Trienamines derived from 5-substituted furfurals: remote ε-functionalization of 2,4-dienals

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Supporting Information

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1. General Methods

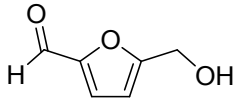
All solvents were freshly dried and distilled before use. All reactions were performed in flame dried glassware under argon atmosphere otherwise notice. Commercially available reagents were used as received without further purification otherwise notice. 3,3'-bis(2,4,6-triisopropylphenyl)-2,2'-binaphtholate (*(R)*-TRIP) was kindly provided by Prof. Dr. Benjamin List.

Flash chromatography was carried out on silica gel 60M purchased from MN (Ref. 815381). Reaction mixtures were analyzed by TLC using ALUGRAM SIL G/UV254 from MN (Ref. 818133, silica gel 60), and visualization by UV and phosphomolybdic acid stain.

NMR spectra were recorded at room temperature in a Bruker AMX 300 or Bruker AMX 400 using $CDCl_3$, D_2O or DMSO-d_6 as solvents and $(CH_3)_4Si(^1H)$ as internal standard. All coupling constants are expressed in Hz. Electrospray ionization (ESI) mass spectra were recorded in a mass spectrometer (Micromass Quattro Micro API, Waters, Ireland) with a Triple Quadrupole (TQ) and with an electrospray ion source operating in positive mode. Elemental analysis was performed in a Flash 2000 CHNS-O analyzer (ThermoScientific, UK).

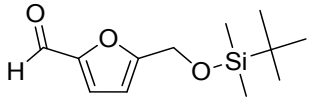
HPLC analysis was performed on a VWR Hitachi apparatus with a diode array detector L-2455 coupled to a pump L-2130 and using a KROMASIL 100 SIL 5.0 column, manual injector with 20 µL loop. Mobile phase gradient from 100:0 to 98:2 in 30 min n-hexane/2-propanol, flow 1 mL/min.

2. Synthesis of furfurals



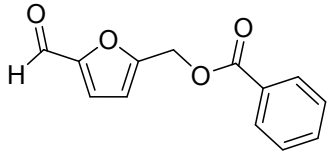
5-(Hydroxymethyl)furfural, HMF[4], 4

To a round-bottom flask D-fructose (2 g, 11.1 mmol), tetraethylamonium bromide (18 mL) and water (2 mL) were added and the mixture and was allowed to stir at 80ºC until a homogeneous solution is obtained (around 15 min). Then Amberlyst-15-powder (200 mg, 10% w/w) was added and the mixture and was allowed to stir for 10 min, from 80ºC to 100ºC, followed by an additional 15 min at 100ºC. Isolation of HMF was performed by dissolution of the reaction mixture in ethanol followed by precipitation with ethyl acetate, filtration, and removal of ammonium salt traces by filtration with silica to yield the product (1.4 g, quantitative yield) as a dark orange oil that crystalizes in the freezer (0ºC). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.59 (s, 1H), 4.71 (s, 2H), 6.51 (d, *J* = 3.5 Hz, 1H), 7.21 (d, *J* = 3.5 Hz, 1H), 9.58 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 57.7, 110.1, 123.1, 152.4, 160.8, 177.9.



5-(((tert-Butyldimethylsilyl)oxy)methyl)furan-2-carbaldehyde[1], 1

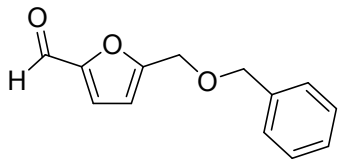
To a solution of 5-hydroxymethylfurfural (HMF) (1.6 g, 12.7 mmol) in DMF (3.2 mL) were added imidazole (2.2 g, 31.7 mmol, 2.5 equiv.) and *tert*-butyldimethylsilyl chloride (2.3 g, 15.2 mmol, 1.2 equiv.). The solution was stirred for 22 h. The silylated compound was extracted with hexane (5 x 20 mL). The collected organic layers were washed with brine, dried over Na_2SO_4, and the solvent removed to give the crude product that was distilled (100 ºC/0.8 mbar) giving the product (1.9 g, 63 % yield) as a light yellow liquid that solidifies in the freezer (0 ºC). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.08 (s, 6H), 0.89 (s, 9H), 4.71 (s, 2H), 6.44 (d, *J* = 3.52 Hz, 1H), 7.18 (d, *J* = 3.54 Hz, 1H), 9.56 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -5.3, 18.4, 25.8, 58.7, 109.5, 122.6, 152.3, 161.5, 177.6.



(5-Formylfuran-2-yl)methyl benzoate[2], 2

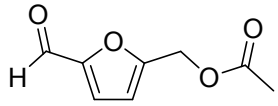
To a flame dried round-bottom flask, HMF (1.0 g, 7.9 mmol) and anhydrous pyridine (4 mL) were added followed by benzoyl chloride (1 mL, 8.7 mmol, 1.1 equiv.). The reaction mixture was allowed to stir at reflux for 1.5 h under argon atmosphere. The mixture was quenched with

cold water (50 mL), acidified with HCl 1M and extracted with Et_2O. The combined organic layers were dried over MgSO4, filtered and the solvent removed to give the crude product that was recrystallized from Et_2O/hexane as a pale orange solid (0.86 g, 47% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.38 (s, 2H), 6.68 (d, *J* = 3.55 Hz, 1H), 7.24 (d, *J* = 3.56 Hz, 1H), 7.46 (t, *J* = 7.7 Hz, 2H), 7.58 (tt, *J* = 7.45, 1.30 Hz, 1H), 8.07 (m, 2H), 9.65 (s, 1H).



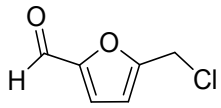
5-((Benzyloxy)methyl)furan-2-carbaldehyde[3], 3

Benzyl bromide (3.8 g, 22.2 mmol) and silver oxide (2.6 g, 11.1 mmol) were successively added to a stirred solution of HMF (1.4 g, 11.1 mmol) dissolved in anhydrous DMF (15 mL). The mixture was stirred for 50 h at RT. The solution was evaporated under reduced pressure and the residue was purified by column chromatography (silica; hexane-EtOAc, 1:1) to give the desired product (1.2 g, 50 % yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.87 (t, *J* = 6.9 Hz, 3H), 1.27-1.31 (m, 4H), 1.63 (quint, *J* = 7.4 Hz, 2H), 2.35 (t, *J* = 7.6, 2H), 5.12 (s, 2H), 6.58 (d, *J* = 3.55 Hz, 1H), 7.21 (d, *J* = 3.55 Hz, 1H), 9.63 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 64.2, 73.0, 111.4, 122.0, 128.0, 128.1, 128.6, 137.3, 152.7, 158.5, 177.8.



(5-Formylfuran-2-yl)methyl acetate[3], 5

To a flame dried round-bottom flask, HMF (3.5 g, 27.8 mmol), anhydrous MeCN (50 mL) and acetic anhydride (4.3 mL, 45.6 mmol) were added followed by catalytic amount of pyridine (0.5 mL, 6.2 mmol). The reaction mixture was allowed to stir at room temperature for 22h under argon atmosphere. The solvent was removed and the product purified by column chromatography with silica gel (hexane/ethyl acetate 8:2) to give the product (4.3 g, 93% yield) as a pale yellow oil that crystallized in the freezer (0ºC). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.11 (s, 3H), 5.12 (s, 2H), 6.58 (d, *J* = 3.55 Hz, 1H), 7.21 (d, *J* = 3.55 Hz, 1H), 9.64 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.8, 57.9, 112.7, 121.8, 153.0, 155.6, 170.5, 178.0.



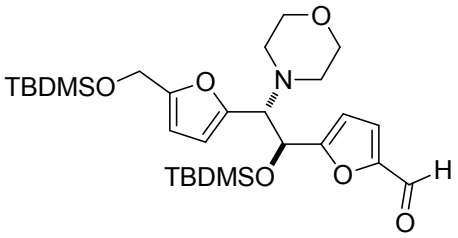
5-(Chloromethyl)furan-2-carbaldehyde[5], CMF

To a flame dried round-bottom flask, HMF (1 g, 7.9 mmol) and anhydrous $CHCl_3$ were added. Trimethylsilyl chloride (6 mL, 47.3 mmol, 6 equiv.) was added dropwise at 45 ºC and the resulting mixture stirred for 24 h at 45ºC under inert atmosphere. The mixture was then quenched with saturated aqueous solution of $NaHCO_3$ and extracted with DCM. The collected organic layers were dried over Na_2SO_4 and the solvent removed. The crude product was purified by dissolution in hot hexane and filtration through a pad of celite and activated carbon. The solvent was removed under vacuum to give the desired product (0.7 g, 61% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.59 (s, 2H), 6.57 (d, J = 3.57 Hz, 1H), 7.19 (d, J = 3.57 Hz, 1H), 9.60 (s, 1H).

3. Synthesis and characterization of 6a

5-(1-((tert-butyldimethylsilyl)oxy)-2-(5-(((tert-butyldimethylsilyl)oxy)methyl)furan-2-yl)-2-morpholinoethyl)furan-2-carbaldehyde

To a solution of **1** (90 mg, 0.375 mmol) in anhydrous acetonitrile, morpholine (1 equiv., 0.375 mmol) was added via gas-tight syringe followed by the addition of $Dy(OTf)_3$ (10 mol%) in one portion. The reaction mixture was allowed to stir at 40 ºC for 2 days. The solvent was then evaporated and the two diastereoisomers **6a-I** (R_f=0.55, 8:2 Hex/AcOEt) and **6a-II** (R_f=0.65, 8:2 Hex/AcOEt) were purified by flash chromatography using hexane/ethyl acetate.



Diastereoisomer 6a-I

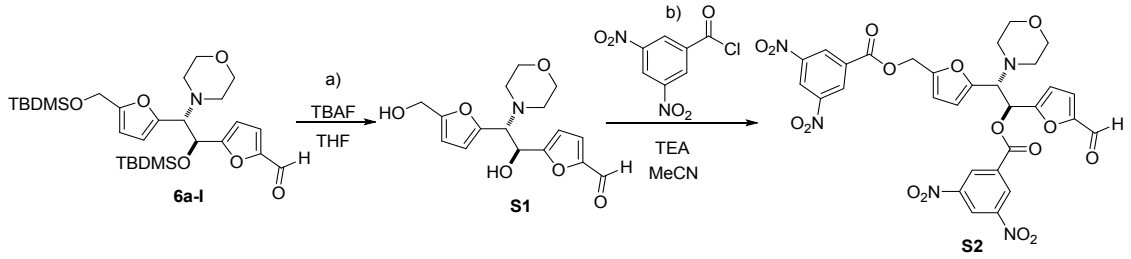
^{1}H NMR (400 MHz, $CDCl_3$) δ -0.17 (s, 3H), -0.13 (s, 3H), 0.09 (s, 3H), 0.10 (s, 3H), 0.69 (s, 9H) 0.91 (s, 9H), 2.29 (m, 2H), 2.59 (m, 2H), 3.46 (m, 4H), 3.82 (d, *J* = 9.04 Hz, 1H), 4.60 (s, 2H), 5.24 (d, *J* = 9.07 Hz, 1H), 6.18 (s, 2H), 6.44 (d, *J* = 3.53 Hz, 1H), 7.22 (d, *J* = 3.47 Hz, 1H), 9.61 (s, 1H).

6-I and 6-II ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.7, 177.6, 163.8, 162.3, 153.9, 153.8, 151.8, 151.8, 150.2, 150.1, 122.8, 122.0, 110.9, 110.1, 110.1, 109.5, 107.8, 107.6, 68.7, 68.3, 68.2, 67.5, 67.5, 67.4, 58.3, 58.2, 50.9, 50.8, 26.0, 25.9, 25.8, 25.5, 18.5, 18.5, 18.3, 18.0, -4.8, -4.9, -5.0, -5.0, -5.4, -18.7.

HRMS Calculated for $C_{28}H_{47}NO_6Si_2Na$: 572.283414 m/z, found: 572.283506 m/z.

ESI$^+$ Calculated for $[C_{28}H_{47}NO_6Si_2]^+$: 550.3020 m/z, found: 550.3015 m/z

Synthesis of the S2 crystals suitable for X-Ray analysis:



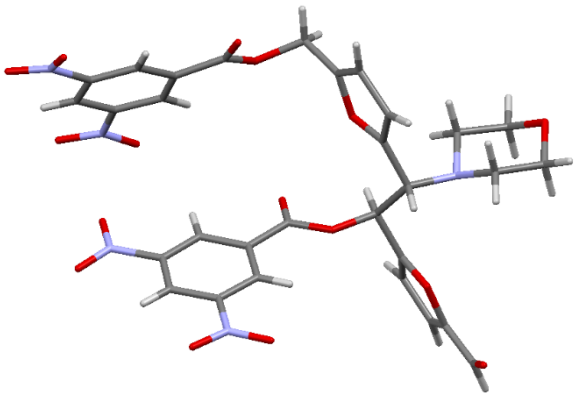
a) To a solution of **6a-I** (100 mg, 0.18 mmol) in anhydrous THF (1 mL), tetrabutylammonium fluoride ($TBAF{\cdot}3H_2O$, 4 equiv., 215 mg) was added at 0ºC and the mixture was allowed to stir for 15 min. The product was purified by chromatography column to yield the product a pale yellow oil (58 mg, 99% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.54 (m, 4H), 3.66 (m, 4H), 3.87 (d, *J* = 6.11 Hz, 1H), 4.54 (d, *J* = 5.87 Hz, 2H), 5.33 (d, *J* = 6.08 Hz, 1H), 6.14 (dd, *J* = 9.96, 2.85, 2H), 6.39 (d, *J* = 3.48 Hz, 1H), 7.13 (d, *J* = 3.50 Hz, 1H), 9.51 (s, 1H).

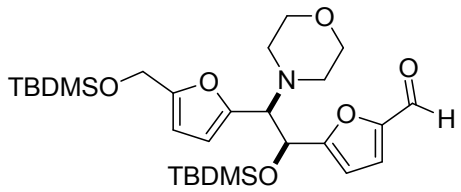
b) To a mixture of compound **S1** (58 mg, 0.18 mmol) in anhydrous MeCN (1 mL) 3,5-dinitrobenzoyl chloride (2.2 equiv.) was added and the reaction mixture was allowed to stir at room temperature (RT). After 1 h, triethylamine (2.2 equiv.) was added slowly and the reaction mixture was allowed to stir for 1 h. The product was then purified by flash chromatography to yield a yellow solid (83.6 mg, 65% yield) that was recrystallized from hexane/ethyl acetate.

X-ray Crystallographic Analysis:

Crystals of **S2** suitable for X-ray diffraction studies were mounted on a loop with protective oil. X-ray data were collected at 150K on a Bruker AXS-KAPPA APEX II diffractometer using graphite monochromated Mo-Kα radiation (λ=0.71069 Å) and operating at 50kV and 30 mA. Cell parameters were retrieved using Bruker SMART software and refined using Bruker SAINT[6] on all observed reflections. Absorption corrections were applied using SADABS[7]. Structure solution and refinement were performed using direct methods with program SIR97[8] and SHELXL97[9], both included in the package of programs WINGX-Version 1.80.05[10]. A full-matrix least-squares refinement was used for the non-hydrogen atoms with anisotropic thermal parameters. All hydrogen atoms connected to carbons were inserted in idealized positions and allowed to refine riding in the parent carbon atom.

Crystallographic data for **S2** (CCDC 1011693): $C_{30}H_{23}N_5O_{16}$, fw=709.53, monoclinic, space group $P2_1$, a=6.462(3) Å, b=21.405(2) Å, c=11.722(4) Å, β= 105.001(1) °, V =1566.1(9) $Å^3$, Z=2, T=150K, d_{calc}=1.505 $mg.m^{-3}$, μ =0.125 mm^{-1}, F(000)=732. Of 22063 reflections collected, 6354 were independent (R_{int}= 0.0725); 461 variables refined with 6354 reflections to final R indices $R_1(I > 2\sigma(I))$=0.0544, $wR_2(I>2\sigma(I))$=0.1136, R_1(all data)=0.0988, wR_2(all data)=0.1284, GOF= 0.967.





Diastereoisomer 6a-II

^{1}H NMR (400 MHz, $CDCl_3$) δ -0.13 (s, 3H), 0.07 (s, 9H), 0.86 (s, 9H) 0.89 (s, 9H), 2.50 (m, 2H), 2.70 (m, 2H), 3.66 (m, 4H), 3.96 (d, *J* = 8.20 Hz, 1H), 4.54 (s, 2H), 5.19 (d, *J* = 8.21 Hz, 1H), 5.96 (d, *J* = 2.98 Hz, 1H), 6.03 (d, *J* = 2.92 Hz, 1H), 6.32 (d, *J* = 3.49 Hz, 1H), 7.06 (d, *J* = 3.55 Hz, 1H), 9.53 (s, 1H). Calculated for $C_{28}H_{47}NO_6Si_2Na$: 572.283414 m/z, found: 572.283506 m/z.

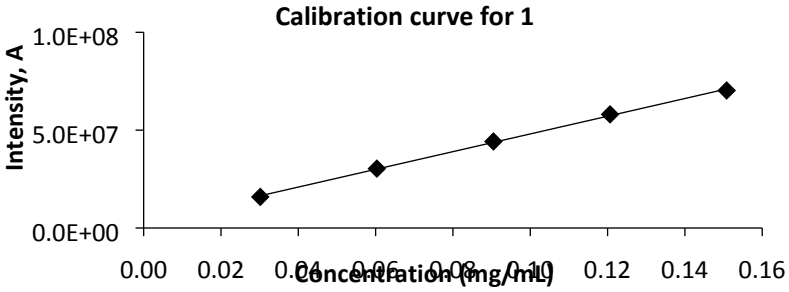
4. Reaction conditions optimization

General Protocol for reaction conditions optimization

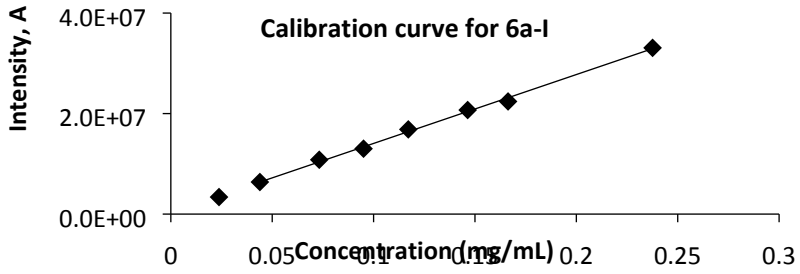
To a solution of **1** (30 mg, 0.125 mmol) in the desired anhydrous solvent, morpholine was added via gas-tight syringe. The catalyst was added in one portion and the mixture was allowed to stir at the mentioned temperature and time. The solvent was then evaporated and the crude reaction mixture was filtered through a small pad of silica gel using 10 mL hexane/ethyl acetate 7:3. The solvent was evaporated and hexane was used to dilute the mixture to the appropriate concentration for HPLC analysis.

R_t (**1**) = 4.78 min., λ_{max}=275 nm; R_t (**6a-II**) = 5.21 min., 282 nm; R_t (**6a-I**) = 7.05 min., λ_{max}=282 nm.

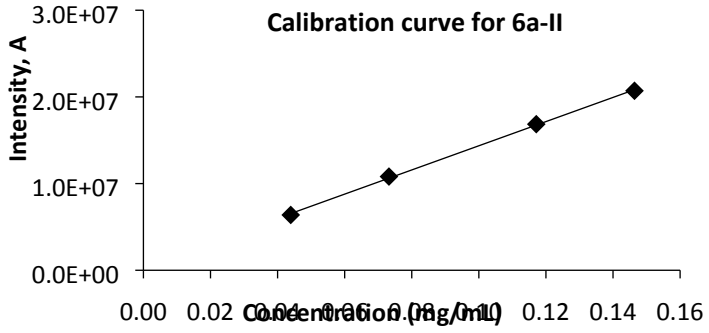
Calibration curves for quantitative HPLC analysis



A = 452574652 [TBDMSOMF] + 2813791; R^2 = 0.9991

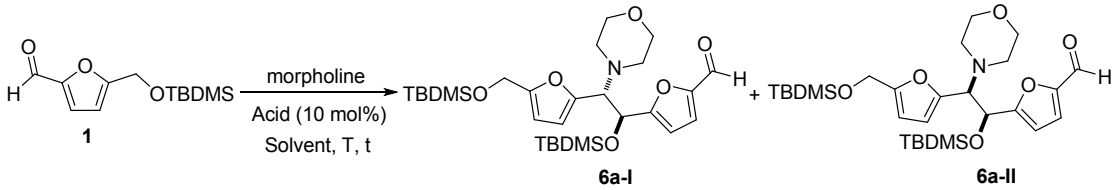


A = 137079868 [6a-I] + 351493; R^2 = 0.9981



A = 139453696 [6a-II] + 417249; R^2 = 0.9993

Results



1 **6a-I** **6a-II**

Catalyst	Cat. Amount (mol%)	Amine quant. (equiv.)	Solvent	Conc. (M)	Temp. (ºC)	t (h)	Conv. (%)[a]	Yield (%)[b]	*d.r.*[c]
$ZrCl_4$	10	2	MeCN	0.08	80	16	70	48	1:1.4
$GdCl_3$	10	2	MeCN	0.08	80	16	68	64	1:1.3
$Dy(OTf)_3$	10	2	MeCN	0.08	80	16	96	6	1:0.6
$FeCl_3$	10	2	MeCN	0.08	80	16	76	13	1:0.1
$CeCl_3$	10	2	MeCN	0.08	80	16	67	42	1:1.3
$AlCl_3$	10	2	MeCN	0.08	80	16	96	35	1:2.6
$ScOf_3$	10	2	MeCN	0.08	80	16	100	6	1:5.5
$ZrCl_4$	10	2	MeCN	0.08	50	16	47	23	1:0.8
$GdCl_3$	10	2	MeCN	0.08	50	16	51	18	1:0.8
$DyOTf_3$	10	2	MeCN	0.08	50	16	93	42	1:1.5
$FeCl_3$	10	2	MeCN	0.08	50	16	67	25	1:0.9
$CeCl_3$	10	2	MeCN	0.08	50	16	31	11	1:0.8
$AlCl_3$	10	2	MeCN	0.08	50	16	32	17	1:0.8
$Dy(OTf)_3$	10	2	MeCN	0.08	40	16	47	47	1:0.9
$Dy(OTf)_3$	10	2	MeCN	0.08	30	16	21	11	1:0.8
$Dy(OTf)_3$	10	2	MeCN	0.08	40	48	73	73	1:1.0
$GdCl_3$	10	2	MeCN	0.08	80	6	63	34	1:1.0
$GdCl_3$	10	2	MeCN	0.08	80	48	95	33	1:2.6
$Sc(OTf)_3$	10	2	MeCN	0.08	40	16	44	44	1:0.9
H_2SO_4	10	2	MeCN	0.08	80	16	46	23	1:0.9
TFA	10	2	MeCN	0.08	80	16	97	20	1:2.3
PTSA	10	2	MeCN	0.08	80	16	82	59	1:1.4
HCOOH	10	2	MeCN	0.08	80	16	38	8	1:0.8
$Dy(OTf)_3$	5	2	MeCN	0.08	40	48	57	57	1:0.9
$Dy(OTf)_3$	20	2	MeCN	0.08	40	48	85	85	1:1.1
$Dy(OTf)_3$	10	1	MeCN	0.08	40	48	74	74	1:1.0
$Dy(OTf)_3$	10	0.55	MeCN	0.08	40	48	51	38	1:1.1
$Dy(OTf)_3$	10	1	Hexane	0.08	40	48	25	traces	-
$Dy(OTf)_3$	10	1	MeOH	0.08	40	48	62	3	1:0.3
$Dy(OTf)_3$	10	1	DCE	0.08	40	48	91	33	1:1.8
$Dy(OTf)_3$	10	1	THF	0.08	40	48	60	22	1:0.9
$Dy(OTf)_3$	10	1	DCM	0.08	40	48	77	59	1:1.3
$Dy(OTf)_3$	10	1	DMSO	0.08	40	48	16	traces	-
$Dy(OTf)_3$	10	1	DMF	0.08	40	48	24	traces	-
$Dy(OTf)_3$	10	1	H_2O	0.08	40	48	71	traces	-
$Dy(OTf)_3$	10	1	MeCN	0.04	40	48	68	68	1:1.3
$Dy(OTf)_3$	**10**	**1**	**MeCN**	**0.17**	**40**	**48**	**88**	**88**	**1:1.1**
$Dy(OTf)_3$	10	1	MeCN[d]	0.08	40	48	77	55	1:1.1
$Dy(OTf)_3$	10	1	MeCN[e]	0.08	40	48	62	62	1:1.3

[a] Conversion determined by HPLC analysis based on starting material that did not react. [b] Total yield of both isomers **6a-I** and **6a-II** determined by HPLC analysis of crude reaction mixture. [c] Determined by HPLC analysis of crude reaction mixture, ratio **6a-II**:**6a-I**. [d] 10% w/w molecular sieves was used as additive. [e] Used comercial HPLC grade MeCN, not dried.

Other catalysts screened by TLC analysis that gave no promising results: $Pd(II)(acac)_2$, $Cu(OTf)_2$, $Au(I)Cl(PPh_3)$, AgOTf, $Ru(III)Cl_3 \cdot xH_2O$, $CoCl_2 \cdot 2H_2O$, $InCl_3$, $Zn(OTf)_2$, $PdCl_2$, CuI, $BaCl_2 \cdot 2H_2O$, $NiCl_2 \cdot 6H_2O$, $FeCl_3 \cdot 6H_2O$, $TiC_{12}H_{28}O_4$, $AlC_9H_{21}O_3$, $LaCl_3 \cdot 7H_2O$, $BF_3 \cdot Et_2O$.

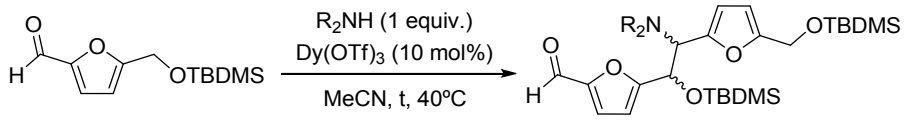
5. Amine scope

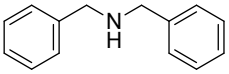
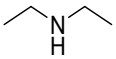
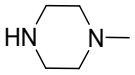
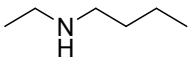
General Protocol

To a solution of **1** (90 mg, 0.375 mmol) in anhydrous acetonitrile (2.25 mL), amine (1 equiv., 0.375 mmol) was added followed by the addition of $Dy(OTf)_3$ (10 mol%) in one portion. The reaction mixture was allowed to stir at 40ºC until full consumption of **1** (followed by TLC). The solvent was then evaporated and the product was purified by flash chromatography using hexane/ethyl acetate.

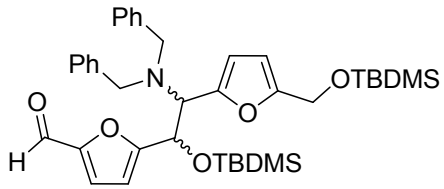
Results

- *N*-methylbutan-1-amine, diallylamine, pyrrolidine, piperazine, proline led to complex mixture and the product was not isolated/identified.
- 2,2,6,6-tetramethylpiperidine, *N*-benzyl-2-methylpropan-2-amine, imidazole, pyrrole, diethanolamine and diphenylamine did not react with **1**.
- Dibenzylamine, diethylamine, methyl-piperazine, ethylbutylamine, piperidine yielded the desired compound:



Entry	Amine	time (h)	Yield (%)
1		41	86
2		24	78
3		24	37
4		20	60
5		24	48
6		48	38

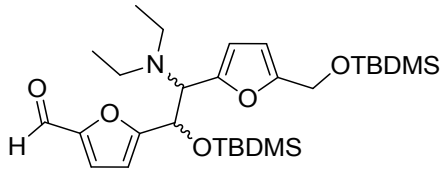
Products characterization



5-(1-((tert-butyldimethylsilyl)oxy)-2-(5-(((tert-butyldimethylsilyl)oxy)methyl)furan-2-yl)-2-(dibenzylamino)ethyl)furan-2-carbaldehyde, 6b

Isolation of the different diastereoisomers, ***6b-I*** *and* ***6b-II*** *(not stable), ratio not determined.*

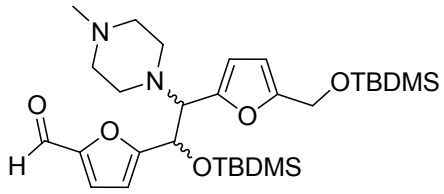
6b-I - ^{1}H NMR (400 MHz, $CDCl_3$) δ -0.24 (s, 3H), -0.19 (s, 3H), 0.16 (s, 3H), 0.16 (s, 3H), 0.60 (s, 9H) 0.96 (s, 9H), 3.13 (d, *J* = 13.78 Hz, 2H), 3.88 (d, *J* = 13.69, 2H), 4.06 (d, *J* = 10.09 Hz, 1H), 4.68 (s, 2H), 5.33 (d, *J* = 10.12 Hz, 1H), 6.20 (d, *J*=2.47 Hz, 1H), 6.27 (d, *J* = 2.50 Hz, 1H), 6.30 (d, *J* = 3.47 Hz, 1H), 7.06 (m, 4H), 7.22 (m, 6 H), 7.29 (d, *J* = 3.36 Hz, 1H), 9.59 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ -5.5, -5.2, -4.9, 18.0, 18.6, 25.5, 26.1, 29.9, 50.0, 55.4, 58.4, 61.7, 67.8, 107.9, 110.4, 111.8, 127.1, 128.3, 128.9, 139.3, 150.4, 152.0, 153.9, 163.2, 178.4. Calculated for $C_{38}H_{53}NO_5Si_2Na$: 682.335451 m/z, found: 682.335489 m/z.



5-(1-((tert-butyldimethylsilyl)oxy)-2-(5-(((tert-butyldimethylsilyl)oxy)methyl)furan-2-yl)-2-(diethylamino)ethyl)furan-2-carbaldehyde, 6c

Isolated as a mixture of diastereoisomers ***6c-I*** *and* ***6c-II****, ratio not determined*

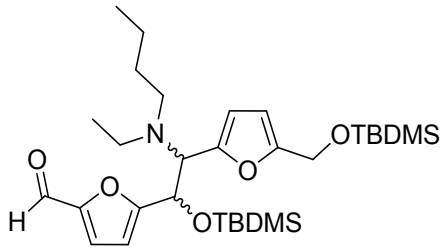
6c-I and 6c-II - ^{1}H NMR (400 MHz, $CDCl_3$) δ -0.20 - -0.15 (6H), 0.00 – 0.12 (6H), 0.75 – 1.00 (18H), 0.5 – 0.7 (6H), 2.00 – 3.00 (4H), 4.03 – 4.13 (1H), 4.59-4.74 (s, 2H), 5.00 – 5.18 (1H), 6.08 - 6.14 (2H), 6.38 - 6.40 (1H), 7.09 - 7.23 (1H), 9.54 - 9.59 (1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ -5.4, -5.2, -4.1, -5.0, 13.9, 18.0, 18.6, 25.6, 25.8, 25.9, 26.0, 44.9, 58.4, 60.6, 63.3, 69.0, 107.7, 107.8, 109.5, 109.6, 109.9, 110.2, 122.2, 151.7, 153.4, 164.3, 177.1, 177.7. Calculated for $C_{28}H_{49}NO_5Si_2Na$: 558.304147 m/z, found: 558.304643 m/z.



5-(1-((tert-butyldimethylsilyl)oxy)-2-(5-(((tert-butyldimethylsilyl)oxy)methyl)furan-2-yl)-2-(4-methylpiperazin-1-yl)ethyl)furan-2-carbaldehyde, 6d

Isolated as a mixture of diastereoisomers, ***6d-I*** *and* ***6d-II****, ratio 1:1.0*

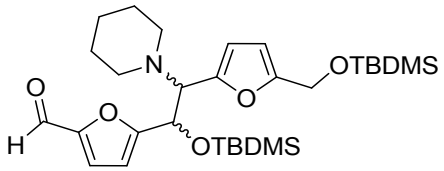
6d-I – ^{1}H NMR (400 MHz, $CDCl_3$) δ -0.18 (s, 3H), -0.15 (s, 3H), 0.07 (s, 3H), 0.08 (s, 3H), 0.68 (s, 9H) 0.90 (s, 9H), 2.14 (s, 3H), 2.30-2.72 (m, 8H), 3.84 (d, *J* = 9.1 Hz, 1H), 4.56 (s, 2H), 5.22 (d, *J* = 9.09 Hz, 1H), 6.14 (m, 2H), 6.44 (d, *J* = 3.46 Hz, 1H), 7.21 (d, *J* = 3.39 Hz, 1H), 9.60 (s, 1H).
6d-II – ^{1}H NMR (400 MHz, $CDCl_3$) δ -0.10 (s, 3H), 0.05 (s, 9H), 0.84 (s, 9H) 0.88 (s, 9H), 1.25-1.55 (m, 6H), 2.24 (s, 3H), 2.30-2.72 (m, 8H), 3.98 (d, *J* = 8.12 Hz, 1H), 4.51 (s, 2H), 5.18 (d, *J* = 8.12 Hz, 1H), 5.94 (d, *J* = 2.4 Hz, 1H), 5.98 (d, *J* = 2.75 Hz, 1H), 6.30 (d, *J* = 3.43 Hz, 1H), 7.05 (d, *J* = 3.46 Hz, 1H), 9.51 (s, 1H).
6d-I + 6d-II – ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.69, 177.67, 164.1, 162.4, 153.8, 153.7, 151.8, 150.1, 149.9, 122.5, 121.0, 110.8, 110.1, 109.4, 107.8, 107.6, 68.5, 67.9, 67.0, 66.6, 58.2, 58.1, 55.4, 55.3, 45.7, 26.1, 26.0, 25.8, 25.6, 18.6, 18.5, 18.3, 18.0, -4.8, -4.9, -5.0, -5.4. Calculated for $C_{29}H_{50}N_2O_5Si_2Na$: 585.315053 m/z, found: 585.315022 m/z.



