Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics.

Supporting Information

Influence of water content on the [2σ+2σ+2π] cycloaddition of dimethyl azodicarboxylate with quadriayclane in mixed methanol-water solvents from QM/MM Monte Carlo simulations

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Content:

Part 1. The other figures

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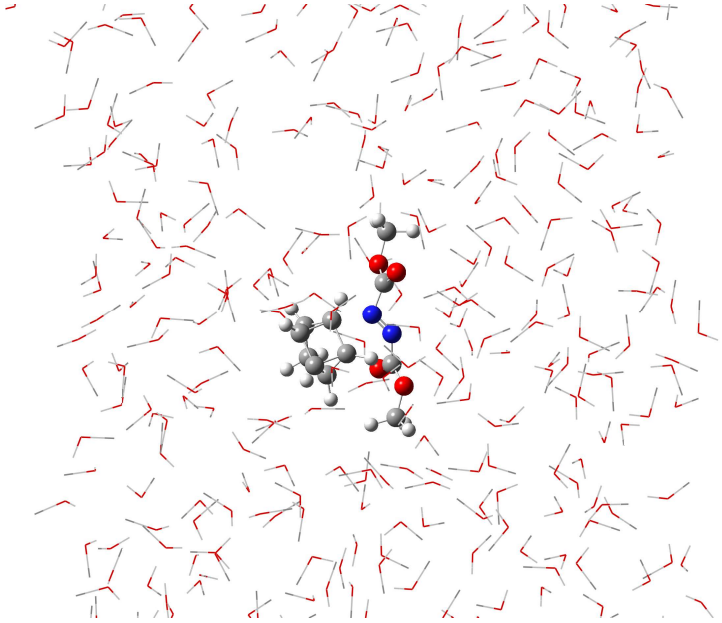

Fig. S1. Illustration MC configuration for the transition structure in methanol for the [2σ+2σ+2π] cycloaddition reaction between quadricyclane and dimethyl azodicarboxylate.

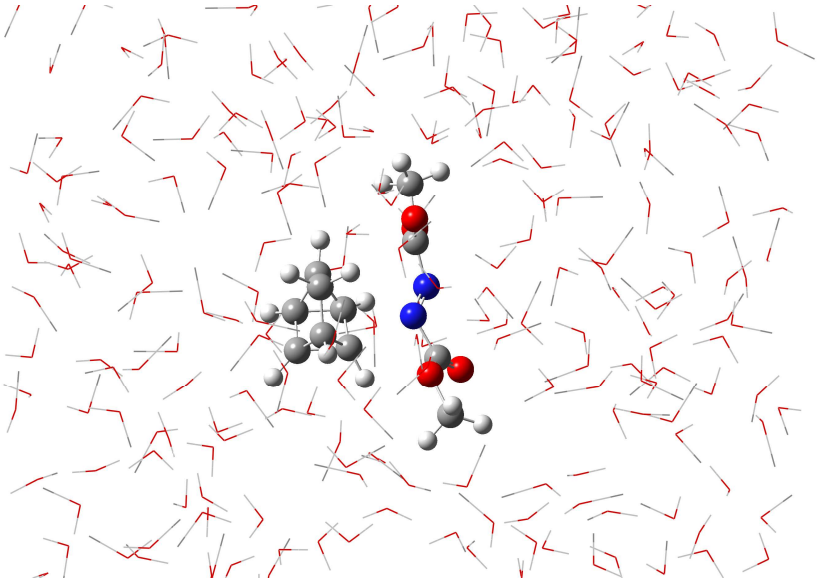

Fig. S2. Illustration MC configuration for the transition structure in methanol-water mixture (MeOH:H_2O=3:1) for the [2σ+2σ+2π] cycloaddition reaction between quadricyclane and dimethyl azodicarboxylate.

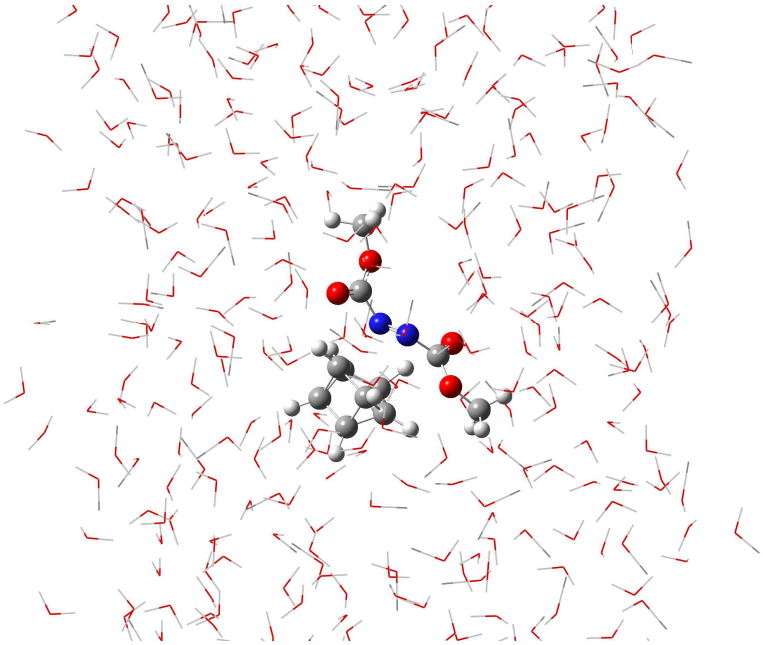

Fig. S3. Illustration MC configuration for the transition structure in methanol-water mixture (MeOH:H_2O=1:1) for the [2σ+2σ+2π] cycloaddition reaction between quadricyclane and dimethyl azodicarboxylate.

