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Model analysis of branching photoreactions with conformationally flexible intermediate

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Abstract

The principal model of multistage branching photoreaction with conformationally flexible intermediate is analyzed. The consideration is restricted to the case of ground-state conformational control. A violation of the reciprocity low as applied to the reactions with alternating photo and dark processes is emphasized. Applications to the reactions of monomolecular photoisomerization of abundant compounds with triene chromophore are discussed. In the specific case of the previtamin D photosynthesis the ways of purposeful influence on the pathway and the products yield of the reaction are exposed. In particular, opportunities connected with an influence on the conformational equilibrium and with the use of high intensity laser irradiation, as well as the possibilities of the temperature control are considered.

Keywords: Conformational flexibility; Provitamin D photosynthesis; Conformational equilibrium; Intensity effect

1. Introduction

It is well known that kinetics and the product yield of branching photochemical reactions may depend perceptibly on the reaction medium, temperature, the radiation characteristics and other factors. A detailed study of the dependences is important both from an academic aspect and for the further development of photochemical technologies.

In the present paper we focus on the analysis of the kinetics set-ups of branching monomolecular photoreactions of structural isomerization characterized by relatively slow dark conformational conversions of the intermediate in the ground electronic state [1]. A good case in point is the photochemistry of small polyenes playing a crucial role in a number of biological processes.

Our approach is based on the concept of "ground-state conformational control", originally advanced as applied to the photochemistry of organic compounds with the triene chromophore [2,3]. Taking as a basis numerous pieces of experimental evidence, it was supposed that, owing to a very short lifetime, thermal equilibrium between singlet excited states of the conformers is not reached; every conformer is then responsible for the advent of specific photoproducts [3].

The most well-known photoreaction of the type is the photosynthesis of previtamin D, which is the first stage of vitamin D synthesis consisting of two consequent stages of photoisomerization and thermoisomerization [2]. In what follows a model of the photoreaction with two different ground-state conformations of the intermediate is considered to find out the possibilities for intentionally influencing the corresponding reaction channels.

2. Principal model

In this section the main characteristic properties of branching monomolecular photoreactions are considered proceeding from the principal model of Fig. 1.

According to the model, the conformationally flexible intermediate photoproduct B is formed from the initial isomer A of the molecule by irradiation. Two stable conformations B_1 and B_2 of the intermediate are then the precursors of the corresponding end products C and D. The rate constants of the transitions into the excited states A^*, B_1^* and B_2^* are proportional to the cross-sections σ_i (cm^2) of the isomer absorption and to the photon flux I (photon cm^{-2} s^{-1}). The radiative and non-radiative transitions from the excited states are characterized by the non-reactive rate constants k_i (s^{-1}) (into the ground state of the same isomer) and by the reactive rate constants γ_i (s^{-1}) (into the ground state of the photoisomers); the ratio $\eta_i \equiv \gamma_i/(k_i+\gamma_i)$ is then the quantum yield of the photoreaction. q_+ and q_- are the corresponding

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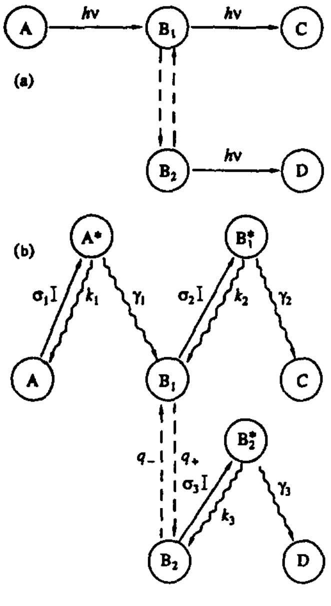

Fig. 1. General scheme of photoreaction with conformationally flexible intermediate photoproduct: (a) A, initial isomer; B_1 and B_2, two conformations of the intermediate isomer; C, D, end photoproducts; (b) the model under study when the excited electronic states are taken into account.

temperature-dependent rate constants of direct and reverse processes of the dark conformational transition $B_1 \leftrightarrow B_2$ (within the ground electronic state). It is worth emphasizing that the dark processes are slow compared with the radiative processes: $q_+, q_- \ll k_i$ [4].

