Supporting Information

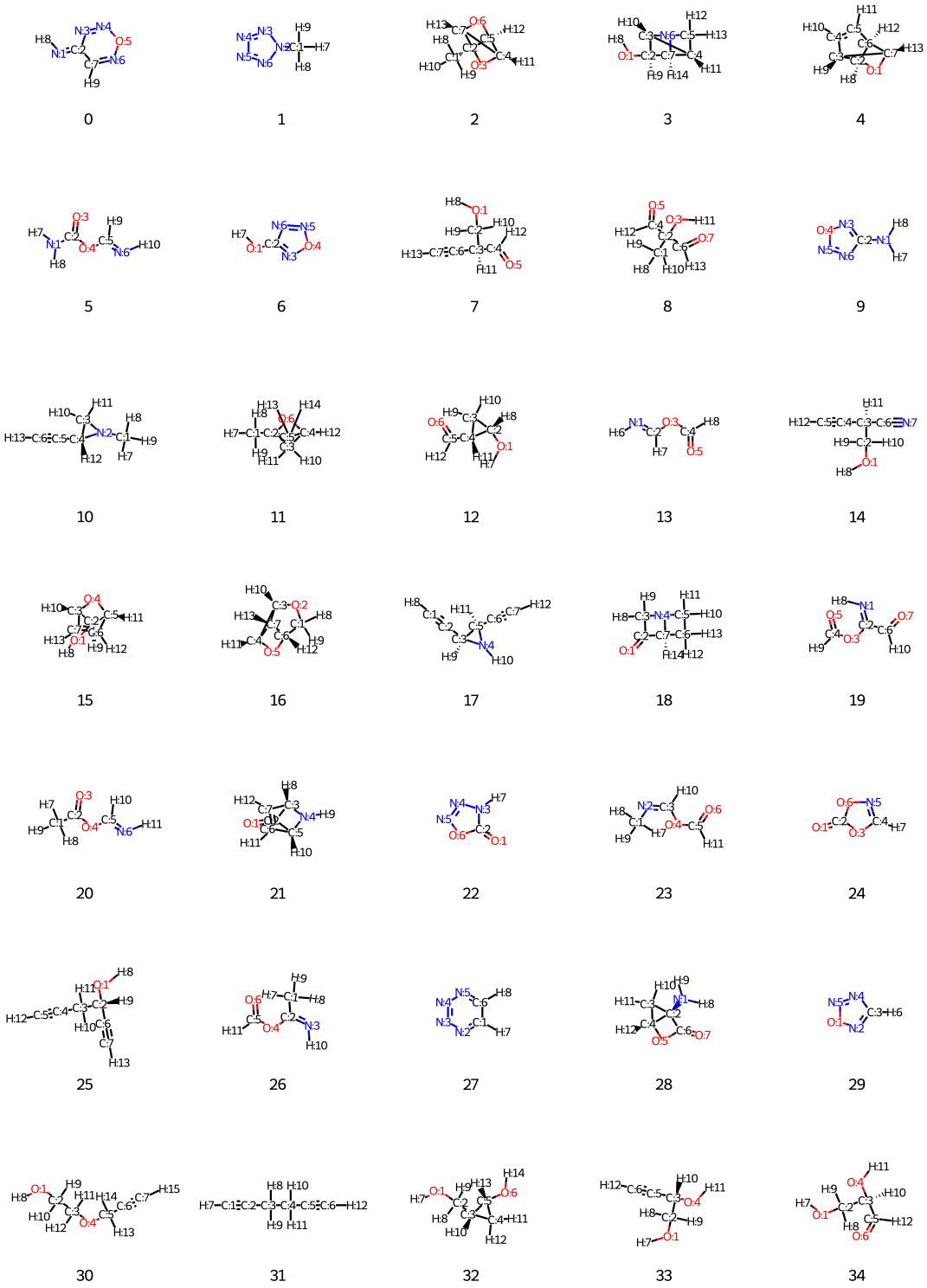


Figure S1: 163 reactants tested - part 1

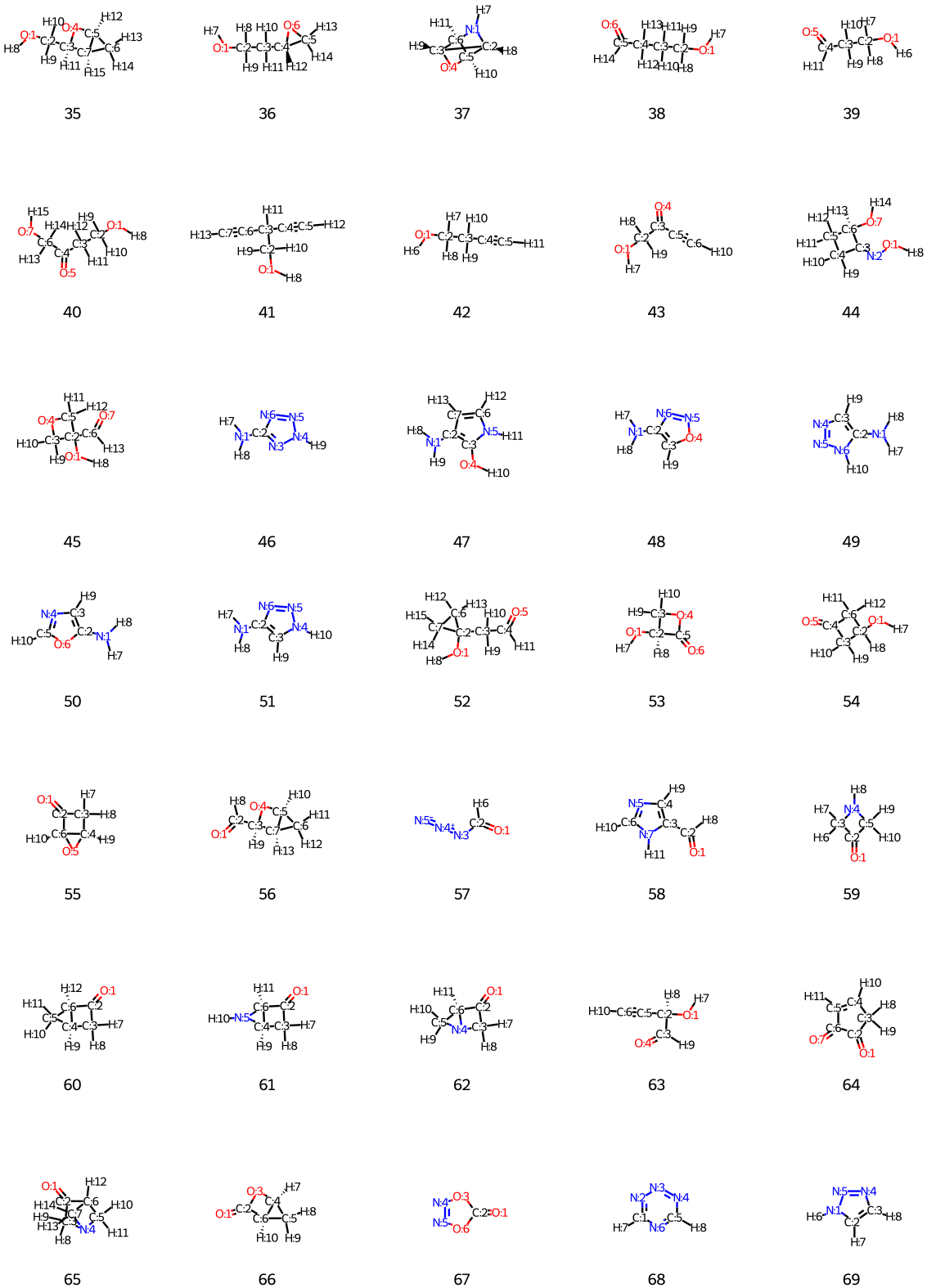


Figure S1: 163 reactants tested - part 2

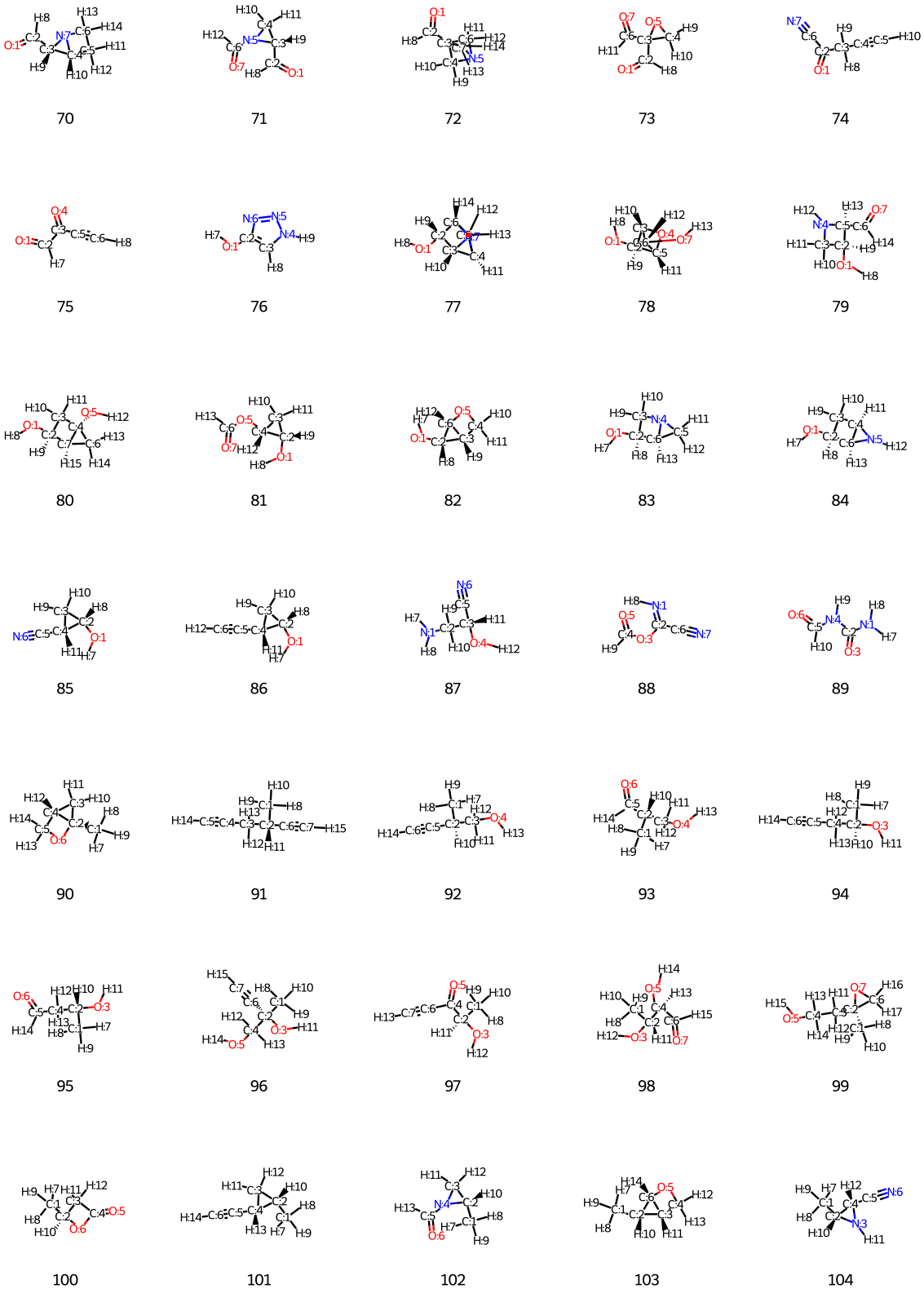


Figure S1: 163 reactants tested - part 3

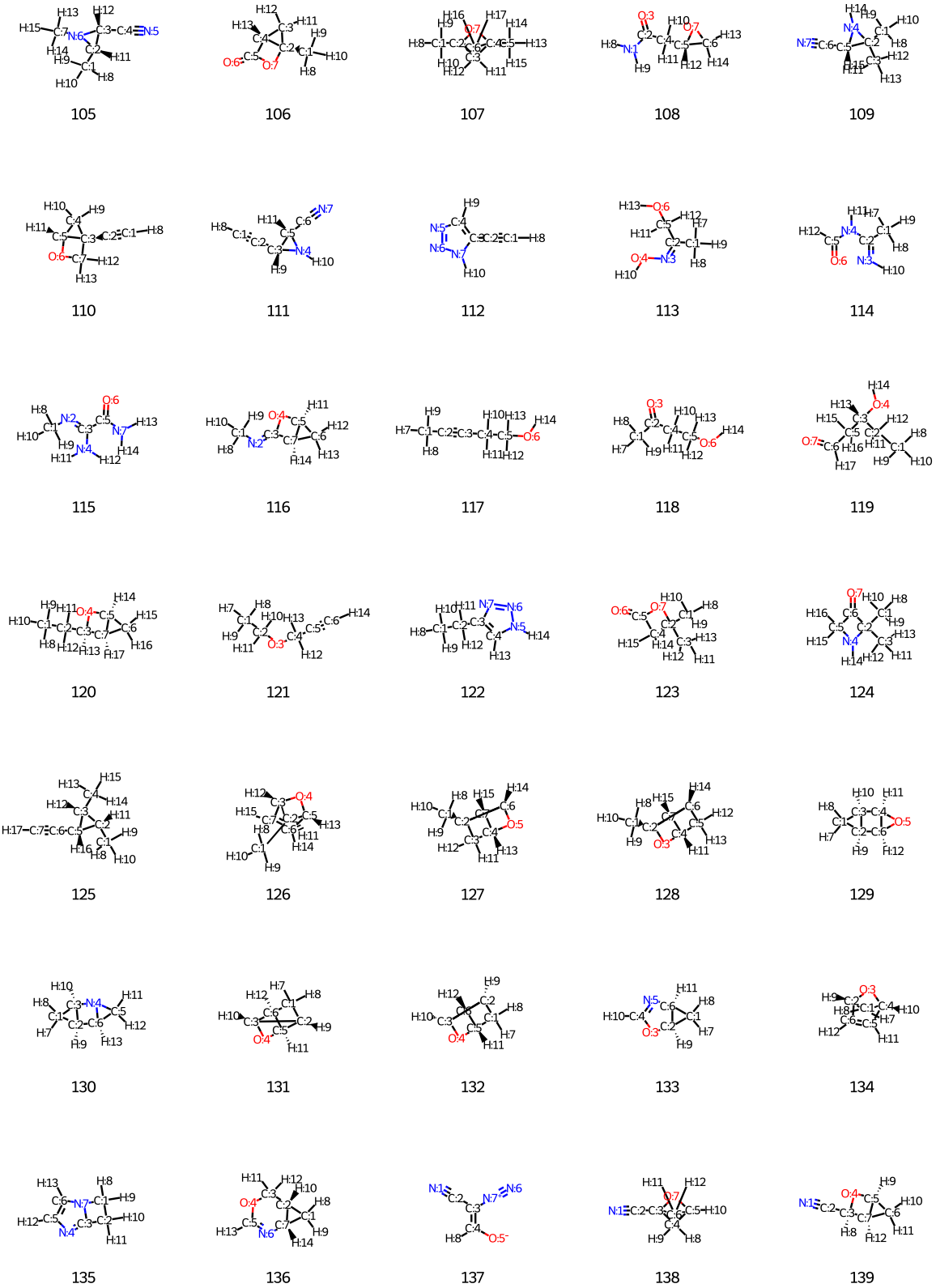


Figure S1: 163 reactants tested - part 4

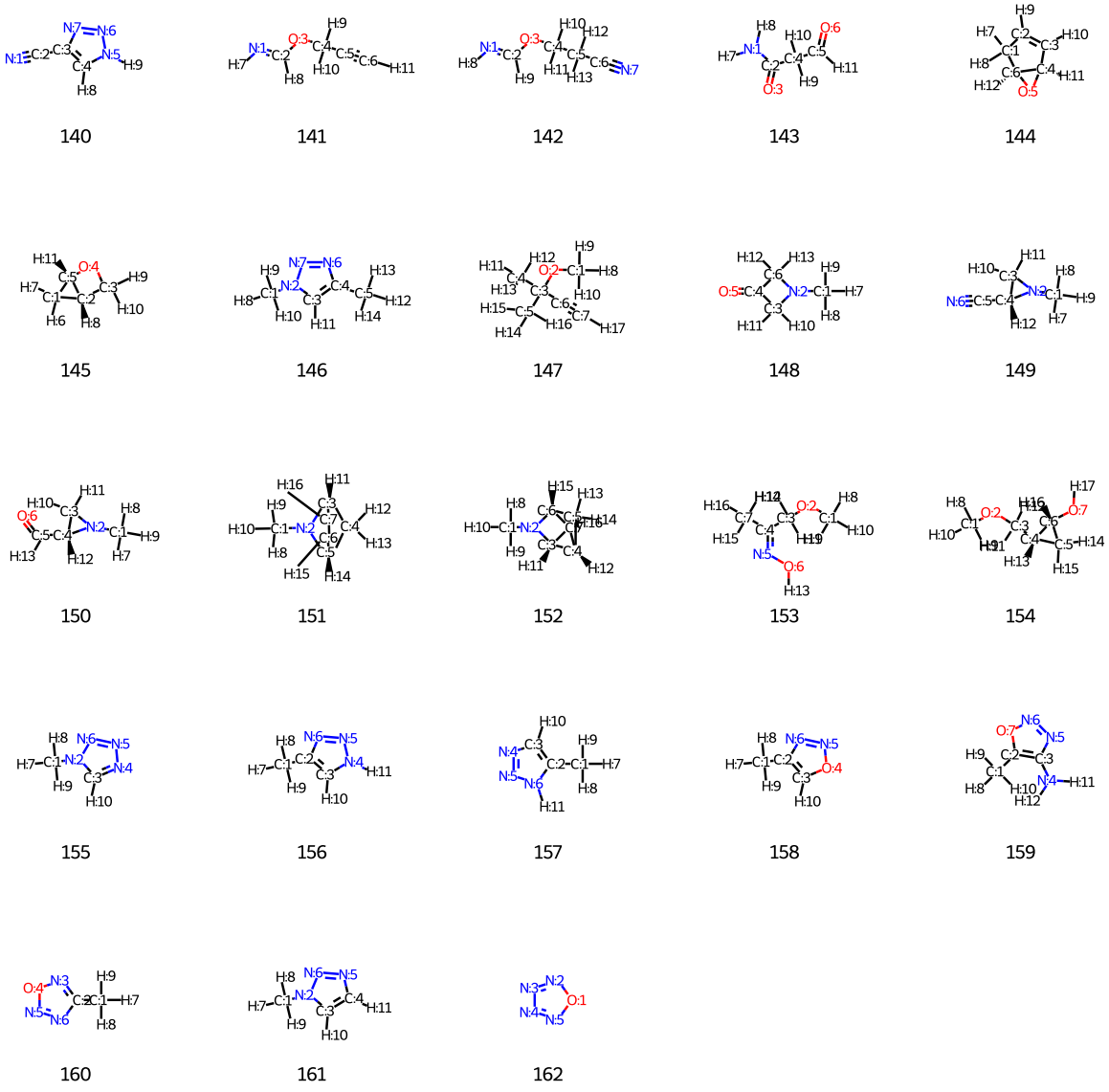
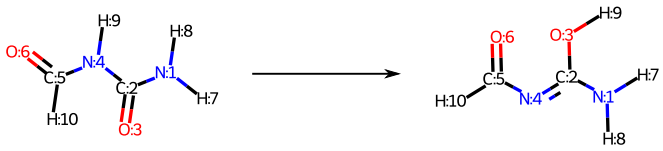
