Synthetic, Functional Thymidine-Derived Polydeoxyribonucleotide Analogues from a Six-Membered Cyclic Phosphoester

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I. Experimental procedures and characterization data

Materials

Thymidine, 4-bromo-1-butene, and phosphorus pentoxide were used as received from Chem-Impex International, Inc. (Wood Dale, IL). 1,5,7-Triazabicyclo[4.4.0]dec-5-ene (TBD) was used as received from TCI America (Portland, OR). *N*,*N*-Dimethylformamide (DMF, ACS grade), tetrahydrofuran (THF, HPLC grade), hexanes (ACS grade), dichloromethane (ACS grade), and acetone (ACS grade) were used as received from VWR International. Anhydrous solvents were obtained after passage through a drying column of a solvent purification system from JC Meyer Solvent Systems (Laguna Beach, CA). All other chemicals were purchased from Sigma-Aldrich (St. Louis, MO) and used without further purification unless otherwise noted.

Instrumentation

^{1}H, ^{13}C, and ^{31}P NMR spectra were recorded on a Varian 500 MHz spectrometer interfaced to a Linux computer using VNMR-J software, while ^{1}H–^{31}P HMBC was performed on a Varian 600 MHz spectrometer interfaced to a Linux computer using VNMR-J software with $^{n}J_{HP}$ = 8 Hz. Chemical shifts were referenced to the solvent residual signals. All ^{1}H NMR spectra were reported in parts per million (ppm) downfield of tetramethylsilane and were measured relative to the signals for residual $CHCl_3$ (7.26 ppm). All ^{13}C NMR spectra were reported in ppm relative to $CDCl_3$ (77.0 ppm), and were obtained with ^{1}H decoupling. For ^{31}P NMR spectroscopy, phosphoric acid (85 wt% in H_2O) at 0 ppm was used as an external standard. The splitting patterns were reported as s (singlet), d (doublet), t (triplet), q (quartet), quin (quintet), m (multiplet), and br (broad). FTIR spectra were recorded on an IR Prestige 21 system using a diamond ATR lens (Shimadzu Corp., Japan) and analyzed using IRsolution v.1.40 software. The polymer molecular weight and molecular weight distribution values were determined by size exclusion chromatography (SEC) performed on a Waters 1515 HPLC pump (Waters Chomatography, Inc.) equipped with a 2414 differential refractometer (Waters, Inc.), a PD2020 dual-angle (15º and 90º) light scattering detector (Precision Detectors, Inc.), and a four-column series of PL gel columns (Polymer Laboratories, Inc.): 5 μm Guard (50 × 7.5 mm), 5 μm Mixed C (300 × 7.5 mm), 5 μm 10^4 Å (300 × 7.5 mm) and 5 μm 500 Å (300 × 7.5 mm). Polymer solutions were prepared at a known concentration and an injection volume of 200 μL was used. The system was equilibrated at 40 ºC in THF, which served as the polymer solvent and eluent (flow rate set to 1.00 mL/min). The differential refractometer was calibrated with Polymer Laboratories, Inc. polystyrene standards (300 to 467,000 Da). Data collection and analysis were performed using the Breeze (version 3.30, Waters, Inc.) software. Thermogravimetric analysis (TGA) was performed under argon atmosphere using a Mettler Toledo model TGA/DSC 1 (Mettler Toledo), with a heating rate of 10 ºC/min. Measurements were analyzed using Mettler Toledo STAR^{e} v. 7.01 software. Glass transition temperature (T_g) and melting temperature (T_m) were measured by differential scanning calorimetry (DSC) on a Mettler Toledo DSC822®, with a heating rate of 10 ºC/min and a cooling rate of 10 ºC/min. Measurements were analyzed using Mettler Toledo STAR^{e} v. 7.01

software. The T_g values were taken as the midpoint of the inflection tangent upon the third heating scan, and T_m values as the onset temperatures upon the first heating scan.

Synthesis of 3-(3-butenyl) thymidine (6)

To a 50-mL round bottom flask equipped with a magnetic stir bar containing 30.0 mL of DMF were added thymidine **4** (5.5880 g, 23.069 mmol, 1 equiv), 4-bromo-1-butene (5.5865 g, 41.381 mmol, 1.7938 equiv) and potassium carbonate (6.3524 g, 45.965 mmol, 1.9925 equiv). The reaction mixture was allowed to stir at 60 ºC for 2 days before it was diluted with 30 mL of water and extracted with dichloromethane (3×20 mL). The organic layer was collected, dried over magnesium sulfate, filtered, concentrated and purified by silica gel column chromatography with acetone/hexane = 1:1 as eluent followed by lyophilization overnight to give **6** as a white solid with a yield of 95%. ^{1}H NMR (500 MHz; $CDCl_3$) δ 7.36 (d, J = 1.0 Hz, 1H, H^A), 6.86 (t, J = 6.8 Hz, 1H, H^B), 5.79 (ddt, J = 17.1, 10.1, 7.0 Hz, 1H, -CCH^C=CH_2), 5.05 (dd, J = 17.1, 1.0 Hz, 1H, -CCH=CH^DH), 5.00 (dd, J = 10.1, 1.0 Hz, 1H, -CCH=CHH^E), 4.58 (dt, J = 6.6, 3.4 Hz, 1H, H^F), 4.00 (m, 3H, H^G and -NCH^H_2-), 3.92 (dd, J = 11.8, 3.1 Hz, 1H, $H^I_{pro\text{-}S}$), 3.83 (dd, J = 11.8, 3.1 Hz, 1H, $H^J_{pro\text{-}R}$), 2.49–2.58 (br, -OH), 2.42–2.29 (m, 4H, H^K and -NCH_2CH^L_2-), 1.91 (d, J = 0.6 Hz, 3H, -CCH^M_3); ^{13}C NMR (126 MHz; $CDCl_3$) δ 163.4, 150.8 134.7, 134.5, 116.9, 110.1, 86.9, 86.6, 71.2, 62.2, 40.5, 40.1, 31.7, 13.2. FTIR (cm^{-1}): 3518, 3443, 3073, 2922, 1666, 1626, 1472, 1402, 1364, 1348, 1294, 1234, 1198, 1097, 989, 920, 770, 631. HR-MS (ESI): calculated $[M + H]^+$ for $C_{14}H_{21}N_2O_5$: 297.1450, found: 297.1481. TGA in Ar: 100–245 ºC, 16% mass loss; 245–330 ºC, 76% mass loss; 330–500 ºC, 4% mass loss; 4% mass remaining above 500 ºC. DSC: no melting observed below 170 ºC.

Synthesis of 3',5'-cyclic 3-(3-butenyl) thymidine ethylphosphate (5)

In a 250-mL round bottom flask equipped with a magnetic stir bar were placed 4-dimethylaminopyridine (807.4 mg, 6.609 mmol, 2.665 equiv) and **6** (735.0 mg, 2.480 mmol, 1 equiv) in 25.0 mL of dichloromethane at –78 ºC. A solution of ethyl dichlorophosphate **7** (404.2 g, 2.481 mmol, 1.000 equiv) in 5.0 mL of dichloromethane was injected *via* syringe in one portion. The reaction mixture was allowed to stir for 1 h while gradually warming up to ambient temperature before it was washed with 5.0 mL of water and purified by silica gel column chromatography with a gradient of hexane and acetone as eluent to give **(*R*)-5** and **(*S*)-5** with yields of 51% and 7% as white solids, respectively. **(*R*)-5.** R_f = 0.12 (acetone/hexane = 2:8); ^{1}H NMR (500 MHz; $CDCl_3$) δ 7.00 (d, J = 1.3 Hz, 1H, H^A), 6.36 (dd, J = 8.8, 2.6 Hz, 1H, H^B), 5.78 (ddt, J = 17.1, 10.1, 7.0 Hz, 1H, -CCH^C=CH_2), 5.04 (dd, J = 17.1, 1.7 Hz, 1H, -CCH=CH^DH), 5.00 (dd, J = 10.2, 1.7 Hz, 1H, -CCH=CHH^E), 4.86 (qd, J = 9.3, 0.9 Hz, 1H, H^F), 4.57 (ddd, J = 16.6, 9.7, 5.5 Hz, 1H, $H^G_{pro\text{-}S}$), 4.52 (ddd, J = 19.7, 8.7, 5.8 Hz, 1H, $H^H_{pro\text{-}R}$), 4.22 (dq, J = 8.9, 7.1 Hz, 2H, -OC$H^I_2$$CH_3$), 3.98 (td, J = 7.4, 3.6 Hz, 2H, -NCH^J_2-), 3.92 (m, 1H, H^K), 2.56 (ddd, J = 13.6, 10.4, 8.9 Hz, 1H, $H^L_{pro\text{-}S}$), 2.43 (ddd, J = 13.6, 8.2, 2.6 Hz, 1H, $H^M_{pro\text{-}R}$), 2.36 (q, J = 7.2 Hz, 2H, -NCH_2CH^N_2-), 1.94 (d, J = 1.2 Hz, 3H, -CCH^O_3), 1.36 (td, J = 7.1, 1.1 Hz, 3H, -OCH_2CH^P_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.7, 150.5, 134.7, 132.7, 117.0, 111.6, 85.3, 76.9 (d, J = 3.9 Hz), 74.0 (d, J = 6.2 Hz), 68.9 (d, J = 7.3

Hz), 65.9 (d, J = 6.3 Hz), 40.7, 35.5 (d, J = 8.3 Hz), 31.9, 16.1 (d, J = 6.3 Hz), 13.3; ^{31}P NMR (202 MHz, $CDCl_3$) δ –3.8. FTIR (cm^{-1}): 3080, 2983, 2916, 1703, 1666, 1639, 1466, 1448, 1359, 1348, 1273, 1165, 1110, 1009, 926, 891, 820, 768. HR-MS (ESI): calculated $[M + H]^+$ for $C_{16}H_{24}N_2O_7P$: 387.1321, found: 387.1482. DSC: T_m = 34 ºC. **(*S*)-5.** R_f = 0.10 (acetone/hexane = 2:8); ^{1}H NMR (500 MHz; $CDCl_3$) δ 6.95 (d, J = 1.1 Hz, 1H, H^A), 6.12 (dd, J = 8.5, 3.2 Hz, H^B), 5.79 (ddt, J = 17.1, 10.1, 7.0 Hz, 1H, -CCH^C=CH_2), 5.05 (dd, J = 17.1, 1.8 Hz, 1H, -CCH=CH^DH), 5.01 (dd, J = 10.2, 1.8 Hz, 1H, -CCH=CHH^E), 4.68 (q, J = 9.1 Hz, 1H, H^F), 4.57 (ddd, J = 21.3, 9.5, 4.7 Hz, 1H, $H^G_{pro\text{-}S}$), 4.34 (td, J = 10.1, 1.1 Hz, 2H, -OC$H^H_2$$CH_3$), 4.26 (ddd, J = 9.0, 7.1, 2.9 Hz, 1H, $H^I_{pro\text{-}R}$), 3.99 (td, J = 7.4, 3.0 Hz, 2H, -NCH^J_2-), 3.91 (ddd, J = 10.4, 9.3, 4.6 Hz, 1H, H^K), 2.56 (m, 2H, $H^L_{pro\text{-}S}$ and $H^M_{pro\text{-}R}$), 2.37 (q, J = 7.3 Hz, 2H, -NCH_2CH^N_2-), 1.95 (d, J = 1.1 Hz, 3H, -CCH^O_3), 1.43 (td, J = 7.1, 0.7 Hz, 3H, -OCH_2CH^P_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.8, 150.3, 134.7, 133.9, 117.0, 111.1, 87.1, 78.0 (d, J = 5.6 Hz), 74.0 (d, J = 6.2 Hz), 69.3(d, J = 9.0 Hz), 64.6 (d, J = 5.7 Hz), 40.6, 35.3 (d, J = 8.3 Hz), 31.9, 16.2 (d, J = 5.9 Hz), 13.3; ^{31}P NMR (202 MHz, $CDCl_3$) δ –6.7. FTIR (cm^{-1}): 3082, 2976, 2908, 1703, 1666, 1639, 1524, 1466, 1449, 1361, 1348, 1274, 1109, 1011, 928, 891, 818, 767. HR-MS (ESI): calculated $[M + H]^+$ for $C_{16}H_{24}N_2O_7P$: 387.1321, found: 387.1498. DSC: T_m = 33 ºC.