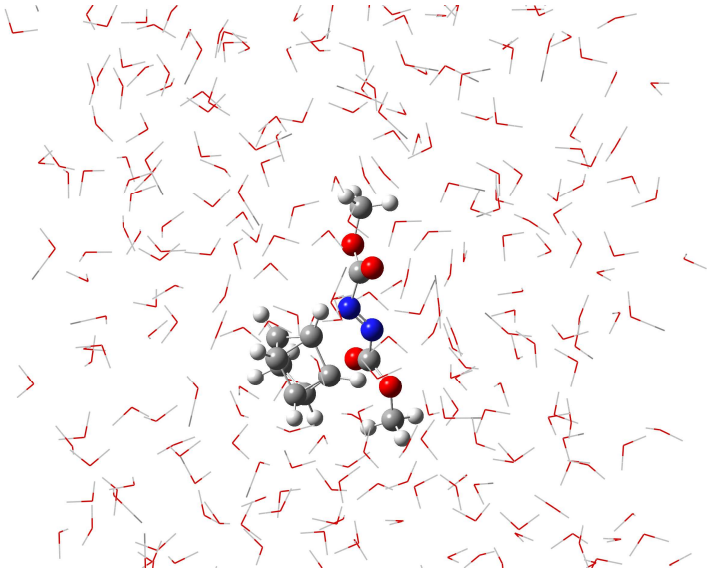

Fig. S4. Illustration MC configuration for the transition structure in methanol-water mixture (MeOH:H_2O=1:3) for the [2σ+2σ+2π] cycloaddition reaction between quadricyclane and dimethyl azodicarboxylate.

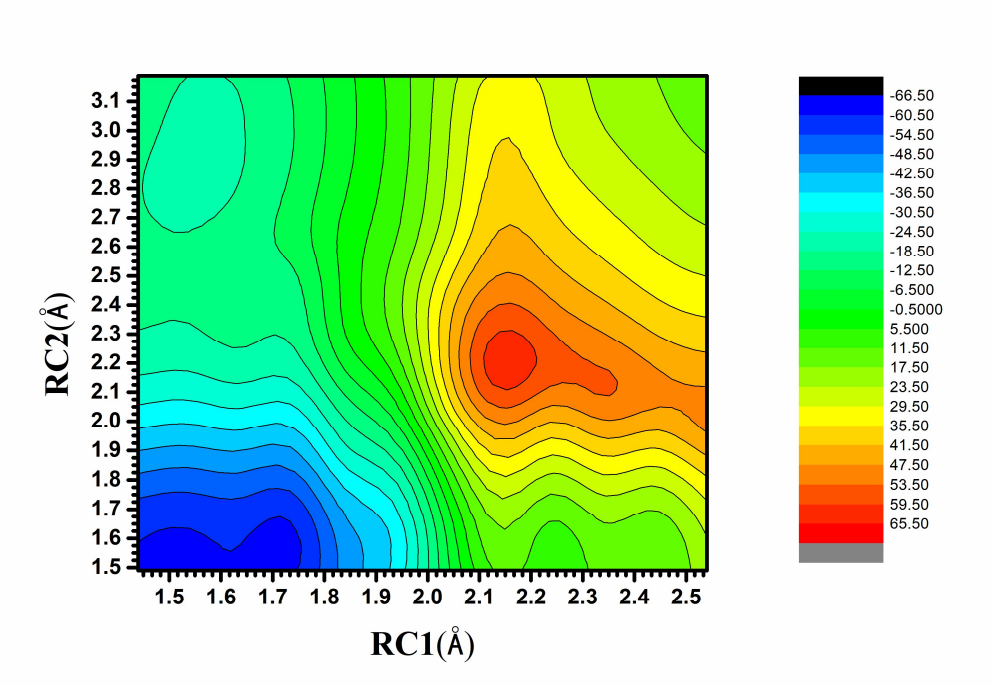

Fig. S5. Two-dimensional free energy map for the quadriayclane with dimethyl azodicarboxylate on the surface of the water slab in 0 °C and 1 atm. RC1 and RC2 are in Angstroms, and the free energies in the legend are relative to the product in kcal.mol^{-1}.

