Supporting Information

Catalytic Mechanisms for Cofactor-Free Oxidase-Catalyzed Reactions: Reaction Pathways of Uricase-Catalyzed Oxidation and Hydration of Uric Acid

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Part 1. The optimized structures of TS1$^{t\prime}$ and INT1$^{t\prime}$and the corresponding free energy profile

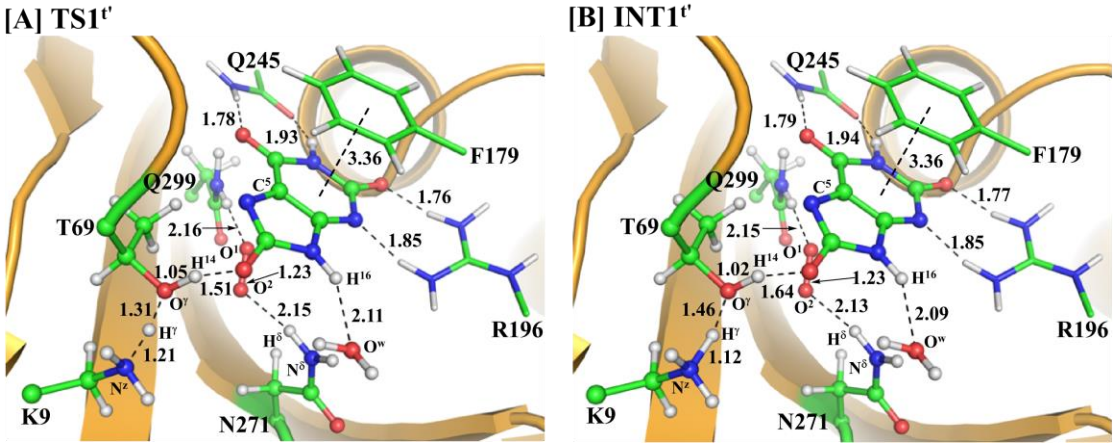


Figure S1. The QM/MM-optimized structures of TS1$^{t\prime}$ (A) and INT1$^{t\prime}$ (B) for uricase-catalyzed oxidation of 8-HX. The color scheme and division of the QM/MM system are teh same as those in Figure 1.

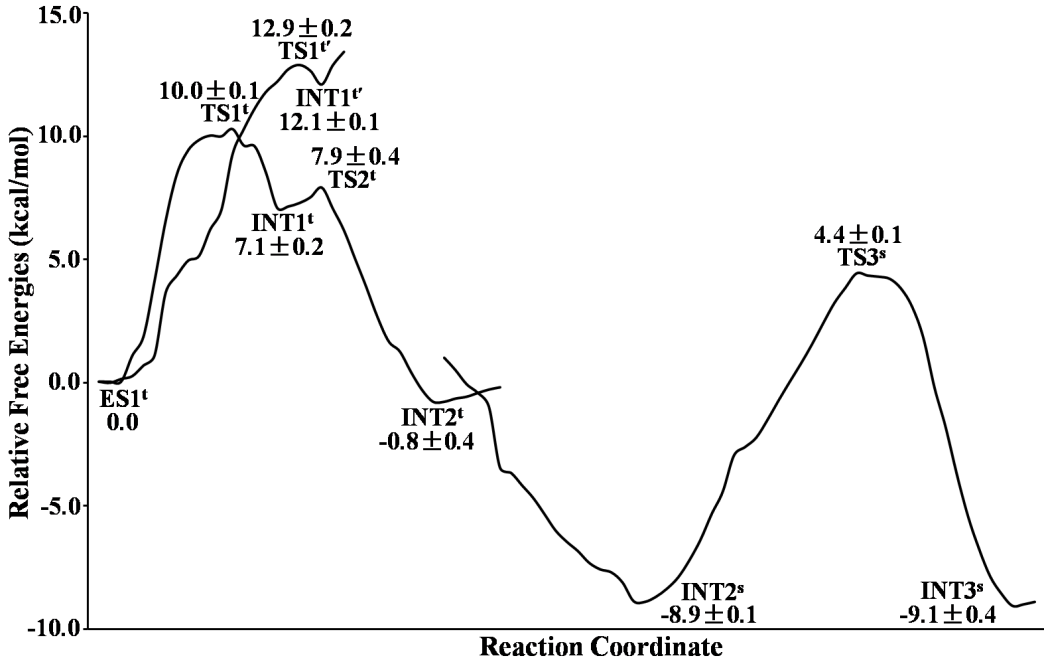


Figure S2. Free energy profiles for uricase-catalyzed oxidation of 8-HX including that of hypothetical pathway associated with TS1$^{t\prime}$ and INT1$^{t\prime}$. The relative free energies were determined with the zero-point and thermal corrections for the QM subsystem. The QM/MM-FE calculations were performed at the B3LYP/6-31+G*:AMBER level for each QM/MM-optimized geometry along the reaction path.

Part 2. Alternative reaction pathways without the participation of residues Lys9 and Thr69 in the chemical reaction process

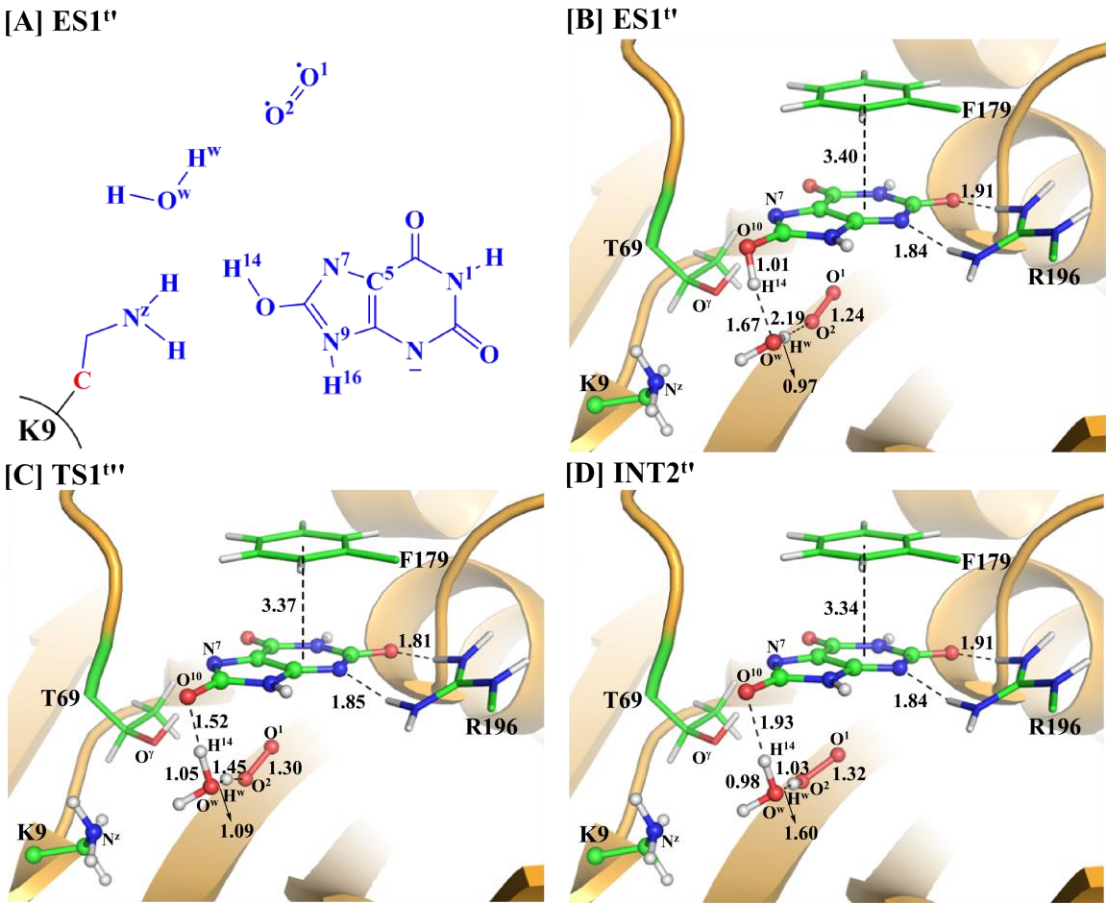


Figure S3. (A) Division of the QM/MM system for the reaction pathway assoicated with ES1ᵗ′. (B-D) Optimized structures of ES1ᵗ′, TS1ᵗ′′ and INT2ᵗ′. The color scheme and division of the QM/MM system are the same as those in Figure 1.

For the oxidation stage, $R_{O10\text{-}H14} + R_{Ow\text{-}Hw} - R_{Ow\text{-}H14} - R_{O2\text{-}Hw}$ was set as the reaction coordinate. As shown in Figure S3 of Supporting Information, $R_{O10\text{-}H14}$ changes from 1.010 Å in ES1ᵗ′ to 1.519 Å in TS1ᵗ′′ and to 1.931 Å in INT2ᵗ′, $R_{Ow\text{-}Hw}$ changes from 0.973 Å in ES1ᵗ′ to 1.087 Å in TS1ᵗ′′ and to 1.604 Å in INT2ᵗ′, $R_{Ow\text{-}H14}$ shortens from 1.670 Å in ES1ᵗ′ to 1.045 Å in TS1ᵗ′′ and to 0.981 Å in INT2ᵗ′, and $R_{O2\text{-}Hw}$ shortens from 2.190 Å in ES1ᵗ′ to 1.451 Å in TS1ᵗ′′ and to 1.034 Å INT2ᵗ′. For the hydration stage, $R_{Ow1\text{-}Hw1} + R_{Ow2\text{-}Hw2} - R_{C5\text{-}Ow1} - R_{Ow2\text{-}Hw1} - R_{N7\text{-}Hw2}$ was set as the reaction coordinate for this reaction stage. As shown in Figure S4 of Supporting Information, $R_{Ow1\text{-}Hw1}$ changes from 0.984 Å in ES2ˢ′′ to 1.183 Å in TS4ˢ′′ and to

1.897 Å in EP$^{s\prime\prime}$, $R_{Ow2\text{-}Hw2}$ changes from 0.990 Å in ES2$^{s\prime\prime}$ to 1.592 Å in TS4$^{s\prime\prime}$ and to 2.101 Å in EP$^{s\prime\prime}$, $R_{C5\text{-}Ow1}$ shortens from 2.944 Å in ES2$^{s\prime\prime}$ to 2.264 Å in TS4$^{s\prime\prime}$ and to 1.478 Å in EP$^{s\prime\prime}$, $R_{Ow2\text{-}Hw1}$ shortens from 1.853 Å in ES2$^{s\prime\prime}$ to 1.256 Å in TS4$^{s\prime\prime}$ and to 0.979 Å in EP$^{s\prime\prime}$, and $R_{N7\text{-}Hw2}$ shortens from 1.783 Å in ES2$^{s\prime\prime}$ to 1.078 Å in TS4$^{s\prime\prime}$ and then to 1.014 Å in EP$^{s\prime\prime}$.

