

ACCELERATION OF THE THERMAL PAUSON-KHAND REACTION BY COORDINATING LIGANDS

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Abstract: Coordinating ligands in the homo- and bishomopropargylic position of a 1,6-enyne have been found to enhance the rate of the thermal Pauson-Khand cycloaddition.

Several methods have been reported to increase the rate of the intramolecular Pauson-Khand cycloaddition.^{2,3} These include performing the reaction in the presence of 4-methylmorpholine N-oxide⁴ or trimethylamine N-oxide⁵ in CH₂Cl₂, or carrying out the reaction in the dry state on silica gel.⁶ In our earlier work⁷ on the ligand directed intermolecular Pauson-Khand reaction, we noted that the use of alkyl sulfides as directing groups gave rise to modestly enhanced reaction rates in addition to providing regioselectivity. Further investigations using enynes with sulfur bearing functionality have led us to discover an unusual rate enhancing effect in the intramolecular reaction.

We have found that the rate of the intramolecular cycloaddition is greatly increased by the presence of a sulfur or oxygen atom in the homopropargylic or bishomopropargylic position of a 1,6-enyne. The results are listed in the Table. A comparison of the cycloaddition of enyne **1** with that of enynes **8** and **10** clearly illustrates the rate enhancement at 71 °C in toluene. Acceleration by the coordinating ligands follows a pattern with sulfur providing more acceleration than oxygen. Sulfur containing functional groups accelerate the reaction to less than 2.5 hours reaction time (entries 4-10, Table), and oxygen bearing functional groups promote the reaction in approximately 5-7 hours (entries 2 and 3, Table).

Table

entry #				time	% yield
1	1	L = CH ₂ CH ₂ CH ₃	11	21 h	30%
2	2	L =	12	7.5 h	67%
3	3	L = CH ₂ OEt	13	5.5 h	81%
4	4	L =	14*	2.25 h	75%
5	5	L =	15*	2.25 h	59%
6	6	L =	16	2 h	60%
7	7	L = CH ₂ SEt	17	1.5 h	59%
8	8	L =	18	1.5 h	58%
9	9	L = CH ₂ -	19	1.25 h	75%
10	10	L = CH ₂ -	20*	0.75 h	69%

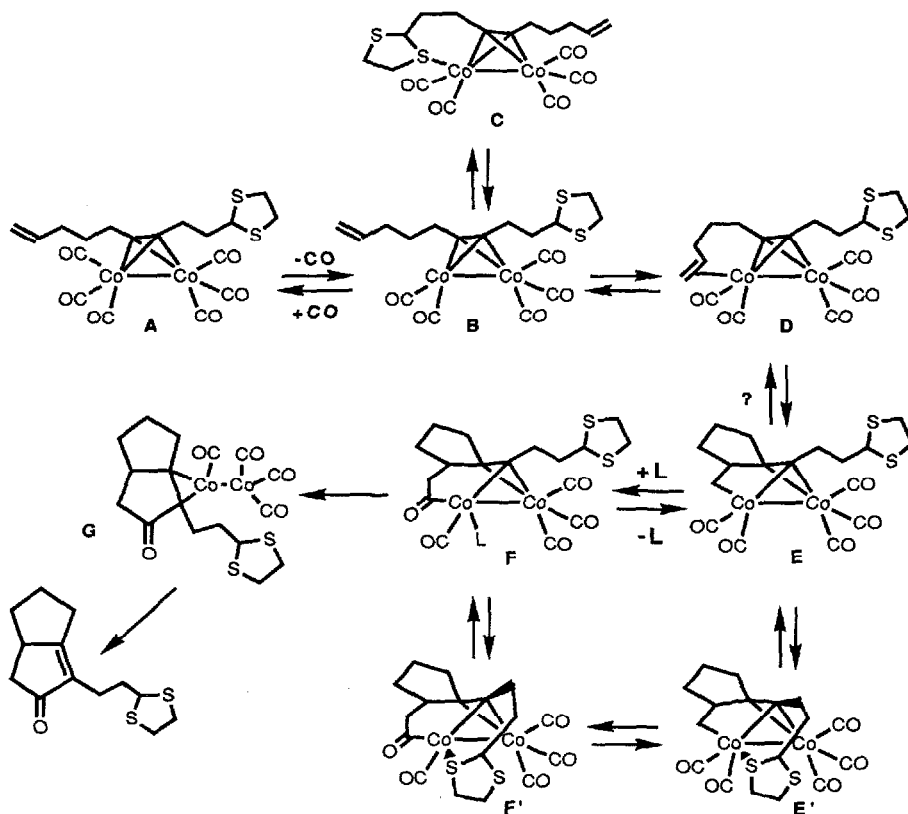
* cyclopentenones = 1:1 mixture of diastereomers

These results can be rationalized within the context of the proposed^{3,8} reaction mechanism which is illustrated in Scheme 1. Initial ligand exchange (**A** to **D**) is usually assumed to take place through a dissociative process via initial loss of carbon monoxide. The next step is metallacycle formation (**D** to **E**), which involves the insertion of the π -complexed alkene into one of the formal cobalt-carbon bonds. This step is proposed³ to be rate limiting and product determining. Subsequent insertion of carbon monoxide into either of the cobalt-carbon bonds (**E** to **F**) and reductive coupling (**F** to **G**) gives the cobalt complexed cyclopentenone.

Three steps in the proposed mechanism, **A** to **B**, **D** to **E**, and **E** to **F**, necessarily generate a vacant coordination site. Judicious placement of a coordinating ligand can be expected to lead to a stabilization of a coordinatively unsaturated complex. Stabilization of **B** by formation of complex **C** may inhibit reincorporation of CO and allow for loss of CO from solution. Transformations **D** to **E** and **E** to **F** may be driven by heteroatom coordination to provide a saturated complex with formation of **E'** or **F'** respectively.

Since sulfur is generally considered to be a better coordinating ligand than oxygen for cobalt complexes, the rates should be more enhanced in those cases with sulfur containing functionality. In addition, the bishomopropargylic ligands would be expected to provide a more stable complex (6 membered chelate ring) than the homopropargylic cases (5 membered chelate ring) due to the strain in a five membered chelate ring caused by the bond angle at the carbon bound to cobalt. The results are consistent with these expectations as the rate is most greatly enhanced with sulfur in the bishomopropargylic position and with sulfur rather than oxygen as the coordinating ligand.

Since the reaction rate, with substrates that bear coordinating ligands, is increased in all our cases, it is likely that complex C is thermally unstable. The observed rate acceleration most probably arises from either intramolecular coordination which stabilizes complexes E or F or an increase in the steady state concentration of complex D caused by the intermediate formation of complex C.



Scheme 1

Further work on rate enhancements in the Pauson-Khand reaction and their mechanistic consequences is in progress and these results will be reported in due course.

Acknowledgments: We are grateful to the National Science Foundation, the National Institutes of Health, the Sloan Foundation, and the Camille and Henry Dreyfus Foundation for partial support of this work.

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(Received in USA 25 March 1992)