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Mechanistic Investigation of Enolate/Stabilized Vinylogous Carbanion-Mediated Organocatalytic Azide (3+2) Cycloaddition Reactions for the Synthesis of 1,2,3-Triazoles.

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1 NMR Experiments for ¹H Monitoring Studies and Intermediates Identification

The relevant chemical shifts of butylidene malononitrile **1** (Figure S1, Table S1) and 4ethyl-1-phenyl-1*H*-1,2,3-triazol (Figure S2, Table S2) in reported in the following Figures and



Figure S1: NMR ¹H spectra of butylidene malononitrile 1 (400 MHz, CDCl₃).

Table S1: Spectroscopic data of butylidene malononitrile 1 (400 MHz, CDCl₃).



(H)	Multiplicity	δ (ppm)	J(Hz)
C4 (CH)	triplet	7.34	J = 8.0
C3 (CH ₂)	quartet	2.58	<i>J</i> = 7.3
C2 (CH ₂)	sextet	1.62	J = 7.4
C1 (CH ₃)	triplet	1.02	J = 7.4



Figure S2: ¹H NMR spectra of 4-ethyl-1-phenyl-1*H*-1,2,3-triazol (400 MHz, DMSO-d6).

Table S2: Spectroscopic data of 4-ethyl-1-phenyl-1*H*-1,2,3-triazol (400 MHz, DMSO-d6).



(H)	Multiplicity	δ (ppm)	J(Hz)	
C-1 (CH ₃)	triplet	1.28	J=7.6	_
C-2 (CH ₂)	quartet	2.74	J = 7.0	
C-4 (CH)	broad simplet	8.57 - 8.58	-	
	multiplet	7.90 - 7.85	-	
Ar	multiplet	7.61 – 7.55	-	
	multiplet	7.48 - 7.43	-	

1.1 Procedure for reaction monitoring experiments

The reaction was carried out in an NMR tube at a concentration 10x lower than the original condition for Paixão's reaction. This is due to the need to match the reaction with the optimal concentration in the NMR. The NMR spectra was acquired using single-pulse experiments, aiming to reduce the quantitative integration problems due to different relaxation times of nucleus. To further ensure this experimental aspect, the time of each pulse varied

around 3 minutes, ensuring that all ¹H nuclei were relaxed. The reaction was performed using DMSO-d6, at the concentrations and quantities as shown in Table S3.

Component	n (mmol)	Concentration (mol L ⁻¹)
butylidene malononitrile 1	0.050	0.083
PhN ₃	0.10	0.17
DBU	0.050	0.083
DMSO-d6 (0.60 mL)		

 Table S3: Reaction conditions for Paixão's reaction.

The NMR tube was filled with a solution of PhN_3 and 1 in DMSO-d6. Next, the temperature was homogenized at 50°C, followed by calibration of the 90° pulse and analysis of a standard containing the chitin molecule (10.3 mg/2 mL) for the use of the ERETIC2 technique, based on the methodology PULCON to determine the concentration of reaction components.¹ Then, the sample was inserted into the equipment for temperature and field homogenization. For the addition of the base, the sample was removed, added the base and the tube returned to the equipment, a process that took about 1min 30s to be done. The zero time of the reaction occurred after the addition of the base.

1.2 First attempt to monitoring the Paixão's reaction

In Figure S3 lies an overview of our first attempt in monitoring the Paixão's reaction. It is observed that the reaction starts from the addition of DBU (Figure S3A versus S3B), presenting an immediate change in the spectrum, due to the reaction of the base with **1**, with total consumption of starting material and formation of the carbanion intermediate. The removal of vinylic proton can be noticeable by the disappearance of chemical shift triplets equivalent to 7.95 ppm (vinyl CH) and 0.92 ppm (-CH₃), and the appearance of vinylic C-H in the range of 5.5 - 4.2 ppm, and a localized triplet at 0.87 ppm. After 2 minutes of reaction (Figure S3C), a spectrum was acquired without the respective "shimming", showing that the introduction of the base did not significantly affect the homogeneity of the field. After 23 minutes (Figure S3D), a large consumption of starting material was observed, but practically no product was formed. The spectrum obtained with 2h 20min of reaction (Figure S3E) showed characteristic signs of the product, whose chemical shifts 8.49 ppm, 2.73 ppm and 1.28 ppm, consisting of a singlet, doublet quartet and triplet, respectively.



Figure S3: Monitoring of reaction by ¹H NMR (400 MHz, DMSO-d6). a) Reagents only; b) 2 minutes after addition of the DBU; c) formation of the triazole nucleus and d) elimination of malonitrile after 5 hours.

1.3 Quantitative monitoring Paixão's reaction

After 5 minutes of the addition of DBU (Figure S4B), it was possible to identify the carbanion intermediates in their *cis* and *trans* isomeric form, represented by **Z-1a** and **E-1a**, in a 1:5 ratio, respectively.



