), oxidant (0.75 mmol, 3.0 equiv) and benzene (556 μL or 1 mL, 25 or 45 equiv respectively). The reaction vessel was then briefly flushed with N_2 and trifluoroacetic acid was then added under N_2 flow and sealed. The reaction mixture was then heated with stirring to 50 ^{o}C in an oil bath for 18 hours. After the allotted reaction time the reaction was then allowed to cool to room temperature, diluted with CH_2Cl_2 (10 mL), filtered through cotton wool and adsorbed onto silica gel *in vacuo*. The sample was then dry loaded onto a silica gel column and purified eluting with hexane/ethyl acetate (100:0 to 95:5). The fractions containing the arylated product were then concentrated *in vacuo* to yield the pure product.



(1.0 equiv) (25 or 45 equiv)

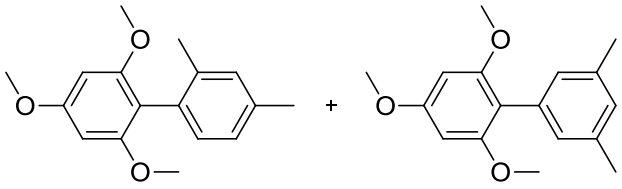
Entry	Benzene equiv	Pd Cat.	X	Y	Oxidant	Isolated Yield (%)	Notes
1	25	$Pd(OAc)_2$	10	50	$K_2S_2O_8$	0	
2	25		10	25	$K_2S_2O_8$	0	
3	25		10	10	$K_2S_2O_8$	0	
4	25		10	5	$K_2S_2O_8$	20	
5	25		10	2.5	$K_2S_2O_8$	12	
6	25		10	1	$K_2S_2O_8$	<5	
7	45		10	5	$(NH_4)_2S_2O_8$	16	
8	45		10	5	$Na_2S_2O_8$	<5	
9	45		5	5	$K_2S_2O_8$	<5	
10	45		10	5	$K_2S_2O_8$	40	
11	45		20	5	$K_2S_2O_8$	18	
12	45		10	5	$K_2S_2O_8$	15	4.5 equiv of oxidant
13	45		10	5	$K_2S_2O_8$	18	6.0 equiv of oxidant
14	45		10	5	$K_2S_2O_8$	<5	12 equiv of oxidant
15	45	Hermann-Beller Palladacycle	5	5	$K_2S_2O_8$	<5	
16	***45***	***$Pd(O_2CCF_3)_2$***	***10***	***5***	***$K_2S_2O_8$***	***45***	
17	45	$Pd(acac)_2$	10	5	$K_2S_2O_8$	16	
18	45	$PdCl_2$	10	5	$K_2S_2O_8$	0	

3 Characterisation Data for Compounds **3a-q**



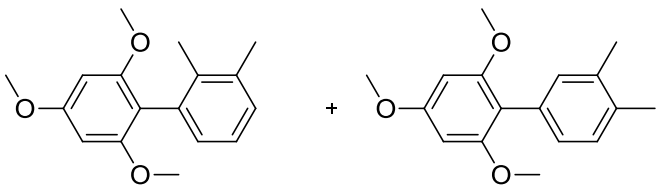
3a

2,4,6-trimethoxy-2',5'-dimethyl-1,1'-biphenyl,[3] **3a**, was synthesised using the general protocol from *para*-xylene (771 μL, 6.25 mmol) and 1,3,5-trimethoxybenzene (42.0 mg, 0.25 mmol); the title compound was isolated as a white crystalline solid (43.4 mg, 159 μmol, 64% yield; this experiment was repeated 5 times with yields ranging from 62 to 66%, average = 64%). M.p. = 121-123 °C (lit. = 125 °C); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.18 (d, *J* = 7.7, 1H), 7.07 (dd, *J* = 7.7, 1.5, 1H), 6.98 (d, *J* = 1.5, 1H), 6.26 (s, 2H), 3.90 (s, 3H), 3.73 (s, 6H), 2.36 (s, 3H), 2.06 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 160.5, 158.3, 134.5, 134.3, 133.8, 131.8, 129.3, 127.9, 111.9, 90.6, 55.8, 55.3, 21.0, 19.3; MS (ESI) m/z = 295 ($M+Na^+$, 100), 273 ($M+H^+$, 40.6); HRMS (ESI, $M+H^+$) 273.1481 (Calcd. for $C_{17}H_{21}O_3$ 273.1485).



3b 1 : 2

2,4,6-trimethoxy-2',4'-dimethyl-1,1'-biphenyl (**A**) and 2,4,6-trimethoxy-3',5'-dimethyl-1,1'-biphenyl (**B**),[4] **3b**, was synthesised using the general protocol from *meta*-xylene (764 μL, 6.25 mmol) and 1,3,5-trimethoxybenzene (42.0 mg, 0.25 mmol); the title compound was isolated as a white solid (Run 1 = 44.7 mg, 164 μmol, 66 % yield; Run 2 = 42.2 mg, 155 μmol, 62% yield; average = 64% yield; ^{1}H NMR analysis revealed that in both cases the samples were a 1:2 ratio of **A**:**B** isomers). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.12 (s, 1H A), 7.06 (m, 2H A), 6.97 (app s, 3H B), 6.26 (s, 2H A), 6.25 (s, 2H B), 3.90 (s, 3H A), 3.89 (s, 3H B), 3.75 (s, 6H B), 3.73 (s, 6H A), 2.38 (s, 3H A), 2.37 (s, 6H B), 2.08 (s, 3H A); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 160.4, 160.2, 158.3, 158.3, 137.5, 136.8, 136.4, 133.7, 131.0, 130.9, 130.4, 128.8, 128.5, 126.0, 112.6, 111.5, 90.7, 90.5, 55.8, 55.7, 55.3, 55.3, 21.4, 21.3, 19.7; MS (ESI) m/z = 295 ($M+Na^+$, 100), 273 ($M+H^+$, 38.4); HRMS (ESI, $M+H^+$) 273.1472 (Calcd. for $C_{17}H_{21}O_3$ 273.1485).

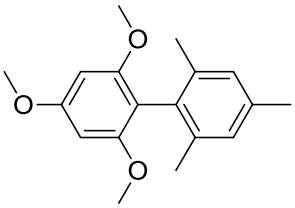


3c 1 : 1

2,4,6-trimethoxy-2',3'-dimethyl-1,1'-biphenyl (**A**), 2,4,6-trimethoxy-3',4'-dimethyl-1,1'-biphenyl (**B**), **3c**, was synthesised using the general protocol from *ortho*-xylene (755 μL, 6.25 mmol) and 1,3,5-trimethoxybenzene (42.0 mg, 0.25 mmol); the title compound was isolated as an off white solid (Run 1 = 23.0 mg, 85 μmol, 34 % yield; Run 2 =

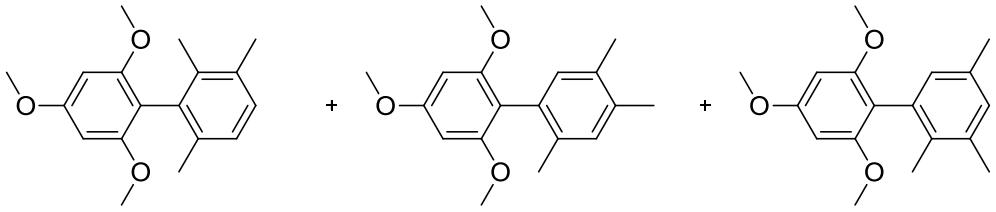
23.0 mg, 85 μmol, 34% yield; average = 34% yield; ^{1}H NMR analysis revealed that in both cases the sample was a 1:1 ratio of **A**:**B** isomers). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.17 (d, *J* = 7.5, 1H B), 7.14 (d, *J* = 4.7, 2H A), 7.11 (d, *J* = 1.7, 1H B), 7.08 (dd, *J* = 1.7, 7.5, 1H B), 7.01 (t, *J* = 4.7, 1H A), 6.24 (s, 2H B), 6.24 (s, 2H A), 3.89 (s, 3H B), 3.88 (s, 3H A), 3.74 (s, 6H A), 7.71 (s, 6H B), 2.34 (s, 3H A), 2.29 (s, 6H B), 1.99 (s, 3H A); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 160.4, 160.2, 158.3, 158.3, 136.3, 136.2, 135.7, 134.8, 133.9, 132.3, 131.3, 129.1, 129.0, 128.8, 128.5, 124.7, 112.4, 112.2, 90.7, 90.5, 55.8, 55.8, 55.3, 55.3, 20.7, 19.9, 19.7, 16.4; MS (ESI) m/z = 295 ($M+Na^+$, 100), 273 ($M+H^+$, 33.2); HRMS (ESI, $M+H^+$) 273.1472 (Calcd. for $C_{17}H_{21}O_3$ 273.1485).

3d



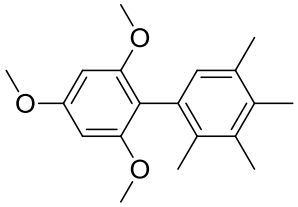
2,4,6-trimethoxy-2',4',6'-trimethyl-1,1'-biphenyl, **3d**, was synthesised using the general protocol from mesitylene (869 μL, 6.25 mmol) and 1,3,5-trimethoxybenzene (42.0 mg, 0.25 mmol); the title compound was isolated as yellow amorphous solid (19.7 mg, ^{1}H NMR analysis of the product sample, post silica gel chromatography, showed that it was a 7:3 mixture of **3d**:residual starting material; 55 μmol, 22 % yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 6.93 (s, 2H), 6.24 (s, 2H), 3.88 (s, 3H), 3.70 (s, 6H), 2.31 (s, 3H), 1.97 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 160.5, 158.1, 137.4, 136.2, 130.8, 127.8, 110.2, 90.5, 55.7, 55.3, 21.3, 20.0; MS (ESI) m/z = 309 ($M+Na^+$), 287 ($M+H^+$, 33.5); HRMS (ESI, $M+H^+$) 287.1638 (Calcd. for $C_{18}H_{23}O_3$ 287.1642).

3e



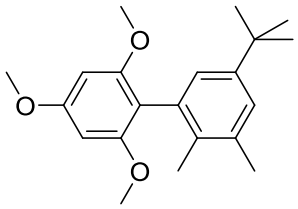
2,4,6-trimethoxy-2',3',6'-trimethyl-1,1'-biphenyl (**A**), 2,4,6-trimethoxy-2',4',5'-dimethyl-1,1'-biphenyl (**B**), 2,4,6-trimethoxy-2',3',5'-dimethyl-1,1'-biphenyl (**C**), **3e**, was synthesised using the general protocol from 1,2,4-trimethylbenzene (856 μL, 6.25 mmol) and 1,3,5-trimethoxybenzene (42.0 mg, 0.25 mmol); the title compounds were isolated as a white crystalline solid (Run 1 = 41.8 mg, 146 μmol, 58% yield; Run 2 = 52.1 mg, 182 μmol, 73% yield; average = 66% yield; ^{1}H NMR analysis revealed that in both cases the samples were a 1:4:5 ratio of **A**:**B**:**C** isomers). ^{1}H NMR analysis revealed that this substance was a). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.08 (d, *J* = 8.0, 1H A), 7.08 (s, 1H B), 7.04 (d, *J* = 8.0, 1H A), 6.99 (d, *J* = 1.7, 2H C), 6.94 (s, 1H B), 6.85 (d, *J* = 1.7, 1H C), 6.27 (s, 2H A), 6.26 (app s, 2H A + 2H B), 3.91 (s, 3H A), 3.90 (s, 3H C), 3.90 (s, 3H B), 3.74 (s, 6H B), 7.73 (s, 6H C), 3.72 (s, 6H A), 2.33 (s, 3H C), 2.32 (s, 3H C), 2.31 (s, 3H A), 2.28 (s, 3H B), 2.26 (s, 3H B), 2.05 (s, 3H B), 1.99 (s, 3H A), 1.97 (s, 3H C), 1.95 (s, 3H A); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 160.3, 158.3, 158.3, 136.0, 135.1, 134.8, 133.8, 133.6, 133.1, 133.0, 132.3, 131.1, 131.0, 129.9, 129.5, 112.3, 111.6, 92.8, 90.5, 55.8, 55.7, 55.3, 21.0, 20.6, 19.6, 19.4, 19.1, 15.9 (Only 28 carbon

resonances observed, these can be attributed to the two major isomers - **B** and **C**); MS (ESI) m/z 309 ($M+Na^+$), 287 ($M+H^+$, 30.1); HRMS (ESI, $M+H^+$) 287.1626 (Calcd. for $C_{18}H_{23}O_3$ 287.1642).



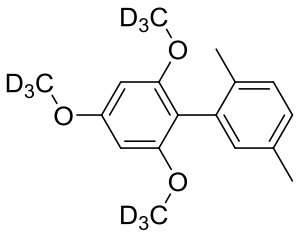
3f

2,4,6-trimethoxy-2',3',4',5'-tetramethyl-1,1'-biphenyl, **3f**, was synthesised using the general protocol from prehenitene (931 μL, 6.25 mmol) and 1,3,5-trimethoxybenzene (42.0 mg, 0.25 mmol); the title compound was isolated as a white crystalline solid (Run 1 = 66.2 mg, 221 μmol, 88% yield; Run 2 = 73.7 mg, 246 μmol, 98% yield; average = 93% yield). M.p. = 118-119 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.90 (s, 1H), 6.29 (s, 2H), 3.93 (s, 3H), 3.77 (s, 6H), 2.34 (s, 3H), 2.31 (s, 3H), 2.28 (s, 3H), 2.05 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 160.2, 158.3, 134.6, 133.7, 133.5, 132.7, 130.7, 130.0, 112.5, 90.4, 55.7, 55.2, 20.8, 17.1, 16.5, 16.2; MS (ESI) m/z = 323 ($M+Na^+$, 100), 301 ($M+H^+$, 38.8); HRMS (ESI, $M+H^+$) 301.1784 (Calcd. for $C_{19}H_{25}O_3$ 301.1798).



3g

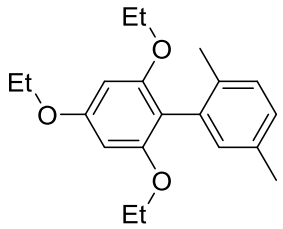
2,4,6-trimethoxy-2',3'-dimethyl-4'-*tert*-butyl-1,1'-biphenyl, **3g**, was synthesised using the general protocol from 3,4-dimethyl-1-*tert*-butylbenzene (1.16 mL, 6.25 mmol) and 1,3,5-trimethoxybenzene (42.0 mg, 0.25 mmol); the title compound was isolated as an off white solid (Run 1 = 45.0 mg, 138 μmol, 55 % yield; Run 2 = 49.7 mg, 152 μmol, 61% yield; average = 58% yield). M.p. = 101-103 °C; ^{1}H NMR (400 MHz, CDCl3) δ = 7.18 (d, *J* = 2.2 Hz, 1H), 7.05 (d, *J* = 2.2 Hz, 1H), 6.26 (s, 2H), 3.89 (s, 3H), 3.72 (s, 6H), 2.35 (s, 3H), 1.98 (s, 3H), 1.34 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 160.41, 158.48, 146.92, 135.43, 133.44, 133.32, 126.55, 125.92, 112.93, 90.78, 55.80, 55.37, 34.19, 31.47, 21.06, 16.10; MS (ESI) m/z = 351 ($M+Na^+$, 100), 329 ($M+H^+$, 23.4); HRMS (ESI, $M+H^+$) 329.2096 (Calcd. for $C_{21}H_{29}O_3$ 329.2111).



3h

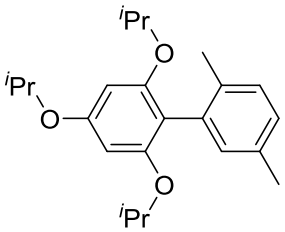
2,4,6-tris(methoxy-d_3)-2',5'-dimethyl-1,1'-biphenyl, **3h**, was synthesised using the general protocol from *para*-xylene (771 μl, 6.25 mmol) and 1,3,5-tris(methoxy-d_3)-benzene (44.3 mg, 0.25 mmol); the title compound was isolated as a white crystalline solid (Run 1 = 36.4 mg, 130 μmol, 52 % yield; Run 2 = 33.1 mg, 118 μmol, 47% yield; average = 50%

yield). M.p. = 114-116 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.18 (d, *J* = 7.7, 1H), 7.07 (dd, *J* = 7.7, 1.5, 1H), 6.98 (d, *J* = 1.5, 1H), 6.24 (s, 2H), 2.35 (s, 3H), 2.06 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ = 160.5, 158.3, 134.6, 134.4, 133.9, 131.9, 129.4, 128.0, 111.9, 90.6, 54.7 (br m), 21.1, 19.3; MS (ESI) m/z = 304 ($M+Na^+$, 100), 282 ($M+H^+$, 47.2); HRMS (ESI, $M+H^+$) 282.2038 (Calcd. for $C_{17}H_{12}D_9O_3$ 282.2050).



3i

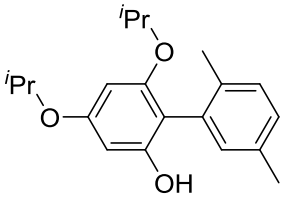
2,4,6-triethoxy-2',5'-dimethyl-1,1'-biphenyl, **3i**, was synthesised using the general protocol from *para*-xylene (771 μl, 6.25 mmol) and 1,3,5-triethoxy-benzene (52.6 mg, 0.25 mmol); the title compound was isolated as a clear oil (Run 1 = 39.8 mg, ^{1}H NMR analysis of the product sample, post preparative thin layer chromatography, showed that it was a 2:1 mixture of **3i**:residual starting material; 93 μmol, 37 % yield; Run 2 = 38.0 mg, ^{1}H NMR analysis of the product sample, post preparative thin layer chromatography, showed that it was a 18:7 mixture of **3i**:residual starting material; 96 μmol, 38% yield; average = 38% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.21 (d, *J* = 7.7, 1H), 7.02 (dd, *J* = 7.7, 1.6, 1H), 6.98 (d, *J* = 1.6, 1H), 6.21 (s, 2H), 4.07 (q, *J* = 7.0, 2H), 3.94 (app qd, *J* = 7.0, 3.1, 4H), 2.32 (s, 3H), 2.06 (s, 3H), 1.45 (t, *J* = 7.0, 3H), 1.21 (t, *J* = 7.0, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ = 159.5, 157.6, 134.4, 134.1, 133.8, 132.0, 129.0, 127.3, 113.3, 92.8, 64.1, 63.4, 21.0, 19.4, 14.9, 14.7; MS (ESI) m/z = 337 ($M+Na^+$, 100), 315 ($M+H^+$, 46.8); HRMS (ESI, $M+H^+$) 315.1937 (Calcd. for $C_{20}H_{27}O_3$ 315.1955).



3j

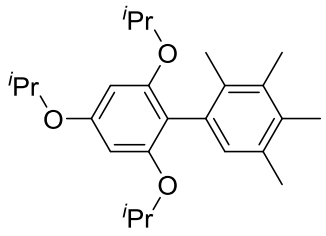
2,4,6-triisopropoxy-2',5'-dimethyl-1,1'-biphenyl, **3j**, To a 10 ml microwave vial or round bottomed flask equipped with a magnetic stirrer bar was palladium(II) acetate (5.6 mg, 25 μmol, 10 mol%), 1,3,5-triisopropoxy-benzene (63.1 mg, 0.25 mmol, 1.0 equiv), potassium peroxodisulfate (203 mg, 0.75 mmol, 3.0 equiv) and *para*-xylene (771 μL, 6.25 mmol, 25 equiv). The reaction vessel was then briefly flushed with N_2 and trifluoroacetic acid (191 μL, 2.5 mmol, 10 equiv) was then added under N_2 flow and sealed. The reaction mixture was then heated with stirring to 50 ^{o}C in an oil bath for 18 hours. After the allotted reaction time the reaction was then allowed to cool to room temperature, diluted with dichloromethane (10 mL), filtered through cotton wool and adsorbed onto silica gel *in vacuo*. The sample was then dry loaded onto a silica gel column and purified eluting with hexane/ethyl acetate (100:0 to 95:5).* The fractions containing the arylated product were then concentrated *in vacuo* to yield a crude sample which was further purified by preparative thin layer chromatography; the title compound was isolated as a colourless oil (25.0 mg, 70 μmol, 28% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.08 (d, *J* = 7.7, 1H), 6.98 (dd, *J* = 7.7, 1.5, 1H), 6.94 (d, *J* = 1.5,

1H), 6.21 (s, 2H), 4.54 (sept, *J* = 6.0, 1H), 4.18 (sept, *J* = 6.0, 2H), 2.30 (s, 3H), 2.06 (s, 3H), 1.37 (d, *J* = 6.0, 6H), 1.10 (d, *J* = 6.0, 12H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 158.0, 157.0, 134.5, 134.4, 133.6, 132.2, 128.8, 127.0, 116.3, 97.4, 71.3, 69.9, 22.2, 22.1, 22.1, 20.9, 19.5; MS (ESI) m/z 379 ($M+Na^+$, 100), 357 ($M+H^+$, 30.5); HRMS (EI, $M+H^+$) 357.2423 (Calcd. for $C_{23}H_{33}O_3$ 357.2424).



