

Capture of Benzotriazole-Based Mannich Electrophiles by *CH*-Acidic Compounds

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1. Generalities

1.1 Experimental

^1H NMR spectra were recorded at 300 MHz and ^{13}C NMR spectra were recorded at 75 MHz on Gemini or Varian spectrometers at room temperature. All solvents were dried according to standard procedures. All commercially available substrates were used as received without further purification.

1.2 Computational

Quantum chemical calculations were performed using the Gaussian 03 package of programs.¹ B3LYP method employing the 6-31+G** basis set with pure *d* functions and gradient techniques using internal coordinates and Newton-Raphson steps with extremely tight optimization convergence criteria were used for geometry optimization and computation of vibrational properties (under STP conditions). Activation and reaction parameters were calculated from the standard thermochemistry output. The PCM model was used to model THF. Electronic properties were studied using the standard NBO keyword.

2. Global electronic properties for iminium species 3a-e

The global electrophilicity (ω) was computed using the procedure introduced by Domingo.² The ω parameter is a measure of the capability of a molecule to accept electrons and allows a quantitative assessment of electrophiles within the unique electrophilicity scale defined by Parr^{4,5} in terms of two static global properties: chemical potential (μ) and chemical hardness (η) (Equation 1).

$$\omega = \frac{\mu^2}{\eta} \quad (1)$$

The chemical potential (μ) and chemical hardness (η) can be estimated from the one-electron energies of the frontier molecular orbitals HOMO and LUMO, ε_H and ε_L according to

Equations 2³ and 3:⁴

$$\mu \approx \frac{\varepsilon_H + \varepsilon_L}{2} \quad (2)$$

$$\eta \approx \varepsilon_L - \varepsilon_H \quad (3)$$

The global electrophilicity (ω) has been computed for iminium species **3a-e** (See Table S1).

Table S1. HOMO and LUMO energies, Chemical potential (μ), global hardness (η) and global electrophilicity (ω) for iminium species **3a-e**.

Iminium	HOMO (u.a.)	LUMO (u.a.)	μ (u.a.)	η (u.a.)	ω (eV)
3a	-0.54957	-0.27198	-0.4108	0.2776	8.3
3b	-0.52027	-0.2587	-0.3862	0.2470	8.2
3c	-0.50969	-0.26271	-0.3733	0.1276	14.9
3d	-0.47003	-0.25432	-0.3996	0.1353	16.1
3e	-0.4371	-0.30953	-0.4303	0.1629	15.5

3. Summary of the thermochemistry for compounds 1a-i and 2a,b

The thermochemistry for compounds **1a-i** and **2a,b** was computed at 298.15 K in gas phase and in THF and at 338.15 K in THF (See Figure S1). In Tables S2-4, 1N refers to the ¹N-isomer of benzotriazole, 2N refers to the ²N-isomer of benzotriazole, R1 refers to a benzotriazole substituted at position C₅ and R2 refers to a benzotriazole substituted at position C₆ (See Figure S1).