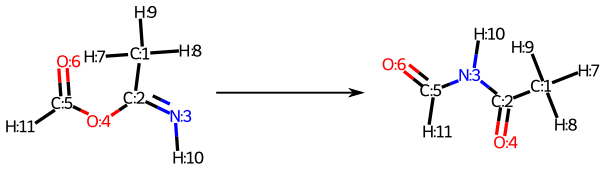
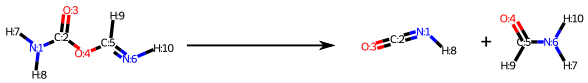
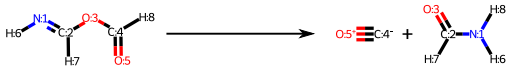
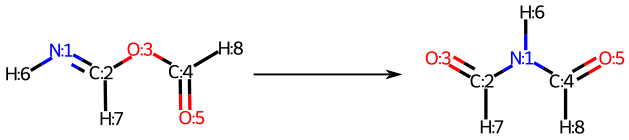
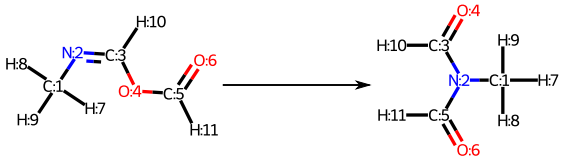
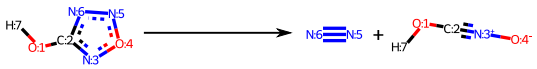
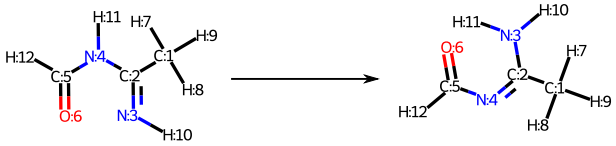
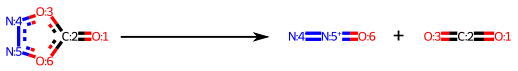
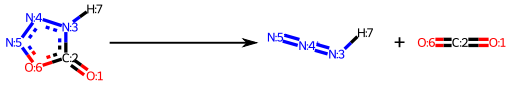
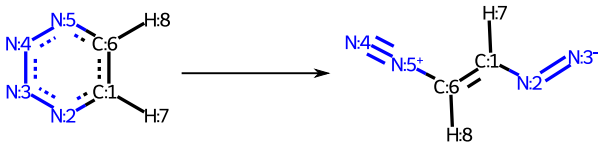
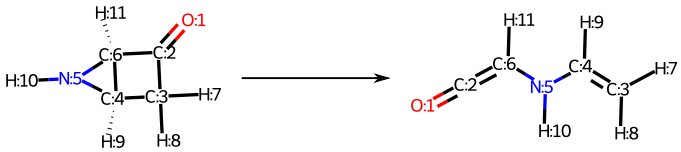