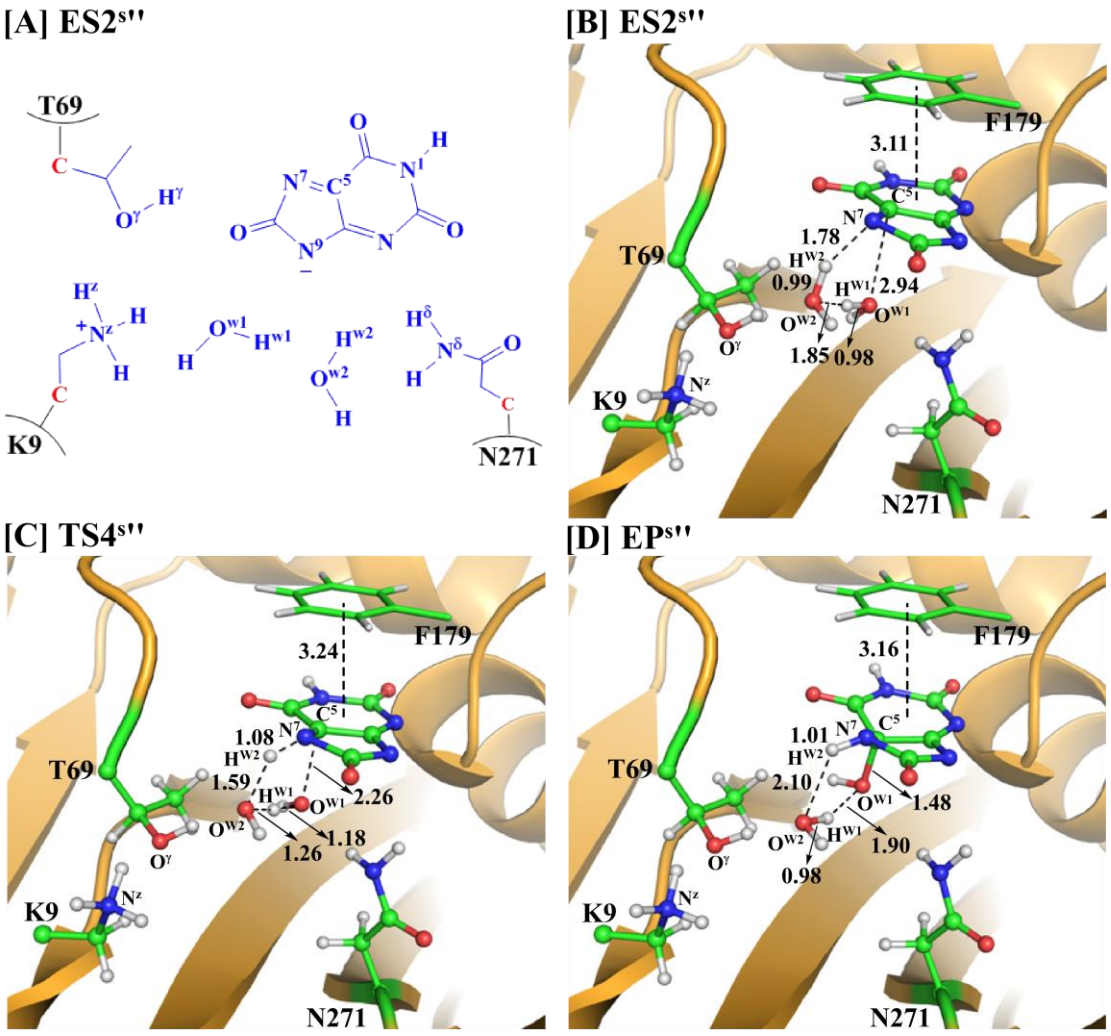


Figure S4. (A) Division of the QM/MM system for the reaction pathway assoicated with ES2$^{s\prime\prime}$. (B-D) Optimized structures of ES2$^{s\prime\prime}$, TS4$^{s\prime\prime}$ and EP$^{s\prime\prime}$. The color scheme and division of the QM/MM system are the same as those in Figure 1.

Part 3. The calculated results with the presence of residue Phe179 in the QM part

We have also recalculated the energy barrier of the first reaction step with the presence of residue Phe179 in the QM part. The reaction coordinate is the same with that pathway *via* transition state $TS1^{t}$. As shown in Figure S5, The key structures are similar to those depicted in Figure 4, and the energy barrier *via* $TS1^{Phe}$ (10.3 kcal/mol, Figure S6) has a tiny difference with that *via* $TS1^{t}$ (10.0 kcal/mol), indicating the set of QM part without residue Phe179 should be adequate for this enzymatic reaction.

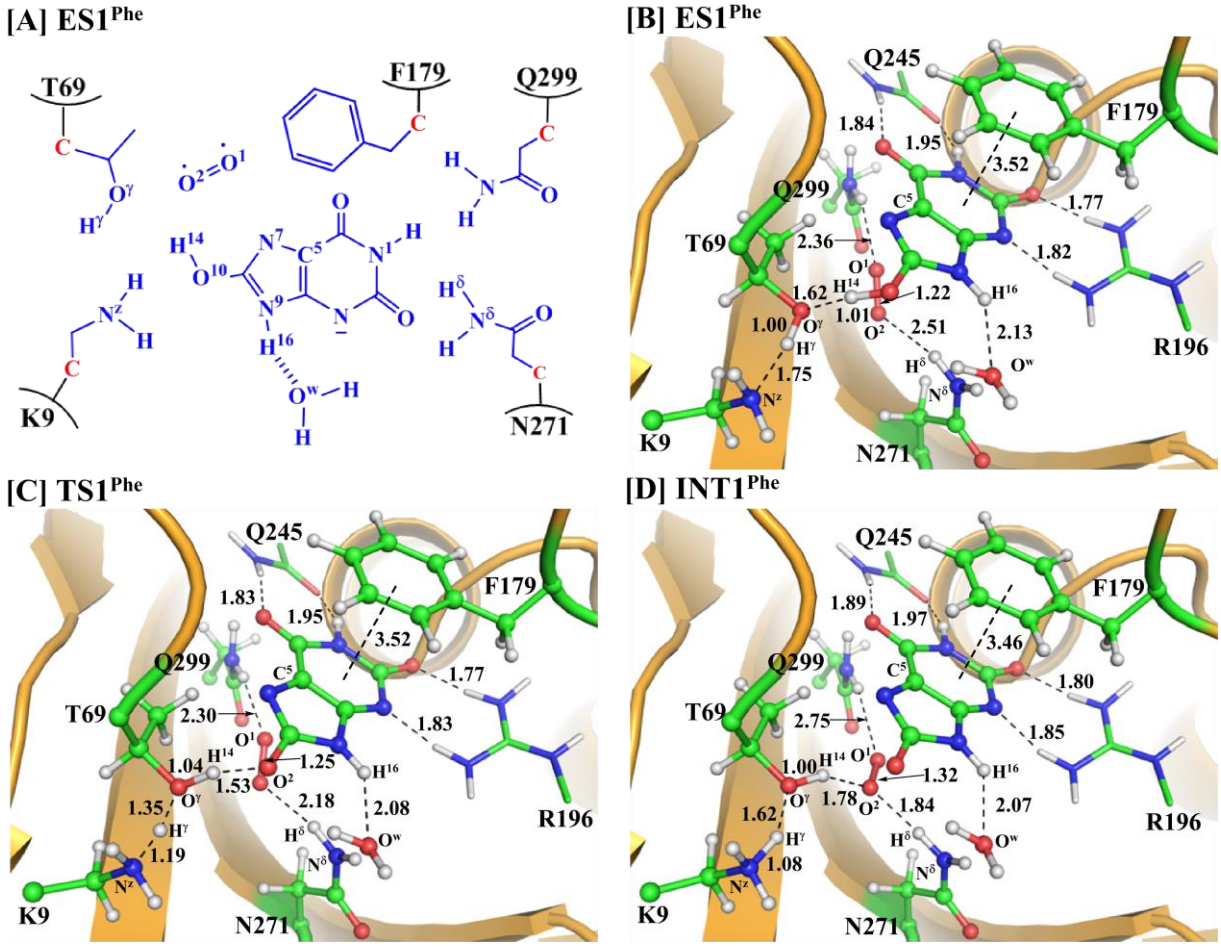


Figure S5. (A) Division of the QM/MM system for the reaction pathway assoicated with $ES1^{Phe}$. (B-D) Optimized structures of $ES1^{Phe}$, $TS1^{Phe}$, and $INT1^{Phe}$. The color scheme and division of the QM/MM system are the same as those in Figure 1.

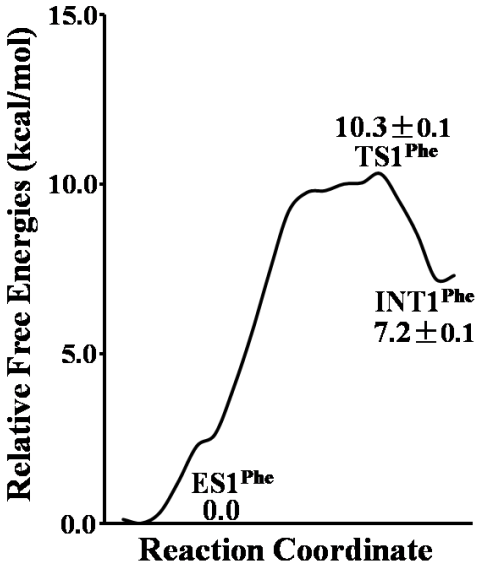


Figure S6. Free energy profile for the pathway associated with transition state $TS1^{Phe}$.

