Major mechanistic differences between the reactions of hydroxylamine with phosphate di- and tri-esters

Michelle Medeiros[†], *Eduardo H. Wanderlind*[†], *José R. Mora*[†], *Raphaell Moreira*[†], *Anthony J. Kirby*[*,§] *and Faruk Nome*[*,†].

[†] Instituto Nacional de Ciência e Tecnologia (INCT) de Catálise, Departamento de Química, Universidade Federal de Santa Catarina (UFSC), CEP 88040-900, Florianópolis, Santa Catarina (SC), Brazil [§] University Chemical Laboratory, Cambridge CB2 1EW, UK.

* Corresponding authors' email addresses: faruk.nome@ufsc.br; ajk1@cam.ac.uk

ELECTRONIC SUPPLEMENTARY INFORMATION

Contents.

2. Reaction of DPP with hydroxylamine

2.1. Kinetic data

Table S.5. Values of k_{obs} as a function of pH in the reaction with [NH_2OH]
Figure S.7. Calculated compositions of **DPP** and hydroxylamine as a function of pH.
Table S.6. Values of k_{obs} as a function of [NH_2OH]
Figure S.8. Plot of k_{obs} *vs*. [NH_2OH]

2.2. NMR data

Figure S.9. Progressive ^{1}H NMR spectra for the reaction with NH_2OH.
Figure S.10. Progressive ^{31}P NMR spectra for the reaction with NH_2OH.

3. Theoretical calculations

3.1. Reaction of TPP with hydroxylamine

3.1.1 Cartesian coordinates for Mechanism 1 (TPP + NH_2OH):
3.1.1.1. Reactant **3.1.1.2. Transition State (TS1)**
3.1.1.3. Intermediate **3.1.1.4. Transition State (TS2)**
3.1.1.5 Product

3.1.2. Cartesian coordinates for Mechanism 2 (TPP + NH_2OH):

Table S.7. Structural parameters of intermediate (**Int**), transition state (**TS2**) and products (**P**) for mechanism **1** in the reaction of **TPP** with hydroxylamine at the B3LYP/6-31++G(d,p) level of theory.

Table S.8. Structural parameters of intermediate (**Int**), alternative transition states (**TS4** and **TS5**) and products (**P**) for Mechanism **2** in the reaction of **TPP** with hydroxylamine at the B3LYP/6-31++G(d,p) level of theory.

3.2. Reaction of DPP with hydroxylamine

3.2.1 Cartesian coordinates for the reaction DPP + NH_2OH:
3.2.1.1 Reactant **3.2.1.2. Transition State (TS)**
3.2.1.3 Product

Table S.9. Structural parameters of reactant (**R2**), transition state (**TS**) and products (**P**) for the reaction of **DPP** with hydroxylamine calculated for mechanism **B** of Scheme 9 of the full paper at the B3LYP/6-31+G(d,p) level of theory

1. Reaction of TPP with hydroxylamine

1.1. Kinetic data

Table S.1. Values of k_{obs} as a function of pH in the reaction of **TPP** with hydroxylamine (0.5M), I=1.0 (KCl), 25°C.

pH	k_{obs}, s^{-1}
4.0	2.30×10^{-3}
4.5	1.79×10^{-3}
5.0	2.61×10^{-3}
5.2	3.23×10^{-3}
5.5	5.30×10^{-3}
6.0	9.77×10^{-3}
6.2	8.79×10^{-3}
6.5	1.14×10^{-2}
6.9	1.14×10^{-2}
7.0	1.25×10^{-2}
7.5	1.08×10^{-2}
7.8	1.00×10^{-2}
8.0	9.04×10^{-3}
8.5	1.03×10^{-2}
8.9	1.03×10^{-2}
9.0	1.08×10^{-2}

S.1a. Curve fitting for the data of Table S.1

These data were fit to equation 2 of the full paper, using values of k_0, k_2 and k_3 and pK_as for **TPPH**$^+$ and $NH_3{}^+OH$ measured in earlier experiments. (Table 1).

$$k_{obs} = k_H.\chi_{TPPH+} + [k_0 + (k_2[NH_2OH].\chi_{NH2OH} + k_3([NH_2OH].(\chi_{NH2OH}))^2 + k_4([NH_2OH]^2.(\chi_{NH2OH}).(\chi_{NH3OH+}))^2].\chi_{TPP} \quad (2)$$

Figure S.1a shows how each of the various reactions contributes to the observed overall rate of release of 2-pyridone as the pH is varied. The coloured curves are calculated using the constants shown in Table 1 of the full paper, for the three separate reactions (k_2, k_3 and k_4) catalyzed by one and two molecules of hydroxylamine reacting with **TPP** and **TPPH**$^+$ in the pH-range studied. The background hydrolysis rate is included in each case, showing how the reactions second order in hydroxylamine in particular dominate above pH 5, where significant amounts of the free base are present.

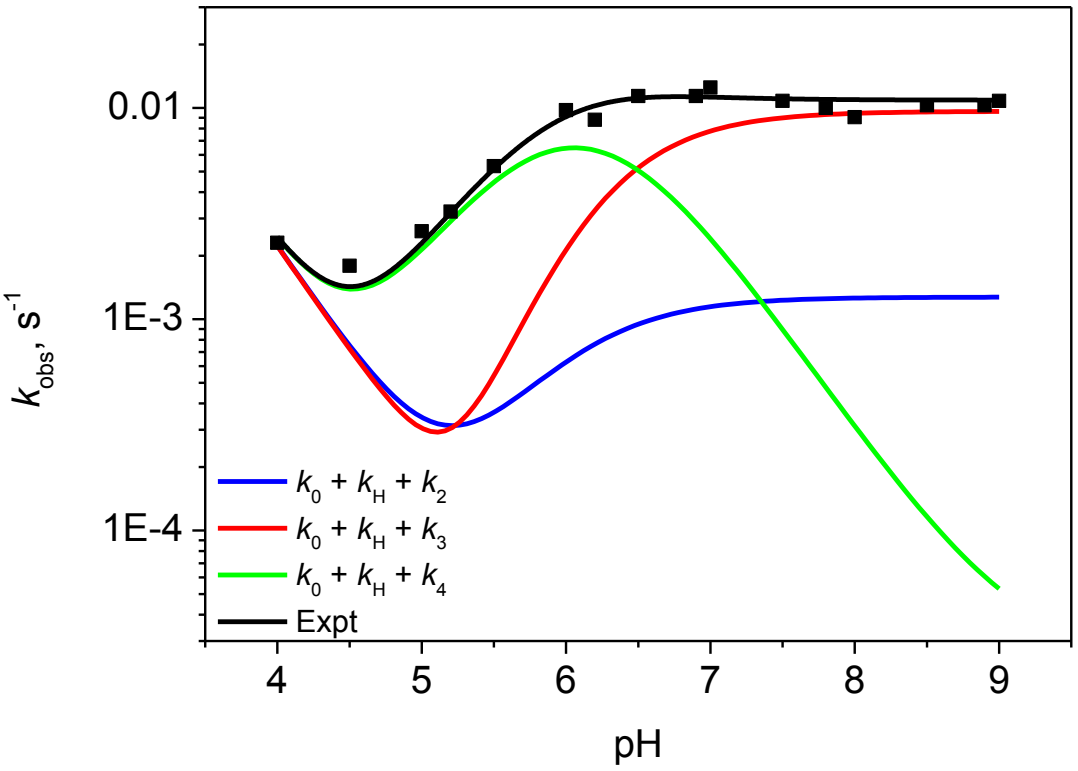


Figure S.1a. Breakdown of k_{obs} (black curve with data points) as a function of pH for the reaction of **TPP** with 0.5M NH_2OH, at 25°C and I = 1M (KCl). Values of k_H and k_4 (full paper, Table 1) were obtained by iterative fit and the errors are presented in the Table. For the 16-point (black) curve Reduced Chisq and R^2 are 7.09645×10^{-7} for 14 degrees of freedom, and 0.949, respectively.

Table S.2. Values of k_{obs} as a function of hydroxylamine concentration in the reaction with **TPP**, I=1.0 (KCl), at pH 8.5 and 25°C.