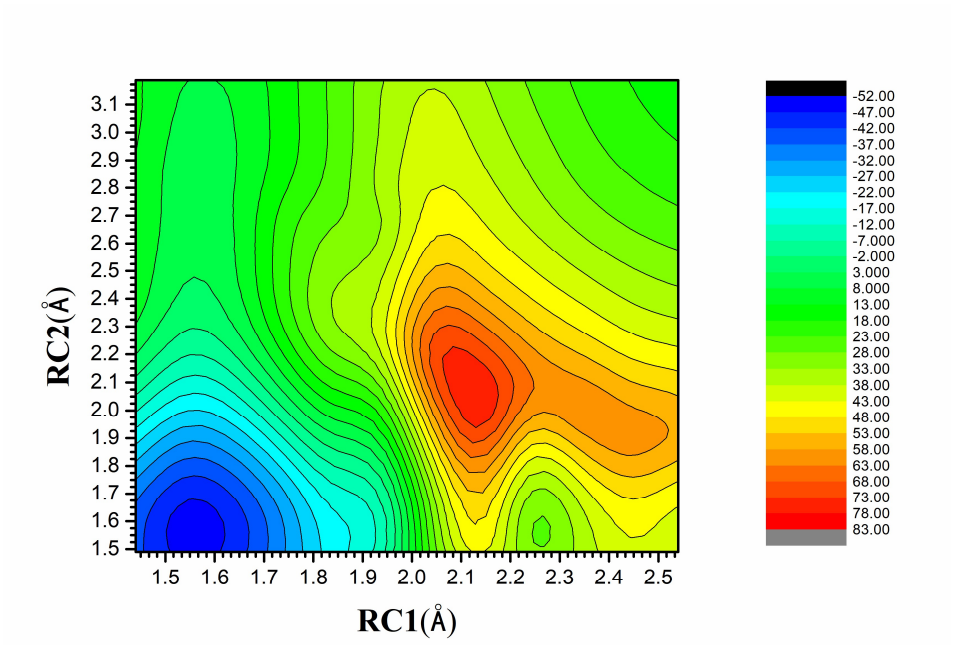

Fig. S6. Two-dimensional free energy map for the quadriayclane with dimethyl azodicarboxylate in methanol at 23 °C and 1 atm. RC1 and RC2 are in Angstroms, and the free energies in the legend are relative to the product in kcal.mol^{-1}.

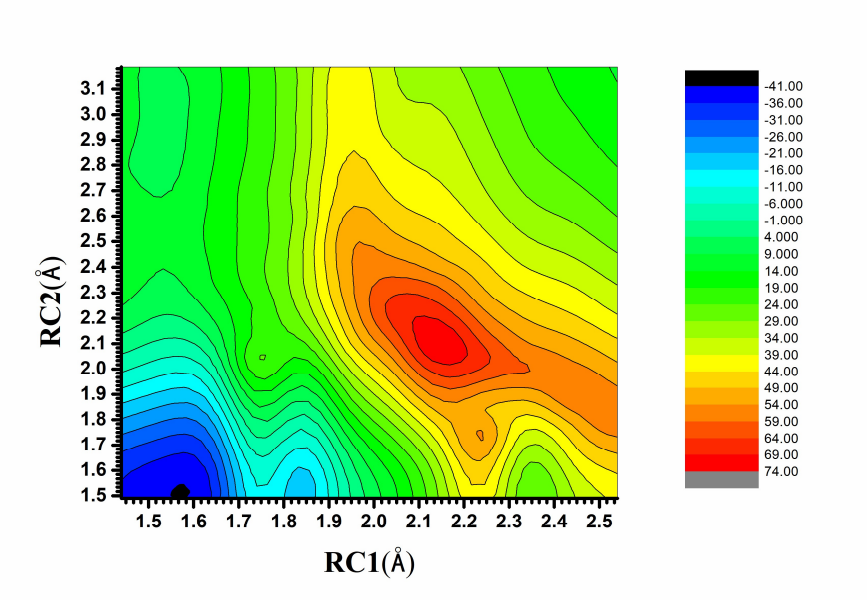

Fig. S7. Two-dimensional free energy map for the quadriayclane with dimethyl azodicarboxylate in methanol-water mixtures (MeOH:H_2O=3:1) at 23 °C and 1 atm. RC1 and RC2 are in Angstroms, and the free energies in the legend are relative to the product in kcal.mol^{-1}.