General procedure for polymerization of 5

A solution of **5** (98.1 mg, 0.254 mmol) and a given amount of 4-methoxybenzyl alcohol (1.2–3.5 mg, 0.00847–0.0254 mmol) in anhydrous dichloromethane (0.90 mL) was transferred into a flame-dried 10-mL Schlenk flask equipped with a magnetic stir bar and a glass stopper on a dual-manifold Schlenk line. A solution of a given amount of TBD (4.7–7.1 mg, 0.0339–0.0508 mmol) in anhydrous dichloromethane (0.10 mL) was injected into the Schlenk flask *via* syringe to initiate the polymerization, while being maintained under a nitrogen gas atmosphere at ambient temperature. After stirring for a predetermined period of time (6 h to 24 h), the reaction was quenched by addition of a solution of acetic acid (excess) in dichloromethane *via* pipette. The poly(3',5'-cyclic 3-(3-butenyl) thymidine ethylphosphate) (**PCBT**, **9**) was purified by precipitation from dichloromethane into diethyl ether (3 times), and dried *in vacuo* to give an average yield of 50%. δ ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.38–7.30 (br), 6.89 (d, J = 8.6 Hz), 6.40–6.20 (br), 5.85–5.72 (br), 5.15–4.95 (br), 4.40–4.22 (br), 4.21–4.12 (br), 4.01–3.91 (br), 3.90 (s), 2.61–2.48 (br), 2.41–2.32 (br), 1.96–1.90 (br), 1.40–1.32 (br); ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.0, 150.7, 134.8, 133.1, 130.0, 117.0, 114.1, 110.8, 85.6, 83.0, 77.6, 66.9, 65.0, 55.3, 46.8, 40.6, 38.3, 31.9, 20.7, 16.2, 13.2; ^{31}P NMR (202 MHz, $CDCl_3$) δ –1.0, –1.7, –1.8, –2.8. FTIR (cm^{-1}): 3078, 2978, 1701, 1666, 1639, 1466, 1450, 1361, 1269, 1195, 1161, 1099, 1011, 910, 833, 768. DSC: T_g = 50 ($\mathbf{PCBT_{10}}$), 55 ($\mathbf{PCBT_{21}}$), and 54 ºC ($\mathbf{PCBT_{32}}$). TGA in Ar: 235–285 ºC, 50% mass loss; 285–500 ºC, 12% mass loss; 38% mass remaining above 500 ºC ($\mathbf{PCBT_{10}}$); 235–285 ºC, 50% mass loss; 285–500 ºC, 13% mass loss; 37% mass remaining above 500 ºC ($\mathbf{PCBT_{21}}$); 235–272 ºC, 60% mass loss; 272–500 ºC, 14% mass loss; 26% mass remaining above 500 ºC ($\mathbf{PCBT_{32}}$).

Synthesis of 3'-thymidine monophosphate diethylester (10)

A solution of **5** (113.8 mg, 0.295 mmol, 1 equiv) in ethanol (0.50 mL) was transferred into a flame-dried 10-mL Schlenk flask equipped with a magnetic stir bar and a glass stopper on a dual-manifold Schlenk line. A solution of TBD (20.1 mg, 0.144 mmol, 0.0488 equiv) in ethanol (0.50 mL) was injected into the Schlenk flask *via* syringe to initiate the reaction, which was stirred under a nitrogen gas atmosphere at ambient temperature for 1 h. Excess ethanol was removed by rotary evaporation before the reaction mixture was purified by silica gel column chromatography with acetone/hexane = 3:7 as eluent to give **10** as a colorless liquid with a yield of 80%. R_f = 0.20 (acetone/hexane = 3:7); ^{1}H NMR (500 MHz; $CDCl_3$) δ 7.47 (d, J = 1.2 Hz, 1H, H^A), 6.23 (t, J = 6.9 Hz, 1H, H^B), 5.79 (ddt, J = 17.1, 10.1, 7.0 Hz, 1H, -CCH=CH^CH), 5.09 (m, 2H, H^D and H^E), 4.99 (dd, J = 10.5, 1.5 Hz, 1H, -CCH=CHH^F), 4.20 (q, J = 2.6 Hz, 1H, H^G), 4.12 (qd, J = 7.4, 1.3 Hz, 4H, -OC$H^H{}_2$CH$_3$), 3.99 (t, J = 7.5 Hz, 2H, -NC$H^I{}_2$-), 3.87 (t, J = 2.4 Hz, 2H, H^J), 3.60–3.40 (br, 1H, -OH^K), 2.54-2.44 (m, 2H, H^L), 2.36 (q, J = 7.2 Hz, 3H, -NCH$_2$C$H^M{}_2$-), 1.91 (d, J = 1.1 Hz, 4H, H^N), 1.34 (td, J = 7.1, 0.9 Hz, 6H, H^O); ^{13}C NMR (126 MHz; $CDCl_3$) δ 163.2, 150.8 134.8, 134.3, 116.9, 110.4, 86.7, 85.6 (d, J = 4.92 Hz), 77.5 (d, J = 5.46 Hz), 64.3 (d, J = 6.18 Hz), 62.0, 40.5, 38.5 (d, J = 5.04 Hz), 31.9, 16.1 (d, J = 6.79 Hz), 13.3; ^{31}P NMR (202 MHz, $CDCl_3$) δ –1.81. FTIR (cm^{-1}): 3387, 3078, 2982, 2924, 2249, 1701, 1666, 1639, 1466, 1362, 1254, 1196, 1161, 1103, 1011, 910, 826, 768, 729. HR-MS (ESI): calculated $[M + Na]^+$ for $C_{18}H_{29}N_2O_8PNa$: 455.1559, found: 455.1545.

II. Figures

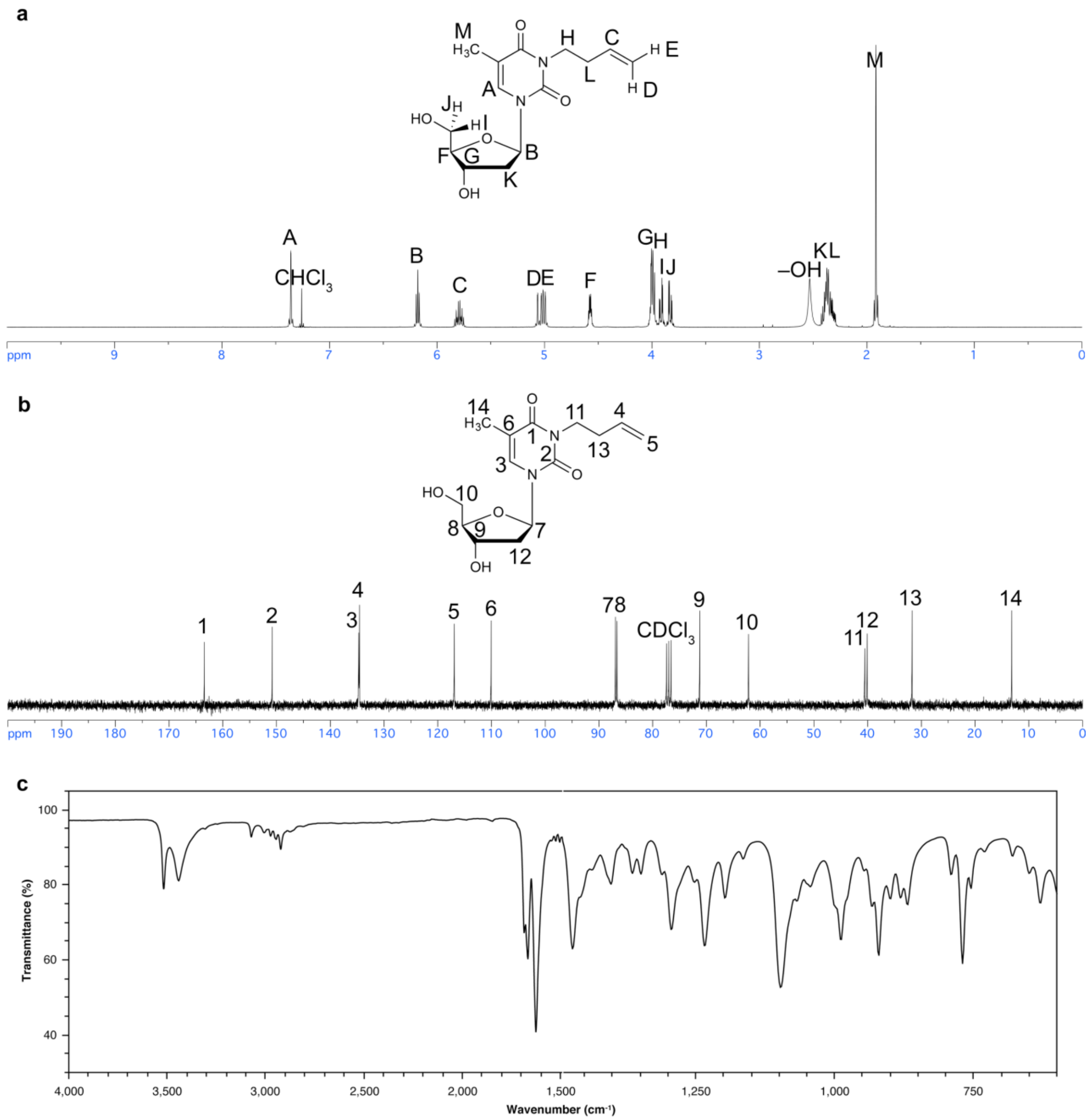

Figure S1. Spectroscopic characterization of 6. a, ^{1}H NMR (500 MHz). **b,** ^{13}C NMR (125 MHz). **c,** IR spectrum.