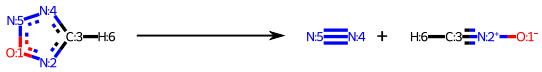
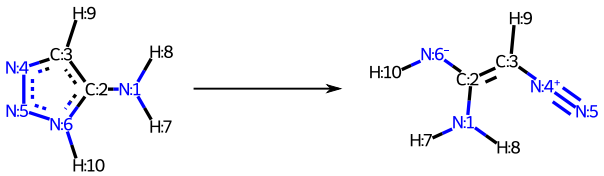
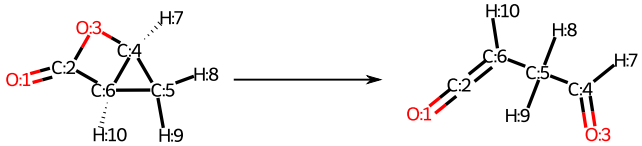
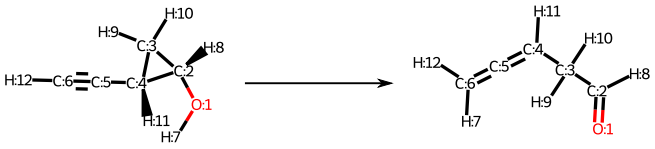
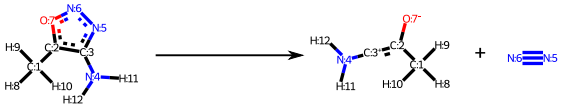
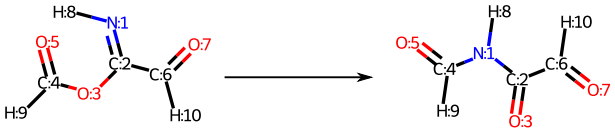
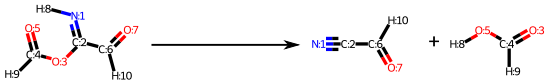
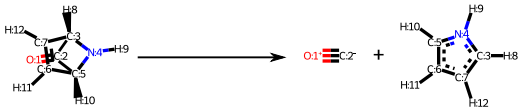
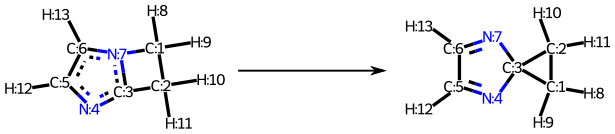
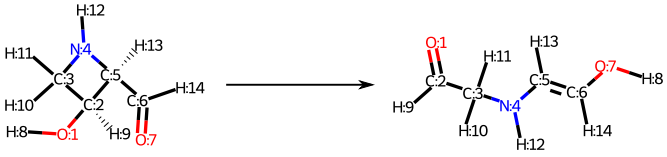
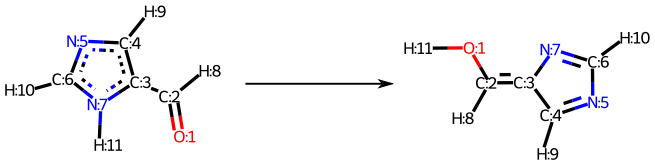


