

**Table I.** Diylphilic Reactivities<sup>a</sup> of Olefins toward Singlet and Triplet States of 2-Isopropylidenecyclopentane-1,3-diyl

Olefin	Rel gross reactivity <sup>b</sup> R	Rel singlet reactivity, <sup>c</sup> $^1R_i = ^1k_i/^1k_M$	Rel triplet reactivity, <sup>c</sup> $^3R_i = ^3k_i/^3k_M$
Maleic anhydride	590	235	
<i>trans</i> -NCCH=CHCN	450	180	
<i>cis</i> -NCCH=CHCN	410	160	
<i>trans</i> -MeO <sub>2</sub> CCH=CHCO <sub>2</sub> Me	170	67	59
CH <sub>2</sub> =C(Me)CN	20		
CH <sub>2</sub> =CHCN	10	4	35
CH <sub>2</sub> =CHCO <sub>2</sub> Me	10	2	11.5
CH <sub>2</sub> =C(Me)CO <sub>2</sub> Me	7		
<i>cis</i> -MeO <sub>2</sub> CCH=CHCO <sub>2</sub> Me	(1)	(1)	(1)

<sup>a</sup> In each column, the value for dimethyl maleate (M) is defined as unity. <sup>b</sup> These values are estimated to be accurate to at least  $\pm 10\%$ . <sup>c</sup> For experimental errors, see ref 6a.

The reactivities toward the singlet (Table I) roughly parallel the Diels–Alder dienophilic reactivity of these olefins toward cyclopentadiene.<sup>7</sup> Data in the literature<sup>7,8</sup> suggest that for a given group of olefins, the monosubstituted ones lie closer to the high end of the reactivity range in copolymerization reactions than they do in Diels–Alder reactions. The observation (Figure 1, Table I) that the reactivity ratio of acrylonitrile (A) *vs.* dimethyl fumarate (F) is greater when measured against the triplet than against the singlet [ $^3R_A/^3R_F \cong 7(^1R_A/^1R_F)$ ] therefore is reasonable if the transition states of the triplet and singlet cycloadditions are imagined to resemble those of a free radical addition and a Diels–Alder reaction, respectively.

(7) J. Sauer, H. Wiest, and A. Mielert, *Chem. Ber.*, **97**, 3183 (1964).

(8) (a) F. R. Mayo and C. Walling, *Chem. Rev.*, **46**, 191 (1950); (b) C. Walling, "Free Radicals in Solution," Wiley, New York, N. Y., 1957, Chapter IV.

(9) National Institute of General Medical Sciences Predoctoral Fellow, 1969–1973 (GM-46,047).

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### Mechanistic Separation of Singlet and Triplet Reactions of a Trimethylenemethane. Stereospecificity and Regiospecificity in the Cycloadditions of 2-Isopropylidenecyclopentane-1,3-diyl to Olefins<sup>1</sup>

Sir:

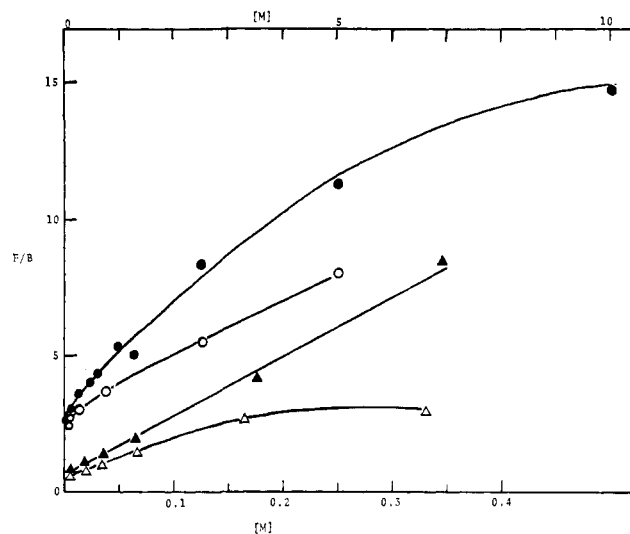
Thermal decomposition of the azo compound **1** releases 2-isopropylidenecyclopentane-1,3-diyl, which can be trapped with conjugated olefins, M (XCH=CHX), to give cycloadducts of the fused type F (bicyclo[3.3.0]octenes), or the bridged type B (7-isopropylidenenorbornenes).<sup>2–4</sup> Supplementing the previous observation<sup>3</sup> that the stereospecificity of formation of *cis* cycloadducts from *cis* olefins diminishes as the initial

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(2) J. A. Berson, D. M. McDaniel, L. R. Corwin, and J. H. Davis, *J. Amer. Chem. Soc.*, **94**, 5508 (1972).

