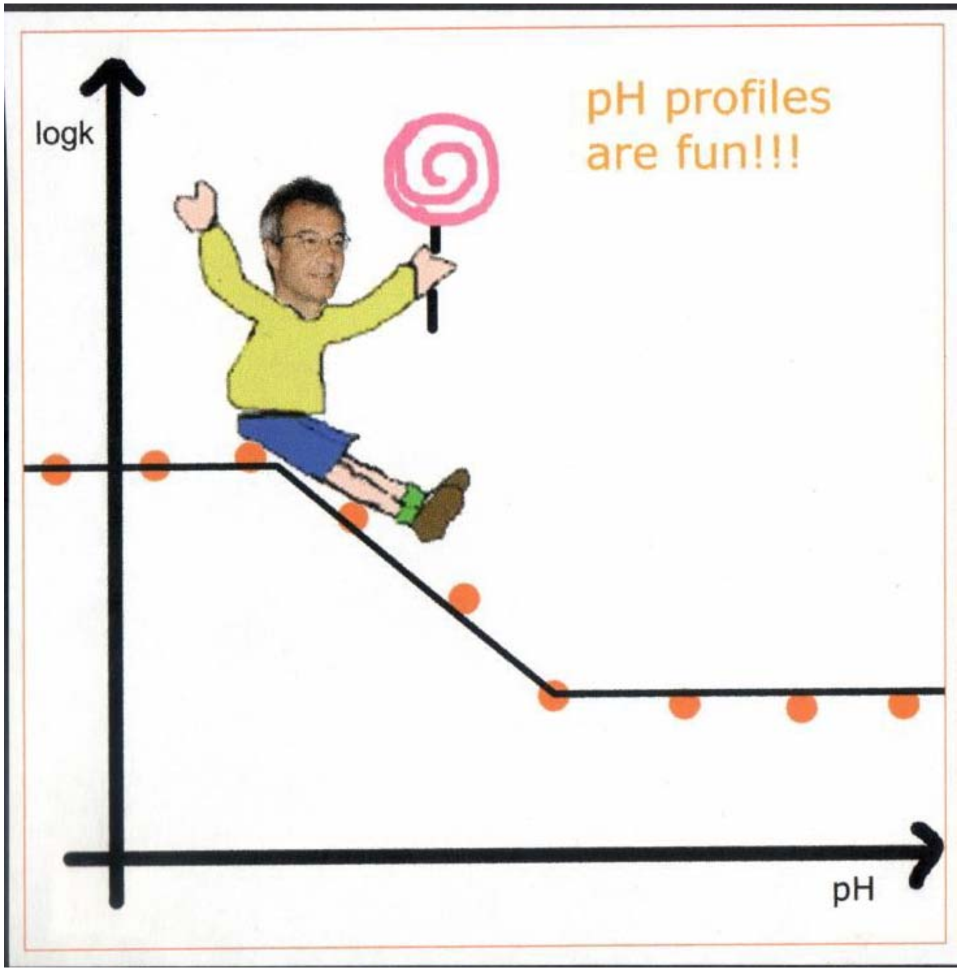
Bringing Light to Dark Reactions:
Acid- and Base Catalysis in Keto–Enol Chemistry

Many reactions of ketones proceed via their enol tautomers. -> Rates of reaction? Equilibria?



Adv. Phys. Org. Chem., *44,* **2010**, 325

Some Preliminaries

We use water as a solvent: Why?

- over 90% of photochemistry on earth occurs in aqueous solution
- well-defined pH-scale
- heterolytic reactions preferred; no H-abstraction from solvent
- biochemistry is mostly “aqueous”

Autoionization: $H_2O\,(aq) \rightleftharpoons H^+(aq) + HO^-(aq)$

Ion product: $K_w^\circ(298\ K) = a_{H^+}a_{HO^-} = \gamma_{H^+}(c_{H^+}/c_{H^+}^\circ)\,\gamma_{HO^-}(c_{HO^-}/c_{HO^-}^\circ)$

$\approx 1.008 \times 10^{-14}$, $pK_w^\circ(298\ K) \approx 14.00$,

Activity coefficients γ depend on ionic strength: $I = \frac{1}{2}\Sigma z_j^2 c_j$

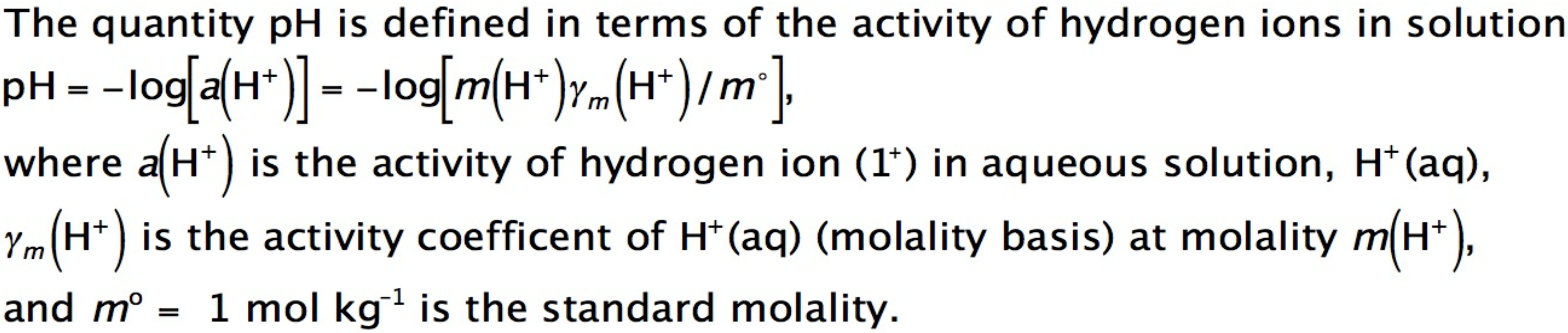
Pure water: $\gamma_j = 1$; brine ($I = 0.1$ M): $\gamma_{H^+} \approx 0.83$, $\gamma_{HO^-} \approx 0.76$,

hence $K_{w,c}(298\ K, I = 0.1\ M) = c_{H^+}\,c_{HO^-}$

$= K_w^\circ(298\ K)\,c_{H^+}^\circ c_{HO^-}^\circ/(\gamma_{H^+}\gamma_{HO^-}) \approx 1.598 \times 10^{-14}\ M^2$,

$p[K_{w,c}(298\ K, I = 0.1\ M)/M^2] \approx 13.80$

The definition of pH (IUPAC Gold Book)



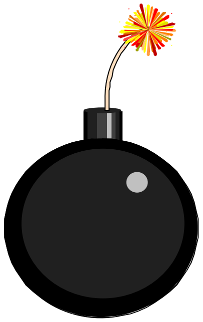
The quantity pH is defined in terms of the activity of hydrogen ions in solution

$$\mathrm{pH} = -\log\left[a\left(\mathrm{H}^+\right)\right] = -\log\left[m\left(\mathrm{H}^+\right)\gamma_m\left(\mathrm{H}^+\right)/m^\circ\right],$$

where $a\left(\mathrm{H}^+\right)$ is the activity of hydrogen ion (1^+) in aqueous solution, $\mathrm{H}^+(\mathrm{aq})$,

$\gamma_m\left(\mathrm{H}^+\right)$ is the activity coefficent of $\mathrm{H}^+(\mathrm{aq})$ (molality basis) at molality $m\left(\mathrm{H}^+\right)$,

and $m^\mathrm{o} = 1\ \mathrm{mol\ kg}^{-1}$ is the standard molality.



Note: pH involves the activity of a single ion, which cannot be measured!
The standard activity of a 1 *m* solution of $\mathrm{H}^+(\mathrm{aq})$ at infinite dilution (!!!) is,
therefore, defined as $a^\mathrm{o} = 1$.

This looks terribly complicated, but …

In practice: be happy, don't worry!

Acidity constants: $\mathrm{HA\,(aq)} \rightleftharpoons \mathrm{H^+(aq)} + \mathrm{A^-(aq)}$

$K_a°(T) = a_{H+}a_{A-}/a_{HA}$

$K_a°(H_2O, 298\ K) = a_{H+}a_{HO-}/a_{H_2O} = a_{H+}a_{HO-} = K_w°(298\ K)$;

$pK_a°(H_2O, 298\ K) = 14.0$ (not 15.74!)

$K_a°(H^+, 298\ K) = a_{H+}/a_{H+} = 1$; $pK_a°(H^+, 298\ K) = 0$ (not –1.74!)

We measure concentrations: $A = \varepsilon c d$ (LFP, spectrophotometry);

hence, we determine concentration quotients: $K_{a,c}(T) = c_{H+}c_{A-}/c_{HA}$

and need to know the hydrogen ion concentrations: c_{H+}

Keep ionic strength I constant, if necessary by addition of, e.g., KCl

We need buffers for $3 < pH < 11$

c_{H+} is best calculated from the buffer ratio c_{HA}/c_{A-} and known $K_{a,c}(I, T)$-values

given in the literature or known $K_a°$-values using known $\gamma_i(I, T)$:

For pH ≤ 3 (.. 4): c_{H+} = nominal concentration of a strong acid ($HClO_4$);

For pH ≥ (10...) 11: $c_{H+} = K_{w,c}(298\ K, I)/(c_{HO-})_{nom}$ Avoid CO_2 in air!

Cross-check for buffer solutions

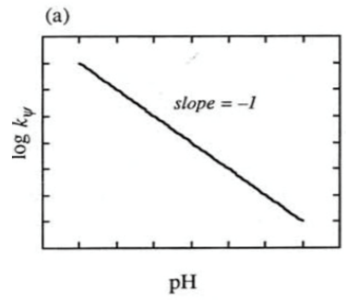
Prepare buffer solution as described in the literature ($I = 0.1$ M)
Measure pH with a glass electrode.
The glass electrode must be calibrated!
(See provider instructions, e.g., Metrohm)
Remarkably, glass electrode readings $(\mathrm{pH})_{\mathrm{meas}}$ are closer to $\mathrm{p}c_{\mathrm{H+}}$ than to $\mathrm{p}a_{\mathrm{H+}}$! 1)
Your results should hold within:

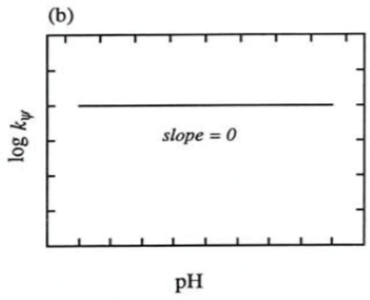
$$(\mathrm{pH})_{\mathrm{meas}} - (\mathrm{p}c_{\mathrm{H+}})_{\mathrm{calc}} = 0.03 \pm 0.02$$

1) H. Sigel, A. D. Zuberbühler, O. Yamauchi, *Anal. Chim. Acta*, **1991**, *255*, 63.

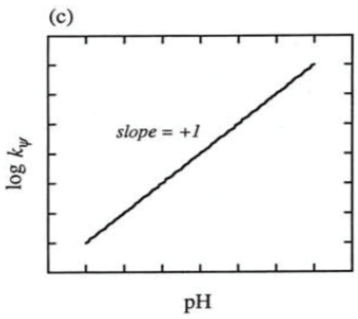
Interpretation of pH–rate profiles: $\log({}^1k_{obs}) = f(pH)$

G. M. Loudon, *J. Chem. Ed.* **1991**, *68*, 973

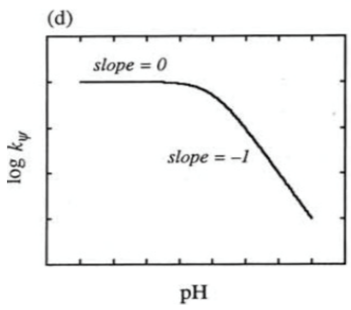


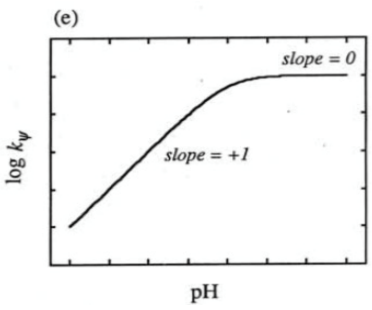


(a) ${}^1k_{obs} = k_{H^+}c_{H^+}$ (b) ${}^1k_{obs} = k_0$



(c) ${}^1k_{obs} = \text{const}/c_{H^+}$





(d) ${}^1k_{obs} = \text{const } c_{H^+}/(\text{const'} + c_{H^+})$
for $c_{H^+} \ll \text{const'}$: ${}^1k_{obs} = (\text{const}/\text{const'})\, c_{H^+}$
for $c_{H^+} \gg \text{const'}$: ${}^1k_{obs} = \text{const}$

(e) ${}^1k_{obs} = \text{const}/(\text{const'} + c_{H^+})$

Downward bends indicate a) the loss or gain of a proton by the substrate or b) a change in the rate-limiting step with pH. The same mechanism operates to the left and right of negative curvature. Upward bends indicate a change of mechanism.

Spectrophotometric determination of acidity constants p$K_{\mathrm{a},c}$

Choose a well-known (preferably monoacid) buffer with known p$K_{\mathrm{a},c}$ near (±1 unit) to that p$K_{\mathrm{a},c}$ which you want to determine.

Titrate with 0.1 M strong base starting with 0.1 M HA plus dye or with 0.1 M strong acid starting with buffer salt plus dye.

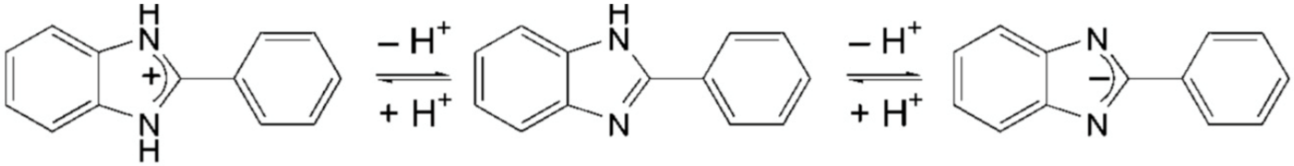
Record spectra and get pH readings between small additions of titrant.

Global analysis (Specfit or Matlab) of the spectral series (number of components) and fit of an appropriate titration function: $K_{\mathrm{a},c} = (c_{\mathrm{A^-}} c_{\mathrm{H^+}} / c_{\mathrm{HA}})$.

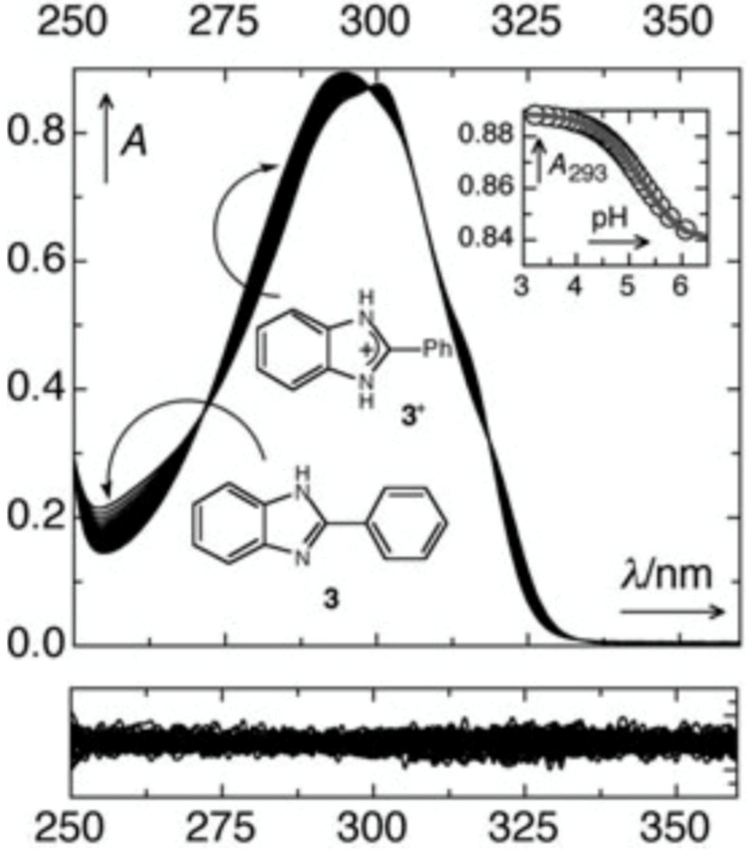
The thermodynamic acidity constant K_a^o can then be estimated using known activity coefficients.

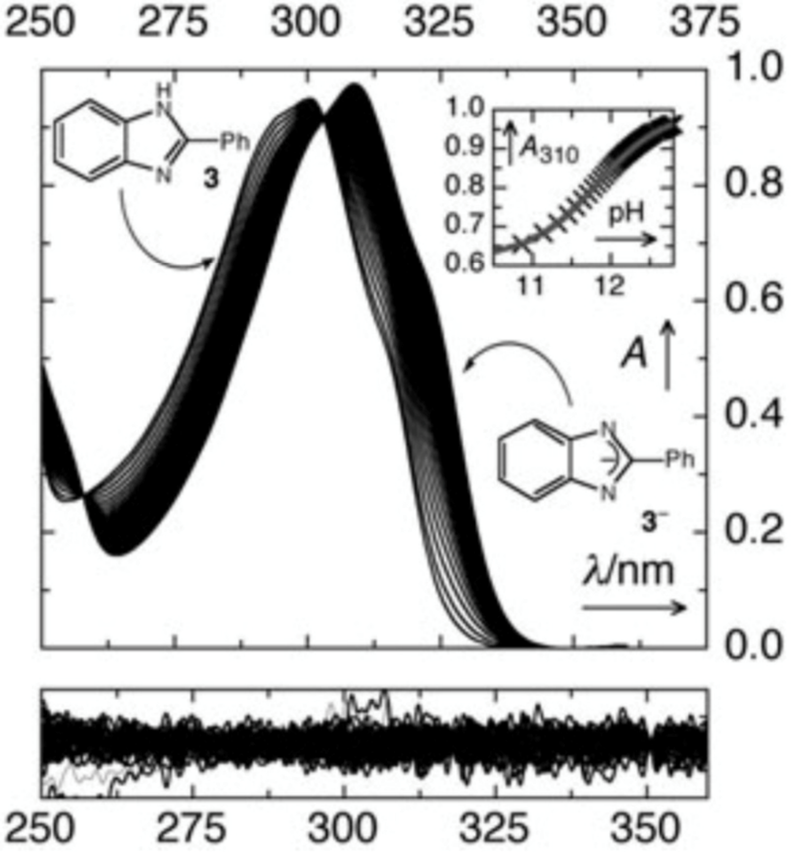
Titration of 2-phenyl-1*H*-benzimidazole (**3**)