Figure S4: Formation of carbanion intermediates *E***-1a** and *Z***-1a**. ¹H NMR spectra after 5 min of reaction (400 MHz, DMSO-d6).

Then, PhN₃ was added, resulting in the formation of intermediates Z-2a and E-2a after 20 minutes of reaction in a 1:3.7 diastereomeric ratio (Figure S5). These intermediates were revealed applying selective total correlation spectroscopy (1D-TOCSY) with a mixing time of 120 ms, by excitation of -CH₃ groups with chemical shifts of 0.97 and 1.18 ppm, which correspond the Z-2a (Figure S6) and E-2a (Figure S7), respectively.



Figure S5: ¹H NMR spectra after 20 minutes of reaction (400 MHz, DMSO-d6).



Figure S6: Selective 1D-TOCSY spectra after 20 minutes of reaction. Excitation of -CH₃ group at 0.97 ppm. (400 MHz, DMSO-d6).



Figure S7: Selective 1D-TOCSY spectra after 20 minutes of reaction. Excitation of -CH₃ group at 1.18 ppm. (400 MHz, DMSO-d6).

Time (min)	[E-1a]	[3a]	[Z-2a]	[E-2a]
5	35.36	0.27	2.60	9.31
8	27.58	0.06	4.34	15.32
11	23.52	0.17	5.19	18.49
14	20.07	0.25	5.64	20.75
17	17.50	0.34	5.74	22.16
20	16.14	0.50	6.07	23.56
23	14.93	0.65	6.19	24.68
26	14.02	0.81	6.34	25.62
29	13.25	1.01	6.39	26.41
32	12.73	1.20	6.46	27.05
35	12.17	1.38	6.50	27.65
38	11.68	1.60	6.55	28.15
41	11.17	1.78	6.56	28.60
44	10.55	1.98	6.59	28.97
47	10.03	2.13	6.62	29.37
50	9.48	2.28	6.63	29.67
53	9.02	2.41	6.63	29.93
56	8.63	2.57	6.67	30.16
59	8.30	2.67	6.69	30.38

Table S4: Reaction monitoring between 1 and PhN_3 using Paixão's methodology.Concentrations [] in mmol L⁻¹

1.4 ¹H NMR monitoring for direct use of butyraldehyde and catalytic amount of DBU (Ramachary's Reaction).

The experimental conditions applied in the Ramachary's reactions are the same as those applied in the Paixão's reactions, differing mostly in the catalytic amount of catalyst (Table S5). The DBU aliquot was added from a 1.7 mol L⁻¹ of a DMSO-d6 stock solution.

Table S5: Ro	eaction	conditions	for	Ramac	hary'	's reaction.
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Component	n(mmol)	Concentration (mol L ⁻¹)
butyraldehyde	0.050	0.083

PhN ₃	0.075	0.13
DBU	0.0050	0.0083
DMSO-d6 (0.60 mL)		

The monitoring from butyraldehyde and PhN_3 revealed the reaction did not proceed with the formation of intermediates or product. In fact, the attempt to reproduce in the original concentration conditions and carried out in a balloon did not produce the product of interest. Figure S8 is the mixture of phenyl azide with butyraldehyde before de DBU addition, which is indicated by 0.87 ppm (CH₃), 9.66 ppm (CHO), 1.90 (CH₂) and 1.96 (CH₂), in DMSO- d6.



Figure S8: ¹H NMR spectra before DBU addition at 25 °C (400 MHz, DMSO-d6).

As can be seen in Figure S9, the addition of DBU does not lead to significant changes in the spectrum and absent of new signals indicating the product after 30 minutes of reaction time.



Figure S9: ¹H NMR spectra after 30 min of DBU addition at 25 °C (400 MHz, DMSO-d6).

Finally, even after 1 h at 50°C, aiming to increase the reaction speed and compatibility with the Paixão's reaction condition, it was observed only a small variation in the chemical shift of the butyraldehyde signals, possibly due to the change of the temperature (Figure S10).



Figure S10: ¹H NMR spectra after 1 h of DBU addition at 50 °C (400 MHz, DMSO-d6).

2 Experimental Section

Reagents, when not synthesized, as well as solvents, were obtained commercially (Merck, Sigma Aldrich), and when necessary were treated using standard laboratory techniques according to methods published by Perrin, Armarego, and Perrin (Pergamon Press, 1966). Butyraldehyde was dried with sodium sulfate and then distilled before use. The 8-Diazabicyclo [5.4.0] undec-7-ene (DBU) base was purified by vacuum distillation and stored in 4Å molecular sieves. The purification of the products was conducted using silica gel Flash (230-400 mesh, 40-63 µm) as stationary phase. ¹H NMR was obtained using 9.4 Tesla equipment (Bruker-AVANCE III-400 MHz). Deuterated dimethyl sulfoxide (DMSO-d6) and chloroform (CDCl₃) were used as commercially available solvents, both with tetramethylsilane (TMS) as internal standard.