[NH_2OH], M	**k_{obs}, s^{-1}**
0.05	$2.60x10^{-4}$
0.1	$3.83x10^{-4}$
0.15	$1.17x10^{-3}$
0.2	$1.73x10^{-3}$
0.3	$3.89x10^{-3}$
0.4	$6.97x10^{-3}$
0.5	$1.06x10^{-2}$
0.6	$1.53x10^{-2}$
0.7	$2.08x10^{-2}$
0.8	$2.68x10^{-2}$

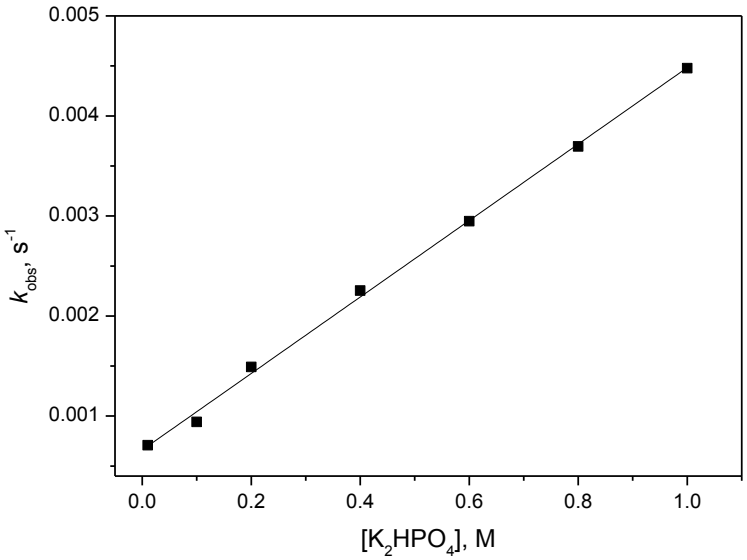
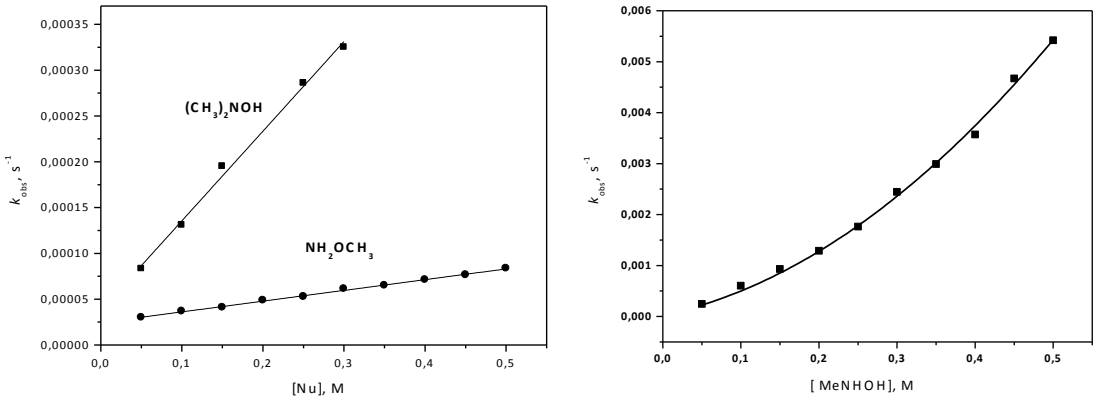


Figure S.1. Values of k_{obs} as a function of buffer [dipotassium hydrogen phosphate] concentration in the reaction of **TPP** with hydroxylamine 0.1M, at pH 8.5 and 25°C. The linear fit gives a k_2 value of $3.82x10^{-3}$ M^{-1} s^{-1}.

Table S.3. Values of k_{obs} as a function of nucleophile concentration for the reactions of **TPP** with hydroxylamine derivatives: all at *I*=1.0 (KCl), pH 8.5 and 25°C.

[Nucleophile], M	k_{obs}, s^{-1}		
	MeNHOH	**NMe_2OH**	**NH_2OMe**
0.05	$2.47x10^{-4}$	$8.32x10^{-5}$	$3.00x10^{-5}$
0.1	$6.03x10^{-4}$	$1.31x10^{-4}$	$3.68x10^{-5}$
0.15	$9.32x10^{-4}$	$1.95x10^{-4}$	$4.09x10^{-5}$
0.2	$1.29x10^{-3}$	-	$4.87x10^{-5}$
0.25	$1.76x10^{-3}$	$2.86x10^{-4}$	$5.28x10^{-5}$
0.3	$2.45x10^{-3}$	$3.25x10^{-4}$	$6.14x10^{-5}$
0.35	$2.99x10^{-3}$	-	$6.41x10^{-5}$
0.4	$3.57x10^{-3}$	-	$7.11x10^{-5}$
0.45	$4.67x10^{-3}$	-	$7.65x10^{-5}$
0.5	$5.42x10^{-3}$	-	$8.35x10^{-5}$



(A) **(B)**

Figure S.2. Plots of k_{obs} *vs*. nucleophile concentration for the reactions of **TPP** with the hydroxylamine derivatives: **(A)** $(Me)_2NOH$ and NH_2OMe and **(B)** MeNHOH: all at *I*=1.0 (KCl), pH 8.5 and 25°C. Lines in **(A)** represent linear fits, curve fit in **(B)** is to eq. 1 (in main article). The derived data appear in **Table 2** in the main article.

Table S.4 Solvent deuterium isotope effect measurements

Conditions: T=25°C, Ionic strength = 1 M (KCl + NH_2OH). [NH_2OH]=0.5 M
pH = 8.5 and pD = 8.5 (based on pD = pH_{rdg} + 0.4); 0.01M TRIS buffer.

k_{obs} (H_2O) = 1.03e-2 s^{-1}

k_{obs} (D_2O) = 6.13e-3 s^{-1} (mean of 3 measurements)

gives **k_{H2O}/ k_{D2O} = 1.7**

Table S.4 Proton inventory for the reaction between hydroxylamine and TPP

Conditions: as above at T=25°C, 0.01M TRIS buffer, [NH_2OH]=0.5 M
Ionic strength = 1 M (KCl + NH_2OH), pH=8.5 and pD=8.5 (based on pD = pH_{rdg} + 0.4);.

V,H_2O (mL)	V, D_2O (mL)	Mols of H_2O	Mols of D_2O	n D_2O	k_n, s^{-1}
-	2.0	0.000	0.110	1.000	$6.24x10^{-3}$
0.5	2.5	0.028	0.138	0.833	$7.11x10^{-3}$
1.0	2.0	0.055	0.110	0.666	$7.30x10^{-3}$
1.5	1.5	0.083	0.083	0.499	$8.41x10^{-3}$
2.0	1.0	0.111	0.055	0.333	$8.96x10^{-3}$
2.5	0.5	0.138	0.028	0.166	$9.67x10^{-3}$
2.0	-	0.111	0.000	0.000	$1.06x10^{-2}$

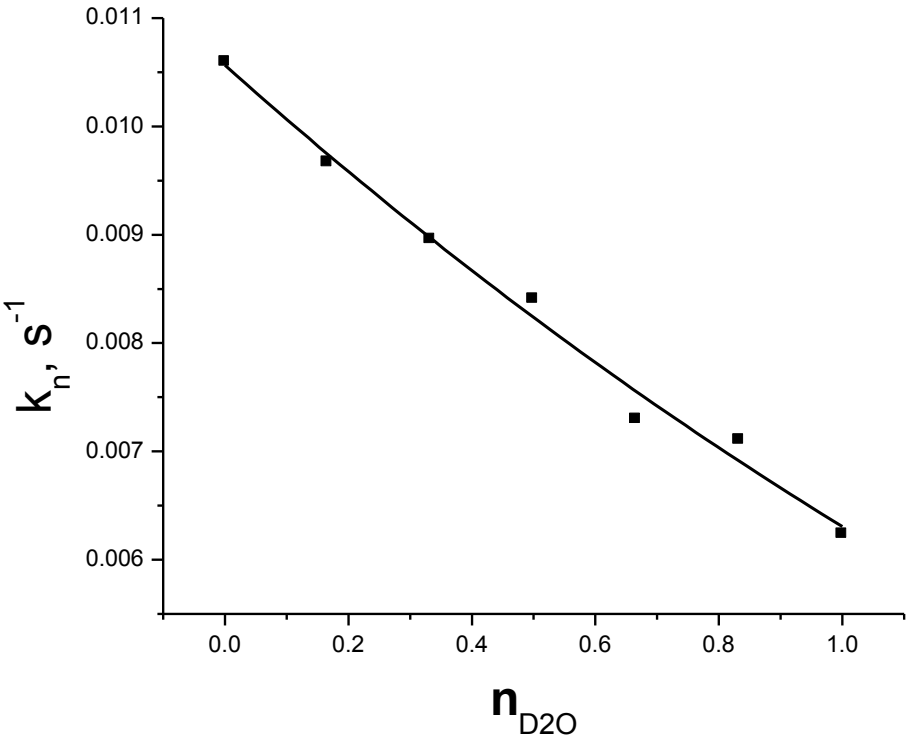


Figure S.3a. Proton inventory plot for the reaction between hydroxylamine and **TPP** at 25°C, pH/ pD= 8.5 and μ = 1.0 M.

Fitting curve to

$$k_n = k_H(1 - n + n.\phi_i^T)^m$$

Gives:

$R^2 = 0.9899$

$\phi_i = 0.87$

$m = 3.6$ (between 3 and 4 protons)

$k_H = 0.0106 \pm 0.0002\ M^{-1}\ s^{-1}$

A test specifically for two in-flight protons shows an equally reasonable fit.

