Synthesis and behavior of DNA oligomers containing the ambiguous Z-nucleobase 5-aminoimidazole-4-carboxamide

Yuhei Nogi[1], Noriko Saito–Tarashima[1],* Sangita Karanjit[1], and Noriaki Minakawa[1,*]

1 Graduate School of Pharmaceutical Science, Tokushima University.

* Correspondence: noriko.tarashima@tokushima-u.ac.jp (N.S.T.); minakawa@tokushima-u.ac.jp (N.M.)

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Figure S1. Synthesis of the **ODN4** containing multiple Z-bases. LC-MS analysis after treatment by (a) ethylenediamine at 50 °C, and (b) 1,3-propanediamine at 50 °C. Samples were analyzed by UPLC using a BEH C18 column (Waters, 2.1×50 mm, 1.7 μm) eluted with linear gradient from 0% to 60% MeOH with 3.5 mM TEA and 40 mM HFIP (0.3 mL/min for 15 min).

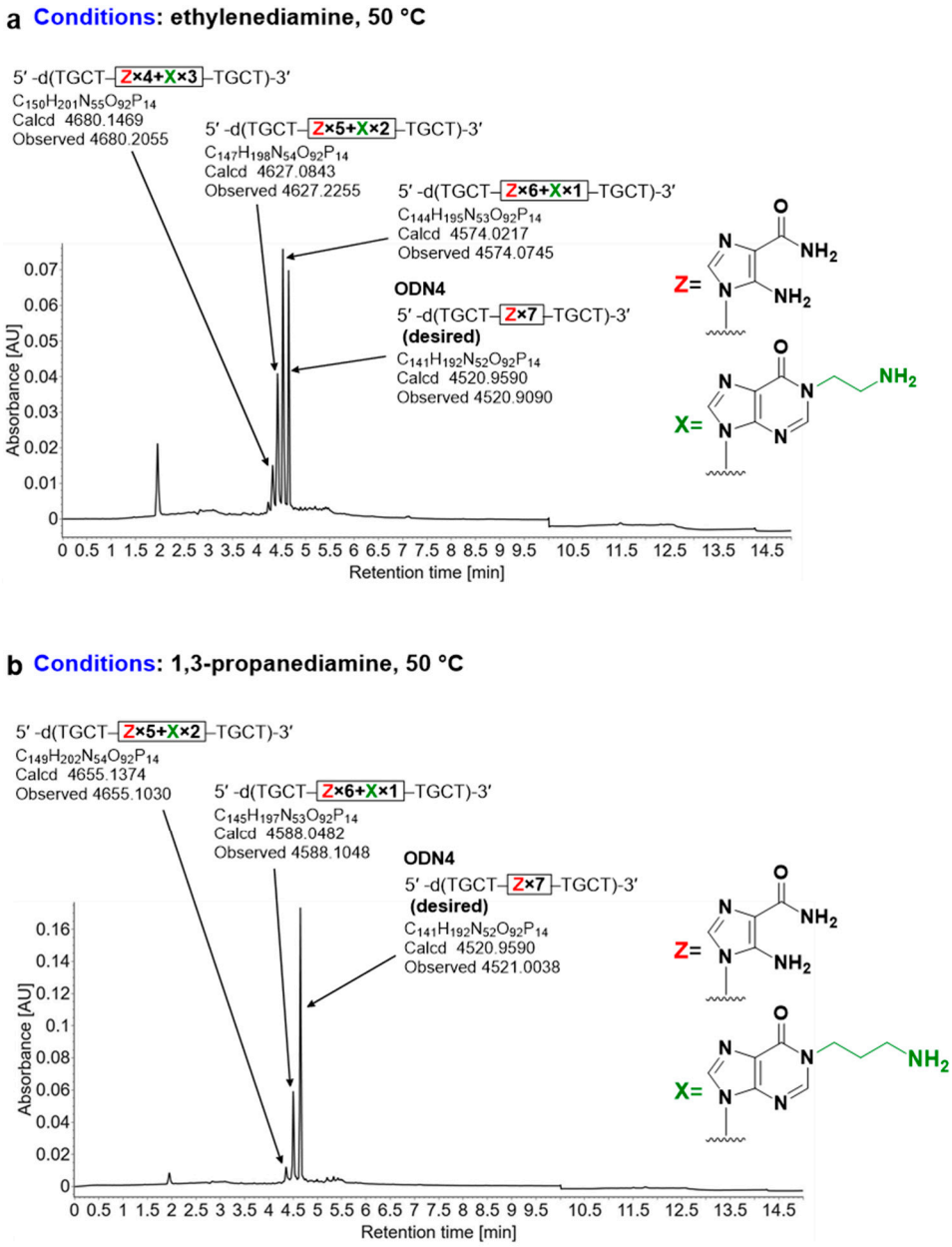


Figure S2. Proposed mechanism of Z-base construction by ring-opening reaction of an Hxa^{DNP}-base (DFT calculation result with the calculated activation barriers).

