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# Temperature Effect on [2 + 2] Intramolecular Photocycloadditions[†]

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**Abstract:** The temperature dependence of intramolecular [2 + 2] photocycloadditions has been studied for two series of cyclohexenones, α- and $\beta$-linked, respectively, to a variously substituted olefin moiety *via* a trimethylene chain. With one exception, the disappearance quantum yield of the starting material decreases sharply in a narrow temperature range to approximately one-half of its initial value. No such sharp temperature effect was observed on the product ratio, which either remains constant or varies monotonically over the entire temperature range. This indicates that the temperature effects on the disappearance rate and on the product distribution refer to two distinct processes. A mechanism rationalizing this behavior is proposed.

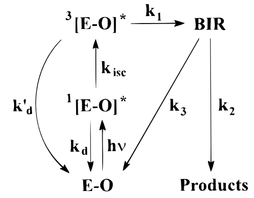
## Introduction

The temperature effect on [2 + 2] *inter*molecular photocycloadditions has been examined in detail by de Mayo.[1,2] Less attention has been paid to the effect of temperature on the corresponding *intra*molecular photocycloadditions; we are aware of only one such communication, published by Jones[3] in 1976.

Loutfy and de Mayo[2] observed a temperature effect on both the product ratio and the product quantum yield in certain [2 + 2] *inter*molecular photocycloadditions. For example, when the temperature is increased from −102 °C to 27 °C, the product quantum yield for the addition of cyclopentenone to cyclohexene drops by a factor of up to 1.6, and the *cis*/*trans* product ratio decreases. In the addition of cyclopentenone to cyclopentene, the product quantum yield decreases by a factor of up to 2.6 when the temperature is increased from −71 °C to 27 °C. In several other [2 + 2] intermolecular photocycloadditions the product quantum yield increases or remains unchanged with increasing temperature, depending on the structures of the enone and olefin. The authors concluded that the temperature effect on the product quantum yield is not related to the greater viscosity at low temperatures, but to the activation energy difference between biradical closure and fission ($k_2/k_3$ in Scheme 1). In contrast, the temperature effect on the product ratio was said to arise from the temperature dependence of the relative rates of closure from different conformations of the biradical, i.e., *cis*-cyclization has the lower activation energy and therefore presumably predominates at lower temperatures.

In contradiction to the findings of Loutfy and de Mayo, Jones,[3] who studied the temperature effect on the [2 + 2] *intra*molecular photocycloaddition of cyclopentenone to an olefin in a rigid system, found that the rate constant for the triplet enone reaction ($k_1$ in Scheme 1) increases as the temperature is increased from 4 °C to 51 °C, whereas the product quantum yield, which depends on the rate difference between biradical closure and fission, is temperature independent.

**Scheme 1**



In this paper we describe a systematic study of the temperature effect on the disappearance rate of the starting material and on the product selectivity in [2 + 2] intramolecular photocycloaddition of cyclohexenones, α- or $\beta$-linked to a variously substituted olefin moiety *via* a trimethylene chain.

## Results

All irradiations were carried out in *n*-hexane at constant concentration (0.5−0.7 mM) under nitrogen at several temperatures (±0.5 °C, internal monitoring) using a uranium glass filter ($\lambda > 330$ nm). The irradiations were continuous, and the disappearance of the starting material was followed by GC analysis of aliquots withdrawn during irradiation at various time intervals. The disappearance rate of the starting material ($v$) at each temperature was determined[4] in triplicate from the slope of the linear plot of $\ln(C)$ versus time, where $C$ is the starting material's concentration. The disappearance rate ($v$) is proportional to the corresponding quantum yield ($\phi$), where $\phi = v/I_{abs}$, and $I_{abs}$ is the intensity of the light absorbed.

It should be emphasized, that the immersion lamp intensity was constant in all irradiations. This was checked by irradiating samples of **1** (Scheme 2) at 20 °C at identical concentration before each irradiation and verifying that the rate of its disappearance was unchanged. The lamp was sufficiently well insulated, so we could assume that its intensity was not affected by changing the temperature of the cooling liquid. Furthermore, the absorbance spectra of all the substances studied in this work were similar due to their common enone chromophor and the remote changes in structure, so that we could assume that the intensity of the light absorbed ($I_{abs}$) in all irradiations was approximately constant. Thus, the ratio of the quantum yields

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[†] Prefatory comment: The study described in this paper is part of a comprehensive experimental investigation of photochemical [2 + 2] cycloadditions carried out in this laboratory, that was discontinued at the death of the senior author. The present results are sufficiently complete, however, to allow novel conclusions to be drawn about the mechanism of intramolecular [2 + 2] photocycloadditions, which are amenable to computational confirmation.

[‡] Deceased, 7/4/1994.

[⊗] Abstract published in *Advance ACS Abstracts,* July 15, 1996.

(1) de Mayo, P. *Acc. Chem. Res.* **1971**, *4*, 41.

(2) Loutfy, R. O.; de Mayo, P. *J. Am. Chem. Soc.* **1977**, *99*, 3559.

(3) Jones, G.; Ramachandran, B. R. *J. Photochem.* **1976**, *5*, 341.

(4) The experimental error in determining the rate is ±10%.

S0002-7863(95)03107-6 CCC: $12.00

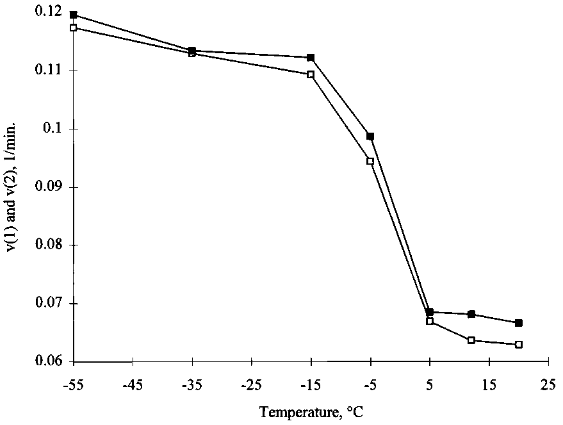


**Figure 1.** Dependence of $v(\mathbf{1})$ (■) and $v(\mathbf{2})$ (□) on temperature.

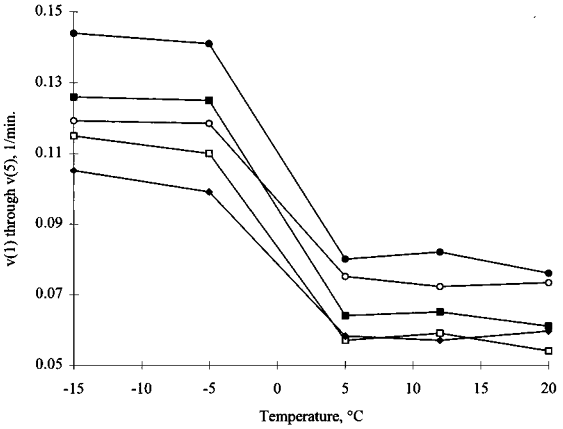
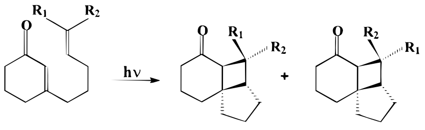


**Figure 2.** Dependence of $v(\mathbf{1})$ (■), $v(\mathbf{2})$ (□), $v(\mathbf{3})$ (●), $v(\mathbf{4})$ (◆) and $v(\mathbf{5})$ (○) on temperature.