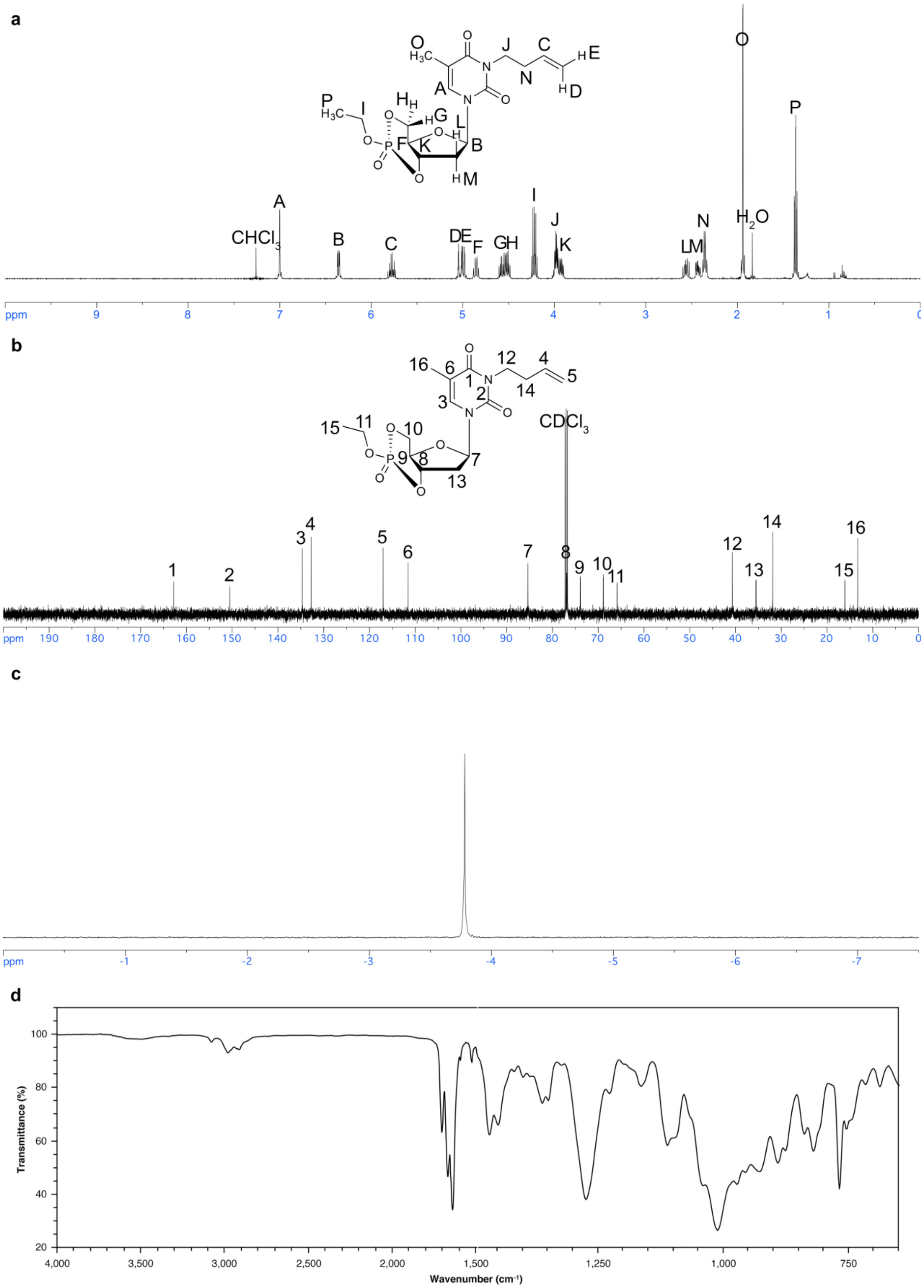

Figure S2. Spectroscopic characterization of (*R*)-5. a, ^{1}H NMR (500 MHz). **b,** ^{13}C NMR (125 MHz). **c,** ^{31}P NMR (202 MHz). **d,** IR spectrum.

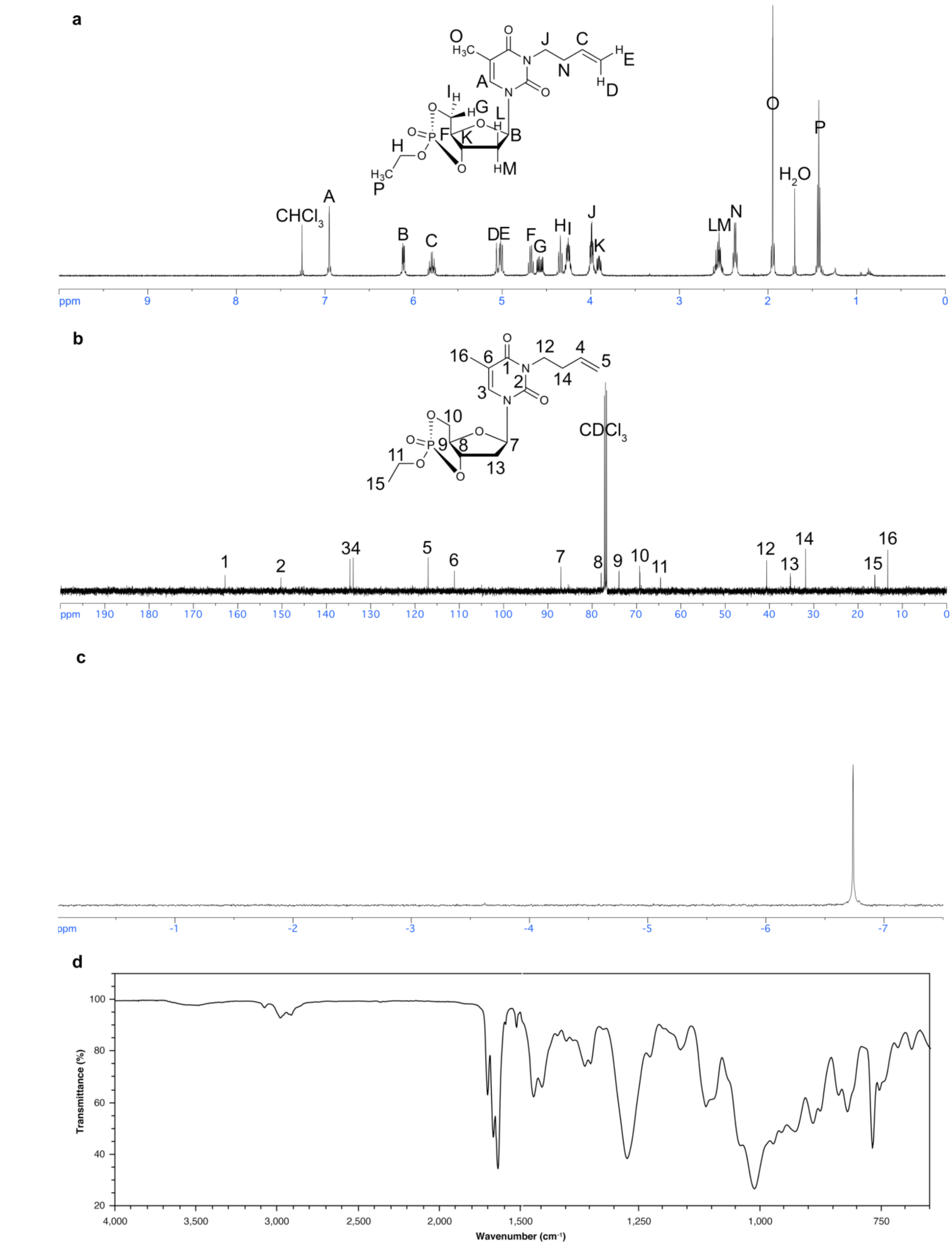

Figure S3. Spectroscopic characterization of (*S*)-5. a, ^{1}H NMR (500 MHz). **b,** ^{13}C NMR (125 MHz). **c,** ^{31}P NMR (202 MHz). **d,** IR spectrum.

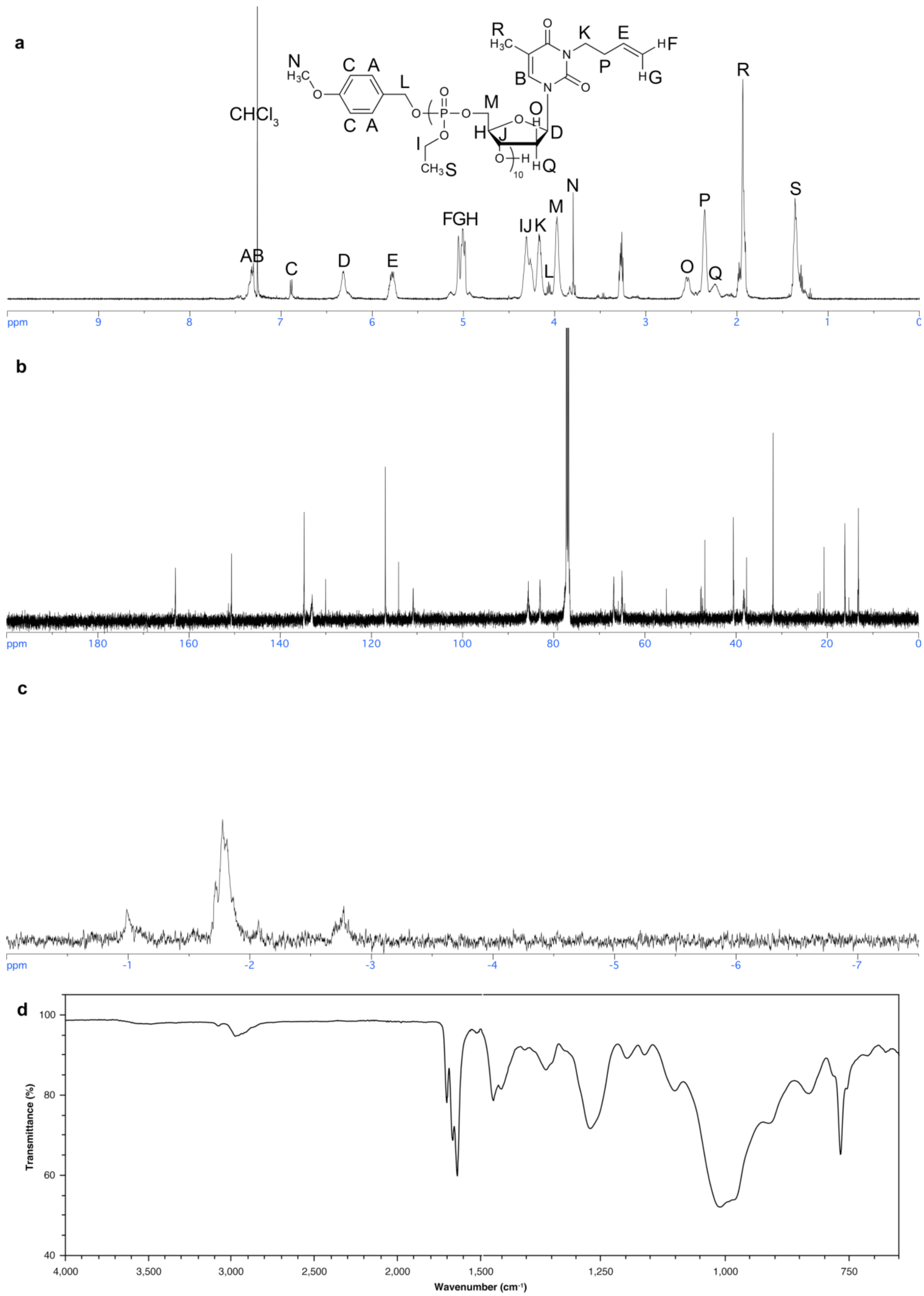

Figure S4. Spectroscopic characterization of PCBT$_{10}$. a, ^{1}H NMR (500 MHz). **b,** ^{13}C NMR (125 MHz). **c,** ^{31}P NMR (202 MHz). **d,** IR spectrum.

