

added. It was then stirred for an additional 63.5 h. The usual workup afforded 2.05 g (100%) of a light yellow sticky solid, which by GLPC (Carbowax 20 M capillary column, 15 m \times 0.25 mm, at 60 °C) was shown to consist of durene (72%), 1,2,4,5-tetramethyl-1,4-cyclohexadiene (17%), and 1,2,4,5-tetramethyl-1,3-cyclohexadiene^{31,32} (10%).

Isomerization of 1,2,4,5-Tetramethyl-1,4-cyclohexadiene by Preformed Amides Derived from Calcium-Methylamine-Ethylenediamine. The same setup described under General Procedure was employed. Into the 200-mL reaction flask was placed 50 mL of methylamine, 50 mL of ethylenediamine, 1.82 g (23.3 mmol) of benzene, and 0.93 g (0.023 mol) of calcium. The mixture was stirred for 28.6 h, during which time a gray solid formed and all the calcium appeared to be consumed. At this point 1,2,4,5-tetramethyl-1,4-cyclohexadiene (1.58 g; 11.6 mmol) was added and the mixture was stirred for an additional 88 h. The usual workup afforded 1.47 g (93%) of a white sticky solid, which by GLPC (Carbowax 20 M capillary column, 15 m \times 0.25 mm, at 60 °C) was shown to consist of durene (4%), 1,2,4,5-tetramethyl-1,4-cyclohexadiene (90%), and 1,2,4,5-tetramethyl-1,3-cyclohexadiene^{31,32} (6%).

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Department of Energy Office of Basic Energy Sciences under Contract DE-AC02-81ER10989. The Varian XL-200 spectrometer used in this work was purchased with funds from NSF Grant CHE-8004246. This support is gratefully acknowledged.

Registry No. Naphthalene, 91-20-3; tetralin, 119-64-2; durene, 95-93-2; anthracene, 120-12-7; *tert*-butylbenzene, 98-06-6; cumene, 98-82-8; *p*-xylene, 106-42-3; *m*-xylene, 108-38-3; *o*-xylene, 95-47-6; norbornadiene, 121-46-0; norbornene, 498-66-8; indan, 496-11-7; mesitylene, 108-67-8; calcium, 7440-70-2; methylamine, 74-89-5; ethylenediamine, 107-15-3; Δ^9 -octalin, 493-03-8; $\Delta^{1(9)}$ -octalin, 1194-95-2; 1,2,4,5-tetramethyl-1,4-cyclohexadiene, 26976-92-1; 1,2,3,4,5,6,7,8,9,10-decahydroanthracene, 3485-60-7; 1-*tert*-butylcyclohexene, 3419-66-7; 1-isopropylcyclohexene, 4292-04-0; 3-isopropylcyclohexene, 3983-08-2; 1,4-dimethylcyclohexene, 2808-79-9; 1,3-dimethylcyclohexene, 2808-76-6; 1,2-dimethylcyclohexene, 1674-10-8; norbornane, 279-23-2; nortricyclene, 279-19-6; 4,5,6,7-tetrahydroindane, 695-90-9; *cis*-1,3,5-trimethylcyclohexene, 24583-97-9; *trans*-1,3,5-trimethylcyclohexene, 86436-70-6; 1,3,4,6-tetramethylcyclohexene, 86436-71-7; 1,2,4,5-tetramethylcyclohexene, 86436-72-8.

Diels-Alder Reactions of Cycloalkenones. 3. Effects of Specific Reaction Parameters¹

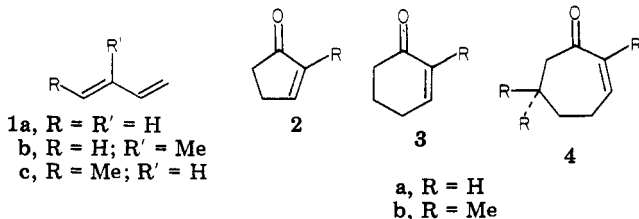
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The effects of the Lewis acid–ketone complexation time and temperature, the nature and amount of catalyst, and the concentrations of ketone and diene on the Diels-Alder reactions of 2-cyclopentenones, 2-cyclohexenones, and 2-cycloheptenones with 1,3-butadiene, isoprene, and (*E*)-piperylene are described.

The recent past has witnessed the widespread use of acid catalysis in Diels-Alder reactions, especially of 2-cycloalkenones with butadienes. Since a survey of the literature reveals the use of a broad range of reaction conditions and the consequent acquisition of a variety of product yields, it became necessary to investigate the reaction parameters responsible for the previous observations and to standardize the reaction conditions at an optimum yield level, thus enhancing the great potential of the cycloaddition process in organic synthesis. The study was initiated with the reactions between the dienes 1,3-butadiene (1a), isoprene (1b), and (*E*)-piperylene (1c) and the cycloalkenones 2-cyclopentenone (2a), 2-methyl-2-cyclopentenone (2b), 2-cyclohexenone (3a), 2-methyl-2-cyclohexenone (3b), 2-cycloheptenone (4a), and 2,6,6-trimethylcycloheptenone (4b) and indicated at an early stage



(1) For previous papers see: (a) Fringuelli, F.; Pizzo, F.; Taticchi, A.; Wenkert, E. *Synth. Commun.* 1979, 9, 391. (b) Fringuelli, F.; Pizzo, F.; Taticchi, A.; Halla, T. D. J.; Wenkert, E. *J. Org. Chem.* 1982, 47, 5056. (c) Fringuelli, F.; Minuti, L.; Pizzo, F.; Taticchi, A.; Halla, T. D. J.; Wenkert, E. *Ibid.* 1983, 48, 1810.

(2) (a) Università di Perugia. (b) University of California—San Diego.

