

Supplementary Information

Understanding the stereoselectivity in Brønsted acid catalysed Povarov reactions generating *cis/trans* CF₃-substituted tetrahydroquinolines: a DFT study

Luis R. Domingo,^{*a} Mar Ríos-Gutiérrez^a and Saeedreza Emamian^b

^a *Department of Organic Chemistry, University of Valencia, Dr. Moliner 50, E-46100
Burjassot, Valencia, Spain.*

^b *Chemistry Department, Shahrood Branch, Islamic Azad University, Shahrood, Iran.*

e-mail: domingo@utopia.uv.es

web: www.luisrdomingo.com

Index

- S2** **Table S1.** M06-2X/6-31G(d) total and relative energies, in gas phase and in DCE, of the stationary points involved in the Povarov reaction between protonated imine **8:H** and VPO **9a**.
- S3** **Table S2.** M06-2X/6-31G(d) enthalpies, entropies and Gibbs free energies, and the relative ones, computed at 298 K and 1 atm in DCE, of the stationary points involved in the Povarov reaction between protonated imine **8:H** and VPO **9a**.
- S4** **Table S3.** M06-2x/6-31G(d) and B3LYP/6-31G(d) total and relative energies of the stereoisomeric TSs associated with the nucleophilic attack of ER ethylenes **9a** and **9b** on protonated imine **8:H**.
- S5** **Figure S1.** M06-2X/6-31G(d) and B3LYP/6-31(d) optimised geometries of the TSs involved in the Povarov reaction of protonated imine **8:H** with ATMS **9b**.
- S6** Theoretical background of NCI analysis.

Table S1. M06-2X/6-31G(d) total (E, in a.u.) and relative^{a, b} (ΔE , in kcal·mol⁻¹) energies, in gas phase and in DCE, of the stationary points involved in the Povarov reaction between protonated imine **8:H** and VPO **9a**.

	<i>Gas phase</i>		<i>Solvent</i>	
	E	ΔE	E	ΔE
8:H	-893.811209		-893.879383	
9a	-363.867846		-363.874647	
MC1n	-1257.701296	-14.0	-1257.766671	-7.9
MC1x	-1257.701283	-13.9	-1257.763900	-6.2
TS1n	-1257.694824	-9.9	-1257.758843	-3.0
TS1x	-1257.691422	-7.8	-1257.755831	-1.1
IN1n	-1257.712118	-20.7	-1257.778102	-15.1
IN1x	-1257.701992	-14.4	-1257.771074	-10.7
TS2n	-1257.710186	-19.5	-1257.774445	-12.8
TS2x	-1257.700278	-13.3	-1257.764540	-6.6
IN2n	-1257.717934	-24.4	-1257.785989	-20.1
IN2x	-1257.717060	-23.8	-1257.784633	-19.2
MC2n	-3084.667577		-3084.691966	
MC2x	-3084.655866		-3084.666075	
TS3n	-3084.656458	7.0 ^b	-3084.680196	7.4 ^b
TS3x	-3084.646881	5.6 ^b	-3084.666075	10.9 ^b
<i>cis</i> - 10a	-3084.689771	-13.9 ^b	-3084.705065	-8.2 ^b
<i>trans</i> - 10a	-3084.693610	-23.7 ^b	-3084.707518	-15.1 ^b

^a Relative to protonated imine **8:H** and VPO **9a**.

^b Relative to the corresponding molecular complex **MC2n** or **MC2x**.

Table S2. M06-2X/6-31G(d) enthalpies (H, in a.u.), entropies (S, in cal·mol⁻¹·K⁻¹) and Gibbs free energies (G, in a.u.), and the relative^{a, b} ones (ΔH in kcal·mol⁻¹, ΔS in cal·mol⁻¹·K⁻¹ and ΔG in kcal·mol⁻¹), computed at 298 K and 1 atm in DCE, of the stationary points involved in the Povarov reaction between protonated imine **8:H** and VPO **9a**.

	H	ΔH	S	ΔS	G	ΔG
8:H	-893.638977		126.6		-893.699124	
9a	-363.720205		84.6		-363.760423	
MC1n	-1257.369442	-6.4	169.8	-41.4	-1257.450125	5.9
MC1x	-1257.366860	-4.8	180.4	-30.8	-1257.452594	4.4
TS1n	-1257.364342	-3.2	160.6	-50.7	-1257.440634	11.9
TS1x	-1257.360533	-0.8	158.3	-52.9	-1257.435763	14.9
IN1n	-1257.381562	-14.0	155.4	-55.9	-1257.455379	2.6
IN1x	-1257.374230	-9.4	160.5	-50.7	-1257.450493	5.7
TS2n	-1257.377043	-11.2	152.3	-59.0	-1257.449391	6.4
TS2x	-1257.368153	-5.6	151.8	-59.5	-1257.440256	12.1
IN2n	-1257.386802	-17.3	158.8	-52.4	-1257.462263	-1.7
IN2x	-1257.385320	-16.4	161.4	-49.8	-1257.462002	-1.5
MC2n	-3084.220492		230.5		-3084.330025	
MC2x	-3084.210838		231.5		-3084.320810	
TS3n	-3084.213197	4.6 ^b	238.0	7.5 ^b	-3084.326294	2.3 ^b
TS3x	-3084.198998	7.4 ^b	227.2	-4.3 ^b	-3084.306945	8.7 ^b
<i>cis</i> - 10a	-3084.233720	-8.3 ^b	239.9	9.4 ^b	-3084.347704	-11.1 ^b
<i>trans</i> - 10a	-3084.235202	-15.3 ^b	231.9	0.4 ^b	-3084.345366	-15.4 ^b

^a Relative to protonated imine **8:H** and VPO **9a**.