(3) J. A. Berson, D. M. McDaniel, and L. R. Corwin, *J. Amer. Chem. Soc.*, **94**, 5509 (1972).

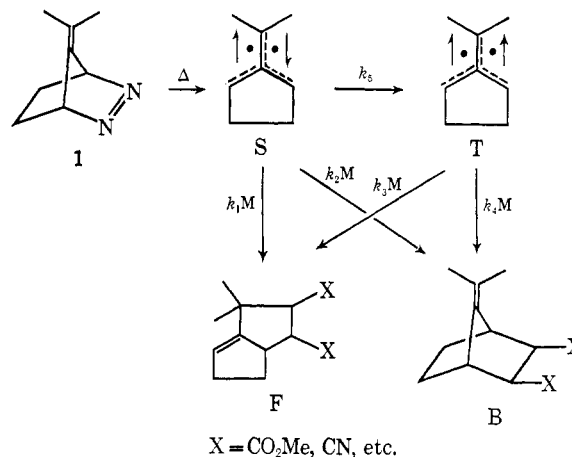
(4) J. A. Berson, C. D. Duncan, and L. R. Corwin, *J. Amer. Chem. Soc.*, **96**, 6175 (1974).



**Figure 1.** Dependence of the ratio of fused to bridged products (F/B) on the olefin concentration [M]. The upper scale refers to methyl acrylate (O), acrylonitrile (●), and dimethyl maleate (Δ). The lower scale refers to dimethyl fumarate (▲).

concentration of olefin is decreased, we now find that the regiospecificity also is concentration dependent. A quantitative treatment of these dilution effects provides the basis for a dissection of the reactions of the diyl into those characteristic of two subspecies, a singlet and a triplet (S and T, Scheme I).

#### Scheme I



The reaction samples are prepared by dilutions of a stock solution of azo compound **1** and olefin (M) in 1:10 molar ratio in CH<sub>3</sub>CN to produce a series in which the initial [M] decreases from 5 to 0.003 M. The solutions are degassed, sealed, pyrolyzed at 60°, and analyzed by gas–liquid chromatography (glc), using 0.125-in. packed or 0.01-in. coated capillary columns in a Perkin-Elmer 900 chromatograph with flame-ionization detector. Figure 1 shows the data on the concentration dependence of the regiospecificity for fused products *vs.* bridged products (F/B) in reactions of four olefins.

Although the solvent composition is unavoidably inconstant over this range, it is the change in concentration of reactants rather than the change of medium that is responsible for the major effects observed. Independent experiments with a dozen other inert solvents (hydrocarbons, alcohols, halogen compounds) show no sig-

**Table I.** Regiospecificity (F/B), Stereospecificity (Retention of Olefin Stereochemistry), and Reactivity<sup>b</sup> in Cycloadditions of Singlet (S) and Triplet (T) 2-Isopropylidene-cyclopentane-1,3-diyli to Olefins

	F/B		Retention of stereochemistry, %		Reactivity (rel) <sup>d, e</sup>		
	S	T	S	T	From dilution <sup>c</sup> S	S	T
<i>trans</i> -MeO <sub>2</sub> CCH=CHCO <sub>2</sub> Me	~75	0.7	>99.9	92	59	67	59
<i>cis</i> -MeO <sub>2</sub> CCH=CHCO <sub>2</sub> Me	>50	0.7	>83	8-11	(1)	(1)	(1)
<i>trans</i> -NCCH=CHCN <sup>a</sup>	>50		>98	>98			
CH <sub>2</sub> =CHCO <sub>2</sub> Me	>55	2.7			1.6	2	11.5
CH <sub>2</sub> =CHCN	31	3.0			3.9	4	35

<sup>a</sup> Observation by D. R. Kelsey. <sup>b</sup> See ref 4. <sup>c</sup>  $(k_1 + k_2)/k_5$ , assuming  $k_5$  invariant. <sup>d</sup> In each column, the reactivities refer to that of dimethyl maleate defined as unity. <sup>e</sup> Estimated experimental error 15% on the first S value, 8% on the second S value, and 20% on the T value. <sup>f</sup> From dissection of gross reactivity (ref 4).

nificant trends that could account for the dilution effect.

