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Review

Cyclophanes obtained by photocyclodimerization reactions

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ABSTRACT

Benzene derivatives, which contain two, three or four photoreactive functionalities, such as vinyl, styryl or cinnamoyl groups, can undergo multiple [2π+2π] 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** → **2**, which consist of two-, three- or fourfold [2π+2π] photocycloadditions, or on analogous intramolecular reactions **3** → **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 [$\pi^2s+\pi^2s$] cycloaddition reactions is thermally forbidden as concerted process. However, two-step reactions *via* zwitterions or diradicals are well-known. 1,4-Bis-(trifluoroethenyl)benzene (**7**) is a compound, which undergoes a thermal cyclodimerization 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_2F_3-groups. Cyclobutane derivatives

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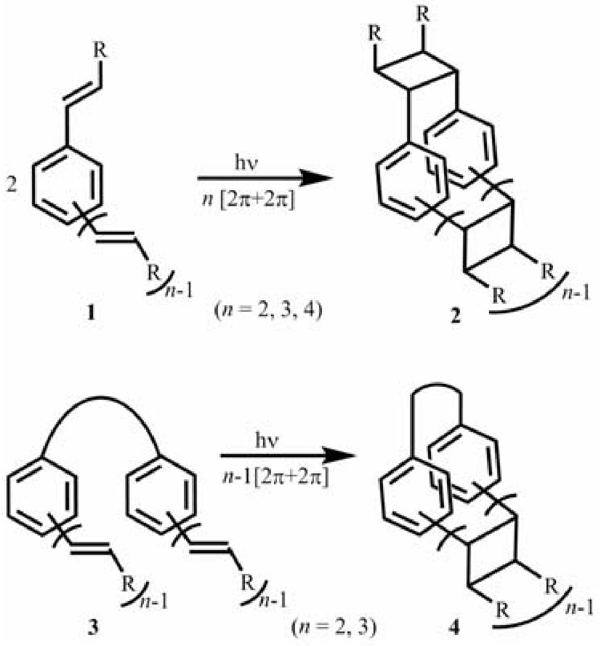
with *cis*- and *trans*-configuration are obtained in this non-stereoselective process. Subsequently, the *cis*-isomer can undergo a second cycloaddition to form cyclophane **8** at a low yield [4].



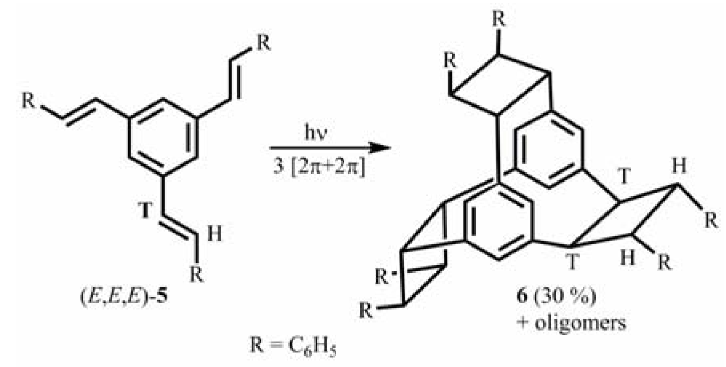
Scheme 1. Inter- and intramolecular photocycloaddition reactions for the generation of cyclophanes.

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.

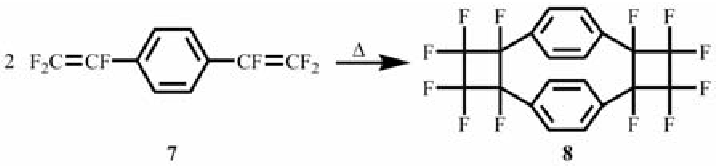
Let us consider again the generation of cyclophane **6** by a threefold [$\pi^2s+\pi^2s$] photocycloaddition [3, 5b, 6-8]. This example shows already the whole scope of problems. The first step has to be a regioselective head-to-head process (H$\cdots$H), in which the two heads adopt *cis* position in 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 *trams* 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 2. First application of a photocyclodimerization reaction for the preparation of cyclophanes.



7 8

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 $[S_0 \ldots S_1]$ are formed, whose stabilization energies can be estimated from first-order and/or second-order perturbation theory [5b, 8]. All pairs of overlapping π 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].

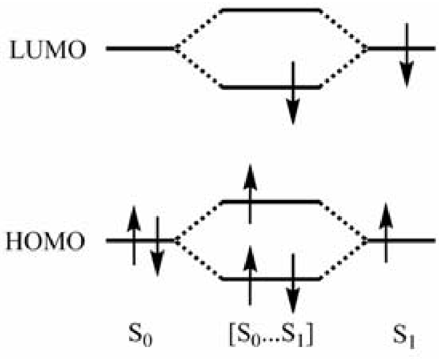
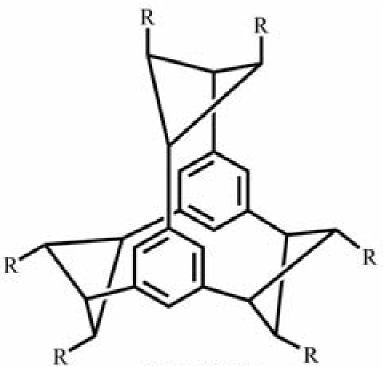


Figure 1. Frontier orbital interactions for the formation of excimers.