Preparation of PhN₃: In a solution of aniline (2.00 mL, 21.9 mmol) in ethyl acetate (40 mL) and H₂O (5 mL) was added a concentrated solution of HCl (12 mL) at 0 °C over a period of 10 minutes. After this time, a solution of NaNO₂ (2.6 g, 37 mmol) in H₂O (7.5 mL) was added dropwise to the reaction mixture. The reaction was kept under vigorous stirring during 30 minutes at 0 °C. A solution of NaN₃ (2.40 g, 37.1 mmol) in water (8 mL) was subsequently added over a period of 5 minutes. After stirring at 0 °C for 30 minutes, the reaction mixture was diluted with water (50 mL) and extracted with ethyl acetate (2x50 mL). The combined organic phase was dried over anhydrous sodium sulfate, filtered, and solvent was removed in vacuo. The crude compound was purified by column chromatography using acetate/hexane as eluent (20:1) providing PhN₃ in 44% yield (888 mg, 7.40 mmol) as a light-yellow oil. ¹H NMR (400 MHz, DMSO) δ 7.45 – 7.39 (m, 2H), 7.23-7.18 (m, 1H), 7.14 – 7.10 (m, 2H).

Preparation of butylidene malononitrile 1:² To a stirred solution of malononitrile (3.0 g, 27 mmol) and butyraldehyde (2.3 mL, 41 mmol) in CHCl₃ (16 mL) was added Al₂O₃ (4.0g, 38 mmol, 1.4 equiv.) (Brockmann I Activated, basic) slowly and carefully, once the reaction is very exothermic. After 2h 30min, Al₂O₃ was removed by vacuum filtration, and dichloromethane was used to rinse the solid (15 mL). The solvent was removed in vacuo, furnishing a yellow oil in 93% yield (2.78g, 23 mmol). The product was used without further purification. ¹H NMR (400 MHz, CDCl₃) δ 7.34 (t, *J* = 8.0 Hz, 1H), 2.58 (q, *J* = 7.3 Hz, 2H), 1.62 (sext, *J* = 7.4 Hz, 2H), 1.02 (t, *J* = 7.4 Hz, 3H).

3 Computational Methods

All DTF calculations were performed using the ultrafine grid in Gaussian 09^3 using default convergence criteria for energy and forces. Geometry optimization and single-point calculations of intermediates and transition states were made using M06-2X functional⁴ using 6-311+g(d,p) basis set for all atoms, except for shielding tensor calculation in which the geometries were calculated at M06-2X/6-31+G(d,p) level of theory, and the shield tensors calculated using MPW1PW91 functional⁵ and 6-311+G(2d,p) basis set, using a method validated elsewhere.⁶ Vibrational analysis was performed at all calculated points to confirm they either as a transition state (only one imaginary frequency) or as a local minimum (zero imaginary frequencies), furnishing also the zero-point vibrational energies, the thermal and entropic correction from which the Gibbs free energies were determined. Solvent effects were accounted for all optimizations using the continuum model IEF-PCM using dimethyl sulfoxide (DMSO) as the solvent. Transition states were submitted to intrinsic reaction coordinate (IRC) calculation to confirm the desired connection between reactants and products. Visualizations were done using GaussView 5.0^7 and PyMOL 2.6.0a0⁸.

4 Electronic Energy and Gibbs Thermal Corrections of calculated intermediates and transition states

Table S6: Electronic and Gibbs Free energies for all intermediates and transition states. (M06-2X/6311+g(d,p) using IEF-PCM DMSO)