Application of the steady-state assumption to the mechanism of Scheme I<sup>5,6</sup> yields eq 1, which predicts

$$F/B = \frac{k_1(k_3 + k_4)[M] + k_5k_3}{k_2(k_3 + k_4)[M] + k_5k_4} \quad (1)$$

that the intercept of a plot of the F/B product ratio *vs.* [M] would be  $k_3/k_4$ , the distribution factor for capture of the triplet T, and that the shape of such a plot would depend upon the relative magnitudes of the distribution factors,  $k_1/k_2$  for S and  $k_3/k_4$  for T. Of the several types of plots possible for such a scheme, the only two observed for these olefins correspond to  $k_1/k_2 > k_3/k_4 > 0$ , with  $k_2 > 0$  for dimethyl maleate, methyl acrylate, and acrylonitrile (convex plots) and  $k_2 \sim 0$  for dimethyl fumarate (linear plot). This implies that in each case, S is captured as a fused product with higher regio-specificity than is T, and moreover, that dimethyl fumarate captures S with essentially complete regio-specificity.

Figure 1 and other methods<sup>9</sup> of treating the dilution effect data provide estimates of  $k_1/k_5 \sim 11$  l. mol<sup>-1</sup>, for the ratio of specific rates of entrapment of S by dimethyl fumarate and intersystem crossing of S to T, and  $k_3/k_4 = 0.66$ , for the distribution ratio from T.

In the cases of dimethyl maleate, acrylonitrile, and methyl acrylate, the curved plots of F/B *vs.* [M] preclude a direct analysis. However, limiting values of the triplet and singlet product distributions may be obtained, respectively, by extrapolation of the product composition to infinite dilution and by the admission to the reaction mixtures of oxygen<sup>7,8</sup> under increasing pressure until no further change in product composition

(5) Scheme I assumes that essentially all of the diyli is trapped as cycloadduct. This is demonstrably the case in the experiments with the more reactive olefins, but the relatively weak diylophile dimethyl maleate<sup>4</sup> permits some diyli to escape capture and dimerize at low [M]. The present evidence cannot distinguish Scheme I from alternatives in which S and T are reversibly interconverted or in which more than two intermediates are formed in sequence, provided that these extra species have distribution factors (F/B) about the same as that of the second intermediate (T). The possibility that S may be 5-isopropylidenebicyclo[2.1.0]pentane will be discussed in a full paper.

(6) Scheme I is a generalization of a very similar treatment used for the analysis of dilution effects in the cycloadditions of nitrenes: J. S. McConaghy, Jr., and W. Lwowski, *J. Amer. Chem. Soc.*, **89**, 2357, 4450 (1967); W. Lwowski and J. S. McConaghy, *ibid.*, **87**, 5490 (1965); W. Lwowski, "Nitrenes," Interscience, New York, N. Y., 1970, p 190.

(7) Selective entrapment of the triplet by triplet O<sub>2</sub> and the effect of dilution on stereospecificity parallel similar observations in carbene chemistry.<sup>8</sup>

(8) (a) For a review, see G. L. Closs, *Top. Stereochem.*, **3**, 193 (1968); (b) M. Jones, Jr., and K. R. Rettig, *J. Amer. Chem. Soc.*, **87**, 4015, 4613 (1965).