5-(2-(butyl(ethyl)amino)-1-((tert-butyldimethylsilyl)oxy)-2-(5-(((tert-butyldimethylsilyl)oxy)methyl)furan-2-yl)ethyl)furan-2-carbaldehyde, 6e

Isolated as a mixture of diastereoisomers, ***6e-I*** *and* ***6e-II****, ratio 1:0.25*

6e-I – ^{1}H NMR (400 MHz, $CDCl_3$) δ -0.20 (s, 3H), -0.17 (s, 3H), 0.09 (s, 3H), 0.10 (s, 3H), 0.66 (s, 9H), 0.74-0.81 (m, 6H), 0.91 (s, 9H), 1.04-1.31 (m, 4H), 2.11 (m, 2H), 2.37 (m, 1H), 2.64 (m, 1H), 4.03 (d, *J* = 9.78 Hz, 1H), 4.59 (s, 2H), 5.18 (d, *J* = 9.79 Hz, 1H), 6.12 (d, *J* = 2.7 Hz, 1H), 6.16 (d, *J* = 2.7 Hz, 1H), 6.44 (d, *J* = 3.52 Hz, 1H), 7.21 (d, *J* = 3.51 Hz, 1H), 9.61 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.7, 164.2, 153.3, 151.7, 151.6, 122.2, 110.4, 109.7, 107.8, 68.7, 63.5, 58.4, 50.7, 45.1, 30.5, 26.0, 25.8, 25.5, 20.4, 20.3, 18.6, 18.1, 18.0, 14.2, 13.9, -5.0, -5.1, -5.5. Calculated for $C_{30}H_{53}NO_5Si_2Na$: 586.335452 m/z, found: 586.335467 m/z.
6e-II – Calculated for $C_{30}H_{53}NO_5Si_2Na$: 586.335452 m/z, found: 586.335797 m/z.



5-(1-((tert-butyldimethylsilyl)oxy)-2-(5-(((tert-butyldimethylsilyl)oxy)methyl)furan-2-yl)-2-(piperidin-1-yl)ethyl)furan-2-carbaldehyde, 6f

Isolation of the different diastereoisomers, 6f-I and 6f-II.

6f-I – ^{1}H NMR (400 MHz, $CDCl_3$) δ -0.17 (s, 3H), -0.15 (s, 3H), 0.09 (s, 3H), 0.10 (s, 3H), 0.68 (s, 9H) 0.91 (s, 9H), 1.20-1.31 (m, 6H), 2.17 (m, 2H), 2.53 (m, 2H), 3.81 (d, *J* = 9.24 Hz, 1H), 4.60 (s, 2H), 5.24 (d, *J* = 9.24 Hz, 1H), 6.13 (d, *J* = 2.93 Hz, 1H), 6.17 (d, *J* = 2.95 Hz, 1H), 6.45 (d, *J* = 3.56 Hz, 1H), 7.21 (d, *J* = 3.55 Hz, 1H), 9.61 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.77, 151.76, 109.49, 107.84, 68.54, 58.33, 51.70, 26.00, 25.57, 18.54, 18.02, -5.00, -5.04, -5.36. $C_{29}H_{49}NO_5Si_2Na$: 570.304151 m/z, found: 570.303693 m/z.
6f-II – ^{1}H NMR (400 MHz, $CDCl_3$) δ -0.07 (s, 3H), 0.06 (s, 6H), 0.09 (s, 3H), 0.85 (s, 9H) 0.89 (s, 9H), 1.25-1.55 (m, 6H), 2.38 (m, 2H), 2.63 (m, 2H), 3.95 (d, *J* = 8.73 Hz, 1H), 4.53 (s, 2H), 5.18 (d, *J* = 8.69 Hz, 1H), 5.90 (d, *J* = 2.94 Hz, 1H), 6.00 (d, *J* = 2.96 Hz, 1H), 6.30 (d, *J* = 3.51 Hz, 1H), 7.05 (d, *J* = 3.56 Hz, 1H), 9.51 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.1, 151.7, 110.0, 107.8, 68.4, 58.2, 51.7, 29.9, 25.8, 18.5, 18.33, -4.73, -5.0, -5.4.

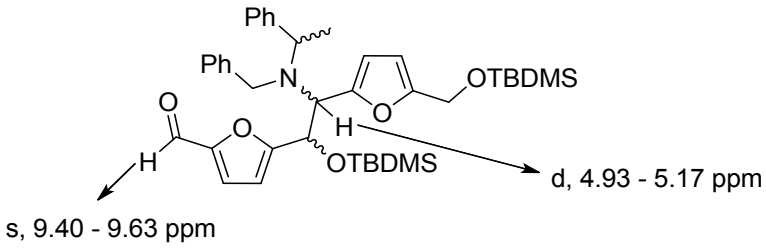
6. Asymmetric version

General Protocol using chiral amines:

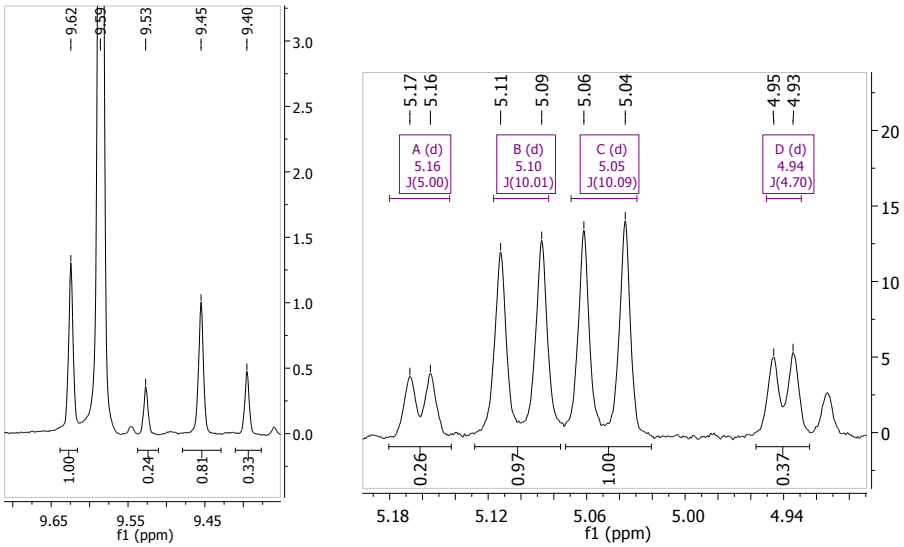
To a solution of **1** (90 mg, 0.375 mmol) in anhydrous acetonitrile (2.25 mL), *N*-benzyl-1-phenylethanamine (1 equiv., racemic, *(R)*- or *(S)*-isomers) was added followed by the addition of $Dy(OTf)_3$ (10 mol%) in one portion. The reaction mixture was allowed to stir at 40ºC for 4 days. The solvent was then evaporated and the catalyst was filtrated through a pad of silica gel using hexane/ethyl acetate and the starting material/products were analyzed by ^1H NMR.

HRMS for the product **6g** using racemic amine: Calculated for $C_{39}H_{56}NO_5Si_2$: 674.3692 m/z, found: 6474.3690 m/z.

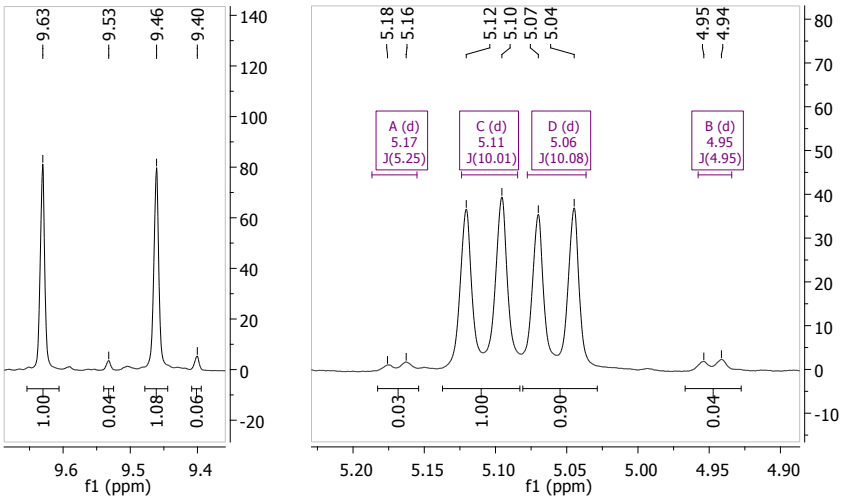
^1H NMR analysis



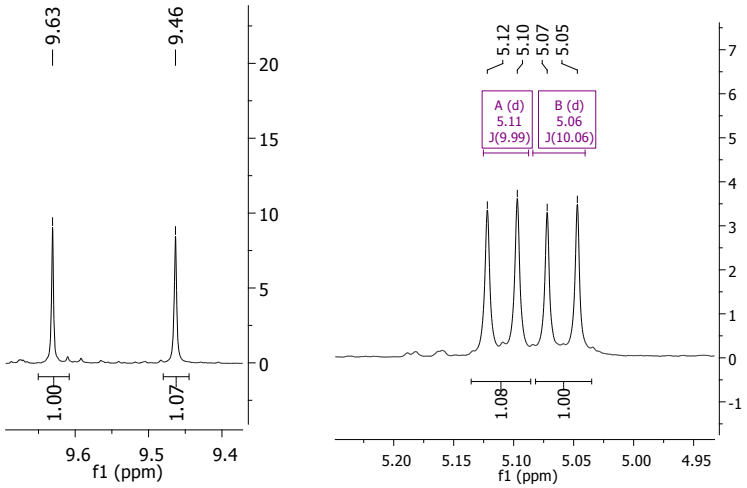
***Using racemic amine** – d.r. 1:1:0.35:0.25*



***Using amine S-isomer** – d.r 1: 1: 0.05: 0.05*



***Using amine R-isomer** – d.r 1:1:0:0*



General protocol for unsuccessful asymmetric version using chiral catalysts

To a solution of **1** (15 mg, 0.06 mmol) in the desired anhydrous solvent (0.4 mL), morpholine (1 equiv., 0.06 mmol), catalyst (10 mol%) and the ligand (for the Lewis acid examples, 10 mol%) were added. The reaction mixture was allowed to stir for the time and temperature described. The solvent was then evaporated and the catalyst was filtrated through a pad of silica gel using hexane/ethyl acetate and the starting material/products were analyzed by HPLC.

HPLC analysis was performed on a Shimadzu apparatus with a diode array detector SPD-M20A coupled to a pump LC-20AT and using a CHIRALCEL OD column, manual injector with 20 µL loop. Mobile phase gradient from 99:1 n-hexane/2-propanol, flow 1 mL/min.

Entry	Catalyst	Ligand	Conditions	Yield[a]	*ee*[b]
1	$Dy(OTf)_3$	*(S)*-BINOL	MeCN, 40ºC, 2d	Good	racemic
2	$Dy(OTf)_3$	BOX	MeCN, 40ºC, 2d	Good	racemic
3	$Dy(OTf)_3$		MeCN, 40ºC, 2d	Good	racemic
4[c]	$Sc(OTf)_3$	PyBOX	MeCN, 40ºC, 2d	Good	racemic
5[c]	$Sc(OTf)_3$		DCM, 40ºC, 2d	Good	racemic
6	*(R)*-BINOL Hydrogenphosphate	-	DCE, 80ºC, 3d	Low	racemic
7[d]	*(R)*-VAPOL Hydrogenphosphate	-	DCE, 80ºC, 5d	Low	racemic
8	*(R)*-TRIP	-	DCE, 70ºC, 5d	Moderate	racemic
9[d]	*(S)*-CSA	-	MeCN, 80ºC, 2d	Moderate	racemic

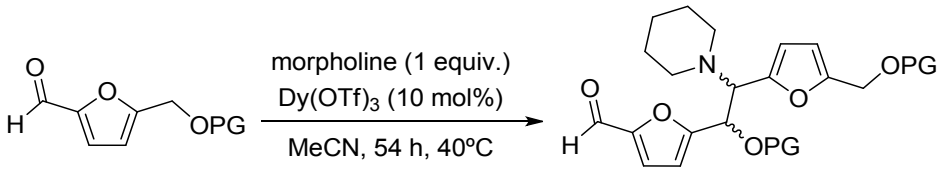
[a]Qualitative yield determined by TLC analysis of crude reaction mixture; [b]Determined by HPLC of crude reaction mixture; [c]The catalyst and the ligand were pre-mixed before for 2h at RT; [d]No reaction observed at 40ºC for 2d. *(S)*-BINOL: (S)-(−)-1,1′-Bi(2-naphthol) (CAS: 18531-99-2); BOX: 2,2′-Isopropylidenebis[(4S)-4-tert-butyl-2-oxazoline] (CAS: 131833-93-7); PyBOX: 2,6-Bis[(4R)-4-phenyl-2-oxazolinyl]pyridine (CAS:128249-70-7); *(R)*-BINOL Hydrogenphosphate: (R)-(−)-1,1′-Binaphthyl-2,2′-diyl hydrogenphosphate (CAS: 39648-67-4); *(R)*-VAPOL Hydrogenphosphate: (R)-2,2′-Diphenyl-3,3′-biphenanthryl-4,4′-diyl phosphate (CAS: 871130-18-6); *(R)*-TRIP: (R)-3,3′-Bis(2,4,6-triisopropylphenyl)-1,1′-binaphthyl-2,2′-diyl hydrogenphosphate; *(S)*-CSA: (1S)-(+)-10-Camphorsulfonic acid (CAS: 3144-16-9).

7. Aldehyde scope

General protocol:

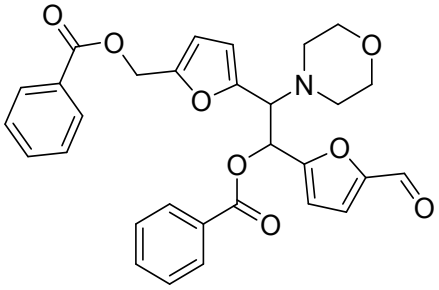
To a solution of aldehyde (0.375 mmol) in anhydrous acetonitrile (2.25 mL), morpholine (1 equiv., 0.375 mmol) was added via gas-tight syringe followed by the addition of $Dy(OTf)_3$ (10 mol%) in one portion. The reaction mixture was allowed to stir at 40 ºC for 54h. The solvent was then evaporated and the product (mixture of diastereoisomers) was purified by flash chromatography using hexane/ethyl acetate.

Results:



Entry	PG	Conversion (%)	Yield (%)
1	Bz	99	58
2	Bn	69	58
3	Ac	80	29
4	H	78	44

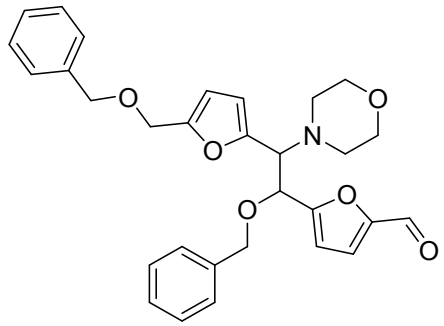
Products characterization



(5-(2-(benzoyloxy)-2-(5-formylfuran-2-yl)-1-morpholinoethyl)furan-2-yl)methyl benzoate, 7a

*Isolated as a mixture of diastereoisomers, **7a**-I and **7a**-II, ratio 1:1.0*

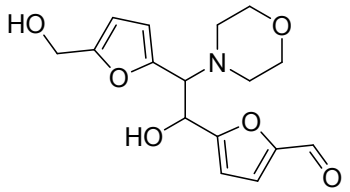
7a-I and **7a-II** – ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.32-2.40 (m, 4H), 2.67 (m, 2H), 3.78 (m, 2H), 3.50 (m, 8H), 4.35 (d, *J* = 10.42 Hz, 1H), 4.47 (d, *J* = 9.97 Hz, 1H), 5.20 (s, 2H), 5.22 (s, 2H), 6.12 (d, *J* = 3.10 Hz, 1H), 6.31 (d, *J* = 2.76 Hz, 2H), 6.40 (d, *J* = 3.11 Hz, 1H), 6.43 (d, *J* = 3.53 Hz, 1H), 6.60 (d, *J* = 9.97 Hz, 1H), 6.63 (d, *J* = 3.53 Hz, 1H), 6.73 (d, *J* = 10.40 Hz, 1H), 6.91 (d, *J* = 3.54 Hz, 1H), 7.18 (d, *J* = 3.53 Hz, 1H), 7.26-7.57 (m, 12H), 7.80 (d, *J* = 7.44 Hz, 2H), 7.90 (d, *J* = 7.41 Hz, 2H), 8.01 (d, *J* = 7.39 Hz, 2H), 8.06 (d, *J* = 7.36 Hz, 2H), 9.49 (s, 1H), 9.61 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.8, 177.8, 166.2, 166.1, 165.6, 165.3, 157.7, 156.4, 152.7, 152.5, 150.7, 149.8, 149.7, 149.7, 133.4, 133.4, 133.1, 130.0, 129.9, 129.9, 129.8, 129.8, 129.3, 128.7, 128.6, 128.6, 128.5, 128.5, 128.4, 127.2, 122.1, 122.1, 121.6, 121.5, 112.3, 112.3, 111.4, 111.3, 111.0, 111.0, 67.3, 67.3, 67.0, 66.1, 64.8, 64.2, 58.6, 58.5, 50.5, 50.3. CHN Calculated for $(C_{30}H_{27}NO_8)_4H_2O$: C: 67.47; H: 5.19; N: 2.62, found: C: 67.45; H: 5.29; N: 2.42.



5-(1-(benzyloxy)-2-(5-((benzyloxy)methyl)furan-2-yl)-2-morpholinoethyl)furan-2-carbaldehyde, 8a

Isolated as a mixture of diastereoisomers, ***8a-I*** *and* ***8a-II****, ratio 1:0.8*

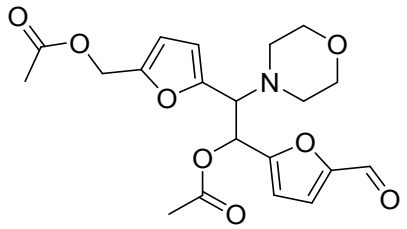
8a **I** – ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.28 (m, 2H), 2.58 (m, 2H), 3.68 (m, 4H), 4.19 (d, *J* = 9.12 Hz, 1H), 4.36 (d, *J* = 12.21 Hz, 1H), 4.39 (d, *J* = 12.14 Hz, 1H), 4.38 (s, 2H), 4.46 (d, *J* = 2.88 Hz, 2H), 4.98 (d, *J* = 9.11 Hz, 2H), 6.02 (d, *J* = 2.99 Hz, 1H), 6.13 (d, *J* = 2.95 Hz, 1H), 6.39 (d, *J* = 3.51 Hz, 1H), 7.03 (d, *J* = 3.51 Hz, 1H), 7.23-7.36 (m, 10H), 9.63 (s, 1H).
8a **II** – ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.28 (m, 2H), 2.58 (m, 2H), 3.68 (m, 4H), 4.01 (d, *J* = 9.12 Hz, 1H), 4.42 (s, 2H), 4.50 (s, 2H), 4.53 (d, *J* = 11.81 Hz, 1H), 4.67 (d, *J* = 12.07 Hz, 1H), 5.04 (d, *J* = 9.16 Hz, 2H), 6.22 (d, *J* = 2.96 Hz, 1H), 6.33 (d, *J* = 2.95 Hz, 1H), 6.50 (d, *J* = 3.49 Hz, 1H), 7.09 (d, *J* = 3 Hz, 1H), 7.23-7.36 (m, 10H), 9.52 (s, 1H).
8a **I** and ***8a*** **II** – ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.8, 177.7, 161.0, 159.5, 152.5, 152.4, 151.4, 151.3, 150.8, 150.8, 150.5, 150.3, 138.0, 137.9, 137.3, 137.2, 128.6, 128.5, 128.4, 128.3, 128.2, 127.9, 127.8, 127.8, 122.2, 122.2, 121.5, 121.5, 111.7, 110.8, 110.6, 110.4, 110.3, 110.1, 74.0, 72.9, 72.1, 71.6, 71.5, 67.3, 66.2, 65.5, 64.0, 63.8, 50.6, 50.3. CHN Calculated for $(C_{30}H_{31}NO_6)_2(H_2O)$: C: 70.57; H: 6.32; N: 2.74, found: C: 70.37; H: 6.12; N: 2.84.



5-(1-hydroxy-2-(5-(hydroxymethyl)furan-2-yl)-2-morpholinoethyl)furan-2-carbaldehyde, 9a

Isolated as a mixture of diastereoisomers, ***9a-I*** *and* ***9a-II****, ratio 1:1.1*

9a-I – ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.50 (m, 4H), 3.6 – 3.7 (m, 4H), 3.50-3.86 (d, 1H), 4.53 (d, *J* = 4.97 Hz, 2H), 5.28 (d, *J* = 6.40 Hz, 1H), 6.14 (dd, *J* = 9.96, 2.85, 2H), 6.39 (d, *J* = 3.48 Hz, 1H), 7.13 (d, *J* = 3.50 Hz, 1H), 9.51 (s, 1H).
9a-II – ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.75 (m, 4H), 3.6 – 3.7 (m, 4H), 3.82 (d, *J* = 9.69 Hz, 1H), 4.54 (s, 2H), 5.12 (d, *J* = 10.51 Hz, 1H), 6.08 (s, 1H), 6.10 (s, 1H), 6.45 (d, *J* = 3.48 Hz, 1H), 7.10 (d, *J* = 3.50 Hz, 1H), 9.45 (s, 1H).
9a-I *and* ***9a-II***– ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.6, 177.5, 161.1, 160.5, 155.0, 154.4, 152.3, 152.0, 149.9, 148.4, 122.6, 119.6, 111.5, 111.4, 110.7, 109.8, 109.1, 108.3, 67.3, 67.2, 67.1, 67.0, 66.8, 66.5, 66.2, 64.1, 57.5, 57.3.



(5-(2-acetoxy-2-(5-formylfuran-2-yl)-1-morpholinoethyl)furan-2-yl)methyl acetate, 10a

*Isolated as a mixture of diastereoisomers, **10a-I** and **10a-II**, ratio 1:1.05*

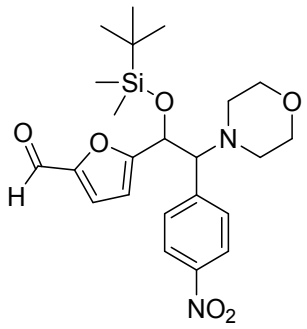
***10a*-I** – ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.90-2.15 (2 x s, 2 x 3H), 3.25-3.80 (m, 4H or 2 x 2H), 3.4-3.7 (m, 4H), 4.16 (d, *J* = 10.56 Hz, 1H), 5.00 (d, *J* = 9.57 Hz, 2H), 6.21 (m, t_{ap}, *J* = 3.0 Hz, 2H), 6.47 (d, *J* = 10.56 Hz, 1H), 6.56 (d, *J* = 3.49 Hz, 1H), 7.20 (d, *J* = 3.52 Hz, 1H), 9.62 (s, 1H).
***10a*-II** –^{1}H NMR (400 MHz, $CDCl_3$) δ 1.90-2.15 (2 x s, 2 x 3H), 3.25-3.80 (m, 4H or 2 x 2H), 3.4-3.7 (m, 4H), 4.27 (d, *J* = 10.34 Hz, 1H), 4.93 (s, 2H), 6.04 (d, *J* = 3.08 Hz, 1H), 6.34 (d, *J* = 3.40 Hz, 1H), 6.37 (d, *J* = 11.02 Hz, 1H), 6.39 (d, *J* = 3.70 Hz, 1H), 7.04 (d, *J* = 3.54 Hz, 1H), 9.53 (s, 1H).
***10a*-I** + ***10a*-II** –^{13}C NMR (100 MHz, $CDCl_3$) δ 177.8, 177.8, 170.7, 170.6, 169.8, 169.5, 157.7, 156.4, 152.6, 152.4, 150.6, 150.5, 149.7, 149.6, 122.0, 121.4, 112.1, 112.0, 111.1, 111.1, 110.9, 110.6, 67.5, 67.2, 66.1, 65.1, 64.6, 63.9, 58.2, 58.0, 50.3, 50.3, 21.1, 21.1, 21.0, 20.7. CHN Calculated for $C_{20}H_{23}NO_8$: C: 59.25; H: 5.72; N: 3.46, found: C: 59.4; H: 5.78; N: 3.18.

8. Cross reaction

General Procedure:

To a solution of **1** (90 mg, 0.375 mmol) and the desired aldehyde (2 equiv., 0.75 mmol) in anhydrous acetonitrile (3 mL), morpholine (2 equiv., 0.75 mmol) was added via gas-tight syringe followed by the addition of $Dy(OTf)_3$ (10 mol%) in one portion. The reaction mixture was allowed to stir at 40 ºC for 3 d. The solvent was then evaporated and the product was purified by flash chromatography using hexane/ethyl acetate. Compound **11** was isolated in 20% yield when 4-nitrobenzaldeyde was used as aldehyde.

Product characterization



5-(1-((tert-butyldimethylsilyl)oxy)-2-morpholino-2-(4-nitrophenyl)ethyl)furan-2-carbaldehyde, 11

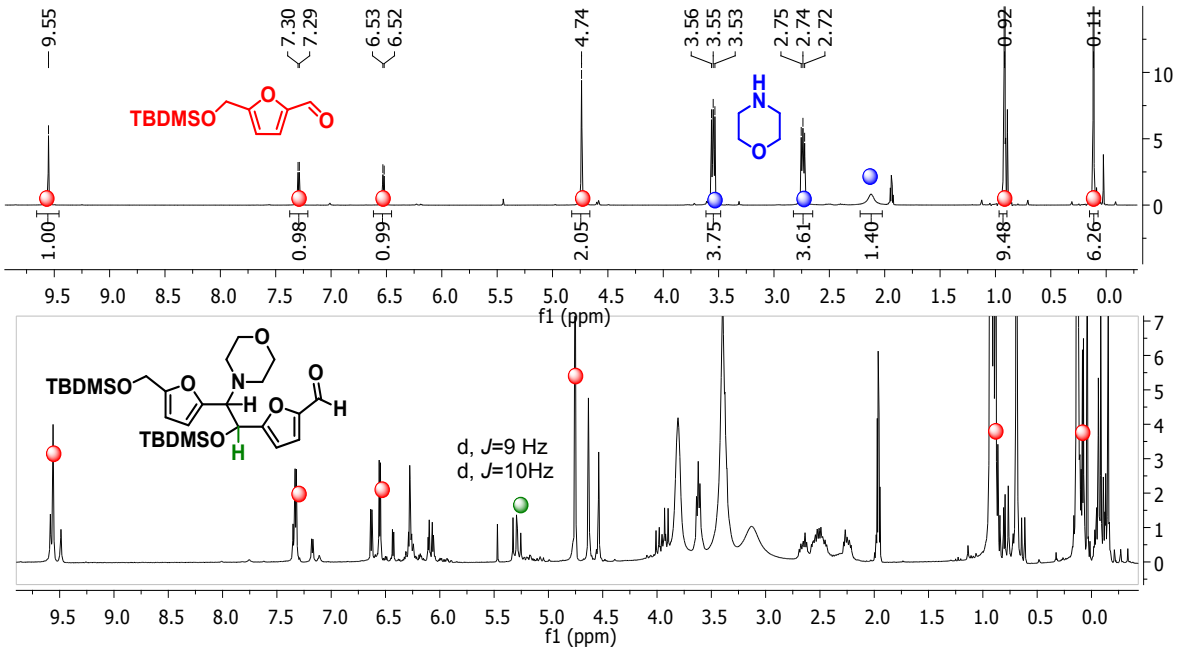
11-I – ^{1}H NMR (400 MHz, $CDCl_3$) δ -0.18 (s, 3H), 0.00 (s, 3H), 0.77 (s, 9H), 2.44 (m, 4H), 3.58 (m, 4H), 3.76 (d, *J* = 5.58 Hz, 1H), 5.35 (d, *J* = 5.58 Hz, 1H), 6.10 (d, *J* = 3.42 Hz, 1H), 7.10 (d, *J* = 3.44 Hz, 1H), 7.34 (d, *J* = 8.43 Hz, 1H), 8.12 (d, *J* = 8.42 Hz, 1H), 9.57 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ -5.1, -4.5, 18.1, 25.6, 51.5, 67.1, 68.3, 74.4, 110.5, 122.8, 130.56, 130.60, 144.0, 147.5, 151.8, 162.3, 177.4. CHN Calculated for $(C_{23}H_{32}N_2O_6Si)_5(CHCl_3)_3$: C: 53.26; H: 6.17; N: 5.26, found: C: 53.53; H: 6.14; N: 5.19.

11-II – ^{1}H NMR (400 MHz, $CDCl_3$) δ -0.12 (s, 3H), 0.05 (s, 3H), 0.86 (s, 9H), 2.45 (m, 2H), 2.66 (m, 2H), 3.58 (m, 4H), 3.69 (d, *J* = 5.5 Hz, 1H), 5.33 (d, *J* = 5.52 Hz, 1H), 6.00 (d, *J* = 3.4 Hz, 1H), 7.07 (d, *J* = 3.4 Hz, 1H), 7.34 (d, *J* = 8.4 Hz, 1H), 8.05 (d, *J* = 8.4 Hz, 1H), 9.55 (s, 1H).

