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AMIDINE MEISENHEIMER COMPLEX
META BRIDGING.
THE CYCLIZATION STEP IN AQUEOUS SOLUTION

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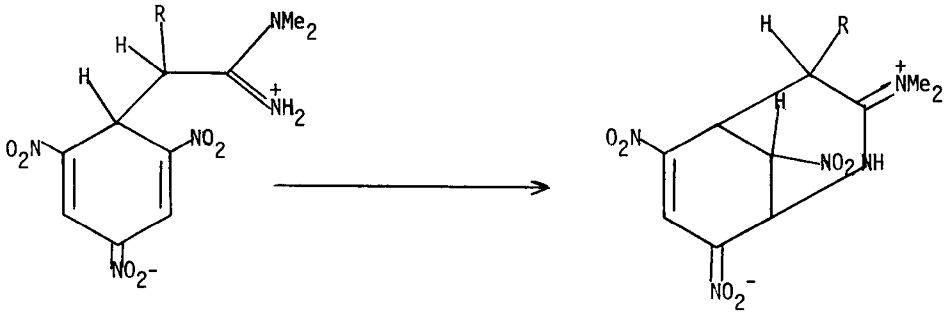
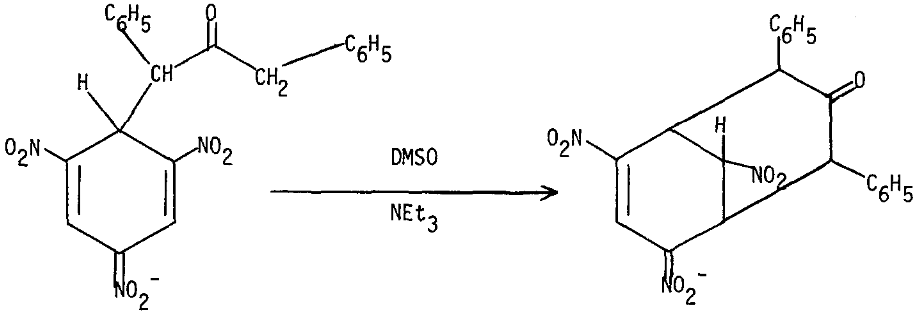
Cyclization of amidinium trinitrocyclohexadienate complexes like 1 to their bicyclic analogues 2 exemplifies the second step of the general process we have described as *meta-bridging*.[1]



1a (R=H)
1b ($R=CH_3$)

2a (R=H)
2b ($R=CH_3$)

Because of the unusual stability of complexes like 1[2,3], we have been able to study the pH dependence of this cyclization in aqueous solution. A previous study of the conversion of the unstable intermediate 3 to 4 in DMSO, catalyzed by NEt_3, has been carried out.[4]



3 4

We report here a study of the cyclization of 1 in aqueous solution which further clarifies the nature of amidine bridging reactions, previously studied only qualitatively.[2,3] There are significant and interesting differences in the chemical reactivity of complexes like 1 and 3.

Both 1a and 1b, as well as the cyclic analogues 2 have previously been prepared and characterized.[2] The rates of cyclization of 1a and 1b in aqueous solution were followed by monitoring the disappearance of absorption maxima for these zwitterions as a function of time. The pH-rate profile for the reactions, as well as a consistent mechanism are summarized in the accompanying diagram. Slopes of the straight lines below pH 10.5 are unity indicating a reaction catalyzed by hydroxide ion. Runs at constant pH, but with varying total buffer concentrations, show no change in rate, substantiating specific rather than general base catalysis. Above pH 10.5 (1b) and 11.5 (1a) the rate is below an extrapolated linear plot because of approach to the amidinium pKa of 1. A consistent rate law is shown in the Figure where K_a is the dissociation constant for **1**, k_b is the rate constant for cyclization of the deprotonated form, and B_{total} represents the sum of the concentrations of the protonated and deprotonated forms. Unfortunately, at 29° accurate rate measurements beyond pH 13 were made difficult because of a secondary reaction of **2** which complicates determination of the final absorbance at t_∞. This difficulty could be overcome (only for **1b**) by lowering the reaction temperature. The pH-rate profile at 5° provides enough curvature for an accurate plot of k_{obs} vs. $k_{obs}[H^+]$. The slope of the resulting line is $-1/Ka$ and the intercept is k_b. Thus at 5°, the pK_a of **1b** = 12.7 and $k_b = 0.45\ sec^{-1} (t_{1/2} \simeq 1.5$ seconds). The pK_a is a bit larger than that expected for N,N-dimethylpropionamidine[5] and this may, in part, explain the unusual stability of such complexes in the presence of free amidine base.[2,3] It should be noted that at high pH the deprotonated form of **2** is the product.