Since a plot of $(k_n/k_H)^{1/2}$ versus n_{D2O} is linear:

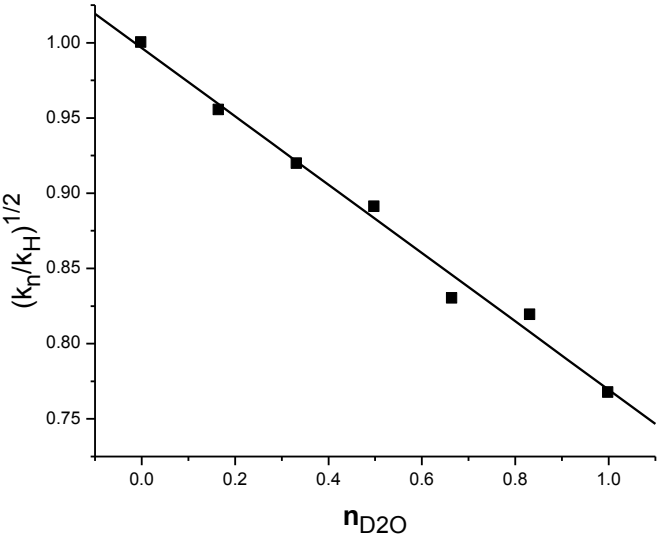


Figure S.3b. Proton inventory plot for the reaction between hydroxylamine and **TPP** with two mobile protons in the rate-determining transition state.

Intercept = 0.997 ± 0.007 Slope = -0.227 ± 0.011 R = 0.9943

1.2. NMR data

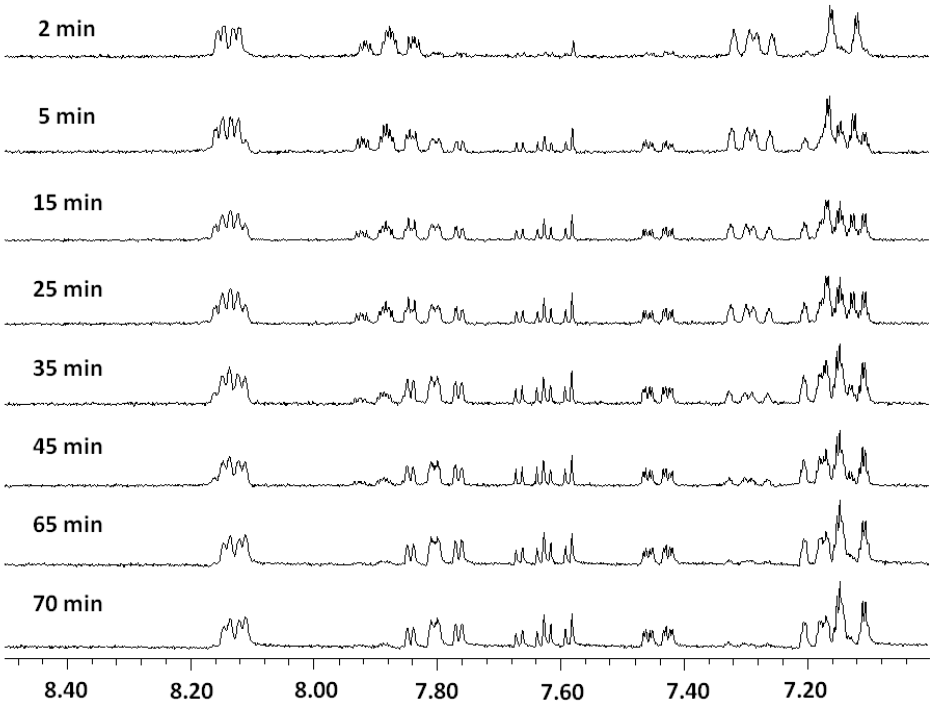


Figure S.4. Progressive ^{1}H NMR spectra for the reaction of **TPP** with hydroxylamine in presence of 0.3M of fumaric acid in D_2O, at pD=7.2 and 25°C.

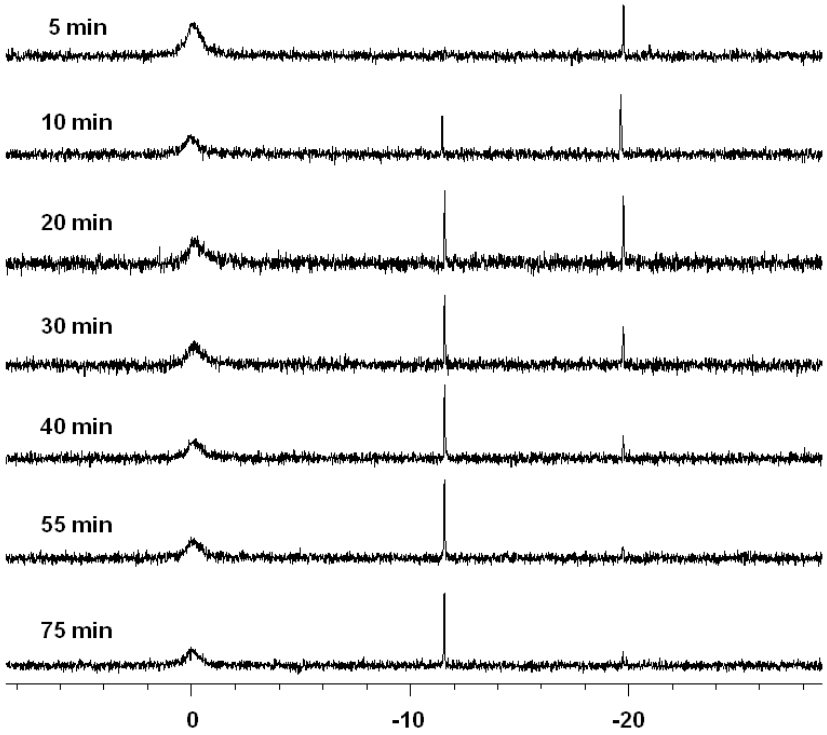


Figure S.5. Typical progressive ^{31}P NMR spectra for the reaction of **TPP** (0.02M) with hydroxylamine (0.1M) in D_2O, at pD=7.2 and 25°C. H_3PO_4 (85%) as external reference.

1.3. Hydrazine and diimine trapping

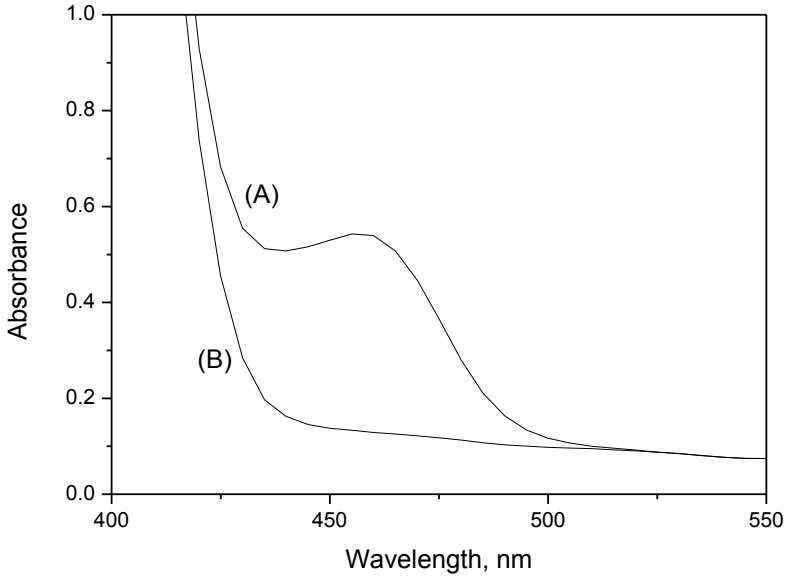


Figure S.6. UV-Vis spectra of solutions of 4-(dimethylamino)benzaldehyde and the product mixture of **TPP** reaction with hydroxylamine: (**A**) in the absence and (**B**) in presence of added fumaric acid. The band with maximum at 454nm in (**A**) is consistent with hydrazone formation.