9. Investigation of reaction mechanism

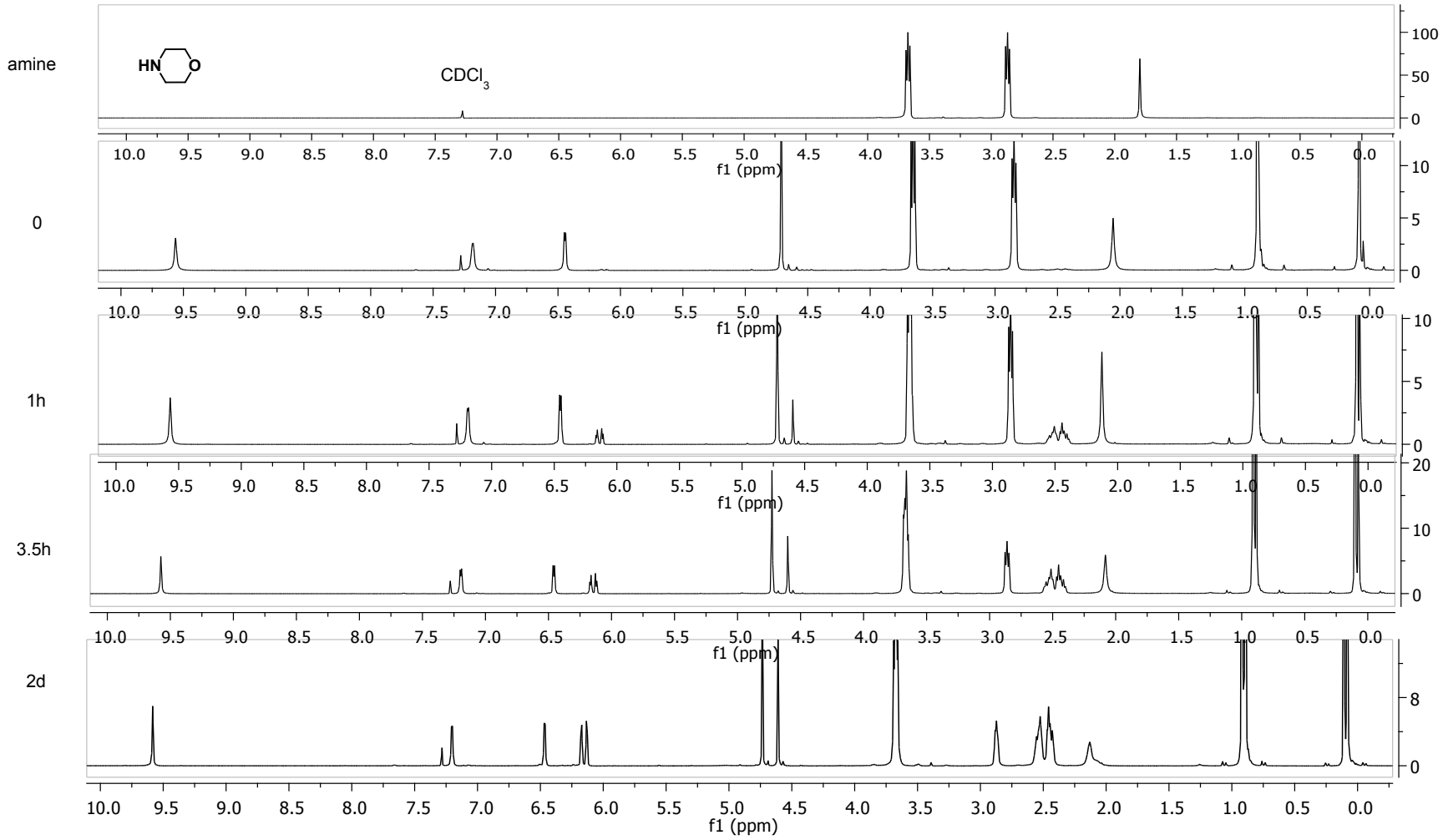
Reaction followed by ^{1}H NMR

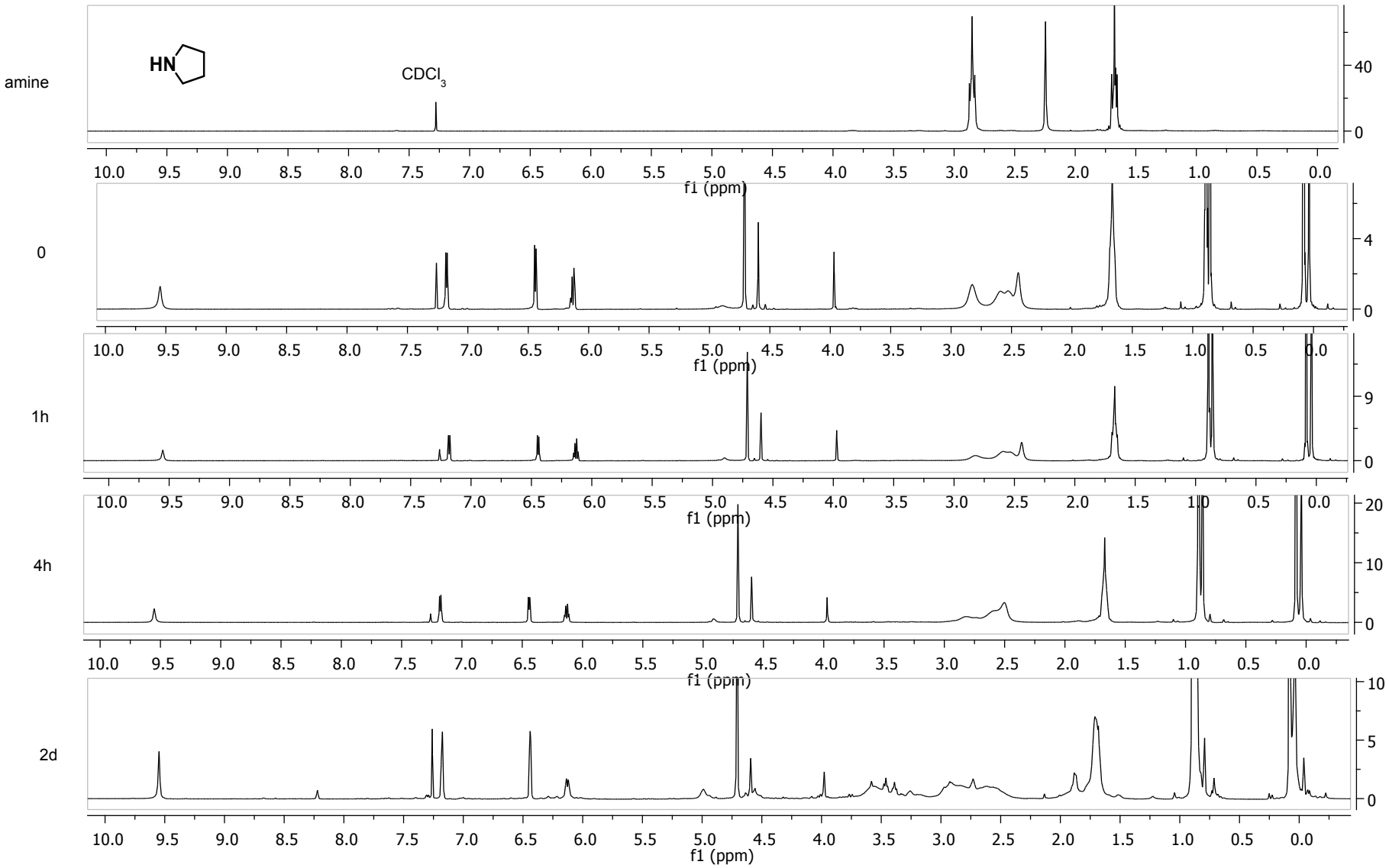
A NMR tube was charged with **1** (30 mg, 0.125 mmol), 0.4 mL acetonitrile-d_3, morpholine (11 µL, 0.125 mmol) and $Sc(OTf)_3$ (10 mol%). The heterogeneous mixture was allowed to react in the NMR at 40ºC. The ^{1}H NMR data was acquired during 16h.



Stability of 1 in presence of amines

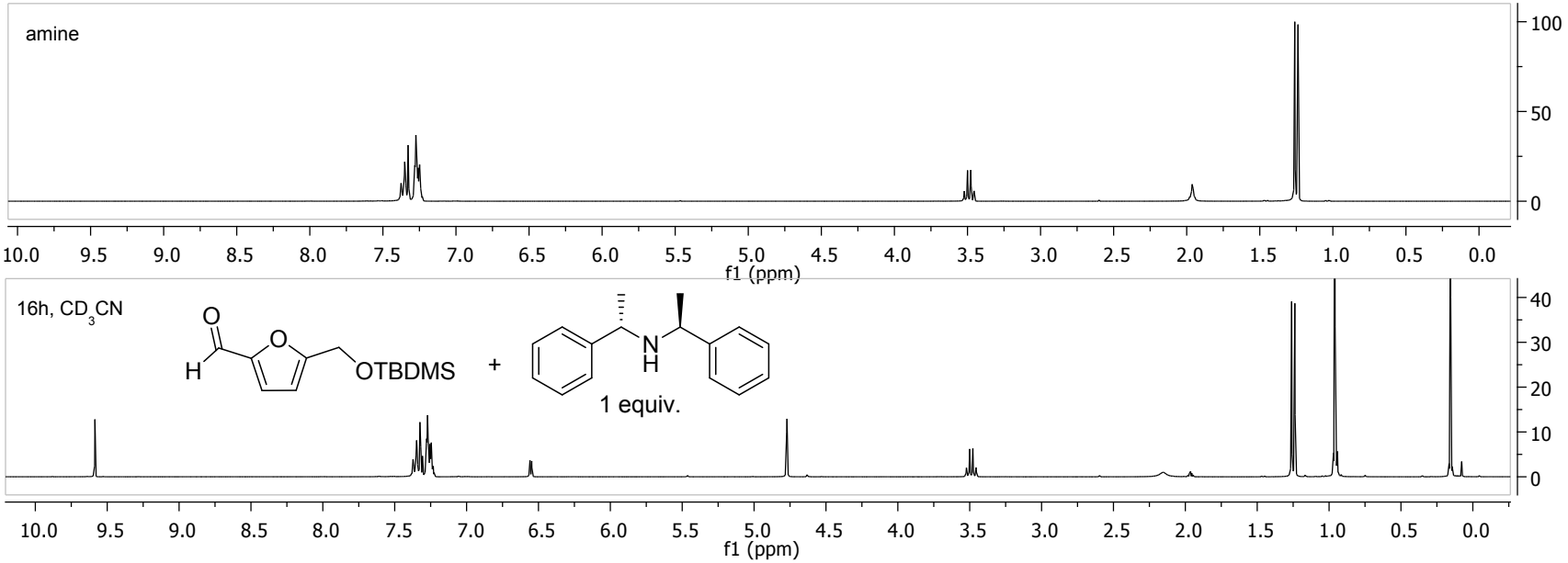
To study the stability of aldehyde **1** in the presence of morpholine or pyrrolidine, NMR tubes were charged with amine, $CDCl_3$ and **1**. The mixture was kept at r.t. and ^1H NMR was performed at 0 min, 1 h, 4 h, 2 d.




amine
HN
CDCl3
0
1h
4h
2d
f1 (ppm)

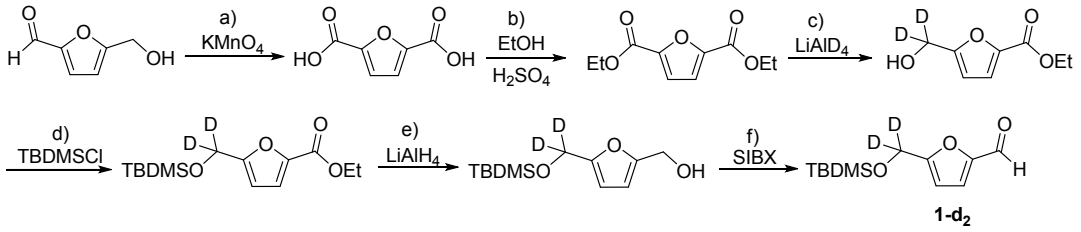
No reactive amines

For non-reactive amines, the formation of the aminal intermediate was not observed after 16h.



Determination of kinetic isotope effect (KIE)

Synthesis of 1-d_2



a) **Furan-2,5-dicarboxylic acid, FDCA.** To a solution of sodium hydroxide (30 g) in water (300 mL), HMF (4.1 g, 32.5 mmol) was added at 20 ºC, followed by the addition of potassium permanganate (11 g, 70 mmol). After 10 minutes stirring at 20ºC the precipitate was filtered off and a concentrated HCl solution was added to the filtrate until pH 1. The resulted precipitate was separated by filtration, washed with water and dried under vacuum to give FDCA (4.26 g, 84% yield) as a white powder. ^{1}H NMR (300 MHz, D_2O) δ 7.25 (s).

b) **Diethyl furan-2,5-dicarboxylate.** To a round bottom flask equipped with a Dean-Stark a solution of FDCA (2.53 g, 16.2 mmol) in ethanol (70 mL) was charged, followed by the addition of a catalytic amount of sulfuric acid (3 drops). The mixture was allowed to stir at reflux for 16h. The mixture was neutralized with a saturated aqueous solution of $NaHCO_3$, extracted with ethyl acetate, dried over $MgSO_4$, filtered and evaporated to give the crude product as a yellow solid. The product was purified by column chromatography to give the product as a white solid (1.36 g, 40% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.39 (t, *J* = 7.12 Hz, 6H), 4.40 (t, *J* = 7.13 Hz, 2H), 7.20 (s_{app}, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.4, 61.8, 118.4, 147.1, 158.2.

c) **Ethyl 5-(hydroxymethyl)furan-2-carboxylate-d_2.** To a suspension of $LiAlD_4$ (19 mg, 2 equiv.) in anhydrous THF (1 mL), a solution of diethyl furan-2,5-dicarboxylate (47.8 mg, 0.225 mmol) in THF (1 mL) was added slowly at 0 ºC. The mixture was allowed to stir for 22h at RT. Water was added and the product extracted with ethyl acetate (3 x 10 mL). The product was then purified by column chromatography to yield the product as a yellow oil (9 mg, 23% yield). *Notes*: Scale up of the reaction was not reproducible, so small scale reactions were performed to synthesize the compound. The full reduction (incorporation of four D atoms) occurred as side reaction to give the diol as a minor product. The low overall yield of the reaction was due to low conversion of the starting material.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.36 (t, *J* = 7.13 Hz, 3H), 2.34 (bs, 1H) 4.35 (t, *J* = 7.13 Hz, 2H), 6.40 (d, *J* = 3.40 Hz, 1H), 7.12 (d, *J* = 3.39 Hz, 1H).

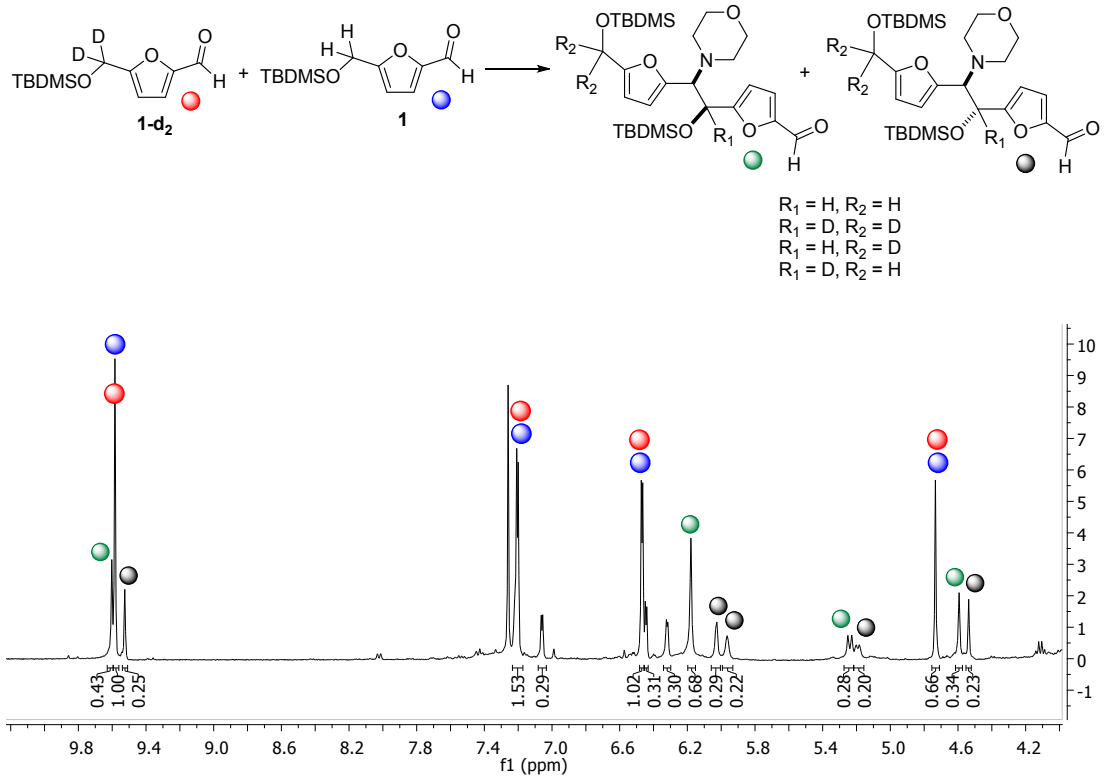
d) **Ethyl 5-(((tert-butyldimethylsilyl)oxy)methyl)furan-2-carboxylate-d_2.** To a solution of ethyl 5-(hydroxymethyl)furan-2-carboxylate-d_2 (43.9 mg, 0.255 mmol) in anhydrous DCM (0.4 mL) were added imidazole (35 mg, 0.5 mmol, 2 equiv.) and *tert*-butyldimethylsilyl chloride (58 mg, 0.382 mmol, 1.5 equiv.) at 0 ºC. The solution was stirred for 15 min at RT. The reaction was quenched with water and the silylated compound was extracted with DCM (5 x 20 mL). The collected organic layers were dried over $MgSO_4$, and the solvent removed to give the crude product as a pale yellow oil that was used without further purification in the next step.

e) **(5-(((tert-butyldimethylsilyl)oxy)methyl)furan-2-yl)methanol-d_2**. To a suspension of $LiAlH_4$ (20 mg, 2 equiv.) in anhydrous THF (1.5 mL), a solution of ethyl 5-(((tert-butyldimethylsilyl)oxy) methyl)furan-2-carboxylate-d_2 (0.255 mmol) in THF (1 mL) was added slowly at 0ºC. The mixture was allowed to stir for 15 minutes at RT and then the reaction was quenched with water. The product was extracted with ethyl acetate (3 x 10 mL), dried over Mg_2SO_4 and filtered to give the crude product (51.4 mg) that was used in the next step without further purification.

f) **5-(((tert-butyldimethylsilyl)oxy)methyl)furan-2-carbaldehyde-d_2**. To a solution of crude (5-(((tert-butyldimethylsilyl)oxy)methyl)furan-2-yl)methanol-d_2 (51.4 mg) in anhydrous THF (1.5 mL), stabilized 2-iodoxybenzoic acid (SIBX, 1.6 equiv.) was added and the mixture was allowed to stir for 8h at 60ºC. The crude product was purified by column chromatography to yield the desired product (22.7 mg, 37% yield - 3 steps).
^{1}H NMR (400 MHz, $CDCl_3$) δ 0.11 (s, 6H), 0.92 (s, 9H), 6.47 (d, J = 3.53 Hz, 1H), 7.20 (d, J = 3.52 Hz, 1H), 9.59 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ -5.2, 18.5, 25.9, 109.6, 122.7, 152.3, 161.5, 177.7.
Calculated for $[C_{12}H_{19}D_2O_3Si]^+$: 243.1380 m/z, found: 243.1380 m/z.

Procedure for determination of kinetic isotope effect (KIE)

To a mixture of **1** (11 mg, 45.76 μmol) and **1-d_2** (9.6 mg, 39.61 μmol), anhydrous acetonitrile (0.5 mL), morpholine (7.3 μL, 2 equiv.) and $DyOTf_3$ (5 mg, 10 mol%) were added. The mixture was allowed to stir for 59 h at 40 ºC. The mixture was filtered through a pad of silica gel and the crude reaction mixture was analyzed by ^{1}H NMR.



Total amount of starting material (SM) initial = 45.8 + 39.6 = 85.4 µmol

Starting material conversion = A(products)/[A(products)+A(SM)/2] = (0.3+0.3)/[0.6+0.5] = 55%

Total amount of SM final = 85.4 × 0.45 = 38.4 µmol

The amount of **1** in the final starting material crude can be calculated using the expression n(**1**)/[n(**1**)+n(**1-d$_2$**)] = 0.66/2 = 33%

Thus, n(**1**) = 12.7 µmol and n(**1-d$_2$**) = 25.7 µmol

Therefore, n(**1**) that reacted is 45.8 – 12.7 = 33.1 µmol and for **1-d$_2$** is 39.6 – 25.7 = 13.9

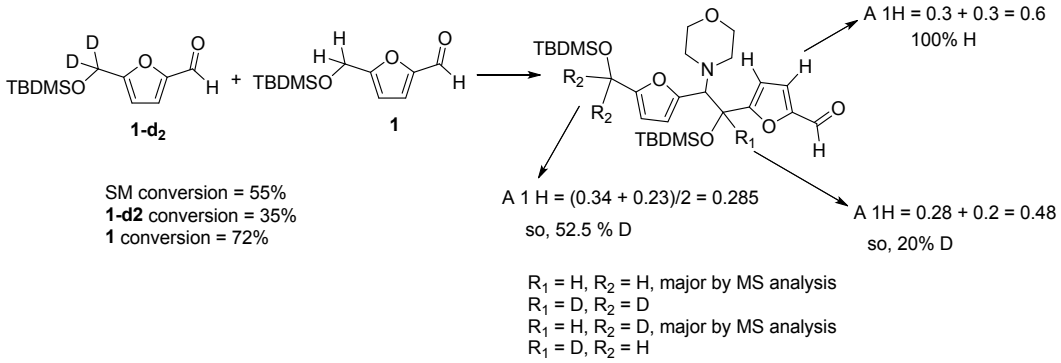
Accordingly, SM KIE = k_H/k_D = 33.1/13.9 = 2.4

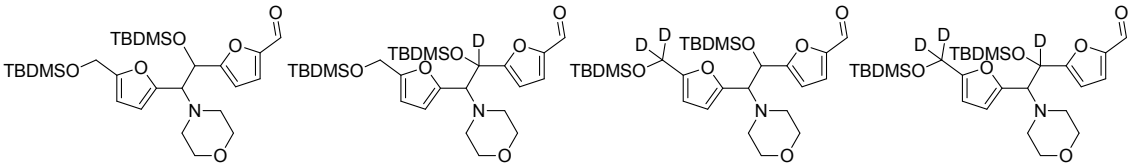
This kinetic isotope effect is relative to the starting material conversion, however this is not the desired KIE since the reaction involves two molecules of the starting material. In fact, the enrichment of the isotope is different for R_1 (trienamine) and for R_2 (iminium) as shown by the different areas of the peaks in the products. To calculate this two different KIE, the area of the corresponding atoms was used.

A 1H furan (products) = 0.3 + 0.3 = 0.6

KIE for R_1 = 0.48/(0.6-0.48) = 4.0

KIE for R_2 = 0.57/(0.6×2-0.57) = 0.9


1-d2
1
SM conversion = 55%
1-d2 conversion = 35%
1 conversion = 72%
A 1H = 0.3 + 0.3 = 0.6
100% H
A 1 H = (0.34 + 0.23)/2 = 0.285
so, 52.5 % D
A 1H = 0.28 + 0.2 = 0.48
so, 20% D
R1 = H, R2 = H, major by MS analysis
R1 = D, R2 = D
R1 = H, R2 = D, major by MS analysis
R1 = D, R2 = H

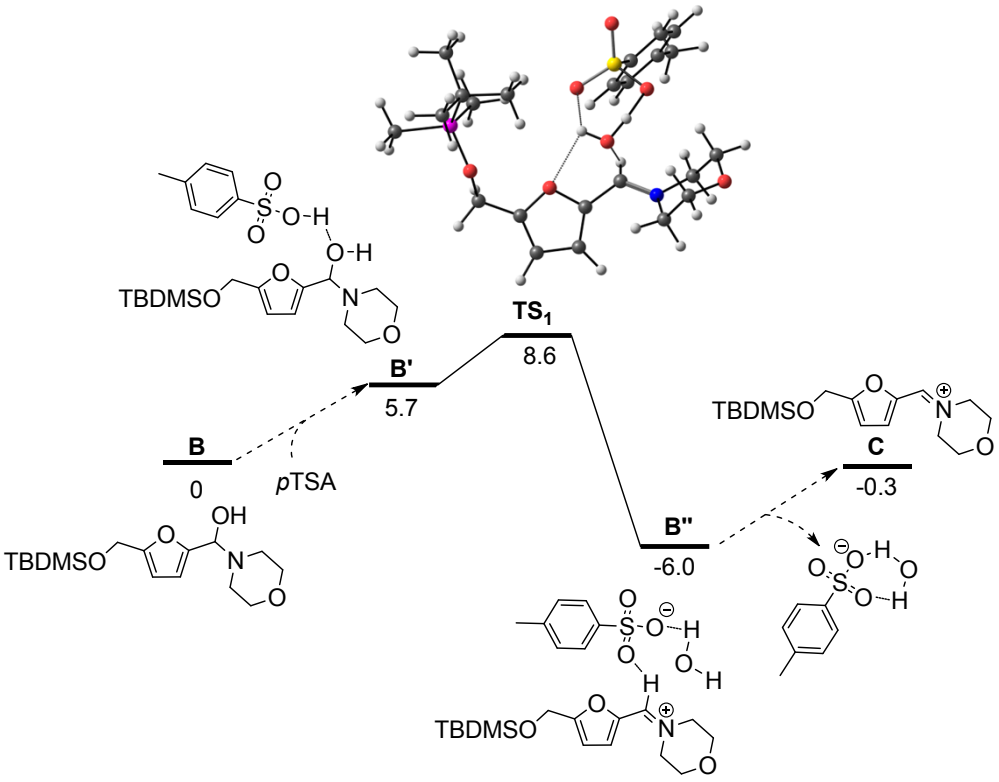

+MS m/z: 550.3020
+MS m/z: 551.3083
+MS m/z: 552.3146
+MS m/z: 553.3208

10. DFT Calculations

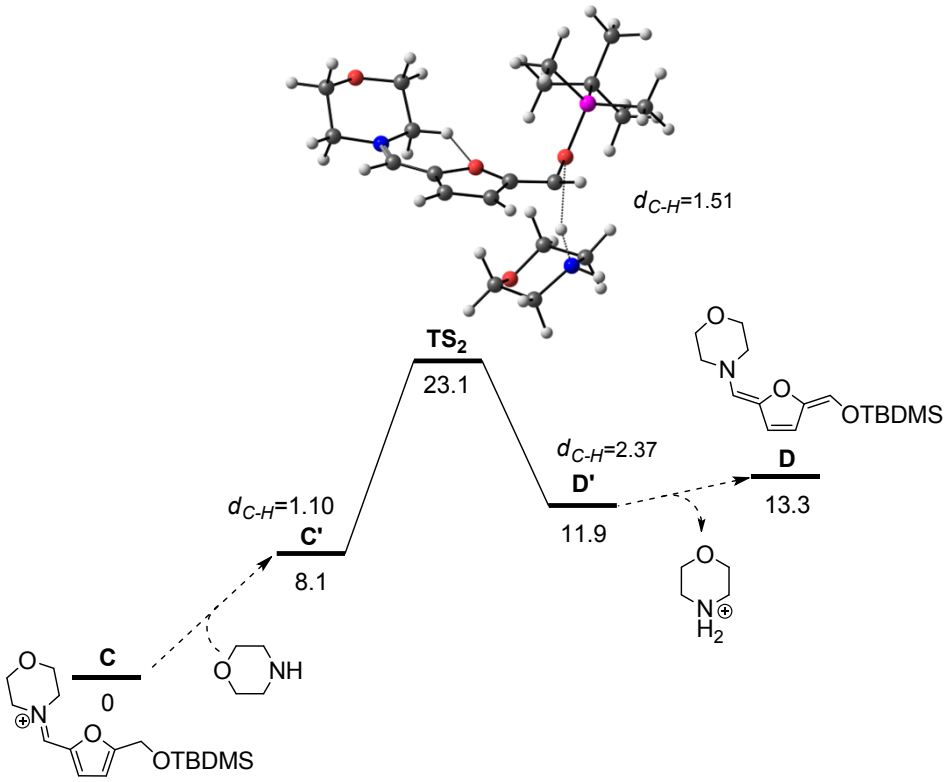
Computational Details

All calculations were performed using the Gaussian 09 software package.[11] The optimized geometries were obtained using B3LYP[12] functional and a standard 6-31G(d,p) basis set,[13] without symmetry constraints. B3LYP functional includes the Becke three parameter hybrid functional devised by Becke in 1993[12] and the correlation functional LYP of Lee, Yang, and Parr, which includes both local and non-local terms[14]. Transition state optimizations were performed with the Synchronous Transit-Guided Quasi-Newton Method (STQN) developed by Schlegel *et al.*,[15] following extensive searches of the potential energy surface. Frequency calculations were performed to confirm the nature of the stationary points, yielding one imaginary frequency for the transition states and none for the minima. Each transition state was further confirmed by following its vibrational mode downhill on both sides and obtaining the minima presented on the energy profile. Single point energy (E2) calculations were performed using M06-2X functional and the 6-311++G(d,p)[16] basis set, with solvent effects (acetonitrile) calculated by means of the Polarizable Continuum Model (PCM) initially devised by Tomasi and coworkers,[17] with radii and non-electrostatic terms of the SMD solvation model, developed by Truhler *et al.*[18] M06-2X is a hybrid meta-GGA functional developed by Truhlar and Zhao,[19] and it was shown to perform very well for main-group kinetics, providing a good description of long range effects such as van der Waals interactions or π–π stacking.[20] The electronic energies (E_1) obtained at the B3LYP/6-31G(d,p) level of theory were converted to free energy at 298.15 K and 1 atm (G_1) by using zero point energy and thermal energy corrections based on structural and vibration frequency data calculated at the same level. The free energy values presented along the text (G_2^{soln}) were derived from the electronic energy values obtained at the M06-2X/6-311++G(d,p)//B3LYP/6-31G(d,p) level, including solvent effects (E_2^{soln}), according to the following expression: $G_2^{soln} = E_2^{soln} + G_1 - E_1$.

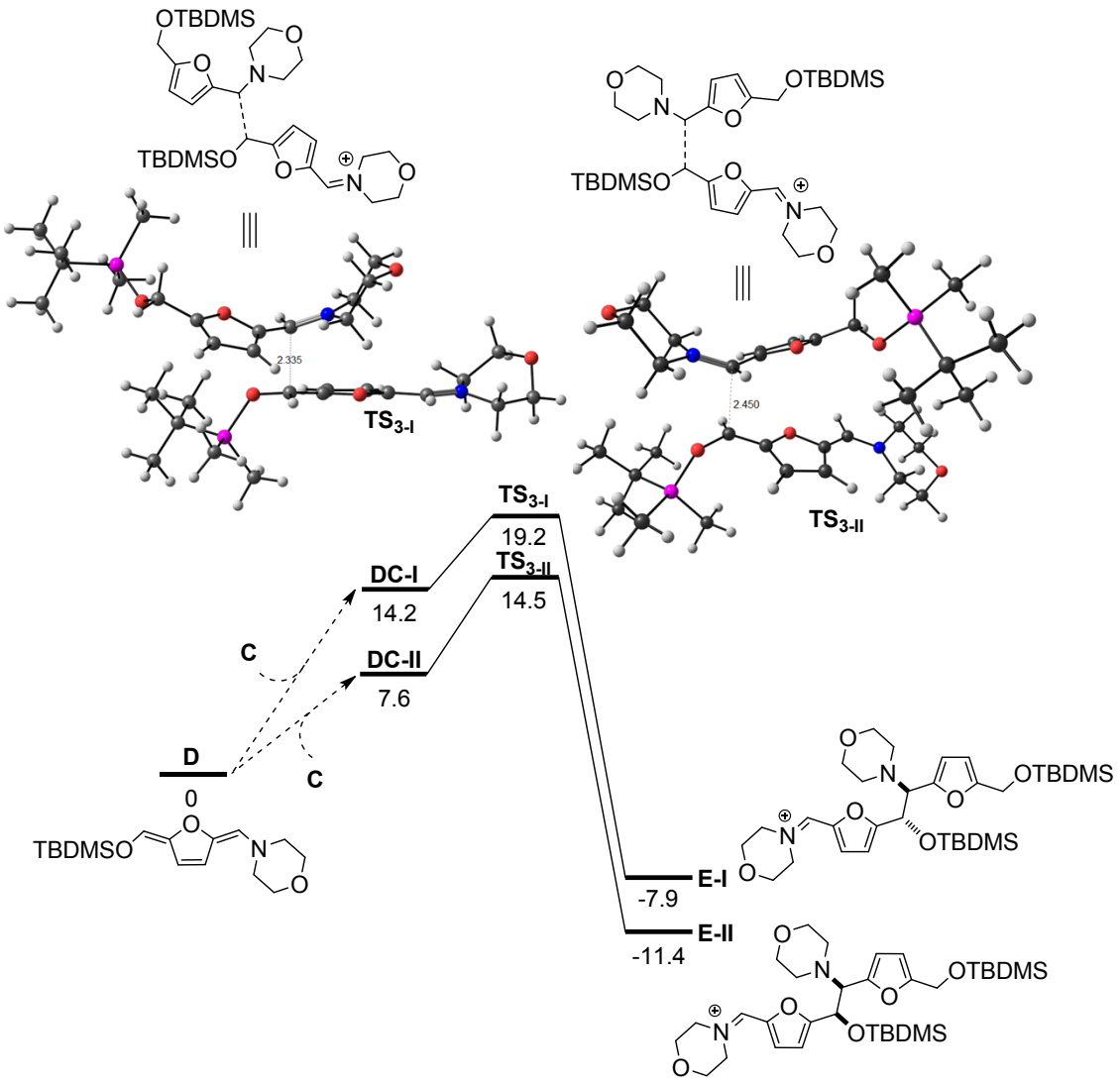
Results



Free energy profile (kcal.mol^{-1}) calculated for the formation of iminium-ion **C** by dehydration of aminal **B** catalyzed by *para*-toluenesulfonic acid (PTSA). The minima and the transition state were optimized and the energy values are referred to **B** after thermal correction to Gibbs Free Energy in acetonitrile. PTSA was used as the acid due to computational convenience.



Free energy profile profile (kcal.mol^{-1}) calculated for the conversion of iminium-ion **C** into trienamine D using morpholine as a base. The minima and the transition state were optimized and the energy values are referred to **C** after thermal correction to Gibbs Free Energy in acetonitrile. The lengths (Å) of the *C-H* that is being broken are indicated for the relevant structures.



Free energy profile (kcal.mol^{-1}) calculated for the reaction of trienamine **D** with iminium-ion **C** to yield the two diastereoisomers **E-I** and **E-II**. The minima and the transition state were optimized and the energy values are referred to **D** after thermal correction to Gibbs Free Energy in acetonitrile.

