Electronic Supplementary Information

Transient changes in aromaticity and their effect on excited-state proton transfer reactions

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1. Computational details

Geometry optimizations of transition states (TSs), frequency calculations on the resulting structures, and intrinsic reaction coordinate (IRC)[1] calculations for the different ESPT reactions in the S_1 state were carried out with the *Gaussian 16*[2] suite of programs using the M06-2X[3] global hybrid meta-GGA density functional in combination with the aug-cc-pVDZ basis set[4,5] in the framework of time-dependent density functional theory (TD-DFT).[6] Numerical integrations in all TD-DFT calculations were performed with the default "UltraFine" grid in *Gaussian16* comprising 99 radial shells and 590 angular points per shell. For the double ESPT reactions in the pyridone homo- and heterodimers, fully relaxed TS structures could not be located. Accordingly, for these reactions, full geometry optimizations and IRC calculations were replaced by performing two-dimensional relaxed scans at the aforementioned TD-M06-2X/aug-cc-pVDZ level of theory. Generating a set of two-dimensional data points between which the relevant N-H and O-H distances vary smoothly (see Fig. S1 and S2), at each point all other geometric degrees of freedom were allowed to relax in these scans. Notably, this modelling showed that while the double ESPT is barrierless for the pyridone homodimer (see Fig. S1), this is not the case for the pyridone heterodimer (see Fig. S2).

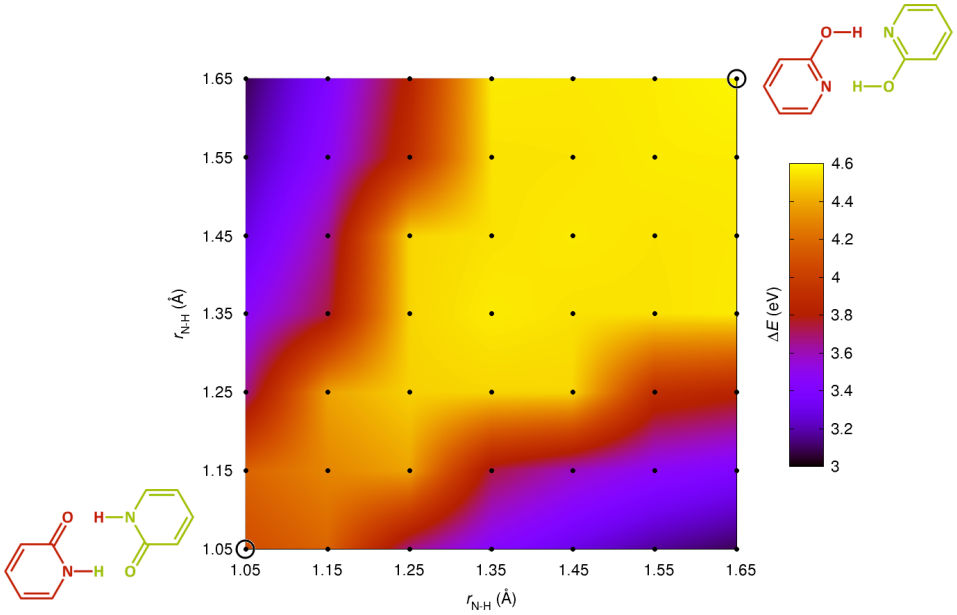


Fig. S1 Two-dimensional relaxed scan for the double ESPT in the pyridone homodimer. The (1.65, 1.65) and (1.05, 1.05) data points correspond to the dienol and diketo forms, respectively. Relative energies in the S_1 state (ΔE) are color coded.

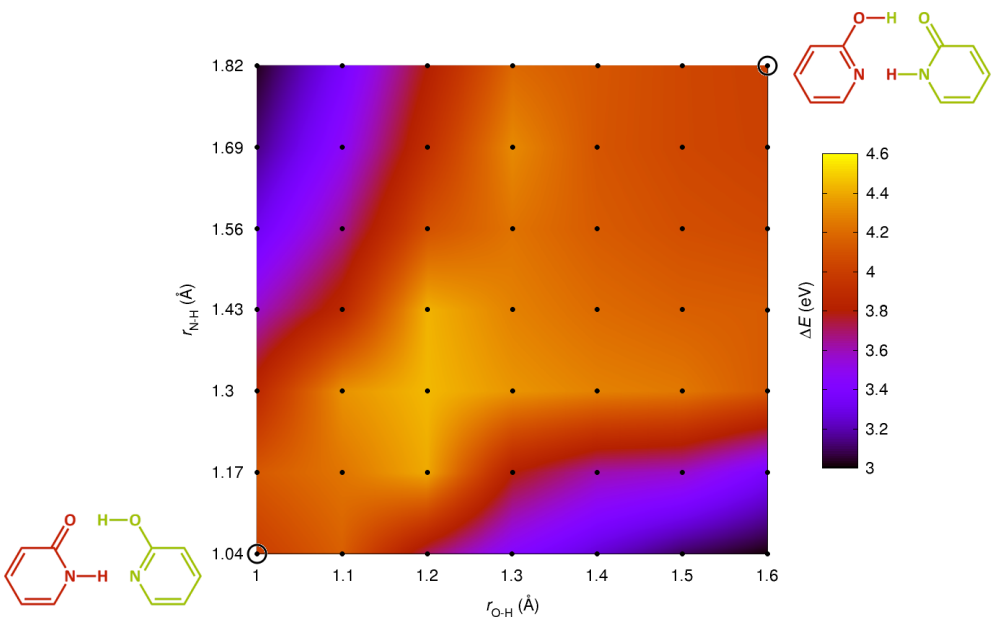


Fig. S2 Two-dimensional relaxed scan for the double ESPT in the pyridone heterodimer. The (1.00, 1.04) and (1.60, 1.82) data points correspond to the keto-A-enol-B and enol-A-keto-B forms, respectively. Relative energies in the S_1 state (ΔE) are color coded.

Based on the resulting S_1 geometries, the final potential energy curves for the ESPT reactions were then derived through single-point calculations with the *BAGEL 1.1.2*[7] suite of programs using the XMS-CASPT2[8] multiconfigurational second-order perturbation theory[9,10] method in combination with the cc-pVDZ basis set.[4] These calculations were done on top of reference wave functions obtained with the CASSCF[11] method and associated state-averaging over the S_0, S_1 and S_2 states (i.e., SA3-CASSCF). The active spaces included the highest occupied and lowest unoccupied π orbitals, corresponding to (12,10) active spaces for the pyridone dimers (see Fig. S3 and S4) and (10,8) active spaces for the pyridone/acetamide (see Fig. S5 and S6) and pyridone/acetic acid (see Fig. S7) systems. For the double ESPT reactions in the pyridone homo- and heterodimers (for which fully relaxed TS structures could not be located), the single-point calculations were carried out at the structures along the main diagonals in Fig. S1 and S2. For all the other ESPT reactions, for which fully relaxed TS structures *could* be located, the single-point calculations were performed at the subsequently obtained IRC structures.

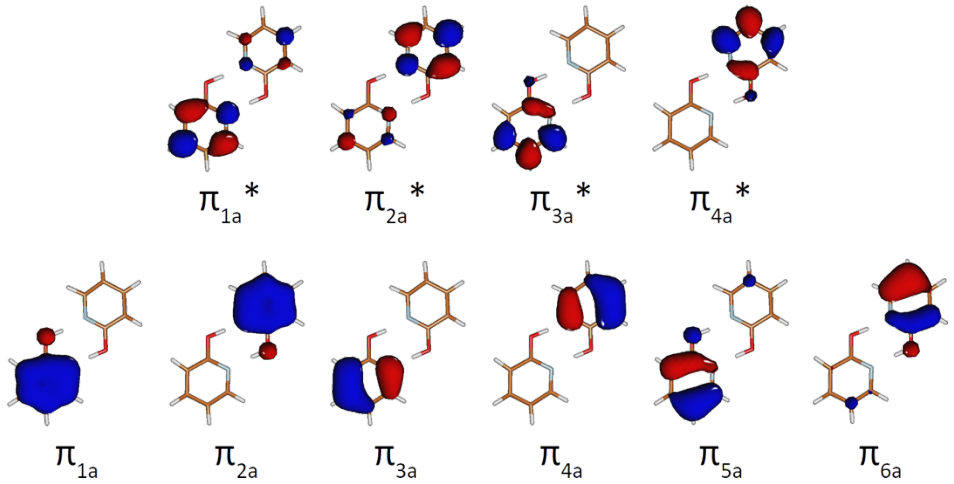


Fig. S3 CASSCF orbitals in the S_1 Franck-Condon region of the pyridone homodimer.

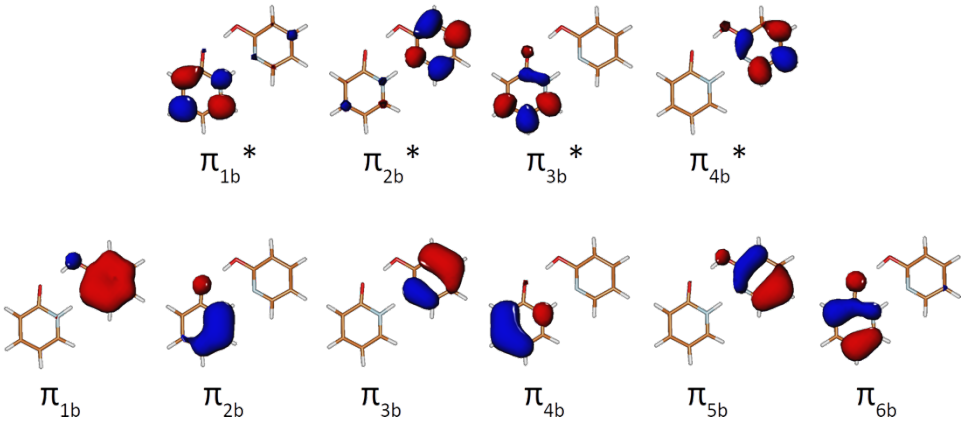


Fig. S4 CASSCF orbitals in the S_1 Franck-Condon region of the pyridone heterodimer.

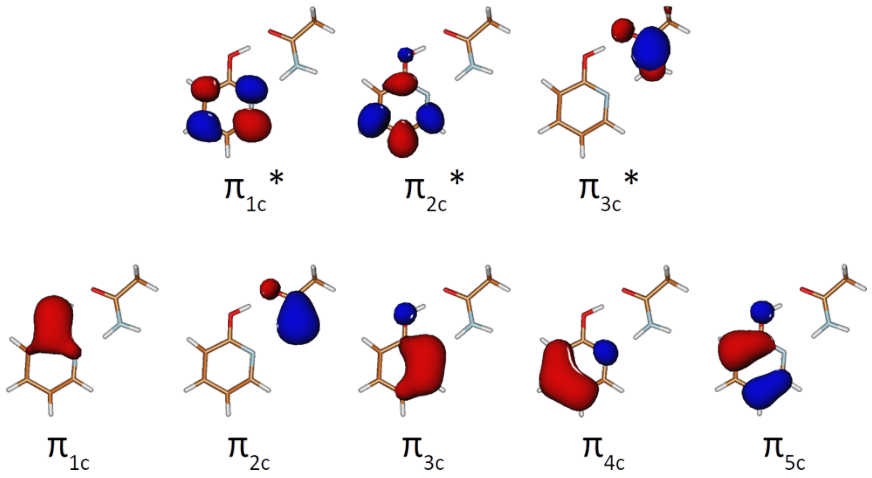


Fig. S5 CASSCF orbitals in the S_1 Franck-Condon region of the pyridone/acetamide (O-H---O / N---H-N hydrogen bond connection) system.

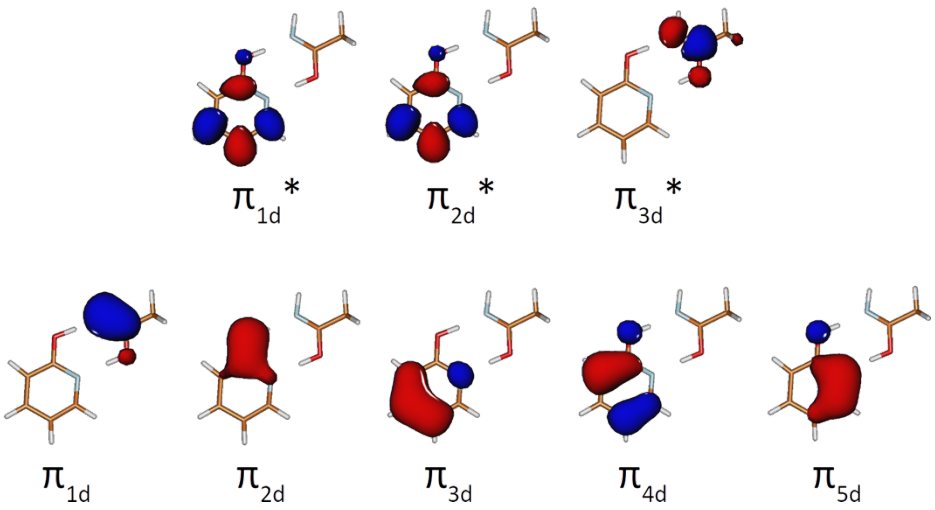


Fig. S6 CASSCF orbitals in the S_1 Franck-Condon region of the pyridone/acetamide (O-H---N / N---H-O hydrogen bond connection) system.

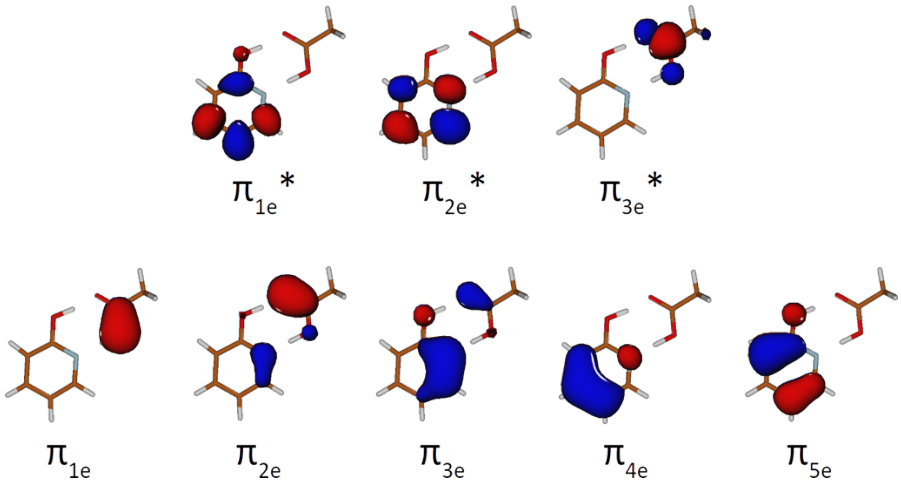
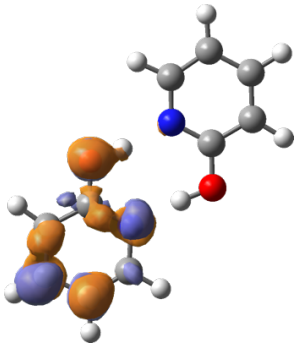
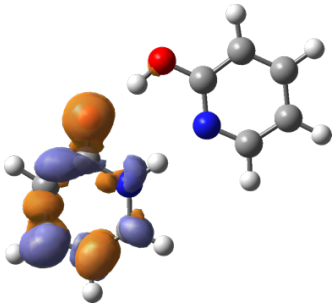
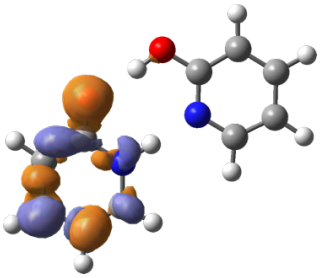
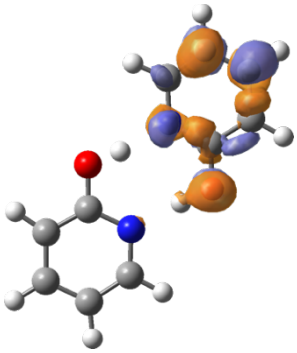
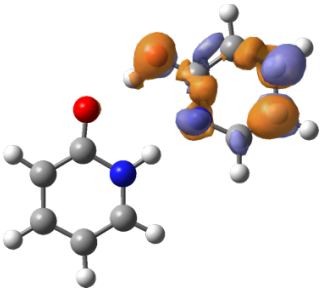
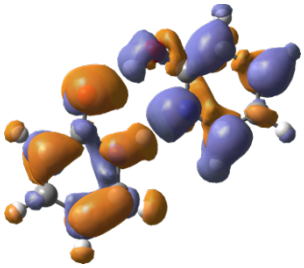


Fig. S7 CASSCF orbitals in the S_1 Franck-Condon region of the pyridone/acetic acid system.