Part 4. List of the Cartesian coordinates of the key stationarary points involved in the possible pathways

ES1^t

F	62.81106500	55.59937100	50.59215600
C	62.93433100	57.12356400	50.60118600
H	62.46383300	57.55927000	49.70837800
H	62.38301200	57.51101900	51.46786800
N	64.26255500	57.69314800	50.65175100
H	64.66549100	57.84752800	49.72413500
H	63.96214000	58.91857900	51.82921400
H	64.90721100	57.17359300	51.24654600
F	64.38383400	57.98841200	54.41705500
C	63.26703300	58.74347600	53.70068500
H	62.57706500	58.00464000	53.26956900
C	62.45392000	59.67570800	54.58911900
H	63.05622000	60.49893400	54.98265500
H	61.62471100	60.10855000	54.02069200
H	62.02620400	59.11876000	55.43103200
O	63.77413100	59.51881500	52.61280200
H	65.23345300	60.24187200	52.64794900
F	60.32212900	63.56265500	48.06797200
C	61.39110500	63.24869400	49.12212100
H	61.15789400	63.69949800	50.10112300
H	61.45601100	62.16639200	49.33905800
C	62.79299100	63.69573200	48.78555200
O	63.06516700	64.17046200	47.67851700
N	63.69868800	63.53579400	49.76789100
H	64.69761300	63.61630000	49.57575400
H	63.42038400	63.14356200	50.66023000
F	56.30115800	64.07602700	56.10222400
C	57.78551600	64.13606300	56.49448800
H	58.05865800	65.17382700	56.77166100
H	57.99954700	63.53719500	57.39390800
C	58.78974400	63.76476000	55.40875000
O	58.50921900	63.83518800	54.21264800
N	60.00411500	63.34831700	55.84968400
H	60.73301500	63.22250900	55.16029200
H	60.32624600	63.48339400	56.80078300
N	63.42641900	65.07774900	55.49542700
H	62.81627400	65.51760400	56.18703300

C	63.92823700	65.88904400	54.46742700
O	63.67764900	67.11222700	54.49500000
N	64.64893800	65.34125000	53.46158300
C	64.89051300	64.04067300	53.61180700
N	65.56760400	63.22859100	52.72437600
H	66.02575800	63.49839500	51.85847700
C	65.53912000	61.95465400	53.27125000
O	65.99421300	60.90621600	52.56603200
N	64.94215300	61.89853700	54.42943500
C	64.49686400	63.18816100	54.65160800
C	63.65812300	63.70629600	55.68592200
O	63.13515500	63.08435900	56.62328000
O	61.85836500	62.54818400	52.18599900
O	61.96954400	62.85612100	53.37174900
O	66.60684100	63.18164800	49.83864800
H	66.54637900	62.23811200	50.06503800
H	67.34052900	63.22431200	49.17057600

TS1^{t}

F	62.82446300	55.63028000	50.59515400
C	62.92517600	57.14998900	50.61867800
H	62.49599600	57.58353800	49.71012400
H	62.36841800	57.54539100	51.47215200
N	64.27918400	57.75704300	50.73280600
H	64.64629000	58.04889900	49.81487100
H	64.14341600	58.65766600	51.56286000
H	64.95692700	57.13894600	51.18714400
F	64.38318300	57.99386800	54.42944800
C	63.29552900	58.76272500	53.69627800
H	62.58265800	58.04724100	53.26634200
C	62.50941400	59.74623300	54.54839100
H	63.13340600	60.56492100	54.91842600
H	61.69396200	60.18465700	53.96676700
H	62.06925700	59.21919400	55.40394100
O	63.82490200	59.44218900	52.52750800
H	64.67183100	60.03960000	52.69805700
F	60.31555800	63.56362600	48.08606200
C	61.37610500	63.21517900	49.13950400
H	61.13743800	63.62115600	50.13664900
H	61.43854600	62.12451700	49.31902300
C	62.78293100	63.66567500	48.82393000

O	63.07530500	64.13970000	47.71776300
N	63.66346800	63.49338300	49.82314300
H	64.66503400	63.58029600	49.65211800
H	63.35696000	63.13149300	50.72468600
F	56.30919200	64.07089500	56.10695700
C	57.79708800	64.12034500	56.49440900
H	58.07290600	65.15081300	56.79439100
H	58.01909200	63.50230000	57.37915100
C	58.78405400	63.77222600	55.38301200
O	58.45734300	63.84055700	54.19793200
N	60.02182700	63.37942400	55.77367000
H	60.71708300	63.25545700	55.04464300
H	60.38172100	63.51420400	56.71158800
N	63.44446700	65.08673500	55.51325000
H	62.83437900	65.52623000	56.20463900
C	63.92989000	65.89118000	54.47644600
O	63.67962200	67.11588800	54.49747200
N	64.64519400	65.34110100	53.46694200
C	64.88108700	64.04054700	53.60627900
N	65.54111300	63.23330800	52.71782800
H	65.98458300	63.51801000	51.85152200
C	65.50643700	61.92003900	53.23246600
O	65.90457900	60.90765100	52.55001600
N	64.92408400	61.89897100	54.43392300
C	64.49420700	63.18080100	54.65535800
C	63.67515200	63.71402000	55.70068100
O	63.16997100	63.09910100	56.65393100
O	62.02245000	62.49860300	52.24097000
O	62.06239500	62.96613900	53.40816300
O	66.58894700	63.17754500	49.86490600
H	66.57691500	62.26908100	50.21412900
H	67.31882800	63.19109900	49.19615200

INT1^{t}

F	62.83805400	55.75139700	50.62289500
C	62.83199300	57.26937300	50.73539400
H	62.33194400	57.71586700	49.87269100
H	62.31588300	57.59295000	51.64112200
N	64.15330600	57.98111300	50.80351400
H	64.46411800	58.30211600	49.87250700
H	63.99066800	58.80558500	51.53321100

H	64.89406900	57.42382700	51.24300900
F	64.30513200	58.02991800	54.47102100
C	63.09862500	58.76852600	53.87870600
H	62.38620700	57.99397200	53.53913700
C	62.35504000	59.68608100	54.84623700
H	62.99890900	60.48103900	55.23776500
H	61.51651500	60.17744500	54.34055900
H	61.96176500	59.11215700	55.69385000
O	63.47197000	59.51438900	52.72909600
H	63.18644600	60.51929500	52.69093000
F	60.27268600	63.59160700	48.17748300
C	61.32682900	63.26109300	49.24425000
H	61.06839300	63.63678500	50.24959400
H	61.42468000	62.17241300	49.41190200
C	62.71576200	63.77230400	48.94075300
O	62.96511900	64.34677000	47.86778200
N	63.60874200	63.54544200	49.91476000
H	64.59806000	63.68236400	49.72248600
H	63.33253000	63.01246200	50.75916100
F	56.32323400	64.06925800	56.11540400
C	57.83554400	64.10706300	56.40273900
H	58.13263000	65.12751300	56.71600100
H	58.11551900	63.46095700	57.24989800
C	58.73971700	63.79360900	55.20845000
O	58.32791200	63.92278700	54.05664700
N	59.99964900	63.37574000	55.48860600
H	60.61889700	63.15314200	54.71326300
H	60.39029400	63.35519800	56.42167500
N	63.44512600	64.92606400	55.44181200
H	62.82184500	65.33451100	56.14345000
C	63.92322400	65.78168200	54.44709900
O	63.67278700	66.99684900	54.51960300
N	64.65574800	65.28697600	53.40938000
C	64.96922100	64.01250300	53.51104100
N	65.73222200	63.29525300	52.64919400
H	66.13876600	63.62069300	51.77660700
C	65.81469600	61.96303400	53.12821200
O	66.39022200	61.06085300	52.51174600
N	65.14978800	61.88101500	54.34412100
C	64.61915500	63.09085800	54.55247900
C	63.73469300	63.56347000	55.59666500

O	63.24858600	62.90985600	56.52791400
O	62.77630700	61.92604300	52.18249800
O	61.62938300	62.37676500	52.70001900
O	66.63001200	63.30900000	49.84334900
H	66.63716800	62.39336300	50.17435200
H	67.37200800	63.34221000	49.18777500

TS2^{t}

F	62.83839900	55.75202800	50.62162000
C	62.82196600	57.27176900	50.72848600
H	62.33358200	57.71078500	49.85468600
H	62.27658100	57.58834800	51.62052900
N	64.12829300	57.99341000	50.82594300
H	64.44820300	58.32569500	49.90323500
H	63.94132000	58.82881300	51.61119400
H	64.86913300	57.43533600	51.26299000
F	64.30707700	58.02907700	54.46945200
C	63.10913900	58.77057800	53.86535800
H	62.39843600	58.00012500	53.51555000
C	62.35966800	59.68759000	54.82804400
H	63.00103500	60.48260000	55.22346400
H	61.52317100	60.17811700	54.31899800
H	61.96410600	59.11126700	55.67304500
O	63.50043500	59.52424500	52.72327300
H	63.18007500	60.54936000	52.63872900
F	60.27313400	63.59295800	48.17987000
C	61.32921500	63.25916900	49.24325900
H	61.07420100	63.63758400	50.24849900
H	61.42455700	62.17030900	49.41084900
C	62.71834200	63.76804000	48.93570100
O	62.96278700	64.34971200	47.86618700
N	63.61816500	63.53302700	49.90213300
H	64.60693100	63.67112500	49.70673900
H	63.34946400	62.99780100	50.74405700
F	56.32074400	64.06794200	56.11558800
C	57.83157400	64.10381000	56.40713500
H	58.12877700	65.12364000	56.72197000
H	58.10819700	63.45670800	57.25449000
C	58.74019800	63.79126100	55.21690400
O	58.33532300	63.91856100	54.06253000
N	59.99963400	63.37638700	55.50459400

