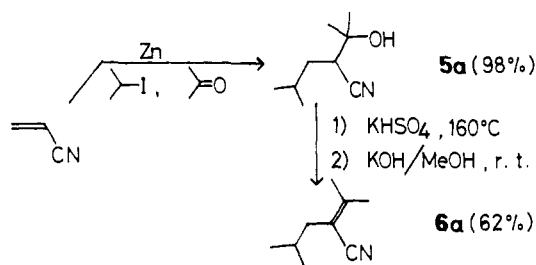


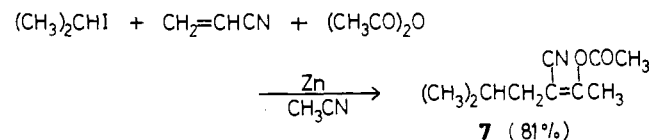
subsequent nucleophilic attack of the intermediate to **4**.

A typical procedure is as follows. Under an atmosphere of nitrogen, a mixture of 2.40 g (37 mmol) of zinc powder,⁶ 0.50 mL (7.6 mmol) of freshly distilled acrylonitrile, 1.70 mL (23 mmol) of acetone, and 14 mL of acetonitrile was refluxed with stirring, and 0.55 mL (5.5 mmol) of isopropyl iodide was added slowly to the mixture. After a short period, an exothermic reaction took place. After the vigorous reaction subsided, an additional 1.65 mL (16.5 mmol) of isopropyl iodide was added dropwise over 10 min, and the mixture was refluxed for 4–5 h. The usual workup gave the β -hydroxy nitrile **5a** in a 98% yield: bp 74–75 °C (1.0 mm); NMR (CCl₄) δ 0.98 (d, 3 H, >CHCH₃), 1.08 (d, 3 H, >CHCH₃), 1.32 (s, 3 H, >C(OH)-CH₃), 1.35 (s, 3 H, >C(OH)CH₃), 1.40–1.75 (m, 2 H, -CH₂-), 1.74–2.10 (m, 1 H, >CH-), 2.60 (d of d, 1 H, >CHCN), 3.00 (br s, 1 H, -OH); IR (neat) 3430–3390, 2240, 1385, 1365, 1140–1160 cm⁻¹. Anal. Calcd for C₉H₁₇ON: C, 69.63; H, 11.04; N, 9.02. Found: C, 69.90; H, 11.24, N, 8.96. In a similar manner, β -hydroxy nitriles **5a–l** and esters **5m,n** were obtained in satisfactory yields as shown in Table I.⁷

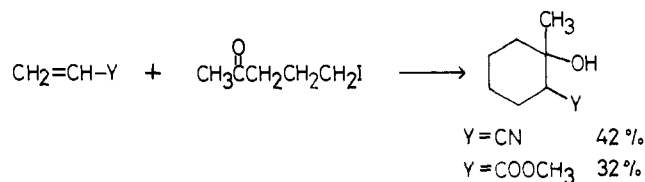
It is noteworthy that the reaction is feasible for a variety of compounds **2** or **4**. The dehydration of the product **5a** gave readily the activated olefin **6a**.⁷



Similar to ketones and aldehydes, acetic anhydride behaved as an electrophile yielding the expected cyanoenol acetate **7**⁷ in a good yield. Furthermore, the pattern of the joining reaction suggests the feasibility of some types of cycloaddition. Indeed,



the zinc-promoted reaction of 5-iodopentan-2-one with acrylonitrile or methyl acrylate gave the corresponding cycloaddition product⁷ in a reasonable yield.



In view of its simplicity and generality, this three-components joining reaction seems one of the promising methods for the synthesis of such selective aldol-type compounds as the conventional condensation between carbonyl compounds and esters or nitriles scarcely yields.⁹ The application of this novel joining reaction to synthesis is in progress.

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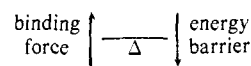
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On Binding to Transition States and Ground States: Remote Catalysis

Sir:

How binding forces increase reaction rates is a crucial question in catalysis, particularly enzymic catalysis. Many recent models use binding forces to reduce entropies of activation *before* a process occurs.¹ In this communication we demonstrate how binding forces may be used *as* a process occurs, with maximum binding at the transition state.² To ensure that binding and activation are simultaneous, we have constructed a molecular lever in which these forces are mechanically coupled.



The design of such a mechanism requires knowledge of transition-state geometry and the racemization of biphenyl derivatives is a process for which reasonable inferences regarding this geometry may be drawn.³ In cyclic systems, e.g., **1**, the transition state for racemization is reached when the two aromatic rings become coplanar. The reaction coordinate is θ , the dihedral angle defined by the aromatic ring planes, and the transition state occurs at $\theta = 0^\circ$. In **1** the process is most easily monitored by DNMR; racemization occurs with inversion of the cycloheptatriene ring and the environments of the *gem*-dimethyl groups are exchanged. Sutherland⁴ has reported that coalescence of the *gem*-dimethyl singlets of **1** occurs at 102 °C with $\Delta G^\ddagger = 18.8$ kcal/mol for the racemization process.

