tically down to a single row of data all the signals from the specified area running across the full width of the CCD in order to minimize readout noise.

Figure 1 shows a typical backscattered ROA spectrum obtained with the CCD detector, that of (+)-*trans*-pinane. The quality of this spectrum, acquired in 10 min, appears to be rather better than that acquired in 30 min under similar conditions but using the intensified diode array detector,[5] which indicates an increase in speed by a factor of perhaps 2 or 3. This constitutes an impressive demonstration of the potential value of CCD detectors in ROA work because the alignment and other optical and electronic parameters were far from the optimum since the detector was only available for a few days. Furthermore, the quantum efficiency, and hence the speed, could be increased significantly by using a backthinned CCD for which quantum efficiencies in excess of 80% in the visible can be achieved[7] (the quantum efficiency of the CCD detector used in this study was approximately 15% in the wavelength range of the measured ROA spectrum). Also, the use of one of the larger CCDs of order 1000 × 1000 elements, which are becoming more readily available, together with an appropriate spectrometer, could provide a complete vibrational ROA spectrum covering 50–4000 cm^{-1} in a single exposure.

The results of this study suggest that, by using a backscattering geometry in conjunction with a large backthinned cooled CCD detector, it is now technically feasible to construct an ROA instrument that could be more than 2 orders of magnitude faster than the existing generation of multichannel instruments that utilize the conventional 90° scattering geometry with an intensified diode array detector. Such an instrument could provide a complete high-quality vibrational ROA spectrum of a favorable sample such as a neat liquid in a minute or two. More importantly, it should render a wide range of new samples, including biologically significant molecules in aqueous media, accessible to ROA studies.

Acknowledgment. We thank the Science and Engineering Research Council and the Wolfson Foundation for Research Grants, and the Deutsche Forschungsgemeinschaft for a Postdoctoral Scholarship (III 02-He 1588/1-1) for L.H.

Registry No. (+)-*trans*-Pinane, 4863-59-6.

Parallel Reactivity Sequences in Cycloadditions of Singlet Biradicals and Diels–Alder Reactions. A Common Physical Basis Manifested as Entropy Control or Enthalpy Control[1a]

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Received August 4, 1989

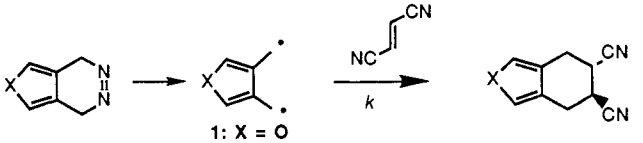
The theoretical rationalizations[2] of the effect of structure on the rates of Diels–Alder reactions and other cycloadditions deal with reactivity sequences that seem to be largely activation enthalpy controlled. For example, the relative reactivities of a series of dienophiles with cyclopentadiene and with 9,10-dimethylanthracene follow $\Delta\Delta H^{\ddagger}$, not $-T\Delta\Delta S^{\ddagger}$. In fact, $\Delta S^{\ddagger}$, is nearly invariant in both of these series, having the value -36 ± 2 cal K^{-1} mol^{-1} for the dienophiles maleic anhydride, fumaronitrile, dimethyl fumarate, and acrylonitrile, the extremes of the range contributing only about 1 kcal/mol (as $-T\Delta\Delta S^{\ddagger}$) to $\Delta\Delta G^{\ddagger}$. The major cause of the >5000-fold range of reactivities of this group of dienophiles is the variation of about 5–6 kcal/mol in $\Delta H^{\ddagger}$.[3]

Table I. Absolute Rate Constants of Reactions of 3,4-Dimethylenefuran **1** and 3,4-Dimethylenethiophene **2** with Alkenes[a,b]

	with **1**[c]		with **2**[d]	
quencher	$k \times 10^{-5}$ M s	temp, °C	$k \times 10^{-5}$ M s	temp, °C
acrylonitrile	3.5	+10		
acrylonitrile	3.7	−10	0.24	−5
acrylonitrile	1.9	−45		
acrylonitrile	1.2	−85		
dimethyl fumarate	440	−10	38	−6
dimethyl fumarate	650	−85	40	−85
fumaronitrile	2200	−10	26	−40
fumaronitrile	2000	−85	46	+20
maleic anhydride	8400	−10	7300	−10
maleic anhydride	3700	−85	5000	−85