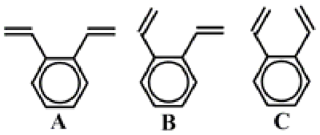
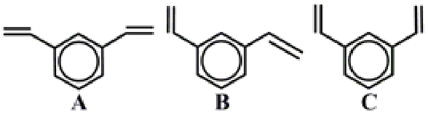
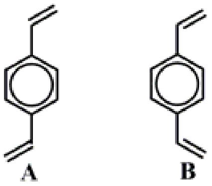
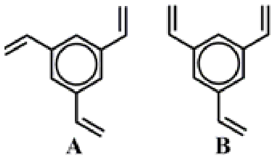
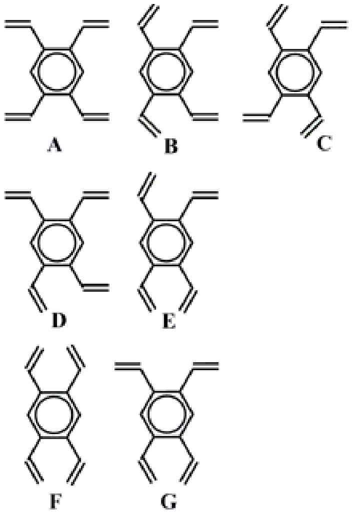
6' ($R=C_6H_5$)

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

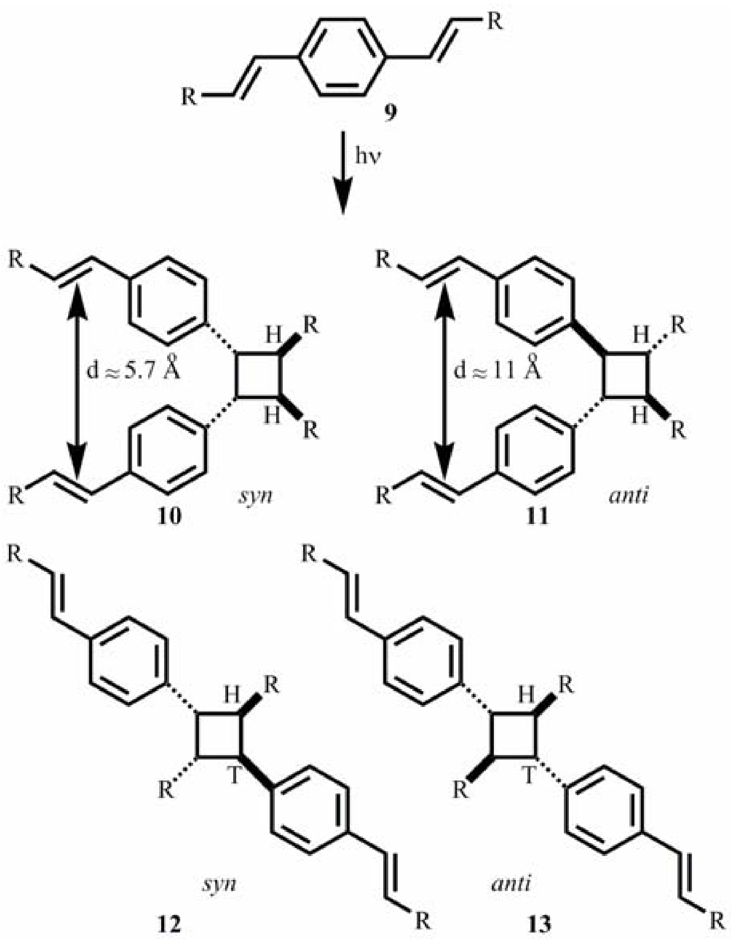
The formation of [2.2](1,4)cyclophane scaffolds by photodimerization of (β-substituted) 1,4-diethenylbenzenes **9** seems to be impossible in solution. Scheme 4 illustrates the situation. When the first cyclobutane ring is closed to a head-to-head (H$\cdots$H) adduct **10** or **11** or to a head-to-tail (H$\cdots$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

Table 1. Possible rotamers of di-, tri- and tetraethenylbenzenes.

Substitution positions in benzene	**Rotamers**	**Number of rotamers**
1,2 ortho		3
1,3 meta		3
1,4 para		2
1,3,5		2
1,2,4,5		7

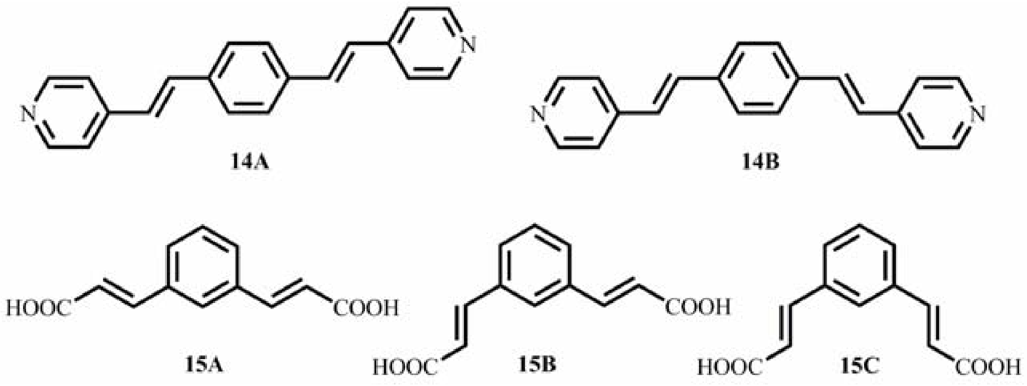
the head-to-tail dimers **11** and **13** (Scheme 4). However, a good chance to yield [2.2](1,4)-cyclophanes is given in the crystalline state, when the olefinic double bonds are lying parallel and close enough in the crystal (Schmidt's rule) [11], and when the crystal has a sufficient stability after the generation of the first four-membered ring. In general, crystalline states are transformed by such processes into amorphous states.

