

A MEDT study of the mechanism and selectivity of the hetero-Diels–Alder reaction between 3-benzoylpyrrolo[1,2-c][1,4]-benzoxazine-1,2,4-trione and vinyl acetate

Soukaina Ameur^{1,2}, Ali Barhoumi¹, Mar Ríos-Gutiérrez³, Anas Ouled Aitouna^{1,2}, Habib El Alaoui El Abdallaoui¹, Nouredine Mazoir², Mohammed Elalaoui Belghiti^{4,5}, Asad Syed⁶, Abdellah Zeroual^{1*}, Luis R. Domingo³

¹ Molecular Modeling and Spectroscopy Research Team, Faculty of Science, Chouaib Doukkali University, P. O. Box 20, 24000 El Jadida, Morocco; e-mail: zeroualabdellah2@gmail.com

² Laboratory of Bioorganic Chemistry, Department of Chemistry Faculty of Sciences, Chouaib Doukkali University, P. O. Box 20, 24000 El Jadida, Morocco

³ Department of Organic Chemistry, University of Valencia, Dr. Moliner 50, 46100 Burjassot, Valencia, Spain

⁴ Laboratory of Physical Chemistry of Materials, Ben M'Sick Faculty of Sciences, Hassan II University, Casablanca, Morocco

⁵ Laboratory of Nernest Technology, 163 Wellington Street, Sherbrooke, QC J1H5C7, Canada

⁶ Department of Botany and Microbiology, College of Science, King Saud University, P. O. Box 2455 Riyadh 11451, Saudi Arabia

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Table S1: Formulae used for calculating global reactivity indices.

Electronic chemical potential (μ)	Electrophilic index (ω)	Nucleophilic index (N)	Chemical hardness (η)
$\eta = \epsilon_{\text{LUMO}} - \epsilon_{\text{HOMO}}$	$\omega = \mu^2/2\eta$	$N = \epsilon_{\text{HOMO}}(\text{Nu}) - \epsilon_{\text{HOMO}}(\text{TCE})$	$\eta = \epsilon_{\text{LUMO}} - \epsilon_{\text{HOMO}}$

TCE – tetracyanoethylene (C₆N₄).

Table S2. Energies of transition states, products and reagents 3-benzoylpyrrolo[1,2-c][1,4]benzoxazine-1,2,4-trione (**1**) and vinyl acetate (**2**) calculated by DFT B3LYP/(6-311G (d, p)).

System	Gas phase		Benzene	
	<i>E</i> (a.u)	<i>E</i> (kcal•mol ⁻¹)	<i>E</i> (a.u)	<i>E</i> (kcal•mol ⁻¹)
1	-1122.466596		-1122.475923	
2	-306.559605		-306.5623921	
1+2	-1429.026201		-1429.038315	
3	-1429.063592	-23.46	-1429.075619	-23.41
TSx1	-1429.001091	15.75	-1429.012759	16.04
6	-1429.057685	-19.75	-1429.06926	-19.42
TSn2	-1428.989117	23.27	-1428.99992	24.09
4	-1429.063797	-23.59	-1429.075952	-23.62
TSn1	-1428.996606	18.57	-1429.008685	18.59
5	-1429.04317	-10.64	-1429.056919	-11.67
TSx2	-1428.966659	37.36	-1428.980742	36.13
7	-1429.034464	-5.18	-1429.045776	-4.68
TS3	-1428.973718	32.93	-1428.983235	34.56

Table S3. B3LYP/6-311G (d,p) thermodynamic data for stationary points involved in the HDA reaction between 3-benzoylpyrrolo[1,2-c][1,4]benzoxazine-1,2,4-trione (**1**) and vinyl acetate (**2**) in the gas phase and in benzene.

System	Gas phase		Benzene	
	<i>G</i> (a.u)	ΔG (kcal•mol ⁻¹)	<i>G</i> (a.u)	ΔG (kcal•mol ⁻¹)
1	-1122.284731		-1122.293672	
2	-306.496969		-306.500006	
1+2	-1428.7817		-1428.793678	
3	-1428.786854	-3.23	-1428.798947	-3.30
TSx1	-1428.730305	32.25	-1428.742377	32.19
6	-1428.780694	0.63	-1428.792701	0.61
TSn2	-1428.717691	40.16	-1428.72971	40.14
4	-1428.787576	-3.68	-1428.799741	-3.80
TSn1	-1428.725624	35.18	-1428.738917	34.36
5	-1428.765855	9.94	-1428.779625	8.81
TSx2	-1428.696866	53.23	-1428.710691	52.07
7	-1428.758729	14.41	-1428.769984	14.86
TS3	-1428.70395	48.78	-1428.714107	49.93

Table S3 (continued). B3LYP/6-311G (d,p) thermodynamic data for stationary points involved in the HDA reaction between 3-benzoylpyrrolo[1,2-*c*][1,4]benzoxazine-1,2,4-trione (**1**) and vinyl acetate (**2**) in the gas phase and in benzene.