Table I. Products of the Aluminum Chloride Catalyzed Reactions of Dienes 1 and Cycloalkenones 2-4 in Toluene Solution

starting materials	products	product ratio	total yield, %
1a-2a	5a (n = 2), 6a (n = 2)	1.2:1	95
1a-3a	5a (n = 3), 6a (n = 3)	9:1	84
1a-2b	6d (n = 2)		92
1a-3b	6d (n = 3)		93
1b-2a	5b (n = 2), 6b (n = 2)	1:1.7	80
1b-3a	5b (n = 3), 6b (n = 3)	18:1	70
1b-4a	5b (n = 4), 6b (n = 4)	1:4.5	73
1b-2b	6e (n = 2), 9 (n = 2)	6.3:1	73
1b-3b	6e (n = 3), 9 (n = 3)	32:1	79
1b-4b	8b		90
1c-2a	5c (n = 2), 6c (n = 2)	200:1	77
1c-3a	5c (n = 3), 6c (n = 3)	1:1.8	81
1c-4a	5c (n = 4), 6c (n = 4)	1:>200	80
1c-3b	6f (n = 3), 7	2.2:1	92
1c-4b	8c		85

that products 5-9 can be obtained in high total yield (Table I) in toluene solution with aluminum chloride catalysis. Whereas an earlier report described the experimental details of these reactions and the structure analysis of the products,^{1b} the present communication illustrates the effect of specific reaction parameters on the product yield.

The Complexation Process. The complexation of the cycloalkenones with the Lewis acids represents a key operation in the catalyzed Diels-Alder reaction and influences the final product yield by its dependence on the

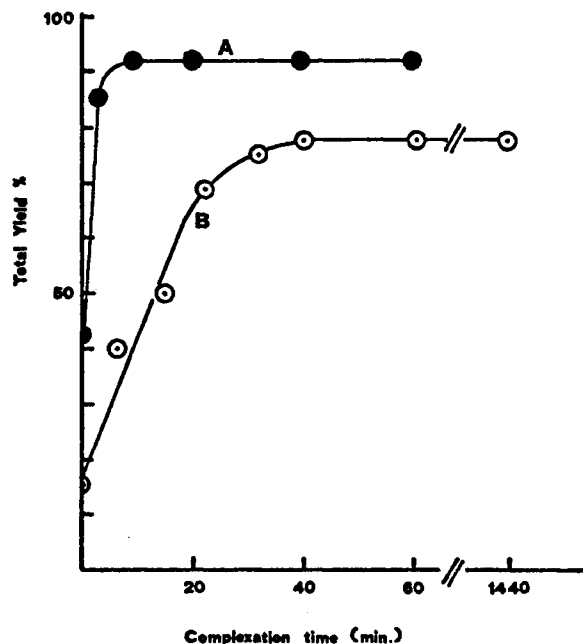


Figure 1. Reactions of 2-methyl-2-cyclohexenone (3b) (curve A) and 2-cyclohexenone (3a) (curve B) in 0.2 and 0.1 M toluene solutions, respectively, with 3 equiv of 1,3-butadiene (1a) in the presence of 0.9 equiv of aluminum chloride (complexation at 22 °C and cycloaddition at 70 °C).

ketone and catalyst ratios, the nature of the catalyst and solvent, and the complexation temperature and time. In view of the intricate interplay of these parameters it has been difficult to prescribe the best conditions for the catalyzed Diels-Alder reaction on a general basis and attain reproducibly high product yields in the past.

The yields of Diels-Alder adducts from reactions in dry toluene under nitrogen and catalyzed by anhydrous aluminum chloride depend on the time and temperature necessary for the buildup of the maximum concentration of the acid-ketone complex prior to the addition of diene.³ Whereas the cycloaddition takes its natural course on the occasion of the diene being added to the solution of the complex only after the appropriate complexation time, the reaction becomes exothermic and the product yield drops precipitously when the complexation constraint is ignored.⁴ Typical examples of the complexation effect in normal reactions, utilizing 0.9:1 aluminum chloride/ketone ratios, are illustrated in Figures 1 and 2.⁵ The reactions of 2-cyclohexenone (3a) and its 2-methyl derivative (3b) at 22 °C require different complexation times, ca. 40 and 12 min, respectively. Heating of a mixture of the acid-ketone complexes and 1,3-butadiene (1a) at 70 °C leads to the highest product yields. The cycloadditions of 2-cyclopentenone (2a) and its 2-methyl derivative (2b) with the same diene require not only diverse complexation times, ca. 15 and 40 min, respectively, but also different complexation temperatures, 70 and 22 °C, respectively; the best product yields being attained by subsequent exposure of mixtures of the complexes and diene to 70 °C. Complexation of 2-cyclopentenone (2a) for only 5 min at 70 °C or 120 min at 22 °C causes a diminution of the product

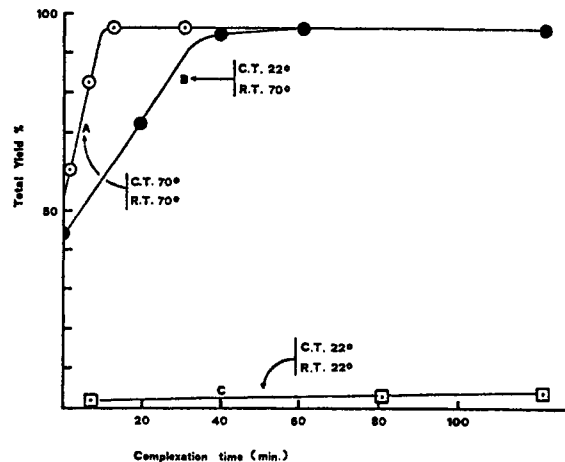


Figure 2. Reactions of 2-cyclopentenone (2a) (curves A and C) and 2-methyl-2-cyclopentenone (2b) (curve B) in 0.1 M toluene solutions with 3 equiv of 1,3-butadiene (1a) in the presence of 0.9 equiv of aluminum chloride (complexation temp C.T., cycloaddition temp R. T.).

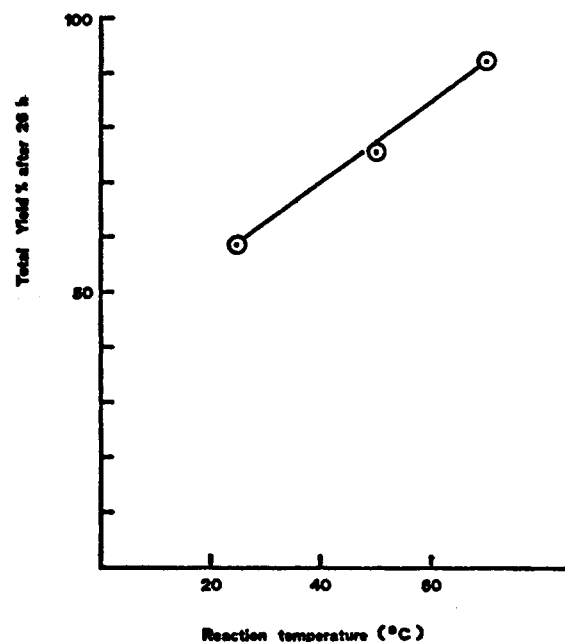


Figure 3. Reactions of 2-cyclopentenone (2a) in 0.1 M toluene solution with 3 equiv of 1,3-butadiene (1a) in the presence of 0.9 equiv of aluminum chloride (complexation at 70 °C for 15 min, cycloaddition for 26 h).

yield to 60 and 5%, respectively, whereas complexation beyond the required time has no effect on the product yield.⁶ As Figure 3 portrays for the reaction of 2-cyclopentenone (2a) with 1,3-butadiene (1a), the catalyzed Diels-Alder reaction proceeds well at even low temperatures as long as the proper complexation conditions have been applied.