The time dependence of the photoisomer concentrations is given by the equations

$$
\begin{aligned}
&[\dot{A}] = -\sigma_1 I[A] + k_1[A^*] \\
&[\dot{A}^*] = -k_1[A^*] + \sigma_1 I[A] - \gamma_1[A^*] \\
&[\dot{B}_1] = \gamma_1[A^*] - \sigma_2 I[B_1] - q_+[B_1] \\
&\qquad + k_2[B_1^*] + q_-[B_2] \\
&[\dot{B}_1^*] = \sigma_2 I[B_1] - k_2[B_1^*] - \gamma_2[B_1^*] \qquad (1) \\
&[\dot{B}_2] = q_+[B_1] - q_-[B_2] - \sigma_3 I[B_2] + k_3[B_2^*] \\
&[\dot{B}_2^*] = \sigma_3 I[B_2] - k_3[B_2^*] - \gamma_3[B_2^*] \\
&[\dot{C}] = \gamma_2[B_1^*] \\
&[\dot{D}] = \gamma_3[B_2^*]
\end{aligned}
$$

Here and below the dots over the symbols denote derivation with respect to time variable *t*.

At $t \to \infty$ the ratio of the end product concentrations is equal to [5]

$$\frac{[C]}{[D]} = \frac{q_-}{q_+} \frac{\sigma_2 \eta_2}{\sigma_3 \eta_3} \left(1 + \frac{I\sigma_3 \eta_3}{q_-}\right) \qquad (2)$$

Let us consider here two extreme cases. In the first, corresponding to low intensity irradiation ($I\sigma_3\eta_3/q_- \ll 1$), the end-product concentrations do not depend on the intensity *I* and are determined by the ratio q_-/q_+ of the rate constants of dark conformational transitions, multiplied by the relative effectiveness $\sigma_2\eta_2/\sigma_3\eta_3$ of the corresponding photoreaction channels. Thus the control of the products yield in this case could be carried on by the use of internal and external factors (nature of the terminal groups, reaction medium characteristics, temperature etc.) affecting the conformational equilibrium.

The model under discussion can, in particular, describe photoisomerization of 3-alkyl-6,6,9,9-tetramethyl-$\Delta^{3,5(10)}$-hexalines (Fig. 2). It has been found [3] that the ratio of the end-product concentrations **1**:**2** increases with increase in the steric bulk of the substituent R. This result has been interpreted in terms of conformational equilibrium between the *s-cis* and *s-trans* triene conformers; an increase in the steric bulk of the R-group gives the corresponding rise in the *cZc*-conformer concentration in the solution and thus promotes the end product **1** accumulation.

In the opposite case of high intensity irradiation ($I\sigma_3\eta_3/q_- \gg 1$), Eq. (2) reduces to

$$\frac{[C]}{[D]} = \frac{I\sigma_2\eta_2}{q_+} \qquad (3)$$

Using the typical values $\sigma \approx 10^{-17}$ cm^2 and $q \approx 10^{10}$ s^{-1} [4], one can evaluate the high intensity criterion as $I > 10^{27}$ photon cm^{-2} s^{-1}, which is within the reach of picosecond laser irradiation [6].

Proportionality of the ratio (3) to the radiation intensity indicates another way to control the yields of products in branching photoreactions with a conformationally flexible intermediate. In particular, this is really important with regard to the triene photoisomerization reactions (see Figs. 1 and 2). A low equilibrium concentration of B_1 conformer (*cZc* conformation of the triene is, as a rule, not easily accessible because of steric strains) is inhibitory to the use of a low intensity (lamp) irradiation to obtain a relatively high yield of the corresponding end product C. At the same time, the use of high intensity laser irradiation (taking into account the above evaluation) makes the task feasible, which, we believe, could be of importance in industrial photochemistry.

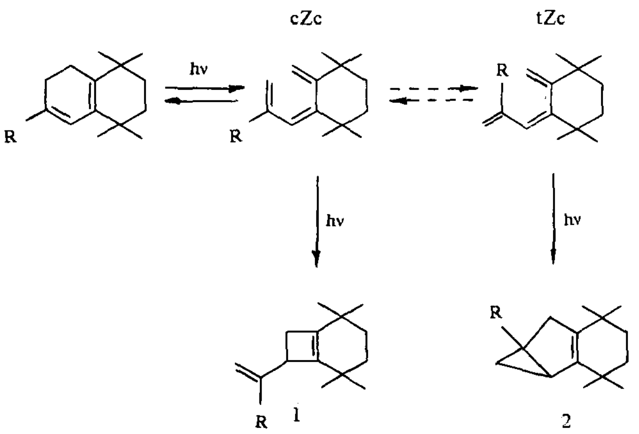

Fig. 2. Photoisomerization scheme of 3-alkyl-6,6,9,9-tetramethyl-$\Delta^{3,5(10)}$-hexalines [3].