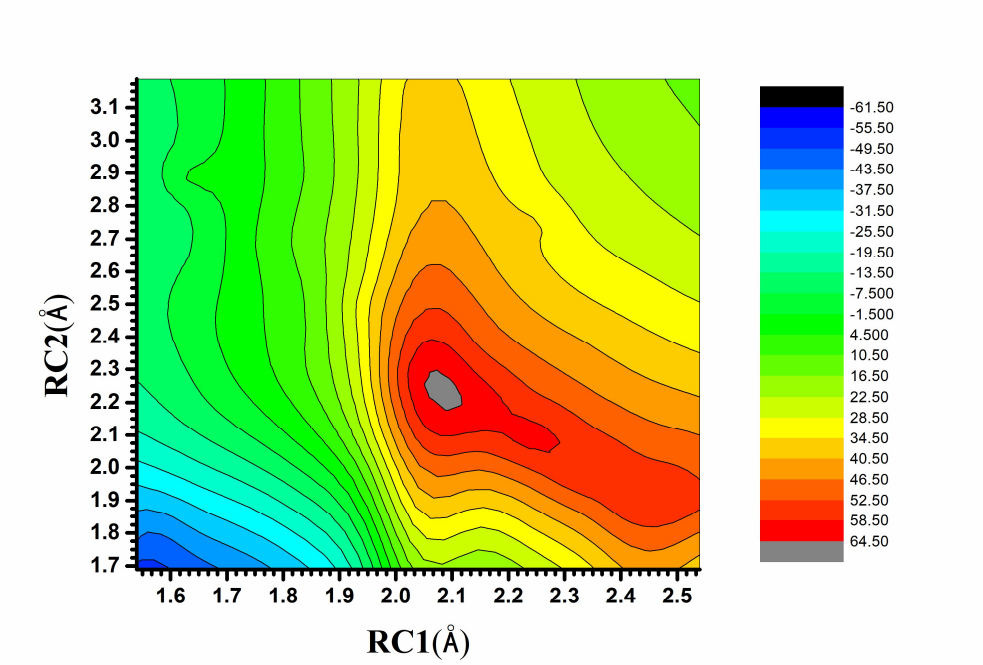

Fig. S8. Two-dimensional free energy map for the quadriayclane with dimethyl azodicarboxylate in methanol-water mixtures (MeOH:H_2O=1:1) at 23 °C and 1 atm. RC1 and RC2 are in Angstroms, and the free energies in the legend are relative to the product in kcal.mol^{-1}.

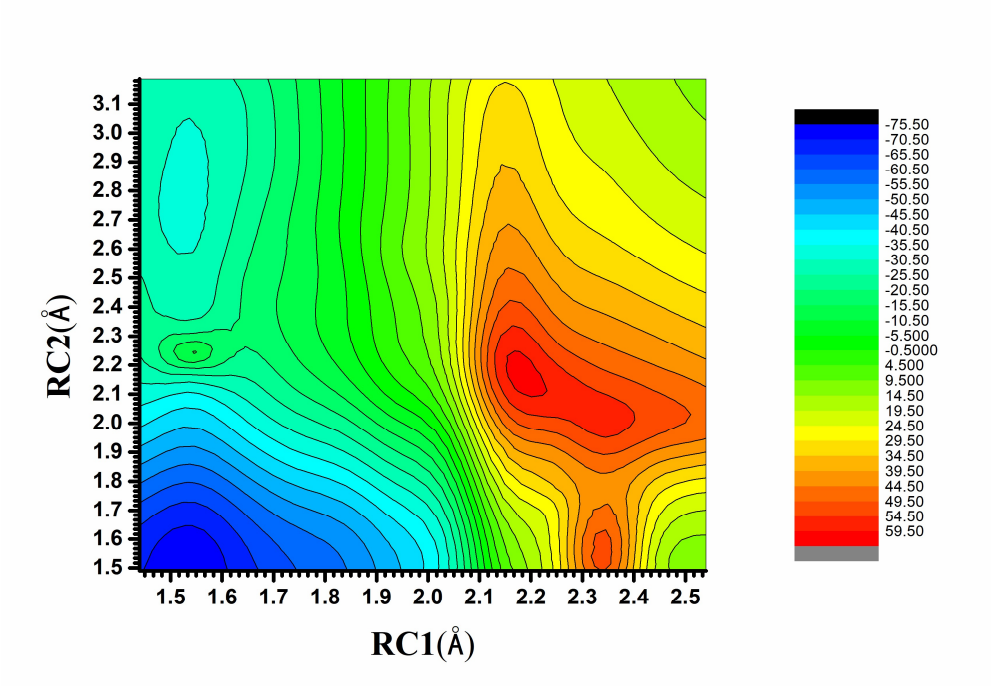

Fig. S9. Two-dimensional free energy map for the quadriayclane with dimethyl azodicarboxylate in methanol-water mixtures (MeOH:H_2O=1:3) at 23 °C and 1 atm. RC1 and RC2 are in Angstroms, and the free energies in the legend are relative to the product in kcal.mol^{-1}.