The use of a lower than 0.9:1 acid/ketone ratio reduces the complexation time. Whereas this result, in principle, is favorable, the consequent increase of the time of reaction between the complex and diene generally lowers the product yield. Thus, for example, the complexation of 2-cyclohexenone (3a) with 0.25 equiv of aluminum chloride in toluene at 22 °C takes only 5 min, but the subsequent cycloaddition with 1,3-butadiene (1a) at 70 °C requires 25

(3) Aluminum chloride is sparingly soluble in toluene and forms complexes of limited solubility with 2-cycloalkenones (2a, 3a, and 4a) and soluble complexes with 2-methyl-2-cycloalkenones (2b, 3b, and 4b).

(4) Exposure of the dienes 1 to a suspension of anhydrous aluminum chloride in toluene leads to a fast exothermic reaction.

(5) None of the figures representing a time dependence of product yield are meant to reflect the exact kinetics of the reactions in view of the limited number of experimental points and the limitation of their accuracy at the early stage of the reactions.

(6) Augmentation of the complexation temperature, however, may cause a reduction of the product yield, presumably due to some decomposition of the intermediate acid-ketone complex.

Table II. Influence of the Lewis Acids on the Product Yield from Reactions of 2-Methyl-2-cyclohexenone (3b) with Dienes 1a-c^a

catalyst (equiv)	diene (equiv)	com-plexa-tion time	reaction		total yield
			temp	time	
AlCl ₃ (0.9)	1a (3)	12	70	10	93
AlBr ₃ (0.9)	1a (3)	12	70	11	85
BF ₃ ·Et ₂ O (0.9)	1a (15)	20 ^d	40 ^b	120	65
ZnCl ₂ (0.9)	1a (15)	25 ^d	70	120	67
SnCl ₄ (0.9)	1a (15)	25 ^d	70	142	50
AlCl ₃ (0.25)	1b (3)	12	25	17	79
AlBr ₃ (0.25)	1b (3)	12	25	14	90
BF ₃ ·Et ₂ O (0.25)	1b (15)	10 ^d	25	120	70
ZnCl ₂ (0.25)	1b (15)	10 ^d	40 ^c	120	15
SnCl ₄ (0.25)	1b (15)	15 ^d	25	96	9
AlCl ₃ (0.25)	1c (3)	12	25	11	92
AlBr ₃ (0.25)	1c (3)	12	25	12	85
BF ₃ ·Et ₂ O (0.25)	1c (15)	10 ^d	25	40	50
ZnCl ₂ (0.25)	1c (15)	10 ^d	40 ^c	72	15
SnCl ₄ (0.25)	1c (15)	15 ^d	25	96	22

^a In 0.2 M toluene solutions of ketone; complexation temperature of 22 °C and time in min; reaction time in h; total yield (by GLC) in %. ^b Yield at 70 °C is 55%. ^c Yield at 25 °C is <10%. ^d No yield change by addition of the diene prior to complete complexation.

h and the yield of adduct is reduced to 66% (vide infra). Much experimentation has shown that a Diels–Alder reaction in toluene solution in the presence of 0.5–0.9 equiv of aluminum chloride requires a complexation time of 20–40 min at 22–40 °C, which may be shortened by an increase of the temperature.

The catalyst–ketone complexation shows also a dependence on the nature of the catalyst and solvent. In toluene solution aluminum bromide behaves similarly to aluminum chloride, whereas the Lewis acids boron trifluoride etherate, zinc chloride, and stannic chloride exhibit different behavior. In the case of the non-aluminum catalysts the complexation time is reduced to a minimum, permitting the addition of diene to the catalyst–ketone complex to take place at an early stage without ill effect to the reaction, i.e., reaction exothermicity or product yield decrease. Thus, for example, the reaction between 2-methyl-2-cyclohexenone (3b) and 1,3-butadiene (1a), catalyzed by boron trifluoride etherate or zinc chloride under the conditions reported in Table II, is as efficient after a 2-min delay of addition of diene to the acid–ketone complex as after a 20-min delay despite the fact of the maximum concentration of the complex being reached only after 10 and 25 min for solutions of 0.25 and 0.9 equiv of boron trifluoride etherate, respectively.⁷ These observations point to a catalyst–diene reaction, present in the case of the aluminum catalysts but absent with the others, which interferes with the Diels–Alder reaction unless the catalyst first is masked as its ketone complex.⁸

The use of solvents in which both the catalyst and its ketone complex are soluble, e.g., acetonitrile or tetra-

hydrofuran, leads to faster complexation than in toluene but also to lower yields of Diels–Alder adducts.