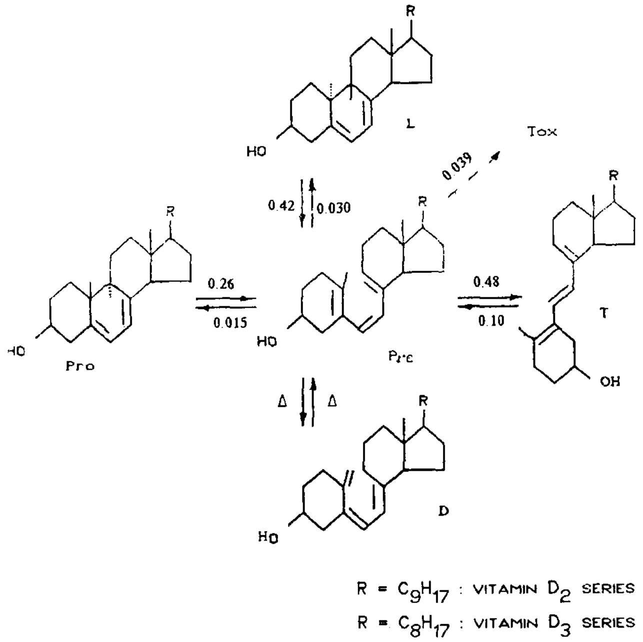

Fig. 3. Reaction scheme of vitamin D synthesis: Pro, provitamin D; Pre, previtamin D; T, tachysterol; L, lumisterol; Tox, toxisterols; D, vitamin D. The numbers associated with the arrows represent the relevant quantum yields [2,7].

Additionally, it is worth emphasizing here the violation of the reciprocity law when using intensive laser irradiation even without taking into account two-stage absorption processes [6]. Equilibrium between the intermediate conformers B_1 and B_2 is violated owing to a high rate of photoinduced transition into the excited electronic state of the B_1 conformer. The yields of end products of the photoreaction can then differ perceptibly compared with the case of low intensity irradiation. In general, it is safe to say that violation of the reciprocity law as applied to any multistage branching photoreaction with alternating photo- and dark processes would thus be expected.

3. Modelling of provitamin D photoisomerization

Let us now consider the photoisomerization reaction of provitamin D which is important for practical purposes. The well-known reaction scheme of vitamin D synthesis is presented in Fig. 3.

Under the influence of UV radiation the cyclohexadiene ring of provitamin D (Pro) opens, and previtamin D (Pre), being a precursor of vitamin D (D), is formed. The end product, vitamin D, is then formed from Pre by thermo-activated intramolecular hydrogen transfer [2].

However, the photoreaction is essentially complicated by a number of parasitic channels of Pre photoconversions. The most effective of the parasitics is the reversible *cis-trans* isomerization of Pre with the formation of tachysterol (T). The reversible ring-closure conversions of Pre with the formation of the initial Pro or its 9,10 *anti* isomer lumisterol (L) are less probable. Also, in due course, UV irradiation results in the accumulation of so-called "over-irradiation products" toxisterols (Tox), being the products of irreversible photoconversions of Pre [2,7]. So, an important problem in the industrial synthesis of vitamin D is the maximization of Pre yield in the photoreaction stage.

There is a good reason to suppose that the complex photochemistry of Pre is consistent with the postulate of the ground-state conformational control of the photoproducts [2,3]. The reaction scheme in Fig. 4(a) [8] illustrates the suggestion. So, *cZc* conformation of Pre could be examined as a precursor of ring-closed products Pro and L, in contrast with *tZc* conformation, regarded as preceding predominantly the *trans* isomer T. Both conformations of Pre could then give rise to Tox formation by irreversible photoconversions [2].

In solution, Pre molecules exhibit a considerable flexibility; by intramolecular rotation around a C(5)–C(6) single bond, they adopt a number of especially different forms not separated by substantial energy barriers [8]. It is shown that approximately equal concentrations of Pre *cZc* and *tZc* conformers exist in solution in the dynamic equilibrium [8].