## Scheme 2



| | | |
|---|---|---|
| **1** $R_1=R_2=H$ | | |
| **2** $R_1=Bu^t$; $R_2=H$ | **6** | **7** |
| **3** $R_1=H$; $R_2=Bu^t$ | **7** | **6** |
| **4** $R_1=Me$; $R_2=H$ | **8** | **9** |
| **5** $R_1=H$; $R_2=Me$ | **9** | **8** |

of two reactions ($\phi$(i)/$\phi$(j)) could be equated with the ratio of the corresponding disappearance rates ($v$(i)/$v$(j)).

As can be seen in Figure 1, the dependence of the disappearance rates of **1** and **2** ($v(\mathbf{1})$ and $v(\mathbf{2})$, respectively) (Scheme 2) on temperature is identical; both of them decreases sharply in a narrow temperature range above −15 °C to approximately one-half of their initial values. The quantum yield for disappearance of **1** ($\phi(\mathbf{1})$) in hexane at 20 °C had been determined[5] actinometrically to be 0.5 ± 0.05, so the 1.8-fold larger value of $v(\mathbf{1})$ at −55 °C brings $\phi(\mathbf{1})$ up to approximately 0.9 at that temperature.

The temperature range between −15 and 5 °C, where the rates decrease sharply, is the interesting one. We therefore irradiated all of the $\beta$-substituted cyclohexenones **1**, **2**, **3**,[6] **4**, and **5** (Scheme 2) in this region, extended to 20 °C. The same temperature effect was found on the disappearance rates of all the $\beta$-substituted cyclohexenones, as can be seen in Figure 2.

We considered the possibility that the temperature effect on the disappearance rates in this region might be related to the decreased viscosity of the solution as the temperature is increased.[2] However, the dependence of the viscosity on the temperature is smoothly exponential, so it would be unreasonable to ascribe the sharp temperature effect on the rates to it. Moreover, irradiation of **1** and **2** at 20 °C in pentane, hexane, decane, dodecane, and tetradecane showed that the temperature effect is not related to viscosity changes. For example, $v(\mathbf{1})$ in decane at 20 °C ($\eta = 0.92$ cp)[7] is *smaller* by a factor of 1.2 than $v(\mathbf{1})$ in hexane at 20 °C ($\eta = 0.33$ cp). The viscosity of hexane at −55 °C is approximately 0.84 cp,[8] so that $v(\mathbf{1})$ in hexane is about twice as large as in decane under comparable conditions of viscosity. Hence, de Mayo's conclusion[2] that decreasing product quantum yield in intermolecular photocycloadditions with increasing temperature is independent of viscosity changes, holds for the disappearance quantum yield of the starting material in the corresponding intramolecular photocycloadditions as well.

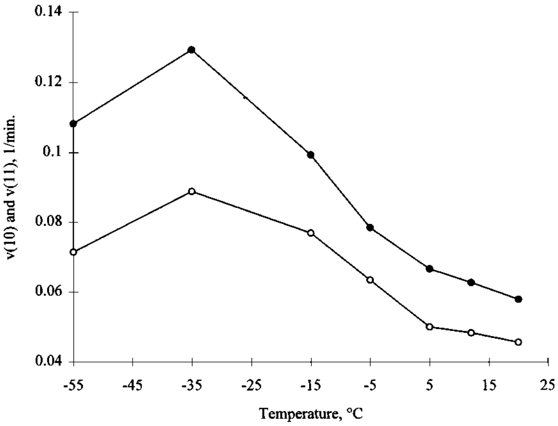
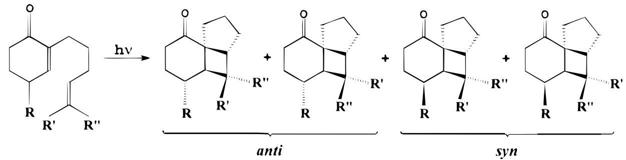


**Figure 3.** Dependence of $v(\mathbf{10})$ (●) and $v(\mathbf{11})$ (○) on temperature.

## Scheme 3



| | *anti* | | *syn* |
|---|---|---|---|
| **10** $R=R'=R''=H$ | | | |
| **11** $R=Bu^t$; $R'=R''=H$ | **18** | | **19** |
| **12** $R=R''=H$; $R'=Me$ | **20** | **21** | |
| **13** $R=R'=H$; $R''=Me$ | **21** | **20** | |
| **14** $R=Bu^t$; $R'=Me$; $R''=H$ | **22** | **23** | *syn* isomers < 6% [a] |
| **15** $R=Bu^t$; $R'=H$; $R''=Me$ | **23** | **22** | |
| **16** $R=R''=H$; $R'=Bu^t$ | **24** | **25** | |

[a] Reference 22.

We also considered the possibility that the temperature effect on the disappearance rates between −15 °C and 5 °C might be related to the decreased absorbance as the temperature is increased. However, the absorbance changes in this narrow temperature range are negligible.

The temperature effect on the disappearance rates of the α-substituted cyclohexenones (Scheme 3) was more variable but, except for **16**, the trends were qualitatively similar to that of the $\beta$-substituted cyclohexenones.

Separate irradiation of **10**−**15** (Scheme 3) were carried out under the usual conditions. Here too, as can be seen in Figure 3, the disappearance rates of **10** and **11** drop to approximately one-half of their initial values as the temperature is increased above −35 °C. Here the maximum is shifted to a lower temperature, so the subsequent drop of the rate with increasing

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(5) Nagler, M. *D. Sc. Thesis* **1978**, Haifa, Israel.

(6) Synthetic restrictions did not permit preparation of **3** in greater than 83% purity, accompanied by 17% of **2** and this mixture was irradiated.

(7) The viscosity values were taken from the *CRC Handbook of Chemistry and Physics*, 72nd ed.; Lide, D. R., Ed. CRC Press, Inc.: Boston 1991−1992, pp *6*−156.

(8) This viscosity value was calculated according to equation (4) in Allan, J. M.; Teja, A. S. *Can. J. Chem. Eng.* **1991**, *69*, 986.