Catalyst Influence. Lewis acids have been known for some time to increase the rate and yield of Diels–Alder reactions and sometimes to influence their regiochemistry.⁹ The effect of the most common Lewis acids on the cycloaddition of 2-methyl-2-cyclohexenone (3b) with the dienes 1a–c in toluene solution is summarized in Table II. The use of magnesium iodide, boron tribromide, and titanium tetrachloride led to discouraging results, while aluminum chloride and bromide gave the highest product yields under the mildest conditions of reactions with a variety of 2-cycloalkenes.^{1b} A large excess of dienes 1 in toluene solution containing the catalysts boron trifluoride etherate, zinc chloride, or stannic chloride improves the adduct yield, while the presence of 3 equiv of the dienes increases the reaction time and decreases the yield. The nature of the catalyst appears not to affect the reaction regioselectivity, as indicated by the lack of significant difference of adduct ratios with catalyst change. All these observations are difficult to rationalize in terms of catalyst solubility,¹⁰ structure,¹¹ and acid strength.¹³

The acid catalyst exerts a strong influence on the regiochemistry of the Diels–Alder reaction. Thus, for example, the reaction of isoprene (1b) with 2-methyl-2-cyclohexenone (3b) without catalyst leads to a 6e:9 (*n* = 3) product ratio of 1.9,^{1b} which increases to 32 in the presence of aluminum chloride (Table I). This catalyst effect differs in magnitude with the ketone ring size. Thus, while the isomer ratios of the products of the uncatalyzed cycloaddition of isoprene (1b) with the cycloalkenes 2b, 3b, and 4b remain nearly constant,^{1b} the 6e:9 ratios change from 6.3 in the tetrahydroindanone case (*n* = 2) to 32 in the octalone case (*n* = 3), becoming infinite in the tetrahydrobenzosuberone case in view of the formation of a single isomer (8b) (Table I). Whereas the Lewis acid affects the regiochemistry of the Diels–Alder reaction, it appears not to influence the stereoselectivity of the reactions of the cycloalkenes, as illustrated by the production of a 2.2:1 mixture of octalone isomers 6f and 7 (*n* = 3) in both the uncatalyzed^{1b} and catalyzed reactions of (*E*)-piperylene (1c) with 2-methyl-2-cyclohexenone (3b) (Table I).

Table III and Figure 4 illustrate the effect of the amount of catalyst on the fate of the Diels–Alder process by focusing on the aluminum chloride catalyzed reactions of ketones 3 with dienes 1a and 1b in toluene solution. The data reveal no simple relationship between catalyst equivalents and yield, a reaction rate drop with decreasing quantity of catalyst, and a cessation of the reaction as soon

(7) The complexation time for boron trifluoride etherate was recorded by the time-dependent diminution of the carbonyl absorption in the infrared spectrum of a 0.12 M benzene solution of ketone 3b (benzene substituting toluene as a solvent to avoid solvent absorption in the carbonyl region of the spectrum).

(8) A tenuous explanation for the nature of the competing reaction between the dienes and aluminum chloride is an electron transfer between the two substances and a subsequent oligomerization or polymerization of the resultant diene cation radical. For a related reaction, a diene dimerization by way of an electron-transfer process see: Bellville, D. J.; Wirth, D. D.; Bauld, N. L. *J. Am. Chem. Soc.* 1981, 103, 718. Bellville, D. J.; Bauld, N. L. *Ibid.* 1982, 104, 2665.

(9) Inter alia: Yates, P.; Eaton, P. *J. Am. Chem. Soc.* 1960, 82, 4436. Inukai, T.; Kasai, M. *J. Org. Chem.* 1965, 30, 3567. Stojanak, Z.; Dickinson, R. A.; Stojanak, N.; Woznow, R. J.; Valenta, Z. *Can. J. Chem.* 1975, 53, 616; Kakushima, M.; Espinosa, J.; Valenta, Z. *Ibid.* 1976, 54, 3304. Trost, B. M.; Ippen, J.; Vladuchick, W. C. *J. Am. Chem. Soc.* 1977, 99, 8117. Kelly, T. R.; Montury, M. *Tetrahedron Lett.* 1978, 4311. Liu, H. J.; Browne, E. N. C. *Can. J. Chem.* 1979, 57, 377.

(10) Zinc chloride is sparingly soluble in toluene, but gives a soluble complex with 2-methyl-2-cyclohexenone (3b). Aluminum bromide, boron trifluoride etherate, boron tribromide, and stannic chloride are soluble in toluene and, except for the latter, form soluble complexes with ketone 3b.

(11) While the boron trihalides and zinc chloride are monomers, aluminum chloride is a polymer and aluminum bromide a dimer.¹² The catalytic species, however, is the monomeric form.¹²

(12) Olah, G. A. "Friedel–Crafts and Related Reactions"; Interscience: New York, 1963; Vol. I.

(13) The following sequence represents a suggested qualitative order of the Lewis acids in decreasing acid strength: BBr₃, BF₃, AlBr₃, AlCl₃, SnCl₄, ZnCl₂.¹⁴

(14) Satchell, D. P. N.; Satchell, R. S. *Chem. Rev.* 1969, 69, 251; *Q. Rev., Chem. Soc.* 1971, 25, 171.

Table III. Influence of the Amount of Aluminum Chloride on the Product Yield from Reactions of Ketones 3a and 3b with Dienes 1a and 1b^a

ketone (M) ^b	catalyst, equiv	diene (equiv)	reaction		total yield
			temp	time	
3a (0.1)	0.25	1a (3)	70	25	66
3a (0.1)	0.5	1a (3)	70	22	84
3a (0.1)	0.9	1a (3)	70	15	72
3a (0.1)	1.25	1a (3)	c	c	0
3b (0.2)	0.25	1a (3)	70	16	77
3b (0.2)	0.5	1a (3)	70	14	83
3b (0.2)	0.9	1a (3)	70	10	93
3b (0.2)	1.25	1a (3)	c	c	0
3b (0.2)	0.25	1b (3)	25	17	79
3b (0.2)	0.5	1b (3)	25	6	54
3b (0.2)	0.9	1b (3)	25	5	54
3b (0.2)	1.25	1b (3)	c	c	0

^a In toluene solution; reaction temperature in °C and time in h; total yield (by GLC) in %. ^b Complexation time of 3a: 40 min at 22 °C and 5 min at 22 °C (in the presence of 0.25 equiv of catalyst); complexation time of 3b: 12 min at 22 °C. ^c Under a variety of experimental conditions.

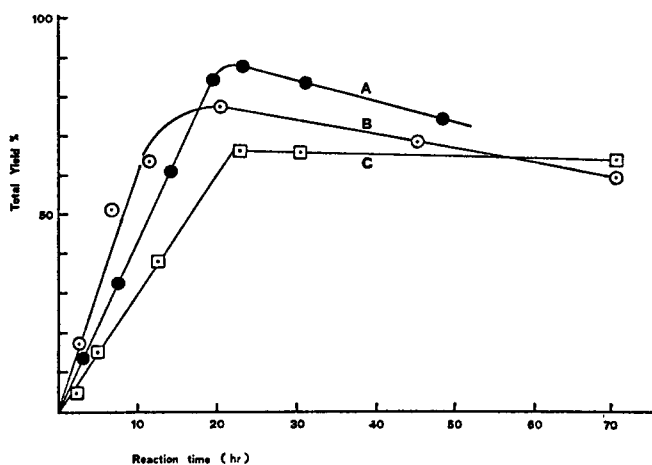


Figure 4. Reactions of 2-cyclohexenone (3a) in 0.1 M toluene solution with 3 equiv of 1,3-butadiene (1a) in the presence of 0.5 (curve A), 0.9 (curve B), and 0.25 equiv (curve C) of aluminum chloride (complexation at 22 °C for 40 min, cycloaddition at 70 °C).