p$K_{a,c}$(**3**$^+$) = 4.18 ± 0.02, p$K_{a,c}$(**3**) = 11.78 ± 0.03; I = 0.1 M

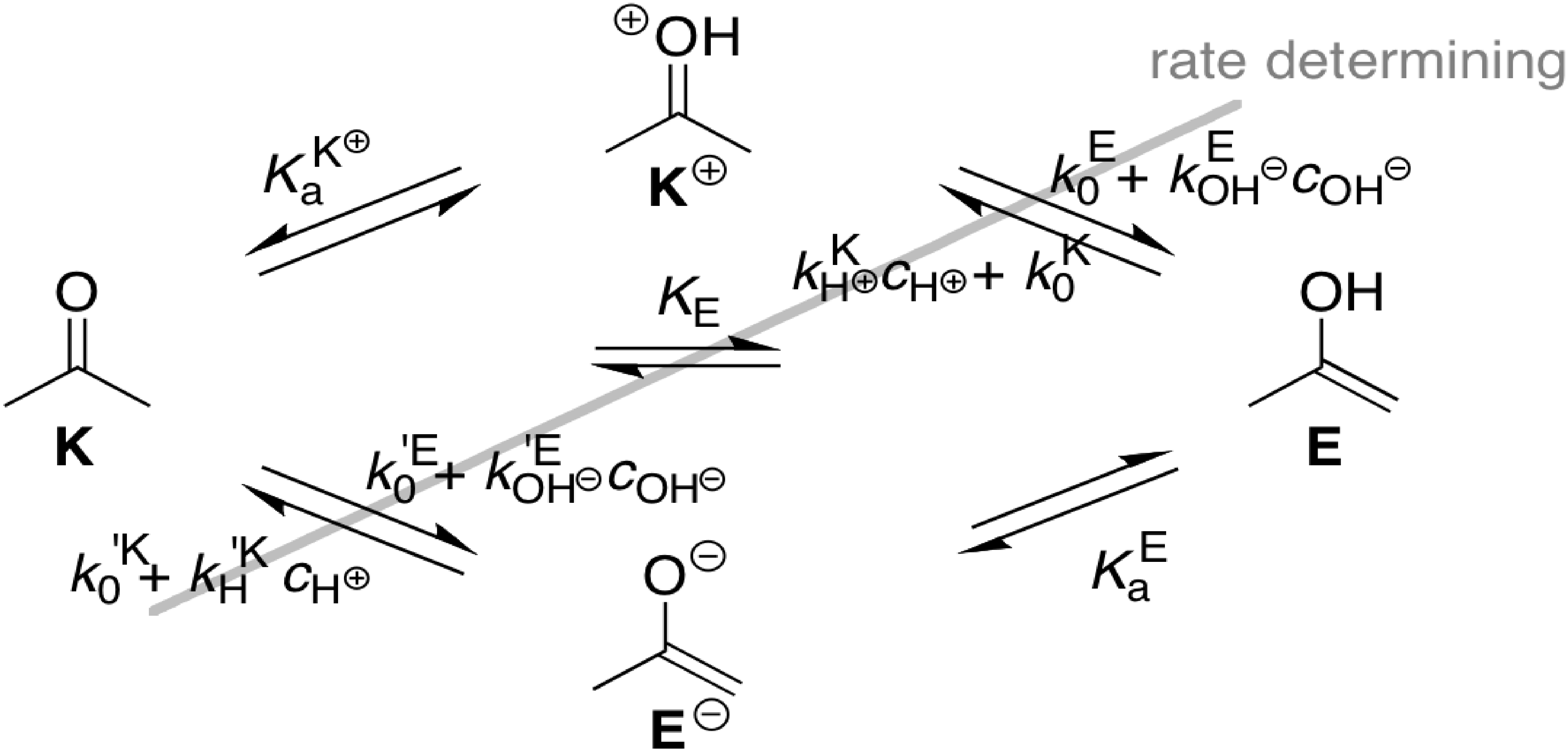


3$^+$ HOAc/NaOAc **3** No buffer **3**$^-$





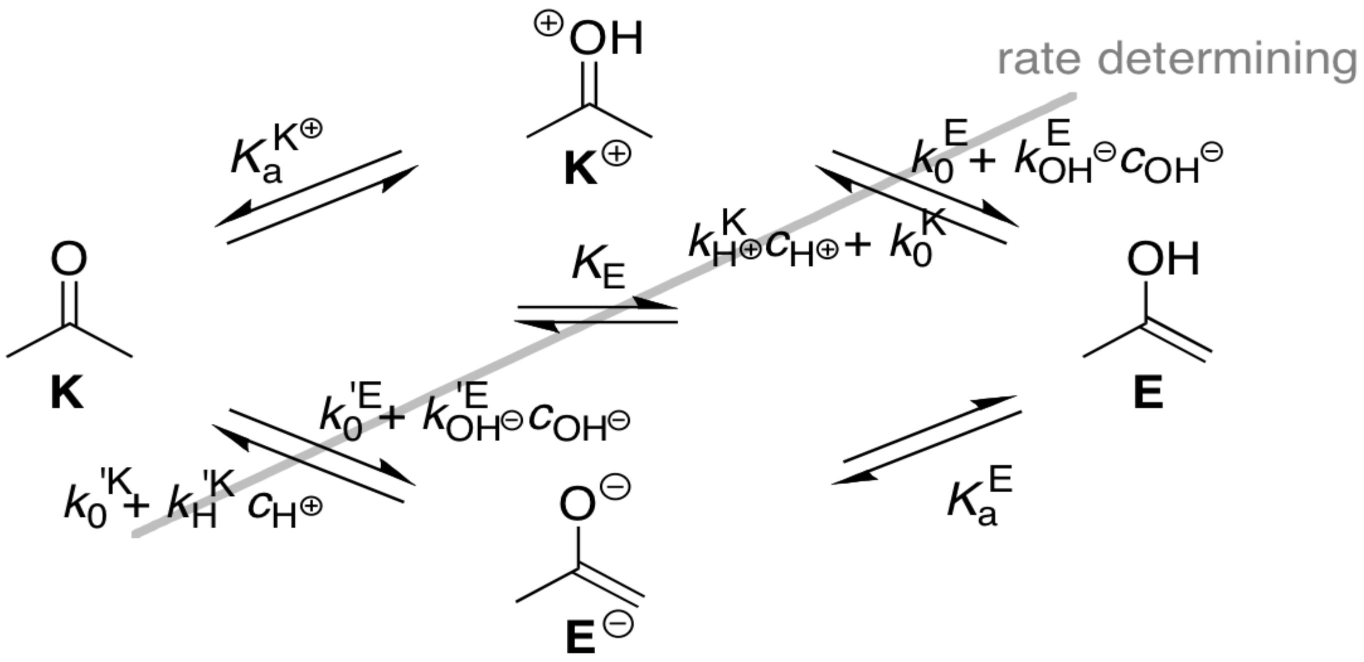
The mechanisms of keto–enol tautomerization



Enolization and ketonization reactions always observe a first-order rate law, but the observed rate constants depend on pH.

Assumption:

Protonation equilibria on oxygen are established at all times during keto–enol tautomerization.



$$\Sigma\Delta_r G^\circ = 2.3RT\Sigma \mathrm{p}K_r = 0$$

e.g., $\mathrm{p}K_a^K = \mathrm{p}K_E + \mathrm{p}K_a^E$

The primed symbols of rate constants, $k^{'E}$ and $k^{'K}$, refer to reactions forming or depleting The enol anion **E**$^{-}$, respectively.
Based on this proposed mechanism we write down the (one-way!) differential rate laws for ketonization of the enol, v^K, and enolization of the ketone, v^E, separately:

$$K_{\mathrm{a}}^{\mathrm{E}} = c_{\mathrm{E}^{\ominus}}(t)c_{\mathrm{H}^{\oplus}}/c_{\mathrm{E}}(t) \quad \text{and} \quad K_{\mathrm{a}}^{\mathrm{K}\oplus} = c_{\mathrm{K}}(t)c_{\mathrm{H}^{\oplus}}/c_{\mathrm{K}^{\oplus}}(t)$$

$$c_{\mathrm{E,tot}}(t) \equiv c_{\mathrm{E}}(t) + c_{\mathrm{E}^{\ominus}}(t)$$

$$c_{\mathrm{E}}(t) = \frac{c_{\mathrm{H}^{\oplus}}}{K_{\mathrm{a}}^{\mathrm{E}} + c_{\mathrm{H}^{\oplus}}} c_{\mathrm{E,tot}}(t) \quad \text{and} \quad c_{\mathrm{E}^{\ominus}}(t) = \frac{K_{\mathrm{a}}^{\mathrm{E}}}{K_{\mathrm{a}}^{\mathrm{E}} + c_{\mathrm{H}^{\oplus}}} c_{\mathrm{E,tot}}(t)$$

Acid cat.:

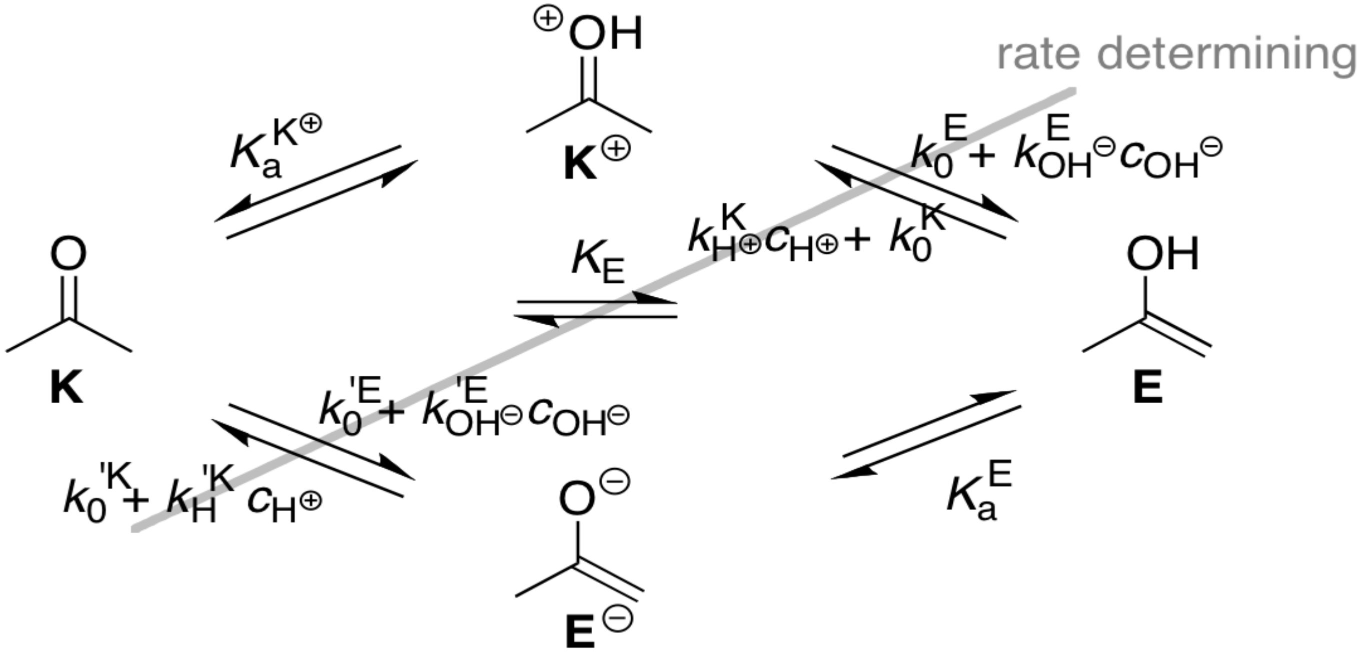
$$v_{\mathrm{H}^{\oplus}}^{\mathrm{K}} = k_{\mathrm{H}^{\oplus}}^{\mathrm{K}} c_{\mathrm{H}^{\oplus}} c_{\mathrm{E}}(t) = k_{\mathrm{H}^{\oplus}}^{\mathrm{K}} c_{\mathrm{H}^{\oplus}} \frac{c_{\mathrm{H}^{\oplus}}}{K_{\mathrm{a}}^{\mathrm{E}} + c_{\mathrm{H}^{\oplus}}} c_{\mathrm{E,tot}}(t)$$

Base cat.:

$$v_{\mathrm{OH}^{\ominus}}^{\mathrm{K}} = k_0'^{\mathrm{K}} c_{\mathrm{E}^{\ominus}}(t) = k_0'^{\mathrm{K}} \frac{K_{\mathrm{a}}^{\mathrm{E}}}{K_{\mathrm{a}}^{\mathrm{E}} + c_{\mathrm{H}^{\oplus}}} c_{\mathrm{E,tot}}(t)$$

“Uncat.”:

$$v_0^{\mathrm{K}} = k_0^{\mathrm{K}} c_{\mathrm{E}}(t) + k_{\mathrm{H}^{\oplus}}'^{\mathrm{K}} c_{\mathrm{H}^{\oplus}} c_{\mathrm{E}^{\ominus}}(t) = \left(k_0^{\mathrm{K}} + k'^{\mathrm{K}}_{\mathrm{H}^{\oplus}} K_{\mathrm{a}}^{\mathrm{E}}\right) \frac{c_{\mathrm{H}^{\oplus}}}{K_{\mathrm{a}}^{\mathrm{E}} + c_{\mathrm{H}^{\oplus}}} c_{\mathrm{E,tot}}(t)$$



$$v^{\mathrm{K}} = \left[\left(k_0^{\mathrm{K}} + k_{\mathrm{H}^\oplus}^{'\mathrm{K}} K_{\mathrm{a}}^{\mathrm{E}} \right) + k_{\mathrm{H}^\oplus}^{\mathrm{K}} c_{\mathrm{H}^\oplus} + k_0^{'\mathrm{K}} \frac{K_{\mathrm{a}}^{\mathrm{E}}}{c_{\mathrm{H}^\oplus}} \right] \frac{c_{\mathrm{H}^\oplus}}{K_{\mathrm{a}}^{\mathrm{E}} + c_{\mathrm{H}^\oplus}} c_{\mathrm{E,tot}}(t) = k^{\mathrm{K}} c_{\mathrm{E,tot}}(t)$$

Three independent rate constants of ketonization, $k_{\mathrm{H}+}^{\mathrm{K}}$, $k_0{}'^{\mathrm{K}}$, and $k_{\mathrm{uc}}^{\mathrm{K}} = k_0^{\mathrm{K}} + k_{\mathrm{H}+}{}'^{\mathrm{K}} K_{\mathrm{a}}^{\mathrm{E}}$, fully determine the kinetic properties of the Scheme, because the rate constants $k_{\mathrm{i}}^{\mathrm{E}}$ for the reverse enolization reactions are related to the former by the principle of microscopic reversibility:
At equilibrium each reaction path is at equilibrium.

$$v^{\mathrm{K}} = \left[\left(k_0^{\mathrm{K}} + k'^{\mathrm{K}}_{\mathrm{H}^\oplus} K_{\mathrm{a}}^{\mathrm{E}} \right) + k^{\mathrm{K}}_{\mathrm{H}^\oplus} c_{\mathrm{H}^\oplus} + k'^{\mathrm{K}}_0 \frac{K_{\mathrm{a}}^{\mathrm{E}}}{c_{\mathrm{H}^\oplus}} \right] \frac{c_{\mathrm{H}^\oplus}}{K_{\mathrm{a}}^{\mathrm{E}} + c_{\mathrm{H}^\oplus}} c_{\mathrm{E,tot}}(t) = k^{\mathrm{K}} c_{\mathrm{E,tot}}(t)$$

$$k_0^{\mathrm{E}} = K_{\mathrm{E}} K_{\mathrm{a}}^{\mathrm{K}^\oplus} k^{\mathrm{K}}_{\mathrm{H}^\oplus}, \qquad \text{b)}\ k^{\mathrm{E}}_{\mathrm{OH}^\ominus} = K_{\mathrm{E}} K_{\mathrm{a}}^{\mathrm{K}^\oplus} k_0^{\mathrm{K}} / K_{\mathrm{w}}$$

$$k'^{\mathrm{E}}_0 = K_{\mathrm{a}}^{\mathrm{K}} k'^{\mathrm{K}}_{\mathrm{H}^\oplus}, \qquad \text{d)}\ k'^{\mathrm{E}}_{\mathrm{OH}^\ominus} = K_{\mathrm{a}}^{\mathrm{K}} k'^{\mathrm{K}}_0 / K_{\mathrm{w}}$$

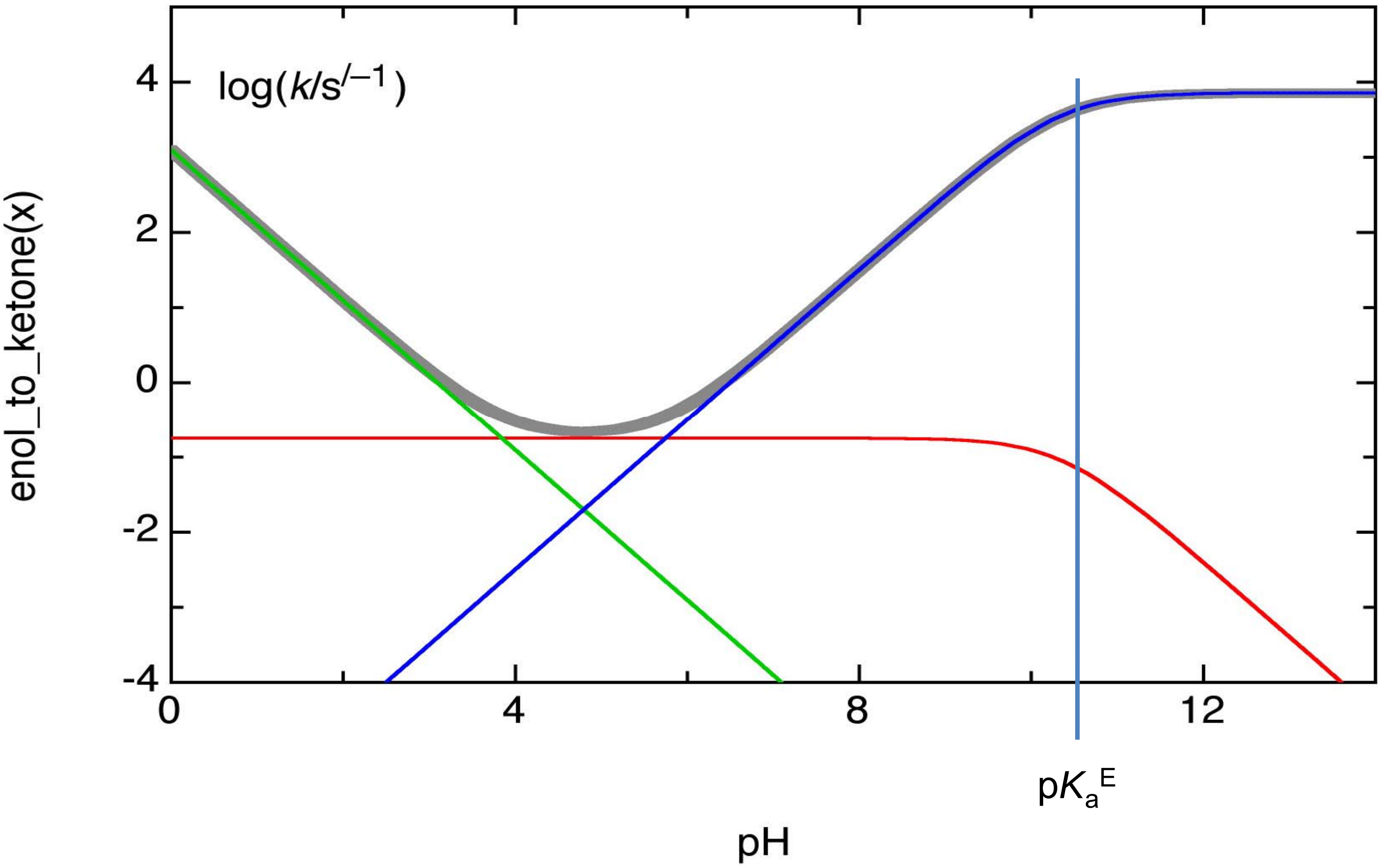
K_w = 1.59 x 10^{-14} M^2 at ionic strength I = 0.1 M

$$v^{\mathrm{E}} = \left[\left(k_0^{\mathrm{K}} + k'^{\mathrm{K}}_{\mathrm{H}^\oplus} K_{\mathrm{a}}^{\mathrm{E}} \right) + k^{\mathrm{K}}_{\mathrm{H}^\oplus} c_{\mathrm{H}^\oplus} + k'^{\mathrm{K}}_0 \frac{K_{\mathrm{a}}^{\mathrm{E}}}{c_{\mathrm{H}^\oplus}} \right] K_{\mathrm{E}} \frac{K_{\mathrm{a}}^{\mathrm{K}^\oplus}}{K_{\mathrm{a}}^{\mathrm{K}^\oplus} + c_{\mathrm{H}^\oplus}} c_{\mathrm{K,tot}}(t) = k^{\mathrm{E}} c_{\mathrm{K,tot}}(t)$$

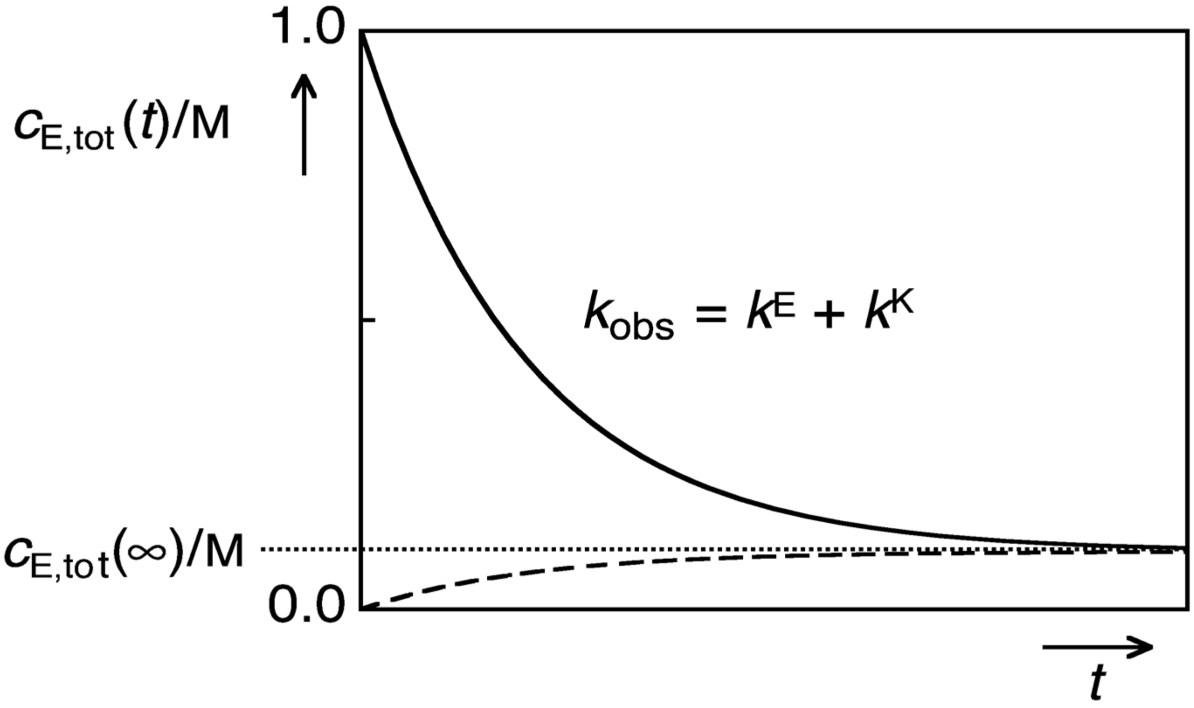
Hence, the total enol concentration obeys the first-order rate law for reversible reactions:

$$c_{\mathrm{E,tot}}(t) = \left[c_{\mathrm{E,tot}}(0) - c_{\mathrm{E,tot}}(\infty) \right] \mathrm{e}^{-\left(k^{\mathrm{E}} + k^{\mathrm{K}}\right)t} + c_{\mathrm{E,tot}}(\infty)$$

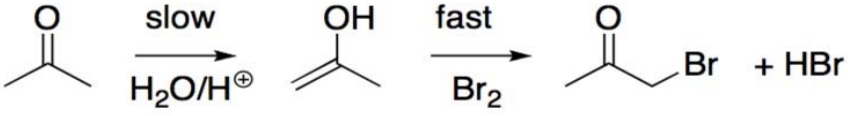
$$v^{\mathrm{K}} = \left[\underline{\left(k_0^{\mathrm{K}} + k_{\mathrm{H}^\oplus}^{'\mathrm{K}} K_{\mathrm{a}}^{\mathrm{E}} \right)} + \underline{k_{\mathrm{H}^\oplus}^{\mathrm{K}} c_{\mathrm{H}^\oplus}} + \underline{k_0^{'\mathrm{K}} \frac{K_{\mathrm{a}}^{\mathrm{E}}}{c_{\mathrm{H}^\oplus}}} \right] \frac{c_{\mathrm{H}^\oplus}}{K_{\mathrm{a}}^{\mathrm{E}} + c_{\mathrm{H}^\oplus}} c_{\mathrm{E,tot}}(t) = k^{\mathrm{K}} c_{\mathrm{E,tot}}(t)$$



Can we measure k^E and k^K separately?