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



Scheme 4. Possible head-to-head (H···H) and head-to-tail (H···T) *syn*- and *anti*-[2π+2π]cyclodimers **10–13** on irradiation of (*E*,*E*)-1,4-diethenylbenzenes **9**.

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.



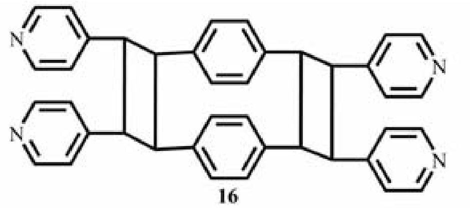
14A **14B**

15A **15B** **15C**

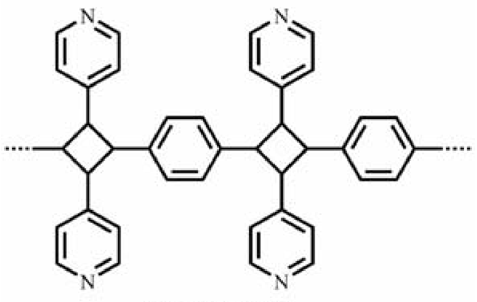
Table 2. Irradiation processes in the coordination polymer: Ratios (%) of the involved components in a typical single crystal UV irradiation with a high-pressure mercury lamp.

Irradiation period (h)	**Component 14A/14B as a guest**			
	Rotamer **14A**	Rotamer **14B**	dimer **16**	Polymer **17**
0	79	21	–	–
1	29	–	–	71
4	21	–	–	79
Component 14A/14B as a ligand				
0	100	–	–	–
1	39	61	–	–
4	33	67	–	–
6	68	–	32	–
Component 15A/15B as a ligand				
	Rotamer **B**	Rotamer **A**	dimer	polymer
0	100	–	–	–
4	100	–	–	–
6	43	57	–	–

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 paracyclophane **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.



16

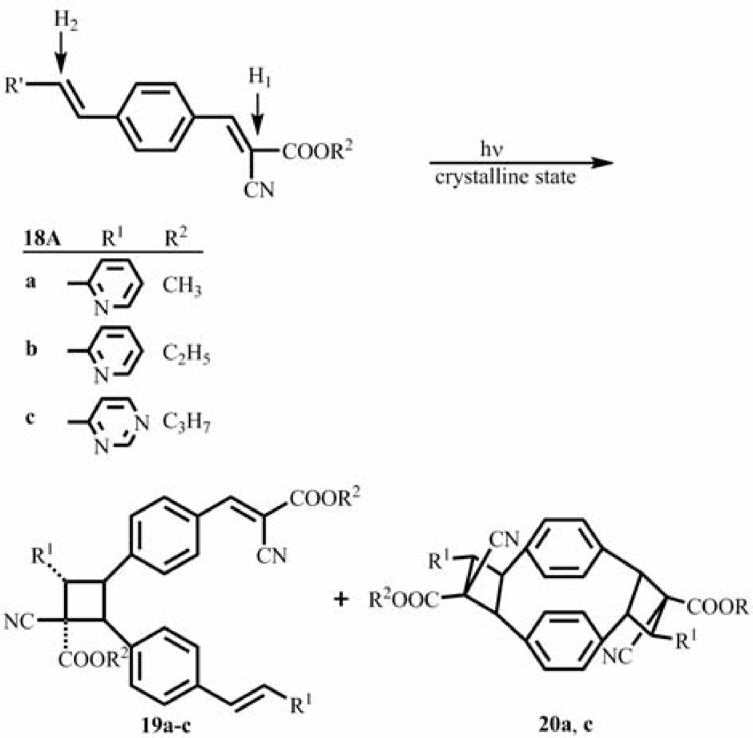


photopolymer 17

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 ($\lambda \geq 410$ 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 $H_1 \cdots H_2$ and stereoselectively to a paracyclophane with *anti*-standing cyclobutane rings (**18A** → **20**).

