ABSTRACT
Benzene derivatives, which contain two, three or four photoreactive functionalities, such as vinyl, styryl or cinnamoyl groups, can undergo multiple \([2\pi+2\pi]\) photocycloaddition reactions on irradiation. The resulting dimers have the substructure of [2.2]- or [4.4]cyclophanes, whose bridges contain cyclobutane rings as distinctive features. Among the variety of synthetic approaches to cyclophanes, this photochemical method provides an easy and versatile preparation mode for many different systems.

KEYWORDS: cyclophanes, photocyclodimerization, rotamers, excimers, regioselectivity, stereoselectivity, topochemistry

1. Introduction
Since the work of Donald Cram in the 50s of the past century, cyclophanes represent a prominent research area of organic chemistry [1]. In the previous decade a variety of reviews on this topic appeared on the basis of new results [2]. Among the synthetic protocols for the generation of cyclophanes, photocycloaddition reactions provide an easy access to this class of compounds with very few steps. This strategy is either based on dimerization processes \(1 \rightarrow 2\), which consist of two-, three- or fourfold \([2\pi+2\pi]\) photocycloadditions, or on analogous intramolecular reactions \(3 \rightarrow 4\) (Scheme 1).

The first variant demands benzene rings with two to four (substituted) ethenyl groups, which permit such photodimerizations. Four-membered rings are then located in the bridges of the resulting [2.2]cyclophanes. The products obtained until now by this strategy have the scaffold of [2.2](1,2)-, [2.2](1,3)-, [2.2](1,4)-, [2.2.2](1,3,5)- or [2.2.2.2](1,2,4,5) cyclophanes.

The second variant requires two correspondingly substituted benzene rings, which are already connected by \(m\) atoms of a hydrocarbon or ether chain, so that a [2.m]- or a [2.2.m]cyclophane scaffold is generated by the photocycloaddition. In principle, the photoreaction can also be started with two benzene rings, which are connected by more than one chain. Instead of (substituted) ethenyl groups (-CH=CHR), cinnamoyl groups (-CO-CH=CH-Ph) can be used for the photocyclodimerization; [4.4](1,3)-, [4.4](1,4)- and [4.4.4](1,3,5)cyclophanes are obtained in the latter case.

The first method, the photodimerization process, is the focus of this review. This synthetic strategy commenced in 1981 with our preparation of cyclophane \(6\) (Scheme 2), which can be regarded as an extended paddlane [3]. The threefold head-to-head (H…H) cycloaddition is highly stereoselective.

2. Mechanistic aspects of the generation of cyclophanes by photodimerization reactions
The formation of cyclobutane rings by \([\pi^2+\pi^2]s\) cycloaddition reactions is thermally forbidden as concerted process. However, two-step reactions via zwitterions or diradicals are well-known. 1,4-Bis-(trifluoroethyl)benzene \(7\) is a compound, which undergoes a thermal cycloaddimerization reaction to form paracyclophane \(8\) (Scheme 3) [4]. The radical reaction for the formation of the first four-membered ring is favored by the effective spin-stabilizing capability of the C\(_2\)F\(_3\)-groups. Cyclobutane derivatives
with cis- and trans-configuration are obtained in this non-stereoselective process. Subsequently, the cis-isomer can undergo a second cycloaddition to form cyclophane 8 at a low yield [4].

Photochemical [2π+2π] cyclodimerizations can be observed as concerted reactions for various compounds with olefinic double bonds. trans-Stilbene and trans-cinnamic acid are prominent examples. Caldwell’s equation provides excellent criteria to determine which CC double bonds are particularly suitable for such photocycloaddition reactions [5]. Two or more such cycloaddition reactions are necessary for the generation of cyclophanes by dimerization of suitable benzene derivatives. It is always a stepwise process. Therefore, the regioselectivity of the formation of the first cyclobutane ring decides whether further four-membered rings can be formed or not.