^b Relative to the corresponding molecular complex **MC2n** or **MC2x**.

Table S3. M06-2X/6-31G(d) and B3LYP/6-31G(d) total (E, in a.u.) and relative (ΔE , in kcal·mol⁻¹) energies of the stereoisomeric TSs associated with the nucleophilic attack of ER ethylenes **9a** and **9b** on protonated imine **8**:H.

	M06-2X/6-31G(d)		B3LYP/6-31G(d)	
	E	ΔE	E	ΔE
TS1n	-1257.694824	0.0	-1258.197913	0.0
TS1x	-1257.691422	2.1	-1258.196269	1.3
TS1n-Si	-1420.221780	0.0	-1420.741061	0.0
TS1x-Si	-1420.221201	0.4	-1420.742513	-0.9

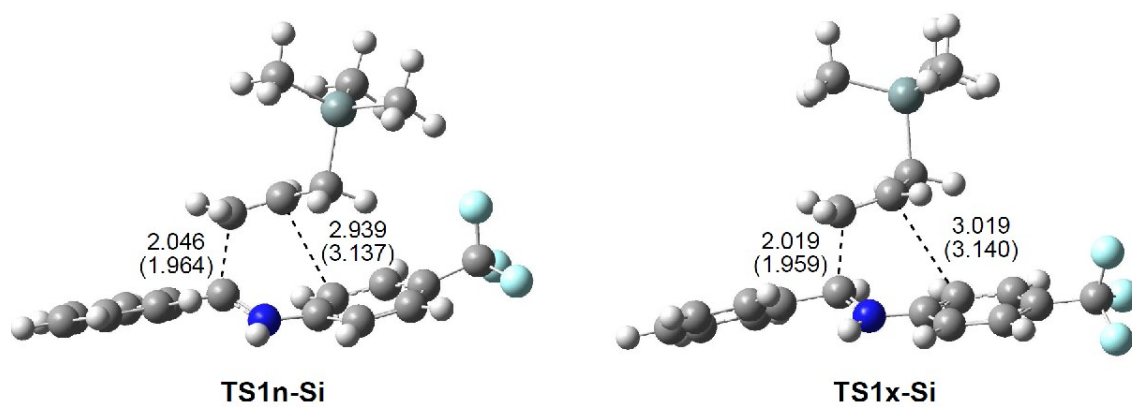


Figure S1. M06-2X/6-31G(d) optimized geometries of the TSs involved in the Povarov reaction of protonated imine **8:H** with ATMS **9b** including the lengths of the C4-C6 and C1-C5 forming bonds in Å. The B3LYP/6-31(d) lengths are given in parenthesis.

Theoretical background of NCI analysis

NCIs have a unique profile and their presence can be revealed solely by means of the electron-density analysis. They are highly non-local and manifest in real space as low-gradient isosurfaces with low densities. The sign of the Laplacian of the density, $\nabla^2\rho$, is a widely used tool to distinguish between different types of strong interactions. To analyse bonding in more detail, the Laplacian is often decomposed into a sum of contributions. These components are the three eigenvalues λ_i of the electron-density Hessian matrix, such that $\nabla^2\rho = \lambda_1 + \lambda_2 + \lambda_3$. Analysis of these components has been widely applied to chemical bonding. The sign of λ_2 can be used to distinguish bonded ($\lambda_2 < 0$) from non-bonded ($\lambda_2 > 0$) interactions. Analysis of the sign of λ_2 thus helps to differentiate between different types of NCIs, whereas the density itself provides information about their strength.

The gradient isosurfaces provide a useful visualisation of NCIs as broad regions of real space, rather than simple pairwise contacts between atoms, and are coloured according to the corresponding values of $\text{sign}(\lambda_2)\rho$. Surfaces with very low density values ($\rho < |0.005|$ a.u.) generally represent weaker dispersion interactions, while surfaces with slightly higher density values ($|0.005| < \rho < |0.05|$ a.u.) represent stronger NCIs, including both attractive HBs and steric clashes. Thus, large negative values of $\text{sign}(\lambda_2)\rho$ are indicative of attractive interactions (such as dipole-dipole or hydrogen bonding) and are coloured in blue, while if $\text{sign}(\lambda_2)\rho$ is large and positive, the interactions are non-bonding and are coloured in red; values near zero indicate very weak van der Waals interactions, and are coloured in green.

E. R. Johnson, S. Keinan, P. Mori-Sanchez, J. Contreras-Garcia, J. Cohen and A. W. Yang, *J. Am. Chem. Soc.*, 2010, **132**, 6498