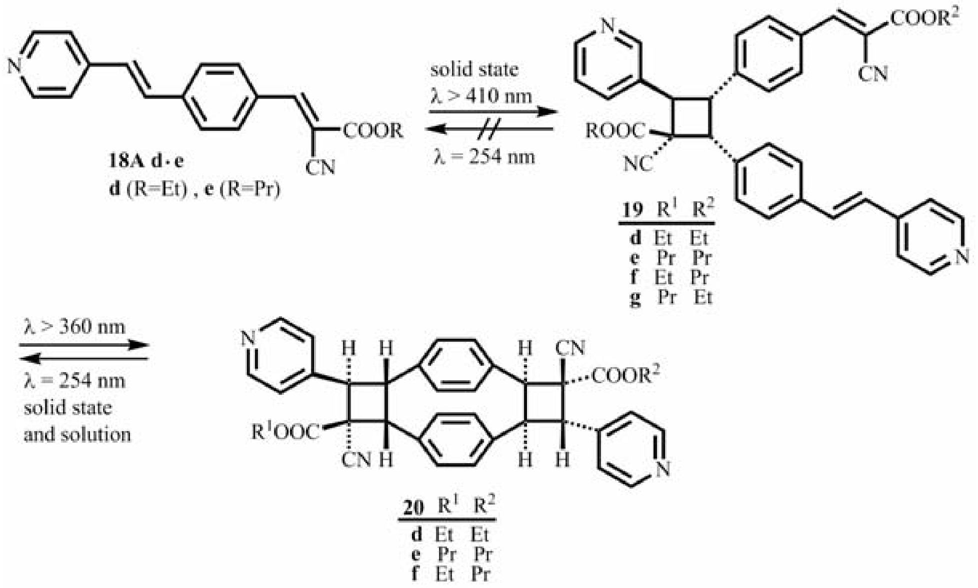
Mixed crystals **18d–18e** (molar ratio 70:30 to 5:95) have a molecular arrangement, which is entirely different from those of pure **18d** and **18e**. They reacted quantitatively to **20d–f** *via* **19d–g** (Scheme 6) [13, 15].



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

Table 3. Photoreactions of **18a–c** in the crystalline state.

Starting compound	Temperature (°C)	Wavelength (nm)	Products (%)	Ref.
18a	-40	≥ 410	**19a** (~100)	[16]
	-40	≥ 300	**19a** (45), **20a** (42), oligomers	[16]
18b	-40	≥ 410	**19b** (~100)	[16]
	-40	≥ 300	**19b** (~100)	[16]
19c	20	≥ 410	**19c** (~100)	[14]
	-78	≥ 300	**20c** (27), oligomers	[14]



Scheme 6. Photodimerization products of the mixed crystal **18d–18e**.

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 **16** could be obtained in a template-directed solid state synthesis. The two resorcinol molecules **21** and **14A** generate a cocrystal through the formation of four hydrogen bonds. This cocrystal acts as a linear template (Scheme 7).

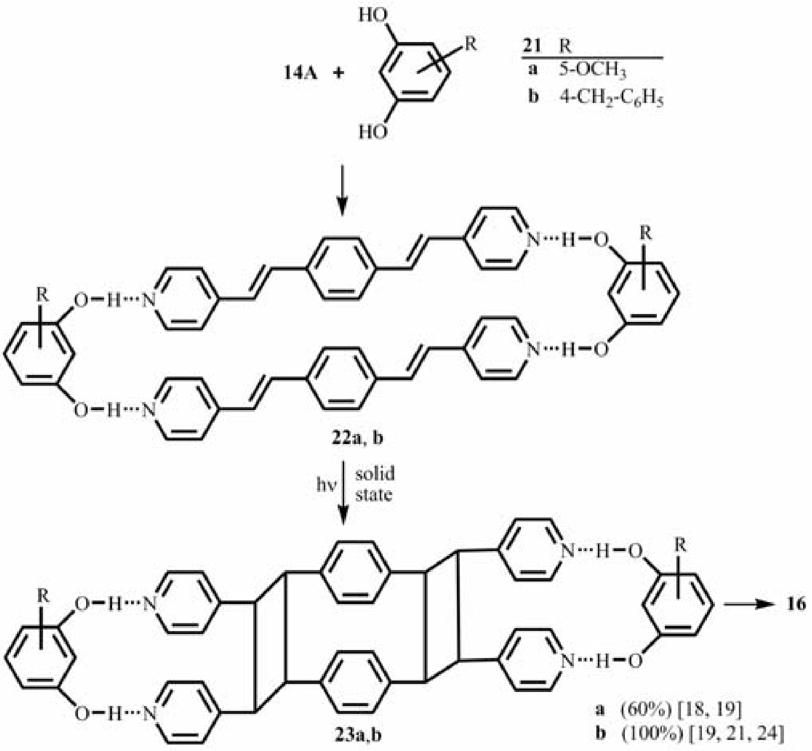
The single-crystal to single-crystal transformation in different templates gave different yields because of different arrangements in the cocrystals and because of different persistence of the crystals.

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

Although the π conjugation, present in **14**, is blocked by the photocycloaddition, the fluorescence of cyclophane **16** (λ_{max} = 414 nm) is red-shifted in comparison to **14** (λ_{max} = 401 nm) [22]. According to DFT calculations [22] HOMO and LUMO of the dimer **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 **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 **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!