Atomic coordinates for all the optimized species

A

6	1.868295000	0.040588000	-0.006053000
6	1.986515000	1.405285000	0.008894000
6	3.382846000	1.673583000	0.014200000
6	4.022322000	0.456795000	0.002026000
8	3.086687000	-0.549952000	-0.010452000
6	0.688293000	-0.878712000	-0.016653000
6	5.433197000	0.117050000	0.001164000
8	5.890121000	-1.012845000	-0.010471000
8	-0.491728000	-0.107297000	-0.011517000
14	-2.054877000	-0.750614000	0.009950000
6	-3.189321000	0.784440000	-0.008627000
6	-2.306102000	-1.839377000	-1.512674000
6	-2.280889000	-1.791435000	1.569612000
6	-4.669149000	0.342733000	0.010140000
6	-2.923638000	1.615377000	-1.282643000
6	-2.907002000	1.662090000	1.230104000
1	1.169073000	2.108824000	0.015611000
1	3.865874000	2.640864000	0.025708000
1	0.746356000	-1.525605000	-0.906401000
1	0.746032000	-1.542323000	0.860890000
1	6.089370000	1.014822000	0.012797000
1	-2.136620000	-1.283182000	-2.440053000
1	-3.324522000	-2.241811000	-1.545483000
1	-1.623247000	-2.696257000	-1.509741000
1	-2.094245000	-1.206926000	2.475928000
1	-3.298878000	-2.191201000	1.632552000
1	-1.598851000	-2.648938000	1.581453000
1	-5.327711000	1.221493000	0.000614000
1	-4.916201000	-0.235946000	0.907615000
1	-4.929772000	-0.265390000	-0.863609000
1	-1.880492000	1.941654000	-1.340476000
1	-3.149383000	1.051745000	-2.194778000
1	-3.556507000	2.513101000	-1.289863000
1	-3.543548000	2.557198000	1.214762000
1	-1.864789000	1.995220000	1.260108000
1	-3.116505000	1.131488000	2.165643000

Morpholine

7	0.000022000	1.364253000	-0.325703000
6	-1.205274000	0.718372000	0.199902000
6	-1.174857000	-0.755696000	-0.198392000
8	0.000057000	-1.394054000	0.291929000
6	1.174829000	-0.755606000	-0.198403000
6	1.205195000	0.718497000	0.199925000
1	-0.000040000	2.351997000	-0.087755000
1	-2.091079000	1.200227000	-0.229801000
1	-1.283322000	0.780981000	1.301533000
1	-1.220631000	-0.836479000	-1.296396000
1	-2.023432000	-1.295895000	0.231513000
1	2.023435000	-1.295620000	0.231659000
1	1.220991000	-0.836766000	-1.296422000
1	1.283057000	0.780508000	1.301600000
1	2.091046000	1.200300000	-0.229639000

B

6	-0.077992000	-2.315595000	-0.204253000
6	0.563378000	-3.032352000	-1.170940000
6	1.957243000	-2.723894000	-1.056179000
6	2.068635000	-1.830792000	-0.032434000
8	0.836016000	-1.581165000	0.505486000
6	-1.505031000	-2.179105000	0.193492000
6	3.239884000	-1.121596000	0.589854000
7	3.451715000	0.224395000	0.047775000
8	-1.988955000	-0.885059000	-0.148615000
14	-3.470346000	-0.231800000	0.311740000
6	-3.351527000	1.590432000	-0.249020000
6	-4.876654000	-1.152583000	-0.552940000
6	-3.699008000	-0.386834000	2.182440000
6	-4.671675000	2.331842000	0.052246000
6	-3.068584000	1.648995000	-1.765855000
6	-2.195128000	2.283874000	0.503087000
6	4.387186000	0.995270000	0.880371000
6	4.753227000	2.293854000	0.169409000
8	3.596488000	3.067261000	-0.119224000
6	2.682882000	2.326930000	-0.918591000
6	2.256309000	1.026955000	-0.239203000
8	4.432104000	-1.866180000	0.400834000
1	0.097500000	-3.704021000	-1.877922000
1	2.769501000	-3.125385000	-1.643456000
1	-2.076335000	-2.962959000	-0.322285000
1	-1.603514000	-2.350099000	1.275334000
1	3.078041000	-1.097057000	1.681453000
1	-4.904669000	-2.205490000	-0.250140000
1	-4.768124000	-1.125132000	-1.641659000
1	-5.850782000	-0.718730000	-0.301500000
1	-4.624766000	0.103497000	2.503714000
1	-3.767670000	-1.435103000	2.494002000
1	-2.871311000	0.070027000	2.734209000
1	-5.521591000	1.893960000	-0.483582000
1	-4.598567000	3.382401000	-0.259942000
1	-4.912476000	2.329475000	1.121704000
1	-2.970308000	2.692544000	-2.095298000
1	-2.140924000	1.127287000	-2.020397000
1	-3.878007000	1.199095000	-2.352052000
1	-2.367649000	2.308014000	1.584824000
1	-1.241104000	1.776520000	0.327644000
1	-2.090419000	3.324486000	0.166764000
1	3.942531000	1.235374000	1.864135000
1	5.282277000	0.391331000	1.052262000
1	5.393271000	2.913205000	0.804474000
1	5.298361000	2.061487000	-0.760352000
1	1.815410000	2.973123000	-1.079870000
1	3.136412000	2.093862000	-1.895955000
1	1.688553000	1.267165000	0.677012000
1	1.593160000	0.473586000	-0.908268000

1	4.731929000	-1.629282000	-0.490395000

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6	2.670598000	0.007596000	0.027725000
6	-0.120429000	-0.007865000	-0.075580000
6	1.959651000	-1.201160000	0.032181000
6	1.948875000	1.208609000	-0.032089000
6	0.568485000	-1.220243000	-0.023088000
6	0.557471000	1.211787000	-0.084576000
6	4.179429000	0.015491000	0.052273000
16	-1.901469000	-0.017587000	-0.131491000
8	-2.280145000	-0.076404000	1.473152000
8	-2.344094000	-1.271457000	-0.724532000
8	-2.384399000	1.277707000	-0.614801000
1	2.503019000	-2.140957000	0.075348000
1	2.483810000	2.154267000	-0.041281000
1	0.021314000	-2.156214000	-0.034537000
1	0.001144000	2.140538000	-0.145112000
1	4.576144000	-0.866846000	0.561962000
1	4.567139000	0.905230000	0.556313000
1	4.585725000	0.014776000	-0.966628000
1	-2.830173000	0.706541000	1.646152000

B’

6	-5.535266000	-2.778504000	-1.179590000
6	-3.532831000	-1.461831000	0.258996000
6	-4.278807000	-2.540457000	-1.753445000
6	-5.763605000	-2.343499000	0.134226000
6	-3.274290000	-1.885534000	-1.044214000
6	-4.771258000	-1.690775000	0.860395000
6	-6.609180000	-3.514457000	-1.943392000
16	-2.264324000	-0.608370000	1.178253000
8	-0.949037000	-0.939707000	0.596738000
8	-2.500818000	-0.821631000	2.602052000
8	-2.576441000	0.927296000	0.800447000
6	2.876569000	0.814999000	-2.096335000
6	3.297901000	2.012748000	-2.591698000
6	2.306827000	2.984859000	-2.232252000
6	1.353382000	2.313704000	-1.528406000
8	1.678159000	0.986382000	-1.450826000
6	3.428285000	-0.569824000	-2.123577000
6	0.029692000	2.692727000	-0.923948000
8	-0.199039000	1.858208000	0.265752000
7	-0.045307000	4.080971000	-0.641838000
6	-1.373350000	4.704764000	-0.595045000
6	-1.956473000	4.762470000	0.821401000
8	-1.044888000	5.399780000	1.708317000
6	0.192192000	4.692611000	1.766416000
6	0.852853000	4.633222000	0.385411000
8	3.698826000	-1.025887000	-0.810383000
14	3.365780000	-2.560243000	-0.189269000
6	3.506769000	-2.329512000	1.700321000
6	1.644156000	-3.125346000	-0.719561000
6	4.642766000	-3.787580000	-0.853448000
6	2.510469000	-1.244291000	2.164029000
6	4.939067000	-1.884840000	2.068064000
6	3.185991000	-3.657260000	2.420247000
1	-4.082494000	-2.875768000	-2.768161000
1	-6.730611000	-2.522618000	0.596445000
1	-2.298456000	-1.715487000	-1.485185000
1	-4.943473000	-1.368797000	1.881311000
1	-6.440991000	-3.462553000	-3.022431000
1	-7.601520000	-3.104806000	-1.732335000
1	-6.630492000	-4.575093000	-1.664555000
1	-1.689113000	1.377515000	0.603312000
1	4.212329000	2.185315000	-3.141086000
1	2.301513000	4.040239000	-2.458620000
1	2.716064000	-1.232941000	-2.636971000
1	4.348844000	-0.553969000	-2.722178000
1	-0.777169000	2.460887000	-1.633975000
1	0.211318000	0.981452000	0.142377000
1	-2.048963000	4.168454000	-1.269869000
1	-1.274965000	5.733038000	-0.968194000
1	-2.200692000	3.751324000	1.183044000
1	-2.872740000	5.361403000	0.833063000
1	0.826815000	5.241266000	2.469413000
1	0.032775000	3.675214000	2.150291000
1	1.126583000	5.652558000	0.081821000
1	1.767043000	4.036451000	0.423443000
1	1.431398000	-4.117884000	-0.306507000
1	1.564138000	-3.214471000	-1.809230000
1	0.859078000	-2.445716000	-0.375024000
1	5.664713000	-3.471953000	-0.621483000
1	4.496332000	-4.788426000	-0.432064000
1	4.566057000	-3.880863000	-1.942978000
1	2.589422000	-1.097112000	3.249983000
1	1.471297000	-1.510678000	1.944947000
1	2.717791000	-0.283423000	1.682180000
1	5.018013000	-1.717660000	3.151119000
1	5.686865000	-2.640377000	1.800838000
1	5.211084000	-0.950469000	1.566648000
1	2.164244000	-3.997430000	2.218172000
1	3.873019000	-4.461400000	2.131040000
1	3.275099000	-3.530569000	3.507618000

TS_1

6	4.813675000	-3.260955000	1.353744000
6	2.855916000	-2.085326000	-0.276284000
6	3.598298000	-2.823157000	1.893648000
6	5.025568000	-3.099845000	-0.024077000
6	2.619568000	-2.238941000	1.088530000
6	4.056958000	-2.522237000	-0.839943000
6	5.858132000	-3.922282000	2.221213000
16	1.624859000	-1.309069000	-1.330347000
8	0.365872000	-1.238898000	-0.522466000
8	1.572485000	-2.079508000	-2.577833000
8	2.152654000	0.121178000	-1.532060000
6	-2.400147000	1.551217000	2.135195000
6	-2.207797000	2.785346000	2.686954000

6	-0.942705000	3.254919000	2.213102000
6	-0.453572000	2.275762000	1.393264000
8	-1.328986000	1.226894000	1.355716000
6	-3.484459000	0.526502000	2.232715000
6	0.800707000	2.053490000	0.655575000
8	0.169729000	1.495641000	-0.937657000
7	1.659302000	3.071206000	0.453228000
6	3.081461000	2.802060000	0.166240000
6	3.441032000	3.184314000	-1.271702000
8	3.062382000	4.530120000	-1.546508000
6	1.661411000	4.696846000	-1.401030000
6	1.218656000	4.413365000	0.039023000
8	-3.953701000	0.177066000	0.949545000
14	-4.134147000	-1.395757000	0.341792000
6	-4.258002000	-1.146336000	-1.546664000
6	-2.665913000	-2.467975000	0.839423000
6	-5.715249000	-2.138256000	1.066935000
6	-2.979461000	-0.451379000	-2.064706000
6	-5.481012000	-0.266070000	-1.883044000
6	-4.408039000	-2.515535000	-2.245338000
1	3.411076000	-2.947058000	2.957441000
1	5.960637000	-3.438343000	-0.463459000
1	1.669119000	-1.919881000	1.501944000
1	4.219010000	-2.419381000	-1.907609000
1	5.732608000	-3.655583000	3.274444000
1	6.870056000	-3.637678000	1.916545000
1	5.795109000	-5.015211000	2.150339000
1	1.024422000	0.995517000	-1.312984000
1	-2.888300000	3.302519000	3.347463000
1	-0.460123000	4.188277000	2.461751000
1	-3.098012000	-0.348584000	2.776969000
1	-4.295579000	0.951937000	2.838876000
1	1.295499000	1.115938000	0.899260000
1	-0.388790000	0.711745000	-0.740011000
1	3.286410000	1.742988000	0.332365000
1	3.681076000	3.400122000	0.863628000
1	2.963645000	2.489876000	-1.976300000
1	4.524023000	3.127233000	-1.409883000
1	1.435294000	5.734950000	-1.661409000
1	1.116630000	4.031526000	-2.088108000
1	1.671152000	5.152291000	0.712021000
1	0.133610000	4.479552000	0.119410000
1	-2.808461000	-3.486733000	0.461087000
1	-2.573787000	-2.550644000	1.928909000
1	-1.715566000	-2.096960000	0.443351000
1	-6.589213000	-1.514401000	0.855580000
1	-5.910204000	-3.138462000	0.664417000
1	-5.636388000	-2.238252000	2.155774000
1	-3.044150000	-0.300671000	-3.150904000
1	-2.078699000	-1.043193000	-1.870569000
1	-2.848064000	0.533244000	-1.602869000
1	-5.538257000	-0.094475000	-2.966707000
1	-6.423497000	-0.735957000	-1.578880000
1	-5.420118000	0.711829000	-1.394358000
1	-3.545926000	-3.166029000	-2.062218000
1	-5.309869000	-3.048572000	-1.921585000
1	-4.484809000	-2.379328000	-3.332377000

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6	-5.790083000	-2.778552000	-0.337409000
6	-3.401931000	-1.306949000	-0.224860000
6	-5.072171000	-2.482026000	-1.504068000
6	-5.289615000	-2.311830000	0.885627000
6	-3.885252000	-1.753297000	-1.455273000
6	-4.103692000	-1.582346000	0.948995000
6	-7.058144000	-3.597138000	-0.394681000
16	-1.835155000	-0.426890000	-0.147076000
8	-1.743865000	0.328438000	-1.442721000
8	-0.766339000	-1.440317000	0.025397000
8	-1.970480000	0.498181000	1.032842000
6	3.503046000	1.265973000	-1.371651000
6	3.922024000	2.553359000	-1.120788000
6	2.760245000	3.311192000	-0.855174000
6	1.685332000	2.442684000	-0.956398000
8	2.159811000	1.196107000	-1.293955000
6	4.237977000	-0.011192000	-1.642553000
6	0.264573000	2.505452000	-0.918388000
8	0.325920000	1.743666000	1.877120000
7	-0.486641000	3.478016000	-0.477486000
6	-1.955839000	3.439935000	-0.690819000
6	-2.694806000	3.683871000	0.624739000
8	-2.247358000	4.890938000	1.236881000
6	-0.875719000	4.783380000	1.568579000
6	-0.005275000	4.623905000	0.310596000
8	4.246558000	-0.820732000	-0.491534000
14	3.559373000	-2.361924000	-0.275738000
6	3.074801000	-2.398244000	1.571630000
6	2.092124000	-2.616196000	-1.424819000
6	4.898379000	-3.636939000	-0.673364000
6	2.201001000	-1.167774000	1.900959000
6	4.341520000	-2.374959000	2.453117000
6	2.264987000	-3.679652000	1.869652000
1	-5.450698000	-2.822044000	-2.465089000
1	-5.838868000	-2.518144000	1.801120000
1	-3.340748000	-1.511050000	-2.361382000
1	-3.727699000	-1.208418000	1.894958000
1	-7.589938000	-3.447790000	-1.339243000
1	-7.738948000	-3.340037000	0.422333000
1	-6.840545000	-4.669419000	-0.310897000
1	-0.479137000	1.224601000	1.645511000
1	4.944388000	2.901478000	-1.124131000
1	2.720169000	4.368935000	-0.644967000
1	3.771335000	-0.508488000	-2.503959000
1	5.267337000	0.244980000	-1.924610000
1	-0.271539000	1.637400000	-1.321741000
1	0.852430000	1.135658000	2.410204000
1	-2.212433000	2.467010000	-1.116401000
1	-2.190087000	4.241631000	-1.401445000
1	-2.556070000	2.820978000	1.286175000
1	-3.760911000	3.805726000	0.417569000
1	-0.590664000	5.707142000	2.080163000

1	-0.686777000	3.922978000	2.224145000
1	-0.059584000	5.523902000	-0.313019000
1	1.023114000	4.437833000	0.612085000
1	1.784848000	-3.667739000	-1.383288000
1	2.343940000	-2.407622000	-2.471372000
1	1.221636000	-2.013526000	-1.146689000
1	5.816961000	-3.448370000	-0.109021000
1	4.563722000	-4.654081000	-0.439842000
1	5.152854000	-3.615701000	-1.739294000
1	1.927680000	-1.185340000	2.966821000
1	1.273858000	-1.157453000	1.319356000
1	2.741943000	-0.235600000	1.705434000
1	4.063498000	-2.365347000	3.516206000
1	4.972878000	-3.255796000	2.290923000
1	4.951911000	-1.485045000	2.263541000
1	1.322470000	-3.699911000	1.313300000
1	2.826309000	-4.591277000	1.630305000
1	2.014246000	-3.727167000	2.938069000

[*p*TSA-OH]$^-$

6	2.878534000	0.176821000	-0.002904000
6	0.107774000	-0.323623000	0.001127000
6	2.385423000	-1.131275000	-0.008203000
6	1.952988000	1.233338000	0.002868000
6	1.010204000	-1.383485000	-0.005788000
6	0.581771000	0.994729000	0.005011000
6	4.364764000	0.454739000	0.003553000
16	-1.681775000	-0.637187000	0.002026000
8	-1.816157000	-2.113383000	0.011197000
8	-2.168715000	0.025738000	-1.247455000
8	-2.169219000	0.040585000	1.243547000
1	3.085455000	-1.965354000	-0.014549000
1	2.316602000	2.259877000	0.005085000
1	0.617803000	-2.394952000	-0.009790000
1	-0.131054000	1.816531000	0.007956000
1	4.943812000	-0.470090000	-0.084372000
1	4.679778000	0.954290000	0.928870000
1	4.657476000	1.110668000	-0.825686000
8	-2.364096000	2.641604000	-0.006774000
1	-2.404604000	1.997396000	0.724343000
1	-2.400134000	2.002809000	-0.742380000

C

6	0.032588000	2.434266000	0.186482000
6	0.654436000	3.650053000	-0.037608000
6	2.002279000	3.364765000	-0.305616000
6	2.139729000	1.980384000	-0.240712000
8	0.919024000	1.426649000	0.069298000
6	-1.369496000	2.073922000	0.570600000
6	3.289522000	1.205242000	-0.467077000
7	3.459840000	-0.097470000	-0.474482000
8	-1.671699000	0.782783000	0.128785000
14	-3.228474000	0.080261000	0.271270000
6	-3.015989000	-1.647470000	-0.503977000
6	-3.692884000	0.016933000	2.097246000
6	-4.454172000	1.160496000	-0.667203000
6	-4.376646000	-2.380285000	-0.499742000
6	-1.995802000	-2.472063000	0.310382000
6	-2.513757000	-1.514015000	-1.958093000
6	4.797785000	-0.687155000	-0.706808000
6	5.147973000	-1.624902000	0.457486000
8	4.147807000	-2.611924000	0.616331000
6	2.889523000	-2.037565000	0.917139000
6	2.418353000	-1.119808000	-0.220201000
1	0.180528000	4.620309000	-0.015507000
1	2.789039000	4.070813000	-0.534564000
1	-1.449640000	2.160161000	1.668815000
1	-2.033597000	2.843206000	0.147698000
1	4.181529000	1.789433000	-0.678495000
1	-3.775542000	1.019360000	2.532300000
1	-2.966147000	-0.546572000	2.690978000
1	-4.668584000	-0.463617000	2.227892000
1	-5.459645000	0.728623000	-0.622239000
1	-4.526900000	2.166682000	-0.239162000
1	-4.185783000	1.264777000	-1.723026000
1	-4.772531000	-2.513277000	0.513256000
1	-4.268664000	-3.380458000	-0.938008000
1	-5.131876000	-1.849816000	-1.089811000
1	-1.862985000	-3.463905000	-0.140730000
1	-1.014387000	-1.984443000	0.338700000
1	-2.322464000	-2.626100000	1.344204000
1	-3.223035000	-0.968995000	-2.590069000
1	-1.552590000	-0.991553000	-2.008140000
1	-2.379792000	-2.507413000	-2.405874000
1	4.753664000	-1.258120000	-1.640016000
1	5.533297000	0.113407000	-0.810282000
1	6.083969000	-2.143571000	0.238526000
1	5.276620000	-1.040340000	1.381786000
1	2.179708000	-2.859247000	1.034010000
1	2.931572000	-1.471483000	1.860416000
1	2.312333000	-1.702775000	-1.141338000
1	1.469938000	-0.643321000	0.013182000

C'

6	-0.313601000	0.478533000	2.193083000
6	0.035689000	0.299383000	3.519567000
6	1.314818000	-0.282906000	3.524864000
6	1.688570000	-0.440646000	2.193348000
8	0.677103000	0.030663000	1.390112000
6	-1.488168000	1.109050000	1.509463000
6	2.904427000	-0.925734000	1.677335000
7	3.307986000	-1.078772000	0.437171000
8	-1.916355000	0.338758000	0.409396000
14	-3.267191000	-0.705749000	0.420935000
6	-3.314145000	-1.415967000	-1.347369000
6	-2.994292000	-2.040065000	1.729326000
6	-4.804491000	0.295587000	0.849327000
6	-4.457350000	-2.451017000	-1.453679000

6	-1.973835000	-2.108433000	-1.676892000
6	-3.559668000	-0.283107000	-2.367866000
6	4.700071000	-1.495755000	0.147297000
6	4.704629000	-2.645211000	-0.865582000
8	4.007993000	-2.267664000	-2.035850000
6	2.648479000	-1.994149000	-1.752285000
6	2.495789000	-0.819176000	-0.776877000
1	-0.568185000	0.562810000	4.375324000
1	1.905194000	-0.562556000	4.386975000
1	-2.269597000	1.273202000	2.263707000
1	-1.168456000	2.096695000	1.134459000
1	3.632748000	-1.191701000	2.439382000
1	-2.860105000	-1.604603000	2.726130000
1	-2.115373000	-2.655768000	1.512505000
1	-3.859604000	-2.708534000	1.789927000
1	-5.699784000	-0.334473000	0.813257000
1	-4.753882000	0.715064000	1.860290000
1	-4.953290000	1.125482000	0.152085000
1	-4.313957000	-3.298146000	-0.773909000
1	-4.505520000	-2.857329000	-2.471966000
1	-5.435997000	-2.008382000	-1.237902000
1	-1.999936000	-2.519759000	-2.694334000
1	-1.136178000	-1.404108000	-1.623745000
1	-1.763318000	-2.941113000	-0.995949000
1	-4.524097000	0.211252000	-2.209557000
1	-2.778005000	0.482688000	-2.320665000
1	-3.567429000	-0.687459000	-3.388392000
1	5.218723000	-0.631349000	-0.281076000
1	5.190273000	-1.781029000	1.080783000
1	5.733780000	-2.869421000	-1.154976000
1	4.261024000	-3.546909000	-0.415112000
1	2.167721000	-1.733416000	-2.697481000
1	2.152231000	-2.887167000	-1.341692000
1	2.845990000	0.117033000	-1.226860000
1	1.454048000	-0.693830000	-0.494995000
7	-0.248720000	3.894772000	-0.414192000
6	1.146123000	4.301596000	-0.206517000
6	2.027382000	3.060598000	-0.313668000
8	1.866299000	2.397137000	-1.567136000
6	0.497376000	2.085838000	-1.850153000
6	-0.397655000	3.317151000	-1.756874000
1	-0.861994000	4.699530000	-0.314584000
1	1.485369000	5.044092000	-0.948984000
1	1.255942000	4.744393000	0.789261000
1	3.085377000	3.329360000	-0.244411000
1	1.779301000	2.373889000	0.511676000
1	0.485639000	1.675013000	-2.863536000
1	0.124869000	1.323351000	-1.150387000
1	-0.119279000	4.027567000	-2.553946000
1	-1.439626000	3.019534000	-1.912528000

TS_2

6	-0.199035000	1.140956000	1.748319000
6	0.319465000	1.947549000	2.798461000
6	1.689612000	1.949551000	2.668321000
6	2.024979000	1.161423000	1.544697000
8	0.835258000	0.679562000	0.991371000
6	-1.526226000	0.896523000	1.344278000
6	3.278509000	0.864651000	1.051556000
7	3.673271000	0.114971000	0.015781000
8	-1.770246000	-0.118756000	0.408872000
14	-2.221714000	-1.703429000	0.880573000
6	-2.311095000	-2.685059000	-0.753912000
6	-0.922407000	-2.388341000	2.064134000
6	-3.887609000	-1.613826000	1.760424000
6	-2.709988000	-4.146579000	-0.445241000
6	-0.936095000	-2.674997000	-1.456368000
6	-3.363403000	-2.065714000	-1.698596000
6	5.099466000	-0.002872000	-0.329059000
6	5.476187000	-1.479201000	-0.485836000
8	4.634951000	-2.109885000	-1.437125000
6	3.276554000	-2.064847000	-1.034568000
6	2.786125000	-0.618894000	-0.901088000
1	-0.270536000	2.429674000	3.564331000
1	2.405413000	2.443679000	3.311951000
1	-2.257848000	0.987184000	2.153670000
1	-1.905330000	2.103898000	0.514245000
1	4.090474000	1.325722000	1.606562000
1	-0.818422000	-1.753409000	2.950498000
1	0.062724000	-2.469359000	1.594952000
1	-1.207937000	-3.385507000	2.415689000
1	-4.215081000	-2.612481000	2.068506000
1	-3.831844000	-1.006098000	2.670353000
1	-4.670731000	-1.191803000	1.122859000
1	-1.983478000	-4.644808000	0.206031000
1	-2.763557000	-4.727831000	-1.374507000
1	-3.692621000	-4.214058000	0.034033000
1	-0.984334000	-3.239375000	-2.396596000
1	-0.612661000	-1.656182000	-1.697429000
1	-0.160193000	-3.140770000	-0.838068000
1	-4.364742000	-2.063117000	-1.254702000
1	-3.110635000	-1.033937000	-1.967095000
1	-3.423924000	-2.641146000	-2.631319000
1	5.276227000	0.519994000	-1.277547000
1	5.701181000	0.472716000	0.449253000
1	6.500148000	-1.566476000	-0.856996000
1	5.409486000	-1.987207000	0.489214000
1	2.698984000	-2.581458000	-1.804961000
1	3.139168000	-2.593027000	-0.077541000
1	2.827702000	-0.129537000	-1.882913000
1	1.763020000	-0.587191000	-0.533531000
7	-2.371186000	2.971536000	-0.240053000
6	-1.394407000	4.090492000	-0.417093000
6	-0.219932000	3.603775000	-1.265780000
8	-0.668979000	3.093384000	-2.508868000
6	-1.524673000	1.972109000	-2.325263000
6	-2.777806000	2.365767000	-1.548725000
1	-3.200776000	3.316854000	0.245398000
1	-1.898177000	4.924009000	-0.917187000
1	-1.062379000	4.414762000	0.572983000
1	0.445557000	4.442581000	-1.483002000

1	0.350861000	2.838248000	-0.717712000
1	-1.803846000	1.618396000	-3.320078000
1	-1.003110000	1.162784000	-1.794316000
1	-3.357796000	3.103903000	-2.112592000
1	-3.398781000	1.493585000	-1.336513000

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6	-0.036755000	0.329949000	2.345086000
6	0.601037000	0.772100000	3.564075000
6	1.939391000	0.817465000	3.331421000
6	2.190436000	0.416561000	1.980951000
8	0.942901000	0.139925000	1.382812000
6	-1.347296000	0.120894000	2.067816000
6	3.395208000	0.267367000	1.360873000
7	3.734588000	-0.215036000	0.132698000
8	-1.777803000	-0.276754000	0.798795000
14	-2.452803000	-1.865956000	0.572140000
6	-2.667612000	-2.028502000	-1.318670000
6	-1.237959000	-3.107853000	1.283439000
6	-4.087012000	-1.915835000	1.501557000
6	-3.331440000	-3.393601000	-1.619101000
6	-1.294823000	-1.971878000	-2.022934000
6	-3.571493000	-0.908490000	-1.876083000
6	5.088449000	0.011499000	-0.385658000
6	5.539306000	-1.191783000	-1.213848000
8	4.599127000	-1.475369000	-2.240952000
6	3.331590000	-1.794335000	-1.691556000
6	2.766437000	-0.622165000	-0.885708000
1	0.080966000	0.995708000	4.484467000
1	2.713092000	1.089847000	4.037210000
1	-2.108262000	0.258259000	2.828223000
1	-1.231834000	2.479933000	0.809187000
1	4.247010000	0.552276000	1.971170000
1	-1.093671000	-2.938165000	2.354803000
1	-0.257373000	-3.044015000	0.802937000
1	-1.608243000	-4.131106000	1.160301000
1	-4.557085000	-2.900076000	1.404464000
1	-3.936260000	-1.739079000	2.571764000
1	-4.800188000	-1.170717000	1.135459000
1	-2.728743000	-4.234545000	-1.259805000
1	-3.453049000	-3.522951000	-2.701847000
1	-4.326809000	-3.476024000	-1.169918000
1	-1.418716000	-2.065325000	-3.109301000
1	-0.772927000	-1.026771000	-1.829730000
1	-0.637745000	-2.785687000	-1.699268000
1	-4.559267000	-0.896749000	-1.403887000
1	-3.125348000	0.085202000	-1.741949000
1	-3.726677000	-1.044434000	-2.953849000
1	5.104288000	0.912482000	-1.018002000
1	5.771895000	0.171614000	0.452966000
1	6.491515000	-0.978301000	-1.705631000
1	5.667098000	-2.067743000	-0.558901000
1	2.671871000	-2.026365000	-2.532131000
1	3.404724000	-2.682936000	-1.044598000
1	2.568989000	0.218493000	-1.571904000
1	1.831125000	-0.906820000	-0.405373000
7	-1.454134000	2.197313000	-0.152827000
6	-2.643653000	2.973600000	-0.649721000
6	-2.245542000	4.435512000	-0.842054000
8	-1.131706000	4.543283000	-1.711120000
6	0.014486000	3.895387000	-1.185340000
6	-0.237016000	2.399344000	-1.017607000
1	-1.670961000	1.167420000	-0.042605000
1	-2.940609000	2.524589000	-1.599942000
1	-3.453090000	2.853944000	0.074132000
1	-3.069804000	4.983368000	-1.303426000
1	-2.027505000	4.903004000	0.132703000
1	0.828674000	4.055480000	-1.895234000
1	0.307774000	4.343958000	-0.221547000
1	-0.455208000	1.932998000	-1.981205000
1	0.591829000	1.876598000	-0.536714000

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6	2.148128000	-0.267342000	-0.198641000
6	1.659992000	1.033010000	0.207805000
6	0.304695000	1.017946000	0.161252000
6	-0.110191000	-0.289686000	-0.283107000
8	1.027185000	-1.052114000	-0.502016000
6	3.358492000	-0.865213000	-0.335467000
6	-1.335418000	-0.812231000	-0.494643000
7	4.643214000	-0.331152000	-0.249943000
8	-2.461155000	-0.043136000	-0.345169000
14	-3.954339000	-0.609042000	0.222182000
6	-5.145317000	0.846465000	-0.104638000
6	-4.440456000	-2.162420000	-0.736308000
6	-3.804063000	-1.025883000	2.055788000
6	-6.554031000	0.502818000	0.426229000
6	-4.627818000	2.113021000	0.610949000
6	-5.224569000	1.124792000	-1.621099000
6	5.636438000	-1.180761000	0.414879000
6	7.044170000	-0.693312000	0.087424000
8	7.204603000	0.675455000	0.436888000
6	6.281568000	1.481434000	-0.281430000
6	4.834188000	1.087914000	0.015782000
1	2.277425000	1.859960000	0.523475000
1	-0.375057000	1.817981000	0.416030000
1	3.341734000	-1.918091000	-0.603848000
1	-1.456822000	-1.833878000	-0.843679000
1	-5.447566000	-2.492624000	-0.458524000
1	-3.759294000	-2.993479000	-0.523104000
1	-4.430552000	-1.992567000	-1.817390000
1	-4.735926000	-1.443888000	2.452108000
1	-3.014899000	-1.769487000	2.211682000
1	-3.548079000	-0.144980000	2.652635000
1	-7.244137000	1.337067000	0.241385000
1	-6.976821000	-0.380418000	-0.066426000
1	-6.553910000	0.316278000	1.506209000
1	-5.300922000	2.959978000	0.420092000
1	-3.630372000	2.393376000	0.258488000
1	-4.575224000	1.978369000	1.697247000

1	-5.884880000	1.980488000	-1.817805000
1	-4.240321000	1.359939000	-2.038414000
1	-5.628592000	0.269341000	-2.174078000
1	5.507475000	-2.211146000	0.065964000
1	5.493337000	-1.176263000	1.509283000
1	7.244763000	-0.836476000	-0.986862000
1	7.786751000	-1.254358000	0.661708000
1	6.462605000	2.515737000	0.024621000
1	6.467306000	1.396193000	-1.364396000
1	4.592890000	1.343604000	1.063400000
1	4.167406000	1.659052000	-0.637032000

[Morpholine-H]$^+$

7	0.002343000	1.381110000	0.224422000
6	1.264451000	0.659536000	-0.230330000
6	1.173054000	-0.801380000	0.207305000
8	-0.002882000	-1.402578000	-0.300732000
6	-1.175838000	-0.796531000	0.208447000
6	-1.261923000	0.663562000	-0.231405000
1	0.002095000	1.441746000	1.249539000
1	0.004306000	2.346140000	-0.121236000
1	2.121359000	1.179267000	0.203903000
1	1.291525000	0.743543000	-1.318550000
1	1.213435000	-0.877659000	1.306347000
1	2.024312000	-1.350579000	-0.200444000
1	-2.029787000	-1.343028000	-0.197267000
1	-1.214851000	-0.870692000	1.307699000
1	-1.286710000	0.745686000	-1.319800000
1	-2.117493000	1.187312000	0.200615000