System	Gas phase		Benzene	
	$S(\text{cal}\cdot\text{mol}^{-1}\cdot\text{K}^{-1})$	$\Delta S(\text{cal}\cdot\text{mol}^{-1}\cdot\text{K}^{-1})$	$S(\text{cal}\cdot\text{mol}^{-1}\cdot\text{K}^{-1})$	$\Delta S(\text{cal}\cdot\text{mol}^{-1}\cdot\text{K}^{-1})$
1	143.8		142.95	
2	81.939		82.141	
1+2	225.739		225.091	
3	169.451	-56.288	169.287	-55.804
TSx1	172.415	-53.324	172.856	-52.235
6	169.734	-56.005	170.257	-54.834
TSn2	170.9	-54.839	172.764	-52.327
4	170.643	-55.096	170.388	-54.703
TSn1	171.795	-53.944	174.065	-51.026
5	168.312	-57.427	168.247	-56.844
TSx2	173.654	-52.085	172.845	-52.246
7	172.761	-52.978	172.362	-52.729
TS3	174.198	-51.541	174.917	-50.174

Systems	Gas phase		Benzene	
	$H(\text{a.u.})$	$\Delta H(\text{kcal}\cdot\text{mol}^{-1})$	$H(\text{a.u.})$	$\Delta H(\text{kcal}\cdot\text{mol}^{-1})$
1	-1122.216407		-1122.225752	
2	-306.458037		-306.460978	
1+2	-1428.674444		-1428.68673	
3	-1428.706342	-20.01	-1428.718513	-19.94
TSx1	-1428.648385	16.35	-1428.660248	16.61
6	-1428.700049	-16.06	-1428.711806	-15.73
TSn2	-1428.636491	23.81	-1428.647624	24.53
4	-1428.706498	-20.11	-1428.718784	-20.11
TSn1	-1428.643998	19.10	-1428.656213	19.14
5	-1428.685884	-26.28	-1428.699686	-8.13
TSx2	-1428.614357	37.70	-1428.628567	36.49
7	-1428.676645	-1.38	-1428.688089	-0.85
TS3	-1428.621183	33.42	-1428.630998	34.97

Table S4. ELF valence basin populations, distances of the forming bonds, of **TSx1** and the selected structures of the IRC involved in the formation of the new single bonds along cycloaddition of 3-benzoylpyrrolo[1,2-*c*][1,4]benzoxazine-1,2,4-trione (**1**) and vinyl acetate (**2**). Electron populations are given in average number of electrons, *e*, and distances in angstroms, Å