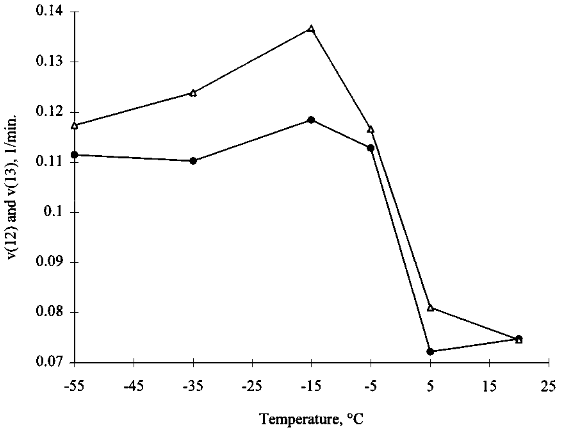

**Figure 4.** Dependence of *v*(**12**) (△) and *v*(**13**) (●) on temperature.

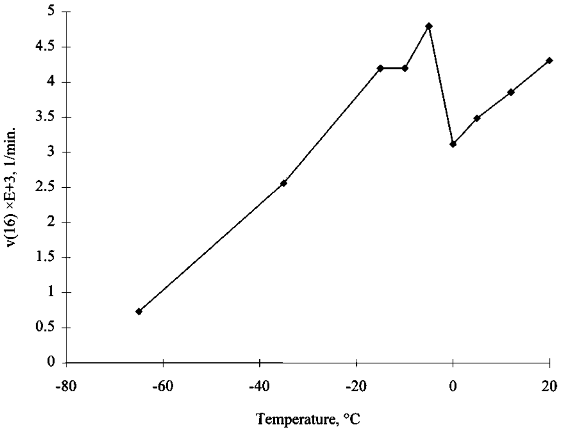

**Figure 5.** Dependence of *v*(**16**) (◆) on temperature.

temperature is more gradual. The quantum yield for the disappearance of **10** ($\phi$(**10**)) in hexane at 20 °C had been determined[9] actinometrically to be 0.5 ± 0.05, so that $\phi$(**10**) exhibits a maximum at −35 °C that is very close to unity.

In the case of the methyl analogues **12**−**15** (Scheme 3), we observed a greater similarity to the temperature dependence of the disappearance rates of the $\beta$-substituted cyclohexenones, as can be seen in Figure 4 for compounds **12** and **13**. Their disappearance rates drop to approximately one-half of their initial values as the temperature is increased above −15 °C. However, a slight increase of the rates was observed between −55 and −15 °C, in contrast to the constant reaction rate, which was observed in the case of the $\beta$-substituted cyclohexenones (Figure 1). Compounds **14** and **15** behaved similarly to **12** and **13**.

This slight increase of the disappearance rate at low temperatures in the case of the α-substituted cyclohexenones is much more pronounced when a bulky *tert*-butyl group is substituted on the olefin, as can be seen in Figure 5 for compound **16** (Scheme 3). *v*(**16**) increases with increasing temperature, except in the limited region between −5 and 0 °C, where a local decrease is observed, presumably due to a vestigial temperature effect, similar to that observed in the other cases. *v*(**16**) is at least one order of magnitude smaller than *v*(**11**) ($\approx$*v*(**14**) $\approx$ *v*(**15**)), which is slightly smaller than *v*(**10**) ($\approx$*v*(**12**) $\approx$ *v*(**13**)) at all temperatures (Figure 3); thus, the quantum yield for the disappearance of **16** is smaller than 0.05 at all temperatures.

## Discussion

In our systems, $k_3$ (see Scheme 1) is insignificant because there is no more than 10% reversion of the 1,4-biradical to the starting material.[10] De Mayo[2] has concluded that biradical closure to products ($k_2$) governs the temperature dependence of the quantum yield for product formation in intermolecular photocycloadditions. This is not the case with respect to the disappearance rate of starting materials, because $k_2$ is irrelevant to it, assuming that the 1,4-biradical does not revert to the triplet. Moreover, as will be discussed below, regardless of whether or not biradical formation is reversible, if $k_2$ were the temperature-dependent rate coefficient we would expect the product ratio to be sharply temperature dependent in the region between −15 and 5 °C, as is the reaction efficiency. However, this is not so: the product ratio varies monotonically with temperature, as can be seen in Figures 6 and 8. Thus, it is obvious that $k_2$ does not represent the rate determining step.

The initial bonding step ($k_1$) is an activated process. If $k_1$ were rate determining for the disappearance of starting material, the normal monotonic increase of rate with temperature should have been observed. Such an increase is approximated only in the case of the α-substituted cyclohexenone **16**, which has a *tert*-butyl group on the olefin (Figure 5), and is manifested residually at the lowest temperatures in the case of the other α-substituted cyclohexenones. We can assume that the temperature-dependent process in these cases is the primary bonding, which is presumably subject to steric effects. In the case of the $\beta$-substituted cyclohexenones, where a constant reaction rate is observed at low temperatures for both the unsubstituted compound **1** and the *tert*-butyl substituted compound **2** (Figure 1), the steric effect on the primary bonding is evidently insufficient to affect the temperature dependence of the disappearance rate.

Regardless of the different behavior at low temperatures, a similar temperature effect on the reaction efficiency in the region between −15 and 5 °C was observed in all cases (except **16**). We can therefore conclude that this temperature effect is roughly independent of the reactant's structure. Consequently, in this region, the temperature-dependent process must *precede* the primary bonding step ($k_1$ in Scheme 1).

Hence, if our model is restricted to Scheme 1, the reduction of the reaction efficiency in the region between −15 and 5 °C must be due either to a decrease in the rate of intersystem crossing ($k_{isc}$) or to an increase in the rate of the thermal decay of the triplet enone to its ground state ($k'_d$),[11] since radiative decay is unlikely to be markedly temperature dependent. The decrease in the disappearance rate in our case is very sharp, and it is unreasonable to assume that thermal decay of the active triplet suddenly becomes efficient at a particular temperature near −15 °C. Furthermore, the decrease in the rate stops at 5 °C, when it has reached one-half of its initial value, and then remains constant or begins to increase slightly. It is unlikely that the efficiency of thermal decay would become constant at an arbitrary temperature.

In intermolecular photocycloadditions, the quantum yield of intersystem crossing from the singlet to the triplet enone ($k_{isc}$ in Scheme 1) is equal to unity,[12] and it is reasonable to assume that it has the same value in intramolecular additions as well. The triplet yield can therefore not be improved by lowering

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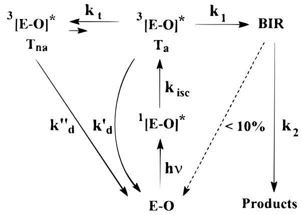
[9] Denekamp, C. *M. Sc. Thesis* 1992, Haifa, Israel.

[10] Becker, D.; Nagler, M.; Sahali, Y.; Haddad, N. *J. Org. Chem.* **1991**, *56*, 4537.

[11] (a) Schuster, D. I.; Dunn, D. A.; Heibel, G. E.; Brown, P. B.; Rao, J. M.; Woning, J.; Bonneau, R. *J. Am. Chem. Soc.* **1991**, *113*, 6245. (b) Schuster, D. I.; Brown, R. H.; Resnick, B. M. *J. Am. Chem. Soc.* **1978**, *100*, 4504. (c) Wagner, P. J.; Bucheck, D. J. *J. Am. Chem. Soc.* **1969**, *91*, 5090.

[12] (a) de Mayo, P.; Pete, J. P.; Tchir, M. F. *Can. J. Chem.* **1968**, *46*, 2535. (b) de Mayo, P.; Nicholson, A. A.; Tchir, M. F. *Can. J. Chem.* **1970**, *48*, 225.