DC-II

6	-0.519046000	1.750778000	-1.529988000
6	-0.115263000	1.558678000	-2.846320000
6	1.291435000	1.495776000	-2.836576000
6	1.687025000	1.656910000	-1.524494000
8	0.608649000	1.796704000	-0.728389000
6	-1.736305000	1.836304000	-0.813944000
7	-2.921987000	2.224969000	-1.273364000
6	3.043248000	1.888809000	-0.928330000
8	3.147361000	1.392514000	0.381019000
6	-4.978911000	3.387226000	-0.568654000
6	-4.116684000	2.135330000	-0.413063000
6	-3.198927000	2.604456000	-2.665904000
6	-4.140035000	3.817112000	-2.699731000
8	-5.307026000	3.593916000	-1.933377000
14	3.963990000	2.243714000	1.615596000
6	3.214049000	3.969546000	1.765942000
6	1.139773000	-1.758368000	-0.909058000
6	1.168375000	-1.741953000	0.521733000
6	-0.083064000	-1.442678000	0.974568000
6	-0.929705000	-1.275203000	-0.171651000
8	-0.172095000	-1.461352000	-1.305612000
6	2.026363000	-1.975447000	-1.931506000
7	3.312022000	-2.428500000	-1.903697000
6	-2.254161000	-0.966601000	-0.280805000
8	-3.039591000	-0.802621000	0.827170000
6	3.681618000	1.199532000	3.185125000
6	5.786444000	2.381983000	1.151323000
6	4.368262000	1.881539000	4.390003000
6	4.283570000	-0.209952000	2.998472000
6	2.168259000	1.075084000	3.465989000
14	-3.970945000	-2.031638000	1.596720000
6	-3.134220000	-3.691105000	1.297636000
6	-5.755958000	-2.002291000	0.903044000
6	-3.924930000	-1.560707000	3.415697000
6	-6.484617000	-0.714631000	1.342553000
6	-6.525928000	-3.223423000	1.457268000
6	-5.741044000	-2.078162000	-0.638713000
6	5.193062000	-3.649789000	-0.895288000
6	4.006134000	-2.714159000	-0.649139000
6	4.181740000	-2.089556000	-3.038393000
6	5.332583000	-3.085792000	-3.148761000
8	6.041137000	-3.163389000	-1.921836000
1	-0.754625000	1.426215000	-3.705845000
1	1.943900000	1.356697000	-3.686112000
1	-1.666273000	1.705919000	0.260222000
1	3.783197000	1.423872000	-1.595207000
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1	-5.918909000	3.257087000	-0.027588000
1	-4.455347000	4.264977000	-0.158803000
1	-3.797243000	1.984395000	0.619501000
1	-4.692226000	1.254952000	-0.720787000
1	-2.261700000	2.859375000	-3.159679000
1	-3.659415000	1.754065000	-3.185067000
1	-4.458189000	3.999235000	-3.728966000
1	-3.602656000	4.707107000	-2.336402000
1	3.687159000	4.520660000	2.585876000
1	3.362504000	4.567692000	0.860141000
1	2.139269000	3.929437000	1.968125000
1	2.041163000	-1.899912000	1.134961000
1	-0.400076000	-1.326729000	2.000183000
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1	6.352775000	2.901134000	1.931907000
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1	6.246502000	1.399870000	1.004252000
1	4.214692000	1.286114000	5.299172000
1	3.962675000	2.880088000	4.586247000
1	5.450056000	1.979898000	4.247888000
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1	5.367456000	-0.176375000	2.843524000
1	1.710483000	2.050182000	3.666172000
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1	1.635786000	0.621585000	2.623740000
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1	-3.153764000	-3.987806000	0.244517000
1	-4.221093000	-0.519016000	3.572891000
1	-2.918008000	-1.687465000	3.826443000

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6	1.673086000	-1.617237000	-0.252086000
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6	-2.844472000	-2.039113000	-1.786151000
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6	4.324067000	-3.756783000	0.936963000
6	3.661868000	-2.378781000	0.948506000
6	3.614890000	-2.496233000	-1.523256000
6	4.323791000	-3.850898000	-1.392906000
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E-II

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DC-I

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1	6.766509000	0.843884000	0.128007000
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1	0.109114000	5.602575000	1.525709000
1	-0.491610000	5.080605000	-0.052761000
1	1.990266000	1.951987000	2.818093000
1	0.495376000	2.729273000	3.367884000
1	1.979188000	3.668737000	3.238921000
1	4.434248000	2.744347000	-0.514326000
1	3.169599000	1.567407000	-0.141014000
1	3.914075000	2.515765000	1.154578000
1	4.024809000	5.232801000	-0.253173000
1	2.432006000	5.862394000	0.173137000
1	3.420079000	5.040345000	1.392352000
1	1.379551000	4.523571000	-1.772255000
1	2.997366000	3.955710000	-2.189670000
1	1.694999000	2.786131000	-1.921445000
1	-9.923443000	-0.367728000	0.071497000
1	-9.382420000	1.073400000	-0.801217000
1	-7.947148000	0.910390000	1.155659000
1	-7.737739000	-0.842891000	0.942787000
1	-5.912054000	0.628464000	-2.341550000
1	-7.181250000	1.759495000	-1.873287000
1	-7.370762000	-1.083725000	-2.939511000
1	-8.387385000	0.327250000	-3.296519000

$TS_{3\text{-}I}$

6	0.676214000	-1.175652000	1.343079000
6	0.902374000	-1.114855000	2.699287000
6	2.312729000	-1.154465000	2.879283000
6	2.865861000	-1.244569000	1.628520000
8	1.884596000	-1.241433000	0.688724000
6	-0.464063000	-1.159308000	0.446048000
7	-1.532996000	-1.971242000	0.565954000
6	4.270628000	-1.475426000	1.166176000
8	4.581328000	-0.690441000	0.040926000
6	-2.789016000	-3.665006000	-0.685355000
6	-2.452525000	-2.176578000	-0.560112000
6	-1.977018000	-2.581607000	1.822871000
6	-2.385224000	-4.040181000	1.582053000
8	-3.332374000	-4.148788000	0.532422000
14	5.544537000	-1.175459000	-1.273368000

6	5.067305000	0.022827000	-2.640160000
6	-4.420791000	0.777284000	-0.192600000
6	-3.914538000	1.438363000	-1.345244000
6	-2.573705000	1.667126000	-1.154727000
6	-2.237065000	1.162579000	0.131579000
8	-3.355769000	0.629325000	0.707502000
6	-5.635720000	0.318735000	0.275729000
6	-1.025124000	1.078269000	0.806644000
8	0.067160000	1.703999000	0.280050000
6	7.401064000	-1.045472000	-0.821689000
6	5.069737000	-2.937577000	-1.767853000
6	8.255668000	-1.464188000	-2.039610000
6	7.744645000	-1.969496000	0.367119000
6	7.743885000	0.411010000	-0.439563000
14	0.690161000	3.189000000	0.894956000
6	-0.684661000	4.476616000	0.803982000
6	2.161661000	3.605773000	-0.236652000
6	1.187524000	2.919669000	2.692433000
6	3.330011000	2.632118000	0.025234000
6	2.628263000	5.049560000	0.061413000
6	1.738081000	3.505710000	-1.718194000
7	-6.831545000	0.224900000	-0.331503000
6	-9.263955000	-0.128523000	-0.378670000
6	-8.025175000	-0.016492000	0.508680000
6	-7.060352000	0.495556000	-1.748565000
6	-8.041241000	-0.533070000	-2.361209000
8	-9.000538000	-1.028690000	-1.436466000
1	0.158898000	-1.008171000	3.476089000
1	2.851356000	-1.124517000	3.815223000
1	-0.202628000	-0.903265000	-0.575625000
1	4.934642000	-1.247098000	2.011188000
1	4.387125000	-2.549936000	0.952878000
1	-3.549837000	-3.811187000	-1.456339000
1	-1.890462000	-4.236946000	-0.964259000
1	-1.985192000	-1.801314000	-1.473722000
1	-3.381966000	-1.621384000	-0.384682000
1	-1.165027000	-2.544218000	2.548253000
1	-2.828842000	-2.009299000	2.213318000
1	-2.855520000	-4.445760000	2.481136000
1	-1.489633000	-4.638643000	1.353833000
1	5.655257000	-0.148282000	-3.547837000
1	4.010451000	-0.096632000	-2.899818000
1	5.217640000	1.061792000	-2.333230000
1	-4.492591000	1.744732000	-2.204418000
1	-1.885002000	2.164849000	-1.820486000
1	-5.632813000	-0.012765000	1.311329000
1	-1.047965000	0.897047000	1.878641000
1	5.566029000	-3.210926000	-2.705435000
1	3.989911000	-3.012275000	-1.936744000
1	5.347136000	-3.694098000	-1.026923000
1	9.323434000	-1.377506000	-1.799800000
1	8.069293000	-0.829493000	-2.913054000
1	8.074219000	-2.503860000	-2.334170000
1	8.817987000	-1.916010000	0.591700000
1	7.213928000	-1.679843000	1.281059000
1	7.511830000	-3.019811000	0.158770000
1	7.575623000	1.103163000	-1.271692000
1	8.802302000	0.492782000	-0.158885000
1	7.148509000	0.760753000	0.410869000
1	-1.581010000	4.142385000	1.337251000
1	-0.360999000	5.413266000	1.270024000
1	-0.974350000	4.703091000	-0.226886000
1	1.884582000	2.083600000	2.799312000
1	0.317507000	2.719489000	3.327489000
1	1.674551000	3.815419000	3.093122000
1	4.171364000	2.870104000	-0.638916000
1	3.058003000	1.588352000	-0.155883000
1	3.702789000	2.708069000	1.052423000
1	3.493753000	5.299576000	-0.565261000
1	1.849596000	5.790283000	-0.150487000
1	2.940458000	5.177898000	1.104427000
1	0.918188000	4.192090000	-1.960589000
1	2.581498000	3.768521000	-2.369735000
1	1.421235000	2.491044000	-1.979642000
1	-10.093078000	-0.541889000	0.199544000
1	-9.577759000	0.858307000	-0.751546000
1	-8.146254000	0.796200000	1.236218000
1	-7.881267000	-0.955399000	1.054846000
1	-6.110729000	0.418692000	-2.278185000
1	-7.428554000	1.521761000	-1.878635000
1	-7.490748000	-1.407057000	-2.721243000
1	-8.538924000	-0.065017000	-3.223014000

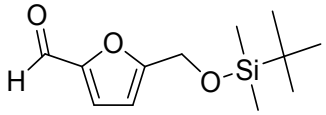
E-I

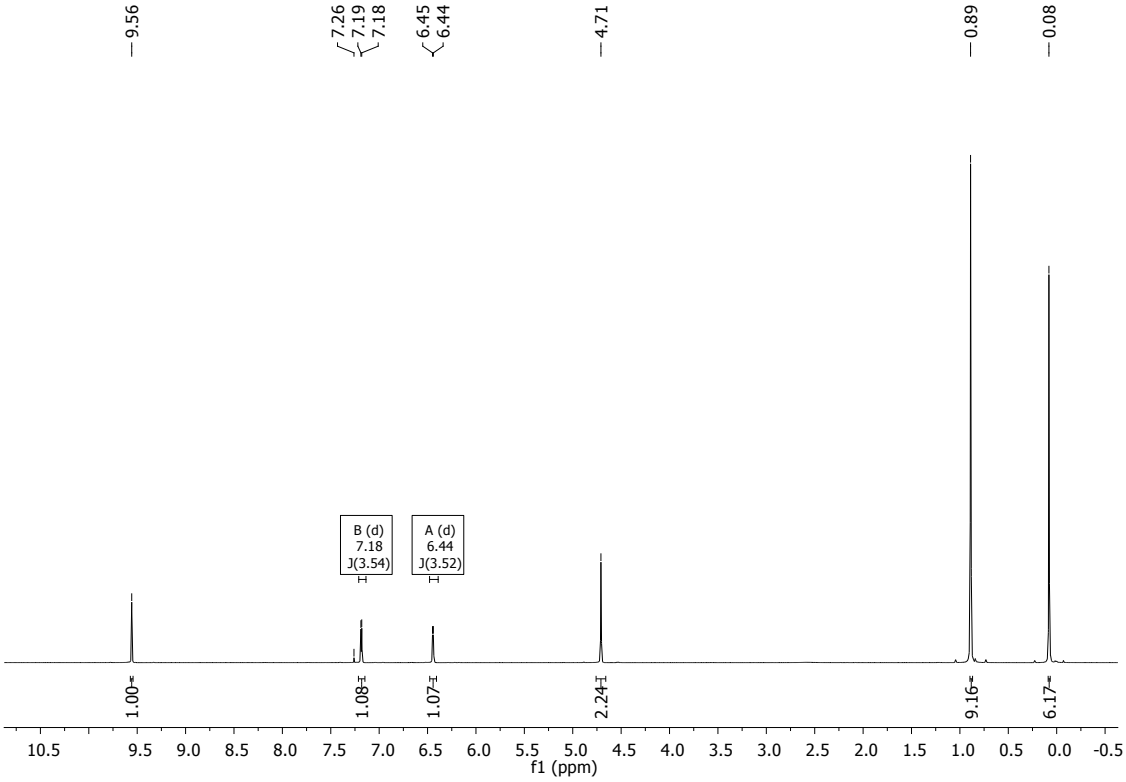
6	0.858853000	-0.860224000	1.300948000
6	1.173824000	-0.651374000	2.614643000
6	2.571156000	-0.935880000	2.747218000
6	3.013931000	-1.298744000	1.509474000
8	1.974184000	-1.257789000	0.620051000
6	-0.395641000	-0.782079000	0.478634000
7	-1.230258000	-1.959973000	0.633962000
6	4.344558000	-1.711864000	0.978480000
8	4.813469000	-0.768604000	0.031147000
6	-2.472156000	-3.829579000	-0.325669000
6	-2.036359000	-2.374897000	-0.509015000
6	-1.859652000	-2.214668000	1.927282000
6	-2.318417000	-3.671594000	1.996985000
8	-3.169224000	-3.991989000	0.901782000
14	5.820757000	-1.069939000	-1.293326000
6	5.331166000	0.245266000	-2.547815000
6	-4.520247000	0.639135000	-0.344775000
6	-3.979432000	1.234287000	-1.490316000
6	-2.602694000	1.351458000	-1.285665000
6	-2.341023000	0.830480000	-0.023315000
8	-3.481763000	0.423869000	0.553350000
6	-5.764054000	0.238749000	0.166309000
6	-1.057003000	0.654475000	0.719175000
8	-0.137761000	1.599078000	0.241797000
6	7.655714000	-0.900545000	-0.767501000
6	5.457598000	-2.788670000	-1.993385000
6	8.575255000	-1.166833000	-1.979540000

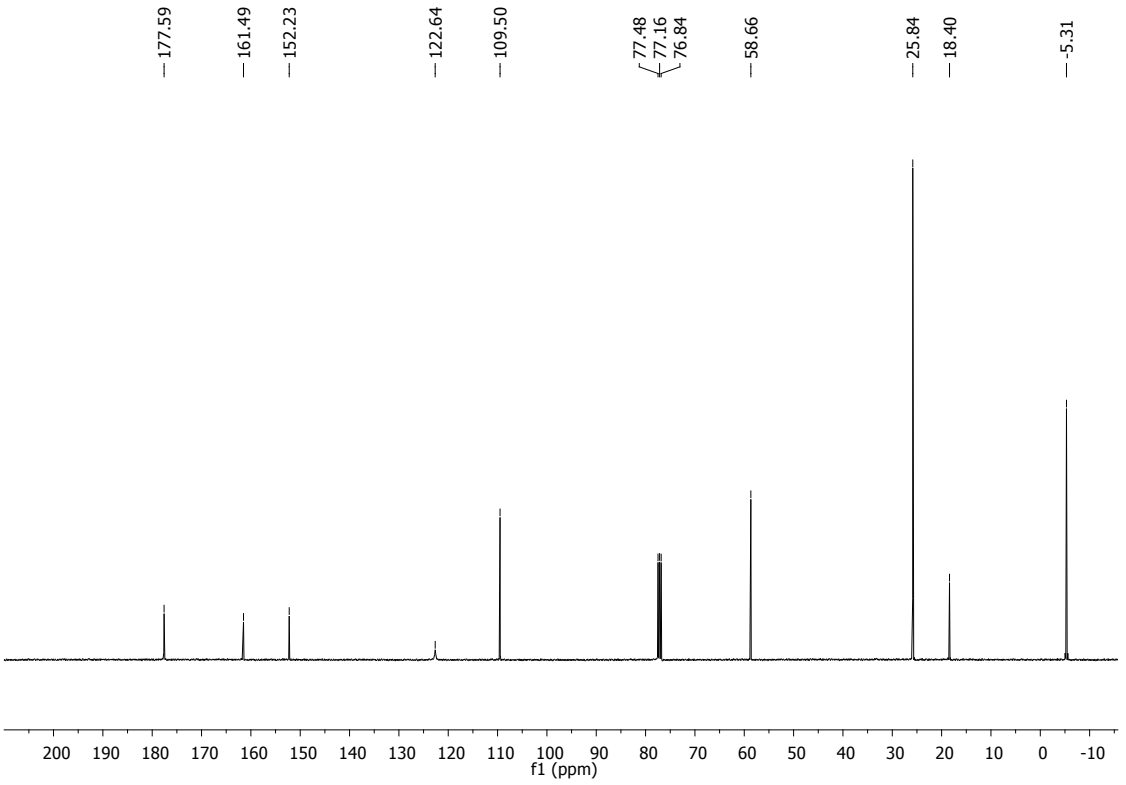
6	7.989340000	-1.914262000	0.348075000
6	7.910854000	0.527378000	-0.239286000
14	0.244658000	3.136636000	0.886196000
6	-1.249687000	4.274133000	0.662456000
6	1.745504000	3.691898000	-0.144992000
6	0.617437000	2.984639000	2.726423000
6	2.953083000	2.771514000	0.140156000
6	2.111959000	5.145823000	0.231124000
6	1.406177000	3.627948000	-1.650306000
7	-6.951362000	0.183161000	-0.400048000
6	-9.305401000	-0.561146000	-0.468063000
6	-8.138089000	-0.152377000	0.437149000
6	-7.233484000	0.443521000	-1.817699000
6	-8.019335000	-0.745127000	-2.430717000
8	-8.819236000	-1.424618000	-1.475814000
1	0.506813000	-0.318962000	3.397207000
1	3.169237000	-0.872689000	3.644789000
1	-0.072842000	-0.754735000	-0.566987000
1	5.032035000	-1.790313000	1.830958000
1	4.263148000	-2.712665000	0.530477000
1	-3.158718000	-4.129016000	-1.122818000
1	-1.588402000	-4.485035000	-0.354041000
1	-1.435423000	-2.283393000	-1.420758000
1	-2.948735000	-1.765041000	-0.644322000
1	-1.128440000	-2.031349000	2.720008000
1	-2.731902000	-1.560979000	2.107844000
1	-2.896475000	-3.849069000	2.907975000
1	-1.439614000	-4.334094000	1.999912000
1	5.976214000	0.229145000	-3.432571000
1	4.301270000	0.081901000	-2.882094000
1	5.382238000	1.247745000	-2.112374000
1	-4.518066000	1.570526000	-2.363637000
1	-1.864914000	1.771950000	-1.951096000
1	-5.736302000	-0.075944000	1.207419000
1	-1.268018000	0.758457000	1.793346000
1	5.996076000	-2.931748000	-2.936510000
1	4.389299000	-2.902055000	-2.208510000
1	5.754041000	-3.604242000	-1.326052000
1	9.628769000	-1.058212000	-1.689240000
1	8.392978000	-0.461797000	-2.798370000
1	8.453052000	-2.180761000	-2.376782000
1	9.046504000	-1.834477000	0.634402000
1	7.397042000	-1.734984000	1.252399000
1	7.818597000	-2.949523000	0.031813000
1	7.738496000	1.284997000	-1.011434000
1	8.952133000	0.633069000	0.093576000
1	7.264727000	0.765208000	0.612599000
1	-2.131140000	3.891838000	1.190401000
1	-1.038323000	5.266381000	1.075587000
1	-1.520078000	4.406713000	-0.389833000
1	1.432193000	2.281889000	2.918181000
1	-0.257028000	2.654464000	3.298730000
1	0.908990000	3.960248000	3.130804000
1	3.811755000	3.081718000	-0.469417000
1	2.744515000	1.723920000	-0.096479000
1	3.268114000	2.821674000	1.187793000
1	2.986767000	5.472756000	-0.345078000
1	1.300073000	5.848955000	0.013701000
1	2.370619000	5.246751000	1.291267000
1	0.559175000	4.273584000	-1.911629000
1	2.264624000	3.966212000	-2.244582000
1	1.169634000	2.606583000	-1.965711000
1	-10.040762000	-1.116937000	0.116953000
1	-9.812342000	0.317528000	-0.893064000
1	-8.398690000	0.713767000	1.056389000
1	-7.858244000	-0.984830000	1.087528000
1	-6.300433000	0.576907000	-2.358720000
1	-7.800674000	1.377954000	-1.885596000
1	-7.326528000	-1.489980000	-2.830086000
1	-8.631262000	-0.360733000	-3.259185000

11. ^{1}H and ^{13}C NMR Spectra

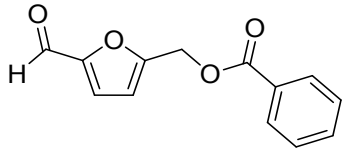
Compound **1**

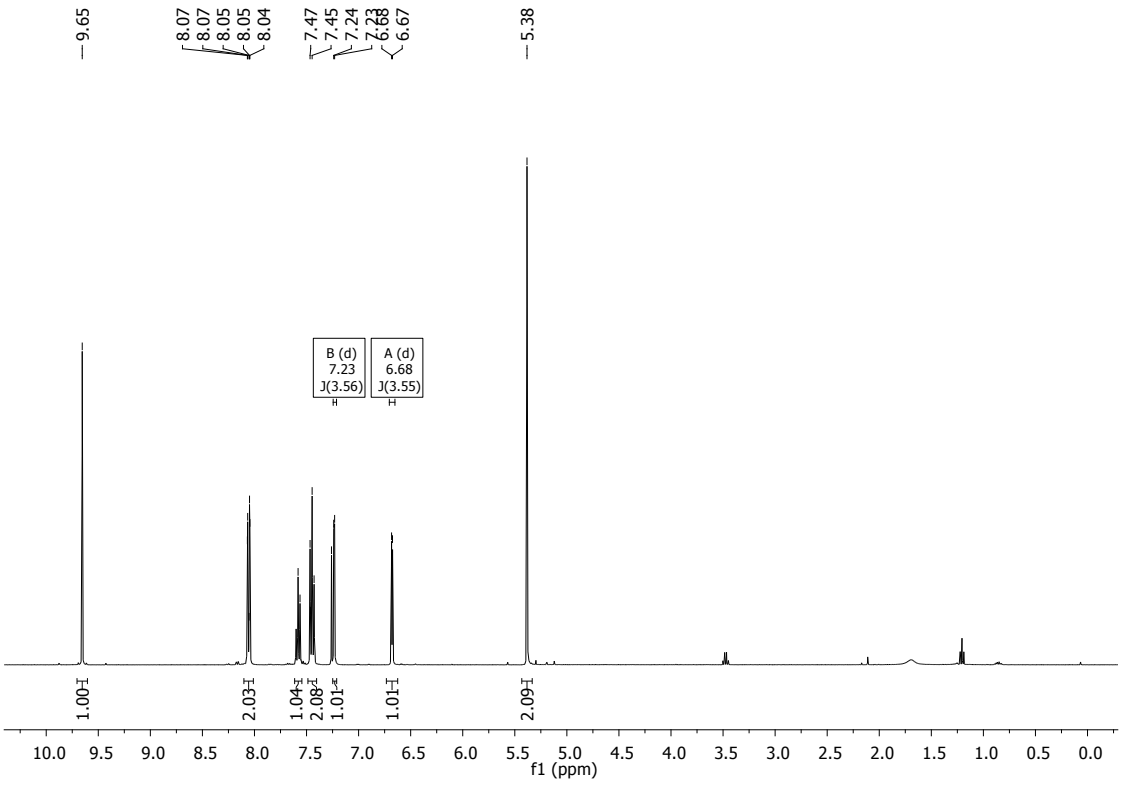




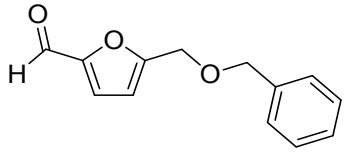


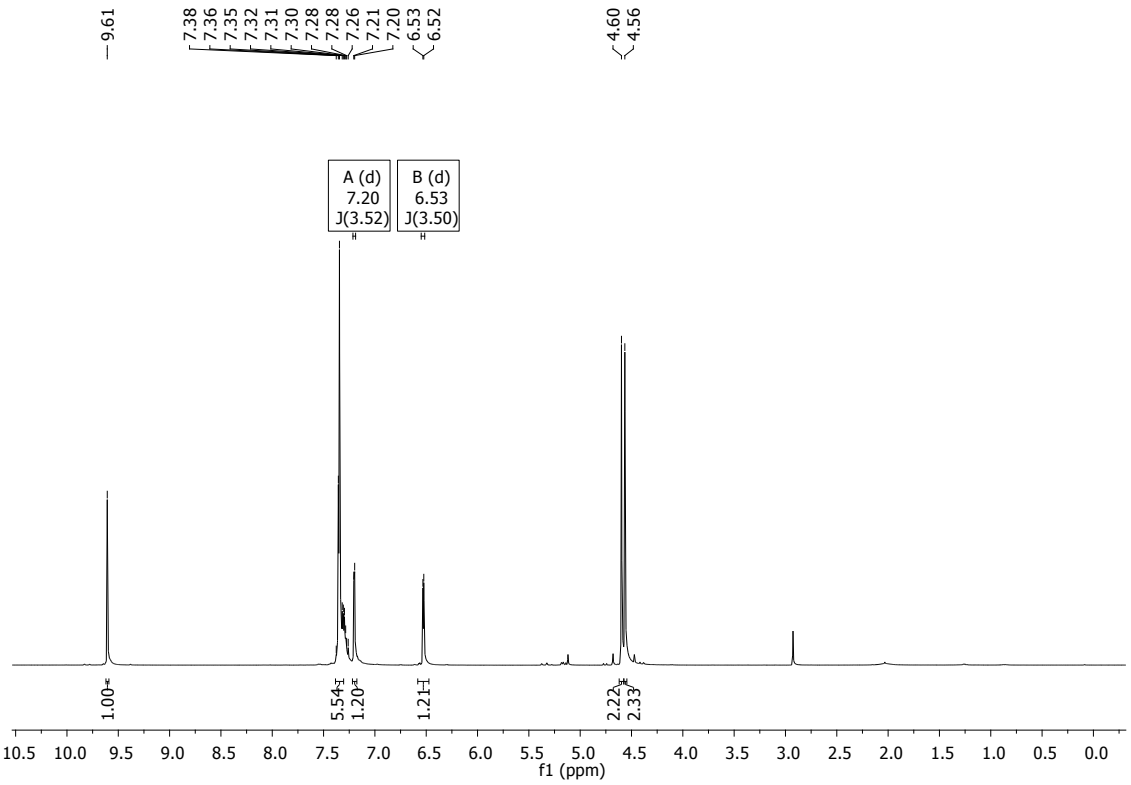
Compound **2**

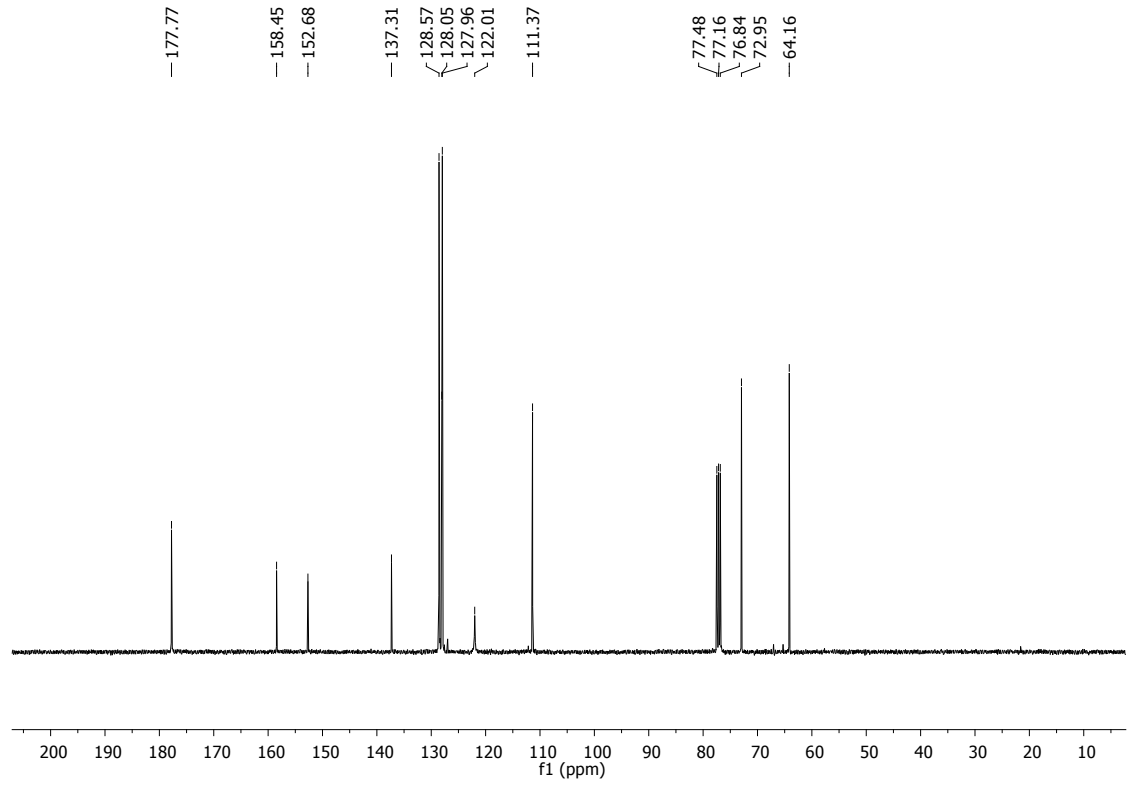

O
O
H
O
O


9.65
8.07
8.07
8.05
8.05
8.04
7.47
7.45
7.24
7.23
6.68
6.67
5.38
B (d)
7.23
J(3.56)
H
A (d)
6.68
J(3.55)
H
1.00
2.03
1.04
2.08
1.01
1.01
2.09
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

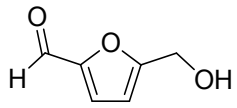
Compound **3**

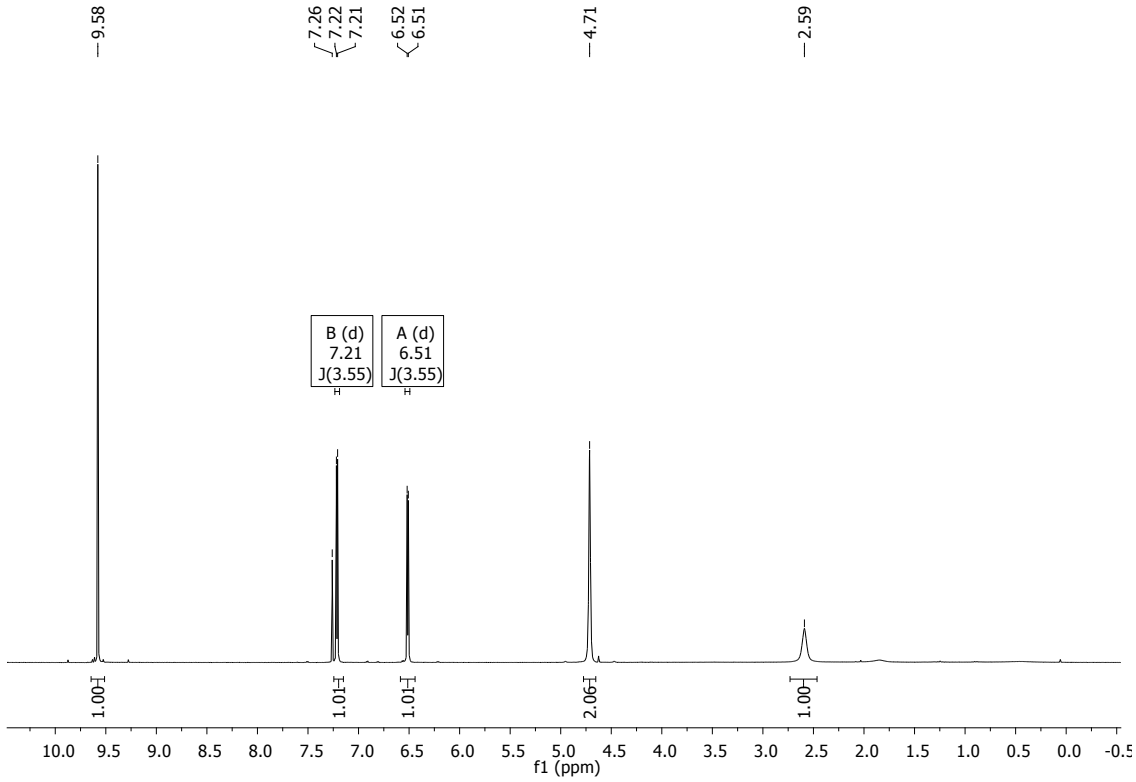

O
O
H
O


9.61
7.38
7.36
7.35
7.32
7.31
7.30
7.28
7.28
7.26
7.21
7.20
6.53
6.52
4.60
4.56
A (d)
7.20
J(3.52)
B (d)
6.53
J(3.50)
1.00
5.54
1.20
1.21
2.22
2.33
f1 (ppm)