2. Reaction of DPP with hydroxylamine

2.1. Kinetic data

Table S.5. Values of k_{obs} as a function of pH in the reaction of **DPP** with hydroxylamine (1M), I=1.0 (KCl), 25°C.

pH	k_{obs}, s^{-1}
5.0	1.23×10^{-4}
5.5	1.10×10^{-4}
6.0	8.27×10^{-5}
6.3	8.59×10^{-5}
6.6	5.57×10^{-5}
7.0	1.92×10^{-5}
7.6	5.55×10^{-6}
8.0	3.24×10^{-6}
8.5	1.02×10^{-6}
9.0	4.27×10^{-7}

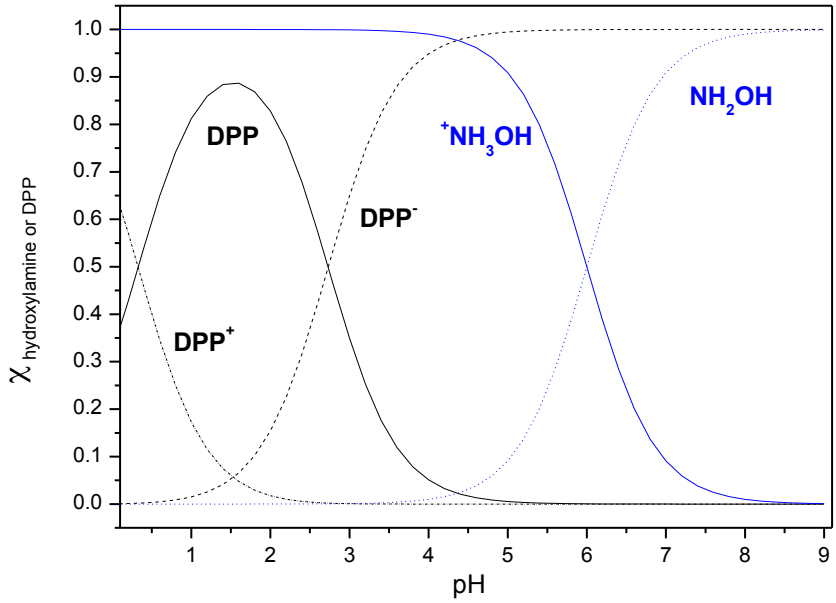


Figure S.7. Calculated compositions of **DPP** and hydroxylamine as a function of pH. Values of pK_a used for **DPP** were: pK_{a1}=0.33 and pK_{a2}=2.73, and for hydroxylamine value was 6.06.

Table S.6. Values of k_{obs} as a function of hydroxylamine concentration in the reaction with **DPP**.

[NH_2OH], M	**k_{obs}, s^{-1}**
0	5.50×10^{-6}
0.1	1.64×10^{-5}
0.2	3.01×10^{-5}
0.3	4.11×10^{-5}
0.4	5.52×10^{-5}
0.5	6.70×10^{-5}
0.6	7.96×10^{-5}
0.7	9.04×10^{-5}
0.8	1.06×10^{-4}
0.9	1.20×10^{-4}

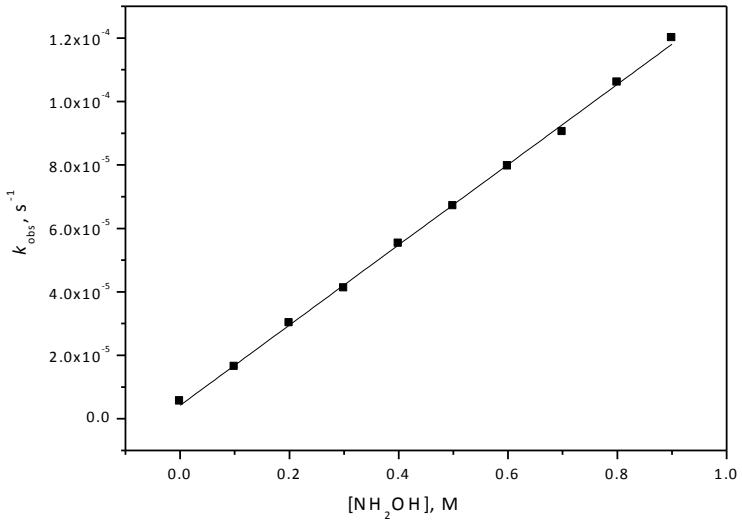


Figure S.8. Plot of k_{obs} *vs*. [NH_2OH] in the reaction of **DPP** at 25ºC.

2.2. NMR data

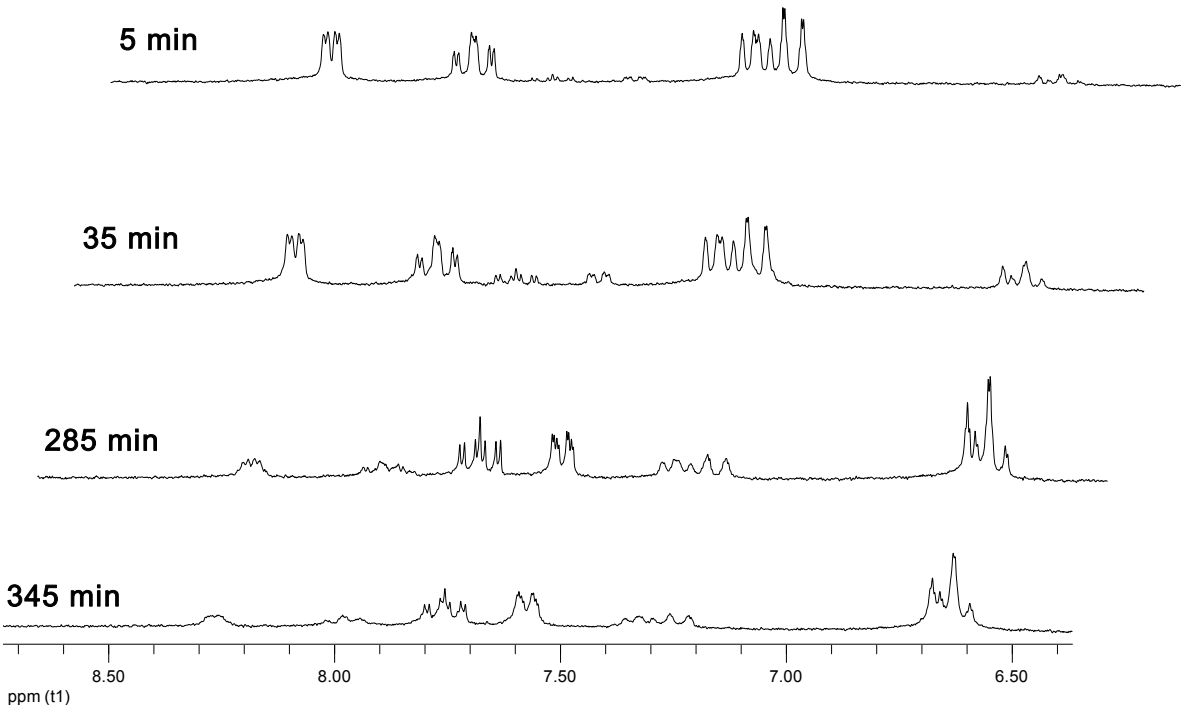


Figure S.9. Progressive ^{1}H NMR spectra for the reaction of **DPP** with hydroxylamine (1M) in D_2O, at pD 5.0 and 25°C.

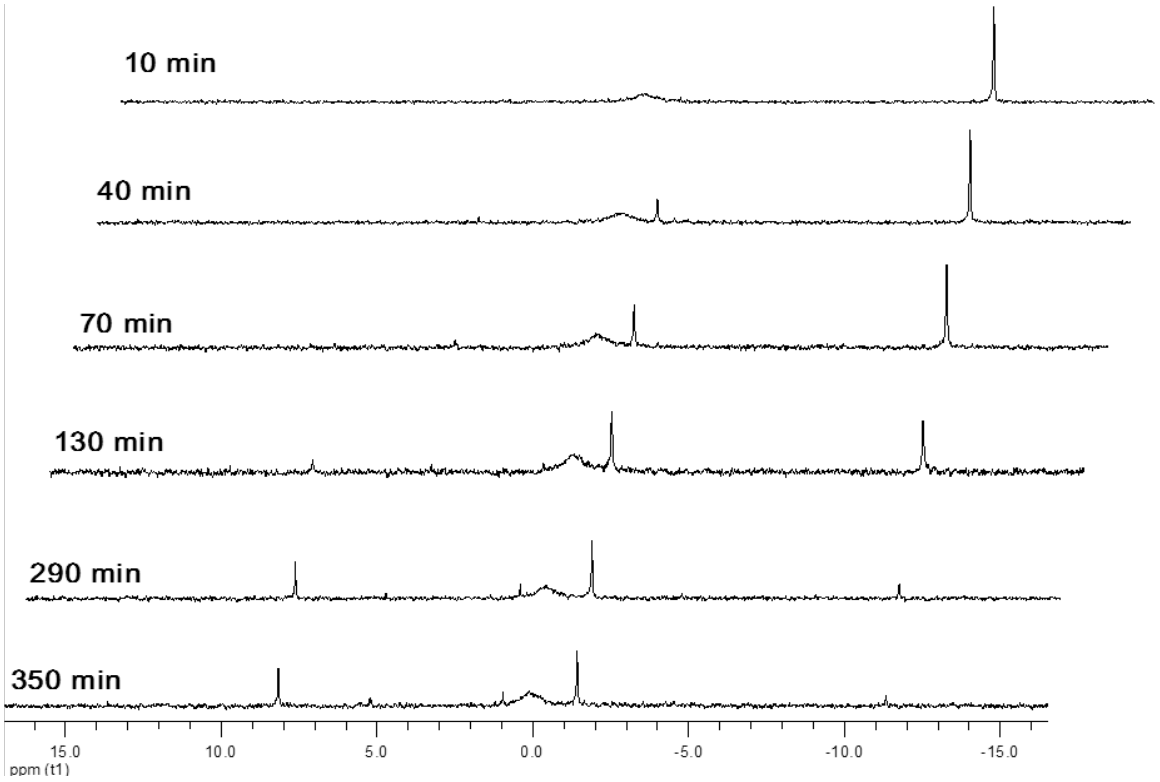


Figure S.10 Progressive ^{31}P NMR spectra for the reaction of **DPP** with hydroxylamine (1M) in D_2O, at pD 5.0 and 25°C. Phosphoric acid (85%) was used as external reference. For assignments see the main text.

