Supporting Information

for

Synthesis of New Beta-Amidophosphonates and Theoretical Evaluation of Related Features

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Experimental

Melting points were measured on an Electrothermal 9100 apparatus. Elemental analyses for C, H, and N were performed using a Heraeus CHN-O-Rapid analyzer. These data were in good agreement with the calculated values. IR spectra were measured on a Shimadzu IR 460 spectrometer. ^{1}H and ^{13}C NMR spectra were measured with BRUKER DRX-500 AVANCE spectrometer at 500.1 and 125.8 MHz, respectively. Mass spectra were recorded with a Finnigan-Matt 8430 mass spectrometer operating at an ionization potential of 70 eV. Triphenylphosphine, triphenylphosphite, theophiline, dimethyl acetylenedicarboxylate were obtained from Fluka (Buchs, Switzerland) and were used without further purification.

Computational method

Full optimizations of **4** taked place at B3LYP/6-311+G* level of theory without any constrains using Guassian 98 program. Optimized structures and heats of formations of two diastereomers of **4** summarized in Tables S3 and S4.

The typical process for Preparation of *7-(Dialkyl-2-[bis(alkyl(aryl)oxy)-phosphoryl])-(1,3-dimethyl-purine-2,6-dione)-butanedioate* **(*4a-i*)**. To a magnetically stirred mixture of 0.36 g theophiline (2 mmol) and trialkyl(aryl) phosphites **(*1a-c*)** (2 mmol) in dried dichloromethane 5 cm^{-3} was added dropwise a solution of dialkyl acetylenecarboxylates **(2)** (2 mmol) in dried dichloromethane (5 cm^{-3}). The solution was stirred at room temperature for 24 hr. The solvent was removed under reduced pressure and the solid residue was washed with 2×5 cm^{-3} cold diethyl ether and the product was obtained as white crystals. The solid was filtered off and dried to give products.

7-(Dimethyl-2-[bis(phenyloxy)-phosphoryl])-(1,3-dimethyl-purine-2,6-dione)-butanedioate (**4a**, $C_{25}H_{25}N_4O_9P$) Yield: 0.76 g (86%). White powder, M.p.: 293-295 °C. IR (KBr): ν = 3062 (C-H), 2900 (C-H), 1711 (OC=O), 1663 (NC=O), 1242 (P=O) cm^{-1}.

7-(Diethyl-2-[bis(phenyloxy)-phosphoryl])-(1,3-dimethyl-purine-2,6-dione)-butanedioate (**4b**, $C_{27}H_{31}N_4O_9P$) Yield: 0.71 g (82%). White powder, M.p.: 282-284 °C. IR (KBr): ν = 3000 (C-H), 2826 (C-H), 1717 (OC=O), 1668 (NC=O), 1242 (P=O) cm^{-1}.

7-(Di-tert-butyl-2-[bis(phenyloxy)-phosphoryl])-(1,3-dimethyl-purine-2,6-dione)-butanedioate (**4c**, $C_{31}H_{37}N_4O_9P$) Yield: 0.74 g (58%). White powder, M.p.: 290-292 °C. IR (KBr): ν = 3064 (C-H), 2975 (C-H), 1720 (OC=O), 1668 (NC=O), 1241 (P=O) cm^{-1}.

7-(Dimethyl-2-[bis(methyloxy)-phosphoryl])-(1,3-dimethyl-purine-2,6-dione)-butanedioate (**4d**, $C_{15}H_{21}N_4O_9P$) Yield: 0.74 g (86%). White powder, M.p.: 286-288 °C. IR (KBr): ν = 3049 (C-H), 2923 (C-H), 1721 (OC=O), 1665 (NC=O), 1242 (P=O) cm^{-1}.

7-(Diethyl-2-[bis(methyloxy)-phosphoryl])-(1,3-dimethyl-purine-2,6-dione)-butanedioate (**4e**, $C_{17}H_{25}N_4O_9P$) Yield: 0.67g (73%). White powder, M.p.: 264-266 °C. IR (KBr): ν = 3064 (C-H), 2960 (C-H), 1726 (OC=O), 1667 (NC=O), 1241 (P=O) cm^{-1}.

7-(Di-tert-butyl-2-[bis(methyloxy)-phosphoryl])-(1,3-dimethyl-purine-2,6-dione)-butanedioate (**4f**, $C_{21}H_{33}N_4O_9P$) Yield: 0.66 g (64%). White powder, M.p.: 251-253 °C. IR (KBr): ν = 3043 (C-H), 2954 (C-H), 1722 (OC=O), 1667 (NC=O), 1238 (P=O) cm^{-1}.

7-(Dimethyl-2-[bis(ethyloxy)-phosphoryl])-(1,3-dimethyl-purine-2,6-dione)-butanedioate (**4g**, $C_{17}H_{25}N_4O_9P$) Yield: 0.68g (76%). White powder, M.p.: 276-277 °C. IR (KBr): ν = 3057 (C-H), 2977 (C-H), 1717 (OC=O), 1667 (NC=O), 1241 (P=O) cm^{-1}.

7-(Diethyl-2-[bis(ethyloxy)-phosphoryl])-(1,3-dimethyl-purine-2,6-dione)-butanedioate (**4h**, $C_{19}H_{29}N_4O_9P$) Yield: 0.62 g (64%). White powder, M.p.: 283-285 °C. IR (KBr): ν = 3064 (C-H), 2975 (C-H), 1716 (OC=O), 1667 (NC=O), 1242 (P=O) cm^{-1}.

7-(Di-tert-butyl-2-[bis(ethyloxy)-phosphoryl])-(1,3-dimethyl-purine-2,6-dione)-butanedioate (**4i**, $C_{23}H_{37}N_4O_9P$) Yield: 0.54 g (50%). White powder, M.p.: 265-267 °C. IR (KBr): ν = 3048 (C-H), 2993 (C-H), 1719 (OC=O), 1667 (NC=O), 1241 (P=O) cm^{-1}.

Table S1. Selected chemical shifts of phosphonates **4** in DMSO-d_6 as the solvents (25°C)