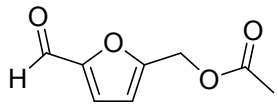

177.77
158.45
152.68
137.31
128.57
128.05
127.96
122.01
111.37
77.48
77.16
76.84
72.95
64.16
f1 (ppm)

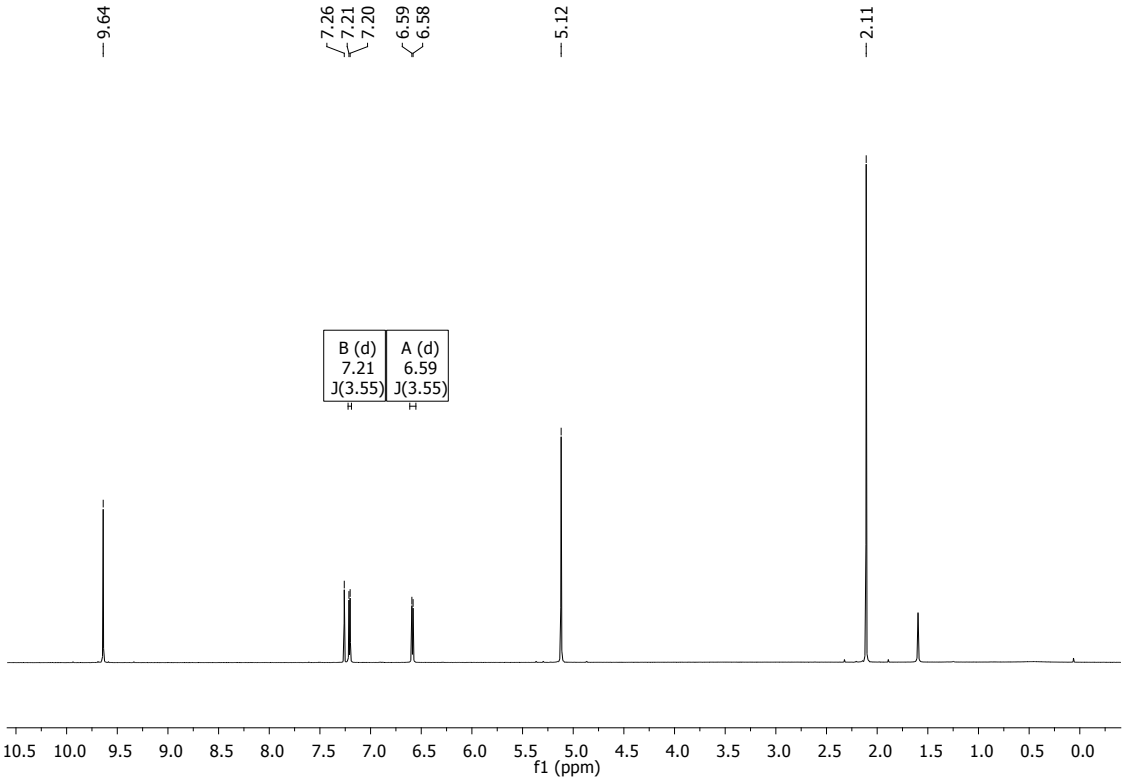
Compound **4**

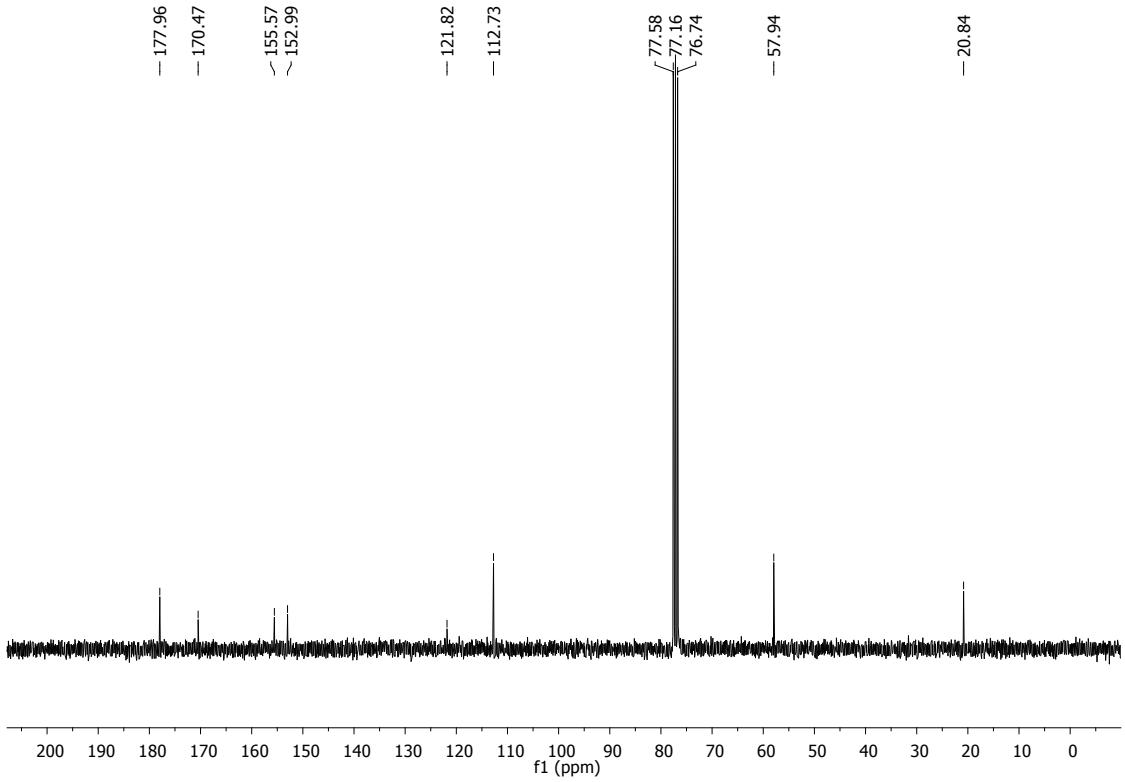

O
O
H
OH


9.58
7.26
7.22
7.21
6.52
6.51
4.71
2.59
B (d)
7.21
J(3.55)
H
A (d)
6.51
J(3.55)
H
1.00
1.01
1.01
2.06
1.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

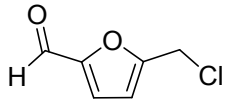
Compound **5**

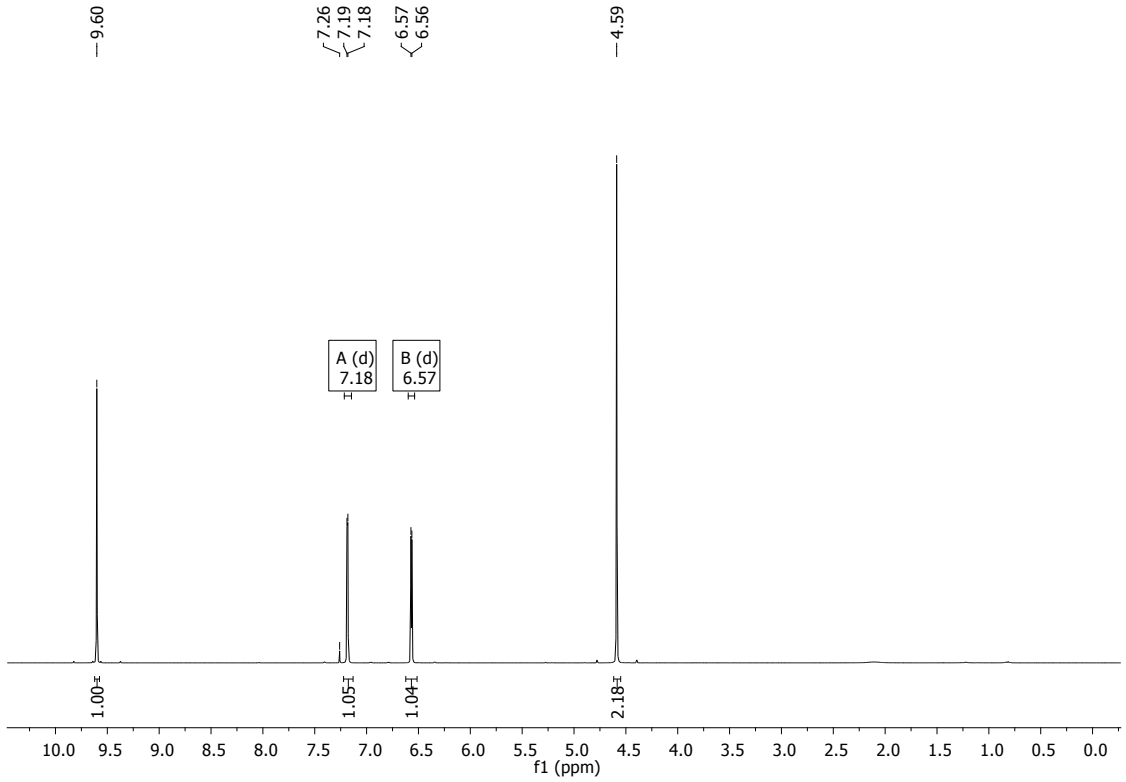



9.64
7.26
7.21
7.20
6.59
6.58
5.12
2.11
B (d)
7.21
J(3.55)
A (d)
6.59
J(3.55)
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

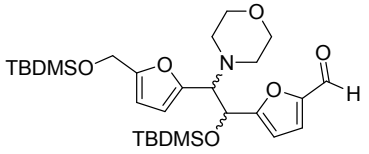

177.96
170.47
155.57
152.99
121.82
112.73
77.58
77.16
76.74
57.94
20.84
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

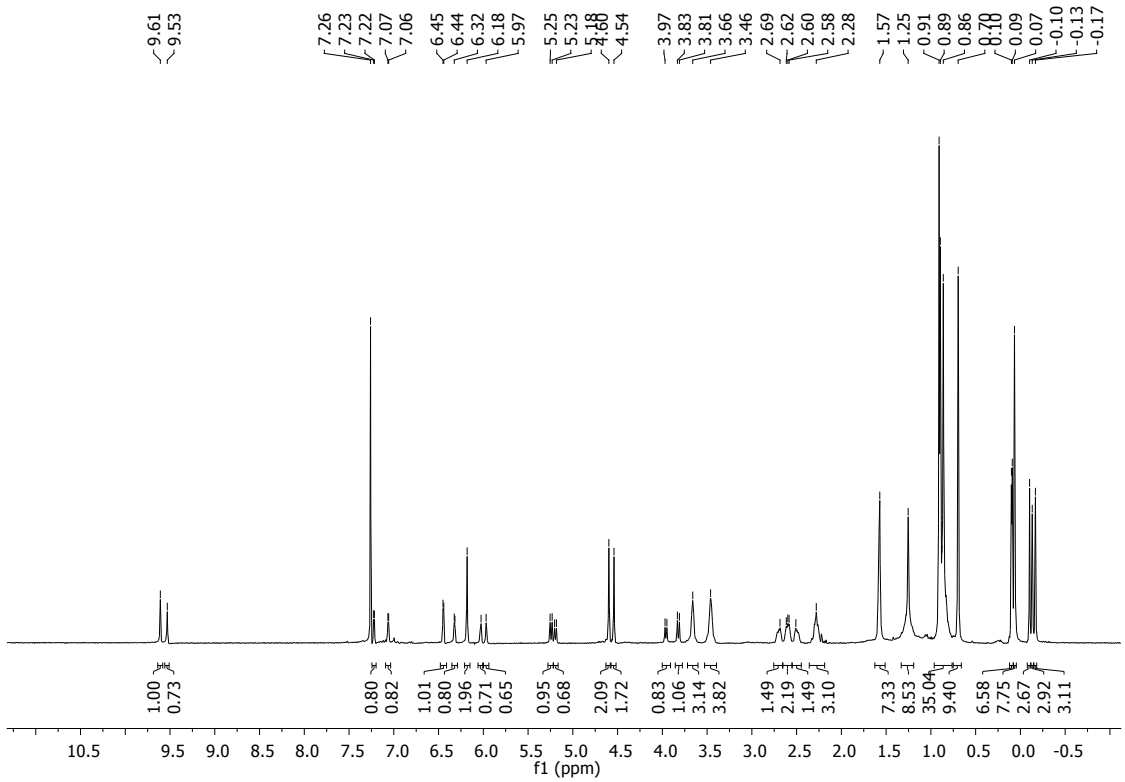
Compound **ClMF**

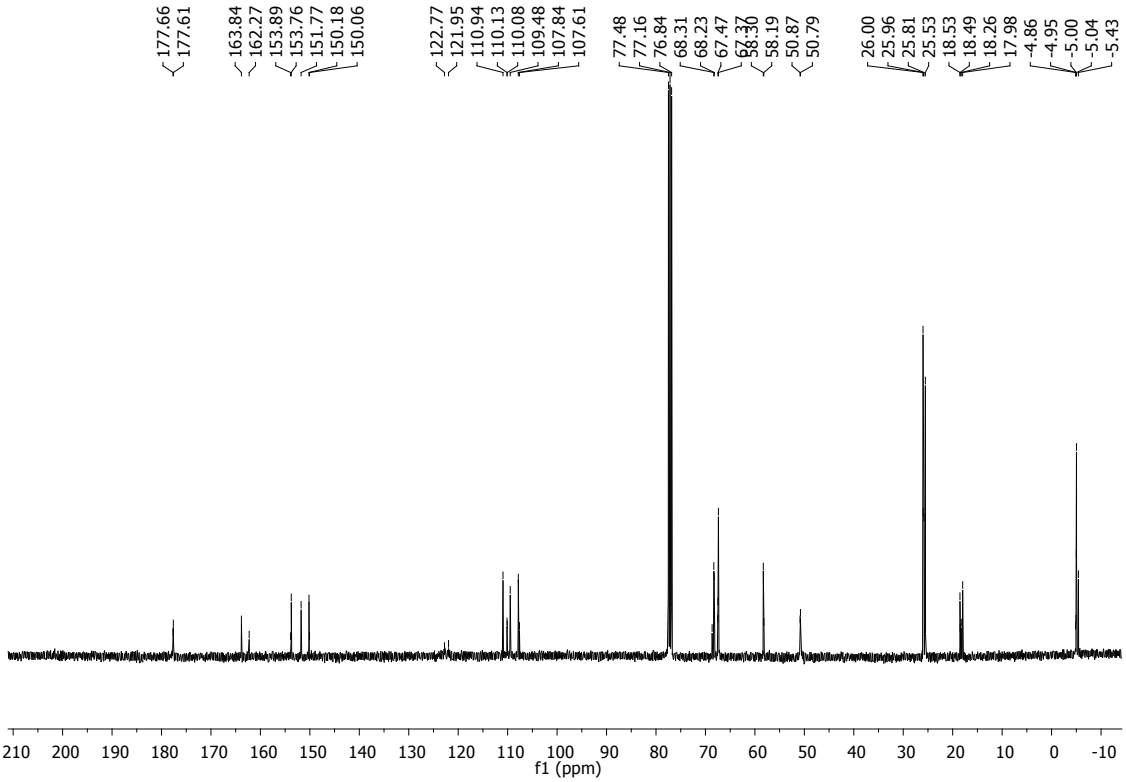




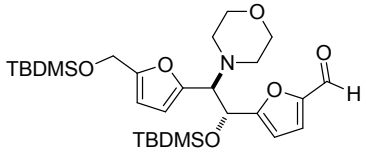
Mixture of compounds **6a-I** and **6a-II**

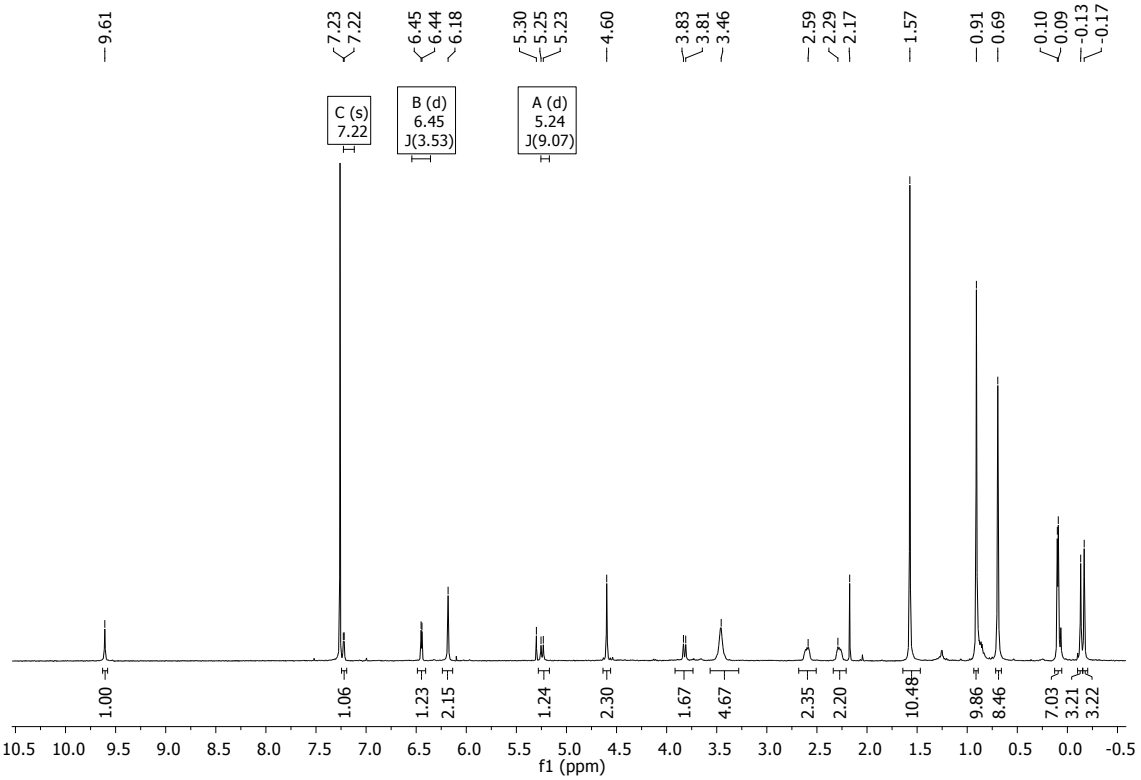




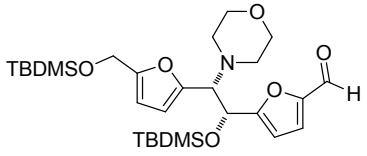


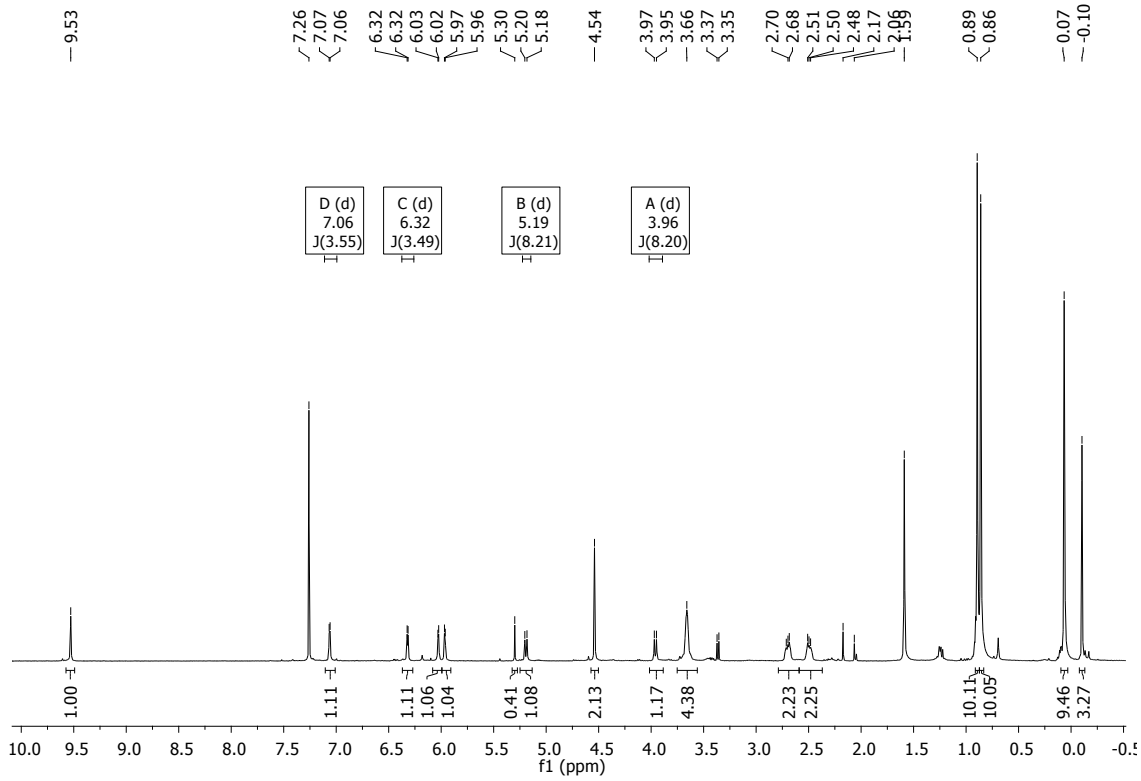
Compound **6a-I**



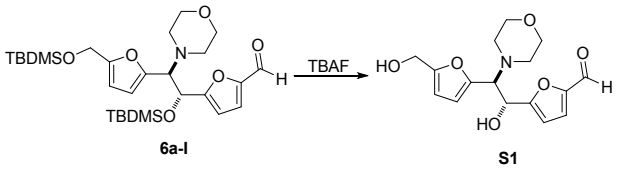


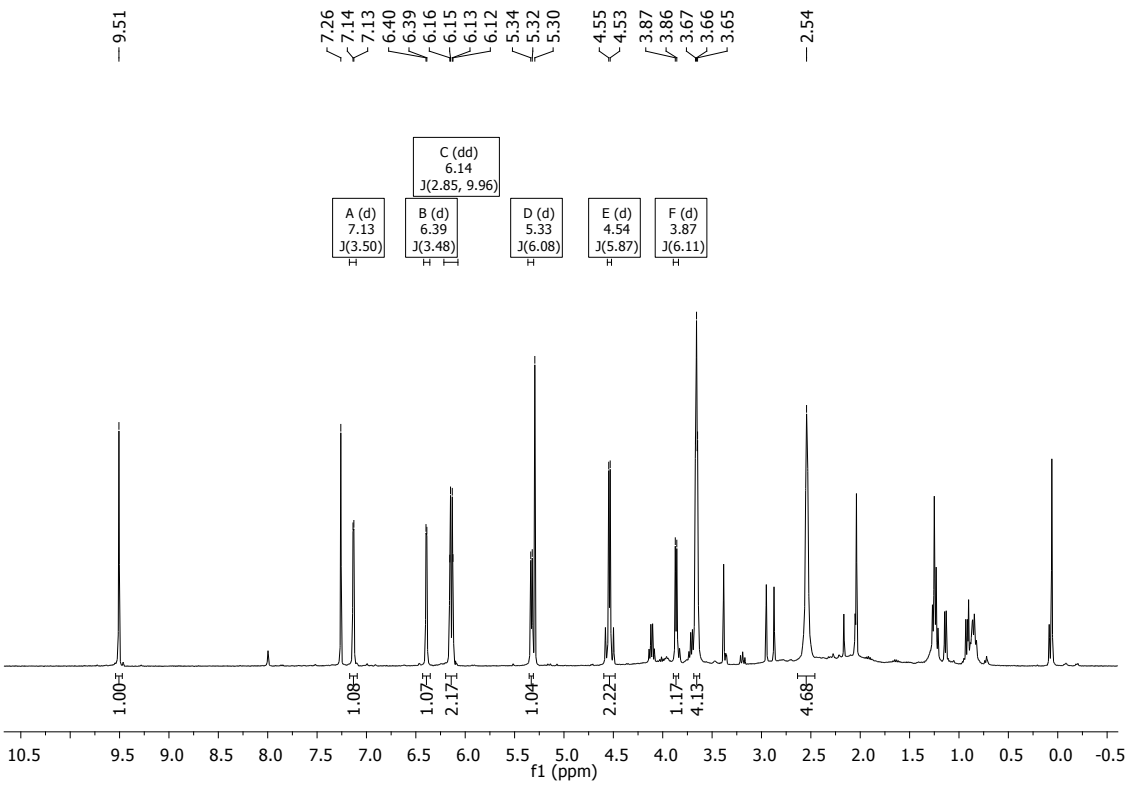
Compound **6a-II**



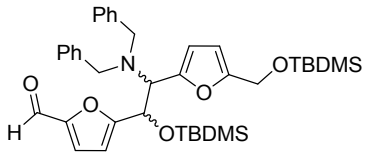


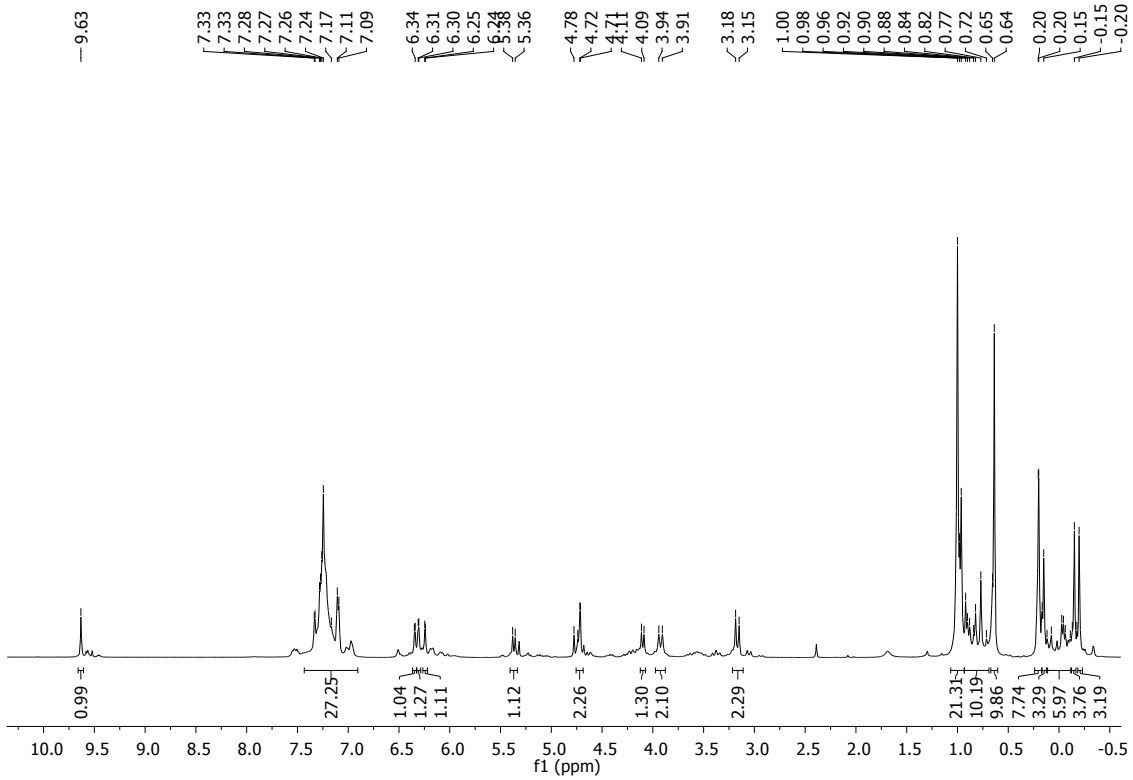
Compound **S1** = **9a-I**

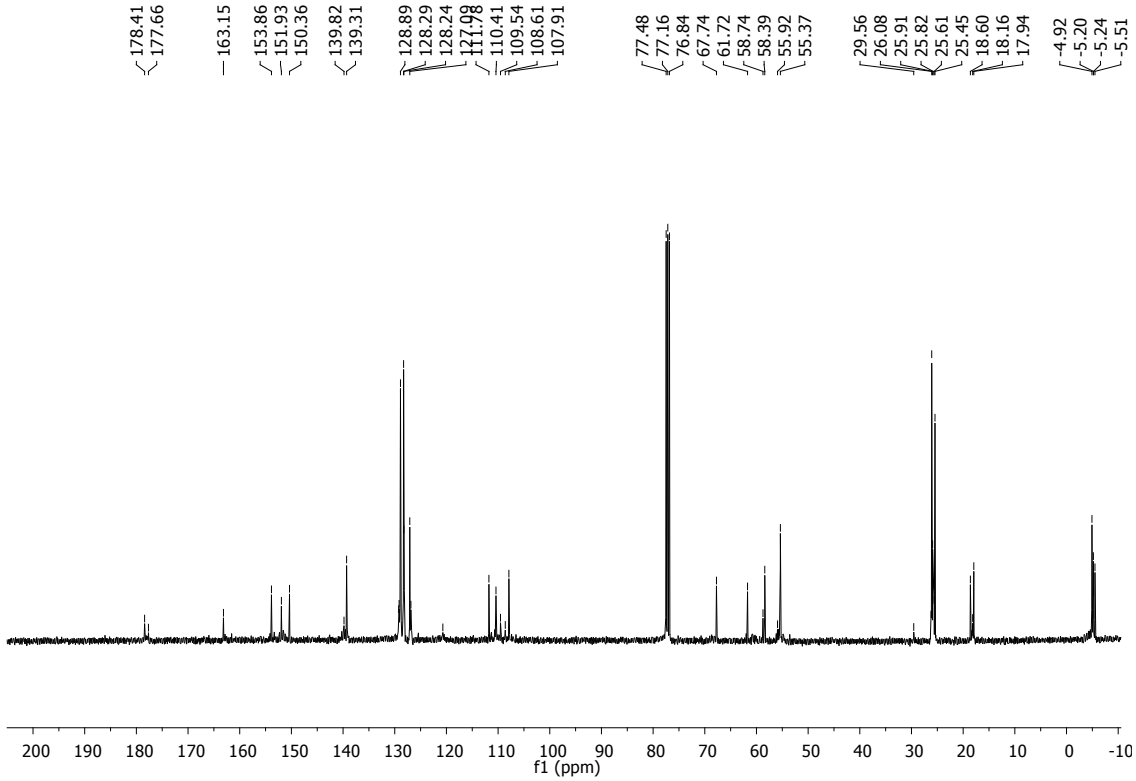




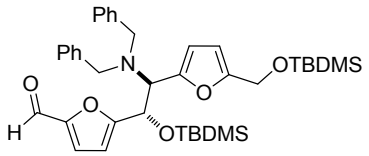
Mixture of compounds **6b-I** and **6b-II**