Table S1 Dominant configurations (DM) in the CASSCF/cc-pVDZ wave functions for the S_1 and S_2 states of the reactant structures in Fig. 2-4 of the main text, and TD-M06-2X/aug-cc-pVDZ electron density difference maps (EDDM) for the corresponding $S_0 \rightarrow S_1$ and $S_0 \rightarrow S_2$ transitions

	Pyridone homodimer (Fig. 2, double ESPT)	**Pyridone heterodimer** (Fig. 3, double ESPT)	**Pyridone heterodimer** (Fig. 4, single ESPT)
DM(S_1)	$\pi_{5a}\pi_{1a}^*$ (LE_A)[a]	$\pi_{6b}\pi_{1b}^*$ (LE_A)[b]	$\pi_{6b}\pi_{1b}^*$ (LE_A)[b]
EDDM($S_0 \rightarrow S_1$)[c]			
DM(S_2)	$\pi_{6a}\pi_{2a}^*$ (LE_B)[a]	$\pi_{5b}\pi_{2b}^*$ (LE_B)[b]	$\pi_{6b}\pi_{2b}^*$ ($CT_{A\rightarrow B}$)[b]
EDDM($S_0 \rightarrow S_2$)[c]			

[a] The orbitals are labelled as in Fig. S3. [b] The orbitals are labelled as in Fig. S4. [c] Orange color indicates a decrease in electron density and blue color indicates an increase in electron density.

Based on the optimized S_1 geometries, NICS[12,13] aromaticity indices were calculated through a NICS-scan procedure[14] at the SA2-CASSCF/cc-pVDZ level of theory using the *Dalton 2016.2*[15] suite of programs, gauge-including atomic orbitals, and the previously defined active spaces. Focusing on isotropic chemical shifts, distances ranging from 0 to 5 Å (in steps of 0.25 Å) above the geometric centers of the rings in question were considered in the calculations. Notably, analogous calculations focusing instead on the zz-component of the magnetic shielding tensor, yielding so-called $NICS_{zz}$ values,[13] were consistently found to produce very similar results. One such comparison, for the particular case of the single ESPT in the pyridone heterodimer, is presented in Fig. S8.

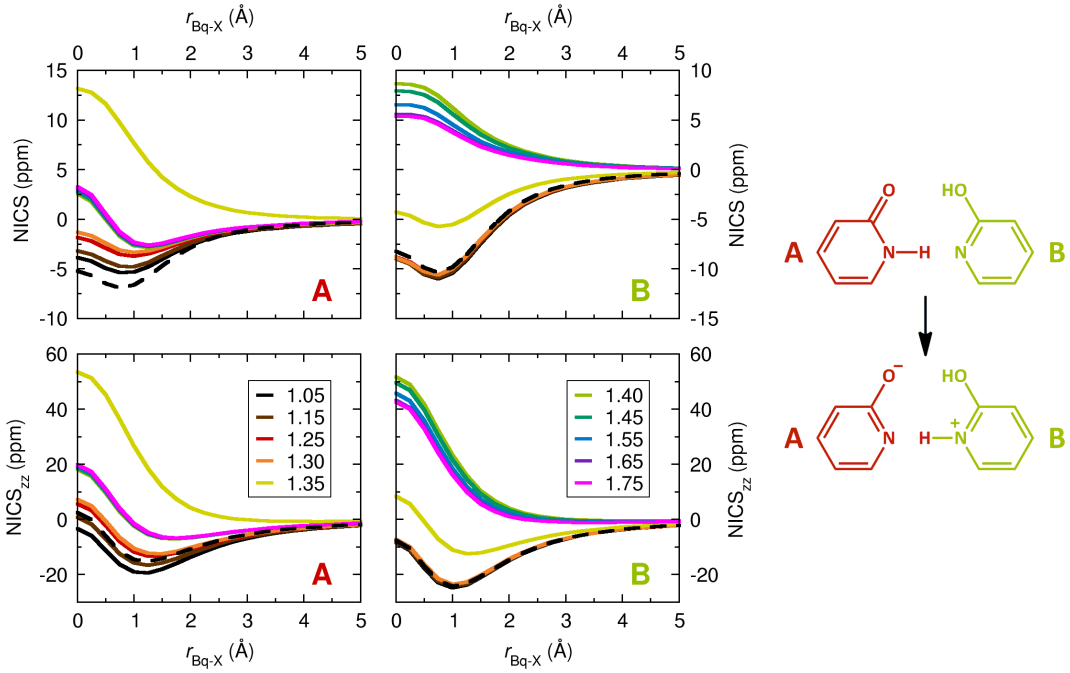


Fig. S8 CASSCF NICS and $NICS_{zz}$ values for rings A and B along the potential energy curve for the single ESPT in the pyridone heterodimer. Full colored curves correspond to values in the S_1 state at different $r_{N\text{-}H}$ distances, whereas dashed, black curves correspond to values in the S_0 state of the initial keto-A-enol-B species. $r_{Bq\text{-}X}$ is the distance between the center of the ring in question and the position of the ghost atom utilized for the NICS-scan calculations. This distance designation is also used in Fig. S9-S15.

In order to corroborate, qualitatively, the conclusions drawn from the NICS calculations, complementary analyses based on HOMA[16] aromaticity indices were also performed. This geometric index probes the deviation of the heavy-atom bond lengths R_i of the ring in question from the ideal R_{opt} reference value shown by the fully aromatic benzene molecule. Specifically, this index is defined as

$$\mathrm{HOMA} = 1 - \frac{\alpha}{n}\sum_{i}^{n}(R_i - R_{opt})^2,$$

where n is the number of bonds in the ring and α is an empirical normalization factor chosen such that the HOMA value approaches 1 (0) for an aromatic (non-aromatic) compound. In this work, the standard parameters[16] α = 257.7 Å^{-2} and R_{opt} = 1.388 Å were used to calculate HOMA values based on the S_1 geometries optimized at the TD-M06-2X/aug-cc-pVDZ level of theory. Importantly, a few points should be noted in connection to these calculations. First, the HOMA index does not distinguish between non-aromaticity and antiaromaticity, which

implies that the comparison of NICS and HOMA values is qualitative. Second, given that HOMA-based analyses are known to depend strongly on the chosen reference parameters,[17] the fact that the currently employed ones have been defined for studies of ground-state compounds is a potential concern. Nonetheless, these parameters could well afford a balanced comparison of HOMA values for a series of different excited-state geometries *of one and the same compound*, for which they are *equally* appropriate. At the same time, it has also been reported that reliable probing of changes in aromaticity along reaction paths using the HOMA index is a difficult task.[18] Against this background, the NICS-scan results in Fig. 2-4 of the main text were not only corroborated in terms of HOMA values, but also by means of the so-called multicenter index (MCI),[19] which has proven accurate in various benchmark tests.[20,21] This electronic index measures the cyclic delocalization of mobile electrons, and the more positive its value, the more aromatic is the ring in question. Using the *Multiwfn 3.7*[22] tool, MCI values were herein calculated from S_1 wave functions obtained at the CASSCF/cc-pVDZ level of theory with the *OpenMolcas 19.11*[23] suite of programs.

The results of the HOMA calculations are summarized in Fig. S16-S22, which also include the corresponding TD-M06-2X potential energy curves for the ESPT reactions. Pleasingly, these curves are very similar to the XMS-CASPT2//TD-M06-2X ones presented in Fig. S9-S15, which reinforces the validity of the computational methodology employed in this work. As for the HOMA values, Fig. S16-S22 support the same overall conclusions as the NICS values presented in Fig. 2-4 of the main text and in Fig. S9-S15. Namely, for the ESPT processes where neither the localization nor the charge-transfer character of the S_1 state changes as the reactions proceed (Fig. S16 and S20-S22), the changes in aromaticity along the reaction coordinate are smooth, whereas they are much less so for the ESPT processes where these requirements are not met (Fig. S17-S19). Indeed, this agreement between NICS and HOMA values is apparent from, e.g., comparing the corresponding results for the double ESPT in the pyridone homodimer on the one hand (both the NICS values in Fig. 2 and the HOMA values in Fig. S16 evolve smoothly along the reaction coordinate), and for the double ESPT in the pyridone heterodimer on the other (both the NICS values in Fig. 3 and the HOMA values in Fig. S17 exhibit sudden and sharp changes as the reaction proceeds). Pleasingly, this trend is fully corroborated by the results from the MCI calculations in Fig. S23-S25. Thus, for the double ESPT in the pyridone homodimer, the MCI values evolve smoothly (see Fig. S23), whereas for the double ESPT in the pyridone heterodimer, they do not (see Fig. S24).

2. XMS-CASPT2//TD-M06-2X potential energy curves and NICS-based analyses for all ESPT reactions

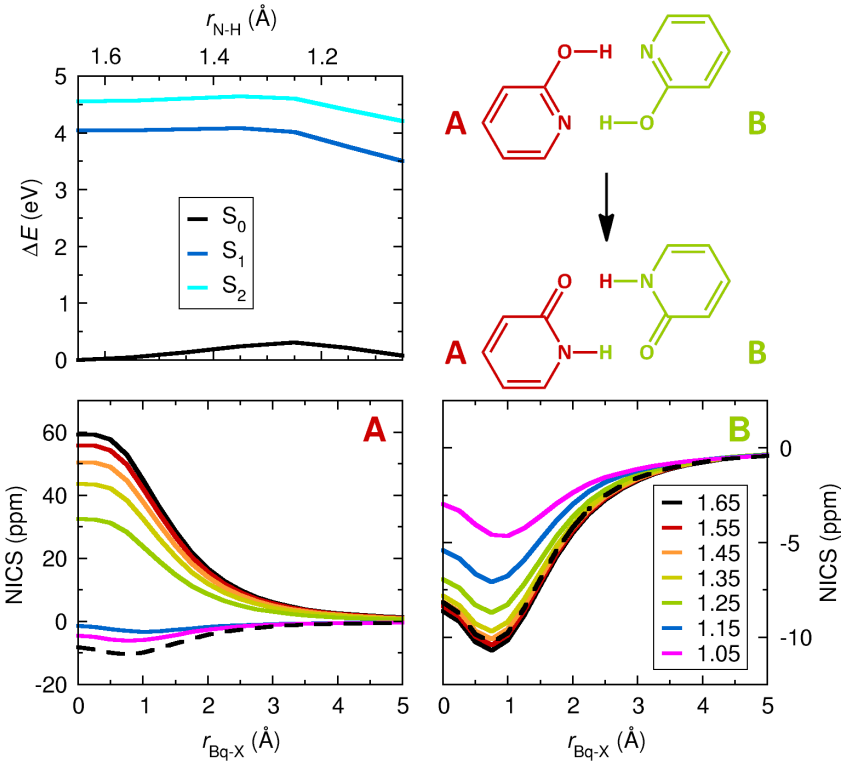


Fig. S9 XMS-CASPT2//TD-M06-2X potential energy (Δ*E*) curves for the double ESPT in the pyridone homodimer and associated CASSCF NICS values for rings A and B. For the NICS values, full colored curves correspond to values in the S_1 state at different r_{N-H} distances, whereas dashed, black curves correspond to values in the S_0 state of the initial dienol species. This figure is identical to Fig. 2 in the main text. Further details are given in the caption for Fig. S8.

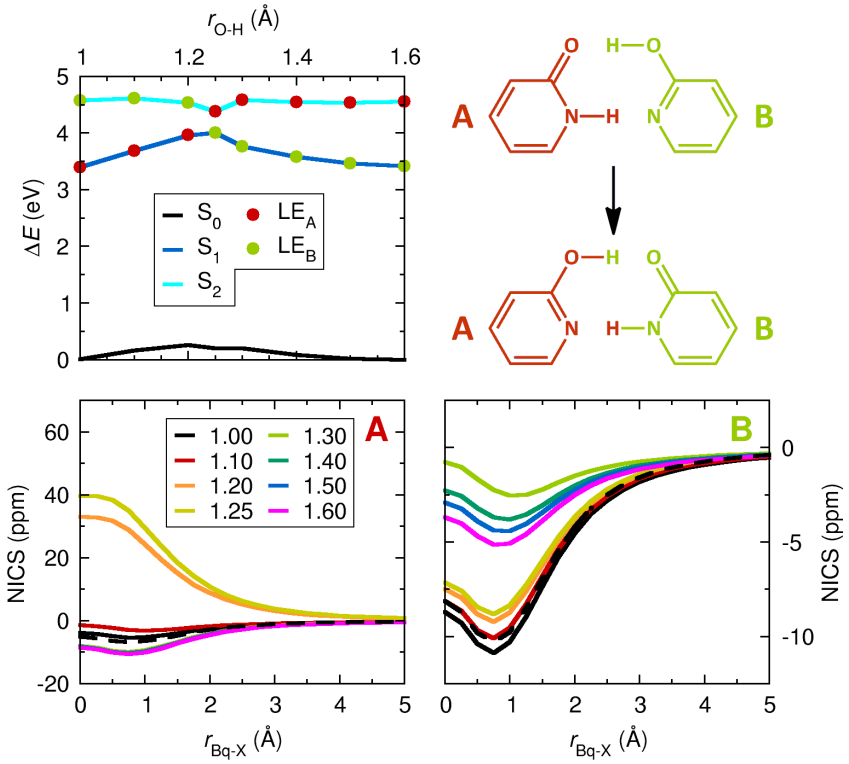


Fig. S10 XMS-CASPT2//TD-M06-2X potential energy (Δ*E*) curves for the double ESPT in the pyridone heterodimer and associated CASSCF NICS values for rings A and B. For the NICS values, full colored curves correspond to values in the S_1 state at different $r_{O\text{-}H}$ distances, whereas dashed, black curves correspond to values in the S_0 state of the initial keto-A-enol-B species. LE = local excitation. This figure is identical to Fig. 3 in the main text. Further details are given in the caption for Fig. S8.

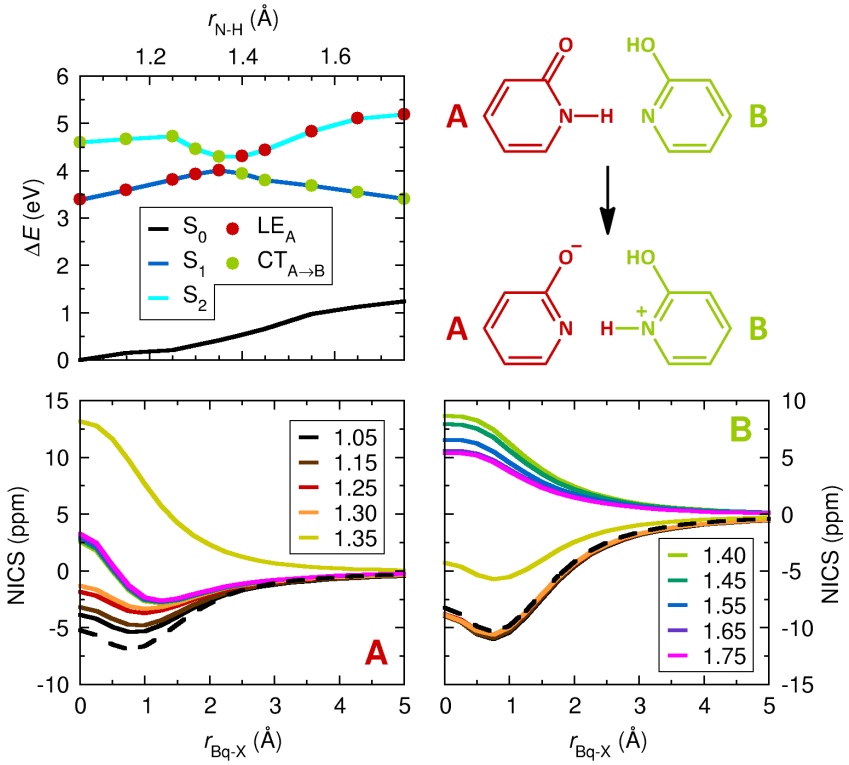


Fig. S11 XMS-CASPT2//TD-M06-2X potential energy (Δ*E*) curves for the single ESPT in the pyridone heterodimer and associated CASSCF NICS values for rings A and B. For the NICS values, full colored curves correspond to values in the S_1 state at different r_{N-H} distances, whereas dashed, black curves correspond to values in the S_0 state of the initial keto-A-enol-B species. LE = local excitation, $CT_{A\rightarrow B}$ = A → B charge-transfer state. This figure is identical to Fig. 4 in the main text. Further details are given in the caption for Fig. S8.

