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Supporting Information

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Selective P–P and P–O–P Bond Formations through Copper-Catalyzed Aerobic Oxidative Dehydrogenative Couplings of H-Phosphonates

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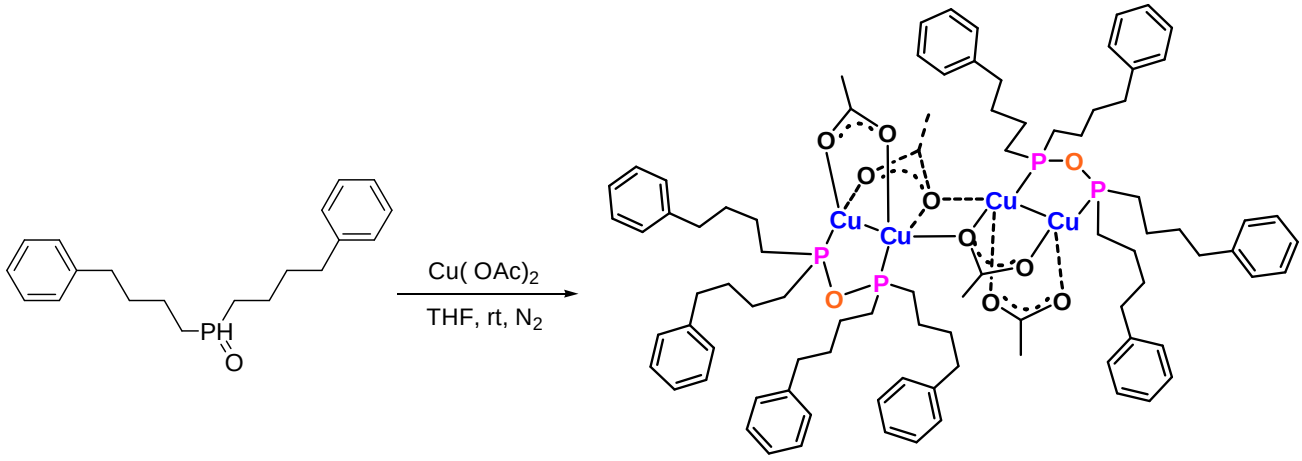
General.

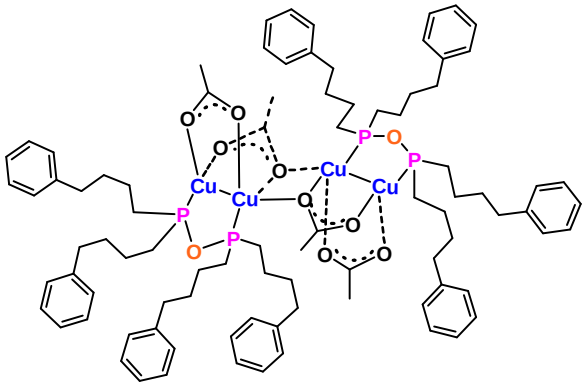
^{1}H, ^{13}C and ^{31}P NMR spectra were recorded on a JEOL LA-500 instrument (500 MHz for ^{1}H, 125.4 MHz for ^{13}C, and 201.9 MHz for ^{31}P NMR spectroscopy) or a JEOL LA-400 instrument (400 MHz for ^{1}H, 100 MHz for ^{13}C, and 162 MHz for ^{31}P NMR spectroscopy). $CDCl_3$ or benzene-d_6 was used as the solvent. Chemical shift values for ^{1}H and ^{13}C were referred to internal Me_4Si (0 ppm), and that for ^{31}P was referred to H_3PO_4 (85% solution in D_2O, 0 ppm). Elemental analysis was performed by the Analytical Center at the National Institute of Advanced Industrial Science and Technology.

Synthesis and characterization of complex 3b



To a capped tube were added the secondary phosphine oxide $(Ph(CH_2)_4)_2P(O)H$ (6 mmol), anhydrous $Cu(OAc)_2$ (4 mmol) and THF (10 mL) under nitrogen atmosphere. The reaction mixture was stirred at room temperature for 2 h. Then volatiles were removed under vacuum. The residue was dissolved in THF (5 mL) and Et_2O (5 mL). Hexane (15 mL) was added. The solution was slowly cooled to -30 ºC to give colorless crystals suitable for X-ray analysis. Yield: 1.45 g, 56%.

Compound **3b**



Colorless solid, m.p.: 77–78 ºC. ^{1}H NMR (benzene-d_6, 400 MHz): δ 7.23-7.14 (m, 32H, C*H*), 7.10-7.06 (m, 8H, C*H*), 2.54 (t, J = 6.8 Hz, 16H, CH_2), 2.32 (s, 12H, CH_3) 1.59-1.51 (m, 40H, CH_2), 1.36-1.30 (m, 8H, CH_2). ^{13}C NMR (benzene-d_6, 100 MHz): δ 177.6 (*C*O), 142.3 (*C*H), 128.8 (*C*H), 128.7 (*C*H), 126.1 (*C*H), 36.0 (*C*H_2), 33.1 (dd, $J_{C\text{-}P}$ = 5.7 Hz, $J_{C\text{-}P}$ = 6.7 Hz, *C*H_2), 32.6 (dd, $J_{C\text{-}P}$ = 2.5 Hz, *C*H_2, overlap), 24.5 (*C*H_3), 22.9 (*C*H_2). ^{31}P NMR (benzene-d_6, 162 MHz): δ 120.77. Anal. Calcd for $C_{88}H_{116}Cu_4O_{10}P_4$: C, 61.74; H, 6.83. Found: C, 61.36; H, 6.66.

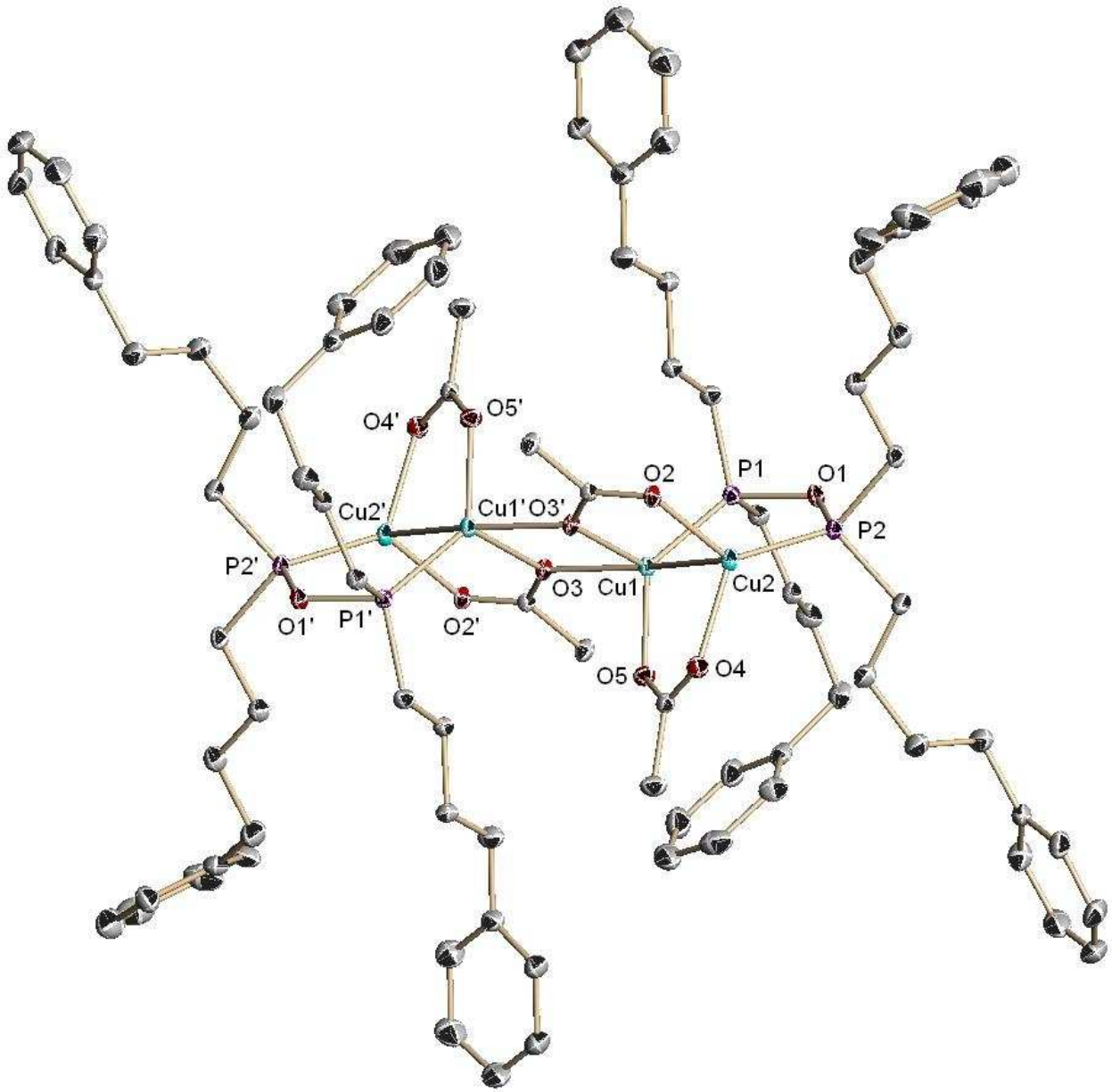


Fig. 1 Molecular structure of complex **3b** (H atoms omitted for clarity).

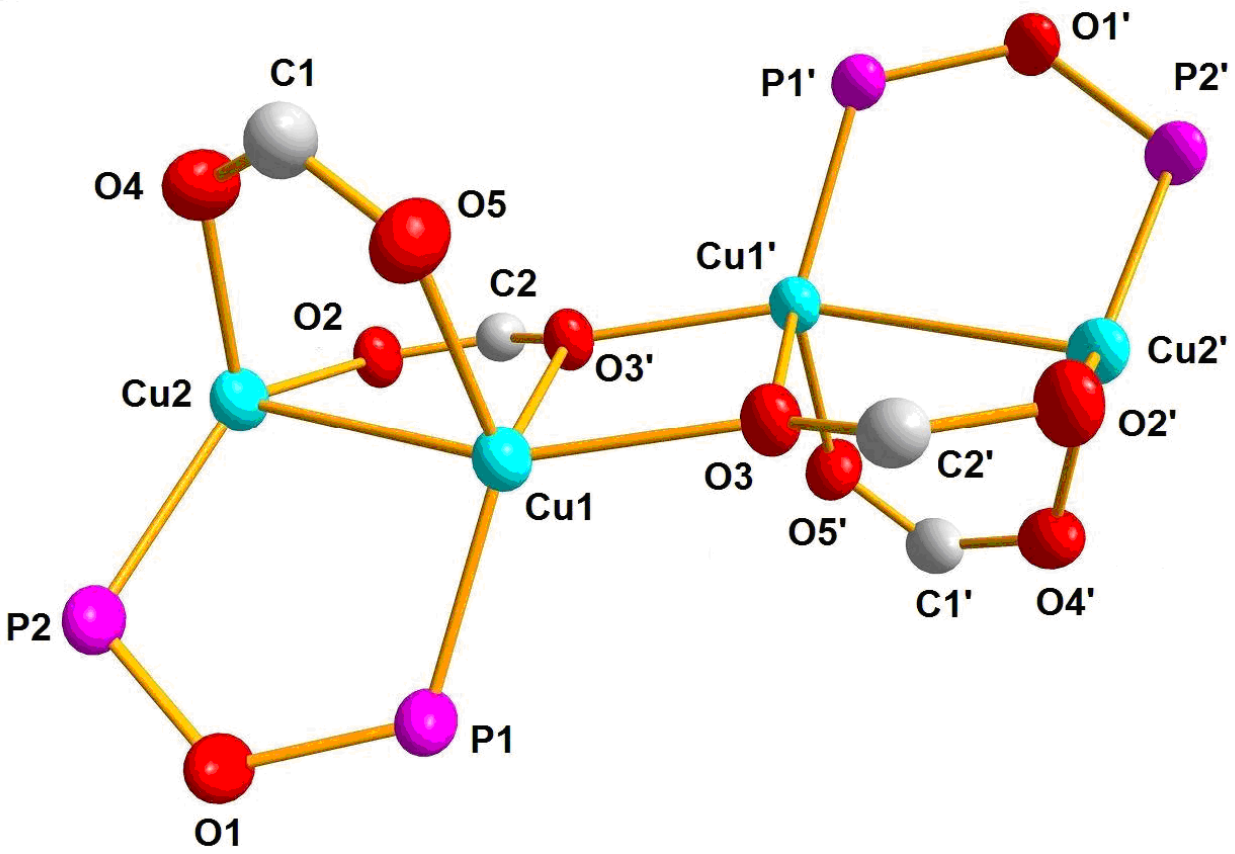
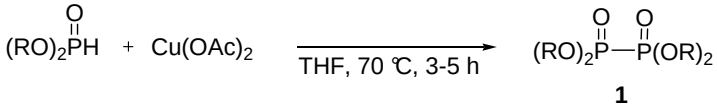


Fig. 2 A simplified diagram showing the coordination geometry of complex **3b**.

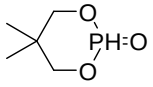
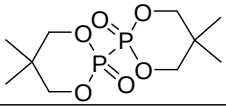
A general procedure for the stoichiometric reaction of *H*-phosphonates with $Cu(OAc)_2$ leading to hypophosphates.

To a capped tube were added *H*-phosphonate (5 mmol), anhydrous $Cu(OAc)_2$ (5 mmol) and THF (10 mL) under nitrogen atmosphere. The reaction mixture was stirred at 70 ºC for the time as shown in Table 1. The precipitate was filtered, washed with THF, and then the filtrate was evaporated under vacuum. 25 mL chilled saturated NH_4Cl solution was added. The product was extracted with $CHCl_3$, dried over $MgSO_4$, and concentrated under vacuum to give NMR spectroscopically pure coupling products.

Table 1. The stoichiometric reaction of *H*-phosphonates with $Cu(OAc)_2$.



1

run	*H*-phosphonate	reaciton time (h)	product	% yield[a](b)
1	$(i\text{-PrO})_2P(O)H$	4	$(i\text{-PrO})_2P(O)-P(O)(Oi\text{-Pr})_2$	99 (93)
2	$(n\text{-BuO})_2P(O)H$	3	$(n\text{-BuO})_2P(O)-P(O)(On\text{-Bu})_2$	99 (92)
3	$(EtO)_2P(O)H$	3	$(EtO)_2P(O)-P(O)(OEt)_2$	99 (90)
4	$(n\text{-}C_{12}H_{25}O)_2P(O)H$	5	$(n\text{-}C_{12}H_{25}O)_2P(O)-P(O)(On\text{-}C_{12}H_{25})_2$	98 (91)
5	$(PhCH_2O)_2P(O)H$	4	$(PhCH_2O)_2P(O)-P(O)(OCH_2Ph)_2$	99 (94)
6		5		98 (90)

[a] ^{31}P NMR yields. [b] Isolated yields.

A general procedure for copper-catalyzed aerobic oxidative coupling of *H*-phosphonates leading to hypophosphates.

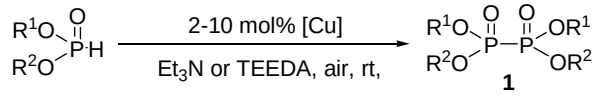
a)

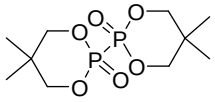
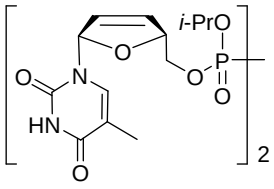
To a tube were added $Cu(OAc)_2$ (3.7 mg, 0.02 mmol) and Et_3N (200 uL). The mixture was stirred at room temperature for 5 min, then *H*-phosphonates (1 mmol) was added. The reaction mixture was stirred under dry air atmosphere at room temperature for the time as shown in Table 2. 10 mL chilled saturated NH_4Cl water solution was added, and the mixture was extracted with $CHCl_3$, dried over $MgSO_4$, filtered, and concentrated under vacuum to give NMR spectroscopically pure coupling products.

b)

To a tube were added CuCl (9.9 mg, 0.1 mmol), TEEDA (52.0 mg, 0.30 mmol) and acetone, and the mixture was stirred at room temperature for 5 min. *H*-phosphonates (1 mmol) was added. The reaction mixture was stirred under dry air atmosphere at room temperature for the time as shown in Table 2. Evaporated the solvent and TEEDA, 10 mL chilled saturated NH_4Cl water solution was added, and the mixture was extracted with $CHCl_3$, dried over $MgSO_4$, filtered, and concentrated under vacuum to give NMR spectroscopically pure coupling products.

Table 2. Copper-catalyzed aerobic oxidative coupling of *H*-phosphonates leading to hypophosphates.



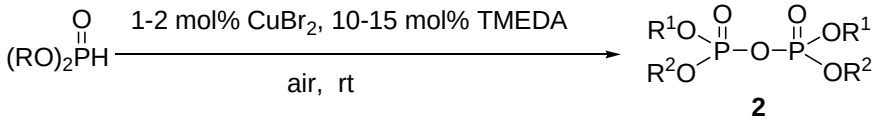
run	[Cu] (mol%)	reaciton time (h)	product **2**	% yield [a]([b])
1[c]	$Cu(OAc)_2$ (2)	4	$(i\text{-PrO})_2P(O)\text{—}P(O)(Oi\text{-Pr})_2$	98 (93)
2[d]	CuCl (10)	1.5	$(n\text{-BuO})_2P(O)\text{—}P(O)(On\text{-Bu})_2$	94 (80)
3[d]	CuCl (10)	1.5	$(EtO)_2P(O)\text{—}P(O)(OEt)_2$	98 (85)
4[c]	$Cu(OAc)_2$ (2)	4	$(n\text{-}C_{12}H_{25}O)_2P(O)\text{—}P(O)(On\text{-}C_{12}H_{25})_2$	95 (84)
5[d]	CuCl (10)	3	$(PhCH_2O)_2P(O)\text{—}P(O)(OCH_2Ph)_2$	96 (83)
6[d]	CuCl (10)	6		96 (84)
7[d]	CuCl (10)	6		95 (78)

[a] ^{31}P NMR yields. [b] Isolated yields. [c] $Cu(OAc)_2$ (2 mol%), Et_3N (0.2 mL), $(RO)_2P(O)H$ (1 mmol).
[d] CuCl (10 mol%), TEEDA (30 mol%), acetone (0.5 mL), and $(RO)_2P(O)H$ (1 mmol).

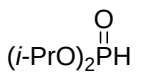
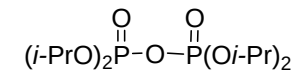
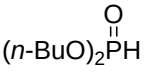
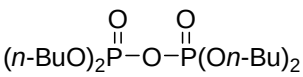
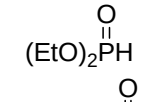
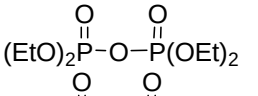
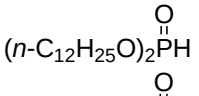
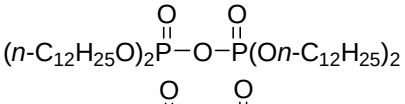
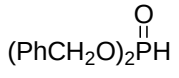
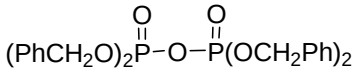
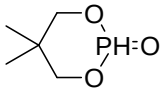
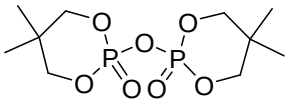
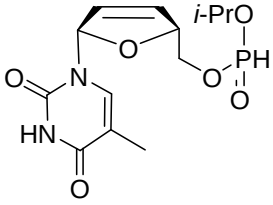
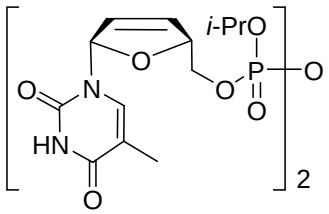
Typical procedure for copper-catalyzed aerobic oxidative coupling of *H*-phosphonates leading to pyrophosphates

To a suspension of $CuBr_2$ (2.2 mg, 0.01 mmol) in 1 mL of acetone, TMEDA (11.6 mg 0.1 mmol) were added. The mixture was stirred at room temperature for 5 min, and then *H*-phosphonates (1 mmol) was added. The mixture was stirred under dry air for the time as shown in Table 3. Chilled saturated NH_4Cl water solution was added, and the mixture was extracted with $CHCl_3$, dried over $MgSO_4$, filtered, and concentrated under vacuum to give NMR spectroscopically pure coupling products.

Table 3. Copper-catalyzed aerobic oxidative coupling of *H*-phosphonates leading to pyrophosphates



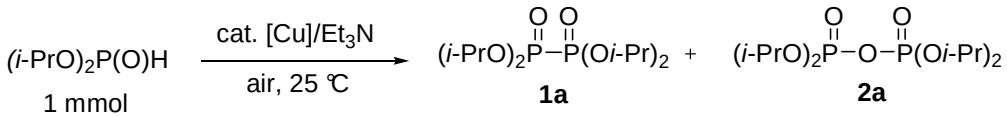
2

run	*H*-phosphonate	reaciton time (h)	product **2**	% yield[a]([b])
1[c]		6		100 (99)
2[c]		6		100 (99)
3[c]		6		100 (99)
4[d]		8		99 (98)
5[d]		15		97 (90)
6[d]		24		99 (96)
7[d]		24		98 (91)

[a] ^{31}P NMR yields. [b] Isolated yields. [c] $CuBr_2$ (1 mol%), TMEDA (10 mol%), acetone (1 mL), $(RO)_2P(O)H$ (1 mmol). [d] $CuBr_2$ (2 mol%), TMEDA (15 mol%), THF (1 mL), $(RO)_2P(O)H$ (1 mmol).

Screening on the catalysts

Table 4-1. Copper-catalyzed aerobic oxidative coupling of *H*-phosphonates with Et_3N.



1a **2a**

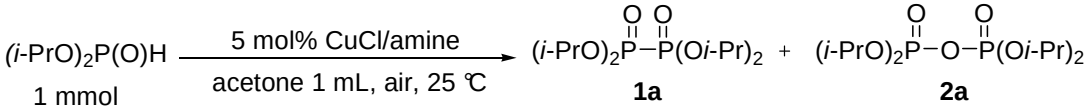
Entry	Cat. [Cu] (mol%)	Et_3N (mL)	Solvent (mL)	Time (h)	% yield **1a**[a] ([b])	% yield **2a**[a] ([b])
1	$Cu(OAc)_2$ (10)	0.2	/	4	**98.4 (99.2)**	**0 (0)**
2	$Cu(OAc)_2$ (5)	0.2	/	4	**98.2 (99.1)**	**0 (0)**
3	$Cu(OAc)_2$ (2)	/	acetone (0.5)	4	0.05	0
				20	0.3	0
4		0.1	/	4	45.4	0.1
				20	76.6	0.3
5		0.2	/	4	**98.0 (98.7)**	**0.03 (0)**
				20	98.1	0.03
6		0.5	/	4	96.8	0.01
				20	97.0	0.01

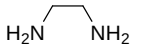
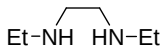
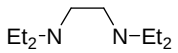
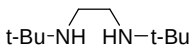
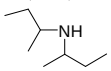
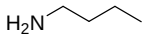
7	$Cu(OAc)_2$ (1)	0.2	/	4	29.7	0.4
				20	72.7	0.5
8	CuCl (2)	0.2	/	2	5.8	0.6
				8	67.1	3.6
				20	92.6	4.1
9	$CuCl_2$ (2)	0.2	/	2	11.1	1.7
				8	41.6	5.7
				20	87.0	**9.4**
10	CuBr (2)	0.2	/	2	37.5	2.2
				8	88.5	4.5
				20	92.7	4.6
11	$CuBr_2$ (2)	0.2	/	2	11.5	3.2
				8	58.7	10.8
				20	78.7	**12.0**
12	CuI (2)	0.2	/	2	33.7	26.2
				8	56.5	41.3
				20	59.1	38.8
13	CuOAc (2)	0.2	/	2	38.5	0.05
				8	96.5	0.06
				20	96.5	0.1
14	$Cu(NO_3)_2 \cdot 3H_2O$ (2)	0.2	/	2	27.3	0.5
				8	90.1	1.5
				20	94.3	1.5
15	$CuSO_4 \cdot 5H_2O$ (2)	0.2	/	2	26.4	0
				8	91.2	0.4
				20	96.1	0.4
16	$CuSO_4$ (2)	0.2	/	2	34.0	0
				8	95.9	0.2
				20	98.0	0.3
17	$Cu(OOCCF_3)_2$ (2)	0.2	/	2	54.5	0.3
				8	97.3	0.5
				20	97.4	0.5
18	$Cu(OH)_2$ (2)	0.2	/	2	0.5	0
				8	2.1	0.1
				20	3.0	0.3
19	CuF_2 (2)	0.2	/	2	0.9	0
				8	8.1	0.2
				20	28.1	0.8
20	$Cu(acac)_2$ (2)	0.2	/	2	0.3	0
				8	0.9	0
				20	18.6	0.1
21	$Cu(acacF_6)_2$ (2)	0.2	/	2	76.9	0.3
				8	77.8	0.3
				20	79.9	0.3
22	$Cu(OTf)_2$ (2)	0.2	/	2	78.0	0.3
				8	79.1	0.3
				20	79.3	0.4
23	$Cu(OAc)_2$ (2)	0.2	/	2	83.2	0.02
				8	98.1	0.03
				20	98.1	0.03
24		0.2	DMF (0.5)	2	10.2	0
				8	31.4	0.1
				20	89.4	0.2
25		0.2	DMSO (0.5)	2	5.7	0
				8	8.5	0
				20	35.3	0.2
26		0.2	THF (0.5)	2	36.0	0.1
				8	90.1	0.2
				20	97.5	0.3
27		0.2	CH_3CN (0.5)	2	79.2	0.5
				8	94.4	0.6
				20	94.9	0.7
28		0.2	Ethanol (0.5)	2	7.6	0
				8	51.3	1.5
				20	65.3	2.0
29		0.2	CH_2Cl_2 (0.5)	2	20.9	0.3
				8	83.0	0.5
				20	93.7	0.7
30		0.2	Toluene (0.5)	2	49.2	0
				8	84.9	0.3

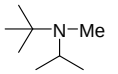
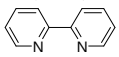
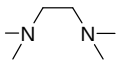
				20	94.2	0.4
31		0.2	$CH_3COOC_2H_5$ (0.5)	2	80.0	0.3
				8	93.8	0.4
				20	96.4	0.4
32		0.2	Acetone (0.2)	2	81.7	0.2
				8	92.1	0.2
				20	97.9	0.2
33		0.2	Acetone(0.5)	2	26.5	0
				8	90.9	0.2
				20	96.6	0.3
34		0.2	Acetone (1.0)	2	19.5	0
				8	58.3	0.2
				20	96.4	0.4
35		0.2	H_20 (0.01)	2	31.2	0.1
				8	58.3	0.7
				20	59.8	0.8
36		0.2	H_20 (0.02)	2	26.2	0.6
				8	55.1	0.9
				20	58.5	0.9
37		0.2	H_20 (0.05)	2	27.0	1.0
				8	28.1	1.1
				20	**31.8**	**1.2**

[a] Determined by GC, [b] ^{31}P NMR yields.