**Scheme 4**



the temperature, so it cannot be responsible for the observed increase in the reaction efficiency with lowering the temperature as well.

Obviously, the model in Scheme 1 cannot explain our experimental results. Consequently, we must assume that there is an additional temperature-dependent process that occurs before the primary bonding step. This may be a partial transition ($k_t$ in Scheme 4) of the active triplet ($T_a$) to an inactive triplet ($T_{na}$), which is more stable than $T_a$, so that the reverse transition from $T_{na}$ to $T_a$ is inefficient. The inactive triplet cannot undergo primary bonding, but can only decay ($k''_d$) to its ground state. If this is the case, then the sharp decrease at −15 °C of the disappearance rate to approximately one-half of its initial value might be due to this transition, where −15 °C is a sufficiently high temperature for it to occur. At temperatures above 5 °C, the two competing processes—primary bonding and the transition from the active triplet to the inactive one—have similar rates, so that they compensate one another and the reaction efficiency remains approximately constant or varies slowly.

The low quantum yield ($<0.05$) in the case of **16** (Figure 5) indicates that at all temperatures, thermal decay of the active triplet ($T_a$) is much more facile than primary bonding, which becomes more favorable as the temperature is increased. At −5 °C we observe a small decrease in the rate, presumably due to a vestigial temperature effect, similar to that described above, which results from a possible partial transition from the active triplet to the inactive one.

Semiempirical calculations at a relatively high level of configuration interaction (MOPAC 93: AM1 (CI = 6))[13] supports the mechanism described in Scheme 4. Two stable triplets formed from **3** (Z) were identified. The first ($T_1$), in which the unpaired spin is concentrated on the cyclohexenone moiety, is separated by a potential barrier of 5 ± 1 kcal/mol from a second triplet ($T_2$), in which the unpaired spin is concentrated on the olefin moiety in the side chain, that is twisted out of planarity. $T_2$ is more stable than $T_1$ by 11 ± 1 kcal/mol, so—if we suppose that $T_1$ is the active triplet ($T_a$) and $T_2$ is the inactive one ($T_{na}$)—then the reverse endothermic transition $T_2 \rightarrow T_1$ is indeed inefficient, as proposed in Scheme 4. The more efficient thermal decay of $T_2$ to the ground state than that of $T_1$ can be explained by their different geometries and location of the spin. Thermal decay of a triplet in an open-chain olefin is more efficient than that of one located in a ring, due to the greater flexibility of the open-chain olefin, that facilitates vibronically induced intersystem crossing from the triplet $T_2$ to the ground state; consequently, $T_2$ has a shorter lifetime.[14] Thus, the reason for the inactivity of $T_2$ is its more rapid thermal decay than reaction with the enone moiety.

Preliminary attempts to measure the lifetime of either triplet formed from **1** by laser experiments were unsuccessful. Only one signal was observed; the lifetime of the species responsible for it is shorter than 1 ns[15] at room temperature and is therefore not measurable within the time resolution of the equipment presently available to us (≈1 ns nitrogen laser). This is not surprising in view of Gleiter's finding that the lifetime of a similarly substituted cyclohexenone is 90 ps.[16] Moreover, it appears that the quantum yield of the phosphorescence in the case of **1** is very low, making lifetime determinations very difficult.

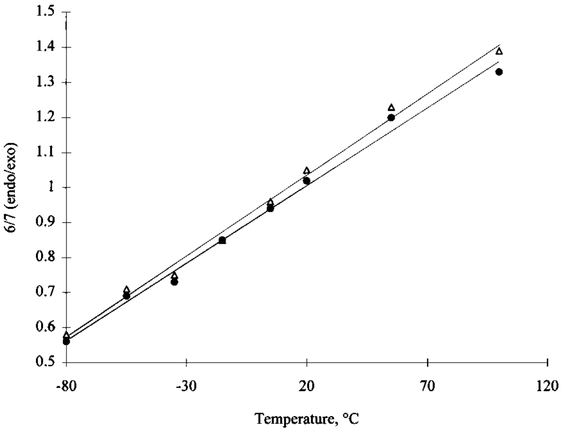


**Figure 6.** Temperature dependence of the photoadduct ratio **6**/**7** (*endo*/*exo*) on irradiation of **2** (*E*-isomer) (●) and **3** (*Z*-isomer) (△).

***β*-Substituted Cyclohexenones.** In the case of **2** and **3** the ratio of photoadducts **6**/**7** (*endo*/*exo*) is similar from irradiation of both isomers at all temperatures (Figure 6),[17] and an identical temperature dependence of the product ratio was obtained for both of them; the *endo*/*exo* ratio increases monotonically with temperature from 0.55 at −80 °C to 1.4 at 100 °C; at approximately 16 °C the ratio is 1.0.

It is reasonable to assume that **2** and **3** undergo primary bonding at the β-carbon, providing the 1,4-biradicals **I** and **II**, respectively (Scheme 5),[18] which are in rapid equilibrium and can close to the *endo* and *exo* products, respectively. Since the product ratio is temperature-dependent, the temperature dependence of the rates of closure to the two stereoisomers *endo* and *exo* must be different.

The excess of the *endo* product in the irradiation of **2** (the *E*-isomer) above 16 °C might have been explained, by primary bonding at the α-carbon of **2** (*E*) at the higher temperatures (>16 °C), in addition to predominant primary bonding at the β-carbon, so that an excess of *endo* product results. Hence, in the case of **3** (*Z*) we would expect an excess of *exo* product above 16 °C. Since this is not the case, as can be seen in Figure 6, the possibility of primary bonding at the α-carbon can be excluded.

Following the modified Eyring approach[19] of eq 1, a linear dependence of the ln($P$) value on the reciprocal of the temperature was found in all of the cases. $P$ is defined by eq 2, where $k$ and $k'$ are the overall rate constants for the formation of the diastereomeric products *endo* and *exo* respectively.

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[13] Full details will be given in a subsequent paper (Halevi, E. A.; Cohen-Arazi, Y.). A referee requested a simulation of the kinetic data in order to verify the "second triplet hypothesis". This will be carried out as soon as all of the potential barriers of the processes along the mechanism have been computed.

[14] This is consistent with Bonneau's conclusion that triplet lifetimes of open-chain alkenones are shorter than those of cyclohexenones: Bonneau, R. *J. Am. Chem. Soc.* **1980**, *102*, 3816.

[15] Very short lifetime in comparison to the lifetime of the triplet formed from 2-cyclohexenone measured by Schuster as 29 ns in cyclohexane: ref 11a.

[16] Gleiter, R.; Fischer, E. *Chem. Ber.* **1992**, *125*, 1899.

[17] The experimental error in determining the product ratio is ±5%.