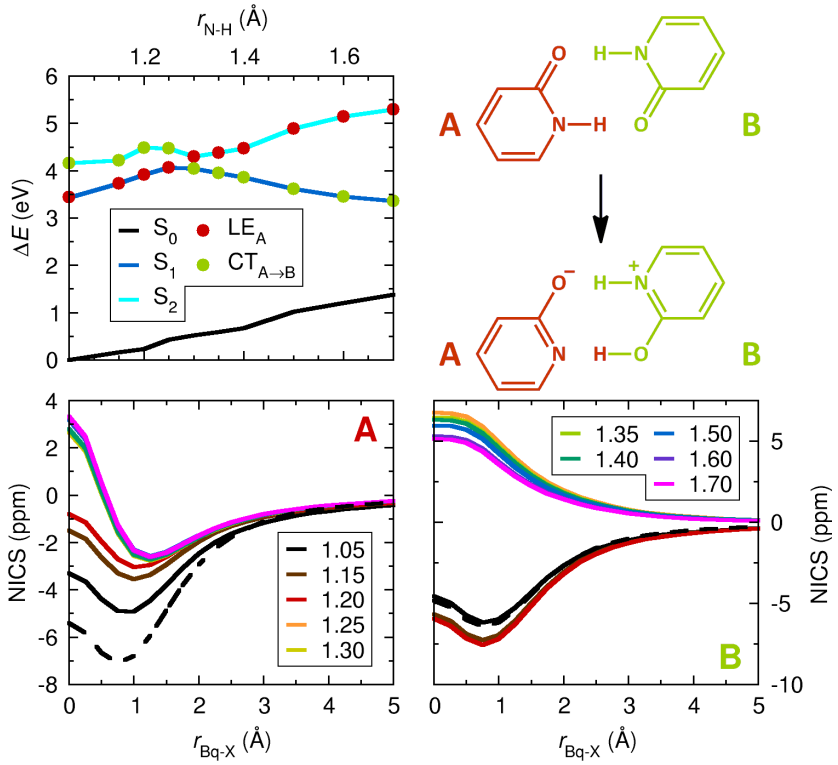


Fig. S12 XMS-CASPT2//TD-M06-2X potential energy (Δ*E*) curves for the single ESPT in the pyridone homodimer and associated CASSCF NICS values for rings A and B. For the NICS values, full colored curves correspond to values in the S_1 state at different r_{N-H} distances, whereas dashed, black curves correspond to values in the S_0 state of the initial diketo species. LE = local excitation, $CT_{A\rightarrow B}$ = A → B charge-transfer state. Further details are given in the caption for Fig. S8.

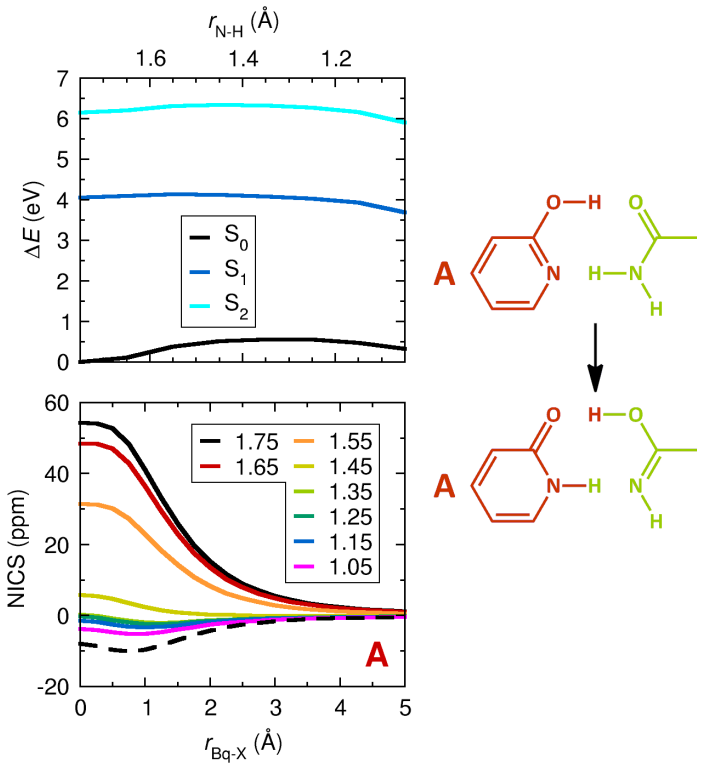


Fig. S13 XMS-CASPT2//TD-M06-2X potential energy (Δ*E*) curves for the double ESPT in the pyridone/acetamide (O-H---O / N---H-N hydrogen bond connection) system and associated CASSCF NICS values for ring A. For the NICS values, full colored curves correspond to values in the S_1 state at different $r_{N\text{-}H}$ distances, whereas dashed, black curves correspond to values in the S_0 state of the initial enol-A species. Further details are given in the caption for Fig. S8.

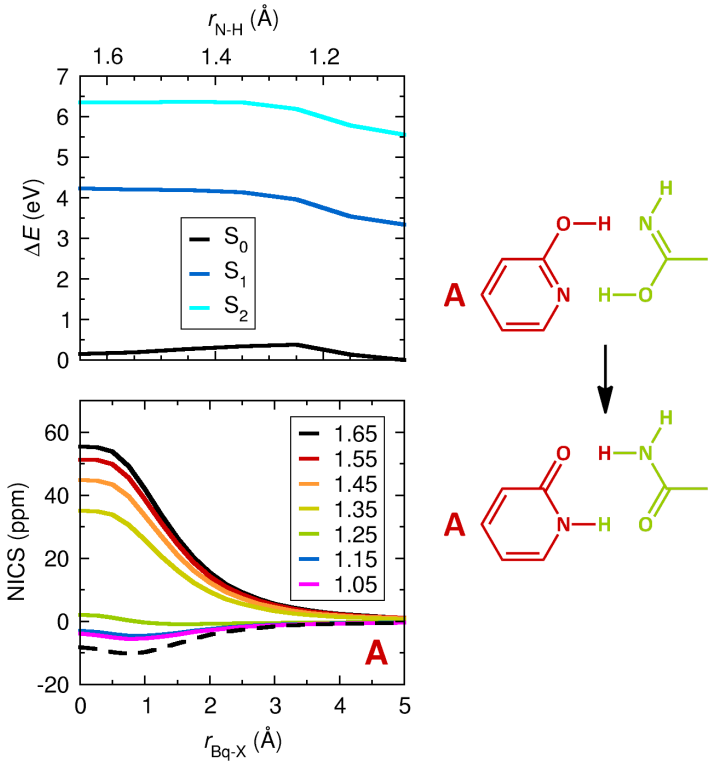


Fig. S14 XMS-CASPT2//TD-M06-2X potential energy (Δ*E*) curves for the double ESPT in the pyridone/acetamide (O-H---N / N---H-O hydrogen bond connection) system and associated CASSCF NICS values for ring A. For the NICS values, full colored curves correspond to values in the S_1 state at different r_{N-H} distances, whereas dashed, black curves correspond to values in the S_0 state of the initial enol-A species. Further details are given in the caption for Fig. S8.

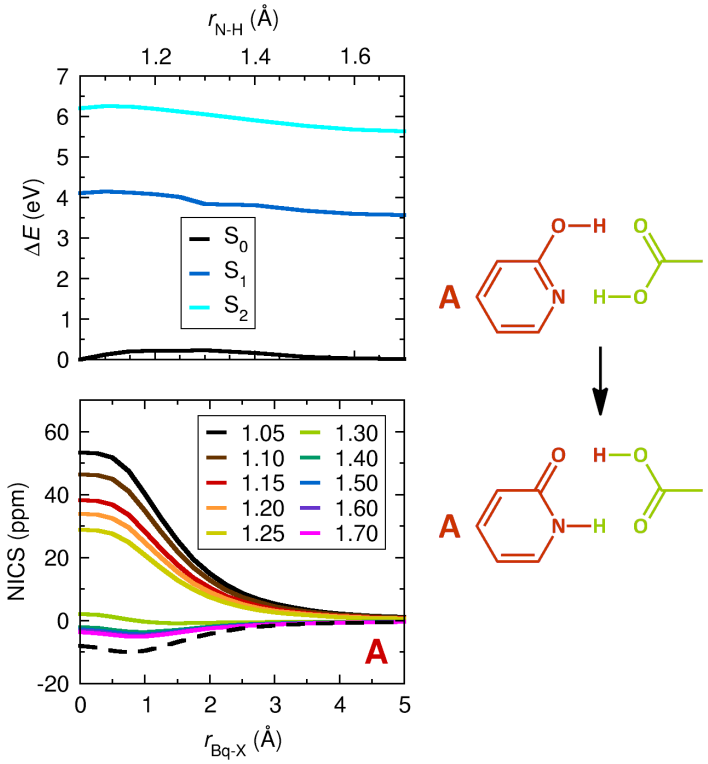


Fig. S15 XMS-CASPT2//TD-M06-2X potential energy (Δ*E*) curves for the double ESPT in the pyridone/acetic acid system and associated CASSCF NICS values for ring A. For the NICS values, full colored curves correspond to values in the S_1 state at different $r_{N\text{-}H}$ distances, whereas dashed, black curves correspond to values in the S_0 state of the initial enol-A species. Further details are given in the caption for Fig. S8.

3. TD-M06-2X potential energy curves and HOMA-based analyses for all ESPT reactions

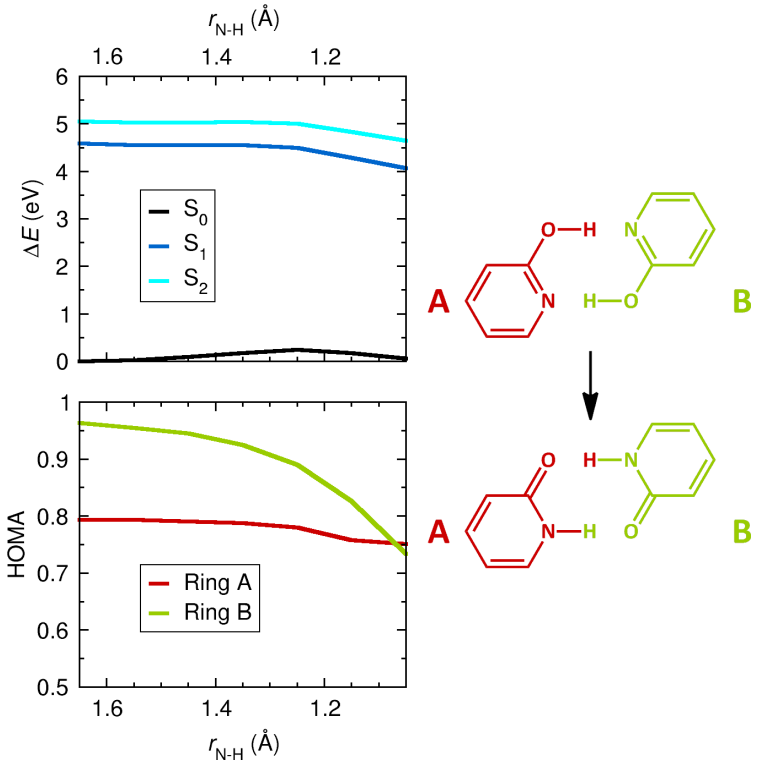


Fig. S16 TD-M06-2X potential energy (Δ*E*) curves for the double ESPT in the pyridone homodimer and associated HOMA values for rings A and B.

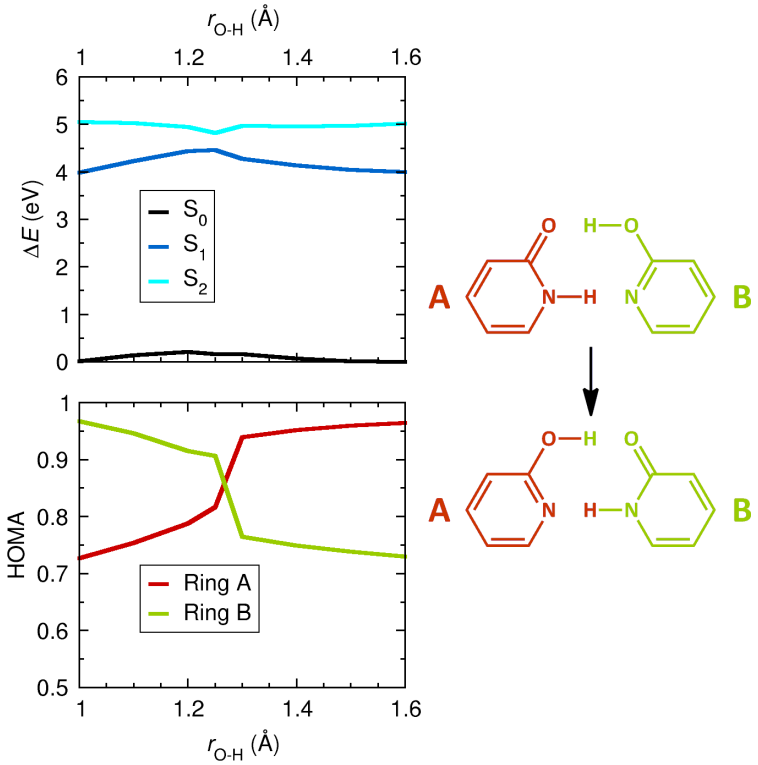


Fig. S17 TD-M06-2X potential energy (Δ*E*) curves for the double ESPT in the pyridone heterodimer and associated HOMA values for rings A and B.

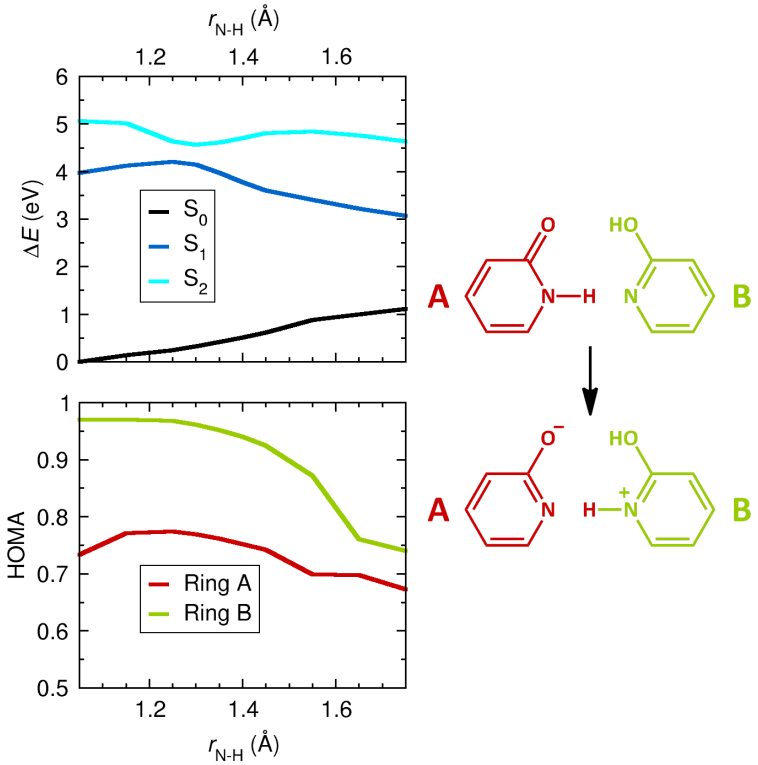


Fig. S18 TD-M06-2X potential energy (Δ*E*) curves for the single ESPT in the pyridone heterodimer and associated HOMA values for rings A and B.

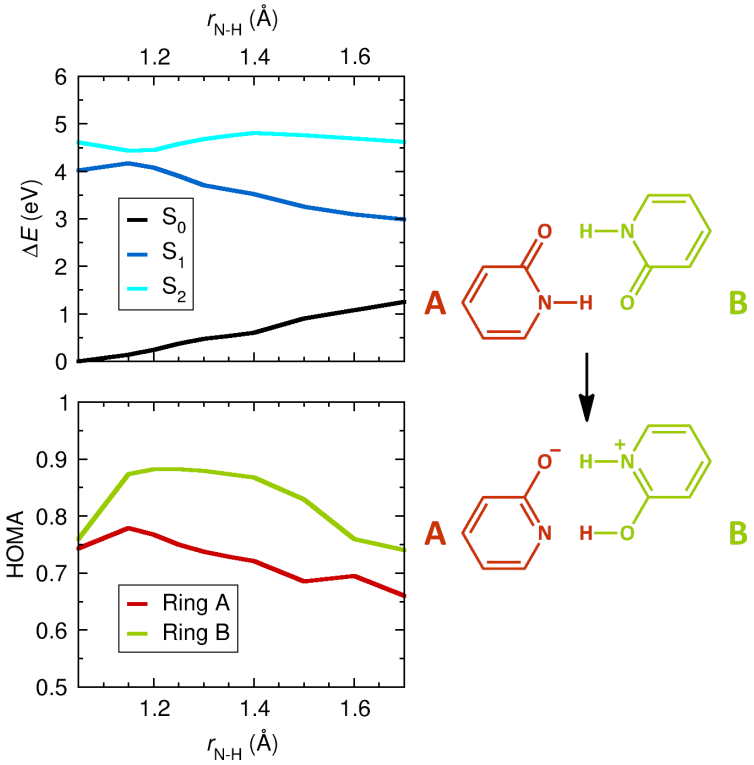


Fig. S19 TD-M06-2X potential energy (Δ*E*) curves for the single ESPT in the pyridone homodimer and associated HOMA values for rings A and B.