		^{1}H NMR (δ / *ppm*)						$^2J_{PH}$, $^3J_{HH}$, $^3J_{PH}$ *(Hz)*
		2 N-CH$_3$	**CH-P**	**N-CH-**	**2 R**	**2 R'**	**N=CH-N**	**HC-CH-P**
4a	(2*S*, 3*R*) or (2*R*, 3*S*)	2.62, 3.19	2.89	5.28	3.40, 3.47	6.7-7.1	7.97	19.8, 7.4, 13.5
	(*2R*, *3R*) or (*2S*, *3S*)	2.60, 3.01	2.91	5.30	3.31, 3.46	6.7-7.1	7.99	21.8, 7.0, 5.6
4b	(2*S*, 3*R*) or (2*R*, 3*S*)	2.80, 2.91	3.26	5.24	1.23, 1.34, 4.1-4.3	6.7-7.7	8.01	18.6, 7.7, 12.9
	(*2R*, *3R*) or (*2S*, *3S*)	2.77, 2.85	3.25	5.23	1.24, 1.35, 4.1-4.3	6.7-7.7	7.98	22.1, 8.6, 6.3
4c	(2*S*, 3*R*) or (2*R*, 3*S*)	2.67, 2.88	4.24	5.12	1.2, 1.6	6.9-7.3	7.84	22.3, 6.9, 13.9
	(*2R*, *3R*) or (*2S*, *3S*)	2.77, 2.91	4.21	5.14	1.3, 1.6	6.9-7.3	7.81	19.4, 8.1, 6.5
4d	(2*S*, 3*R*) or (2*R*, 3*S*)	3.21, 3.29	3.81	5.22	3.41, 3.46	3.51, 3.96	7.99	24.8, 7.7, 9.1
	(*2R*, *3R*) or (*2S*, *3S*)	3.12, 3.18	3.79	5.20	3.37, 3.44	3.52, 3.93	8.01	20.1, 7.8, 5.9
4e	(2*S*, 3*R*) or (2*R*, 3*S*)	2.88, 3.01	3.61	5.15	1.25, 1.35, 4.1-4.3	3.64, 3.73	7.85	23.2, 8.4, 9.1
	(*2R*, *3R*) or (*2S*, *3S*)	2.78, 2.96	3.57	5.13	1.23, 1.34, 4.1-4.3	3.58, 3.97	7.89	19.6, 8.0, 6.5
4f	(2*S*, 3*R*) or (2*R*, 3*S*)	2.92, 3.11	3.68	6.18	1.14, 1.22	3.79, 3.83	8.01	22.7, 7.8, 9.2
	(*2R*, *3R*) or (*2S*, *3S*)	2.88, 3.02	3.66	6.16	1.07, 1.24	3.81, 4.09	7.89	18.9, 6.9, 5.2
4g	(2*S*, 3*R*) or (2*R*, 3*S*)	2.69, 2.83	3.04	5.19	3.90, 4.19	1.01, 1.22, 3.5-3.7	7.99	24.2, 7.6, 13.5
	(*2R*, *3R*) or (*2S*, *3S*)	2.73, 2.98	3.02	5.16	4.01, 4.17	1.81, 1.20, 3.5-3.7	7.97	20.0, 5.3, 6.3
4h	(2*S*, 3*R*) or (2*R*, 3*S*)	2.85, 3.03	3.33	5.70	0.99, 1.21, 3.4-3.9	1.61, 1.71, 3.4-3.9	8.02	21.3, 7.9, 14.3
	(*2R*, *3R*) or (*2S*, *3S*)	2.77, 2.99	3.21	5.73	1.10, 1.24, 3.4-3.9	1.52, 1.77, 3.4-3.9	8.00	19.7, 6.1, 5.9
4i	(2*S*, 3*R*) or (2*R*, 3*S*)	2.69, 2.94	3.26	5.23	0.91, 1.41	1.11, 1.21, 3.3-3.8	8.01	23.8, 8.1, 12.1
	(*2R*, *3R*) or (*2S*, *3S*)	2.76, 2.91	3.25	5.21	1.27, 1.40	1.20, 1.42, 3.3-3.8	7.98	20.2, 6.3, 5.1

Table S2. Selected chemical shifts (δ/ppm) of phosphonates **4** in DMSO-d_6 as the solvents (25°C)

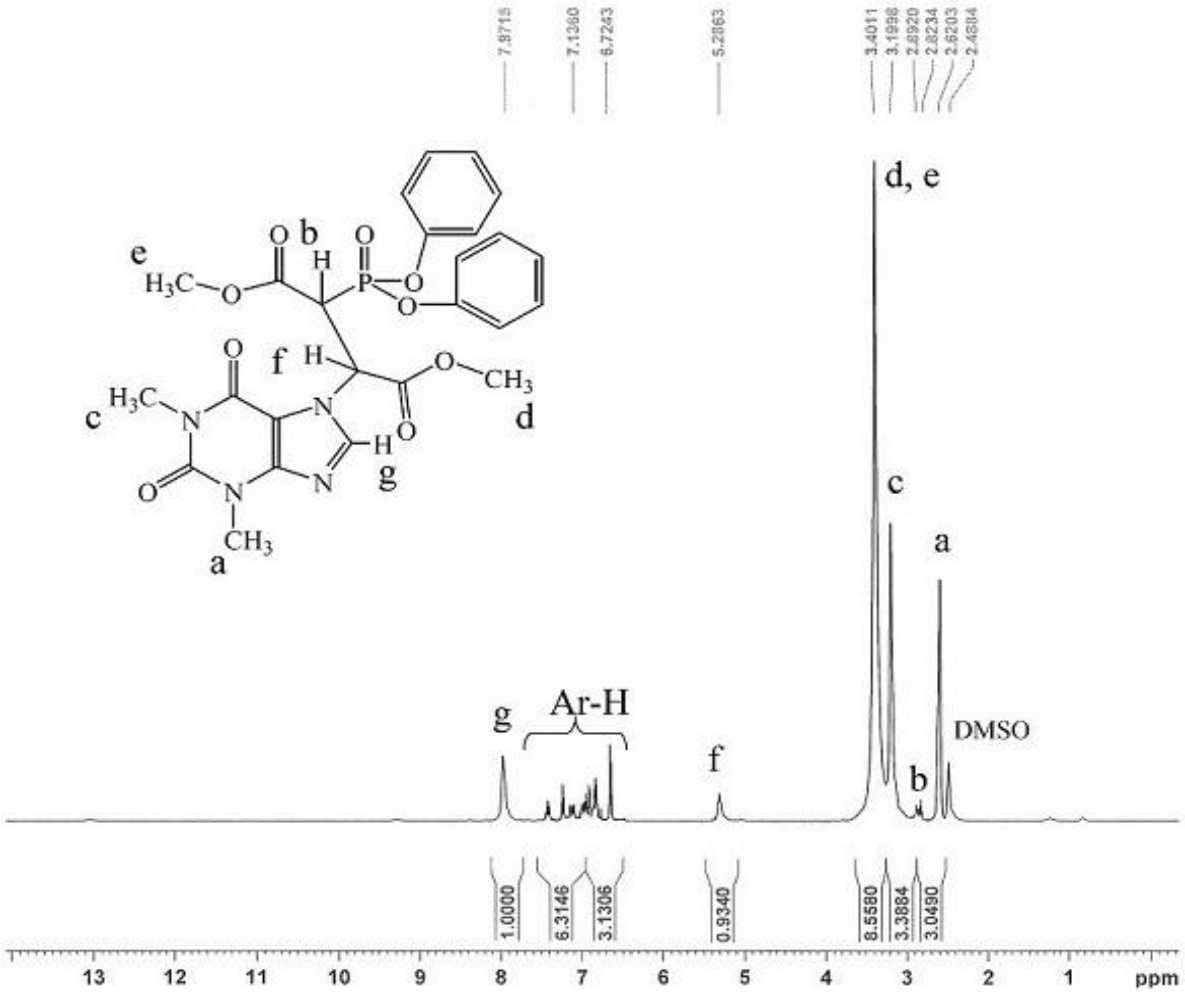
		^{13}C NMR									$^{1}J_{PC}$ (Hz)	^{31}P NMR
		2 N-CH_3	**C-P**	**N-CH-**	**2 C-OC**	**2 C-O-P**	**N=C**	**2 NC=O**	**2 OC=O**	**C=*C*-N**	**C-P**	**C-P**
4a	(2*S*, 3*R*) or (2*R*, 3*S*)	27.7, 29.7	31.1	50.0	50.1, 52.3	114-142	140.4	147.8, 151.2	169.9, 170.0	106.3	136	9.9
	(*2R*, *3R*) or (*2S*, *3S*)	27.8, 29.7	32.2	50.2	49.9, 51.4	115-140	140.4	147.8, 151.2	168.7, 170.2	106.3	136	11.7
4b	(2*S*, 3*R*) or (2*R*, 3*S*)	27.7, 29.8	34.0	54.4	54.5, 56.3	119-140	144.0	146.2, 150.1	168.0, 169.0	107.1	123	9.5
	(*2R*, *3R*) or (*2S*, *3S*)	27.8, 29.7	35.1	54.5	54.6, 57.0	119-140	144.1	146.3, 150.2	168.1, 169.1	107.3	122	11.2
4c	(2*S*, 3*R*) or (2*R*, 3*S*)	27.3, 29.4	33.3	53.7	74.1, 78.3	117-141	147.6	150.9, 151.5	164.3, 170.2	106.3	129	9.6
	(*2R*, *3R*) or (*2S*, *3S*)	27.4, 29.7	33.4	53.8	74.2, 81.2	117-141	147.5	151.2, 151.6	166.4, 170.3	106.2	134	10.9
4d	(2*S*, 3*R*) or (2*R*, 3*S*)	28.6, 29.6	32.2	50.1	49.4, 51.3	51.8, 52.8	138.4	147.2, 147.8	161.4, 167.5	104.3	131	9.9
	(*2R*, *3R*) or (*2S*, *3S*)	28.1, 29.0	32.8	50.4	50.2, 51.5	51.9, 53.5	138.8	147.5, 147.7	161.5, 167.9	104.5	131	10.6
4e	(2*S*, 3*R*) or (2*R*, 3*S*)	27.0, 29.1	32.4	50.1	53.1, 55.7	57.3, 58.8	140.9	146.8, 147.3	161.4, 167.8	106.7	129	9.8
	(*2R*, *3R*) or (*2S*, *3S*)	27.3, 29.5	32.6	50.5	52.6, 53.7	56.3, 58.1	141.9	145.8, 147.8	161.9, 167.9	106.8	130	10.7
4f	(2*S*, 3*R*) or (2*R*, 3*S*)	27.6, 29.6	32.2	50.1	51.3, 51.8	82.1, 84.3	140.4	147.6, 147.8	161.1, 167.3	106.3	131	10.0
	(*2R*, *3R*) or (*2S*, *3S*)	27.7, 29.7	31.2	50.3	51.5, 52.4	82.3, 84.5	140.5	147.7, 147.9	164.2, 167.8	106.4	131	11.9
4g	(2*S*, 3*R*) or (2*R*, 3*S*)	27.2, 28.7	32.4	50.2	55.1, 56.7	57.6, 58.8	141.9	146.8, 147.8	161.9, 166.8	106.9	129	9.8
	(*2R*, *3R*) or (*2S*, *3S*)	27.6, 28.7	32.1	50.4	52.7, 53.7	56.9, 57.8	141.1	147.4, 147.8	161.3, 167.2	106.3	131	11.0
4h	(2*S*, 3*R*) or (2*R*, 3*S*)	27.8, 28.9	32.4	51.1	53.4, 53.8	54.6, 55.9	141.4	147.1, 147.9	161.5, 166.2	106.5	131	9.6
	(*2R*, *3R*) or (*2S*, *3S*)	27.6, 28.7	32.0	51.6	53.2, 54.8	55.3, 56.8	140.8	147.3, 147.5	162.5, 166.7	106.2	130	10.2
4i	(2*S*, 3*R*) or (2*R*, 3*S*)	27.8, 29.3	32.6	50.1	52.3, 53.8	82.3, 84.9	140.0	147.1, 148.2	160.6, 167.0	106.5	130	9.8
	(*2R*, *3R*) or (*2S*, *3S*)	26.6, 26.7	32.3	50.4	52.6, 53.9	82.0, 84.7	140.6	147.5, 148.9	160.3, 167.3	106.2	130	9.4