Table -4-2. CuCl-catalyzed aerobic oxidative coupling of *H*-phosphonates.

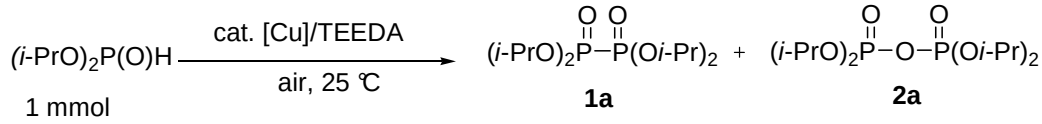


Entry	Amine[a] (20 mol%)	Time (h)	% yield **1a**[b]	% yield **2a**[b]
1		5	0.1	0.4
		20	0.2	2.6
2		5	7.4	34.7
		20	8.5	77.8
3		5	64.3	12.0
		20	**71.5**	**27.4**
4		5	13.3	24.2
		20	16.2	41.6
5		5	5.4	2.6
		20	9.0	15.2
6		5	4.7	3.1
		20	6.3	14.4
7		5	4.1	1.1
		20	9.4	13.7
8		5	2.8	1.6
		20	4.5	9.0
9		5	2.2	0
		20	6.9	0.1
10	$MeNH_2$	5	27.7	3.5
		20	32.9	8.4
11		5	14.3	2.7
		20	23.9	13.7
12		5	24.4	2.7
		20	30.6	7.9

13	Et_3N	5 20	12.7 16.5	0.7 5.7
14		5 20	3.0 4.7	0.16 1.3
15		5 20	1.5 2.3	9.5 **43.8**
16		5 20	3.7 **10.7**	28.9 **48.5**

[a] Based on N atom. [b] Determined by GC.

Table 4-3. Copper-catalyzed aerobic oxidative coupling of *H*-phosphonates with TEEDA.



1 mmol

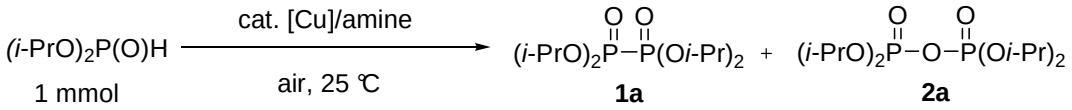
1a **2a**

Entry	Cat. [Cu] (%)	TEEDA (mol%)	Solvent (mL)	Time (h)	% yield **1a**[a] ([b])	% yield **2a**[a] ([b])
1	CuCl (5)	10	acetone (1)	5 20	64.3 71.4	12.0 27.5
2		10	Acetone (1) and H_2O (0.02)	5 20	40.8 54.0	6.3 28.2
3		20	acetone (1)	5 20	76.4 85.5	8.2 11.5
4		30	acetone (1)	5 20	80.6 89.0	7.2 9.3
5		100	/	1 3	87.4 87.5	11.0 11.1
6	$CuCl_2$ (5)	10	acetone (1)	5 20	46.3 47.2	34.2 51.3
7	CuBr (5)	10	acetone (1)	5 20	51.8 70.1	10.2 29.1
8		20	acetone (1)	5 20	24.8 83.2	1.0 8.5
9		30	acetone (1)	5 20	36.9 89.2	2.9 7.4
10	$CuBr_2$ (5)	10	acetone (1)	5 20	57.4 58.4	38.1 41.1
11	CuI (5)	10	acetone (1)	5 20	34.1 39.0	33.7 60.1
12	$Cu(OAc)_2$ (5)	10	acetone (1)	5 20	0.9 2.5	0.1 0.3
13		100	/	5 20	41.2 63.1	0.2 1.1
14	CuBr (2.5)	20	/	5 20	23.3 76.2	1.0 22.3
15	CuBr (10)	20	acetone (1)	5 20	73.3 94.1	2.6 4.8
16	CuBr (10)	20	/	3	90.9	8.0
17	CuBr (10)	30	/	2 4	72.5 93.5 (94.7)	1.1 5.5 (5.3)
18	CuCl (10)	20	acetone (1)	5 20	56.1 95.4	0.5 3.8
19		30	acetone (1)	2 4	66.6 95.7 (97.1)	0.2 2.9 (2.9)
20		20	/	1.5 h	**96.1**	**2.3**
21		30	/	1.5 h	**96.8 (97.5)**	**2.1 (2.0)**
22		100	/	1.5 h	97.0	2.0
23	$Cu(OOCCF_3)_2$ (10)	20	/	4	55.3	0.5

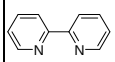
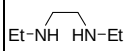
24	$Cu(NO_3)_2 \cdot 3H_2O$ (10)	20	/	4	45.3	0.1

[a] Determined by GC, [b] 31P NMR yields.

Table 4-4. Copper-catalyzed aerobic oxidative coupling of *H*-phosphonates with TMEDA



1 mmol **1a** **2a**

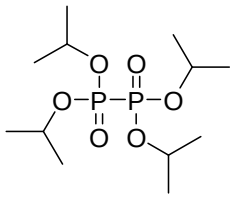
Entry	cat.[Cu] (mol%)	amine (mol%)	solvent (mL)	time (h)	% yield **1a**[a] ([b])	% yield **2a**[a] ([b])
1	$CuBr_2$ (5)	TMEDA (5)	acetone (1)	2	0.5	62.8
2		TMEDA (10)		2	0.4 (0.4)	99.0 (99.3)
3		TMEDA (15)		2	0.3 (0.3)	98.0 (99.4)
4		TMEDA (15)	acetone (1) and H_2O (0.04)	2	2.0 (1.9)	97.3 (97.8)
5		TMEDA (20)	acetone (1)	2	0.3 (0.3)	98.9 (99.3)
6	$CuBr_2$ (2.5)	TMEDA (2.5)		4	0	0.4
7		TMEDA (5)		4	0.3	87.1
8		TMEDA (7.5)		4	0 (0)	99.1 (100)
9		TMEDA (10)		4	0 (0)	99.1 (100)
10	$CuBr_2$ (1)	TMEDA (5)		6 20	1.3 2.4 (2.7)	42.5 72.4 (75.2)
11		TMEDA (7.5)		6 20	0.01 0.06 (0.1)	**96.4** **98.4 (99.9)**
12		TMEDA (10)		6 20	0 (0) 0	**99.2 (100)** **98.9**
13		TMEDA (10)	THF (1)	6 20	0.01 (0) 0	**99.1 (100)** **98.9**
14	$CuBr_2$ (0.5)	TMEDA (5)	acetone (1)	20	0.6	26.9
15	$CuBr_2$ (1)	 (5)		6	0.02	0.05
16	$CuBr_2$ (1)	 (5)		6	0.1	27.6
17	$CuCl_2$ (5)	TMEDA (15)		2 6 20	0.2 1.1 1.4	25.8 62.3 98.4
18	CuCl (10)	TMEDA (100)	neat	3	12.9	86.2
19	CuCl (10)	TMEDA (200)	/	3	9.2	90.3
20	CuCl (5)	TMEDA (100)	/	3	6.4	92.5
21		TMEDA (100)	acetone (1)	3 6	4.1 4.3	95.0 95.2
22		TMEDA (200)		3 6	3.1 3.2	96.1 96.4
23	CuCl (2)	TMEDA (20)		3 6	2.1 2.3	16.9 17.5
24		TMEDA (50)		3 6	3.5 3.8	67.6 88.3
25		TMEDA (50)	acetone (0.5)	3 6	4.6 5.9	55.0 62.0
26		TMEDA (100)	acetone (1)	3 6	2.5 3.5	68.7 90.0
27		TMEDA (200)		3	**2.3**	**97.1**
28		TMEDA (200)	Acetone (2)	3 6	**1.4** **1.6**	**85.8** **97.5**

29	CuCl (1)	TMEDA (100)	acetone (1)	3 6	0.6 0.7	16.5 25.3
30		TMEDA (200)		3 6	0.3 0.4	10.2 15.3
31	CuBr (2)	TMEDA (100)		3 6	1.8 2.5	65.3 77.8
32		TMEDA (200)		3 6	1.8 2.2	96.6 96.9
33	CuBr (1)	TMEDA (200)		3 6	0.01 0.01	2.9 3.6

[a] Determined by GC, [b] 31P NMR yields.

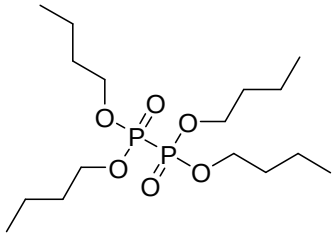
^{1}H NMR, ^{13}C NMR and ^{31}P NMR Spectra

1a[1,2]



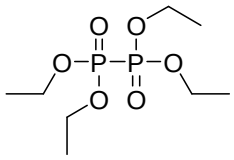
^{1}H NMR ($CDCl_3$, 400 MHz): δ 4.94-4.85 (m, 4H, C*H*), 1.39 (d, 24H, *J* = 6.4 Hz, CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz): 72.9 (dd, $J_{C\text{-}P}$ = 2.8 Hz, $J_{C\text{-}P}$ = 3.8 Hz, *C*H), 24.3 (dd, $J_{C\text{-}P}$ = 2.9 Hz, *C*H_3, overlap), 23.8 (dd, $J_{C\text{-}P}$ = 2.9 Hz, $J_{C\text{-}P}$ = 1.9 Hz, *C*H_3). ^{31}P NMR ($CDCl_3$, 162 MHz): δ 5.01.

1b[1]



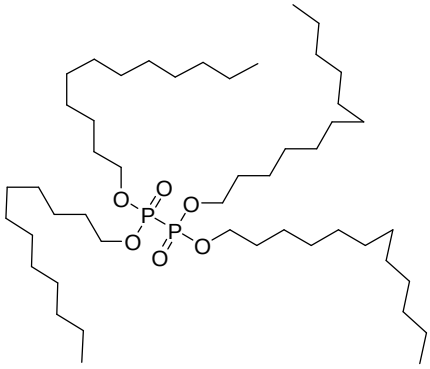
^{1}H NMR ($CDCl_3$, 500 MHz): δ 4.25-4.17 (m, 8H, CH_2), 1.73-1.65 (m, 8H, CH_2), 1.46-1.38 (m, 8H, CH_2), 0.94 (t, 12H, *J* = 7.3 Hz, CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 67.5 (dd, $J_{C\text{-}P}$ = 2.0 Hz, $J_{C\text{-}P}$ = 3.1 Hz, *C*H_2), 32.4 (dd, $J_{C\text{-}P}$ = 3.1 Hz, *C*H_2, overlap), 18.6 (*C*H_2), 13.5 (*C*H_3). ^{31}P NMR ($CDCl_3$, 202 MHz): δ 6.86.

1c[3,4]



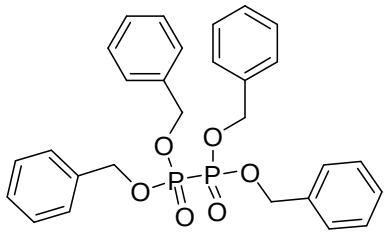
^{1}H NMR ($CDCl_3$, 500 MHz): δ 4.30-4.25 (m, 8H, CH_2), 1.38 (t, 12H, J = 7.0 Hz, CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 63.9 (dd, $J_{C\text{-}P}$ = 3.1 Hz, CH$_2$, overlap), 16.4 (dd, $J_{C\text{-}P}$ = 3.1 Hz, CH$_3$, overlap). ^{31}P NMR ($CDCl_3$, 202 MHz): δ 6.53.

1d



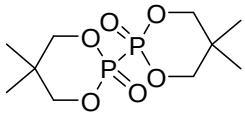
Wax solid. m.p.: 49–50 ºC. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 4.22-4.17 (m, 8H, CH_2), 1.75-1.68 (m, 8H, CH_2), 1.41-1.26 (m, 80H, CH_2), 0.88 (t, 12H, J = 6.8 Hz, CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 67.8 (dd, $J_{C\text{-}P}$ = 3.8 Hz, CH$_2$, overlap), 31.9 (CH$_2$), 30.5 (dd, $J_{C\text{-}P}$ = 2.9 Hz, CH$_2$, overlap), 29.7 (CH$_2$), 29.7 (CH$_2$), 29.6 (CH$_2$), 29.6 (CH$_2$), 29.4 (CH$_2$), 29.2 (CH$_2$), 25.4 (CH$_2$), 22.7 (CH$_2$), 14.1 (CH$_3$). ^{31}P NMR ($CDCl_3$, 162 MHz): δ 6.86. Anal. Calcd for $C_{48}H_{100}O_6P_2$: C, 69.02; H, 12.07. Found: C, 68.72; H, 12.36.

1e[5]



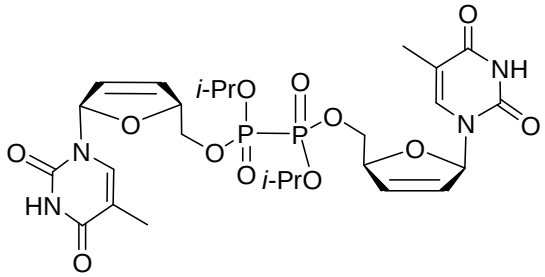
^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.33-7.29 (m, 20H, CH), 5.18-5.08 (m, 8H, CH_2). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 135.3 (dd, $J_{C\text{-}P}$ = 2.8 Hz, $J_{C\text{-}P}$ = 3.8 Hz, CH), 128.7(CH), 128.6(CH), 128.2(CH), 69.2 (dd, $J_{C\text{-}P}$ = 2.9 Hz, CH$_2$, overlap). ^{31}P NMR ($CDCl_3$, 162 MHz): δ 6.56.

1f[6]



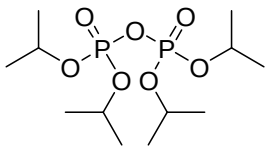
^{1}H NMR ($CDCl_3$, 400 MHz): δ 4.67 (d, 4H, J = 10.4 Hz, CH_2), 4.00 -3.92 (m, 4H, CH_2), 1.35 (s, 6H, CH_3), 0.89 (s, 6H, CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 78.8 (dd, $J_{C\text{-}P}$ = 3.8 Hz, CH$_2$, overlap), 32.7 (dd, $J_{C\text{-}P}$ = 3.8 Hz, $J_{C\text{-}P}$ = 4.8 Hz, (CH$_2$)$_2$$C$(CH$_3$)$_2$), 22.0 ($CH_3$), 20.2 ($CH_3$). ^{31}P NMR ($CDCl_3$, 162 MHz): δ -1.32.

1g



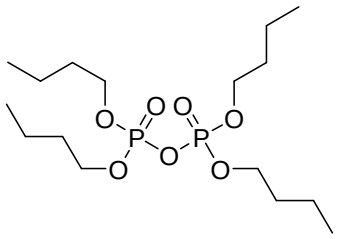
White solid. m.p.: 99–111 ºC. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.30, 9.25 and 9.23 (3s, 2H, NH), 7.28, 7.25 and 7.22 (3d, 2H, J = 1.2 Hz, H6-thymine), 7.01 (s, broad, 2H, H1'), 6.34-6.29 (m, 2H, H3'), 5.92-5.90 (m, 2H, H2'), 5.00 (s, broad, 2H, H4'), 4.94-4.91 (m, 2H, CH-isopropyl), 4.38-4.32 (m, 4H, H5'), 1.92, 1.92 and 1.91 (3s, broad, 6H, CH_3-thymine), 1.40-1.36 (m, 12H, CH_3-isopropyl). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 163.9 and 163.8 (2s, broad, C4-thymine), 150.9 and 150.8 (2s, broad, C2-thymine), 135.7 (d, $J_{C\text{-}P}$ = 2.9 Hz, C6-thymine), 135.6 and 135.5 (2s, broad, C6-thymine), 132.8 and 132.8 (2s, broad, C3'), 132.7 (d, $J_{C\text{-}P}$ = 2.8 Hz, C3',), 127.9 (dd, $J_{C\text{-}P}$ = 3.8 Hz, C2', overlap), 127.7 (s, broad, C2'). 111.5 and 111.4 (2s, broad, C5-thymine), 89.7 and 89.6 (2s, broad, C1'), 84.5, 84.4 and 84.3 (3d, $J_{C\text{-}P}$ = 3.8 Hz, C4'), 74.5, 74.5 and 74.3 (3s, broad, CH-isopropyl), 68.0, 67.8 and 67.7 (3s, broad, C5'), 24.3 and 23.8 (2s, broad, CH-isopropyl), 12.4 (s, broad, CH$_3$-thymine). ^{31}P NMR ($CDCl_3$, 162 MHz): δ 6.33 and 5.91 (broad). Anal. Calcd for $C_{26}H_{36}N_4O_{12}P_2$: C, 47.42; H, 5.51; N, 8.51. Found: C, 47.71; H, 5.35; N, 8.28.

2a[7,8]



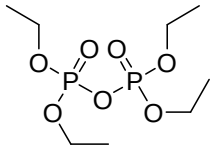
^{1}H NMR ($CDCl_3$, 400 MHz): δ 4.84-4.70 (m, 4H, C*H*), 1.38 (d, 24H, *J* = 6.0 Hz CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 74.1 (dd, $J_{C\text{-}P}$ = 3.1 Hz, *C*H, overlap), 23.6 (dd, $J_{C\text{-}P}$ = 3.1 Hz, *C*H_3, overlap), 23.5 (dd, $J_{C\text{-}P}$ = 3.1 Hz, *C*H_3, overlap). ^{31}P NMR ($CDCl_3$, 202 MHz): δ -15.09.

2b[9,10]



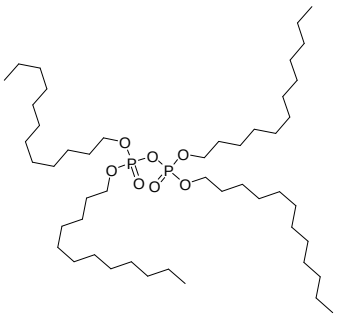
^{1}H NMR ($CDCl_3$, 500 MHz): δ 4.19-4.15 (m, 8H, CH_2), 1.72-1.66 (m, 8H, CH_2), 1.45-38 (m, 8H, CH_2), 0.94 (t, 12H, *J* = 7.3 Hz, CH_3). ^{31}P NMR ($CDCl_3$, 202 MHz): δ -12.79.

2c[8, 11]



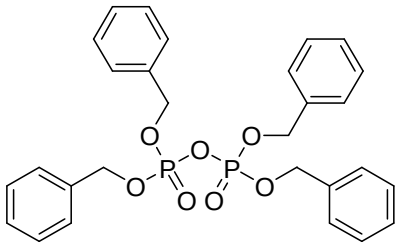
^{1}H NMR ($CDCl_3$, 400 MHz): δ 4.25-4.17 (m, 8H, CH_2), 1.34 (t, 12H, *J* = 7.0 Hz, CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 65.1 (dd, $J_{C\text{-}P}$ = 2.8 Hz, *C*H_2, overlap), 15.9 (dd, $J_{C\text{-}P}$ = 2.8 Hz *C*H_3, $J_{C\text{-}P}$ = 3.8 Hz). ^{31}P NMR ($CDCl_3$, 162 MHz): δ -13.12.

2d



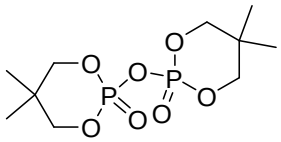
Wax solid. m.p.: 51–52 ºC. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 4.20-4.13 (m, 8H, CH_2), 1.74-1.67 (m, 8H, CH_2), 1.40-1.26 (m, 80H, CH_2), 0.89 (t, 12H, $J_{C\text{-}P}$ = 6.8 Hz, CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 69.2 (dd, $J_{C\text{-}P}$ = 2.9 Hz, *C*H_2, overlap), 32.0 (*C*H_2), 30.2 (dd, $J_{C\text{-}P}$ = 2.8 Hz, $J_{C\text{-}P}$ = 3.8 Hz, *C*H_2), 29.8 (*C*H_2), 29.7 (*C*H_2), 29.7 (*C*H_2), 29.6 (*C*H_2), 29.4 (*C*H_2), 29.2 (*C*H_2), 25.4 (*C*H_2), 22.7 (*C*H_2), 14.2 (*C*H_3). ^{31}P NMR ($CDCl_3$, 162 MHz): δ -12.77. Anal. Calcd for $C_{48}H_{100}O_7P_2$: C, 67.73; H, 11.84. Found: C, 68.01; H, 12.02.

2e[8]



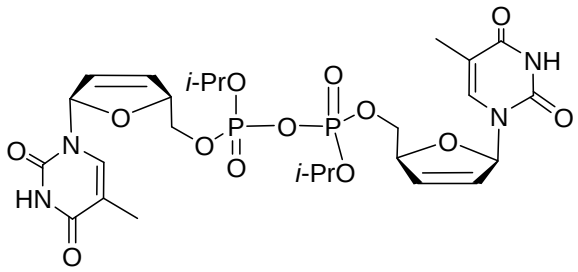
^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.34-7.29 (m, 20H, C*H*), 5.10-5.08 (m, 8H, CH_2). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 134.9 (dd, $J_{C\text{-}P}$ = 3.8 Hz, *C*H, overlap), 128.7 (CH), 128.5 (*C*H), 128.0 (*C*H), 70.4 (dd, $J_{C\text{-}P}$ = 2.9 Hz, *C*H_2, overlap). ^{31}P NMR ($CDCl_3$, 162 MHz): δ -12.97.

2f[12,13]



^{1}H NMR ($CDCl_3$, 400 MHz): δ 4.48 (d, 4H, *J* = 10.8 Hz, CH_2), 4.06 -3.90 (m, 4H, CH_2), 1.32 (s, 6H, CH_3), 0.90 (s, 6H, CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 79.0 (dd, $J_{C\text{-}P}$ = 3.8 Hz, *C*H_2, overlap), 32.2 (dd, $J_{C\text{-}P}$ = 2.9 Hz, $J_{C\text{-}P}$ = 3.8 Hz, $(CH_2)_2C(CH_3)_2$), 21.9 (*C*H_3), 19.9 (*C*H_3). ^{31}P NMR ($CDCl_3$, 162 MHz): δ -21.02.

2g



White solid. m.p.: 102–112 ºC. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.50, 9.47 and 9.44 (3s, 2H, N*H*), 7.29, 7.28 and 7.22 (3s, broad, *H*6-thymine), 7.02, 7.01 and 7.00 (3s, broad, 2H, *H*1'), 6.35-6.29 (m, 2H, *H*3'), 5.90 (s, broad, 2H, *H*2'), 4.99 (s, broad, 2H, *H*4'), 4.82-4.78 (m, 2H, C*H*-isopropyl), 4.39-4.29 (m, 4H, *H*5'), 1.91, and 1.91 (2s, broad, 6H, CH_3-thymine), 1.38-1.34 (m, 12H, CH_3-isopropyl). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 164.0 and 163.9 (2s, broad, *C*4-thymine), 150.9 and 150.9 (2s, broad, *C*2-thymine), 135.8 and 135.7 (2s, broad, *C*6-thymine), 132.8 and 132.7 (2s, broad, *C*3'), 132.6 (d, $J_{C\text{-}P}$ = 4.8 Hz, *C*3'), 127.8, 12.7 and 127.6 (3s, broad, C2'), 111.4, 11.4 and 111.3 (3s, broad, C5-thymine), 89.6 and 89.5 (2s, broad, *C*1'), 84.3, 84.2 and 84.1 (3s, broad, *C*4'), 75.7 (s, broad, *C*H-isopropyl), 75.6 (d, $J_{C\text{-}P}$ = 4.8 Hz, *C*H-isopropyl), 75.5 (s, broad, *C*H-isopropyl), 68.6, 67.5 and 68.5 (3s, broad, *C*5'), 23.6 and 23.4 (2s, broad, C*H*-isopropyl), 12.4 and 12.3 (2s, broad, *C*H_3-thymine). ^{31}P NMR ($CDCl_3$, 162

MHz): δ -13.26 (broad) and -13.65. Anal. Calcd for $C_{26}H_{36}N_4O_{13}P_2$: C, 46.30; H, 5.38; N, 8.31. Found: C, 46.01; H, 5.15; N, 8.54.