3j'

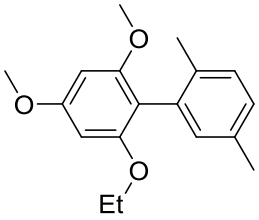
2,4,6-diisopropoxy-2',5'-dimethyl-1,1'-biphen-2-ol, **3j'**, * - from the same reaction mixture as described above, the dealkylated product **3j'** was isolated during column chromatography as a pale oil (9.6 mg, 31 μmol, 12% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.19 (d, *J* = 7.7, 1H), 7.09 (dd, *J* = 7.7, 1.5, 1H), 6.99 (d, *J* = 1.5, 1H), 6.19 (d, *J* = 2.2, 1H), 6.12 (d, *J* = 2.2, 1H), 4.76 (br s, 1H), 4.53 (sept, *J* = 6.0, 1H), 4.33 (sept, *J* = 6.0, 1H), 2.33 (s, 3H), 2.08 (s, 3H), 1.36 (d, *J* = 6.0, 6H), 1.16 (d, *J* = 6.0, 3H), 1.12 (d, *J* = 6.0, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 158.8, 156.6, 154.2, 135.9, 135.6, 131.9, 131.7, 130.3, 128.8, 110.6, 95.7, 94.2, 70.6, 69.8, 22.2, 22.1, 22.1, 22.0, 20.9, 19.2; MS (EI) m/z = 315 ($M+H^+$, 100); HRMS (EI, $M+H^+$) 315.1954 (Calcd. for $C_{20}H_{27}O_3$ 315.1955).

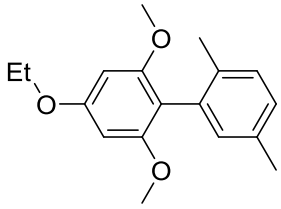


3k

2,4,6-tri-isopropoxy-2',3',4',5'-dimethyl-1,1'-biphenyl, **3k**, To a 10 ml microwave vial or round bottomed flask equipped with a magnetic stirrer bar was added palladium(II) acetate (5.6 mg, 25 μmol, 10 mol%), 1,3,5-triisopropoxy-benzene (63.1 mg, 0.25 mmol, 1.0 equiv), potassium peroxodisulfate (203 mg, 0.75 mmol, 3.0 equiv) and prehenitene (931 μL, 6.25 mmol). The reaction vessel was then briefly flushed with N_2 and trifluoroacetic acid (191 μL, 2.5 mmol, 10 equiv) was then added under N_2 flow and sealed. The reaction mixture was then heated with stirring to 50 ^{o}C in an oil bath for 18 hours. After the allotted reaction time, the reaction was allowed to cool to room temperature, diluted with dichloromethane (10 mL), filtered through cotton wool and adsorbed onto silica gel *in vacuo*. The sample was then dry loaded onto a silica gel column and purified eluting with hexane/ethyl acetate (100:0 to 95:5). The fractions containing the arylated product were then concentrated *in vacuo* to yield a crude sample which was further purified by preparative thin layer chromatography; the title compound was isolated as a colourless oil (38.6 mg, ^{1}H NMR analysis revealed that the product was a mixture of 11:1 **3m**:residual starting material: product = 102 μmol, 41% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.81 (s, 1H), 6.22 (s, 2H), 4.55 (sept, *J* = 6.0, 1H), 4.19 (sept, *J* = 6.0, 2H), 2.26 (s, 3H), 2.23 (s, 3H), 2.23 (s, 3H), 2.01 (s, 3H), 1.38 (d, *J* = 6.0, 6H), 1.11 (d, *J* = 6.0, 6H), 1.11 (d, *J* = 6.0, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 157.7, 157.1, 133.8, 133.2, 132.4, 131.9, 131.4, 130.4, 117.0,

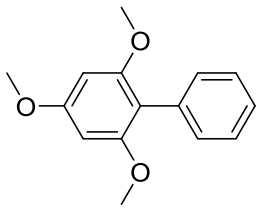
97.3, 71.2, 69.8, 22.2, 22.1, 20.6, 17.7, 16.4, 16.0.; MS (ESI) m/z = 407 ($M+Na^+$, 100), 385 ($M+H^+$, 41.5); HRMS (ESI, $M+H^+$) 385.2726 (Calcd. for $C_{25}H_{37}O_3$ 385.2737).





3m 5 : 3

2-ethoxy-4,6-dimethoxy-2',5'-dimethyl-1,1'-biphenyl (**A**), 4-ethoxy-2,6-dimethoxy-2',5'-dimethyl-1,1'-biphenyl (**B**), **3m**, was synthesised using the general protocol from *para*-xylene (771 µl, 6.25 mmol) and 1-ethoxy-3,5-dimethoxy-benzene (45.6 mg, 0.25 mmol); after silica gel column chromatography the compound was further purified by preparative thin layer chromatography, the title compounds were isolated as a colourless oil (31.0 mg, 108 µmol, 43% yield; ^{1}H NMR analysis revealed that the sample was a 5:3 ratio of **A**:**B** isomers). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.18-7.13 (m, 1H A + 1H B), 7.08-7.02 (m, 1H A + 1H B), 6.97-6.95 (m, 1H A + 1H B), 6.25-6.22 (m, 2H A + 2H B), 4.11 (q, *J* = 7.0, 2H B), 3.96 (app qd, *J* = 7.0, 1.7, 2H A), 3.87 (s, 3H A), 3.71 (s, 3H A), 3.71 (6H, B), 2.34 (br s, 3H A + 3H B), 2.06 (s, 3H A), 2.05 (s, 3H B), 1.48 (t, *J* = 7.0, 3H B), 1.21 (t, *J* = 7.0, 3H A); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 160.4, 159.9, 158.4, 158.3, 157.6, 134.6, 134.5, 134.3, 134.1, 134.0, 133.9, 132.0, 131.9, 129.3, 129.2, 128.0, 127.7, 112.7, 111.8, 92.1, 91.2, 90.9, 64.2, 63.5, 55.8, 55.8, 55.3, 21.1, 21.1, 19.4, 19.3, 15.0, 14.7; MS (ESI) m/z = 309 ($M+Na^+$, 100), 287 ($M+H^+$, 35.4); HRMS (ESI, $M+H^+$) 287.1629 (Calcd. for $C_{18}H_{23}O_3$ 287.1642).

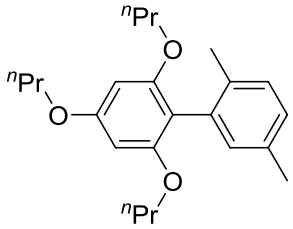


3n

2,4,6-trimethoxy-1,1'-biphenyl,[6] **3n**, To a 10 ml microwave vial or round bottomed flask equipped with a magnetic stirrer bar was palladium(II) trifluoroacetate (8.3 mg, 25 µmol, 10 mol%), 1,3,5-trimethoxybenzene (42.0 mg, 0.25 mmol, 1.0 equiv), potassium peroxodisulfate (203 mg, 0.75 mmol, 3.0 equiv) and benzene (1.00 mL, 11.25 mmol, 45 equiv). The reaction vessel was then briefly flushed with N_2 and trifluoroacetic acid (96 µL, 1.25 mmol, 5 equiv) was then added under N_2 flow and sealed. The reaction mixture was then heated with stirring to 50 ^{o}C in an oil bath for 18 hours. After the allotted reaction time the reaction was then allowed to cool to room temperature, diluted with CH_2Cl_2 (10 mL), filtered through cotton wool and adsorbed onto silica gel *in vacuo*. The sample was then dry loaded onto a silica gel column and purified eluting with hexane/ethyl acetate (100:0 to 95:5). The fractions containing the arylated product were then concentrated *in vacuo* to yield the title compound as a white crystalline solid (27.6 mg, 113 µmol, 45 % yield). M.p. = 151-153 °C (lit. = 152-154 °C)[5]; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.42 – 7.36 (m, 2H), 7.35 – 7.26 (m, 3H), 6.23 (s, 2H), 3.87 (s, 3H), 3.72 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 160.5, 158.3, 134.1, 131.2, 127.6,

126.5, 112.4, 90.8, 55.9, 55.4; MS (ESI) m/z = 267 ($M+Na^+$, 100), 245 ($M+H^+$, 32.9); HRMS (ESI, $M+H^+$) 245.1167 (Calcd. for $C_{15}H_{17}O_3$ 245.1172).

Additional CDC products not in Scheme 2 of paper (**3o**, **3p**, and **3q**).



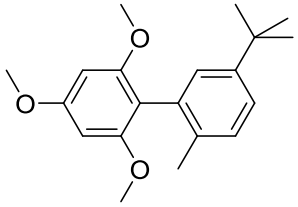
3o

2,4,6-tri-*n*-propoxy-2',5'-dimethyl-1,1'-biphenyl, **3o**, was synthesised using the general protocol from *para*-xylene (771 μl, 6.25 mmol) and 1,3,5-tri-*n*-propoxy-benzene (63.1 mg, 0.25 mmol); the title compound was isolated as a clear oil (Run 1 = 41.8 mg, ^{1}H NMR analysis of the product sample, post preparative thin layer chromatography, showed that it was a 11:9 mixture of **3o**:residual starting material; 72 μmol, 29 % yield; Run 2 = 40.0 mg, ^{1}H NMR analysis of the product sample, post preparative thin layer chromatography, showed that it was a 3:2 mixture of **3o**:residual starting material; 74 μmol, 30% yield; average = 29% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.10 (d, *J* = 7.7, 1H), 7.00 (dd, *J* = 7.7, 1.6, 1H), 6.94 (d, *J* = 1.6, 1H), 6.21 (s, 2H), 3.96 (t, *J* = 6.5, 2H), 3.82 (app td, *J* = 6.5, 1.0, 4H), 2.30 (s, 3H), 2.04 (s, 3H), 1.85 (sext, *J* = 7.0, 2H), 1.59 (sext, *J* = 7.0, 4H), 1.08 (t, *J* = 7.0, 3H), 0.81 (t, *J* = 7.0, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ = 159.7, 157.7, 134.4, 134.1, 133.7, 132.1, 128.8, 127.2, 113.1, 92.6, 70.1, 22.7, 22.5, 20.9, 19.4, 10.6, 10.4 (17 out of a possible 18 carbon resonances observed, it is likely the remaining O-CH_2- signal lies at 69.6 ppm under the residual starting material peak); MS (ESI) m/z = 379 ($M+Na^+$, 100), 357 ($M+H^+$, 37.3); HRMS (ESI, $M+H^+$) 357.2411 (Calcd. for $C_{23}H_{33}O_3$ 357.2424).

3p 2 : 3

2-isopropoxy-4,6-dimethoxy-2',5'-dimethyl-1,1'-biphenyl (**A**), 4-isopropoxy-2,6-dimethoxy-2',5'-dimethyl-1,1'-biphenyl (**B**), **3p**, was synthesised using the general protocol from *para*-xylene (771 μl, 6.25 mmol) and 1-isopropoxy-3,5-dimethoxy-benzene (42.0 mg, 0.25 mmol); after silica gel column chromatography the compound was further purified by preparative thin layer chromatography, the title compounds were isolated as a yellow oil (18.4 mg, 61 μmol, 25% yield; ^{1}H NMR analysis revealed that the sample was a 2:3 ratio of **A**:**B** isomers). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.15 (d, *J* = 7.7, 1H B), 7.12 (d, *J* = 7.7, 1H A), 7.07–7.00 (m, 1H A + 1H B), 6.96 (br s, 1H B), 6.94 (br s, 1H A), 6.25–6.20 (m, 2H A + 2H B), 4.61 (sept, *J* = 6.0, 1H B), 4.23 (sept, *J* = 6.0, 1H A), 3.85 (s, 3H A), 3.70 (s, 3H A), 3.69 (6H, B), 2.33 (s, 3H B), 2.32 (s, 3H A), 2.05 (s, 3H A), 2.04 (s, 3H B), 1.40 (d, *J* = 6.0, 6H B), 1.11 (d, *J* = 6.0, 3H A), 1.11 (d, *J* = 6.0, 3H A); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 160.1, 158.7, 158.5, 158.3, 156.9, 134.6, 134.5, 134.3, 134.1, 134.0, 133.9,

132.0, 131.9, 129.3, 129.1, 127.9, 127.5, 114.2, 111.8, 94.7, 92.5, 91.4, 71.5, 70.0, 55.8, 55.7, 55.3, 22.2, 22.1, 22.0, 21.1, 21.0, 19.3, 19.3; MS (ESI) m/z = 323 ($M+Na^+$, 100), 301 ($M+H^+$, 22.0); HRMS (ESI, $M+H^+$) 323.1606 (Calcd. for $C_{20}H_{26}O_3Na$ 323.1618).



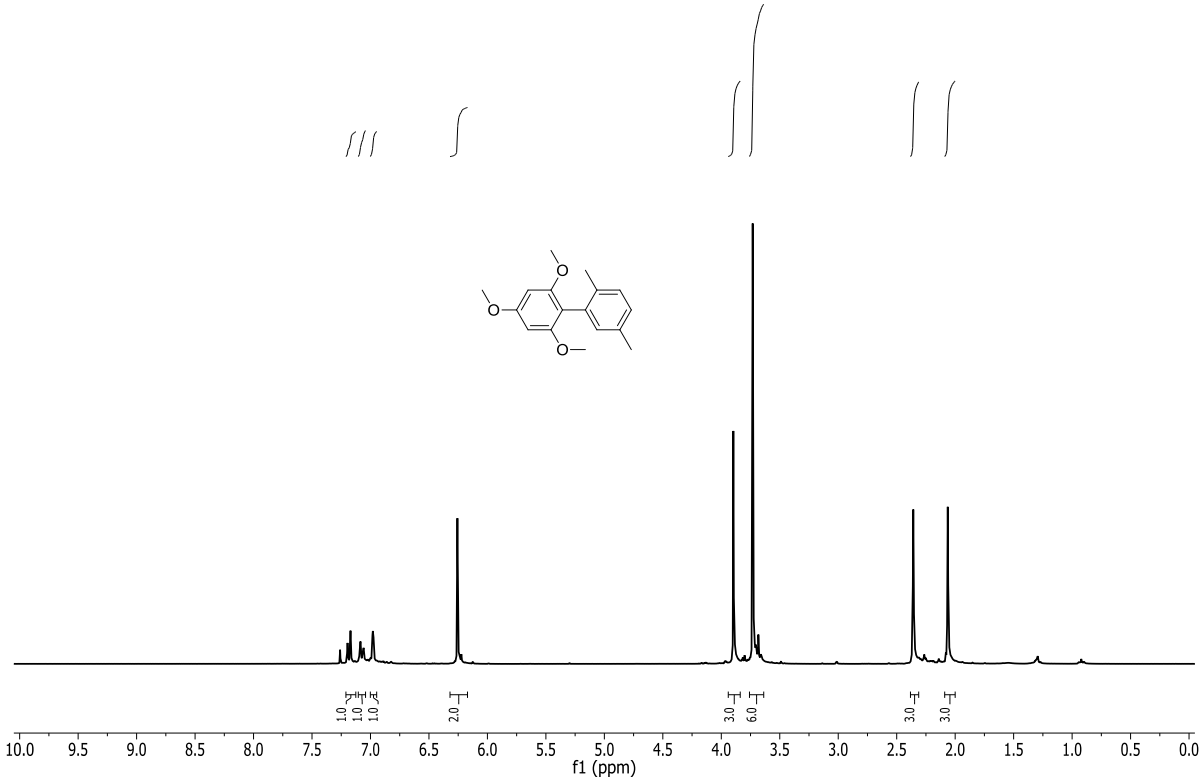
3q

2,4,6-trimethoxy-2'-methyl-4'-*tert*-butyl-1,1'-biphenyl, **3q**, was synthesised using the general protocol from 4-*tert*-butyltoluene (1.08 mL, 6.25 mmol) and 1,3,5-trimethoxybenzene (42.0 mg, 0.25 mmol); the title compound was isolated as a yellow oil (Run 1 = 9.3 mg, 29.6 μmol, 12 % yield; Run 2 = 9.2 mg, 29.3 μmol, 12% yield; average = 12% yield). ^1H NMR (500 MHz, $CDCl_3$) δ = 7.26 (dd, *J* = 8.0, 2.1, 1H), 7.19 (d, *J* = 8.0, 1H), 7.16 (d, *J* = 2.1, 1H), 6.24 (s, 2H), 3.88 (s, 3H), 3.70 (s, 6H), 2.06 (s, 3H), 1.32 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ = 160.5, 158.4, 147.4, 134.7, 133.4, 129.0, 128.8, 123.9, 112.4, 90.8, 55.8, 55.4, 34.3, 31.4, 19.2; MS (ESI) m/z = 337 ($M+Na^+$, 100), 315 ($M+H^+$, 44.0); HRMS (ESI, $M+H^+$) 315.1938 (Calcd. for $C_{20}H_{27}O_3$ 315.1955).

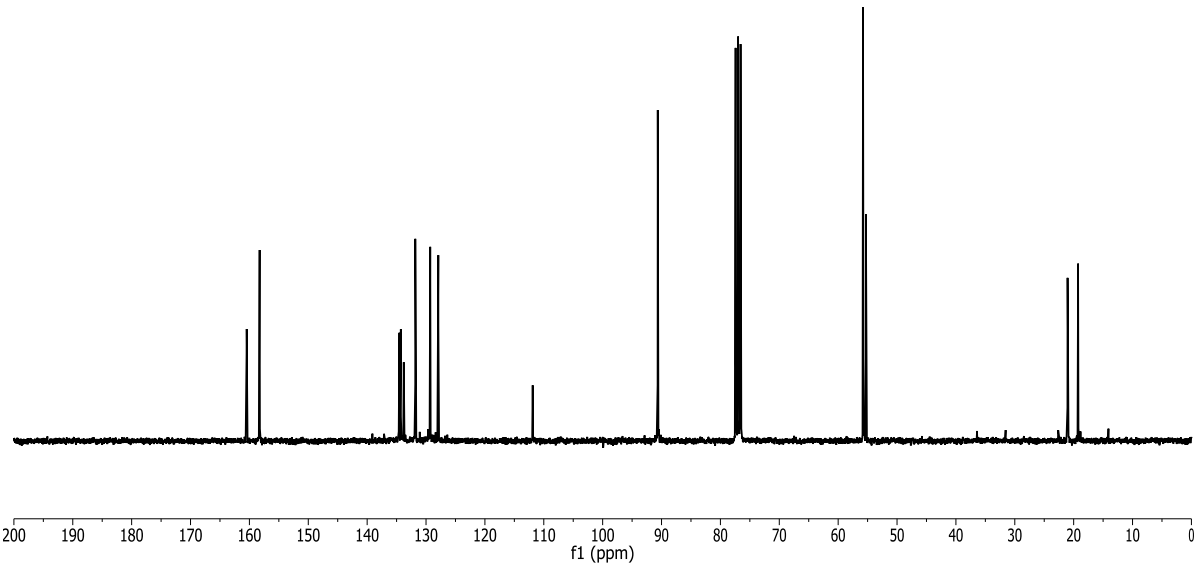
4 NMR Spectra for Compounds **3a-q**

2,4,6-trimethoxy-2',5'-dimethyl-1,1'-biphenyl, **3a**

^{1}H NMR (300 MHz, $CDCl_3$)

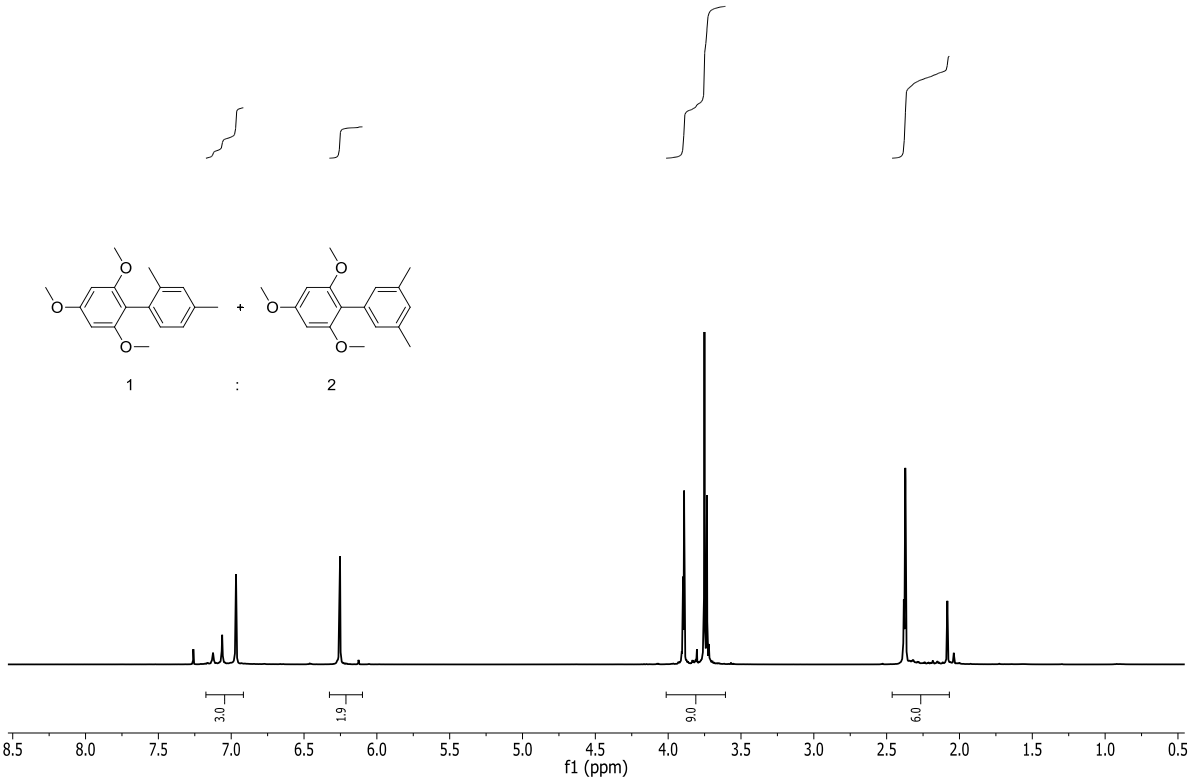


^{13}C NMR (75 MHz, $CDCl_3$)