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 **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 **14A**. The out-of-phase arrangement is suitable for



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

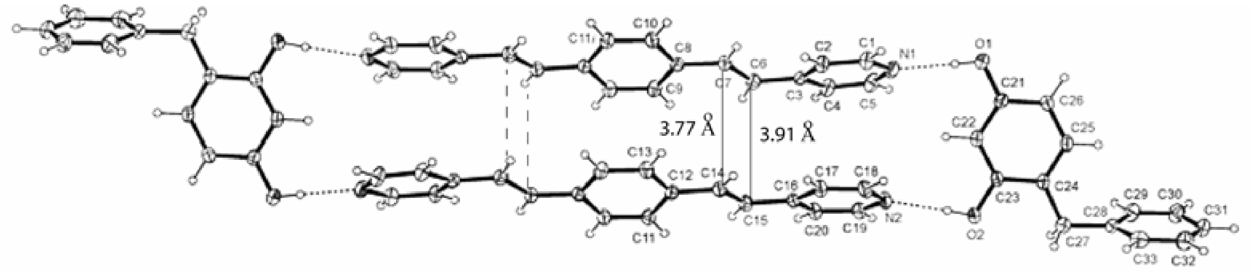
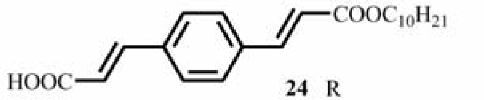


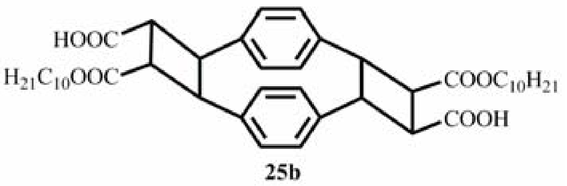
Figure 2. ORTEP3 representation of the cocrystals **22b** (Reproduced from Friscic, T. and MacGillivray, L. R. 2003, Chem. Commun., 1306-1307 with permission of The Royal Society of Chemistry).

head-to-tail cycloaddition, whereas the in-phase arrangement yielded cyclophane **16** on irradiation (λ = 280 nm). This type of dimerization was realized in the coordination polymer [Cd_2(1,3-phenylene diacetic acid)$_2$ (**14A**)$_2$]$_n$ (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].



24	R
a	C_2H_5
b	$C_{10}H_{21}$



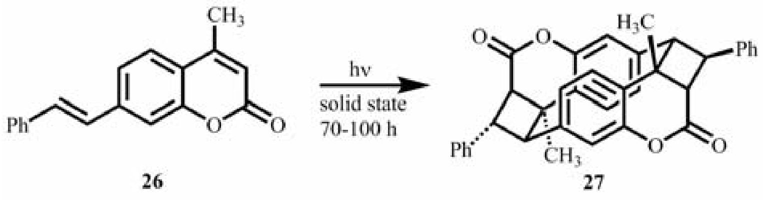
25b

Finally, an example should be discussed, in which one of the two involved olefinic double bonds is located in a ring system.

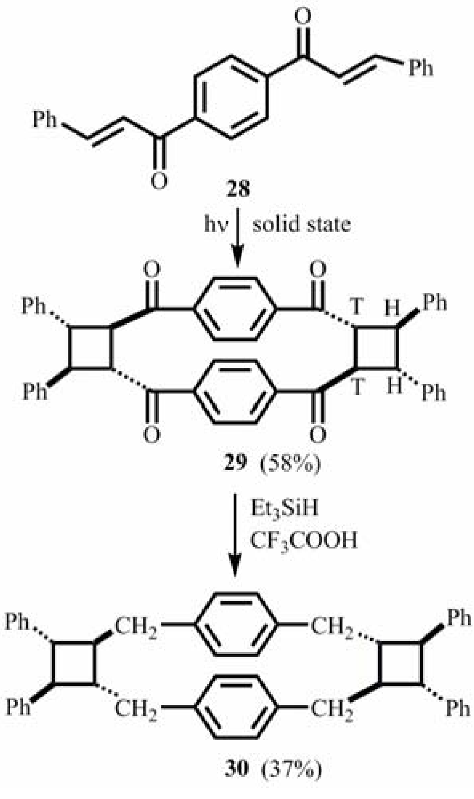
4-Methyl-7-(*E*)-styrylcourmarin (**26**) underwent a twofold, topochemically controlled stereospecific [2+2] photocycloaddition to the polycyclic compound **27,** which has a paracyclophane substructure [27]. The yield was determined by the crystal modification in plates (72%) or needles (45%). An amorphous powder or a solution of the isolated monocycloadduct did not yield **27** on irradiation. This result demonstrates the strict control of the crystal lattice present in **26** (Scheme 8) [27].

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



Scheme 8. Photodimerization of the coumarin derivative **26**.