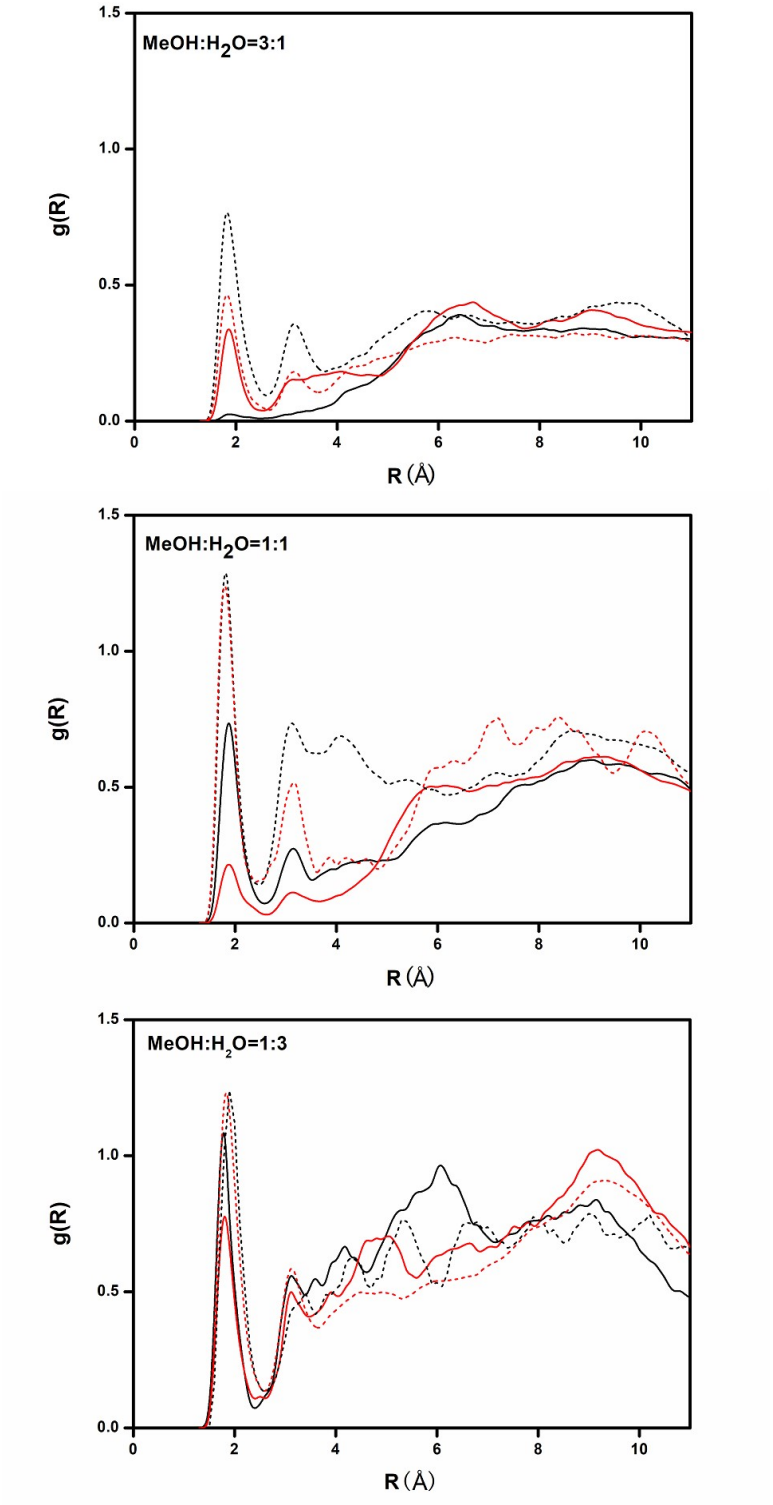

Fig. S10. Computed O (in C=O of dimethyl azodicarboxylate)-H(solvent) radial distribution functions for the reaction of **1** an **2**: 7O atom in transition structure (dash black), 7O atom in reactant (solid black), 4O atom in transition structure (dash red), and 4O atom in reactant (solid red) at 23 ^{o}C and 1 atm.

Part 2. Reaction mechanism and solvent effects studied by DFT calculations

2.1 Computational details

The density functional theory (DFT) B3LYP [1,2] method with the 6-31+G(d,p) basis set was used to characterize the ground state structures and the transition state structures in the solvent phases by Gaussian 09 program.[3] The harmonic frequencies were computed at the same level of theory as that used in geometry optimizations to identify all stationary points as minima with zero imaginary frequency or transitions states with only one imaginary frequency and derive the thermochemical corrections at a temperature of 296.15 K (23 ^{o}C) or 273.15 K (0 ^{o}C) and pressure of 1 atm. The energy profiles connecting transition structures to the two associated minima were checked by the intrinsic reaction coordinate (IRC).[4] The solvent effects in two pure solvents (water and methanol) were simulated by the self-consistent reaction field (SCRF) based on the solvation SMD polarizable continuum model.[5,6] What's more, the single-point energy calculations were performed at the M06-2X/SMD/6-311++G(d,p) level by using the B3LYP/SMD/6-31+G(d,p) optimized structures.

2.2 Discussion

The reaction mechanism for the [2σ+2σ+2π] cycloaddition reaction between quadriayclane and dimethyl azodicarboxylate in two different solvents (water and methanol) were simulated by using the DFT method. The free energy profile and the stationary point structures of the reaction in water are depicted in **Fig. S11**. The bond lengths of RC1 and RC2 are 2.24 and 2.78 Å in water, respectively. According to the geometric changes along the IRC, the two new bonds are formed in an asynchronous manner that the RC1 attack occurs first, and followed by the RC2. Consequently, the reaction occurs through a collaborative asynchronous mechanism, and the RC1 forming is obviously more prior than the forming of RC2. The computed results also show the reaction in methanol has the same

one–step mechanism as in water. The bond lengths of RC1 and RC2 for transition state in methanol are 2.22 and 2.77 Å, respectively. The free energy barriers of activation , $\Delta G^{\neq}$, for the reaction in different solvents are listed in **Table S1**.