[a] See ref 4 for experimental procedures and references to the nanosecond flash kinetic instrumentation. [b] All measurements were carried out in deoxygenated butyronitrile solvent. In earlier work,[4] we found that the rates were insensitive to solvent, the values in acetonitrile and toluene agreeing to within a factor of 2. [c] Excitation with a 337-nm laser pulse. [d] Excitation with a 355-nm laser pulse, except for the maleic anhydride data, which were derived from 337-nm experiments. The yield of transient per pulse (and hence the signal-to-noise ratio) was substantially greater from the 355-nm irradiations, which fall in a stronger absorption region of the diazene precursors of **1** and **2**.

A strong correlation exists between these relative dienophilic reactivities and the relative diylophilic reactivities of the same alkenes toward the singlet biradicals 3,4-dimethylenefuran **1** and 3,4-dimethylenethiophene **2** (generated from the corresponding diazenes.)[4,5] The orders and magnitudes of the relative rates are



1: X = O
2: X = S

essentially the same, despite the factor of 10^{10} in *absolute* rates favoring the biradical reactions. We now find that, in contrast to the diene reactions, the relative rates of the diyl reactions are under activation *entropy* control and are but little influenced by variations in activation enthalpy. Nevertheless, we suggest that although they express themselves here in entropic guise, the causes of the rate order of the biradical cycloadditions are the same as those of the Diels–Alder reactions.

Table I shows that, for all the alkenes, the rates of the biradical cycloadditions are virtually independent of temperature. The acrylonitrile/**1** data cover four temperatures over a 95 °C range and can be expressed in terms of the Arrhenius parameters E_a = 1.3 kcal/mol and $A = 4 \times 10^6$ s^{-1}. Despite the small (in the case of dimethyl fumarate, apparently even slightly negative) activation energies, the rates themselves span a range of about 2200 and 30000 for **1** and **2**, respectively. The reactivities therefore are largely controlled by the entropies of activation.

Why does the same reactivity order appear in the diene and diyl cycloadditions, even though one series is enthalpy controlled

(1) (a) Issued as NRCC 30483. (b) National Research Council of Canada. (c) Yale University.

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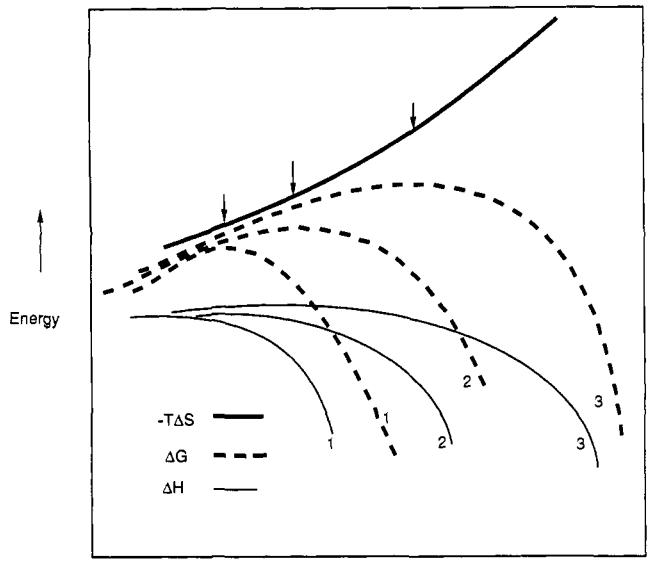

Figure 1. Schematic diagram of energy terms as functions of reaction coordinate for a series of three entropy-controlled cycloadditions with little or no enthalpic barrier, presented in the manner of Houk.[6] In each case, the value of $-T\Delta S$ at the transition state (maximum of ΔG) is marked with an arrow.