Let us consider again the generation of cyclophane 6 by a threefold [π2s+π2s] photocycloaddition [3, 5b, 6-8]. This example shows already the whole scope of problems. The first step has to be a regioselective head-to-head process (H … H), in which the two heads adopt cis position in the formed cyclobutane ring. Owing to the stereoselectivity of the concerted reaction, the two tails T are then also in cis position to each other but in trans position to the heads H, because the original trans configuration of H and T is always maintained.

Several questions arise at this point:

Why are photochemically generated cis-configurations of 7 not involved in the dimerization step?

Scheme 1. Inter- and intramolecular photocycloaddition reactions for the generation of cyclophanes.

Scheme 2. First application of a photocyclodimerization reaction for the preparation of cyclophanes.

Scheme 3. Thermal dimerization 7 → 8.
Why is the head-to-head addition preferred to head-to-tail?

Why are the two heads cis-arranged in the cyclobutane ring?

The starting compound 5 exhibits an aggregation tendency in the ground state $S_0$ itself, which is particularly present in polar solvents. Therefore, the photodimerization works even at low concentrations of $10^{-5}$ M [5b]. ($E$)-Stilbene itself does not photodimerize in such diluted solutions. Irradiation of 5 produces excited singlet states $S_1$, which have average lifetimes of 9.4 and 13.6 ns in toluene at 293 K [9]. They were attributed to the two rotamers of 5, which do not interchange in the $S_1$ state – according to the NEER principle (nonequilibrium of excited rotamers) [10]. Excimers $[S_0...S_1]$ are formed, whose stabilization energies can be estimated from first-order and/or second-order perturbation theory [5b, 8]. All pairs of overlapping $\pi$ centers have to be considered, in particular the HOMO–HOMO and LUMO–LUMO interactions (Figure 1).

By far the largest stabilization energy is achieved by the maximum overlap that occurs when both molecules have a parallel arrangement. This explains the head-to-head selectivity and the fact that exciplexes of the type $S_1[(E,E,E)]-5...S_0[(E,E,Z)]-5$ and $S_1[(E,E,Z)]-5...S_0[(E,E,E)]-5$ are unfavorable. Consequently, cis-isomers do not take part in this reaction.

The formed excimers do not fluoresce. They are in a flat minimum of the energy hypersurface and collapse fast to the photoproduct via the pericyclic minimum as intermediate [8]. ($E,E,E$)-1,3,5-tristyrylbenzene (5) yields [2.2.2](1,3,5)cyclophane 6 and various higher oligomers. A [3.3.3](1,3,5)scaffold as drawn in structure 6' would be less strained than 6, but the stabilization energy for the corresponding excimer is zero [5b, 8].

The next stereochemical problem concerns the mutual orientation of the newly formed cyclobutane rings. Table 1 shows the possible rotamers of di-, tri- and tetraethenylbenzenes. The direction of the double bonds characterizes the orientations of the cyclobutane rings (viewed as cross-section). Since the steric demands are similar for the starting compounds, the excimers and the photoproducts, it can be assumed that each rotamer can lead to the corresponding cyclophane stereoisomer. Thus, the conformation of the starting compound determines the configuration of the product. The ratio of the rotamers has therefore a big influence on the ratio of the stereoisomers of the product. In contrast to the photodimerization in solution, the rotamers and consequently the stereoisomers of the products are fixed in the crystalline state (topochemical control).