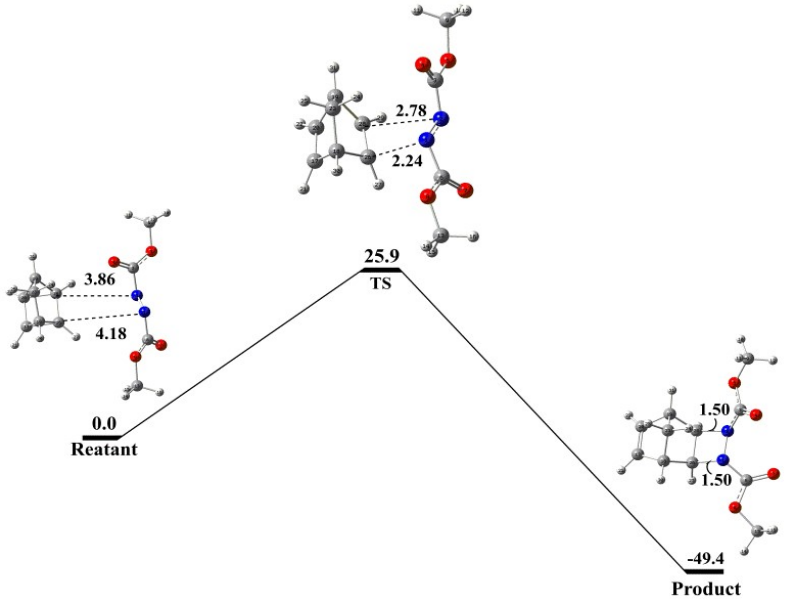

Fig. S11. Free energy profile for [2σ+2σ+2π] cycloaddition reaction of quadricyclane with dimethyl azodicarboxylate in water. Energies are given in kcal mol^{-1} and the bond lengths in Å.

Table S1. Free energies of activation, $\Delta G^{\neq}$（kcal.mol^{-1}), for the [2σ+2σ+2π] cycloaddition reaction of **1** with **2** in solution phases.

solvent	SMD [a]	Time to completion[b]
CH_3OH	25.2	18 h
CH_3OH/H_2O (3:1)	—	4 h
CH_3OH/H_2O (1:1)	—	10 min
CH_3OH/H_2O (1:3)	—	10 min
H_2O (T=23 ℃)	25.9	10 min
H_2O (T=0 ℃)	24.8	1.5 h

a: Obtained by using the M06-2X/SMD/6-311++G(d,p)// B3LYP/SMD/6-31+G(d,p) method.

b: The experimental results are taken from Reference 7.

One can see from **Table S1** that the $\Delta G^{\neq}$ values have the order of 25.9 (in H_2O (T=23℃)) > 25.2 (in CH_3OH) > 24.8 kcal/mol (in H_2O (T=0 ℃)). There is no doubt that this order of activation free energy is disagreed with the change trend of reaction rate observed in the experiment,[7] where the reaction time at the same reaction progress in the different

solvent conditions has the sequence of "in CH_3OH" > "on H_2O (T=0 ℃)" > "on H_2O (T=23℃)". This indicates that the DFT calculations using the implicit SMD model are unsuited to reproduce the experimental rate trend of the [2σ+2σ+2π] cycloaddition reaction between quadriayclane and dimethyl azodicarboxylate in water and CH_3OH. In fact, some investigations using the DFT methods and the polarizable continuum solvation models also failed to represent the accurate sequence of rates of reactions for the 1,3-dipolar cycloadditions,[8] Claisen rearrangements,[9] the uncatalyzed aldol reaction,[10] and the allyl *p*-tolyl ether rearrangement[11] in solutions. Thus, it should be realized that the continuum treatment of the solvent effects could not reflect the specific changes of hydrogen bond interactions between molecules of reaction system and solvents along the reaction pathway, which are important to the reaction under an "on water" environment. Therefore, the QM/MM/MC simulations were performed for the title reaction under the different solution conditions: on water, in CH_3OH, and in the mixed methanol-water solvents with three proportions to gain the detailed and explicit solvent representation.

1.3 References

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Rendell, J.C. Burant, S.S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J.M. Millam, M. Klene, J.E. Knox, J.B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R.E. Stratmann, O. Yazyev, A.J. Austin, R. Cammi, C. Pomelli, J.W. Ochterski, R.L. Martin, K. Morokuma, V.G. Zakrzewski, G.A. Voth, P. Salvador, J.J. Dannenberg, S. Dapprich, A.D. Daniels, O. Farkas, J.B. Foresman, J.V. Ortiz, J. Cioslowski, D.J. Fox, *Gaussian 09, Revision D.01*, Gaussian, Wallingford CT, 2010.

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Part 3. Cartesian coordinates of all stationary points optimized in condensed-phases at the B3LYP/SMD/6-31+G(d,p) level

in water

Quadricyclane(QDC)

at 23 °C

Sum of electronic and zero-point Energies= -271.340539
Sum of electronic and thermal Energies= -271.335949
Sum of electronic and thermal Enthalpies= -271.335011
Sum of electronic and thermal Free Energies= -271.368218

at 0 °C

Sum of electronic and zero-point Energies= -271.340539
Sum of electronic and thermal Energies= -271.336645
Sum of electronic and thermal Enthalpies= -271.335780
Sum of electronic and thermal Free Energies= -271.365671

C	-0.77567	0.71043	0.75923
C	-1.15454	-0.55156	-0.00004
C	1.15426	-0.55199	0.00011
C	0.77585	0.71004	0.75937
H	-1.42816	1.23311	1.44912
H	1.42867	1.23284	1.44884
C	-0.00038	-1.54016	0.00003
H	-0.00023	-2.18064	-0.89070
H	-0.0006	-2.18146	0.89015
C	-0.77554	0.71036	-0.75938
H	-1.42793	1.23312	-1.44930
C	0.77602	0.70997	-0.75927
H	1.42882	1.23249	-1.44897
H	-2.19085	-0.87523	0.00029
H	2.19023	-0.87676	0.00029

