

Electronic Supporting Information

for

Fast Transimination in Organic Solvents in the Absence of Proton and Metal Catalysts. A Key to Imine Metathesis Catalyzed by Primary Amines under Mild Conditions

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Derivation of the kinetic equation for imine metathesis mediated by primary amines ESI 2

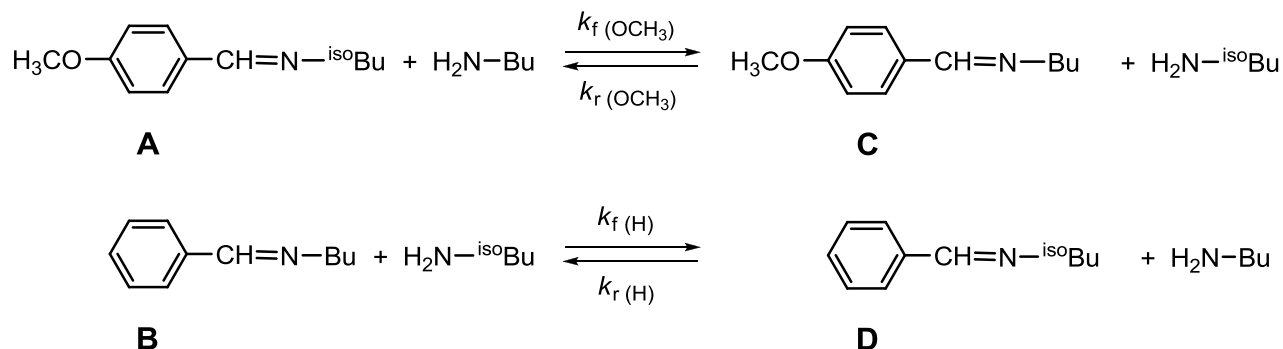
Basicity of imines and amines ESI 5

Cartesian coordinates, electronic energies, and zero-point vibrational energies obtained from ab initio calculations ESI 6

Derivation of the kinetic equation for imine metathesis mediated by primary amines

Background metathesis reaction is not taken into account in the following kinetic treatment.

Scheme ESI 1



When

$$[\text{A}]_0 = [\text{B}]_0$$

and

$[\text{isoBuNH}_2]_0 = 0$, and, as a consequence,

$$[\text{BuNH}_2]_0 = [\text{BuNH}_2] + [\text{isoBuNH}_2]$$

and when the equilibrium constants for the two coupled equilibria are both unity,

that is, $k_f(\text{OCH}_3) = k_r(\text{OCH}_3) = k_{\text{OCH}_3}$, and $k_f(\text{H}) = k_r(\text{H}) = k_{\text{H}}$, the following equation can be written:

$$\begin{aligned} \frac{d[\text{isoBuNH}_2]}{dt} &= k_{\text{OCH}_3} [\text{A}][\text{BuNH}_2] - k_{\text{H}} [\text{B}][\text{isoBuNH}_2] - k_{\text{OCH}_3} [\text{C}][\text{isoBuNH}_2] + k_{\text{H}} [\text{D}][\text{BuNH}_2] = \\ &= [\text{BuNH}_2] (k_{\text{OCH}_3} [\text{A}] + k_{\text{H}} [\text{D}]) - [\text{isoBuNH}_2] (k_{\text{OCH}_3} [\text{C}] + k_{\text{H}} [\text{B}]) = \\ &= [\text{BuNH}_2] (k_{\text{OCH}_3} [\text{A}] + k_{\text{H}} [\text{D}]) - [\text{BuNH}_2]_0 (k_{\text{OCH}_3} [\text{C}] + k_{\text{H}} [\text{B}]) + [\text{BuNH}_2] (k_{\text{OCH}_3} [\text{C}] + k_{\text{H}} [\text{B}]) \end{aligned}$$

At the stationary state:

$$\begin{aligned} \frac{d[\text{isoBuNH}_2]}{dt} &= 0 \\ [\text{BuNH}_2]_0 (k_{\text{OCH}_3} [\text{C}] + k_{\text{H}} [\text{B}]) &= [\text{BuNH}_2]_{\text{SS}} (k_{\text{OCH}_3} [\text{A}] + k_{\text{H}} [\text{D}] + k_{\text{OCH}_3} [\text{C}] + k_{\text{H}} [\text{B}]) \end{aligned}$$