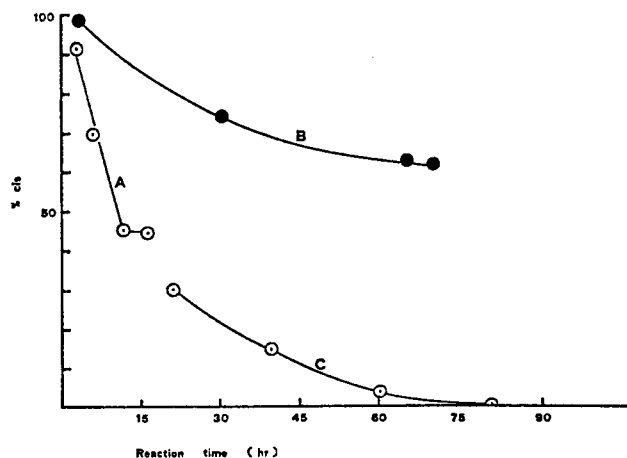
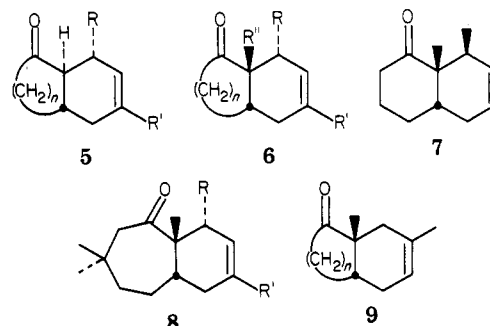


Figure 5. Percent yield of products 6a ($n = 2$) (curve A), 6b ($n = 2$) (curve B), and 6c ($n = 2$) (curve C) in the aluminum chloride catalyzed reactions of 2-cyclopentenone (2a) with 3 equiv of 1,3-butadiene (1a), 15 equiv of isoprene (1b), and 9 equiv of (*E*)-piperylene (1c), respectively, in toluene solution (experimental conditions listed in Table IV of this communication and Table VI of ref 1b).



- a, R = R' = R'' = H
 b, R = R'' = H; R' = Me
 c, R = Me; R' = R'' = H
 d, R = R' = H; R'' = Me
 e, R = H; R' = R'' = Me
 f, R = R'' = Me; R' = H

as the amount of aluminum chloride exceeds 1 equiv. In the latter event the reactions with any 2-cycloalkenone become exothermic and lead to no Diels-Alder adduct irrespective of the length of complexation time or size of excess of diene used.⁸ Since the diene-catalyst side reaction takes place only in the presence of uncomplexed aluminum chloride, it is not surprising that replacement of toluene by the coordinating solvent acetonitrile permits the use of excess catalyst and under these conditions converts ketones 3 into Diels-Alder adducts, albeit in yields lower than those of normal reactions in toluene. Finally, the cycloaddition tolerates an excess of the catalysts boron trifluoride etherate, zinc chloride, and stannic chloride even in toluene solution, but the product yields are distinctly lower than those of aluminum chloride catalyzed reactions.

The cis-bicyclic, primary Diels-Alder adducts 6 without angular substituent suffer partial or total transformation into their trans isomers 5 in the presence of aluminum chloride in toluene solution. No significant differences appear on change of the catalyst, but different cis-trans product ratios are obtained in uncatalyzed reactions.^{1b} The data for some aluminum chloride induced isomerizations are exhibited in Figures 5 and 6.

Effects of Ketone Concentration and Structure and Reaction Time. Figure 7, depicting the catalyzed reactions of 1,3-butadiene (1a) with ketones 3, portrays two typical examples of the product yield dependence on ketone concentration.¹⁵ In view of the strong interrelationship of this parameter with those discussed heretofore it is impossible to predict the ideal ketone concentration needed for attaining the best product yield. The parameter interdependence is shown dramatically by a comparison of the best product yields obtained in reactions of 3 equiv of 1,3-butadiene (1a) in 0.1 M vs. 1 M toluene solutions of 2-cyclohexenone (3a) in the presence of 0.5 and 0.9 equiv of aluminum chloride. The dilute ketone solutions lead to yields of 84 and 72%, respectively (Table III), whereas the more concentrated ketone solutions afford 12% (at 25 °C after 142 h) and 65% yields (at 25 °C after 4 h), respectively.

As Figures 8 and 9 illustrate, the Diels-Alder adduct yields depend also on the length of the reaction time. The yields either stay constant or actually drop after a certain time period. This unusual yield decrease reflects the

(15) The cycloalkenone concentration in the complexation process is approximately twice that in the cycloaddition process. The best product yields resulted from the use of 0.1–0.4 M toluene solutions of ketone as the "final" ketone concentration. Since a concentration increase generally lowers the yield, it is not possible to study the complexation time dependence on the ketone concentration.

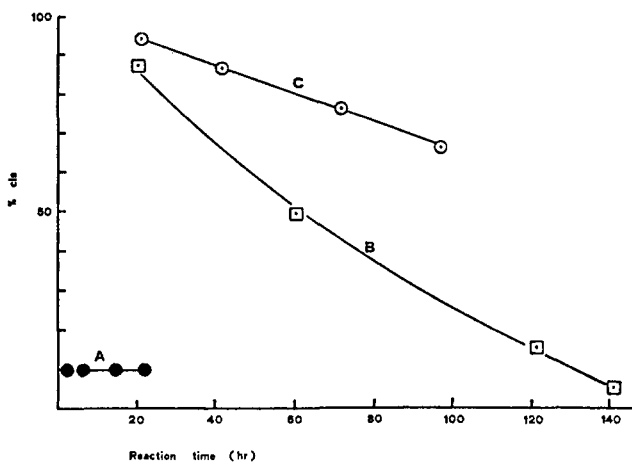


Figure 6. Percent yield of products **6a** ($n = 3$) (curve A), **6b** ($n = 3$) (curve B), and **6c** ($n = 3$) (curve C) in the aluminum chloride catalyzed reactions of 2-cyclohexenone (**3a**) with 3 equiv of 1,3-butadiene (**1a**), isoprene (**1b**), and (*E*)-piperylene (**1c**), respectively, in toluene solution (experimental conditions listed in Table VI of ref 1b).