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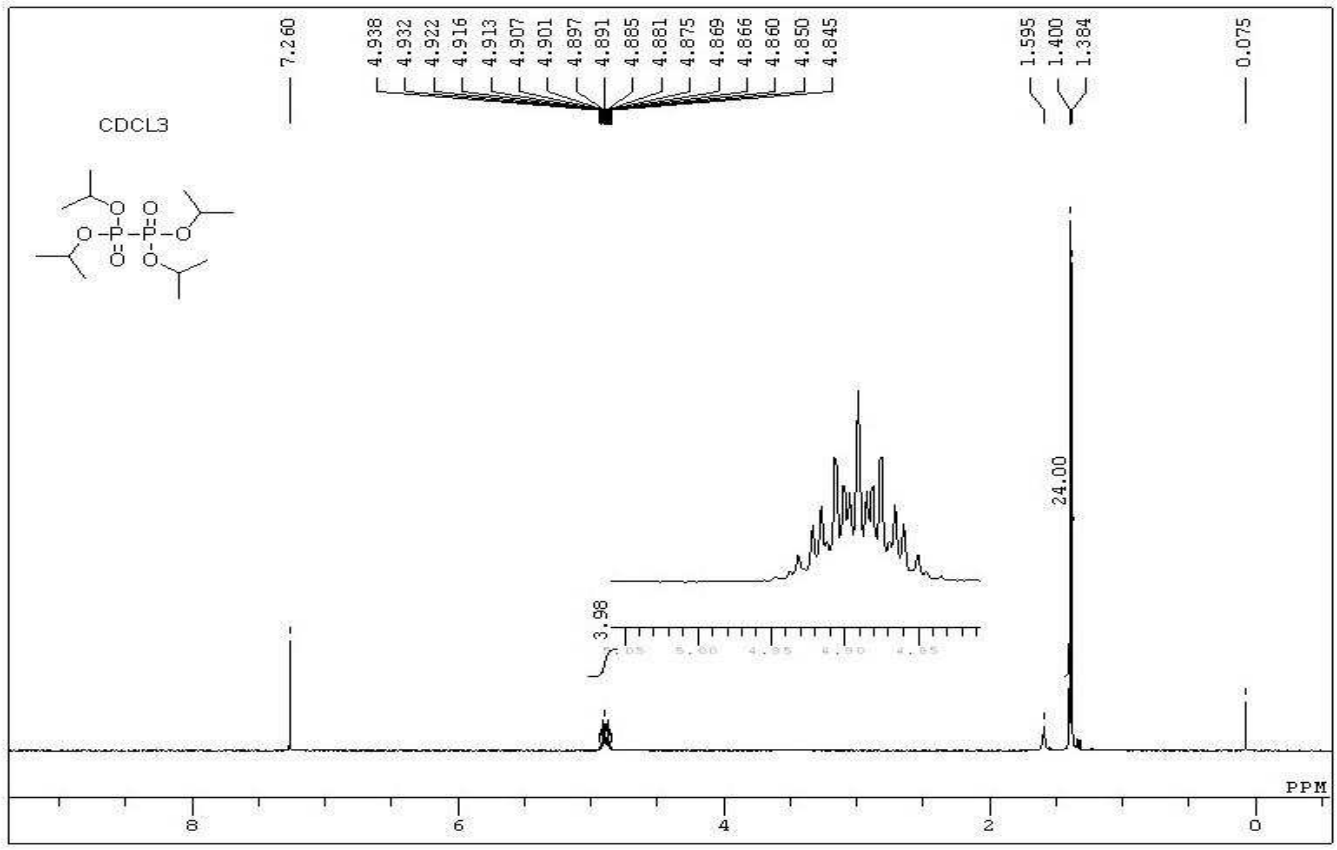
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4.869
4.866
4.860
4.850
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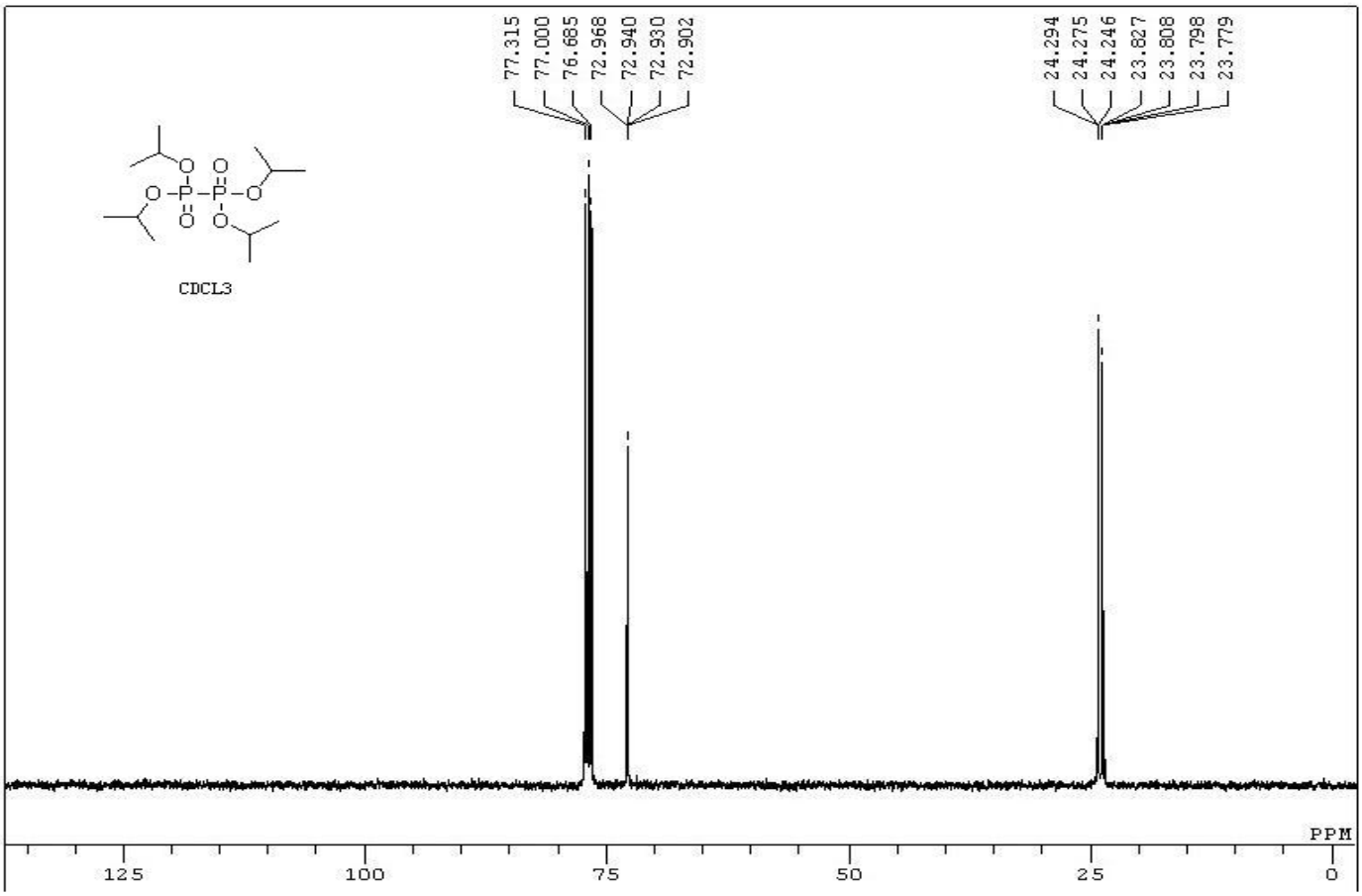
6
4
2
0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25
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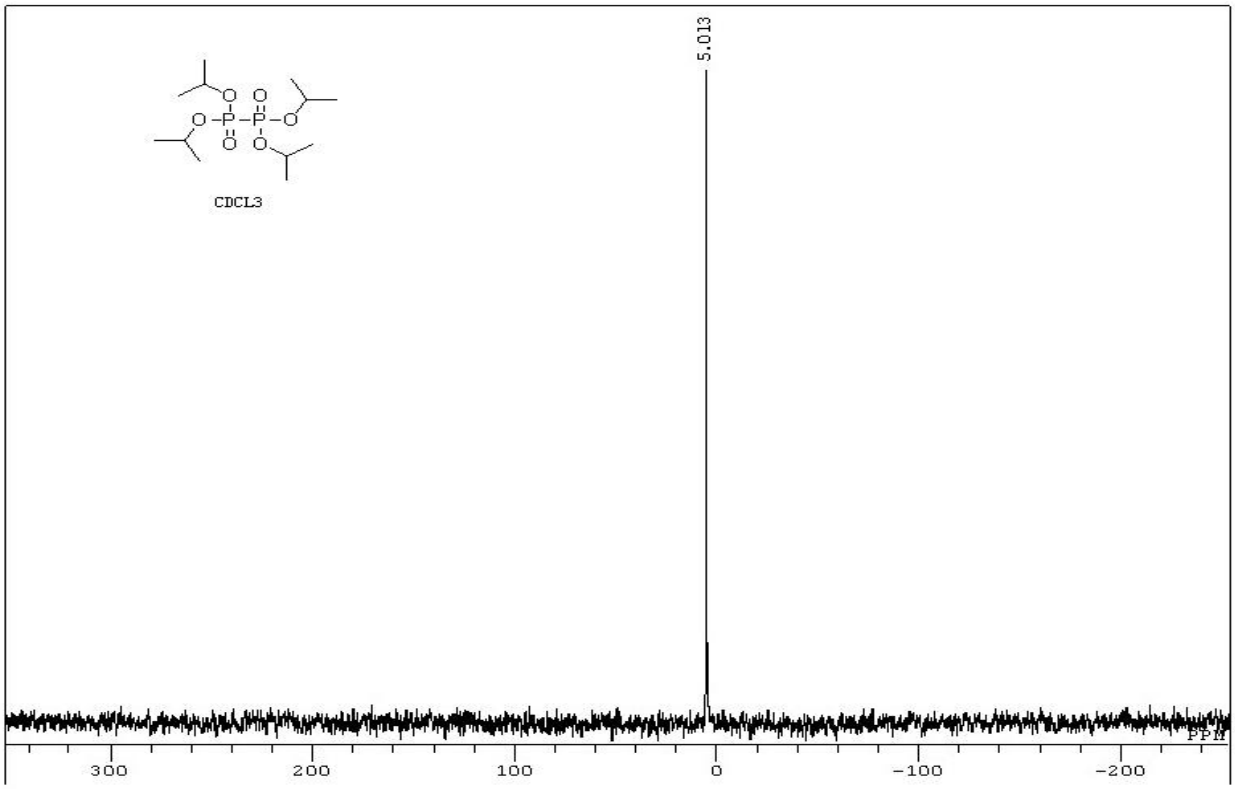
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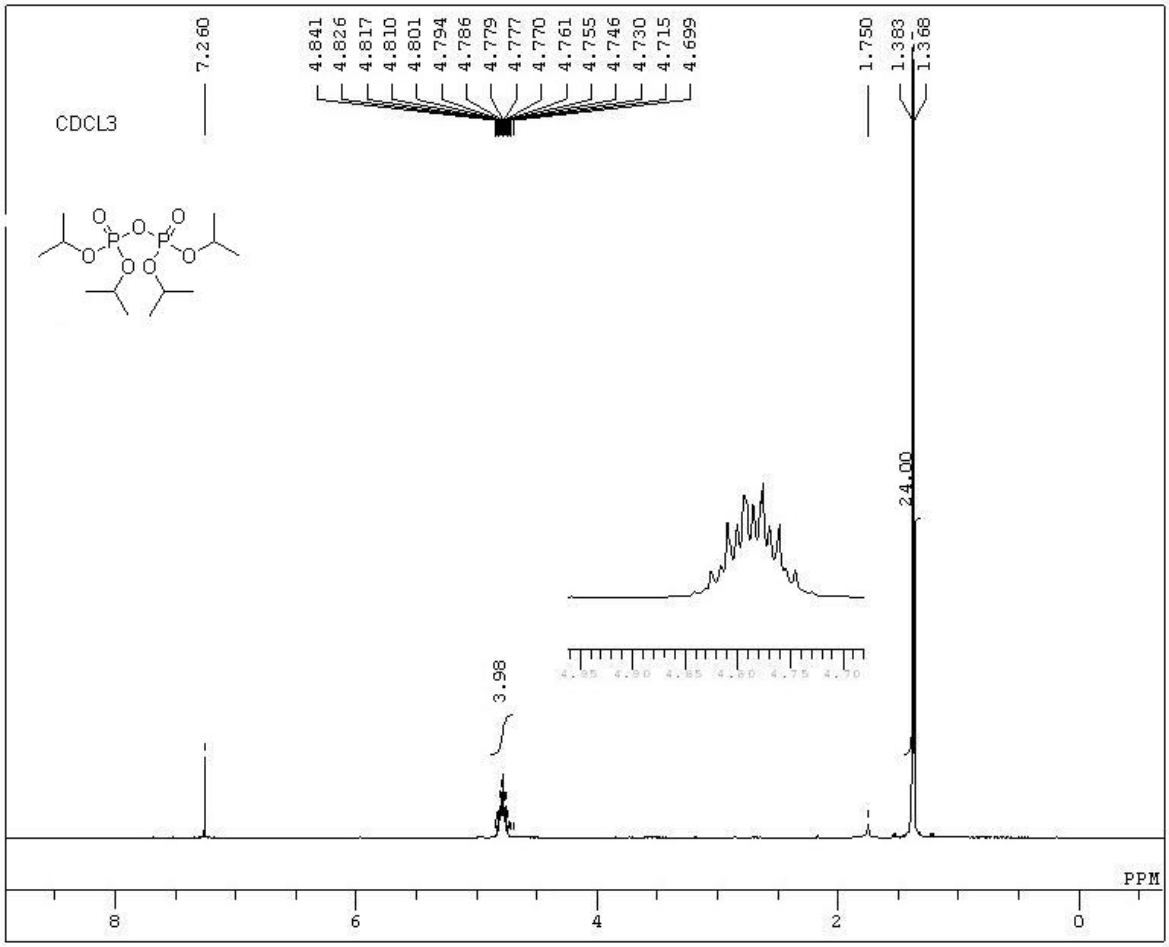
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4.730
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4
2
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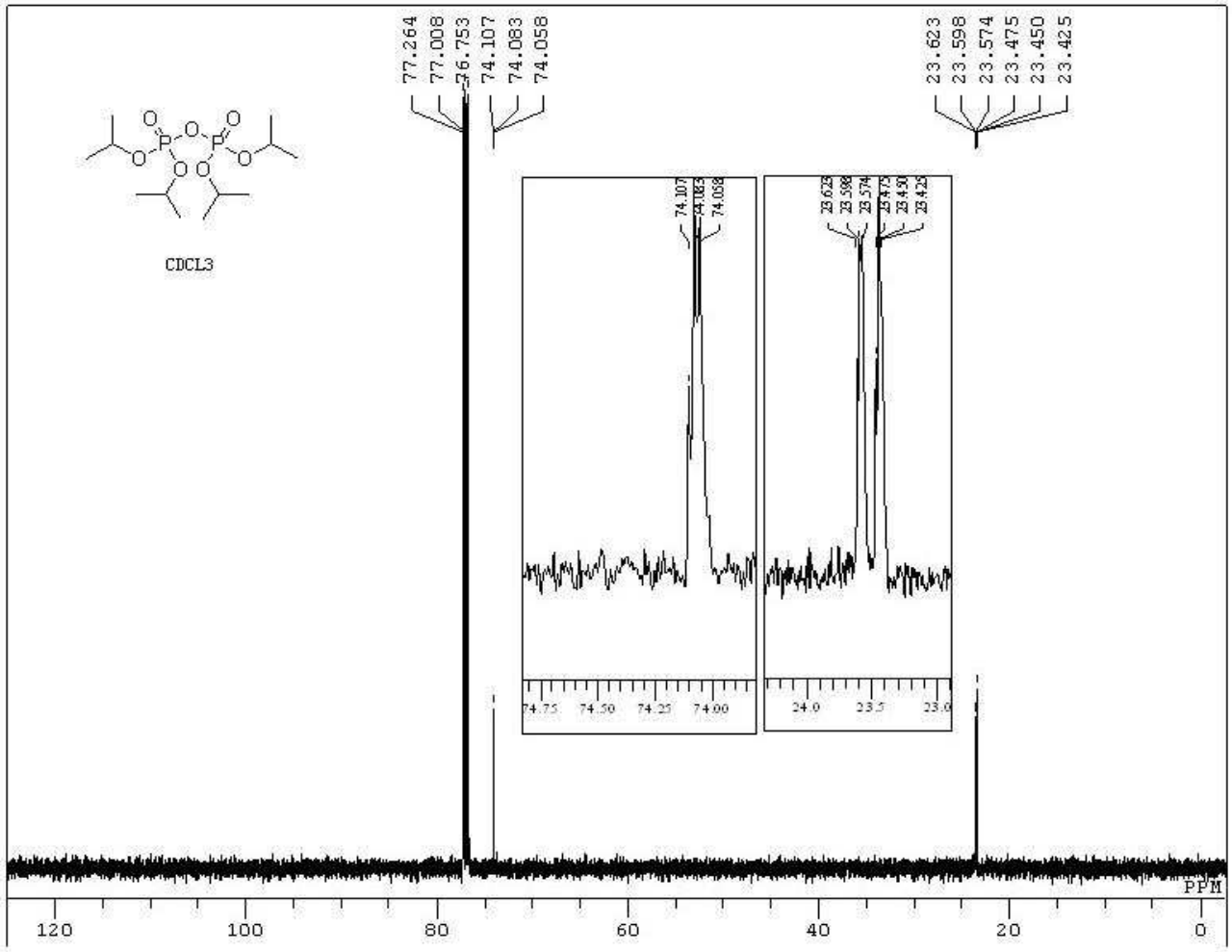
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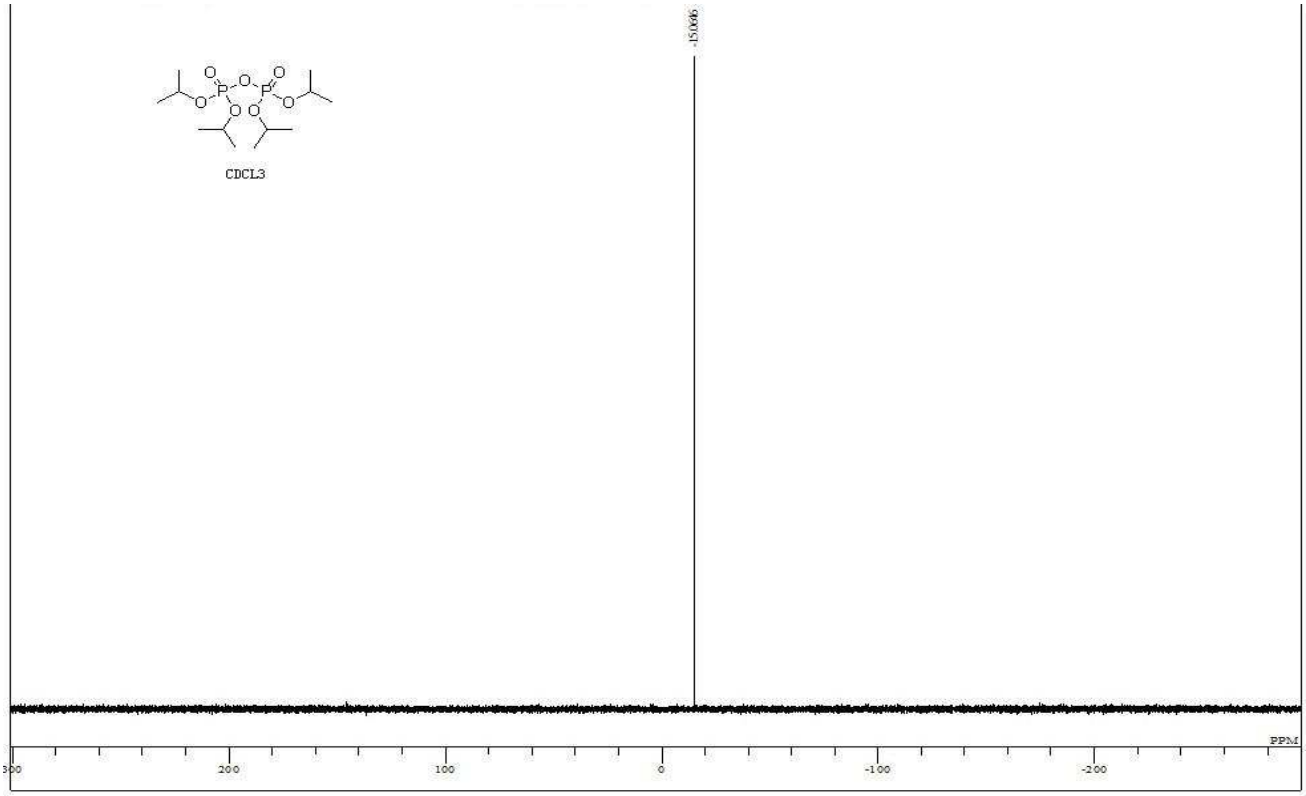
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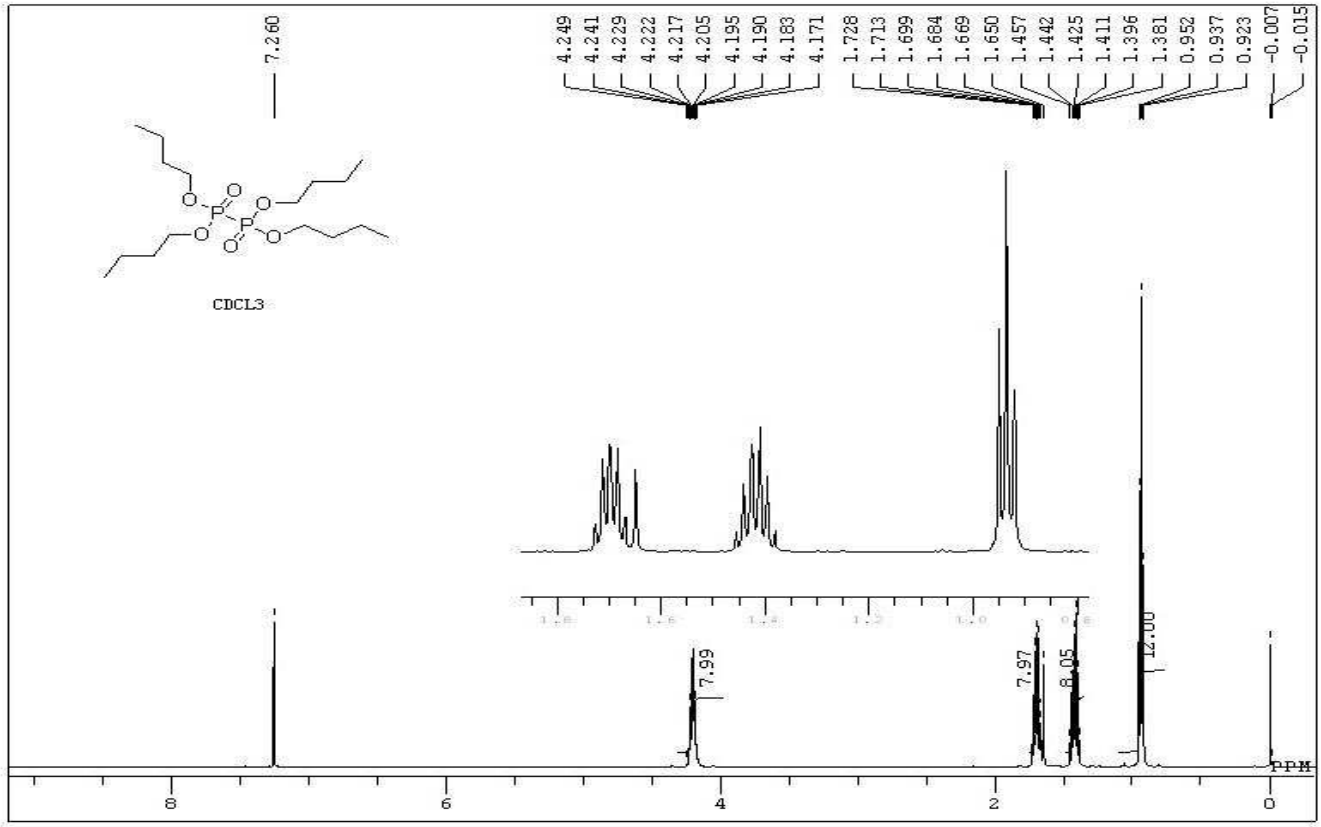
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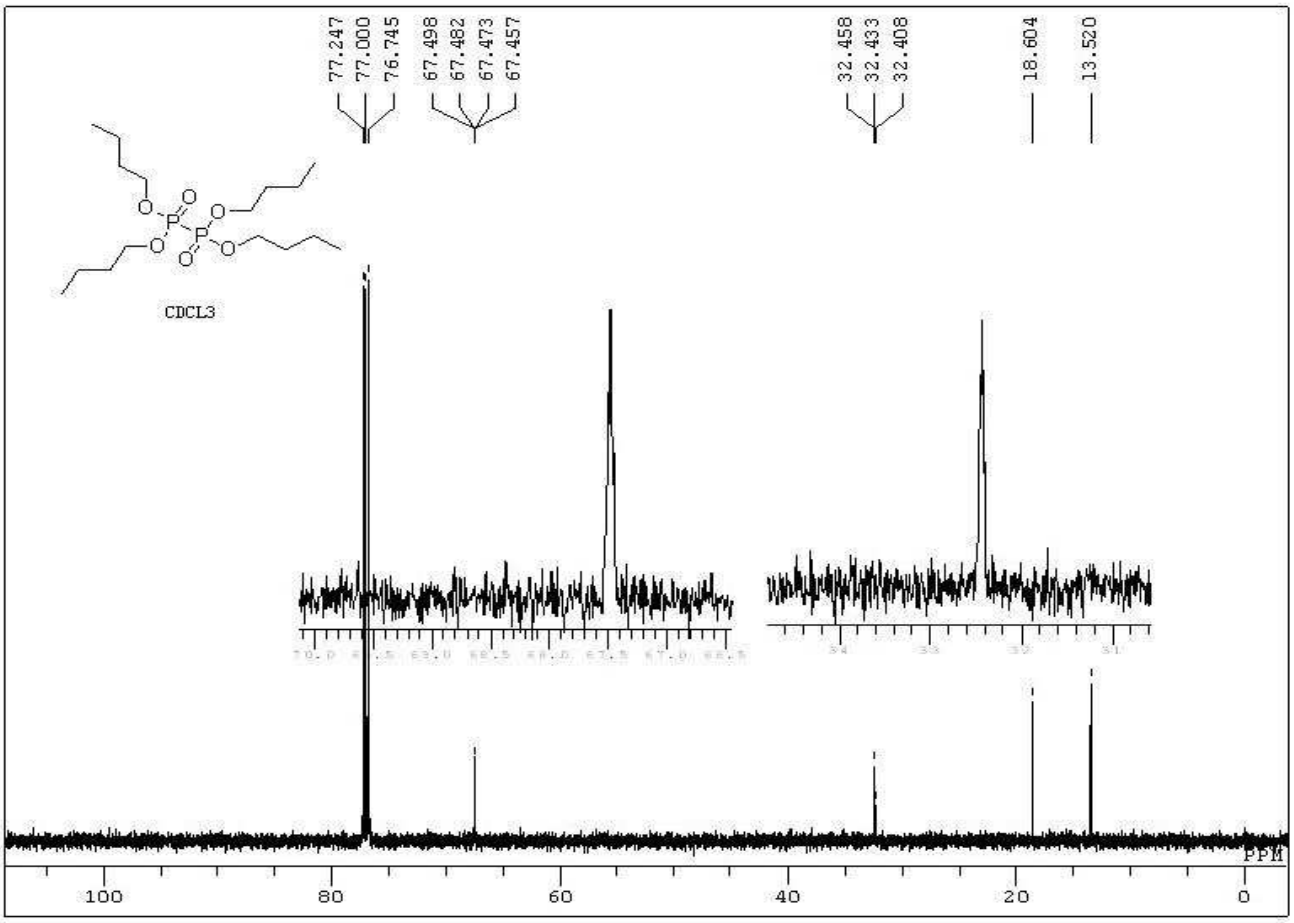
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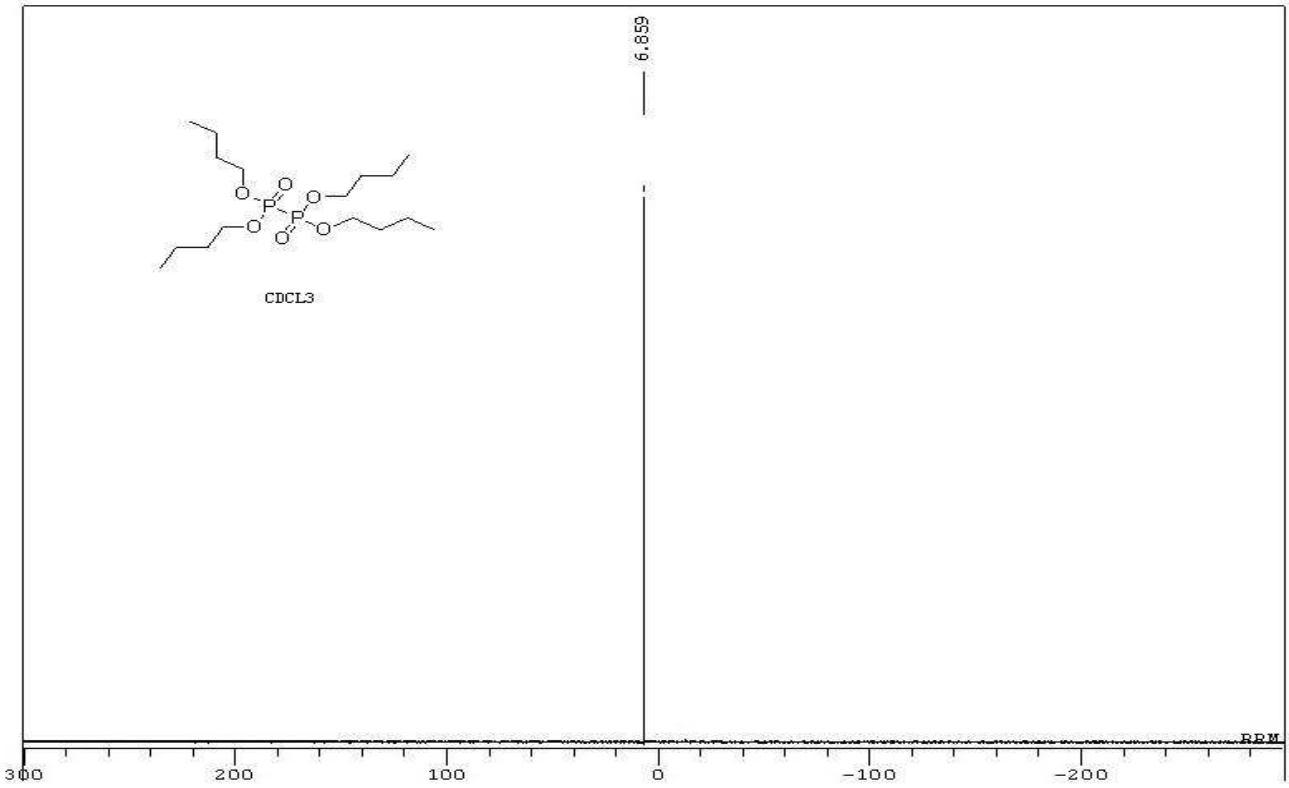
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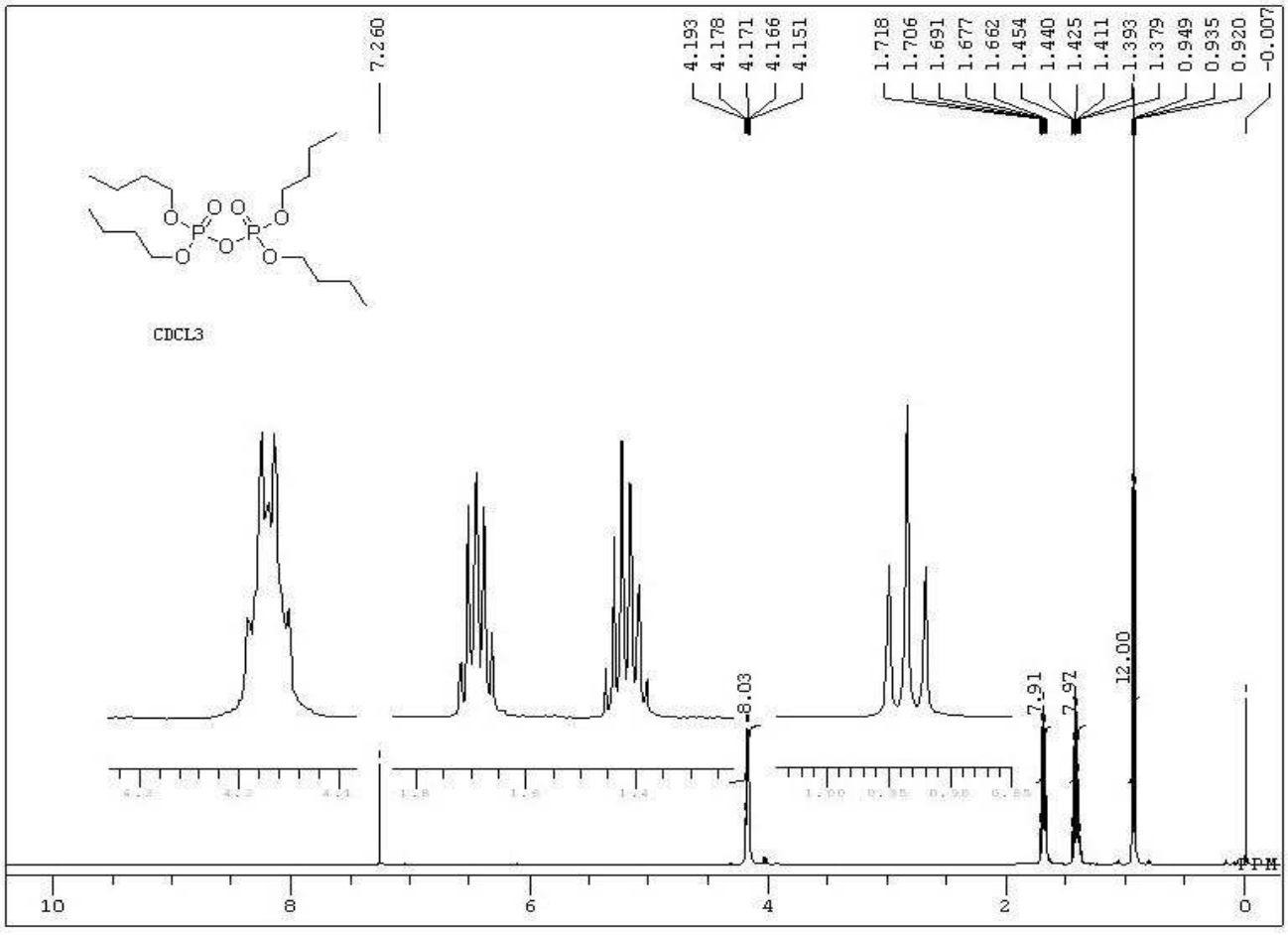
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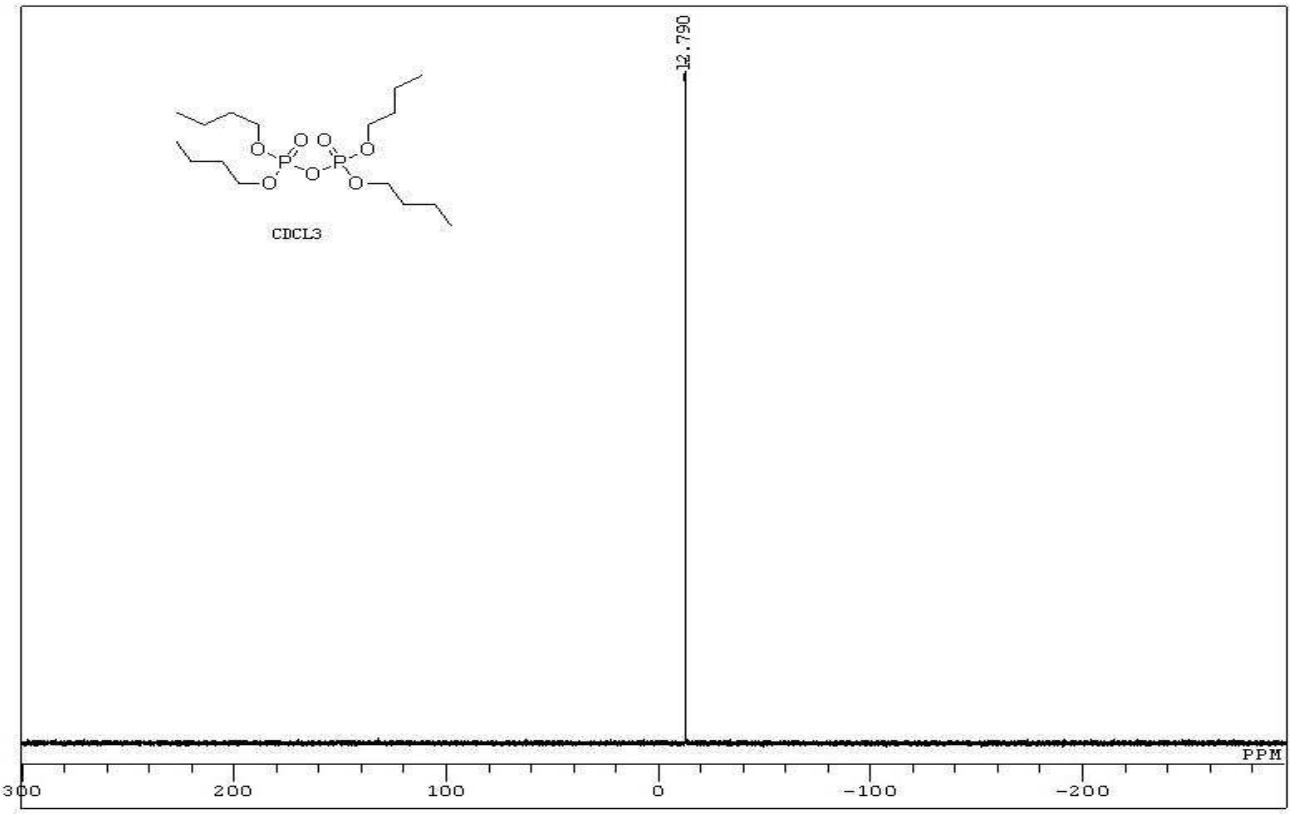
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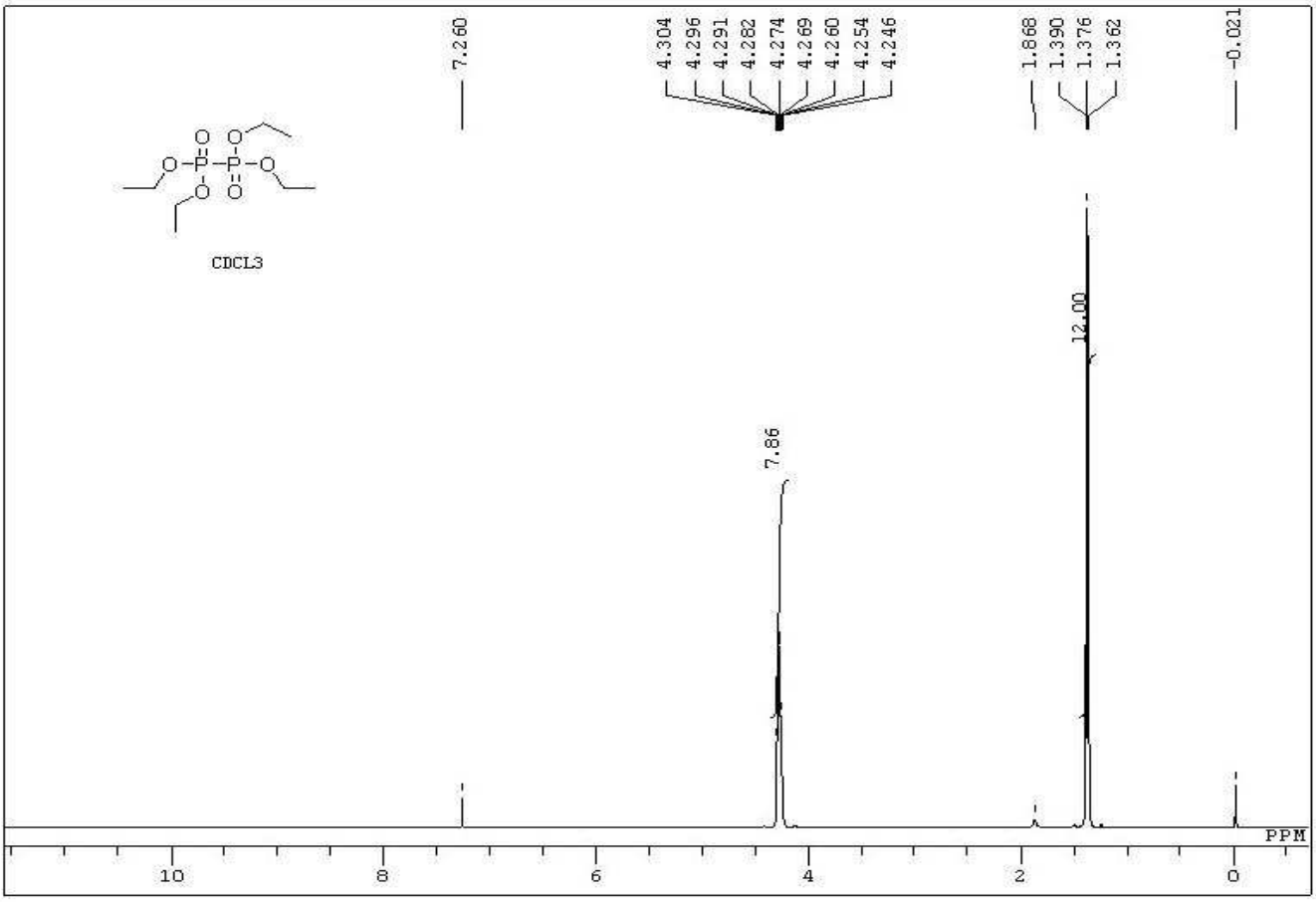