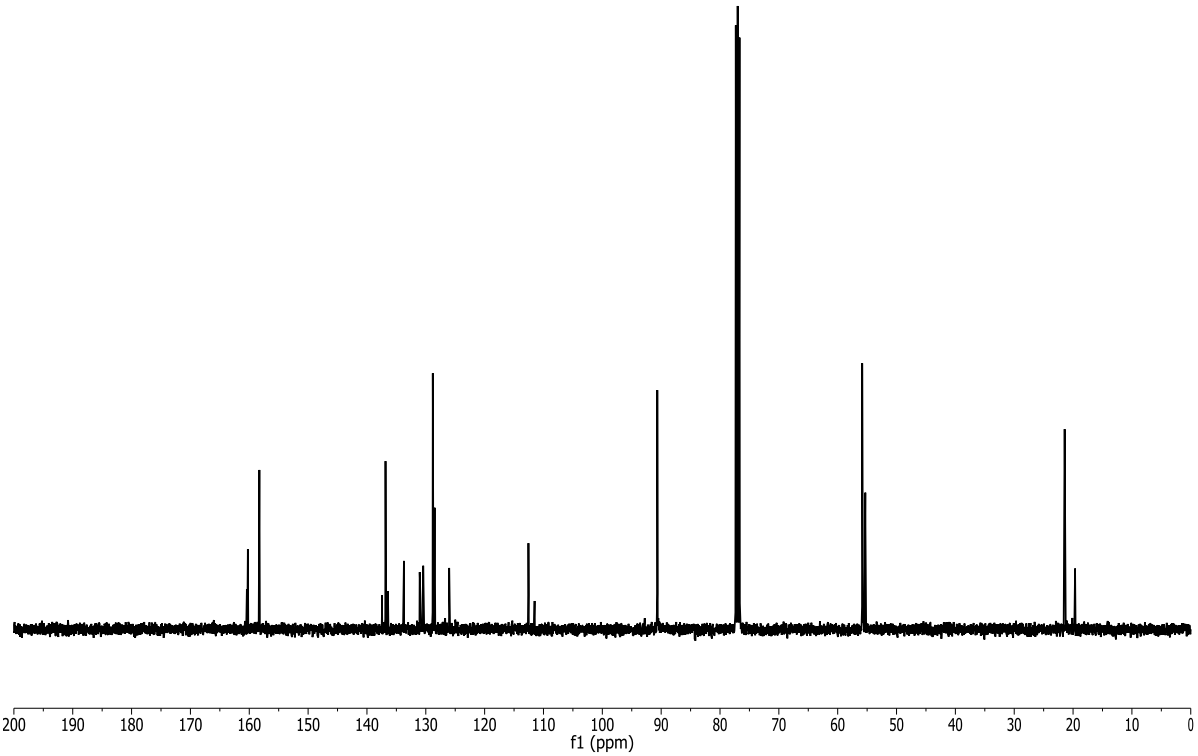


2,4,6-trimethoxy-2',4'-dimethyl-1,1'-biphenyl, and 2,4,6-trimethoxy-3',5'-dimethyl-1,1'-biphenyl, **3b**

^{1}H NMR (400 MHz, $CDCl_3$)

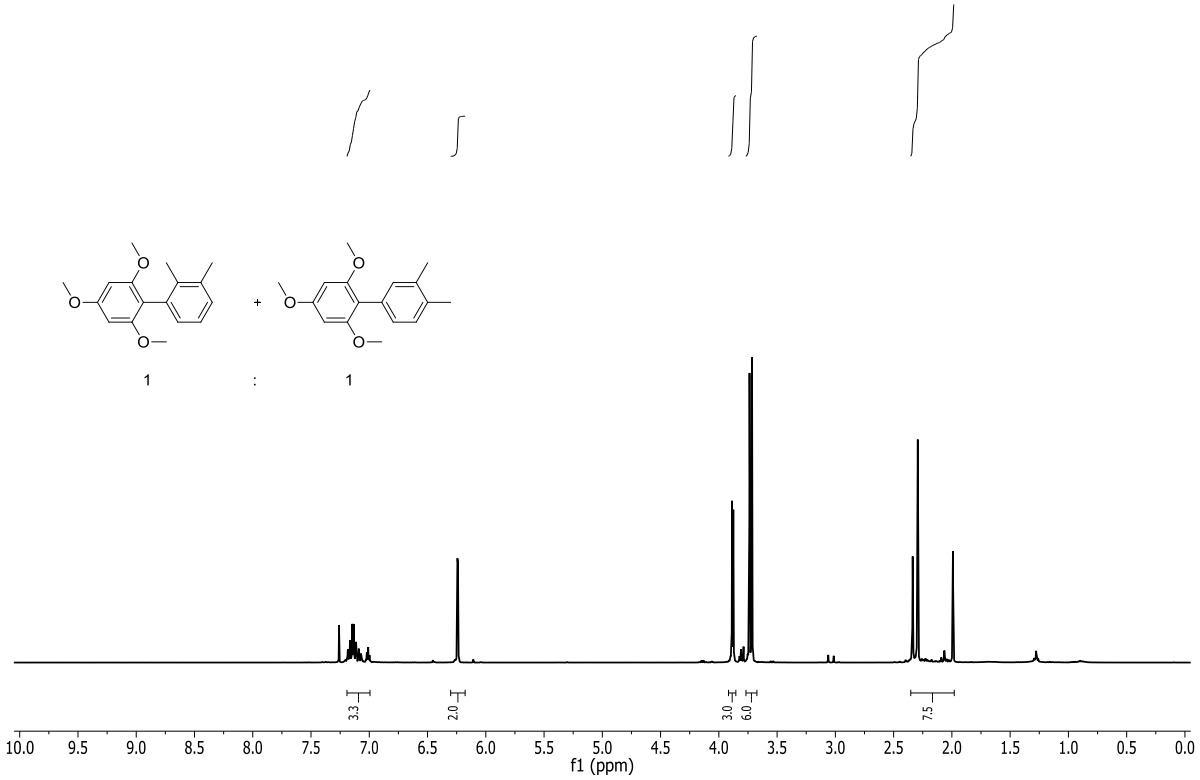


^{13}C NMR (101 MHz, $CDCl_3$)

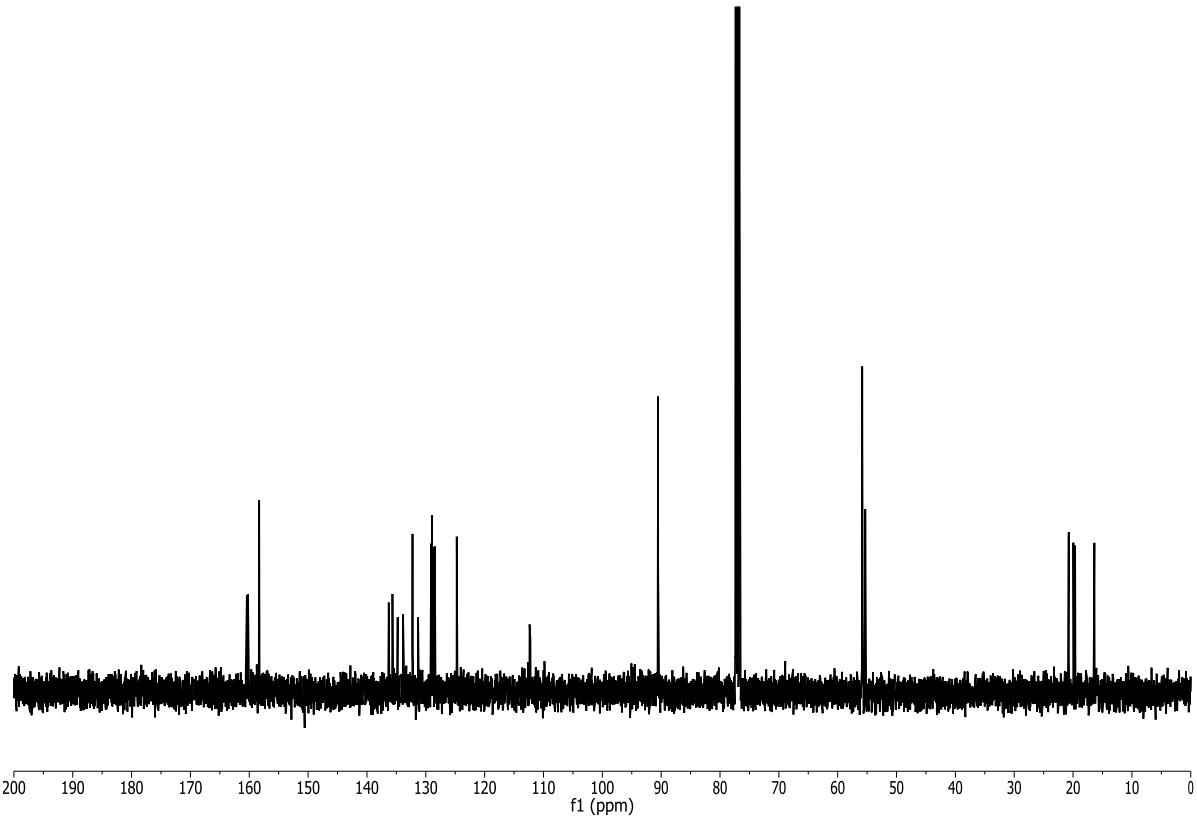


2,4,6-trimethoxy-2',3'-dimethyl-1,1'-biphenyl, 2,4,6-trimethoxy-3',4'-dimethyl-1,1'-biphenyl, **3c**

^{1}H NMR (400 MHz, $CDCl_3$)

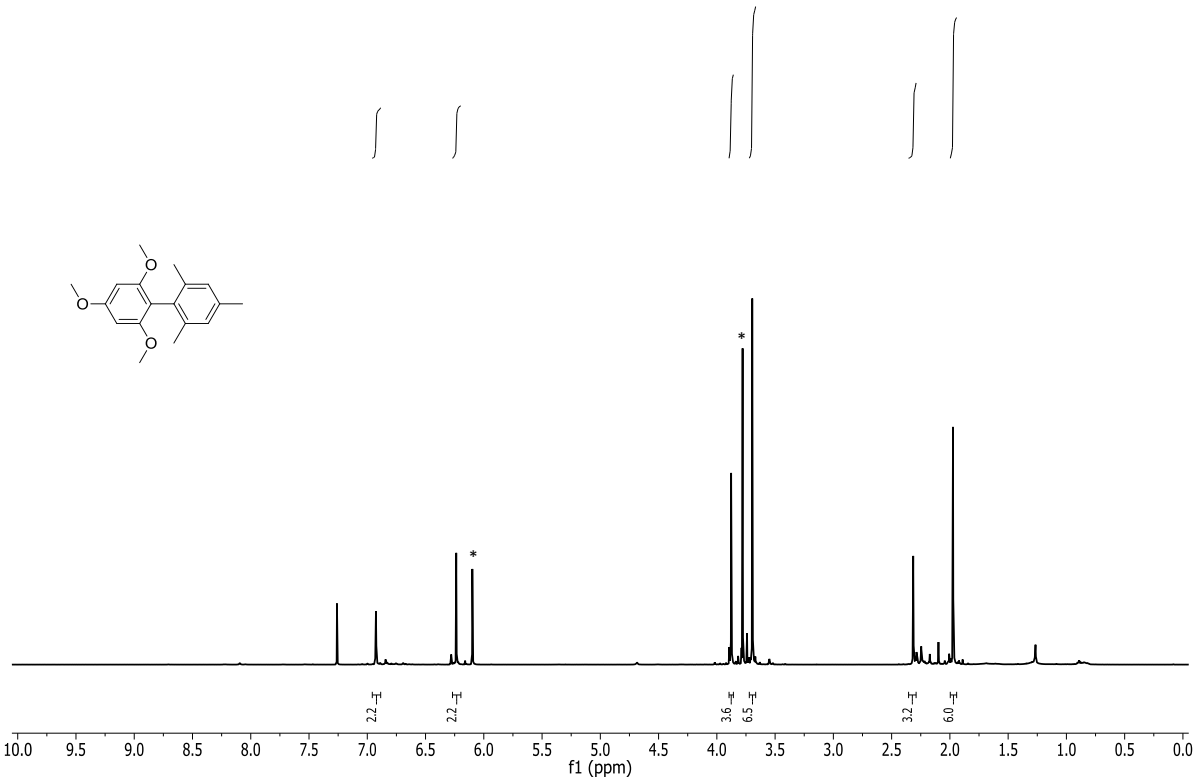


^{13}C NMR (101 MHz, $CDCl_3$)

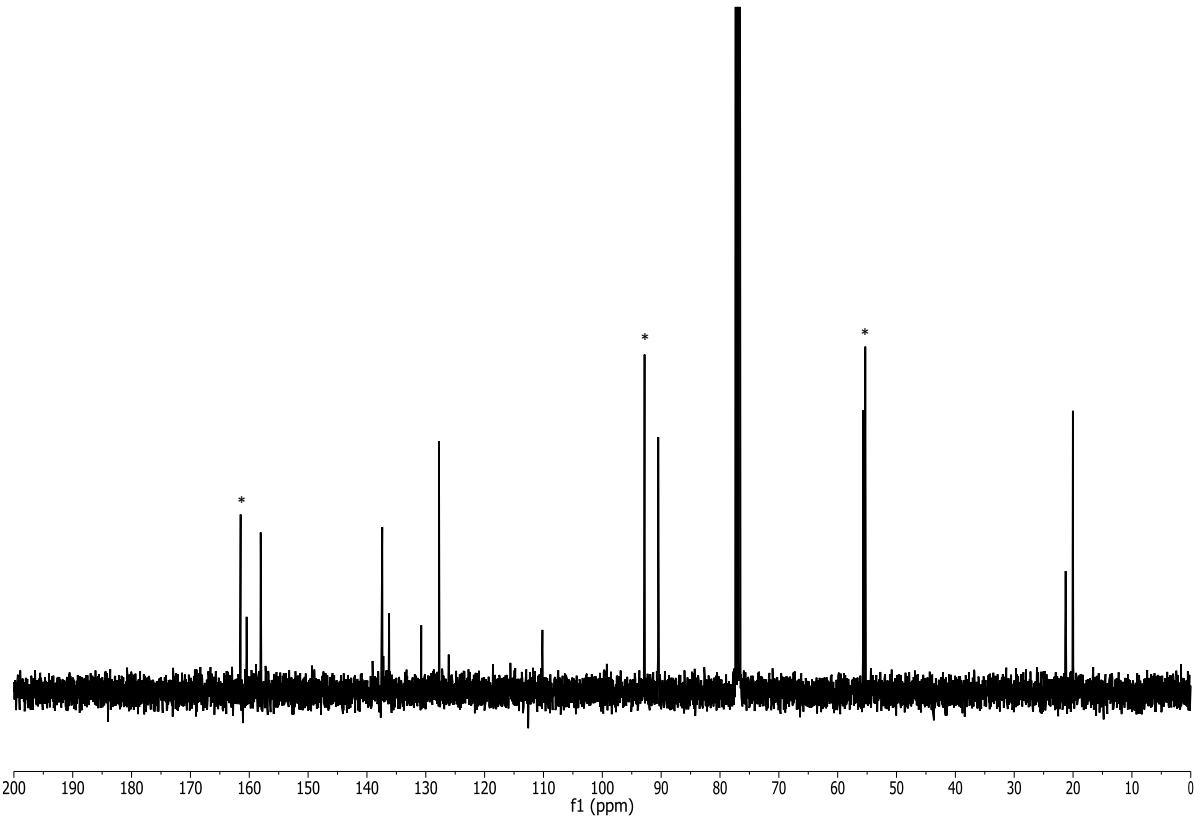


2,4,6-trimethoxy-2',4',6'-trimethyl-1,1'-biphenyl, **3d**

^{1}H NMR (500 MHz, $CDCl_3$)



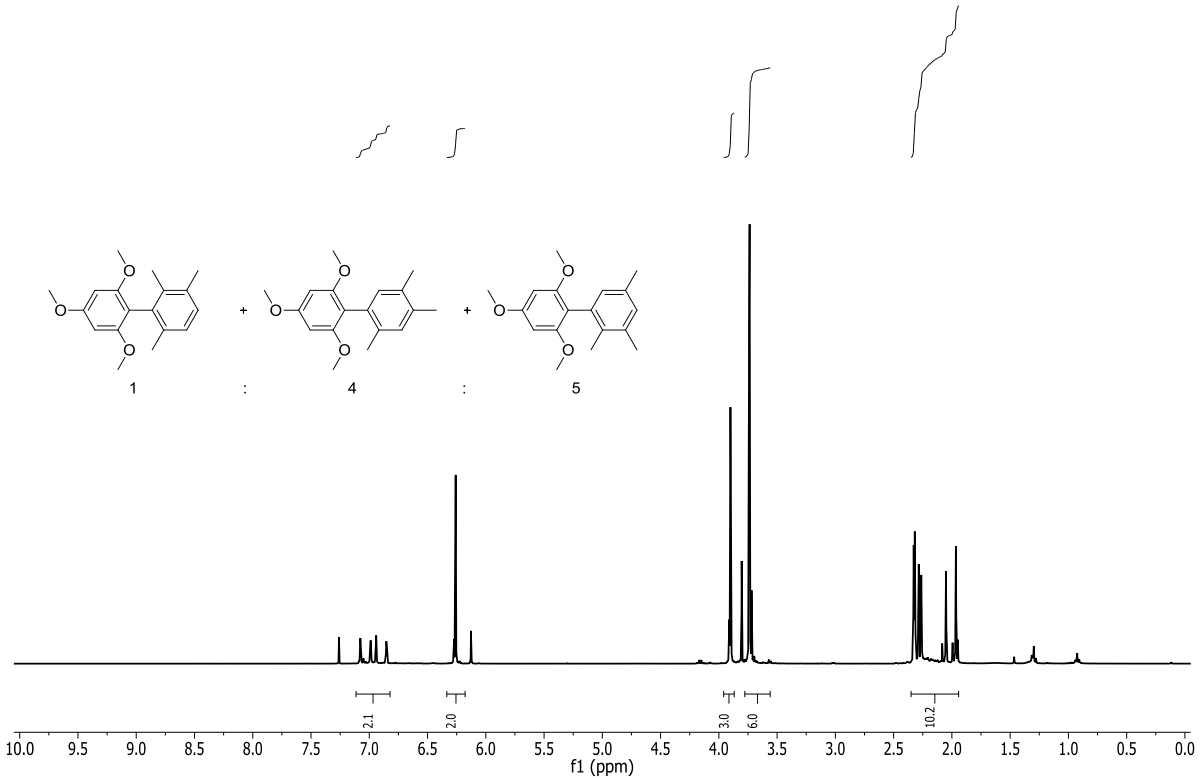
^{13}C NMR (101 MHz, $CDCl_3$)



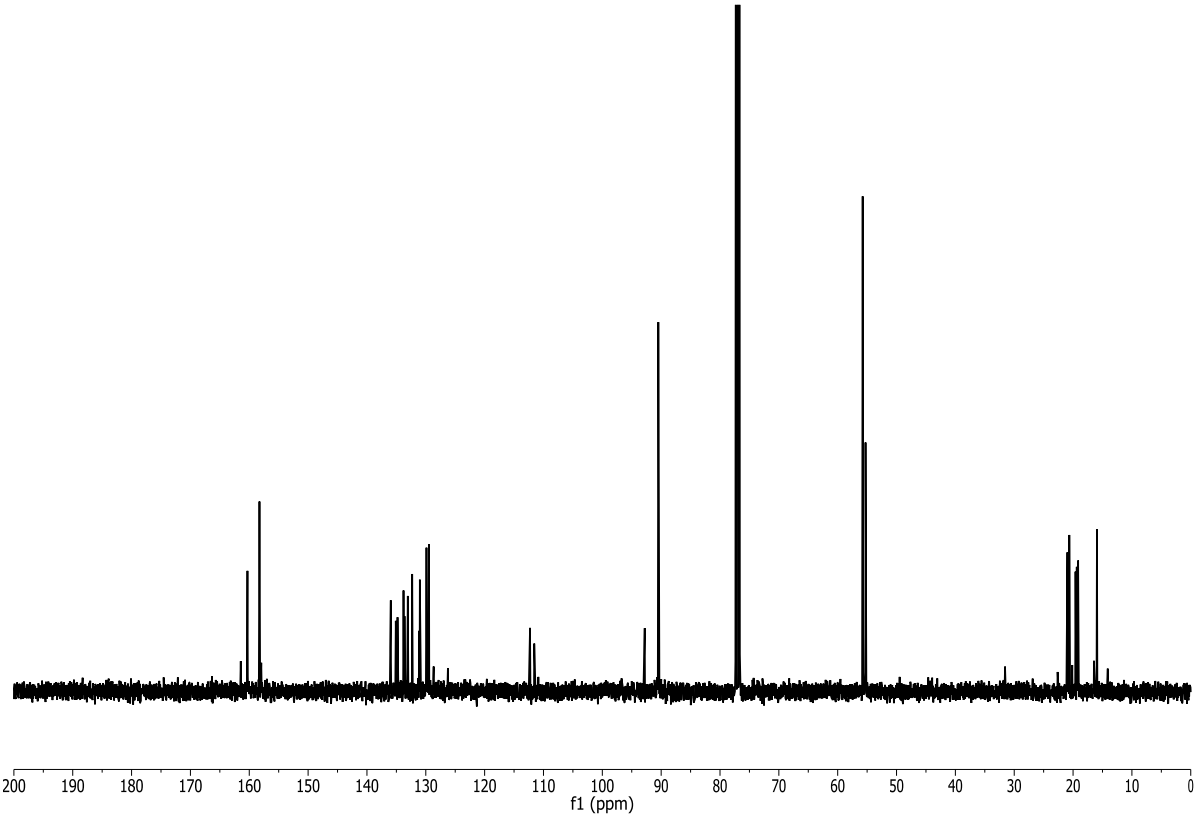
* - Residual 1,3,5-trimethoxybenzene starting material present in the ^{1}H NMR at 6.08, and 3.75 ppm and ^{13}C NMR at 161.7, 93.0 and 55.2 ppm.