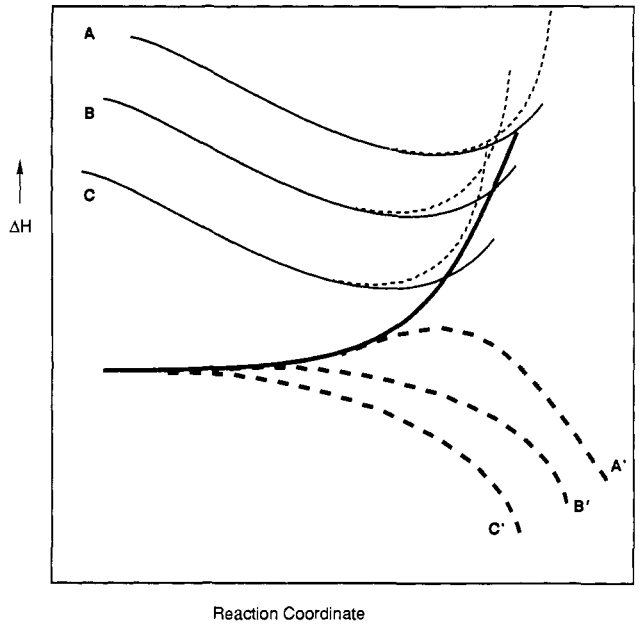

Figure 2. Schematic diagram of configurational interaction of ground level (heavy solid line) with charge-transfer configurations of decreasing energy A, B, and C to produce ground state reaction profiles A′, B′, and C′, respectively.

and the other is entropy controlled? A detailed treatment remains to be given, but we point out that just this result can be deduced qualitatively as a corollary from Houk's model[6] for entropy control, according to which the contribution of the $-T\Delta S^{\ddagger}$ term to $\Delta G^{\ddagger}$ depends on the position of the transition state (maximum in ΔG) along the reaction coordinate. In the ordinary Diels–Alder series, all of the reactions have substantial enthalpic barriers, but to a good approximation, the reaction exothermicities hardly vary. Therefore, by the Hammond postulate, the Diels–Alder transition states all should have about the same location, and hence all should have about the same value of $-T\Delta S^{\ddagger}$. The major contributor to $\Delta\Delta G^{\ddagger}$ thus will be the $\Delta\Delta H^{\ddagger}$ term.

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In contrast, the diyl cycloadditions have little or no enthalpic barrier, but in terms of Figure 1, the variation in their relative rates must result from shifts of the position of the transition state along the reaction coordinate, which in turn produces a monotonic variation of $-T\Delta S^{\ddagger}$.[6] What causes these shifts? For didactic convenience, we offer an interpretation based on a configuration interaction (CI) treatment[2c,d,7,8] of cycloadditions, although the same result would be obtained in any formalism that takes into account the idea[6] that the more reactive the system, the faster the drop of the floor of the potential energy pass. In the CI formalism, the wave function for the transition state can be described as the result of quantum mechanical mixing of ground and excited, notably charge transfer (CT), wave functions (Figure 2). The deeper the CT energy minimum, the stronger the interaction with the ground level. With reference to Figure 2, one sees that this will cause a steeper descent of the ΔH profile to lower energy, which in turn, as Figure 1 shows, will result in a shift to an earlier, lower maximum in ΔG. In this view, a single physical basis underlies both the changes of transition-state energy that produce enthalpy control of the Diels–Alder sequence and the shifts of transition-state location that produce entropy control of the biradical addition sequence.

Acknowledgment. Acknowledgement is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this work. We also thank the National Science Foundation for partial support and Mr. Richard Heath for the generous gift of a synthetic intermediate.

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(8) Although usually couched in frontier molecular orbital or lowest charge transfer state formalism, this is recognized[2b,c] to be a sometimes inadequate approximation.

Nonenzymatic Ligation of Oligodeoxyribonucleotides on a Duplex DNA Template by Triple-Helix Formation

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Received August 2, 1989

We report that a double-stranded DNA template can direct the sequence-specific formation of a phosphodiester linkage between oligodeoxyribonucleotides in aqueous solution by juxtaposing the termini head-to-tail in a triple-helical complex (Figure 1).[1] A triple-stranded complex can be formed when a pyrimidine oligodeoxynucleotide binds in the major groove of duplex DNA parallel to the purine Watson–Crick strand. In the complex, sequence specificity for the condensation of oligodeoxynucleotides

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