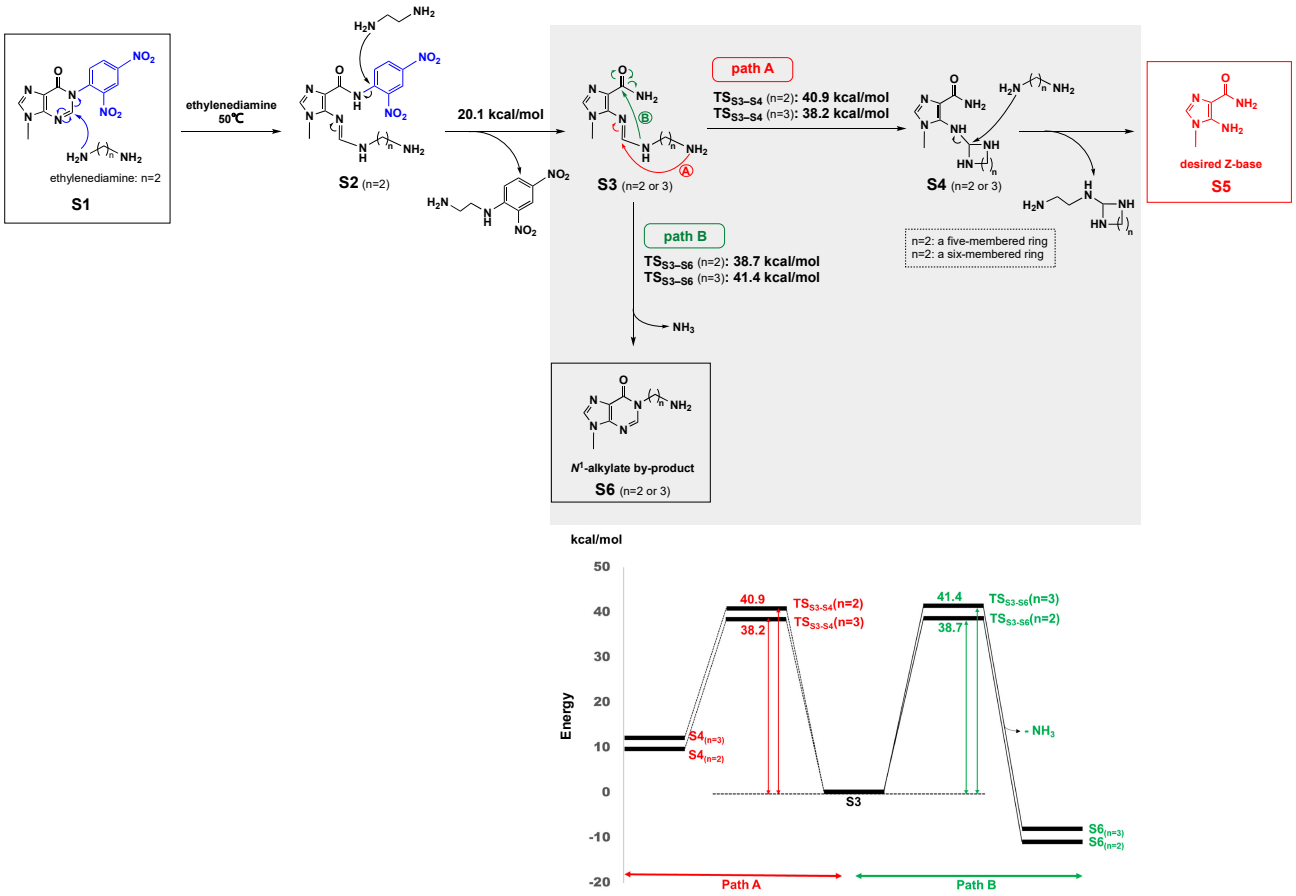


Figure S3. Possible formation of a Hoogsteen-type Z:G pair similar to a natural A:G pair.

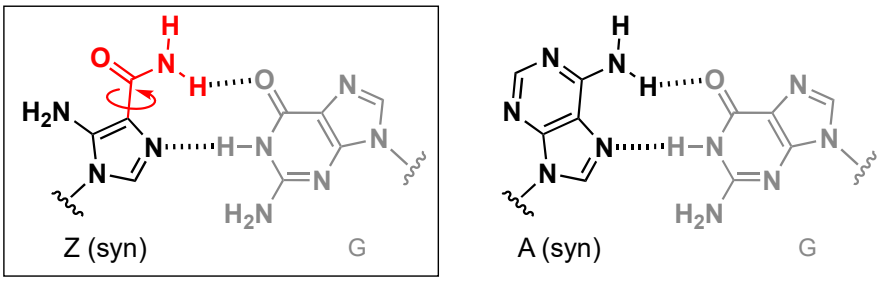
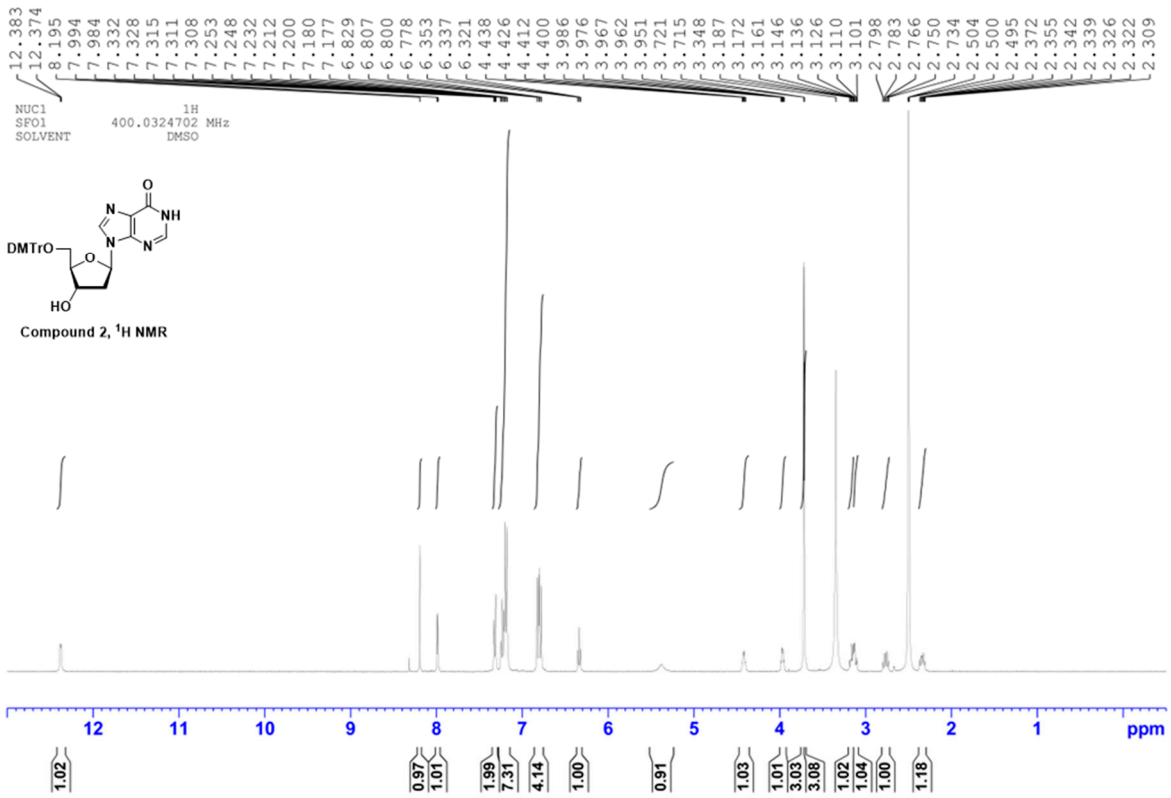


Table S1. Characterization of ODNs containing Z-bases.