2,4,6-trimethoxy-2',3',6'-trimethyl-1,1'-biphenyl, 2,4,6-trimethoxy-2’,3',5'-dimethyl-1,1'-biphenyl, 2,4,6-trimethoxy-2’,4',5'-dimethyl-1,1'-biphenyl, **3e**

^{1}H NMR (400 MHz, $CDCl_3$)

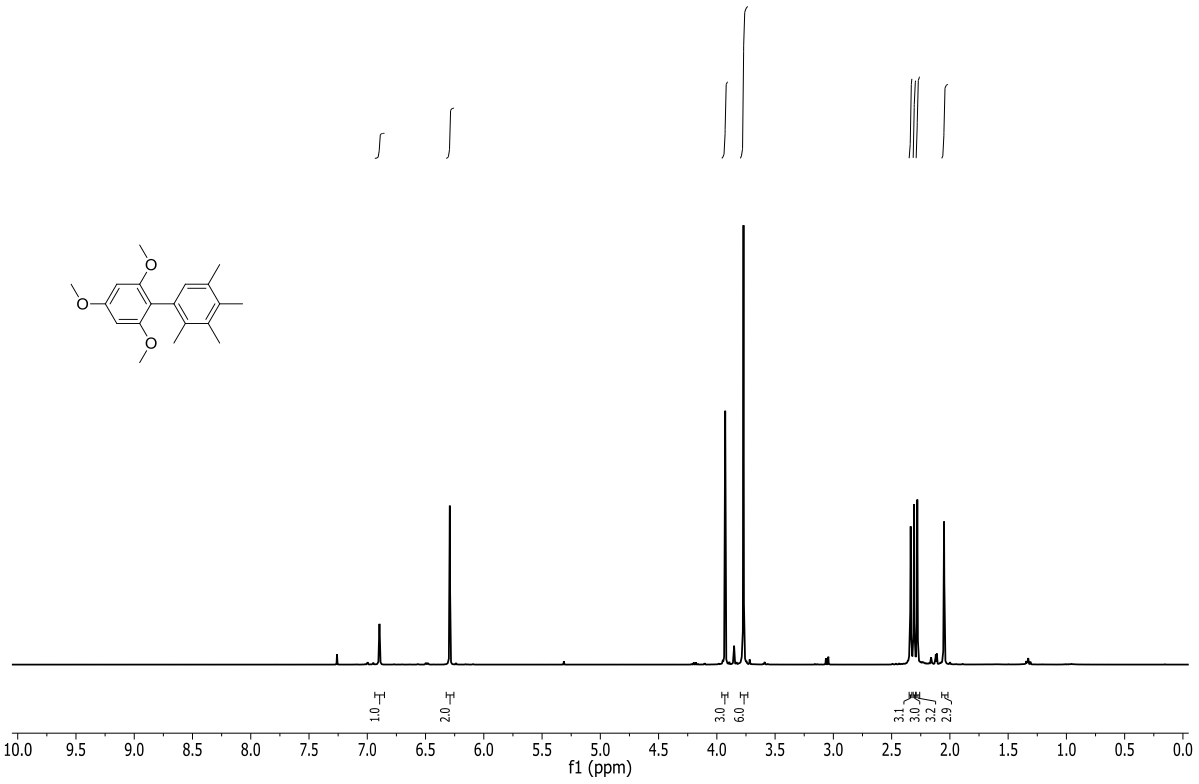


^{13}C NMR (101 MHz, $CDCl_3$)

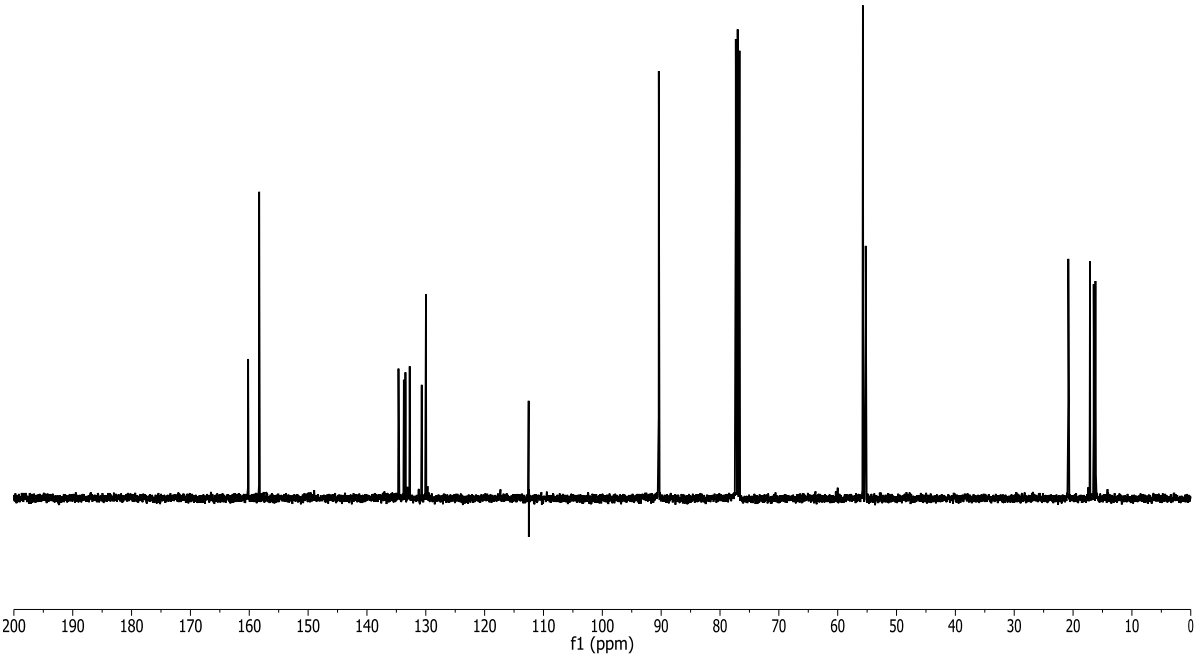


2,4,6-trimethoxy-2',3',4',5'-tetramethyl-1,1'-biphenyl, **3f**

^{1}H NMR (400 MHz, $CDCl_3$)

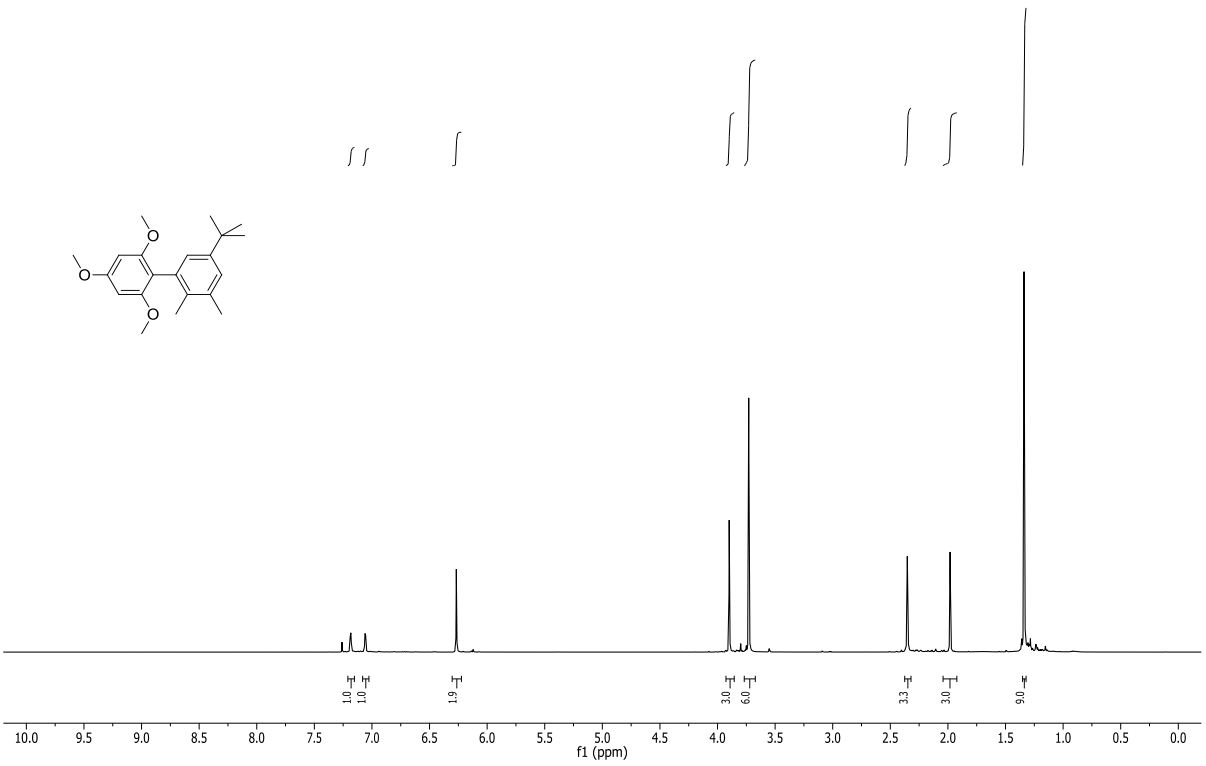


^{13}C NMR (101 MHz, $CDCl_3$)

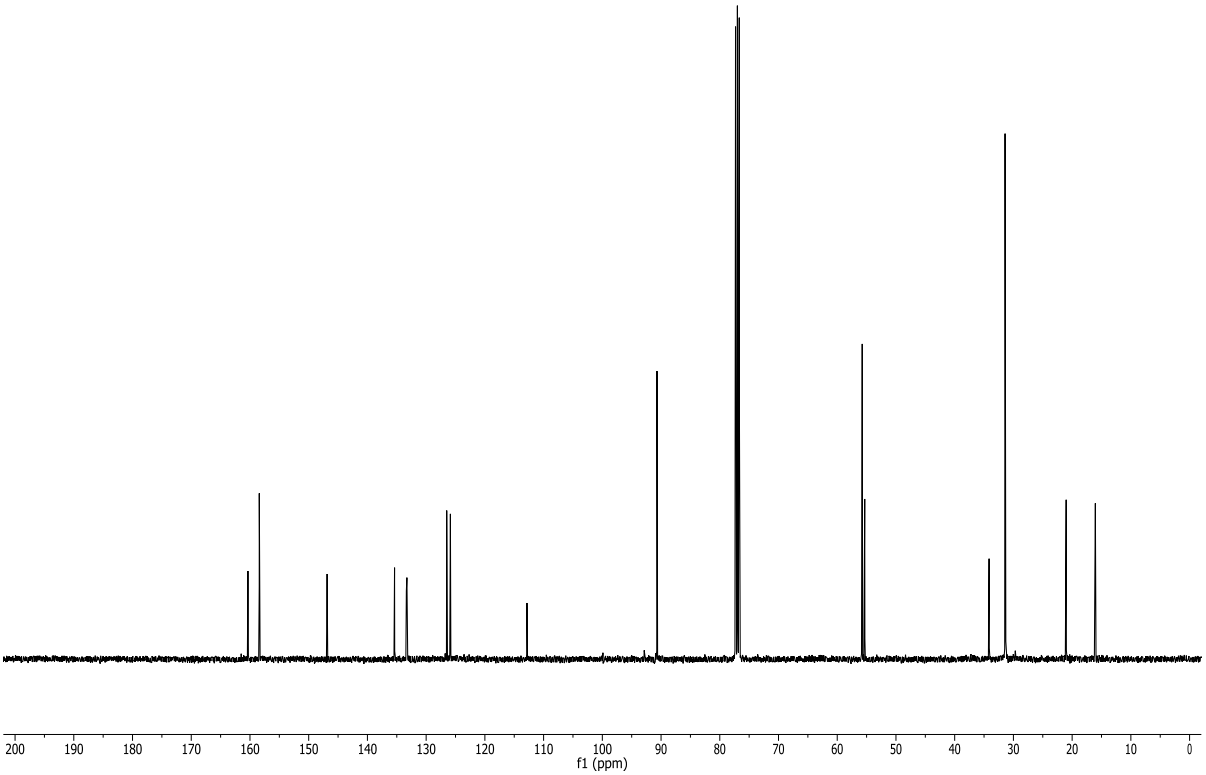


2,4,6-trimethoxy-2', -methyl-4'-*tert*-butyl-1,1'-biphenyl, **3g**

^{1}H NMR (400 MHz, $CDCl_3$)

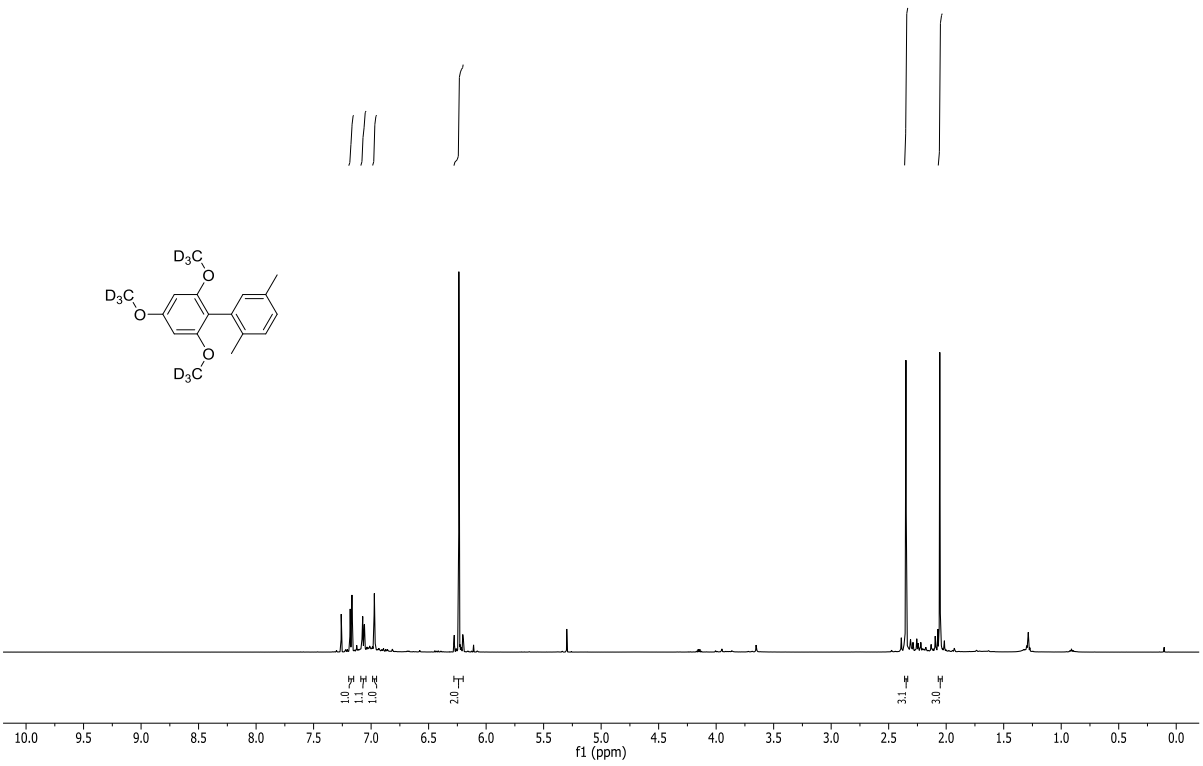


^{13}C NMR (101 MHz, $CDCl_3$)

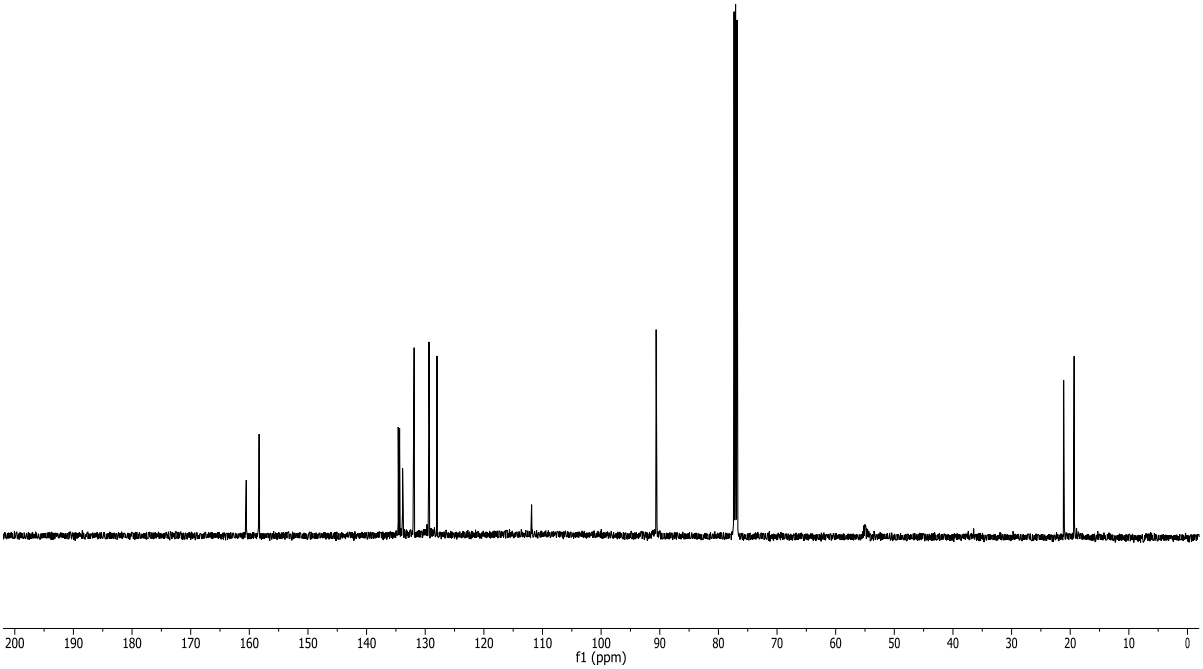


2,4,6-tris(methoxy-d_3)-2',5'-dimethyl-1,1'-biphenyl, **3h**

^{1}H NMR (500 MHz, $CDCl_3$)