Figure S1: 163 reactants tested - part 5

R_{ID}	Reactant	Energetics	Reaction
R1084	89	$\Delta E^{\dagger}$ = 28 kcal/mol ΔE = 8 kcal/mol	
R1108	26	$\Delta E^{\dagger}$ = 21 kcal/mol ΔE = −13 kcal/mol	
R1110	26	$\Delta E^{\dagger}$ = 20 kcal/mol ΔE = −8 kcal/mol	
R1334	20	$\Delta E^{\dagger}$ = 26 kcal/mol ΔE = −16 kcal/mol	
R1689	5	$\Delta E^{\dagger}$ = 15 kcal/mol ΔE = −5 kcal/mol	
R1957	13	$\Delta E^{\dagger}$ = 29 kcal/mol ΔE = −13 kcal/mol	
R1958	13	$\Delta E^{\dagger}$ = 25 kcal/mol ΔE = −18 kcal/mol	
R2399	23	$\Delta E^{\dagger}$ = 21 kcal/mol ΔE = −19 kcal/mol	

R2514	6	$\Delta E^{\dagger}$ = 23 kcal/mol ΔE = −3 kcal/mol	
R2523	114	$\Delta E^{\dagger}$ = 30 kcal/mol ΔE = −2 kcal/mol	
R2552	67	$\Delta E^{\dagger}$ = 16 kcal/mol ΔE = −49 kcal/mol	
R3096	22	$\Delta E^{\dagger}$ = 19 kcal/mol ΔE = −24 kcal/mol	
R3504	27	$\Delta E^{\dagger}$ = 25 kcal/mol ΔE = 8 kcal/mol	
R3648	61	$\Delta E^{\dagger}$ = 29 kcal/mol ΔE = −3 kcal/mol	
R3725	29	$\Delta E^{\dagger}$ = 17 kcal/mol ΔE = −21 kcal/mol	
R4612	49	$\Delta E^{\dagger}$ = 26 kcal/mol ΔE = 13 kcal/mol	
R4808	66	$\Delta E^{\dagger}$ = 26 kcal/mol ΔE = −10 kcal/mol	

R5847	86	$\Delta E^{\dagger}$ = 25 kcal/mol ΔE = −20 kcal/mol	
R6490	159	$\Delta E^{\dagger}$ = 11 kcal/mol ΔE = −14 kcal/mol	
R7201	19	$\Delta E^{\dagger}$ = 28 kcal/mol ΔE = −8 kcal/mol	
R7207	19	$\Delta E^{\dagger}$ = 27 kcal/mol ΔE = 0 kcal/mol	
R7885	21	$\Delta E^{\dagger}$ = 13 kcal/mol ΔE = −47 kcal/mol	
R7931	135	$\Delta E^{\dagger}$ = 28 kcal/mol ΔE = −2 kcal/mol	
R8367	79	$\Delta E^{\dagger}$ = 24 kcal/mol ΔE = −2 kcal/mol	
R8701	58	$\Delta E^{\dagger}$ = 27 kcal/mol ΔE = 19 kcal/mol	