The reaction model of Pro photoisomerization is given in Fig. 4(b). It includes the initial isomer Pro (A), two planar conformations B_1 (*cZc*) and B_2 (*tZc*) of the intermediate Pre (which is the target product in the case), the main side product, the *trans* isomer T (C), and the side products Tox. The UV photons induce isomer transitions from the ground into the excited S_1 electronic state: $A \rightarrow A^*$; $B_1 \rightarrow B_1^*$; $B_2 \rightarrow B_2^*$; $C \rightarrow C^*$. The transition rates are then proportional to the cross-sections σ_i of the isomer absorption and to the radiation intensity I. The non-reactive rate constants k_i (s^{-1}) characterize radiative and non-radiative decay of the excited states into the ground state; the processes of reversible and irreversible photoconversion are characterized by the rate constants γ_i (s^{-1}) and γ_{ir} (s^{-1}); q_+ and q_- (s^{-1}) are the rate constants of the dark transitions between the Pre conformers.

The model is described by the system of kinetic equations

$$\begin{aligned}
[\dot{A}] &= -\sigma_1 I[A] + k_1[A] + \gamma_2[B_1] \\
[\dot{A}^*] &= \sigma_1 I[A] - (k_1 + \gamma_1)[A^*] \\
[\dot{B}_1] &= \gamma_1[A^*] - (q_+ + \sigma_2 I)[B_1] + k_2[B_1^*] + q_-[B_2] \\
[\dot{B}_1^*] &= \sigma_2 I[B_1] - (\gamma_2 + k_2 + \gamma_{ir})[B_1^*] \\
[\dot{B}_2] &= q_+[B_1] - (\sigma_3 I + q_-)[B_2] + k_3[B_2^*] + \gamma_4[C^*] \\
[\dot{B}_2^*] &= \sigma_3 I[B_2] - (\gamma_3 + k_3 + \gamma_{ir})[B_2^*] \\
[\dot{C}] &= \gamma_3[B_2^*] - \sigma_4 I[C] + k_4[C^*] \\
[\dot{C}^*] &= \sigma_4 I[C] - (k_4 + \gamma_4)[C^*]
\end{aligned} \tag{4}$$

Taking account of relationships between the real values of the parameters, one can simplify the general kinetic set-up of the problem (4) to a great extent. Thus all the cross-section values σ_i, as well as the non-reactive rate constants k_i, could for simplicity be assumed to be equal:

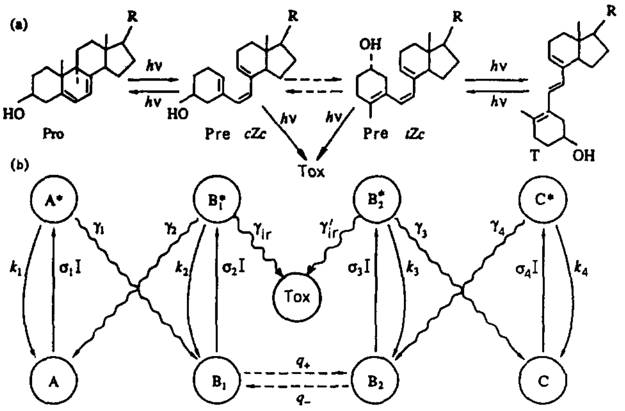

Fig. 4. (a) Scheme of provitamin D photoisomerization with regard to the two planar Pre conformers; (b) the model under study.

$$\sigma_i = \sigma \qquad k_i = k \tag{5}$$

The values of the rate constants of photochemical conversions allow (for the actual time of the reaction) us to set [7]

$$\gamma_1 \approx \gamma_3 = \gamma \qquad \gamma_2 \approx \gamma_4 \approx \gamma_{\text{ir}} \approx 0 \tag{6}$$

It is worth mentioning here that within the approximation the T isomer is the only end product of the photoreaction. At the same time, from a utilitarian aspect, only the accumulation of the intermediate *cZc*-Pre conformer is of importance.