Structure	ructure Electronic Energy / Eh Free Energy / Eh		iv / cm ⁻¹
1m	-341.658375816	-341.584638	-
3a	-192.613692539	-192.569966	-
3b	-192.612643369	-192.567976	-
4	-588.430427534	-588.289913	-
5a	-588.444059872	-588.298023	-
5b	-588.933409056	-588.774415	-
6	-1050.94376555	-1050.553778	-
E-1am	-341.195505306	-341.135066	-
E-2am	-737.022959923	-736.861569	-
E-2bm	-737.475637563	-737.301413	-
Z-1am	-341.192948879	-341.13264	-
Z-2am	-737.022747449	-736.861102	-
Z-2bm	-737.472547467	-737.297547	-
T1	-512.524657581	-512.392323	-
T2	-512.525288769	-512.391869	-
a1	-395.77833085	-395.705885	-
a2	-510.291799632	-510.190202	-
a3	-600.273124312	-600.202433	-
r 1	-193.115295967	-193.057493	-
r2	-224.966751006	-224.949037	-
r3a	-462.014579829	-461.801815	-
r3b	-462.487011437	-462.259349	-
E-TS1	-736.953706195	-736.801773	-443.7541
E-TS1b	-851.466143986	-851.284784	-449.4332
E-TS1c	-941.453999899	-941.304312	-429.8121
E-TS2	-1199.46937401	-1199.067228	-1137.8266
E-TS3	-736.940372237	-736.78657	-498.1741
E-TS4	-655.108598984	-654.823347	-1218.433
TS-8	-1050.93735599	-1050.547068	-419.5329
Z-TS1	-736.95140985	-736.799756	-427.3996
Z-TS2	-1199.47350251	-1199.06839	-1283.1688
Z-TS4	-655.110256225	-654.825417	-1253.7555
Z-TS5	-588.384925398	-588.251094	-376.5495
Z-TS5b	-702.897500263	-702.733527	-384.0941
Z-TS5c	-792.88423459	-792.751868	-358.2967
Z-TS6	-588.430611487	-588.287165	-74.7174
Z-TS7	-1050.92661684	-1050.541489	-1115.4904
Z-TS9	-588.360558647	-588,223563	-403.4219

5 Electronic Energies calculated for Distortion/Interaction Activation Strain (DIAS) analysis

Reaction coordinate / A	ΔE _{dist, dipole} / kcal mol ⁻¹	ΔE _{dist,dipolarophile} / kcal mol ⁻¹	ΔE _{dist,total} / kcal mol ⁻¹	ΔE _{int} / kcal mol ⁻¹
2.9333	0.0550	0.2487	0.3038	-1.4719
2.9245	0.0697	0.1970	0.2668	-1.3408
2.8864	0.0920	0.2099	0.3019	-1.1123
2.8442	0.0980	0.3204	0.4184	-0.9653
2.8015	0.1010	0.4471	0.5481	-0.7876
2.7577	0.0970	0.6227	0.7197	-0.6140
2.7127	0.0860	0.8588	0.9448	-0.4375
2.6665	0.0709	1.1790	1.2499	-0.3034
2.6198	0.0567	1.6072	1.6639	-0.2279
2.5726	0.0510	2.1810	2.2320	-0.2627
2.5252	0.0653	2.9343	2.9996	-0.4718
2.4780	0.1160	3.8958	4.0118	-0.9130
2.4310	0.2174	5.1102	5.3276	-1.7017
2.3843	0.3897	6.5766	6.9663	-2.9073
2.3377	0.6477	8.3101	8.9578	-4.6040
2.2912	1.0012	10.3200	11.3212	-6.8669
2.2448	1.4491	12.5901	14.0392	-9.6916
2.1981	1.9973	15.1025	17.0998	-13.0660
2.1513	2.6331	17.8028	20.4358	-16.9291
2.1041	3.3736	20.6688	24.0424	-21.2636
2.0565	4.1786	23.6519	27.8305	-25.9679
2.0087	5.0605	26.6756	31.7361	-30.9716
1.9608	5.9973	29.7511	35.7484	-36.2640
1.9127	6.9972	32.7957	39.7930	-41.7643
1.8646	8.0257	35.7815	43.8073	-47.3976
1.8165	9.0827	38.6622	47.7449	-53.0796
1.7688	10.1506	41.3970	51.5475	-58.7083
1.7217	11.2277	43.8933	55.1210	-64.1329
1.6755	12.2806	46.1405	58.4211	-69.2214
1.6309	13.3118	48.0528	61.3647	-73.8090
1.5894	14.2596	49.5273	63.7869	-77.6305
1.5542	15.0455	50.4377	65.4832	-80.4312
1.5309	15.5334	50.8548	66.3882	-82.1708
1.5190	15.7442	51.1730	66.9172	-83.3775
1.5117	15.8910	51.4244	67.3155	-84.3719
1.5086	15.7674	51.6703	67.4377	-85.0715
1.5058	15.6804	51.8571	67.5376	-85.6168
1.5043	15.6504	52.0636	67.7140	-86.2577
1.5018	15.7110	52.7510	68.4620	-87.4511
1.5010	15.4637	52.0396	67.5033	-86.9379

Table S7: Calculated Electronic Energies (M06-2X/6311+g(d,p) using IEF-PCM DMSO) forDIAS analysis of Z-TS5.

Reaction coordinate / A	ΔE _{dist, dipole} / kcal mol ⁻¹	ΔE _{dist,dipolarophile} / kcal mol ⁻¹	ΔE _{dist,total} / kcal mol ⁻¹	ΔE _{int} / kcal mol ⁻¹
1.5011	15.3476	53.1191	68.4667	-88.2528
1.4972	15.4246	54.2231	69.6476	-89.6032

Table S8: Calculated Electronic Energies (M06-2X/6311+g(d,p) using IEF-PCM DMSO) forDIAS analysis of Z-TS9.