[18] The biradical conformations in Scheme 5 are analogous to those in Griesbeck's work, where triplet−singlet biradical inversion geometries were taken in account: (a) Griesbeck, A. G.; Mauder, H.; Stadtmüller, S. *Acc. Chem. Res.* **1994**, *27*, 70. (b) Griesbeck, A. G.; Stadtmüller, S. *J. Am. Chem. Soc.* **1991**, *113*, 6923. (c) Griesbeck, A. G.; Stadtm¸ller, S.; Busse, H.; Bringmann, G.; Buddrus, J. *Chem. Ber.* **1992**, *125*, 933.

[19] Eyring, H. *J. Chem. Phys.* **1935**, *3*, 107.

$$\ln(P) = -\frac{\Delta\Delta H^{\ddagger}}{R} \times \frac{1}{T} + \frac{\Delta\Delta S^{\ddagger}}{R} \qquad (1)$$

$$P = \frac{k(endo)}{k'(exo)} \qquad (2)$$

Figure 7 shows the temperature dependence of diastereoselectivity on irradiation of **2** in the form of an Eyring diagram.[20] The values of the activation parameter differences $\Delta\Delta H^{\ddagger}$ and $\Delta\Delta S^{\ddagger}$ (Tables 1 and 2) were derived from the slope and the intercept on the *y*-axis, respectively.

According to the values referring to **2** and **3** in Table 1, the activation enthalpy ($\Delta H^{\ddagger}$) for *exo* closure is smaller than that for *endo* closure. This is consistent with the excess of the *exo* product at low temperatures and its decrease with temperature (Figure 6). At higher temperatures (>16 °C) the *endo* product is in excess, because the activation entropy ($\Delta S^{\ddagger}$) for *endo* closure is more positive than that for *exo* closure (Table 1). Presumably, this is so because the rotation of the *tert*-butyl group, and/or of its methyl groups, is more restricted during *exo* closure, as can be seen in Scheme 5.

Contrary to **2** and **3**, in the case of **4** and **5** the ratio of photoadducts **8**/**9** (*endo*/*exo)* is identical for both isomers (≈1.1) at all temperatures. The methyl group is probably insufficiently bulky to cause a significant difference in either the activation enthalpy or entropy of closure to either the *endo* or the *exo* product (see Table 1), so the *endo*/*exo* ratio is near unity and essentially temperature independent.

**α-Substituted Cyclohexenones.** A monotonic temperature effect on the product ratio was also observed in several irradiations of α-substituted cyclohexenones. The ratio of photoadducts **20**/**21** (*endo*/*exo*) on irradiation of **12** (the *E*-isomer) was dependent on the temperature, decreasing monotonically from 9.3 at −55 °C to 6.5 at 20 °C;[10,21] approximately a 1.4-fold decrease (Figure 8). On irradiation of **13** (the *Z*-izomer) the ratio **20**/**21** was also temperature dependent, decreasing monotonically from 2.7 at −55 °C to 1.8 at 20 °C;[10,21] a 1.5-fold decrease, similar to that obtained for the *E*-isomer.

On irradiation of **14** (the *E*-isomer), the ratio of photoadducts **22**/**23** (*endo*/*exo*) was dependent on the temperature, decreasing monotonically from 7.0 at −55 °C to 4.3 at 20 °C;[22] a 1.6-fold decrease, similar to that obtained for **12** and **13**. On irradiation of **15** (the *Z*-izomer) the ratio **22**/**23**, which had been determined[22] to be 1.8 at 20 °C, remained essentially constant throughout the temperature range, and on irradiation of **16** the ratio **24**/**25** (*endo*/*exo*), which had been determined[9] to be 3.3 at 20 °C, also remained constant at all temperatures. On irradiation of **11**, the ratio of photoadducts **18**/**19** (*anti*/*syn*), which had been determined[22] to be 2.3 at 20 °C, remained constant throughout the temperature range as well.

Thus, in the case of the α-substituted cyclohexenones a large excess of *endo* product is observed, and this excess decreases with temperature in the case of **12**, **13**, and **14**. The α-substituted cyclohexenones probably undergo primary bonding at the α-carbon of the enone (Scheme 6) to yield two biradical rotamers, which can close either to the *endo* or to the *exo* product (in analogy to biradicals **I** and **II** in Scheme 5).

According to Table 2, the activation enthalpy for *endo* closure is smaller than that for *exo* closure in the case of **12**, **13**, and **14**. This is consistent with the excess of the *endo* product and its decrease with temperature. In the case of **11**, **15**, and **16**, where no temperature effect was observed (the activation enthalpy is equal for both products), the excess product (*anti* or *endo*, respectively) must be ascribed to the entropy difference (Table 2).

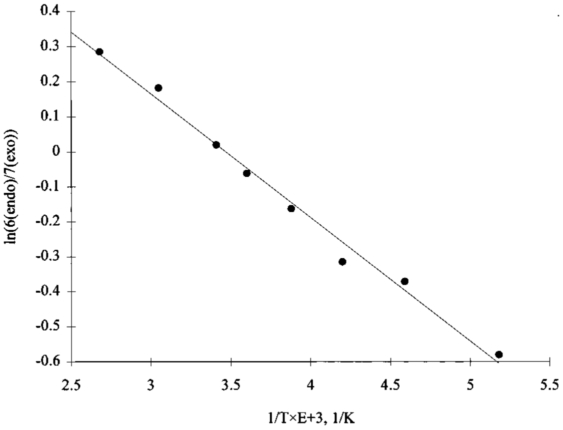

**Figure 7.** Temperature dependence of diastereoselectivity on irradiation of **2** (●) in the form of an Eyring diagram.

**Table 1.** Activation Parameter Differences for the $\beta$-Substituted Cyclohexenones: $\Delta\Delta H^{\ddagger} = \Delta H^{\ddagger}(endo) - \Delta H^{\ddagger}(exo)$; $\Delta\Delta S^{\ddagger} = \Delta S^{\ddagger}(endo) - \Delta S^{\ddagger}(exo)$

| | $\Delta\Delta H^{\ddagger}$ (kJ/mol) | $\Delta\Delta S^{\ddagger}$ (J/mol × K) |
|---|---|---|
| **2** | 2.9 | 10.2 |
| **3** | 2.9 | 10.4 |
| **4** | 0.0 ± 0.1 | 0.0 ± 0.1 |
| **5** | 0.0 ± 0.1 | 0.0 ± 0.1 |

**Table 2.** Activation Parameter Differences for the α-Substituted Cyclohexenones: $\Delta\Delta H^{\ddagger} = \Delta H^{\ddagger}(endo) - \Delta H^{\ddagger}(exo)$; $\Delta\Delta S^{\ddagger} = \Delta S^{\ddagger}(endo) - \Delta S^{\ddagger}(exo)$

| | $\Delta\Delta H^{\ddagger}$ (kJ/mol) | $\Delta\Delta S^{\ddagger}$ (J/mol × K) |
|---|---|---|
| **11** | 0.0 ± 0.1 | 0.8 |
| **12** | −2.3 | 8.1 |
| **13** | −2.3 | −2.5 |
| **14** | −3.2 | 1.4 |
| **15** | 0.0 ± 0.1 | 0.6 |
| **16** | 0.0 ± 0.1 | 1.2 |

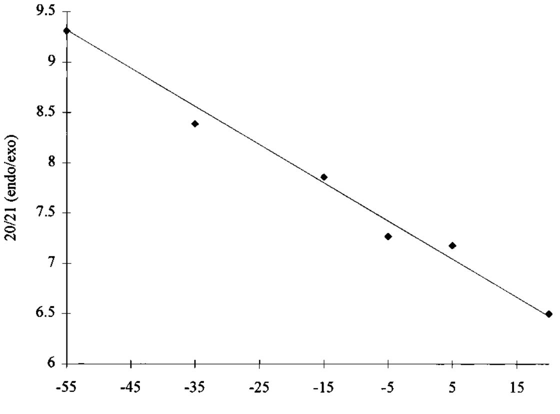

**Figure 8.** Temperature dependence of the photoadduct ratio **20**/**21** (*endo*/*exo*) on irradiation of **12** (*E*-isomer) (◆).