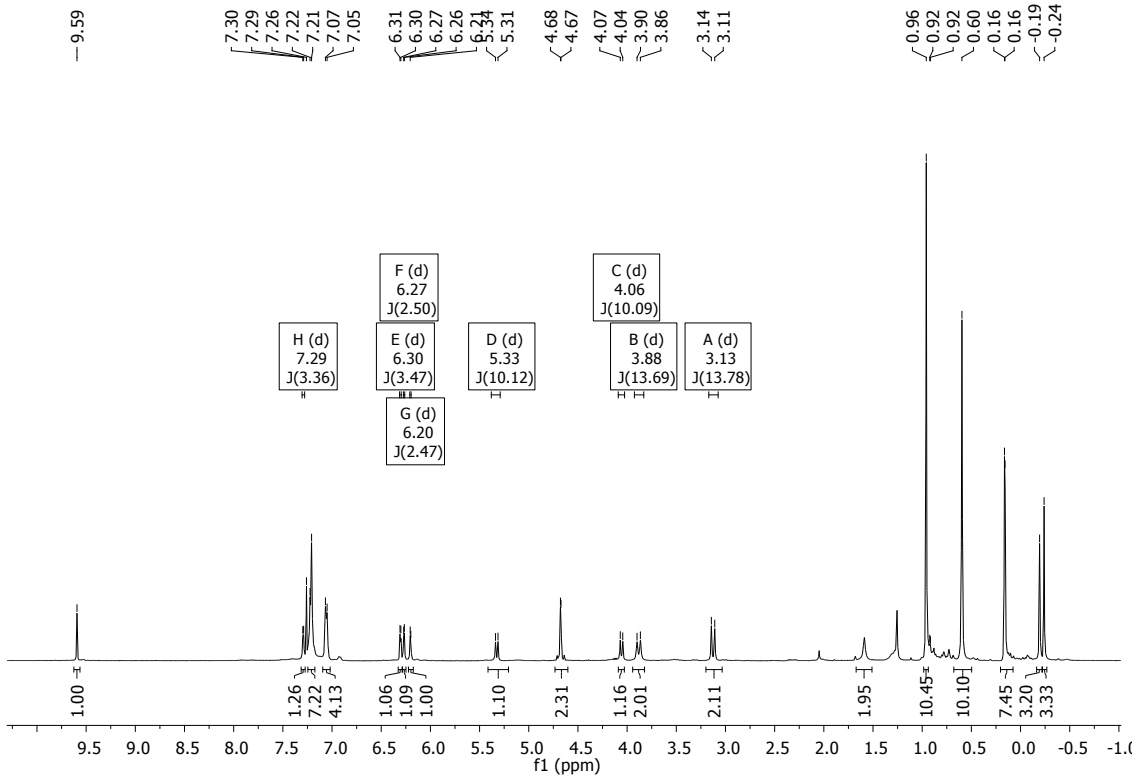


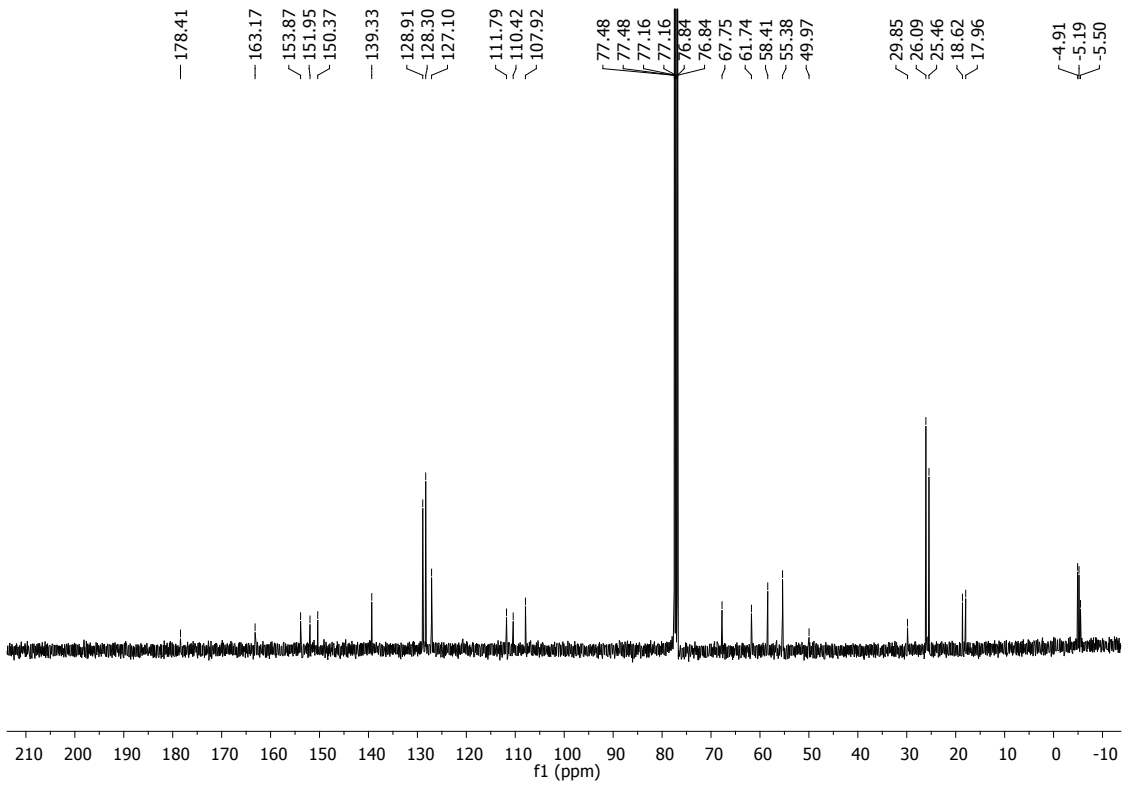




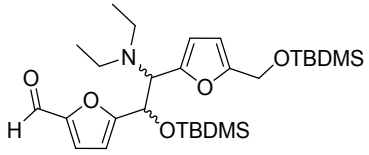
Compound **6b-I**

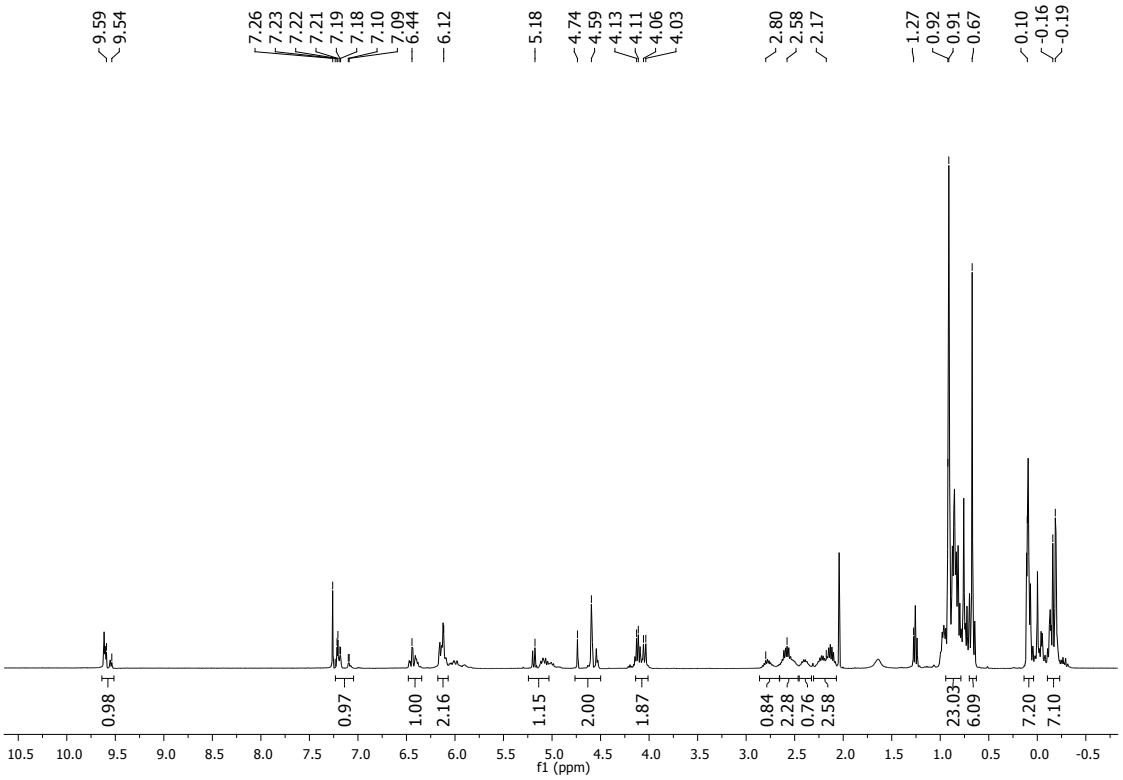


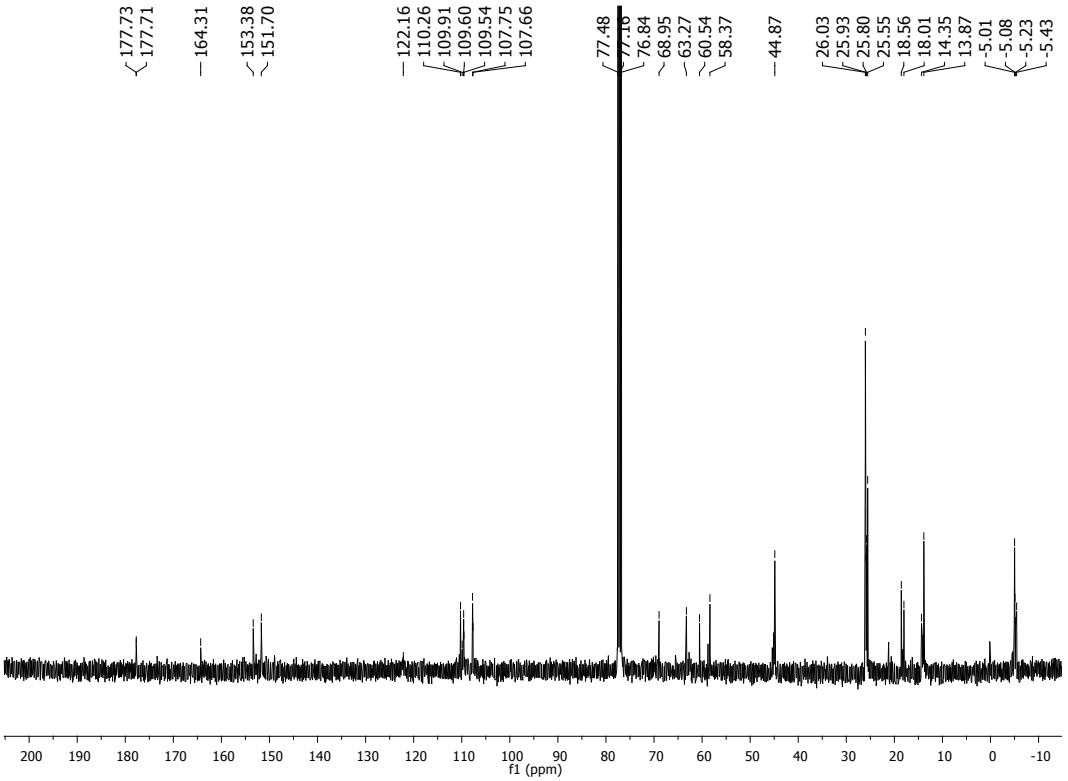




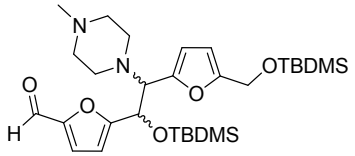
Mixture of compounds **6c-I** and **6c-II**

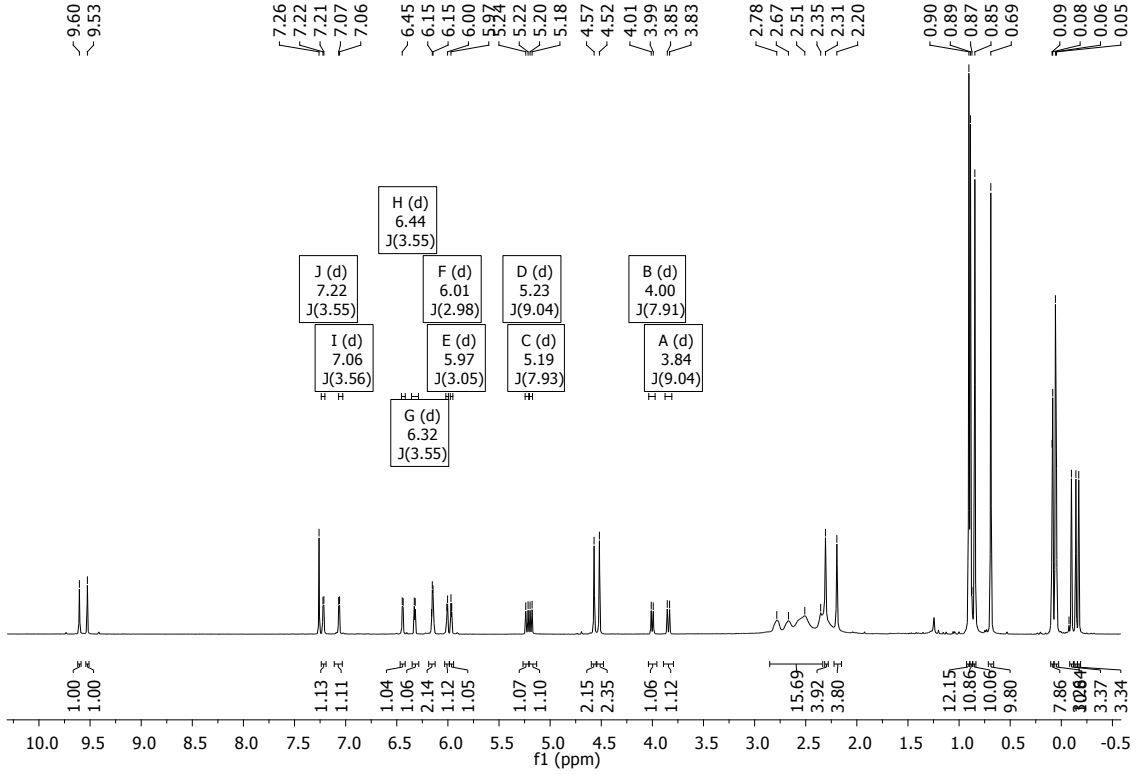


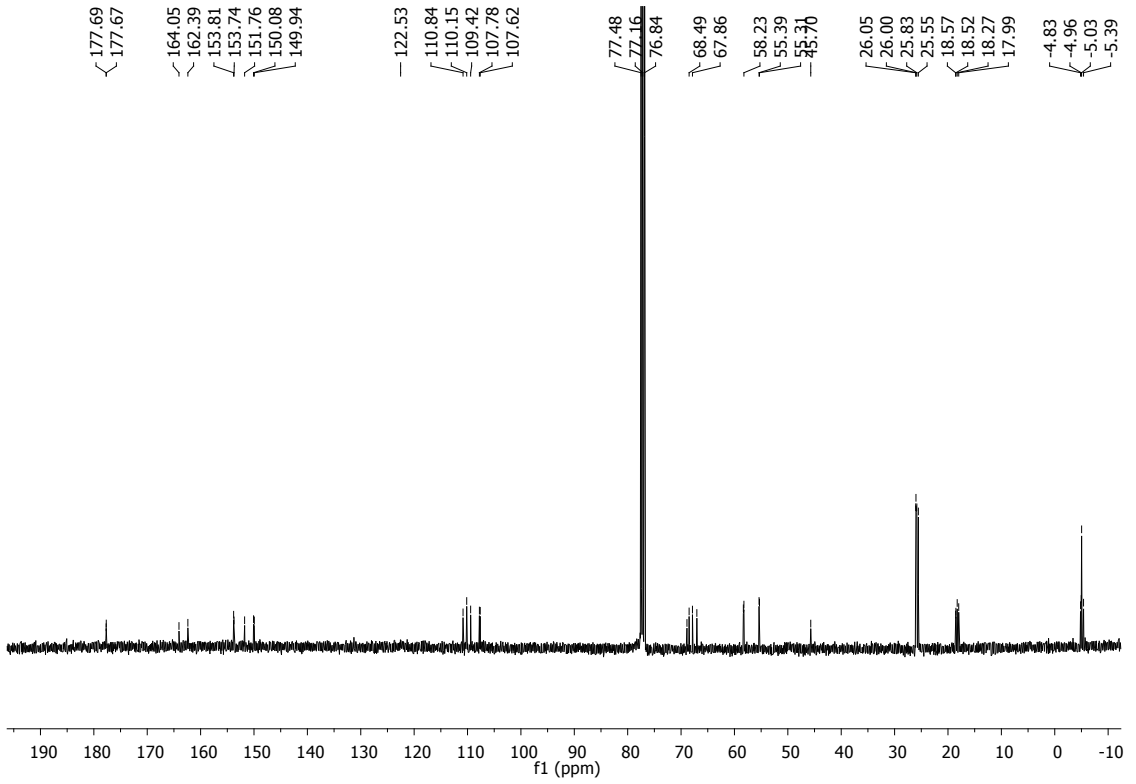




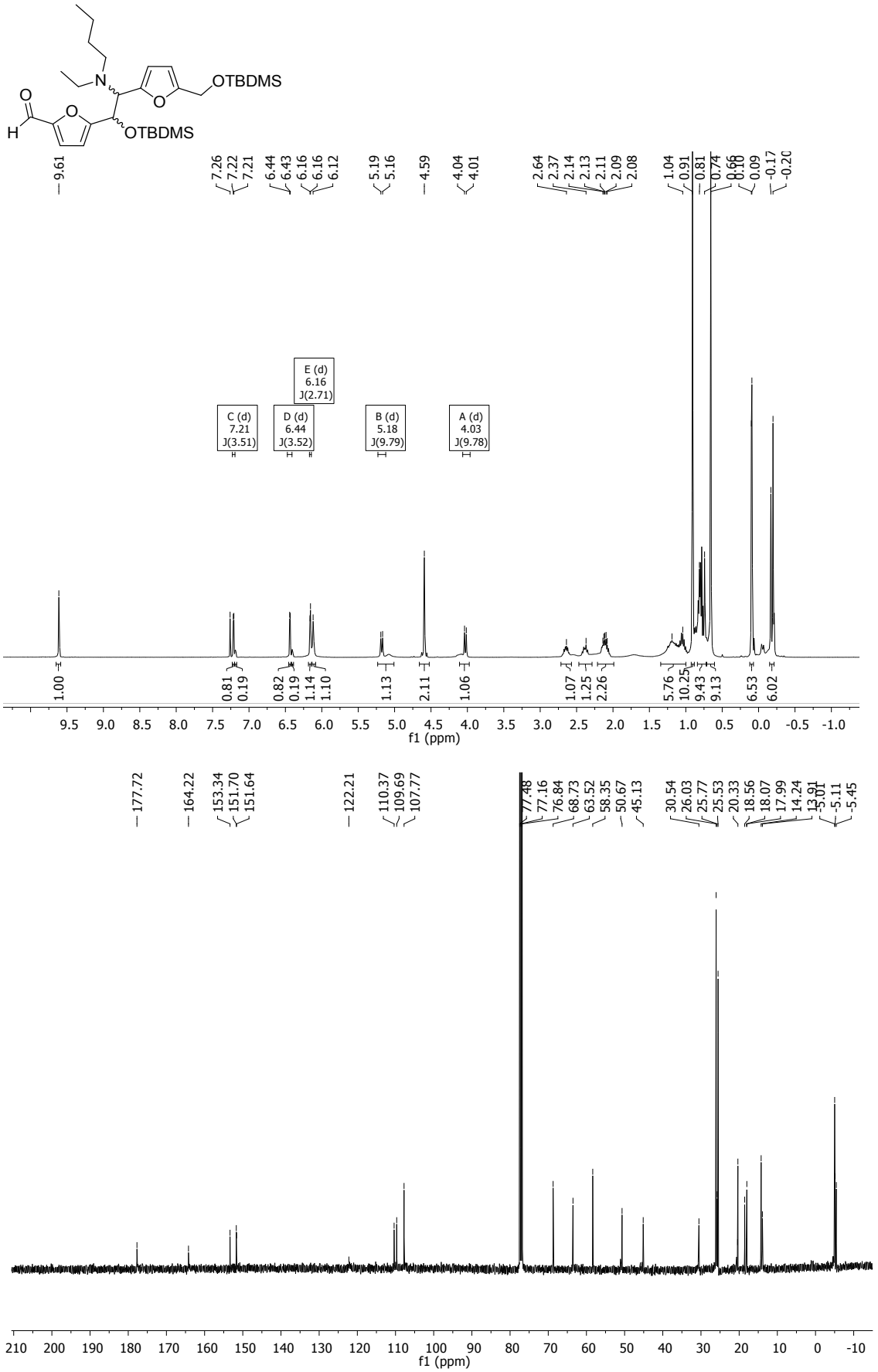
Mixture of compounds **6d-I** and **6d-II**



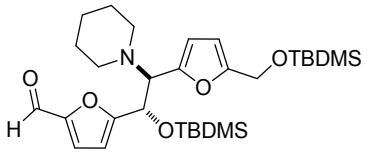


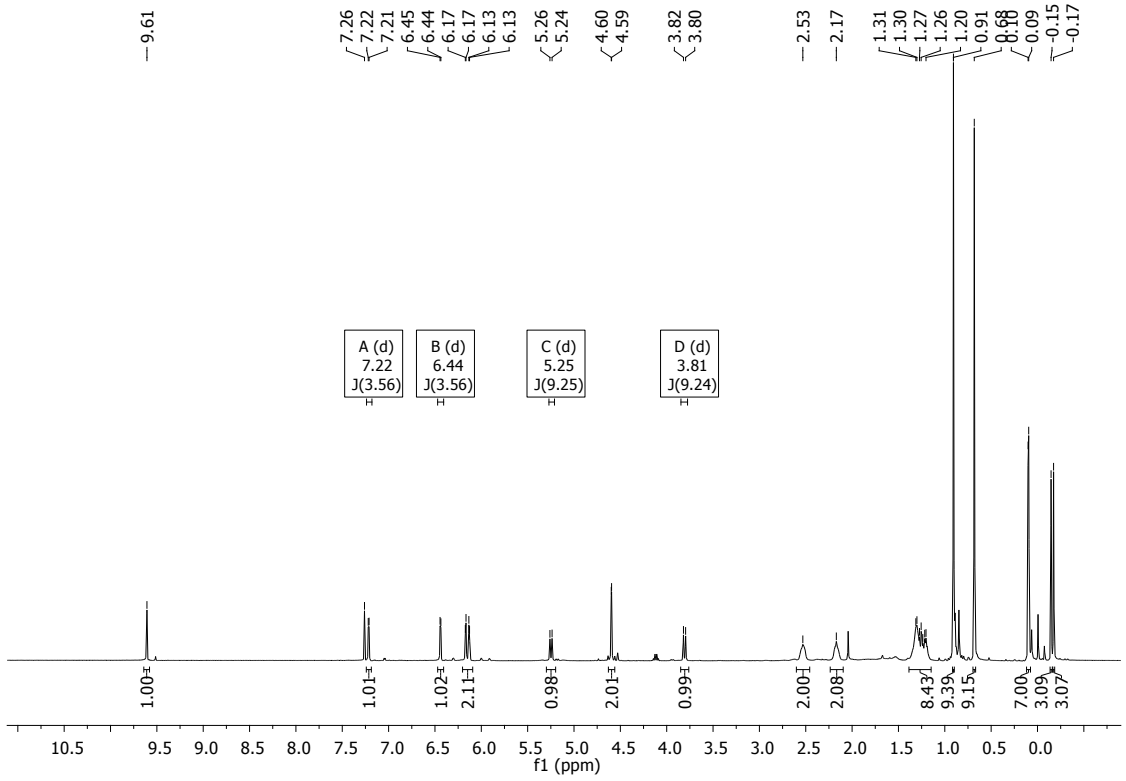


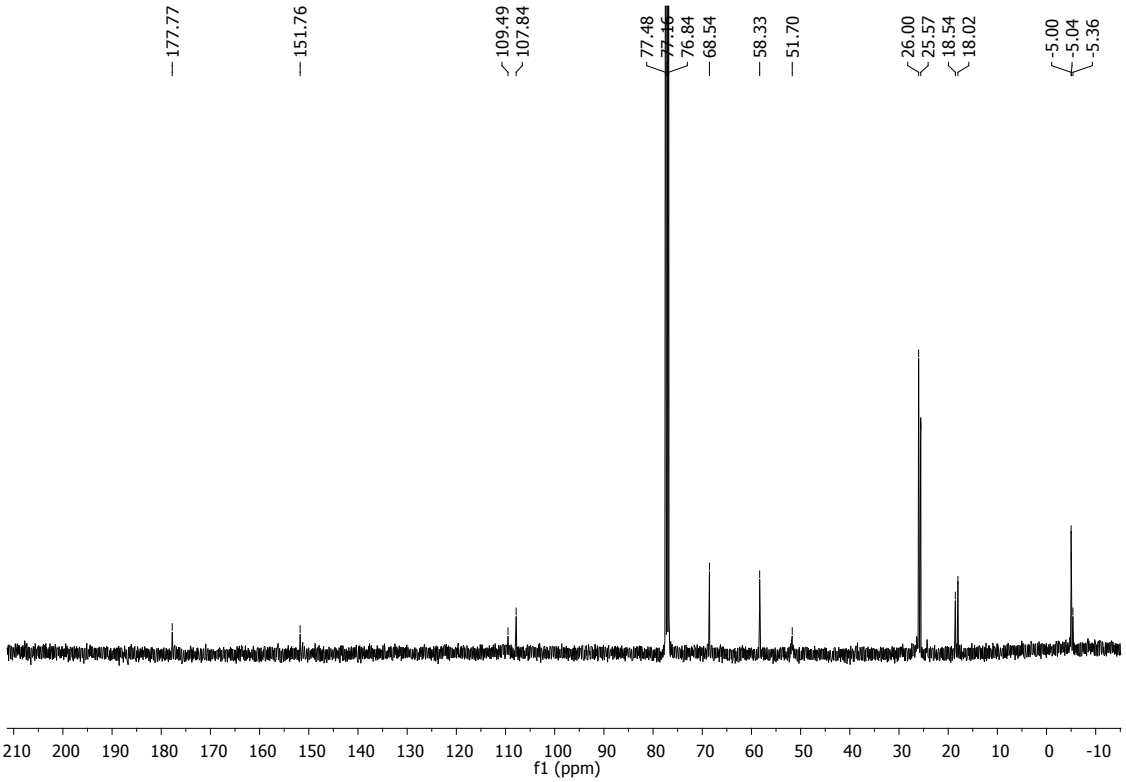
Mixture of compounds **6e-I** and **6e-II**