### 3. Paracyclophanes

The formation of [2.2](1,4)cyclophane scaffolds by photodimerization of ($\beta$-substituted) 1,4-diethenylbenzenes 9 seems to be impossible in solution. Scheme 4 illustrates the situation. When the first cyclobutane ring is closed to a head-to-head (H–H) adduct 10 or 11 or to a head-to-tail (H–T) adduct 12 or 13, the distance of the remaining CC double bonds is far too large to permit the second photocycloaddition. This statement is valid for the head-to-head dimers 10 and 12 and even more for

![Figure 1. Frontier orbital interactions for the formation of excimers.](image-url)
Using single-crystal X-ray crystallography, recently Yang et al. [12] studied the irradiation of a highly complex coordination polymer (2D net), which contained different photoreactive sites as host ligands as well as guest molecules in the nanopores of the host. 1,4-Bis[(E)-2-(4-pyridyl)ethenyl]benzene 14A/14B and (E,E)-1,3-phenylenediacrylic acid 15B were fixed as ligands to Mn(II) ions. A porous coordination polymer

<table>
<thead>
<tr>
<th>Substitution positions in benzene</th>
<th>Rotamers</th>
<th>Number of rotamers</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,2 ortho</td>
<td><img src="image1" alt="Diagram" /></td>
<td>3</td>
</tr>
<tr>
<td>1,3 meta</td>
<td><img src="image2" alt="Diagram" /></td>
<td>3</td>
</tr>
<tr>
<td>1,4 para</td>
<td><img src="image3" alt="Diagram" /></td>
<td>2</td>
</tr>
<tr>
<td>1,3,5</td>
<td><img src="image4" alt="Diagram" /></td>
<td>2</td>
</tr>
<tr>
<td>1,2,4,5</td>
<td><img src="image5" alt="Diagram" /></td>
<td>7</td>
</tr>
</tbody>
</table>
photodimerization of \(14\) and \(15\) could be ruled out in the crystalline state, but not the light-triggered formation of rotamers.

resulted, in whose 1D channels two rows of guest molecules \(14A\) were accommodated. This complex contained several photocenters. *Cis-trans* photoisomerizations of \(14\) and \(15\) could be ruled out in the crystalline state, but not the light-triggered formation of rotamers.
The most interesting photoresponse concerned the photoreactivity of the olefinic double bonds of 14 (and 15) in cyclodimerization and polymerization processes: 14A → 16 and 14A → 17, respectively. A regioselective [2+2] photopolymerization could be observed for 14A as guest molecule. Its CC double bonds have an average distance of 3.6776 Å and are lying in almost parallel planes. The distance of the olefinic double bonds in 14B is also in accordance with Schmidt’s distance rule [11], but the molecular planes of the double bonds include a large angle, that prevented a [2\pi+2\pi] process. Moreover, density functional theory (DFT) calculations predicted a higher dimerization propensity of 14A than of 14B due to energetic reasons [12]. Component 14A as a ligand dimerized to paracyclopohane 16. The ligand 15B has locations in the coordination polymer, which did not permit a [2\pi+2\pi] process. However, when the photoreactivity of 14 had reached a certain state, rotamer 15A was formed by UV irradiation. The third rotamer 15C could not be observed [12]. Table 2 summarizes the light-triggered processes.

### Table 2. Irradiation processes in the coordination polymer: Ratios (%) of the involved components in a typical single crystal UV irradiation with a high-pressure mercury lamp.

<table>
<thead>
<tr>
<th>Irradiation period (h)</th>
<th>Component 14A/14B as a guest</th>
<th>Component 14A/14B as a ligand</th>
<th>Component 15A/15B as a ligand</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Rotamer 14A</td>
<td>Rotamer 14B</td>
<td>dimer 16</td>
</tr>
<tr>
<td>0</td>
<td>79</td>
<td>21</td>
<td>–</td>
</tr>
<tr>
<td>1</td>
<td>29</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>4</td>
<td>21</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>6</td>
<td>68</td>
<td>–</td>
<td>32</td>
</tr>
</tbody>
</table>

The results indicate a strong interplay and coupling of the light-induced processes within the framework of the coordination polymer.