Dimethyl azodicarboxylate(DMAD)

at 23 °C

Sum of electronic and zero-point Energies= -566.310069
Sum of electronic and thermal Energies= -566.299246
Sum of electronic and thermal Enthalpies= -566.298308
Sum of electronic and thermal Free Energies= -566.348450

at 0 °C

Sum of electronic and zero-point Energies= -566.310069
Sum of electronic and thermal Energies= -566.300510
Sum of electronic and thermal Enthalpies= -566.299645
Sum of electronic and thermal Free Energies= -566.344609

N	-0.42172	0.03754	0.65557
N	0.35122	0.03719	-0.3155
C	1.72321	-0.28367	0.08167
O	2.01332	-1.1667	0.86072
O	2.53544	0.49171	-0.60806
C	-1.78433	0.36016	0.28547
O	-2.24971	1.44639	0.56361
O	-2.38365	-0.67223	-0.26761
C	3.96421	0.31224	-0.37721
H	4.44549	1.03429	-1.03311
H	4.19281	0.52093	0.66889
H	4.24612	-0.70776	-0.64251
C	-3.79637	-0.50687	-0.60587
H	-4.09342	-1.46443	-1.02774
H	-4.36293	-0.28447	0.29929
H	-3.8981	0.29396	-1.33913

Transition state

at 23 ℃

Sum of electronic and zero-point Energies= -837.631547

Sum of electronic and thermal Energies= -837.615495

Sum of electronic and thermal Enthalpies= -837.614557

Sum of electronic and thermal Free Energies= -837.675802

at 0 ℃

Sum of electronic and zero-point Energies= -837.631547

Sum of electronic and thermal Energies= -837.617612

Sum of electronic and thermal Enthalpies= -837.616747

Sum of electronic and thermal Free Energies= -837.671134

N	-0.5288	-0.93603	0.31952
N	0.4611	-1.37692	-0.41382
C	1.68961	-1.27991	0.24643
O	1.91099	-0.98633	1.42148
O	2.6668	-1.65324	-0.61324
C	-1.78788	-1.3721	-0.18085
O	-1.99837	-2.06508	-1.16883
O	-2.74733	-0.9616	0.66372
C	4.00558	-1.71342	-0.07523
H	4.6303	-2.05864	-0.89829
H	4.32971	-0.72398	0.25571
H	4.04893	-2.42027	0.75671
C	-4.10344	-1.33534	0.3241
H	-4.72323	-0.90092	1.10711
H	-4.37589	-0.92349	-0.65002

H	-4.20422	-2.42263	0.31741
C	-0.84127	2.94129	-0.47464
C	-0.90296	2.08426	0.72013
C	1.32321	2.13966	0.08947
C	0.55831	2.91573	-0.96146
H	-1.6861	3.39842	-0.97387
H	0.97426	3.53953	-1.74024
C	0.48431	2.11555	1.36676
H	0.67543	1.23564	1.98242
H	0.62157	3.02158	1.96481
C	-0.79521	1.13882	-0.47121
H	-1.61935	0.86858	-1.11745
C	0.61703	1.34678	-0.97948
H	1.07312	0.79244	-1.78885
H	-1.81686	2.04498	1.30314
H	2.40579	2.18159	0.09229

Product

at 23 ℃

Sum of electronic and zero-point Energies= -837.742846

Sum of electronic and thermal Energies= -837.727879

Sum of electronic and thermal Enthalpies= -837.726941

Sum of electronic and thermal Free Energies= -837.784989

at 0 ℃

Sum of electronic and zero-point Energies= -837.742846

Sum of electronic and thermal Energies= -837.729903

Sum of electronic and thermal Enthalpies= -837.729038

Sum of electronic and thermal Free Energies= -837.780566

N	-0.86782	-0.08938	0.12526
N	0.26752	-0.66578	-0.5433
C	0.96785	-1.67745	0.07806
O	0.51514	-2.3975	0.96359
O	2.18365	-1.80922	-0.47872
C	-2.10943	-0.6484	-0.11171
O	-2.2982	-1.81367	-0.44621
O	-3.07634	0.24729	0.14757
C	3.01025	-2.88343	0.03582
H	3.93478	-2.82654	-0.53673
H	3.20877	-2.72705	1.09781
H	2.52096	-3.84587	-0.12551
C	-4.43979	-0.22941	0.02019
H	-5.06312	0.63299	0.25147
H	-4.62315	-0.57148	-0.99999

H	-4.62406	-1.03557	0.73287
C	0.77068	3.32825	-0.01743
C	0.08258	2.23063	0.79229
C	1.94723	1.32866	-0.14089
C	1.87237	2.79329	-0.57225
H	0.36523	4.32092	-0.18119
H	2.5461	3.25941	-1.28317
C	1.31745	1.42861	1.27129
H	1.07448	0.46733	1.73237
H	1.94268	2.004	1.95778
C	-0.48285	1.2979	-0.3119
H	-1.23008	1.75239	-0.9595
C	0.79194	0.68254	-0.96129
H	0.91771	0.74599	-2.0404
H	-0.64698	2.54765	1.53781
H	2.91508	0.83959	-0.24018

in methanol at 23 ℃

Quadricyclane(QDC)