H	60.62552600	63.16665000	54.73239700
H	60.38769200	63.36161100	56.43891400
N	63.43714800	64.92804000	55.43750400
H	62.81413600	65.33701500	56.13920000
C	63.91644300	65.78292500	54.44263100
O	63.66753200	66.99823200	54.51453200
N	64.64822200	65.28715800	53.40505300
C	64.96741100	64.01443000	53.51116800
N	65.73294000	63.29747300	52.65204300
H	66.14070200	63.62197600	51.77963800
C	65.82565600	61.96806300	53.13934600
O	66.40710500	61.06741500	52.52808500
N	65.16062400	61.88812200	54.35568300
C	64.62191100	63.09535300	54.55674700
C	63.73301500	63.56725100	55.59751700
O	63.24723000	62.91380100	56.52875600
O	62.80128400	61.87718400	52.17863300
O	61.65146100	62.29471000	52.71705400
O	66.63204700	63.31247500	49.84204500
H	66.64383600	62.39642300	50.17174100
H	67.37324500	63.34830500	49.18537600

INT2^{t}

F	62.83716300	55.72653000	50.60929900
C	62.87331200	57.25470600	50.71129900
H	62.34256500	57.70354800	49.86124300
H	62.33402200	57.55587800	51.61842600
N	64.15630100	57.91999400	50.74463300
H	64.51763700	58.13124900	49.81127800
H	63.83223300	59.10864000	52.02501500
H	64.86110300	57.43473200	51.30021100
F	64.32277800	58.00989800	54.45966400
C	63.10995200	58.73131300	53.87602700
H	62.42820700	57.97056900	53.46652200
C	62.33308000	59.58284500	54.87594700
H	62.94548400	60.39689200	55.27945100
H	61.45633100	60.03358600	54.39978700
H	61.98657700	58.96835600	55.71406100
O	63.47079400	59.60963500	52.81600300
H	62.95746100	61.07051200	52.56783200
F	60.28403400	63.58767400	48.15627900

C	61.36513200	63.27043900	49.19694100
H	61.12277300	63.65322600	50.20380900
H	61.48477800	62.18288300	49.35511200
C	62.73613100	63.80798400	48.85566800
O	62.93581500	64.38632400	47.78138000
N	63.67989000	63.61436600	49.79385100
H	64.66739800	63.72703800	49.56843000
H	63.44764200	63.10099100	50.64021000
F	56.32218700	64.06686000	56.10928700
C	57.82962000	64.09346500	56.41088900
H	58.13382200	65.11511000	56.71245400
H	58.09087000	63.45630200	57.27010900
C	58.75951200	63.75734800	55.24708800
O	58.39874400	63.87279500	54.07749800
N	60.00408000	63.32999300	55.58507500
H	60.66416800	63.15564300	54.83728600
H	60.37145300	63.35521300	56.52765600
N	63.42890300	64.91981800	55.41825600
H	62.80546100	65.33255200	56.11743800
C	63.91744700	65.77088500	54.42382900
O	63.66580300	66.98528700	54.49152400
N	64.65114000	65.26769900	53.38855900
C	64.97645900	63.99649500	53.50470000
N	65.73027800	63.26351700	52.64541500
H	66.16797900	63.57939000	51.78314100
C	65.84088400	61.94080500	53.16267200
O	66.43249200	61.03687900	52.57401300
N	65.16472600	61.87764000	54.37467600
C	64.62838300	63.08775600	54.55935300
C	63.72607900	63.56115800	55.58784100
O	63.22400500	62.90723200	56.50948900
O	62.69031100	62.00891600	52.23572000
O	61.51239800	62.30627700	52.77803200
O	66.63210700	63.29547500	49.80448800
H	66.61773500	62.36190000	50.08008400
H	67.38293600	63.34109700	49.15551400

TS1$^{t'}$

F	62.82462300	55.63072900	50.59512300
C	62.92696600	57.15011100	50.61756500
H	62.49906500	57.58365100	49.70847400

H	62.37344500	57.54833300	51.47151600
N	64.28356300	57.75626700	50.73073700
H	64.65003400	58.05034700	49.81292900
H	64.15084000	58.64623100	51.54670500
H	64.96175000	57.13786100	51.18431000
F	64.38299800	57.99407800	54.42925500
C	63.29495400	58.76332600	53.69563900
H	62.58084000	58.04648300	53.26849300
C	62.50823900	59.74489200	54.55057500
H	63.13154800	60.56557200	54.91773500
H	61.68907700	60.17937000	53.97076800
H	62.07118200	59.21793700	55.40779500
O	63.82147800	59.44174400	52.52836100
H	64.66971900	60.03958500	52.69718900
F	60.31631700	63.56379400	48.08628200
C	61.37863000	63.21793200	49.13902300
H	61.14213500	63.63044900	50.13403800
H	61.43958000	62.12811600	49.32349000
C	62.78598700	63.66535800	48.81914700
O	63.07418300	64.14091300	47.71296500
N	63.67193300	63.48984500	49.81307200
H	64.67359800	63.57578700	49.63971400
H	63.37217600	63.12740900	50.71534400
F	56.30889400	64.07107500	56.10688500
C	57.79592400	64.12267200	56.49655300
H	58.07061100	65.15473700	56.79224700
H	58.01577400	63.50881900	57.38472000
C	58.78758200	63.77008400	55.39132700
O	58.46887900	63.83378500	54.20376800
N	60.02238800	63.37858500	55.79276700
H	60.72512600	63.25771000	55.07178000
H	60.37682600	63.51991800	56.73190000
N	63.44204800	65.08855300	55.50991400
H	62.83423000	65.52845900	56.20283700
C	63.92931400	65.89384000	54.47433400
O	63.67973900	67.11949100	54.49706300
N	64.64237900	65.34317800	53.46520400
C	64.87745200	64.04088300	53.60624700
N	65.53354700	63.23293000	52.71434400
H	65.98578800	63.52128800	51.85410400
C	65.50004200	61.91879700	53.22870400

O	65.89956100	60.90654700	52.54325900
N	64.91697200	61.89678000	54.42754500
C	64.48999900	63.18233200	54.65287300
C	63.66997200	63.71436400	55.69575500
O	63.15824600	63.09946400	56.64688100
O	62.01187700	62.49767100	52.25267800
O	62.04249700	62.95857300	53.39264800
O	66.59180500	63.17543000	49.86527300
H	66.58493800	62.27170300	50.22721000
H	67.32295400	63.18614100	49.19780100

INT1$^{t'}$

F	62.82272700	55.62302400	50.59698700
C	62.93563100	57.13987600	50.61792200
H	62.49922400	57.57720300	49.71569000
H	62.41598100	57.55047200	51.48560700
N	64.31013500	57.73899600	50.70259200
H	64.66127500	58.03574300	49.77741900
H	64.20433100	58.58258600	51.43933600
H	64.99437500	57.12041200	51.14861700
F	64.38576000	57.99151400	54.42758300
C	63.27678000	58.75806600	53.71772300
H	62.55356000	58.03799000	53.30701900
C	62.50257300	59.73166900	54.59617000
H	63.12935000	60.55349200	54.95521200
H	61.67359900	60.16892700	54.03211700
H	62.08048400	59.20093400	55.45884700
O	63.77196800	59.43382900	52.54618600
H	64.57610800	60.03498000	52.72954500
F	60.31894000	63.56093400	48.07535000
C	61.37851200	63.22622900	49.13493600
H	61.13688800	63.64578900	50.12563200
H	61.43993500	62.13810800	49.32895800
C	62.78728700	63.67113400	48.81980300
O	63.08425200	64.12848700	47.70792500
N	63.66448900	63.51292600	49.82395800
H	64.66767100	63.58753300	49.65407000
H	63.35691800	63.15932900	50.72797200
F	56.30870400	64.07311100	56.10737100
C	57.79636900	64.12785600	56.49565000
H	58.06881700	65.15962700	56.79446200

H	58.01964300	63.51152500	57.38131600
C	58.78546500	63.78060800	55.38583200
O	58.45959600	63.84479900	54.20006000
N	60.02343500	63.39309400	55.77943900
H	60.72138000	63.26655600	55.05413300
H	60.38217300	63.52832800	56.71770900
N	63.44466200	65.08058900	55.50967600
H	62.83721700	65.51512400	56.20617700
C	63.93031800	65.89432600	54.48104700
O	63.68023700	67.12000300	54.51049800
N	64.64528700	65.35156100	53.46972900
C	64.88164900	64.04896800	53.60055300
N	65.54515000	63.25518300	52.70429400
H	65.99565800	63.55460400	51.84722700
C	65.51647600	61.93159600	53.20074300
O	65.92619900	60.93591400	52.50904200
N	64.92548800	61.89659900	54.40067000
C	64.49238100	63.17757000	54.63771800
C	63.67083600	63.70353800	55.68416300
O	63.15620700	63.08624000	56.63297800
O	62.00001800	62.52110300	52.23737600
O	62.03922000	62.95508800	53.38760200
O	66.58414500	63.16778800	49.87512100
H	66.57859200	62.27667800	50.26908500
H	67.31795100	63.16355100	49.21153500

INT2^{s}

F	62.90413700	55.66081000	50.55955800
C	62.97570800	57.18622100	50.71573400
H	62.42010400	57.66142200	49.89665800
H	62.47414400	57.46921100	51.64954700
N	64.26007400	57.84466200	50.71899300
H	64.66694400	57.90581900	49.78035600
H	63.75674100	59.02449500	52.20861100
H	64.93743800	57.41634700	51.35251900
F	64.49099300	57.82375300	54.49334400
C	63.17870300	58.44300900	54.02887100
H	62.54820200	57.63913200	53.61818000
C	62.40720900	59.13233400	55.15143100
H	62.97229600	59.97534700	55.56295600
H	61.44743000	59.51992000	54.79883000