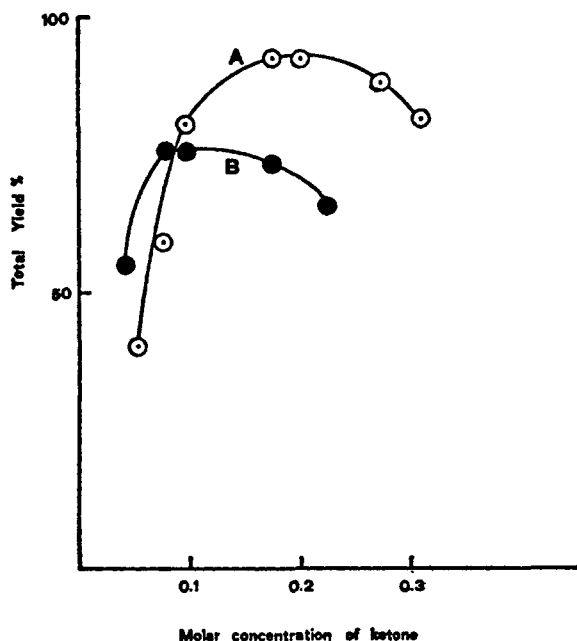


Figure 7. Reactions of 2-methyl-2-cyclohexenone (**3b**) (curve A) and 2-cyclohexenone (**3a**) (curve B) with 3 equiv of 1,3-butadiene (**1a**) in the presence of 0.9 equiv of aluminum chloride in toluene solution (see Experimental Section and Table VI of ref 1b).

product instability under the reaction conditions, as attested by an experiment involving the exposure of a pure product sample to the reaction environment in the absence of diene and the observation of a measurable decomposition of the compound.

Figure 8 would suggest that 2-methyl-2-cyclohexenone (**3b**) is more reactive than its unmethylated analogue (**3a**), a fact in opposition to the known deactivation of a dienophile by electron-releasing substituents on its olefinic carbons.¹⁶ The cause of this discrepancy lies in the complexation stage and is associated with the unequal solubility of the ketone-catalyst complexes.³ The anomaly disappears in reactions in which the aluminum chloride-ketone complexes are fully in solution. Thus 2-cyclohexenone (**3a**) is twice as reactive as its 2-methyl derivative (**3b**) in acetonitrile solution and 4,4-dimethyl-2-cyclo-

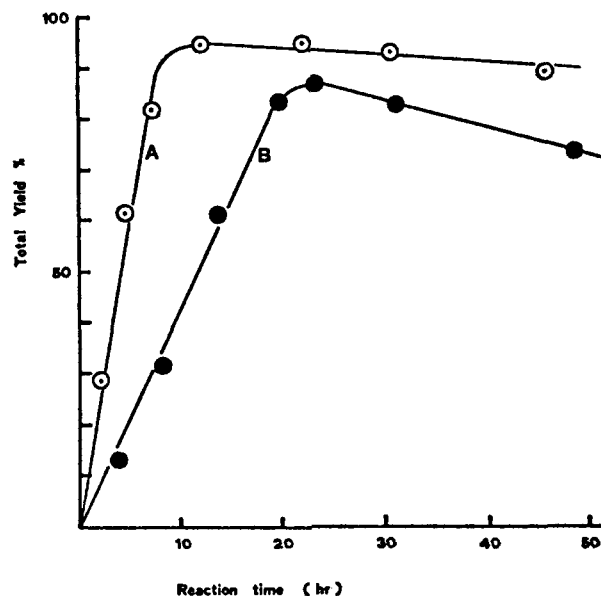


Figure 8. Reactions of 2-methyl-2-cyclohexenone (**3b**) (curve A) and 2-cyclohexenone (**3a**) (curve B) with 3 equiv of 1,3-butadiene (**1a**) in the presence of 0.9 and 0.5 equiv of aluminum chloride, respectively, in toluene solution (see Experimental Section and Table VI of ref 1b).

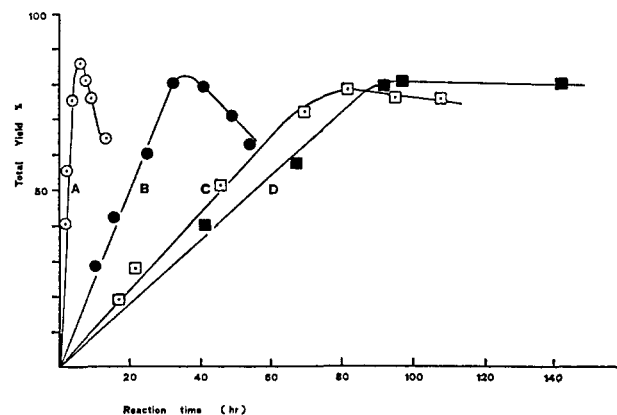


Figure 9. Reactions of 2,6,6-trimethylcycloheptenone (**4b**) (curve A), 2-cycloheptenone (**4a**) (curve B), 2-cyclopentenone (**2a**) (curve C), and 2-cyclohexenone (**3a**) (curve D) with (*E*)-piperylene (**1c**) under the experimental conditions reported in Table VI of ref 1b.

hexenone is approximately twice as reactive as its 2-methylated form in reactions with 1,3-butadiene (**1a**) in toluene solution.^{1b}

The introduction of a methyl group into the β -position of an α,β -unsaturated, cyclic ketone leads to complete blockage of the Diels-Alder reaction. Thus neither 2,3-dimethyl-3-cyclohexenone¹⁷ nor 3-methyl-2-cyclohexenone and 3-methyl-2-cyclopentenone undergo the reaction by either catalytic or noncatalytic means, despite their otherwise normal behavior, i.e., forming ketone-catalyst complexes¹⁸ and exhibiting exothermicity in reactions with excess aluminum chloride. On the other hand, the introduction of an electron-withdrawing substituent on the β -carbon of the conjugated enone system enhances Diels-Alder reactivity, e.g., 3-carbomethoxy-2-cyclohexenone undergoing a ready, uncatalyzed reaction with 1,3-butadiene (**1a**) (at 130–140 °C for 3 h, giving a 55%