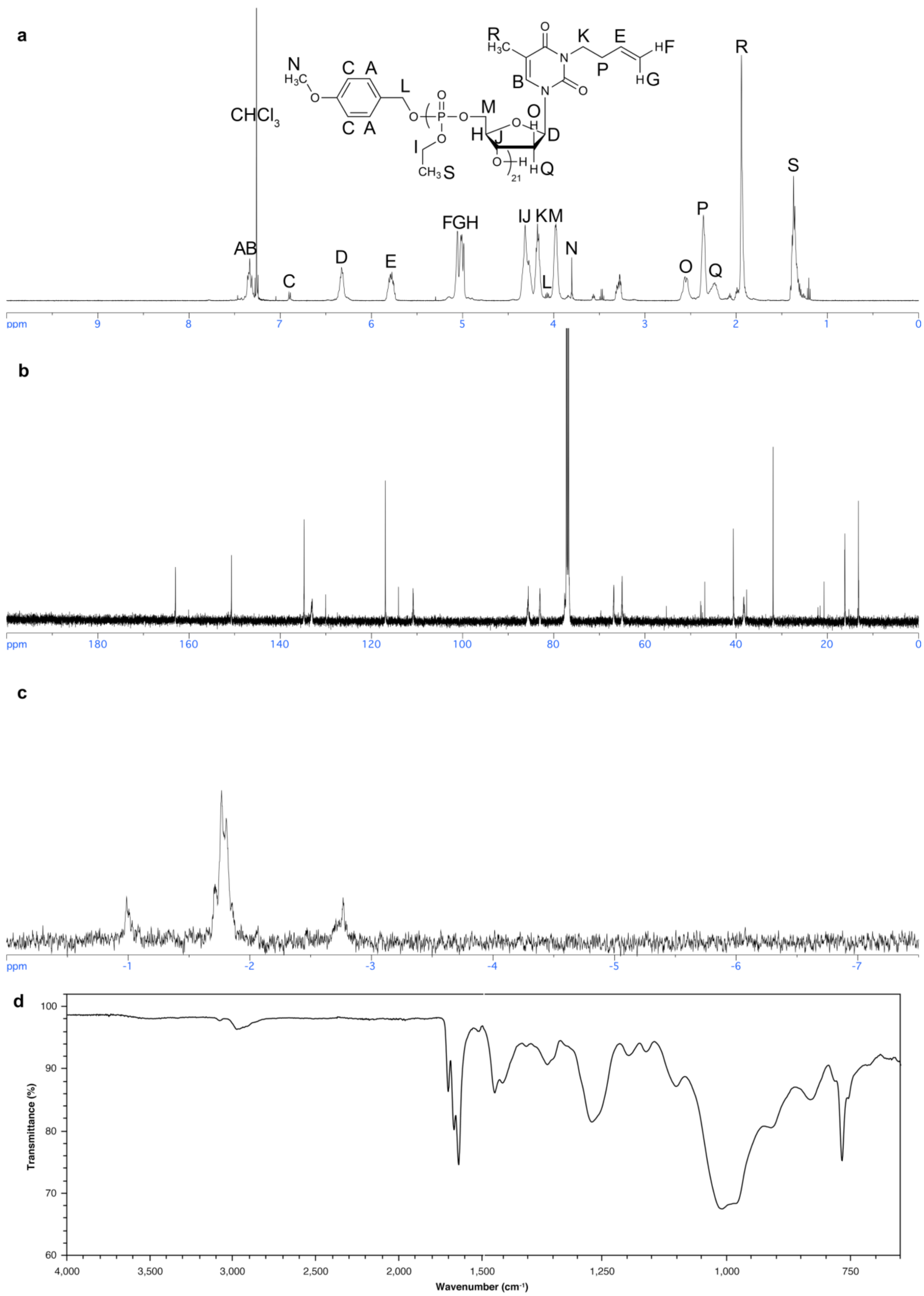

Figure S5. Spectroscopic characterization of PCBT$_{21}$. a, ^{1}H NMR (500 MHz). **b,** ^{13}C NMR (125 MHz). **c,** ^{31}P NMR (202 MHz). **d,** IR spectrum.

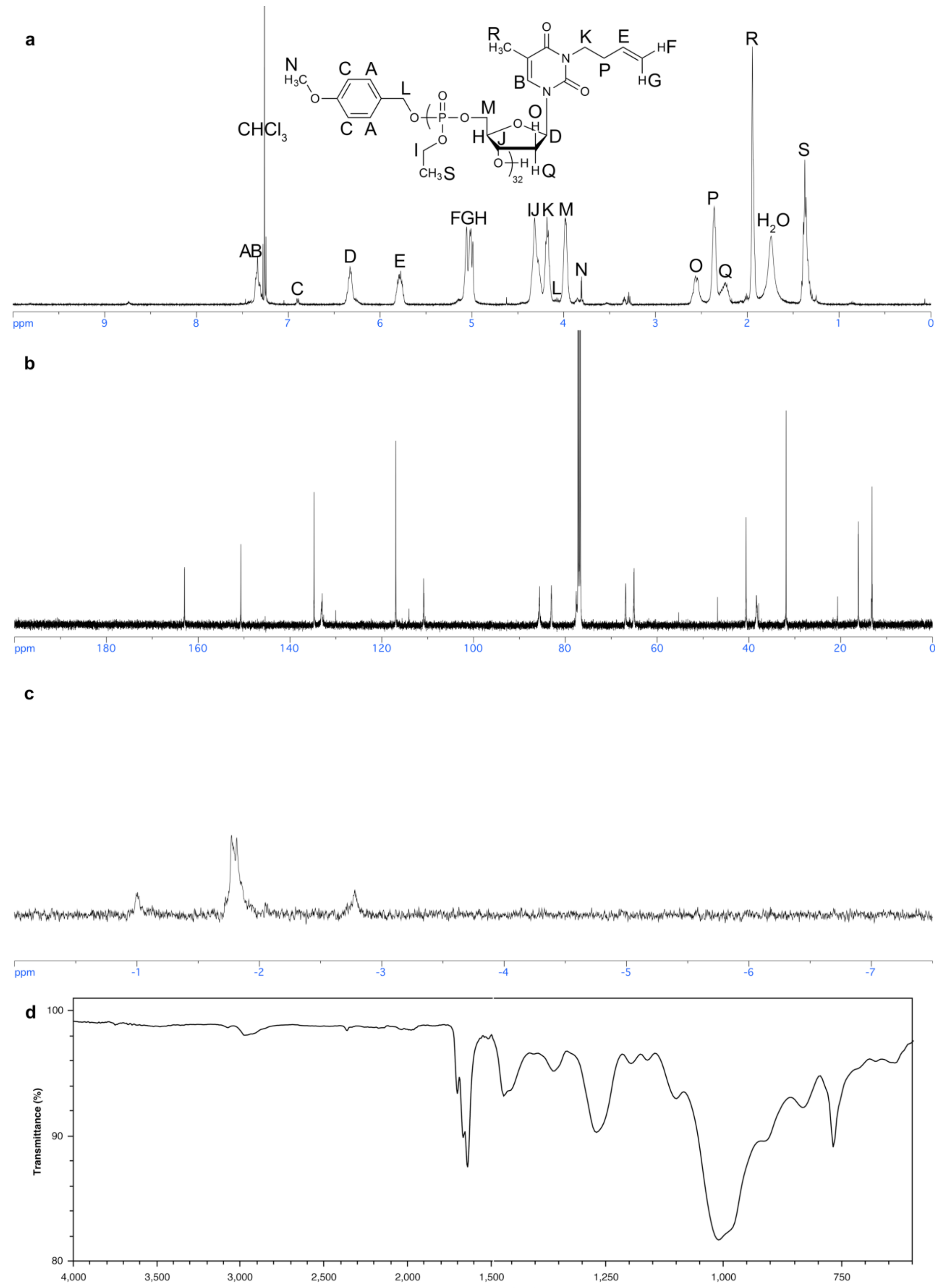

Figure S6. Spectroscopic characterization of $PCBT_{32}$. a, ^{1}H NMR (500 MHz). **b,** ^{13}C NMR (125 MHz). **c,** ^{31}P NMR (202 MHz). **d,** IR spectrum.

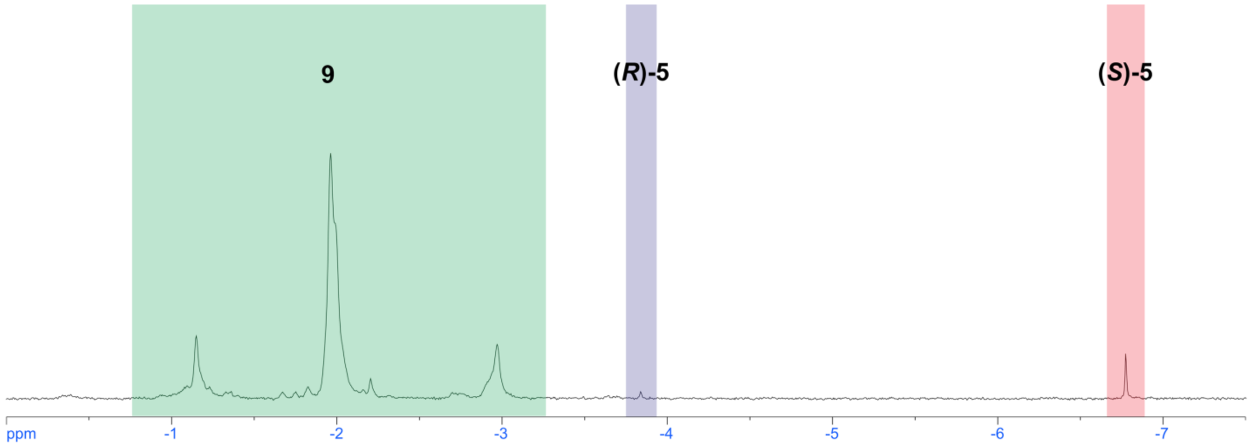

Figure S7. Crude ^{31}P NMR (202 MHz) spectrum of the copolymerization of a 88:12 diastereomeric mixture of 5.

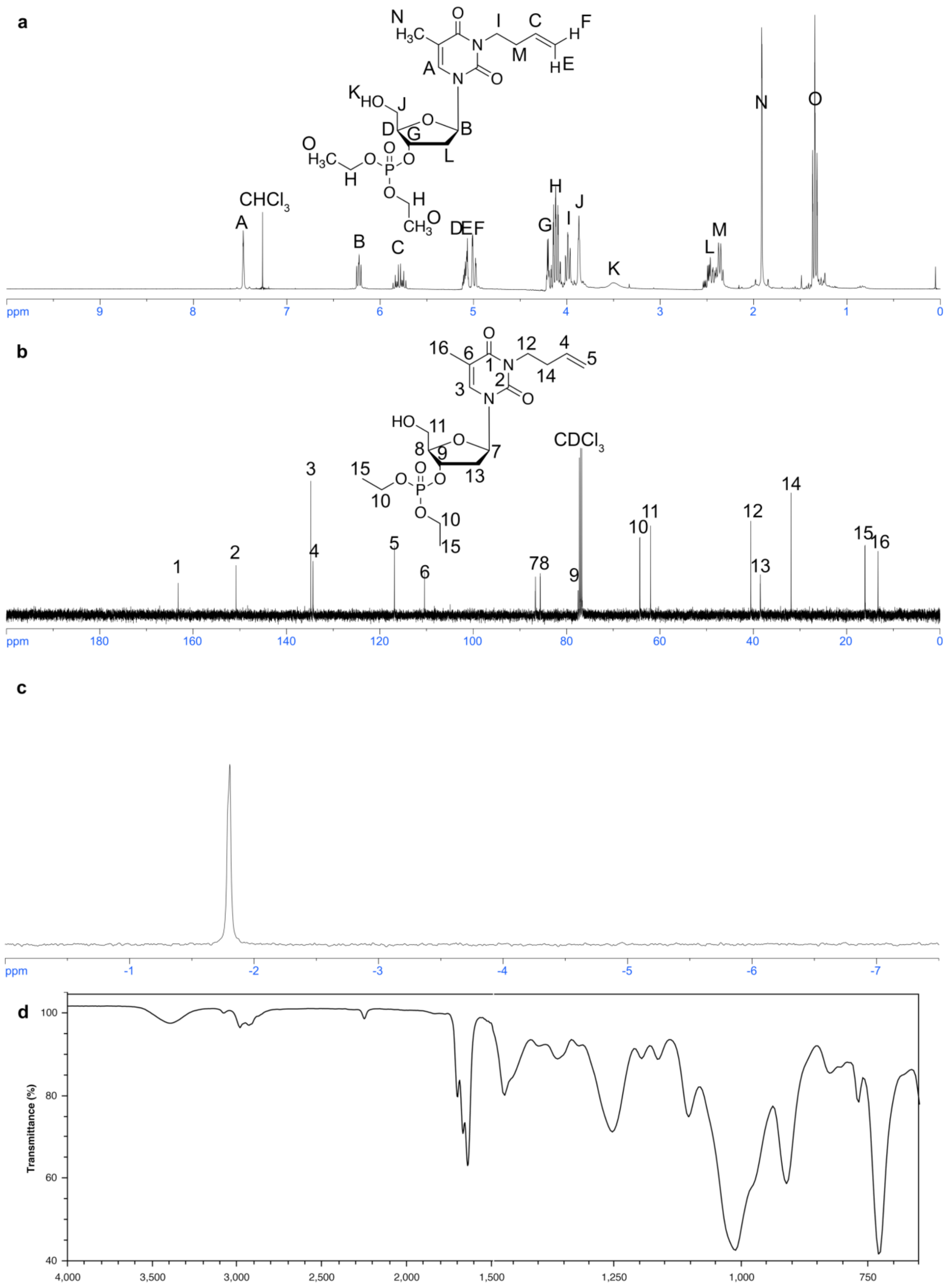

Figure S8. Spectroscopic characterization of 10. a, ^{1}H NMR (500 MHz). **b,** ^{13}C NMR (125 MHz). **c,** ^{31}P NMR (202 MHz). **d,** IR spectrum.