In the 80s and 90s of the previous century the “classical” work on the [2.2](1.4)cyclophane synthesis...
by photodimerization reactions in the solid state was started by Hasegawa et al. [13-17]. It was shown that the irradiation of the cinnamates 18a–c (conformation A) depend on the wavelength and the temperature [14, 16]. A cut-off filter (λ ≥ 410 nm) permitted the selective excitation of 18a–c and excluded the excitation of the primary photoproducts 19a–c. The formation of the first cyclobutane ring changed the crystal structure; however, low temperatures could prevent the crystal from changing its structure to an extent that the second cycloaddition fails. Scheme 5 and Table 3 give a survey of the product formation. According to the crystal structure of 18, the topochemical control of the photoreaction led regioselectively to head-to-head adducts H$_1$⋯H$_2$ and stereoselectively to a paracyclophane with anti-standing cyclobutane rings (18A → 20).

Mixed crystals 18d–18e (molar ratio 70:30 to 5:95) have a molecular arrangement, which is entirely different from those of pure 18d and 18e. They reacted quantitatively to 20d–f via 19d–g (Scheme 6) [13, 15].

![Scheme 5. Photodimerization of (E,E)-18a–c in the solid state.]

<table>
<thead>
<tr>
<th>Starting compound</th>
<th>Temperature (°C)</th>
<th>Wavelength (nm)</th>
<th>Products (%)</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>18a</td>
<td>-40</td>
<td>≥ 410</td>
<td>19a (~100)</td>
<td>[16]</td>
</tr>
<tr>
<td></td>
<td>-40</td>
<td>≥ 300</td>
<td>19a (45), 20a (42), oligomers</td>
<td>[16]</td>
</tr>
<tr>
<td>18b</td>
<td>-40</td>
<td>≥ 410</td>
<td>19b (~100)</td>
<td>[16]</td>
</tr>
<tr>
<td></td>
<td>-40</td>
<td>≥ 300</td>
<td>19b (~100)</td>
<td>[16]</td>
</tr>
<tr>
<td>19c</td>
<td>20</td>
<td>≥ 410</td>
<td>19c (~100)</td>
<td>[14]</td>
</tr>
<tr>
<td></td>
<td>-78</td>
<td>≥ 300</td>
<td>20c (27), oligomers</td>
<td>[14]</td>
</tr>
</tbody>
</table>
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Electron-deficient pyridine rings. This effect is even more strengthened in the pyridinium salt obtained by tetrafold N-alkylation [22]. Nanocrystals of the cyclophane \( \text{16} \), prepared by sonication in water, exhibit an intense fluorescence emission at 490 nm. The respective surfactant crystallization was performed with sodium dodecyl sulfate (SDS) as antisolvent [23]. In MeOH, dimer \( \text{16} \) and cobalt (II) acetate (1:1) generate a 2D organometallic framework with multiple cavities (squares and hexagons). Addition of toluene led within two weeks to pink crystals (yield of 70%) [20]. Each Co(II) ion is coordinated to four pyridyl N-atoms and two O atoms of the monodentate acetate ions. The crystal structure analysis of this net of vertex type reveals the incorporation of MeOH and toluene as guests in the grid [20]. Other guests should be welcome!

\( \text{1,4-Bis[(E)-2-(4-pyridyl)ethenyl]benzene (14)} \) was also irradiated in two 3D coordination polymers [25]. Single-crystal to single-crystal structural transformations were achieved for 3D networks, in which Zn\(^{2+}\) or Cd\(^{2+}\) carboxylates (5-sulfoisophthalic acid and 1,3-phenylenediacetic acid) are linked by parallel ligands \( \text{14} \). The olefinic centers have sufficiently small distances (between 3.61 and 4.03 Å) in these coordination polymers. However, one has to distinguish between in-phase and out-of-phase orientations of neighboring molecules \( \text{14A} \). The out-of-phase arrangement is suitable for

MacGillivray et al. solved the steric problem of the second cyclobutane ring formation for the synthesis of paracyclophanes in an elegant way [18-24]. Cyclophane \( \text{16} \) could be obtained in a template-directed solid state synthesis. The two resorcinol molecules \( \text{21} \) and \( \text{14A} \) generate a cocrystal through the formation of four hydrogen bonds. This cocrystal acts as a linear template (Scheme 7).