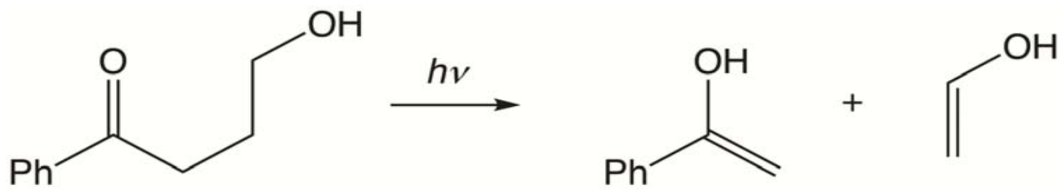


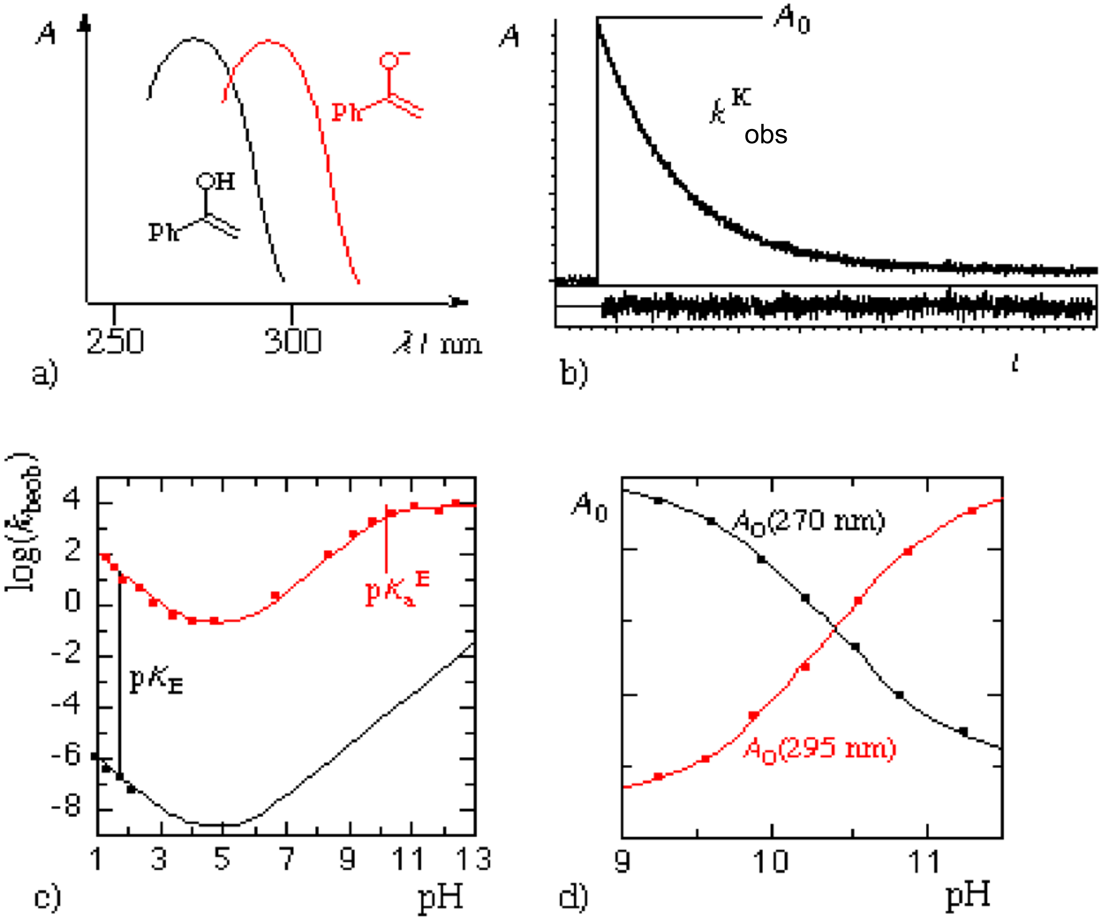
If $K^K = c_K/c_E >> 1$, then $k_{obs} \sim k^K$. The reverse rate constant can be measured by, e.g., acid-catalyzed bromination:

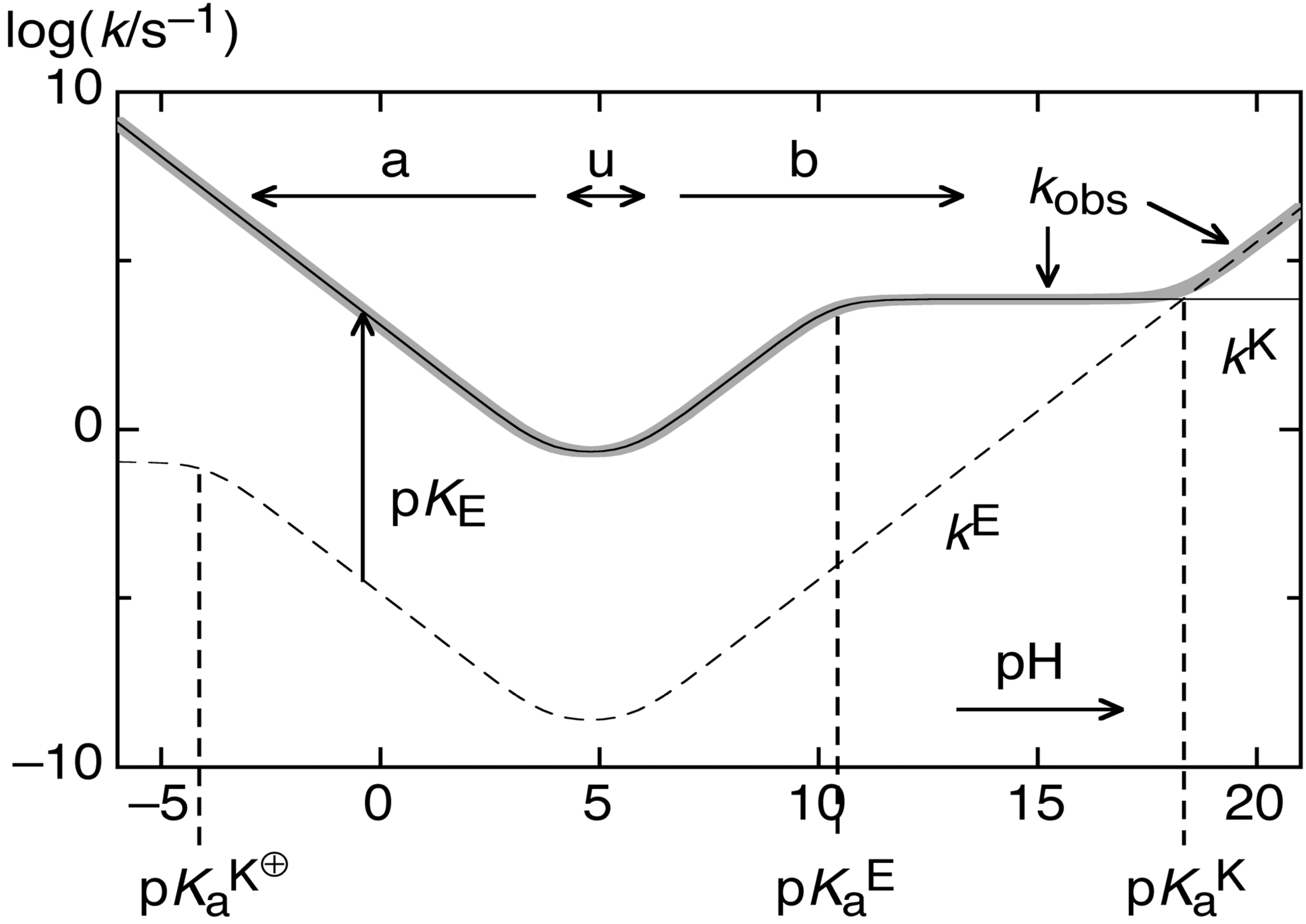


The rate law is independent of bromine conc. (Lapworth 1906)

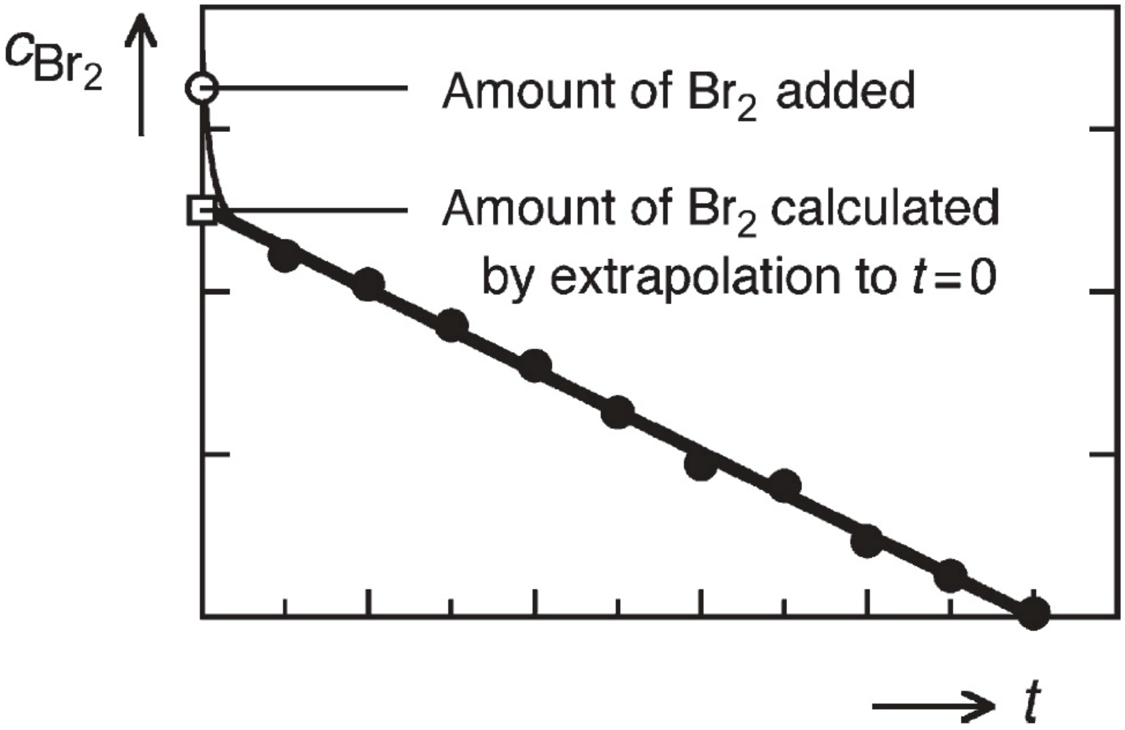
Acetophenone

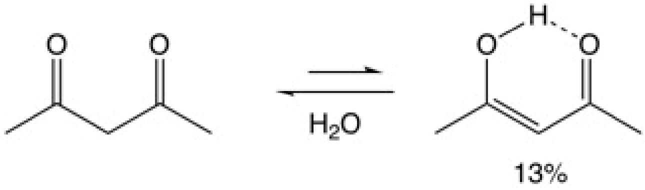





log(k/s−1)
10
0
−10
−5
0
5
10
15
20
a
u
b
kobs
kK
pKE
kE
pH
pKaK⊕
pKaE
pKaK

The bromine titration method





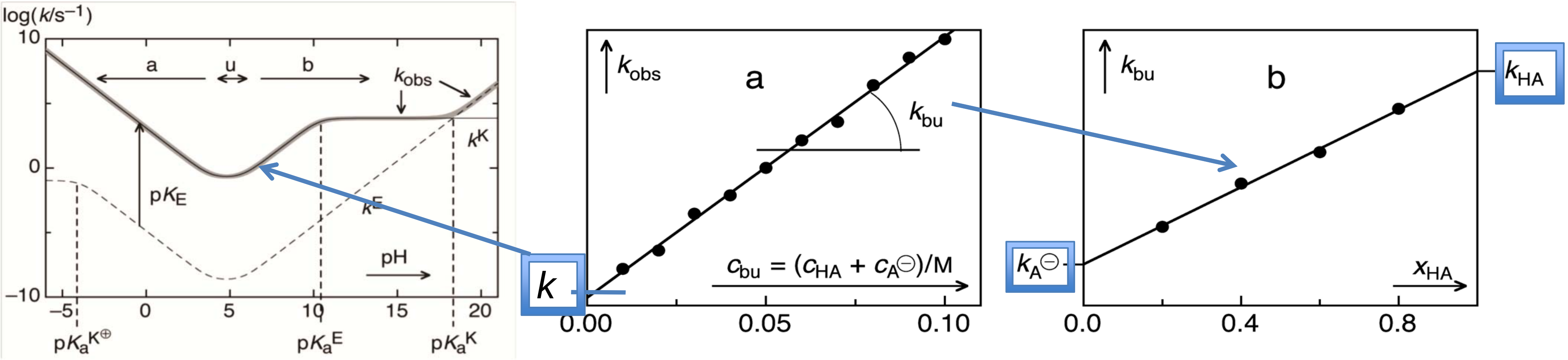
Acetylacetone: 13 %

Acetone: 2.5 x 10^{-4} %, i.e., pK^{E} = 5.6

In fact (flash photolysis): pK^{E} = 8.3 ± 0.1

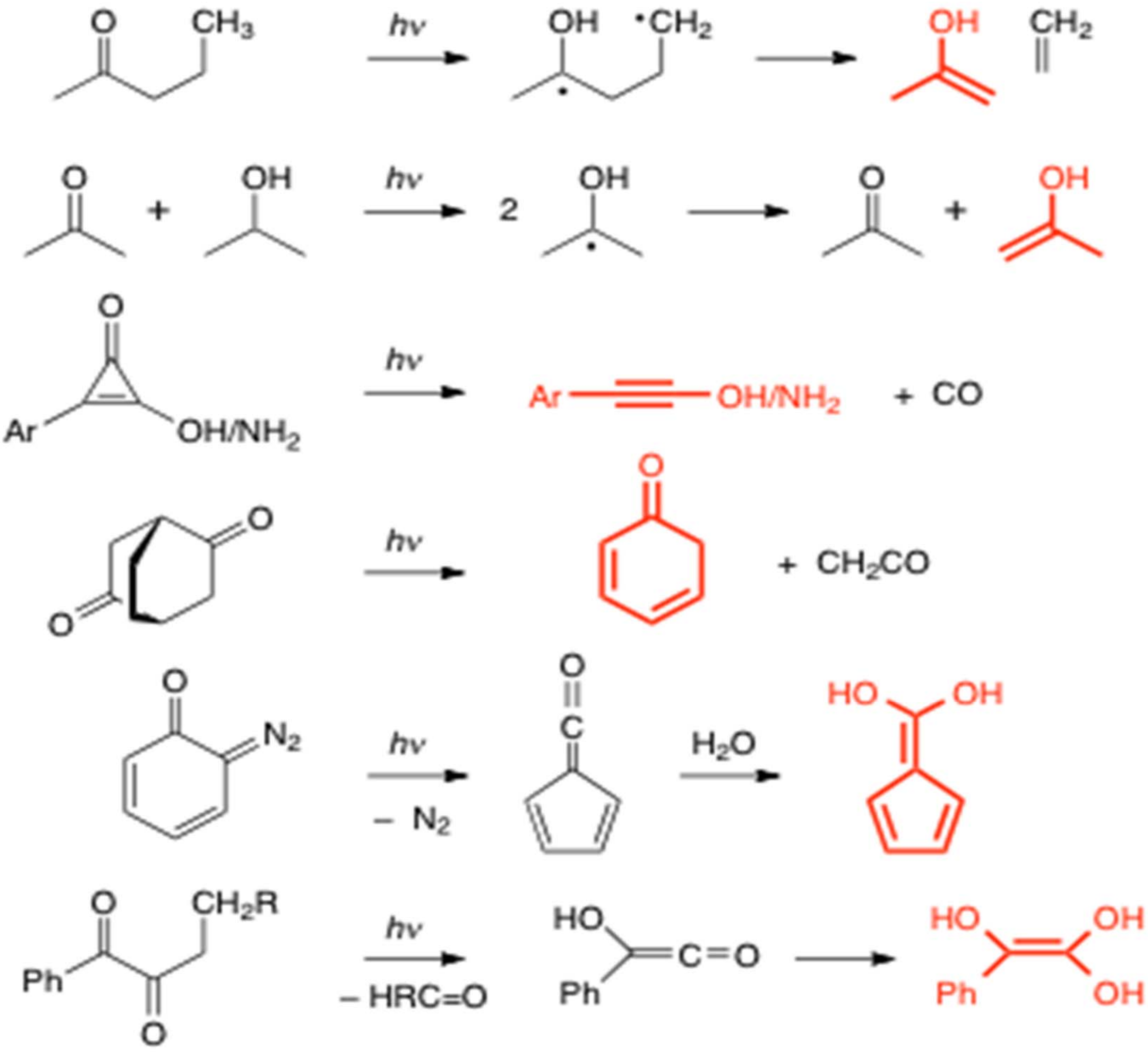
Buffer catalysis

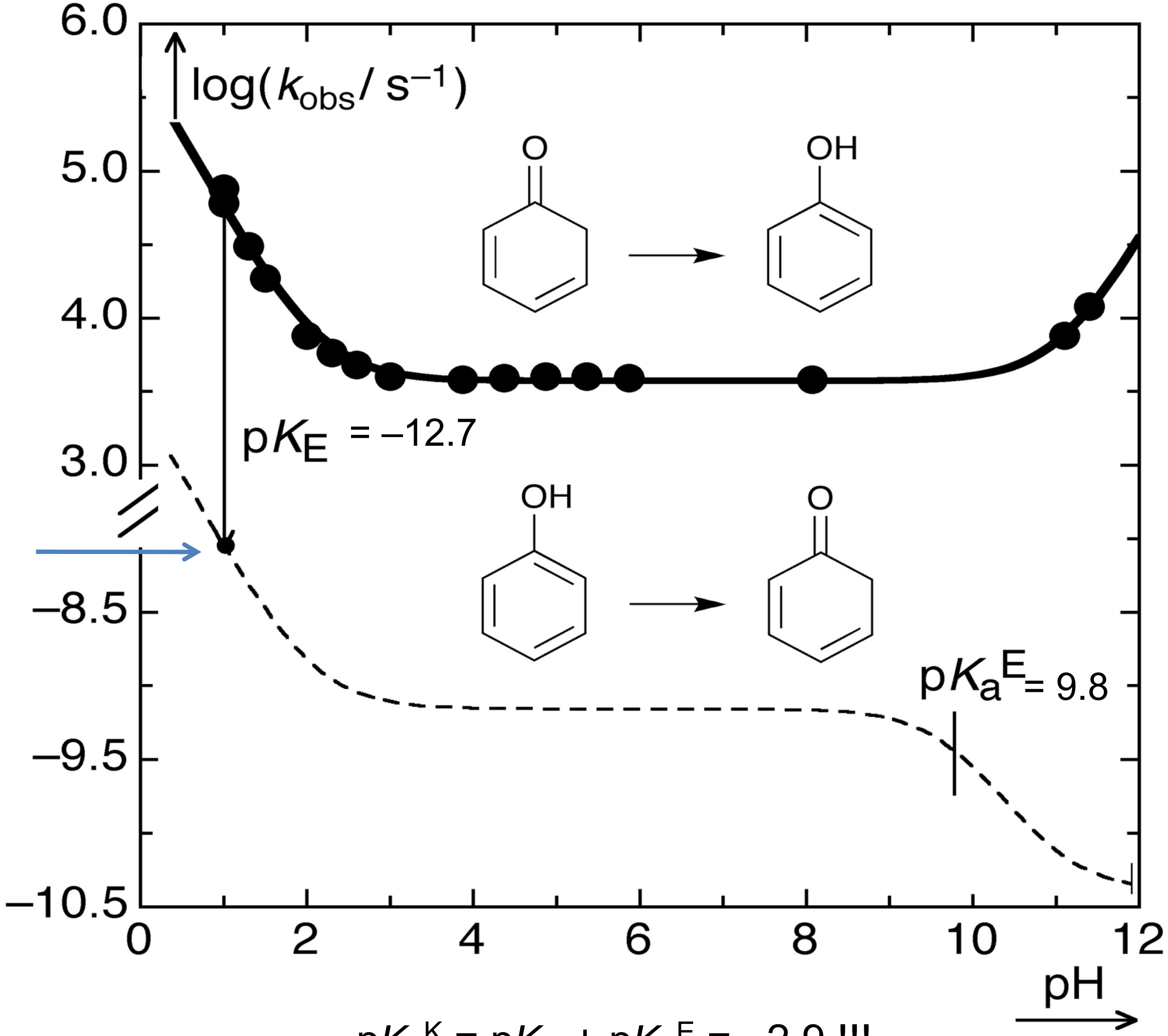
The determination of rate constants for a pH-rate profile in solutions with buffers (pH = 3 –11) requires extrapolation to zero buffer concentration.