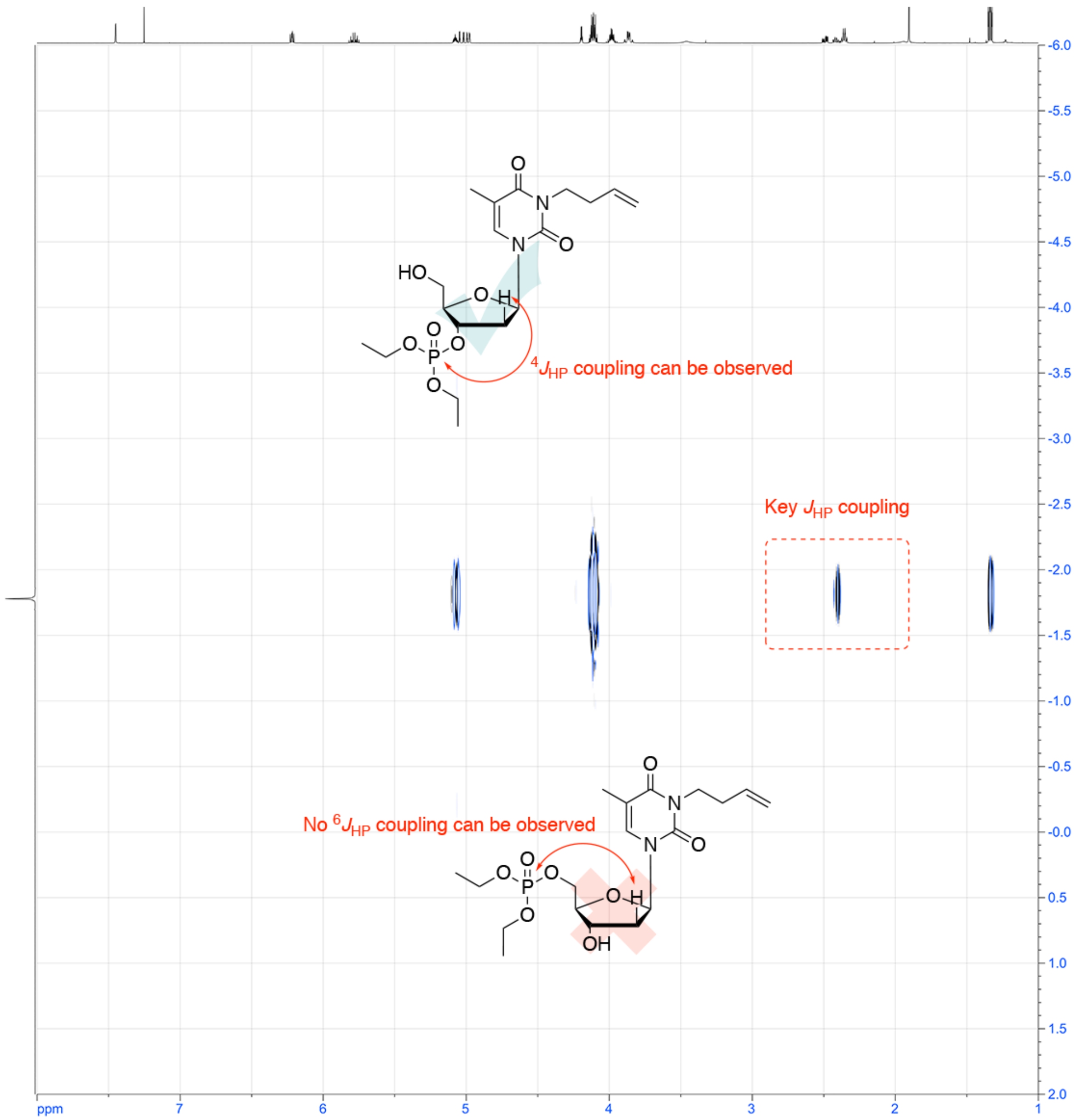

Figure S9. **[1]H–[31]P HMBC spectrum of 10.**

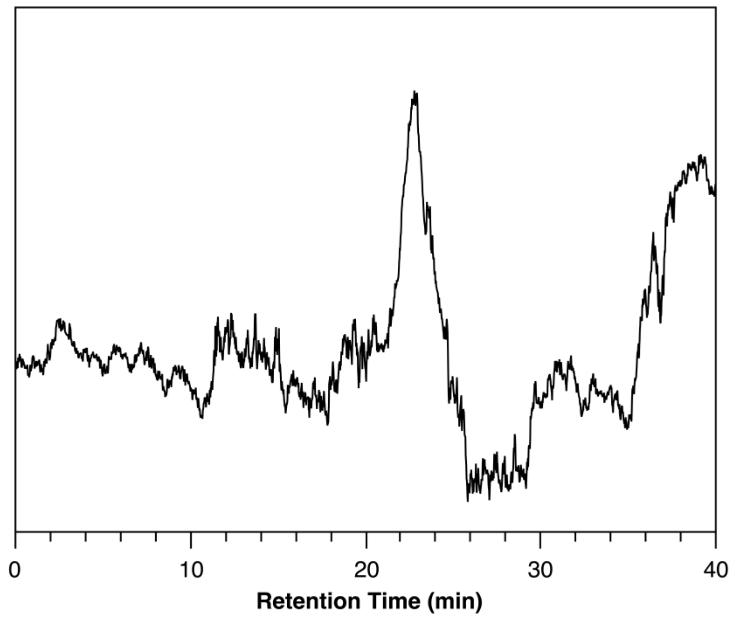

Figure S10. Light scattering detector trace (90º) for $PCBT_{32}$ from THF SEC, demonstrating poor signal-to-noise ratio.

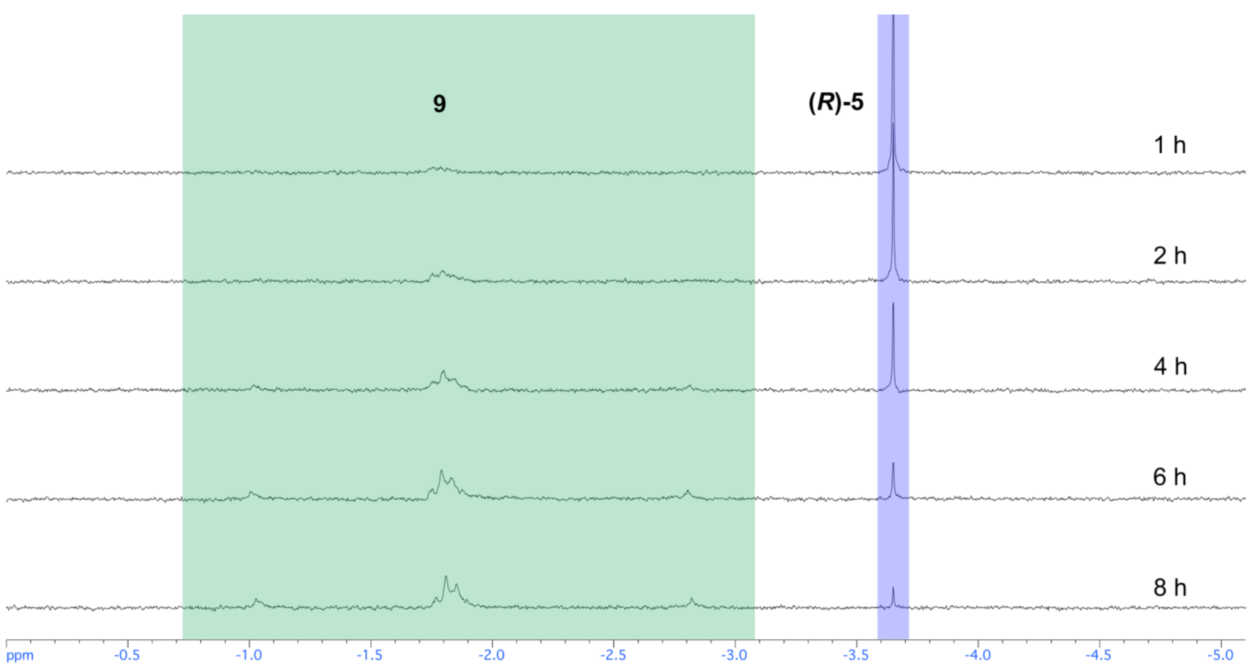

Figure S11. ^{31}P NMR (202 MHz) spectra for the calculations of conversions in the kinetic study.

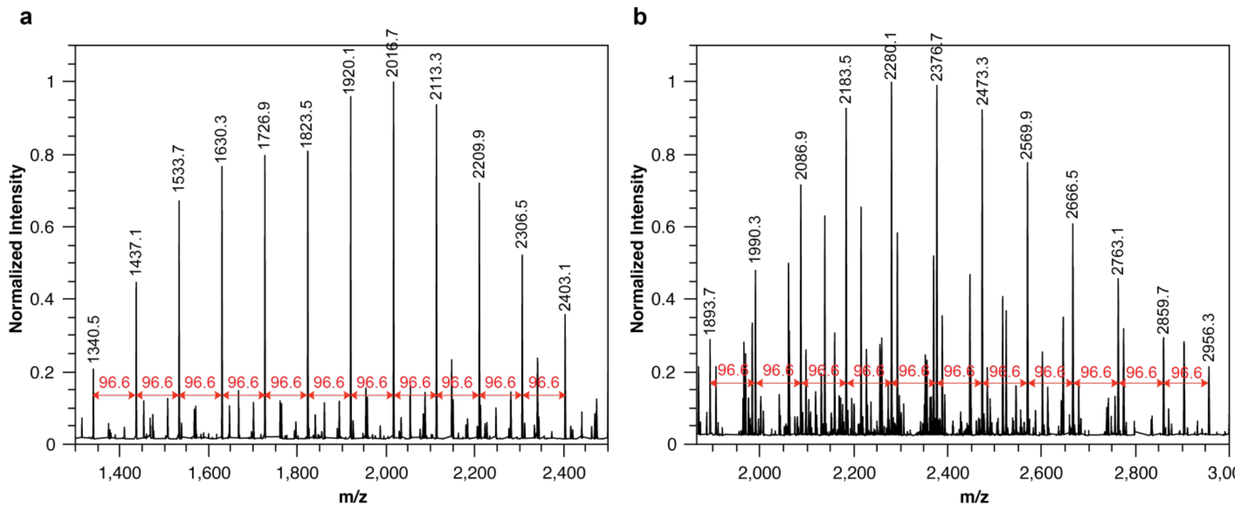

Figure S12. ESI-MS analysis for $PCBT_{21}$ and $PCBT_{32}$. a, $PCBT_{21}$ (z = 4, repeating unit = 386.1 Da or 96.5 Th). **b, $PCBT_{32}$** (z = 4, repeating unit = 386.1 Da or 96.5 Th), both indicating that chain end analyses (M_n = 8,200 and 12,400 Da, respectively) provided more accurate molecular weight estimations than did THF SEC (M_n = 4,800 and 6,200 Da, respectively).

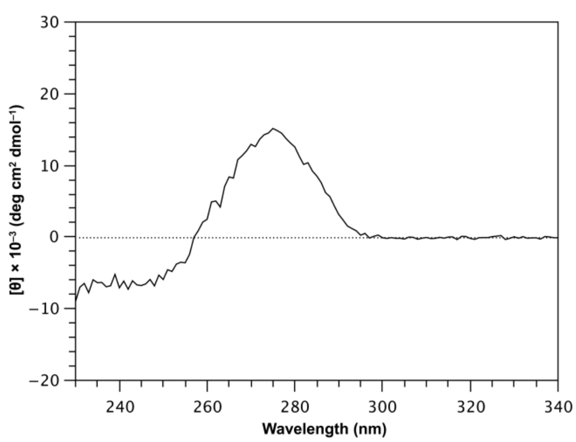

Figure S13. Circular dichroism spectrum of $PCBT_{20}$ (0.01 mg/mL in dichloromethane), demonstrating stacking behavior of N^3-butenylthymine bases.