The single-crystal to single-crystal transformation in different templates gave different yields because of different arrangements in the cocrystals and because of different persistence of the crystals.

A quantitative yield and a perfect topochemical control of the regio- and stereoselectivity is provided by 5-benzylresorcinol (21b) as hydrogen bond donor. The anti-position of the two cyclobutane rings is indicated by the arrangement of \( \text{14A} \) in the cocrystal (Figure 2).

Although the \( \pi \) conjugation, present in \( \text{14} \), is blocked by the photocycloaddition, the fluorescence of cyclophane \( \text{16} \) (\( \lambda_{\text{max}} = 414 \text{ nm} \)) is red-shifted in comparison to \( \text{14} \) (\( \lambda_{\text{max}} = 401 \text{ nm} \)) [22]. According to DFT calculations [22] HOMO and LUMO of the dimer \( \text{16} \) are preferentially localized on the cyclophane core. The bathochromic shift can be attributed to an intramolecular charge transfer (ICT) from the strained cyclophane scaffold to the electron-deficient pyridine rings. This effect is even more strengthened in the pyridinium salt obtained by tetrafold N-alkylation [22]. Nanocrystals of the cyclophane \( \text{16} \), prepared by sonication in water, exhibit an intense fluorescence emission at 490 nm.

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Scheme 6. Photodimerization products of the mixed crystal 18d–18e.
head-to-tail cycloaddition, whereas the in-phase arrangement yielded cyclophane 16 on irradiation ($\lambda = 280$ nm). This type of dimerization was realized in the coordination polymer $[\text{Cd}_2(\text{1,3-phenylene diacetic acid})_2]_n$ (yield of 83%), from which 16 could be obtained (yield of 70%) [25].

The photoreactivity of the monoesters $(E,E)$-24a,b in the crystalline state depends on the steric demand of the ester groups. Whereas the ethylester 24a is photostable, the more planar, better aligned $n$-decyl ester 24b reacted to cyclophane 25b [26].

**Scheme 7.** Photodimerization of $(E,E)$-14A fixed by resorcinol cramps.

**Figure 2.** ORTEP3 representation of the cocrystals 22b (Reproduced from Friscic, T. and MacGillivray, L. R. 2003, Chem. Commun., 1306-1307 with permission of The Royal Society of Chemistry).
Due to photocyclodimerization reactions in constrained media, all the \([2.2](1,4)\)cyclophanes, namely 16, 20a, c-f, 25b and 27, discussed herein, have anti-standing cyclobutane rings. Obviously, conformer A (Table 1) of all the \((E,E)\)-1,4-diethenylbenzenes involved is either the only conformer present or the exclusively reacting conformer.

Irradiation of \((E,E)\)-1,4-dicinnamoylbenzene (28) in the crystalline state led to \([4.4]\)paracyclophane 29 in good yields (Scheme 9) [28]. The crystal structure of 28 revealed that the reacting molecular pairs are arranged in skewed positions, in which

\[
\text{28} \xrightarrow{hv \text{ solid state } 70-100 \text{ h}} \text{29 (58%)}
\]

Scheme 9. Preparation of the \([4.4](1,4)\)cyclophanes 29 and 30.
the olefinic carbon centers have distances between 3.90 and 4.09 Å. The morphology changed from the crystalline state to a nearly amorphous state during the reaction. The topochemical control, valid in the reaction period, provided an unusual stereochemistry of the dimerization, in which each of the two reacting heads H of one molecule is in trans position to the reacting head H of the second molecule. The corresponding tails T also have the trans arrangement. Reduction of 30 furnished the corresponding [4.4]cyclophane 30. The racemates 29 and 30 could be resolved into pairs of enantiomers by chiral affinity chromatography [28].