At any time:

$$[\text{A}] + [\text{C}] = [\text{A}]_0 \quad \text{and} \quad [\text{B}] + [\text{D}] = [\text{B}]_0$$

Furthermore

$$[\text{A}] = [\text{B}] \quad \text{and} \quad [\text{C}] = [\text{D}]$$

thus

$$[\text{BuNH}_2]_0 (k_{\text{OCH}_3} [\text{C}] + k_{\text{H}} [\text{B}]) = [\text{BuNH}_2]_{\text{SS}} (k_{\text{OCH}_3} [\text{A}]_0 + k_{\text{H}} [\text{B}]_0)$$

and finally

$$[\text{BuNH}_2]_{\text{SS}} = \frac{k_{\text{OCH}_3} [\text{C}] + k_{\text{H}} [\text{B}]}{k_{\text{OCH}_3} [\text{A}]_0 + k_{\text{H}} [\text{B}]_0} [\text{BuNH}_2]_0$$

For

$$[\text{A}]_0 = [\text{B}]_0 = a$$

$$[\text{BuNH}_2]_{\text{SS}} = \frac{k_{\text{OCH}_3} [\text{C}] + k_{\text{H}} [\text{B}]}{a(k_{\text{H}} + k_{\text{OCH}_3})} [\text{BuNH}_2]_0$$

and

$$[\text{iso BuNH}_2]_{\text{SS}} = \left(1 - \frac{k_{\text{OCH}_3} [\text{C}] + k_{\text{H}} [\text{B}]}{a(k_{\text{H}} + k_{\text{OCH}_3})} \right) [\text{BuNH}_2]_0$$

Thus, for the reaction rate:

$$\frac{d[\text{C}]}{dt} = k_{\text{OCH}_3} [\text{A}] [\text{BuNH}_2]_{\text{SS}} - k_{\text{OCH}_3} [\text{C}] [\text{iso BuNH}_2]_{\text{SS}}$$

$$\begin{aligned} \frac{d[\text{C}]}{dt} &= k_{\text{OCH}_3} [\text{A}] \frac{k_{\text{OCH}_3} [\text{C}] + k_{\text{H}} [\text{B}]}{a(k_{\text{H}} + k_{\text{OCH}_3})} [\text{BuNH}_2]_0 - k_{\text{OCH}_3} [\text{C}] [\text{BuNH}_2]_0 + k_{\text{OCH}_3} [\text{C}] \frac{k_{\text{OCH}_3} [\text{C}] + k_{\text{H}} [\text{B}]}{a(k_{\text{H}} + k_{\text{OCH}_3})} [\text{BuNH}_2]_0 = \\ &= k_{\text{OCH}_3} [\text{BuNH}_2]_0 \frac{k_{\text{OCH}_3} [\text{C}] + k_{\text{H}} [\text{B}]}{a(k_{\text{H}} + k_{\text{OCH}_3})} ([\text{A}] + [\text{C}]) - k_{\text{OCH}_3} [\text{C}] [\text{BuNH}_2]_0 \end{aligned}$$

Since

$$[\text{A}]_0 = [\text{A}] + [\text{C}] = a$$

$$\frac{d[\text{C}]}{dt} = \frac{k_{\text{OCH}_3} [\text{BuNH}_2]_0}{k_{\text{OCH}_3} + k_{\text{H}}} \{k_{\text{H}} [\text{B}] + k_{\text{OCH}_3} [\text{C}] - [\text{C}] (k_{\text{OCH}_3} + k_{\text{H}})\}$$

$$\frac{d[\text{C}]}{dt} = \frac{k_{\text{OCH}_3} k_{\text{H}} ([\text{B}] - [\text{C}])}{k_{\text{OCH}_3} + k_{\text{H}}} [\text{BuNH}_2]_0$$

with

$$[\text{C}] = x; \quad [\text{A}] = [\text{B}] = a - x; \quad [\text{B}] - [\text{C}] = a - 2x$$

$$\frac{dx}{dt} = \frac{k_{\text{OCH}_3} k_{\text{H}}}{k_{\text{OCH}_3} + k_{\text{H}}} [\text{BuNH}_2]_0 (a - 2x)$$

$$\int_0^x \frac{dx}{a-2x} = \frac{k_{\text{OCH}_3} k_{\text{H}}}{k_{\text{OCH}_3} + k_{\text{H}}} [\text{BuNH}_2]_0 \int_0^t dt$$

$$\ln \frac{a}{a-2x} = 2 \left(\frac{k_{\text{OCH}_3} k_{\text{H}}}{k_{\text{OCH}_3} + k_{\text{H}}} [\text{BuNH}_2]_0 \right) t$$