On irradiation of **13** and **15** (the *Z*-isomers), the *endo*/*exo* product ratio is smaller than that obtained from the *E*-isomers **12** and **14**. A possible explanation might be that the *Z*-isomers undergo primary bonding at the $\beta$-carbon of the enone, yielding

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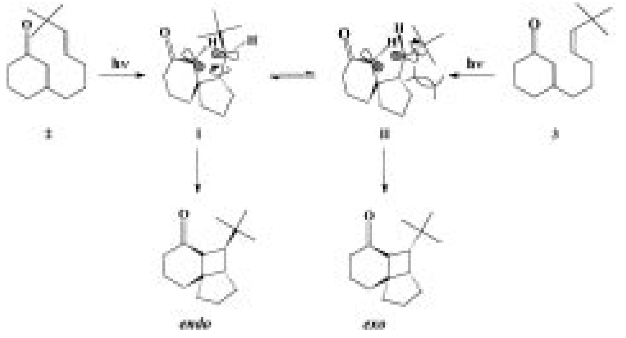
[20] (a) Pelzer, R.; Scharf, H.-D.; Buschmann, H.; Runsink, J. *Chem. Ber.* **1989**, *122*, 1187. (b) Buschmann, H.; Scharf, H.-D.; Hoffmann, N.; Plath, M. W.; Runsink, J. *J. Am. Chem. Soc.* **1989**, *111*, 5367.

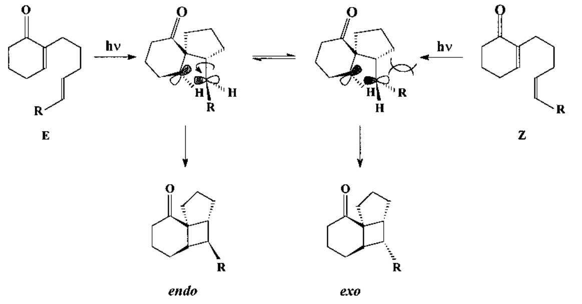
[21] The ratio of photoadducts published in ref 10 were found to be incorrect, and were redetermined in this work according to NMR, GC, and GC-MS data.

[22] Becker, D.; Haddad, N. *Tetrahedron* **1993**, *49*, 947.

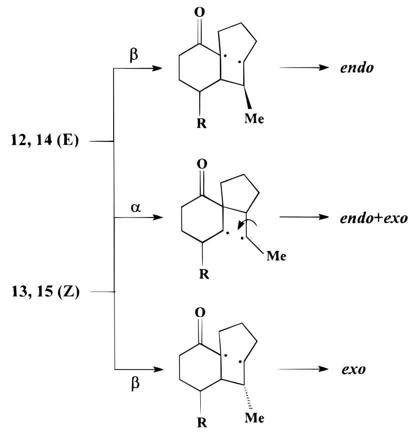
**Scheme 5**



**Scheme 6**



**Scheme 7**



only the *exo* product, in addition to primary bonding at the α-carbon (Scheme 7). If so the *E*-isomers might also undergo primary bonding at the *β*-carbon, increasing the excess of the *endo* product.

Obviously, further investigation is needed in order to clarify the mechanism of this reaction. The computations that are now in progress[13] may indicate the direction that it should take.

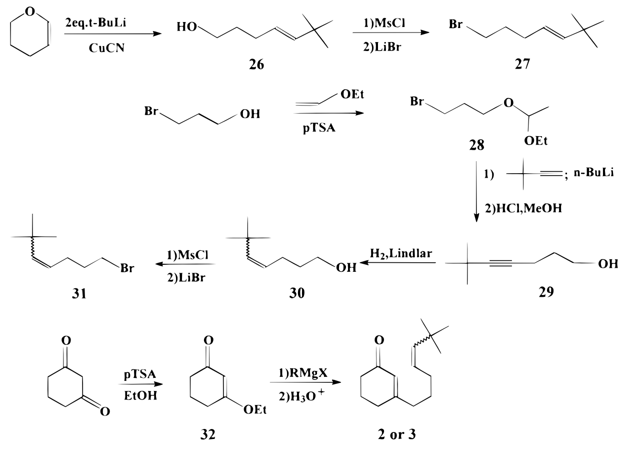
## Preparation of Materials

The synthesis of **2** and **3** by the reaction of the corresponding Grignard reagent with the enol ether **32** followed by hydrolysis, is shown in Scheme 8, as well as the synthesis of the *E*- and *Z*-bromo-olefins (**27** and **31**, respectively) substituted with a bulky *tert*-butyl group.

Syntheses of compounds **1**, **4**, **5**, and **10**−**15** and experimental data for their photoproducts are available in refs 10 and 22. Compound **16** was synthesized according to ref 10 using the *E*-bromoolefin **27**.

## Experimental Section

**Scheme 8**



**General Data.** Nuclear magnetic resonance spectra were obtained on a Bruker AM-400 400-MHz instrument equipped with an Aspect 3000 computer and on a Bruker AM-200 200-MHz instrument. High-resolution MS were measured on a Varian MAT-711 instrument, and GC analyses were carried out on an HP 5890 instrument using the capillary column DB210, 30 m, 0.25 mm with helium as carrier gas. A Perkin-Elmer 298 instrument was used for IR, and a Hewlett Packard-diode array spectrophotometer-8452 ≈ was used for UV.

**Irradiations.** Irradiations were carried out in hexane as a solvent under a nitrogen atmosphere. The commercial hexane was purified by shaking with concentrated sulfuric acid and then with 10% sodium carbonate, irradiation through quartz for 4 h using a 450-W Hanovia lamp, repeated shaking with concentrated sulfuric acid, and distillation. The photoreactions were carried out in concentrations of 0.5−0.7 mM using an 80W Hanau mercury vapor lamp (Q-81) with an uranium glass filter ($\lambda$ > 330 nm). The photoreactions were followed by GC analysis. A HAAKE F3 circulator was used for cooling the irradiating solution using methanol as the cooling liquid. The temperature monitoring (±0.5 °C) was internal using a thermocouple (type K).