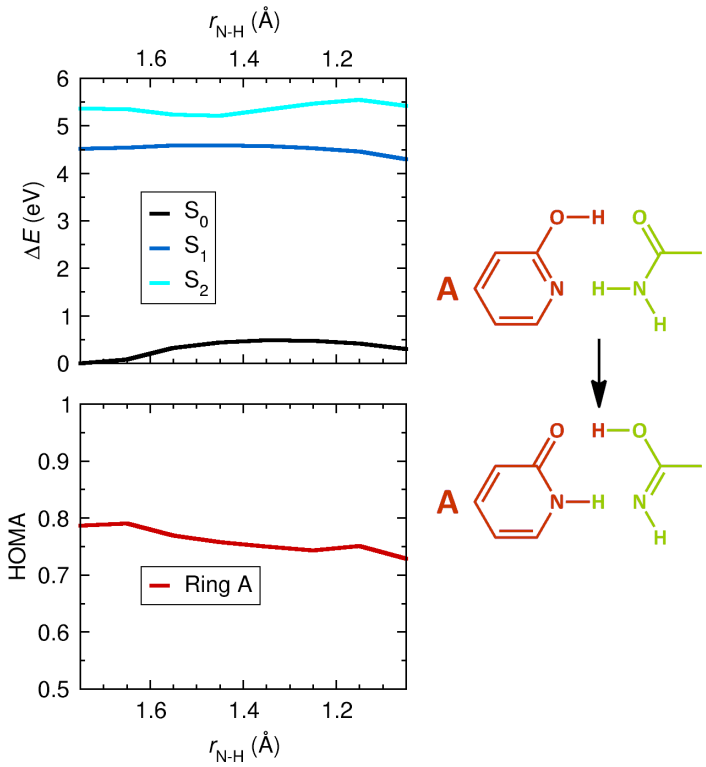


Fig. S20 TD-M06-2X potential energy (Δ*E*) curves for the double ESPT in the pyridone/acetamide (O-H---O / N---H-N hydrogen bond connection) system and associated HOMA values for ring A.

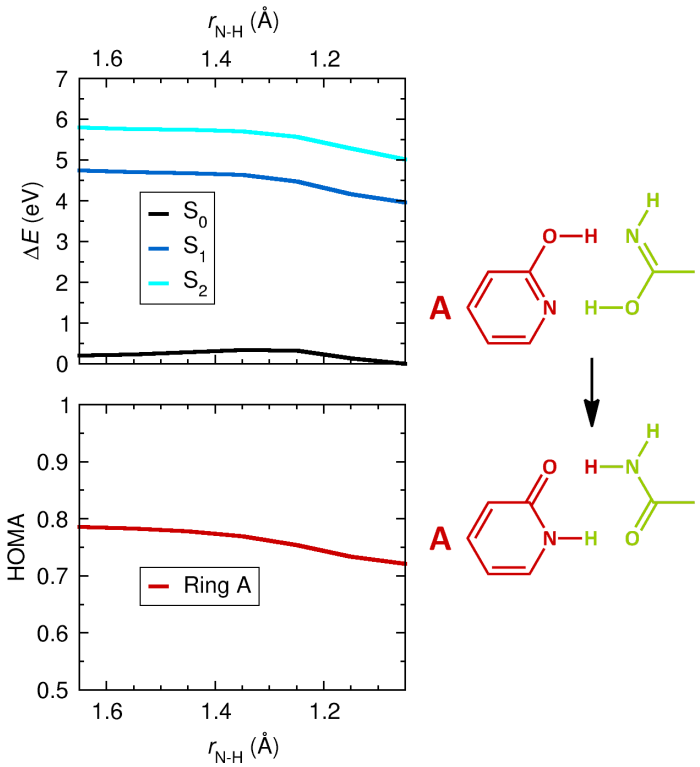


Fig. S21 TD-M06-2X potential energy (Δ*E*) curves for the double ESPT in the pyridone/acetamide (O-H---N / N---H-O hydrogen bond connection) system and associated HOMA values for ring A.

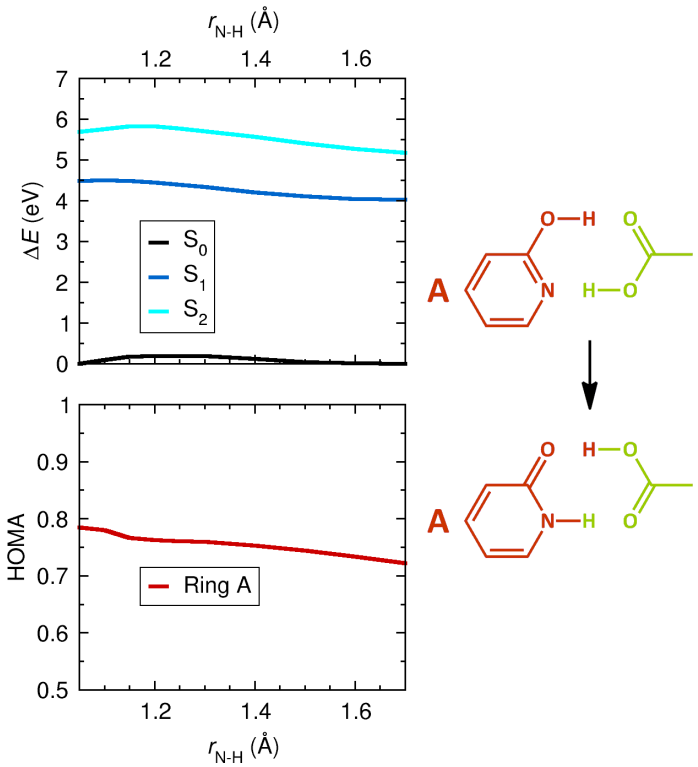


Fig. S22 TD-M06-2X potential energy (Δ*E*) curves for the double ESPT in the pyridone/acetic acid system and associated HOMA values for ring A.

4. XMS-CASPT2//TD-M06-2X potential energy curves and MCI-based analyses for the ESPT reactions in Fig. 2-4 of the main text

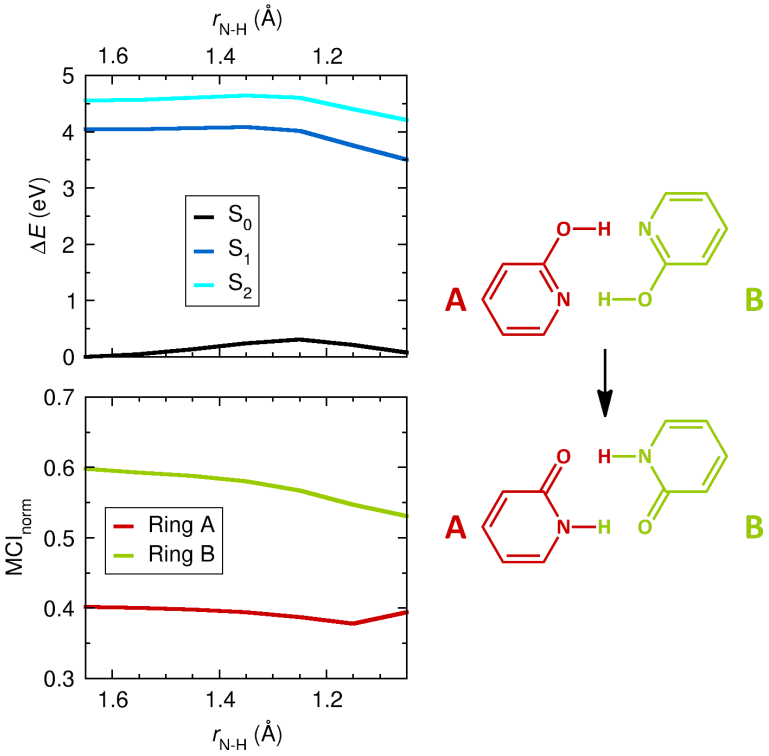


Fig. S23 XMS-CASPT2//TD-M06-2X potential energy (Δ*E*) curves for the double ESPT in the pyridone homodimer and associated CASSCF MCI values for rings A and B.

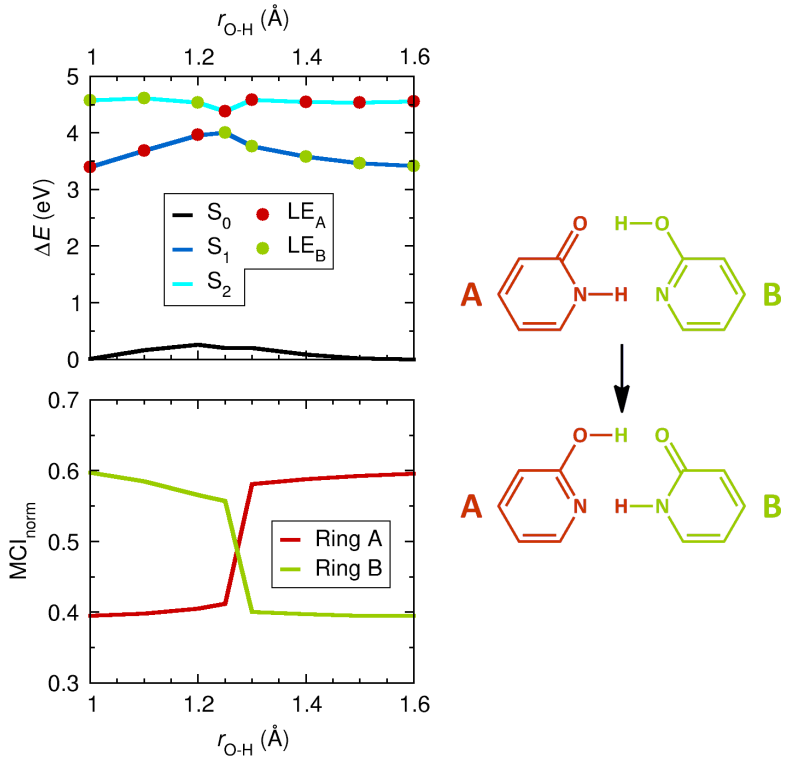


Fig. S24 XMS-CASPT2//TD-M06-2X potential energy (Δ*E*) curves for the double ESPT in the pyridone heterodimer and associated CASSCF MCI values for rings A and B. LE = local excitation.

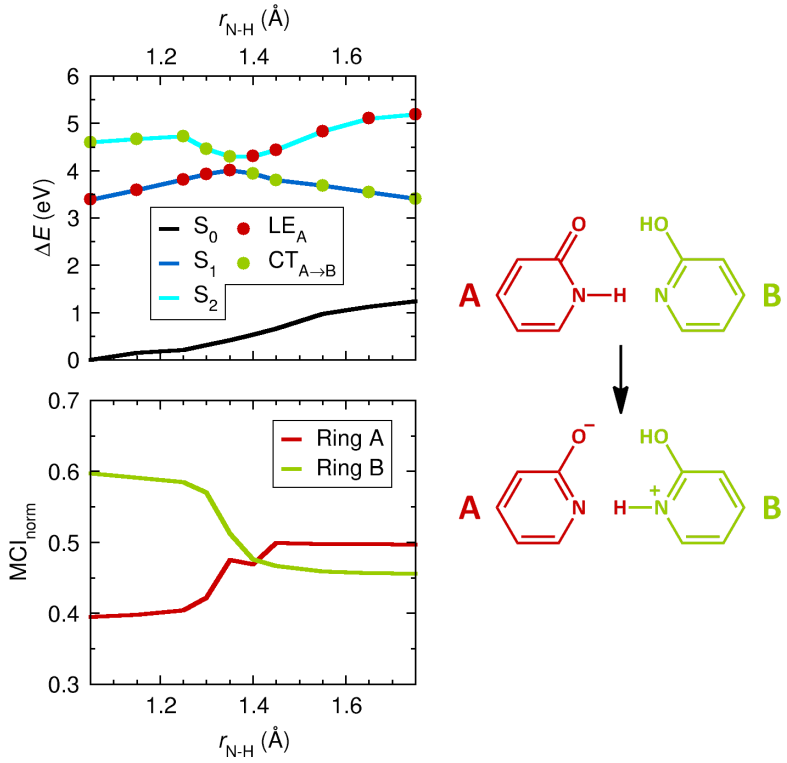


Fig. S25 XMS-CASPT2//TD-M06-2X potential energy (Δ*E*) curves for the single ESPT in the pyridone heterodimer and associated CASSCF MCI values for rings A and B. LE = local excitation, $CT_{A\rightarrow B}$ = A → B charge-transfer state.

5. Cartesian coordinates and energies of molecular geometries

We provide in this section Cartesian coordinates of the S_1 molecular geometries used for the calculations summarized in the different figures. The coordinates are given in the same order as the corresponding geometries appear from left to right in the corresponding figures. Coordinates for fully relaxed TS structures (indicated as "TS") are also provided. For each geometry, the total S_1 electronic energy ($E(S_1)$) calculated at the TD-M06-2X/aug-cc-pVDZ level of theory is also given (in a.u.).

5.1. Double ESPT in the pyridone homodimer (Fig. 2, S9, S16 and S23)

$E(S_1)$ = -646.735543024

C	-1.873190	0.797439	-0.001335
C	-3.206645	1.254839	-0.000915
C	-4.224543	0.322604	0.000659
C	-3.914114	-1.046332	0.001848
C	-2.578828	-1.402304	0.001363
H	-3.391219	2.325802	-0.001824
H	-5.263385	0.650843	0.001007
H	-4.688585	-1.808438	0.003104
H	-2.275916	-2.449827	0.002265
N	-1.575045	-0.507989	-0.000244
H	-0.037806	-1.107484	-0.000549
O	-0.892327	1.682563	-0.002869
O	0.862239	-1.602632	-0.000913
C	1.864432	-0.767287	-0.000572
C	3.174316	-1.293969	-0.000585
N	1.528868	0.574397	-0.000110
C	4.288654	-0.400934	-0.000509
H	3.277730	-2.376129	-0.000263
C	2.599426	1.401979	0.002187
H	0.010051	1.219140	-0.001846
C	3.954801	0.965959	0.001920
H	5.314881	-0.751315	-0.000854
H	2.382566	2.469733	0.003669
H	4.729792	1.731410	0.003653

$E(S_1)$ = -646.736479667

C	1.829001	0.799005	-0.001067
C	3.162065	1.263191	-0.000715
C	4.186811	0.339715	0.000643
C	3.888919	-1.033248	0.001740

C	2.558138	-1.400819	0.001365
H	3.338334	2.335507	-0.001534
H	5.222831	0.676892	0.000928
H	4.669855	-1.788570	0.002881
H	2.261598	-2.450086	0.002196
N	1.547230	-0.513248	-0.000046
H	0.107430	-1.087248	-0.000969
O	0.842449	1.668534	-0.002334
O	-0.815775	-1.593205	-0.001870
C	-1.822972	-0.770768	-0.000748
C	-3.131117	-1.300265	-0.000956
N	-1.501043	0.577873	0.000670
C	-4.250181	-0.413112	0.000266
H	-3.229791	-2.382842	-0.001965
C	-2.575084	1.400222	0.001718
H	-0.077542	1.191178	-0.001137
C	-3.926566	0.955365	0.001631
H	-5.274293	-0.769922	0.000247
H	-2.362546	2.468851	0.002666
H	-4.706660	1.715525	0.002688

$E(S_1)$ = -646.736648851

C	1.790792	0.801460	-0.001591
C	3.123933	1.271982	-0.000984
C	4.156099	0.358061	0.001127
C	3.871933	-1.019355	0.002619
C	2.546401	-1.400029	0.001827
H	3.291196	2.345741	-0.002171
H	5.188978	0.704715	0.001641
H	4.660094	-1.766977	0.004276
H	2.256551	-2.450980	0.002914
N	1.528104	-0.519422	-0.000288
H	0.183780	-1.062831	-0.001321
O	0.797868	1.651730	-0.003855
O	-0.775454	-1.582990	-0.002545
C	-1.788162	-0.776122	-0.000943
C	-3.095015	-1.306236	-0.001666
N	-1.482064	0.581382	0.001481
C	-4.218475	-0.424402	0.000511
H	-3.190231	-2.389126	-0.003602
C	-2.558413	1.399071	0.002623

H	-0.151019	1.156545	-0.001575
C	-3.905840	0.945403	0.002325
H	-5.240222	-0.788271	0.000426
H	-2.349288	2.468311	0.003868
H	-4.690946	1.700229	0.003302

$E(S_1)$ = -646.736543038

C	1.763206	0.805033	-0.000435
C	3.098174	1.281516	-0.000142
C	4.137528	0.378107	0.000423
C	3.869429	-1.004968	0.000667
C	2.550778	-1.400896	0.000266
H	3.256429	2.356590	-0.000280
H	5.167011	0.734955	0.000760
H	4.666334	-1.743017	0.001112
H	2.267053	-2.453131	0.000437
N	1.525223	-0.526361	-0.000341
H	0.273129	-1.031100	-0.000406
O	0.763908	1.630894	-0.000828
O	-0.749025	-1.573656	-0.000504
C	-1.766599	-0.785077	-0.000318
C	-3.073924	-1.311718	0.000086
N	-1.478067	0.582014	-0.000419
C	-4.199212	-0.431759	0.000279
H	-3.168957	-2.394551	0.000272
C	-2.553418	1.399982	0.000454
H	-0.236121	1.111230	-0.000428
C	-3.896618	0.938814	0.000725
H	-5.219774	-0.799474	0.000417
H	-2.343401	2.468781	0.000770
H	-4.686919	1.688041	0.001290