The determination of the coefficients of general acid catalysis, k_{HA}, and of general base catalysis, k_{A^-}, requires measurements in buffer solutions with different mole ratios of general acid, x_{HA}, and extrapolation to x_{HA} = 0 and 1, respectively.

Photochemical generation of unstable enols and ketones





Isotopic exchange

pK_a^K = pK_E + pK_a^E = –2.9 !!!

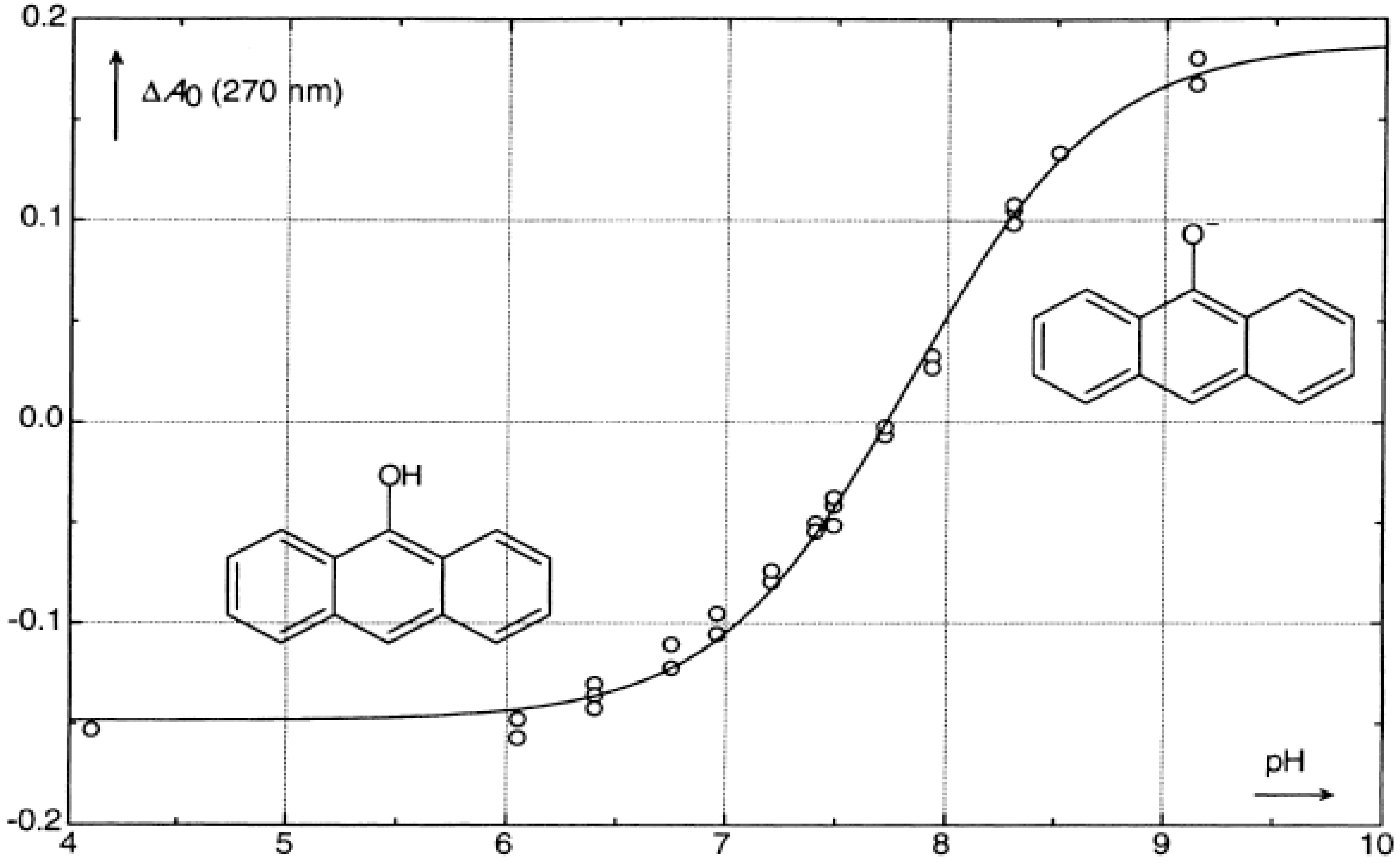
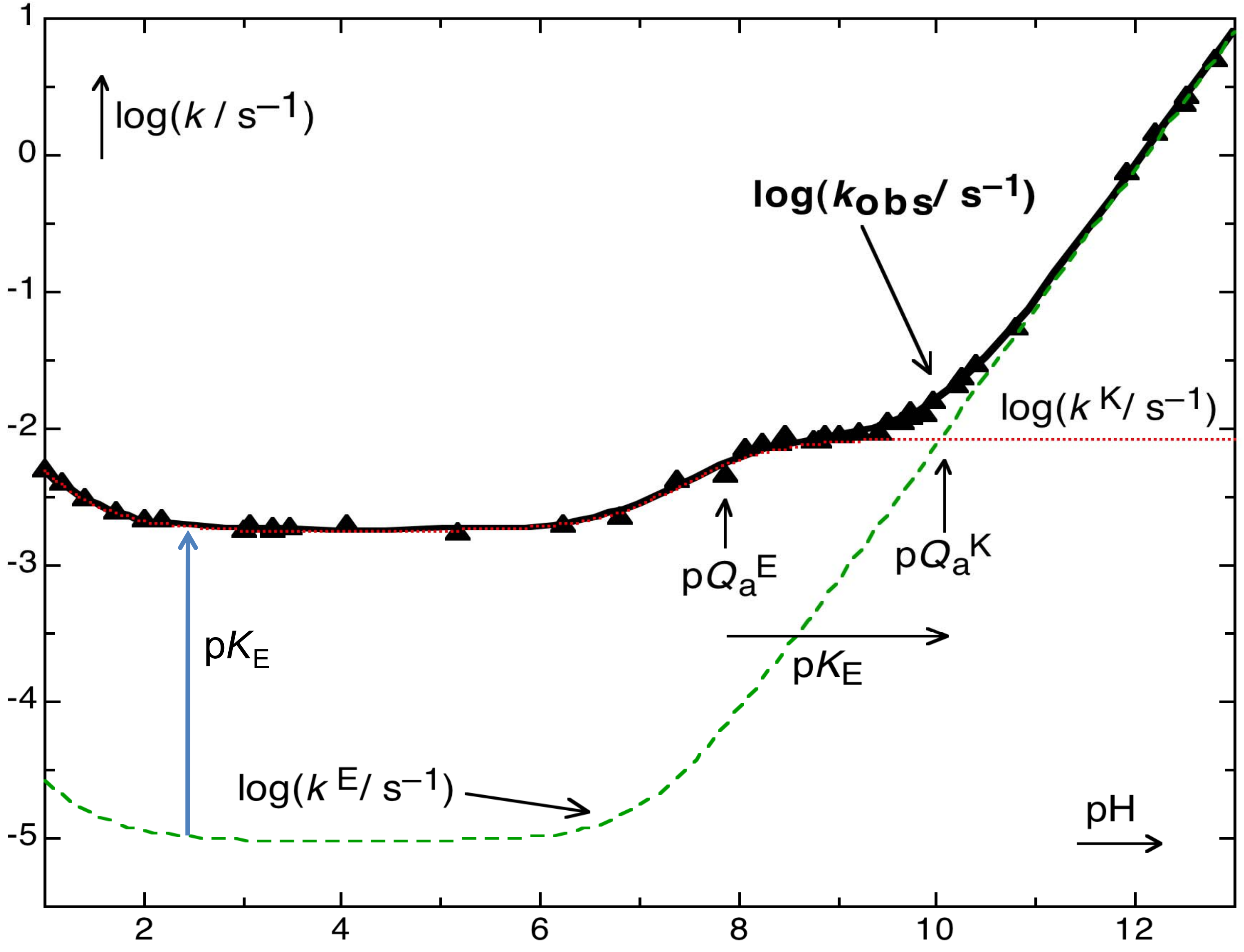
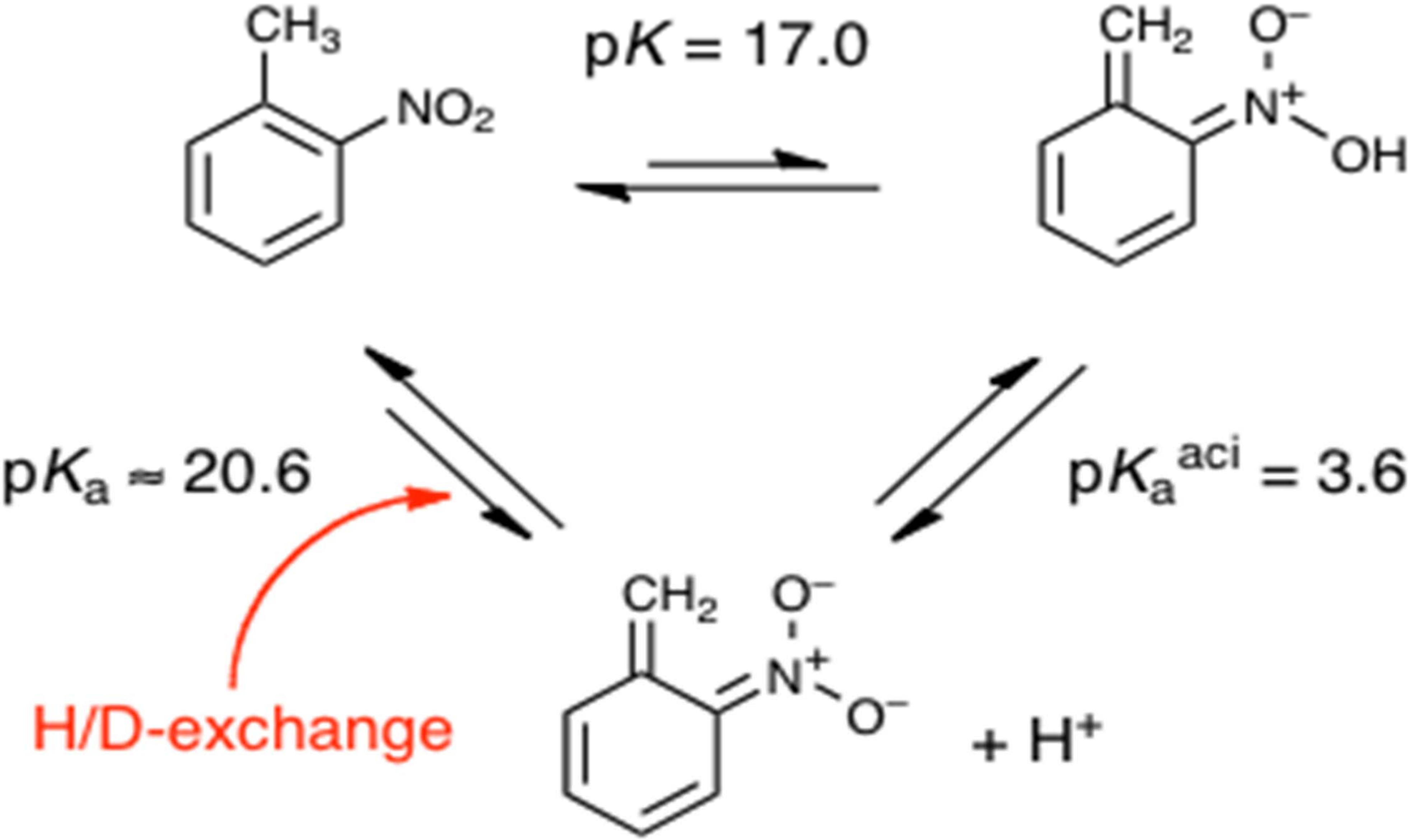


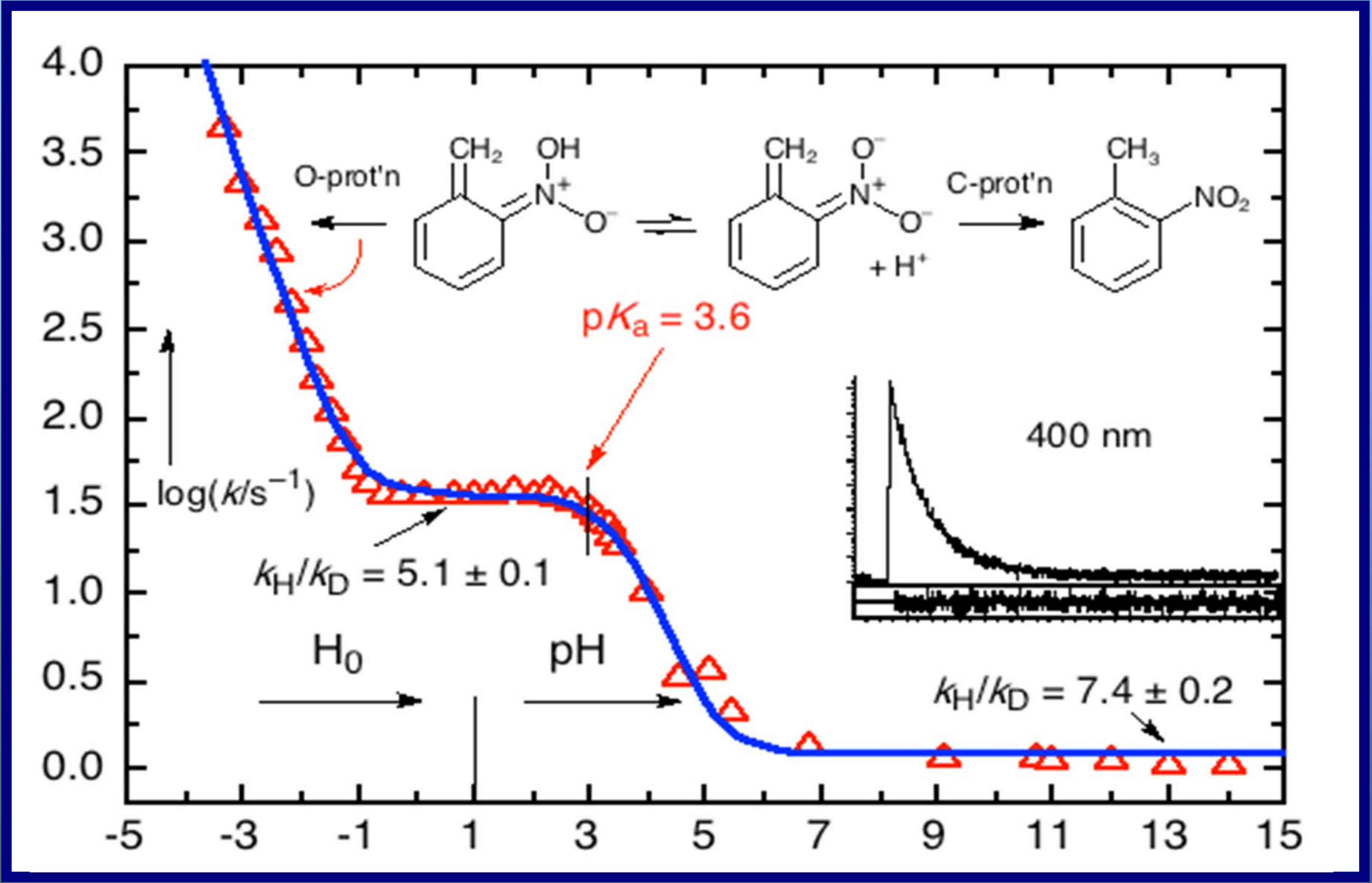
Fig. 2. *Titration curve for the ionization of* **E** *determined by flash photolysis.* The data points are initial absorbances A_0 at 270 nm immediately after the flash. The solid line is the best fit of *Eqn. 5* to the data points.

pH–rate profile for 9-Anthrole –>10*H*-Anthr-9-one



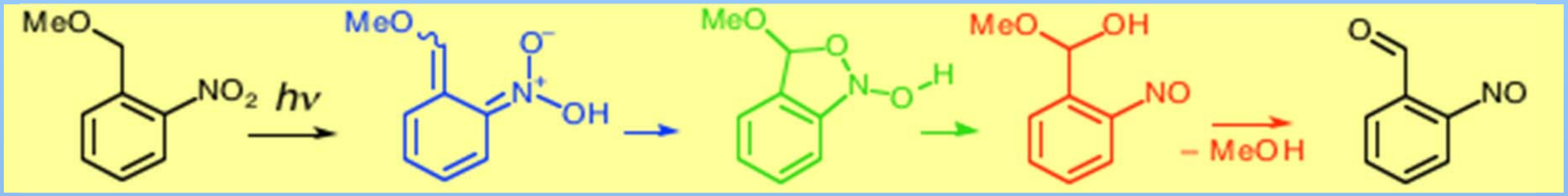

CH3
NO2
pK = 17.0
CH2
O−
N+
OH
pKa ≈ 20.6
pKa aci = 3.6
H/D-exchange
CH2
O−
N+
O−
+ H+