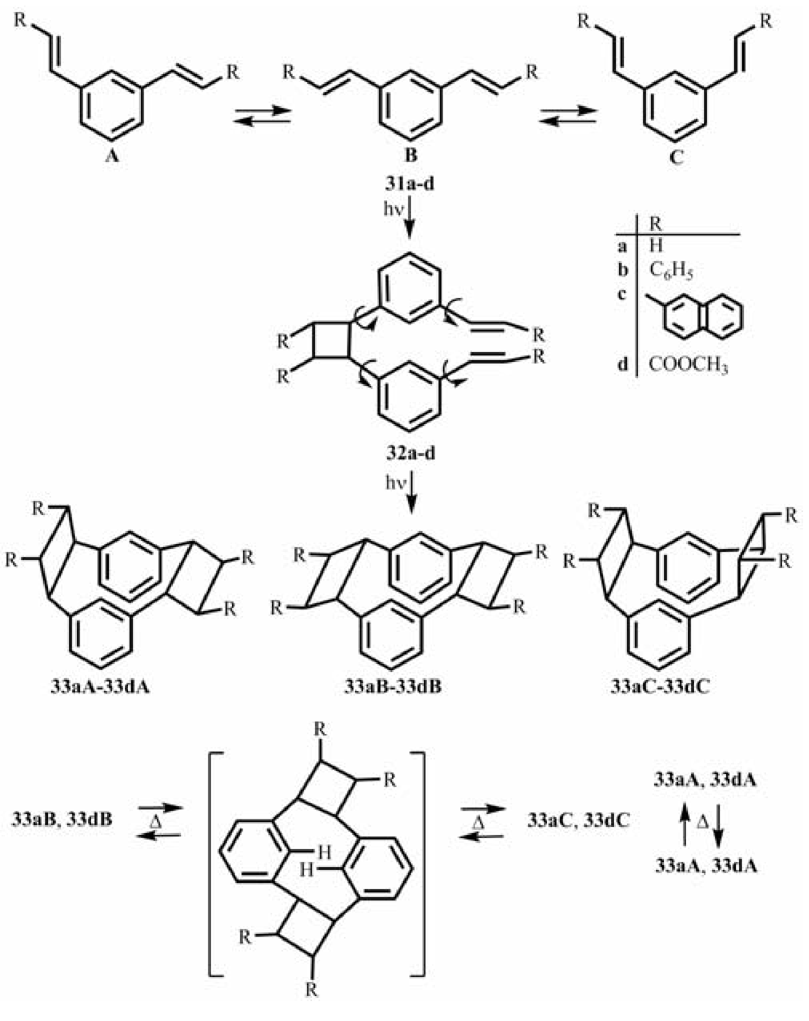
Scheme 9. Preparation of the [4.4](1,4)cyclophanes **29** and **30**.

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

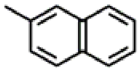
In contrast to 1,4-diethenylbenzenes, the 1,3-isomers can photodimerize in solution to yield the stereoisomeric [2.2](1,3)cyclophanes **33** *via* the primary adducts **32**. Nishimura *et al.* found that even the unsubstituted 1,3-diethenylbenzene **31a** showed this reaction (Scheme 10) [29-31]. The 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.

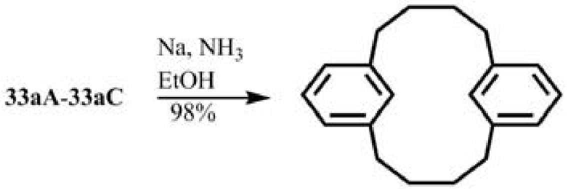
33aB and **33aC** as well as **33dB** and **33dC** interconvert slowly at room temperature. The



Scheme 10. Photodimerization of the 1,3-diethenylbenzenes **31a-c** to the stereoisomeric metacyclophanes **33a-d** (A,B,C).

Table 4. Photocyclodimerization products **33a-d**.

Comp. 33	**-R**	**Total yield (%)**	**Ratio (photodimerization) A : B : C**	**Thermal equilibrium A : B : C**	**Ref.**
a	-H	18	56 : 28 : 16	56 : 26 : 18	29-31
b	-C_6H_5	59	50 : 45 : 5		32, 33
c		53	66 : 31 : 3		33
d	-$COOCH_3$	53	64 : 16 : 20	64 : 27 : 9	33



34

Scheme 11. Reduction of the metacyclophanes **33a**.

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 photoreactions (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_2Cl_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].