Table S3. The relative energies (ΔE) and dihedral angles for the structures compared to those diastereomers at B3LYP/6-311+G* level of theory.

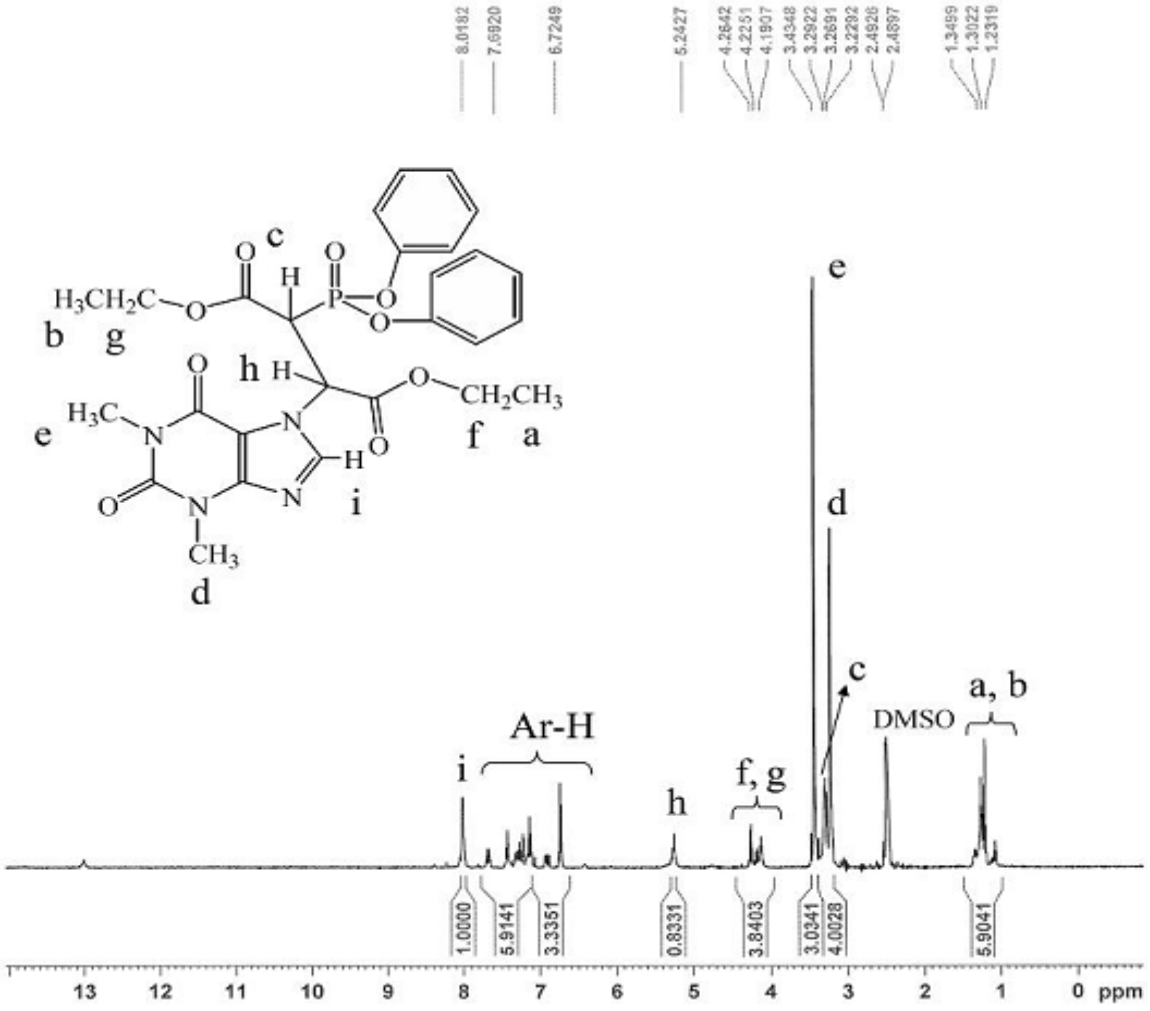
Compound	**Dihedral angle** (Degree) **H-C-C-H**		**(Δ*E*)** (*Kcal/mol*)	
	(*2R, 3R*) or (*2S, 3S*)	**(*2R, 3S*) or (*2S, 3R*)**	**(*2R, 3R*) or (*2S, 3S*)**	**(*2R, 3S*) or (*2S, 3R*)**
4a	56.8	176.8	(0.00)	(22.17)
4b	83.8	176.9	(0.00)	(27.43)
4c	64.9	173.5	(0.00)	(24.77)
4d	174.9	69.8	(0.00)	(15.81)
4e	176.3	70.6	(0.00)	(18.48)
4f	173.3	70.1	(0.00)	(24.38)
4g	168.4	91.2	(0.00)	(25.40)
4h	166.1	74.0	(0.00)	(26.67)
4i	173.1	71.0	(0.00)	(27.69)