H	62.21231800	58.42128200	55.95764900
O	63.35618200	59.42014900	53.01975100
H	62.61618500	61.00268900	53.51315900
F	60.22302000	63.65822200	47.83136300
C	61.42655700	63.46947500	48.76089800
H	61.23548700	63.86085100	49.77741800
H	61.69510300	62.41523900	48.92571100
C	62.64783300	64.21649100	48.27813600
O	62.53383100	65.06584800	47.38323300
N	63.81143500	63.93047600	48.88922400
H	64.64504300	64.37444900	48.52857200
H	63.88485500	63.14674100	49.55089100
F	56.40915800	64.05761800	56.04449400
C	57.91507800	64.08705600	56.35685100
H	58.22629000	65.11967000	56.61209100
H	58.16282900	63.48908200	57.24883800
C	58.85264500	63.68255900	55.22166300
O	58.52239800	63.78622000	54.04133200
N	60.07079200	63.22427400	55.60127400
H	60.70567200	62.85977700	54.89822500
H	60.36366800	63.17146300	56.56655200
N	63.34417700	64.96579000	55.40073200
H	62.77266800	65.43339200	56.11033700
C	63.89132100	65.75746000	54.38433000
O	63.63754800	66.96470300	54.38147900
N	64.74220800	65.22766800	53.44066900
C	64.93554600	63.93786300	53.50499900
N	65.81301400	63.17128100	52.88264200
H	66.56219200	63.48497300	52.27924100
C	65.72123700	61.76384700	53.46521700
O	66.46380300	60.89936000	53.02982200
N	64.77873600	61.76579600	54.40907600
C	64.08883700	62.95777200	54.30413000
C	63.48523200	63.59318500	55.54099300
O	63.08493200	62.99054100	56.52094700
O	62.90325400	62.88685800	53.32864500
O	62.04748700	61.79408800	53.71298900
O	63.55270800	61.78926100	50.73262600
H	63.32950200	62.18963800	51.59837700
H	64.19677100	61.09222300	50.93748000

TS3^{s}

F	62.90568300	55.66611400	50.56659600
C	62.98433400	57.18625300	50.75263800
H	62.41481800	57.67741000	49.95397600
H	62.50209200	57.45234200	51.70147300
N	64.27061100	57.83901000	50.74632100
H	64.66657400	57.91012200	49.80367900
H	63.84341800	59.06142300	52.21722100
H	64.95274400	57.39803600	51.36637900
F	64.48948900	57.83256400	54.50793200
C	63.21096500	58.50231400	54.02292600
H	62.56096500	57.72911100	53.58615300
C	62.43098600	59.21081200	55.12847200
H	62.99824300	60.04896600	55.54959500
H	61.48266400	59.60918200	54.75810500
H	62.21355200	58.50978300	55.93907400
O	63.47314500	59.48482100	53.03227500
H	62.51071200	61.01468500	53.26821200
F	60.23238000	63.66057900	47.87061800
C	61.45875800	63.46706100	48.77100900
H	61.29742700	63.85277800	49.79340300
H	61.72967100	62.40948000	48.92405600
C	62.66860200	64.21005800	48.24167300
O	62.51242700	65.09345100	47.38071300
N	63.85487900	63.86219800	48.75068800
H	64.66576000	64.36767500	48.41871000
H	63.93807700	63.17772300	49.53662100
F	56.41434100	64.04803300	56.04454200
C	57.92737600	64.05971500	56.33346400
H	58.24958800	65.08356400	56.60815600
H	58.18750700	63.44032500	57.20678900
C	58.84617500	63.68248000	55.16849900
O	58.48014600	63.79653600	54.00105700
N	60.09157500	63.25165700	55.50199100
H	60.69918500	62.89182600	54.76828500
H	60.38725500	63.13339300	56.46086800
N	63.37143900	64.90298400	55.49713900
H	62.72072000	65.37220400	56.13604100
C	63.84978500	65.64057000	54.39743900
O	63.60427000	66.84827600	54.35916400
N	64.58053600	65.03926400	53.39190600

C	64.87408500	63.78216500	53.57838100
N	65.64100600	62.96727300	52.79315700
H	65.28180500	62.79585500	51.80232800
C	65.82049500	61.76461300	53.52413800
O	66.38602600	60.77829000	53.11945000
N	65.19551600	61.87175700	54.82869000
C	64.59787000	63.00674500	54.80085100
C	63.68851500	63.59571100	55.81134400
O	63.26361300	63.00423600	56.79019700
O	62.72029000	62.89936500	52.92509700
O	61.91198300	61.79375300	53.37402500
O	63.96849700	62.27520800	50.92728000
H	63.20699000	62.54855000	51.93417600
H	64.06696900	61.31443700	50.83033200

INT3^{s}

F	62.90983000	55.67462200	50.56684000
C	62.99913700	57.19814400	50.74782300
H	62.43125600	57.68790300	49.94665000
H	62.52026400	57.47115900	51.69589700
N	64.28618200	57.85554500	50.73690500
H	64.69009200	57.89938800	49.79575600
H	63.82816000	59.10031000	52.25297200
H	64.96495100	57.43522700	51.37512100
F	64.48834000	57.83297900	54.51096700
C	63.20434800	58.50392000	54.04150200
H	62.55536900	57.73530200	53.59463800
C	62.42795700	59.19667600	55.15981500
H	62.99838100	60.03041400	55.58734800
H	61.47485400	59.59439300	54.79991800
H	62.21516200	58.48775300	55.96376200
O	63.45174000	59.50778200	53.06884000
H	62.40352000	61.02835700	53.38220100
F	60.24077800	63.66152000	47.86860800
C	61.47280500	63.48133600	48.76590800
H	61.30452600	63.85171000	49.79344300
H	61.76613800	62.42654100	48.90047500
C	62.66774900	64.25848000	48.25141900
O	62.49833800	65.13802800	47.39466200
N	63.86885400	63.96564900	48.77592000
H	64.66833300	64.47901100	48.42857700

H	64.01718200	63.19035900	49.42990100
F	56.41382300	64.04947700	56.04223500
C	57.92450700	64.06380300	56.33847300
H	58.24421700	65.08877900	56.61157100
H	58.17906900	63.44674600	57.21492600
C	58.84777200	63.67989400	55.18139400
O	58.48878900	63.78876800	54.01069000
N	60.08570200	63.24047400	55.52614000
H	60.69401800	62.87605200	54.79628000
H	60.39085800	63.15914000	56.48605400
N	63.40394600	64.92846700	55.53878300
H	62.74203500	65.39798200	56.16510800
C	63.89815600	65.66981800	54.43474300
O	63.61985000	66.87403900	54.40001400
N	64.64219600	65.09026800	53.44452200
C	64.99465800	63.83129600	53.62404200
N	65.71526500	63.05014000	52.82179600
H	64.89988500	62.44078300	51.35921500
C	65.85103700	61.84827700	53.51799600
O	66.39114600	60.83527900	53.12479600
N	65.17576600	61.88779000	54.84678300
C	64.63972600	63.04328100	54.84877000
C	63.71240300	63.62343300	55.84918500
O	63.26301800	63.01825000	56.81196000
O	62.48907300	62.86595600	52.83641800
O	61.71476400	61.73148800	53.30757500
O	64.19832800	62.00829500	50.79134200
H	62.87418800	62.52349300	51.99476900
H	64.45743100	61.07205900	50.74468000

ES2^{s}

F	63.79252000	54.33911000	50.01926000
C	63.94357000	55.83643000	49.81311000
H	63.58726000	56.12735000	48.82523000
H	63.40950000	56.40602000	50.57370000
N	65.37293000	56.39016000	49.88876000
H	66.06259000	55.67368000	50.13522000
H	65.65920000	56.84506000	49.00164000
H	65.41691000	57.12427000	50.65005000
F	65.58675000	56.53518000	53.62586000
C	64.44056000	57.30517000	52.99992000

H	63.77218000	56.61106000	52.48437000
C	63.61176000	58.12936000	53.97357000
H	63.16737000	57.48311000	54.73769000
H	64.19982000	58.90228000	54.48050000
H	62.78706000	58.62178000	53.44768000
O	64.92236000	58.14782000	51.93772000
H	65.60621000	58.76083000	52.31407000
N	65.04679000	63.02833000	54.26254000
H	64.59986000	63.37785000	55.10563000
C	65.40709000	64.03219000	53.31678000
O	65.04235000	65.18289000	53.56005000
N	66.11585000	63.69737000	52.19178000
C	66.50918000	62.44358000	52.04877000
N	67.21216000	61.92238000	51.05098000
C	67.34266000	60.58733000	51.36504000
O	67.85472000	59.69802000	50.70757000
N	66.70138000	60.24353000	52.68647000
C	66.19183000	61.35986000	53.04128000
C	65.40029000	61.69375000	54.25922000
O	65.10802000	60.91396000	55.15072000
O	63.90777000	60.96406000	51.47553000
H	64.31040000	60.73031000	50.59425000
H	63.85115000	60.08624000	51.88810000

TS4^{s}

F	63.78485000	54.36933000	50.02363000
C	63.87319000	55.88330000	49.83935000
H	63.57318000	56.16213000	48.82741000
H	63.23082000	56.40010000	50.55332000
N	65.23243000	56.54492000	50.04001000
H	65.94201000	55.89226000	50.38781000
H	65.57743000	56.96544000	49.16040000
H	65.18328000	57.35464000	50.82193000
F	65.56407000	56.54971000	53.61568000
C	64.45376000	57.35584000	52.94323000
H	63.82370000	56.63668000	52.39462000
C	63.53873000	58.08137000	53.92650000
H	63.06573000	57.37545000	54.61715000
H	64.08030000	58.82390000	54.52147000
H	62.73859000	58.60307000	53.38966000
O	64.98220000	58.26271000	52.00703000

H	66.21330000	59.22849000	52.51773000
N	64.94550000	62.91878000	54.16538000
H	64.57709000	63.24855000	55.05449000
C	65.32748000	63.95462000	53.26163000
O	64.97984000	65.10086000	53.53587000
N	66.06629000	63.64746000	52.14695000
C	66.45705000	62.39955000	51.96063000
N	67.27806000	61.94100000	51.02642000
C	67.42450000	60.59294000	51.26420000
O	68.02885000	59.75316000	50.63254000
N	66.68702000	60.20268000	52.50016000
C	65.97844000	61.26005000	52.81906000
C	65.29352000	61.58361000	54.11292000
O	65.12301000	60.79464000	55.02132000
O	64.17083000	60.77556000	51.76026000
H	64.46862000	60.75455000	50.80321000
H	64.27262000	59.77953000	51.95810000