Reaction coordinate / A	ΔE _{dist, dipole} / kcal mol ⁻¹	ΔE _{dist,dipolarophile} / kcal mol ⁻¹	ΔE _{dist,total} / kcal mol ⁻¹	ΔE _{int} / kcal mol ⁻¹
2.8752	0.1127	1.2691	1.3818	0.2023
2.8752	0.1127	1.2691	1.3818	0.2022
2.8673	0.1331	1.2129	1.3461	0.5015
2.8440	0.1747	1.3245	1.4992	0.9760
2.8168	0.2014	1.4881	1.6895	1.4257
2.7881	0.2153	1.7099	1.9252	1.8802
2.7589	0.2302	2.0106	2.2408	2.3176
2.7291	0.2476	2.4121	2.6597	2.7395
2.6991	0.2705	2.9371	3.2076	3.1204
2.6691	0.3024	3.6198	3.9223	3.4285
2.6391	0.3482	4.4749	4.8231	3.6509
2.6089	0.4127	5.5246	5.9373	3.7477
2.5788	0.5031	6.7906	7.2937	3.6715
2.5488	0.6259	8.2659	8.8918	3.3911
2.5186	0.7920	9.9733	10.7654	2.8479
2.4883	1.0110	11.9004	12.9115	1.9881
2.4576	1.2976	14.0492	15.3467	0.7639
2.4265	1.6609	16.3695	18.0303	-0.8404
2.3951	2.1109	18.8656	20.9764	-2.8703
2.3629	2.6555	21.4941	24.1496	-5.3281
2.3302	3.2922	24.1858	27.4779	-8.1419
2.2968	4.0163	26.9346	30.9509	-11.3074
2.2628	4.8351	29.6704	34.5055	-14.7616
2.2283	5.7383	32.4048	38.1431	-18.4996
2.1934	6.7199	35.0630	41.7828	-22.4342
2.1580	7.7995	37.6816	45.4811	-26.6219
2.1222	8.9646	40.1946	49.1592	-30.9903
2.0861	10.2145	42.6355	52.8500	-35.5722
2.0496	11.5661	44.9852	56.5513	-40.3716
2.0131	13.0037	47.2421	60.2458	-45.3775
1.9761	14.5133	49.4118	63.9252	-50.5880
1.9390	16.0889	51.4732	67.5621	-55.9694
1.9018	17.7262	53.4014	71.1276	-61.4739
1.8648	19.4005	55.2311	74.6315	-67.0925
1.8279	21.1142	56.9071	78.0213	-72.7475
1.7913	22.8578	58.4542	81.3120	-78.4102
1.7554	24.6110	59.8617	84.4727	-84.0119

Reaction coordinate / A	ΔE _{dist, dipole} / kcal mol ⁻¹	ΔE _{dist,dipolarophile} / kcal mol ⁻¹	ΔE _{dist,total} / kcal mol ⁻¹	ΔE _{int} / kcal mol ⁻¹
1.7202	26.3799	61.1338	87.5137	-89.5127
1.6863	28.1521	62.2880	90.4401	-94.8863
1.6539	29.9463	63.2806	93.2269	-100.0514
1.6238	31.7388	64.1637	95.9025	-105.0110
1.5963	33.5301	64.9106	98.4406	-109.6952
1.5722	35.3295	65.6004	100.9299	-114.1925
1.5518	37.1133	66.1969	103.3102	-118.4365
1.5352	38.8456	66.7644	105.6099	-122.4555
1.5220	40.5210	67.3507	107.8717	-126.2986
1.5118	42.1066	67.8864	109.9930	-129.8569
1.5036	43.5486	68.3997	111.9484	-133.0798
1.4970	44.7670	68.8487	113.6157	-135.8264
1.4916	45.7256	69.1417	114.8673	-137.9503
1.4872	46.2755	69.2590	115.5345	-139.2889
1.4839	46.4359	69.2225	115.6584	-139.9022
1.4813	46.7081	69.2055	115.9135	-140.5150
1.4808	46.0473	68.7703	114.8176	-139.7203
1.4816	45.7857	68.3722	114.1579	-139.1547

Table S9: Calculated Electronic Energies (M06-2X/6311+g(d,p) using IEF-PCM DMSO) forDIAS analysis of E-TS2.