(9) L. R. Corwin, Ph.D. Dissertation, Yale University, 1974.

occurs.<sup>9</sup> The product compositions (not only F *vs.* B but also *cis vs. trans*) at any finite [M] may then be reproduced by assuming (from Scheme I) that each observed composition is a linear combination of the triplet and singlet compositions, with the fraction from S

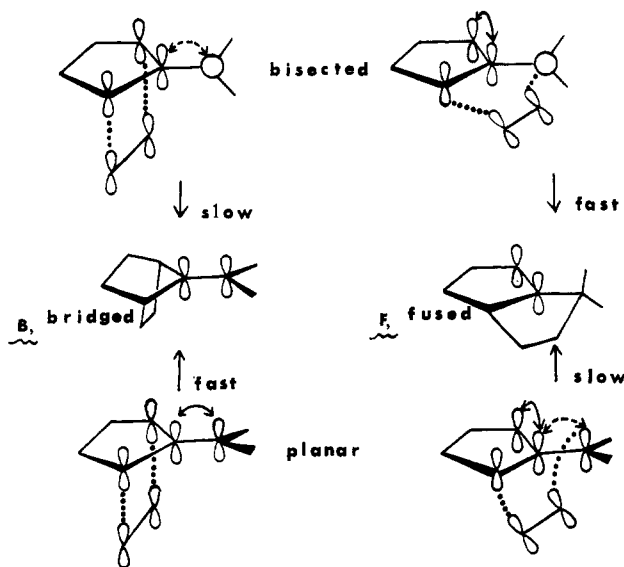
$$f_S = (k_1 + k_2)[M]/[(k_1 + k_2)[M] + k_5]$$

and the fraction from T,  $f_T = 1 - f_S$ . Values of  $(k_1 + k_2)/k_5$  are chosen empirically to minimize the least-squares error in a linear plot of the yield of each product *vs.*  $f_S$ .

Two independent checks of this procedure are available. First, the oxygen-saturated dimethyl fumarate reaction mixtures give 98.7% of the two *trans*-fused adducts F. The high preference for fused product is in agreement with the above deduction that  $k_2 \cong 0$ . Second, the values of  $(k_1 + k_2)/k_5$  deduced from the dilution curves characterize the singlet in terms of its relative rates of entrapment and intersystem crossing. Scheme I assumes that the intersystem crossing rate  $k_5$  is independent of the trapping agent and thus predicts that the ratio of the  $(k_1 + k_2)/k_5$  values for two different olefins should be identical with the ratio of their reactivities toward the singlet. The latter ratio is available from direct competition experiments,<sup>4</sup> and as Table I shows, in each of the four cases examined, it is in good agreement with the value derived here from the dilution studies.

The cycloadditions of the triplet T are sterically and

Scheme II



orientationally nonspecific. The singlet S adds to olefins with high cis stereospecificity, as expected, but also with high regiospecificity for the fused type of cycloadduct (F). We suggest that the cause of the striking and unanticipated regiospecificity is that S has a "bisected" geometry, like that predicted<sup>10-12</sup> for the parent trimethylenemethane. This would produce a low bond order at the developing  $\pi$  bond in the transition state leading to bridged adduct B (Scheme II) but not in that leading to fused adduct F. One might expect a tendency for the regiospecificity to be reversed in reactions of a planar singlet trimethylenemethane (Scheme II).

(10) M. J. S. Dewar and J. S. Wasson, *J. Amer. Chem. Soc.*, **93**, 308 (1971).

(11) W. T. Borden and L. Salem, *J. Amer. Chem. Soc.*, **95**, 932 (1973).

(12) D. R. Yarkony and H. F. Schaefer, III, *J. Amer. Chem. Soc.*, **96**, 3754 (1974).

(13) National Institute of General Medical Sciences Predoctoral Fellow, 1969-1973 (4-F01-GM-46,047-04).

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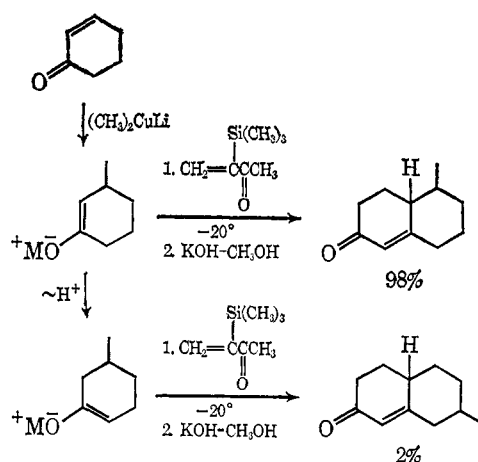
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### Regiospecificity in Enolate Reactions with $\alpha$ -Silyl Vinyl Ketones. An Application to Steroid Total Synthesis

Sir:

Recently,  $\alpha$ -silylated vinyl ketones have been introduced as useful reagents for annelation reactions under strongly basic conditions.<sup>1</sup> These reagents have also been utilized in conjunction with diorganocuprate reagents in an efficient conjugate addition annelation sequence.<sup>2</sup> The observed successful trapping of the enolate intermediate in organocuprate additions under aprotic conditions, even in situations where rapid equilibration to a more stable enolate (eq 1) is possible, led us to investigate this process further.