EP^{s}

F	63.75655000	54.33157000	50.01118000
C	63.84556000	55.83267000	49.80503000
H	63.46208000	56.11372000	48.82362000
H	63.30379000	56.38238000	50.57573000
N	65.25245000	56.43595000	49.85884000
H	65.95964000	55.75919000	50.16186000
H	65.54260000	56.85170000	48.95429000
H	65.25186000	57.20591000	50.57826000
F	65.51474000	56.56282000	53.62180000
C	64.32018000	57.28280000	53.01353000
H	63.67850000	56.52876000	52.54854000
C	63.46918000	58.11681000	53.95859000
H	62.99550000	57.48139000	54.71219000
H	64.04514000	58.89345000	54.47204000
H	62.66407000	58.61498000	53.40558000
O	64.77454000	58.11522000	51.93043000
H	66.46410000	59.35033000	52.56571000
N	64.96323000	63.00802000	54.18998000
H	64.66741000	63.33557000	55.10578000
C	65.30084000	64.04678000	53.26552000
O	64.96150000	65.19388000	53.56519000
N	66.00143000	63.73808000	52.13870000

C	66.37258000	62.47750000	51.94065000
N	67.27357000	62.05037000	51.07596000
C	67.45144000	60.68943000	51.34322000
O	68.09684000	59.88411000	50.68817000
N	66.74979000	60.32298000	52.52886000
C	65.71428000	61.29925000	52.66957000
C	65.26900000	61.66966000	54.08179000
O	65.13784000	60.86913000	54.99188000
O	64.49123000	60.92218000	51.97954000
H	64.71312000	60.78415000	51.01680000
H	64.47235000	59.04672000	52.03180000

ES2$^{s'}$

F	63.64205000	54.05117000	50.10541000
C	63.78135000	55.49615000	49.65935000
H	63.28583000	55.64098000	48.70002000
H	63.36753000	56.19822000	50.38672000
N	65.20254000	55.99674000	49.45595000
H	65.84622000	55.24565000	49.19795000
H	65.23207000	56.70391000	48.69153000
H	65.52804000	56.51163000	50.31393000
F	65.85042000	56.35296000	53.41110000
C	64.72704000	57.09965000	52.72245000
H	64.00104000	56.37704000	52.33595000
C	63.98686000	58.08663000	53.61591000
H	63.62266000	57.57576000	54.51332000
H	64.63343000	58.91143000	53.93966000
H	63.11344000	58.49051000	53.09563000
O	65.19606000	57.74480000	51.52015000
H	65.97440000	58.31855000	51.71089000
F	61.03730000	62.63966000	47.06966000
C	62.25996000	62.39346000	47.95585000
H	62.06486000	62.62363000	49.02138000
H	62.57829000	61.33741000	47.96722000
C	63.45713000	63.24682000	47.59254000
O	63.40042000	64.09469000	46.69311000
N	64.55582000	63.04027000	48.33818000
H	65.38699000	63.57919000	48.13966000
H	64.58465000	62.26804000	48.99916000
N	65.30212000	63.36532000	54.83230000
H	64.89650000	63.77530000	55.66981000

C	65.50255000	64.25288000	53.75505000
O	65.16231000	65.42625000	53.90730000
N	66.06308000	63.80832000	52.56101000
C	66.40825000	62.54660000	52.49571000
N	66.91980000	61.87580000	51.44313000
C	67.09379000	60.59272000	51.90937000
O	67.38446000	59.59892000	51.23951000
N	66.74024000	60.42620000	53.33259000
C	66.26475000	61.57447000	53.63101000
C	65.60819000	62.01494000	54.88919000
O	65.36043000	61.29535000	55.83705000
O	63.70040000	61.41563000	52.88973000
H	63.74349000	61.23108000	51.92987000
H	63.46789000	60.56991000	53.29924000
O	64.54086000	60.83811000	50.24106000
H	65.41221000	61.23297000	50.48116000
H	64.75221000	59.91759000	50.01150000

TS4$^{s'}$

F	63.65564000	54.06690000	50.09463000
C	63.79877000	55.51177000	49.65282000
H	63.29287000	55.66158000	48.69998000
H	63.40281000	56.21322000	50.38933000
N	65.22167000	55.99672000	49.43290000
H	65.84726000	55.24342000	49.13842000
H	65.24975000	56.72862000	48.69080000
H	65.56125000	56.47517000	50.30223000
F	65.83369000	56.35490000	53.44520000
C	64.69652000	57.07383000	52.75185000
H	63.97917000	56.33241000	52.38705000
C	63.95228000	58.06543000	53.63333000
H	63.58270000	57.55774000	54.53031000
H	64.59875000	58.88770000	53.96250000
H	63.08611000	58.47596000	53.10781000
O	65.14196000	57.69561000	51.53233000
H	65.90932000	58.28134000	51.70519000
F	61.03724000	62.63915000	47.09884000
C	62.24819000	62.35508000	47.98698000
H	62.05718000	62.56500000	49.05641000
H	62.54185000	61.29097000	47.98171000
C	63.46397000	63.18279000	47.63007000

O	63.43265000	64.02892000	46.72271000
N	64.54557000	62.94127000	48.37951000
H	65.37798000	63.47990000	48.18716000
H	64.50933000	62.24358000	49.14418000
N	65.26819000	63.34663000	54.79417000
H	64.89888000	63.75764000	55.64793000
C	65.43309000	64.22728000	53.71970000
O	65.12311000	65.40580000	53.86041000
N	65.96318000	63.76221000	52.50058000
C	66.26066000	62.50725000	52.45532000
N	66.77561000	61.79523000	51.38825000
C	67.02237000	60.49294000	51.90196000
O	67.36485000	59.54297000	51.21363000
N	66.71959000	60.39642000	53.28547000
C	66.13938000	61.52450000	53.55714000
C	65.55018000	61.98412000	54.84139000
O	65.34260000	61.27933000	55.80618000
O	63.95794000	61.48235000	52.80024000
H	64.10641000	61.28568000	51.65079000
H	63.70403000	60.62672000	53.18348000
O	64.46536000	61.13746000	50.43589000
H	66.03436000	61.67774000	50.62194000
H	64.48098000	60.19776000	50.19587000

EP$^{s\prime}$

F	63.64168000	54.06297000	50.10791000
C	63.77733000	55.52097000	49.69161000
H	63.34199000	55.66733000	48.70342000
H	63.29468000	56.19693000	50.40035000
N	65.19166000	56.09121000	49.58301000
H	65.89755000	55.36785000	49.42697000
H	65.25127000	56.75324000	48.77943000
H	65.44036000	56.66291000	50.42938000
F	65.84357000	56.35108000	53.41968000
C	64.65366000	57.06989000	52.81725000
H	63.98103000	56.33134000	52.36841000
C	63.86063000	57.90137000	53.82182000
H	63.46707000	57.26072000	54.61698000
H	64.47990000	58.67154000	54.29956000
H	63.00912000	58.38396000	53.33267000
O	65.06260000	57.87462000	51.71137000

H	65.57418000	58.64397000	52.08342000
F	61.02891000	62.63705000	47.07219000
C	62.21987000	62.36722000	47.99583000
H	61.99471000	62.59157000	49.05718000
H	62.51412000	61.30644000	48.01750000
C	63.44464000	63.19305000	47.67921000
O	63.45152000	64.01101000	46.74966000
N	64.49546000	63.00968000	48.50436000
H	65.35119000	63.48600000	48.25711000
H	64.51591000	62.20291000	49.13754000
N	65.33135000	63.24902000	54.78587000
H	65.17183000	63.58866000	55.73077000
C	65.42707000	64.24112000	53.78843000
O	65.11285000	65.39838000	54.04937000
N	65.96933000	63.89232000	52.55331000
C	66.13857000	62.62203000	52.33911000
N	66.88169000	62.02933000	51.40348000
C	66.97447000	60.58765000	51.69082000
O	67.64922000	59.85095000	50.97534000
N	66.24184000	60.29648000	52.76874000
C	65.55327000	61.47192000	53.16001000
C	65.52755000	61.87804000	54.63843000
O	65.52263000	61.09341000	55.56446000
O	64.12044000	61.41290000	52.83683000
H	64.03805000	60.87319000	51.02815000
H	63.80888000	60.59849000	53.27630000
O	64.14513000	60.66660000	50.07720000
H	67.47632000	62.49464000	50.73073000
H	64.76523000	59.92178000	50.04747000

ES1$^{t\prime}$

F	62.87250000	55.84598000	50.57265000
C	63.01203000	57.37082000	50.42540000
H	62.39177000	57.72377000	49.58640000
H	62.64690000	57.86343000	51.33895000
N	64.31805000	57.91420000	50.16032000
H	65.02533000	57.59451000	50.81681000
H	66.00986000	61.11661000	51.56305000
H	64.62360000	57.79008000	49.19653000
N	63.43852000	65.09490000	55.38263000
H	62.80528000	65.50789000	56.06956000

C	63.97423000	65.95777000	54.41899000
O	63.69533000	67.17031000	54.47107000
N	64.76517000	65.44858000	53.43842000
C	65.02057000	64.15260000	53.55759000
N	65.78812000	63.40353000	52.69081000
H	66.38567000	63.75145000	51.95454000
C	65.77141000	62.09884000	53.15774000
O	66.39347000	61.12321000	52.50474000
N	65.04605000	61.95846000	54.24559000
C	64.55975000	63.23114000	54.51360000
C	63.66348000	63.71396000	55.53044000
O	63.10109000	63.07146000	56.42271000
O	62.57974000	62.33452000	52.00261000
O	62.35475000	63.12425000	52.93248000
O	64.95244000	61.30412000	50.32685000
H	64.16946000	61.57955000	50.83983000
H	64.75120000	60.36331000	50.10352000