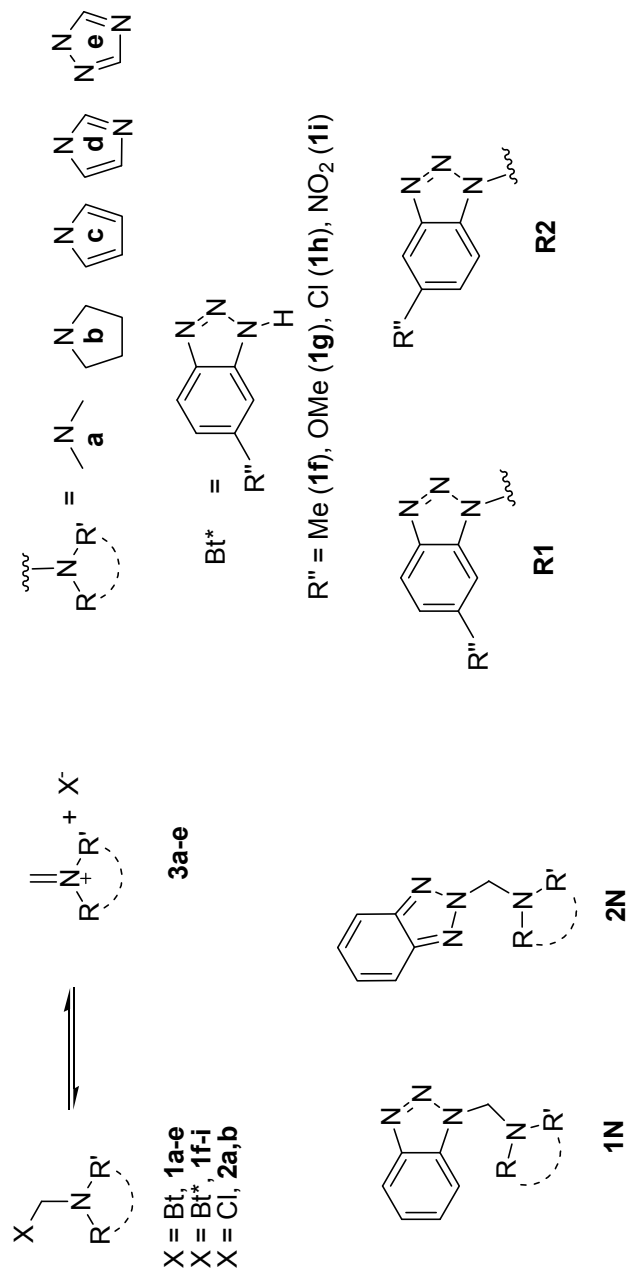


Figure S1. Summary of the structures computed (see Tables S2-S4).

Table S2. Thermochemistry computed at 298.15 K in gas phase

Cpds	Reactant (1a-i, and 2a,b)		Product (3a-e)		Product (X)		ΔG° kcal·mol ⁻¹	ΔH° kcal·mol ⁻¹
	G	H	G	H	G	H		
1a1N	-569.002725	-568.952521	-173.548834	-173.515254	-395.274882	-395.238226	112.3	124.9
1a2N	-569.001861	-568.951385	-173.548834	-173.515254	-395.274882	-395.238226	111.8	124.2
1b1N	-646.392085	-646.338773	-250.945748	-250.909682	-395.274882	-395.238226	107.6	119.8
1b2N	-646.394943	-646.34154	-250.945748	-250.909682	-395.274882	-395.238226	109.4	121.5
1c1N	-644.016462	-643.964387	-248.519088	-248.485391	-395.274882	-395.238226	139.6	151.1
1c2N	-644.017657	-643.96602	-248.519088	-248.485391	-395.274882	-395.238226	140.4	152.1
1d1N	-660.072928	-660.020928	-264.55451	-264.520872	-395.274882	-395.238226	152.8	164.3
1d2N	-660.074747	-660.023456	-264.55451	-264.520872	-395.274882	-395.238226	154.0	165.9
1e1N	-676.120775	-676.069949	-280.586287	-280.552978	-395.274882	-395.238226	162.9	174.9
1e2N	-676.119739	-676.068464	-280.586287	-280.552978	-395.274882	-395.238226	162.3	174.0
1fR1	-685.687563	-685.62993	-250.945748	-250.909682	-434.568457	-434.527569	110.9	119.1
1fR2	-685.687068	-685.629439	-250.945748	-250.909682	-434.568457	-434.527569	106.3	114.1
1gR1	-760.889489	-760.82996	-250.945748	-250.909682	-509.771154	-509.726954	108.8	120.9
1gR2	-760.887129	-760.82759	-250.945748	-250.909682	-509.771154	-509.726954	108.5	120.6
1hR1	-1105.99415	-1105.9374	-250.945748	-250.909682	-854.886056	-854.845901	108.3	121.3
1hR2	-1105.99354	-1105.93677	-250.945748	-250.909682	-854.886056	-854.845901	106.8	119.8
1iR1	-850.899147	-850.838857	-250.945748	-250.909682	-599.790485	-599.748672	101.9	114.1
1iR2	-850.899444	-850.839236	-250.945748	-250.909682	-599.790485	-599.748672	101.5	113.7
2a	-634.012014	-633.974186	-173.548834	-173.515254	-460.286486	-460.269103	102.2	113.3
2b	-711.401713	-711.360613	-250.945748	-250.909682	-460.286486	-460.269103	102.4	113.5