#	Squence (5′→3′)	Fomula	Calcd. mass	Observed mass	Correspond duplexes
ODN2	d(TGCTACA**Z**ACATGCT)	$C_{145}H_{186}N_{54}O_{88}P_{14}$	4526.9700	4526.9759 (ethylenediamine) 4526.9641 (1,3-propandiamine)	#1–#4 (Table 1)
ODN4	d(TGCT**ZZZZZZZ**TGCT)	$C_{141}H_{192}N_{52}O_{92}P_{14}$	4520.9590	4521.0038	–
ODN5	d(TGCTACC**Z**CCATGCT)	$C_{143}H_{186}N_{50}O_{90}P_{14}$	4478.9206	4478.9618	#10–#13 (Table 1)
ODN6	d(**Z**CGCGCG)	$C_{66}H_{86}N_{28}O_{40}P_{6}$	2097.3952	2097.3912	#3 (Table 2)
ODN7	d(GTGGGCAAG**Z**GTGCGCTGACCATCCAGAAC)	$C_{291}H_{366}N_{121}O_{175}P_{29}$	9256.9645	9256.9596	Figure 3a
ODN8	d(GGGACTAGCTACGAGTGCTCCCTGTATACTTACTCGTA**Z**GTCGTCGAACTACCACGGCCACTTCAGACCACCAGCTTATATTCCGTC)	$C_{841}H_{1068}N_{312}O_{523}P_{86}$	26578.9987	26578.1173	Figure 3d