Sum of electronic and zero-point Energies= -271.347081
Sum of electronic and thermal Energies= -271.342482
Sum of electronic and thermal Enthalpies= -271.341544
Sum of electronic and thermal Free Energies= -271.374767

C	-0.77567	-0.71043	-0.75923
C	-1.15454	0.55156	0.00004
C	1.15427	0.55199	-0.00011
C	0.77584	-0.71004	-0.75937
H	-1.42817	-1.2331	-1.44912
H	1.42866	-1.23285	-1.44884
C	-0.00037	1.54016	-0.00003
H	-0.00022	2.18064	0.8907
H	-0.00059	2.18146	-0.89015
C	-0.77555	-0.71035	0.75938
H	-1.42794	-1.23312	1.4493
C	0.77602	-0.70997	0.75927
H	1.42882	-1.2325	1.44897
H	-2.19084	0.87524	-0.00029
H	2.19024	0.87675	-0.00029

Dimethyl azodicarboxylate(DMAD)

Sum of electronic and zero-point Energies= -566.306828
Sum of electronic and thermal Energies= -566.296090
Sum of electronic and thermal Enthalpies= -566.295153

Sum of electronic and thermal Free Energies= -566.344818

N	-0.42398	0.03141	0.65706
N	0.35196	0.04365	-0.31068
C	1.7233	-0.27999	0.08738
O	2.0122	-1.15543	0.87405
O	2.53444	0.48648	-0.61108
C	-1.7848	0.35854	0.28614
O	-2.24909	1.44312	0.5686
O	-2.38233	-0.67031	-0.27241
C	3.96356	0.30689	-0.38827
H	4.44171	1.02446	-1.05224
H	4.20056	0.52215	0.65516
H	4.24404	-0.71525	-0.64919
C	-3.79424	-0.50705	-0.61234
H	-4.09467	-1.47165	-1.01687
H	-4.36133	-0.26699	0.28855
H	-3.89477	0.28062	-1.36079

Transition state

Sum of electronic and zero-point Energies= -837.634641
Sum of electronic and thermal Energies= -837.618529
Sum of electronic and thermal Enthalpies= -837.617591
Sum of electronic and thermal Free Energies= -837.679458

N	-0.52944	-0.91827	0.30715
N	0.4612	-1.36194	-0.42292
C	1.68677	-1.28152	0.24524
O	1.90028	-1.01816	1.42804
O	2.6666	-1.63038	-0.61685
C	-1.78715	-1.36941	-0.18438
O	-1.99261	-2.08524	-1.1554
O	-2.74687	-0.94393	0.64915
C	4.00232	-1.70927	-0.0748
H	4.63454	-2.00517	-0.91201
H	4.3178	-0.73677	0.31142
H	4.04585	-2.46026	0.71827
C	-4.10163	-1.33205	0.32365
H	-4.72111	-0.8818	1.09872
H	-4.3813	-0.94585	-0.65956
H	-4.19827	-2.42008	0.34349
C	-0.83425	2.94673	-0.46786
C	-0.90541	2.07878	0.71801

C	1.32397	2.12892	0.09854
C	0.56738	2.91792	-0.94938
H	-1.67512	3.41117	-0.96801
H	0.9904	3.54884	-1.71915
C	0.47874	2.09494	1.37186
H	0.65995	1.20524	1.97719
H	0.61916	2.99272	1.98243
C	-0.79553	1.14022	-0.4789
H	-1.61833	0.87813	-1.13084
C	0.61887	1.35062	-0.98233
H	1.07548	0.79852	-1.79349
H	-1.82214	2.03726	1.29714
H	2.40712	2.16584	0.10737

Product

Sum of electronic and zero-point Energies=	-837.746896
Sum of electronic and thermal Energies=	-837.731841
Sum of electronic and thermal Enthalpies=	-837.730904
Sum of electronic and thermal Free Energies=	-837.789443

N	-0.86432	-0.07197	0.12595
N	0.2724	-0.65853	-0.52203
C	0.95166	-1.68589	0.09189
O	0.48666	-2.39973	0.97489
O	2.16308	-1.83699	-0.46781
C	-2.10396	-0.63294	-0.11719
O	-2.28748	-1.79363	-0.46549
O	-3.07128	0.25659	0.15131
C	2.96263	-2.94323	0.01889
H	3.88942	-2.89403	-0.55171
H	3.1655	-2.82202	1.08508
H	2.45085	-3.88974	-0.1681
C	-4.4344	-0.21787	0.01938
H	-5.05745	0.6436	0.25735
H	-4.61921	-0.55231	-1.00361
H	-4.62052	-1.02955	0.72604
C	0.79651	3.33444	-0.03744
C	0.0879	2.25154	0.77494
C	1.95881	1.32449	-0.12171
C	1.90212	2.78481	-0.56961
H	0.40167	4.32884	-0.21864
H	2.58999	3.23837	-1.27582
C	1.30882	1.44452	1.28019
H	1.04948	0.49034	1.748

H	1.92895	2.0217	1.97049
C	-0.47037	1.30881	-0.32482
H	-1.20967	1.75727	-0.98662
C	0.81024	0.677	-0.9525
H	0.9513	0.72709	-2.03119
H	-0.64898	2.58346	1.50724
H	2.9245	0.82646	-0.20132