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LARGE RATE ENHANCEMENTS THROUGH PREFERENTIAL BINDING TO TRANSITION STATES

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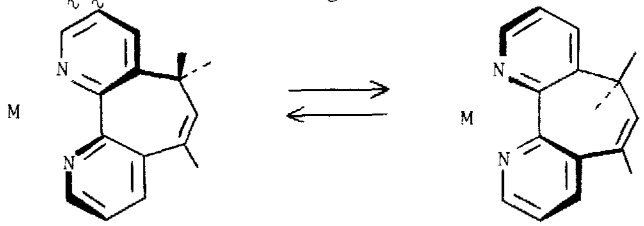
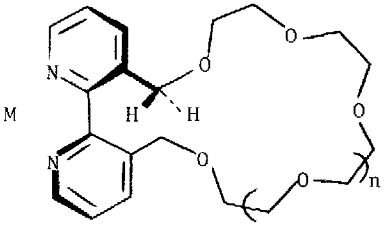
Summary: The racemization rate of chiral bipyridines can be increased by more than six decades through binding to $PdCl_2$.

We recently reported that the activation barrier for the racemization of 1 could be lowered ∼4 kcal by chelation with metal ions.[1] This enhancement is caused by the increase in binding between the bipyridyl and the metal as the coplanar transition state for racemization is attained. We have now examined the racemization behavior of the bipyridyl crown ethers[2] 3-5 and find even larger rate enhancements.



1 M = -
2 M = $HgCl_2$, $ZnCl_2$, $PdCl_2$



3 n = 0 a M = -
4 n = 1 b M = $PdCl_2$
5 n = 2

Racemization rates were studied by dynamic nmr at 90 MHz. The benzyl protons of 3a, for example, appear as an AB quartet (δ4.2, J = 13 Hz) at 25°. On heating up to 165°C, neither coalescence nor line broadening is observed and a lower limit of 24 kcal/mole can be placed on the barrier to racemization. Both 4a and 5a exhibited only singlets in the benzyl region, but it is unlikely that this equivalence is due to their rapid racemization. In contact with the chiral shift reagent, Eufacam, binding at oxygen is observed and each gave two sets of AB quartets.[3] Moreover, the related 6 does not racemize at a significant rate even at 200°, and an $\Delta G^{\neq}$ of ∼ 30 kcal/mole for this process can be estimated from the published spectra.[4] Thus it is reasonable to assume that the barriers to racemization of 3a, 4a and 5a all exceed 24 kcal/mole.

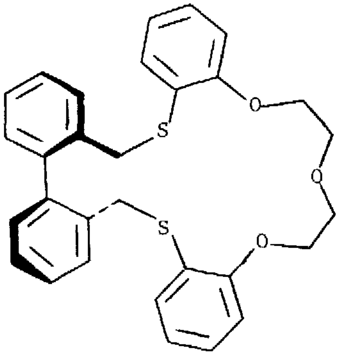


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Table

	$\Delta G^{\neq}_c$	T_c
3a	>24	
3b	14.6	34°
4a	>24	
4b	14.0	10°
5a	>24	
5b	13.9	4°

Benzyl protons in the spectra of all the PdCl$_2$ complex showed the expected temperature dependence: coupled AB systems at -50° to singlets at +50°. Activation barriers, $\Delta G^{\neq}_c$, were calculated[5] at the appropriate coalescence temperature, T_c, and are reported in the Table.

The lowering of the $\Delta G^{\neq}$ for racemization is seen to be at least 8.4 kcal which represents a factor of 10^6 in rate enhancement at room temperature. The magnitude of this increase exceeds that of most model systems and supports the view that catalysis is most effective in cases that offer maximum binding at the transition state.[6]

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