Taking further into account that at the values of the radiation intensity in use the inequality $\sigma I \ll k$ is valid (for any of the isomers), the concentrations of the excited molecules could be considered as time independent at $t \gg k^{-1}$:

$$[\dot{A}^*] = [\dot{B}_1^*] = [\dot{B}_2^*] = [\dot{C}^*] = 0$$

Thus, according to Eq. (4), one obtains

$$\begin{aligned} &\frac{[A^*]}{[A]} = \frac{[B_2^*]}{[B_2]} = \frac{\sigma I}{k+\gamma} (\ll 1) \\ &\frac{[B_1^*]}{[B_1]} = \frac{[C^*]}{[C]} = \frac{\sigma I}{k} (\ll 1) \end{aligned} \tag{7}$$

The final reduced version of the set of evolution equations with respect to the ground-state isomer concentrations could then be presented as

$$\begin{aligned} &[\dot{A}] = -Q[A] \\ &[\dot{B}_1] = Q[A] - rq[B_1] + q[B_2] \\ &[\dot{B}_2] = rq[B_1] - (q+Q)[B_2] \\ &[\dot{C}] = Q[B_2] \end{aligned} \tag{8}$$

Here $Q = \sigma I \gamma/(k+\gamma)$ is the effective rate constant of the radiative conversions; $r = q_+/q_-$ is a temperature-dependent constant of the conformational equilibrium (then $q_- = q$ and $q_+ = rq$).

We also assume the initial condition in the form

$$[A] = A_0 \approx 1 \qquad [B_1] = [B_2] = [C] = 0 \text{ at } t = 0 \tag{9}$$

Later we consider in detail an explicit form of the time dependences of the concentrations, being the solution of Eq. (8), in the extreme cases of low and high intensity irradiation. The criterion that we use is the ratio Q/q of the rate constants of radiative and dark processes.

3.1. *Low intensity irradiation*

In this case using the first-order approximation with respect to the small parameter Q/q, one obtains

$$\begin{aligned} &[A] = A_0 \exp(-Qt) \\ &[C] = A_0 - [A] - [B_1] - [B_2] \end{aligned} \tag{10}$$

and

$$\begin{aligned} [B_1] = A_0 \Bigg\{ &-\left(1 + \frac{Q}{q}\frac{r}{(r+1)^2}\right)\exp(-Qt) \\ &+\left(1 + 2\frac{Q}{q}\frac{r}{(r+1)^2}\right)\exp\left(-\frac{Qtr}{(r+1)}\right) \\ &-\frac{Q}{q}\frac{r}{(r+1)^2}\exp\left[-\left((r+1)q + \frac{Q}{(r+1)}\right)t\right]\Bigg\} \\ [B_2] = A_0 r - \Bigg\{ &-\left(1 + \frac{Q}{q}\frac{r}{(r+1)^2}\right)\exp(-Qt) \\ &+\left(1 + \frac{Q}{q}\frac{(r-1)}{(r+1)^2}\right)\exp\left(-\frac{Qtr}{(r+1)}\right) \\ &-\frac{Q}{q}\frac{1}{(r+1)^2}\exp\left[-\left((r+1)q + \frac{Q}{(r+1)}\right)t\right]\Bigg\} \end{aligned} \tag{11a}$$

The concentrations (10) and (11a) as functions of time are given in Fig. 5. According to the plots, during the photoreaction the concentrations of Pre conformers are approximately proportional to each other: $[B_2] = r[B_1]$. Special attention has to be paid here to the conformational effect displaying itself in a perceptible dependence of the maximal B_1 concentration on the r value [9]. In particular, the most considerable effect is characteristic of small values of the equilibrium constant ($r \ll 1$), corresponding to a high share of *cZc*-Pre conformation (Fig. 5(a)). Thus, one has to look for specific factors having marked influence on the conformational equilibrium.

As has been established earlier [10], the use of heterogeneous media such as silica-gel suspensions, water–ethanol mixtures, synthetic lipid multibilayers and liposomes shows promise with that end in view [11]. The same mechanism is evidently responsible for the low yield of *trans* isomer during in-vivo vitamin D synthesis.