$E(S_1)$ = -646.738723109

C	1.761005	0.810405	-0.000193
C	3.100277	1.292155	-0.000242
C	4.147420	0.401123	-0.000014
C	3.900336	-0.989503	0.000199
C	2.591132	-1.405423	0.000260
H	3.248588	2.368642	-0.000435
H	5.172570	0.770441	-0.000072

H	4.708411	-1.714932	0.000291
H	2.313919	-2.458608	0.000406
N	1.558969	-0.535429	0.000085
H	0.394685	-0.990339	-0.000072
O	0.754608	1.602218	-0.000311
O	-0.751621	-1.563959	-0.000215
C	-1.774346	-0.798942	-0.000068
C	-3.084441	-1.315981	-0.000288
N	-1.508917	0.579938	0.000569
C	-4.209297	-0.433671	-0.000046
H	-3.183734	-2.398282	-0.000585
C	-2.577851	1.404784	0.000285
H	-0.350130	1.048673	0.000261
C	-3.916808	0.936416	0.000042
H	-5.229153	-0.804125	-0.000133
H	-2.362649	2.471878	0.000349
H	-4.711332	1.680850	0.000025

$E(S_1)$ = -646.746317484

C	-1.800325	-0.817658	-0.000319
C	-3.148067	-1.301413	0.000058
C	-4.199972	-0.421569	0.000469
C	-3.974732	0.977683	0.000571
C	-2.676597	1.413750	0.000255
H	-3.289042	-2.378895	-0.000027
H	-5.221178	-0.802193	0.000737
H	-4.794294	1.689581	0.000924
H	-2.404440	2.467290	0.000337
N	-1.639930	0.544675	-0.000190
H	-0.563579	0.949603	-0.000270
O	-0.788201	-1.569829	-0.000820
O	0.799397	1.554624	-0.000795
C	1.827937	0.817809	-0.000328
C	3.143558	1.318674	-0.000037
N	1.586036	-0.572709	-0.000128
C	4.263822	0.425702	0.000562
H	3.253790	2.399611	-0.000337
C	2.641036	-1.415297	0.000206
H	0.507479	-0.971728	-0.000248
C	3.977725	-0.942159	0.000582
H	5.284785	0.793982	0.000888

H	2.413388	-2.478702	0.000182
H	4.774490	-1.683806	0.000852

$E(S_1)$ = -646.754421918

C	1.914792	0.831384	-0.000333
C	3.234636	1.319390	-0.000370
C	4.349530	0.414583	-0.000211
C	4.066668	-0.950680	0.000572
C	2.730333	-1.426800	0.000822
H	3.355359	2.398893	-0.000578
H	5.372085	0.779181	-0.000460
H	4.864123	-1.691193	0.001039
H	2.491440	-2.486814	0.001523
N	1.688366	-0.566804	-0.000014
H	0.694525	-0.905595	0.000086
O	0.878857	1.542084	-0.000529
O	-0.854124	-1.536746	-0.000238
C	-1.871223	-0.818454	-0.000109
C	-3.225529	-1.307604	-0.000016
N	-1.745541	0.558138	-0.000064
C	-4.282861	-0.439887	0.000137
H	-3.357660	-2.386266	-0.000068
C	-2.790941	1.422186	0.000087
H	-0.763507	0.929766	-0.000134
C	-4.078296	0.967216	0.000194
H	-5.299953	-0.831862	0.000211
H	-2.528239	2.477547	0.000116
H	-4.908468	1.666290	0.000314

5.2. Double ESPT in the pyridone heterodimer (Fig. 3, S10, S17 and S24)

$E(S_1)$ = -646.751580099

C	-2.055835	-0.854147	-0.000348
C	-3.458611	-0.945087	0.000069
C	-4.264841	0.245266	0.001362
C	-3.605152	1.470856	0.000492
C	-2.186817	1.545544	-0.000598
N	-1.438808	0.419526	0.000268
O	-1.259701	-1.824709	-0.001313
H	-3.884877	-1.943934	-0.000404

H	-5.349106	0.190151	0.002277
H	-4.158000	2.408124	0.000498
H	-1.658424	2.494860	-0.001702
H	-0.398825	0.425512	-0.000190
C	2.095647	-0.794100	0.000193
C	3.503573	-0.839253	0.000620
C	4.198109	0.353740	0.000384
C	3.491736	1.565545	-0.000274
C	2.110122	1.503344	-0.000640
N	1.414492	0.353411	-0.000412
O	1.435302	-1.947376	0.000425
H	0.445522	-1.804778	-0.000115
H	3.997671	-1.807250	0.001117
H	5.287549	0.350525	0.000701
H	4.001726	2.525156	-0.000482
H	1.514581	2.417505	-0.001141

$E(S_1)$ = -646.742643705

C	-1.973032	-0.836388	-0.000445
C	-3.376979	-0.922173	-0.000069
C	-4.175159	0.269602	0.000893
C	-3.492434	1.486071	0.000566
C	-2.073089	1.535406	-0.000111
N	-1.321850	0.413114	-0.000030
O	-1.211246	-1.846757	-0.001202
H	-3.807283	-1.919691	-0.000486
H	-5.259700	0.226777	0.001500
H	-4.029459	2.432891	0.000788
H	-1.543548	2.485303	-0.000502
H	-0.151867	0.406794	-0.000296
C	1.987070	-0.809578	0.000242
C	3.400325	-0.857226	0.000758
C	4.108080	0.325513	0.000495
C	3.420377	1.551967	-0.000277
C	2.041612	1.511822	-0.000705
N	1.336087	0.365572	-0.000446
O	1.310502	-1.931618	0.000461
H	0.218964	-1.795440	-0.000229
H	3.883950	-1.830427	0.001339
H	5.197426	0.307722	0.000874
H	3.945338	2.503095	-0.000522

H	1.451842	2.429077	-0.001294

$E(S_1)$ = -646.735171014

C	-1.936939	-0.815240	-0.000046
C	-3.342909	-0.897221	0.000151
C	-4.131276	0.294371	0.000460
C	-3.425827	1.501984	-0.000070
C	-2.006603	1.523572	-0.000431
N	-1.249144	0.406095	0.000010
O	-1.213407	-1.868089	-0.000335
H	-3.777485	-1.893291	0.000037
H	-5.216062	0.263749	0.000812
H	-3.946903	2.457973	-0.000255
H	-1.475899	2.474470	-0.000876
H	0.050856	0.407380	0.000131
C	1.923139	-0.826653	0.000053
C	3.341367	-0.883566	0.000040
C	4.068393	0.286447	0.000041
C	3.405073	1.530898	0.000066
C	2.028916	1.523517	0.000085
N	1.309717	0.382615	0.000074
O	1.215137	-1.903737	-0.000005
H	0.020828	-1.787004	-0.000080
H	3.809626	-1.864158	0.000019
H	5.157186	0.249418	0.000036
H	3.950349	2.470192	0.000067
H	1.449631	2.446273	0.000155

$E(S_1)$ = -646.734263527

C	-1.937188	-0.805845	-0.000006
C	-3.343742	-0.887956	0.000045
C	-4.126544	0.302044	0.000047
C	-3.415756	1.508590	-0.000022
C	-1.998442	1.520287	-0.000062
N	-1.239980	0.403774	-0.000044
O	-1.227303	-1.875766	-0.000021
H	-3.780062	-1.883384	0.000069
H	-5.211513	0.274753	0.000079
H	-3.932887	2.466716	-0.000051
H	-1.465605	2.470629	-0.000159

H	0.124936	0.418914	0.000130
C	1.910245	-0.831757	-0.000012
C	3.329006	-0.900865	-0.000033
C	4.072177	0.261543	-0.000004
C	3.424191	1.515055	0.000036
C	2.047356	1.530524	0.000046
N	1.316139	0.396287	0.000019
O	1.180150	-1.882854	-0.000009
H	-0.065600	-1.779865	0.000113
H	3.785018	-1.887130	-0.000056
H	5.160253	0.211501	-0.000015
H	3.982228	2.446823	0.000041
H	1.479537	2.459852	0.000046

$E(S_1)$ = -646.741053986

C	1.926601	-0.805779	0.000124
C	3.340540	-0.876063	-0.000061
C	4.070198	0.293037	-0.000349
C	3.404923	1.532716	-0.000421
C	2.025703	1.518362	-0.000198
N	1.297775	0.386072	0.000058
O	1.226251	-1.906063	0.000433
H	3.806154	-1.858023	0.000015
H	5.159063	0.255534	-0.000525
H	3.947538	2.473880	-0.000643
H	1.453766	2.447076	-0.000261
H	-0.131465	0.432669	0.000039
C	-1.919775	-0.825611	-0.000087
C	-3.321402	-0.928308	-0.000414
C	-4.132836	0.253115	-0.001246
C	-3.461302	1.476927	0.000310
C	-2.043433	1.539326	0.001279
N	-1.276927	0.427354	-0.000262
O	-1.148468	-1.832911	0.000480
H	0.150506	-1.781260	0.000495
H	-3.740052	-1.930854	-0.000013
H	-5.216767	0.198542	-0.002286
H	-4.007560	2.418454	0.000919
H	-1.524692	2.495466	0.002758

$E(S_1)$ = -646.746327262

C	1.966499	-0.797240	0.000218
C	3.377874	-0.867899	0.000614
C	4.102894	0.304996	0.000508
C	3.430515	1.538783	-0.000090
C	2.049837	1.515005	-0.000569
N	1.324957	0.381936	-0.000357
O	1.275355	-1.914520	0.000163
H	3.847299	-1.848083	0.001032
H	5.191932	0.272672	0.000888
H	3.967135	2.483545	-0.000175
H	1.476223	2.443051	-0.000924
H	-0.233833	0.443371	-0.000563
C	-1.946647	-0.833144	-0.000399
C	-3.347455	-0.941967	0.000322
C	-4.166168	0.237083	0.000549
C	-3.508826	1.466762	0.000526
C	-2.091354	1.545617	0.000039
N	-1.324670	0.433515	-0.000749
O	-1.156014	-1.818438	-0.000785
H	0.243450	-1.779702	-0.000347
H	-3.761520	-1.946206	0.000558
H	-5.249739	0.173881	0.000878
H	-4.065019	2.402282	0.000927
H	-1.575678	2.502716	0.000142

$E(S_1)$ = -646.749653505

C	-2.014065	-0.789664	0.000003
C	-3.423260	-0.865341	0.000251
C	-4.148482	0.308088	0.000190
C	-3.474807	1.539749	-0.000013
C	-2.093081	1.514194	-0.000154
N	-1.367587	0.382375	-0.000199
O	-1.325042	-1.916474	0.000257
H	-3.892212	-1.845786	0.000519
H	-5.237509	0.276284	0.000345
H	-4.010306	2.485288	-0.000092
H	-1.520809	2.443142	-0.000404
H	0.320667	0.459166	-0.000475
C	1.984661	-0.837114	-0.000267
C	3.384858	-0.953699	0.000241

C	4.211537	0.221320	0.000179
C	3.567791	1.456939	0.000320
C	2.150989	1.551183	0.000113
N	1.380993	0.440907	-0.000631
O	1.178673	-1.804681	-0.000383
H	-0.320962	-1.771598	-0.000055
H	3.793154	-1.960137	0.000512
H	5.294659	0.149159	0.000281
H	4.133646	2.386507	0.000640
H	1.639935	2.510303	0.000378

$E(S_1)$ = -646.751132911

C	-2.066526	-0.783623	-0.000089
C	-3.473986	-0.864994	0.000770
C	-4.200795	0.308182	0.000725
C	-3.527584	1.539155	-0.000072
C	-2.144905	1.514389	-0.000716
N	-1.418025	0.384002	-0.000807
O	-1.376331	-1.915931	-0.000026
H	-3.941427	-1.846177	0.001456
H	-5.289787	0.275577	0.001342
H	-4.063584	2.484508	-0.000132
H	-1.574455	2.444434	-0.001334
H	0.399536	0.478191	-0.000562
C	2.028049	-0.838310	-0.000177
C	3.427554	-0.964501	0.000100
C	4.263451	0.204898	0.000567
C	3.633497	1.446590	0.000441
C	2.217622	1.556104	0.000036
N	1.441515	0.449553	0.000072
O	1.208970	-1.791000	-0.000756
H	-0.390745	-1.760778	-0.000112
H	3.828742	-1.973698	0.000024
H	5.345947	0.122732	0.000841
H	4.209021	2.370110	0.000567
H	1.712953	2.518314	-0.000190

5.3. Single ESPT in the pyridone heterodimer (Fig. 4, S11, S18 and S25)

TS

$E(S_1)$ = -646.742655181

C	-1.972269	-0.859447	-0.000051
C	-3.392204	-0.882994	-0.000199
C	-4.127559	0.328679	-0.000177
C	-3.402545	1.519232	0.000023
C	-1.979470	1.501186	0.000152
N	-1.274332	0.365676	0.000085
O	-1.264859	-1.892005	-0.000025
H	-3.866190	-1.860929	-0.000315
H	-5.213996	0.330854	-0.000288
H	-3.902881	2.485390	0.000079
H	-1.418232	2.433923	0.000308
H	-0.036637	0.295989	0.000086
C	2.022198	-0.837016	0.000139
C	3.417285	-0.791732	0.000091
C	4.053015	0.448870	-0.000080
C	3.274182	1.616209	-0.000198
C	1.901149	1.491897	-0.000129
N	1.273885	0.284886	0.000041
O	1.411043	-2.016661	0.000287
H	0.429003	-1.922273	0.000220
H	3.963441	-1.730834	0.000186
H	5.139558	0.508011	-0.000126
H	3.729275	2.603225	-0.000340
H	1.247630	2.362743	-0.000210

$E(S_1)$ = -646.751208465

C	-2.040725	0.873048	0.000041
C	-3.445517	0.921060	0.000174
C	-4.211282	-0.296273	0.000182
C	-3.515553	-1.501618	-0.000001
C	-2.096414	-1.530342	-0.000149
N	-1.388676	-0.380507	-0.000096
O	-1.269402	1.865028	0.000024
H	-3.905184	1.904730	0.000258
H	-5.296755	-0.275831	0.000307
H	-4.040544	-2.454782	-0.000035
H	-1.537619	-2.461620	-0.000299
H	-0.339015	-0.353553	-0.000108
C	2.087019	0.815418	-0.000128
C	3.494200	0.800952	-0.000087

C	4.135616	-0.422800	0.000072
C	3.382061	-1.605850	0.000183
C	2.005479	-1.485911	0.000120
N	1.366325	-0.305576	-0.000035
O	1.462647	1.989817	-0.000264
H	0.483121	1.874371	-0.000192
H	4.031985	1.745317	-0.000173
H	5.224192	-0.464972	0.000111
H	3.853394	-2.584907	0.000312
H	1.367610	-2.371046	0.000197

$E(S_1)$ = -646.745604738

C	-1.975042	0.859966	0.000052
C	-3.388138	0.885956	0.000199
C	-4.129449	-0.330327	0.000177
C	-3.402196	-1.517988	-0.000022
C	-1.980365	-1.504565	-0.000152
N	-1.270985	-0.362703	-0.000085
O	-1.261480	1.893357	0.000025
H	-3.861876	1.863091	0.000312
H	-5.214773	-0.331257	0.000288
H	-3.901411	-2.485163	-0.000079
H	-1.419403	-2.435601	-0.000308
H	-0.141813	-0.303403	-0.000087
C	2.019069	0.835495	-0.000139
C	3.421461	0.789035	-0.000091
C	4.050949	-0.447128	0.000080
C	3.274838	-1.617653	0.000198
C	1.900678	-1.488055	0.000129
N	1.281610	-0.286295	-0.000041
O	1.412745	2.015110	-0.000287
H	0.420338	1.922425	-0.000214
H	3.967744	1.728550	-0.000185
H	5.138779	-0.507607	0.000125
H	3.730747	-2.603841	0.000339
H	1.246343	-2.360365	0.000210

$E(S_1)$ = -646.742655102

C	-1.972269	0.859447	0.000051
C	-3.392204	0.882994	0.000199

C	-4.127559	-0.328679	0.000177
C	-3.402545	-1.519232	-0.000023
C	-1.979470	-1.501186	-0.000152
N	-1.274332	-0.365676	-0.000085
O	-1.264859	1.892005	0.000025
H	-3.866190	1.860929	0.000315
H	-5.213996	-0.330854	0.000288
H	-3.902881	-2.485390	-0.000079
H	-1.418232	-2.433923	-0.000308
H	-0.036637	-0.295989	-0.000086
C	2.022198	0.837016	-0.000139
C	3.417285	0.791732	-0.000091
C	4.053015	-0.448870	0.000080
C	3.274182	-1.616209	0.000198
C	1.901149	-1.491897	0.000129
N	1.273885	-0.284886	-0.000041
O	1.411043	2.016661	-0.000287
H	0.429003	1.922273	-0.000220
H	3.963441	1.730834	-0.000186
H	5.139558	-0.508011	0.000126
H	3.729275	-2.603225	0.000340
H	1.247630	-2.362743	0.000210