III. Details of computational chemistry

Methods

All calculations were performed with Gaussian 09.[1] All geometries for ring-strain energies were optimized using the B3LYP/6-31+G*, B97-D/6-31+G*, and M06-2X/6-31+G* levels of theory. These levels of theory have been used in numerous studies based on the emphasis on medium-range electron correlation or dispersion correction. The strain energy of a given cyclic molecule relative to another structurally related cyclic reference compound can be calculated by directly comparing the DFT electronic energies of the two molecules given the energy of the fragment, by which the two species differ from each other, is known. A similar theoretical approach to ring strain energy was previously described by Lim and co-workers[2] with *ab initio* calculations at the HF/6-31+G* and MP2/6-31+G* levels of theory. Relative ring strain energies were obtained from the differences between total electronic energies of the targeted molecule and the reference molecule. The QST2 option implemented in Gaussian 09 with the Synchronous Transit-Guided Quasi-Newton (STQN) method at the B3LYP/6-31+G* level of theory was used to locate the transition state, and the electronic energies were reported to explain the diastereoselective cyclization of **6**.

Cartesian coordinates and energies (in Hartrees) for all optimized structures

1-acyclic (B3LYP), *E* = –915.9305667

O	3.83679	1.41256	-0.39115
C	3.91072	0.06529	0.08762
C	2.59168	-0.26865	0.77424
C	1.41105	-0.22545	-0.18580
O	0.21661	-0.56523	0.57149
P	-1.14449	-0.94005	-0.21722
O	-2.03837	-1.54293	0.99221
O	-1.89672	0.43855	-0.51848
C	-2.23043	1.39312	0.52640
C	-2.77776	2.64025	-0.14159
O	-0.96399	-1.79465	-1.41121
H	4.66296	1.63702	-0.84509
H	4.73536	-0.04391	0.80696
H	4.09308	-0.62936	-0.74732
H	2.66473	-1.27282	1.21132
H	2.42283	0.43736	1.59643
H	1.52967	-0.94807	-1.00024
H	1.28762	0.77421	-0.61274
H	-1.84628	-2.47997	1.16010

H	-1.32699	1.61056	1.10690
H	-2.97093	0.93094	1.18711
H	-2.03073	3.08816	-0.80524
H	-3.05020	3.37746	0.62319
H	-3.66998	2.40530	-0.73118

1-cyclic (B3LYP), *E* = –839.5019251

O	0.46587	2.22431	-0.10461
P	-0.01788	0.83749	0.01495
O	1.10446	-0.29280	0.30387
C	2.40408	-0.20106	-0.34240
C	3.31194	-1.24399	0.28195
O	-1.05267	0.56405	1.21535
C	-1.78248	-0.68982	1.25396
C	-2.49912	-0.94243	-0.07055
C	-1.52052	-0.93474	-1.24343
O	-0.79913	0.32074	-1.30827
H	2.79132	0.81198	-0.19858
H	2.27350	-0.37644	-1.41718
H	3.43162	-1.06156	1.35503
H	4.30099	-1.20131	-0.18960
H	2.90734	-2.25261	0.14314
H	-2.48726	-0.58304	2.08129
H	-1.07756	-1.49587	1.49162
H	-3.26386	-0.17230	-0.22682
H	-3.00542	-1.91581	-0.02740
H	-2.03825	-1.01799	-2.20161
H	-0.79593	-1.75543	-1.16201

1-acyclic (B97D), *E* = –915.5485664

O	-3.65430	1.10953	0.40499
C	-3.74183	-0.25747	-0.04147
C	-2.43486	-0.60949	-0.75426
C	-1.24163	-0.56204	0.19750
O	-0.05398	-0.92509	-0.57434
P	1.37641	-0.86633	0.19731
O	2.35548	-1.18731	-1.07458

O	1.60765	0.70334	0.53226
C	1.46448	1.71058	-0.52006
C	1.66194	3.07687	0.12407
O	1.56524	-1.73649	1.38995
H	-4.47718	1.32872	0.87482
H	-4.58823	-0.38408	-0.74210
H	-3.89892	-0.93592	0.82005
H	-2.52271	-1.62334	-1.17794
H	-2.27242	0.09341	-1.58705
H	-1.36219	-1.28208	1.02309
H	-1.11481	0.44688	0.61682
H	2.96975	-1.90137	-0.82215
H	0.46176	1.61697	-0.96707
H	2.22009	1.51236	-1.29646
H	0.90434	3.24988	0.90375
H	1.56354	3.86067	-0.64503
H	2.66161	3.15036	0.57880

1-cyclic (B97D), *E* = –839.1612228

O	0.40198	2.28056	-0.22956
P	-0.04283	0.88350	-0.01630
O	1.09538	-0.19865	0.43659
C	2.35308	-0.22016	-0.31155
C	3.26159	-1.25176	0.34578
O	-1.14307	0.67053	1.15688
C	-1.79290	-0.63725	1.25888
C	-2.41663	-1.04786	-0.08112
C	-1.36016	-1.08231	-1.19357
O	-0.72631	0.22378	-1.35183
H	2.79435	0.78767	-0.28177
H	2.13609	-0.48385	-1.36045
H	3.45988	-0.97863	1.39356
H	4.22071	-1.29336	-0.19611
H	2.80064	-2.25187	0.32143
H	-2.55360	-0.51211	2.04031
H	-1.04281	-1.37299	1.59273
H	-3.21226	-0.33620	-0.35229

H	-2.86591	-2.05014	0.02357
H	-1.80730	-1.30261	-2.17194
H	-0.58102	-1.83217	-0.97173

1-acyclic (M06-2X), *E* = –915.6484964

O	3.62592	1.22170	-0.45900
C	3.77012	-0.08694	0.07452
C	2.47741	-0.43301	0.79106
C	1.29713	-0.41734	-0.16083
O	0.12863	-0.79075	0.59511
P	-1.25403	-0.91080	-0.20081
O	-2.23273	-1.32037	1.00556
O	-1.65555	0.59405	-0.54166
C	-1.70616	1.58174	0.50542
C	-2.14017	2.88911	-0.11999
O	-1.27668	-1.80240	-1.36943
H	4.43764	1.47723	-0.91687
H	4.60886	-0.13045	0.78183
H	3.96121	-0.81301	-0.72970
H	2.56373	-1.42816	1.24159
H	2.30357	0.28790	1.59786
H	1.43493	-1.13635	-0.97708
H	1.15321	0.58055	-0.58920
H	-2.68578	-2.15538	0.81115
H	-0.71274	1.66417	0.96119
H	-2.41452	1.24441	1.26963
H	-1.42713	3.20087	-0.88799
H	-2.19404	3.66890	0.64587
H	-3.12516	2.78209	-0.58179

1-cyclic (M06-2X), *E* = –839.2567353

O	0.43117	2.24322	-0.21353
P	-0.04193	0.87290	-0.01328
O	1.06399	-0.21276	0.41287
C	2.31582	-0.21105	-0.30248
C	3.21156	-1.24944	0.33623
O	-1.12922	0.66256	1.13567

C	-1.75826	-0.62784	1.24854
C	-2.38646	-1.03357	-0.07792
C	-1.34653	-1.05350	-1.19067
O	-0.72529	0.23589	-1.32393
H	2.74822	0.79212	-0.24202
H	2.11892	-0.44444	-1.35603
H	3.38875	-1.00467	1.38688
H	4.17442	-1.28189	-0.18249
H	2.75328	-2.24117	0.28099
H	-2.50809	-0.51677	2.03291
H	-1.00502	-1.35530	1.57452
H	-3.18074	-0.32484	-0.33660
H	-2.83467	-2.02856	0.02198
H	-1.79815	-1.26346	-2.16156
H	-0.56986	-1.80349	-0.99025

2-acyclic (B3LYP), *E* = –876.6156213

O	-4.24859	0.82851	0.03849
C	-2.87683	1.07954	-0.25081
C	-2.02500	-0.15483	0.03272
O	-0.66406	0.17208	-0.33388
P	0.54251	-0.80168	0.09304
O	0.45853	-1.98183	-1.00934
O	1.81709	0.02742	-0.40113
C	2.30187	1.15621	0.37950
C	3.62592	1.59670	-0.21497
O	0.53836	-1.26882	1.50269
H	-4.37301	0.79627	0.99969
H	-2.83090	1.32638	-1.31484
H	-2.49254	1.93924	0.31593
H	-2.37046	-1.00237	-0.56866
H	-2.06000	-0.42726	1.09428
H	0.77727	-2.82340	-0.64239
H	2.41159	0.83948	1.42186
H	1.55410	1.95541	0.32557
H	4.36346	0.78902	-0.16357
H	4.01239	2.45608	0.34577

H	3.50404	1.89168	-1.26238

2-cyclic (B3LYP), E = –800.1804188

O	-0.34338	-1.56246	-0.98691
P	0.15222	-0.42014	-0.19073
O	-0.97384	0.36318	0.63924
C	-2.36094	-0.08445	0.67237
C	-3.21641	0.78213	-0.23508
O	1.33965	-0.76686	0.87245
C	2.34181	0.26859	0.87715
C	2.31859	0.84728	-0.54406
O	0.93633	0.79018	-0.95156
H	-2.66007	0.01076	1.71993
H	-2.40346	-1.13656	0.37939
H	-4.26770	0.48086	-0.14644
H	-2.91543	0.66832	-1.28191
H	-3.13486	1.83877	0.04160
H	3.29773	-0.19156	1.13647
H	2.07587	1.02157	1.62830
H	2.91735	0.24575	-1.23723
H	2.63890	1.89049	-0.58714

2-acyclic (B97D), E = –876.2616679

O	-4.25064	0.83105	0.04958
C	-2.87890	1.08481	-0.27572
C	-2.00967	-0.13363	0.05884
O	-0.64426	0.20109	-0.32428
P	0.54857	-0.81837	0.09146
O	0.43866	-1.98709	-1.04324
O	1.84656	0.00133	-0.40361
C	2.29346	1.14727	0.39622
C	3.59594	1.64898	-0.21342
O	0.53479	-1.31227	1.50109
H	-4.33052	0.80011	1.01949
H	-2.85292	1.27901	-1.35671
H	-2.49132	1.97640	0.25083
H	-2.34628	-1.01382	-0.51057

H	-2.04289	-0.35962	1.13785
H	0.72561	-2.83799	-0.66192
H	2.43260	0.81730	1.43759
H	1.50844	1.91947	0.36001
H	4.36590	0.86293	-0.18326
H	3.95507	2.51799	0.36212
H	3.44203	1.95633	-1.25911

2-cyclic (B97D), *E* = –799.8676365

O	-0.42560	-1.19196	-1.40483
P	0.11884	-0.39545	-0.27413
O	-0.93828	-0.06436	0.90881
C	-2.37748	-0.24087	0.67794
C	-2.96156	0.93002	-0.10804
O	1.41590	-1.02733	0.51211
C	2.36390	0.02456	0.82722
C	2.20904	1.05544	-0.30788
O	0.79262	1.07217	-0.61783
H	-2.79655	-0.29910	1.69188
H	-2.53867	-1.19608	0.15743
H	-4.05455	0.80615	-0.19071
H	-2.53944	0.96278	-1.12420
H	-2.75114	1.88380	0.40023
H	3.36349	-0.42867	0.86134
H	2.10612	0.45828	1.80738
H	2.76853	0.75104	-1.20749
H	2.49915	2.07064	-0.00541

2-acyclic (M06-2X), *E* = –876.3536623

O	-4.19617	0.81611	0.05861
C	-2.84859	1.06047	-0.28944
C	-1.97715	-0.13545	0.05962
O	-0.63885	0.18890	-0.34288
P	0.54121	-0.79945	0.08504
O	0.43494	-1.98486	-0.98748
O	1.82220	-0.00152	-0.40614
C	2.24471	1.14847	0.35718