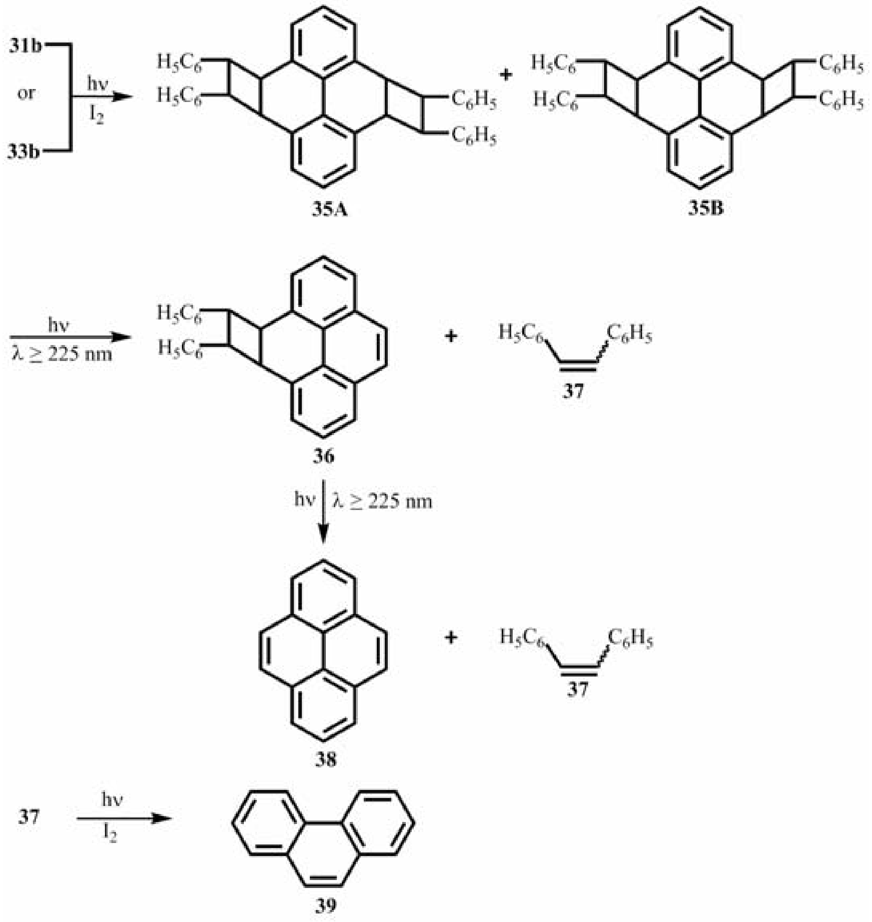
5. Orthocyclophanes

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 [$2\pi+2\pi$] 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].

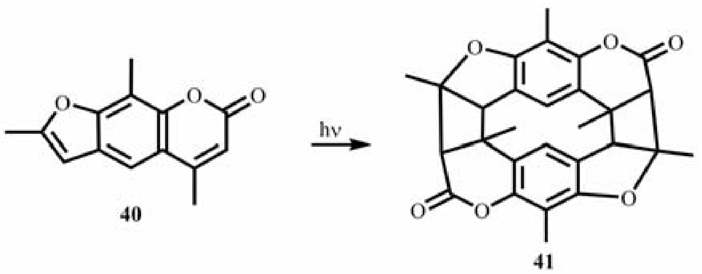
Table 5 gives a survey of other examples of this reaction type. All identified products corresponded to the boat configuration **43**.

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



Scheme 12. Photooxidation and degradation processes of metacyclophane **33b** (or its precursor **31b**).

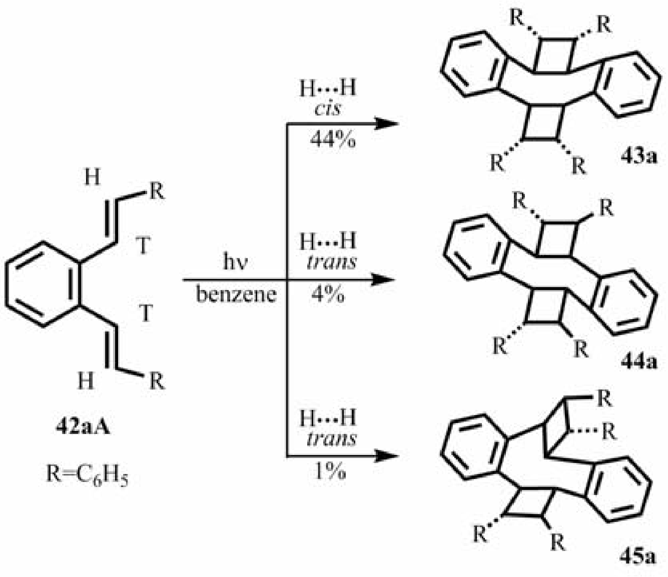


Scheme 13. Heterodimerization of **40** to **41**.

compounds **49b** and **49c** almost quantitatively yielded the products **50b** and **50c**/**50c'**, respectively [42].

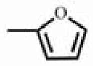
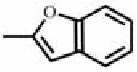
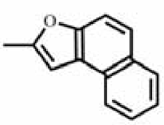
A special situation is given, when both reacting 2π components belong to the same naphthalene ring (Scheme 17). Photocyclodimerization of the compound **52** yields the cubane-related systems **53**. Many different substituents R tolerate this photoreaction.

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].



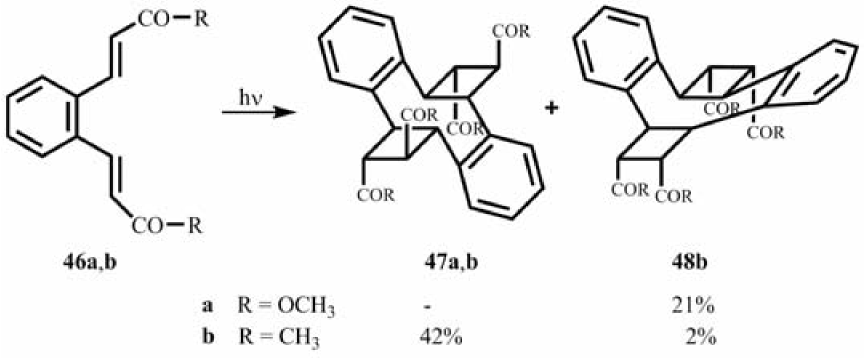
Scheme 14. Photocyclodimerization reactions of conformer **A** of (*E*,*E*)-1,2-distyrylbenzene **42a**.