$E(S_1)$ = -646.745565658

C	-1.970426	0.859554	0.000051
C	-3.394599	0.881246	0.000199
C	-4.126464	-0.327773	0.000177
C	-3.402858	-1.519829	-0.000023
C	-1.978693	-1.499368	-0.000152
N	-1.277249	-0.367452	-0.000085
O	-1.266813	1.891139	0.000025
H	-3.867947	1.859875	0.000316
H	-5.213757	-0.330779	0.000288
H	-3.903513	-2.485426	-0.000079
H	-1.417772	-2.432921	-0.000307
H	0.020295	-0.292642	-0.000085
C	2.024356	0.837429	-0.000139
C	3.414727	0.793564	-0.000091
C	4.054238	-0.450090	0.000080
C	3.273857	-1.615388	0.000198
C	1.901657	-1.494047	0.000129

N	1.269798	-0.283837	-0.000041
O	1.409819	2.017604	-0.000287
H	0.437524	1.922166	-0.000221
H	3.961461	1.731868	-0.000186
H	5.139624	-0.508152	0.000126
H	3.728733	-2.602942	0.000340
H	1.248692	-2.363755	0.000210

$E(S_1)$ = -646.751233491

C	-1.968810	0.859718	0.000051
C	-3.396573	0.879857	0.000199
C	-4.125607	-0.327081	0.000177
C	-3.403156	-1.520287	-0.000023
C	-1.977989	-1.497957	-0.000151
N	-1.279988	-0.368856	-0.000085
O	-1.268412	1.890410	0.000025
H	-3.869177	1.859056	0.000316
H	-5.213662	-0.330782	0.000288
H	-3.903955	-2.485418	-0.000079
H	-1.417517	-2.432054	-0.000306
H	0.065225	-0.290203	-0.000085
C	2.026136	0.837568	-0.000139
C	3.412620	0.795159	-0.000091
C	4.055227	-0.451176	0.000081
C	3.273607	-1.614722	0.000198
C	1.902126	-1.495805	0.000130
N	1.266789	-0.282862	-0.000041
O	1.408727	2.018388	-0.000287
H	0.445910	1.922228	-0.000220
H	3.959960	1.732593	-0.000186
H	5.139489	-0.508245	0.000126
H	3.728392	-2.602728	0.000340
H	1.249721	-2.364441	0.000210

$E(S_1)$ = -646.758458895

C	-1.967209	0.859599	0.000051
C	-3.398661	0.878453	0.000199
C	-4.124740	-0.326400	0.000177
C	-3.403452	-1.520837	-0.000023
C	-1.977393	-1.496415	-0.000151

N	-1.283076	-0.370305	-0.000085
O	-1.270118	1.889675	0.000025
H	-3.870870	1.857980	0.000316
H	-5.213216	-0.330747	0.000288
H	-3.904635	-2.485503	-0.000078
H	-1.417229	-2.431137	-0.000305
H	0.117982	-0.286541	-0.000084
C	2.027826	0.837965	-0.000139
C	3.410467	0.796746	-0.000091
C	4.056268	-0.452247	0.000081
C	3.273355	-1.614000	0.000198
C	1.902541	-1.497777	0.000130
N	1.263937	-0.281907	-0.000042
O	1.407933	2.019248	-0.000287
H	0.448966	1.922093	-0.000220
H	3.958045	1.733590	-0.000185
H	5.139788	-0.508433	0.000126
H	3.727836	-2.602330	0.000340
H	1.250782	-2.365402	0.000211

$E(S_1)$ = -646.765032152

C	-1.965767	0.859269	0.000051
C	-3.400746	0.877070	0.000200
C	-4.123835	-0.325688	0.000177
C	-3.403752	-1.521408	-0.000023
C	-1.976930	-1.494788	-0.000151
N	-1.286263	-0.371793	-0.000086
O	-1.271847	1.888963	0.000026
H	-3.872884	1.856704	0.000317
H	-5.212509	-0.330612	0.000288
H	-3.905556	-2.485626	-0.000078
H	-1.417063	-2.430069	-0.000304
H	0.170958	-0.281710	-0.000084
C	2.029465	0.838669	-0.000139
C	3.408357	0.798179	-0.000092
C	4.057345	-0.453252	0.000081
C	3.273105	-1.613277	0.000198
C	1.902880	-1.499875	0.000130
N	1.261657	-0.281109	-0.000042
O	1.407297	2.020128	-0.000287
H	0.449911	1.921979	-0.000219

H	3.955837	1.734815	-0.000185
H	5.140454	-0.508736	0.000127
H	3.727105	-2.601861	0.000340
H	1.251650	-2.366686	0.000211

$E(S_1)$ = -646.772306133

C	-1.961688	0.857286	0.000050
C	-3.406880	0.872974	0.000200
C	-4.120435	-0.323343	0.000176
C	-3.404396	-1.523217	-0.000023
C	-1.976158	-1.489730	-0.000150
N	-1.296480	-0.376118	-0.000087
O	-1.277301	1.886712	0.000026
H	-3.880726	1.851803	0.000318
H	-5.209213	-0.329484	0.000288
H	-3.908908	-2.485792	-0.000077
H	-1.416313	-2.425627	-0.000300
H	0.253457	-0.263126	-0.000086
C	2.034930	0.842047	-0.000139
C	3.402759	0.802169	-0.000092
C	4.061428	-0.456282	0.000082
C	3.272928	-1.611165	0.000197
C	1.904002	-1.507369	0.000131
N	1.263907	-0.279023	-0.000042
O	1.405994	2.023286	-0.000288
H	0.450134	1.922195	-0.000216
H	3.948093	1.739582	-0.000185
H	5.144019	-0.510535	0.000128
H	3.725012	-2.600541	0.000339
H	1.253979	-2.372696	0.000212

$E(S_1)$ = -646.779032697

C	-1.979399	0.847973	0.000047
C	-3.429370	0.869944	0.000204
C	-4.124309	-0.319378	0.000171
C	-3.421762	-1.527486	-0.000021
C	-1.999321	-1.487088	-0.000145
N	-1.330703	-0.380831	-0.000101
O	-1.307998	1.879882	0.000029
H	-3.919255	1.840190	0.000334

H	-5.212336	-0.321556	0.000282
H	-3.937361	-2.483713	-0.000069
H	-1.430842	-2.416963	-0.000280
H	0.314786	-0.221341	-0.000120
C	2.065318	0.864357	-0.000141
C	3.421535	0.815442	-0.000093
C	4.076943	-0.465209	0.000081
C	3.286330	-1.618484	0.000198
C	1.915945	-1.535767	0.000134
N	1.317649	-0.273461	-0.000040
O	1.411032	2.040933	-0.000296
H	0.455561	1.923436	-0.000189
H	3.965913	1.753167	-0.000176
H	5.159606	-0.530061	0.000128
H	3.745881	-2.604558	0.000339
H	1.253705	-2.390891	0.000220

$E(S_1)$ = -646.784482789

C	-2.027252	0.842835	0.000042
C	-3.479804	0.871367	0.000208
C	-4.181572	-0.313411	0.000173
C	-3.480271	-1.522105	-0.000010
C	-2.055890	-1.486421	-0.000145
N	-1.371819	-0.386943	-0.000126
O	-1.356535	1.874891	0.000039
H	-3.962568	1.845203	0.000347
H	-5.269621	-0.312191	0.000285
H	-3.996894	-2.477828	-0.000047
H	-1.496934	-2.422330	-0.000277
H	0.369624	-0.205333	-0.000142
C	2.123678	0.874568	-0.000142
C	3.481044	0.814412	-0.000086
C	4.122267	-0.476860	0.000082
C	3.328084	-1.628972	0.000198
C	1.958586	-1.536354	0.000137
N	1.371462	-0.265553	-0.000037
O	1.457565	2.048791	-0.000307
H	0.502786	1.920542	-0.000172
H	4.040488	1.743309	-0.000161
H	5.204500	-0.549041	0.000127
H	3.784711	-2.616328	0.000335

H	1.284955	-2.382334	0.000225

5.4. Single ESPT in the pyridone homodimer (Fig. S12 and S19)

TS

$E(S_1)$ = -646.748321752

C	-1.900478	0.871681	-0.000082
C	-3.266734	1.271846	-0.000038
C	-4.299861	0.308765	0.000071
C	-3.930536	-1.038657	0.000149
C	-2.561472	-1.409138	0.000095
H	-3.459359	2.341410	-0.000083
H	-5.345540	0.603963	0.000110
H	-4.677165	-1.829591	0.000259
H	-2.256145	-2.453952	0.000154
N	-1.580429	-0.505021	-0.000040
H	-0.480316	-0.852048	-0.000105
O	-0.942223	1.667929	-0.000150
O	0.720678	-1.450230	-0.000166
C	1.799008	-0.772927	-0.000079
C	3.092442	-1.336056	-0.000051
N	1.717495	0.607738	-0.000007
C	4.220575	-0.523094	0.000056
H	3.158612	-2.420314	-0.000118
C	2.820199	1.421669	0.000105
H	0.783286	1.022198	-0.000047
C	4.078887	0.883750	0.000141
H	5.213117	-0.969488	0.000075
H	2.620368	2.489149	0.000163
H	4.943868	1.541028	0.000231

$E(S_1)$ = -646.753709054

C	-1.927581	0.881039	-0.000074
C	-3.273740	1.290691	-0.000026
C	-4.330799	0.317231	0.000071
C	-3.972675	-1.030521	0.000143
C	-2.612010	-1.424457	0.000095
H	-3.462391	2.360196	-0.000055
H	-5.373109	0.620894	0.000104
H	-4.727665	-1.814221	0.000240

H	-2.302820	-2.465933	0.000146
N	-1.629784	-0.500406	-0.000034
H	-0.625326	-0.808393	-0.000102
O	-0.925503	1.640941	-0.000146
O	0.797618	-1.493587	-0.000176
C	1.826006	-0.792249	-0.000084
C	3.160274	-1.324213	-0.000047
N	1.732641	0.587365	-0.000012
C	4.243810	-0.492063	0.000063
H	3.252412	-2.406869	-0.000108
C	2.807880	1.417525	0.000098
H	0.780439	0.986404	-0.000055
C	4.079156	0.920383	0.000142
H	5.248518	-0.914355	0.000091
H	2.580695	2.480890	0.000149
H	4.930398	1.593634	0.000231

$E(S_1)$ = -646.748321704

C	-1.900478	0.871681	-0.000082
C	-3.266734	1.271846	-0.000038
C	-4.299861	0.308765	0.000071
C	-3.930536	-1.038657	0.000149
C	-2.561472	-1.409138	0.000095
H	-3.459359	2.341410	-0.000083
H	-5.345540	0.603963	0.000110
H	-4.677165	-1.829591	0.000259
H	-2.256145	-2.453952	0.000154
N	-1.580429	-0.505021	-0.000040
H	-0.480316	-0.852048	-0.000105
O	-0.942223	1.667929	-0.000150
O	0.720678	-1.450230	-0.000166
C	1.799008	-0.772927	-0.000079
C	3.092442	-1.336056	-0.000051
N	1.717495	0.607738	-0.000007
C	4.220575	-0.523094	0.000056
H	3.158612	-2.420314	-0.000118
C	2.820199	1.421669	0.000105
H	0.783286	1.022198	-0.000047
C	4.078887	0.883750	0.000141
H	5.213117	-0.969488	0.000075
H	2.620368	2.489149	0.000163

H	4.943868	1.541028	0.000231

$E(S_1)$ = -646.751539393

C	-1.897644	0.871790	-0.000082
C	-3.269807	1.271005	-0.000037
C	-4.297987	0.310061	0.000071
C	-3.931032	-1.038612	0.000150
C	-2.559979	-1.407036	0.000095
H	-3.460929	2.341213	-0.000083
H	-5.345049	0.604711	0.000110
H	-4.677760	-1.828770	0.000259
H	-2.255478	-2.453094	0.000154
N	-1.583568	-0.505918	-0.000039
H	-0.433875	-0.869952	-0.000106
O	-0.944569	1.667621	-0.000149
O	0.716232	-1.450348	-0.000166
C	1.803591	-0.772948	-0.000078
C	3.088051	-1.336679	-0.000051
N	1.714918	0.607299	-0.000007
C	4.223099	-0.521288	0.000057
H	3.157061	-2.420315	-0.000117
C	2.821486	1.423695	0.000106
H	0.794976	1.018770	-0.000046
C	4.078561	0.882929	0.000141
H	5.213448	-0.968654	0.000076
H	2.621224	2.489439	0.000164
H	4.943610	1.541289	0.000231

$E(S_1)$ = -646.757927115

C	-1.895060	0.871680	-0.000082
C	-3.272590	1.270437	-0.000037
C	-4.296445	0.310998	0.000071
C	-3.931768	-1.038401	0.000150
C	-2.558395	-1.405201	0.000095
H	-3.462460	2.340964	-0.000083
H	-5.344535	0.605233	0.000110
H	-4.678427	-1.827994	0.000259
H	-2.254966	-2.452208	0.000153
N	-1.586870	-0.506449	-0.000039
H	-0.384481	-0.888958	-0.000107

O	-0.946798	1.667349	-0.000149
O	0.712066	-1.450480	-0.000166
C	1.807610	-0.772561	-0.000078
C	3.084097	-1.337324	-0.000051
N	1.712813	0.606579	-0.000007
C	4.225294	-0.519476	0.000057
H	3.155625	-2.420230	-0.000117
C	2.822630	1.425643	0.000106
H	0.804547	1.016262	-0.000047
C	4.078285	0.882152	0.000141
H	5.213744	-0.967850	0.000076
H	2.621953	2.489758	0.000164
H	4.943309	1.541476	0.000231

$E(S_1)$ = -646.765082806

C	-1.893879	0.871058	-0.000082
C	-3.274564	1.270174	-0.000037
C	-4.295524	0.311494	0.000071
C	-3.932451	-1.038266	0.000150
C	-2.557344	-1.403691	0.000094
H	-3.464713	2.340555	-0.000083
H	-5.343467	0.605492	0.000110
H	-4.679553	-1.827424	0.000258
H	-2.254704	-2.451143	0.000153
N	-1.589018	-0.506766	-0.000038
H	-0.328125	-0.910748	-0.000109
O	-0.948499	1.667322	-0.000149
O	0.708172	-1.450542	-0.000166
C	1.810455	-0.771601	-0.000078
C	3.081282	-1.337722	-0.000051
N	1.712197	0.605731	-0.000007
C	4.226661	-0.518099	0.000057
H	3.153935	-2.420397	-0.000117
C	2.823200	1.427074	0.000106
H	0.801315	1.018463	-0.000048
C	4.078121	0.881739	0.000141
H	5.214723	-0.967278	0.000076
H	2.622434	2.491057	0.000163
H	4.942770	1.541474	0.000231

$E(S_1)$ = -646.768688100

C	-1.893123	0.870775	-0.000082
C	-3.275703	1.269954	-0.000037
C	-4.294878	0.311851	0.000071
C	-3.932746	-1.038247	0.000150
C	-2.556759	-1.402799	0.000094
H	-3.465756	2.340401	-0.000083
H	-5.343078	0.605647	0.000110
H	-4.680051	-1.827133	0.000258
H	-2.254625	-2.450693	0.000152
N	-1.590398	-0.506940	-0.000038
H	-0.301268	-0.920503	-0.000110
O	-0.949452	1.667274	-0.000149
O	0.706144	-1.450678	-0.000166
C	1.812239	-0.771191	-0.000078
C	3.079637	-1.337959	-0.000051
N	1.711482	0.605453	-0.000007
C	4.227555	-0.517378	0.000057
H	3.153163	-2.420478	-0.000117
C	2.823619	1.427882	0.000106
H	0.802977	1.018059	-0.000048
C	4.078029	0.881499	0.000141
H	5.215052	-0.966999	0.000076
H	2.622660	2.491507	0.000163
H	4.942580	1.541514	0.000231

$E(S_1)$ = -646.772142222

C	-1.892367	0.870491	-0.000082
C	-3.276843	1.269730	-0.000037
C	-4.294233	0.312206	0.000071
C	-3.933040	-1.038231	0.000150
C	-2.556173	-1.401909	0.000094
H	-3.466800	2.340244	-0.000083
H	-5.342690	0.605798	0.000110
H	-4.680548	-1.826844	0.000258
H	-2.254544	-2.450245	0.000152
N	-1.591778	-0.507116	-0.000038
H	-0.274410	-0.930259	-0.000111
O	-0.950405	1.667226	-0.000149
O	0.704118	-1.450813	-0.000166
C	1.814024	-0.770779	-0.000078