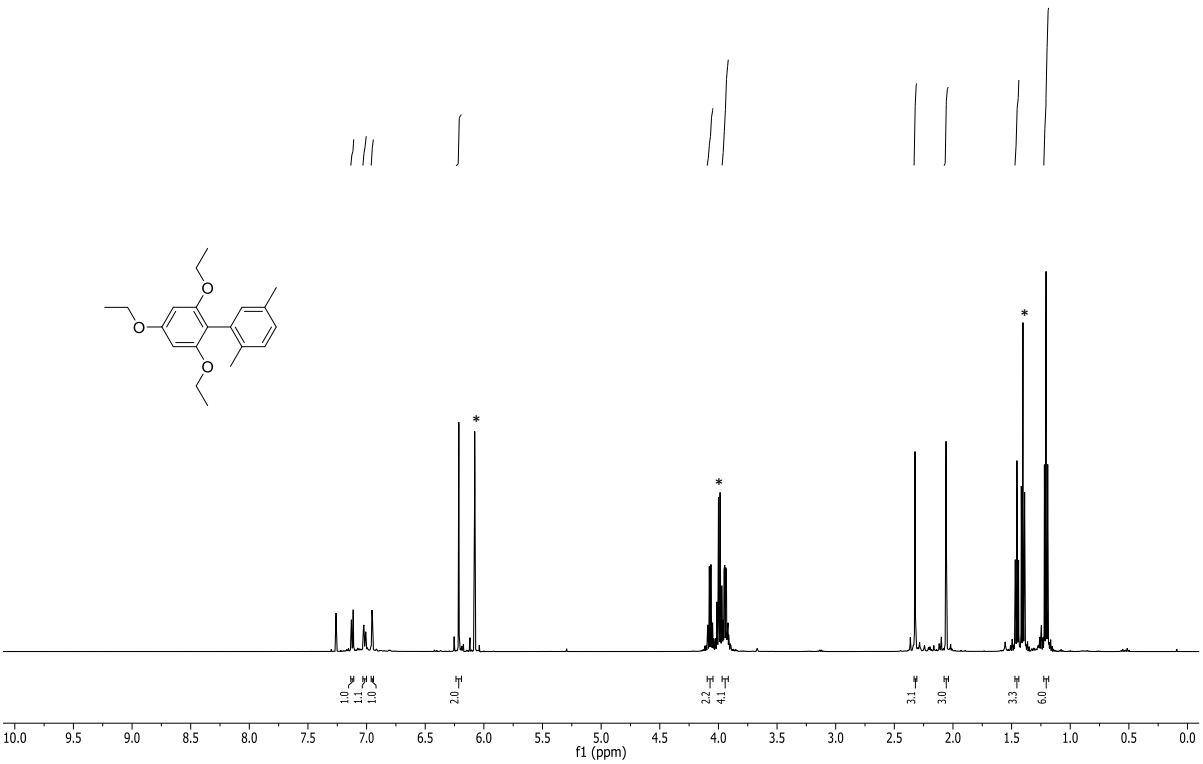


^{13}C NMR (126 MHz, $CDCl_3$)

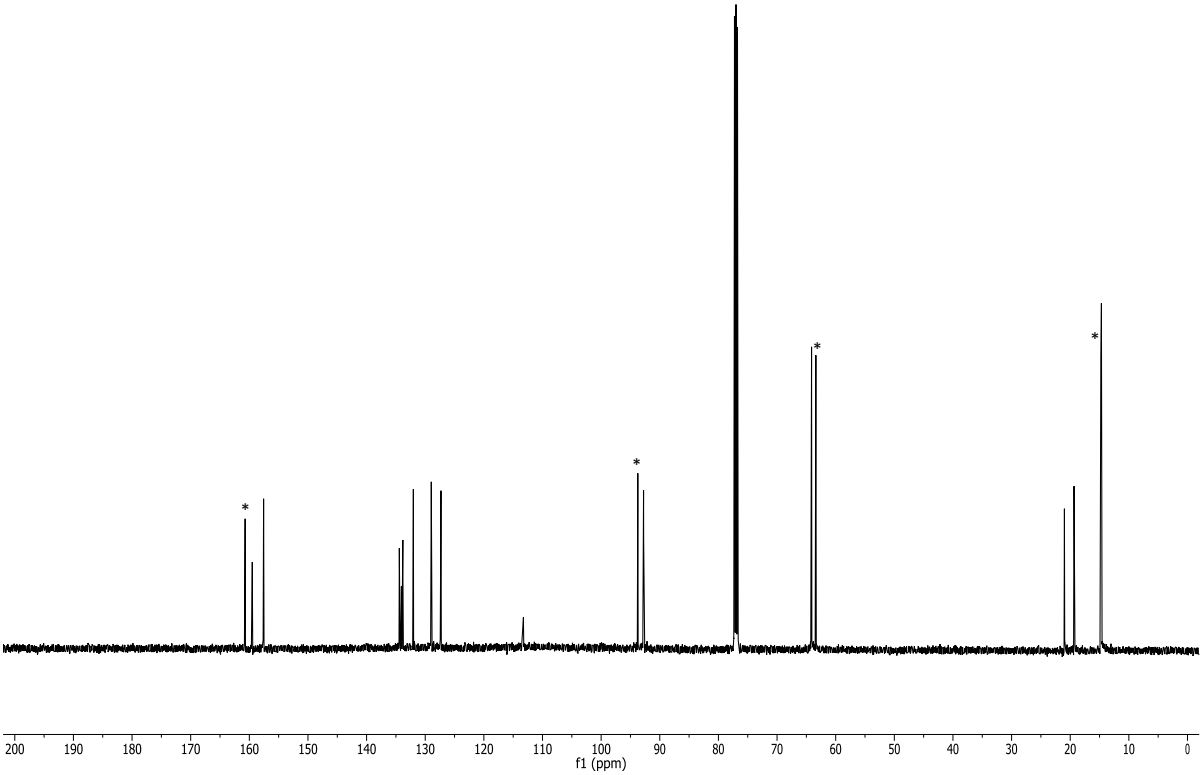


2,4,6-triethoxy-2',5'-dimethyl-1,1'-biphenyl, **3i**

^{1}H NMR (500 MHz, $CDCl_3$)



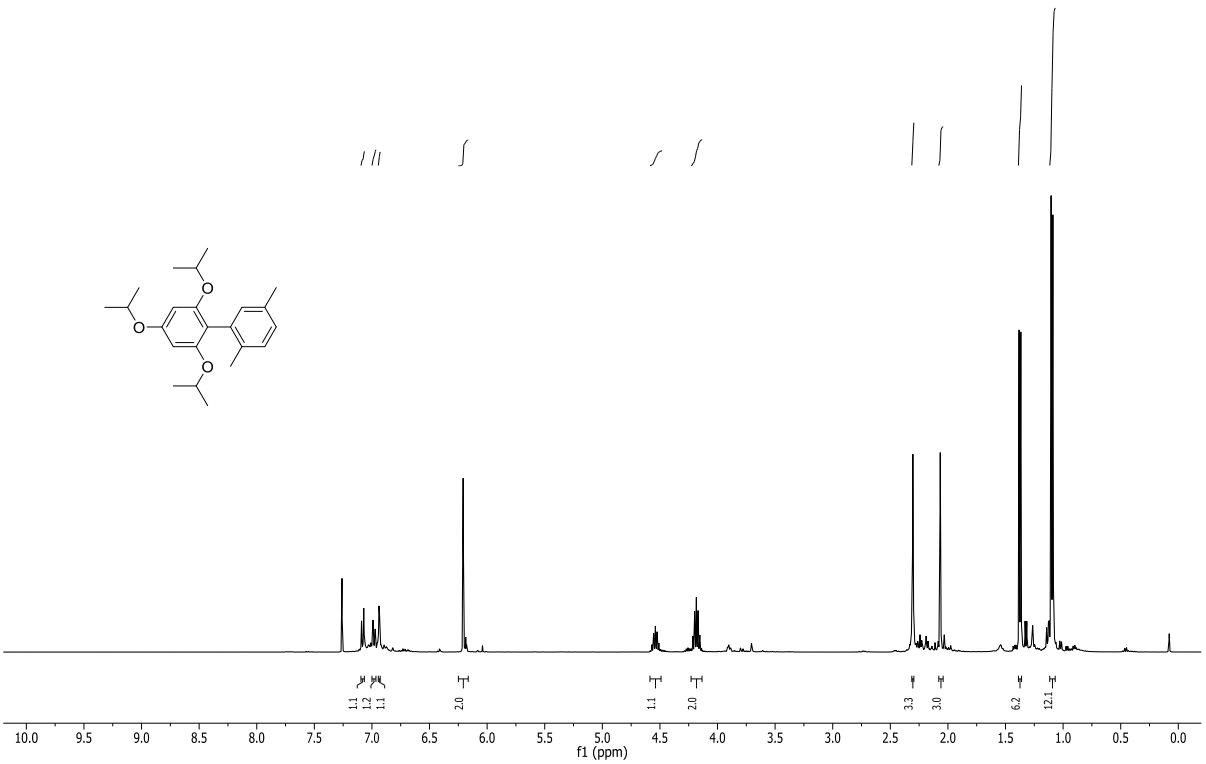
^{13}C NMR (126 MHz, $CDCl_3$)



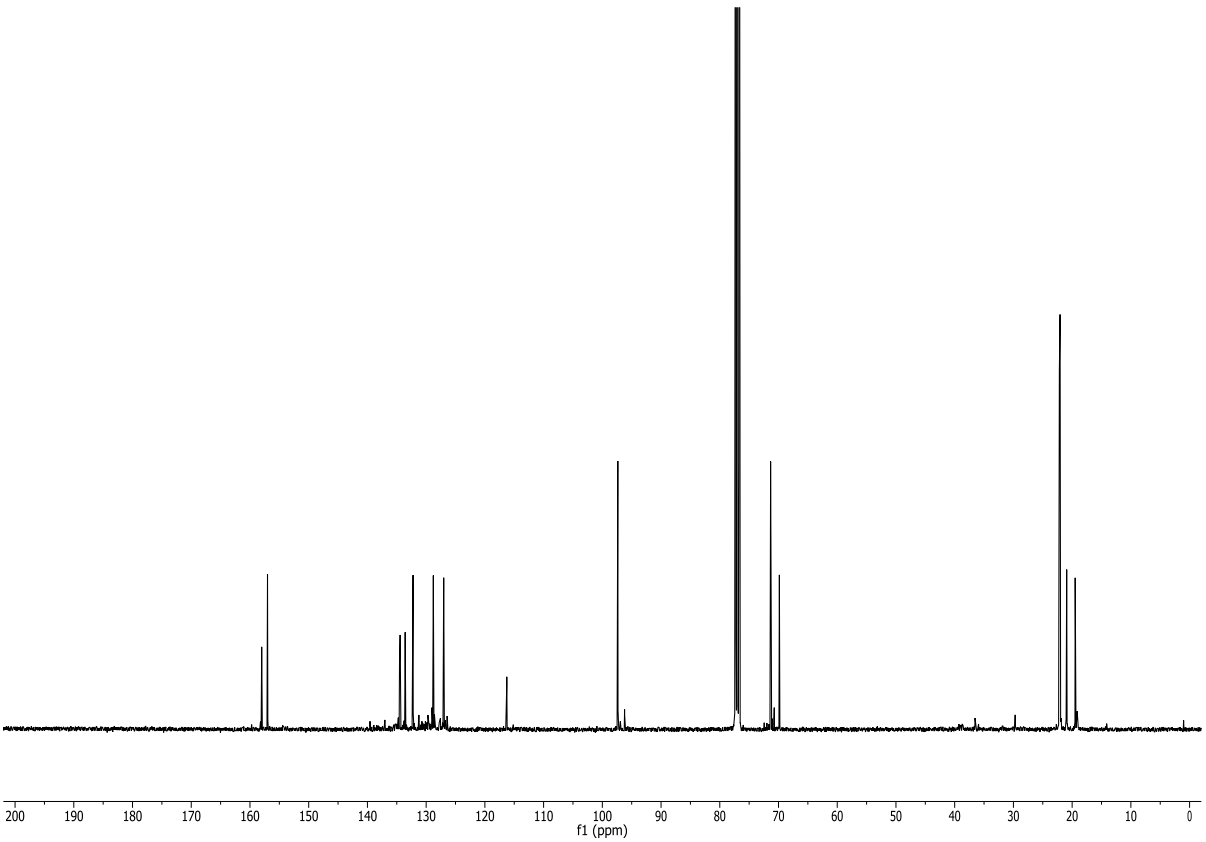
* - Residual 1,3,5-triethoxybenzene starting material present in the ^{1}H NMR at 6.08, 3.99 and 1.40 ppm and ^{13}C NMR at 160.7, 93.8, 63.4 and 14.8 ppm.

2,4,6-triisopropoxy-2',5'-dimethyl-1,1'-biphenyl, **3j**

^{1}H NMR (400 MHz, $CDCl_3$)

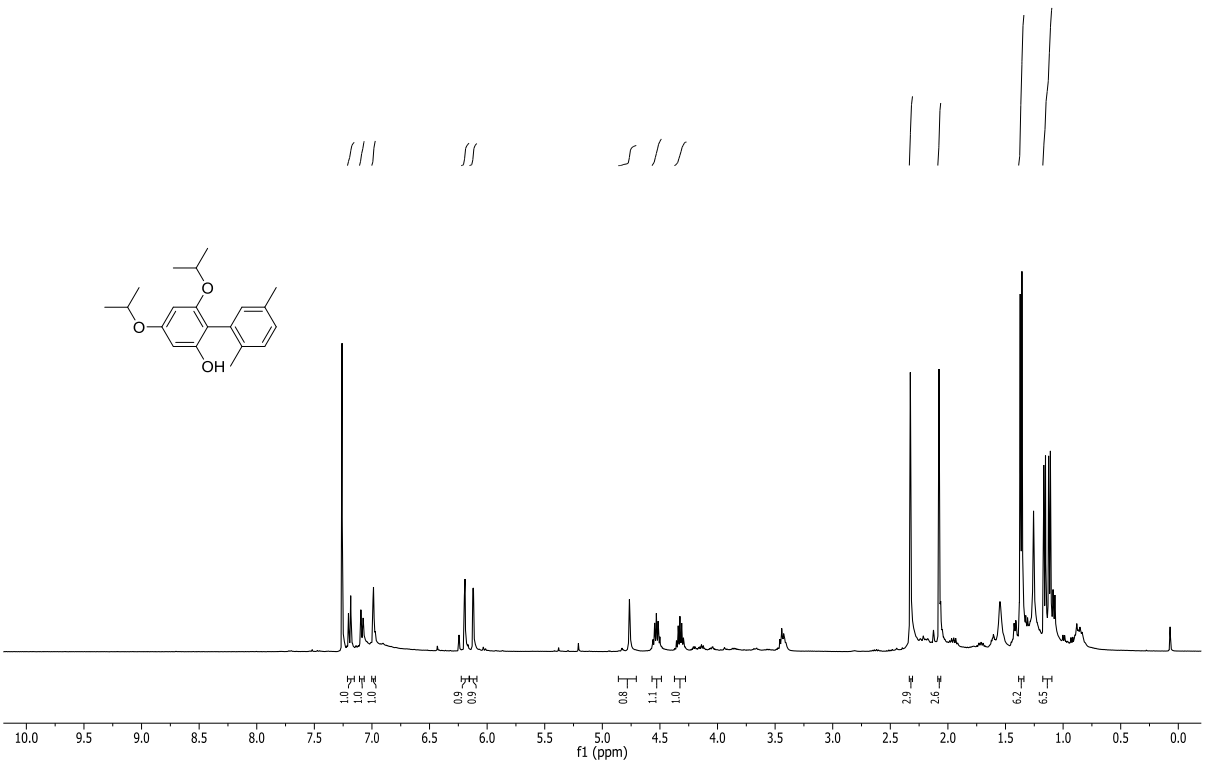


^{13}C NMR (101 MHz, $CDCl_3$)

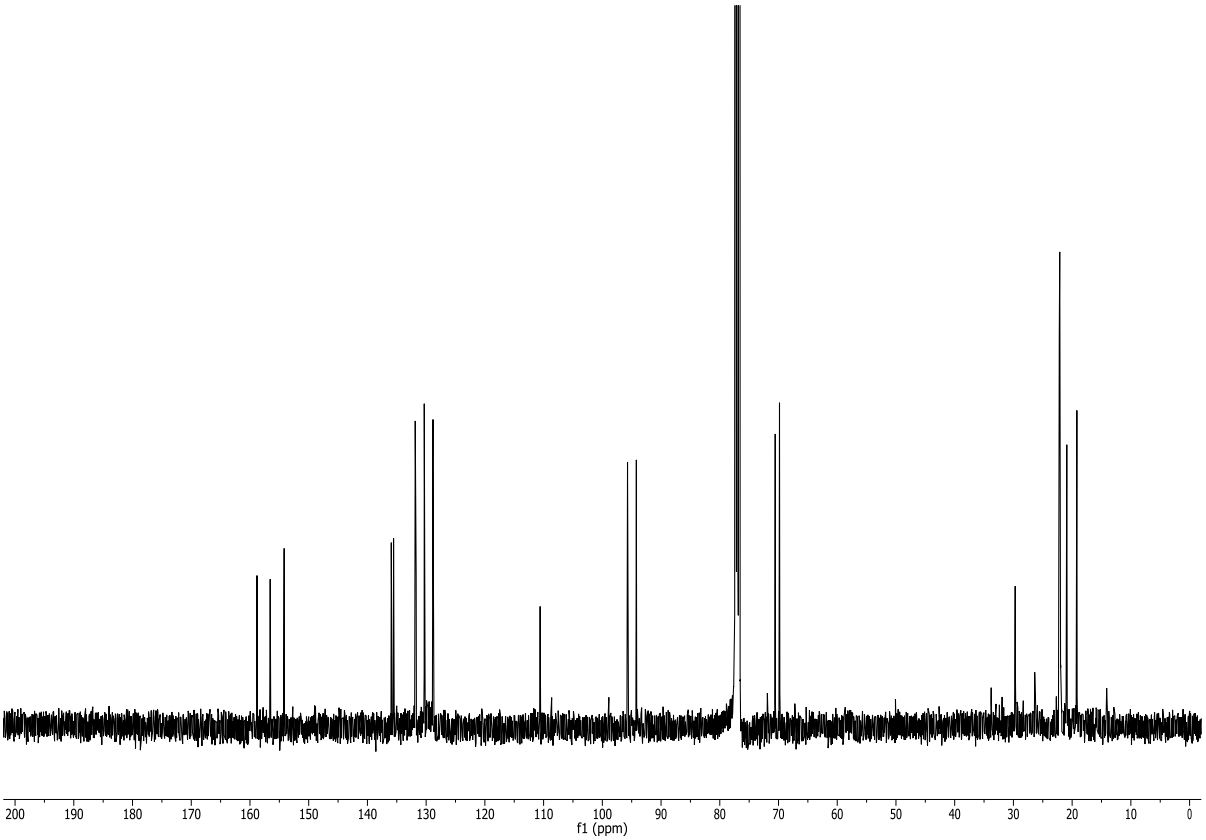


2,4,6-diisopropoxy-2',5'-dimethyl-1,1'-biphen-2-ol, **3j'**

^{1}H NMR (400 MHz, $CDCl_3$)

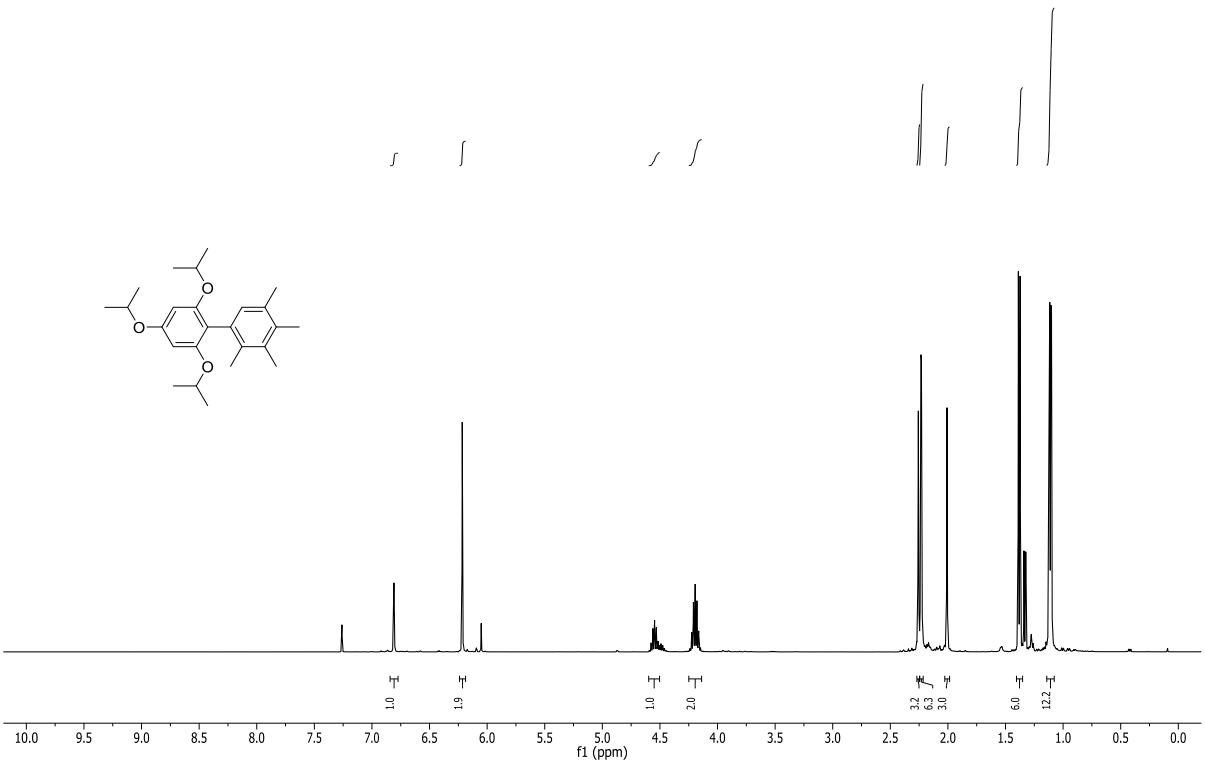


^{13}C NMR (101 MHz, $CDCl_3$)