ΔE (kcal.mol ⁻¹)	Struc- ture	<i>d</i> (O4-C12)	<i>d</i> (C1-C11)	V (C12,C11)	V' (C12,C11)	V (C12)	V (C11)	V (C1,C2)	V (C2,C3)	V (C3,O4)	V (C1)	V(C2)	V(O4)	V'(O4)	V(N)	V'(N)	V (O4,C12)	V (C1,C11)
-	S1	3.262932	3.863299	1.78	1.76	-	-	3.35	2.27	2.31	-	-	2.63	2.62	0.56	0.93	-	-
0,15	S2	3.226161	3.824794	1.78	1.76	-	-	3.36	2.27	2.31	-	-	2.63	2.61	0.55	0.95	-	-
0,52	S3	3.140945	3.722938	1.78	1.76	-	-	3.35	2.28	2.31	-	-	2.62	2.61	0.53	0.94	-	-
0,84	S4	3.074715	3.628848	1.77	1.76	-	-	3.35	2.28	2.31	-	-	2.63	2.61	0.55	0.93	-	-
1,24	S5	3.003331	3.520322	1.76	1.76	-	-	3.35	2.28	2.30	-	-	2.62	2.62	0.56	0.92	-	-
1,77	S6	2.930509	3.396092	1.77	1.73	-	-	3.34	2.29	2.30	-	-	2.64	2.61	0.58	0.89	-	-
2,73	S7	2.833606	3.221993	1.75	1.74	-	-	3.32	2.30	2.31	-	-	2.67	2.59	0.63	0.86	-	-
4,21	S8	2.732225	3.034699	1.75	1.71	-	-	3.30	2.32	2.29	-	-	2.68	2.59	0.68	0.81	-	-
5,97	S9	2.646974	2.871001	1.71	1.75	-	-	3.28	2.32	2.28	-	-	2.68	2.59	0.77	0.72	-	-
9,26	S10	2.536662	2.638529	1.69	1.71	-	-	3.22	2.34	2.26	-	-	2.71	2.58	0.74	0.77	-	-
10,09	S11	2.513735	2.587395	1.69	1.70	-	-	3.21	2.35	2.26	-	-	2.71	2.57	0.73	0.79	-	-
10,98	S12	2.490391	2.534446	1.65	1.71	-	-	2.95	2.36	2.25	-	0.24	2.71	2.57	0.74	0.78	-	-
12,91	S13	2.442542	2.423049	3.32	-	-	-	2.89	2.39	2.23	-	0.28	2.73	2.57	0.76	0.79	-	-
15,84	S14	2.368586	2.243493	3.25	-	-	-	2.79	2.44	2.17	-	0.36	2.78	2.54	0.81	0.79	-	-
17,16	S15	2.318062	2.118594	2.84	-	-	0.38	2.55	2.50	2.12	0.25	0.40	2.80	2.55	0.88	0.79	-	-
17,36	S16	2.292043	2.055659	2.73	-	-	0.47	2.45	2.53	2.09	0.35	0.42	2.81	2.56	0.90	0.79	-	-
17,14	S17	2.265098	1.992898	2.63	-	-	0.57	2.37	2.58	2.05	0.42	0.45	2.89	2.49	0.93	0.78	-	-
16,42	S18	2.237077	1.930670	2.55	-	-	-	2.31	2.63	2.01	-	0.46	2.94	2.47	0.98	0.78	-	1.15
13,62	S19	2.174978	1.810381	2.40	-	-	-	2.19	2.75	1.93	-	0.46	3.04	2.41	1.04	0.77	-	1.40
11,75	S20	2.139027	1.754565	2.35	-	-	-	2.16	2.80	1.89	-	0.46	3.08	2.38	1.06	0.79	-	1.49
9,78	S21	2.097647	1.705158	2.31	-	-	-	2.13	2.86	1.84	-	0.45	3.20	2.27	1.08	0.79	-	1.60
7,82	S22	2.051354	1.663457	2.30	-	-	-	2.10	2.91	1.81	-	0.44	3.31	2.17	1.08	0.77	-	1.67
5,89	S23	2.000343	1.631892	2.23	-	0.06	-	2.08	2.95	1.77	-	0.42	3.41	2.09	1.09	-	-	1.72
3,95	S24	1.946336	1.609740	2.20	-	0.11	-	2.07	2.99	1.72	-	0.40	5.52	-	1.08	0.79	-	1.75
1,96	S25	1.891018	1.594436	2.16	-	0.16	-	2.06	3.04	1.69	-	0.37	5.54	-	1.07	0.79	-	1.78

Table S4 (continued).