Original ^{1}H NMR spectrum

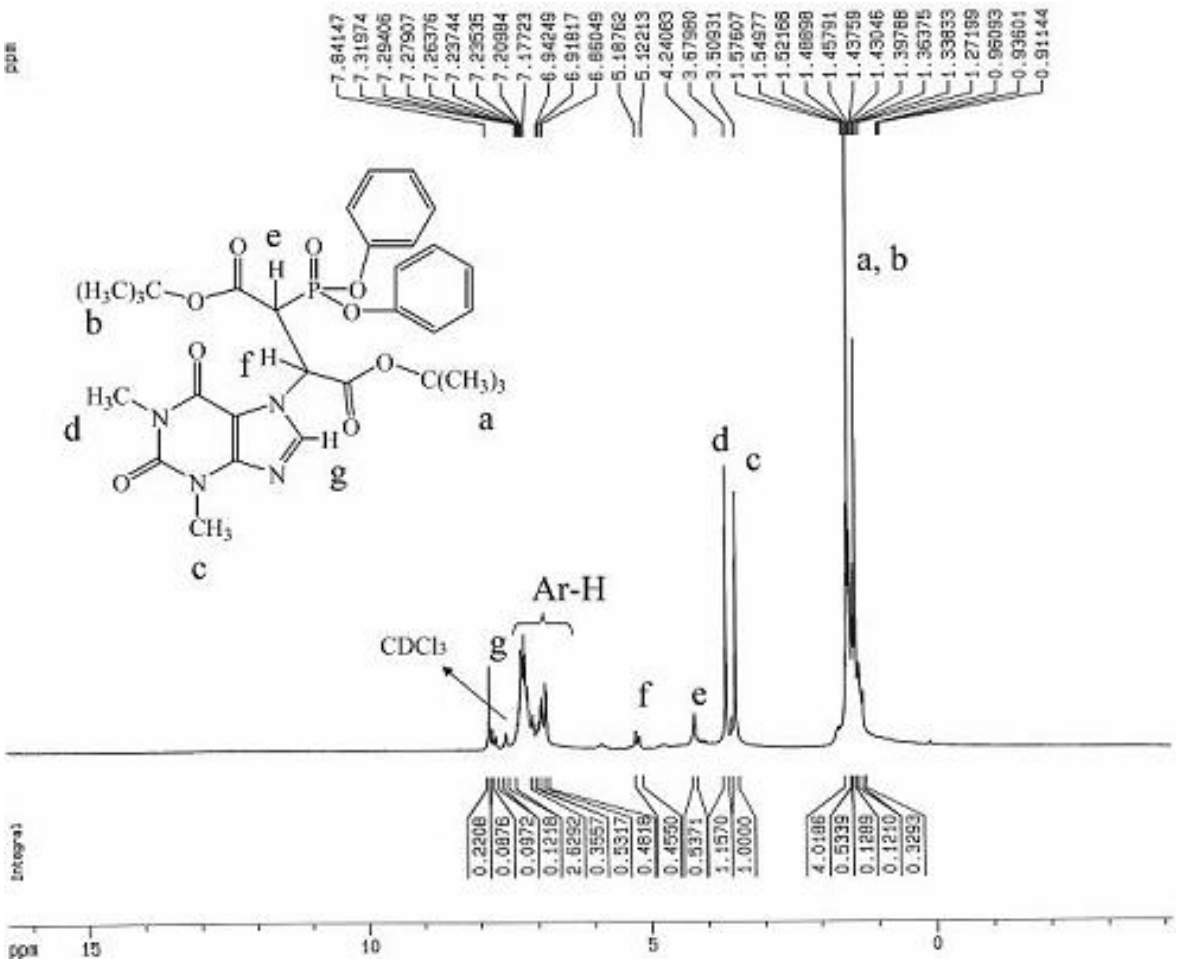
1. *7-(Dimethyl-2-[bis(phenyloxy)-phosphoryl])-(1,3-dimethyl-purine-2,6-dione)-butanedioate* (**4a**, $C_{25}H_{25}N_4O_9P$)



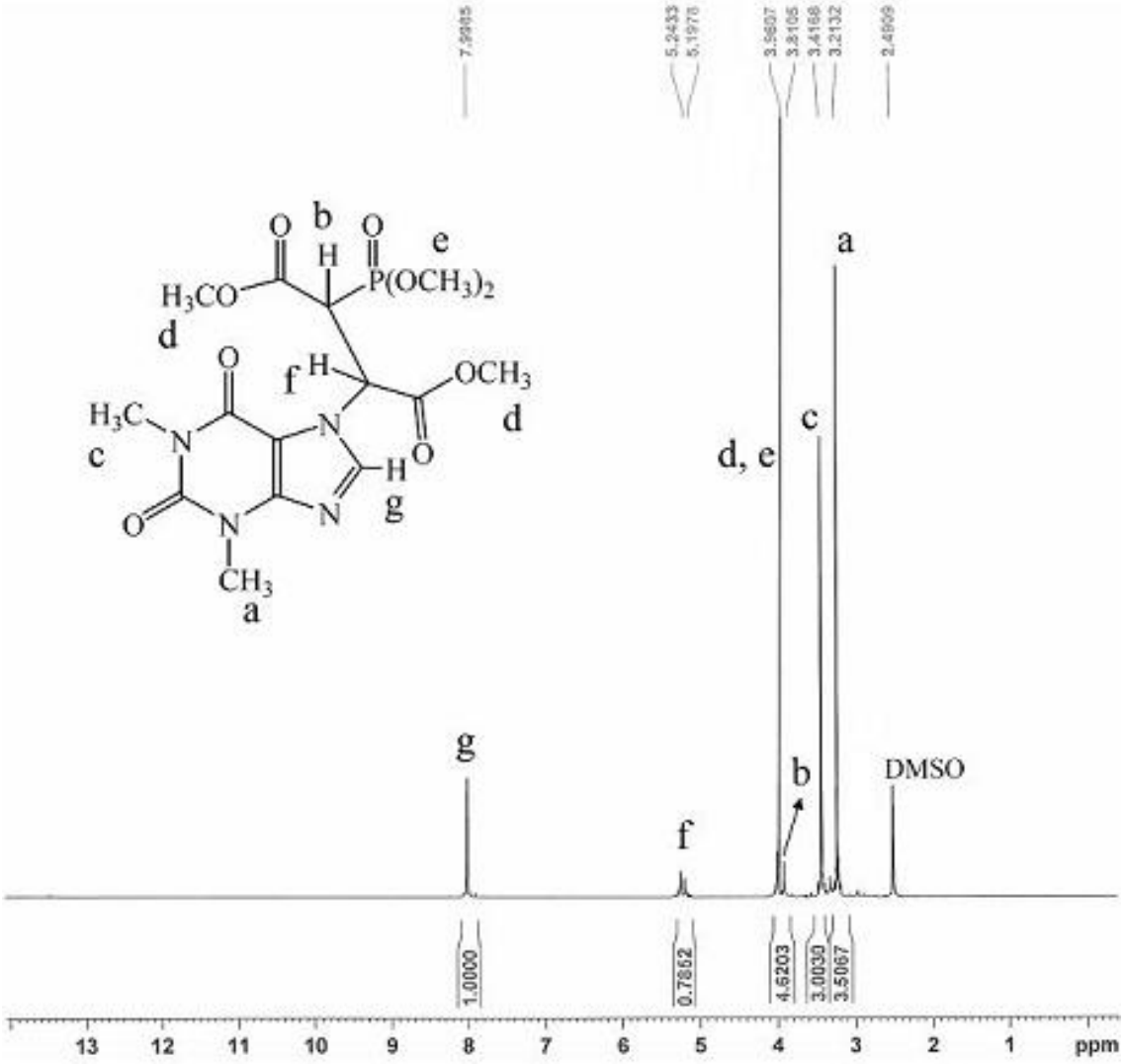
2. *7-(Diethyl-2-[bis(phenyloxy)-phosphoryl])-(1,3-dimethyl-purine-2,6-dione)-butanedioate* (**4b**, $C_{27}H_{31}N_4O_9P$)