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Table IV. Influence of the Amount of Diene on the Product Yield from Reactions of Ketones 2-4 with Dienes 1^a

ketone (M)	diene (equiv)	reaction		total yield
		temp	time	
2a (0.1)	1a (3)	70	16	92
2a (0.1)	1a (13)	70	5	95
2a (0.15)	1c (3)	40	40	30
2a (0.15)	1c (9)	40	81	77
2a (0.15)	1c (14)	40	70	65
2b (0.2)	1b (3)	40	60	45
2b (0.2)	1b (15)	40	40	73
3a (0.1)	1a (1)	70	10	43
3a (0.1)	1a (2)	70	20	82
3a (0.1)	1a (3)	70	15	78
3b (0.2)	1a (1)	70	5	30
3b (0.2)	1a (2)	70	5	50
3b (0.2)	1a (3)	70	10	93
4a (0.2)	1a (3)	25	41 ^b	65
4a (0.2)	1a (6)	25	15	98
4a (0.2)	1b (3)	25	60	53
4a (0.2)	1b (6)	25	87	73

^a With aluminum chloride in toluene solution; amount of catalyst and complexation conditions as in Table VI of ref 1b, except for the reaction of 3a in which 0.9 equiv of catalyst were used; reaction temperature in °C and time in h; total yield (by GLC) in %. ^b A 0.4 M ketone concentration lowers the reaction time to 19 h without affecting the yield.^{1a}

product yield).¹⁹ The abnormal lack of reactivity of 3-methyl-2-cyclohexenone, especially in comparison with that of 2-methyl-2-cyclohexenone (3b), will require a future theoretical analysis.

Influence of the Quantity of Diene. Usually both uncatalyzed and catalyzed Diels-Alder reactions are carried out with the use of an excess of diene in view of diene-based side reactions, e.g., polymerization.²⁰ In the cycloadditions of cycloalkenones 2-4 with dienes 1 in toluene solution under the influence of aluminum chloride, the amount of diene used affects the product yield and reaction rate (see Table IV), albeit without regularity, but does not influence the regiochemistry or ratio of the adducts. The use of a stoichiometric quantity of diene leads to products in low yield; good yields being achieved by the introduction of at least 3 equiv of diene into the reaction mixture. An increase of the quantity of 1,3-butadiene (1a) beyond 3 equiv augments the product yields and the rates of the reactions of 2-cyclopentenone (2a) and 2-cycloheptenone (4a). Whereas this trend is observed also in the reaction between 2-methyl-2-cyclopentenone (2b) and isoprene (1b), it is not followed by the reactions of 2-cycloheptenone (4a) and 2-cyclopentenone (2a) with isoprene (1b) and (*E*)-piperylene (1c), respectively.

Conclusions. The poor dienophilicity of 2-cycloalkenones is overcome by their interaction with Lewis acids, especially aluminum chloride. The use of this catalyst in the Diels-Alder reactions of enones 2-4 with dienes 1 in toluene solution leads to high yields of adducts. The stage of ketone-catalyst complexation is a key step, influencing dramatically the product yield. The regiochemistry of the cycloaddition is affected by the presence of a catalyst but not by its structure. The product yield and reaction rate depend on the ketone concentration, the quantity of diene and catalyst used, and the latter's ability to coordinate with the solvent. Under the reaction conditions the primary, cis-bicyclic product may undergo

partial decomposition and isomerization into trans bicycles (in the absence of angular substituents). A methyl group attached to the β -carbon of the α,β -unsaturated ketone exerts a stronger deactivating effect on the dienophilic behavior of the enone than one bonded to the α -carbon.

Experimental Section

Since the preparation and structure analysis of the Diels-Alder adducts have been described previously,^{1b} the following procedures pertain only to the study of the effect of specific reaction parameters on the product yield. Standard solutions of soluble catalysts were prepared before use, while insoluble catalysts were weighed in the reaction vessel. Standard toluene solutions of dienes 1 could be kept at 0 °C for a week. GLC analyses were carried out on a Carlo Erba GI chromatograph with the use of 1-, 2-, or 3-m 20% LAC728 columns and *m*- and *p*-methoxyacetophenone and *p*-chloroacetophenone as internal standards. All preparations of starting mixtures were done in a drybox.

Diels-Alder Reaction of 2-Methyl-2-cyclohexenone (3b) with 1,3-Butadiene (1a). A solution of 220 mg (2.0 mmol) of ketone 3b in 1 mL of toluene was added to a suspension of 240 mg (1.8 mmol) of anhydrous aluminum chloride in 4 mL of toluene and the mixture stirred at 22 °C for 15 min. The catalyst disappeared quickly, making the solution clear. After 12 min a solution of 324 mg (6 mmol) of diene 1a in 5 mL of toluene was added, the reaction flask stoppered, and the mixture heated at 70 °C. At different times during the reaction a standard toluene solution of internal standard *p*-chloroacetophenone (correction factor 0.794) was poured into ice water, a 1-mL aliquot of the reaction mixture added thereto, and the mixture extracted with ether. The extract was washed with 10% sodium bicarbonate solution, dried (Na₂SO₄), and evaporated. The residue was injected into the gas chromatograph, giving the following time-yield relationships for adduct 6d (*n* = 3): 3 h-48%, 5 h-52%, 7 h-82%, 10 h-93%, 22 h-93%, 30 h-91%, 43 h-88% (Figure 8, curve A).

This procedure was followed in six separate experiments of the addition of diene 1a to the aluminum chloride-ketone 3b mixture after 2, 5, 12, 20, 40, and 60 min and subsequent heating at 70 °C. These experiments led to 43%, 85%, 93%, 92%, 93%, and 92% of adduct 6d (*n* = 3), respectively (Figure 1, curve A).

A toluene solution of 3 equiv of diene 1a was added to toluene solutions of 0.9 equiv of aluminum chloride and enough ketone to create final concentrations (i.e., concentrations calculated to include the diene solution) of 0.05, 0.075, 0.1, 0.175, 0.2, 0.25 and 0.3 M after a complexation period of 12 min at 22 °C and the mixture heated at 70 °C. Workup as above led to 40%, 60%, 82%, 93%, 91%, 88%, and 82% yields of ketone 6d (*n* = 3) (Figure 7, curve A).