NMR spectra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3.967
3.962
3.951
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3.348
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3.172
3.161
3.146
3.136
3.126
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3.101
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2.504
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2.495
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2.355
2.342
2.339
2.326
2.322
2.309
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SOLVENT DMSO
DMTrO
HO
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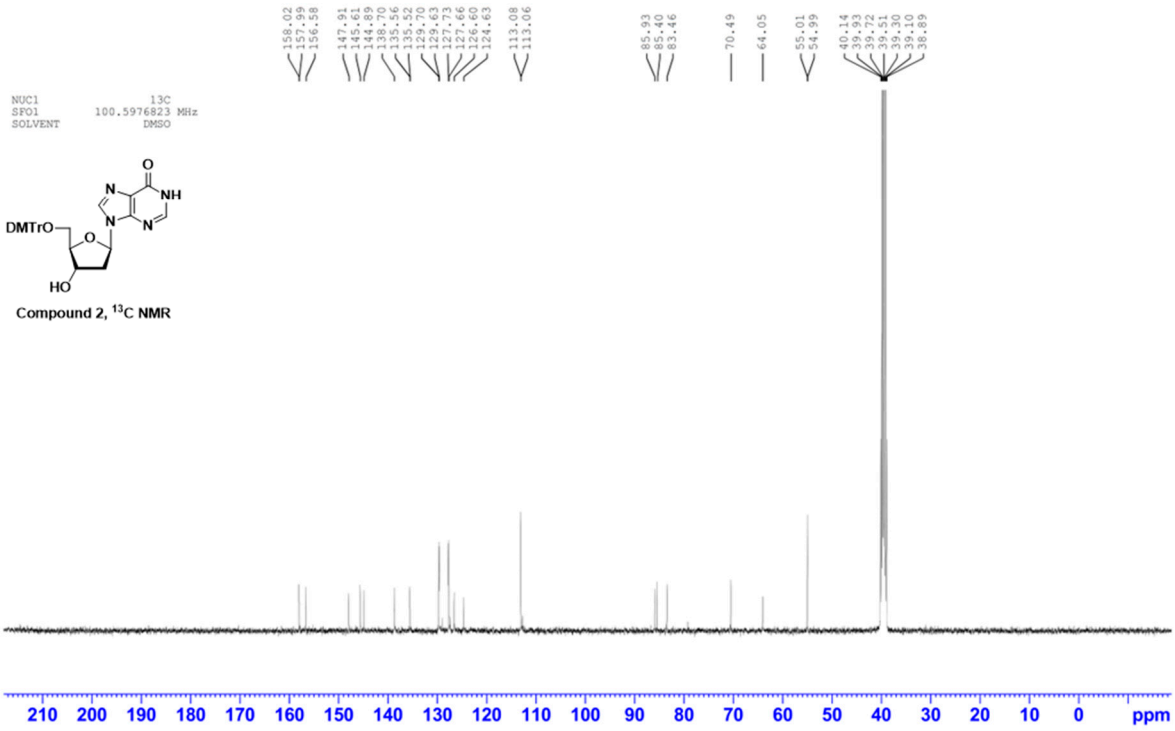