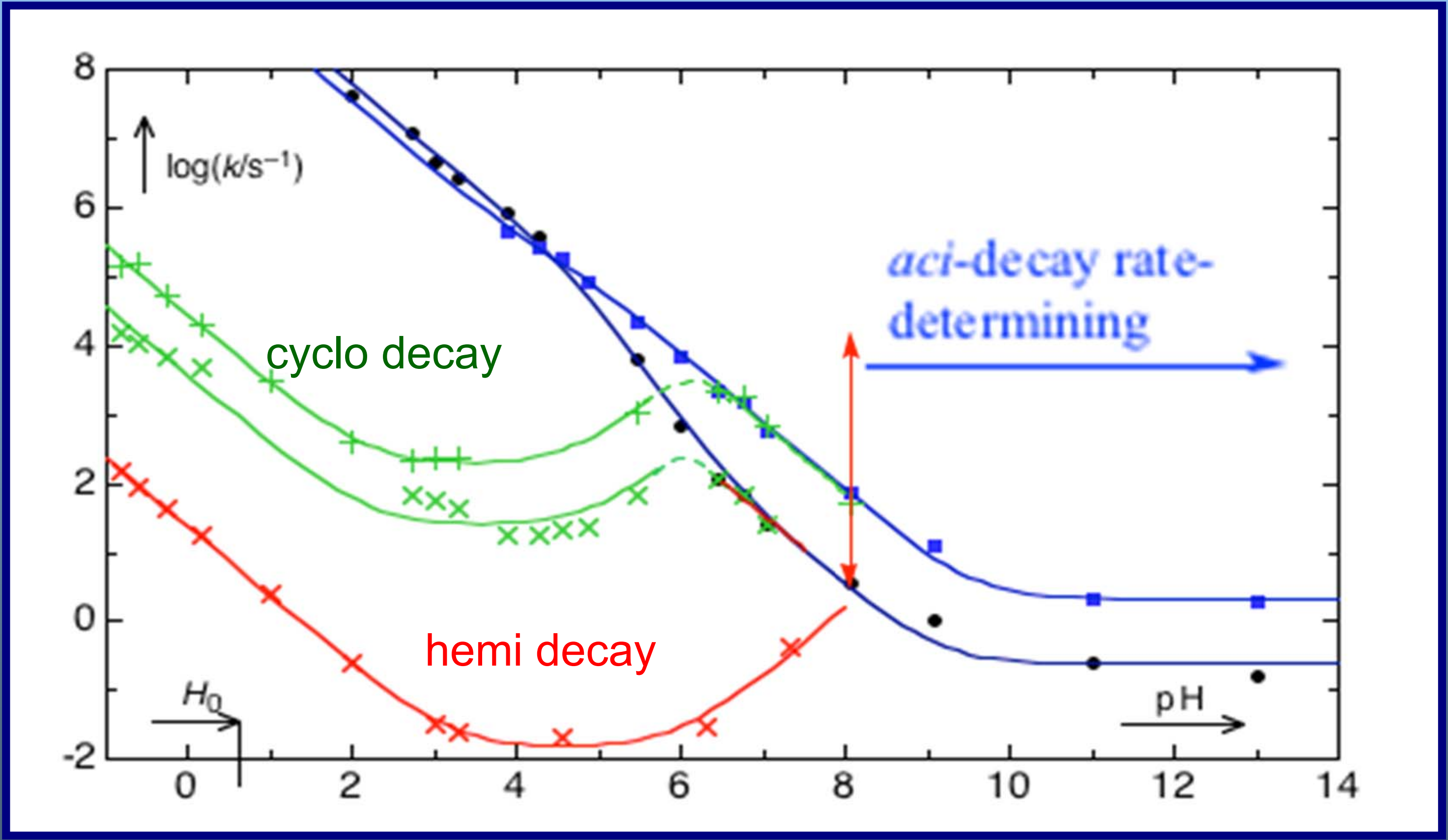
pH-rate profile: *o*-nitrotoluene



Helv. Chim. Acta **2001**, *84*, 1441

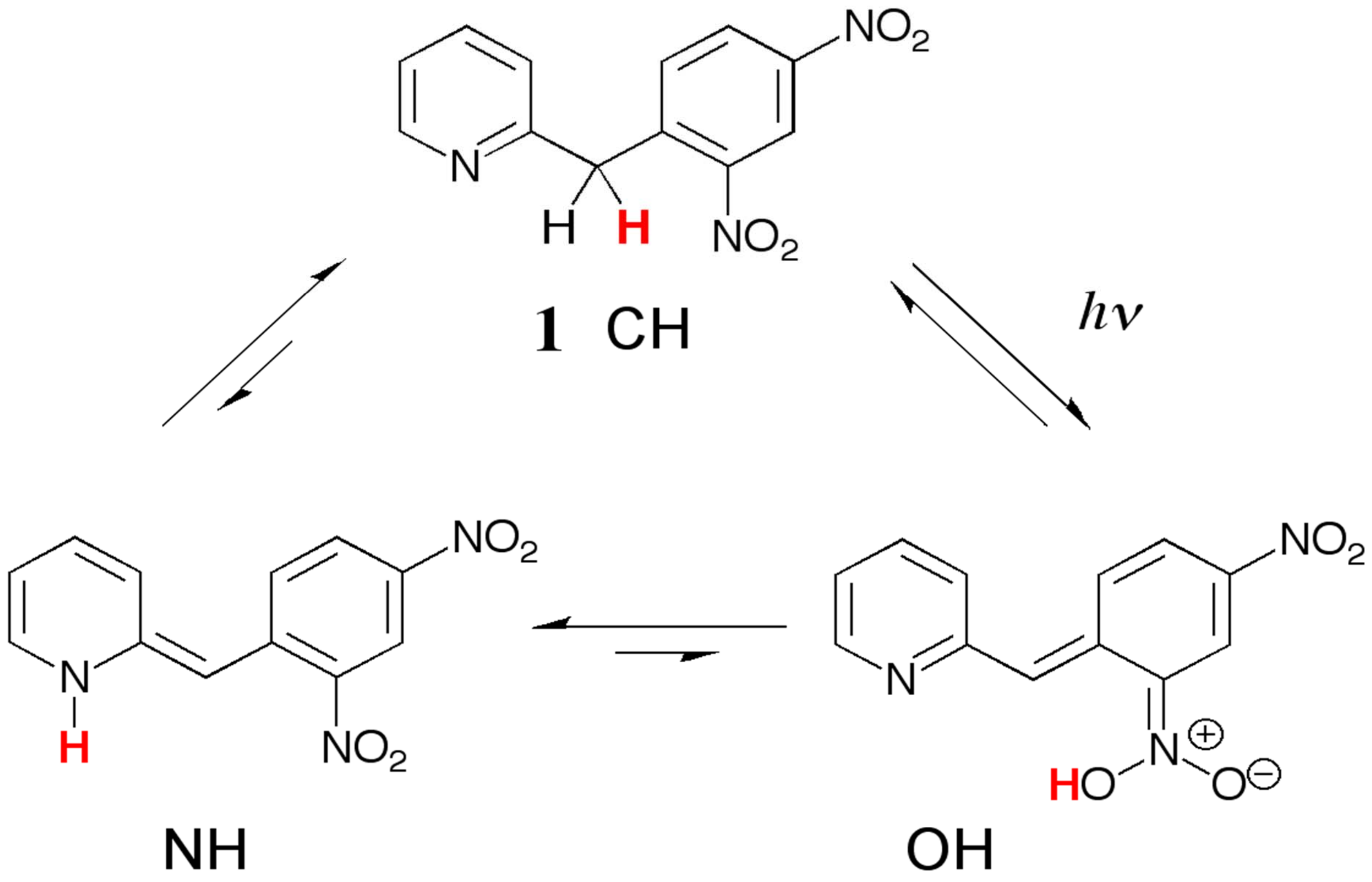
o-Nitrobenzyl methyl ether: pH-profile



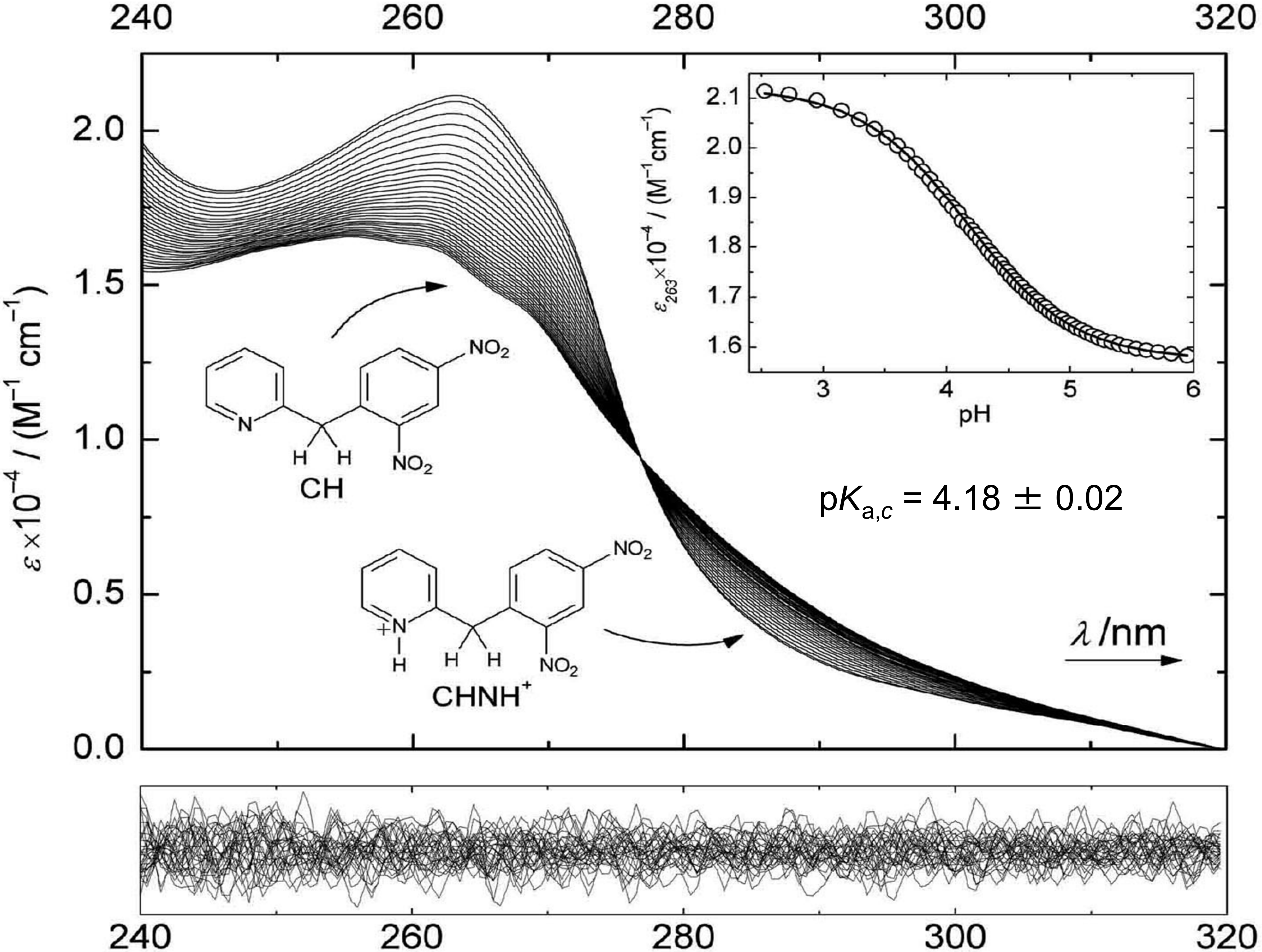


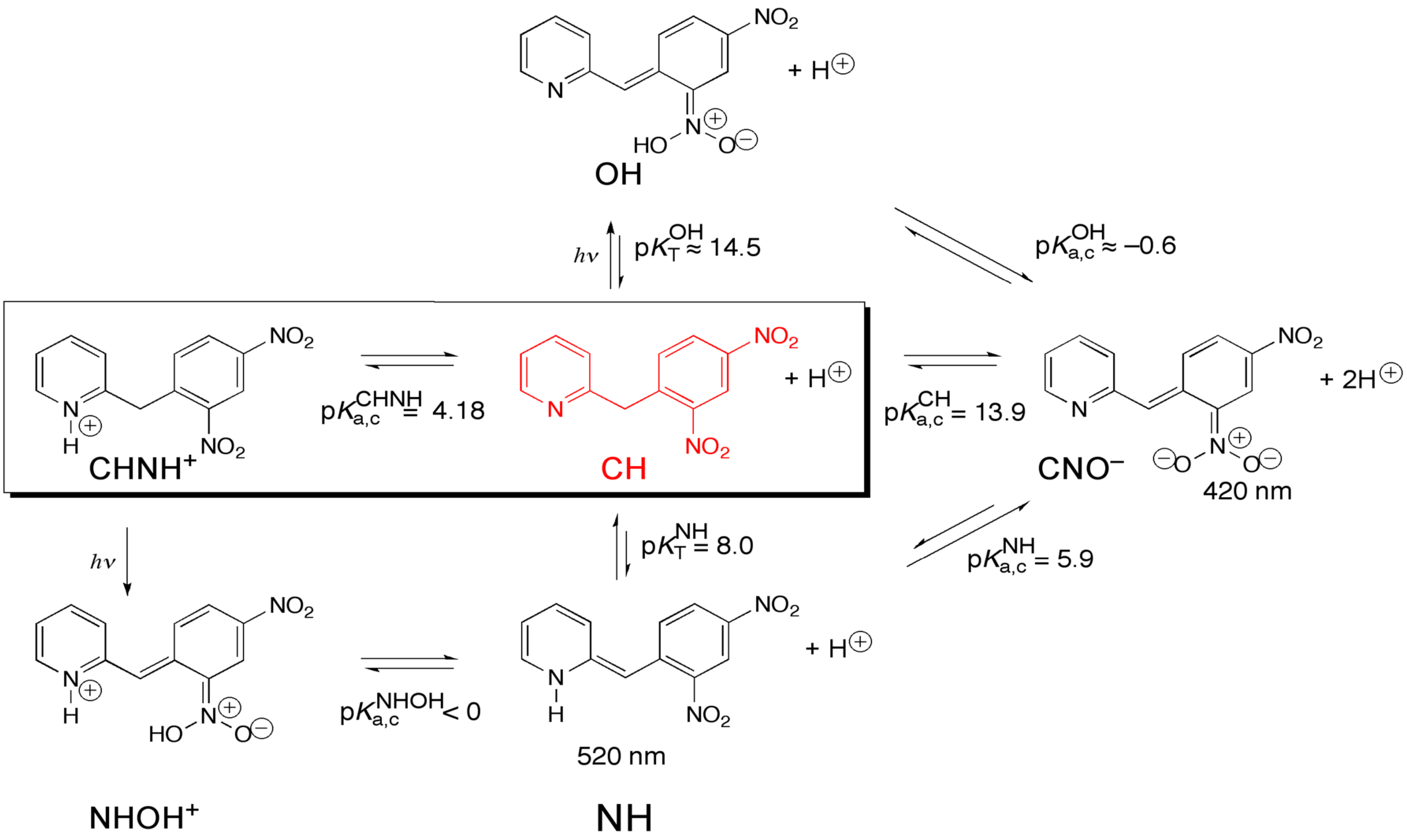
JACS, **2004**, *126*, 4581

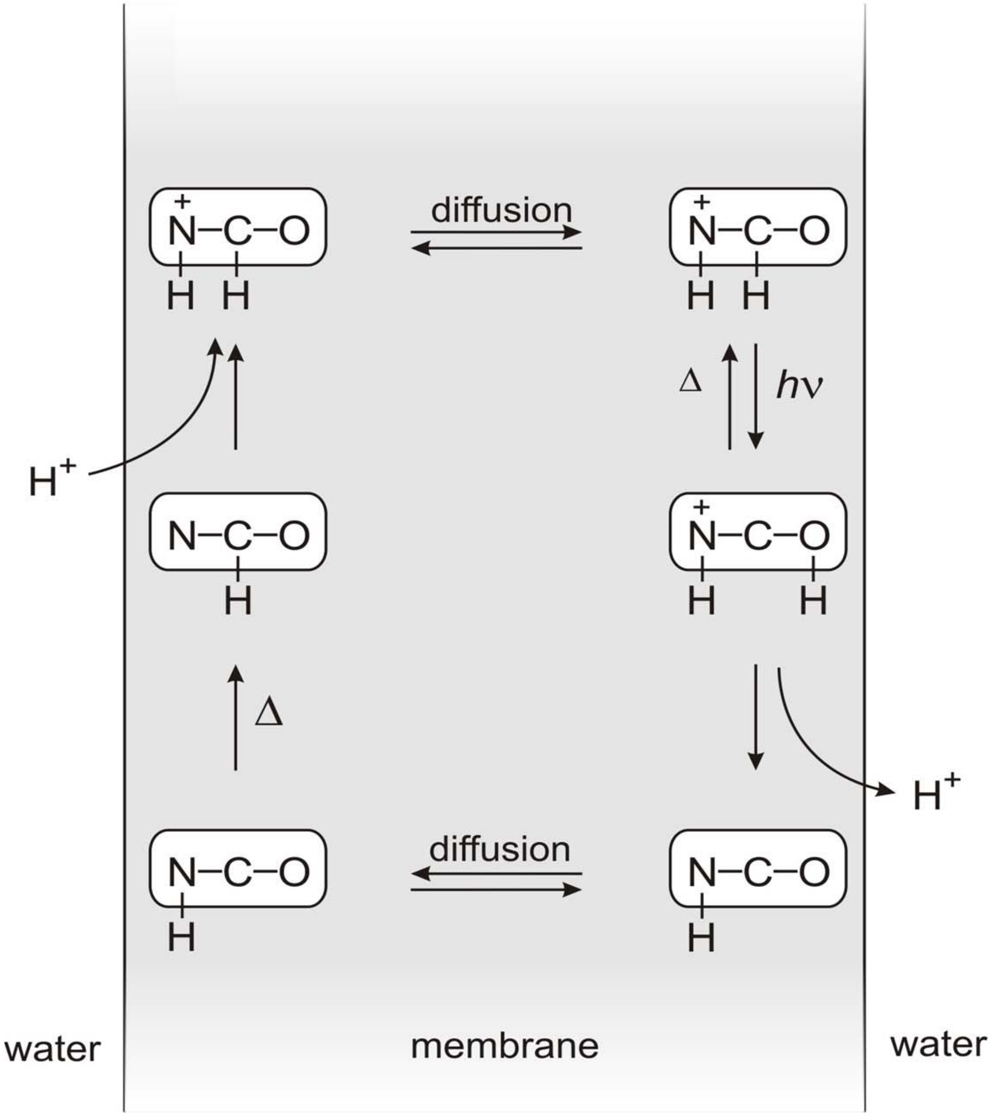
2-(2,4-Dinitrobenzyl)pyridine: A light activated proton shuttle

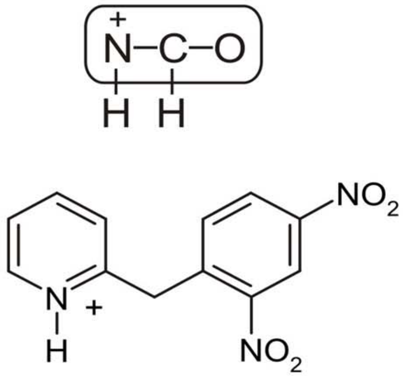


Helv. Chim. Acta, **2009**, *92,* 1909

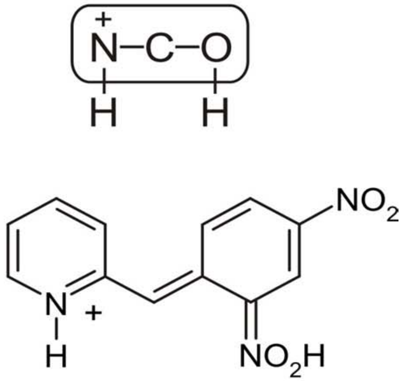

240
260
280
300
320
ε ×10⁻⁴ / (M⁻¹ cm⁻¹)
2.0
1.5
1.0
0.5
0.0
NO2
N
H
H
NO2
CH
NO2
+N
H
H
H
NO2
CHNH+
λ /nm
ε263×10⁻⁴ / (M⁻¹cm⁻¹)
2.1
2.0
1.9
1.8
1.7
1.6
3
4
5
6
pH
pKa,c = 4.18 ± 0.02
240
260
280
300
320


OH
+ H⊕
hν
pK_T^OH ≈ 14.5
pK_a,c^OH ≈ –0.6
CHNH+
pK_a,c^CHNH = 4.18
CH
+ H⊕
pK_a,c^CH = 13.9
CNO–
+ 2H⊕
420 nm
hν
pK_T^NH = 8.0
pK_a,c^NH = 5.9
NHOH+
pK_a,c^NHOH < 0
NH
+ H⊕
520 nm