Diels-Alder Reaction of 2-Cyclopentenone (2a) with 1,3-Butadiene (1a). A solution of 82 mg (1 mmol) of ketone 2a in 1 mL of toluene was added to a suspension of 120 mg (0.9 mmol) of anhydrous aluminum chloride in 4 mL of toluene. The catalyst disappeared and a sparingly soluble complex was formed. A solution of 162 mg (3 mmol) of diene 1a in 5 mL of toluene then was added under the following, separate experimental conditions. (a) After 10, 80, and 120 min of complexation at 22 °C the cycloaddition at 22 °C afforded adducts 5a (*n* = 2) and 6a (*n* = 2) in 2% and 3% and 5% yields, respectively (Figure 2, curve C). (b) After 2, 10, 15, 30, and 60 min of complexation at 70 °C and addition of the diene solution to the cooled mixtures, the cycloaddition at 70 °C, and the above workup gave adducts 5a (*n* = 2) and 6a (*n* = 2) in total yields of 60%, 82%, 92%, 92%, and 90%, respectively (Figure 2, curve A). (c) After 15 min of complexation at 70 °C and addition of the diene solution to the cooled mixture the cycloaddition was carried out for 26 h in three separate experiments at 20, 50, and 70 °C, leading to adducts 5a (*n* = 2) and 6a (*n* = 2) in 58%, 75%, and 92% yields, respectively (Figure 3). In the last case the cycloaddition is complete after 16 h (Table IV). The use of 13 equiv of diene 1a under conditions of 15 min of complexation at 70 °C and cycloaddition also at 70 °C produces a mixture of 5a (*n* = 2) and 6a (*n* = 2) after 5 h in 95% total yield.

A Qualitative Rate Comparison of the Reactions of 1,3-Butadiene (1a) with Ketones 3a and 3b. A solution of 0.5 mmol of ketones 3a and 3b in 0.5 mL of dry acetonitrile was added to a freshly prepared solution of 0.9 mmol of anhydrous aluminum

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chloride in 2 mL of dry acetonitrile. The clear solution was kept at 22 °C for 40 min and then a solution of 3 mmol of diene 1a in 2.5 mL of dry acetonitrile added. The reaction flask was stoppered and the mixture heated at 70 °C. Workup as above yielded 3a-3b adduct ratios of 2.1 and 1.9 after 1- and 2-h reaction times, respectively.

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Solvent Effects upon the Thermal Cis-Trans Isomerization and Charge-Transfer Absorption of 4-(Diethylamino)-4'-nitroazobenzene

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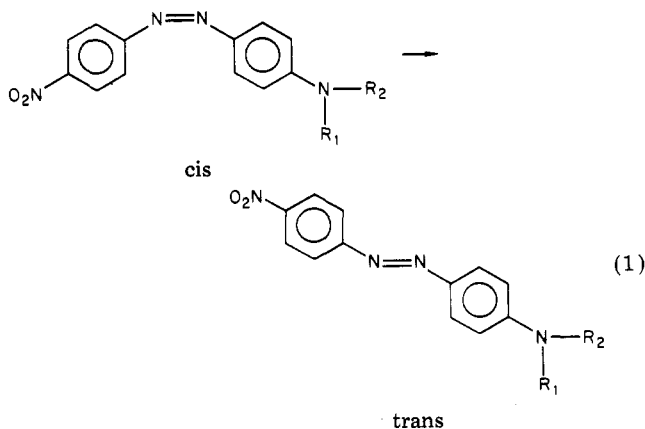
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A comprehensive study of the solvent effects on the rate of the thermal cis-trans isomerization and the position of the charge-transfer absorption of the trans isomer of 4-(diethylamino)-4'-nitroazobenzene (DENAB) is presented. The isomerization rates, the activation parameters, and the absorption maxima have been measured in a variety of protic and aprotic solvents. The data are analyzed and interpreted by using the Taft and Kamlet multiparameter approach and the pyrene fluorescence parameter P_y . The results of the correlations suggest that the isomerization reaction is accelerated in hydrogen-bonding solvents relative to aprotic solvents of similar polarity due to a hydrogen-bonding interaction between the solvent and the nitro group of the dye. Correlation of the absorption maxima with the Taft-Kamlet π^* parameter shows a similar dependence in protic and aprotic media. It is apparent that the absorption process is not affected by hydrogen bonding as strongly as the rate of isomerization. A linear correlation of the rate of isomerization with the position of the CT absorption in different solvents is suggestive of the fact that a similar degree of charge transfer exists in the transition state for the isomerization reaction and in the Frank-Condon excited state.

Introduction

The thermal cis-trans isomerization of azobenzenes was first noted by Hartley in 1937.^{1,2} Since Hartley's initial investigation, numerous groups have studied various aspects of the isomerization mechanism, including solvent, substituent, and temperature dependence effects upon the rate of the cis-trans reaction.³⁻⁸ In a previous investigation we reported that k_{ct} (eq 1) for the 4-(dialkylamino)-4'-



nitrobenzenes was extremely sensitive to solvent polarity.⁹ A general trend of increasing k_{ct} with increasing solvent dielectric constant was attributed to the transition state having considerable dipolar character.

In a recent paper¹⁰ it was shown that a quantitative correlation results when ΔG_{ct}^\ddagger (25 °C) for 4-(diethylamino)-4'-nitroazobenzene (DENAB) is plotted as a function of Kosower's Z value^{11,12} of solvent polarity for 14 solvents. It was noted that the correlation breaks up into two linear regions (aprotic solvents and protic solvents) and the effect is attributed to the presence of specific solvent-solute (hydrogen-bond) interactions in the protic solvent medium.

A substantial number of studies in the field of physical organic chemistry have addressed the problem of understanding the general phenomena of solvent effects upon the physical and chemical properties of solute molecules.¹³ Due to the failure of parameters based upon macroscopic properties of solvents (i.e., dielectric constant, refractive index, etc.) to correlate well with solute molecular properties, considerable effort has aimed at development of empirical scales that can be used to predict solvent effects on solute properties.¹⁴ Several groups have developed spectroscopic probes that serve to correlate remarkably well a variety of solvent effects on chemical reactivity and solvatochromism.^{11,14-17} However, as has been recently

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