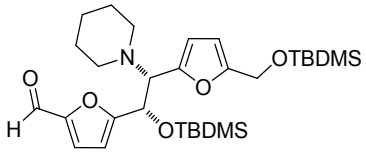
Compound **6f-I**

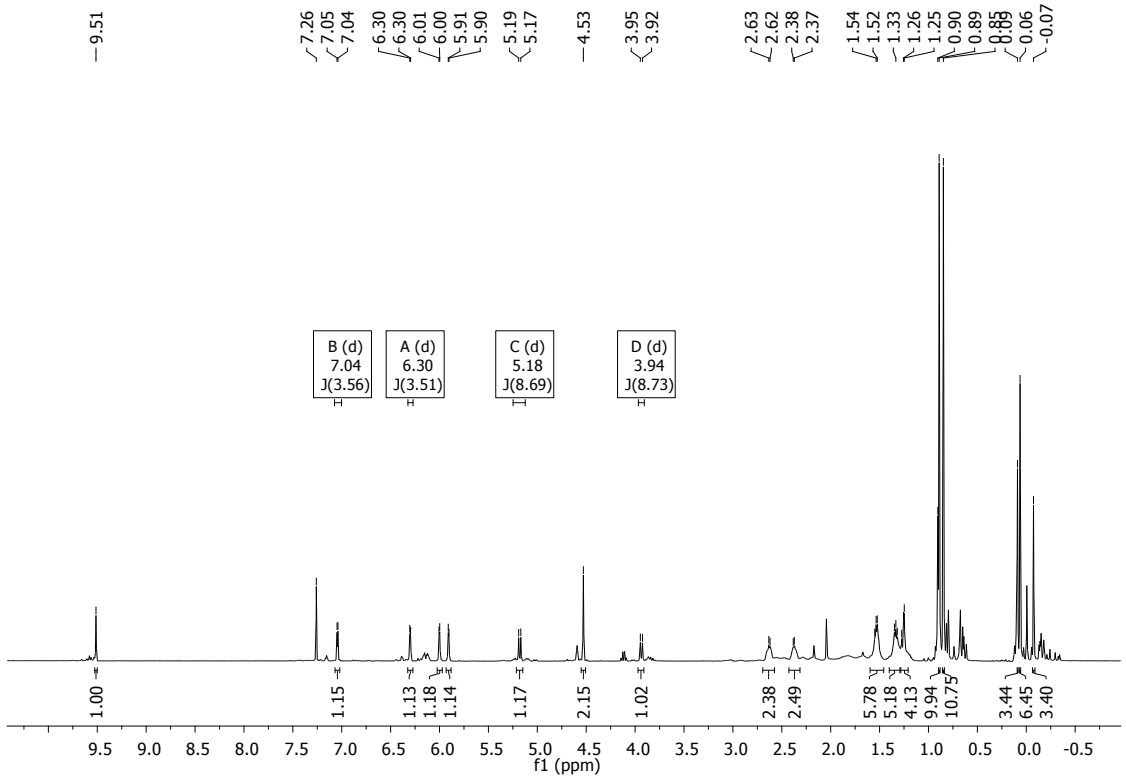


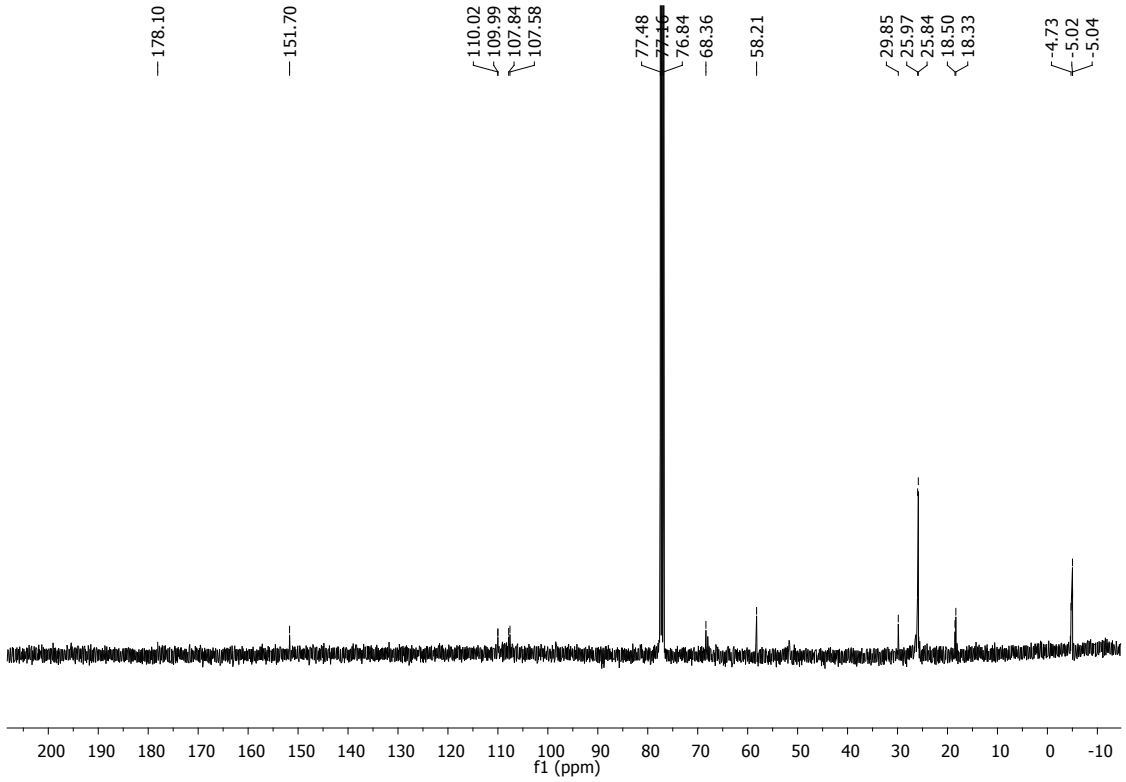




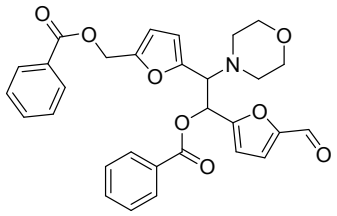
Compound **6f-II**

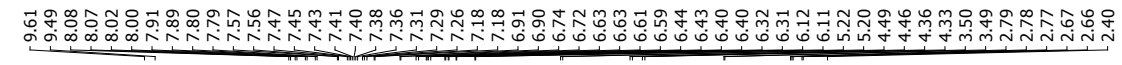


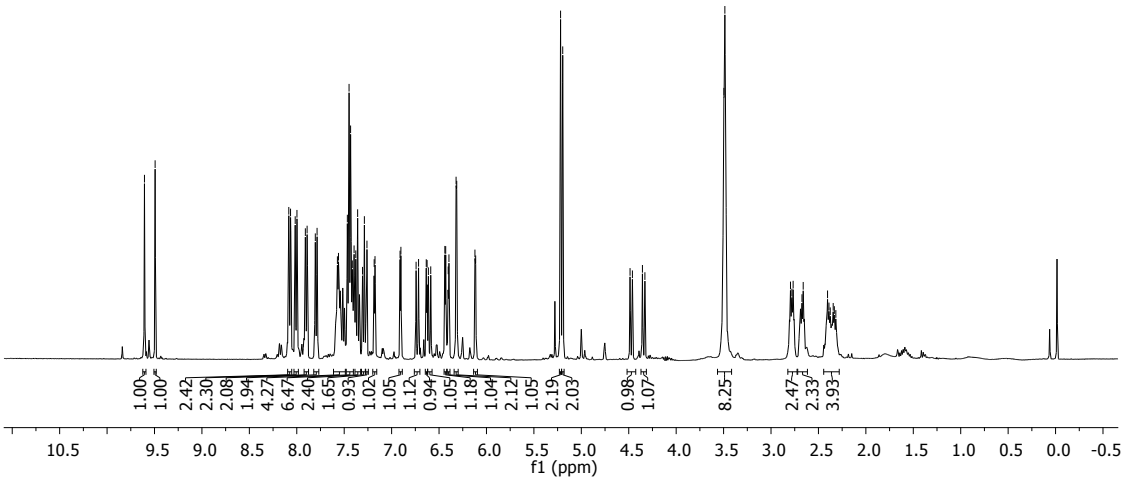


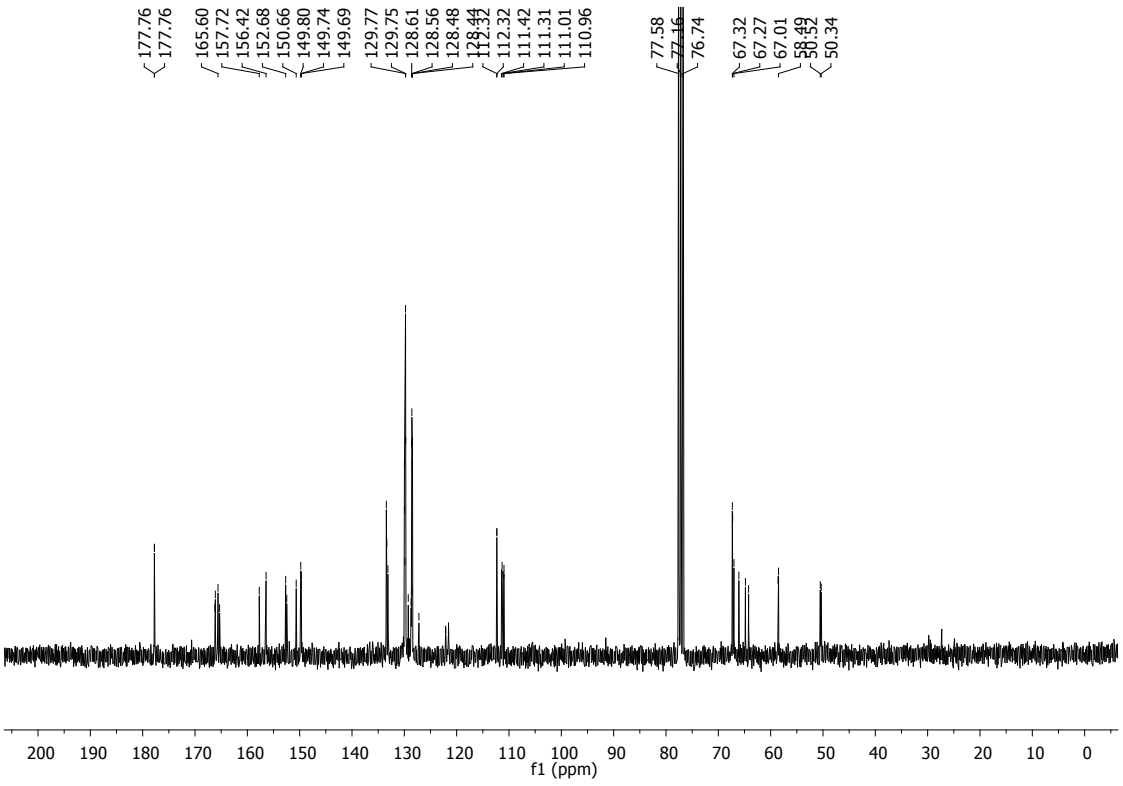


Mixture of compounds **7a-I** and **7a-II**

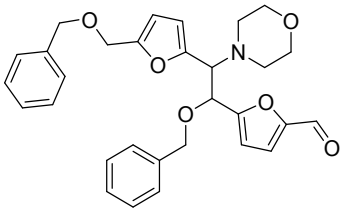


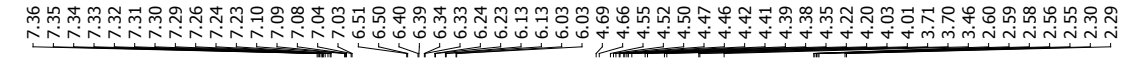


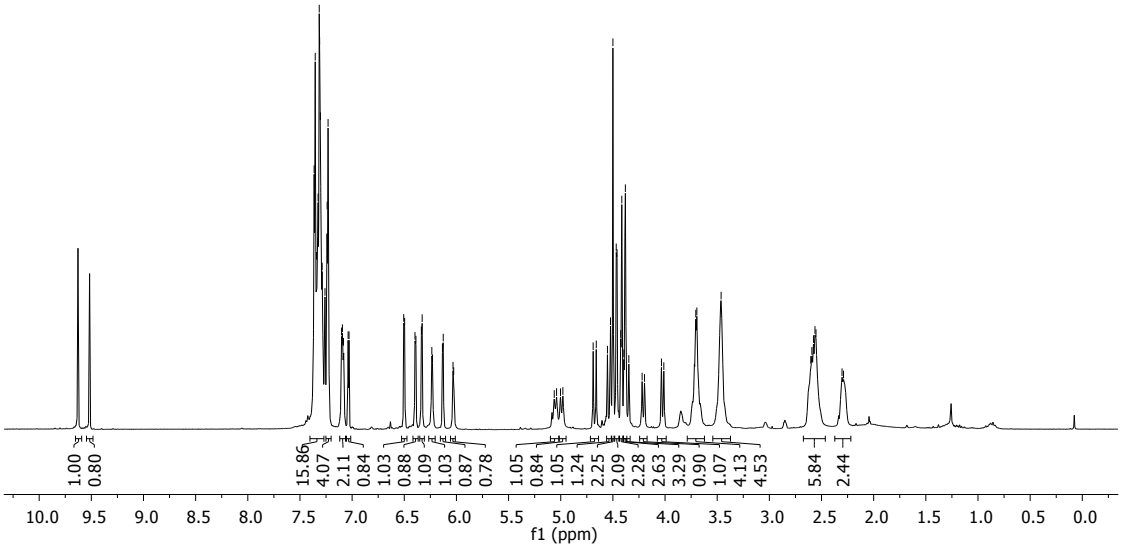


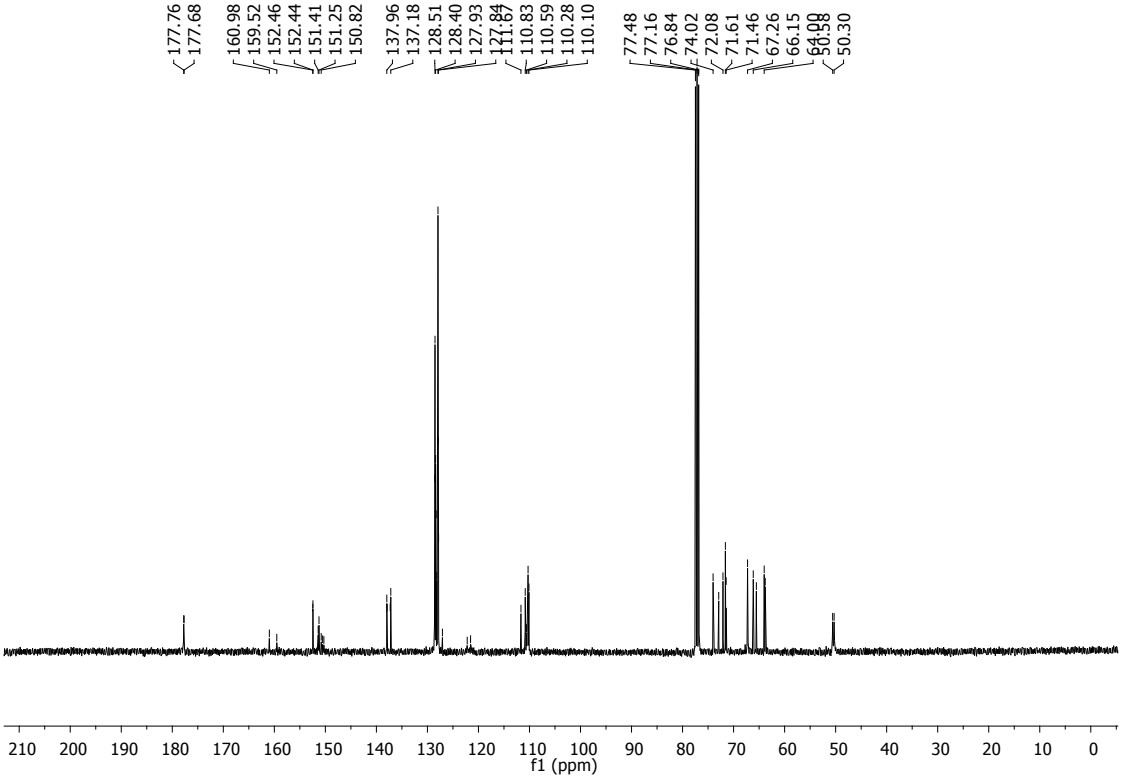


Mixture of compounds **8a-I** and **8a-II**

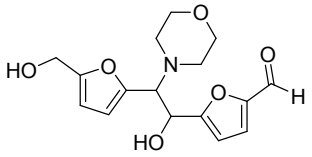


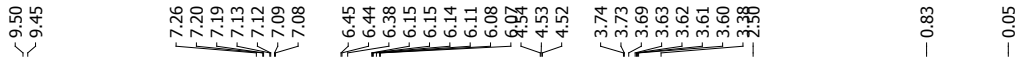


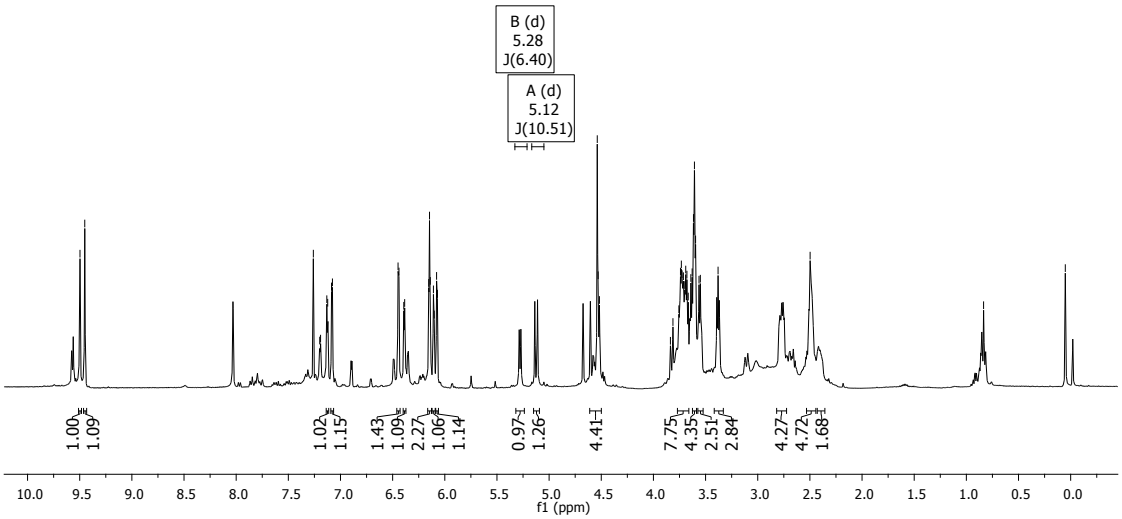


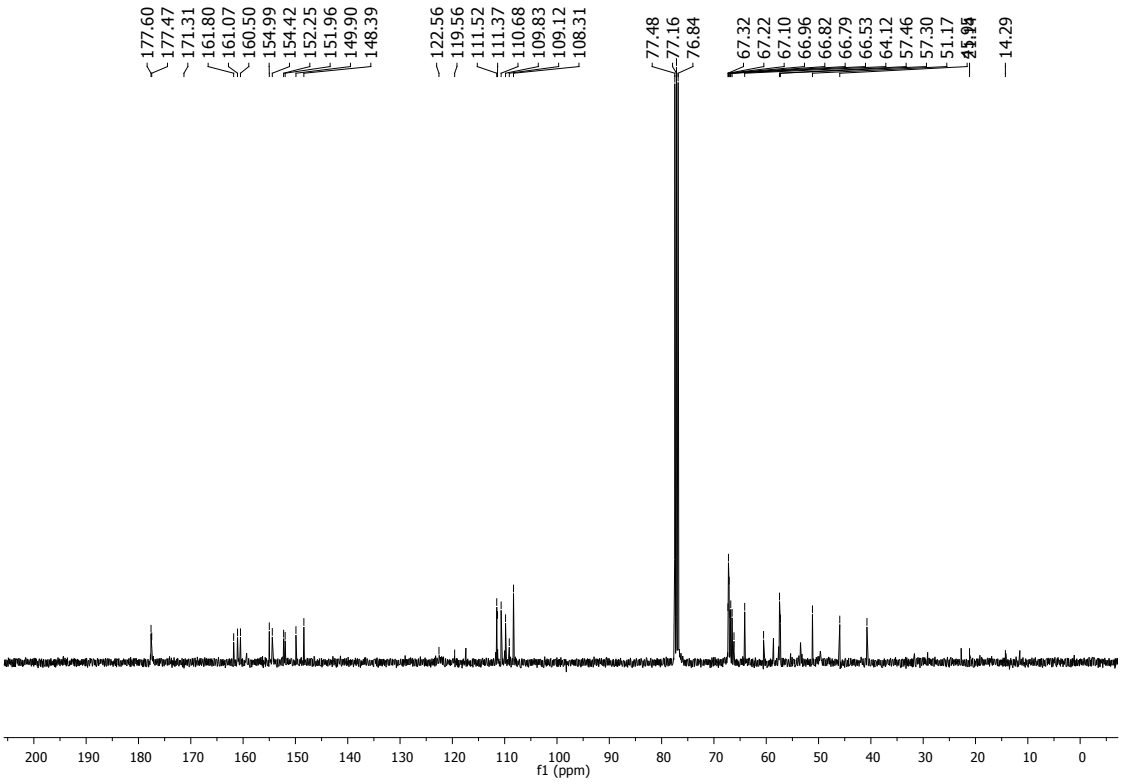


Mixture of compounds compound **9a-I** and **9a-II**

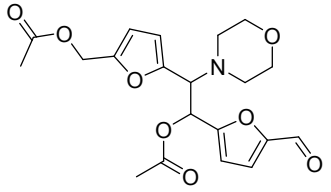


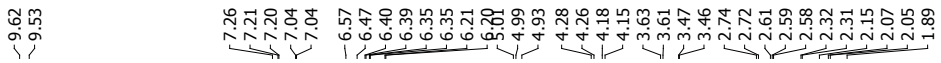


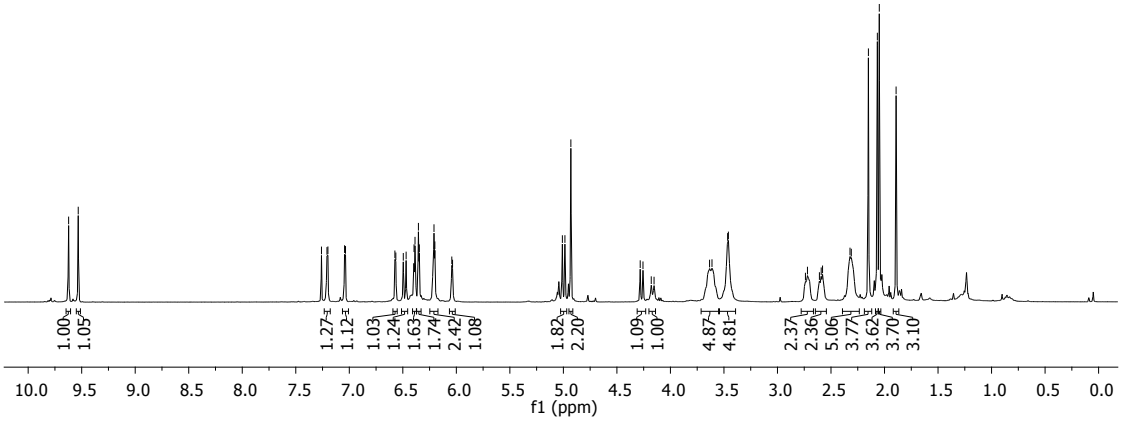


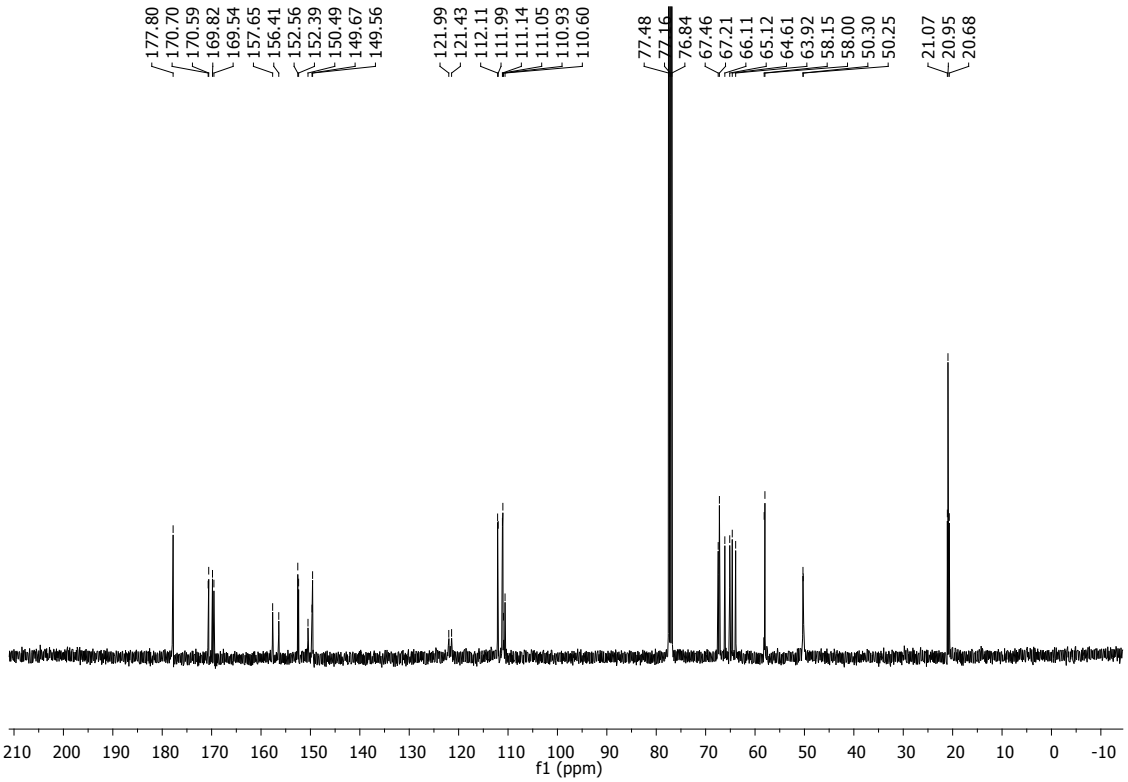


Compound **10a-I** and **10a-II**

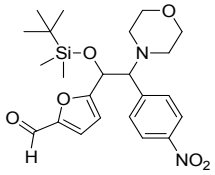




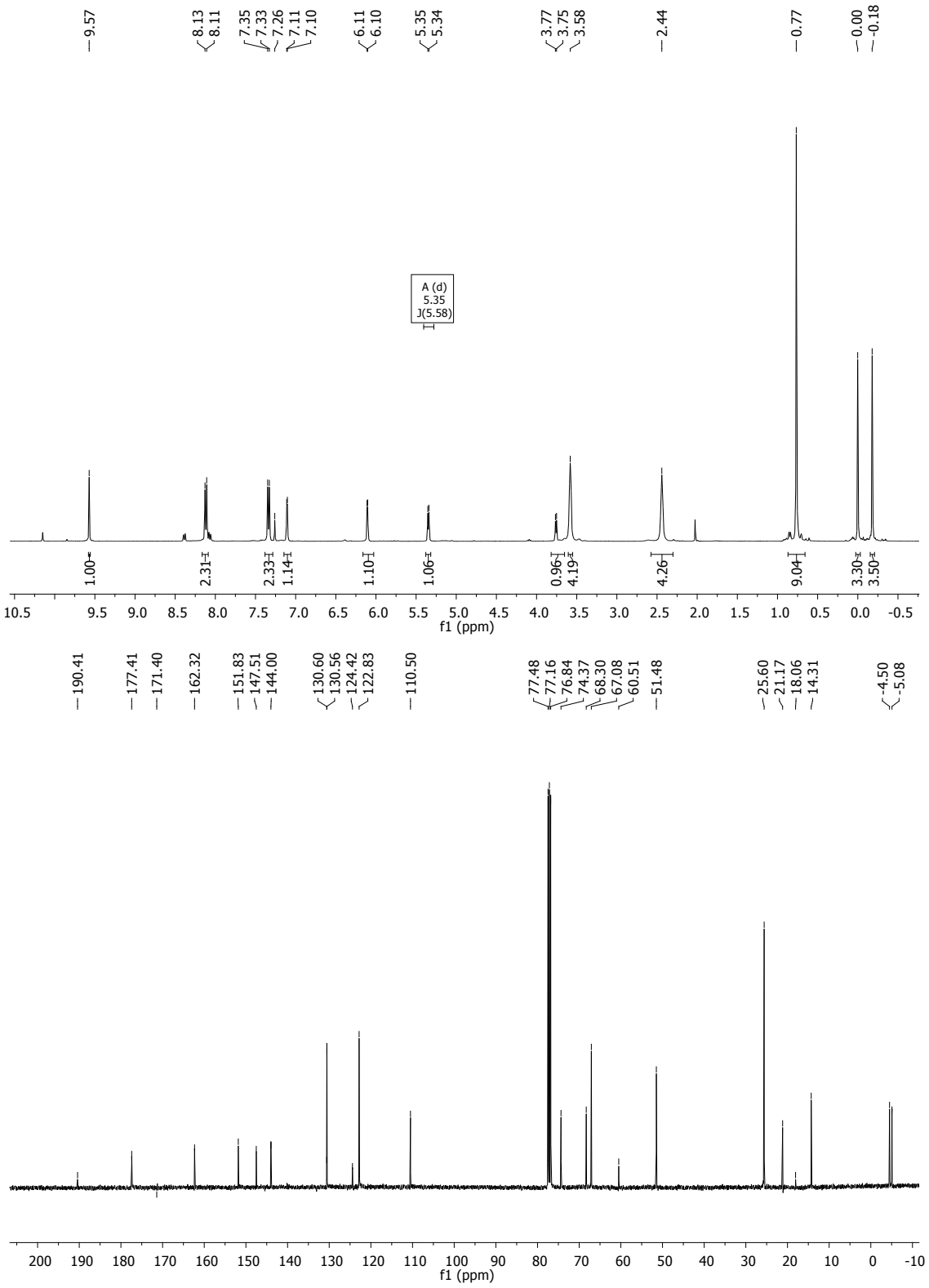




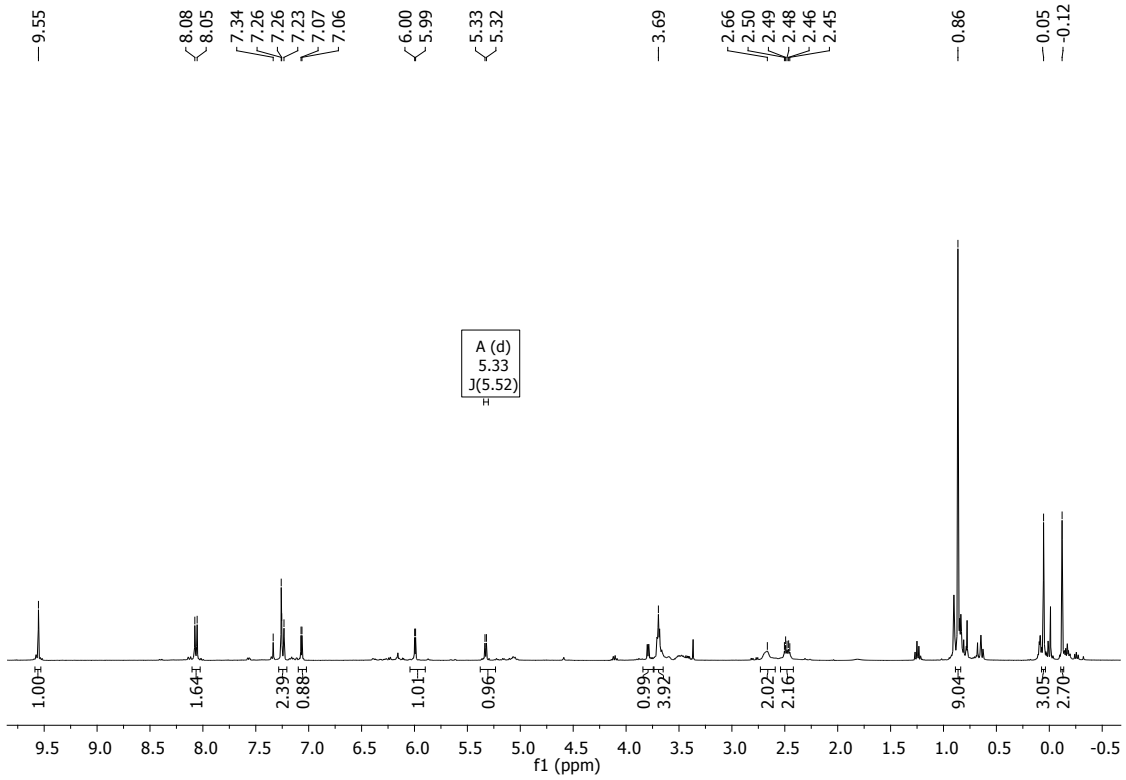
Compound **11-I**



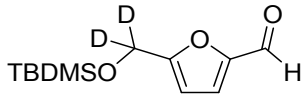
11-I

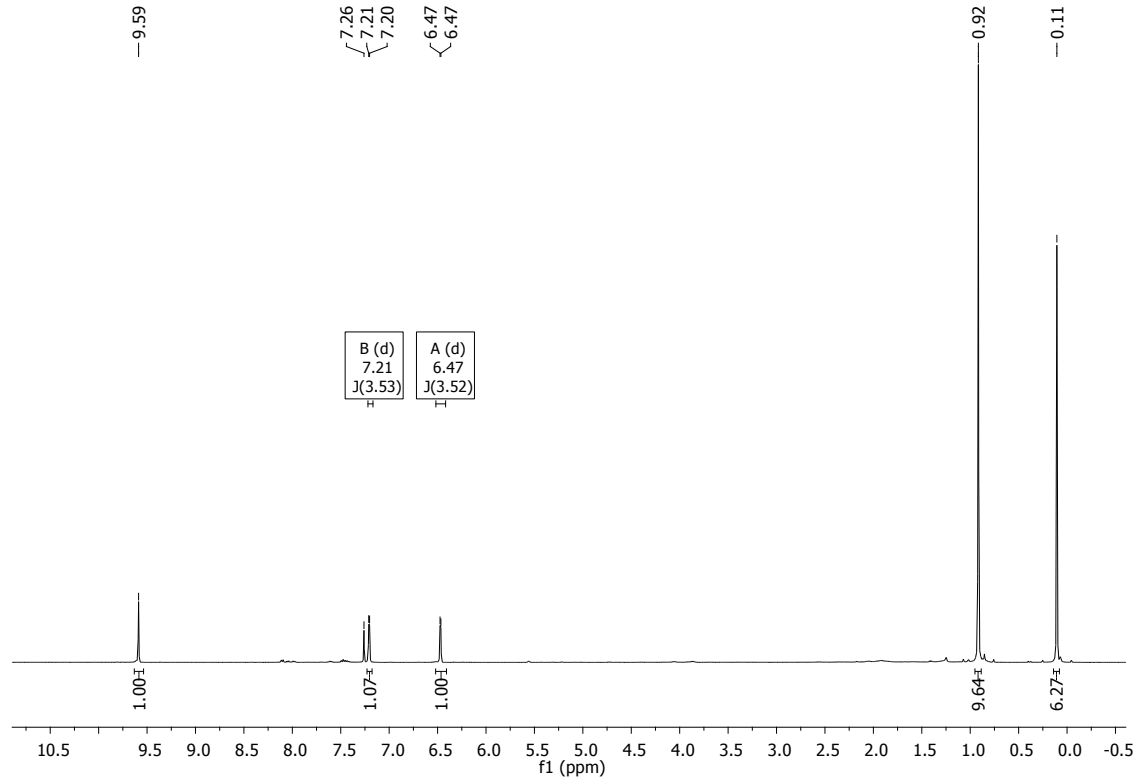


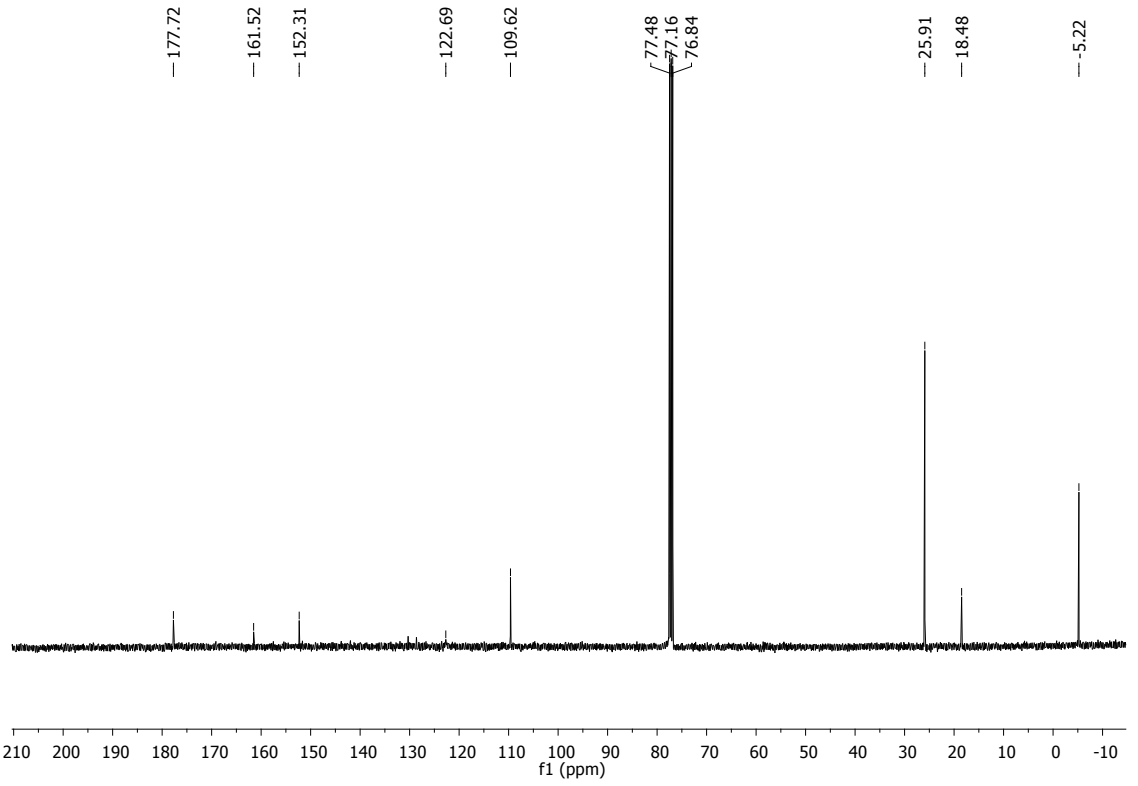
Compound **11-II**



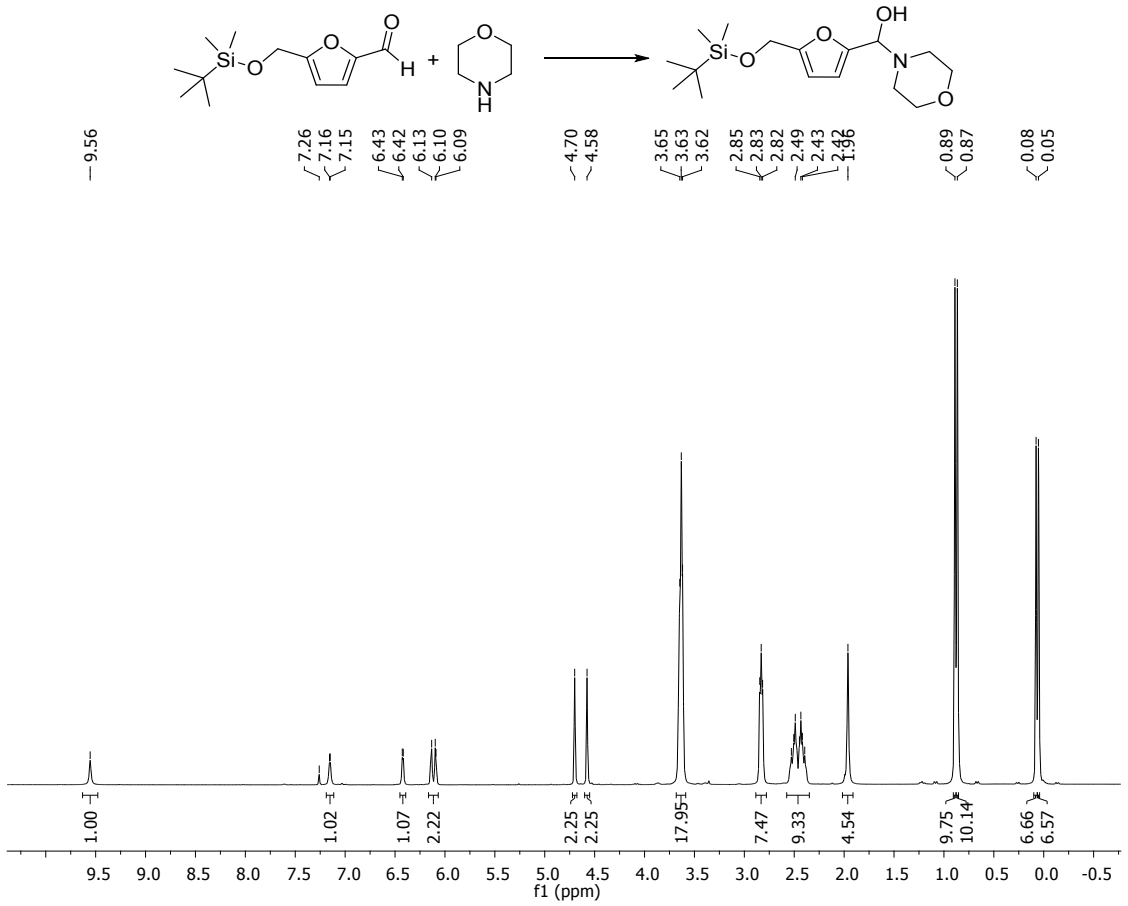
Compound **1-d_2**







Identification of the aminal of 1 and morpholine



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