3. Theoretical calculations

3.1. Reaction of TPP with hydroxylamine

3.1.1 Cartesian coordinates for Mechanism **1** (**TPP** + NH_2OH):

3.1.1.1. Reactant

Atom	X	Y	Z
P	0.48017300	0.09257000	-0.18130200
O	-0.07396400	0.10100700	1.20406000
O	-0.18974000	1.14185500	-1.18819200
O	0.41393900	-1.30241700	-0.96511100
O	2.02937900	0.47121500	-0.34188700
C	-0.70875000	-2.15605000	-0.95775900
C	-1.66705600	-1.99831600	-1.95352400
C	-1.72112500	-3.97680100	-0.05706600
C	-2.71336400	-2.92013900	-1.96875200
H	-1.58757700	-1.19706900	-2.67860200
C	-2.74248800	-3.93084200	-1.00337700
H	-1.70695600	-4.74608000	0.70891500
H	-3.48959500	-2.85061300	-2.72401700
H	-3.53766400	-4.66798000	-0.98216500
C	3.13750700	-0.24692000	0.12496900
C	5.39905100	-0.48168900	-0.09569000
C	4.24113300	-1.83372300	1.50368200
C	5.43906200	-1.46568400	0.88668200
H	6.30110700	-0.15812200	-0.60585100
H	4.22606200	-2.59417700	2.27781200
C	-0.98181300	2.23720800	-0.79247300
C	-0.44342900	3.23917600	0.00959400
C	-1.28014800	4.30918600	0.32313300
H	0.57888000	3.18498700	0.36559800
C	-2.99462700	3.26860500	-0.98988800
C	-2.58342400	4.32504400	-0.18125200
H	-0.91531200	5.11809400	0.94793500
H	-3.99519000	3.24680200	-1.41042800
H	-3.26459600	5.13920500	0.04031000
C	3.05191500	-1.21227300	1.12525700
H	2.11111200	-1.46758500	1.59688900
O	-5.46237100	-0.87396600	0.80625000
H	6.38112800	-1.92791500	1.15909200
N	-2.20151000	2.22437100	-1.29993500
N	4.25771700	0.12320900	-0.47762800
N	-0.69908600	-3.09902500	-0.03204800
N	-4.27024900	-1.32911100	1.40898100
H	-3.73979800	-1.93418400	0.77088700
H	-3.66020400	-0.53099100	1.68001800
H	-4.46862100	-1.88006300	2.25160700
O	-2.63415000	0.93258500	2.13101100
H	-2.92101900	1.70440500	1.61970200
H	-1.75566700	0.70244400	1.76679800
O	1.21429700	1.03336100	3.61767500
H	0.82298100	0.74769900	2.77061600
H	1.46141800	1.95837500	3.47678500
O	4.27766700	2.02737500	-2.64815900
H	4.27212000	1.40226000	-1.88669300
H	4.88157800	2.73704300	-2.38766500

3.1.1.2. Transition State (TS1)

Atom	X	Y	Z
P	-0.14898500	-0.12874200	0.49757400
O	-0.65599100	-0.44495800	1.92651800
O	0.80929400	-1.15787700	-0.37544800
O	-0.71200800	1.15919400	-0.37777600
O	-1.43744300	-1.04296900	-0.26933300
C	-0.14465600	2.41789100	-0.52853900
C	0.46697500	2.71705300	-1.74624100
C	0.13485100	4.53872800	0.26966200
C	0.93100000	4.01693300	-1.92907900
H	0.56726300	1.95320100	-2.50878900
C	0.76459600	4.95046700	-0.90035200
H	-0.01582900	5.23016700	1.09363400
H	1.41576000	4.29668600	-2.85919600
H	1.11298200	5.97240700	-1.00228700
C	-2.77345900	-0.90069600	-0.11173400
C	-4.81324400	-1.82025100	-0.69849900
C	-4.79262700	0.11924600	0.68980400
C	-5.52510000	-0.86132000	0.01180800
H	-5.32698800	-2.60786100	-1.24338200
H	-5.30039900	0.89167500	1.25990400
C	2.10150900	-1.55585200	-0.07690400
C	2.40454700	-2.18474800	1.13288600
C	3.70492700	-2.64820500	1.30738500
H	1.64625600	-2.30559800	1.89785000
C	4.22255000	-1.85074200	-0.88961400
C	4.63821100	-2.47944300	0.27818100
H	3.98433500	-3.14255000	2.23261100
H	4.90536100	-1.70277000	-1.72104100
H	5.65901400	-2.83172200	0.37605600
C	-3.40270900	0.11050300	0.63530900
H	-2.82711300	0.86314600	1.15532200
O	1.33498500	0.72424300	0.90868400
H	-6.60898900	-0.88219800	0.03358200
N	2.96772700	-1.39024300	-1.06960500
N	-3.46958300	-1.84639500	-0.76303000
N	-0.32831000	3.28582400	0.45943100
N	1.45333400	1.50556800	2.11591500
H	0.90883100	2.36237200	1.96668700
H	1.11382900	0.68158300	3.31828700
H	2.43906900	1.77390100	2.10221200
O	0.61017000	-0.05339900	3.91937800
H	1.23854300	-0.76502500	4.12663800
H	-0.02706200	-0.35038500	2.99122000
O	-1.83332100	-3.72022000	-2.13912300
H	-0.93364200	-3.38922700	-2.00437800
H	-2.40805800	-3.06903100	-1.66221600
O	2.40401000	-0.36709400	-3.66347800
H	2.11939900	0.55394100	-3.57903000
H	2.54824100	-0.67759600	-2.73609100

3.1.1.3. Intermediate

Atom	X	Y	Z
P	-0.21754000	-0.31768900	1.01844800
O	-0.42902700	-0.16484300	2.59497500
O	-1.31330900	0.08215500	-0.13491200
O	1.30639900	-0.75908400	0.55697000
O	0.34419900	1.34271100	0.95898000
C	1.69562300	-1.79805600	-0.27008400
C	2.79779400	-2.55534400	0.13564600
C	1.55999800	-2.85413200	-2.28665000
C	3.28821500	-3.50103300	-0.76054300
H	3.24511200	-2.39426600	1.10970200
C	2.65878200	-3.65777700	-2.00060500
H	1.03821900	-2.94372000	-3.23520300
H	4.14846100	-4.10740100	-0.49426700
C	0.20351100	2.20310700	-0.09163700
C	1.07615300	3.12512600	-2.01125900
C	-1.01280700	3.95458100	-1.18923700
C	-0.00052400	3.99148900	-2.15610800
H	1.89374100	3.12807800	-2.72691100
H	-1.86847300	4.61960200	-1.25709100
C	-2.60984600	-0.35917500	-0.33320200
C	-2.95735500	-0.74129100	-1.62962600
C	-4.29630400	-1.03813400	-1.86933600
H	-2.20557200	-0.78718400	-2.40874500
C	-4.74312600	-0.57000700	0.43687300
C	-5.21256900	-0.95387500	-0.81576800
H	-4.61839000	-1.33181300	-2.86357200
H	-5.42054700	-0.49180600	1.28234000
C	-0.91166900	3.05086300	-0.13823300
H	-1.67154300	2.97816600	0.63142600
O	-0.85140000	-1.88723500	1.00248100
H	-0.23195000	0.74547300	2.97346600
O	0.05031200	2.21081800	3.68531100
H	-0.74349800	2.56764000	4.11336000
H	0.16974200	2.74355200	2.88255200
H	-0.04000500	4.67973800	-2.99326400
N	1.18425600	2.24007800	-0.99815000
H	-6.26401300	-1.17664200	-0.96071700
N	-3.45481100	-0.26136900	0.68445900
H	3.00999300	-4.38271300	-2.72672700
N	1.08254300	-1.92090100	-1.43983000
N	-0.28255430	-2.72712460	1.87803798
H	-0.99344030	-2.83380860	2.60412398
H	-0.27464330	-3.60530460	1.35743798
O	3.77305600	1.15934400	-0.91588000
H	2.81746200	1.43278100	-0.91455200
H	3.76536200	0.19150500	-0.88424500
O	4.85471200	2.13548700	1.44613500
H	4.44680300	1.77006600	0.62616800
H	4.16030500	2.07708900	2.11749500