TS1$^{t''}$

F	62.87635000	55.84567000	50.57111000
C	63.03612000	57.36871000	50.42212000
H	62.41664000	57.73308000	49.58792000
H	62.68916000	57.86434000	51.33947000
N	64.34957000	57.89967000	50.14503000
H	65.06813000	57.56028000	50.77930000
H	65.57512000	61.21918000	51.25094000
H	64.63765000	57.80445000	49.17204000
N	63.41123000	65.07081000	55.36016000
H	62.75302000	65.47384000	56.03023000
C	63.97220000	65.94146000	54.42302000
O	63.68320000	67.14875000	54.46545000
N	64.81412000	65.44979000	53.46819000
C	65.07921000	64.16474000	53.56779000
N	65.88870000	63.43641000	52.74318000
H	66.49100000	63.79293000	52.01511000
C	65.87619000	62.09842000	53.18534000
O	66.41121000	61.17420000	52.51907000
N	65.10268000	61.97672000	54.29612000
C	64.59851000	63.21682000	54.52176000
C	63.65343000	63.69645000	55.50870000
O	63.08378000	63.04411000	56.38633000

O	62.70913000	62.17867000	51.72854000
O	62.65055000	63.10875000	52.63984000
O	64.78021000	61.29811000	50.57735000
H	63.95287000	61.69435000	51.16039000
H	64.55499000	60.34779000	50.35872000

INT2$^{t\prime}$

F	62.89951000	55.85897000	50.55133000
C	63.08644000	57.38237000	50.42370000
H	62.48593000	57.75990000	49.58104000
H	62.72609000	57.87185000	51.33987000
N	64.40560000	57.90582000	50.18357000
H	65.09797000	57.60355000	50.86437000
H	65.45581000	61.24745000	51.03591000
H	64.73841000	57.77468000	49.22992000
N	63.42857000	65.07123000	55.35794000
H	62.75091000	65.48066000	56.00462000
C	64.00068000	65.92426000	54.41313000
O	63.69263000	67.12581000	54.41829000
N	64.87634000	65.42230000	53.48606000
C	65.16762000	64.14882000	53.61926000
N	65.99708000	63.41054000	52.83096000
H	66.56095000	63.73872000	52.06005000
C	65.93959000	62.06290000	53.25547000
O	66.48203000	61.13242000	52.65553000
N	65.11159000	61.96980000	54.36236000
C	64.64827000	63.21216000	54.57599000
C	63.66880000	63.70057000	55.52712000
O	63.07394000	63.05101000	56.38778000
O	62.54115000	62.01375000	51.78870000
O	62.66465000	63.20400000	52.35682000
O	64.68870000	61.33817000	50.42971000
H	63.42232000	61.80382000	51.28713000
H	64.50629000	60.39576000	50.19895000

ES2$^{s\prime\prime}$

F	63.49909000	53.80952000	50.10953000
C	63.76418000	55.19441000	49.53775000
H	63.36554000	55.27618000	48.52867000
H	63.34830000	55.98212000	50.16692000
N	65.22174000	55.61277000	49.43361000

H	65.84470000	54.85293000	49.15171000
H	65.33526000	56.38163000	48.73806000
H	65.49116000	56.04253000	50.35179000
F	65.74289000	56.28364000	53.46327000
C	64.51151000	56.89562000	52.82359000
H	63.75721000	56.10478000	52.74173000
C	63.90032000	58.06486000	53.58418000
H	63.66754000	57.76264000	54.61054000
H	64.57372000	58.92963000	53.64040000
H	62.96677000	58.37847000	53.11212000
O	64.76585000	57.25130000	51.47006000
H	65.29363000	58.08812000	51.41076000
F	61.18978000	62.55881000	47.50942000
C	62.23785000	62.28065000	48.59184000
H	61.91572000	62.63361000	49.59221000
H	62.42359000	61.20227000	48.74879000
C	63.57489000	62.94118000	48.36399000
O	63.80507000	63.60144000	47.35509000
N	64.50200000	62.71887000	49.35556000
H	65.24926000	63.40193000	49.44341000
H	64.15995000	62.38149000	50.26144000
N	65.38349000	62.79017000	55.20725000
H	65.08529000	62.62849000	56.16483000
C	65.26149000	64.14816000	54.76608000
O	64.77968000	64.94653000	55.55575000
N	65.65633000	64.50181000	53.48876000
C	66.23738000	63.57347000	52.77184000
N	66.70809000	63.68666000	51.52801000
C	67.28820000	62.48296000	51.22668000
O	67.79822000	62.13338000	50.17814000
N	67.16302000	61.51216000	52.36533000
C	66.49883000	62.17123000	53.23380000
C	65.96540000	61.73037000	54.54856000
O	66.02726000	60.59263000	54.98580000
O	63.99587000	61.32519000	52.00194000
H	64.60003000	60.61082000	51.68700000
H	63.18515000	60.87373000	52.28422000
O	65.95267000	59.56205000	51.02369000
H	66.66278000	60.02640000	51.53911000
H	66.06982000	59.84129000	50.07863000

TS4$^{s''}$

F	63.49306000	53.81093000	50.11293000
C	63.73170000	55.20187000	49.54115000
H	63.34129000	55.26851000	48.52763000
H	63.27856000	55.97913000	50.15874000
N	65.17420000	55.65701000	49.46284000
H	65.82751000	54.90052000	49.25204000
H	65.29386000	56.38725000	48.72901000
H	65.39391000	56.15874000	50.37014000
F	65.73800000	56.28186000	53.45232000
C	64.51081000	56.89045000	52.79397000
H	63.78110000	56.08060000	52.66754000
C	63.84055000	58.00854000	53.58214000
H	63.54656000	57.64651000	54.57268000
H	64.50447000	58.86984000	53.72265000
H	62.93736000	58.34606000	53.06904000
O	64.79052000	57.30426000	51.46979000
H	65.25286000	58.20734000	51.43007000
F	61.18171000	62.55435000	47.49753000
C	62.22447000	62.26647000	48.58022000
H	61.89487000	62.60315000	49.58375000
H	62.41360000	61.18680000	48.72013000
C	63.55572000	62.93917000	48.36359000
O	63.78787000	63.60885000	47.36057000
N	64.48115000	62.72477000	49.35739000
H	65.22184000	63.41490000	49.42888000
H	64.16133000	62.37668000	50.26703000
N	65.30214000	62.70805000	55.11385000
H	65.02997000	62.54188000	56.07903000
C	65.19202000	64.07730000	54.69121000
O	64.70703000	64.86589000	55.48584000
N	65.62195000	64.44670000	53.43227000
C	66.17414000	63.52350000	52.69016000
N	66.70969000	63.67861000	51.47872000
C	67.28895000	62.49572000	51.12529000
O	67.84217000	62.17832000	50.09530000
N	67.12569000	61.51820000	52.24402000
C	66.32101000	62.09036000	53.09250000
C	65.86612000	61.65150000	54.43931000
O	65.99608000	60.52279000	54.88075000
O	64.40552000	61.38702000	52.11217000

H	65.01072000	60.49095000	51.63235000
H	63.72584000	60.97110000	52.67004000
O	65.83669000	59.64405000	51.20963000
H	66.96474000	60.49637000	51.94162000
H	65.94892000	59.80768000	50.24543000

EP$^{s''}$

F	63.48064000	53.79288000	50.13150000
C	63.72023000	55.14982000	49.49061000
H	63.33085000	55.16993000	48.47617000
H	63.28394000	55.95818000	50.07655000
N	65.17012000	55.58610000	49.38174000
H	65.79915000	54.84023000	49.07619000
H	65.26474000	56.37288000	48.70366000
H	65.43756000	55.99111000	50.31099000
F	65.75910000	56.24058000	53.44673000
C	64.48688000	56.80557000	52.84219000
H	63.74868000	55.99410000	52.81776000
C	63.86923000	57.97766000	53.59293000
H	63.61201000	57.67818000	54.61352000
H	64.56329000	58.82577000	53.67227000
H	62.95510000	58.31201000	53.09925000
O	64.66983000	57.12576000	51.47191000
H	65.08704000	58.01733000	51.34139000
F	61.21001000	62.55431000	47.42875000
C	62.28714000	62.28249000	48.47874000
H	61.97446000	62.58342000	49.49852000
H	62.52275000	61.20724000	48.58267000
C	63.58890000	63.00219000	48.22645000
O	63.79964000	63.61720000	47.18762000
N	64.52720000	62.87327000	49.22533000
H	65.28391000	63.55088000	49.24189000
H	64.19033000	62.65470000	50.15861000
N	65.42096000	62.87336000	55.27457000
H	65.31525000	62.77738000	56.28025000
C	65.18121000	64.20068000	54.76951000
O	64.73699000	65.01116000	55.57046000
N	65.49127000	64.49733000	53.46812000
C	65.94640000	63.52428000	52.71293000
N	66.51759000	63.65749000	51.52180000
C	67.12962000	62.44514000	51.22532000

O	67.70735000	62.16330000	50.18550000
N	67.00026000	61.55784000	52.32902000
C	65.89673000	62.03925000	53.08667000
C	65.84831000	61.78327000	54.57990000
O	66.02473000	60.66585000	55.05121000
O	64.60585000	61.51355000	52.58997000
H	65.13058000	60.22553000	51.31442000
H	64.32466000	60.80955000	53.20446000
O	65.66023000	59.49934000	50.92274000
H	67.02778000	60.57146000	52.08505000
H	65.84510000	59.79593000	49.99165000

