(9) The well-known and clinically useful nitrogen mustard N-methylbis(2-chloroethyl)amine was synthesized over 40 years ago: V. Prelog and Z. Blazek, *Collect. Czech. Chem. Commun.*, 6, 211-224 (1934). The utility of such nitrogen mustards in cancer chemotherapy began to be evaluated in earnest about 30 years ago but this lead still needs further development.

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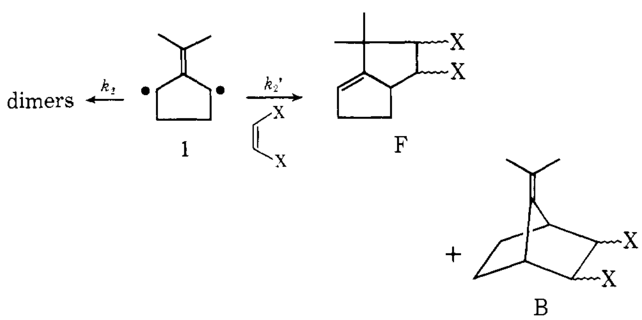
Absolute Rates of Triplet–Triplet Dimerization and Cycloaddition of Trimethylenemethane Biradicals[1]

Sir:

Previous studies[2-4] have shown that the triplet molecules which constitute the ground state[4,5] of the trimethylenemethane (TMM), **1**, dimerize or, in the presence of olefins, are intercepted as fused (F) or bridged (B) cycloadducts. Competition experiments[3] establish an order of *relative* reactivities for a series of olefins, but absolute rates of dimerization or cycloaddition reactions of TMM species heretofore have not been reported. The present description of such measurements is among the very few absolute rates available for biradical reactions.[6,7]

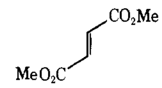
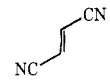
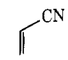
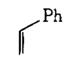
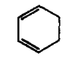


The dimerization and entrapment can be followed by monitoring the intensity of the electron spin resonance (ESR) signal of the $\Delta m_s = 1$ transition in the spectrum[4,5] of triplet **1**. The rates themselves can be made to fall into a convenient range by the choice of the moderately viscous solvent system three parts *i*-PrOH:two parts PrOH, which has $\eta = 2 \times 10^3$ poise[8] at the temperature of our observations, 143.5 K.

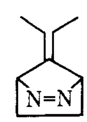
One might imagine that, in fluid media, the quality of the triplet spectrum could be degraded by tumbling of the molecule, which if fast enough, could either collapse the six-line $\Delta m_s = 1$ transitions to a single line by averaging of the direct magnetic dipolar coupling between the two electrons, or produce broad, difficultly observable lines through spin-lattice relaxation. However, for most organic triplet molecules, the rotational correlation time, τ_c, would have to be in the range 10^{-11} to 10^{-12} s in order for these effects to become important.[9] From the Debye theory,[10] we can estimate $\tau_c \sim 8.5 \times 10^{-7}$ s under our conditions, so that a safety factor of 5-6 orders of magnitude protects the experiment.

Irradiation at 360 nm of a 1-2 M solution of the diazene **2**, a precursor of **1**,[4] under these conditions in the cavity of a Varian E-line ESR spectrometer balances the formation and decay of **1** and generates a spectrum which is essentially the same as that previously reported for triplet **1** in rigid glasses.[4,5] The steady-state concentration (±25%) of triplet **1**, usually 10^{-5} to 10^{-4} M, is established by calibration of the spectrometer response against known concentrations of diphenylpicrylhydrazyl (DPPH) and di-*tert*-butylnitroxyl (DTBN).[11,12]

Table I. Second-Order Rate Constants for Cycloaddition of 1 to Olefins at 143.5 K[d]

Olefin	k'_2, l. M^{-1} s^{-1} [b,c]
	3.2
	1.0
	0.20[a]
	0.12
	0.16

[a] At initial olefin concentration = 1.07 M. The values at 1.78 and 1.42 M are 0.21 and 0.20, respectively. [b] The values are probably accurate to ±20%. The major uncertainty is contributed by the solvent contraction, which is assumed to be the same throughout (20% volume decrease relative to the volume at room temperature). [c] Calculated from the equations $\ln (I/I_0) = k_1 t$ and $k'_2 = k_1$ [olefin]$^{-1}$. [d] Material balance of dimer plus cycloadducts in each case is >90% based on azo compound 1. No other products are observed.