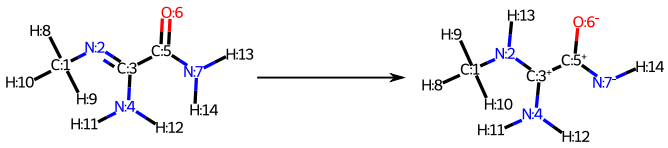
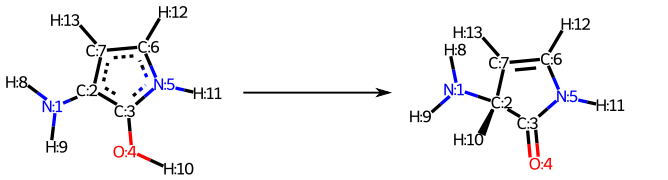
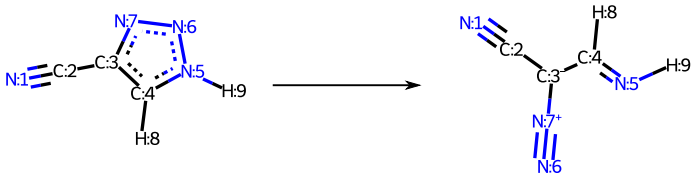
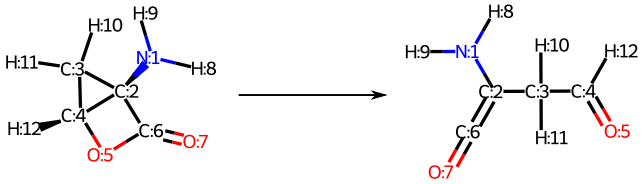
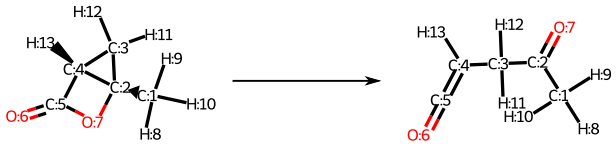
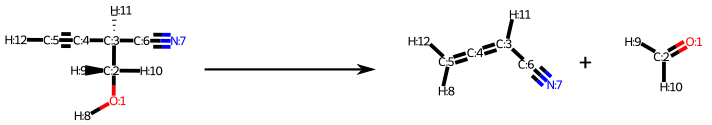
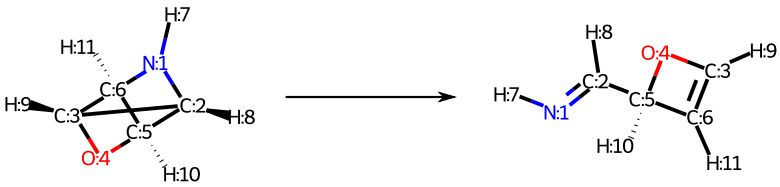
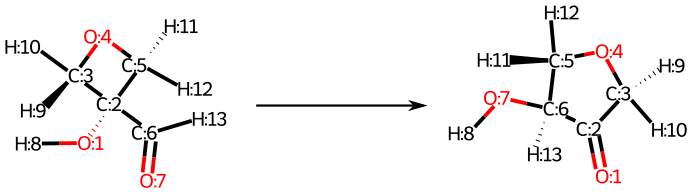
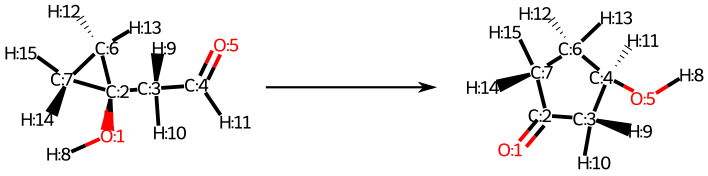
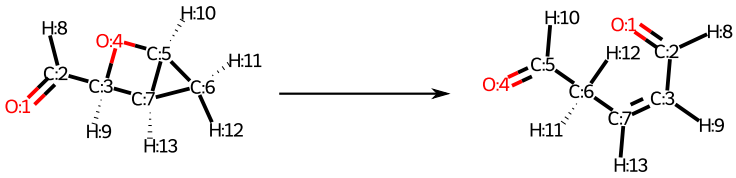
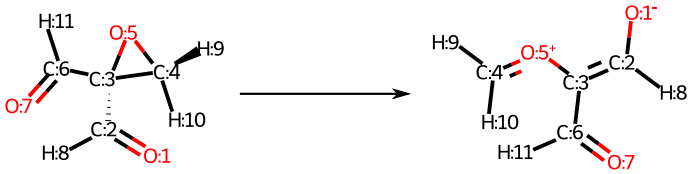
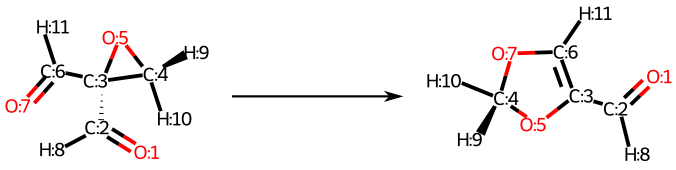
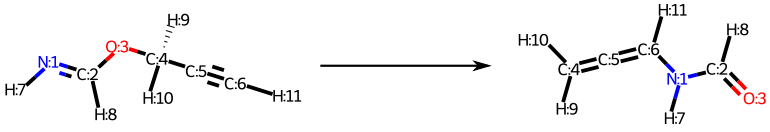
R8713	115	$\Delta E^{\dagger}$ = 20 kcal/mol ΔE = 17 kcal/mol	
R8816	47	$\Delta E^{\dagger}$ = 28 kcal/mol ΔE = −2 kcal/mol	
R9011	140	$\Delta E^{\dagger}$ = 30 kcal/mol ΔE = 21 kcal/mol	
R11611	28	$\Delta E^{\dagger}$ = 25 kcal/mol ΔE = −3 kcal/mol	
R11630	106	$\Delta E^{\dagger}$ = 23 kcal/mol ΔE = −10 kcal/mol	

Table S1: 30 target reactions with one-fragment reactants and barriers below 30 kcal/mol
Reactions colored in red: IRC following re-optimization of the TS led to different reactant/product pair than the one stated.
Reactions colored in blue: IRC following re-optimization of the TS led to a different stereoisomer of the reactant (rotation around C=N bond).
R_{ID} refers to the reaction labelling in [19] while the Reactant index refers to the indexing in Figure S1

r_{ID}	Reactant	Energetics	Reaction
N11	14	$\Delta E^{\dagger}$ = 37 kcal/mol ΔE = 4 kcal/mol	
N12	37	$\Delta E^{\dagger}$ = 43 kcal/mol ΔE = −44 kcal/mol	
N13	45	$\Delta E^{\dagger}$ = 35 kcal/mol ΔE = −18 kcal/mol	
N14	52	$\Delta E^{\dagger}$ = 39 kcal/mol ΔE = −21 kcal/mol	
N15	56	$\Delta E^{\dagger}$ = 37 kcal/mol ΔE = −34 kcal/mol	
N16	73	$\Delta E^{\dagger}$ = 42 kcal/mol ΔE = 32 kcal/mol	
N17	73	$\Delta E^{\dagger}$ = 42 kcal/mol ΔE = −7 kcal/mol	
N18	141	$\Delta E^{\dagger}$ = 33 kcal/mol ΔE = −22 kcal/mol	

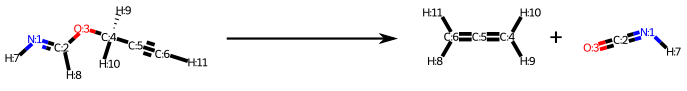
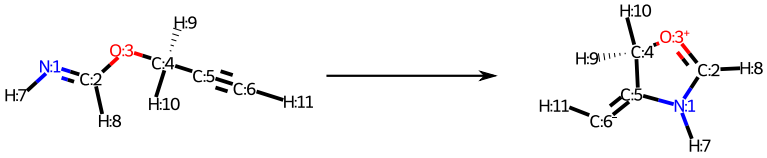
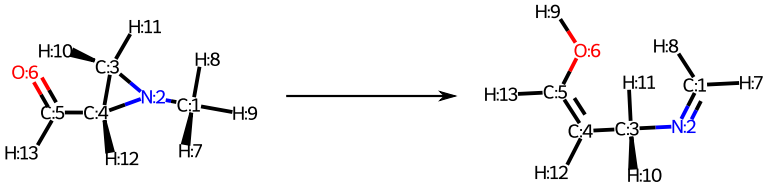
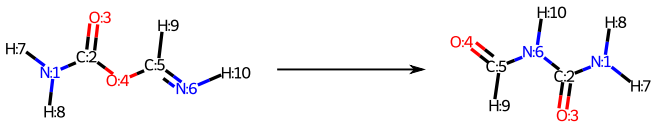
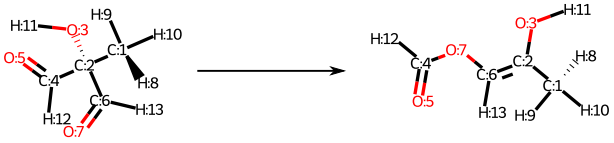
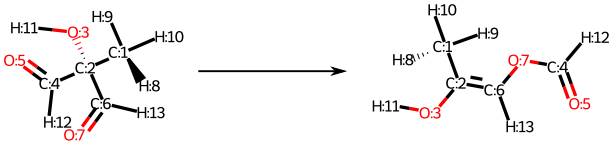
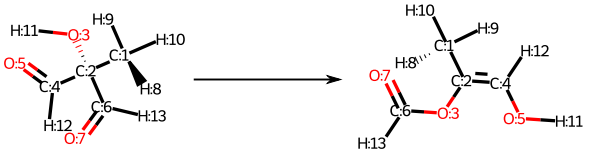
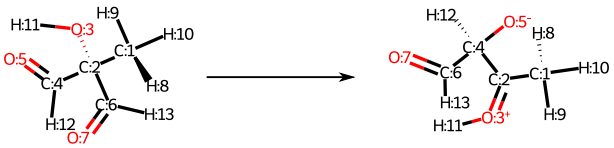
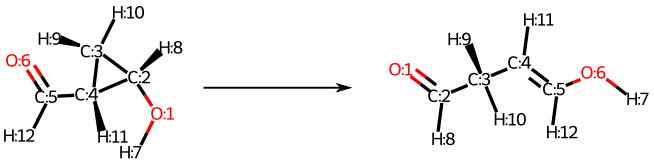
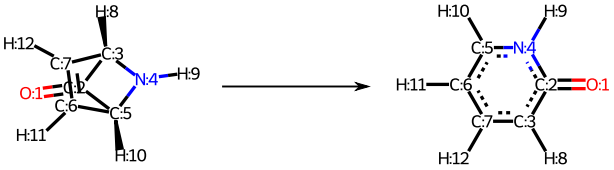
N19	141	$\Delta E^{\dagger}$ = 43 kcal/mol ΔE = −31 kcal/mol	
N20	141	$\Delta E^{\dagger}$ = 38 kcal/mol ΔE = 33 kcal/mol	
N21	150	$\Delta E^{\dagger}$ = 34 kcal/mol ΔE = −3 kcal/mol	