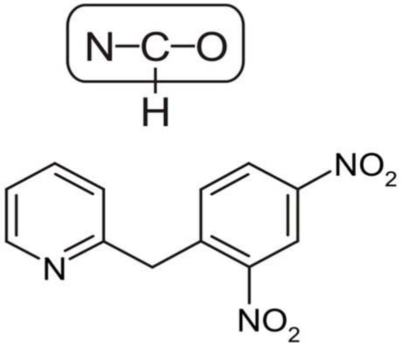




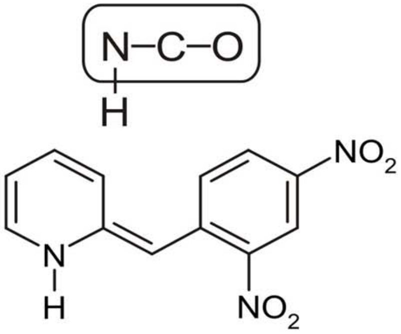
CHNH+



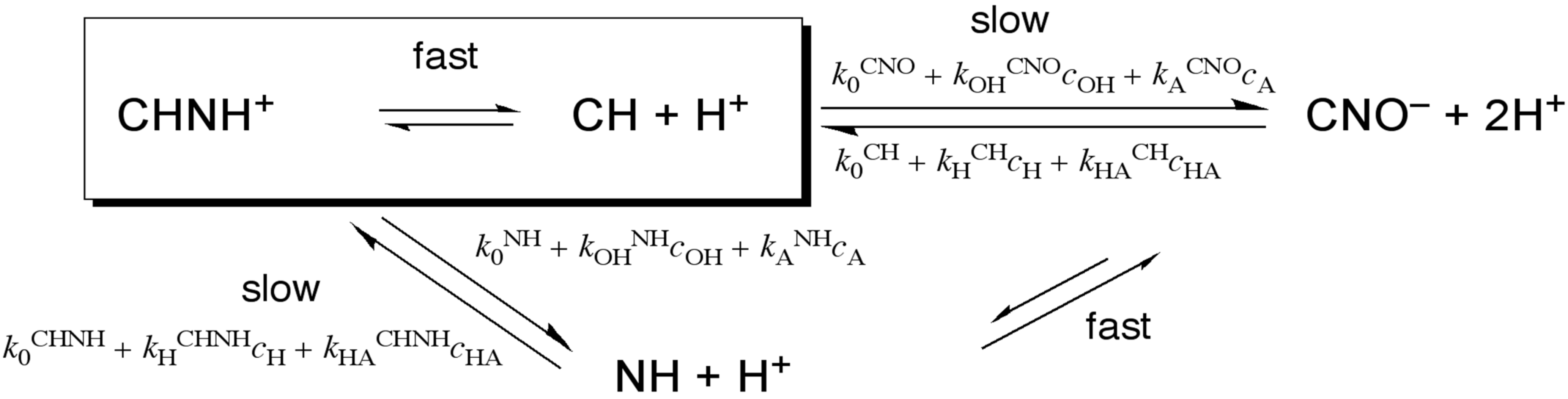
NHOH+

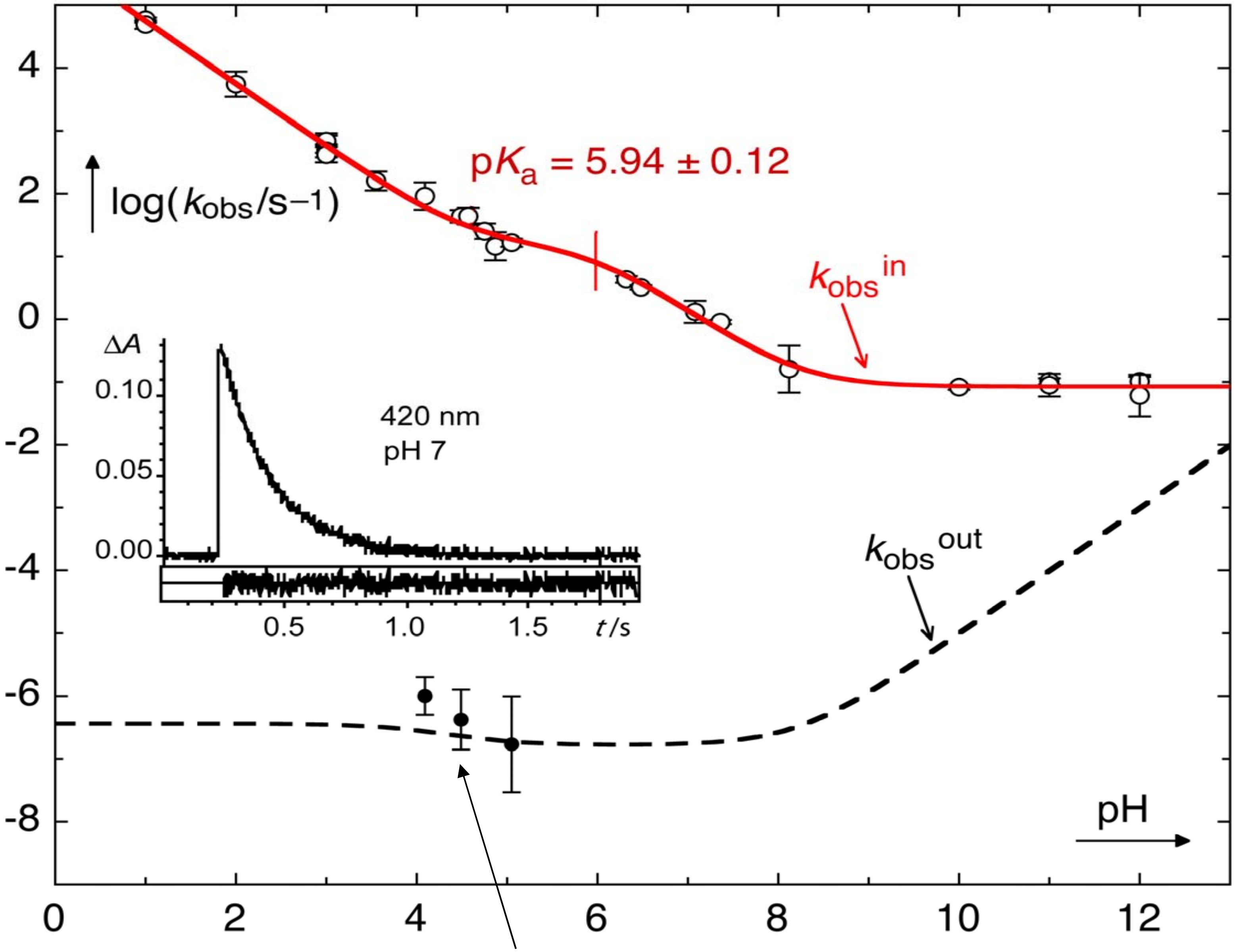


CH

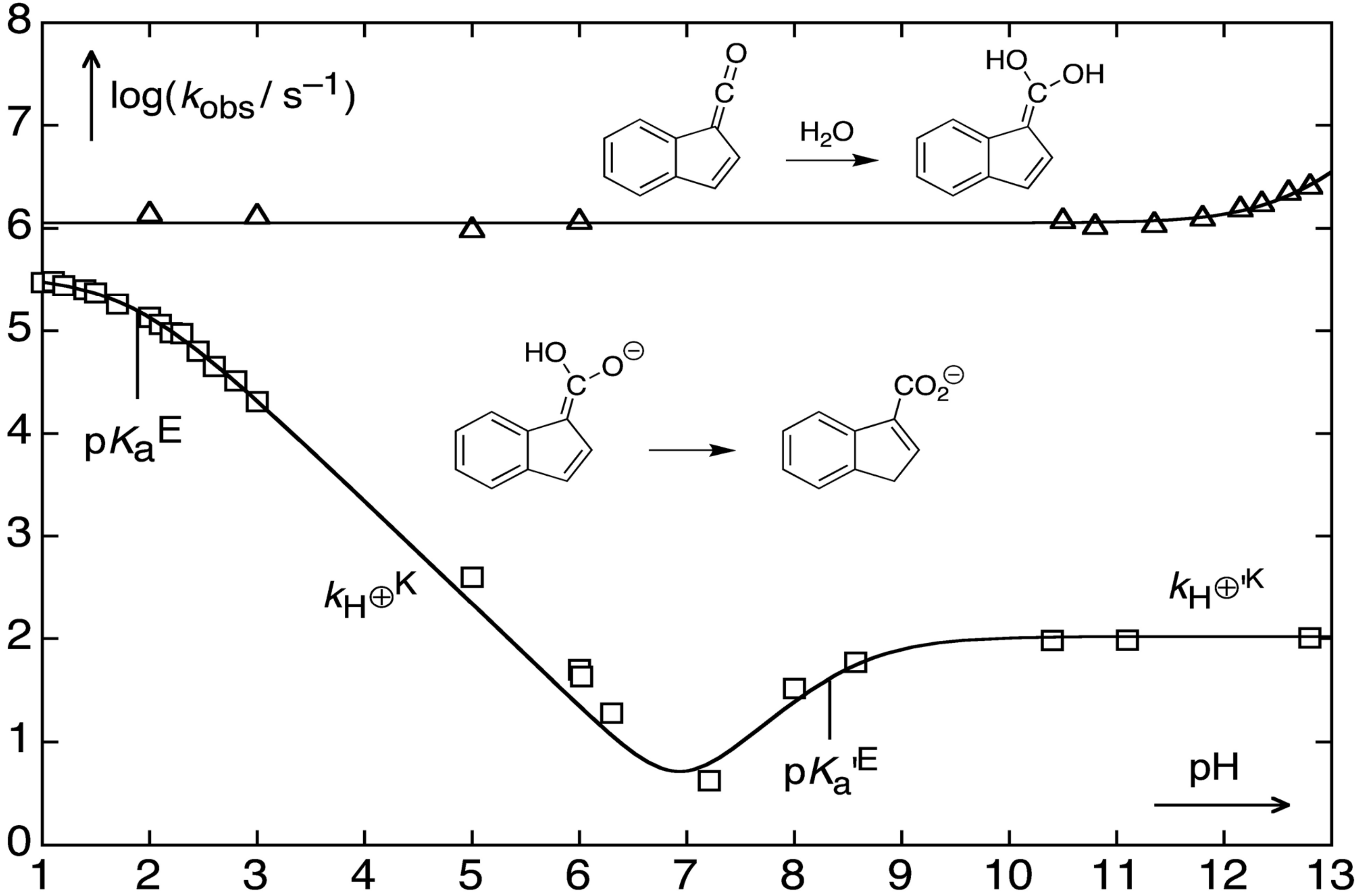


NH


CHNH$^+$
fast
CH + H$^+$
slow
$k_0^{\mathrm{CNO}} + k_{\mathrm{OH}}^{\mathrm{CNO}} c_{\mathrm{OH}} + k_{\mathrm{A}}^{\mathrm{CNO}} c_{\mathrm{A}}$
CNO$^-$ + 2H$^+$
$k_0^{\mathrm{CH}} + k_{\mathrm{H}}^{\mathrm{CH}} c_{\mathrm{H}} + k_{\mathrm{HA}}^{\mathrm{CH}} c_{\mathrm{HA}}$
$k_0^{\mathrm{NH}} + k_{\mathrm{OH}}^{\mathrm{NH}} c_{\mathrm{OH}} + k_{\mathrm{A}}^{\mathrm{NH}} c_{\mathrm{A}}$
slow
$k_0^{\mathrm{CHNH}} + k_{\mathrm{H}}^{\mathrm{CHNH}} c_{\mathrm{H}} + k_{\mathrm{HA}}^{\mathrm{CHNH}} c_{\mathrm{HA}}$
fast
NH + H$^+$

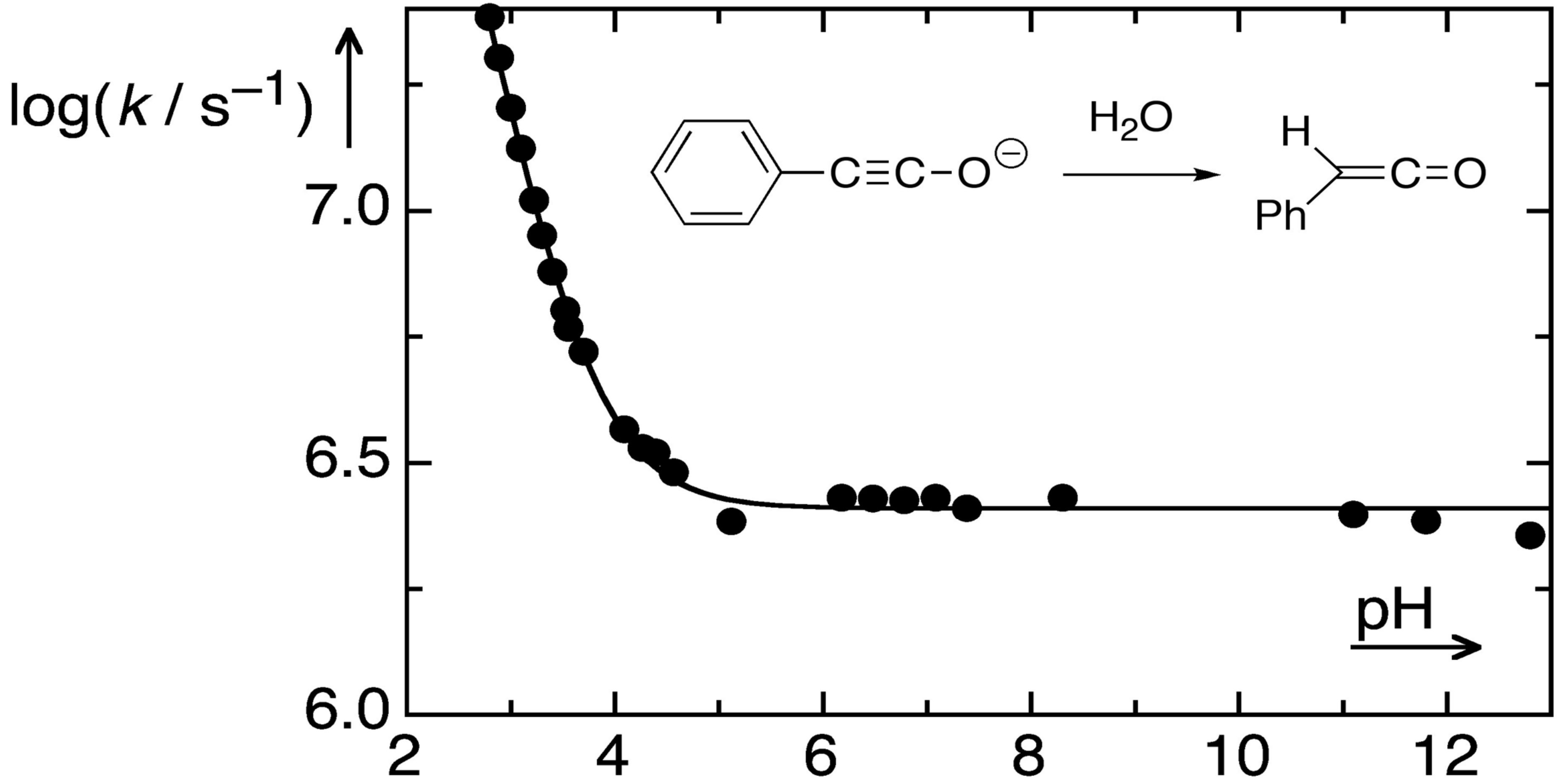


Intercepts of buffer dilution plots

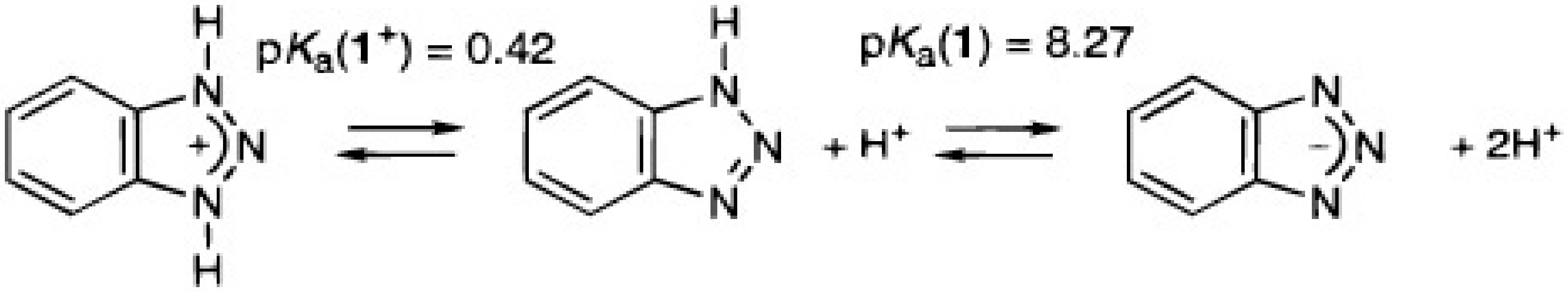


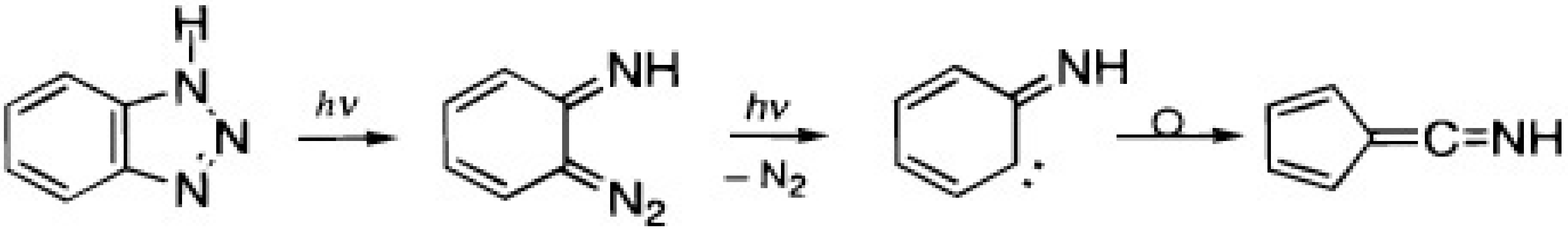
$\uparrow \log(k_{obs} / s^{-1})$
8
7
6
5
4
3
2
1
0
1
2
3
4
5
6
7
8
9
10
11
12
13
O
C
H_2O
HO
OH
C
HO
C
$O^{\ominus}$
$CO_2^{\ominus}$
pK_a^E
$k_{H^{\oplus}}^K$
$k_{H^{\oplus}}'^K$
$pK_a'^E$
pH

pH–Rate profile for the ketonization of phenylynol



pK_a(phenylynol) ≤ 2.8 !


pKa(1+) = 0.42
pKa(1) = 8.27
+ H+
+ 2H+


hν
hν
− N2
NH
N2
C=NH

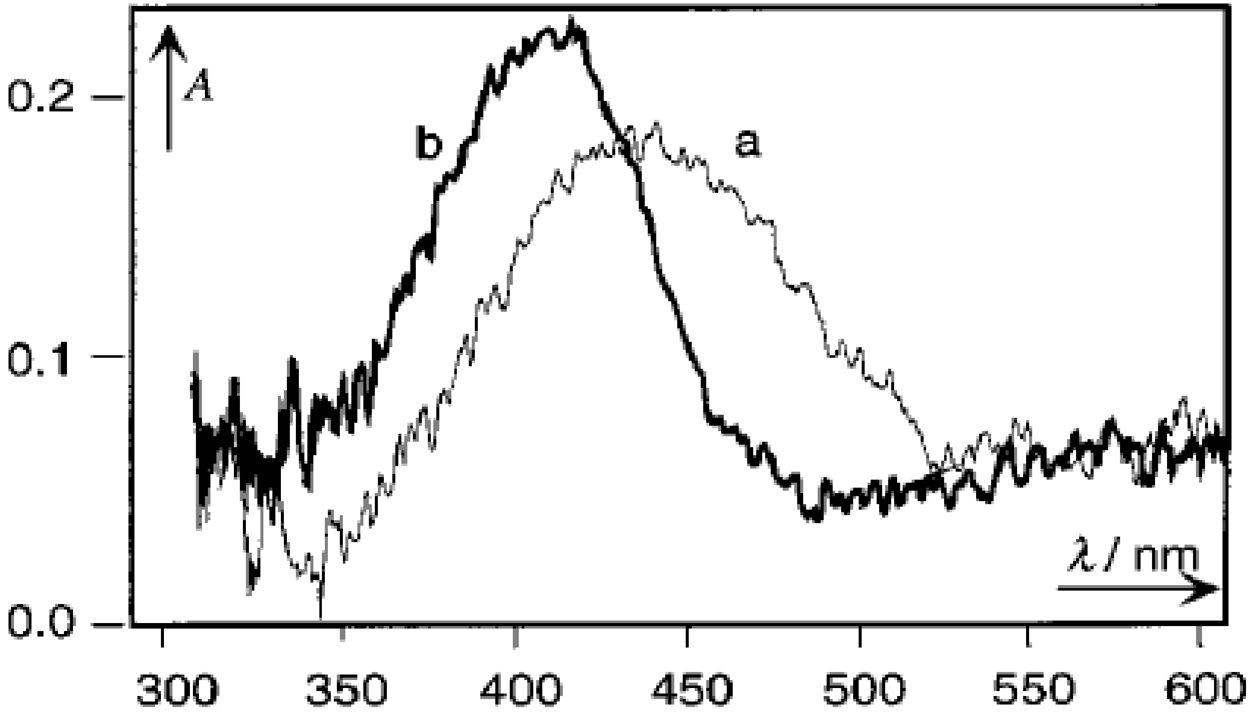
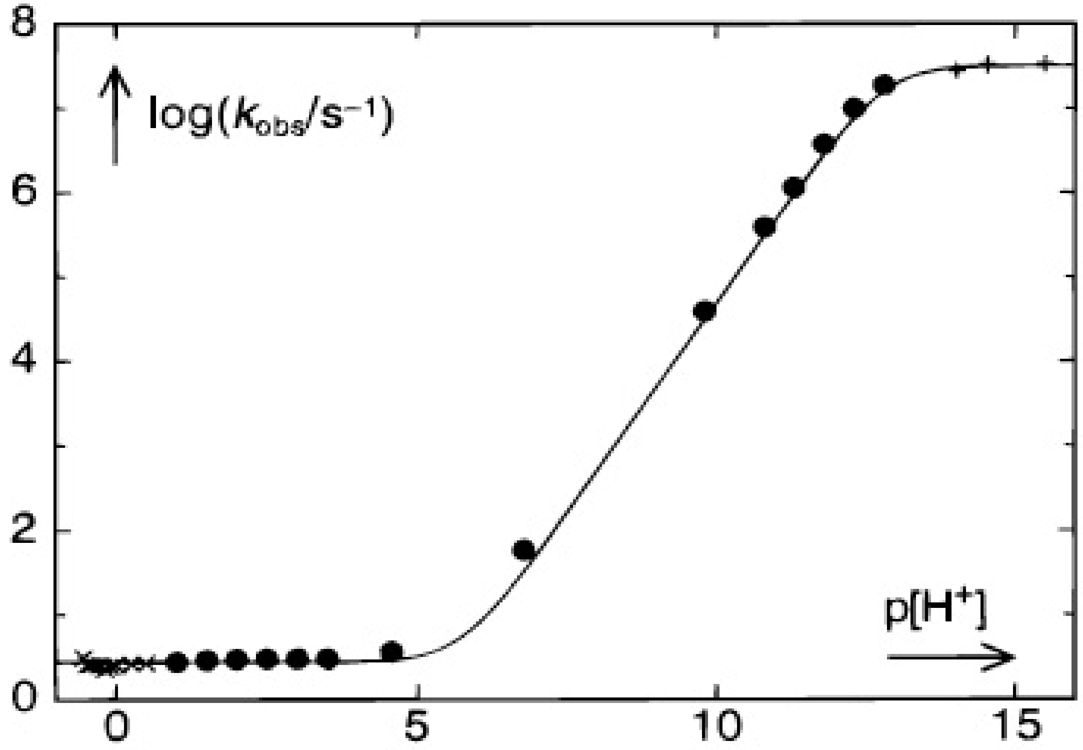
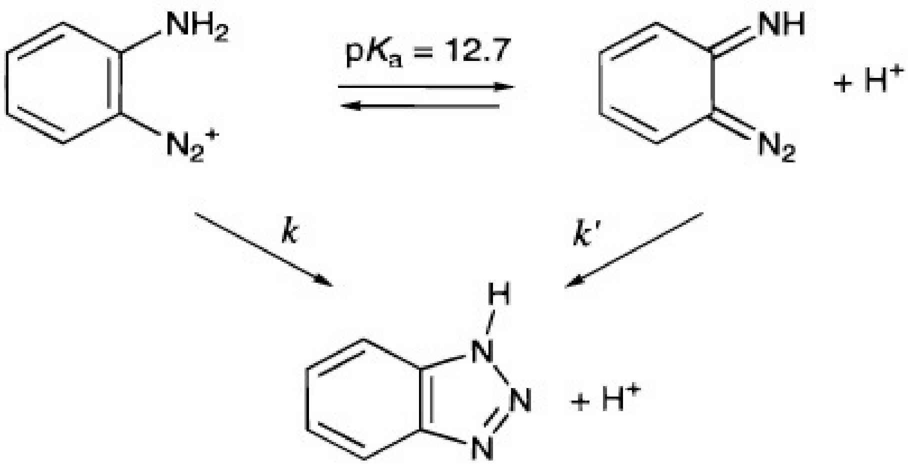


Figure 1. Absorption spectra of the transient generated by flash photolysis of **1** using an excitation pulse from a KrF-excimer-laser (λ_{exc} = 248 nm, 100 mJ per pulse, pulse width ~25 ns, delay after the pulse maximum ~30 ns). Spectrum a: 1.0 N aqueous NaOH. Spectrum b: 0.001 N aqueous NaOH.