A first order kinetic equation is obtained:

$$\ln \frac{a}{a-2x} = 2 k_{\text{obs}}^* t$$

with

$$k_{\text{obs}}^* = \frac{k_{\text{OCH}_3} k_{\text{H}}}{k_{\text{OCH}_3} + k_{\text{H}}} [\text{BuNH}_2]_0$$

The symbol k_{obs}^* was introduced in the main text of the article as the observed rate constant value (k_{obs}) corrected for background reaction (k_0). Background reaction has not been taken into account in this kinetic treatment.

$$k_{\text{obs}}^* = k_{\text{obs}} - k_0$$

Basicity of imines and amines

In the presence of BuNH₂ the acid impurity is partitioned between the amines and imines present in solution, according to the relative basicity.

Here we use the p*K*_a values of *N*-(4-methoxybenzylidene)-*tert*-butylamine and *N*-benzylidene-*tert*-butylamine^{1ESI} as reasonable estimates of the unknown p*K*_a values of **A** and **B**, respectively. The latter assumption is strongly supported by the close similarity of the p*K*_a values of the corresponding amines.^{2ESI} Furthermore, under the assumption that the relative basicities of the two imines in CD₃CN are the same as in water, we calculate [AH⁺]_o = 2.3 μM, [BH⁺]_o = 0.23 μM, and [BuNH₃⁺] = 23 μM in the run carried out in the presence of 0.60 mM BuNH₂.

N-(4-methoxybenzylidene)-*tert*-butylamine, p*K*_a = 7.70

N-benzylidene-*tert*-butylamine, p*K*_a = 6.70

tert-butylamine, p*K*_a = 10.68

butylamine, p*K*_a = 10.66

isobutylamine, p*K*_a = 10.72

MP4/6-311++G(3df,2pd)//MP2/6-311+G(d,p) calculations

Cartesian Coordinates, energies, ZPVE (unscaled)

Stationary points found for the formaldehyde-methylamine condensation reaction (Figure 6, top)

H₂C=O + MeNH₂ complex

E = -210.0465533 a.u., ZPVE = 0.094271 a.u.

C	1.507450	0.550997	0.000093
O	1.739745	-0.641657	-0.000070
H	1.409212	1.129925	-0.933364
H	1.409071	1.129624	0.933711
C	-1.460530	-0.733797	0.000025
N	-1.296962	0.726109	0.000013
H	-0.960496	-1.147923	0.877628
H	-2.504631	-1.071196	-0.000510
H	-0.959473	-1.148028	-0.876999
H	-1.756650	1.127358	-0.811405
H	-1.757777	1.127537	0.810700

TS1

E = -210.0038964 a.u., ZPVE = 0.094363 a.u.

C	-0.819818	0.605222	-0.097100
O	-1.587994	-0.499358	-0.174590
H	-1.147070	1.400923	0.596745
H	-0.489598	1.060886	-1.048955
C	1.671821	-0.089796	-0.276418
N	0.437937	-0.074298	0.523687
H	2.104155	0.910534	-0.344309
H	2.396025	-0.773849	0.169000
H	1.412271	-0.440549	-1.276758
H	-0.352750	-0.933277	0.383539
H	0.603340	0.197726	1.492758

Carbinolamine

E = -210.0668010 a.u., ZPVE = 0.099383 a.u.

N	0.618859	-0.676088	-0.219250
H	1.542237	0.568815	1.175110
H	1.193434	1.401092	-0.360287
H	2.511493	0.218595	-0.260197

C	1.501499	0.444645	0.088148
C	-0.713577	-0.538196	0.299881
H	0.577048	-0.828796	-1.221992
O	-1.478223	0.557604	-0.215449
H	-0.642509	-0.464592	1.391945
H	-1.286271	-1.427375	0.034696
H	-1.129190	1.365353	0.170900

TS2

E = -210.9729889 a.u., ZPVE = 0.090167 a.u.