Table S2: 11 new reactions found with barriers above 30 kcal/mol - lower than existing reactions.
r_{ID} refers to the reaction labelling used for new reactions while the Reactant index refers to the indexing of reactants in Figure S1

r_{ID}	Reactant	Energetics	Reaction
N22	5	$\Delta E^{\dagger}$ = 32 kcal/mol ΔE = −21 kcal/mol	
N23	8	$\Delta E^{\dagger}$ = 46 kcal/mol ΔE = −7 kcal/mol	
N24	8	$\Delta E^{\dagger}$ = 48 kcal/mol ΔE = −4 kcal/mol	
N25	8	$\Delta E^{\dagger}$ = 47 kcal/mol ΔE = 1 kcal/mol	
N26	8	$\Delta E^{\dagger}$ = 49 kcal/mol ΔE = 43 kcal/mol	
N27	12	$\Delta E^{\dagger}$ = 42 kcal/mol ΔE = −5 kcal/mol	
N28	19	$\Delta E^{\dagger}$ = 66 kcal/mol ΔE = −1 kcal/mol	
N29	21	$\Delta E^{\dagger}$ = 39 kcal/mol ΔE = −65 kcal/mol	

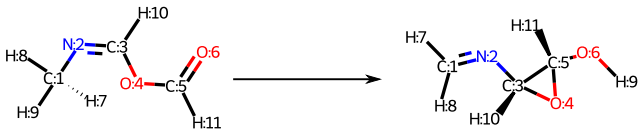
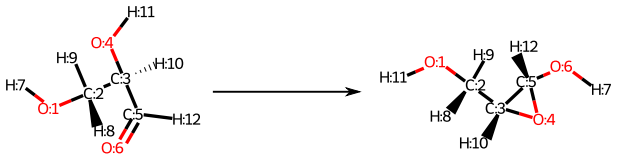
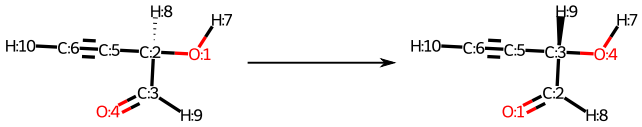
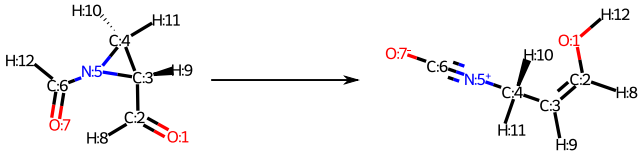
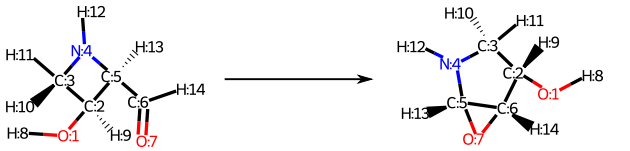
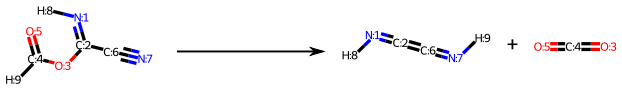
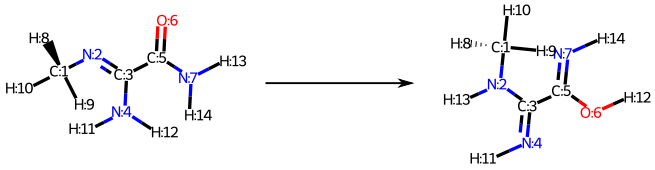
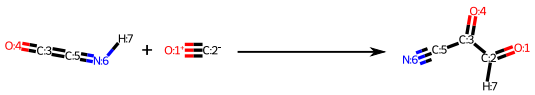
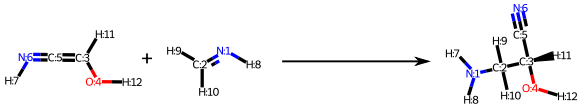
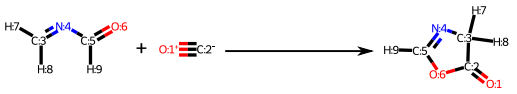
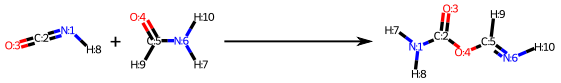
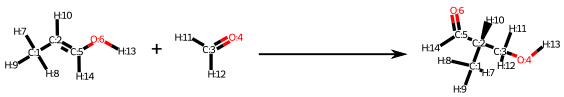
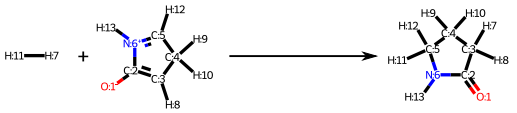
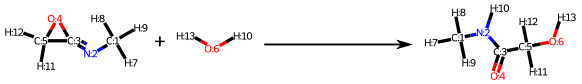
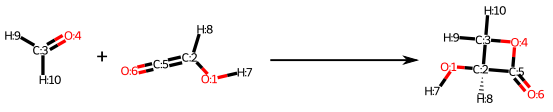
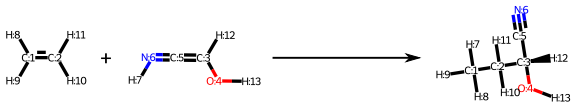
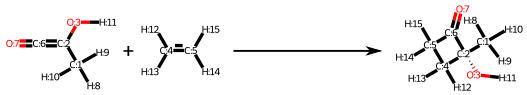
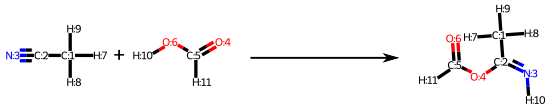
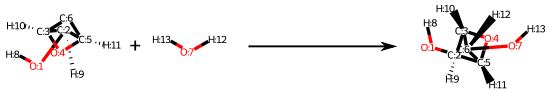
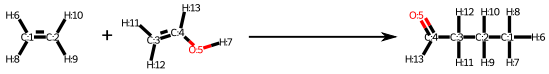
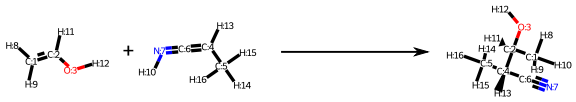
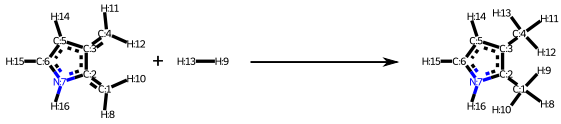
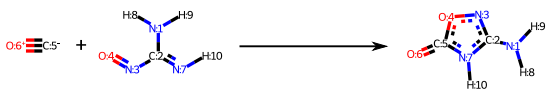
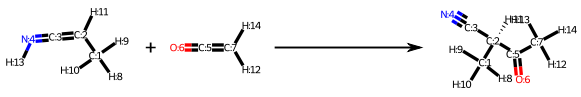
N30	23	$\Delta E^{\dagger}$ = 58 kcal/mol ΔE = 30 kcal/mol	
N31	34	$\Delta E^{\dagger}$ = 40 kcal/mol ΔE = 14 kcal/mol	
N32	63	$\Delta E^{\dagger}$ = 47 kcal/mol ΔE = 0 kcal/mol	
N33	71	$\Delta E^{\dagger}$ = 53 kcal/mol ΔE = −21 kcal/mol	
N34	79	$\Delta E^{\dagger}$ = 36 kcal/mol ΔE = −3 kcal/mol	
N35	88	$\Delta E^{\dagger}$ = 63 kcal/mol ΔE = 13 kcal/mol	
N36	115	$\Delta E^{\dagger}$ = 37 kcal/mol ΔE = 13 kcal/mol	