Table S3. Thermochemistry computed at 298.15 K in THF

Cpds	Reactant (1a-i, and 2a,b)		Product (3a-e)		Product (X)		ΔG° kcal·mol ⁻¹	ΔH° kcal·mol ⁻¹
	G Hartree	H Hartree	G Hartree	H Hartree	G Hartree	H Hartree		
1a1N	-569.011259	-568.961148	-173.624841	-173.59134	-395.351318	-395.314714	22.0	34.6
1a2N	-569.008684	-568.958446	-173.624841	-173.59134	-395.351318	-395.314714	20.4	32.9
1b1N	-646.400599	-646.347396	-251.017491	-250.981252	-395.351318	-395.314714	19.9	32.3
1b2N	-646.400752	-646.347517	-251.017491	-250.981252	-395.351318	-395.314714	20.0	32.3
1c1N	-644.025498	-643.974278	-248.592779	-248.559245	-395.351318	-395.314714	51.1	63.0
1c2N	-644.025235	-643.973685	-248.592779	-248.559245	-395.351318	-395.314714	50.9	62.6
1d1N	-660.085278	-660.034806	-264.635402	-264.602004	-395.351318	-395.314714	61.8	74.1
1d2N	-660.085627	-660.034506	-264.635402	-264.602004	-395.351318	-395.314714	62.1	73.9
1e1N	-676.133097	-676.082254	-280.669089	-280.635966	-395.351318	-395.314714	70.7	82.6
1e2N	-676.130544	-676.079811	-280.669089	-280.635966	-395.351318	-395.314714	69.1	81.0
1fR1	-685.696263	-685.638813	-251.017491	-250.981252	-434.645209	-434.604419	21.1	33.3
1fR2	-685.695664	-685.638258	-251.017491	-250.981252	-434.645209	-434.604419	20.7	33.0
1gR1	-760.899522	-760.84013	-251.017491	-250.981252	-509.848161	-509.803888	21.3	34.5
1gR2	-760.897545	-760.838272	-251.017491	-250.981252	-509.848161	-509.803888	20.0	33.3
1hR1	-1106.00238	-1105.94578	-251.017491	-250.981252	-854.957315	-854.917239	17.3	29.7
1hR2	-1106.0021	-1105.94549	-251.017491	-250.981252	-854.957315	-854.917239	17.1	29.5
1iR1	-850.91054	-850.850495	-251.017491	-250.981252	-599.860165	-599.818365	20.6	31.9
1rR2	-850.911635	-850.851617	-251.017491	-250.981252	-599.860165	-599.818365	21.3	32.6
2a	-634.02227	-633.982132	-173.624841	-173.59134	-460.382725	-460.365341	9.2	16.0
2b	-711.413535	-711.370878	-251.017491	-250.981252	-460.382725	-460.365341	8.4	15.2

Table S4. Thermochemistry computed at 338.15 K in THF

Cpds	Reactant (1a-i, and 2a,b)		Product (3a-e)		Product (X)		ΔG° kcal·mol ⁻¹	ΔH° kcal·mol ⁻¹
	G Hartree	H Hartree	G Hartree	H Hartree	G Hartree	H Hartree		
1a1N	-569.018204	-568.958027	-173.629419	-173.590026	-395.356335	-395.313021	20.4	34.5
1a2N	-569.015468	-568.955372	-173.629419	-173.590026	-395.356335	-395.313021	18.6	32.8
1b1N	-646.407951	-646.344	-251.022455	-250.979628	-395.356335	-395.313021	18.3	32.2
1b2N	-646.408107	-646.344129	-251.022455	-250.979628	-395.356335	-395.313021	18.4	32.3
1c1N	-644.032569	-643.971113	-248.597366	-248.557841	-395.356335	-395.313021	49.5	62.9
1c2N	-644.032349	-643.970526	-248.597366	-248.557841	-395.356335	-395.313021	49.4	62.5
1d1N	-660.092242	-660.031735	-264.639966	-264.600669	-395.356335	-395.313021	60.2	74.1
1d2N	-660.092678	-660.031442	-264.639966	-264.600669	-395.356335	-395.313021	60.5	73.9
1e1N	-676.140105	-676.079272	-280.67361	-280.634723	-395.356335	-395.313021	69.1	82.5
1e2N	-676.137536	-676.076839	-280.67361	-280.634723	-395.356335	-395.313021	67.5	81.0
1fR1	-685.70421	-685.635013	-251.022455	-250.979628	-434.650813	-434.602326	19.4	33.3
1fR2	-685.703605	-685.634458	-251.022455	-250.979628	-434.650813	-434.602326	19.0	32.9
1gR1	-760.907742	-760.836115	-251.022455	-250.979628	-509.854246	-509.801571	19.5	34.5
1gR2	-760.90575	-760.834258	-251.022455	-250.979628	-509.854246	-509.801571	18.2	33.3
1hR1	-1106.010196	-1105.942137	-251.022455	-250.979628	-854.962815	-854.915296	15.6	29.6
1hR2	-1106.009919	-1105.941848	-251.022455	-250.979628	-854.962815	-854.915296	15.5	29.4
1iR1	-850.918845	-850.84653	-251.022455	-250.979628	-599.880102	-599.828511	10.2	24.1
1rR2	-850.919937	-850.847653	-251.022455	-250.979628	-599.880102	-599.828511	10.9	24.8
2a	-634.027761	-633.980459	-173.629419	-173.590026	-460.385077	-460.365025	8.3	15.9
2b	-711.419383	-711.368892	-251.022455	-250.979628	-460.385077	-460.365025	7.4	15.2

4. Mannich-type capture experiments: reaction of **4a** with iminium releasing compounds **1a-i** and **2a,b**

Compound **4a** (1 mmol) was added to a solution of electrophile (1 mmol of **1a-1i** or **2a,b**; see Table 4 in manuscript) in anhydrous THF (20 mL) and heated under reflux conditions for 18 hours. The solvent was then removed under reduced pressure. The sample was then dissolved in CDCl₃ (2 mL) and analyzed by ¹H NMR. Completeness of the reaction was monitored by integration of the relevant signals of the Mannich-type capture product.

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