The high regiostability of this enolate intermediate could conceivably result from the incorporation of a copper atom, and we therefore set out to discover whether there was a dependence upon the presence of copper species in the reaction medium. Enol silyl ether **1** was prepared from cyclohexenone by addition

(1) G. Stork and B. Ganem, *J. Amer. Chem. Soc.*, **95**, 6152 (1973).

(2) R. K. Boeckman, Jr., *J. Amer. Chem. Soc.*, **95**, 6867 (1973).

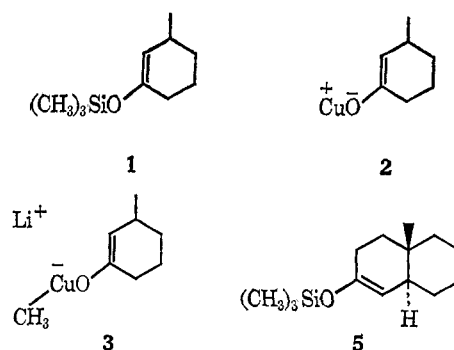
of lithium dimethyl cuprate in ether followed by quenching with trimethylsilyl chloride.<sup>3a</sup> The required lithium enolate was regenerated with methyl lithium (1.1 equiv) in ether (2-3 hr at room temperature or 1 hr at reflux). As the results in Table I indicate, reaction of the lithium

Table I

substrate <sup>a</sup>	products <sup>b</sup>	Yield, % <sup>c</sup>
1	99:1	85 (50)
2 + CuI (1 equiv)	75:25	30
3 + CuI + CH3Li (1 equiv each)	75:25	50
4 + (CuCH3)n (1 equiv preprepared)	98:2	50
5 (DME)	80:20	64
6 (THF)	95:5	48

<sup>a</sup> Reactions were run in dry ether unless specified otherwise on a 1 mmol scale with a 1:1 molar ratio of silyl ether to  $\alpha$ -silylvinyl ketone excepting case 1 which was run with 1.5 equiv of vinyl ketone. The yield with 1 equiv is given in parentheses. <sup>b</sup> Ratio of products determined by vpc (20% Carbowax-20-M, 10 ft at 170°) by comparison with authentic materials; cf. ref 2. <sup>c</sup> Yields of distilled materials.

enolate (1 equiv) with  $\alpha$ -trimethylsilyl methyl vinyl ketone (1.5 equiv) at  $-78^\circ$  (initially) produced regio-specifically, the desired octalone in 85% yield.<sup>4</sup> The addition of CuI (1 equiv) in order to produce cuprous enolate (**2**), prior to the addition of silyl vinyl ketone, reduced the reactivity markedly and had a somewhat detrimental effect upon the regioselectivity. Further addition of an equivalent of methyl lithium to the cuprous enolate to produce a proposed "ate" enolate species (**3**) had no significant effect nor did the addition of independently prepared methyl copper (1 equiv). While these experiments do not rule out the intermediacy of a "copper" enolate, they indicate that the "copper" enolate is operationally indistinguishable in this case from a simple lithium enolate.



We have made the observation that the partial loss of regiospecificity<sup>1,3a</sup> may be eliminated by changing the solvent from 1,2-dimethoxyethane (DME)

(3) (a) B. Ganem, Ph.D. Thesis, Columbia University, 1972. (b) The results reported by Professor Stork and his coworker in the accompanying communication indicate that this conclusion may not be entirely valid (G. Stork and J. Singh, *J. Amer. Chem. Soc.*, **96**, 6181 (1974)). Traces of protic impurities may be the cause of the observed partial equilibration in our experiments. However, we find that DME seems to offer no particular advantage over ether, and parenthetically, ether is easier to prepare and keep anhydrous. We thank Professor Stork for making his results available to us prior to publication.

(4) Distilled yield and identified by comparison with authentic material (cf. ref 2).