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When the irradiation is switched off, the ESR signal intensity (I) declines with a rate that is cleanly second order, $-dI/dt = k_2[\text{triplet } \mathbf{1}]^2$. The products are the previously reported[4] dimers of **1**. The rate-constant, $k_2 = (2 \pm 0.8) \times 10^3$ l. M^{-1} s^{-1}, is about 0.13 times the bimolecular encounter rate constant k_d calculated from the Stokes-Einstein diffusion theory.

The rates of the diyl + olefin cycloaddition are followed by the same experimental technique used in the dimerization studies, except that the reaction mixtures initially contain a 10-20-fold molar excess of olefin (0.1-1 M) over diazene (0.01-0.1 M). At low light intensity, the reaction in each case is first-order in triplet **1**.[13] The order in olefin is established for the case of acrylonitrile by the observation that the pseudo-first-order rate constant is directly proportional to the acrylonitrile concentration. Table I summarizes the data.

If we assume that a lower Arrhenius activation energy is responsible for the entire factor of 15.2 ± 3 favoring cycloaddition of dimethyl fumarate over acrylonitrile at 143.5 K, we may extrapolate to a corresponding ratio of 3.3 ± 0.7 at 333 K. Direct competition experiments[2,3] at 333 K in fluid medium give a ratio of 1.7 ± 0.4, which in view of the uncertainties in the extrapolation, may be considered to be in satisfactory agreement with the ratio of absolute values.

The rate constants k'_2 at seven temperatures between 120.8 and 143.5 K for the reaction of **1** with acrylonitrile give Arrhenius parameters (least-squares rms = 0.0788) $E_a = 6.3$ kcal/mol, $\log A = 8.9$ (A in s). These are very similar to those observed[14] for free radical-olefin additions.

Is the dimerization a triplet–triplet reaction? The chemically induced nuclear polarization (CIDNP) signals previously observed[4] in the dimerization of **1** could arise from either a triplet–triplet or a triplet–singlet combination.[16] Moreover, the second-order rate-law now found for the dimerization is a necessary but insufficient condition for a triplet–triplet reaction. A triplet–singlet reaction also would produce this behavior if the singlet (S) were generated from the triplet (Tr) by a rapid equilibrium Tr $\rightleftharpoons$ S, with equilibrium constant K. The observed rate constant, k_2, then would be related by eq 1 to the S + Tr mechanistic reaction rate constant k by the rate law $-d[\mathrm{Tr}]/dt = kK[\mathrm{Tr}]^2$.

$$k_2 = kK \tag{1}$$

However, the energy of the singlet conservatively may be placed at least 600 cal/mol above that of the triplet,[15] which means that the singlet concentration at 143.5 K would be small. Quantitatively, $K = [\mathrm{S}]/[\mathrm{Tr}] = (1/3)[\exp(-\Delta E/RT)] \lessapprox 0.041$, taking into account the statistical factor favoring the triplet. Since we already know that $k_2 = 0.13k_d$, we may calculate from eq 1 that $k \geqslant 3k_d$. In other words, the alleged S + Tr reaction would have to occur much faster than the diffusion-controlled encounter frequency. This suggests that at least under the conditions in this study, the reaction Tr + Tr is the major dimerization pathway.[17]

References and Notes

(1) The support of this work by the National Science Foundation (GP 33909X and CHE 76-00416) is gratefully acknowledged.
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(7) For reviews of absolute rates of monoradical reactions, see (a) J. A. Kerr in "Free Radicals", Vol. I, J. K. Kochi, Ed., Wiley, New York, N.Y., 1973, p 1; (b) K. U. Ingold, *ibid.*, p 37.
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(9) S. I. Weissman, *J. Chem. Phys.*, **29**, 1189 (1958).
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(11) Digitization of the derivative trace by a computer program and double integration give the areas for use in the equations [DPPH] = c_1 (area$_{\mathrm{DPPH}}$) and [DTBN] = c_2 (area$_{\mathrm{DTBN}}$). The areas and c values are determined for a series of specific temperatures in the same cavity and sample tube.[12] The areas are reproducible to a few percent, but the radical concentrations are accurate to only about 25%. The radical concentrations are corrected for the fact that the signal of the $\Delta m_s = 1$ transition of a triplet is inherently 8/3 as intense as that of a doublet. We thank Professor J. M. McBride for the use of his computer program and for pointing out the necessary intensity factor.
(12) The technique is essentially that of K. Adamic, J. A. Howard, and K. U. Ingold, *Can. J. Chem.*, **47**, 3803 (1969).
(13) High light intensities lead to a high steady-state concentration of triplets, whereupon dimerization becomes competitive and the reaction order in triplet becomes >1.
(14) J. M. Tedder and J. C. Walton, *Acc. Chem. Res.*, **9**, 183 (1976), and references cited therein.
(15) From the linearity of the Curie plot[5] over the range 14–268 K. A gap smaller than 600 cal/mol would have led to at least 10% deviation from the Curie line.
(16) G. L. Closs, *J. Am. Chem. Soc.*, **93**, 1546 (1971).
(17) The possibility remains that a small amount of S + Tr reaction could account for some or all of the CIDNP effect. Also, since the cycloaddition of olefins is much slower than diffusion-controlled, a singlet–olefin reaction cannot be ruled out on kinetic grounds alone.