8
6
4
2
0
0
5
10
15
log(k_{obs}/s^{-1})
p[H$^+$]


NH$_2$
N$_2^+$
pK_a = 12.7
NH
N$_2$
+ H$^+$
k
k'
H
N
N
N
+ H$^+$

Bronsted equation

$$\log\left(\frac{k_{HA}}{p}\right) = \log G_A + \alpha \log\left(\frac{qK_a^{HA}}{p}\right)$$

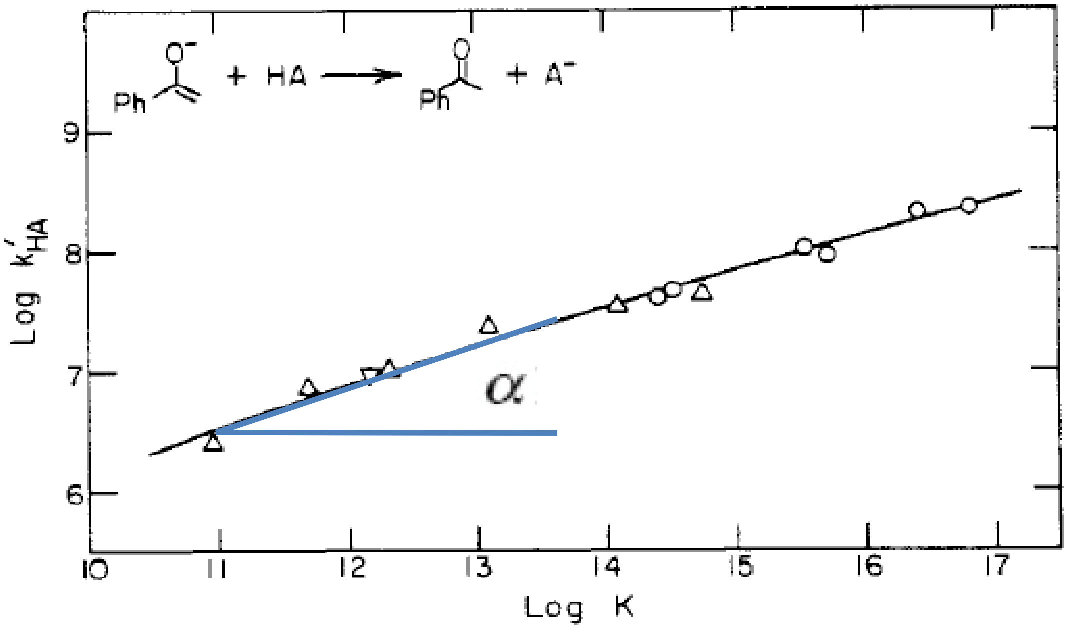
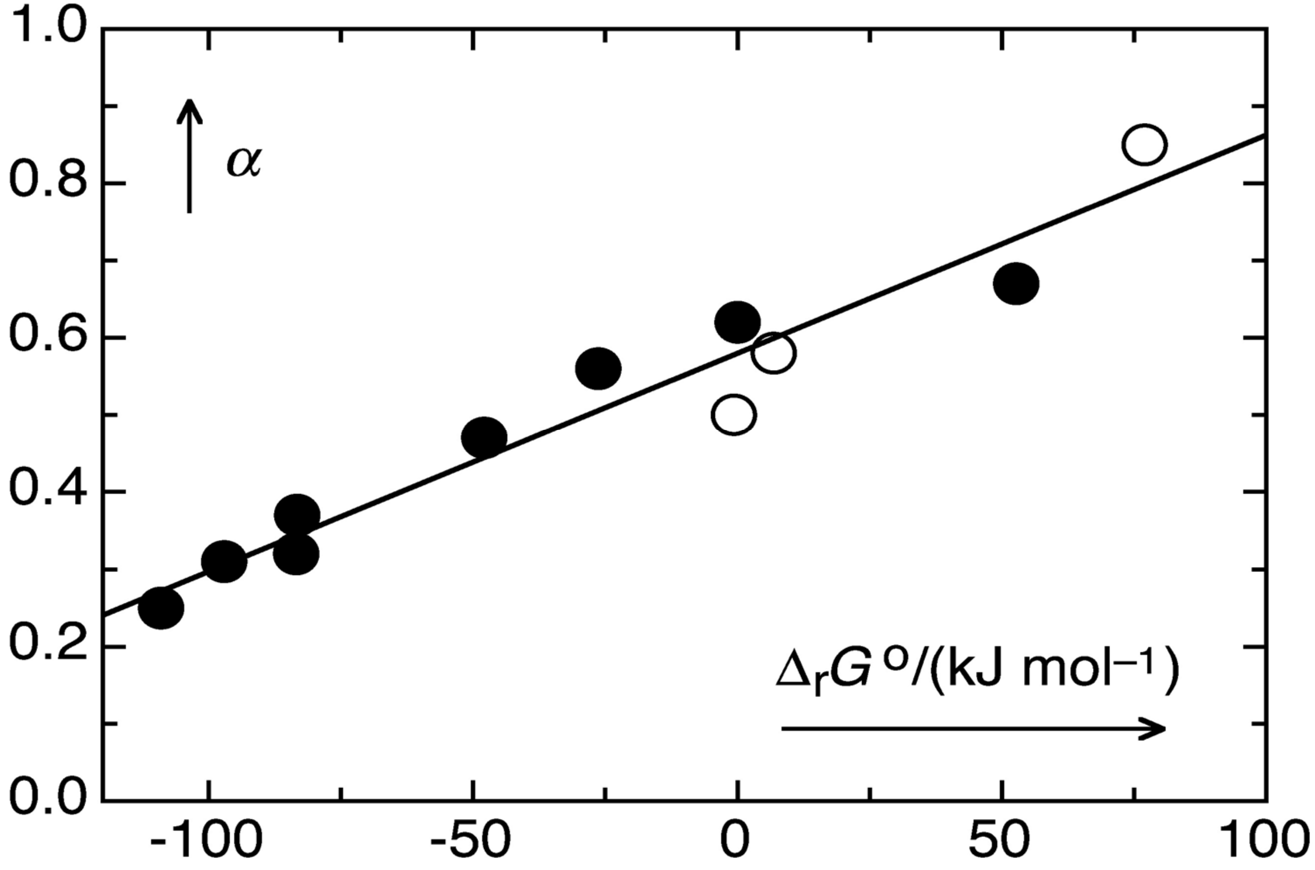
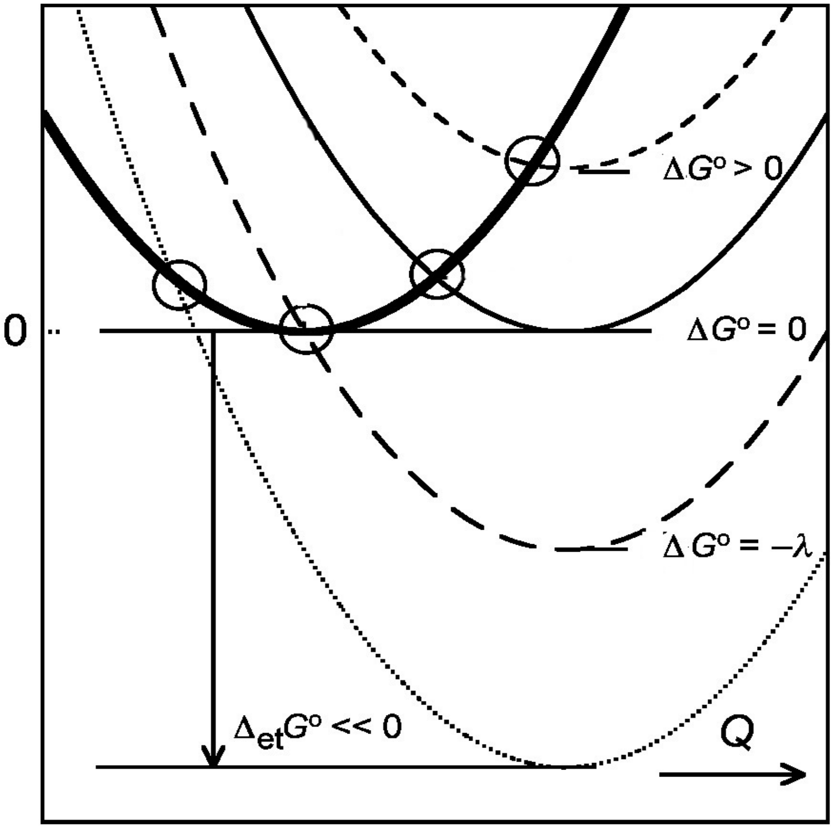


Figure 1. Rate–equilibrium relation for the ketonization of acetophenone enolate ion in aqueous solution at 25 °C catalyzed by RCO_2H (○) and RPO_3H^- (including $HOPO_3H^-$) (△). The points represent "chemical" rate and equilibrium constants with symmetry-induced contributions removed by using the following statistical factors: $p = 1$, $q = 2$ for RCO_2H; $p = 1$, $q = 3$ for RPO_3H^-; $p = 2$, $q = 3$ for $H_2PO_4^-$; $p = 3$, $q = 1$ for $PhCOCH_3$.

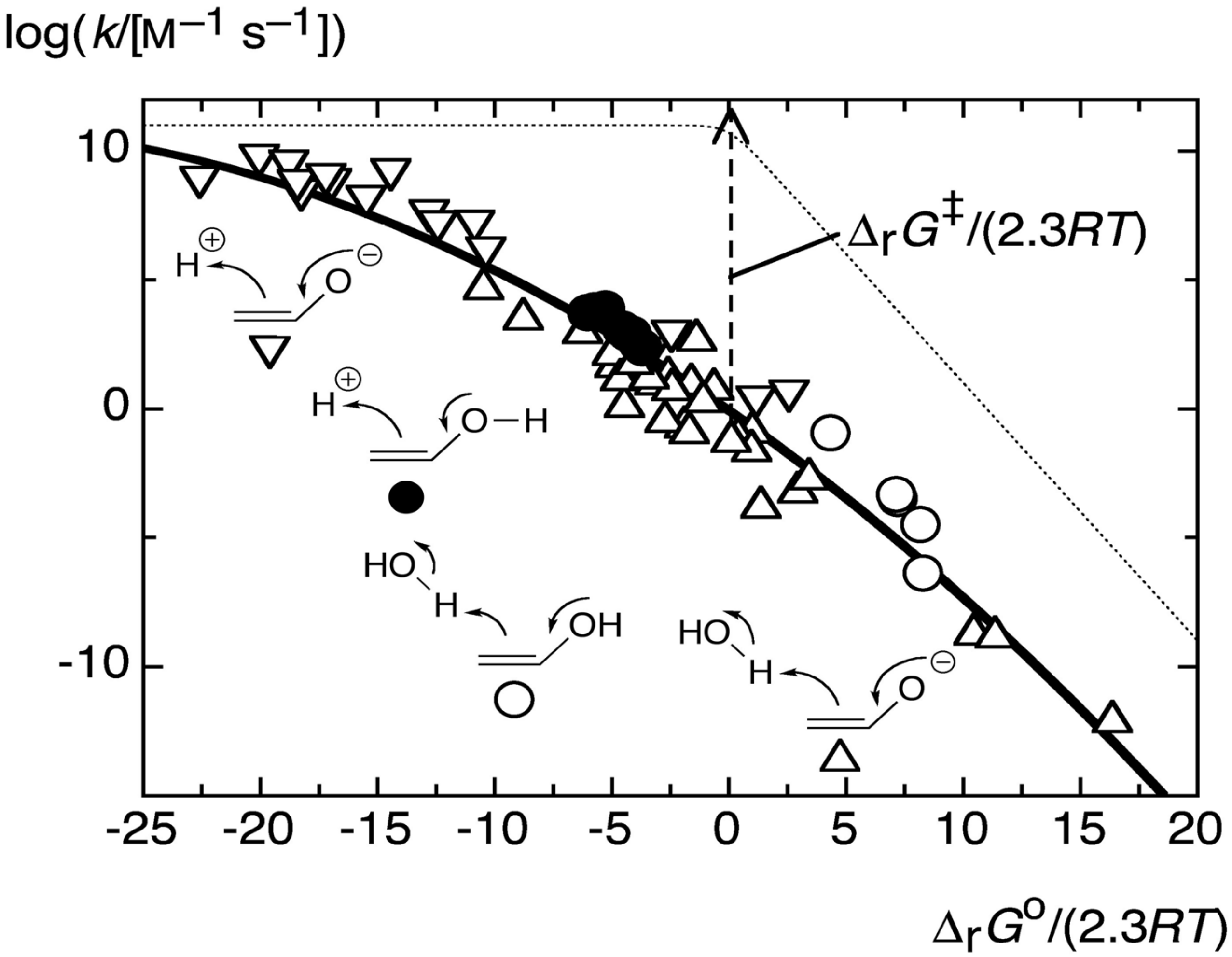
Bronsted α variation with ΔG^o



Marcus theory



$$\log\frac{k}{k_\mathrm{d}} = \left(\frac{-\Delta_\mathrm{r}G^\ddagger}{\ln(10)RT}\right), \text{ where } \Delta_\mathrm{r}G^\ddagger = \Delta_\mathrm{r}G_0^\ddagger\left(1+\frac{\Delta_\mathrm{r}G^\circ}{4\Delta_\mathrm{r}G_0^\ddagger}\right)^2$$



Solid line: Marcus eq. $$\log\frac{k}{k_\mathrm{d}} = \left(\frac{-\Delta_\mathrm{r}G^\ddagger}{\ln(10)RT}\right),\ \text{where } \Delta_\mathrm{r}G^\ddagger = \Delta_\mathrm{r}G_0^\ddagger\left(1+\frac{\Delta_\mathrm{r}G^\mathrm{o}}{4\Delta_\mathrm{r}G_0^\ddagger}\right)^2$$

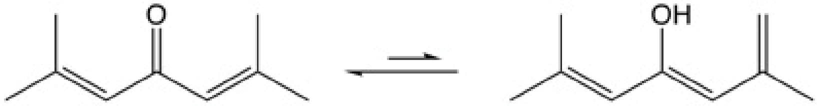
The parameter $\Delta_\mathrm{r}G_0{}^\ddagger$ is called the “intrinsic” barrier, the barrier of a thermoneutral reaction, $\Delta_\mathrm{r}G^\circ = 0$. The rate of diffusion was assumed as $k_\mathrm{d} = 1 \times 10^{11}$ M^{-1} s^{-1}. Nonlinear least-squares fitting of Equation (19) to the set of data gave $\Delta_\mathrm{r}G_0{}^\ddagger = 55.6 \pm 0.7$ kJ mol^{-1}.

What is the mechanism of the “uncatalyzed” reaction?

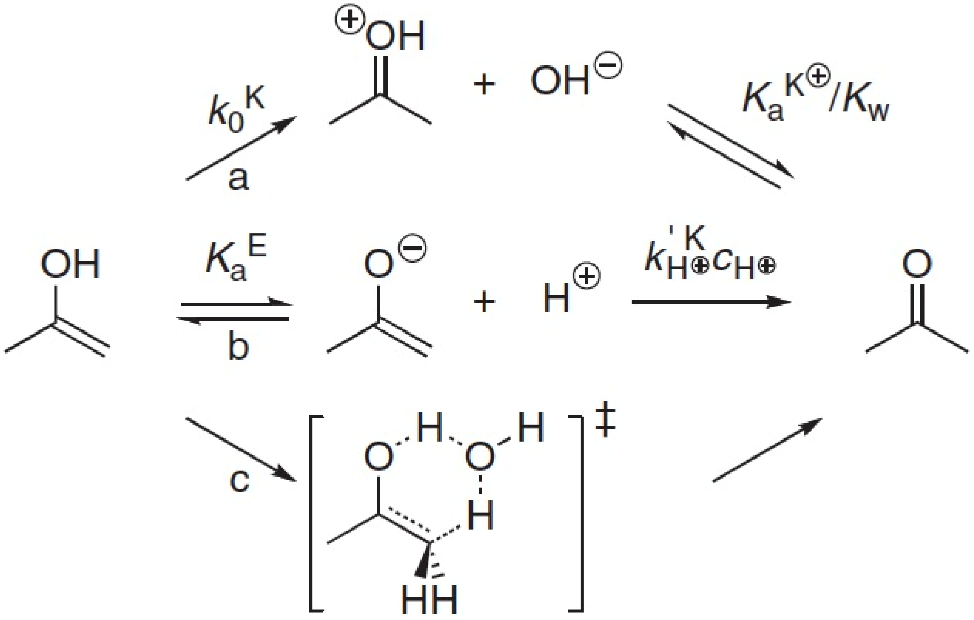
Flat portion of pH–rate profile near pH 7 (catalyzed neither by acid nor by base)

Several mechanisms may be considered:

- Intramolecular 1,5-H shift in the ketonization of 1,3-dienols:

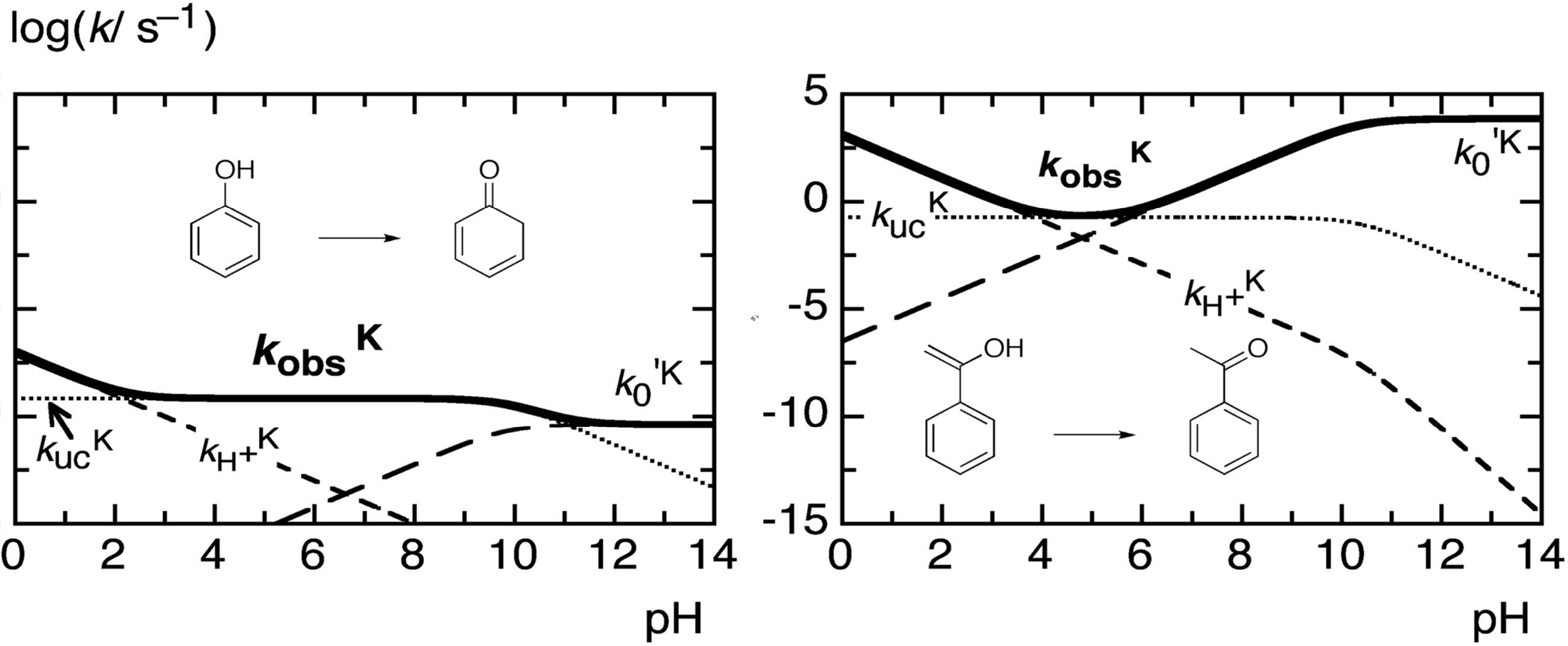


- a) water as a general acid
- b) water as a general base
- c) concerted transfer of two protons



Bronsted eqn: b)

The rate constant of the “uncatalyzed” reaction dominates around pH 7, if $\Delta_r G^o$ >> 0



Is carbon protonation of enols always rate-determining?