ES1^{Phe}

F	62.77179500	55.49386000	50.58997500
C	62.94254300	57.01309500	50.53280900
H	62.49029600	57.42134100	49.61735200
H	62.39868500	57.45506200	51.37729500
N	64.28539100	57.54844200	50.57218900
H	64.72543900	57.60782100	49.64978000
H	64.00342400	58.84026400	51.71293900
H	64.89740400	57.05765000	51.22424800
F	64.43436400	57.97758300	54.31227600
C	63.30664200	58.70359200	53.58708600
H	62.62454300	57.94757400	53.17445900
C	62.49086300	59.64120800	54.46514100
H	63.08869700	60.47779200	54.83572200
H	61.64875700	60.05503700	53.90243500
H	62.08171800	59.09245700	55.32133200
O	63.79821600	59.45960600	52.47570200
H	65.19123300	60.29271400	52.48847900
F	68.99625600	68.45047300	55.38326200
C	68.11999700	67.38698400	54.69471900
H	67.18509600	67.84190500	54.32928400
H	68.61024700	66.96723200	53.79654700
C	67.67871100	66.25077300	55.55790000
C	66.91069100	66.49022000	56.70696900
H	66.66758000	67.51295400	56.98497000
C	66.44947200	65.43156600	57.48582200
H	65.84477600	65.63213500	58.36452700
C	66.74432500	64.11500000	57.11854600
H	66.36307400	63.28736100	57.70775700

C	67.50144300	63.86775600	55.97424900
H	67.71558900	62.85106400	55.66468300
C	67.97201600	64.93236800	55.20782400
H	68.56727200	64.74528100	54.31651200
F	60.35899400	63.53013500	47.91826800
C	61.40598400	63.24045300	48.99980500
H	61.17932300	63.76155400	49.94550900
H	61.42147400	62.17177200	49.28565500
C	62.83268500	63.59574900	48.66537400
O	63.16399000	63.97659600	47.53803200
N	63.70117000	63.45520900	49.68324100
H	64.70942400	63.44295400	49.51427000
H	63.37927000	63.12741500	50.58588800
F	56.35491900	64.08561300	56.13503400
C	57.81510600	64.13561700	56.61203500
H	58.08426700	65.17607100	56.88309100
H	57.96655500	63.55498400	57.53628000
C	58.88065000	63.73021600	55.59862100
O	58.69600500	63.82447900	54.38593700
N	60.03368300	63.25418700	56.13414700
H	60.84030900	63.14828700	55.53386700
H	60.27335400	63.40712100	57.10688600
N	63.34475700	65.11077400	55.44895600
H	62.78803400	65.54760400	56.18528600
C	63.85217000	65.94476700	54.44231900
O	63.65887100	67.17669100	54.52511800
N	64.51688600	65.40465400	53.39836300
C	64.74020400	64.09674500	53.50903100
N	65.40852200	63.30813900	52.59338600
H	65.89086700	63.60131400	51.74987500
C	65.41117300	62.02699900	53.11969400
O	65.90315800	61.00664600	52.39098800
N	64.81872600	61.93688900	54.27649700
C	64.36013900	63.22263500	54.53165000
C	63.56121600	63.73066200	55.60065300
O	63.05707000	63.10518800	56.55024100
O	61.47258700	62.62247000	52.13350400
O	61.61837900	62.77814000	53.33700200
O	66.54425400	62.96831600	49.81874500
H	66.50178900	62.08262900	50.22035800
H	67.24985900	62.90629500	49.12365100

TS1^{Phe}

F	62.77948200	55.51237800	50.59530200
C	62.91975600	57.02777000	50.52982000
H	62.52643600	57.41736000	49.58515500
H	62.35959200	57.49158200	51.34524800
N	64.29302600	57.60281200	50.64949200
H	64.70516000	57.82710600	49.73030200
H	64.17762300	58.51816700	51.39887500
H	64.93397300	56.98752100	51.15890300
F	64.43953600	57.98629000	54.31982900
C	63.32748400	58.71393300	53.57834400
H	62.62537200	57.96838800	53.17886300
C	62.53042700	59.69340600	54.42450300
H	63.14429200	60.52933400	54.77202300
H	61.69879500	60.10931600	53.84940500
H	62.11144300	59.17038000	55.29286000
O	63.81934100	59.36551900	52.38372700
H	64.61089000	60.03339800	52.52329800
F	68.98229600	68.45801300	55.36895800
C	68.08807800	67.40531700	54.68780100
H	67.14876600	67.86789400	54.34552800
H	68.55769900	66.98842000	53.77751500
C	67.65891400	66.27250500	55.55708100
C	66.90432900	66.51906900	56.71321200
H	66.65577300	67.54304300	56.98181000
C	66.46405000	65.46489200	57.50886900
H	65.86722200	65.66772100	58.39203200
C	66.76643300	64.14776800	57.15040200
H	66.40193800	63.32349200	57.75423900
C	67.50549400	63.89399700	55.99580900
H	67.71836900	62.87608600	55.69013800
C	67.95639800	64.95445800	55.21262400
H	68.53475100	64.76529900	54.31077300
F	60.35142600	63.52980100	47.93269600
C	61.38902100	63.22345700	49.02019200
H	61.14734200	63.70327600	49.98420200
H	61.41223900	62.14637900	49.27530300
C	62.81637500	63.59693900	48.70806000
O	63.16019200	63.97784800	47.58063100
N	63.66095900	63.45697700	49.74189700

H	64.67106700	63.43211000	49.58962100
H	63.31517200	63.14079600	50.64524700
F	56.36021100	64.08239800	56.14166800
C	57.82432900	64.12748500	56.61324700
H	58.08988300	65.16087400	56.91286500
H	57.99144300	63.52198000	57.51883000
C	58.86679600	63.75698100	55.56201500
O	58.62072700	63.85932000	54.36102800
N	60.05510200	63.29665800	56.02910400
H	60.80617900	63.18448800	55.35881600
H	60.36253400	63.44798200	56.98329700
N	63.38515000	65.10241400	55.48656300
H	62.82889800	65.53603600	56.22456800
C	63.86876400	65.93504700	54.47189200
O	63.66944600	67.16771100	54.54944800
N	64.52541800	65.39791400	53.42011000
C	64.73991000	64.08951800	53.51152500
N	65.37073100	63.30946600	52.58017800
H	65.82718400	63.61476900	51.72870800
C	65.36381300	61.98518300	53.05914800
O	65.78100700	61.00345800	52.33535900
N	64.80451600	61.92181200	54.26774000
C	64.37377600	63.20117100	54.54176900
C	63.60119300	63.71968800	55.62991500
O	63.11681100	63.09973700	56.59436700
O	61.89227000	62.50733200	52.17329800
O	61.89815600	62.93191900	53.34922800
O	66.48989500	62.90270900	49.88793600
H	66.44618400	62.07055200	50.40042200
H	67.20511700	62.79931500	49.21641700

INT1^{Phe}

F	62.81183700	55.58986900	50.61168500
C	62.96712000	57.10675300	50.66963800
H	62.48650400	57.57639200	49.80807900
H	62.52600800	57.50908700	51.58112700
N	64.35248800	57.71645600	50.67062400
H	64.71968200	57.89395800	49.71991200
H	64.25822800	58.61594400	51.26387100
H	65.04178900	57.17641900	51.20879700
F	64.44986900	58.00788700	54.33107000

C	63.27807100	58.77019400	53.71776900
H	62.53300400	58.02385600	53.39632900
C	62.58886600	59.75488600	54.65785700
H	63.25309700	60.57907800	54.94283200
H	61.71151900	60.19920000	54.17894000
H	62.26127600	59.24267400	55.56995200
O	63.67805900	59.44929700	52.52839200
H	63.65246400	60.44646300	52.62205800
F	69.05055500	68.50494400	55.42528900
C	68.15930200	67.44700300	54.75845000
H	67.20063100	67.89312900	54.45014100
H	68.61360100	67.05179100	53.83155600
C	67.79280400	66.29968400	55.63372100
C	67.08303100	66.52026900	56.82268100
H	66.81811100	67.53528600	57.10937400
C	66.71210700	65.44887900	57.63040600
H	66.15142200	65.62712600	58.54171500
C	67.03792500	64.14360900	57.25050300
H	66.73611800	63.30673400	57.87195400
C	67.73665300	63.91822600	56.06527100
H	67.98668600	62.91209700	55.75234000
C	68.12291700	64.99538100	55.27130000
H	68.68134400	64.83132800	54.35238700
F	60.38348800	63.51770100	47.93973700
C	61.43028200	63.24327300	49.03650800
H	61.19568500	63.75539400	49.98688400
H	61.46015700	62.17729100	49.33050100
C	62.85612300	63.62229400	48.70029300
O	63.14536300	64.06230900	47.57668000
N	63.73214300	63.43686200	49.69573300
H	64.73792300	63.48963800	49.52798900
H	63.42875900	62.98423600	50.57048200
F	56.42325000	64.08340800	56.15376900
C	57.91296500	64.12454200	56.55706600
H	58.18644500	65.15043100	56.87511400
H	58.12753400	63.49843400	57.43819900
C	58.92319100	63.79636500	55.45552400
O	58.61804000	63.88567000	54.26820000
N	60.15915100	63.39977700	55.86045200
H	60.87970900	63.30481400	55.15238700
H	60.49780800	63.52309700	56.80817000

N	63.55326200	65.04235300	55.54457600
H	62.95069500	65.43266100	56.27072800
C	63.99267700	65.92325900	54.55831900
O	63.69398800	67.13094500	54.63128400
N	64.73539400	65.45752200	53.52392900
C	65.04780500	64.17815200	53.58860100
N	65.79732700	63.50081600	52.68405300
H	66.17270900	63.85294500	51.81060600
C	65.83448400	62.14018400	53.06581900
O	66.37814000	61.27086200	52.35666800
N	65.18731200	61.99130000	54.27456900
C	64.68800900	63.21276700	54.57774800
C	63.83448300	63.66593000	55.65548100
O	63.34999600	63.01452500	56.59383200
O	63.02144200	62.01996000	52.08429400
O	62.26780400	62.77955700	52.83610500
O	66.67421500	63.08779800	49.95196400
H	66.68695600	62.30433400	50.54464100
H	67.34344700	62.91077400	49.24814500

Table S1. Experimentally measured enzyme activity (V_{max})

Enzyme (wild-type or mutant)	Uricase activity (U/mg)	Activity relative to wild-type
Wild-type uricase	0.3080	100%
Gln299Ile	0.0233	8%
Asn271Leu	0.0	0% or <1%[a]
Lys9His	0.0	0% or <1% [a]
Lys9Arg	0.0	0% or <1% [a]
Lys9Glu	0.0	0% or <1% [a]

[a] The estimated detection limit (1%) of our activity assays.