C	3.58121	1.59592	-0.19168
O	0.52005	-1.24209	1.49250
H	-4.29137	0.85177	1.02039
H	-2.83045	1.22643	-1.36916
H	-2.45409	1.96063	0.20071
H	-2.31934	-1.02503	-0.48025
H	-1.99334	-0.33905	1.13714
H	0.68519	-2.83550	-0.59420
H	2.31493	0.86264	1.41176
H	1.48508	1.92997	0.24750
H	4.32475	0.80217	-0.08206
H	3.92866	2.47898	0.35311
H	3.49354	1.84993	-1.25137

2-cyclic (M06-2X), *E* = –799.9539636

O	-0.46888	-1.11195	-1.41954
P	0.10684	-0.38475	-0.28207
O	-0.91075	-0.11726	0.91545
C	-2.33143	-0.24809	0.68954
C	-2.86791	0.93537	-0.09056
O	1.39813	-1.03670	0.43075
C	2.33334	-0.02000	0.80471
C	2.16735	1.06667	-0.26111
O	0.77066	1.06524	-0.57220
H	-2.76097	-0.30122	1.69168
H	-2.51751	-1.18989	0.16615
H	-3.95530	0.85539	-0.18844
H	-2.43716	0.95968	-1.09665
H	-2.63002	1.87251	0.42076
H	3.32945	-0.46412	0.81429
H	2.07719	0.35112	1.80301
H	2.73238	0.82873	-1.16798
H	2.43807	2.06083	0.09708

3-acyclic (B3LYP), *E* = –1068.5646549

O	2.00924	0.56867	1.97190
C	2.27287	0.75714	0.58664

H	1.66246	1.58806	0.20256
C	2.01409	-0.50690	-0.26700
H	2.20057	-1.39196	0.36530
C	0.62162	-0.59369	-0.87001
O	-0.30633	-0.49029	0.24478
P	-1.84581	-0.96748	0.06415
O	-2.32932	-0.95058	1.61014
O	-2.61860	0.28079	-0.56645
C	-2.65720	1.58955	0.06802
C	-3.43063	2.52396	-0.84247
O	-2.03550	-2.23113	-0.67794
O	2.95767	-0.43958	-1.32597
C	4.18326	0.01936	-0.73258
C	3.77316	1.03675	0.35480
H	1.07061	0.33230	2.06148
H	0.46360	-1.53934	-1.39495
H	0.45143	0.24107	-1.55961
H	-2.36376	-1.84715	1.98287
H	-1.62852	1.93585	0.21971
H	-3.14174	1.48366	1.04391
H	-2.94206	2.61258	-1.81836
H	-3.48250	3.52018	-0.38737
H	-4.45107	2.15872	-0.99664
H	4.79169	0.44118	-1.53588
H	4.71800	-0.83766	-0.29718
H	3.93725	2.06701	0.02567
H	4.32093	0.88759	1.29023

(*R*)-3-cyclic (B3LYP), *E* = –992.1260383

O	-1.19776	0.54844	1.81900
P	-0.92103	0.22491	0.39830
O	-2.15247	-0.23580	-0.49779
C	-3.52364	0.07958	-0.11221
C	-4.43240	-0.97176	-0.71952
O	-0.27798	1.44560	-0.46660
C	1.12680	1.78234	-0.30310
C	1.90060	0.50168	-0.57687

C	1.47823	-0.60493	0.39011
H	1.56037	-0.24033	1.42305
O	0.11682	-1.00818	0.14637
C	2.54210	-1.66080	0.12033
C	3.78076	-0.76587	-0.16826
O	3.29715	0.59188	-0.36754
H	-3.75099	1.07909	-0.49801
H	-3.58829	0.09734	0.97909
H	-4.33247	-0.99375	-1.80980
H	-5.47533	-0.74041	-0.47167
H	-4.19487	-1.96612	-0.32734
H	1.31044	2.16133	0.70884
H	1.32955	2.57044	-1.03033
H	1.67455	0.17685	-1.60676
H	2.25839	-2.25319	-0.75638
H	2.70045	-2.34103	0.96155
H	4.31976	-1.08884	-1.06659
H	4.48298	-0.73206	0.66944

(*S*)-3-cyclic (B3LYP), *E* = –992.1266317

O	1.96345	0.17800	1.81587
P	1.01067	0.12910	0.69259
O	1.59007	-0.34996	-0.73638
C	2.90145	0.10243	-1.18630
C	3.98084	-0.89488	-0.80202
O	0.32439	1.57539	0.40207
C	-0.84051	1.71928	-0.45466
C	-1.86597	0.71151	0.03598
C	-1.31290	-0.70942	-0.05160
H	-0.94066	-0.89715	-1.06665
O	-0.22949	-0.89916	0.87749
C	-2.56455	-1.53517	0.21736
C	-3.65179	-0.65434	-0.46150
O	-3.04746	0.64011	-0.73934
H	3.10709	1.09512	-0.77182
H	2.80388	0.19337	-2.27184
H	4.06605	-0.97224	0.28581

H	4.94616	-0.56473	-1.20608
H	3.75546	-1.88525	-1.21228
H	-0.56575	1.53663	-1.50020
H	-1.16633	2.75455	-0.33878
H	-2.09687	0.93946	1.09052
H	-2.72626	-1.61555	1.29761
H	-2.51699	-2.54405	-0.20139
H	-4.52489	-0.50955	0.18530
H	-3.98801	-1.05850	-1.42034

3-acyclic (B97D), *E* = –1068.0803405

O	2.73691	0.71822	1.87075
C	2.09882	0.62482	0.58684
H	1.16409	1.21201	0.58730
C	1.83169	-0.84813	0.15698
H	1.87427	-1.51304	1.03956
C	0.48629	-1.03010	-0.54812
O	-0.54107	-0.88517	0.47881
P	-2.09490	-0.83501	-0.02008
O	-2.84783	-0.75642	1.42944
O	-2.28886	0.64852	-0.63318
C	-2.00083	1.83630	0.17374
C	-2.00409	3.04005	-0.75936
O	-2.53323	-1.91840	-0.93893
O	2.85685	-1.21713	-0.78188
C	3.86761	-0.18555	-0.78845
C	3.09991	1.10581	-0.47470
H	2.14759	0.29855	2.52332
H	0.41283	-2.02709	-1.00438
H	0.35392	-0.26109	-1.32783
H	-3.30909	-1.59746	1.60456
H	-1.02133	1.70844	0.66231
H	-2.77789	1.91702	0.94903
H	-1.22275	2.93910	-1.52845
H	-1.80961	3.95456	-0.17518
H	-2.97975	3.14037	-1.25852
H	4.34256	-0.20261	-1.77948

H	4.62307	-0.39194	-0.00897
H	2.55584	1.45030	-1.36850
H	3.73107	1.92193	-0.09507

(*R*)-3-cyclic (B97D), *E* = –991.681869

O	-1.16607	0.51028	1.85726
P	-0.91755	0.17522	0.42512
O	-2.16472	-0.32647	-0.45336
C	-3.52542	0.04715	-0.04027
C	-4.49131	-0.82766	-0.82777
O	-0.32065	1.41681	-0.47694
C	1.08429	1.78288	-0.28945
C	1.89344	0.52071	-0.58610
C	1.50635	-0.60705	0.38278
H	1.59956	-0.24407	1.42127
O	0.14509	-1.05297	0.15206
C	2.59153	-1.63889	0.08398
C	3.81135	-0.70573	-0.19972
O	3.29384	0.65268	-0.38043
H	-3.66723	1.11528	-0.26781
H	-3.62188	-0.10582	1.04442
H	-4.36376	-0.67458	-1.91039
H	-5.52551	-0.56241	-0.55285
H	-4.32607	-1.89126	-0.59724
H	1.25283	2.13555	0.74101
H	1.27509	2.59579	-1.00107
H	1.66477	0.19368	-1.62064
H	2.31004	-2.21710	-0.80920
H	2.77461	-2.33218	0.91654
H	4.35181	-1.00686	-1.11228
H	4.51757	-0.66537	0.64200

(*S*)-3-cyclic (B97D), *E* = –991.6844212

O	1.99481	-0.59131	1.72964
P	1.02170	-0.20637	0.68052
O	1.54418	-0.16706	-0.86297
C	2.79646	0.53655	-1.16883

C	4.00326	-0.37750	-0.97380
O	0.39631	1.29272	0.93848
C	-0.74593	1.75237	0.14708
C	-1.82960	0.68626	0.28599
C	-1.34170	-0.65455	-0.27774
H	-0.97674	-0.50833	-1.30744
O	-0.26647	-1.20321	0.52694
C	-2.63616	-1.46465	-0.27406
C	-3.67385	-0.35432	-0.63387
O	-3.00685	0.94021	-0.46880
H	2.87032	1.44312	-0.54580
H	2.68289	0.84001	-2.21951
H	4.09019	-0.67772	0.07991
H	4.91903	0.16076	-1.27209
H	3.90524	-1.27909	-1.59820
H	-0.44992	1.88148	-0.90681
H	-1.03339	2.71911	0.57911
H	-2.05723	0.55814	1.36367
H	-2.81152	-1.86850	0.73442
H	-2.63520	-2.29265	-0.99637
H	-4.55523	-0.38913	0.02725
H	-4.00476	-0.40757	-1.68098

3-acyclic (M06-2X), *E* = –1068.2288891

O	2.99903	-0.11551	1.89869
C	2.19336	0.34511	0.82655
H	1.28630	0.83090	1.20900
C	1.84934	-0.78189	-0.16663
H	1.92544	-1.76037	0.32860
C	0.46091	-0.63609	-0.76488
O	-0.47386	-0.82085	0.31034
P	-2.03405	-0.86833	-0.05898
O	-2.65641	-0.99143	1.41560
O	-2.37670	0.61996	-0.51369
C	-2.09865	1.73250	0.35660
C	-2.40455	3.00093	-0.40952
O	-2.45534	-1.89003	-1.02559

O	2.78509	-0.70236	-1.23138
C	3.78475	0.26476	-0.90982
C	3.06253	1.26981	-0.01942
H	2.49697	-0.76188	2.41591
H	0.29603	-1.38758	-1.54274
H	0.33281	0.36442	-1.20061
H	-3.20664	-1.78625	1.49580
H	-1.04493	1.69261	0.65966
H	-2.72144	1.63794	1.25215
H	-1.78354	3.06363	-1.30740
H	-2.20342	3.87404	0.21855
H	-3.45470	3.01992	-0.71200
H	4.15518	0.67979	-1.84933
H	4.61095	-0.21559	-0.37095
H	2.43560	1.93217	-0.62650
H	3.72548	1.87220	0.60554

(*R*)-3-cyclic (M06-2X), *E* = –991.8256795

O	-1.12503	0.46275	1.81433
P	-0.90361	0.15944	0.38937
O	-2.15600	-0.30221	-0.45530
C	-3.48448	0.06722	-0.01699
C	-4.46510	-0.80615	-0.76693
O	-0.31115	1.39217	-0.46956
C	1.06497	1.77083	-0.26199
C	1.88030	0.52866	-0.56645
C	1.47696	-0.61549	0.35678
H	1.54677	-0.27999	1.40166
O	0.13889	-1.03956	0.08813
C	2.56612	-1.62648	0.05322
C	3.77727	-0.68502	-0.16986
O	3.25863	0.65183	-0.32846
H	-3.63458	1.12759	-0.24376
H	-3.54945	-0.07533	1.06503
H	-4.36245	-0.66127	-1.84572
H	-5.48781	-0.54904	-0.47493
H	-4.28958	-1.86057	-0.53771

H	1.21588	2.10697	0.77058
H	1.26308	2.59302	-0.95027
H	1.67604	0.22682	-1.60813
H	2.30504	-2.17312	-0.85842
H	2.73135	-2.34482	0.85842
H	4.34654	-0.95749	-1.06432
H	4.45443	-0.66565	0.68727