ΔE (kcal.mol ⁻¹)	Struc- ture	d (O4-C12)	d (C1-C11)	V (C12,C11)	V' (C12,C11)	V (C12)	V (C11)	V (C1,C2)	V (C2,C3)	V (C3,O4)	V (C1)	V(C2)	V(O4)	V'(O4)	V(N)	V'(N)	V (O4,C12)	V (C1,C11)
-0,11	S26	1.835437	1.583453	2.14	-	-	-	2.05	3.07	1.65	-	0.35	5.74	-	1.07	0.78	-	1.80
-4,42	S27	1.725872	1.568271	2.10	-	-	-	2.04	3.44	1.59	-	-	4.84	-	1.04	0.79	0.98	1.82
-6,57	S28	1.672993	1.562469	2.07	-	-	-	2.03	3.45	1.56	-	-	4.83	-	1.03	-	1.05	1.83
-10,39	S29	1.576880	1.553966	2.06	-	-	-	2.03	3.47	1.53	-	-	4.74	-	1.02	-	1.18	1.84
-11,91	S30	1.538713	1.551206	2.05	-	-	-	2.03	3.47	1.52	-	-	4.72	-	1.02	0.75	1.23	1.85
-13,14	S31	1.511420	1.549622	2.05	-	-	-	2.03	3.47	1.51	-	-	4.69	-	1.01	0.75	1.27	1.85
-16,40	S32	1.470945	1.549017	2.04	-	-	-	2.03	3.22	1.54	-	0.24	4.60	-	1.00	0.85	1.35	1.86
-17,80	S33	1.457866	1.548767	2.04	-	-	-	2.02	3.19	1.54	-	0.28	4.55	-	0.96	0.89	1.38	1.87
-19,56	S34	1.447713	1.548632	2.03	-	-	-	2.02	3.23	1.54	-	0.23	4.52	-	0.87	1.01	1.41	1.88
-20,57	S35	1.443466	1.546981	2.04	-	-	-	2.03	3.44	1.54	-	-	4.52	-	0.77	1.11	1.42	1.88
-21,02	S36	1.439787	1.545004	2.04	-	-	-	2.03	3.45	1.53	-	-	4.53	-	0.71	1.17	1.43	1.89
-21,18	S37	1.438753	1.544499	2.04	-	-	-	2.03	3.45	1.54	-	-	4.52	-	0.67	1.20	1.43	1.89
-21,32	S38	1.438412	1.543801	2.04	-	-	-	2.03	3.45	1.53	-	-	4.52	-	0.66	1.21	1.43	1.89

At **S17**, $d(\text{C3-C2}) = 1.992 \text{ \AA}$, $d(\text{O6-C1}) = 2.265 \text{ \AA}$. This is the structure just before the formation of the $\text{C}_3\text{-C}_2$ single bond. We observe a monosynaptic $V(\text{C}_3)$ pool integrating 0.42 e. The most relevant ELF topology change observed in **S17** is the presence of a new monosynaptic $V(\text{C11})$ pool on the ethylene fragment that integrates 0.57e. In contrast, the disynaptic pool $V(\text{C12}, \text{C11})$ decreased significantly to 2.63e.

At **S18**, $d(\text{C1-C11}) = 1.93 \text{ \AA}$ and $d(\text{O4-C12}) = 2.237 \text{ \AA}$. The two monosynaptic pools $V(\text{C1})$ and $V(\text{C11})$ are merged into a new disynaptic pool $V(\text{C1}, \text{C11})$ that integrates the initial population at 1.15 e. This associated change in topology may be related to the formation of the first C1-C11 single bond at a C-C distance of approximately 1.93 \AA .

At **S26**, $d(\text{C1-C11}) = 1.583 \text{ \AA}$ and $d(\text{O4-C12}) = 1.835 \text{ \AA}$, which is the structure just before the formation of the second C-O single bond, the monosynaptic $V(\text{C12})$ has disappeared and the population of the monosynaptic pool $V(\text{O4})$ has increased to 5.74e, while the disynaptic pool $V(\text{C2}, \text{C2})$ incorporates 3.07e and can already be considered a C2-C3 double bond.

At **S27**, $d(\text{C1-C11}) = 1.568 \text{ \AA}$ and $d(\text{O4-C12}) = 1.725 \text{ \AA}$, with the disappearance of the monosynaptic pool $V(\text{C2})$, a new disynaptic pool $V(\text{O4}, \text{C12})$, associated with the O4-C12 single bond formation, is created with an initial population of 0.98e.

Finally, at **S38**, $d(\text{C1-C11}) = 1.543 \text{ \AA}$ and $d(\text{O4-C12}) = 1.438 \text{ \AA}$, only changes in the populations of the ELF valence basins associated with the complete relaxation of the molecular system are observed. The two disynaptic basins $V(\text{C1}, \text{C11})$ and $V(\text{O4}, \text{C12})$ reach populations of 1.89e and 1.43e, respectively. The disynaptic pool $V(\text{C2}, \text{C3})$ ends with population of 3.45e, while the monosynaptic pool $V(\text{O4})$ incorporates a population of 4.52e. Similarly, the population of the disynaptic pool $V(\text{C12}, \text{C11})$ is 2.04e, while that of the two disynaptic pools $V(\text{C1-C2})$ and $V(\text{C3-O4})$ are 2.03e and 1.53e, respectively.