Table S3: 15 new reactions found with barriers over 30 kcal/mol. Note that Grambow et al reported a reaction to another diastereomer of the product of N32. We include it here because we saw a significantly lower barrier than the reported (55 kcal/mol).
r_{ID} refers to the reaction labelling used for new reactions while the Reactant index refers to the indexing of reactants in Figure S1

R_{ID}	Reactant	Energetics	Reaction
R129	1	$\Delta E^{\dagger}$ = 8 kcal/mol ΔE = −34 kcal/mol	
R5946	2	$\Delta E^{\dagger}$ = 14 kcal/mol ΔE = −44 kcal/mol	
R2793	3	$\Delta E^{\dagger}$ = 10 kcal/mol ΔE = −24 kcal/mol	
R1689	4	$\Delta E^{\dagger}$ = 20 kcal/mol ΔE = 5 kcal/mol	
R4870	5	$\Delta E^{\dagger}$ = 15 kcal/mol ΔE = −19 kcal/mol	
R2042	6	$\Delta E^{\dagger}$ = 19 kcal/mol ΔE = −62 kcal/mol	
R2191	7	$\Delta E^{\dagger}$ = 19 kcal/mol ΔE = −46 kcal/mol	
R2353	8	$\Delta E^{\dagger}$ = 20 kcal/mol ΔE = −39 kcal/mol	

R2858	9	$\Delta E^{\dagger}$ = 19 kcal/mol ΔE = −52 kcal/mol	
R6677	10	$\Delta E^{\dagger}$ = 20 kcal/mol ΔE = −34 kcal/mol	
R1110	11	$\Delta E^{\dagger}$ = 28 kcal/mol ΔE = 8 kcal/mol	
R7854	12	$\Delta E^{\dagger}$ = 21 kcal/mol ΔE = −58 kcal/mol	
R73	13	$\Delta E^{\dagger}$ = 28 kcal/mol ΔE = −33 kcal/mol	
R11240	14	$\Delta E^{\dagger}$ = 26 kcal/mol ΔE = −38 kcal/mol	
R11355	15	$\Delta E^{\dagger}$ = 25 kcal/mol ΔE = −48 kcal/mol	
R11396	16	$\Delta E^{\dagger}$ = 28 kcal/mol ΔE = −56 kcal/mol	
R11478	17	$\Delta E^{\dagger}$ = 25 kcal/mol ΔE = −44 kcal/mol	

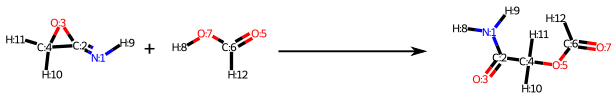
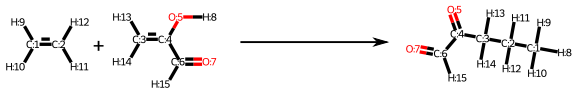
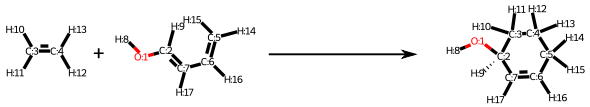
R10077	18	$\Delta E^{\dagger}$ = 10 kcal/mol ΔE = −39 kcal/mol	
R10514	19	$\Delta E^{\dagger}$ = 25 kcal/mol ΔE = −33 kcal/mol	
R8426	20	$\Delta E^{\dagger}$ = 26 kcal/mol ΔE = −39 kcal/mol	

Table S4: 20 target reactions with two-fragment reactants and barriers below 30 kcal/mol. R_{ID} refers to the reaction labelling in [19] while the Reactant index will be used to refer to the reactant of the reaction