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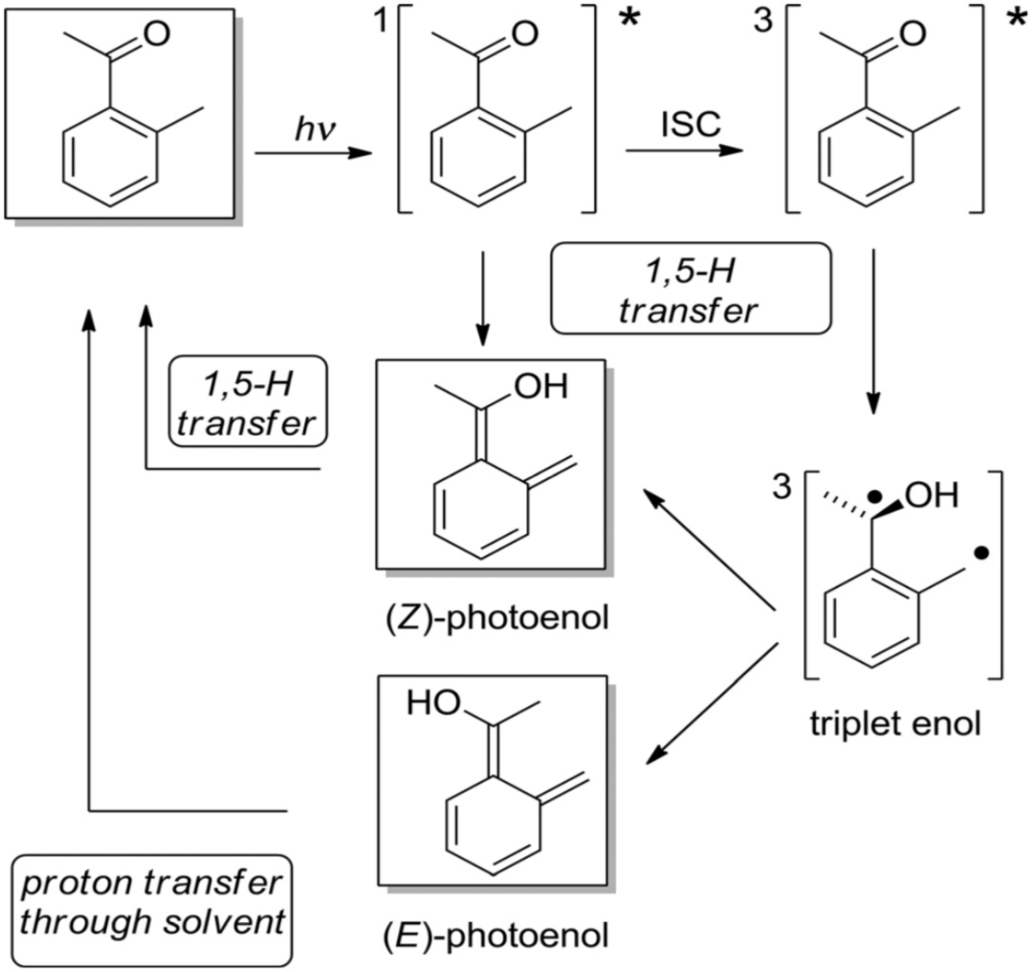


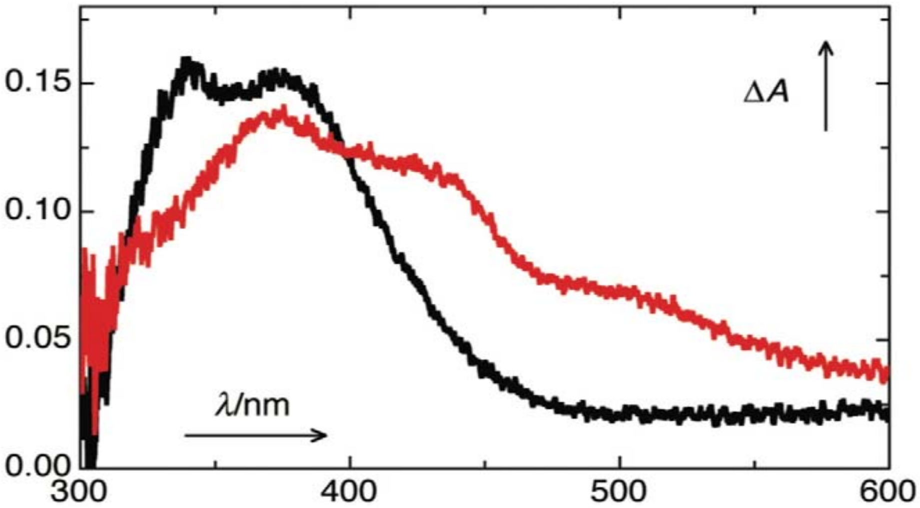


Fig. 1 Transient absorption spectra obtained by LFP of **MA** in water (black line) and in 0.1 N aqueous NaOH (red line). Excitation 266 nm, delay ~20 ns, window 10 ns.

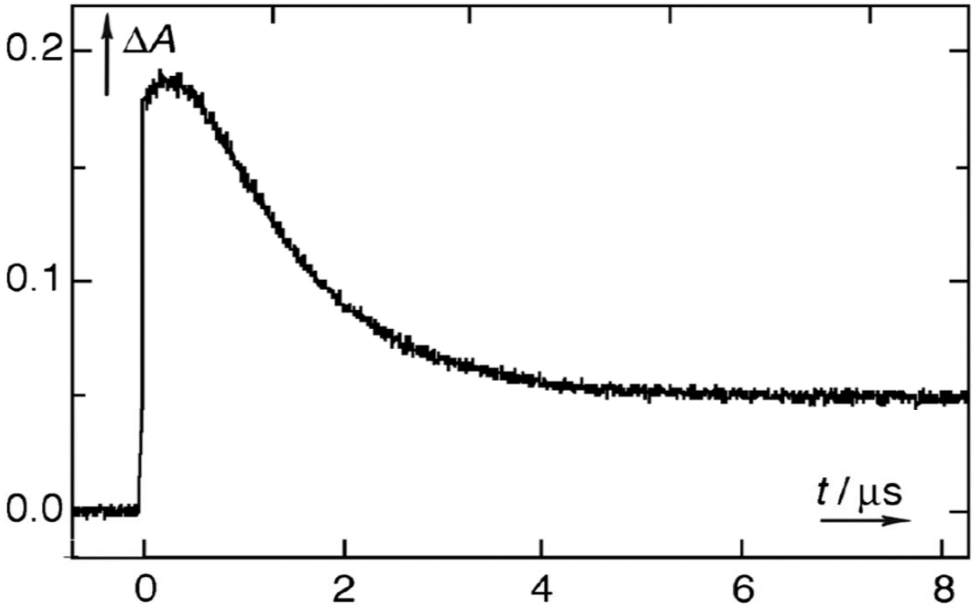
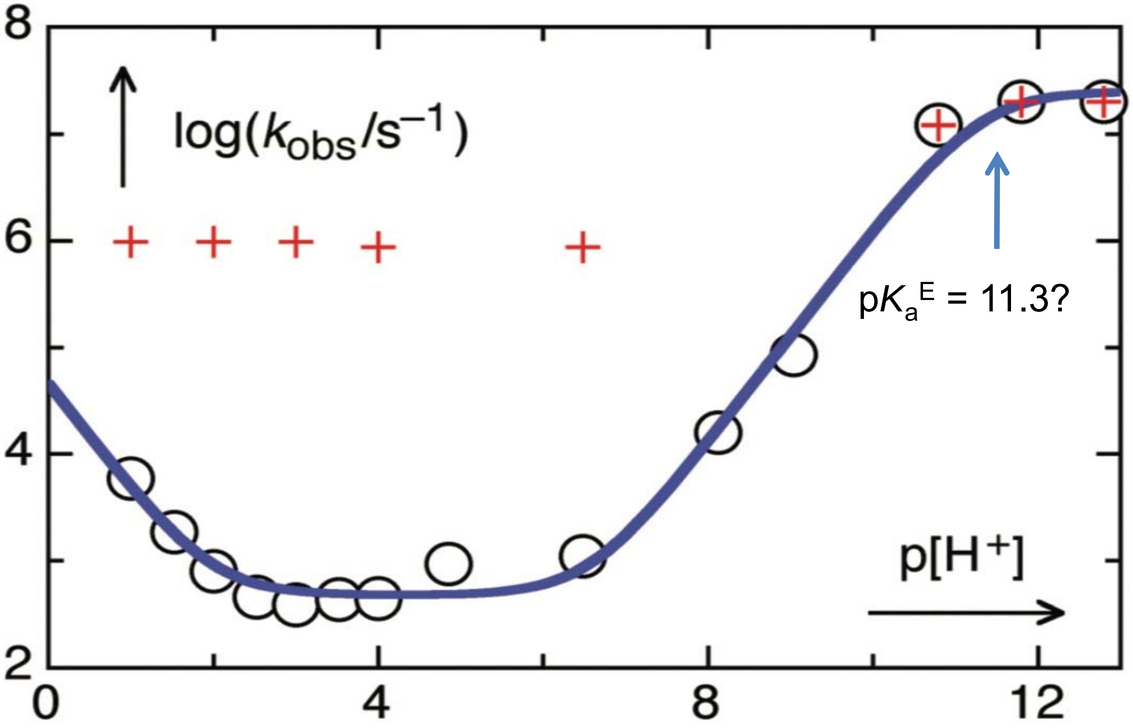


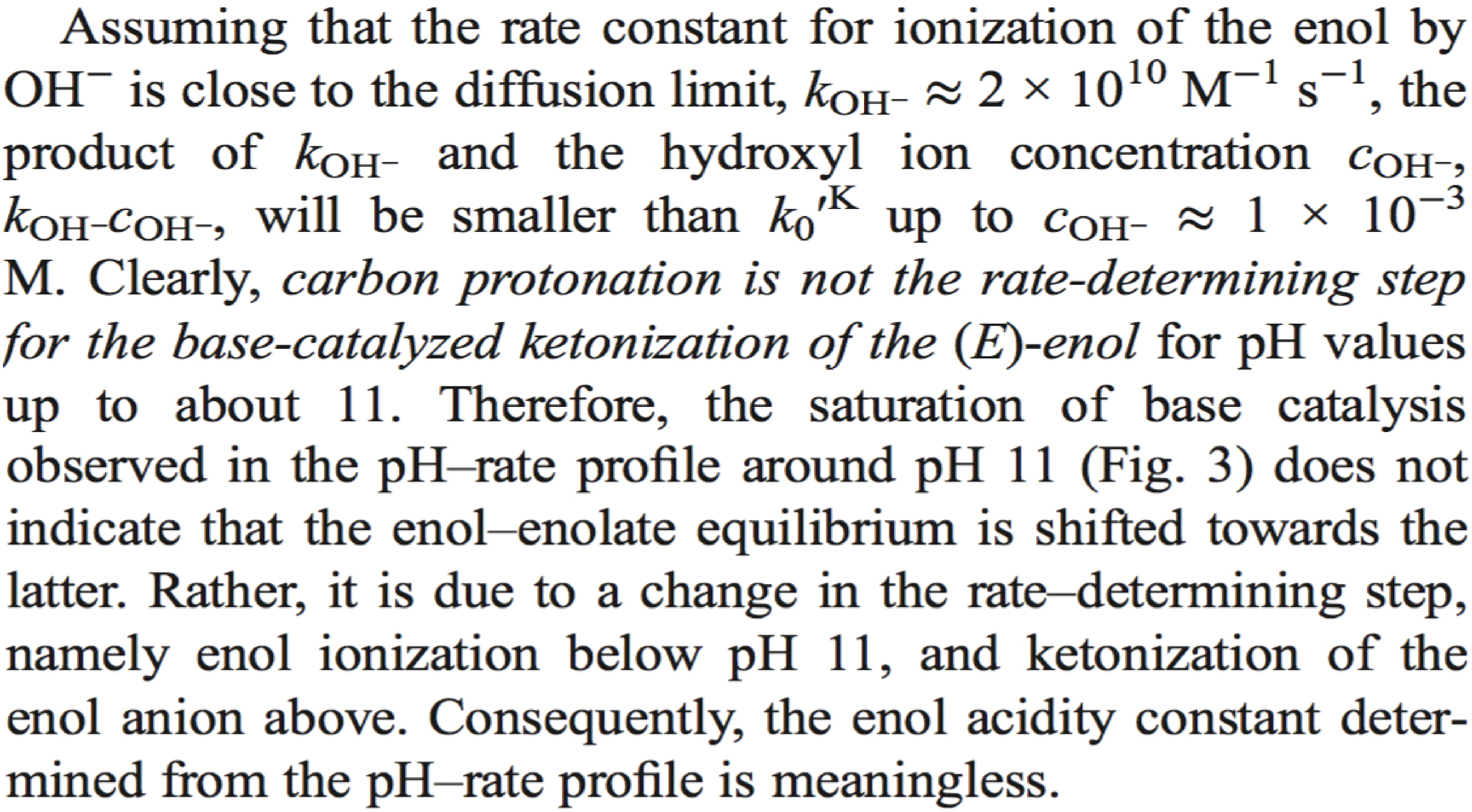
Fig. 2 Kinetic trace observed at 390 nm by LFP (308 nm) of **MA** in water. The resolved absorbance growth (0–0.2 μs) is due to enol formation from the triplet enol. The decay is assigned to reketonization of the (*Z*)-enol, and the residual absorption to the (*E*)-enol, which decays on a millisecond timescale (not shown).



$k_0{}'^{\mathrm{K}}$ = 2x10^7 s^{-1}

pK_a^{E} = 11.3?

Fig. 3 pH–rate profiles of the (*Z*)-enol (+) and of the (*E*)-enol (○) of **MA**. The solid line was obtained by fitting of eqn (1).



Assuming that the rate constant for ionization of the enol by OH^- is close to the diffusion limit, $k_{OH^-} \approx 2 \times 10^{10}\ M^{-1}\ s^{-1}$, the product of k_{OH^-} and the hydroxyl ion concentration c_{OH^-}, $k_{OH^-}c_{OH^-}$, will be smaller than $k_0{'}^{K}$ up to $c_{OH^-} \approx 1 \times 10^{-3}$ M. Clearly, *carbon protonation is not the rate-determining step for the base-catalyzed ketonization of the* (*E*)-*enol* for pH values up to about 11. Therefore, the saturation of base catalysis observed in the pH–rate profile around pH 11 (Fig. 3) does not indicate that the enol–enolate equilibrium is shifted towards the latter. Rather, it is due to a change in the rate–determining step, namely enol ionization below pH 11, and ketonization of the enol anion above. Consequently, the enol acidity constant determined from the pH–rate profile is meaningless.

The pK_a^E is about 9.6 (from spectrographic flash photolysis in conc. buffer solutions.

Buffer dilution plot

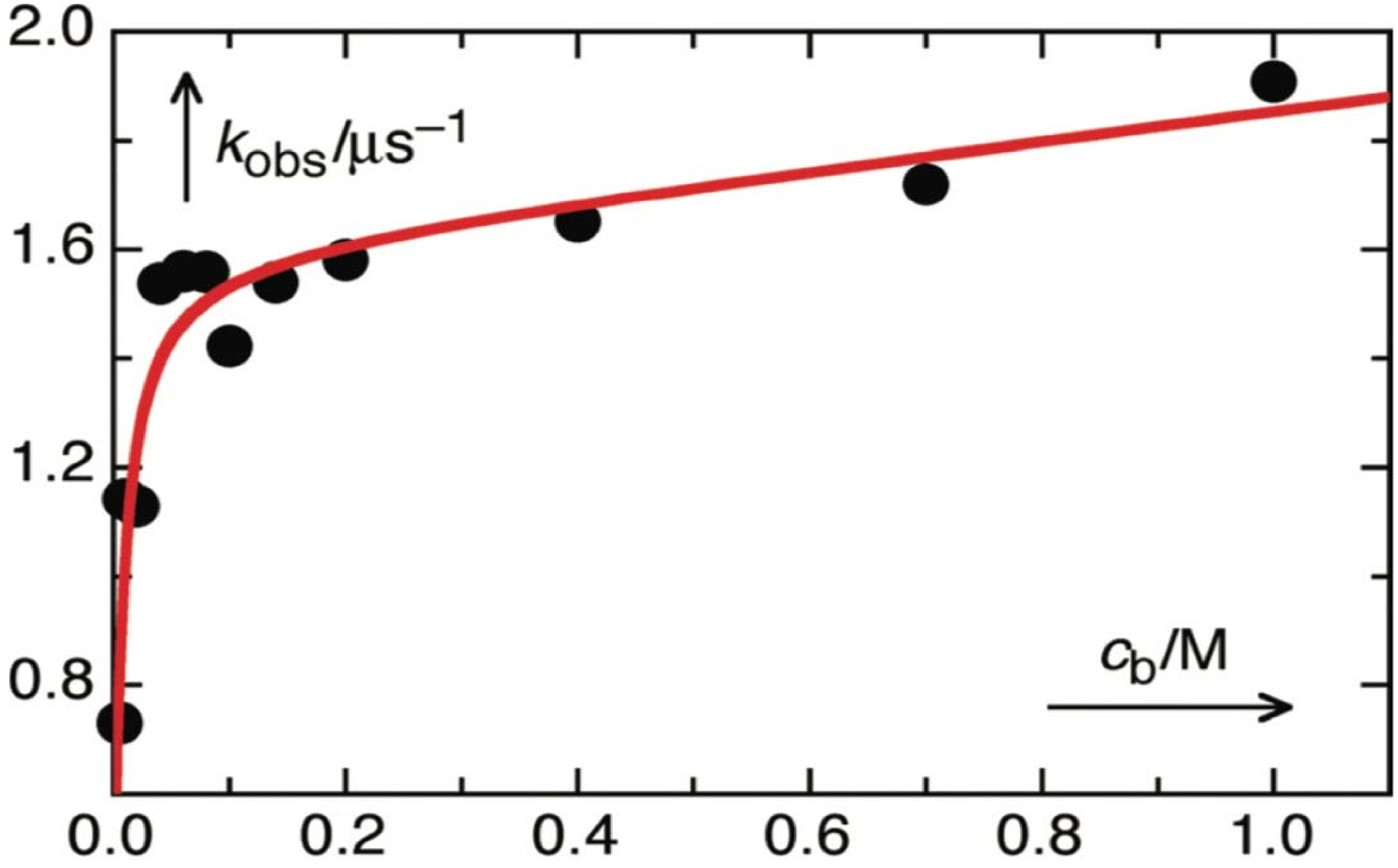


Fig. 4 Buffer dilution plot for the rate constants k_{obs} observed for the decay of the (*E*)-enol of **MA** ($\lambda_{obs} = 390$ nm) in Tris buffer with a buffer ratio of 0.1 (HCl:Tris); ionic strength was kept constant at $I = 0.1$ M.

Exercises

1. From the data shown in the pH–rate profile of cyclohexa-2,4-dienone, calculate the (CH) acidity constant of cyclohexa-2,4-dienone.
2. Explain the curvature in the buffer dilution plot of the observed rate constant of ketonization of 2-methylacetophenone-*E*-enol.
3. How can you tell that phenylynol ionizes to phenylynolate at all pH-values ≥ 2.8? Why is phenynol at least 7 orders more acidic than the corresponding enol, PhCH=CHOH, $pK_a = 9.5$?
4. Show that the four proposed mechanisms for the "uncatalyzed ketonization reaction correspond to a rate law $v_K = k_{uc}c_{enol}$ that is independent of acid or base.
5. Discuss the pH–rate profile for the decay of 1-indene-2-carboxylic acid enol.

Conclusions

- When will YOU do flash photolysis?

- beware of artefacts
- buffer catalysis
- experts in reading pH–rate profiles

- equilibrium constants K_E spanning 30 orders magnitude
- assignments of elementary reactions
- LFER