C	3.077992	-1.338195	-0.000051
N	1.710766	0.605177	-0.000007
C	4.228450	-0.516655	0.000057
H	3.152393	-2.420557	-0.000116
C	2.824036	1.428692	0.000106
H	0.804639	1.017656	-0.000048
C	4.077936	0.881262	0.000141
H	5.215381	-0.966716	0.000076
H	2.622884	2.491960	0.000164
H	4.942390	1.541557	0.000231

$E(S_1)$ = -646.781618806

C	-1.890600	0.867771	-0.000082
C	-3.281820	1.268775	-0.000037
C	-4.291421	0.313171	0.000071
C	-3.934347	-1.038646	0.000150
C	-2.553843	-1.397717	0.000093
H	-3.474147	2.338854	-0.000083
H	-5.340078	0.606137	0.000109
H	-4.683667	-1.825529	0.000257
H	-2.254253	-2.447435	0.000150
N	-1.597804	-0.507445	-0.000037
H	-0.166492	-0.958538	-0.000113
O	-0.954959	1.667172	-0.000149
O	0.698221	-1.454098	-0.000166
C	1.822335	-0.767697	-0.000077
C	3.071184	-1.339112	-0.000052
N	1.708638	0.603939	-0.000007
C	4.232373	-0.513521	0.000058
H	3.147358	-2.421115	-0.000116
C	2.825619	1.432447	0.000107
H	0.802475	1.018632	-0.000050
C	4.077730	0.880694	0.000141
H	5.218024	-0.965081	0.000077
H	2.624070	2.495159	0.000164
H	4.941518	1.541874	0.000231

$E(S_1)$ = -646.787592487

C	-1.919415	0.859156	-0.000080
C	-3.311823	1.263671	-0.000038

C	-4.301206	0.302328	0.000075
C	-3.944002	-1.047892	0.000149
C	-2.560372	-1.389575	0.000086
H	-3.519596	2.330224	-0.000093
H	-5.350388	0.589309	0.000110
H	-4.693141	-1.834725	0.000247
H	-2.254440	-2.436760	0.000133
N	-1.614045	-0.500093	-0.000029
H	-0.081430	-0.970892	-0.000109
O	-0.998626	1.673720	-0.000153
O	0.747039	-1.502374	-0.000174
C	1.856087	-0.757176	-0.000076
C	3.088605	-1.333073	-0.000050
N	1.711390	0.608651	-0.000003
C	4.255837	-0.498429	0.000058
H	3.149092	-2.415789	-0.000104
C	2.830434	1.452646	0.000107
H	0.796277	1.012295	-0.000088
C	4.083306	0.891934	0.000140
H	5.247451	-0.938815	0.000078
H	2.628611	2.515719	0.000165
H	4.944149	1.557217	0.000229

$E(S_1)$ = -646.791415509

C	-1.962956	0.862883	-0.000077
C	-3.363801	1.251791	-0.000035
C	-4.343187	0.283334	0.000079
C	-3.964517	-1.060958	0.000147
C	-2.575015	-1.385573	0.000086
H	-3.583488	2.316067	-0.000092
H	-5.395938	0.557981	0.000118
H	-4.702449	-1.858333	0.000241
H	-2.264409	-2.431666	0.000128
N	-1.630780	-0.494000	-0.000020
H	-0.014664	-1.023338	-0.000111
O	-1.060675	1.695993	-0.000159
O	0.807051	-1.543958	-0.000186
C	1.904188	-0.768733	-0.000078
C	3.146500	-1.318265	-0.000046
N	1.725792	0.595401	0.000001
C	4.300976	-0.463656	0.000062

H	3.218760	-2.400368	-0.000097
C	2.833858	1.459010	0.000106
H	0.802130	0.982111	-0.000101
C	4.097755	0.922157	0.000141
H	5.300726	-0.883782	0.000085
H	2.615541	2.518526	0.000162
H	4.944893	1.604775	0.000228

5.5. Double ESPT in the pyridone/acetamide (O-H---O / N---H-N hydrogen bond connection) system (Fig. S13 and S20)

TS

$E(S_1)$ = -532.444672226

C	-1.082560	0.743190	-0.000148
C	-2.421755	1.194668	0.000124
C	-3.497021	0.251655	0.002725
C	-3.117684	-1.096243	-0.000497
C	-1.747602	-1.478087	-0.002246
N	-0.714979	-0.607886	0.000800
H	-4.537440	0.560030	0.004490
H	-2.577923	2.270480	-0.001674
H	-3.864113	-1.889830	-0.001809
H	-1.492199	-2.538242	-0.004538
O	-0.121643	1.588346	-0.001483
H	0.772449	-0.996509	0.000848
C	2.672028	-0.116875	0.000291
O	2.226493	1.078213	-0.000544
H	1.096860	1.218360	-0.000864
C	4.161321	-0.277253	0.000503
H	4.566537	0.226849	0.884967
H	4.460454	-1.328755	0.001242
H	4.566630	0.225612	-0.884623
N	1.869498	-1.154122	0.000917
H	2.287956	-2.072752	0.001643

$E(S_1)$ = -532.447242962

C	1.131231	-0.727866	-0.005317
C	2.471576	-1.177021	0.008781
C	3.534585	-0.221858	0.017733
C	3.126279	1.121558	0.004414

C	1.747748	1.478076	-0.011391
N	0.723204	0.594978	-0.013347
H	4.579299	-0.512796	0.030179
H	2.636724	-2.251284	0.011751
H	3.856954	1.929768	0.005647
H	1.478375	2.534278	-0.020885
O	0.193533	-1.626807	-0.012102
H	-0.953910	1.097182	-0.007563
C	-2.723577	0.085899	0.001766
O	-2.208448	-1.049367	-0.006487
H	-0.787657	-1.261036	-0.021036
C	-4.222552	0.208873	0.014590
H	-4.604338	-0.310037	0.900330
H	-4.560239	1.249279	0.021075
H	-4.619070	-0.304034	-0.868391
N	-1.988742	1.195888	0.000069
H	-2.439793	2.096040	0.007092

$E(S_1)$ = -532.446314998

C	1.100493	-0.726462	-0.000105
C	2.435611	-1.186328	0.000133
C	3.507640	-0.241722	0.002885
C	3.119282	1.106511	-0.000600
C	1.746455	1.481460	-0.002317
N	0.716104	0.607017	0.000872
H	4.549290	-0.545092	0.004586
H	2.590406	-2.262065	-0.002297
H	3.862031	1.903612	-0.002191
H	1.487080	2.540024	-0.004607
O	0.154817	-1.608393	-0.001542
H	-0.871330	1.050194	0.001079
C	-2.690423	0.091452	0.000284
O	-2.215739	-1.069767	-0.000530
H	-0.881908	-1.248254	-0.001050
C	-4.183184	0.252462	0.000491
H	-4.588140	-0.252418	0.884490
H	-4.491846	1.302002	0.001210
H	-4.588276	-0.251252	-0.884109
N	-1.921391	1.170848	0.001003
H	-2.358158	2.079232	0.001709

$E(S_1)$ = -532.444669810

C	1.084422	-0.741468	-0.000143
C	2.423189	-1.193811	0.000125
C	3.498120	-0.250633	0.002742
C	3.117850	1.097303	-0.000508
C	1.747483	1.478434	-0.002253
N	0.715094	0.607795	0.000808
H	4.538667	-0.558490	0.004500
H	2.579215	-2.269613	-0.001738
H	3.863900	1.891254	-0.001849
H	1.491669	2.538425	-0.004545
O	0.125065	-1.590434	-0.001489
H	-0.782650	1.002110	0.000872
C	-2.673940	0.114254	0.000290
O	-2.225373	-1.077343	-0.000542
H	-1.074637	-1.221558	-0.000883
C	-4.163589	0.274699	0.000502
H	-4.568778	-0.229483	0.884918
H	-4.463709	1.326002	0.001239
H	-4.568876	-0.228253	-0.884570
N	-1.874855	1.155877	0.000926
H	-2.295212	2.073455	0.001650

$E(S_1)$ = -532.444763968

C	1.080806	-0.752047	-0.000179
C	2.422045	-1.194923	0.000277
C	3.494020	-0.248721	0.002528
C	3.113531	1.096835	-0.000357
C	1.742859	1.479040	-0.002153
N	0.713760	0.604778	0.000463
H	4.535367	-0.554243	0.004251
H	2.580618	-2.270094	-0.001140
H	3.858806	1.891421	-0.001382
H	1.485624	2.538102	-0.004367
O	0.120946	-1.588837	-0.001409
H	-0.697793	0.953490	0.000789
C	-2.668318	0.128161	0.000269
O	-2.255215	-1.089262	-0.000618
H	-1.189514	-1.219558	-0.000890
C	-4.154641	0.304269	0.000518

H	-4.566364	-0.194702	0.885065
H	-4.439888	1.359439	0.001210
H	-4.566547	-0.193603	-0.884560
N	-1.837042	1.135087	0.000982
H	-2.244997	2.059798	0.001699

$E(S_1)$ = -532.445258924

C	1.079062	-0.758514	-0.000194
C	2.421428	-1.194289	0.000336
C	3.491404	-0.244835	0.002414
C	3.108337	1.098674	-0.000297
C	1.736901	1.480691	-0.002085
N	0.710955	0.600945	0.000360
H	4.533832	-0.546458	0.004051
H	2.583014	-2.268836	-0.000686
H	3.850296	1.896196	-0.001100
H	1.473852	2.537906	-0.004183
O	0.121005	-1.591482	-0.001390
H	-0.603274	0.916314	0.000636
C	-2.665024	0.135638	0.000265
O	-2.270012	-1.094639	-0.000658
H	-1.234028	-1.223545	-0.000903
C	-4.151385	0.319883	0.000541
H	-4.568459	-0.172763	0.885872
H	-4.424331	1.378631	0.001150
H	-4.568685	-0.171825	-0.885199
N	-1.817858	1.123455	0.000948
H	-2.226184	2.049069	0.001705

$E(S_1)$ = -532.446818099

C	1.077596	-0.762009	-0.000195
C	2.420179	-1.194067	0.000359
C	3.490222	-0.243623	0.002373
C	3.106008	1.098464	-0.000273
C	1.734253	1.482280	-0.002064
N	0.709465	0.599175	0.000331
H	4.533052	-0.543482	0.003980
H	2.581861	-2.268401	-0.000511
H	3.845799	1.897778	-0.000999
H	1.468109	2.538175	-0.004152

O	0.120666	-1.592521	-0.001387
H	-0.507002	0.889308	0.000555
C	-2.663733	0.141742	0.000266
O	-2.278348	-1.096108	-0.000669
H	-1.251906	-1.225278	-0.000907
C	-4.151069	0.325887	0.000546
H	-4.569017	-0.165288	0.886083
H	-4.421309	1.385440	0.001098
H	-4.569271	-0.164462	-0.885323
N	-1.809941	1.119485	0.000935
H	-2.226258	2.042570	0.001693

$E(S_1)$ = -532.449586861

C	1.078388	-0.768636	-0.000191
C	2.420356	-1.194313	0.000374
C	3.488967	-0.241589	0.002346
C	3.105205	1.099260	-0.000252
C	1.734995	1.486315	-0.002053
N	0.719918	0.594495	0.000325
H	4.531804	-0.541280	0.003988
H	2.582402	-2.268323	-0.000499
H	3.845219	1.897926	-0.000999
H	1.462068	2.539559	-0.004205
O	0.121848	-1.593566	-0.001387
H	-0.399664	0.871360	0.000480
C	-2.666021	0.148968	0.000272
O	-2.287895	-1.097597	-0.000673
H	-1.266986	-1.221683	-0.000896
C	-4.153429	0.327962	0.000550
H	-4.571542	-0.164458	0.885497
H	-4.425907	1.386696	0.001092
H	-4.571793	-0.163644	-0.884726
N	-1.813805	1.121184	0.000931
H	-2.250780	2.035601	0.001680

$E(S_1)$ = -532.455546165

C	1.169226	-0.812433	-0.000177
C	2.521099	-1.200081	0.000210
C	3.562670	-0.209153	0.001755
C	3.175899	1.128306	-0.000013

C	1.805237	1.500394	-0.001560
N	0.834185	0.561735	0.000413
H	4.610589	-0.492474	0.003140
H	2.724125	-2.266813	-0.000394
H	3.913766	1.928226	-0.000398
H	1.489004	2.539686	-0.003462
O	0.189212	-1.598779	-0.001165
H	-0.190494	0.799032	0.000162
C	-2.796124	0.170229	0.000175
O	-2.447991	-1.108591	-0.000592
H	-1.462421	-1.212554	-0.000767
C	-4.286155	0.348740	0.000647
H	-4.705926	-0.144288	0.884965
H	-4.559027	1.407118	0.001073
H	-4.706429	-0.143722	-0.883742
N	-1.918259	1.105508	0.000458
H	-2.365555	2.018043	0.001145

5.6. Double ESPT in the pyridone/acetamide (O-H---N / N---H-O hydrogen bond connection) system (Fig. S14 and S21)

$E(S_1)$ = -532.440367374

C	-1.188675	0.791275	-0.000039
C	-2.568028	1.095623	0.000510
C	-3.524084	0.033331	0.000955
C	-2.973771	-1.260373	-0.000085
C	-1.565462	-1.470685	-0.000772
N	-0.642226	-0.481149	-0.000341
H	-4.593652	0.212512	0.001546
H	-2.844896	2.146842	0.000456
H	-3.614099	-2.141739	-0.000400
H	-1.179636	-2.489815	-0.001472
O	-0.340949	1.778544	-0.000349
H	0.959988	-0.875371	-0.000163
O	1.938573	-1.154806	0.000061
C	2.708341	-0.087777	-0.000134
H	0.648713	1.456992	-0.000710
C	4.172544	-0.415295	0.000872
H	4.402292	-1.017150	0.887569
H	4.402381	-1.023244	-0.881596
H	4.784506	0.490261	-0.002069

N	2.207996	1.098336	-0.000776
H	2.927830	1.813916	-0.000873

$E(S_1)$ = -532.441818205

C	-1.156691	0.797560	-0.000065
C	-2.535430	1.101193	0.000257
C	-3.494931	0.041360	0.000767
C	-2.951611	-1.254062	-0.000102
C	-1.545027	-1.470621	-0.000615
N	-0.619914	-0.483591	-0.000101
H	-4.563841	0.224898	0.001245
H	-2.810514	2.152867	-0.000009
H	-3.595909	-2.132462	-0.000424
H	-1.161024	-2.490421	-0.001199
O	-0.303372	1.773626	-0.000422
H	0.884381	-0.857216	0.000160
O	1.884010	-1.149174	0.000367
C	2.662632	-0.097723	0.000056
H	0.718392	1.447181	-0.000520
C	4.126256	-0.428633	0.000384
H	4.353147	-1.033637	0.885589
H	4.353190	-1.035467	-0.883549
H	4.742400	0.474189	-0.000502
N	2.177474	1.099217	-0.000441
H	2.900561	1.810633	-0.000662

$E(S_1)$ = -532.442807150

C	-1.131228	0.806567	-0.000036
C	-2.509789	1.106646	0.000184
C	-3.471320	0.047743	0.000573
C	-2.934820	-1.248925	-0.000131
C	-1.530027	-1.471053	-0.000498
N	-0.605140	-0.484733	-0.000029
H	-4.539787	0.234633	0.000948
H	-2.784985	2.158266	-0.000041
H	-3.582777	-2.124532	-0.000414
H	-1.146089	-2.490785	-0.000980
O	-0.271607	1.768861	-0.000306
H	0.802587	-0.832301	0.000260
O	1.835791	-1.140564	0.000362

C	2.625956	-0.109655	0.000038
H	0.800969	1.434126	-0.000292
C	4.088958	-0.444760	0.000230
H	4.312327	-1.051095	0.885327
H	4.312266	-1.052538	-0.883887
H	4.710329	0.454645	-0.000499
N	2.160783	1.101102	-0.000326
H	2.885807	1.809240	-0.000534

$E(S_1)$ = -532.444497802

C	1.119761	0.820665	-0.000021
C	2.499429	1.111128	0.000386
C	3.459636	0.049471	0.001196
C	2.928657	-1.247137	-0.000035
C	1.525508	-1.472785	-0.000803
N	0.605920	-0.482529	0.000052
H	4.528162	0.237170	0.001951
H	2.778942	2.161518	-0.000034
H	3.579025	-2.120777	-0.000468
H	1.137322	-2.490572	-0.001696
O	0.253745	1.765885	-0.000523
H	-0.707647	-0.794040	-0.000027
O	-1.800911	-1.125278	0.000448
C	-2.608295	-0.124819	-0.000012
H	-0.912551	1.419268	-0.000785
C	-4.070292	-0.467543	0.000216
H	-4.288011	-1.076942	-0.884031
H	-4.288015	-1.075691	0.885325
H	-4.700021	0.426239	-0.000405
N	-2.174184	1.105769	-0.000599
H	-2.898453	1.812406	-0.000958