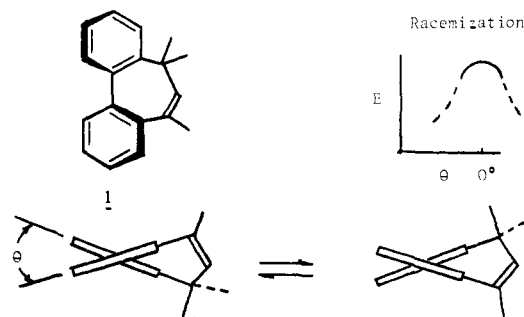
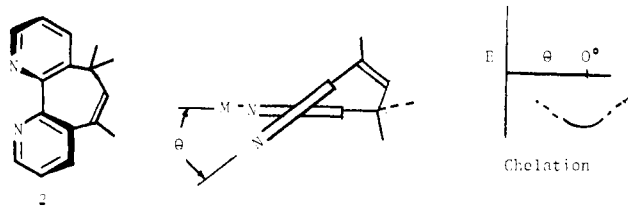


Table I. Racemization of **2**

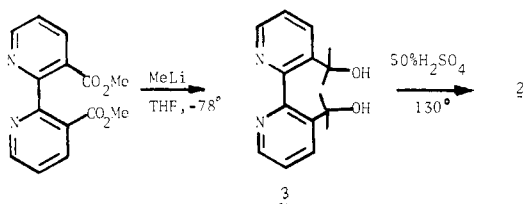
	ΔG^\ddagger	$T_c, ^\circ\text{C}$
2	14.5	2
2 ·HgCl ₂	10.5	-60
2 ·ZnCl ₂	10.5	-60
2 + 1 equiv of CF ₃ SO ₃ H	10.1	-65
2 + excess CF ₃ SO ₃ H	16.8	+68

Consider now the corresponding process in bipyridyl **2**. Again, θ defines the racemization coordinate and the transition state occurs at $\theta = 0^\circ$. The parent 2,2'-bipyridyl has been much admired for its ability to form chelates with metal ions. X-ray structures of such complexes reveal near coplanarity of the aromatic rings; i.e., maximum binding between metal and bipyridyl occurs at $\theta = 0^\circ$. Chelation and racemization share the



same coordinate, and metal ions could apply a binding force to the transition state for racemization.

We have prepared **2** from the dimethyl ester of 2,2'-binicotinic acid,⁵ readily available from the oxidation of *o*-phen-



anthroline. Excess MeLi afforded the diol **3** which cyclized to **2** under the influence of hot H₂SO₄.

The NMR spectrum of **2** showed the expected temperature effect; the dimethyl signal appeared as a broadened singlet at ambient temperature but was resolved into two singlets ($\Delta\delta = 47$ Hz) at low temperature. From the coalescence temperature ($T_c = 2^\circ\text{C}$) a barrier of 14.5 kcal/mol can be calculated. Complexes of **2** with ZnCl₂ and HgCl₂ were obtained in crystalline form and their racemization rates were determined. The kinetic parameters obtained from ¹H or ¹³C NMR spectra are presented in Table I.

As expected, the rate of racemization is enhanced in the metal complexes. The degree of enhancement reflects the difference in energy of binding in the ground-state vs. the transition-state complex. The behavior of **2** in the presence of protic acids is of special interest since true *catalysis* of racemization occurs. Observed rates increase as acid is added with the maximum rate occurring at 1 equiv. As more acid is added, rates decrease and at ~8 equiv the racemization rate is nearly that observed in neat CF₃SO₃H.⁶ Evidently, the dipole-dipole repulsive forces which contribute to the racemization barrier of **2** are replaced by stabilizing forces in the monoprotonated form. On diprotonation, the coplanar arrangement is destabilized and racemization is inhibited.

The present examples demonstrate how remote binding forces may stabilize a transition state. Applications to chemical processes are underway.

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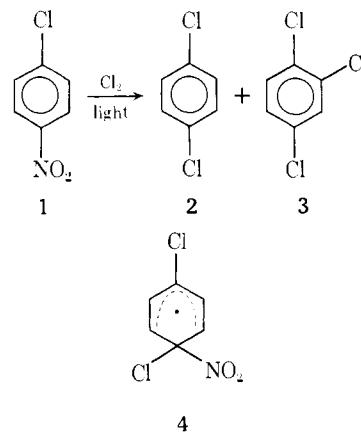
Formation and Rearrangement of Ipso Intermediates in Aromatic Free-Radical Chlorination Reactions¹

Sir:

Only during the past decade has the importance of ipso attack in aromatic substitution reactions been appreciated.² Although replacements of a substituent during aromatic free radical substitution reactions have been reported by several investigators during the past 75 years,^{3,4} the substantial volume of current literature about ipso attack has been largely confined to electrophilic substitutions.² Cationic ipso intermediates have been trapped, and their rearrangements have been shown to account for as much as half of the ortho-substitution products obtained in some nitrations.² In this communication, we report evidence for the formation and rearrangement of an ipso intermediate during free-radical chlorination of *p*-bromonitrobenzene.

Ipso attack in some free-radical aromatic substitution reactions has recently been advocated,⁵⁻⁷ but firm evidence for any behavior of the proposed ipso intermediate other than loss of one of the geminal substituents (which might occur by a mechanism other than formation of an ipso intermediate) was lacking. Rearrangement of the original bromo substituent in the present case appears to require the ipso-intermediate mechanism.

Photoinitiated chlorination of *p*-chloronitrobenzene (**1**) in



carbon tetrachloride at room temperature produces mainly *p*-dichlorobenzene (**2**) plus a small amount (2% of the amount of **2** at 57% reaction) of 1,2,4-trichlorobenzene (**3**).⁸ The reaction is mainly one of chlorodenitration, perhaps through an ipso intermediate (**4**). Photoinitiated chlorination of *p*-bromonitrobenzene (**5**) under the same conditions and at about