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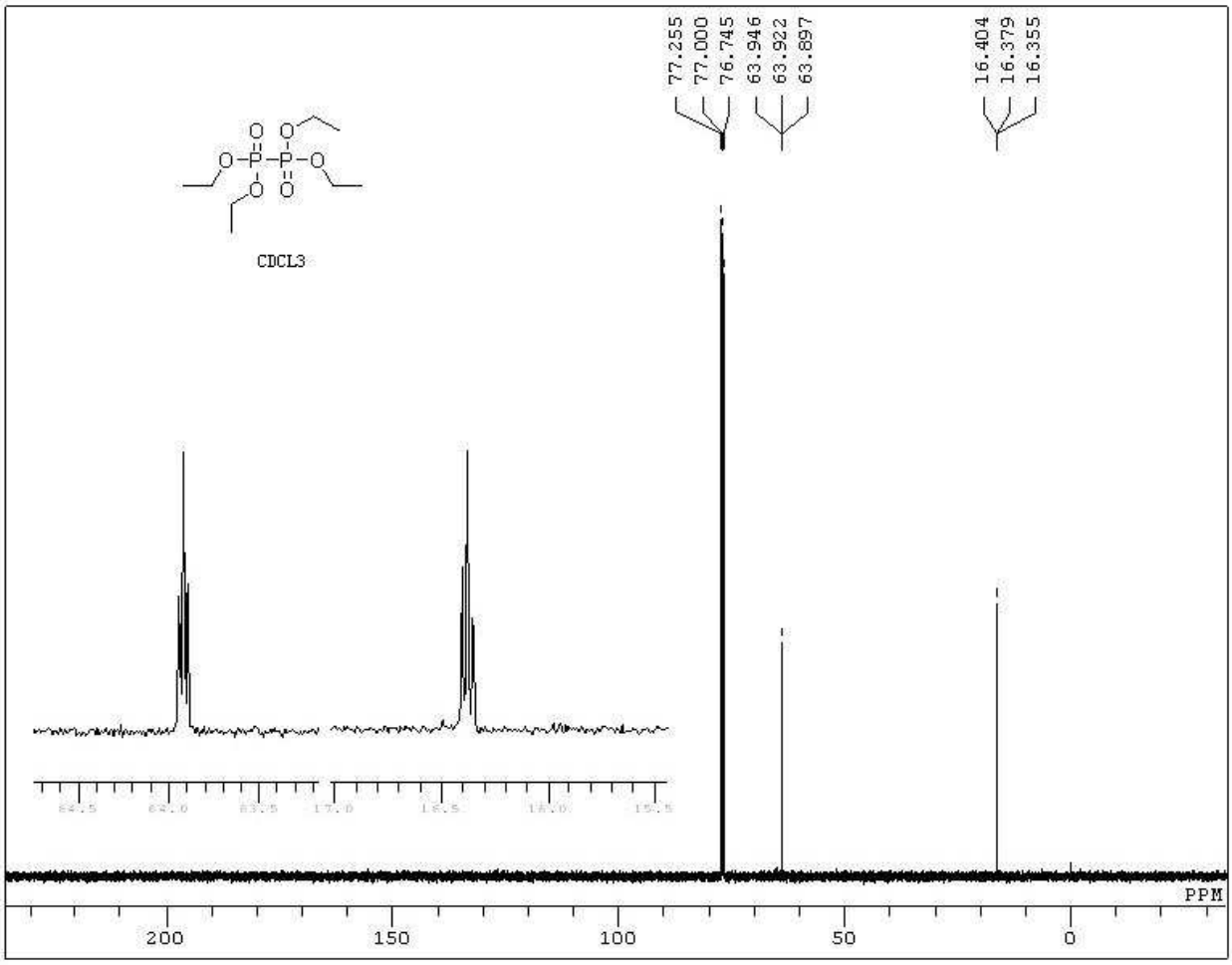
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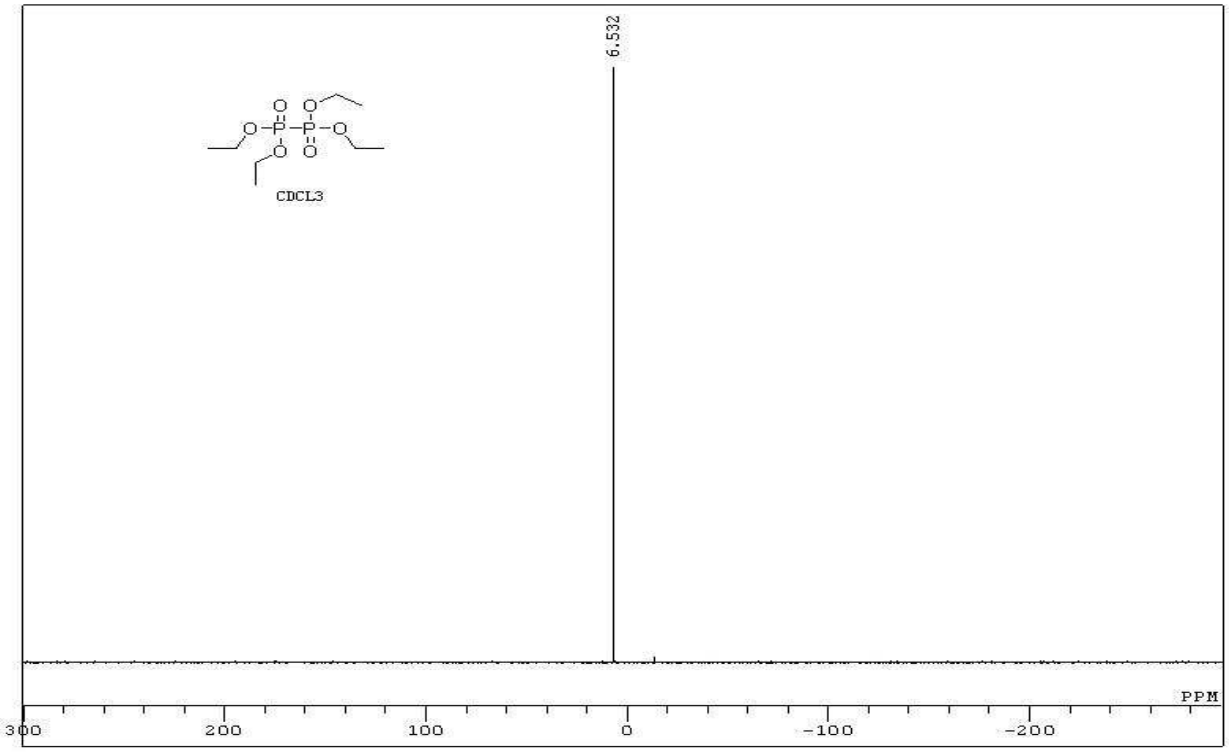
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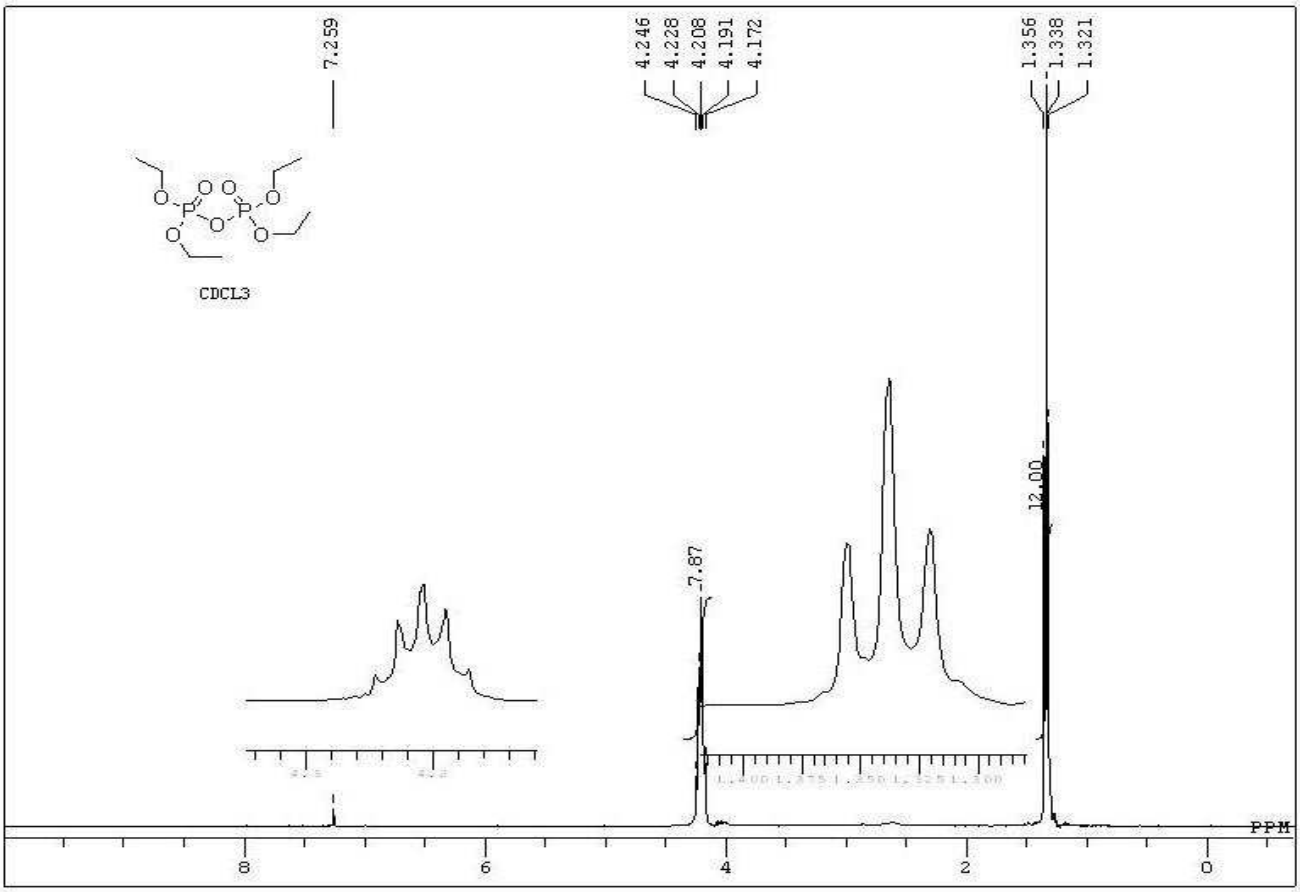
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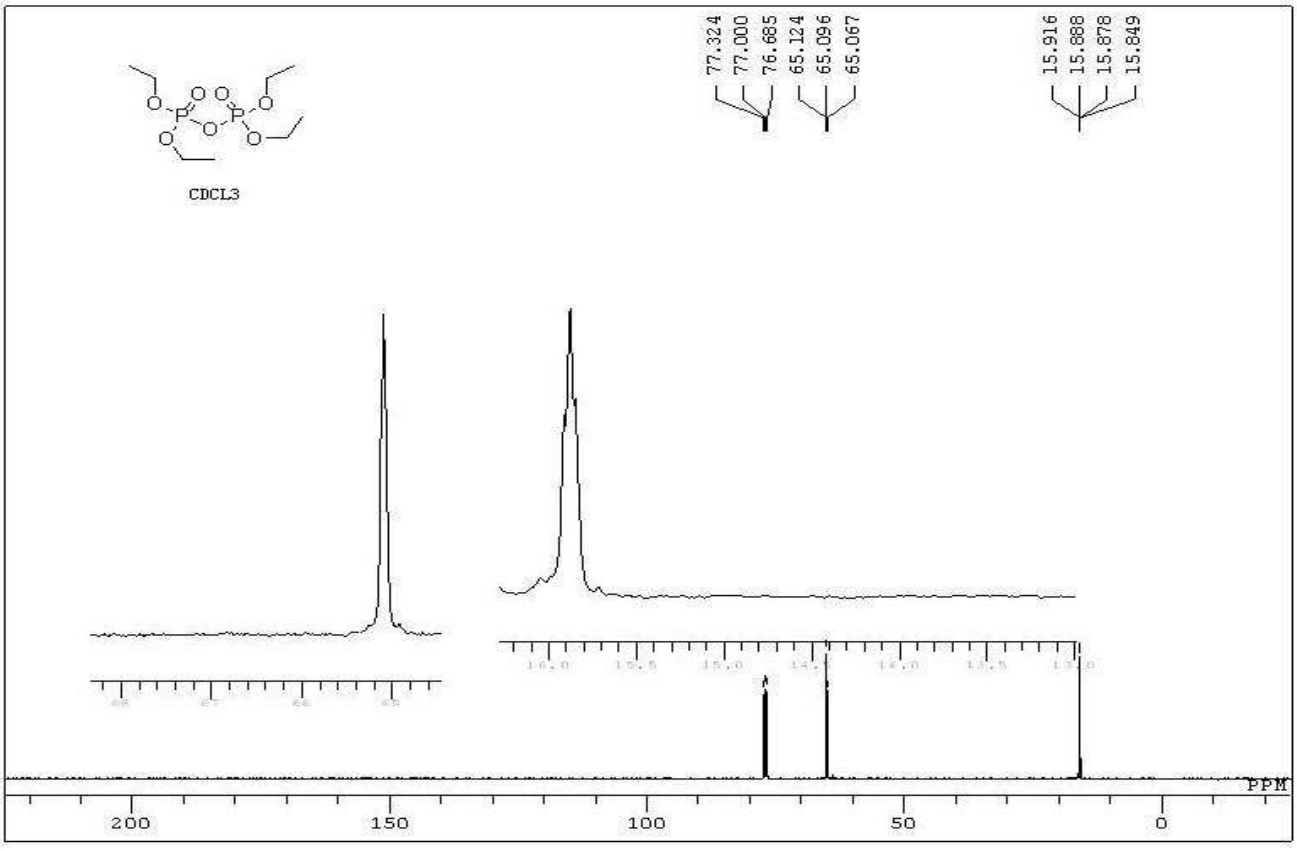
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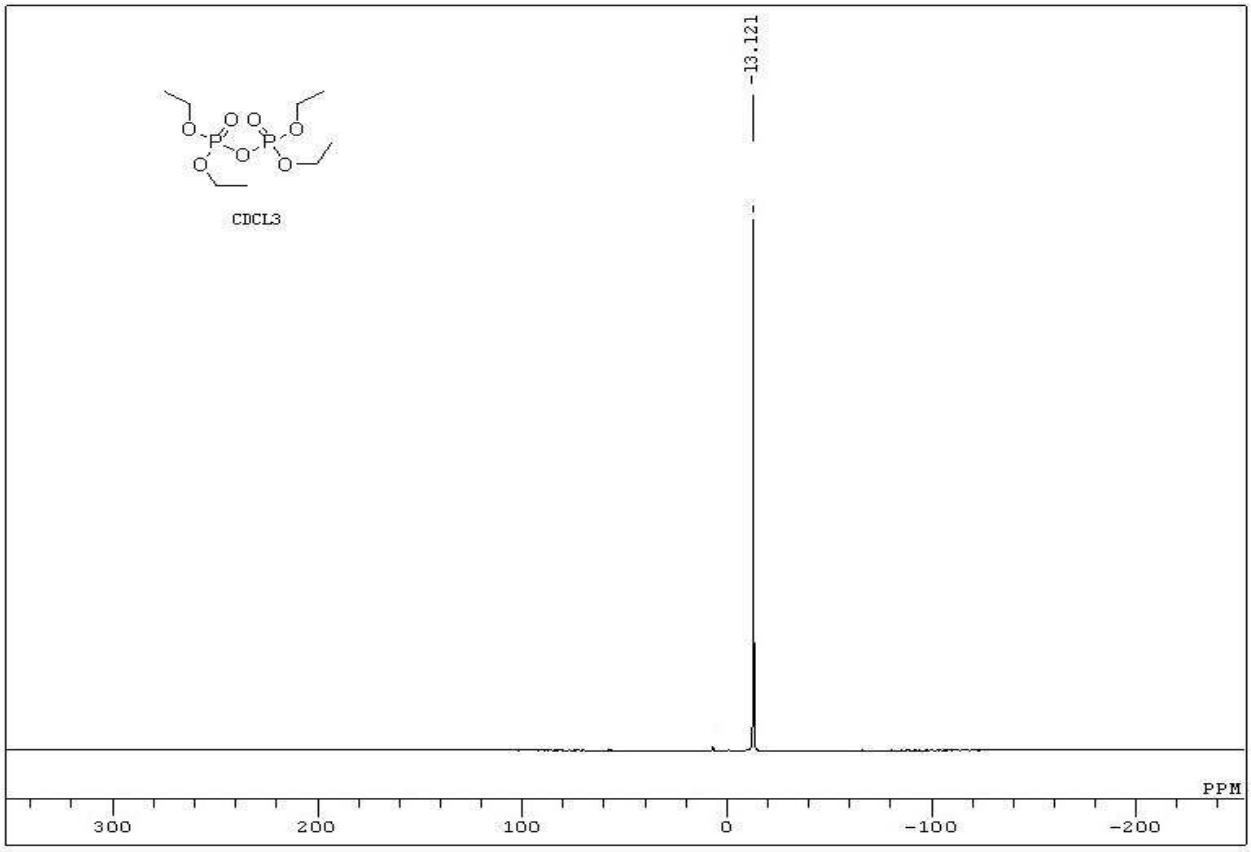
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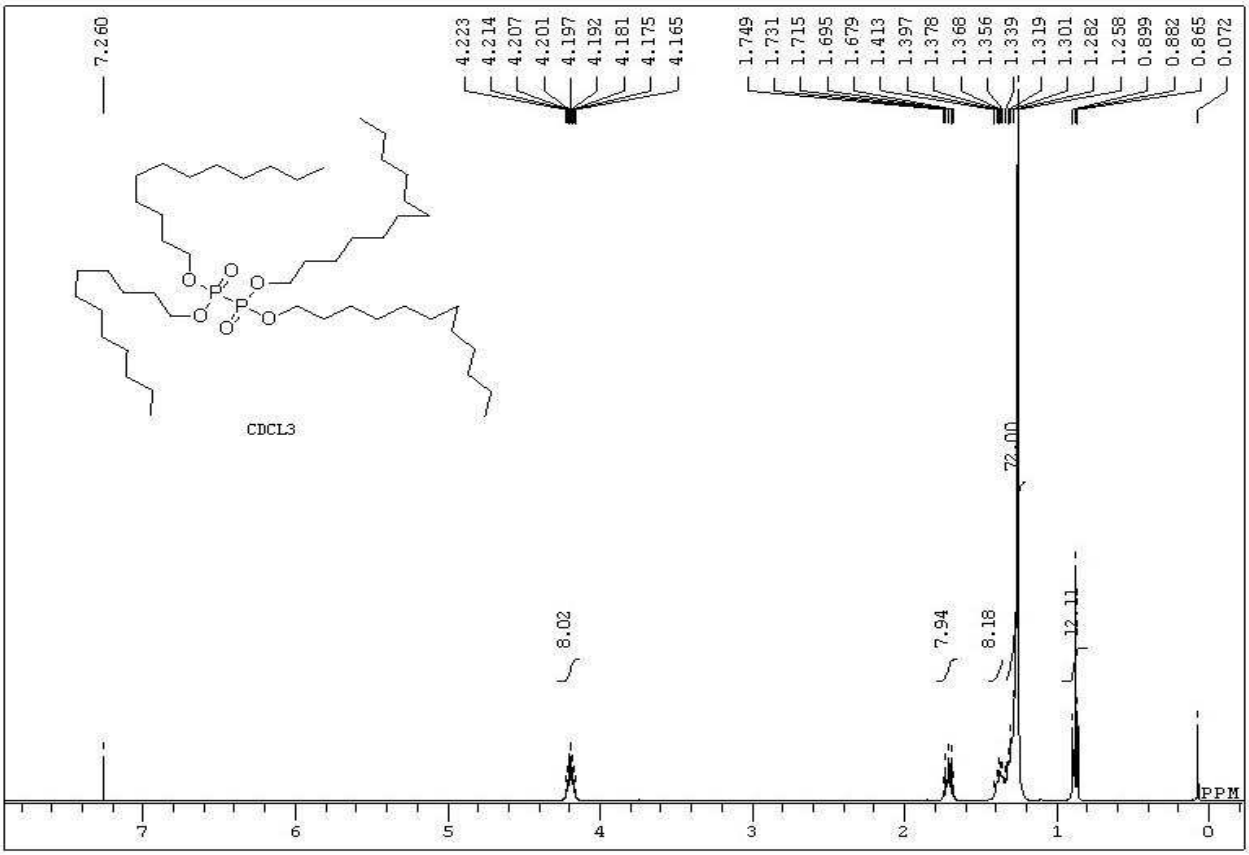
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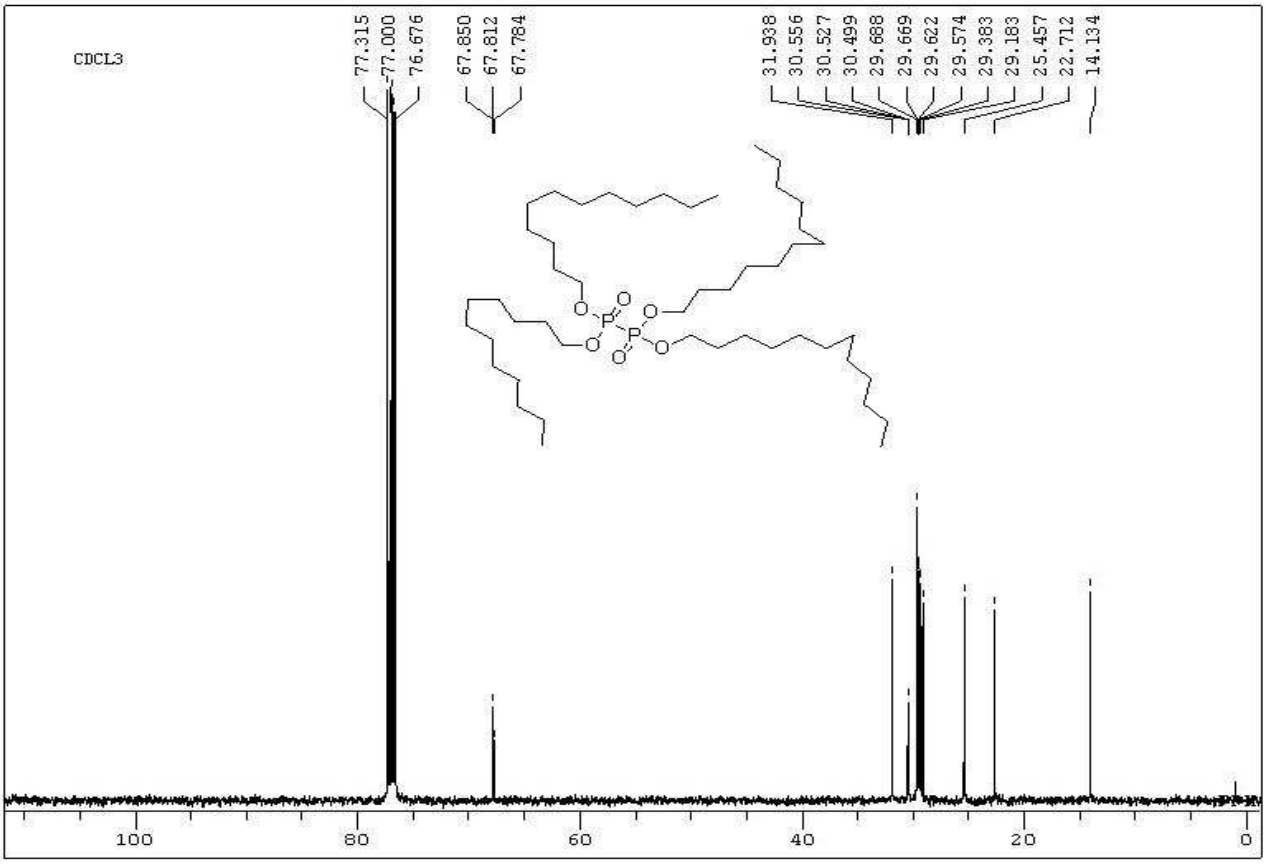
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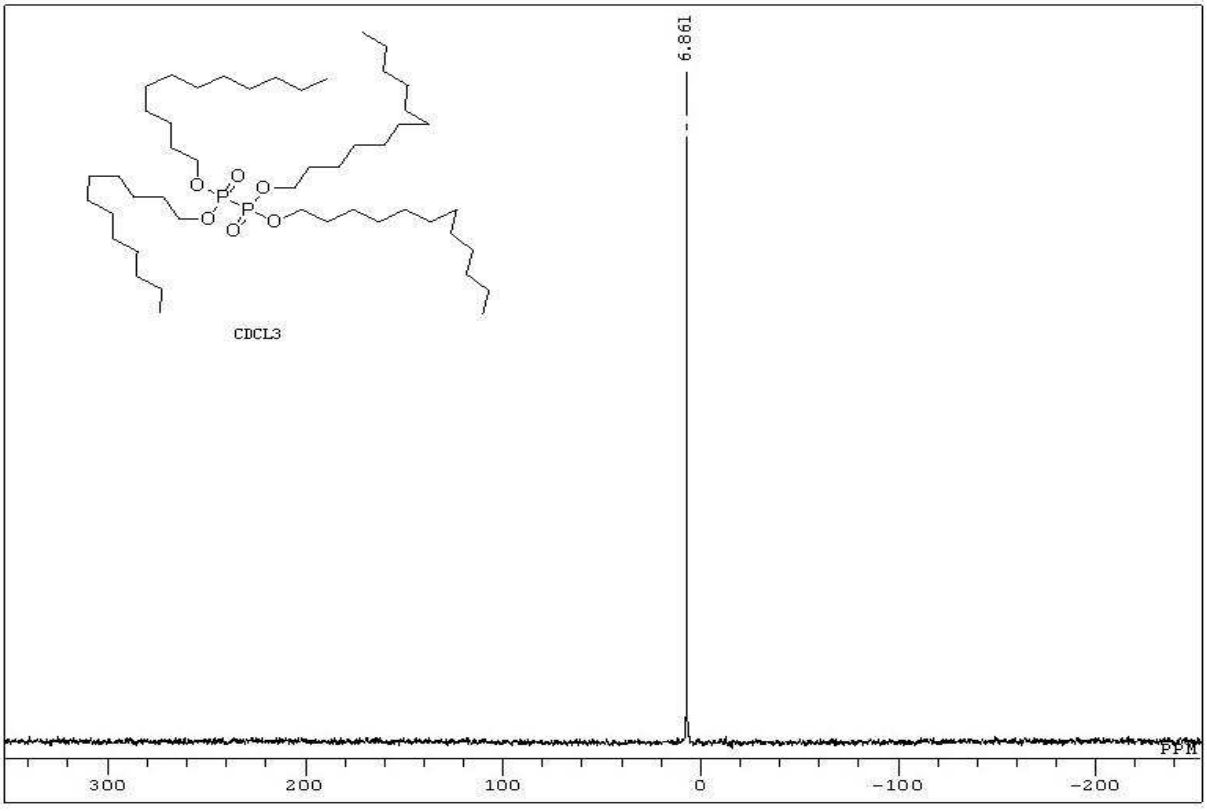
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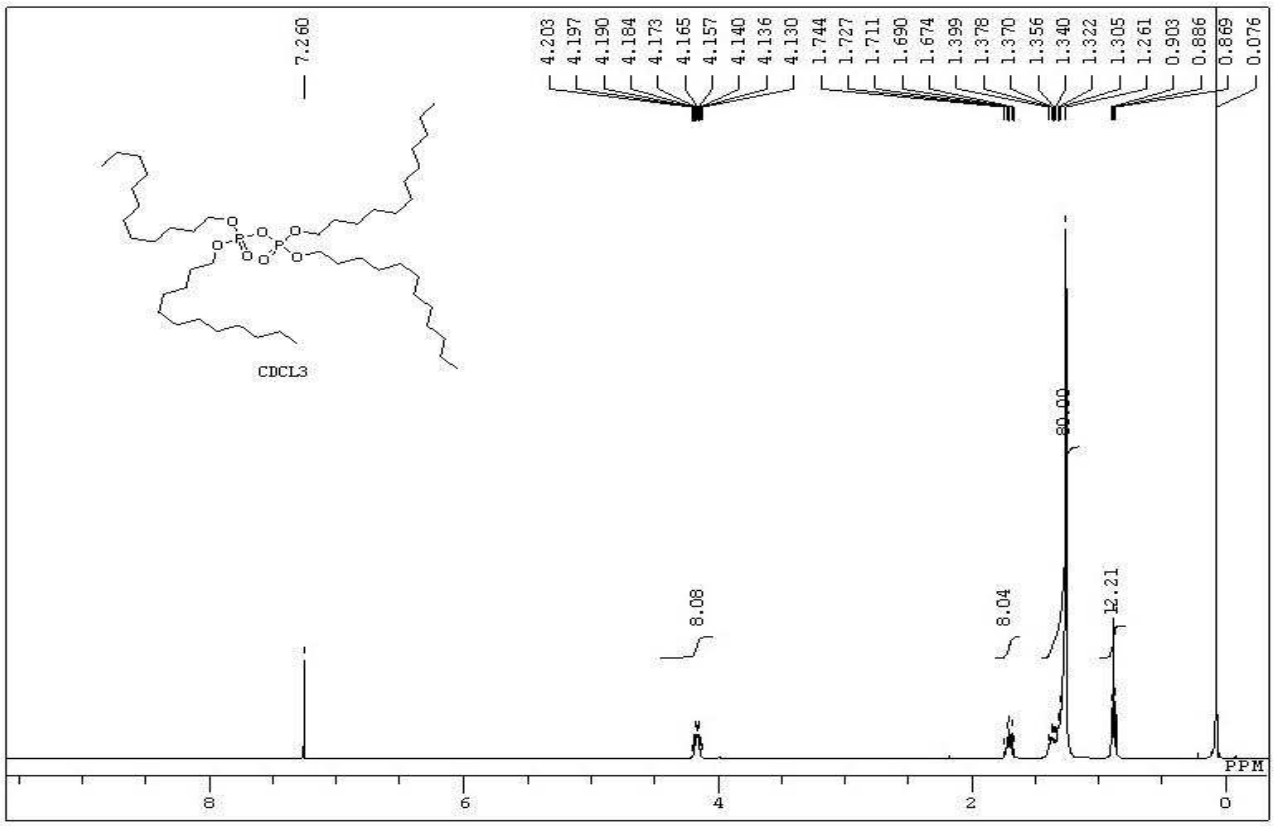
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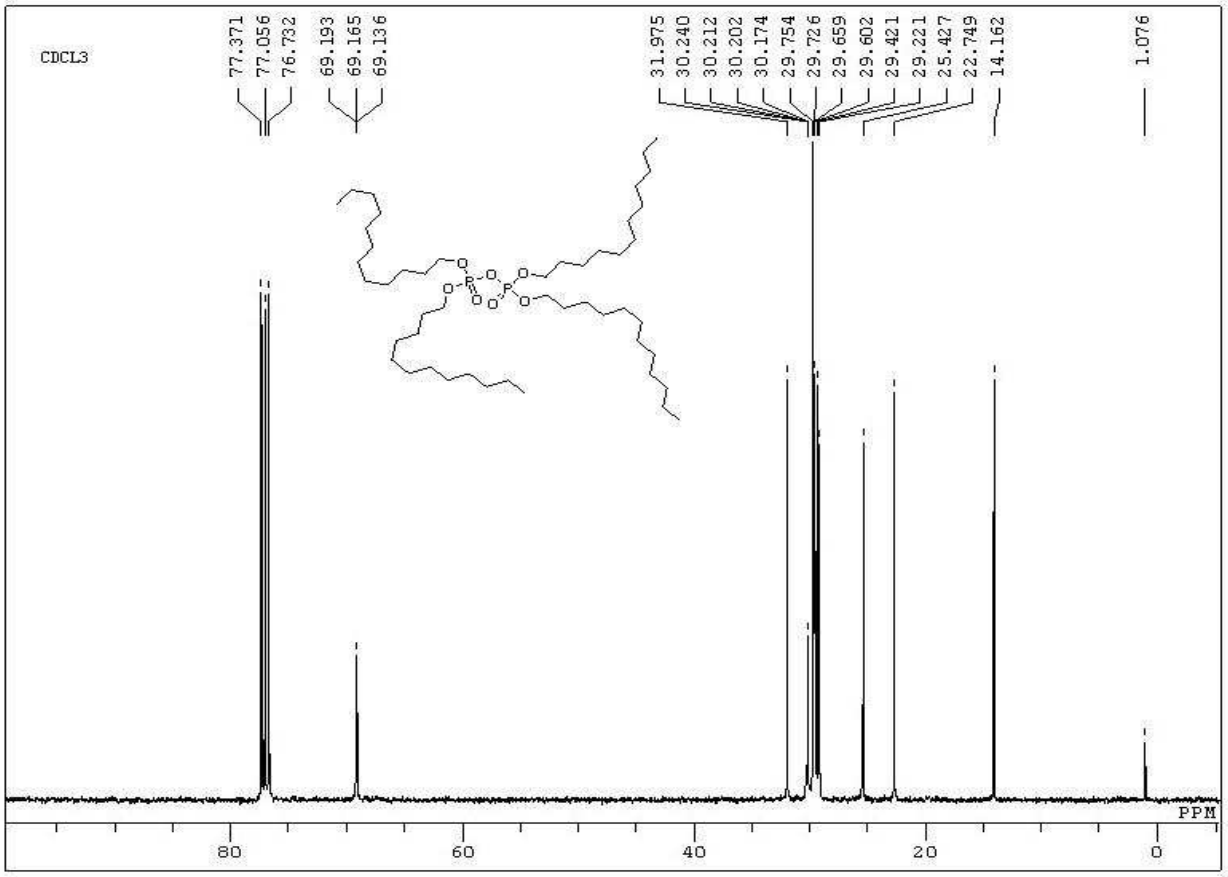
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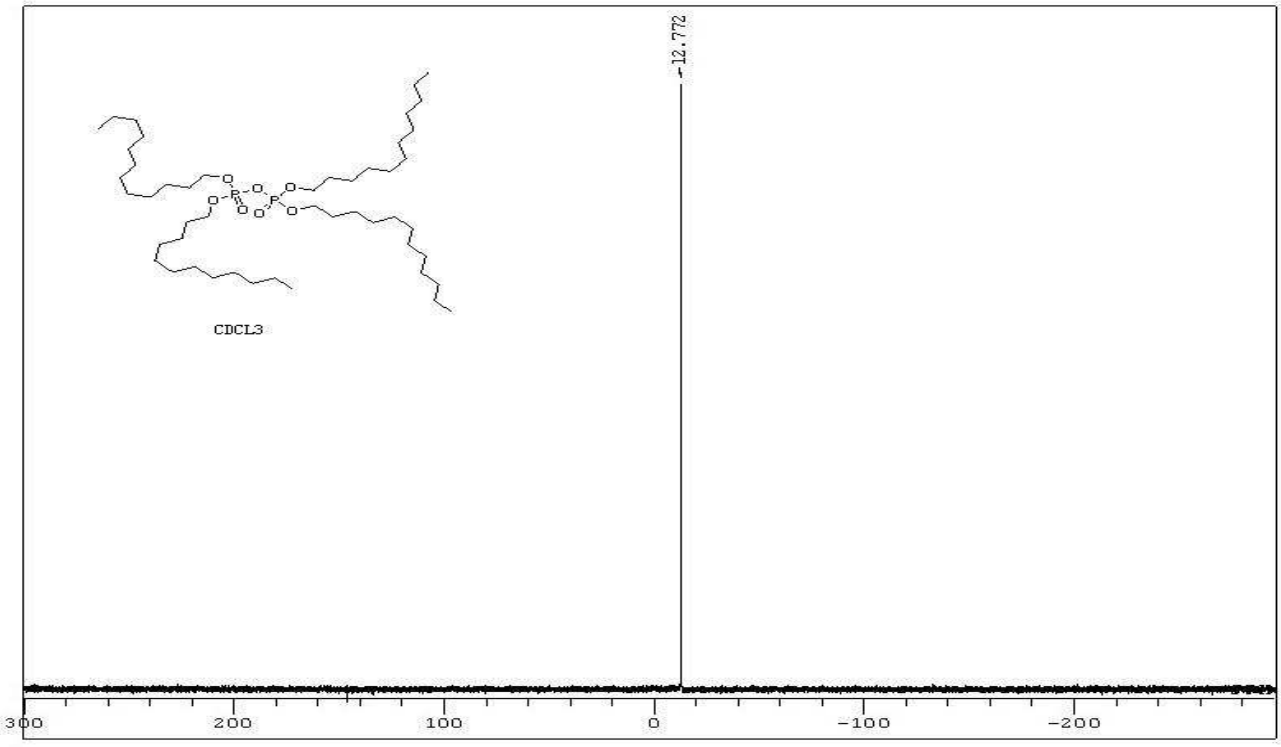
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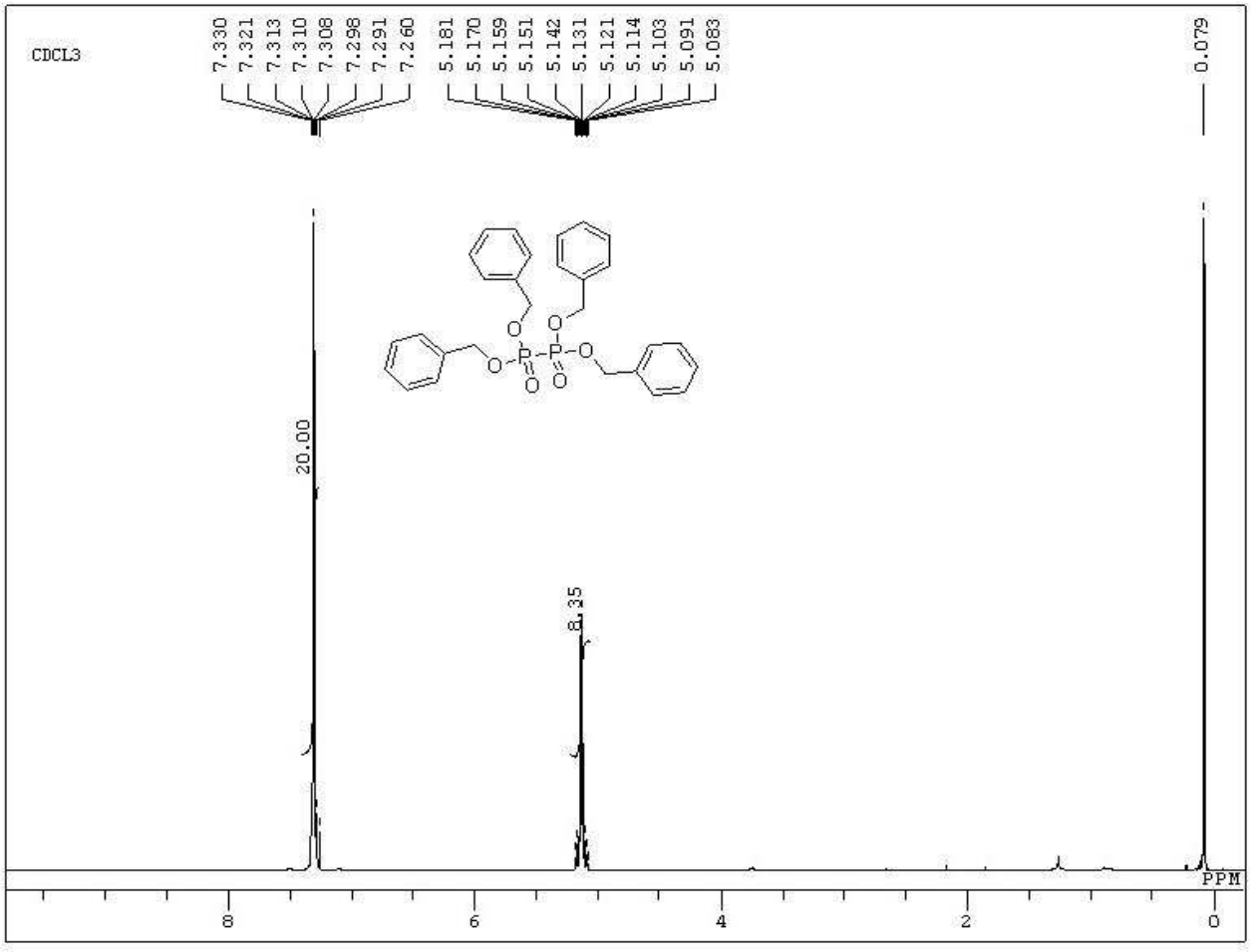
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5.170
5.159
5.151
5.142
5.131
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5.103
5.091
5.083
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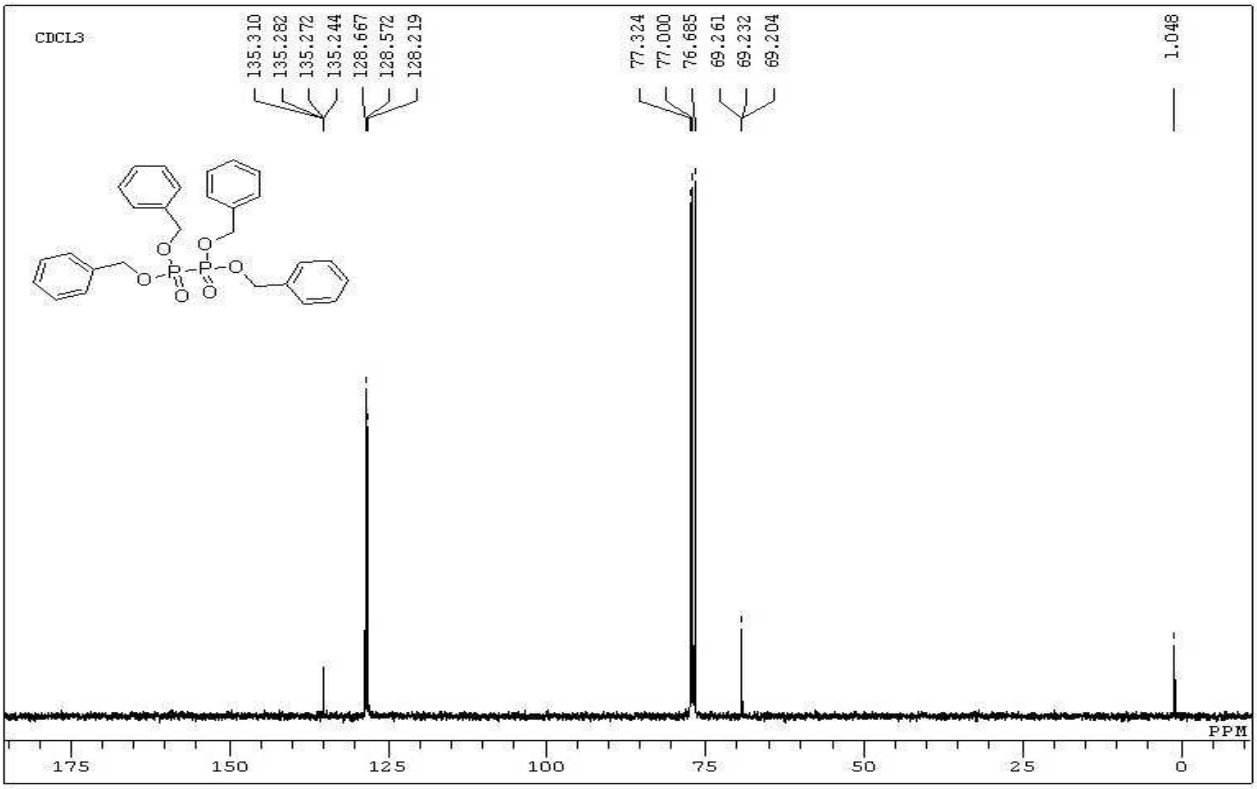
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128.219