Reaction coordinate / A	ΔE _{dist, dipole} / kcal mol ⁻¹	ΔE _{dist,dipolarophile} / kcal mol ⁻¹	ΔE _{dist,total} / kcal mol ⁻¹	ΔE _{int} / kcal mol ⁻¹
2.7478	0.4017	0.9442	1.3459	-1.9733
2.7415	0.4140	0.9400	1.3540	-1.7680
2.7168	0.4649	1.0558	1.5206	-1.3950
2.6770	0.4713	1.2791	1.7504	-1.0224
2.6339	0.4614	1.5870	2.0484	-0.6804
2.5896	0.4512	1.9865	2.4376	-0.3417
2.5450	0.4495	2.4871	2.9366	-0.0124
2.5001	0.4635	3.1234	3.5869	0.2723
2.4550	0.5020	3.9164	4.4184	0.4699
2.4098	0.5788	4.8950	5.4738	0.5377
2.3647	0.7079	6.0767	6.7846	0.4129
2.3195	0.9134	7.4753	8.3887	0.0011
2.2745	1.2106	9.1122	10.3229	-0.7785
2.2293	1.6321	10.9922	12.6243	-2.0445
2.1840	2.1857	13.1124	15.2981	-3.8524
2.1386	2.8966	15.4817	18.3783	-6.2863
2.0928	3.7726	18.0839	21.8565	-9.3629
2.0467	4.8273	20.9002	25.7275	-13.0958
2.0003	6.0745	23.9193	29.9938	-17.5002
1.9535	7.5111	27.0912	34.6023	-22.5354
1.9062	9.1376	30.3605	39.4981	-28.1528

Reaction coordinate / A	ΔE _{dist, dipole} / kcal mol ⁻¹	ΔE _{dist,dipolarophile} / kcal mol ⁻¹	ΔE _{dist,total} / kcal mol ⁻¹	ΔE _{int} / kcal mol ⁻¹
1.8585	10.9270	33.6727	44.5996	-34.2583
1.8108	12.8315	36.9774	49.8089	-40.7163
1.7630	14.7953	40.1265	54.9219	-47.2474
1.7154	16.7784	43.1216	59.9000	-53.7316
1.6684	18.7263	45.8029	64.5293	-59.8418
1.6229	20.6275	48.1520	68.7794	-65.4159
1.5803	22.3541	50.0250	72.3791	-70.0761
1.5468	23.7177	51.1681	74.8858	-73.3044
1.5307	24.5074	51.8021	76.3096	-75.2051
1.5245	24.7506	52.0176	76.7682	-76.0527
1.5177	25.4862	52.8513	78.3375	-77.9797
1.5190	25.2284	52.7320	77.9604	-77.9038
1.5227	24.9804	52.1812	77.1616	-77.2243

Table S10: Calculated Electronic Energies (M06-2X/6311+g(d,p) using IEF-PCM DMSO) forDIAS analysis of E-TS3.

Reaction coordinate / A	ΔE _{dist, dipole} / kcal mol ⁻¹	ΔE _{dist,dipolarophile} / kcal mol ⁻¹	ΔE _{dist,total} / kcal mol ⁻¹	ΔE _{int} / kcal mol ⁻¹
2.7824	0.9315	1.3068	2.2383	-2.3298
2.7788	0.9800	1.3049	2.2848	-2.1630
2.7591	1.0674	1.3743	2.4416	-1.7739
2.7350	1.0992	1.5052	2.6044	-1.3844
2.7092	1.1070	1.6678	2.7748	-0.9712
2.6821	1.0956	1.8733	2.9689	-0.5127
2.6538	1.0700	2.1303	3.2003	-0.0225
2.6248	1.0358	2.4586	3.4944	0.4991
2.5950	0.9966	2.8808	3.8774	1.0260
2.5650	0.9634	3.4124	4.3758	1.5441
2.5345	0.9401	4.0804	5.0205	2.0289
2.5043	0.9399	4.9013	5.8411	2.4570
2.4737	0.9693	5.8963	6.8657	2.7816
2.4432	1.0426	7.0746	8.1173	2.9795
2.4126	1.1718	8.4515	9.6233	2.9921
2.3819	1.3773	10.0291	11.4064	2.7589
2.3513	1.6726	11.8148	13.4874	2.2090
2.3203	2.0865	13.8029	15.8894	1.2627
2.2892	2.6303	15.9841	18.6144	-0.1633
2.2577	3.3292	18.3453	21.6745	-2.1441
2.2261	4.1794	20.8548	25.0343	-4.6944
2.1938	5.2019	23.5114	28.7132	-7.8839
2.1613	6.3849	26.2732	32.6582	-11.6594
2.1281	7.7452	29.0880	36.8332	-16.0039
2.0945	9.2793	31.9535	41.2329	-20.9055
2.0605	10.9733	34.8199	45.7932	-26.3130