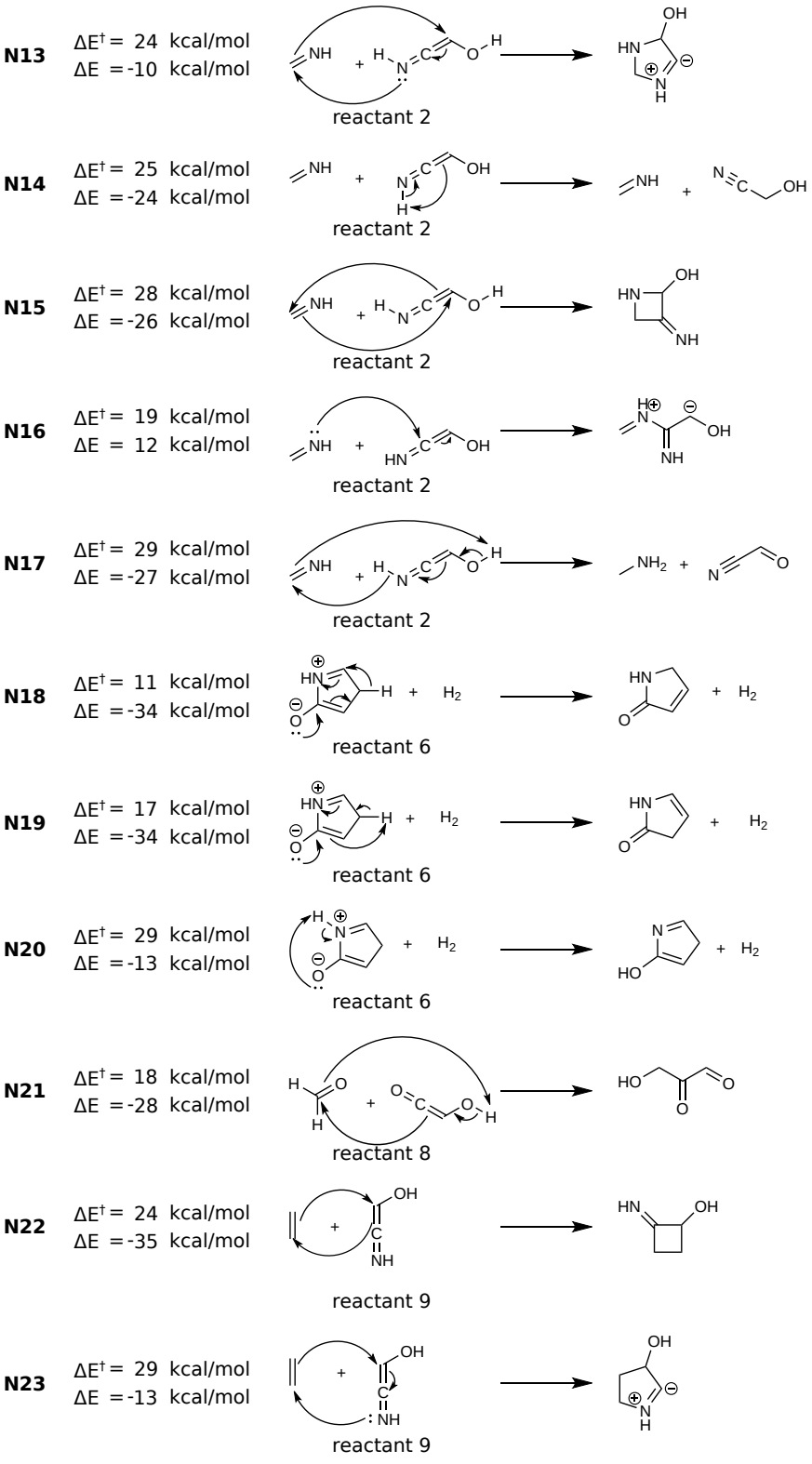

N13
ΔE† = 24 kcal/mol
ΔE = -10 kcal/mol
reactant 2
N14
ΔE† = 25 kcal/mol
ΔE = -24 kcal/mol
reactant 2
N15
ΔE† = 28 kcal/mol
ΔE = -26 kcal/mol
reactant 2
N16
ΔE† = 19 kcal/mol
ΔE = 12 kcal/mol
reactant 2
N17
ΔE† = 29 kcal/mol
ΔE = -27 kcal/mol
reactant 2
N18
ΔE† = 11 kcal/mol
ΔE = -34 kcal/mol
reactant 6
N19
ΔE† = 17 kcal/mol
ΔE = -34 kcal/mol
reactant 6
N20
ΔE† = 29 kcal/mol
ΔE = -13 kcal/mol
reactant 6
N21
ΔE† = 18 kcal/mol
ΔE = -28 kcal/mol
reactant 8
N22
ΔE† = 24 kcal/mol
ΔE = -35 kcal/mol
reactant 9
N23
ΔE† = 29 kcal/mol
ΔE = -13 kcal/mol
reactant 9

Figure S2

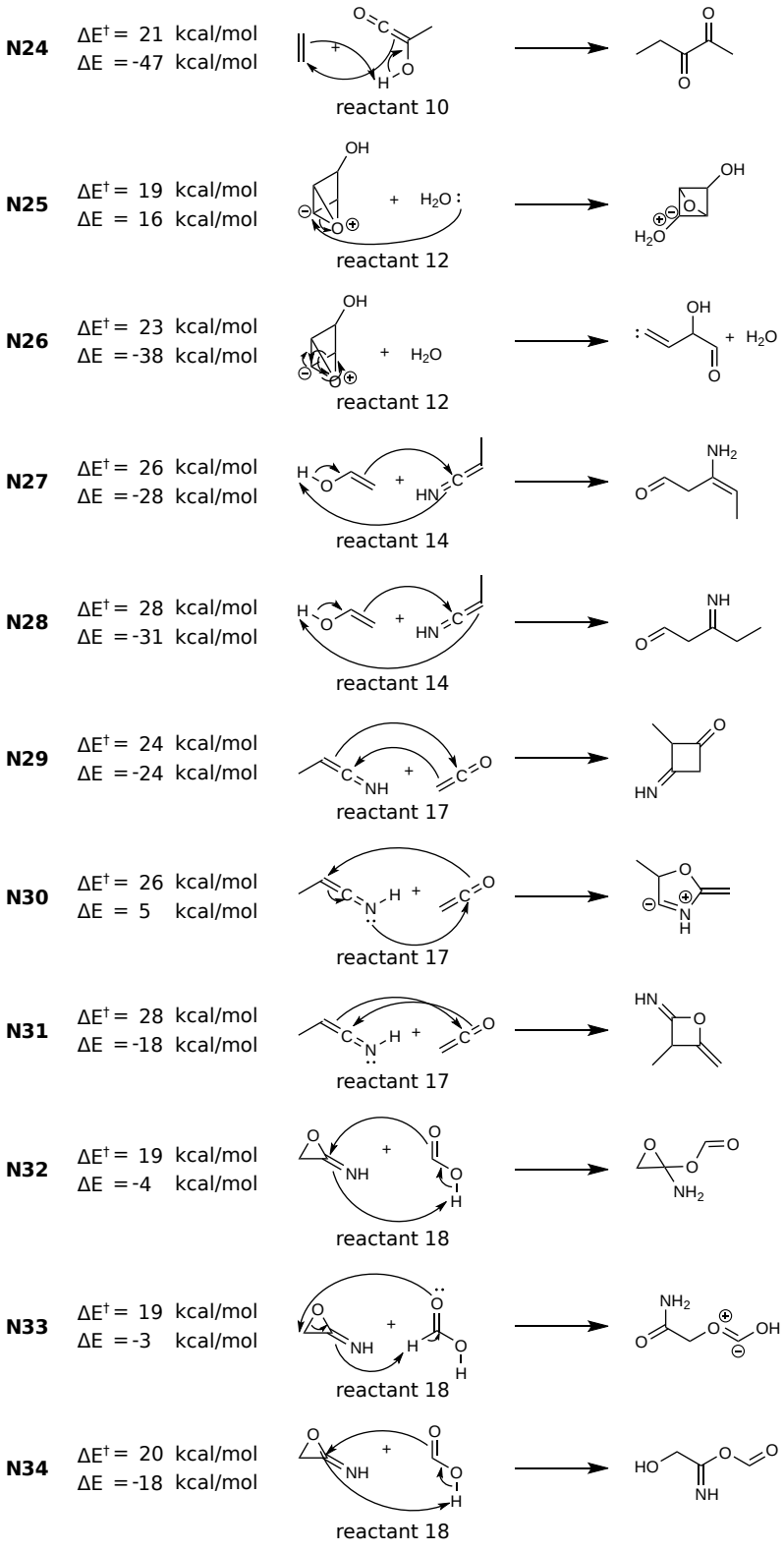


Figure S2: (continued)

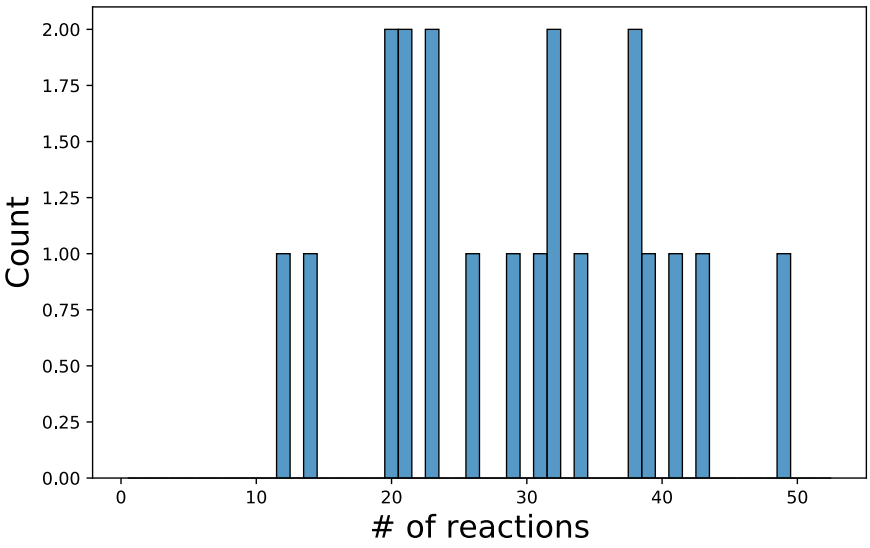


Figure S3: Distribution of the number of different reactions found during the 100 meta-MD runs (with default hyperparameter set) for the 20 bimolecular reactants. The average is 29.3 reactions/reactant.