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69.232
69.204
1.048
PPM
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50
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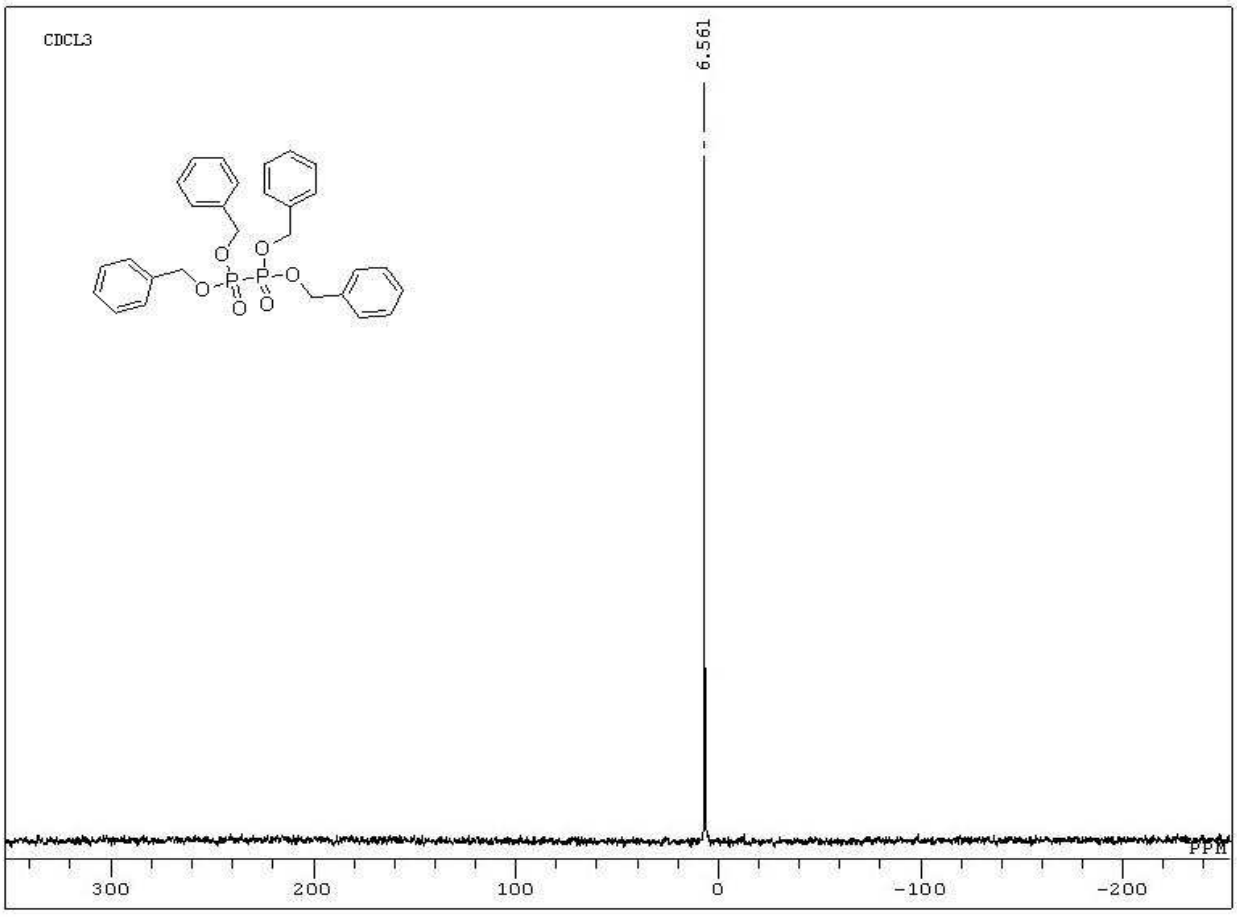
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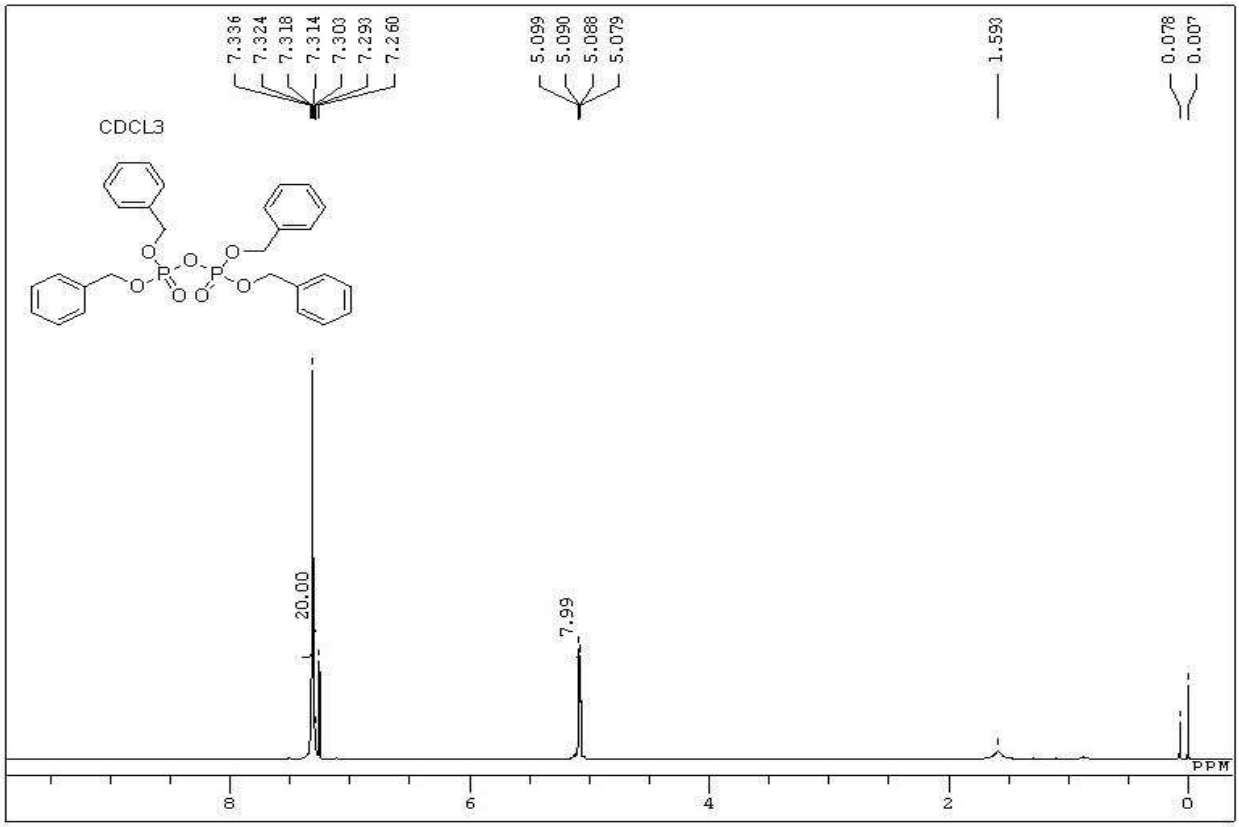
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7.318
7.314
7.303
7.293
7.260
5.099
5.090
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0.078
0.007
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7.99
PPM
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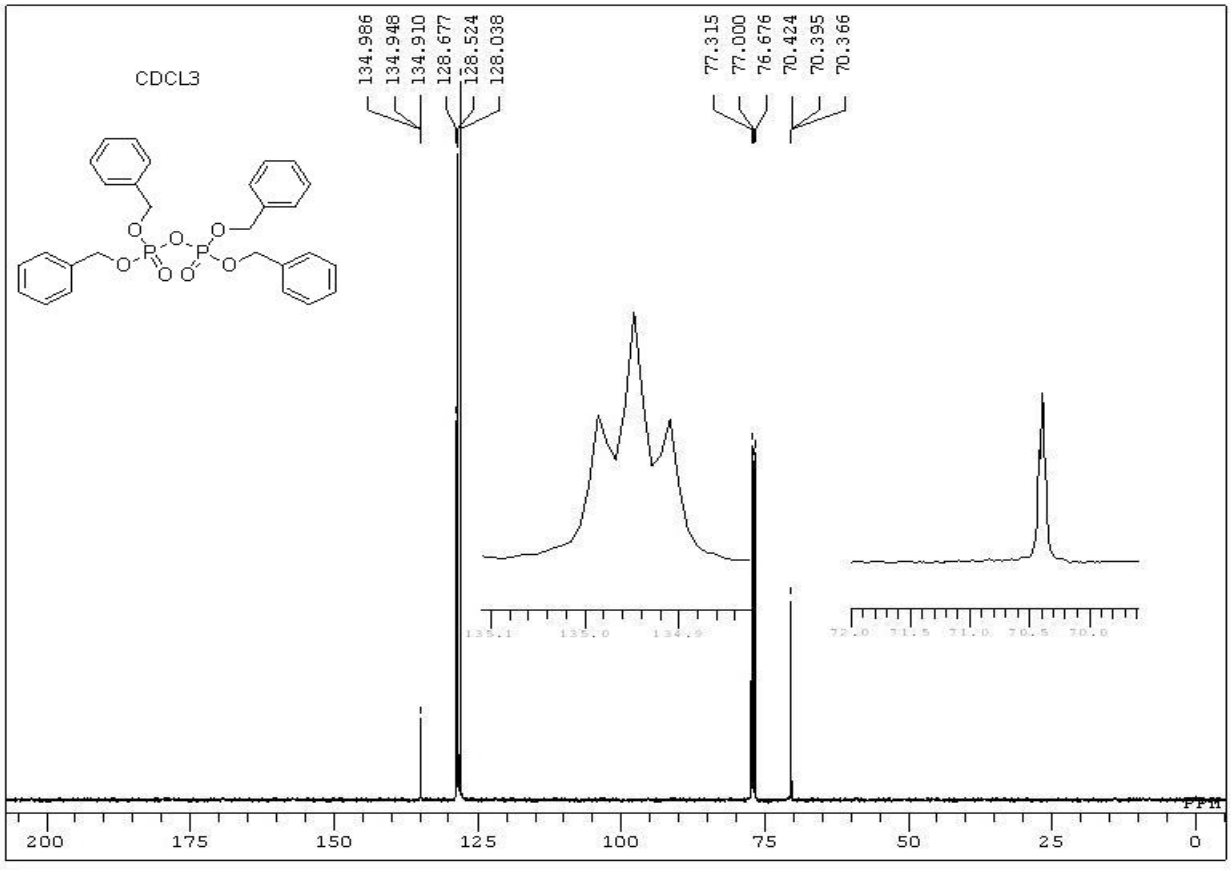
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PPM
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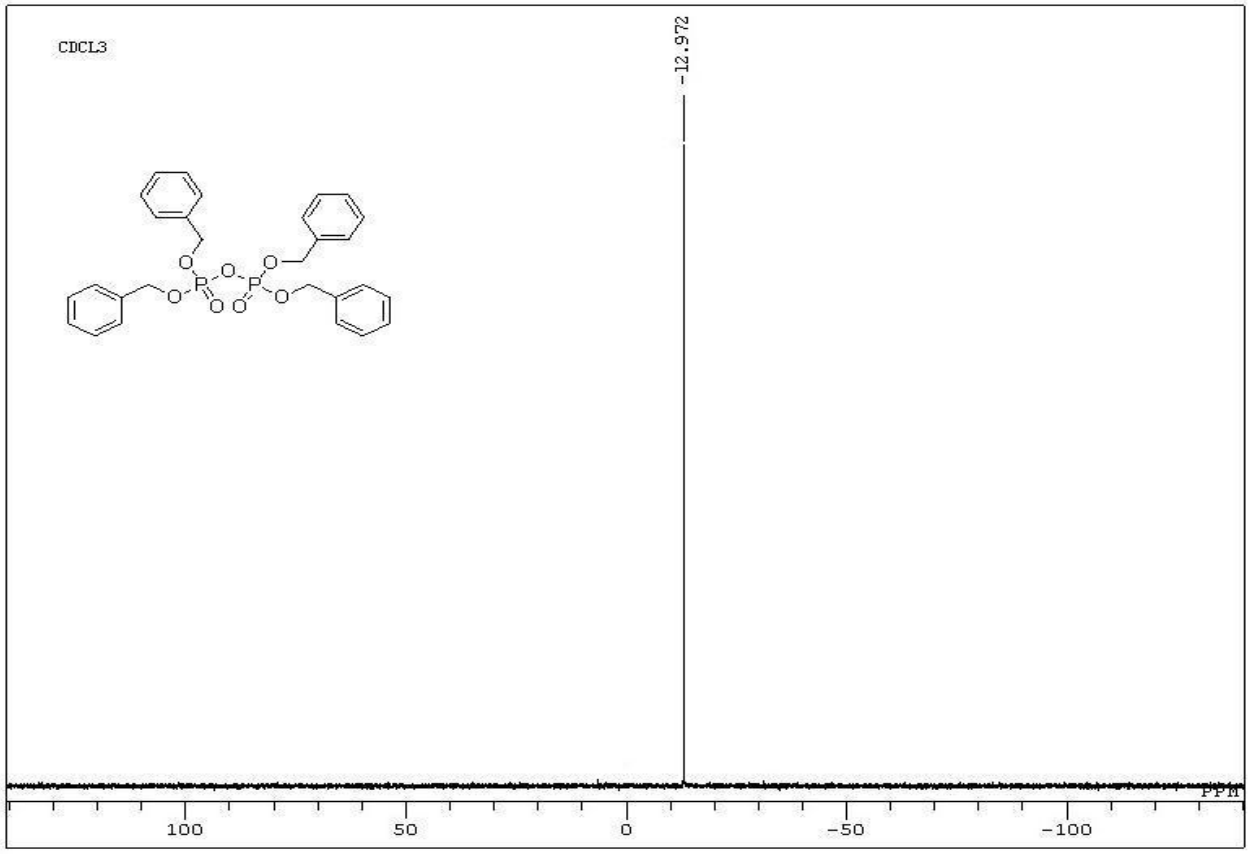
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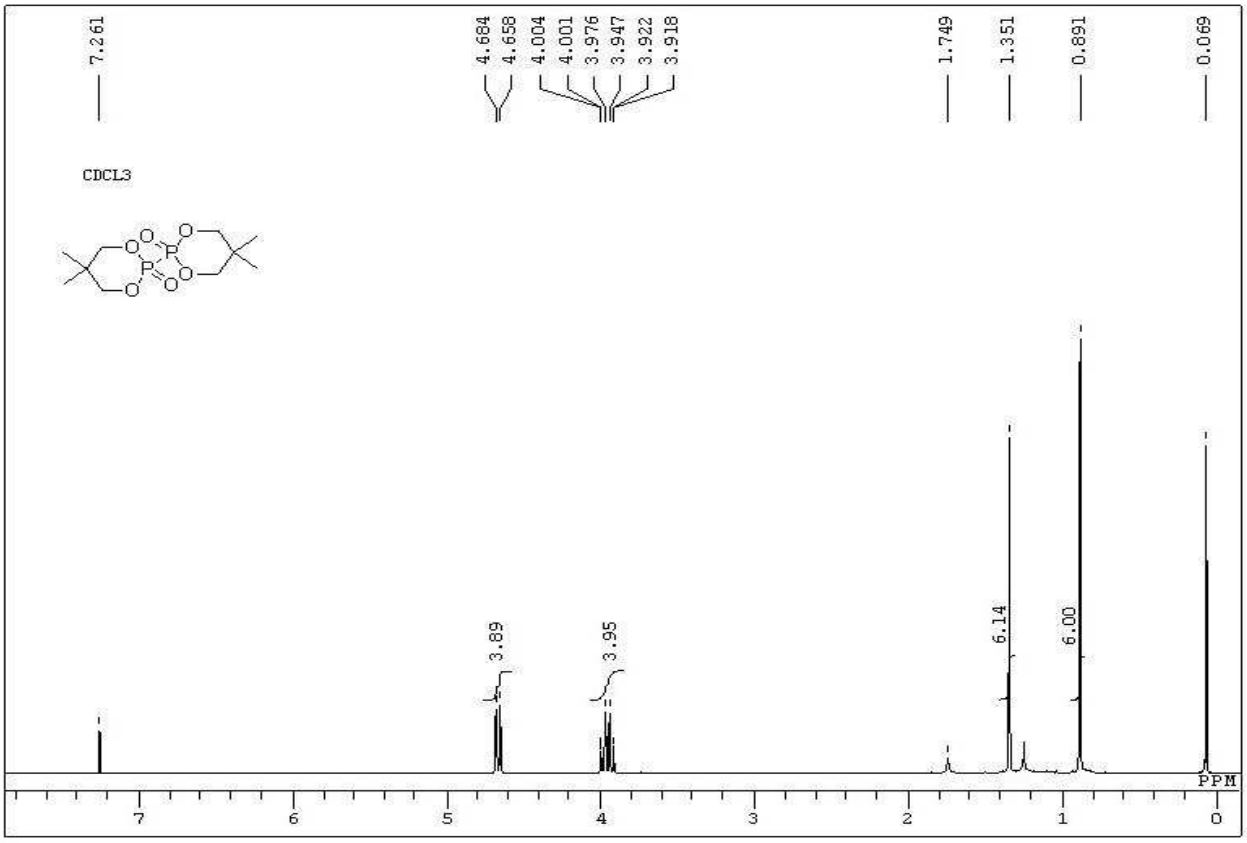
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4.001
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3.922
3.918
1.749
1.351
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3.95
6.14
6.00
PPM
7
6
5
4
3
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1
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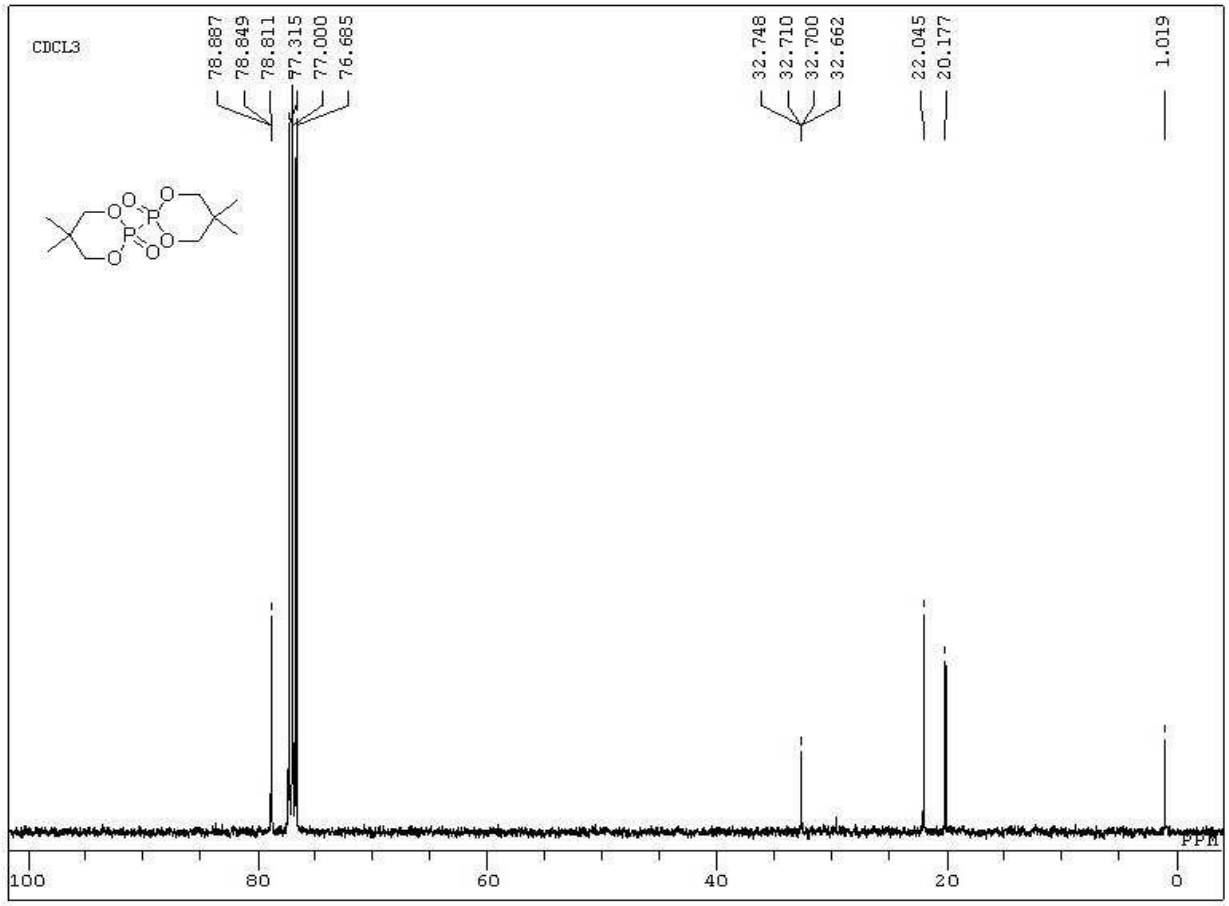
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77.000
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32.700