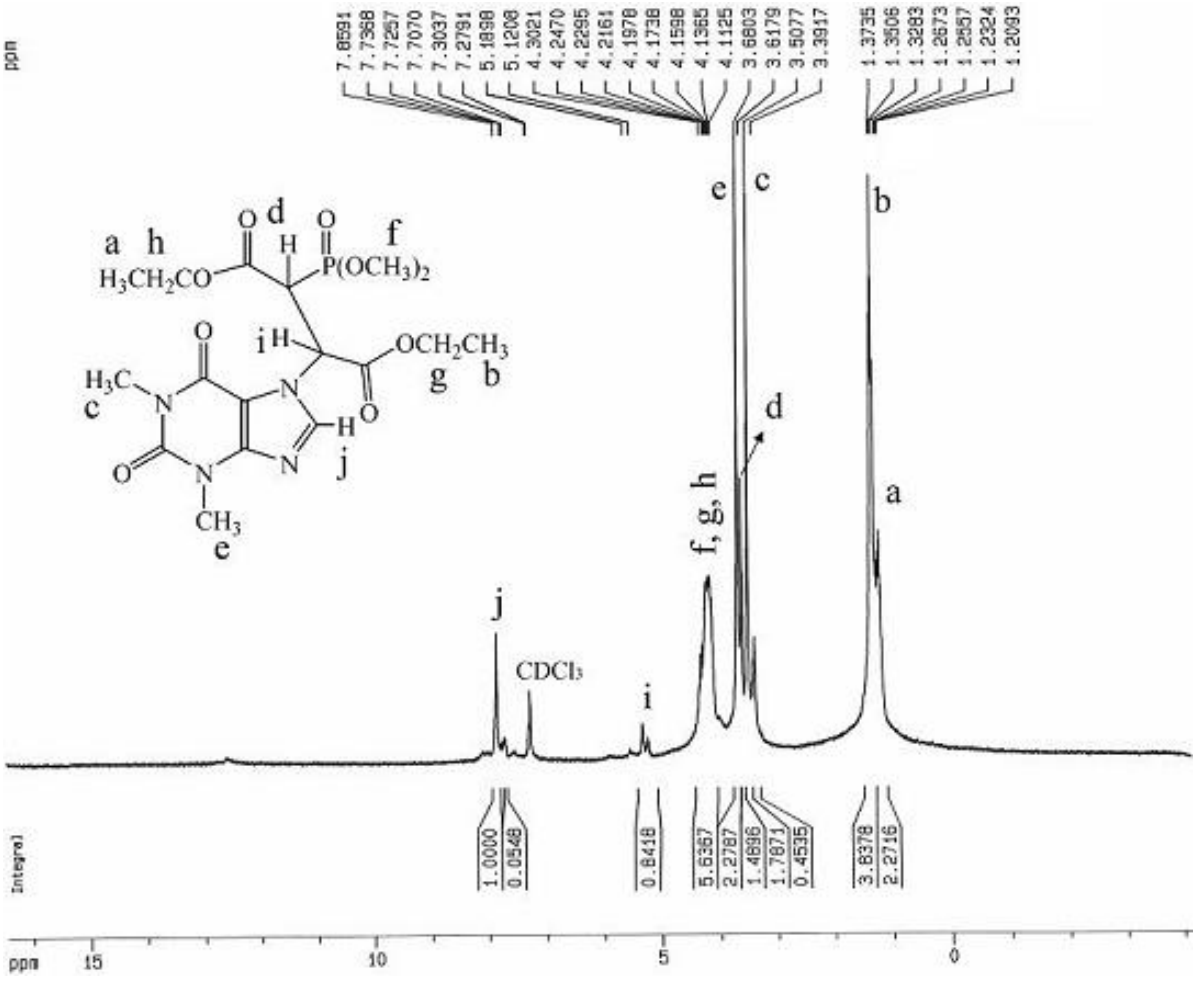
3. *7-(Di-tert-butyl-2-[bis(phenyloxy)-phosphoryl])-(1,3-dimethyl-purine-2,6-dione)-butanedioate* (**4c**, $C_{31}H_{37}N_4O_9P$)



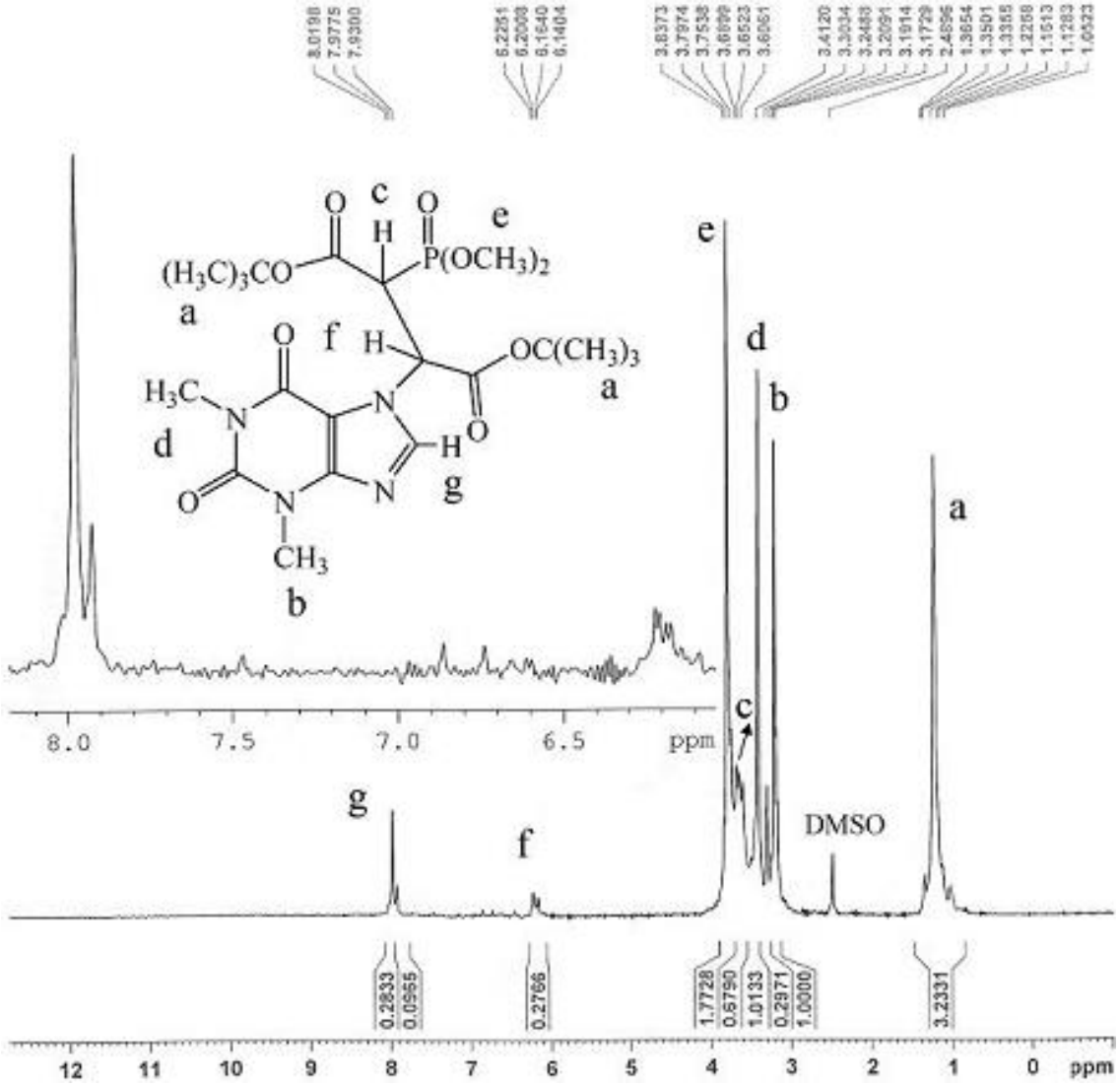
4. *7-(Dimethyl-2-[bis(methyloxy)-phosphoryl])-(1,3-dimethyl-purine-2,6-dione)-butanedioate* **(4d,** $C_{15}H_{21}N_4O_9P$)