3.1.1.4. Transition State (**TS2**)

Atom	X	Y	Z
P	-0.30152400	-0.56567000	1.10568200
O	-0.46064500	-0.21926000	2.60972300
O	-1.25982800	0.03015100	-0.02943300
O	1.22134900	-0.82046300	0.66050600
O	0.49156400	1.56948500	0.97800100
C	1.66634400	-1.80696500	-0.23195200
C	2.78843500	-2.53343200	0.16113400
C	1.54401700	-2.81367500	-2.26496300
C	3.29316500	-3.45261800	-0.75587700
H	3.23346200	-2.37966800	1.13710400
C	2.65931400	-3.60019000	-1.99415500
H	1.02105700	-2.89469600	-3.21310100
H	4.16670600	-4.04581500	-0.50464900
C	0.28620700	2.34964800	-0.07083700
C	1.04787400	3.19080000	-2.10490400
C	-1.05530900	3.96736200	-1.27918800
C	-0.07031100	3.99521700	-2.27896900
H	1.84342200	3.18109600	-2.84656000
H	-1.94739900	4.58158200	-1.36711400
C	-2.59092400	-0.34439200	-0.27591400
C	-2.91172500	-0.68323500	-1.58721100
C	-4.25023800	-0.96664600	-1.85084100
H	-2.14844300	-0.71782000	-2.35501000
C	-4.72984600	-0.54620900	0.45977200
C	-5.17987300	-0.90228800	-0.80828000
H	-4.55951000	-1.23700400	-2.85546600
H	-5.41815600	-0.47957000	1.29685900
C	-0.88083400	3.14688000	-0.17502100
H	-1.62134200	3.09626000	0.61647000
O	-0.93302000	-2.07651600	1.06656500
H	-0.27908900	0.74061000	3.00303800
O	0.01384100	2.08469100	3.45045600
H	-0.80493000	2.56025300	3.66080800
H	0.21219500	2.26812600	2.48873300
H	-0.16688700	4.62232400	-3.15853000
N	1.23384000	2.38722800	-1.03745900
H	-6.22957000	-1.11875000	-0.97341300
N	-3.44097800	-0.25824800	0.73135000
H	3.02092000	-4.30656700	-2.73322600
N	1.04877700	-1.91054300	-1.39470700
N	-0.30949800	-2.97966100	2.03709800
H	-1.08605600	-3.20328600	2.66278700
H	-0.14912800	-3.81462200	1.47074100
O	3.71767600	1.21810400	-0.91184300
H	2.77940400	1.57729700	-0.93046300
H	3.62864300	0.25448200	-0.88135600
O	4.83979800	2.12133100	1.44484000
H	4.41655100	1.77873900	0.62104000
H	4.14236800	2.08894400	2.11482900

3.1.1.5 Product

Atom	X	Y	Z
P	-0.42418600	-0.95222500	1.21881500
O	-0.50933900	-0.34156100	2.57335800
O	-1.21739500	-0.21619300	0.02907200
O	1.10344000	-0.94888000	0.71301800
O	1.08118600	2.28438900	1.05739800
C	1.64592300	-1.83744500	-0.23150600
C	2.80025600	-2.51700000	0.15115200
C	1.60608300	-2.77555600	-2.30087500
C	3.36207300	-3.38125600	-0.78640700
H	3.22199100	-2.37588500	1.13935000
C	2.75244400	-3.51910900	-2.03752600
H	1.10278600	-2.84875800	-3.26029500
H	4.25881200	-3.94100300	-0.54016400
C	0.57205400	2.81606500	-0.07503000
C	0.92270300	3.17239900	-2.32528000
C	-1.06196400	4.04899000	-1.32110500
C	-0.25935300	3.88915100	-2.45929400
H	1.57759000	3.00996300	-3.17704900
H	-1.99841300	4.59583900	-1.37896800
C	-2.57824100	-0.41058700	-0.25243000
C	-2.91236700	-0.63992500	-1.58480800
C	-4.26401100	-0.81521900	-1.87165600
H	-2.14576500	-0.68482900	-2.34881500
C	-4.73443000	-0.50512400	0.45848400
C	-5.19616800	-0.75187800	-0.83084400
H	-4.58239700	-1.00408600	-2.89191900
H	-5.42384400	-0.44291400	1.29501300
C	-0.65287000	3.50462600	-0.10998500
H	-1.24508000	3.60976800	0.79255800
O	-0.99354600	-2.45437800	1.06478200
H	-0.41207500	1.35335900	3.25880700
O	-0.19325400	2.29190700	3.43720700
H	-1.04591300	2.74838300	3.49758400
H	0.51046300	2.44728300	1.85316000
H	-0.54502800	4.30370900	-3.41932400
N	1.33887200	2.64243200	-1.15801100
H	-6.25645800	-0.88780400	-1.01347800
N	-3.43037800	-0.33093200	0.75447200
H	3.15594000	-4.18492500	-2.79248900
N	1.05099300	-1.93202900	-1.40751500
N	-0.45624539	-3.27679103	2.01968768
H	-1.28606739	-3.58786903	2.52851868
H	-0.14878439	-4.07026403	1.45403868
O	3.75687300	1.24962700	-0.96867300
H	2.87570500	1.71255000	-1.02999100
H	3.54782400	0.30657100	-0.89200400
O	4.82755100	2.11974700	1.43717600
H	4.42555700	1.79436400	0.59714000
H	4.09321100	2.14884900	2.06678400
H	3.54782400	0.30657100	-0.89200400
O	4.82755100	2.11974700	1.43717600
H	4.42555700	1.79436400	0.59714000

3.1.2. Cartesian coordinates for Mechanism 2 (**TPP** + NH_2OH):

3.1.2.1 Reactant

Atom	X	Y	Z
P	-0.40844600	-0.35924600	-0.52060900
O	0.67273600	0.20798300	-1.36851200
O	-0.80182500	0.46341100	0.81192500
O	-0.10785100	-1.80395900	0.11555300
O	-1.74481500	-0.61182800	-1.36304200
C	1.17231600	-2.22121100	0.52766800
C	2.94193400	-2.24320600	2.10929300
C	2.95701100	-3.56109600	0.10598100
C	3.59115200	-3.16179800	1.28022600
H	3.39784500	-1.91172900	3.03664400
H	3.42287100	-4.28051500	-0.56039800
H	4.56397100	-3.56579500	1.53818300
C	-3.04362200	-0.91851600	-0.92598000
C	-3.29692300	-1.55350400	0.28824400
C	-4.63065200	-1.82774600	0.58836200
H	-2.50117300	-1.83404900	0.96604800
C	-5.24324600	-0.84736600	-1.50605900
C	-5.62753700	-1.47059400	-0.32232700
H	-4.88080700	-2.32123300	1.52212900
H	-5.98140300	-0.55543100	-2.24662800
C	-1.15753000	1.81381500	0.84596500
C	-1.75958600	3.72409500	-0.22978100
C	-1.61013200	3.73289300	2.16273900
C	-1.87753500	4.41605200	0.97052200
H	-1.95559800	4.21340300	-1.17911600
H	-1.68972400	4.23736800	3.12035700
H	-2.17023800	5.46009600	0.97157000
C	1.69087800	-1.75603700	1.73260700
H	1.14081200	-1.04589800	2.33855400
C	-1.23653200	2.39311400	2.11111200
H	-1.01422100	1.81400700	2.99969800
H	-6.67456400	-1.67083800	-0.12370700
N	-1.40295900	2.42481000	-0.29906800
N	-3.96204600	-0.56722900	-1.81106800
N	1.75048900	-3.09840300	-0.27566600
O	3.80808000	1.07347600	0.42986200
N	3.58826900	0.23642600	-0.69674600
H	3.86912800	-0.72835300	-0.49025900
H	2.58901100	0.22435000	-0.95250700
H	4.16246700	0.60441200	-1.49481900
O	5.32887400	1.75775200	-2.22386200
N	5.54370700	2.54085600	-1.05963800
H	4.94429700	2.14558900	-0.28236700
H	6.53007900	2.51970500	-0.78106600
H	5.29015300	3.52033900	-1.22470500