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1.019
PPM
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20
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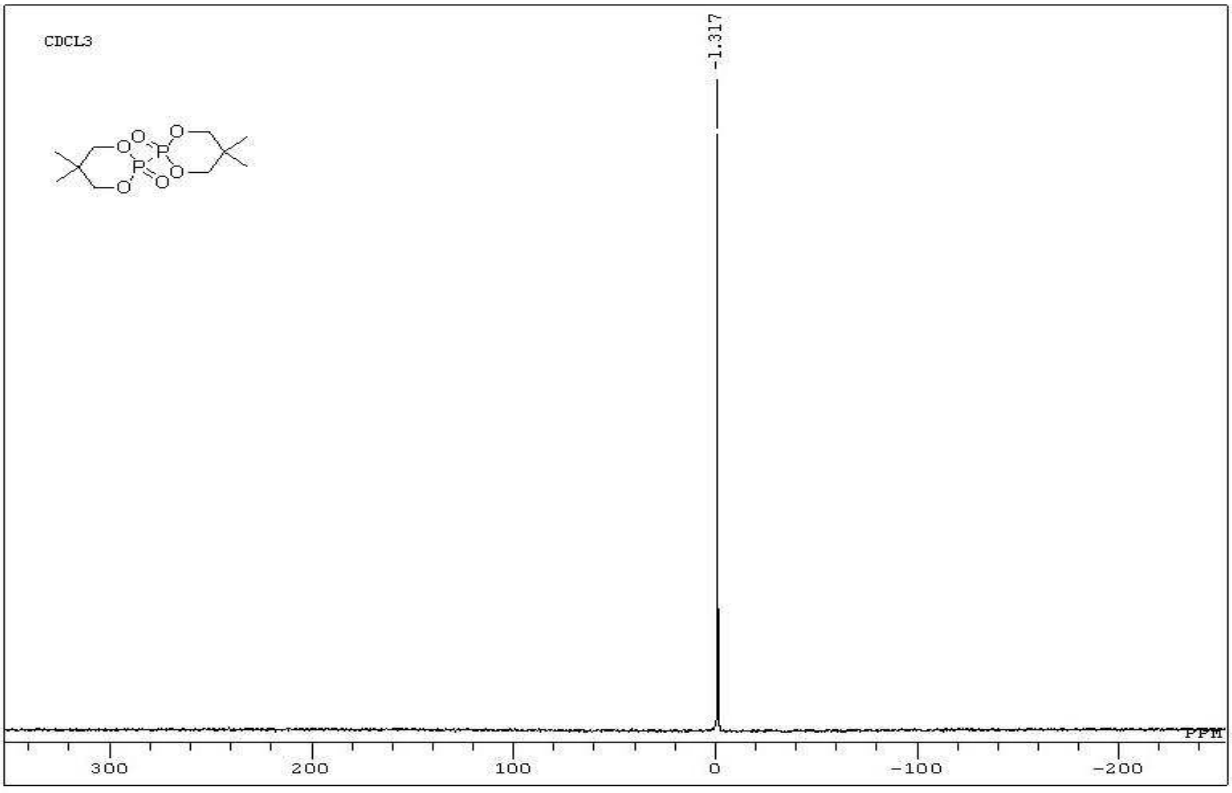
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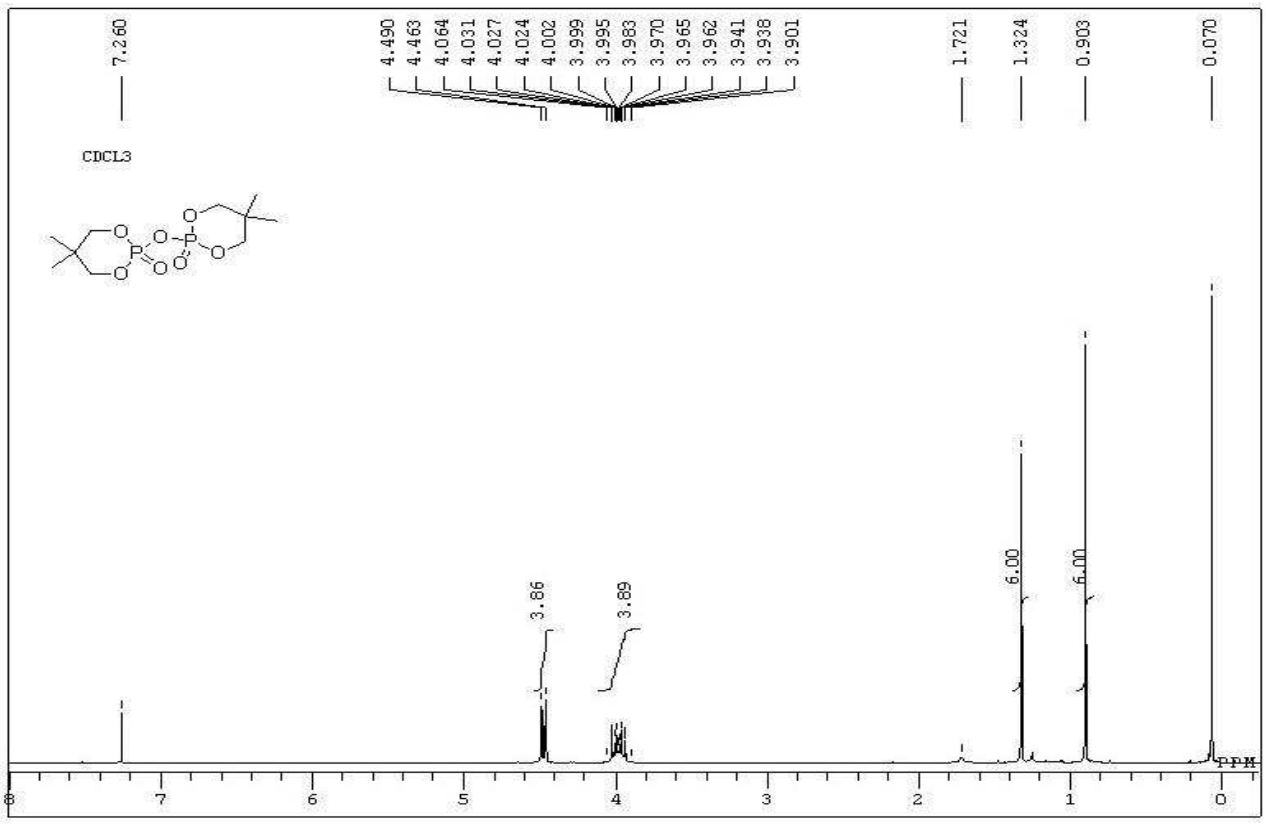
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4.463
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4.002
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3.995
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3.965
3.962
3.941
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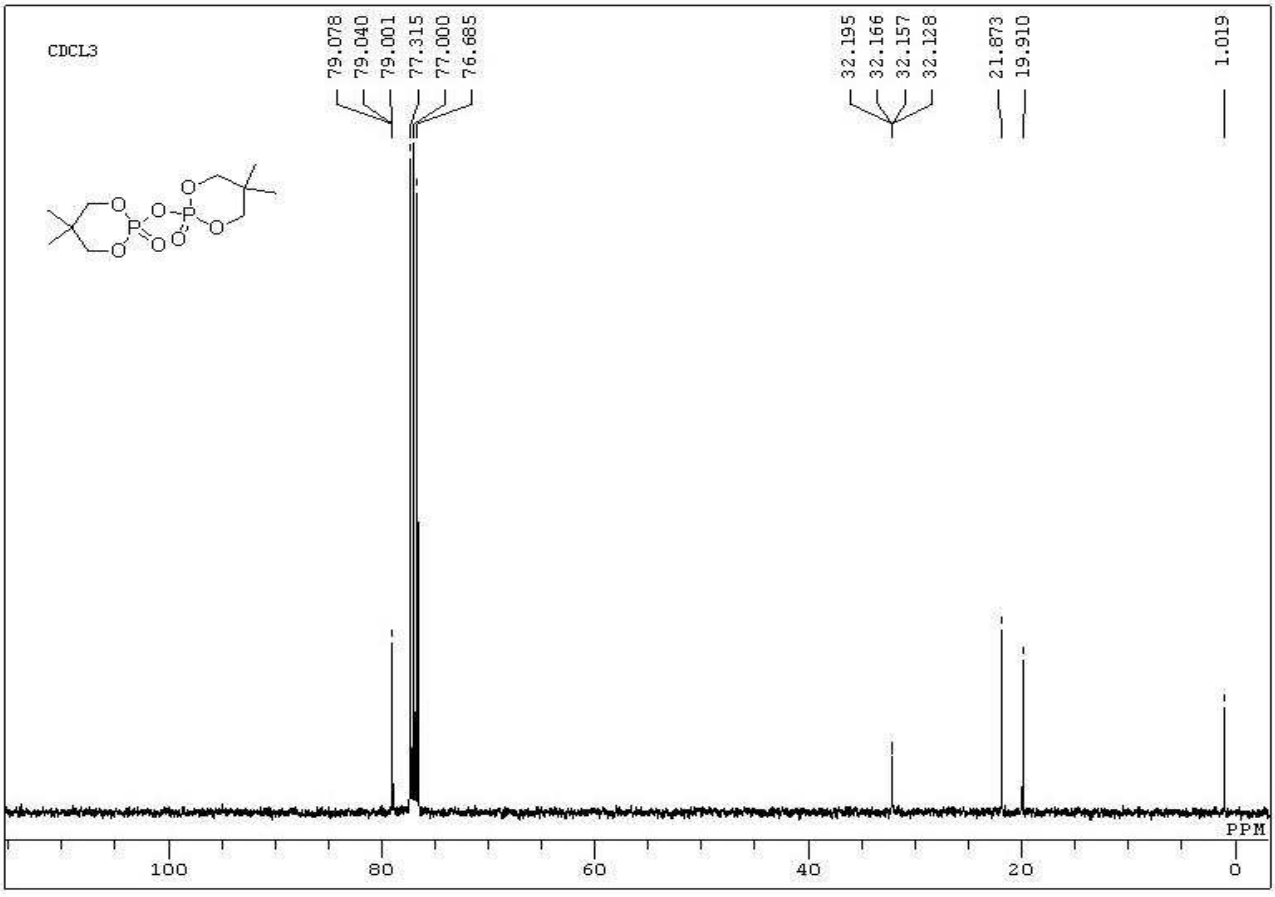
6.00
PPM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77.000
76.685
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32.166
32.157
32.128
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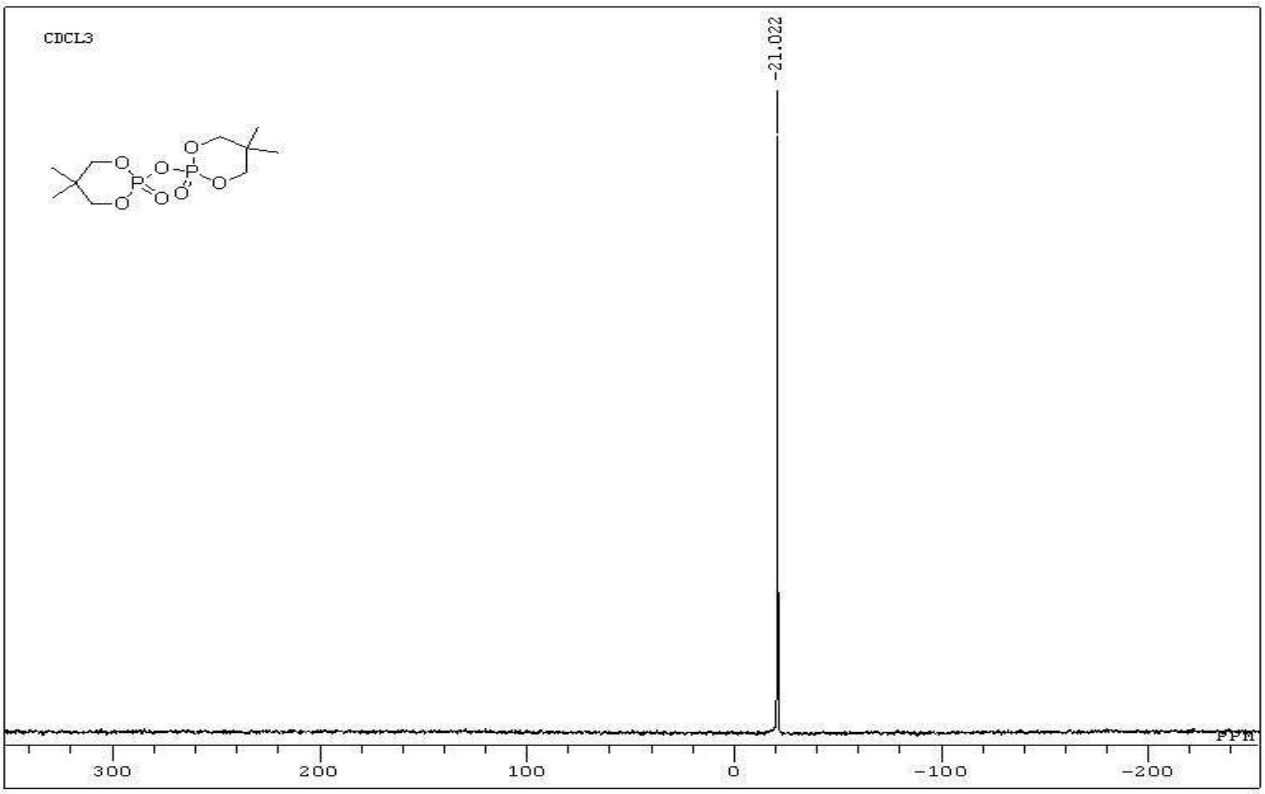
19.910
1.019
PPM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PPM
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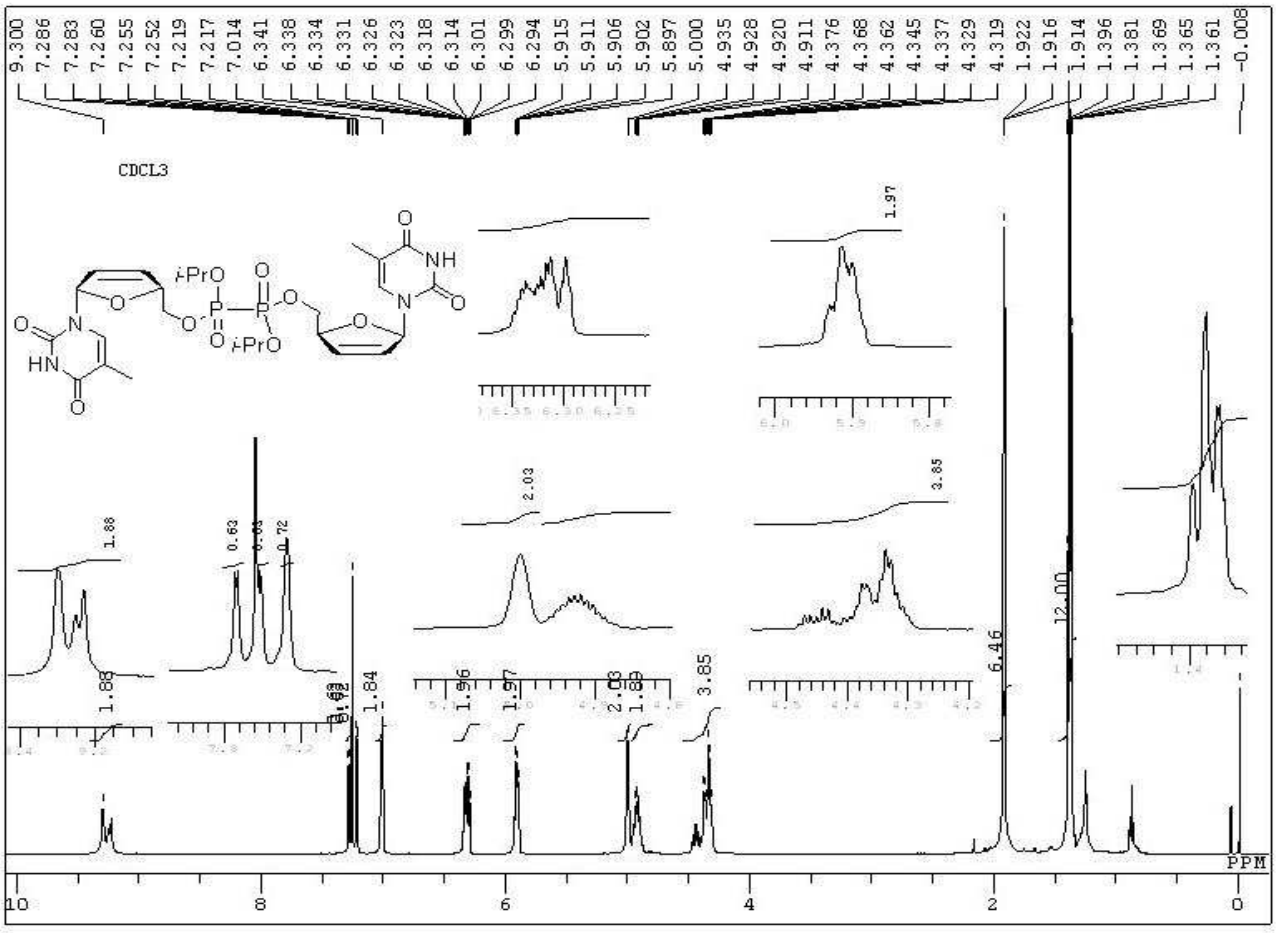
-200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PPM
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8
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4
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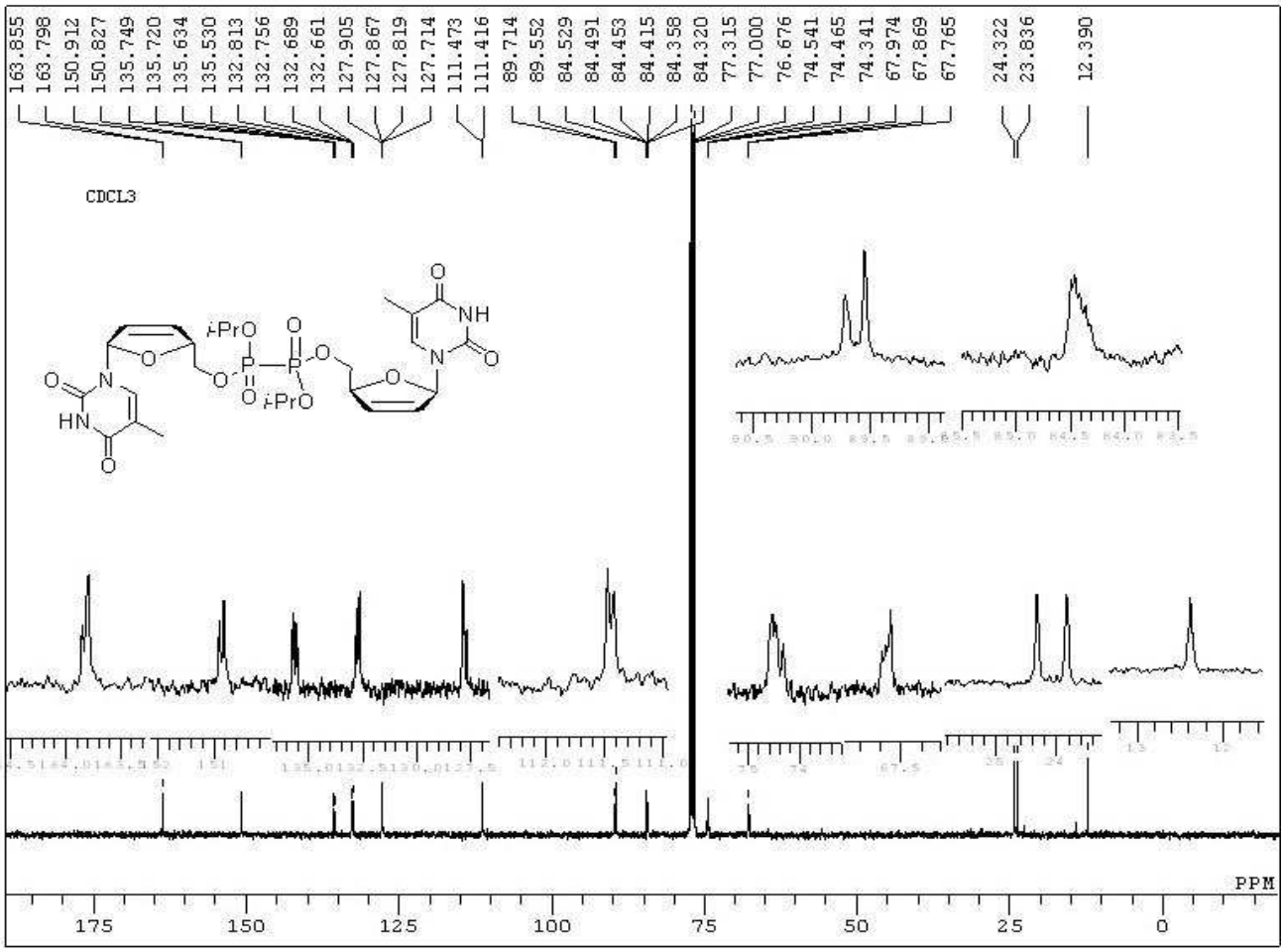
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127.714