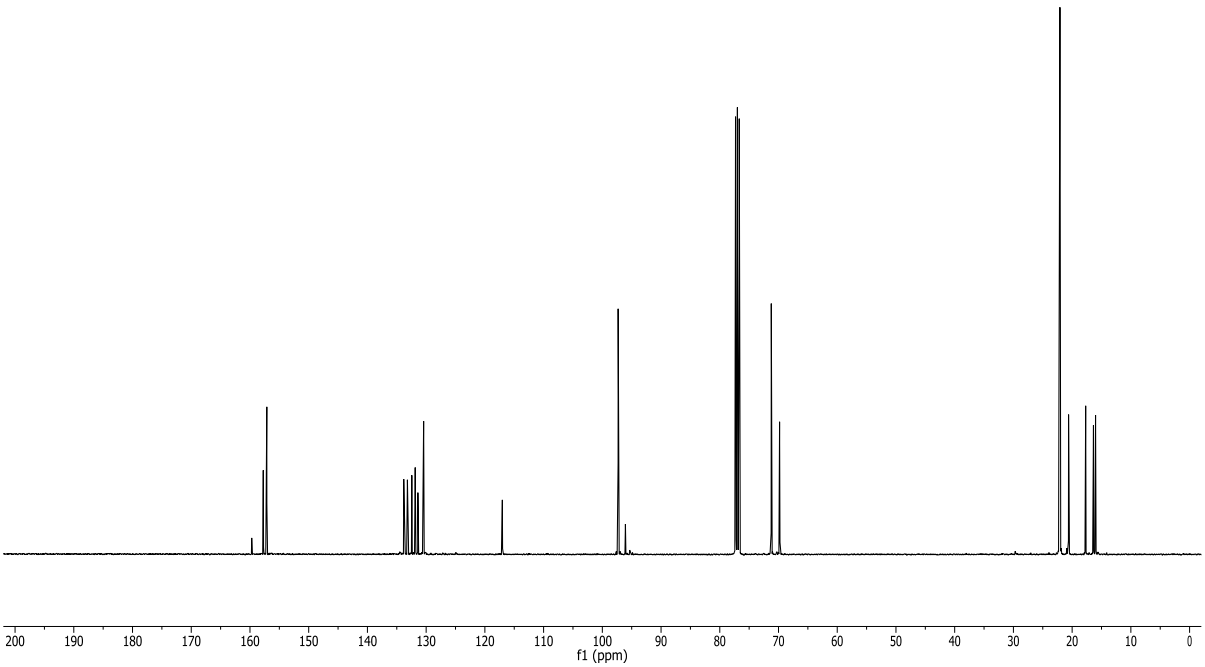


2,4,6-triisopropoxy-2',3',4',5'-dimethyl-1,1'-biphenyl, **3k**

^{1}H NMR (400 MHz, $CDCl_3$)

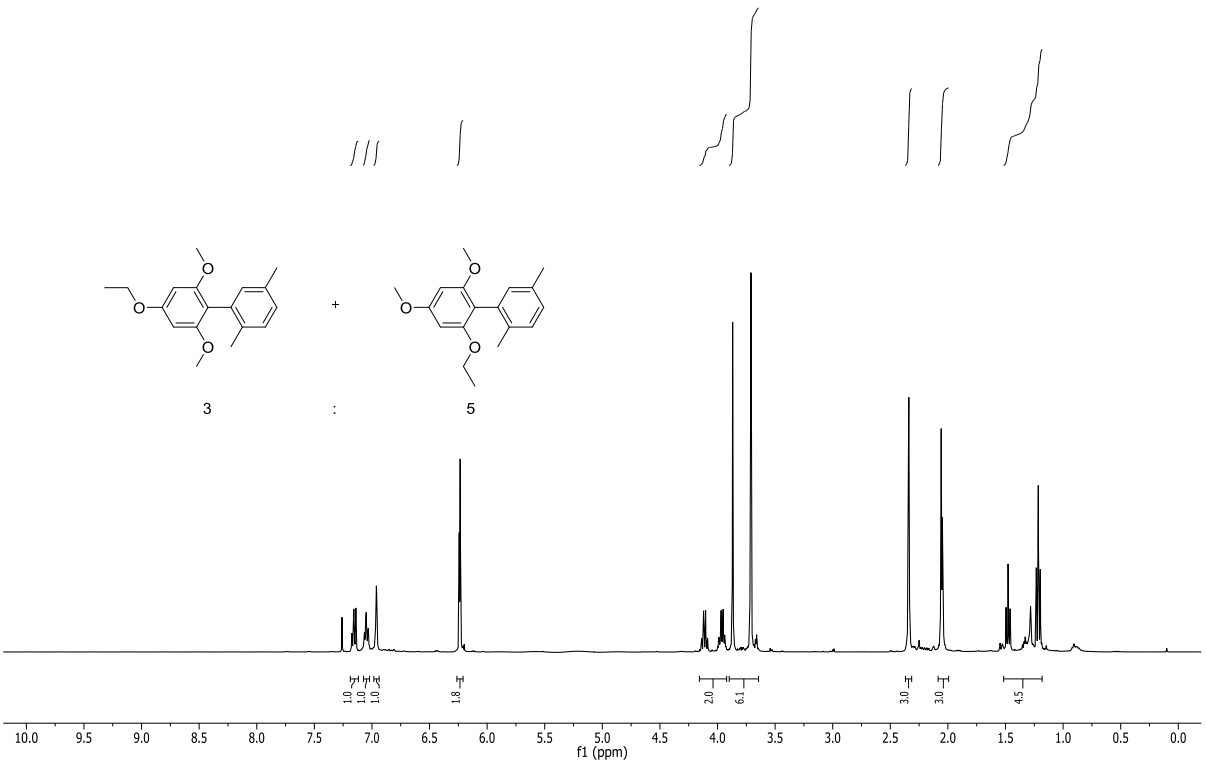


^{13}C NMR (101 MHz, $CDCl_3$)

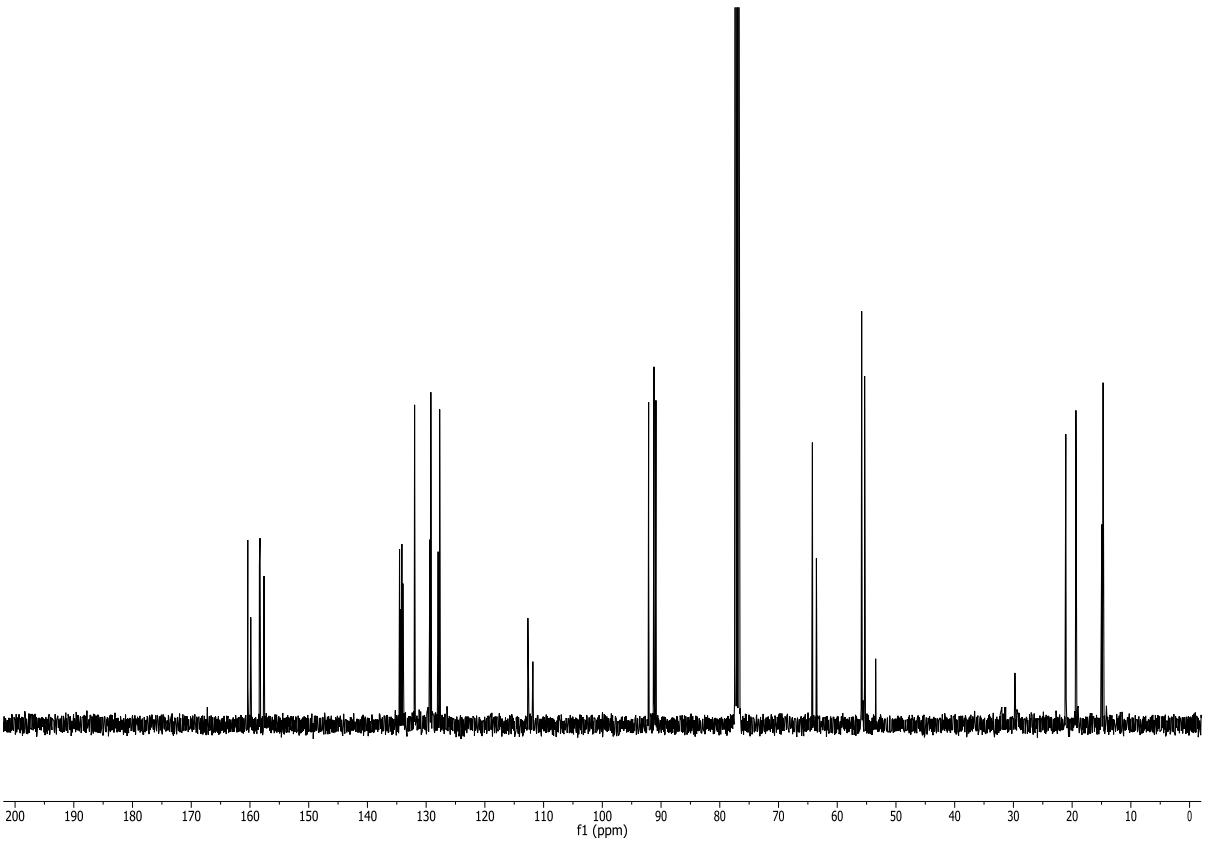


2-ethoxy-4,6-dimethoxy-2',5'-dimethyl-1,1'-biphenyl and 4-ethoxy-2,6-dimethoxy-2',5'-dimethyl-1,1'-biphenyl, **3m**

^{1}H NMR (400 MHz, $CDCl_3$)

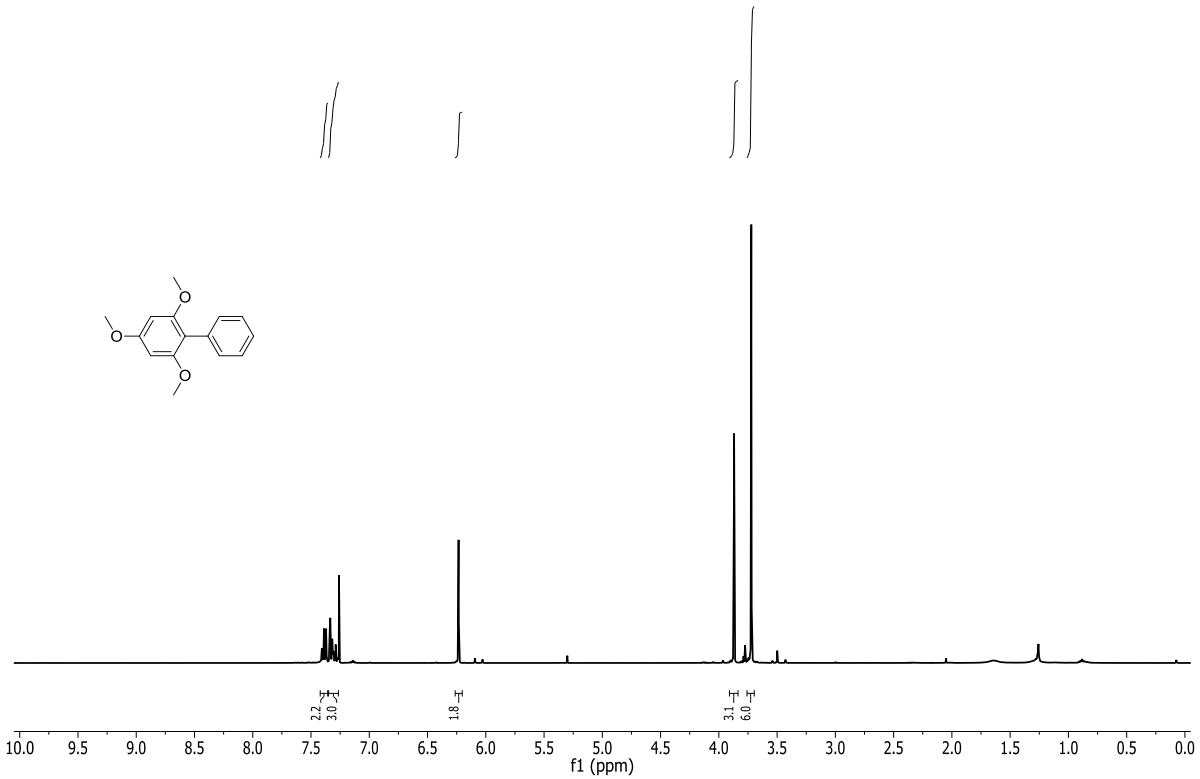


^{13}C NMR (101 MHz, $CDCl_3$)

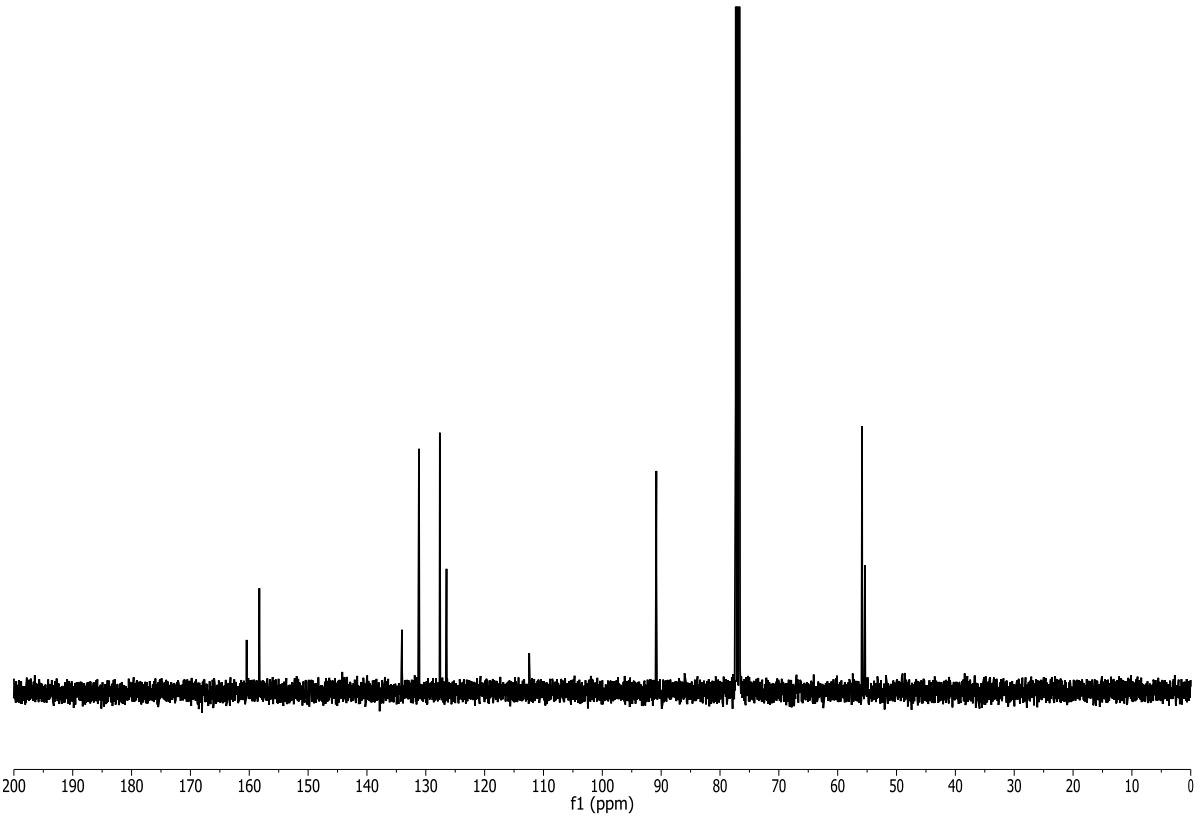


2,4,6-trimethoxy-1,1'-biphenyl, **3n**

^{1}H NMR (400 MHz, $CDCl_3$)

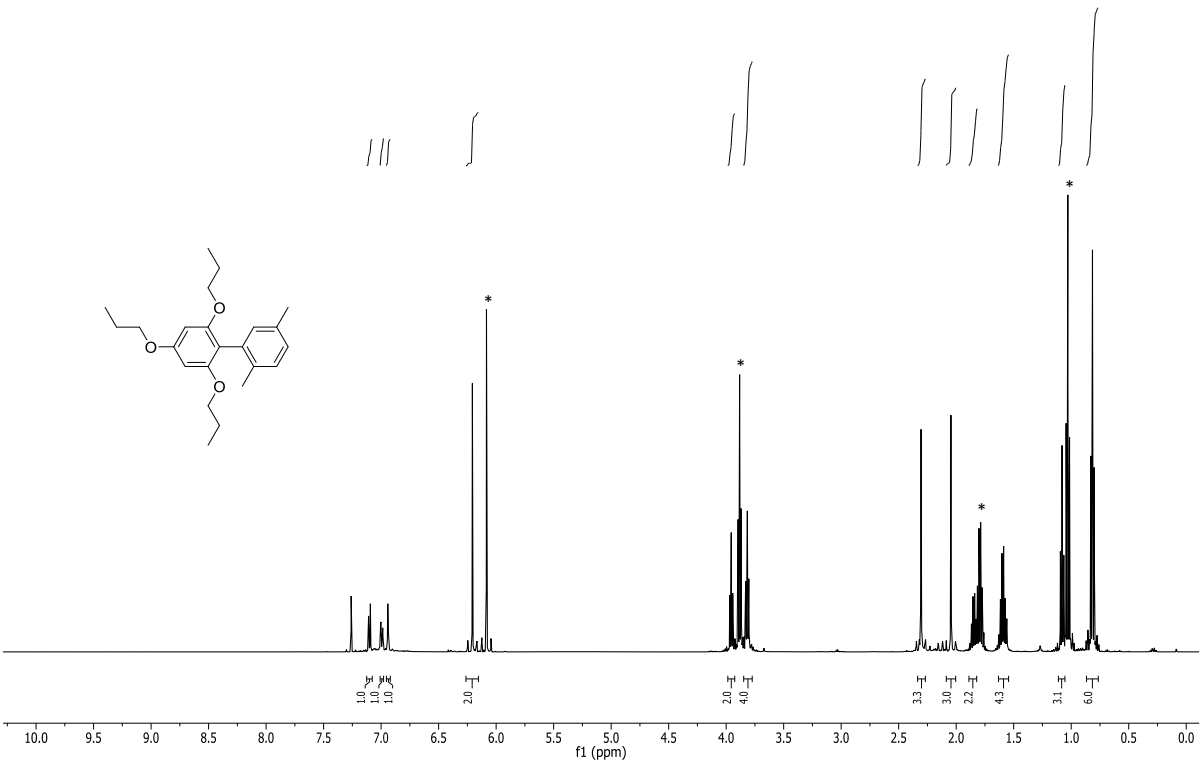


^{13}C NMR (101 MHz, $CDCl_3$)

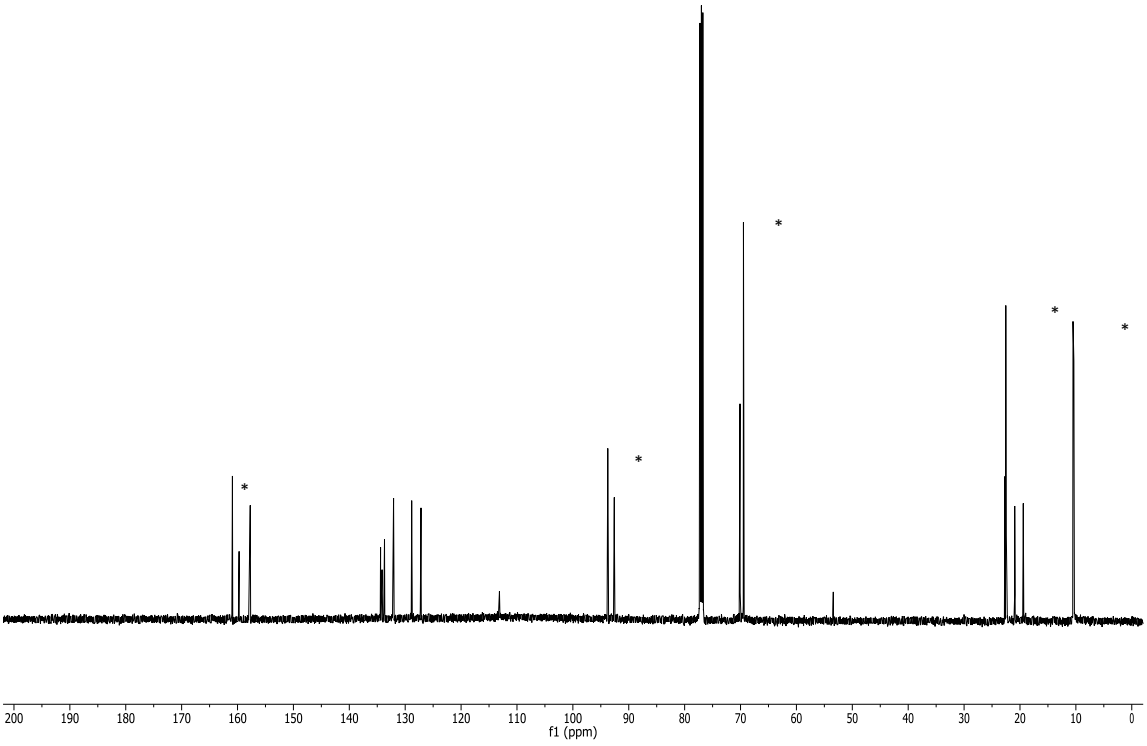


2,4,6-tripropoxy-2',5'-dimethyl-1,1'-biphenyl, **3o**

^{1}H NMR (500 MHz, $CDCl_3$)