0.97
1.01
1.99
7.31
4.14
1.00
0.91
1.03
1.01
3.03
3.08
1.02
1.04
1.00
1.18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39.51
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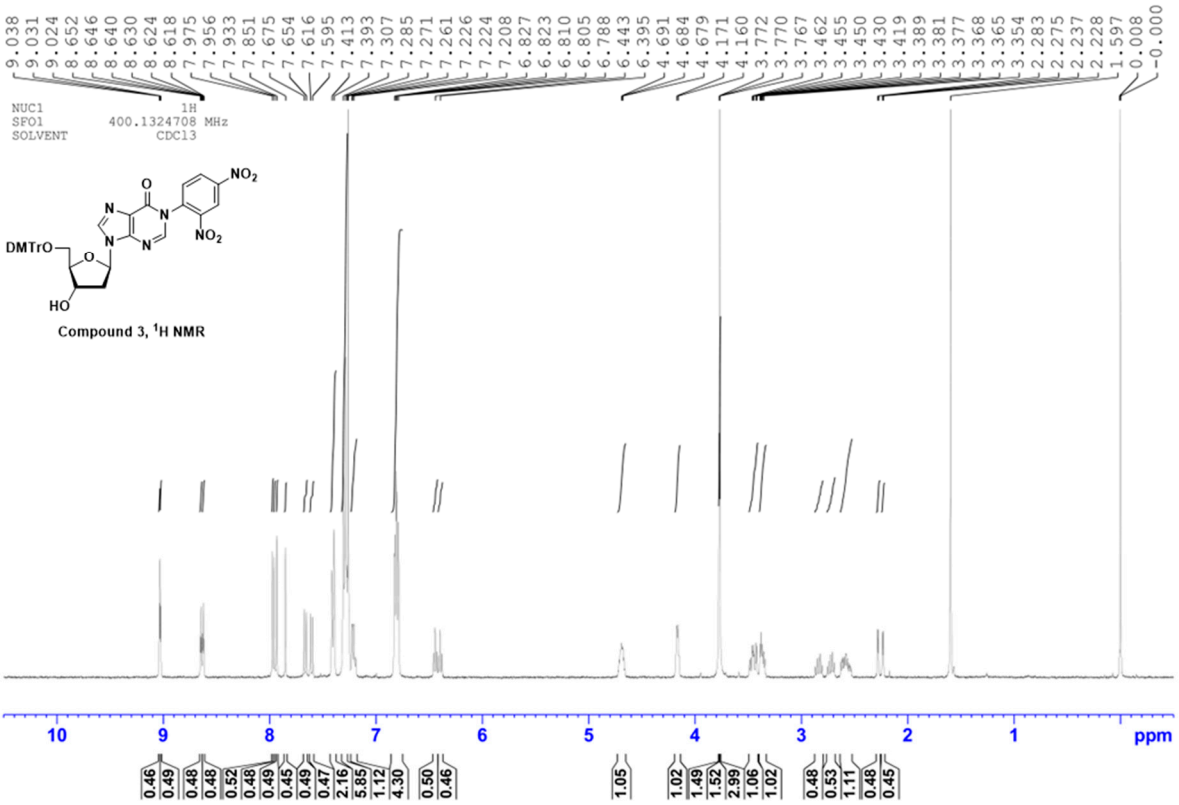
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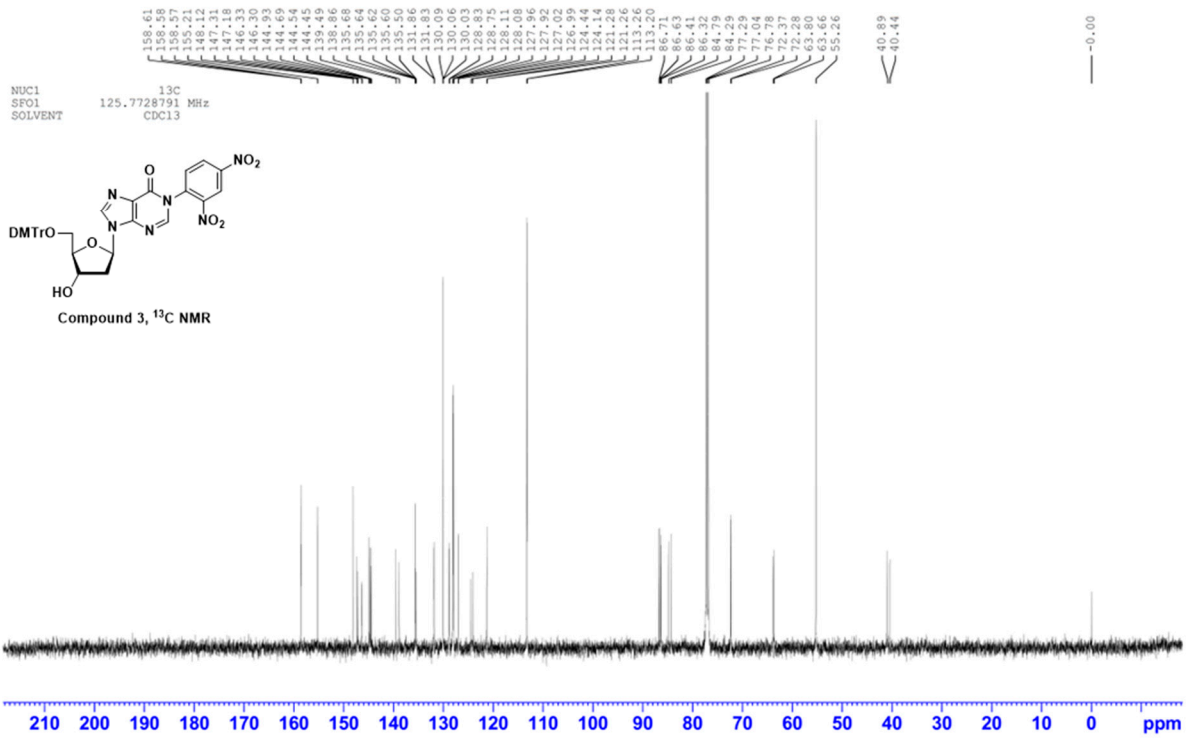
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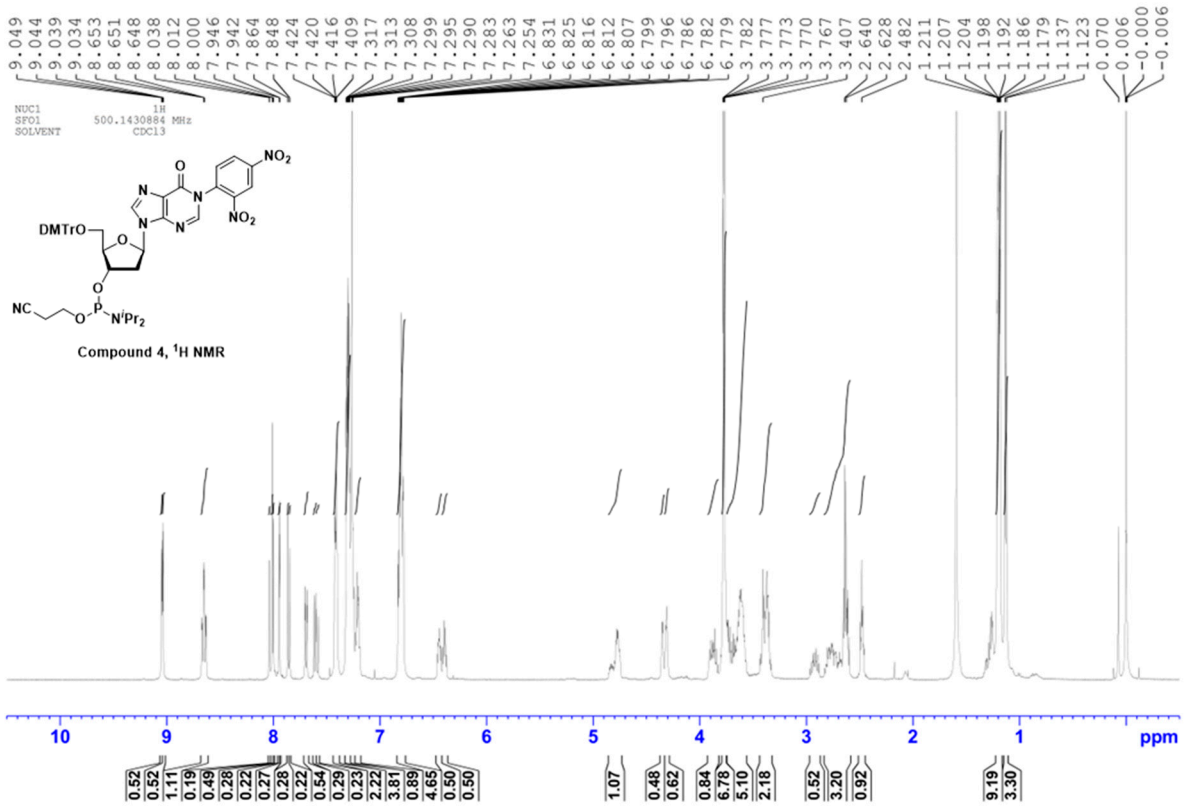
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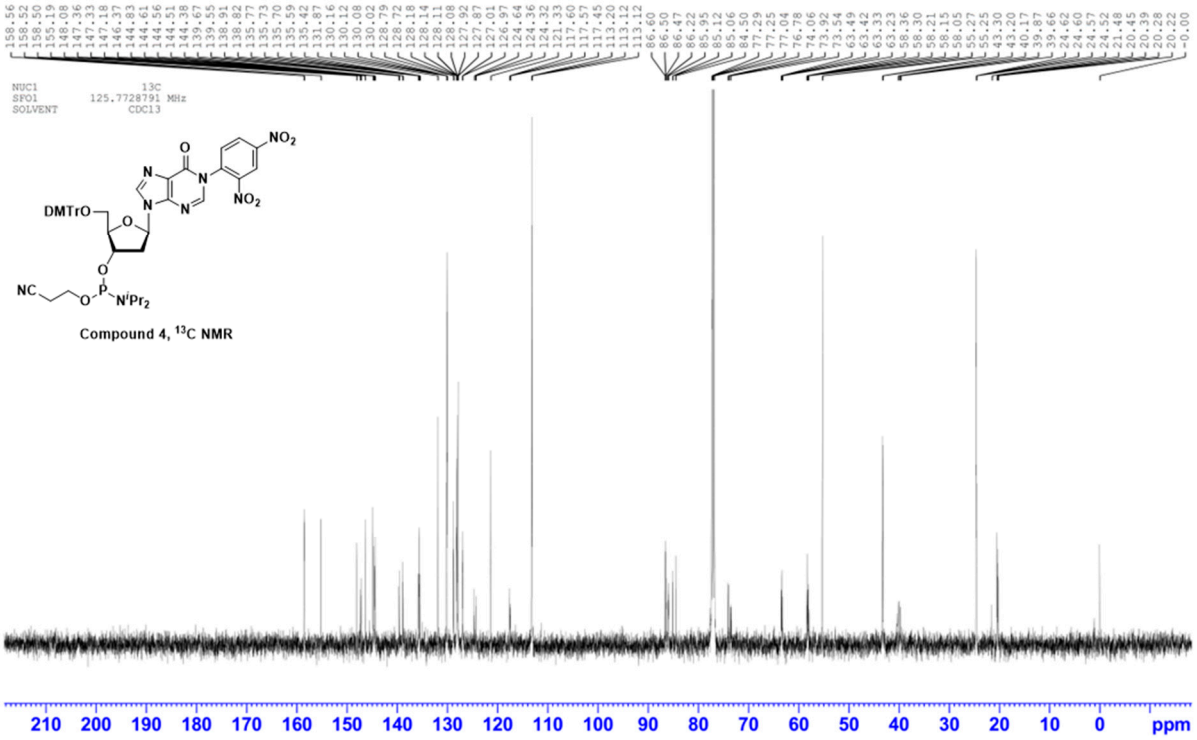
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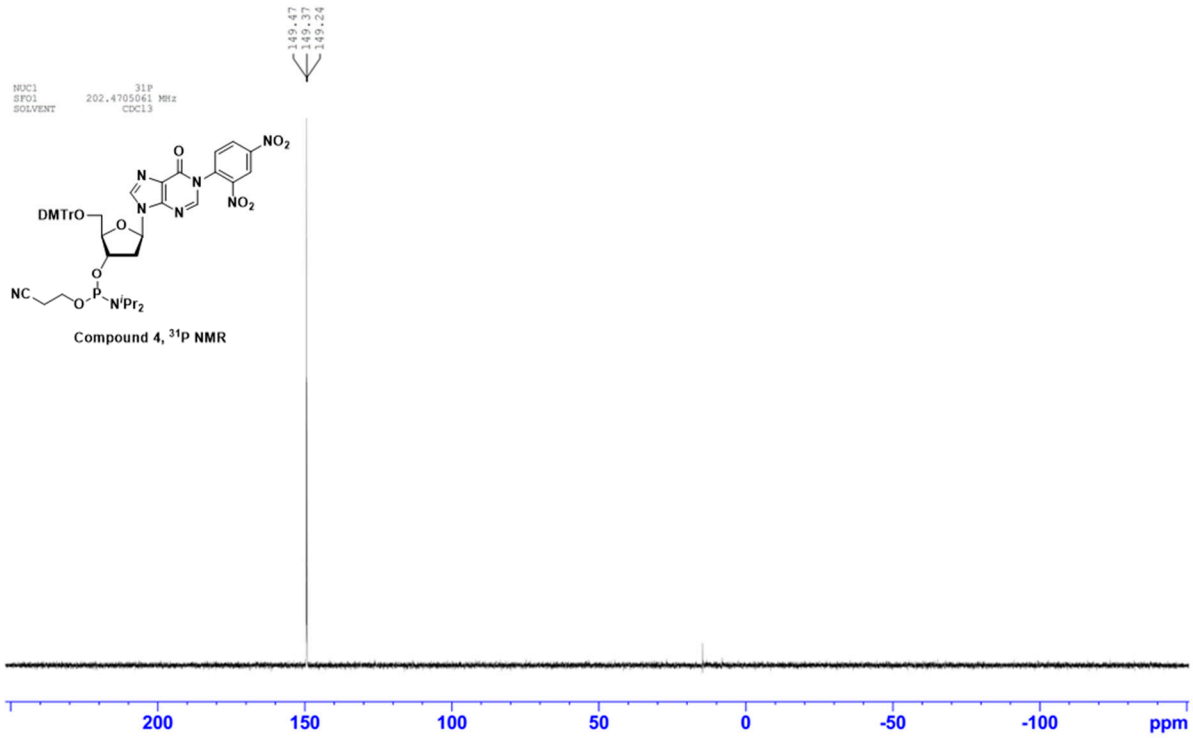