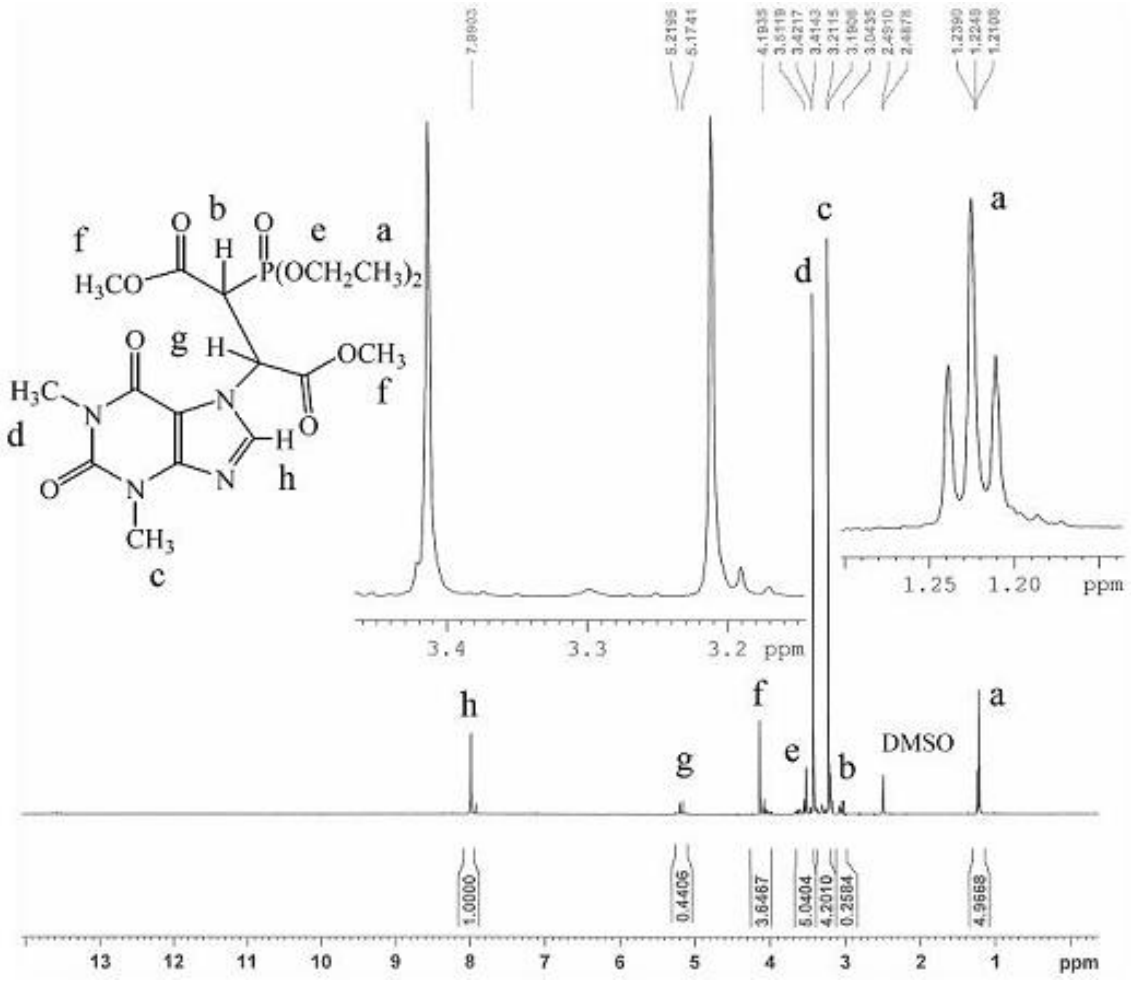
5. *7-(Diethyl-2-[bis(methyloxy)-phosphoryl])-(1,3-dimethyl-purine-2,6-dione)-butanedioate* (**4e**, $C_{17}H_{25}N_4O_9P$)



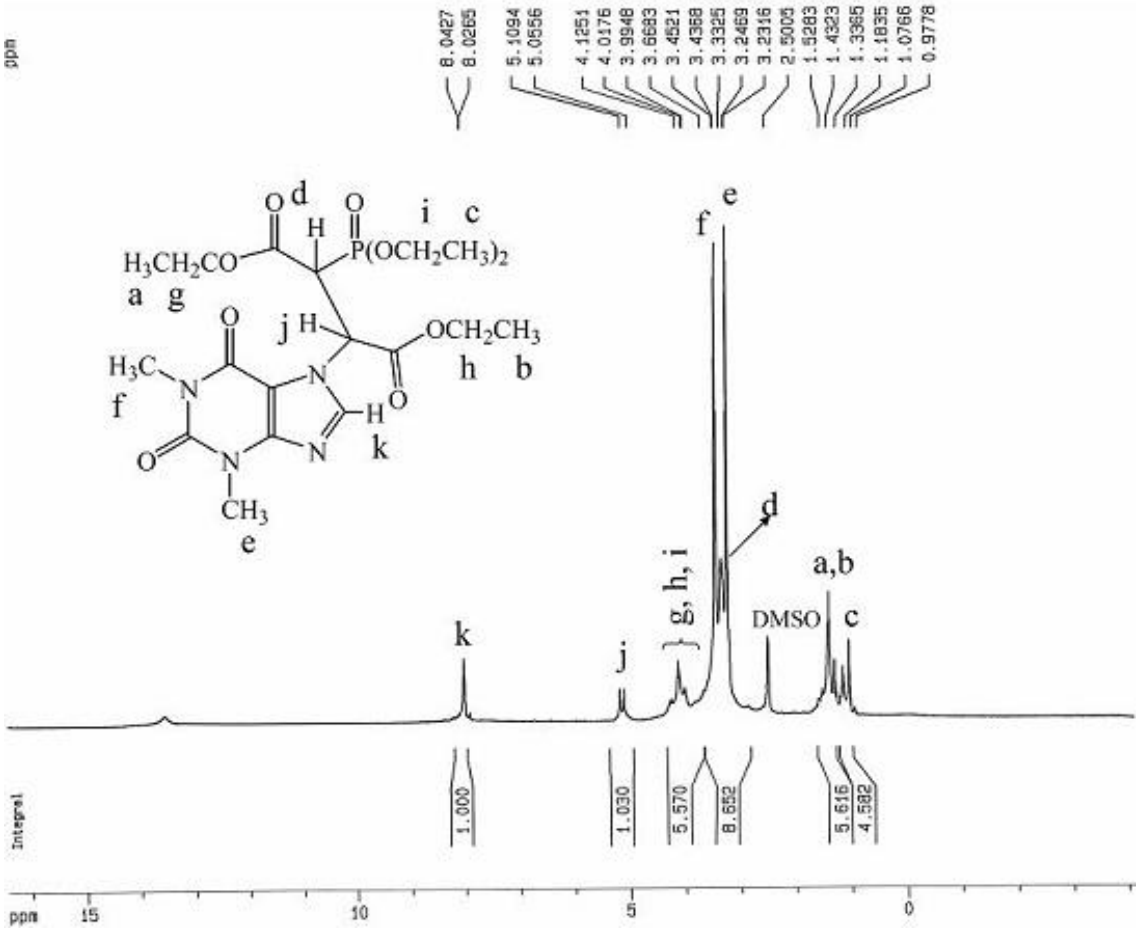
6. *7-(Di-tert-butyl-2-[bis(methyloxy)-phosphoryl])-(1,3-dimethyl-purine-2,6-dione)-butanedioate* (**4f**, $C_{21}H_{33}N_4O_9P$)



7. *7-(Dimethyl-2-[bis(ethyloxy)-phosphoryl])-(1,3-dimethyl-purine-2,6-dione)-butanedioate* (**4g**, $C_{17}H_{25}N_4O_9P$)