**(*E*)-6,6-Dimethyl-4-hepten-1-ol (26).** Kocien'nski's[23] procedure was used for the preparation of **26**. *n*-Butyllithium (43.5 mL, 1.7 M in hexane, 74 mmol) was added dropwise to a suspension of CuCN (1.8 g, 12.8 mmol) in dry ether (45 mL) at −40 °C under nitrogen. The resultant mixture was slowly warmed to −20 °C and 3,4-dihydro-[2*H*]pyrane (2.25 mL, 24.6 mmol) in dry ether (30 mL) was added. The reaction mixture was stirred for 30 min at −20 °C and 2 h at room temperature. Water (2 mL) was added, and the resultant mixture was poured into a 10% solution of ammonia in a saturated aqueous solution of ammonium chloride (60 mL). The product was extracted with ether (3 × 25 mL) and dried over $MgSO_4$, and the solvent was removed under reduced pressure. The resultant oil was purified by distillation (40 °C, 0.1 mmHg) to give 2.3 g of pure **26** in 65% yield: $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 0.96 (s, 9 H), 1.61 (qu, 2 H), 2.05 (q, 2 H), 3.62 (t, 2 H), 5.3 (dt, 1 H), 5.42 (d, 1 H).

**(*E*)-7-Bromo-2,2-dimethyl-3-heptene (27).** Methanesulfonyl chloride (3.5 mL, 45 mmol) was added dropwise to a solution of **26** (3.96 g, 27.9 mmol) and triethylamine (9.7 mL, 70 mmol) in THF (28 mL) at 0 °C under nitrogen. The reaction mixture was stirred for 1 h at 0 °C and 30 min at room temperature and then quenched with water (14 mL). The solvent was removed under reduced pressure, and the product was extracted with $CH_2Cl_2$ (3 × 15 mL), washed with 5% HCl (10 mL) and $NaHCO_3$ saturated aqueous solution (5 mL), and dried over $MgSO_4$. The solvent was removed to give 4.9 g of crude mesylate, which was used in the next step without further purification. LiBr (anhydrous, 3.6 g, 41.4 mmol) was added to a solution of this mesylate (4.9 g) in THF (12 mL), and the reaction mixture was stirred overnight under nitrogen. Water (14 mL) was added, and the solvent was removed under reduced pressure. The product was extracted with $CH_2Cl_2$ (3 × 15 mL). The organic phases were combined, washed with water (10 mL), and dried over $MgSO_4$. The crude bromide was chromatographed over silica gel (eluent hexane) to give 4.0 g of pure **27** in 70% yield: $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 0.96 (s, 9 H), 1.88 (qu, 2 H), 2.09 (q, 2 H), 3.41 (t, 2 H), 5.26 (dt, 1 H), 5.52 (d, 1 H).

**Ethanal-3-bromopropylethylacetal (28).** *p*-TSA·$H_2O$ (12 mg) and 3-bromopropanol (8 g, 85 mmol) were added to a flask containing ethyl

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[23] Kocien'nski, P.; Wadman, S. *J. Am. Chem. Soc.* **1989**, *111*, 2363.

vinyl ether (12.2 g, 169 mmol) at 0 °C under nitrogen. The reaction mixture was warmed to 20 °C and stirred for 1 h. An additional amount of *p*-TSA·$H_2O$ (9 mg) was added slowly. The reaction mixture was cooled to 10 °C, and a saturated aqueous solution of $K_2CO_3$ (0.9 mL) was added. After stirring for 5 min the solution was dried with $K_2CO_3$ powder and filtered, and the solvent was removed under reduced pressure. The crude product was purified by distillation (50 °C, 0.2 mmHg) to give 11.8 g of **28** in 84% yield: $^1H$ NMR (200 MHz, $CDCl_3$) $\delta$ 1.2 (t, 3 H), 1.3 (d, 3 H), 2.09 (qu, 2 H), 3.51 (t, 2 H), 3.64 (m, 4 H), 4.67 (q, 1 H).

**Ethanal-6,6-dimethyl-4-heptynethylacetal.** *n*-Butyllithium (26 mL, 1.15 M in hexane, 30 mmol) and HMPA (6 mL) were added dropwise to a solution of *tert*-butyl acetylene (2 g, 24.4 mmol) in THF (10 mL) at −40 °C under nitrogen. After stirring for 1 h, **28** (6.3 g, 30 mmol) was added slowly. The reaction mixture was stirred for 1 h, after which the cooling bath was removed and the reaction mixture was kept at room temperature overnight. The reaction flask was cooled (5 °C), and aqueous 5% HCl (25 mL) was added. The solvent was removed under reduced pressure, and the product was extracted with ether (3 × 15 mL), washed with saturated $NaHCO_3$ (10 mL), and dried over $MgSO_4$. The solvent was removed under reduced pressure to give 5.6 g of the desired product in 90% yield: $^1H$ NMR (200 MHz, $CDCl_3$) $\delta$ 1.16 (s, 9 H), 1.2 (t, 3 H), 1.3 (d, 3 H), 1.7 (qu, 2 H), 2.22 (t, 2 H), 3.51 (t, 2 H), 3.6 (q, 2 H), 4.68 (q, 1 H).

**6,6-Dimethyl-4-heptyn-1-ol (29).** A mixture of ethanal-6,6-dimethyl-4-heptynethylacetal (4.6 g, 22 mmol) in methanol (50 mL) and 32% HCl (11 mL) was stirred for 24 h at room temperature. Water (25 mL) was added, and the solvent was removed under reduced pressure. The product was extracted with $CH_2Cl_2$ (3 × 20 mL), washed with saturated $NaHCO_3$ (10 mL), and dried over $MgSO_4$. The crude alcohol was chromatographed over silica gel (eluent hexane:$CH_2Cl_2$ = 1:1) to give 2.7 g of **29** in 88% yield: $^1H$ NMR (200 MHz, $CDCl_3$) $\delta$ 1.16 (s, 9 H), 1.7 (qu, 2 H), 2.6 (t, 2 H), 3.74 (t, 2 H).

**(*Z*)-6,6-Dimethyl-4-hepten-1-ol (30).** 6,6-Dimethyl-4-heptyn-1-ol **29** (0.39 g, 2.8 mmol) was reduced in methanol (150 mL) under hydrogen pressure (4 atm) by using a Lindlar catalyst (Fluka AG) (39 mg). The reaction was stopped after 36 h, the catalyst was filtered off, and the solvent was removed under reduced pressure to give 0.36 g (91% yield) of a *Z*/*E*-isomer mixture in a 80:20 ratio, respectively, by GC analysis. Spectral data of the *Z* isomer **30**: $^1H$ NMR (200 MHz, $CDCl_3$) $\delta$ 1.09 (s, 9 H), 1.59 (qu, 2 H), 2.25 (q, 2 H), 3.67 (t, 2 H), 5.12 (dt, 1 H), 5.31 (d, 1 H).

**(*Z*)-7-Bromo-2,2-dimethyl-3-heptene (31).** The *Z*-alcohol **30** was converted to the corresponding bromide **31** in 68% yield as described for the *E*-isomer **27**. $^1H$ NMR (200 MHz, $CDCl_3$) $\delta$ 1.09 (s, 9 H), 1.9 (qu, 2 H), 2.32 (q, 2 H), 3.38 (t, 2 H), 5.08 (dt, 1 H), 5.36 (d, 1 H).