4. Metacyclophanes

In contrast to 1,4-diethenylbenzenes, the 1,3-isomers can photodimerize in solution to yield the stereoisomeric [2.2](1,3)cyclophanes 33 via the primary adducts 32. Nishimura et al. found that even the unsubstituted 1,3-diethenylbenzene 31a showed this reaction (Scheme 10) [29-31]. The styryl compound 31b, the naphthyl system 31c and the ester 31d represent further examples [32, 33]. All starting compounds 31a-d exist in solution in an equilibrium of three rotamers A−C (Table 1). Each conformer generated a specific product configuration. Owing to similar steric interactions, it can be presumed that the rotameric distribution of the primary adduct 32a-d corresponds approximately to that of 31a-d. All obtained products were syn-metacyclophanes. 33aB and 33aC as well as 33dB and 33dC interconvert slowly at room temperature. The

![Scheme 10. Photodimerization of the 1,3-diethenylbenzenes 31a-c to the stereoisomeric metacyclophanes 33a-d (A,B,C).](image-url)
Table 4. Photocyclodimerization products 33a-d.

<table>
<thead>
<tr>
<th>Comp. 33</th>
<th>-R</th>
<th>Total yield (%)</th>
<th>Ratio (photodimerization) A : B : C</th>
<th>Thermal equilibrium A : B : C</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>-H</td>
<td>18</td>
<td>56 : 28 : 16</td>
<td>56 : 26 : 18</td>
<td>29-31</td>
</tr>
<tr>
<td>b</td>
<td>-C\textsubscript{6}H\textsubscript{5}</td>
<td>59</td>
<td>50 : 45 : 5</td>
<td></td>
<td>32, 33</td>
</tr>
<tr>
<td>c</td>
<td></td>
<td>53</td>
<td>66 : 31 : 3</td>
<td>64 : 27 : 9</td>
<td>33</td>
</tr>
<tr>
<td>d</td>
<td>-COOCH\textsubscript{3}</td>
<td>53</td>
<td>64 : 16 : 20</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The olefinic double bonds of a 1,3-diethenylbenzene moiety can also be part of a polycyclic system. 4,5',8-trimethylpsoralen (trioxasalen, 2,5,9-trimethylfuro[3,2-g]benzopyran-7-one) 40, a natural product, is an interesting example. It is used as a drug against different epidermal proliferative diseases. Irradiation of 40 in CH\textsubscript{2}Cl\textsubscript{2} yielded three dimers. The furan and the pyrone ring are capable of homodimerization and heterodimerization reactions. The latter process yielded the polycyclic compound 41, which has a metacyclophane substructure (Scheme 13) [34, 35].

5. Orthocyclophanes

Cyclophanes of the type [n.m](1,2) can be regarded as condensed ring systems of benzene. Their preparation mode by photodimerization reactions is closely related to the synthesis of metacyclophanes discussed in section 4. In an early study, the photochemistry of (E,E)-1,2-distyrylbenzene (42a) was investigated [36]. The primary photoproducts contain cyclobutane rings obtained by head-to-head H⋯H or head-to-tail H⋯T addition. Rotamer A of 42a is best suited for twofold [2π+2π] head-to-head cycloadditions. The cis-adduct 43a was the major product. In addition two isomeric head-to-head trans-adducts 44a and 45a were obtained in low yields (Scheme 14) [36].

Table 5 gives a survey of other examples of this reaction type. All identified products corresponded to the boat configuration 43.

The irradiations listed in table 5 were performed in solution. On the contrary, diester 46a and diketone 46b were irradiated by Kaupp et al. in the crystalline state (Scheme 15) [40].