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89.714
89.552
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84.453
84.415
84.358
84.320
77.315
77.000
76.676
74.541
74.465
74.341
67.974
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PPM
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75
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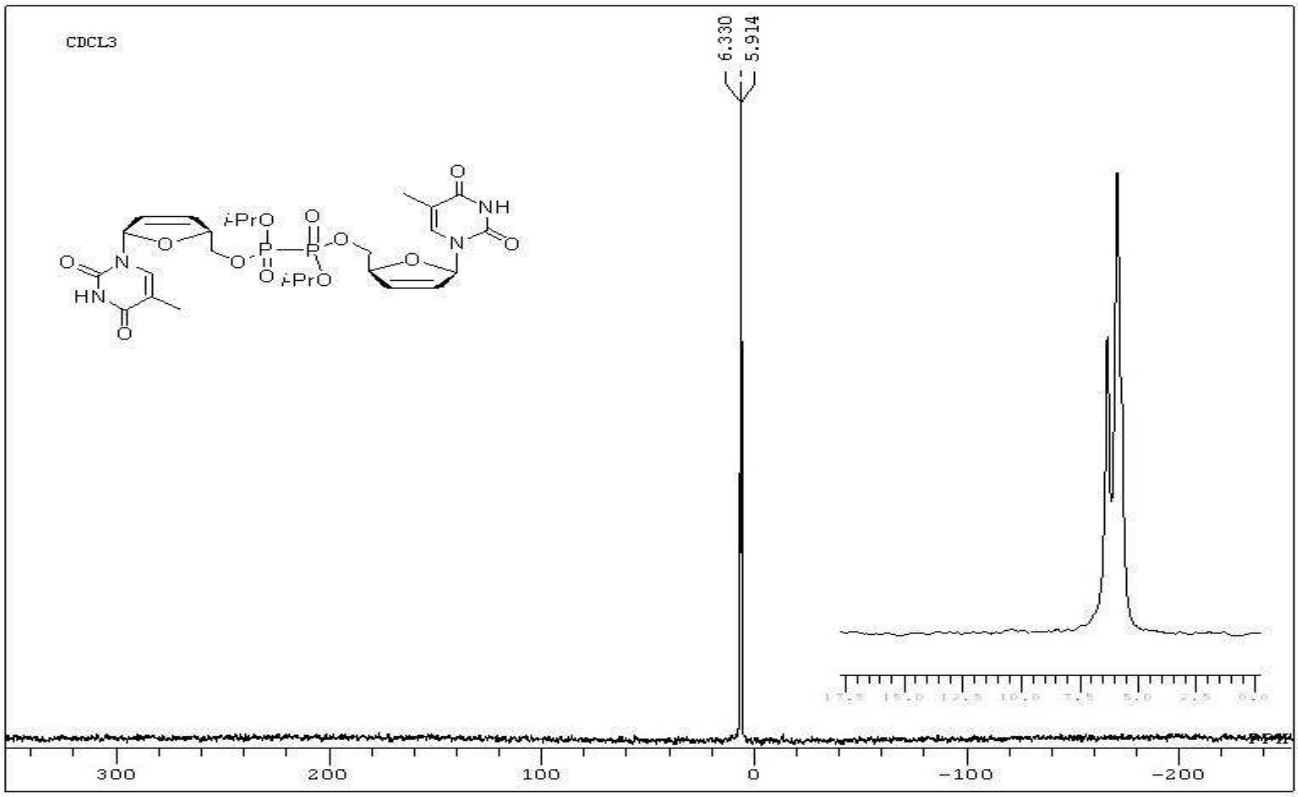
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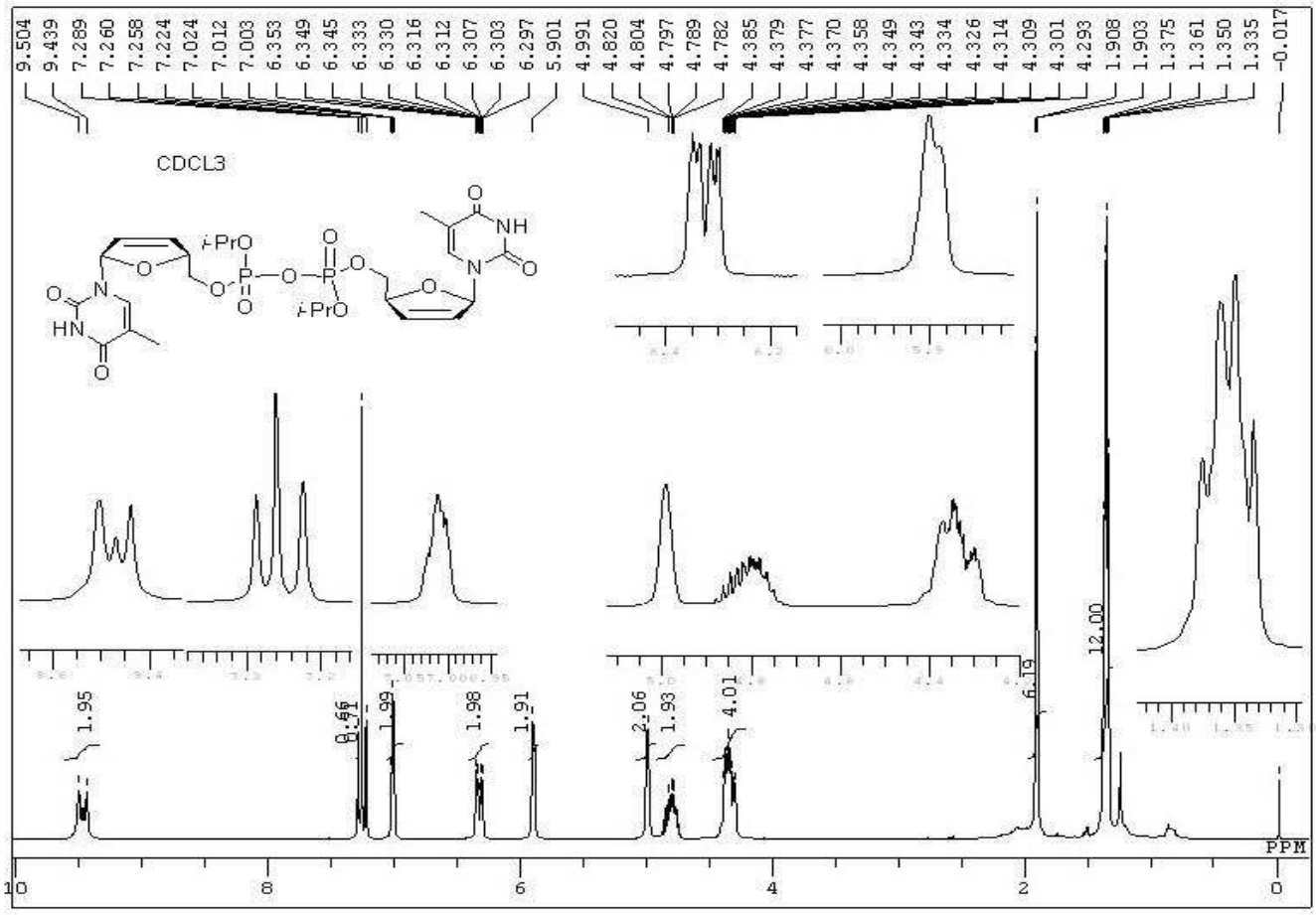
-100
-200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6.349
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6.333
6.330
6.316
6.312
6.307
6.303
6.297
5.901
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4.820
4.804
4.797
4.789
4.782
4.385
4.379
4.377
4.370
4.358
4.349
4.343
4.334
4.326
4.314
4.309
4.301
4.293
1.908
1.903
1.375
1.361
1.350
1.335
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CDCL3
1.95
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2.06
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4.01
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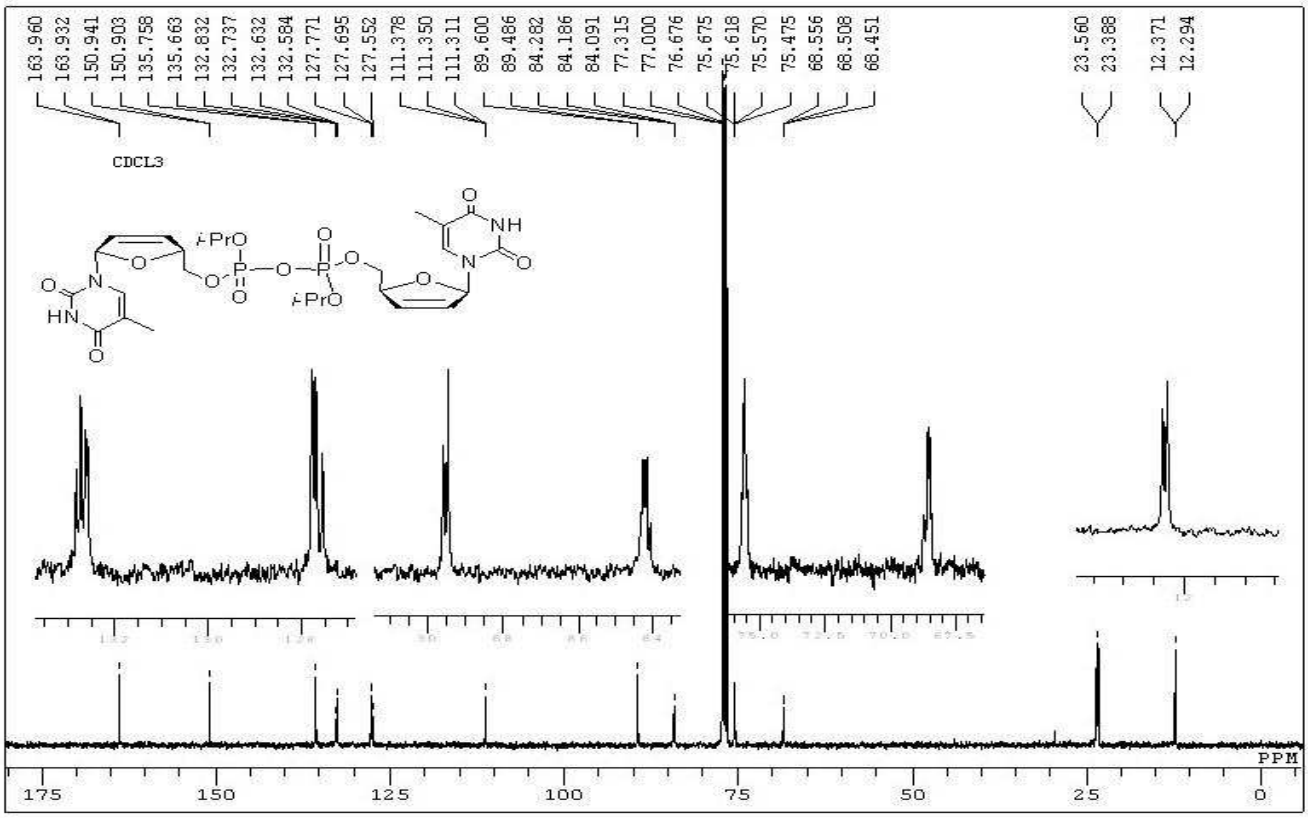
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135.663
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132.632
132.584
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127.695
127.552
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111.350
111.311
89.600
89.486
84.282