3.2. *High intensity irradiation*

In the extreme case of high intensity irradiation the use of the first-order approximation with respect to the ratio q/Q gives in addition to (10) the expressions

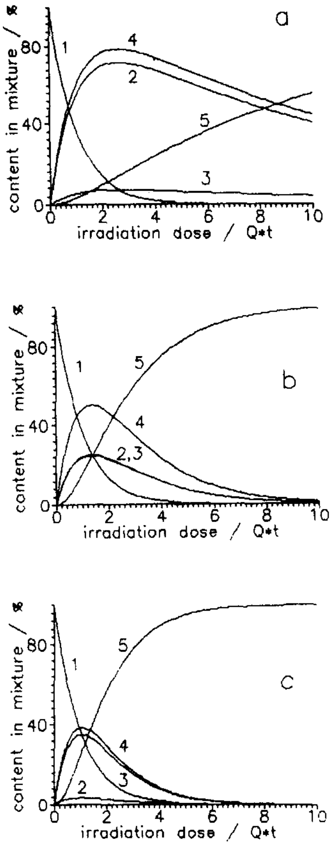

Fig. 5. The low intensity kinetics calculated in accordance with Eqs. (10) and (11a). Here $Q/q = 0.01$ and (a) $r = 0.1$, (b) $r = 1$ and (c) $r = 10$: curves 1, A (Pro); curves 2, B (*cZc*-Pre); curves 3, B′ (*tZc*-Pre); curves 4, Σ (B + B′) (Pre); curves 5, C (T).

$$[B_1] = A_0\left(1 + \frac{rq}{Q}\right)(\exp(-rqt) - \exp(-Qt))$$

$$[B_2] = A_0\left[-\left(1 + \frac{q}{Q}\right)\exp(-Qt) + \left(1 + (r-1)\frac{q}{Q}\right)\exp[-(Q+q)t] + \frac{q}{Q}\exp(-rqt)\right] \quad (11b)$$

Restricting ourselves, for simplicity, to the particular case $r = 1$ (characteristic of solutions [8]), let us present the plots of the concentrations as functions of time for two different values of the ratio Q/q (Fig. 6). On account of the low relative rate of the dark conformational conversions, the share of the initially formed *cZc* conformation is dominant in the case under consideration. Therefore, an increase in the Q/q ratio gives rise to an increase in the maximal $[B_1]$ value.

Thus additional opportunities to control the reaction arise, connected with the application of powerful lasers as well as with a temperature decrease, causing corresponding deactivation of the dark conversion processes.

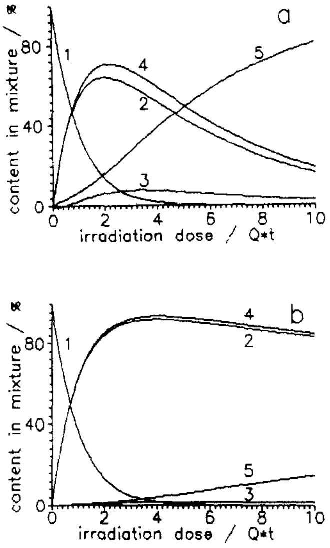

Fig. 6. The high intensity kinetics calculated in accordance with Eqs. (10) and (11b). Here $r = 1$, (a) $Q/q = 5$ and (b) $Q/q = 50$.

It should be noted that factors omitted or neglected during the above consideration may also influence the experimental results in some way. In a particular case of high intensity irradiation the processes of two-step light absorption via singlet excited states of the isomers could cause the advent of new competitive reaction channels [6]. The ring-closure processes and that of Tox formation could in principle become more significant at higher *cZc* conformer concentrations. The pulsed character of picosecond laser irradiation is also not considered.

At present we have convincing experimental evidence of the validity of the model considered [12a]. A detailed study of the intensity effect on the provitamin D photoisomerization under the irradiation of a picosecond laser is in progress now [12b].

4. Conclusions

In this paper we have analyzed a model of multistage branching photoreactions with a conformationally flexible intermediate. The consideration is restricted to the case of ground-state conformational control, when the reaction pathways and the yields of end products are determined by the intermediate conformation. The model is highly applicable to the reactions of monomolecular photoisomerization of abundant compounds with the triene chromophore.

Proceeding from the analysis of the principal model and the specific case of the previtamin D photosynthesis we have found ways of deliberately influencing the pathway and the yields of the reaction products. In particular, opportunities connected with the influence of the conformational equilibrium and the use of high intensity laser irradiation, as well as the possibilities of the temperature control are considered. We believe that thorough experiments have to be carried out to determine additional possibilities for and restrictions on controlling the photoreaction pathways, in a specific way.

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