Reaction coordinate	ΔE _{dist, dipole} / kcal mol ⁻¹	ΔE _{dist,dipolarophile} / kcal	ΔE _{dist,total} / kcal mol ⁻¹	ΔE _{int} / kcal mol ⁻¹
2.02(0	12.9450	27 (550	50,5017	22.2012
2.0260	12.8459	37.0339	50.5017	-32.2012
1.9912	14.8594	40.4389	55.2983	-38.5101
1.9562	17.0206	43.1273	60.1479	-45.2045
1.9212	19.3009	45.7023	65.0032	-52.2059
1.8860	21.6777	48.1992	69.8769	-59.5018
1.8512	24.1024	50.5043	74.6067	-66.8984
1.8167	26.5859	52.6736	79.2595	-74.4126
1.7828	29.0836	54.6778	83.7614	-81.9202
1.7497	31.5763	56.5322	88.1085	-89.3609
1.7175	34.0579	58.2177	92.2756	-96.6592
1.6866	36.4993	59.7466	96.2459	-103.7356
1.6569	38.8909	61.0985	99.9894	-110.5099
1.6289	41.2264	62.3043	103.5307	-116.9503
1.6027	43.4712	63.3425	106.8137	-122.9378
1.5785	45.6091	64.2111	109.8202	-128.3916
1.5566	47.5589	64.9556	112.5145	-133.2194
1.5371	49.2631	65.4810	114.7442	-137.2186
1.5202	50.5427	65.8379	116.3806	-140.2292
1.5064	51.2499	66.0449	117.2948	-142.1537
1.4967	51.3349	66.2820	117.6169	-143.1912
1.4905	51.0342	66.5059	117.5401	-143.6289
1.4859	50.6165	66.9657	117.5822	-144.0413
1.4857	50.3791	66.2653	116.6445	-143.4236
1.4865	50.2365	65.5748	115.8113	-142.6845

6 Electronic Energy Benchmark

Using the optimized geometries for the main intermediates and transition states for both the malononitrile-catalyzed and DBU-catalyzed mechanisms at M062X/6-311+g(d,p) (referred below as reference level) we performed several single-point calculations using different levels of theory in order to assess the reliability of our calculations. For these tests, we employed the hybrid-GGA functionals B3LYP, B3PW91 and PBE1PBE, the GGA functional BP86 and also the range-separated wB97XD functional with the Pople basis set 6-311+g(d,p). Also, we changed the basis set to Alrichs def2-TZVP and the diffusion-augmented def2-TZVPD using M062X functional.

As shown by **Figure S11** and **Figure S13** when using different DFT functionals, the overall shape of the reaction profile is retained, and a good agreement is found for the relative energy of the neutral intermediates. The anionic intermediates, however, show major discrepancies from the reference level. The GGA functional BP86 overstabilize all anionic intermediates, immediately followed by the three hybrid-GGA functionals B3LYP, B3PW91 and PBE1PBE. The hybrid-GGA with range separation wB97XD also overstabilize the anionic intermediates, but to a lesser extent. Regarding the basis set, as shown in **Figure S12** and **Figure S14**, we found that using Alrich def2-TZVP basis set gives very similar results in comparison to 6-311+g(d,p), although the former lacks diffusion functions. The use of diffusion-augmented def2-TZVPD, while retaining the overall shape of the reference level potential energy diagram, leads to overstabilization of anionic intermediates.

As shown by **Table S11**, for the malononitrile-catalyzed reaction, we found that the energy difference between the intermediates E-1am and Z-1am is consistently close to the -1.6 kcal/mol, obtained with the reference level. In fact, considering the thermal correction for the free energy of both structures (from Table S6), the free energy difference between these intermediates is $\Delta \Delta G = -1.604$ kcal/mol, from which we predict a ratio of 1:11 favoring the Z isomer Z-1am at 50°C (the NMR monitoring temperature). It is worth noting that the malononitrile mechanism was calculated for a simplified substrate, so the direct comparison to the experimental ratio of 1:5 is not possible. However, the favored isomer is correct predicted in our simplified model. Also, we found that the cycloaddition barrier calculated using wB97XD functional is close to the reference level result. Nevertheless, the ΔE between the most stable intermediate E-2am (Z-2am) and the highest transition state E-TS2 (Z-TS2) is severely overestimated by the tested functionals, because of overstabilization of the charged intermediate 2am (either Z or E). As for the Table S12 below, even there is not much of an agreement for the relative energy of the charged intermediates, considering the tested levels and the reference level. The rection barriers using wb97xd or the basis-sets def2-TZVP and def2-TZVPD are consistent with the M062X/6-311+g(d,p) results.



Figure S11: Single Point Calculations using different DFT functionals and 6-311+g(d,p) basisset for the *E*-pathway (A) and *Z*-pathway (B) of the proposed mechanism for the malononitrile-catalyzed reaction. Geometries optimized at M062X/6-311+g(d,p) level of theory. Relative total energies reported in kcal/mol.



Figure S12: Single Point Calculations using different basis-sets and M062X DFT functional for the *E*-pathway (A) and *Z*-pathway (B) of the proposed mechanism for the malononitrile-catalyzed reaction. Geometries optimized at M062X/6-311+g(d,p) level of theory. Relative total energies reported in kcal/mol.