84.186
84.091
77.315
77.000
76.676
75.675
75.618
75.570
75.475
68.556
68.508
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23.388
12.371
12.294
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PPM
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150
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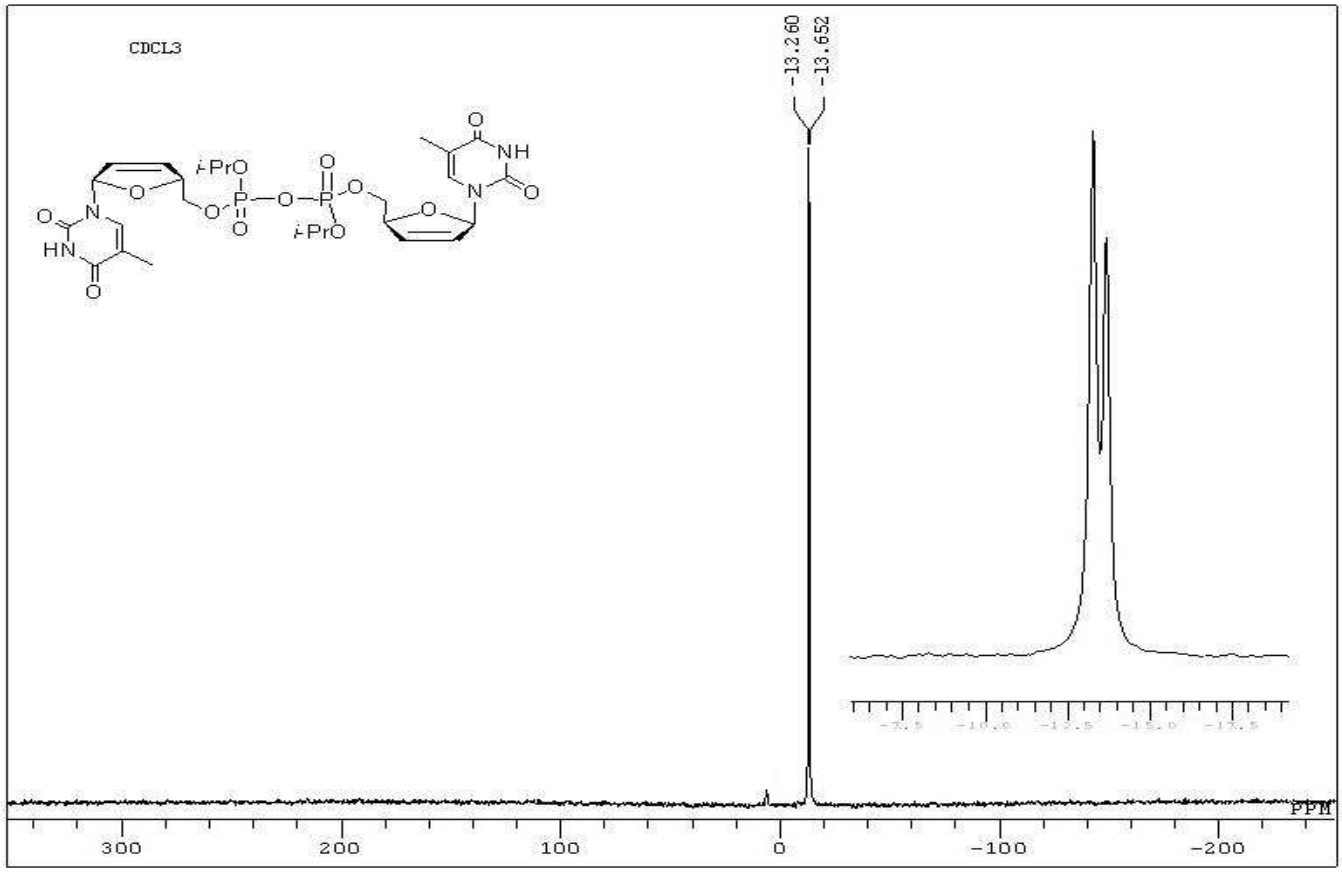
100
75
50
25
0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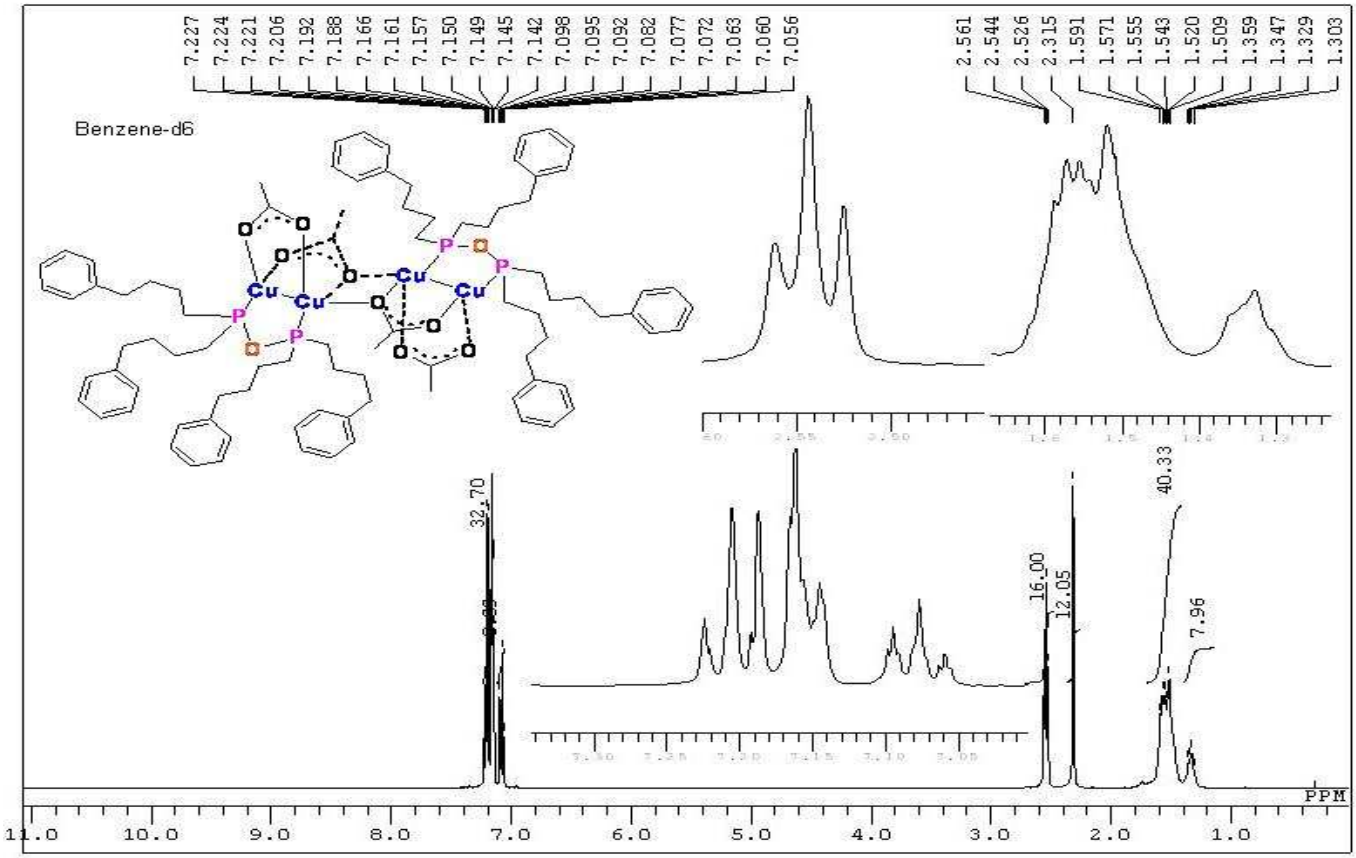
Benzene-d6
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7.188
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7.161
7.157
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7.145
7.142
7.098
7.095
7.092
7.082
7.077
7.072
7.063
7.060
7.056
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2.544
2.526
2.315
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1.571
1.555
1.543
1.520
1.509
1.359
1.347
1.329
1.303
32.70
16.00
12.05
40.33
7.96
PPM
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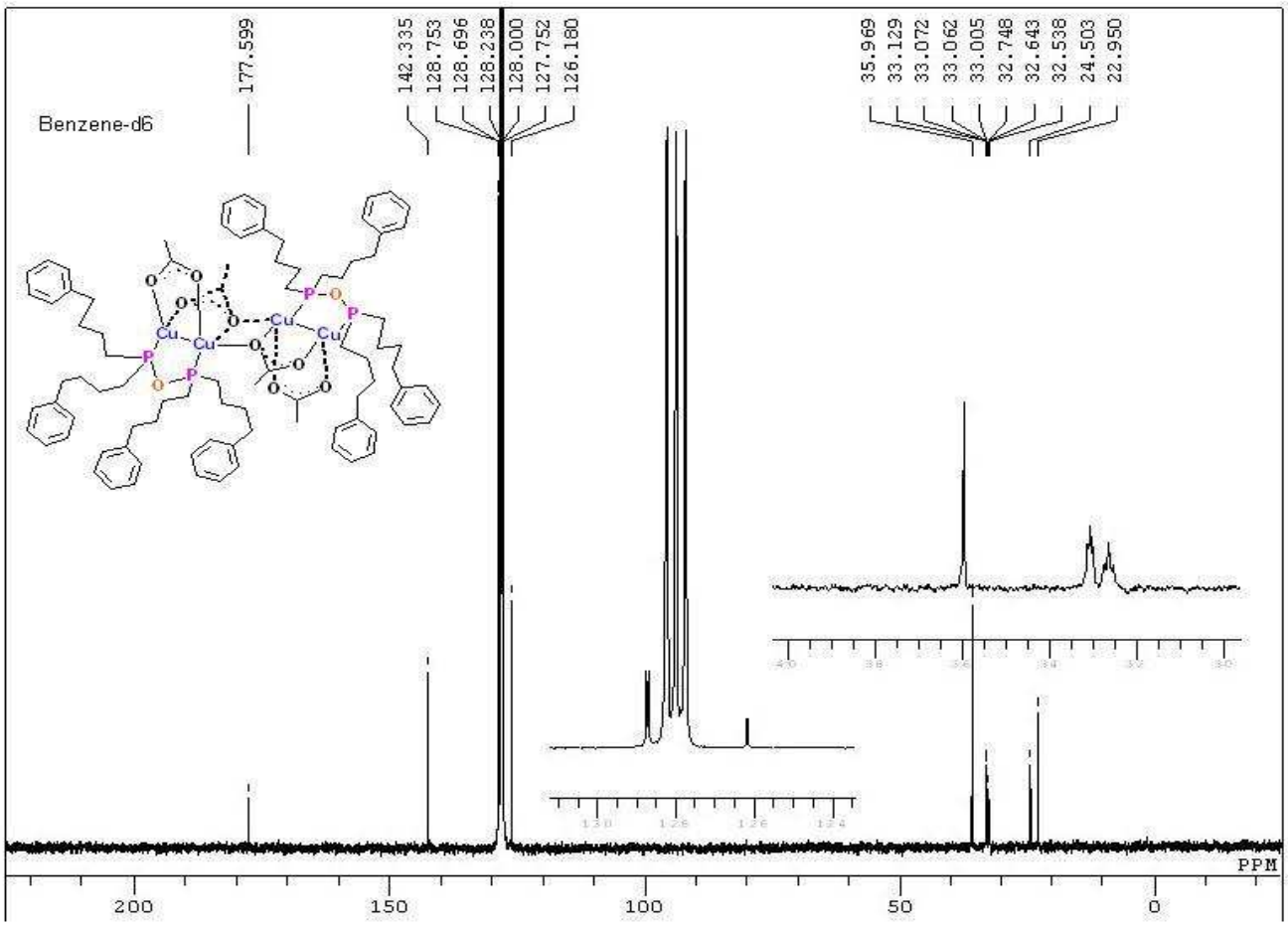
Benzene-d6
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126.180
35.969
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33.005
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32.643
32.538
24.503
22.950
PPM
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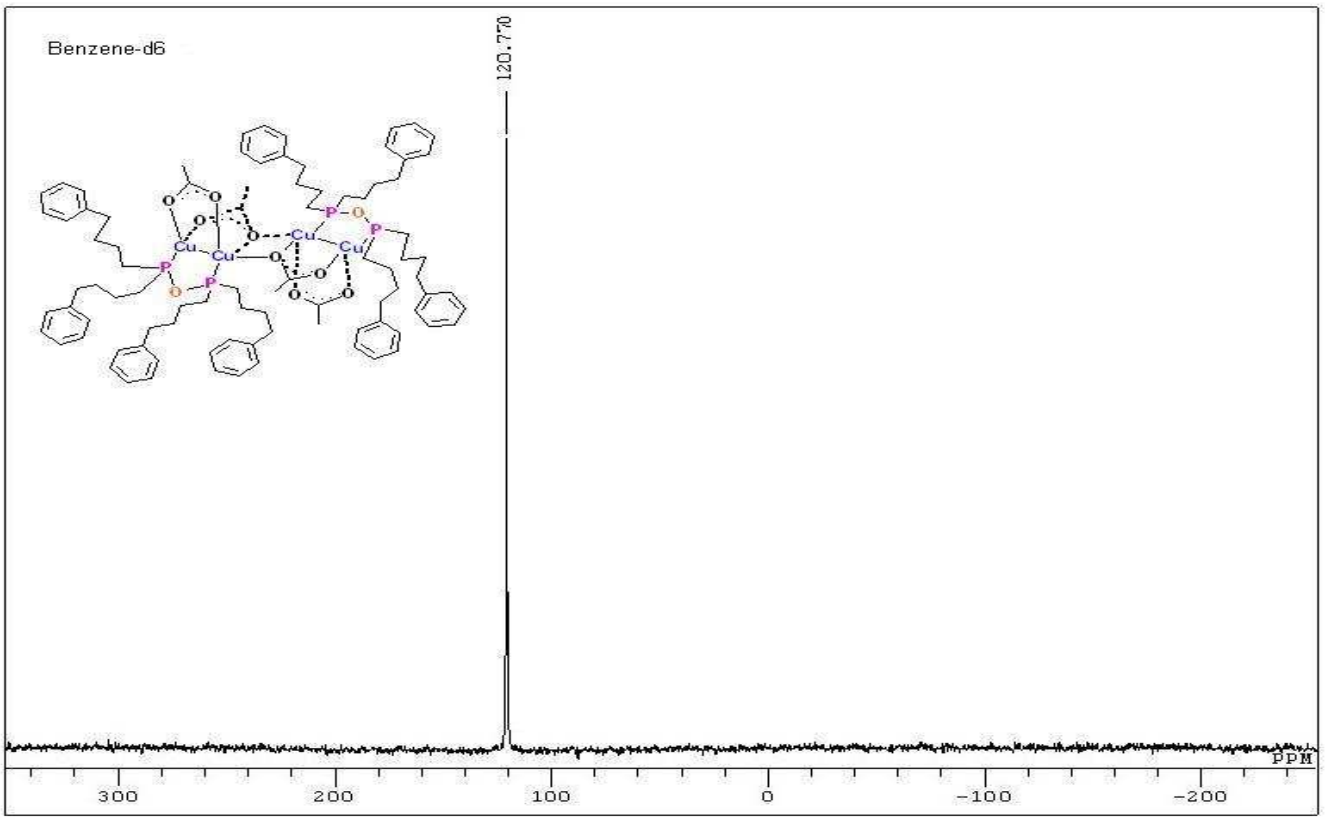
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-200