8. *7-(Diethyl-2-[bis(ethyloxy)-phosphoryl])-(1,3-dimethyl-purine-2,6-dione)-butanedioate* (**4h**, $C_{19}H_{29}N_4O_9P$)



9. *7-(Di-tert-butyl-2-[bis(ethyloxy)-phosphoryl])-(1,3-dimethyl-purine-2,6-dione)-butanedioate* (**4i**, $C_{23}H_{37}N_4O_9P$)

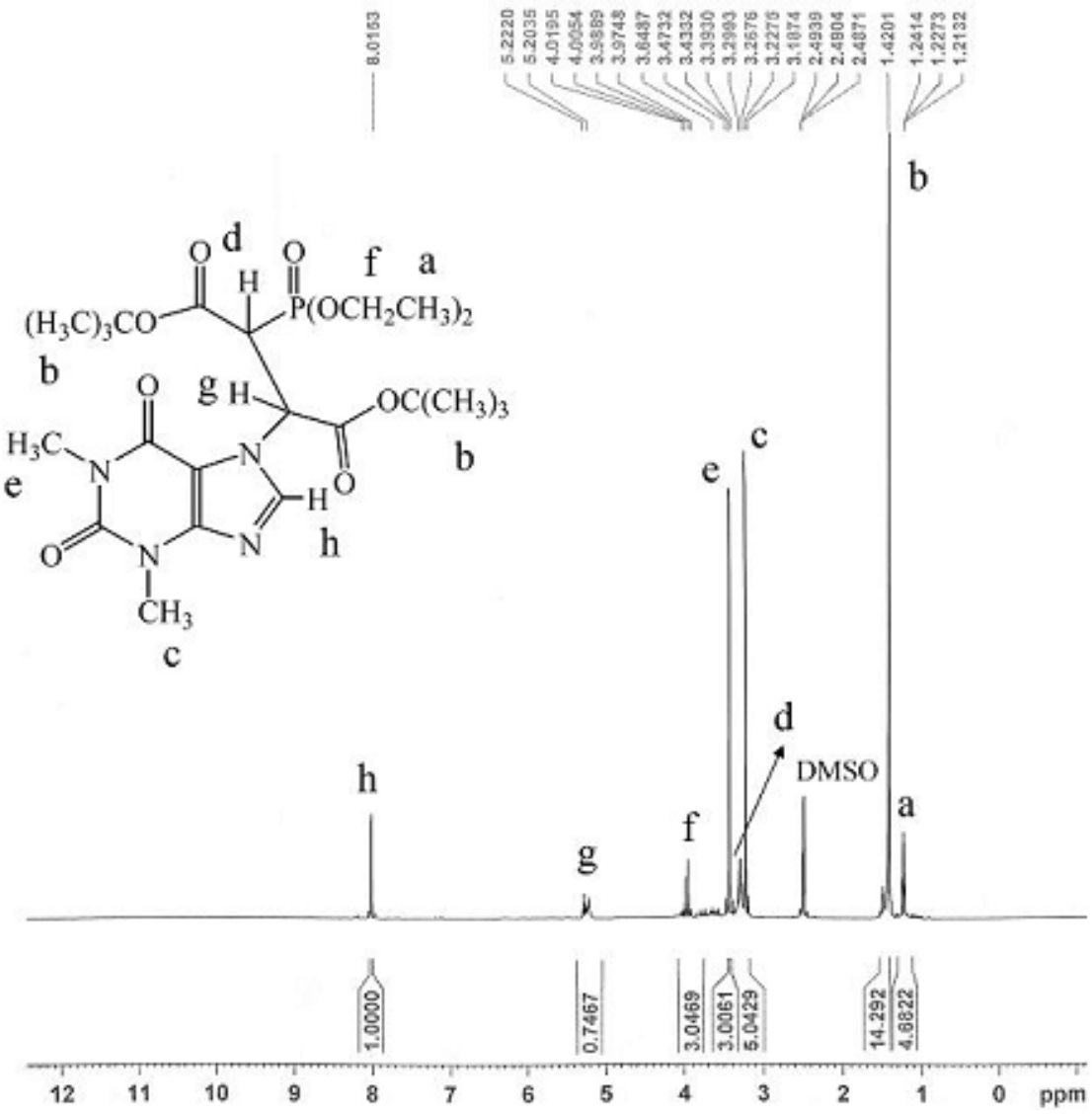
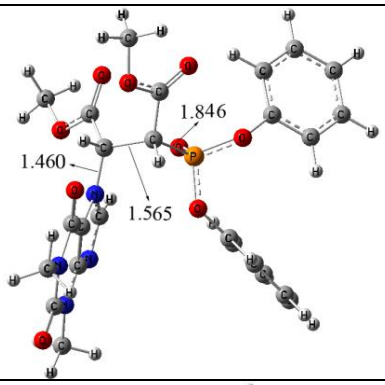
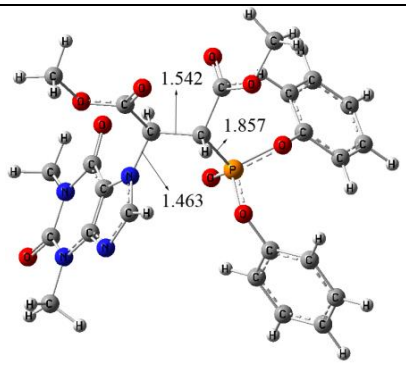
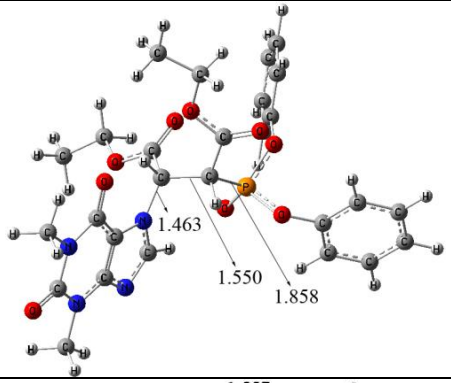
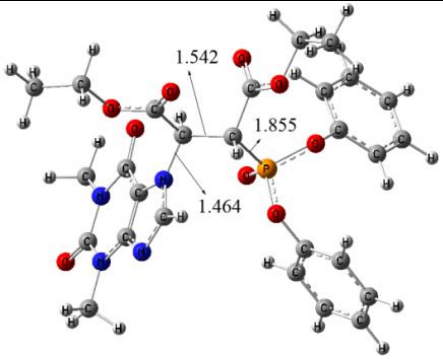
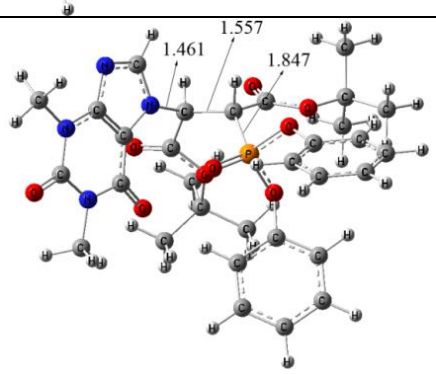
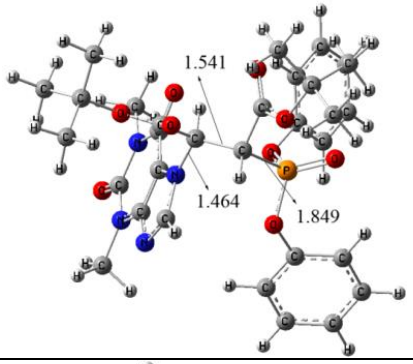
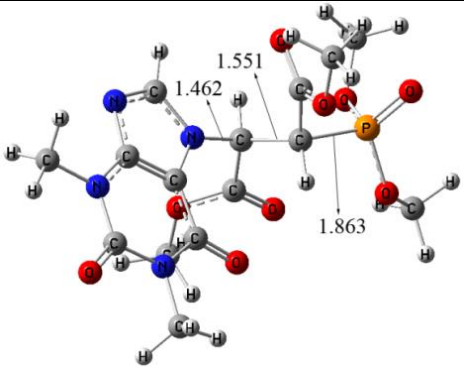
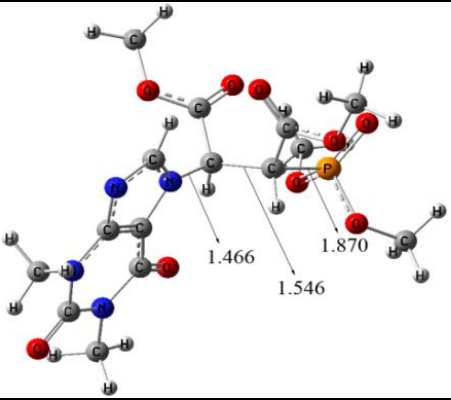
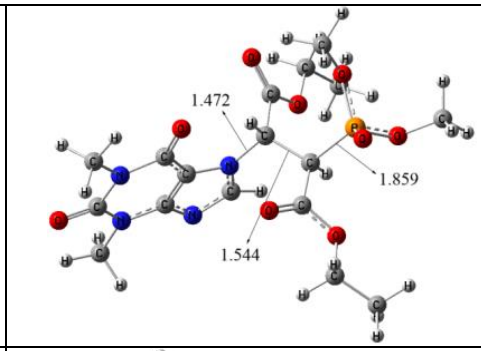
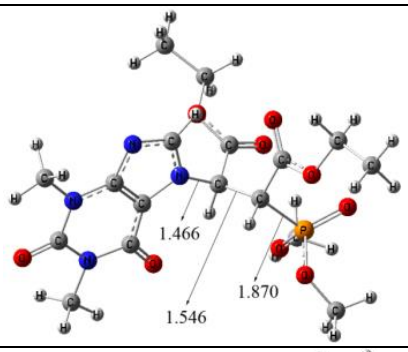
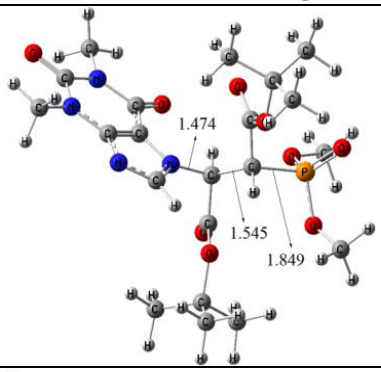
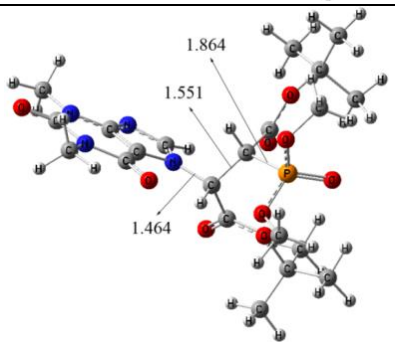
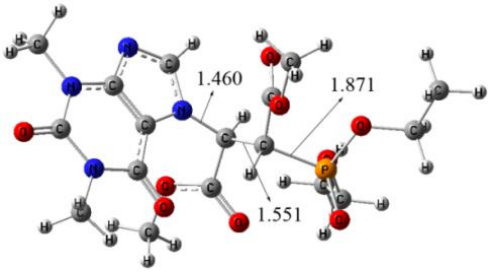
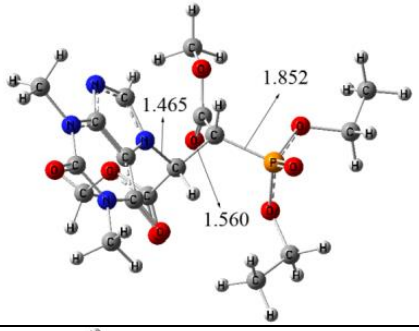
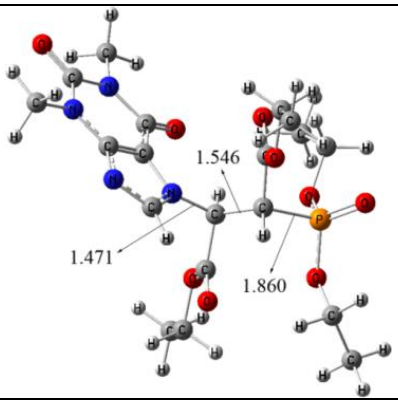
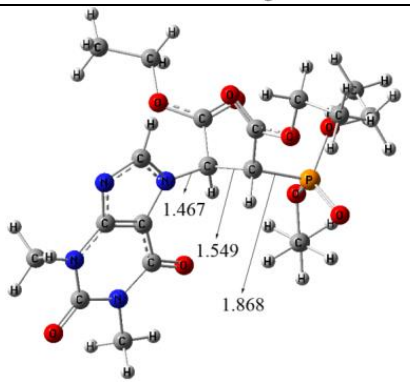