3.1.2.2. Transition State (**TS4**)

Atom	X	Y	Z
P	-0.03672100	-0.57344300	0.18269800
O	-0.54979200	-0.73172900	1.60976600
O	1.05133600	-1.64779200	-0.46061300
O	-0.54836500	0.54802700	-0.92941900
O	-1.19889500	-1.66655000	-0.58270400
C	-0.22526900	1.89367000	-1.04521200
C	0.63375600	2.27532300	-2.07808000
C	-0.62823500	4.05204200	-0.42770700
C	0.85833500	3.63686600	-2.25876100
H	1.09981700	1.52569900	-2.70659500
C	0.21877900	4.54965700	-1.41277100
H	-1.15270300	4.72585100	0.24379800
H	1.52005800	3.98023300	-3.04795800
H	0.36676300	5.61902800	-1.51761900
C	-2.55013900	-1.59247500	-0.50915400
C	-4.51103400	-2.61987800	-1.15136200
C	-4.64998300	-0.62313900	0.14406900
C	-5.30295200	-1.66337100	-0.52478100
H	-4.96858200	-3.45023800	-1.68318600
H	-5.21734200	0.15105600	0.65275400
C	2.43622600	-1.62200700	-0.37179900
C	3.05603900	-2.23352700	0.71957700
C	4.44805500	-2.29173800	0.72209700
H	2.46098300	-2.64748700	1.52621100
C	4.42368300	-1.18522300	-1.40170200
C	5.15142600	-1.75364200	-0.35938400
H	4.97286000	-2.75656400	1.55095200
H	4.93142200	-0.76779900	-2.26653500
H	6.23492400	-1.78008600	-0.40036400
C	-3.25988600	-0.57708400	0.15907600
H	-2.74347300	0.21748700	0.67799800
O	1.29518500	0.56727300	0.58485300
H	-6.38483600	-1.73214400	-0.55788600
N	3.07866200	-1.11930000	-1.41990300
N	-3.16603400	-2.59733700	-1.15117600
N	-0.86207000	2.73717300	-0.24345600
N	1.68208500	0.66926900	1.95218800
H	2.57615200	1.16600900	1.91994600
H	0.85277000	1.28327400	2.66176800
H	1.86546600	-0.26627500	2.32585600
O	0.07492500	1.92824100	3.39396800
N	-1.16707100	1.25601000	3.37937400
H	-1.91237400	1.90611100	3.11062600
H	-1.11876400	0.46789700	2.68760000
H	-1.37928900	0.88629500	4.31152800

3.1.2.3 Intermediate

Atom	X	Y	Z
P	-0.16470200	-0.40895500	0.35044200
O	0.54534700	-0.90406500	1.69885900
O	0.23681600	1.00152100	-0.39903000
O	-1.20180700	-1.48140600	-0.35518500
O	1.00673300	-1.18635600	-0.68169500
C	-2.57625500	-1.38737900	-0.52091900
C	-3.35087100	-2.43972300	-0.02872600
C	-4.36931700	-0.35348000	-1.47510000
C	-4.71545800	-2.41114100	-0.29891300
H	-2.88992500	-3.23786200	0.54123400
C	-5.24182100	-1.34305600	-1.03438000
H	-4.73403200	0.49037800	-2.05361900
H	-5.35848000	-3.20806400	0.06156100
C	2.26257100	-0.75832400	-1.01193500
C	3.89007600	-0.82319200	-2.63290900
C	4.36011600	0.32705100	-0.59443200
C	4.77916000	-0.07829900	-1.86552300
H	4.17251300	-1.17007600	-3.62330000
H	5.01829100	0.90220400	0.05008600
C	-0.04551200	2.30710900	-0.00297200
C	-0.86235100	3.07336700	-0.83445300
C	-1.04850800	4.41042900	-0.49170300
H	-1.32370200	2.63317000	-1.71031800
C	0.38575400	4.05427900	1.39340300
C	-0.41639000	4.91480900	0.64918900
H	-1.67656100	5.04741200	-1.10675300
H	0.90243700	4.40725200	2.28134300
C	3.08795900	-0.01845400	-0.15011500
H	2.74841600	0.27022000	0.83624600
O	-1.35323000	0.43710800	1.20689700
H	1.23315700	-1.62413300	1.59329600
O	2.31267600	-2.88464900	1.69370700
H	2.66761900	-3.08782700	0.81395400
H	5.76341500	0.16945800	-2.24776000
N	2.65125700	-1.15932400	-2.22683700
H	-0.53616100	5.94914800	0.95262100
N	0.58223000	2.76060900	1.07299700
H	-6.30004200	-1.28069700	-1.26368700
N	-3.04225400	-0.37315700	-1.23586900
N	-2.03997100	-0.34310700	2.22303100
H	-1.65847100	0.01995500	3.09895500
H	-2.99418300	0.01474200	2.15844800
N	3.49357800	-2.61589800	2.50213100
H	3.41445300	-1.62369200	2.73435900
H	3.30070700	-3.12232600	3.36701600

3.1.2.4. Transition State (**TS5**)

Atom	X	Y	Z
P	0.47937300	-0.24424700	-0.78386900
O	-0.15709200	-0.93861300	-2.02237200
O	-0.35149000	0.76652300	0.13444400
O	1.53334800	-1.18631700	-0.02992300
O	-0.86088000	-1.70713700	0.44104200
C	2.75472300	-0.78984300	0.53604600
C	3.83444900	-1.64294800	0.31913600
C	3.94391400	0.62633600	1.85374800
C	5.03514700	-1.30076400	0.93586500
H	3.72779600	-2.52393700	-0.30256400
C	5.09550200	-0.14205300	1.71762300
H	3.94521800	1.53243400	2.45203800
H	5.91068400	-1.92850000	0.80432700
C	-2.02078200	-1.33592900	0.96771900
C	-3.32604600	-1.05857200	2.86402200
C	-4.29762000	-0.53093700	0.74773300
C	-4.42741800	-0.61204200	2.14205900
H	-3.38199100	-1.13959900	3.94764800
H	-5.12745500	-0.19048100	0.13382200
C	-0.64123000	2.11036800	-0.16819900
C	-0.31268500	3.05211300	0.80204400
C	-0.67953600	4.37119300	0.54231400
H	0.20095000	2.75791000	1.70939500
C	-1.61435700	3.63524400	-1.53910700
C	-1.34044700	4.67279000	-0.65236100
H	-0.44967200	5.15019200	1.26214400
H	-2.12838000	3.82431700	-2.47665800
C	-3.09652800	-0.89365400	0.15561200
H	-2.96472900	-0.84607200	-0.92049300
O	1.40763700	0.89708600	-1.48673000
H	-0.51561600	-1.91346300	-1.92802500
O	-0.93324600	-3.29168900	-1.60833300
H	-1.08702900	-2.97427500	-0.67392600
H	-5.34748800	-0.33985700	2.64842000
N	-2.14773500	-1.41015700	2.31339200
H	-1.64015300	5.68722100	-0.89128500
N	-1.27335800	2.35294700	-1.30149600
H	6.01289200	0.15855600	2.21159900
N	2.76966500	0.30492900	1.27273600
N	2.35740600	0.34663000	-2.45689400
H	2.03550600	0.75532100	-3.33669100
H	3.21457600	0.84341100	-2.20707000
N	-2.22730700	-3.73114400	-2.11185400
H	-2.51471200	-2.99103300	-2.75603000
H	-1.98041600	-4.52751600	-2.70034800

3.1.2.5 Product

Atom	X	Y	Z
P	-1.25696100	0.26620000	0.91391300
O	-0.14613000	-0.21766600	1.78331800
O	-0.85916100	1.19549200	-0.33630700
O	-1.93056100	-1.00786500	0.20387200
O	2.67121300	-2.91325000	-0.46587900
C	-3.07094700	-1.08149300	-0.60310300
C	-3.48178300	-2.37265600	-0.93429300
C	-4.74863300	-0.09300200	-1.77324100
C	-4.60867500	-2.48494700	-1.74237500
H	-2.93747800	-3.23586300	-0.56965300
C	-5.25971300	-1.32255800	-2.17234300
H	-5.22105000	0.83415400	-2.08387300
H	-4.97382800	-3.46522800	-2.03176500
C	3.59228100	-1.92566800	-0.63534500
C	5.31468800	-1.13032400	-1.92395300
C	4.65720600	0.12498600	0.00115900
C	5.49612900	-0.01648600	-1.11180100
H	5.94179400	-1.28207100	-2.79838700
H	4.75816600	0.97815700	0.66555000
C	-0.10511000	2.37125900	-0.27322900
C	0.28749800	2.91093000	-1.49686200
C	1.02531400	4.09029500	-1.45126000
H	0.02298400	2.42319500	-2.42771000
C	0.88111700	4.02136400	0.94044300
C	1.33203200	4.65961200	-0.20965200
H	1.35783500	4.55782200	-2.37255400
H	1.09327900	4.42715200	1.92495500
C	3.68782700	-0.83857600	0.25188400
H	3.01687400	-0.76279600	1.10078800
O	-2.40003700	1.14837400	1.62595800
H	0.57275200	-1.83035600	1.66763800
O	1.03654800	-2.70188800	1.65580000
H	2.11285200	-2.76188000	0.34382100
H	6.26511100	0.71291700	-1.34139200
N	4.38209900	-2.07711900	-1.70176300
H	1.90653700	5.57625300	-0.13551500
N	0.15974400	2.88155600	0.91547000
H	-6.14094000	-1.36837100	-2.80268000
N	-3.65597600	0.03631800	-0.99112400
N	-2.96959700	0.42906700	2.78107700
H	-2.79209000	1.08235100	3.54660400
H	-3.97029400	0.48318600	2.58111900
N	1.73794600	-2.84806800	2.91496300
H	2.28127800	-1.98978600	3.03168800
H	1.01076900	-2.82609300	3.63205700

Table S.7. Structural parameters of intermediate (**Int**), transition state (**TS2**) and products (**P**) for Mechanism **1** in the reaction of **TPP** with hydroxylamine at the B3LYP/6-31++G(d,p) level of theory.