Figure S13: Single Point Calculations using different DFT functionals and 6-311+g(d,p) basisset for the main pathway of the proposed mechanism for the DBU-catalyzed reaction. Geometries optimized at M062X/6-311+g(d,p) level of theory. Relative total energies reported in kcal/mol.



Figure S14: Single Point Calculations using different basis-sets and M062X DFT functional for the main pathway of the proposed mechanism for the DBU-catalyzed reaction. Geometries optimized at M062X/6-311+g(d,p) level of theory. Relative total energies reported in kcal/mol.

Table S11:Relevant energies differences from	single point calculations using several levels of
theory for the malononitrile-catalyzed reaction.	. Geometries optimized at M062X/6-311+g(d,p)
level of theory. Energies reported in kcal/mol.	

Level of Theory	(E-1am-Z-1am) ((E-TS1-Z-TS1)	(E-TS1-E-1am)	(Z-TS1-Z-1am)	(E-TS2-E-2am)	(Z-TS2-Z-2am)
M062X ^(a,b)	-1.6	-1.4	12.6	12.5	25.5	22.8
B3LYP ^(b,c)	-1.9	-1.7	7.3	7.1	61.6	59.1
B3PW91 ^(b,c)	-1.8	-2.0	6.3	6.6	59.8	56.4
BP86 ^(b,c)	-1.8	-2.1	1.2	1.5	66.1	62.5
PBE1PBE ^(b,c)	-2.0	-1.9	7.5	7.4	59.3	56.6
$\omega B97 XD^{(b,d)}$	-1.8	-1.8	12.5	12.5	42.5	39.0
def2-TZVP ^(e)	-1.8	-1.4	15.9	15.5	35.5	33.0
def2-TZVPD ^(e)	-1.8	-1.4	16.0	15.6	60.4	57.8
def2-07VPD(e)	-1.8	-	-	-	_	-

(a) Level employed for geometry optimization (b) 6-311+g(d,p) basis set (c) Complemented with Grimme's dispersion D3 with Becke-Johnson damping (GD3BJ) (d) This functional has a built-in version of Grimme's dispersion D2 (e) With M062X functional

Table S12: Relevant energies differences from single point calculations using several levels of theory for the DBU-catalyzed reaction. Geometries optimized at M062X/6-311+g(d,p) level of theory. Energies reported in kcal/mol.

Level of Theory	(Z-TS5-3a)	(Z-TS6-4)	(Z-TS7-5b)	(TS8-6)
M062X ^(a,b)	4.5	-0.1	13.4	4.0
B3LYP ^(b,c)	0.2	-1.2	9.7	0.8
B3PW91 ^(b,c)	0.0	-2.5	7.5	1.6
BP86 ^(b,c)	-4.3	-2.8	3.6	-0.4
PBE1PBE ^(b,c)	0.6	-2.1	8.2	2.7
$\omega B97 XD^{(b,d)}$	4.6	-0.5	10.7	2.4
def2-TZVP ^(e)	6.6	0.1	15.0	4.2
def2-TZVPD(e)	6.9	0.0	15.0	4.0

(a) Level employed for geometry optimization (b) 6-311+g(d,p) basis set (c) Complemented with Grimme's dispersion D3 with Becke-Johnson damping (GD3BJ) (d) This functional has a built-in version of Grimme's dispersion D2 (e) With M062X functional



Figure S15 – Intrinsic Reaction Coordinate for E-TS4.



Figure S16 – Intrinsic Reaction Coordinate for Z-TS4.



Figure S17 – Intrinsic Reaction Coordinate for Z-TS5.



Figure S18 – Intrinsic Reaction Coordinate for Z-TS6.



Figure S19 – Intrinsic Reaction Coordinate for Z-TS7.



Figure S20 – Intrinsic Reaction Coordinate for TS-8.



Figure S21 – Intrinsic Reaction Coordinate for Z-TS9.



Figure S22 – Intrinsic Reaction Coordinate for Z-TS5b.



Figure S23 – Intrinsic Reaction Coordinate for Z-TS5c.



Figure S24 – Intrinsic Reaction Coordinate for E-TS1.



Figure S25 – Intrinsic Reaction Coordinate for E-TS1 downhill.



Figure S26 – Intrinsic Reaction Coordinate for Z-TS1.



Figure S27 – Intrinsic Reaction Coordinate for E-TS2.



Figure S28 – Intrinsic Reaction Coordinate for Z-TS2.



Figure S29 – Intrinsic Reaction Coordinate for E-TS3.



Figure S30 – Intrinsic Reaction Coordinate for E-TS1b.



Figure S31 – Intrinsic Reaction Coordinate for E-TS1b downhill.



Figure S32 – Intrinsic Reaction Coordinate for E-TS1c.



Figure S33 – Intrinsic Reaction Coordinate for E-TS1c downhill.

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