Table S4. Optimized calculated structures (bond length/Å) of diastereomeric phosphonates **4**

	(2R, 3S)* or *(2S, 3R)	***(2S, 3S)* or *(2R, 3R)***
4a		
4b		
4c		
4d		

4e	 1.472 1.859 1.544	 1.466 1.870 1.546
4f	 1.474 1.545 1.849	 1.864 1.551 1.464
4g	 1.460 1.871 1.551	 1.852 1.465 1.560
4h	 1.546 1.471 1.860	 1.467 1.549 1.868

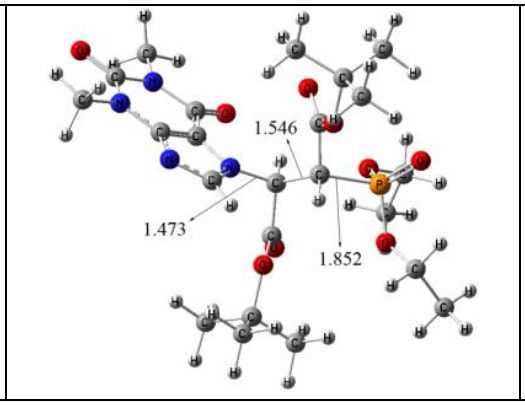
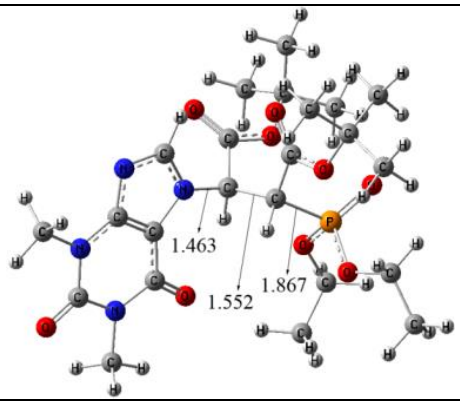
4i		

Table S5. Results of C, H, N Analyses for phosphonates **4**.

	Formala	***Calculated (%)***			***Found(%)***		
		C	H	N	C	H	N
4a	$C_{25}H_{25}N_4O_9P$	53.96	4.53	10.07	54.02	4.60	10.11
4b	$C_{27}H_{31}N_4O_9P$	55.48	5.00	9.58	55.39	5.03	9.62
4c	$C_{31}H_{37}N_4O_9P$	58.12	5.82	8.75	58.20	5.77	8.71
4d	$C_{15}H_{21}N_4O_9P$	41.67	4.90	12.96	41.71	4.95	13.02
4e	$C_{17}H_{25}N_4O_9P$	44.35	5.47	12.17	44.30	5.44	12.22
4f	$C_{21}H_{33}N_4O_9P$	48.84	6.44	10.85	48.61	6.31	10.77
4g	$C_{17}H_{25}N_4O_9P$	44.35	5.47	12.17	44.10	5.23	12.32
4h	$C_{19}H_{29}N_4O_9P$	46.72	5.98	11.47	46.61	5.88	11.55
4i	$C_{23}H_{37}N_4O_9P$	50.73	6.85	10.29	50.78	6.77	10.22