C	-0.407264	0.897630	0.213733
O	-1.581081	-0.557968	-0.028925
H	-0.227338	1.049165	1.284558
H	-1.128859	1.564662	-0.246736
C	1.575601	-0.374361	0.157550
N	0.495160	0.298394	-0.570955
H	1.204614	-1.187103	0.800814
H	2.274999	-0.803193	-0.561472
H	2.122491	0.338268	0.783068
H	-0.498296	-0.496401	-0.728205
H	-1.575109	-1.230022	0.668368

H₂C=NMe + H₂O complex

E = -210.0594676 a.u., ZPVE = 0.093690 a.u.

C	-0.665492	1.263356	0.009231
H	-1.669885	1.685459	-0.122913
H	0.177390	1.948808	0.077769
C	-1.599181	-0.876578	-0.027379
N	-0.445037	0.006686	0.082093
H	-1.446452	-1.547368	-0.876527
H	-1.661046	-1.489722	0.875227
H	-2.542494	-0.328944	-0.160733
H	1.482963	-0.284288	-0.004994
O	2.445911	-0.203559	-0.108852
H	2.795534	-0.722945	0.617227

Stationary points found for methylenemethylamine-methylamine transimination (Figure 6, bottom)

H₂C=NMe + MeNH₂ complex

E = -229.4178852 a.u., ZPVE = 0.135584 a.u.

C	-1.159543	1.147670	-0.251309
H	-2.047109	1.671886	-0.632208
H	-0.217136	1.689788	-0.193382
C	2.600010	-0.427962	-0.482843
N	1.912387	0.279866	0.599414
H	3.576991	0.030961	-0.656270
H	2.754021	-1.502270	-0.307291
H	2.017800	-0.319812	-1.401547
H	0.992806	-0.131454	0.744995
H	2.428507	0.176254	1.466605
N	-1.187279	-0.073291	0.128101
C	-2.472484	-0.754652	0.037348
H	-3.272492	-0.111440	-0.357764
H	-2.363082	-1.630824	-0.607252
H	-2.753964	-1.109451	1.032327

TS1 = TS2

E = -229.3461442 a.u., ZPVE = 0.134352 a.u.

C	0.122798	0.652567	0.340510
H	0.443328	1.679259	0.054528
H	-0.180041	0.675452	1.408175
C	-2.167654	-0.437002	0.230509
N	-1.107739	0.297771	-0.484237
H	-2.699097	0.222268	0.919103
H	-2.867526	-0.860714	-0.491733
H	-1.676053	-1.238939	0.782187
H	-0.348434	-0.364085	-1.021213
H	-1.472164	1.078167	-1.029139
N	0.926296	-0.413588	-0.132778
C	2.346126	-0.202932	0.018849
H	2.694148	-0.256517	1.067072
H	2.884493	-0.979394	-0.533281
H	2.683832	0.779426	-0.375808

aminal

E = -229.4364777 a.u., ZPVE = 0.140864 a.u.

N	-1.096849	0.290234	-0.615973
H	-2.151549	-0.104589	1.139072
H	-1.091864	-1.450796	0.666057
H	-2.587456	-1.127371	-0.236246
C	-1.749494	-0.654646	0.281858
C	0.000000	1.030153	0.000001
H	-0.777024	-0.184008	-1.454144
N	1.096848	0.290233	0.615973
H	-0.430556	1.672547	0.775553
H	0.430557	1.672544	-0.775552
H	0.777023	-0.184010	1.454143
C	1.749495	-0.654645	-0.281858
H	2.587441	-1.127388	0.236254
H	2.151572	-0.104585	-1.139060
H	1.091860	-1.450782	-0.666076

¹ESI Cordes, E. H.; Jencks, W. P. *J. Am. Chem. Soc.* **1962**, *84*, 826–831.

²ESI . *IUPAC Dissociation Constants of Organic Bases in Aqueous Solution*; Perrin, D. D., Ed.; Butterworths: London, 1965.