$E(S_1)$ = -532.450291649

C	1.135782	0.840611	-0.000058
C	2.517742	1.115926	0.000034
C	3.473071	0.047093	0.000090
C	2.948899	-1.248919	-0.000047
C	1.547387	-1.478746	-0.000162
N	0.640787	-0.477191	-0.000102
H	4.542115	0.233684	0.000191

H	2.805838	2.163757	0.000057
H	3.601977	-2.120269	-0.000067
H	1.149737	-2.492005	-0.000286
O	0.261109	1.762725	-0.000105
H	-0.581789	-0.737592	-0.000103
O	-1.799432	-1.100302	-0.000096
C	-2.631141	-0.144432	0.000076
H	-1.081207	1.408829	0.000012
C	-4.091977	-0.499222	0.000226
H	-4.301560	-1.109926	-0.884813
H	-4.301287	-1.110327	0.885049
H	-4.733766	0.386301	0.000515
N	-2.244603	1.114701	0.000080
H	-2.965348	1.821729	0.000248

$E(S_1)$ = -532.461981617

C	-1.193132	0.862216	0.000030
C	-2.577710	1.121002	0.000536
C	-3.523836	0.040365	0.001384
C	-3.006117	-1.254391	0.000218
C	-1.605606	-1.489017	-0.000850
N	-0.719317	-0.469081	0.000245
H	-4.593892	0.223232	0.002253
H	-2.877990	2.165018	0.000429
H	-3.661889	-2.123292	-0.000073
H	-1.193913	-2.495299	-0.002024
O	-0.304403	1.754598	-0.000719
H	0.413435	-0.667504	-0.000843
O	1.848381	-1.061275	-0.001886
C	2.712190	-0.162590	-0.000689
H	1.330712	1.426025	-0.001114
C	4.169874	-0.542748	0.002265
H	4.366208	-1.148820	0.893316
H	4.365819	-1.166068	-0.876770
H	4.832487	0.327717	-0.005964
N	2.390405	1.130981	-0.001105
H	3.115610	1.830087	0.000287

$E(S_1)$ = -532.469270895

C	-1.242973	0.867570	0.000543

C	-2.625393	1.132936	0.000713
C	-3.576734	0.054519	0.000291
C	-3.076999	-1.245044	-0.000480
C	-1.679687	-1.498433	-0.000676
N	-0.795297	-0.475861	-0.000039
H	-4.645421	0.246405	0.000492
H	-2.922150	2.177674	0.001160
H	-3.743891	-2.105092	-0.000943
H	-1.269999	-2.504686	-0.001273
O	-0.332245	1.729069	0.000880
H	0.241496	-0.641874	0.000004
O	1.916110	-1.038804	-0.000024
C	2.795510	-0.172438	-0.001036
H	1.551392	1.434472	-0.001459
C	4.252653	-0.564310	0.001576
H	4.446511	-1.160224	0.899960
H	4.439535	-1.200925	-0.869677
H	4.925572	0.298397	-0.020042
N	2.507414	1.141178	-0.002407
H	3.242958	1.827715	-0.003533

5.7. Double ESPT in the pyridone/acetic acid system (Fig. S15 and S22)

TS

$E(S_1)$ = -552.324556232

C	-1.073914	0.791106	0.000017
C	-2.438341	1.139382	0.000050
C	-3.437725	0.115039	0.000045
C	-2.952836	-1.200787	0.000032
C	-1.558302	-1.479315	-0.000036
N	-0.602800	-0.522631	-0.000017
H	-4.498138	0.342570	0.000097
H	-2.675532	2.200105	0.000082
H	-3.634015	-2.050491	0.000087
H	-1.208079	-2.510440	-0.000080
O	-0.173651	1.714416	0.000017
H	0.705206	-0.833261	-0.000075
O	1.809348	-1.130905	-0.000134
C	2.578211	-0.107090	-0.000129
O	2.165393	1.076073	-0.000166
H	0.872245	1.352555	-0.000061

C	4.054349	-0.379161	0.000185
H	4.304508	-0.974300	0.885593
H	4.304344	-0.978748	-0.882227
H	4.611693	0.558718	-0.002036

$E(S_1)$ = -552.324825360

C	-1.101701	0.782520	0.000013
C	-2.468320	1.128552	0.000063
C	-3.460439	0.099196	0.000070
C	-2.959702	-1.212379	0.000025
C	-1.560823	-1.476215	-0.000025
N	-0.607096	-0.516569	-0.000031
H	-4.522688	0.317098	0.000109
H	-2.709298	2.188328	0.000095
H	-3.631742	-2.069529	0.000026
H	-1.208614	-2.506628	-0.000059
O	-0.215744	1.729805	0.000005
H	0.824301	-0.865711	-0.000080
O	1.857795	-1.143022	-0.000113
C	2.611324	-0.089953	-0.000117
O	2.172134	1.070813	-0.000191
H	0.779197	1.377674	-0.000079
C	4.087236	-0.358402	0.000195
H	4.340543	-0.952471	0.885472
H	4.340464	-0.956349	-0.882458
H	4.638583	0.582887	-0.001732

$E(S_1)$ = -552.324555756

C	-1.073914	0.791106	0.000017
C	-2.438341	1.139382	0.000050
C	-3.437725	0.115039	0.000045
C	-2.952836	-1.200787	0.000032
C	-1.558302	-1.479315	-0.000036
N	-0.602800	-0.522631	-0.000017
H	-4.498138	0.342570	0.000097
H	-2.675532	2.200105	0.000082
H	-3.634015	-2.050491	0.000087
H	-1.208079	-2.510440	-0.000080
O	-0.173651	1.714416	0.000017
H	0.705206	-0.833261	-0.000075

O	1.809348	-1.130905	-0.000134
C	2.578211	-0.107090	-0.000129
O	2.165393	1.076073	-0.000166
H	0.872245	1.352555	-0.000061
C	4.054349	-0.379161	0.000185
H	4.304508	-0.974300	0.885593
H	4.304344	-0.978748	-0.882227
H	4.611693	0.558718	-0.002036

$E(S_1)$ = -552.325273517

C	-1.068989	0.797216	0.000017
C	-2.434373	1.140433	0.000049
C	-3.435587	0.117418	0.000048
C	-2.952806	-1.196956	0.000029
C	-1.558373	-1.480288	-0.000032
N	-0.601757	-0.524480	-0.000019
H	-4.495683	0.346310	0.000095
H	-2.668947	2.201303	0.000084
H	-3.633970	-2.046538	0.000067
H	-1.210112	-2.510671	-0.000074
O	-0.166498	1.710617	0.000017
H	0.612383	-0.809965	-0.000073
O	1.804968	-1.128540	-0.000134
C	2.572662	-0.117394	-0.000129
O	2.162811	1.077837	-0.000165
H	0.933526	1.337006	-0.000064
C	4.052381	-0.381154	0.000185
H	4.302393	-0.976434	0.885485
H	4.302226	-0.980889	-0.882115
H	4.610745	0.556286	-0.002040

$E(S_1)$ = -552.326501417

C	-1.067821	0.799682	0.000017
C	-2.433518	1.140568	0.000049
C	-3.435273	0.117833	0.000049
C	-2.952790	-1.196045	0.000029
C	-1.558713	-1.480764	-0.000031
N	-0.602553	-0.524588	-0.000019
H	-4.495416	0.346976	0.000095
H	-2.667706	2.201665	0.000083

H	-3.633732	-2.045732	0.000062
H	-1.209640	-2.511063	-0.000074
O	-0.165739	1.709715	0.000016
H	0.563777	-0.798189	-0.000072
O	1.806546	-1.128206	-0.000134
C	2.571503	-0.121582	-0.000129
O	2.161808	1.079035	-0.000165
H	0.970234	1.326687	-0.000067
C	4.052309	-0.381372	0.000185
H	4.301897	-0.976817	0.885441
H	4.301725	-0.981271	-0.882070
H	4.611633	0.555593	-0.002040

$E(S_1)$ = -552.328322756

C	-1.066842	0.802355	0.000017
C	-2.432864	1.140732	0.000049
C	-3.435015	0.118171	0.000049
C	-2.952971	-1.195089	0.000029
C	-1.559170	-1.481276	-0.000031
N	-0.604299	-0.524435	-0.000020
H	-4.495199	0.347503	0.000094
H	-2.666502	2.201883	0.000083
H	-3.633692	-2.044893	0.000060
H	-1.209578	-2.511195	-0.000073
O	-0.165498	1.708865	0.000016
H	0.524211	-0.788571	-0.000070
O	1.808183	-1.127871	-0.000135
C	2.570348	-0.125833	-0.000129
O	2.160741	1.080351	-0.000164
H	1.015335	1.313574	-0.000070
C	4.052091	-0.381467	0.000185
H	4.301245	-0.977072	0.885400
H	4.301069	-0.981527	-0.882029
H	4.612325	0.555021	-0.002040

$E(S_1)$ = -552.330577366

C	-1.065978	0.806134	0.000017
C	-2.432342	1.140898	0.000051
C	-3.434681	0.118296	0.000053
C	-2.953295	-1.194119	0.000030

C	-1.560002	-1.482184	-0.000031
N	-0.607873	-0.523750	-0.000022
H	-4.494996	0.347693	0.000099
H	-2.665663	2.202116	0.000086
H	-3.633821	-2.043981	0.000060
H	-1.209202	-2.511685	-0.000075
O	-0.166311	1.708004	0.000015
H	0.488228	-0.779639	-0.000072
O	1.810303	-1.127398	-0.000133
C	2.569329	-0.131515	-0.000129
O	2.161331	1.082027	-0.000167
H	1.064933	1.296499	-0.000078
C	4.051831	-0.381193	0.000187
H	4.300583	-0.977025	0.885325
H	4.300404	-0.981484	-0.881946
H	4.612890	0.554794	-0.002040

$E(S_1)$ = -552.335230908

C	-1.082372	0.815701	0.000016
C	-2.448784	1.146942	0.000016
C	-3.450467	0.121828	0.000016
C	-2.977514	-1.191875	0.000023
C	-1.586498	-1.486787	-0.000003
N	-0.641140	-0.522641	0.000009
H	-4.510522	0.353395	0.000048
H	-2.685013	2.207371	0.000327
H	-3.662785	-2.037707	0.000056
H	-1.232187	-2.514756	-0.000290
O	-0.173063	1.698863	0.000053
H	0.417376	-0.763891	-0.000044
O	1.830040	-1.120220	-0.000115
C	2.597786	-0.143857	-0.000057
O	2.205754	1.087112	-0.000044
H	1.163028	1.272303	0.000039
C	4.080489	-0.388585	-0.000005
H	4.330018	-0.983788	0.885254
H	4.329509	-0.988495	-0.882180
H	4.640867	0.547801	-0.002445

$E(S_1)$ = -552.338942496

C	-1.107142	0.816235	0.000026
C	-2.469875	1.161337	0.000026
C	-3.481888	0.144152	0.000026
C	-3.033767	-1.176867	0.000027
C	-1.648318	-1.494415	-0.000006
N	-0.697863	-0.534721	0.000015
H	-4.538827	0.390158	0.000053
H	-2.698564	2.223234	0.000258
H	-3.734531	-2.009744	0.000048
H	-1.302888	-2.524939	-0.000224
O	-0.174737	1.669271	0.000068
H	0.344171	-0.770237	-0.000121
O	1.863149	-1.102515	-0.000408
C	2.653090	-0.152412	-0.000226
O	2.288367	1.096476	-0.000013
H	1.263903	1.260329	0.000163
C	4.134070	-0.406397	0.000186
H	4.381434	-0.999079	0.887693
H	4.380538	-1.009882	-0.880166
H	4.698548	0.527559	-0.005328

$E(S_1)$ = -552.341230470

C	-1.130916	0.816045	0.000045
C	-2.489614	1.175782	0.000045
C	-3.512500	0.167242	0.000045
C	-3.090114	-1.160878	0.000040
C	-1.710806	-1.501785	0.000001
N	-0.754701	-0.547142	0.000030
H	-4.565970	0.428277	0.000067
H	-2.710118	2.239227	0.000198
H	-3.806619	-1.980086	0.000050
H	-1.374894	-2.534989	-0.000149
O	-0.175908	1.637794	0.000091
H	0.270695	-0.777599	-0.000186
O	1.895556	-1.083523	-0.000698
C	2.707387	-0.160645	-0.000407
O	2.371370	1.105757	0.000009
H	1.365674	1.249558	0.000277
C	4.186428	-0.424762	0.000344
H	4.431328	-1.015047	0.890082
H	4.429930	-1.031964	-0.878174

H	4.755553	0.506394	-0.008269

E(S_1) = -552.342143637

C	-1.153689	0.815127	0.000073
C	-2.507981	1.190221	0.000073
C	-3.542235	0.191028	0.000073
C	-3.146451	-1.143917	0.000062
C	-1.773883	-1.508846	0.000017
N	-0.811617	-0.559834	0.000054
H	-4.591866	0.467640	0.000089
H	-2.719684	2.255271	0.000146
H	-3.878887	-1.948743	0.000061
H	-1.448098	-2.544827	-0.000067
O	-0.176667	1.604450	0.000123
H	0.197002	-0.785845	-0.000238
O	1.927286	-1.063246	-0.000986
C	2.760615	-0.168546	-0.000600
O	2.454679	1.114883	0.000025
H	1.468200	1.239860	0.000379
C	4.237492	-0.443619	0.000471
H	4.479653	-1.031620	0.892420
H	4.477628	-1.054666	-0.876205
H	4.811777	0.484378	-0.011267

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6. References

1 H. P. Hratchian and H. B. Schlegel, *J. Chem. Phys.*, 2004, **120**, 9918–9924.

2 M. J. Frisch, et al., *Gaussian 16, Revision C.01*, Gaussian, Inc., Wallingford CT, USA, 2019.

3 Y. Zhao and D. G. Truhlar, *Theor. Chem. Acc.*, 2008, **120**, 215–241.

4 T. H. Dunning Jr., *J. Chem. Phys.*, 1989, **90**, 1007–1023.

5 R. A. Kendall, T. H. Dunning Jr. and R. J. Harrison, *J. Chem. Phys.*, 1992, **96**, 6796–6806.

6 M. E. Casida and M. Huix-Rotllant, *Annu. Rev. Phys. Chem.*, 2012, **63**, 287–323.

7 T. Shiozaki, *WIREs Comput. Mol. Sci.*, 2018, **8**, e1331.

8 T. Shiozaki, W. Győrffy, P. Celani and H.-J. Werner, *J. Chem. Phys.*, 2011, **135**, 081106.

9 K. Andersson, P.-Å. Malmqvist and B. O. Roos, *J. Chem. Phys.*, 1992, **96**, 1218–1226.

10 J. Finley, P.-Å. Malmqvist, B. O. Roos and L. Serrano-Andrés, *Chem. Phys. Lett.*, 1998, **288**, 299–306.

11 B. O. Roos, P. R. Taylor and P. E. M. Siegbahn, *Chem. Phys.*, 1980, **48**, 157–173.

12 P. v. R. Schleyer, C. Maerker, A. Dransfeld, H. Jiao and N. J. R. van Eikema Hommes, *J. Am. Chem. Soc.*, 1996, **118**, 6317−6318.

13 H. Fallah-Bagher-Shaidaei, C. S. Wannere, C. Corminboeuf, R. Puchta and P. v. R. Schleyer, *Org. Lett.*, 2006, **8**, 863–866.

14 A. Stanger, *J. Org. Chem.*, 2006, **71**, 883–893.

15 K. Aidas, et al., *WIREs Comput. Mol. Sci.*, 2014, **4**, 269–284.

16 J. Kruszewski and T. M. Krygowski, *Tetrahedron Lett.*, 1972, **13**, 3839−3842.

17 I. Casademont-Reig, E. Ramos-Cordoba, M. Torrent-Sucarrat and E. Matito, in *Aromaticity: Modern Computational Methods and Applications*, Ed. I. Fernández, Elsevier, 2021, pp. 235–258.

18 E. Matito, J. Poater, M. Duran and M. Solà, *J. Mol. Struct. (Theochem)*, 2005, **727**, 165–171.

19 P. Bultinck, M. Rafat, R. Ponec, B. Van Gheluwe, R. Carbó-Dorca and P. Popelier, *J. Phys. Chem. A*, 2006, **110**, 7642–7648.

20 F. Feixas, E. Matito, J. Poater and M. Solà, *J. Comput. Chem.*, 2008, **29**, 1543–1554.

21 M. Solà, F. Feixas, J. O. C. Jiménez-Halla, E. Matito and J. Poater, *Symmetry*, 2010, **2**, 1156–1179.

22 T. Lu and F. Chen, *J. Comput. Chem.*, 2012, **33**, 580–592.

23 I. Fdez. Galván, et al., *J. Chem. Theory Comput.*, 2019, **15**, 5925–5964.