Pre-equilibrium deprotonation of **1** followed by slow cyclization is a mechanism quite distinct from that observed for the **3** to **4** conversion in DMSO catalyzed by triethylamine.[4] In this latter case the rates of cyclization and reprotonation are competitive resulting in a steady-state formation of a dianionic precursor to **4**. These differences are not unexpected since the case at hand involves proton transfer to and from a nitrogen base in aqueous solution. Cyclization of **3** initially involves deprotonation of carbon in DMSO by a weak base. At present we have no explanation of the 7-fold greater reactivity of **1b** relative to **1a**.

References

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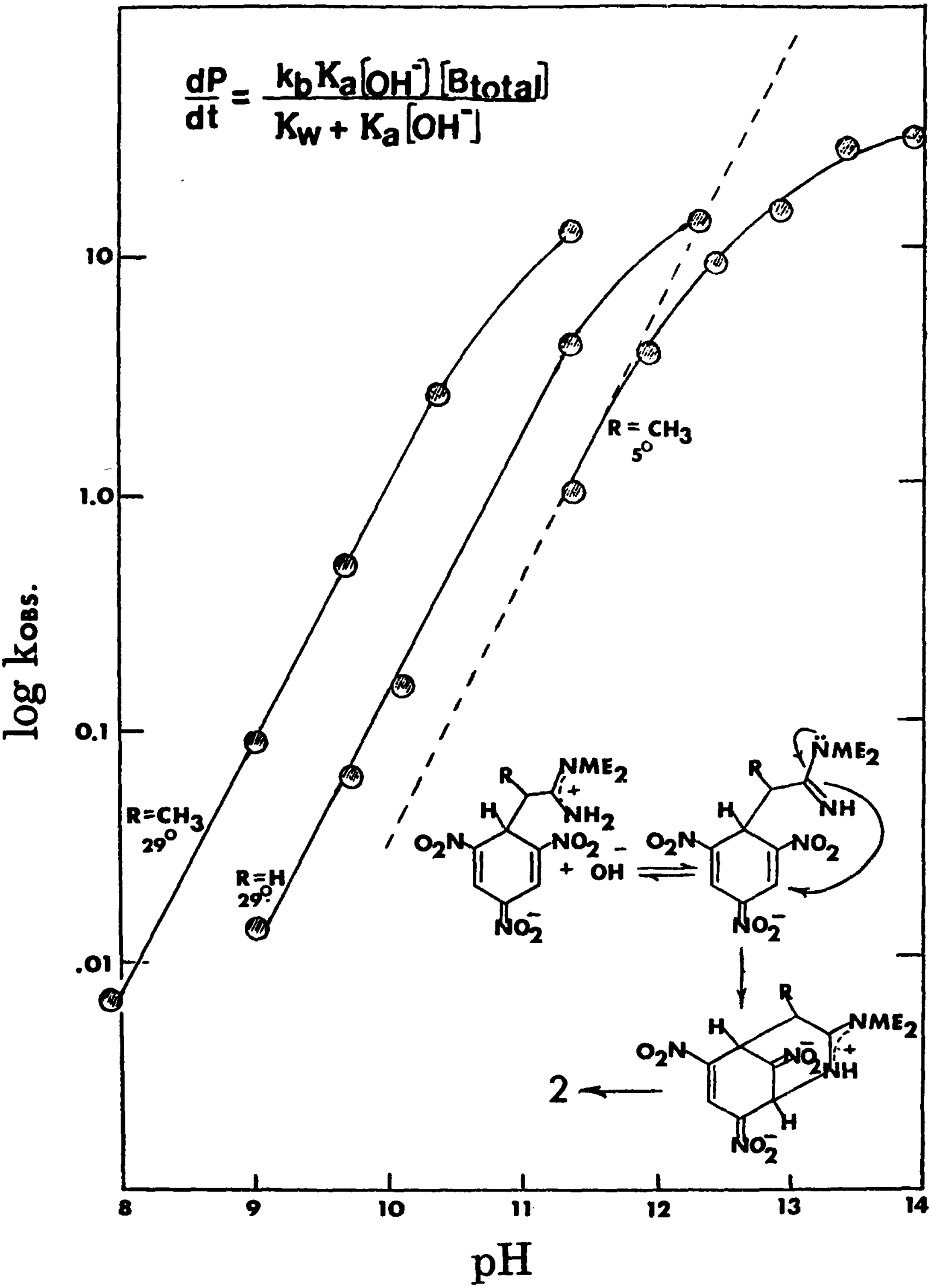
$\frac{dP}{dt} = \frac{k_b K_a [OH^-] [B_{total}]}{K_w + K_a [OH^-]}$
log $k_{OBS.}$
10
1.0
0.1
.01
pH
8
9
10
11
12
13
14
R=CH3 29°
R=H 29°
R = CH3 5°
R
NME2
+
NH2
H
O2N
NO2
NO2⁻
+ OH⁻
ÑME2
NH
NME2
+
NH
NO2⁻
2