Compound 4, ^{31}P NMR

Cartesian coordinates of intermediates and transition states.

S1

Atom	x	y	z
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H	5.95509300	-1.18382600	0.87862300
N	3.86688600	-1.53468700	1.10827400
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C	1.40041900	-1.13589000	0.62129400
O	0.79567500	-1.90991500	1.34087300
N	0.66672500	-0.23810200	-0.27147600
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C	1.26784700	0.67010600	-1.12241100
H	0.58884500	1.25825400	-1.73343400
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C	-2.79731800	-1.55823500	-0.56862300
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H	5.43243600	1.90213500	-0.81940600
H	6.59781700	0.55406700	-0.80695100

S2

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N	-0.44476800	4.73699800	-0.15247400
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H	0.09147500	4.16911200	-0.80481500
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H	-5.35987100	0.24016900	-0.85120900

H	-6.30477800	-1.26173200	-0.85884800

$TS_{S2\text{-}S3}$

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C	2.71001000	1.92656300	-0.08707100
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H	2.93298800	1.59408400	2.01880500
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O	1.95962700	-0.06408400	3.39839100
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C	-2.31012500	2.95815200	-0.39761100
H	-1.53229100	3.05111500	-1.16141100
H	-1.89458600	3.36426900	0.53145300

C	-3.54262100	3.76967100	-0.82395100
H	-3.94241100	3.34442800	-1.75208900
H	-4.32711100	3.65697600	-0.05607100
N	-3.14875000	5.15087800	-1.09307000
H	-3.87033700	5.65716900	-1.59553900
H	-2.95047300	5.66318300	-0.23803000

S3 (n=2)

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C	3.09776000	-1.49394500	-0.24632100
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N	3.42677800	-0.23136200	-0.16838300
C	2.23922700	0.46015400	-0.05325500
C	2.21805700	1.94430200	0.02960000
O	3.23795200	2.62545000	0.06136000
N	-0.19786200	-0.17660100	-0.00543600
C	1.16764000	-0.43161200	-0.04202200
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H	-0.55870200	-1.49214500	1.59516900
N	-2.29654000	-0.66271300	0.86801300
H	-2.77512800	-1.03980300	1.67362500
C	-3.02886000	0.26220300	0.00902400
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H	-5.30933600	1.78172500	-0.36088400
N	0.96449700	2.51183400	0.08424100
H	0.14400000	1.95735800	-0.12611700
H	0.92720800	3.51501000	-0.02104500
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H	0.77647400	-3.41663600	0.61790300
H	0.15263900	-2.82957700	-0.94516400
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S3 (n=3)

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N	3.74607900	-0.29513700	-0.30198000
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C	2.47763800	1.83960000	-0.23694900
O	3.41560800	2.56868900	0.06198400
N	0.13418900	-0.51188600	0.16937300
C	1.50848000	-0.57578400	0.00430400
C	-0.33561400	0.32025900	1.04168600
H	0.30241400	0.91253300	1.70449500
N	-1.66028500	0.53424700	1.20019600
H	-1.94773200	1.14904400	1.94666100

C	-2.68918800	-0.14006600	0.41559300
H	-2.39543700	-0.08614700	-0.63781800
H	-2.72221500	-1.20561900	0.68638900
C	-4.05583000	0.50972900	0.63727500
H	-4.01884100	1.55852900	0.31910500
H	-4.29597500	0.49092800	1.71014500
N	1.26631800	2.37071800	-0.65857300
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C	-5.18635600	-0.19573200	-0.12087700
H	-5.26385800	-1.23890600	0.23301200
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C	-1.65625000	-0.33605500	0.05914200

C	-1.61476300	-1.79484100	-0.05942100
O	-2.16218200	-2.58525900	0.70502100
C	-0.69100400	0.63116400	-0.30904700
N	0.59277900	0.65701000	-0.75172800
H	2.62892800	1.20685100	-1.12094400
C	1.38365900	-0.45991100	-0.62118400
H	1.34748600	-1.24930200	-1.39079600
C	3.60030200	0.19586700	0.47399400
C	2.45762500	-0.20331400	1.45064300
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H	4.07716200	1.14802200	0.71565900
H	2.83782700	-0.73930000	2.32260700
H	1.92306600	0.68488100	1.79573400
N	1.56356900	-1.04280500	0.67008600
H	1.85948900	-2.01400900	0.61964300
N	2.92883800	0.26507200	-0.85648900
H	3.47192900	-0.15875000	-1.60940900
N	-0.87690900	-2.28746100	-1.15968200
H	-1.06060600	-3.27398100	-1.30762200
H	-0.95693500	-1.73667300	-2.00694000
C	-0.72218300	3.14897900	-0.24691400
H	-1.44365700	3.91251300	0.05307300
H	0.18393400	3.25528500	0.36019800
H	-0.45069800	3.30532800	-1.29596000