Both olefinic double bonds can also be a part of a polycyclic system. Kinder and Margaretha [41] studied first the twofold isocoumarin 49a (Scheme 16). Irradiation in benzene or acetonitrile led to the head-to-head-cis adduct 50a as major product. The minor product 51a (ratio 10:90) was the corresponding head-to-head-trans compound. Irradiation of a suspension of 49a in hexane gave the ratio 15:85 for 51a/50a [41]. The starting transition state resembles an anti-metacyclophane structure [33]. The same molecular mobility causes an automerization for 33aA and 33dA. 33b and 33c form three rigid diastereomers each. Table 4 summarizes the yields and ratios of the isomers. Moreover, metacyclophanes are intermediates in the photodimerization of tri- and tetrastyrylbenzenes (see section 6). Birch reduction (Scheme 11) converted the mixture of stereoisomers 33a to [4.4](1,3)-cyclophane (34) [29]. Selective cleavage of the “inner” bond of the cyclobutane rings significantly decreases the cyclophane strain.

When the starting compounds 31b or when the cyclophanes 33b were irradiated in the presence of iodine, pyrene derivatives were obtained, which underwent further photo-reactions (Scheme 12). Finally, a complete aromatization to pyrene (38) and phenanthrene (39) occurred [32, 33].

The olefinic double bonds of a 1,3-diethenylbenzene moiety can also be part of a polycyclic system. 4,5',8-trimethylpsoralen (trioxasalen, 2,5,9-trimethylfuro[3,2-g]benzopyran-7-one) 40, a natural product, is an interesting example. It is used as a drug against different epidermal proliferative diseases. Irradiation of 40 in CH\textsubscript{2}Cl\textsubscript{2} yielded three dimers. The furan and the pyrone ring are capable of homodimerization and heterodimerization reactions. The latter process yielded the polycyclic compound 41, which has a metacyclophane substructure (Scheme 13) [34, 35].
compounds 49b and 49c almost quantitatively yielded the products 50b and 50c/50c', respectively [42].

A special situation is given, when both reacting 2π components belong to the same naphthalene ring (Scheme 17). Photocyclodimerization of the compound 52 yields the cubane-related systems 53. Many different substituents R tolerate this photoreaction.

The original concept of this process was already published by Sasse et al. in the 70s [43]. A detailed discussion of this reaction type is beyond the scope of this article. However, a few recent papers on this photoreaction and its applications shall be quoted here [44-51].
Higher cyclophanes

The (2,2,2)(1,3,5)cyclophane 6a is described in the ‘Introduction’ section as a model to demonstrate how photodimerization reactions provide an easy access to cyclophanes. The crystal structure analysis of 6a confirmed the C₃h structure, which can be deduced from conformer A (Table 1) of (E,E,E)-1,3,5-tristyrylbenzene 5a [3, 6]. Conformer B gave rise to the formation of the stereoisomer 54a, which was found in a small yield of 1% (Scheme 18) [6]. When, however, the trimethoxy compound 5b was used as starting compound, the product ratio changed in favor of 54b [52]. The statistical ratio A:B for 5a,b is 1:3. This ratio was exactly found by Nishimura et al. [53], who studied the photochemistry of unsubstituted

Table 5. Photodimerization of β-substituted 1,2-diethenylbenzenes (E,E)-43b-43g.

<table>
<thead>
<tr>
<th>Photodimer</th>
<th>-R</th>
<th>Yield (%)</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>43b</td>
<td>-H</td>
<td>11</td>
<td>[37]</td>
</tr>
<tr>
<td>43c</td>
<td></td>
<td>38</td>
<td>[38]</td>
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<td>43d</td>
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<td>25</td>
<td>[39]</td>
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<td>43e</td>
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<td>31</td>
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<td>43f</td>
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<td>33</td>
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<td>43g</td>
<td></td>
<td>87</td>
<td>[38]</td>
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</tbody>
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Scheme 14. Photocyclodimerization reactions of conformer A of (E,E)-1,2-distyrylbenzene 42a.
1,3,5-triethenylbenzene (R=H). However, the total yield of cyclophanes 6c and 53c was very low [53].