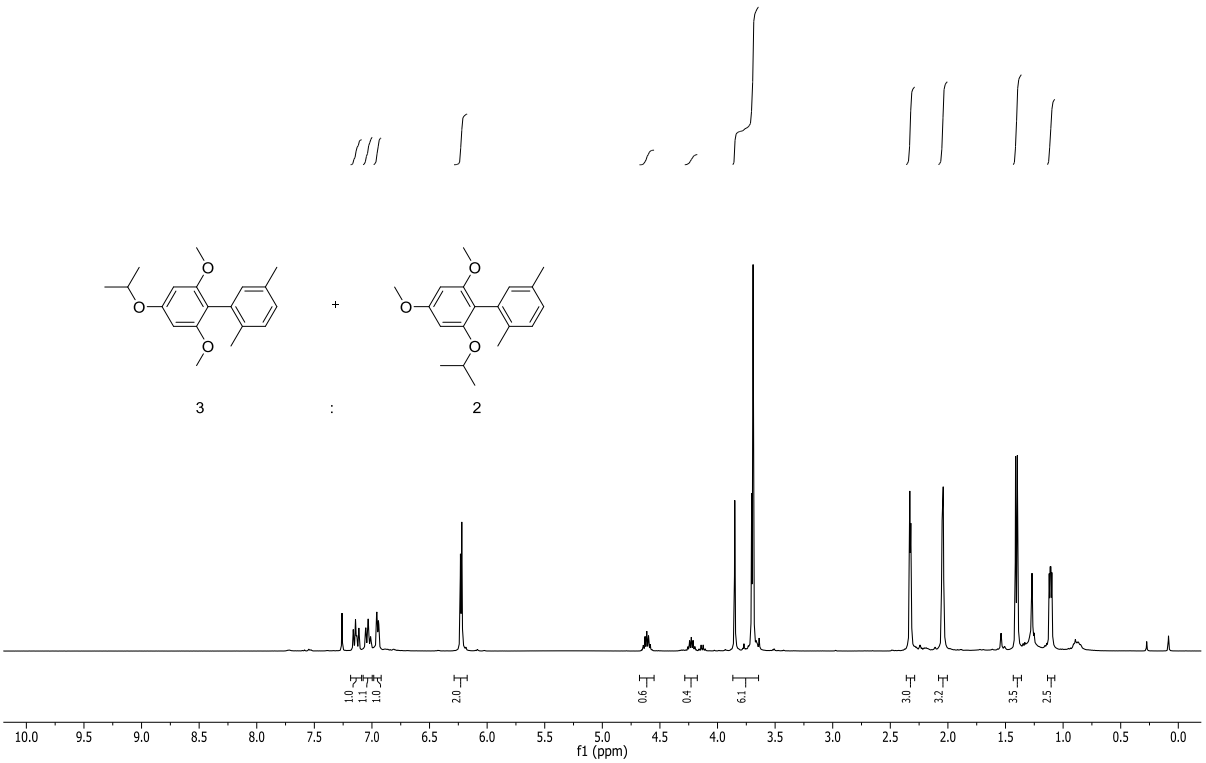
^{13}C NMR (126 MHz, $CDCl_3$)



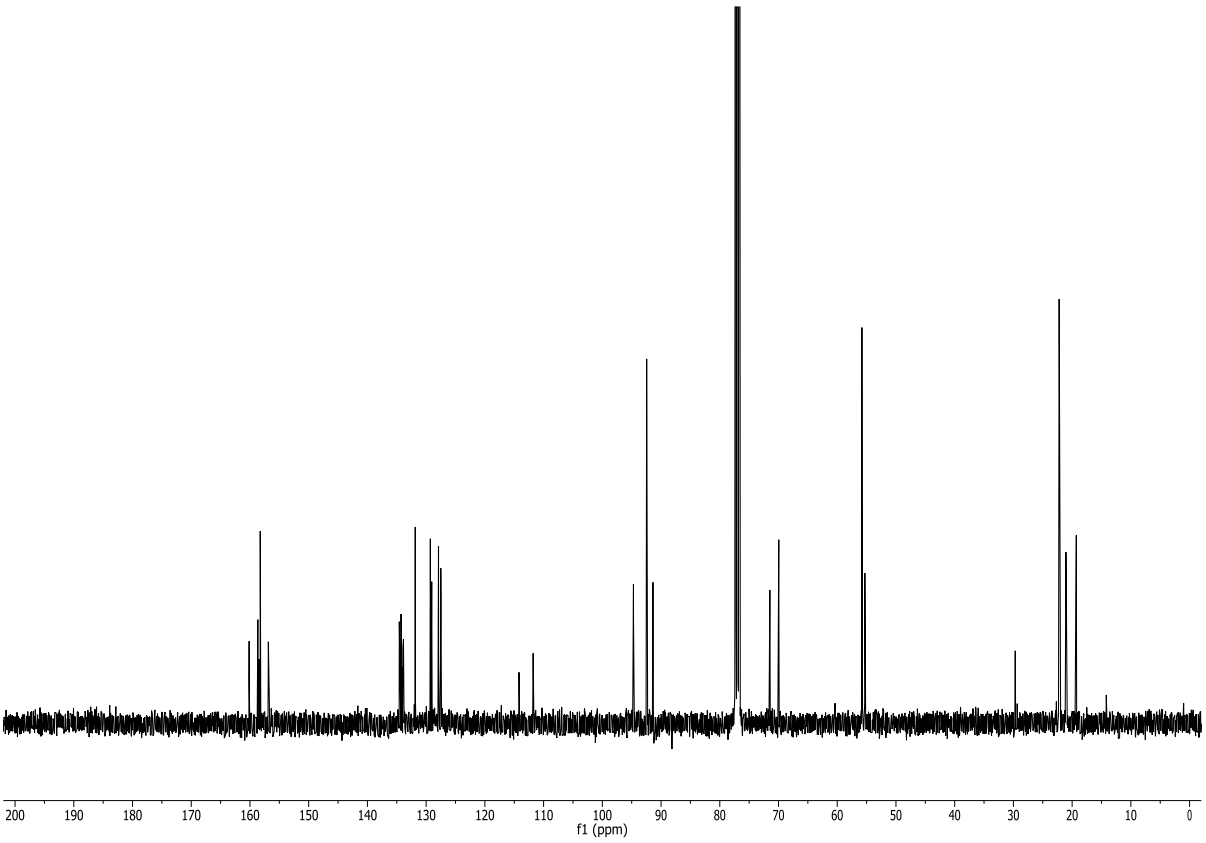
* - Residual 1,3,5-tripropoxybenzene starting material present in the ^{1}H NMR at 6.08, 3.88, 1.79 and 1.03 ppm and ^{13}C NMR at 160.9, 93.8, 69.5, 22.6 and 10.5. ppm.

2-isopropoxy-4,6-dimethoxy-2',5'-dimethyl-1,1'-biphenyl and 4-isopropoxy-2,6-dimethoxy-2',5'-dimethyl-1,1'-biphenyl, **3p**

^{1}H NMR (400 MHz, $CDCl_3$)

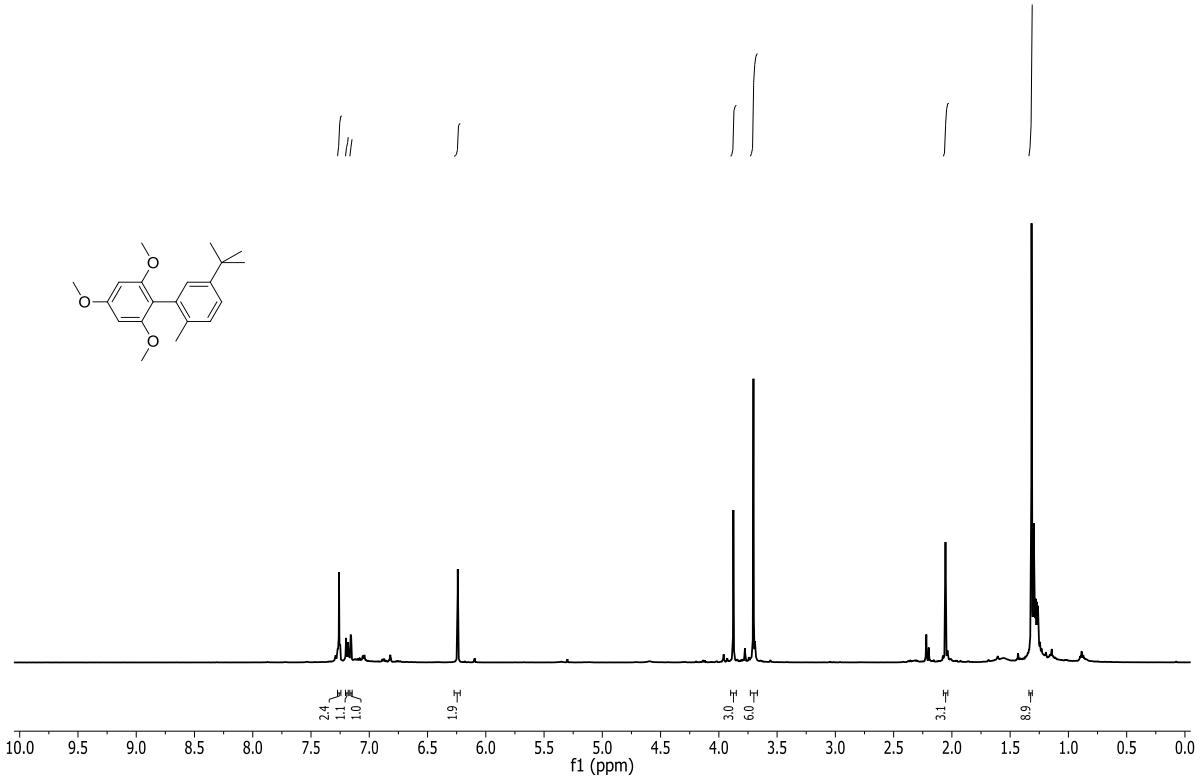


^{13}C NMR (101 MHz, $CDCl_3$)

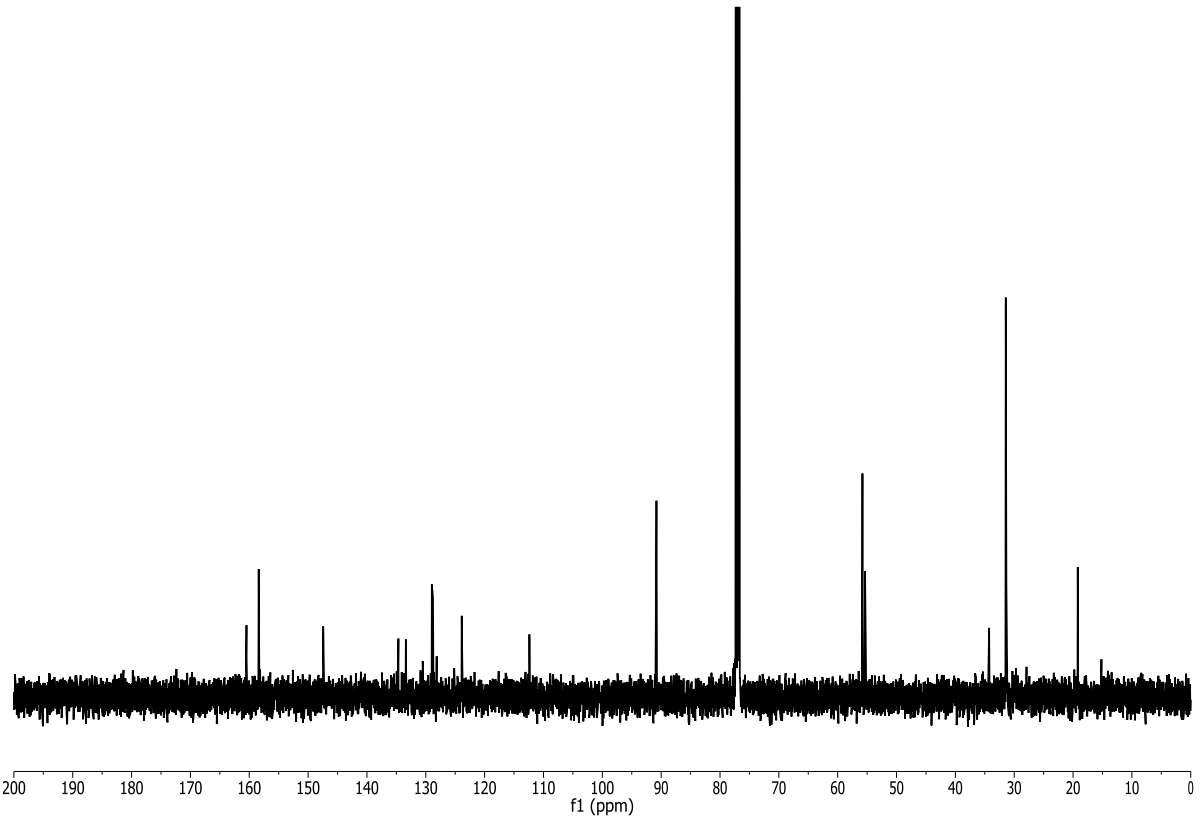


2,4,6-trimethoxy-2'-methyl-4'-*tert*-butyl-1,1'-biphenyl, **3q**

^{1}H NMR (500 MHz, $CDCl_3$)

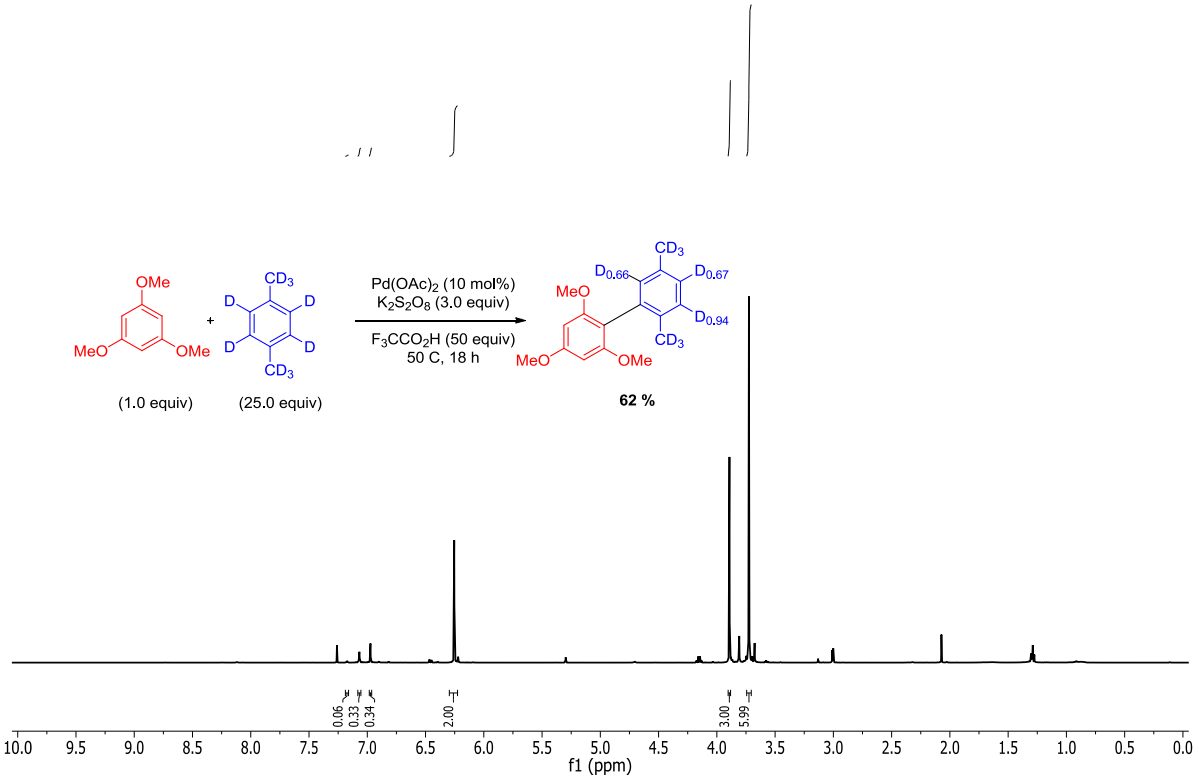


^{13}C NMR (126 MHz, $CDCl_3$)

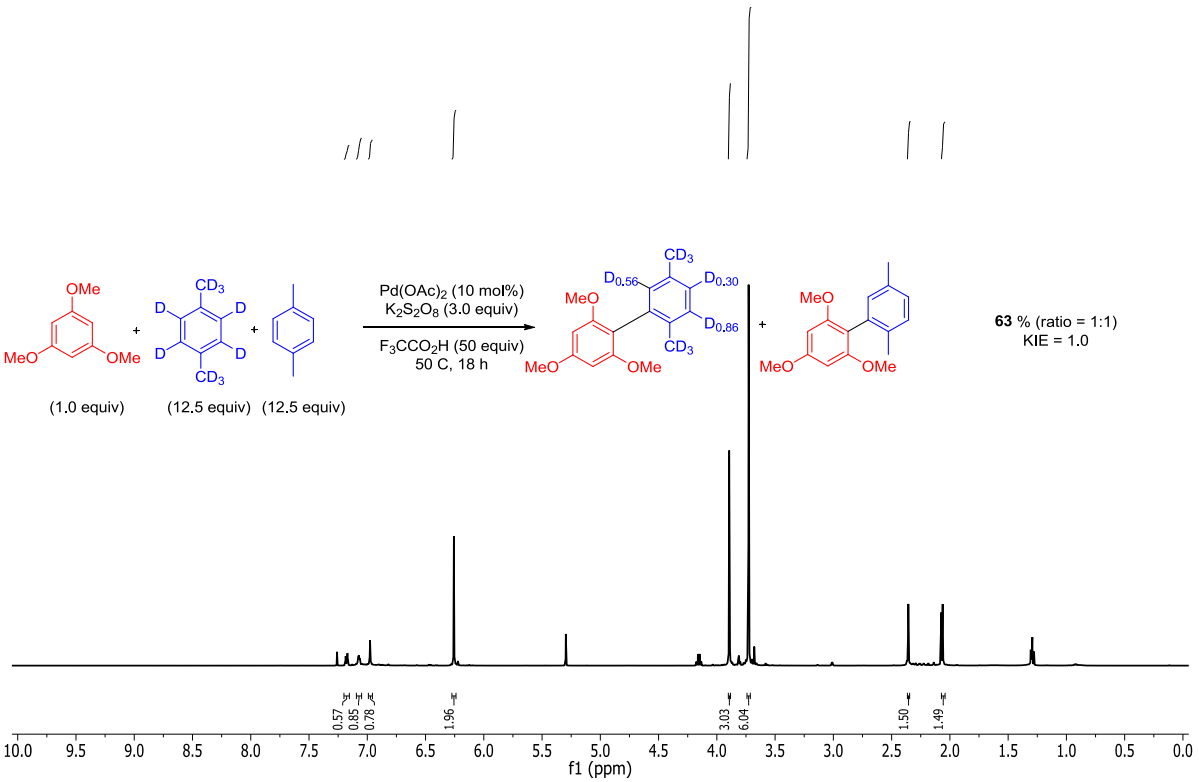


5 Deuterium Kinetic Isotope Experiments

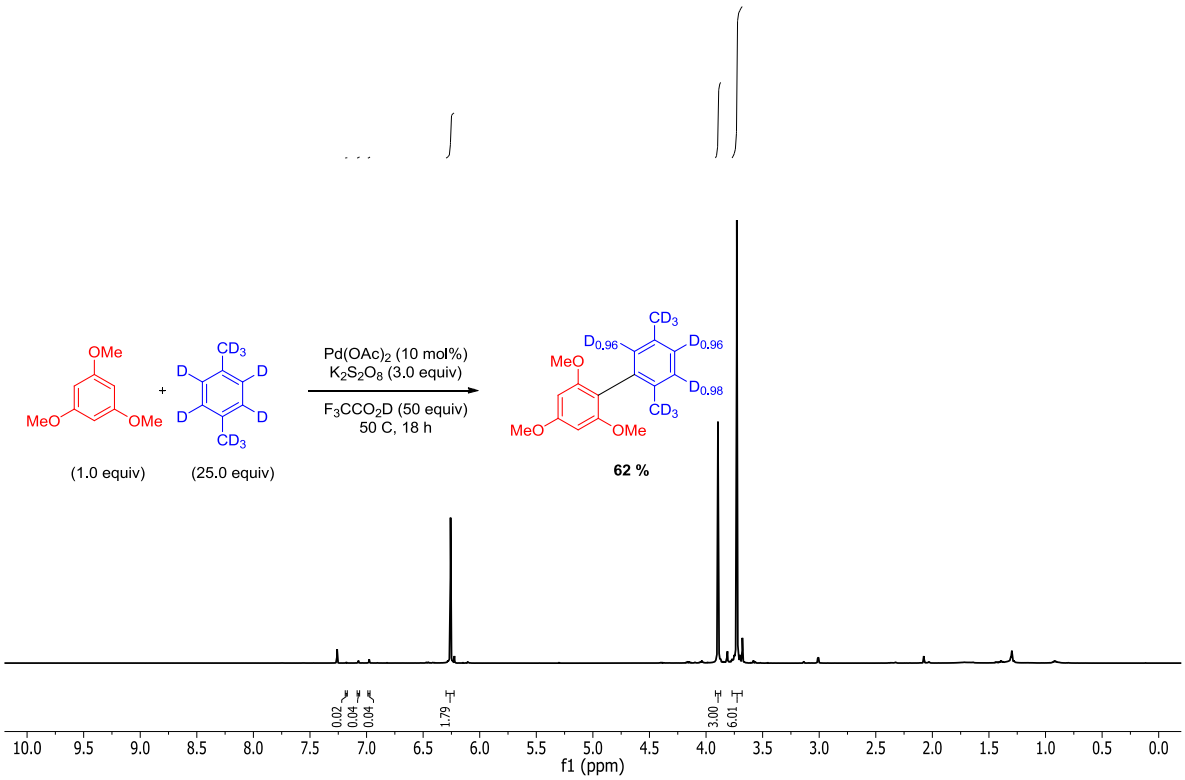
Experiment 1 – Reaction of **1a** with D_{10}-**2a** under the benchmark conditions.