**3-Ethoxy-2-cyclohexen-1-one (32).** 3-Ethoxy-2-cyclohexen-1-one was prepared according to the following procedure.[24] A solution of 1,3-cyclohexadione (5.3 g, 47 mmol) and *p*-TSA·$H_2O$ (0.23 g, 1.2 mmol) in ethanol (25 mL) and benzene (90 mL) was refluxed for 1 h, and the azeotrope composed of benzene, alcohol, and water was removed. When the temperature of the vapor reached 78 °C, the distillation was stopped, and the residual solution was washed with 10% aqueous NaOH saturated with NaCl (4 × 10 mL) and water (3 × 5 mL). The resulting oil was distilled (67 °C, 0.4 mmHg) to give 4.9 g of pure **32** in 75% yield: $^1H$ NMR (200 MHz, $CDCl_3$) $\delta$ 1.32 (t, 3 H), 1.93 (qu, 2 H), 2.33 (m, 4 H), 3.85 (q, 2 H), 5.29 (s, 1 H).

**3-[(*E*)-6,6-Dimethyl-4-heptenyl]-2-cyclohexen-1-one (2).** A solution of **27** (0.89 g, 4.3 mmol) in dry ether (2 mL) was added dropwise to magnesium (0.15 g, 6.25 mmol) in dry ether (3 mL) at room temperature under nitrogen. After stirring the reaction mixture for 0.5 h, **32** (0.55 g, 3.9 mmol) in dry ether (3 mL) was added slowly. After additional stirring for 1 h, the reaction mixture was quenched with 5% hydrochloric acid (10 mL) at 0 °C. The product was extracted with ether (3 × 20 mL), washed with water, and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the crude oil was chromatographed over silica gel (eluent hexane:$CH_2Cl_2$ = 1:1) to give 0.61 g of pure **2** in 70% yield: IR ($CHCl_3$) 1660 $cm^{-1}$; UV (hexane) $\lambda_{max} = 266$ nm ($\epsilon = 12\,000$); $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 0.96 (s, 9 H), 1.25 (qu, 2 H), 1.95 (q, 4 H), 2.20 (m, 2 H), 2.35 (m, 4 H), 5.26 (dt, 1 H), 5.41 (d, 1 H), 5.80 (s, 1 H); HRMS calcd for $C_{15}H_{24}O$ 220.3540, found 220.1812. Anal. Calcd for $C_{15}H_{24}O$: C, 81.76; H, 10.98. Found: C, 82.11; H, 11.26.

**3-[(*Z*)-6,6-Dimethyl-4-heptenyl]-2-cyclohexen-1-one (3).** Enone **3** was prepared from **31** in 73% yield as described for **2**: $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 1.03 (s, 9 H), 1.53 (qu, 2 H), 1.96 (q, 2H), 2.21 (m, 4 H), 2.33 (m, 2 H), 5.07 (td, 1 H), 5.33 (d, 1 H), 5.86 (s, 1 H); HRMS calcd for $C_{15}H_{24}O$ 220.3540, found 220.1838. Anal. Calcd for $C_{15}H_{24}O$: C, 81.76; H, 10.98. Found: C, 81.75; H, 11.19.

**2-[(*E*)-6,6-Dimethyl-4-heptenyl]-2-cyclohexen-1-one (16).** Enone **16** was prepared from **27** in 60% yield as described for **12** in ref 10: $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 0.96 (s, 9 H), 1.43 (qu, 2 H), 1.95 (qu, 4 H), 2.14 (t, 2 H), 2.30 (q, 2 H), 2.39 (t, 2 H), 5.26 (dt, 1 H), 5.41 (d, 1 H), 6.67 (t, 1 H); HRMS calcd for $C_{15}H_{24}O$ 220.3540, found 220.1841. Anal. Calcd for $C_{15}H_{24}O$: C, 81.76; H, 10.98. Found: C, 82.15; H, 11.20.

**Irradiation of Enone Olefin 2.** Enone **2** (2.7 mg, 12.3 $\mu$mol) was dissolved in 20 mL of purified hexane and irradiated for 1 h. The photoadducts **6** and **7** were formed in an approximately 1:1 ratio at 16 °C and were isolated in 93% yield. The two isomers were separated on silica gel (eluent hexane:$CH_2Cl_2$ = 8:1). **6**: $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 0.86 (s, 9 H), 1.30−1.51 (m, 3 H), 1.52−1.66 (m, 4 H), 1.72−1.90 (m, 3 H), 2.01-2.10 (m, 2 H), 2.42 (t, 1 H), 2.52 (bd, 1 H), 2.66 (d, 1 H). **7**: $^1H$ NMR (400 MHz, $CDCL_3$) $\delta$ 0.87 (s, 9 H), 1.31 (m, 1 H), 1.51−1.65 (m, 3 H), 1.67−1.76 (m, 2 H), 1.77−1.89 (m, 2 H), 2.03−2.26 (m, 3 H), 2.30 (d, 1 H), 2.43 (t, 1 H), 2.53 (dd, 1 H), 2.57 (d, 1 H).

**Irradiation of Enone Olefin 3.** A mixture of 83% enone **3** and 17% enone **2**[6] (2.8 mg, 12.7 $\mu$mol) was irradiated as described for **2**. The photoadducts **6** and **7** were formed in approximately 1:1 ratio at 16 °C and were isolated in 92% yield.

**Irradiation of Enone Olefin 16.** Enone **16** (2.7 mg, 12.3 $\mu$mol) was irradiated for 5 h as described for **2**. The photoadducts **24** and **25** were formed in a 3.3:1 ratio, respectively, at 20 °C and were isolated in 90% yield. The two isomers were separated on silica gel (eluent hexane:$CH_2Cl_2$ = 9:1). **24**: $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 0.86 (s, 9 H), 1.50 (dd, 1 H), 1.62 (m, 1 H), 1.66−1.75 (m, 4 H), 1.85−2.03 (m, 4 H), 2.23 (m, 1 H), 2.39 (m, 1 H), 2.45 (m, 1 H), 2.78 (t, 1 H). **25**: $^1H$ NMR (400 MHz, $CDCL_3$) $\delta$ 0.87 (s, 9 H), 1.50 (dd, 1 H), 1.62 (m, 1 H), 1.66−1.75 (m, 4 H), 1.85−2.03 (m, 4 H), 2.23 (m, 1 H), 2.39 (m, 1 H), 2.45 (m, 1 H), 2.83 (t, 1 H).

**Acknowledgment.** Y.C.-A. would like to express her deep gratitude to Professor E. A. Halevi for the semiempirical calculations and for very useful advice, to Professor M. Rubin for valuable discussions, and to Professor M. Ottolenghi for making his nitrogen laser available to her.

JA9531079

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[24] Gannon, W. F.; House, H. O. *Organic Syntheses*; Wiley: New York, Collect. Vol. 5, p 539.