(*S*)-3-cyclic (M06-2X), *E* = –991.827853

O	2.00241	-0.38690	1.73679
P	1.01096	-0.11702	0.69406
O	1.50987	-0.20778	-0.82698
C	2.76264	0.42575	-1.17290
C	3.91942	-0.53150	-0.96873
O	0.37691	1.36279	0.80799
C	-0.74520	1.74827	-0.00906
C	-1.81362	0.69837	0.21733
C	-1.30909	-0.67612	-0.20043
H	-0.93911	-0.62887	-1.23348
O	-0.25126	-1.11301	0.65386
C	-2.59086	-1.48503	-0.12832
C	-3.62233	-0.42974	-0.60427
O	-2.96933	0.85645	-0.56344
H	2.88522	1.33785	-0.57697
H	2.65347	0.71103	-2.22192
H	4.00458	-0.80508	0.08591
H	4.85300	-0.05755	-1.28899
H	3.76770	-1.43848	-1.56081
H	-0.45052	1.78941	-1.06475
H	-1.04225	2.74151	0.32925
H	-2.05332	0.67323	1.29440
H	-2.76890	-1.78488	0.90910
H	-2.57944	-2.37856	-0.75522
H	-4.50620	-0.40397	0.04104
H	-3.94325	-0.59264	-1.63583

(*R*)-5 (B3LYP), *E* = –1601.1014865

O	4.88792	2.17007	-0.06990
C	3.81854	1.57026	-0.11557
C	2.51977	2.21241	0.08789
C	2.49449	3.69261	0.34504
C	1.41060	1.44497	0.03314
N	1.43874	0.08094	-0.20032
C	0.19958	-0.67302	-0.27729
H	0.49129	-1.69174	-0.53055
C	-0.69278	-0.63651	1.00892
C	-1.94752	0.07153	0.51259
H	-1.83464	1.16008	0.60505
O	-3.18407	-0.31002	1.13835
P	-4.44403	0.52219	0.48317
O	-5.71143	-0.33678	0.87912
C	-5.89569	-1.74751	0.55665
C	-7.01337	-1.89958	-0.45876
O	-4.50054	1.94880	0.85944
C	-1.95413	-0.31642	-0.96714
H	-2.22868	-1.38112	-1.05261
C	-2.97879	0.49825	-1.74253
O	-4.26056	0.22489	-1.11362
O	-0.60302	-0.12065	-1.35151
N	3.78729	0.17977	-0.37833
C	5.07732	-0.50334	-0.60408
C	5.68916	-1.04535	0.70134
C	7.06080	-1.61960	0.46717
C	7.39583	-2.90222	0.63865
C	2.64183	-0.60628	-0.41729
O	2.67479	-1.81512	-0.61676
H	3.07186	3.94432	1.24201
H	1.46835	4.05081	0.47755
H	2.95187	4.24154	-0.48613
H	0.41930	1.86567	0.15837
H	-0.19990	-0.12660	1.84016
H	-0.93396	-1.65585	1.32712
H	-6.14357	-2.22517	1.50828
H	-4.95360	-2.16588	0.19168

H	-7.94025	-1.45380	-0.08351
H	-7.19377	-2.96491	-0.64862
H	-6.75002	-1.41694	-1.40513
H	-3.08062	0.18071	-2.78160
H	-2.76346	1.57214	-1.70719
H	5.74121	0.23385	-1.05807
H	4.89815	-1.31783	-1.30648
H	5.02586	-1.80831	1.12486
H	5.75562	-0.21643	1.41924
H	7.82068	-0.91321	0.12713
H	6.67154	-3.64215	0.97550
H	8.40630	-3.25770	0.45255

(*R*)-5-TS (B3LYP), *E* = –1983.0638224, negative frequency = –140.61 cm^{-1}

O	-2.24463	0.63517	0.30253
C	-3.25503	0.50181	-0.38078
N	-4.48430	1.01249	-0.01641
C	-4.55721	1.76193	1.25984
C	-4.86626	0.84933	2.46089
C	-4.83611	1.62314	3.75294
C	-5.89316	1.82981	4.54382
C	-5.69294	0.82828	-0.73769
C	-5.58537	0.06692	-1.98732
C	-6.83729	-0.15376	-2.78595
C	-4.37474	-0.39990	-2.35343
O	-6.74225	1.28859	-0.31431
N	-3.21440	-0.17693	-1.61371
C	-1.98859	-0.80695	-2.03506
H	-2.16499	-1.16641	-3.05168
O	-1.74296	-1.97660	-1.18752
C	-0.68016	0.04401	-1.98870
C	0.15249	-0.62226	-0.88445
H	-0.17615	-0.33773	0.12054
C	-0.37838	-2.15420	-1.09793
H	0.06936	-2.48948	-2.04464
C	0.15241	-2.96283	0.07300
O	1.58070	-2.87976	0.00897

P	2.40384	-1.54296	0.62004
O	1.66291	-1.03708	1.80684
N	3.49272	-0.04623	0.20352
C	4.45999	-0.06953	-0.74803
C	5.23631	1.02620	-1.03369
C	5.05086	2.24778	-0.31865
N	5.80389	3.34265	-0.56228
C	6.85252	3.31014	-1.58598
C	5.59137	4.57296	0.20620
C	4.02407	2.23770	0.67056
C	3.28251	1.10270	0.89569
O	3.79733	-2.35095	0.68953
C	3.96831	-3.76686	1.03633
C	3.68145	-4.02605	2.50398
O	1.49180	-0.68580	-1.01722
H	-5.34473	2.50608	1.13831
H	-3.59789	2.26422	1.39148
H	-4.11597	0.04711	2.49299
H	-5.84942	0.38656	2.32002
H	-3.86771	2.03806	4.03932
H	-6.87738	1.43454	4.29885
H	-5.81163	2.39777	5.46691
H	-7.28431	0.80277	-3.07911
H	-7.58985	-0.68032	-2.18845
H	-6.63307	-0.73772	-3.68866
H	-4.23386	-0.97727	-3.26147
H	-0.87319	1.09489	-1.76882
H	-0.16012	-0.03132	-2.94897
H	-0.09058	-4.02473	-0.04586
H	-0.22763	-2.59283	1.02928
H	4.59947	-1.00890	-1.26802
H	5.99103	0.92967	-1.80296
H	6.43342	3.08916	-2.57469
H	7.33311	4.28664	-1.63197
H	7.61838	2.56289	-1.34605
H	5.75743	4.40433	1.27673
H	4.57686	4.96166	0.05834

H	6.29835	5.32920	-0.13279
H	3.80933	3.11101	1.27211
H	2.50413	1.05490	1.64792
H	5.01798	-3.95029	0.79497
H	3.33829	-4.36393	0.37630
H	4.30667	-3.39601	3.14459
H	3.90462	-5.07517	2.73187
H	2.63145	-3.83963	2.75102

(*S*)-5 (B3LYP), *E* = –1601.1036394

O	4.38673	2.48633	-0.43295
C	3.44156	1.70466	-0.39578
C	2.04190	2.12887	-0.35318
C	1.74842	3.60228	-0.38101
C	1.08635	1.17721	-0.29456
N	1.36121	-0.17823	-0.26523
C	0.27446	-1.14284	-0.22726
H	0.74871	-2.12214	-0.28195
C	-0.67744	-1.03574	1.01090
C	-2.00598	-0.65310	0.36787
H	-2.08164	0.43711	0.25716
O	-3.18350	-1.12692	1.03577
P	-4.57617	-0.83615	0.22179
O	-4.69759	0.77274	0.18750
C	-5.35764	1.47757	1.28043
C	-5.61151	2.90353	0.83078
O	-5.72208	-1.57802	0.77332
C	-1.87236	-1.29065	-1.01449
H	-1.97082	-2.38369	-0.91431
C	-2.96581	-0.79647	-1.94540
O	-4.22674	-1.15713	-1.32096
O	-0.55278	-0.93888	-1.39974
N	3.66497	0.30775	-0.39561
C	5.06415	-0.16212	-0.45739
C	5.68583	-0.33949	0.94063
C	7.14813	-0.68549	0.84943
C	7.69182	-1.83614	1.25824

C	2.67539	-0.66593	-0.31711
O	2.92704	-1.86440	-0.28554
H	2.21926	4.11186	0.46752
H	0.66979	3.78853	-0.34663
H	2.15394	4.06503	-1.28809
H	0.03167	1.42765	-0.28157
H	-0.31782	-0.31176	1.74626
H	-0.76599	-2.00939	1.50283
H	-4.70201	1.44342	2.15864
H	-6.28842	0.95397	1.51625
H	-6.26394	2.92317	-0.04824
H	-4.67391	3.41192	0.58073
H	-6.10067	3.46101	1.63828
H	-2.96286	-1.29748	-2.91469
H	-2.91997	0.28844	-2.09221
H	5.61616	0.58711	-1.02692
H	5.06781	-1.10930	-0.99732
H	5.14426	-1.12263	1.48361
H	5.56482	0.60269	1.49242
H	7.79087	0.07760	0.40602
H	7.09008	-2.62595	1.70498
H	8.75780	-2.02833	1.16466

(*S*)-5-TS (B3LYP), *E* = –1983.0441073, negative frequency = –204.11 cm^{-1}

O	-4.43563	-0.49326	-1.75084
C	-4.11699	0.08158	-0.72166
N	-4.98241	0.86380	0.01949
C	-6.36981	1.00351	-0.48658
C	-7.30184	-0.10160	0.04325
C	-8.72371	0.13382	-0.39345
C	-9.41769	-0.67542	-1.20014
C	-4.65936	1.50512	1.23799
C	-3.27577	1.34643	1.71018
C	-2.89638	2.00556	3.00234
C	-2.42288	0.60584	0.96693
O	-5.49887	2.15375	1.84514
N	-2.79092	0.00174	-0.22051

C	-1.85950	-0.81726	-0.95065
H	-2.42336	-1.26317	-1.77011
O	-1.37019	-1.87757	-0.06985
C	-0.58006	-0.08104	-1.47482
C	0.57838	-0.81881	-0.76994
H	0.75475	-0.40979	0.24042
C	-0.12003	-2.23423	-0.55815
H	-0.17830	-2.71581	-1.54404
C	0.79728	-3.03701	0.35628
O	2.03578	-3.12669	-0.34043
P	3.25387	-1.96145	-0.43718
O	4.16229	-2.42697	-1.50564
N	3.72191	-0.11726	-0.31198
C	4.21996	0.44082	-1.44991
C	4.63294	1.74830	-1.50614
C	4.55004	2.58592	-0.35436
N	4.95626	3.87315	-0.37123
C	5.52389	4.45474	-1.59281
C	4.87731	4.69374	0.84110
C	4.01985	1.97151	0.82017
C	3.63386	0.65183	0.80286
O	3.67555	-2.04832	1.13318
C	3.92886	-3.34875	1.76737
C	4.82951	-3.10727	2.96251
O	1.73011	-1.01561	-1.45444
H	-6.32162	0.97522	-1.57539
H	-6.71521	1.98597	-0.16196
H	-7.24848	-0.10329	1.14069
H	-6.95281	-1.07738	-0.31404
H	-9.19790	1.03856	-0.00931
H	-8.98601	-1.58964	-1.60395
H	-10.44485	-0.45624	-1.47937
H	-3.52506	1.64029	3.82256
H	-3.05715	3.08844	2.94882
H	-1.84754	1.81527	3.25158
H	-1.40030	0.42428	1.27850
H	-0.58817	0.98846	-1.24675

H	-0.49596	-0.19973	-2.55894
H	0.43799	-4.06511	0.47313
H	0.89732	-2.56928	1.34408
H	4.29648	-0.22562	-2.30068
H	5.03587	2.11148	-2.44232
H	4.80007	4.42813	-2.41544
H	5.78360	5.49519	-1.40192
H	6.43333	3.92405	-1.89814
H	3.84407	4.77003	1.19912
H	5.23099	5.69831	0.61265
H	5.50526	4.28277	1.64073
H	3.93209	2.51484	1.75201
H	3.26948	0.16021	1.69506
H	4.39945	-4.00611	1.03119
H	2.96932	-3.78008	2.06548
H	5.78743	-2.67850	2.65252
H	5.02612	-4.06228	3.46328
H	4.35769	-2.43443	3.68681

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