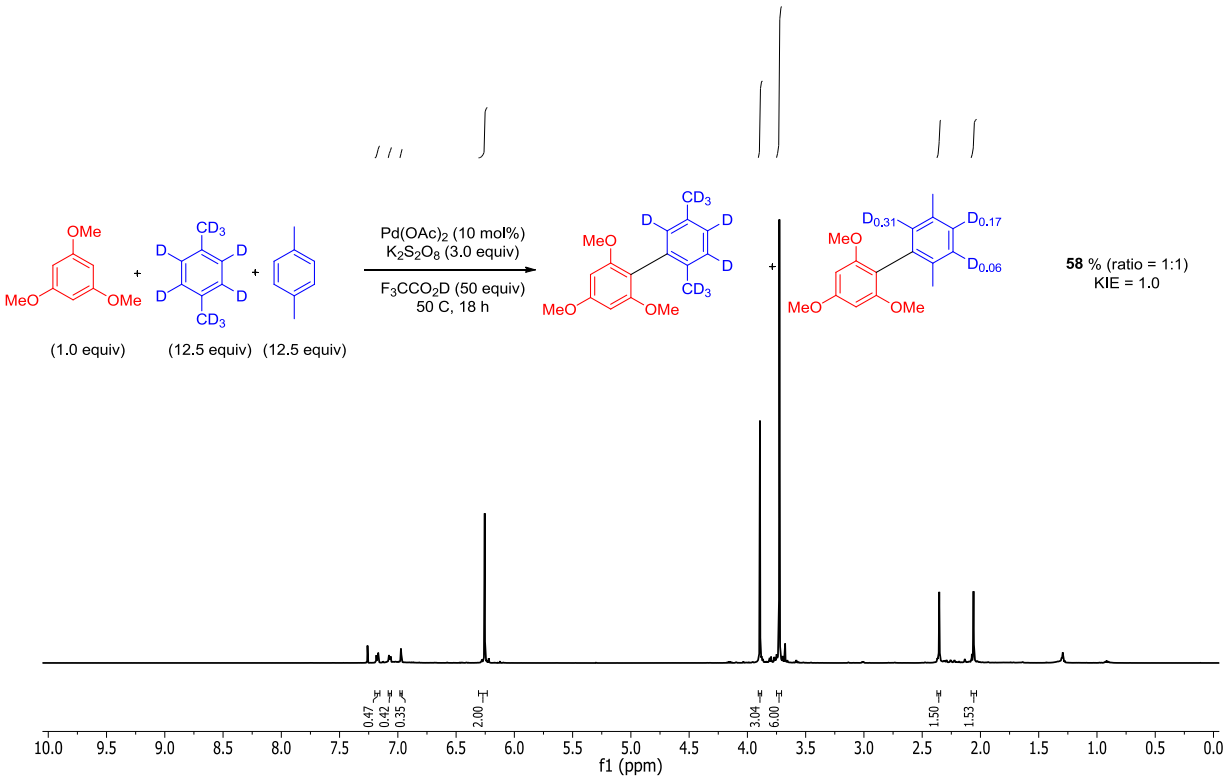
Experiment 2 – Reaction of **1a** with **2a**:D_{10}-**2a** (1:1) under the benchmark conditions.



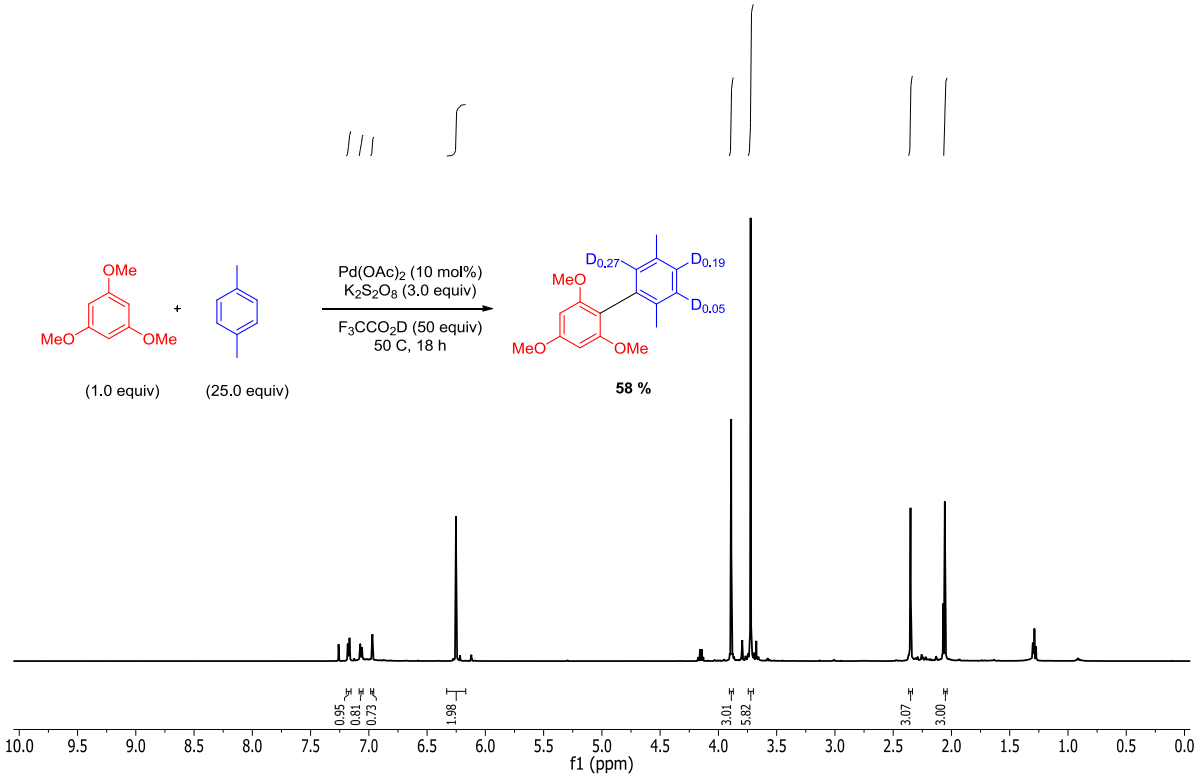
Experiment 3 – Reaction of **1a** with D_{10}-**2a** under the benchmark conditions with deuteriotrifluoroacetic acid.



Experiment 4 – Reaction of **1a** with **2a**:D_{10}-**2a** under the benchmark conditions with deuteriotrifluoroacetic acid.



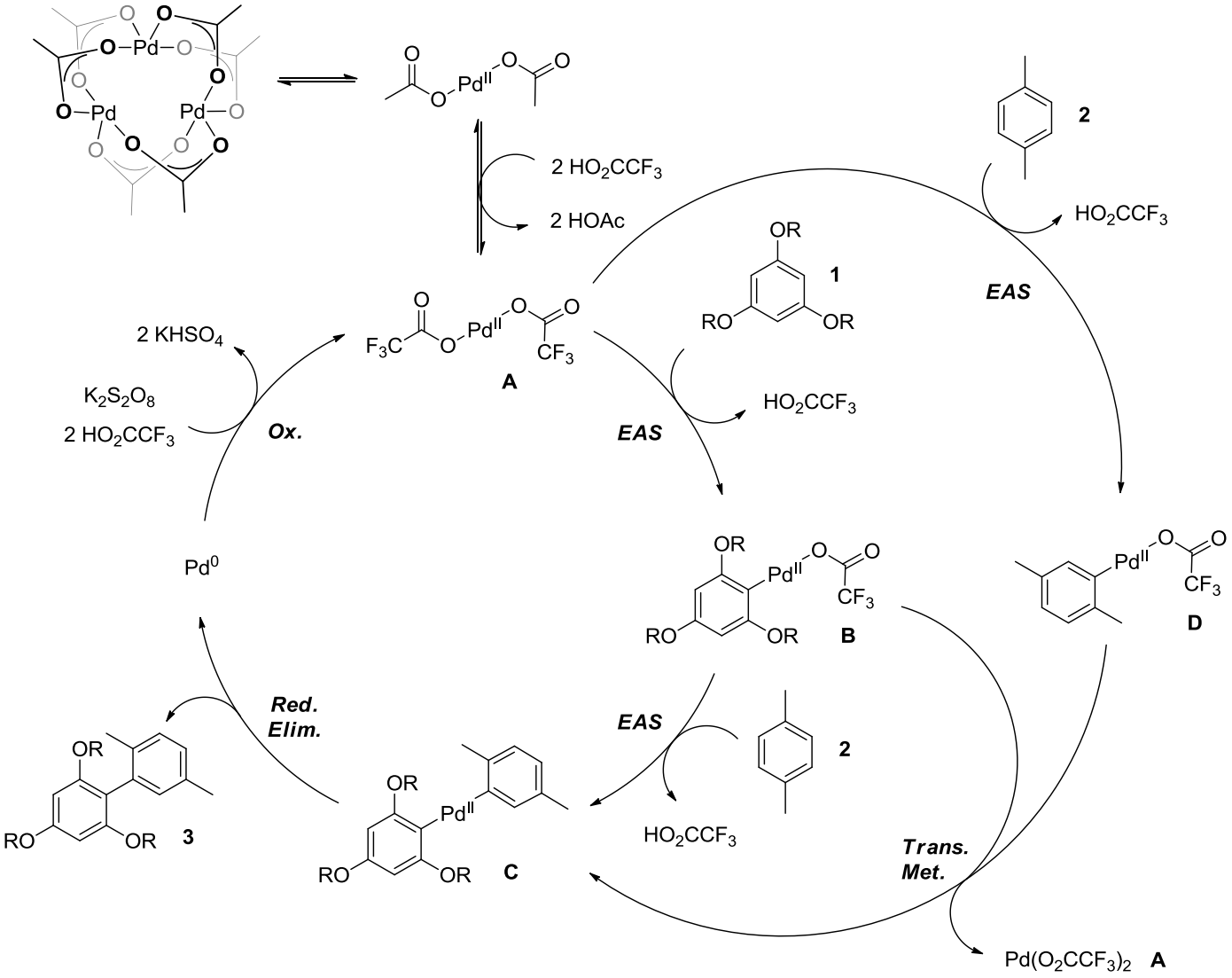
Experiment 5 – Deuterium incorporation control; benchmark conditions with deuteriotrifluoroacetic acid.



6 Plausible Mechanisms for the CDC of **1** and **2**

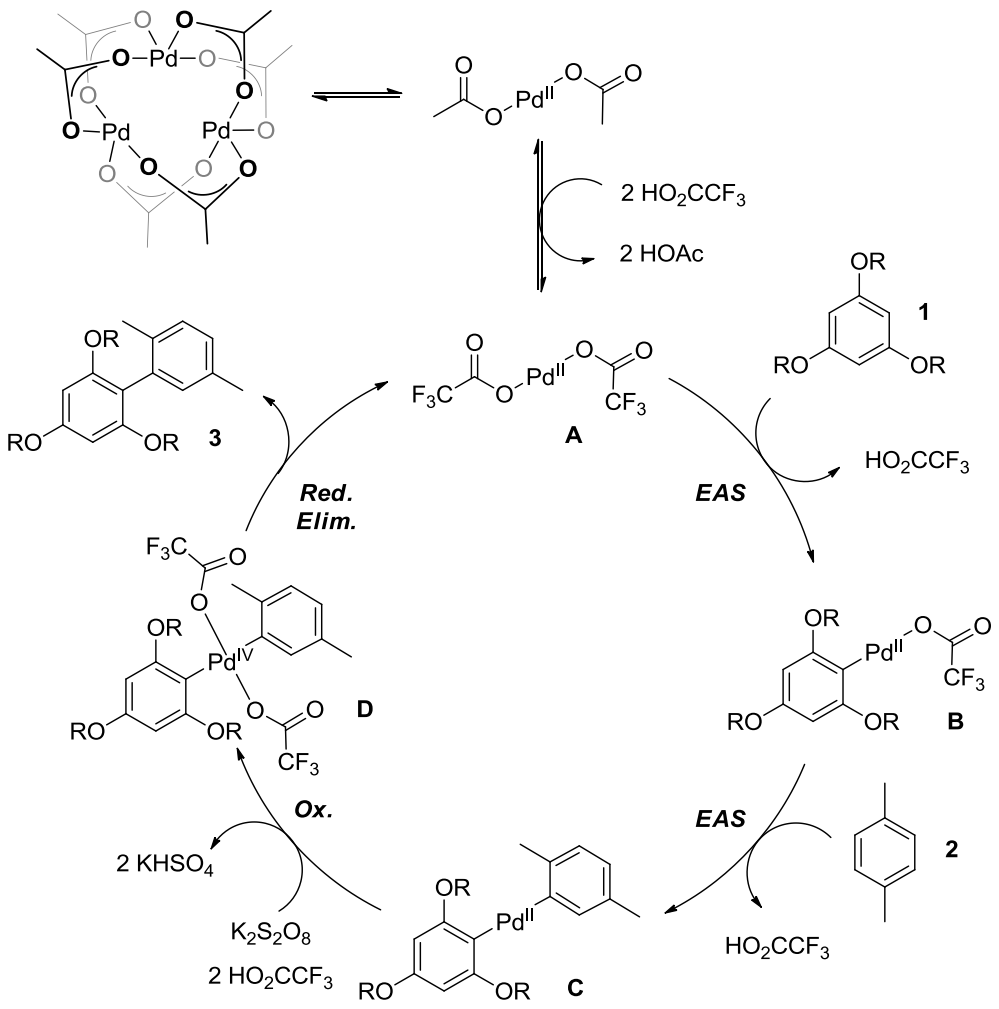
6.1 Palladium(II/0) Cycles

The formation of complex **C** could feasibly occur via sequential C-H palladations of the two arene components (**A** $\rightarrow$**B**$\rightarrow$**C**) or via two different palladations followed by a palladium(II)/palladium(II) transmetallation (2**A**$\rightarrow$**B**+**D**$\rightarrow$**C**+**A**).

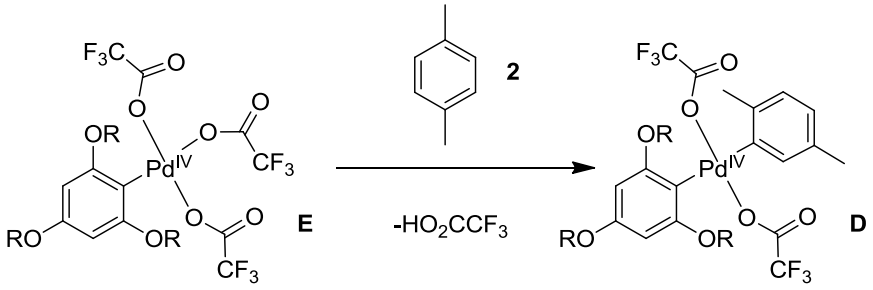


6.2 Palladium(II/IV) Cycles

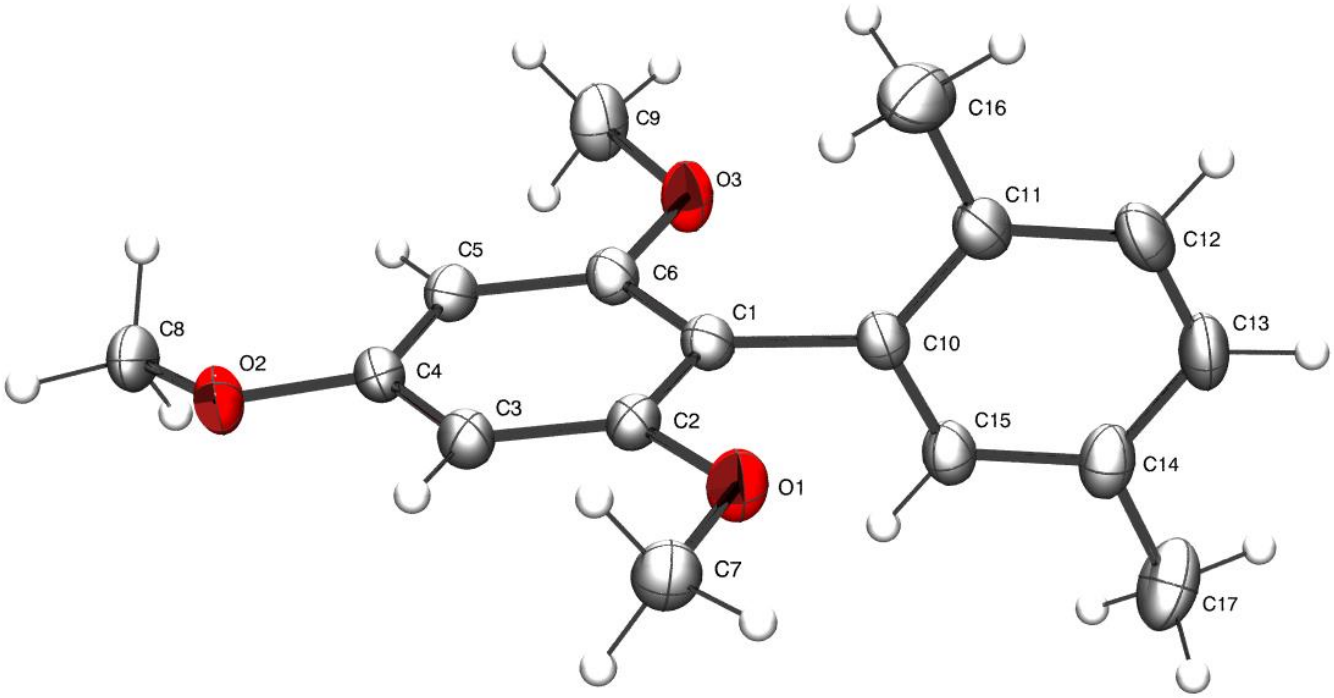
After the formation of complex **C** it is possible that oxidation of the palladium(II) centre could occur generating the palladium(IV) complex **D** which would have a high propensity for reductive elimination.



An alternative route to the formation of complex **D** is *via* an intermediate palladium(IV) species such as **E**, although there is less precedent for this class of palladation.



7 Crystal Structure of **3a**



Slow evaporation of a solution of 3a in EtOAc provided crystals suitable for X-ray crystallographic analysis. X-ray data for 2,4,6-trimethoxy-2',5'-dimethyl-1,1'-biphenyl: $C_{17}H_{20}O_3$ M_w = 272.33; T = 150(2) K; λ = 1.54178 Å; Triclinic; P1 space group; a 8.1003(2) Å = b = 9.2891(2) Å c = 10.3849(2) Å; α = 74.6760(10)°, β = 77.4230(10)°, γ = 79.3020(10)°; V = 728.70(3) $Å^3$; Z = 2; D = 1.241 Mg/m^3; size = 0.19 x 0.18 x 0.15 mm^3; R = 0.0547, wR = 0.1788; GoF = 1.093.

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8 References

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