It is of interest to note that the photocycloaddition of 5a could be stopped after the formation of the second cyclobutane ring, when the irradiation was performed in the presence of iodine. The remaining styryl groups in the obtained pyrene derivative 55 cannot react with each other due to steric reasons (Scheme 19) [3, 6].

Although seven rotamers can be drawn for 1,2,4,5-tetraethenylbenzene 56 (Table 1), only one \([2.2.2.2](1,2,4,5)\) cyclophane 57 was obtained in 0.6% yield (Scheme 20) [53].

Irradiation of 58a,b in CH₂Cl₂ led to the \([4.4.4]\) (1,3,5)cyclophanes 59a,b in high yield (Scheme 21). Three cisoid and three transoid conformers of 58a,b have to be considered. The product is formally derived from the drawn threefold cisoid conformer 58 by a threefold head-to-head trans cycloaddition [54, 55].

When a 2:1 mixture of 58a and 58b was irradiated, three \([4.4.4](1,3,5)\)cyclophanes were obtained: 59a, 59b and the mixed dimer 59a/b (total yield 85%, ratio 59a:59b:59a/b = 1:4:trace). Obviously, the
Scheme 18. Threefold photocycloaddition of \((E,E,E)-1,3,5\)-tristyryl- and 1,3,5-trivinylbenzenes.

Scheme 19. Generation of pyrene derivative 55.

Scheme 20. Photodimerization of 1,2,4,5-tetraethenylbenzene 56 (conformer A).

Scheme 21. Threefold photocycloaddition of \((E,E,E)-1,3,5\)-tricinnamoylbenzenes 58a,b.
Another promising project would be the extension of the photochemical preparation mode to higher numbers ‘n’ of bridges between the decks. A facile superphane synthesis on the basis of β-substituted hexaethenylbenzenes certainly represents an outstanding goal. Furthermore, novel selective cleavages of the cyclobutane rings (such as \(33 \rightarrow 34\) shown in scheme 11), would serve to transform the [2.2]- to higher (cyclo)phanes. Rigid crystals or other constrained media, such as templates or (coordination) polymers seem to be a good choice for the preparation of highly strained (cyclo)phanes (see for example ref. [12, 18-25]).

7. Conclusion and outlook

Multiple \([2\pi + 2\pi]\) photocycloaddition reactions can be applied for the synthesis of \([2.2]\), \([2.2.2]\), \([2.2.2.2]\), \([4.4]\) or \([4.4.4]\) cyclophanes. The resulting products are dimers of easily accessible benzene derivatives, which contain two, three or four photoreactive (β-substituted) ethenyl groups. Owing to this preparation mode, all cyclophane bridges contain cyclobutane rings, whose mutual orientation is determined by the reacting rotamers of the starting compounds. Thus, the configurations of the dimer are decided by the conformation of the monomers – a rare effect! Regio- and stereochemistry of the photodimerizations can be explained by the generation of the energy-lowest excimers.

This synthetic strategy can be extended to the preparation of higher phanes, which contain for example naphthalene instead of benzene decks [56], and to belt cyclophanes [57]. The structures 61 [56] and 62 [57c, d] depict two examples. Another promising project would be the extension of the photochemical preparation mode to higher numbers ‘n’ of bridges between the decks. A facile superphane synthesis on the basis of β-substituted hexaethenylbenzenes certainly represents an outstanding goal.

Furthermore, novel selective cleavages of the cyclobutane rings (such as \(33 \rightarrow 34\) shown in scheme 11), would serve to transform the [2.2]- to higher (cyclo)phanes. Rigid crystals or other constrained media, such as templates or (coordination) polymers seem to be a good choice for the preparation of highly strained (cyclo)phanes (see for example ref. [12, 18-25]).

CONFLICT OF INTEREST STATEMENT

There are no conflicts of interest.

REFERENCES