$TS_{S3\text{-}S4}$ (n=3)

N	-0.93043800	2.00874200	-0.09373500
C	-2.11767900	2.03476400	0.61429000
H	-2.54598300	2.96448000	0.96698600
N	-2.63367000	0.84891200	0.76696500
C	-1.77469800	-0.02494500	0.10920800
C	-2.15535900	-1.42843700	-0.05567300
O	-2.93844700	-2.03584200	0.67028600
C	-0.66652600	0.68070300	-0.42172300
N	0.44530300	0.38566400	-1.13826300
H	2.87485400	0.36036000	-1.82269400
C	1.17270400	-0.75751200	-0.98909100
H	1.21863400	-1.41672700	-1.87270500
N	1.19386100	-1.60318000	0.18731700
H	0.36299600	-2.18887700	0.18196400
N	2.79638400	-0.24135800	-1.00265100
H	3.39216000	-1.06449100	-1.11469900
N	-1.53859600	-2.10509800	-1.13012600
H	-2.01902400	-2.97072200	-1.34741100
H	-1.32437800	-1.53881800	-1.94392800
C	-0.10566200	3.14442900	-0.44716300
H	-0.67879500	4.06025300	-0.28471000
H	0.80457600	3.19132000	0.16344200
H	0.18598700	3.08233100	-1.49866900
C	1.42829500	-0.91515500	1.46079500
H	1.30888700	-1.64886400	2.26263900

H	0.71086100	-0.10416800	1.65118000
C	2.86267300	-0.36978500	1.46669300
H	3.57227500	-1.20756200	1.47944700
H	3.04375400	0.22639800	2.36785200
C	3.12804700	0.51118300	0.24441800
H	2.47239700	1.38540400	0.23969200
H	4.16769900	0.84918000	0.19225100

S4 (n=2)

N	0.74357400	1.85555800	0.20304900
C	2.01571100	2.13926700	-0.21359100
H	2.34233000	3.15463500	-0.39484900
N	2.75556900	1.06229100	-0.35410800
C	1.93440400	0.01306700	-0.00639800
C	2.40391900	-1.39557800	-0.09008500
O	3.07659400	-1.83135000	-1.01446100
C	0.67057400	0.48238900	0.34601300
N	-0.53327200	-0.14824200	0.71334500
H	-0.37823900	-0.93801100	1.33000700
C	-1.38532300	-0.62811800	-0.39944900
H	-0.76299800	-1.04623800	-1.20286700
C	-3.67736900	-1.07915900	0.11260300
C	-3.43564100	0.42270500	-0.14362500
H	-4.27070200	-1.52054800	-0.70162000
H	-4.20502000	-1.25942600	1.05504500
H	-4.25274800	0.91038600	-0.68026800

H	-3.27869600	0.94938600	0.80308300
N	-2.18705800	0.47631100	-0.92578400
H	-2.38830900	0.29381700	-1.90684100
N	-2.30774600	-1.63074700	0.15335700
H	-2.23025500	-2.51512700	-0.33431800
N	1.96380200	-2.21884300	0.93912600
H	2.37147600	-3.14594200	0.93275700
H	1.84234600	-1.80880700	1.85548200
C	-0.31417500	2.81655700	0.48933000
H	-1.17571600	2.61961100	-0.15054900
H	-0.61782200	2.73678500	1.53677700
H	0.07491900	3.81919700	0.30215500

S4 (n=3)

N	-1.13176000	1.84359300	-0.24105400
C	-2.34592600	2.02617600	0.37553400
H	-2.71576300	3.01357300	0.61961500
N	-2.96972000	0.89671100	0.60486400
C	-2.15418400	-0.08891600	0.09260000
C	-2.56885900	-1.52024200	0.11353000
O	-3.55601500	-1.91931700	0.71952900
C	-0.99902000	0.47648400	-0.43878100
N	0.12068700	-0.12919800	-1.03266000
H	0.53623700	0.40489100	-1.79014900
C	1.19091800	-0.64860900	-0.14792000
H	0.76861300	-1.53203800	0.35851800

N	1.63004200	0.35930400	0.82567600
H	0.85334300	0.57883700	1.44435300
N	2.31933800	-1.05191000	-0.97091100
H	2.48132500	-2.04922900	-0.90725900
N	-1.75019300	-2.37452500	-0.59328700
H	-2.10875400	-3.30743300	-0.73863500
H	-1.07862000	-1.99511500	-1.25121000
C	-0.20554000	2.88176000	-0.67151400
H	0.81216500	2.60729500	-0.38389800
H	-0.25595100	3.03189100	-1.75581800
H	-0.47828700	3.81683900	-0.17880900
C	3.55703000	-0.28441800	-0.78470300
H	3.39410200	0.72718400	-1.16760500
H	4.32530100	-0.73954500	-1.41672900
C	4.01602500	-0.20973200	0.68783100
H	4.65615900	0.67027700	0.82294200
H	4.61803000	-1.08790800	0.94905800
C	2.77636500	-0.13487200	1.60761700
H	2.94382200	0.54980700	2.44352300
H	2.56677900	-1.12839900	2.04229600

Desired product S5

N	-1.70115800	-0.19516600	0.03815800
C	-1.32348700	-1.51955100	0.16771900
H	-2.05688900	-2.30779800	0.27277600
N	-0.02690200	-1.66922900	0.16664100

C	0.49762700	-0.39278500	0.06134600
C	1.95081800	-0.14811700	-0.03168500
O	2.75701800	-0.95385200	-0.47122800
C	-0.53728600	0.53569900	-0.02406400
N	-0.56451700	1.90291700	-0.29845100
H	-1.09422000	2.47092400	0.35434400
H	0.36578100	2.28027500	-0.44232800
C	-3.05016700	0.32972000	-0.08830400
H	-3.35910500	0.86624000	0.81595900
H	-3.10486800	1.00798200	-0.94445700
H	-3.73657600	-0.50332600	-0.24870800
N	2.35457100	1.13852000	0.36323900
H	1.90676000	1.51342900	1.19140700
H	3.36397500	1.23400100	0.37364700

$TS_{S3\text{-}S6}$ (n=2)