Interatomic distances (Å)						
	P_1-O_2	O_2-H_3	H_3-O_4	O_4-H_5	H_5-O_6	H_6-O_1
Int	1.598	1.005	1.653	0.971	2.386	1.754
TS2	1.552	1.053	1.447	0.999	1.688	2.281
P	1.488	1.831	0.980	1.740	0.992	3.573
Dihedral angles						
	P_1-O_2-H_3-O_4	O_2-H_3-O_4-H_5	H_3-O_4-H_5-O_6	O_4-H_5-O_6-P_1	H_5-O_6-P_1-O_2	O_6-P_1-O_2-H_3
TS2	-11.3	11.6	-13.3	18.2	-8.1	5.4
Imaginary frequency (cm^{-1})						
193.10						

Table S.8. Structural parameters of intermediate (**Int**), alternative transition states (**TS4** and **TS5**) and products (**P**) for Mechanism **2** in the reaction of **TPP** with hydroxylamine at the B3LYP/6-31++G(d,p) level of theory.

Interatomic distances (Å)						
	P_1-O_2	O_2-H_3	H_3-O_4	O_4-H_5	H_5-O_6	H_6-O_1
Int	1.602	1.001	1.663	0.970	2.935	1.744
TS4	1.556	1.043	1.475	0.999	1.703	2.332
TS5	1.510	1.601	1.070	1.027	2.938	2.228
P	1.491	1.770	0.987	1.698	0.995	5.239
Dihedral angles						
	P_1-O_2-H_3-O_4	O_2-H_3-O_4-H_5	H_3-O_4-H_5-O_6	O_4-H_5-O_6-P_1	H_5-O_6-P_1-O_2	O_6-P_1-O_2-H_3
TS4	-8.7	38.4	-10.9	-6.0	24.4	-25.6
	P_1-O_2-H_3-N_4	O_2-H_3-N_4-H_5	H_3-N_4-H_5-O_6	N_4-H_5-O_6-P_1	H_5-O_6-P_1-O_2	O_6-P_1-O_2-H_3
TS5	149.5	-151.7	24.0	-39.6	29.6	-28.7
Imaginary frequency (cm^{-1})						
TS4				**TS5**		
168.9				160.0i		

3.2. Reaction of DPP with hydroxylamine

3.2.1 Cartesian coordinates for the reaction DPP + NH_2OH:

3.2.1.1 Reactant

Atom	X	Y	Z
P	-0.43922800	-0.71497900	-0.07807800
O	-0.41432600	-1.88861900	0.86083900
O	1.04840500	-0.65967600	-0.89727300
O	-0.35637200	0.62157700	0.86716800
O	-1.43739300	-0.55758400	-1.18832500
C	2.26963900	-0.73723900	-0.36267000
C	2.61713100	-0.72499100	0.98892300
C	4.56958400	-0.88254500	-0.98089100
C	3.96376000	-0.79214300	1.32772400
H	1.84981700	-0.66098500	1.74784900
C	4.95742600	-0.87008700	0.33985500
H	5.24957900	-0.94130200	-1.82086500
H	4.24382500	-0.78087200	2.37580000
H	6.00853900	-0.92061500	0.59394700
C	-0.59918100	1.93192100	0.46256700
C	-0.09367700	2.44189500	-0.73494000
C	-0.35451500	3.78062500	-1.01952700
H	0.48501200	1.82478000	-1.41111700
C	-1.52932600	3.92810000	1.05897600
C	-1.08771400	4.54471000	-0.10764200
H	0.01716400	4.21971600	-1.94006800
H	-2.09704400	4.48351300	1.79969100
H	-1.30850100	5.59040400	-0.29176600
N	-1.29503300	2.63364500	1.34839700
N	3.25141700	-0.81890500	-1.29079500
N	-3.84075800	-2.24209100	-0.98160600
H	-3.06349700	-1.59433500	-1.19518900
H	-3.51994800	-2.83267400	-0.19245800
O	-5.02255300	-1.54205200	-0.64499600
H	-3.98946800	-2.84454300	-1.79769600
H	2.96974800	-0.82781000	-2.27100800
O	-2.61819900	-3.54281700	1.35439500
H	-1.85007900	-2.93805900	1.25479500
H	-3.09136800	-3.22918800	2.13855800

3.2.1.2. Transition State (TS)

Atom	X	Y	Z
P	0.76825900	-0.91439900	0.31669500
O	0.44002900	-2.16876200	-0.46397800
O	-0.91432100	-0.59833100	1.03472400
O	0.64919700	0.40544800	-0.66634900
O	1.44671200	-0.81798100	1.66171900
C	-2.05927600	-0.59764500	0.40252800
C	-2.28872300	-0.60175200	-0.98786800
C	-4.43586500	-0.55758100	0.77198700
C	-3.59074000	-0.58408200	-1.45983700
H	-1.44717700	-0.61199700	-1.66528900
C	-4.68866100	-0.56176500	-0.57785700
H	-5.20046900	-0.54055900	1.53826000
H	-3.76251900	-0.58486700	-2.53161600
H	-5.70902600	-0.54664800	-0.93919500
C	0.77601600	1.74008800	-0.34454000
C	0.85440600	2.21652500	0.96891000
C	0.96269200	3.59377100	1.14616700
H	0.83564500	1.54051900	1.81323700
C	0.89599900	3.84766200	-1.22807800
C	0.98580700	4.43449100	0.03015700
H	1.02722200	4.00189400	2.15025900
H	0.90701200	4.45803100	-2.12667400
H	1.06861600	5.51114900	0.13029000
N	0.79300600	2.52011200	-1.42337200
N	-3.15257400	-0.57806000	1.21667100
N	3.64798700	-1.63337300	0.21748300
H	3.38925700	-1.47250500	1.20263900
H	3.53030300	-2.64122800	0.00300200
O	2.79248800	-0.86908500	-0.59463300
H	4.62360200	-1.35795900	0.07082700
H	-2.97584800	-0.57723600	2.22009100
O	2.39438600	-4.12324200	-0.58359700
H	1.64814900	-3.47915400	-0.61826400
H	2.58456100	-4.34685900	-1.50596300

3.2.1.3 Product

Atom	X	Y	Z
P	1.48141200	-0.95620900	0.12943100
O	0.75734600	-2.17791600	-0.37444400
O	-1.92378300	-0.27212000	1.61721800
O	0.77983000	0.32440400	-0.58887700
O	1.81879500	-0.77187400	1.58102300
C	-2.88289900	-0.39992500	0.80973900
C	-2.78446000	-0.37667300	-0.62278400
C	-5.28554300	-0.72586000	0.52905300
C	-3.90210800	-0.52204200	-1.41006500
H	-1.79895000	-0.23795500	-1.05143600
C	-5.18817500	-0.70072500	-0.83572000
H	-6.21646900	-0.85697800	1.06715600
H	-3.79946300	-0.49947800	-2.49136800
H	-6.07375300	-0.81472800	-1.44811800
C	0.98568000	1.67715700	-0.32293500
C	0.91454600	2.18439800	0.97551000
C	1.05611100	3.56203900	1.12879200
H	0.74839800	1.52855800	1.82030300
C	1.28447900	3.74072000	-1.24744400
C	1.24286700	4.36182300	-0.00250200
H	1.00823900	4.00269300	2.11985500
H	1.42095000	4.32271800	-2.15422700
H	1.34882900	5.43829900	0.07578100
N	1.16157400	2.40973300	-1.41552600
N	-4.16968200	-0.58185400	1.30018600
N	3.99842300	-1.64557500	-0.24031200
H	4.18149700	-1.42636500	0.74875000
H	3.72548500	-2.66278900	-0.36400400
O	2.96384500	-0.81233100	-0.74164900
H	4.83000700	-1.42409800	-0.79885000
H	-4.26679600	-0.60445900	2.31169900
O	2.79500600	-4.11420800	-0.54923400
H	1.92471100	-3.65991200	-0.56721700
H	2.91272100	-4.49090400	-1.43419700

Table S.9. Structural parameters of reactant (R2), transition state (TS) and products (P) for the reaction of **DPP** with hydroxylamine at the B3LYP/6-31+G(d,p) level of theory, calculated for mechanism **B** of Scheme 9.

Interatomic distances (Å)								
	O_1-P_2	P_2-O_3	P_2-O_6	P_2-O_7	P_2-O_8	O_3-N_4	N_4-H_5	O_9-H_{10}
R2	1.693	5.917	1.508	1.635	1.500	1.412	1.041	0.983
TS	1.840	2.234	1.518	1.648	1.508	1.405	1.037	0.985
P	3.880	1.710	1.505	1.710	1.505	1.360	1.000	0.960

Dihedral angles						
	O_1-P_2-O_3-O_6	O_1-P_2-O_3-N_4	O_3-N_4-H_5-O_9	N_4-H_5-O_9-H_{10}	H_5-O_9-H_{10}-O_6	O_6-P_2-O_3-N_4
TS	-140.18	131.96	-30.61	-5.09	-28.16	-87.87

Imaginary frequency (cm^{-1})
215.24