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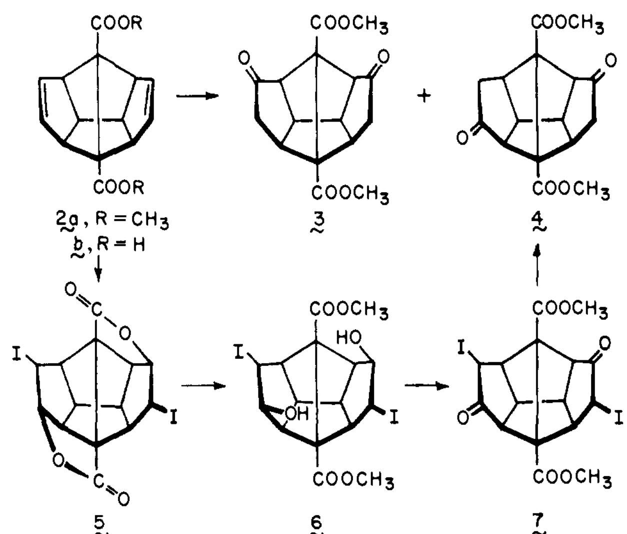
A Functionalized Trisecododecahedrane Having C_2 Symmetry

Sir:

From among the regular polyhedral hydrocarbons based upon the perfect solids of antiquity, dodecahedrane (**1**) holds a preeminent position because its relatively strain-free array of 12 polyfused cyclopentane rings generate the highest known point group symmtery (I_h), a completely enclosed cavity lacking solvation capacity, and an aesthetically appealing topology. Although numerous synthetic approaches to **1** are conceivable, some of which have already been reduced to practice in part,[1] we have viewed with especial interest a scheme which would capitalize on the inherent symmetry of the target molecule. We now describe the essence of this plan as it relates to the ready elaboration of the functionalized trisecododecahedrane **14,** the most highly condensed precursor of **1** presently known.

Diester **2a,** available in one step by Domino Diels-Alder reaction of 9,10-dihydrofulvalene with dimethyl acetylenedicarboxylate,[2] possesses four suitably arrayed cyclopentanoid rings and adequate symmetry (C_{2v}) to serve as our molecular cornerstone. The unnecessary central bond in **2** may be cleaved by a variety of methods but is presently retained to maintain norbornene character and thereby guarantee excellent stereochemical control in later stages. Elaboration of the pivotal diketo diester **4** (C_2 symmetry) was initially attempted by reaction of **2a** with disiamylborane followed by sequential alkaline peroxide and Jones oxidation. However, the principal product proved to be the unwanted isomer **3** (49%) rather than **4** (30%).



3 **4** **5** **6** **7**

To circumvent this complication, the following "cross-corner" oxygenation sequence was developed. Iodolactonization of diacid **2b,** available in 98% yield from alkaline hydrolysis of **2a,** proceeded with high efficiency (96%) to give **5** (ν_{max}^{KBr} 1780 and 1792 cm^{-1}) which underwent cleavage to **6** in the presence of methanolic sodium methoxide at room temperature. Importantly, the iodohydrin part structures survive such treatment because intramolecular S$_N$2 displacement of iodide by the transient alkoxide ions (epoxide formation) is precluded by the rigid superstructure which maintains these groups in a geometric relationship approaching 120°. The oxidation of **6** was brought about with Jones reagent (92% from **5**) and reductive removal of the iodine atoms in **7** was conveniently effected with zinc-copper couple and ammonium chloride in methanol solution.[3] This four-step procedure, which can be performed on large scale quantities, delivers exclusively **4** in