N	2.78093200	-0.56814100	0.25801400
C	3.09407500	0.61151500	0.89090900
H	4.07564900	0.78962500	1.30987000
N	2.10055800	1.46609300	0.89654300
C	1.07527700	0.81763600	0.22108300
O	-0.88141800	2.20039000	0.66126600
N	0.84437800	-1.57158900	-0.67861100
C	1.46490200	-0.47718100	-0.16953200
C	-0.47412400	-1.48918800	-0.82773500
H	-0.97767300	-2.44222700	-1.03773100

C	-2.64816600	-0.53610200	-0.59057900
H	-3.14335600	0.36273900	-0.98674600
H	-3.02837700	-1.38817300	-1.17514000
C	-3.06911900	-0.71673100	0.87646100
H	-2.67414900	-1.67330500	1.23780500
H	-2.60243600	0.07646300	1.47889400
N	-4.53437000	-0.76325500	0.97690300
H	-4.82596400	-1.08106200	1.89662600
H	-4.93538100	0.16183600	0.84248200
C	-0.18516400	1.49620300	-0.01436200
N	-1.20505200	-0.38672200	-0.74333400
H	-0.72913600	0.99106600	-2.00478100
N	-0.32296300	1.87629600	-1.65757600
H	-0.96448800	2.66347100	-1.76086500
H	0.58163500	2.08050200	-2.08194700
C	3.60570900	-1.76037900	0.15444300
H	4.60490100	-1.52630000	0.52739000
H	3.17547600	-2.57563100	0.74272500
H	3.66991600	-2.08554500	-0.88640300

$TS_{S3\text{-}S6}$ (n=3)

N	2.12236800	-1.80981500	-0.08360800
C	3.46580100	-1.57264100	-0.25934800
H	4.17806700	-2.38154300	-0.35476300
N	3.74607900	-0.29513700	-0.30198000
C	2.53815000	0.35910500	-0.15157100

C	2.47763800	1.83960000	-0.23694900
O	3.41560800	2.56868900	0.06198400
N	0.13418900	-0.51188600	0.16937300
C	1.50848000	-0.57578400	0.00430400
C	-0.33561400	0.32025900	1.04168600
H	0.30241400	0.91253300	1.70449500
N	-1.66028500	0.53424700	1.20019600
H	-1.94773200	1.14904400	1.94666100
C	-2.68918800	-0.14006600	0.41559300
H	-2.39543700	-0.08614700	-0.63781800
H	-2.72221500	-1.20561900	0.68638900
C	-4.05583000	0.50972900	0.63727500
H	-4.01884100	1.55852900	0.31910500
H	-4.29597500	0.49092800	1.71014500
N	1.26631800	2.37071800	-0.65857300
H	0.64945900	1.80495000	-1.22540800
C	1.46684100	-3.09948600	0.05700700
H	1.16970900	-3.28075600	1.09484700
H	0.57547300	-3.13348900	-0.57313500
H	2.16326700	-3.87966000	-0.25643600
C	-5.18635600	-0.19573200	-0.12087700
H	-5.26385800	-1.23890600	0.23301200
H	-6.13081800	0.29420400	0.13776700
N	-5.01574300	-0.08206000	-1.57441700
H	-4.29883200	-0.71224800	-1.92255400
H	-5.87611900	-0.31169800	-2.06238300

H	1.29656200	3.35799400	-0.87546200

By-product S6 (n=2)

N	2.87503800	-0.22311700	0.16119000
C	3.03651500	1.14597200	0.24723400
H	4.01297000	1.58436300	0.40631900
N	1.91601600	1.81832400	0.11599000
C	0.95630700	0.84712800	-0.06416500
C	-0.46622800	0.97563300	-0.25919800
O	-1.15634400	1.98547300	-0.30782400
N	-1.07388900	-0.32550100	-0.40789000
N	0.91236700	-1.62455000	-0.18441700
C	1.53153200	-0.42379700	-0.03814000
C	-0.37572600	-1.50193500	-0.36381700
H	-0.97147600	-2.40074200	-0.49806700
C	-2.53204300	-0.35776700	-0.60773100
H	-2.78911400	0.49872300	-1.23488500
H	-2.79239000	-1.27296600	-1.14486700
C	-3.30601400	-0.28513000	0.71448400
H	-3.09867900	-1.18673100	1.30283500
H	-2.94426900	0.57898900	1.28985100
N	-4.74125300	-0.25360600	0.41900900
H	-5.29106400	-0.42520900	1.25520700
H	-5.01639600	0.65726000	0.05978000
C	3.89643200	-1.25369500	0.27167600
H	3.72095600	-1.87439300	1.15433400

H	3.88648700	-1.89148900	-0.61537400
H	4.87112600	-0.77089900	0.35822300

By-product S6 (n=3)

N	3.26851400	-0.30210400	0.30249700
C	3.46983500	1.05375500	0.47321200
H	4.44226500	1.44451900	0.74291800
N	2.39057800	1.77550600	0.27581600
C	1.41788500	0.85342800	-0.04110400
C	0.02459000	1.04948400	-0.35650900
O	-0.62022100	2.08745600	-0.41484700
N	-0.61260900	-0.21845600	-0.62703500
N	1.29783200	-1.60528200	-0.29396800
C	1.94308800	-0.43894600	-0.02896800
C	0.03665700	-1.42160100	-0.58117400
H	-0.57529900	-2.28911000	-0.81367600
C	-2.05308400	-0.18598000	-0.93800400
H	-2.23261000	0.73434900	-1.49774600
H	-2.26994900	-1.03662800	-1.59207600
C	-2.92823700	-0.22124400	0.31961900
H	-2.72925000	-1.14958100	0.87428900
H	-2.66235100	0.61301500	0.97544900
C	4.23737800	-1.37700400	0.45738300
H	3.97906500	-2.00739700	1.31269300
H	4.25875700	-1.99529400	-0.44303500
H	5.22341600	-0.93764900	0.61748400

C	-4.41969200	-0.13722600	-0.01808700
H	-4.67339500	-0.91981900	-0.75658800
H	-4.62477200	0.82745200	-0.49695100
N	-5.22560800	-0.20517400	1.20470500
H	-6.20485500	-0.01652500	1.01203300
H	-5.17073400	-1.12640200	1.63167700