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

Photodimer	-R	Yield (%)	References
43b	-H	11	[37]
43c		38	[38]
43d		25	[39]
43e		31	[39]
43f		33	[38]
43g		87	[38]

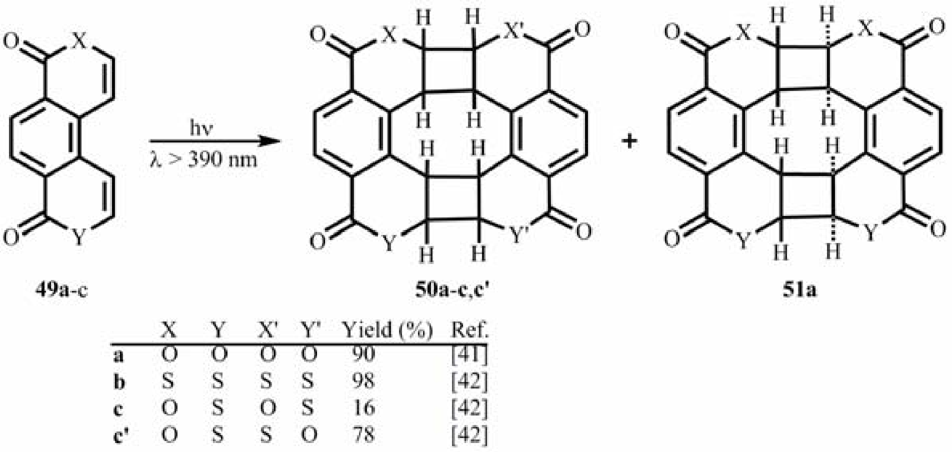
6. Higher cyclophanes

[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 C_{3h} 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



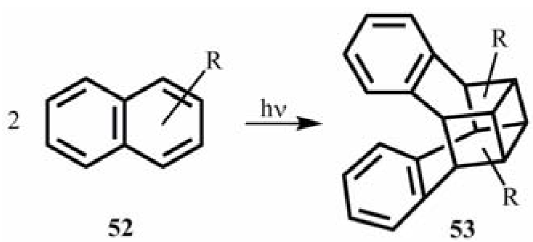
		47a,b	48b
a	R = OCH_3	-	21%
b	R = CH_3	42%	2%

Scheme 15. Photodimerization of (*E*,*E*)-**46a**,**b** in solid state.



	X	Y	X'	Y'	Yield (%)	Ref.
a	O	O	O	O	90	[41]
b	S	S	S	S	98	[42]
c	O	S	O	S	16	[42]
c'	O	S	S	O	78	[42]

Scheme 16. Photodimerization of the lactones/thiolactones **49a**-**c**.



Scheme 17. Photodimerization of the naphthalene systems **52**.

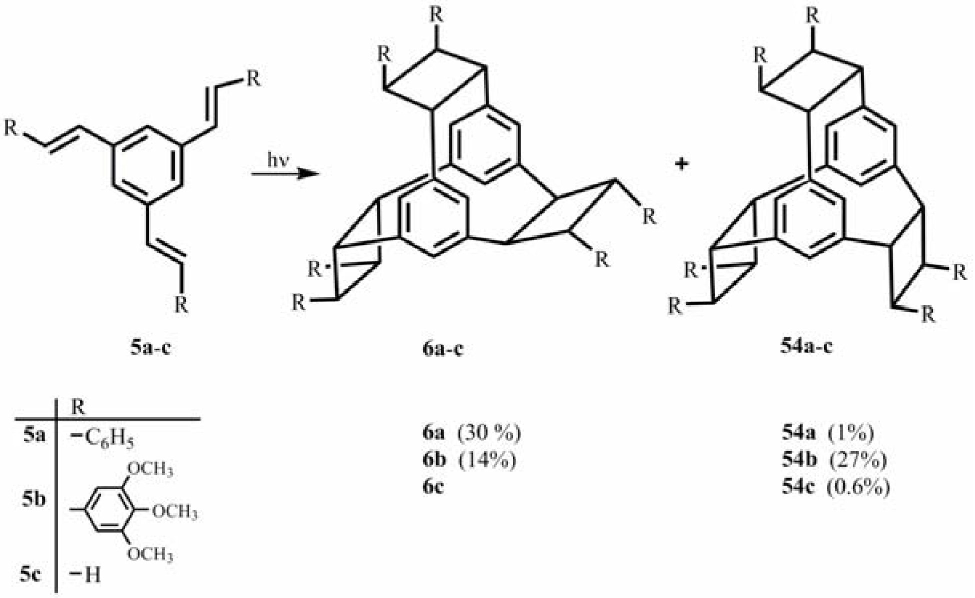
1,3,5-triethenylbenzene (R=H). However, the total yield of cyclophanes **6c** and **53c** was very low [53].

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].

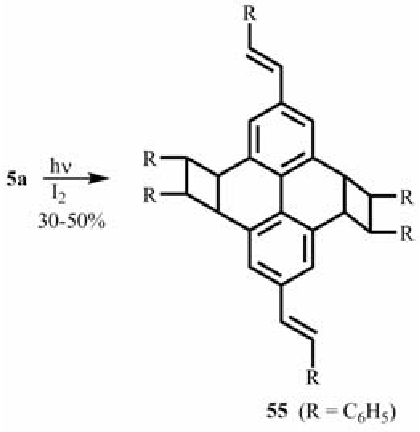
Although seven rotamers can be drawn for 1,2,4,5-tetraethenylbenzene **56** (Table 1), only one [2.2.2.2](1,2,4,5) cyclophane **57** was obtained in 0.6% yield (Scheme 20) [53].

Irradiation of **58a**,**b** in CH_2Cl_2 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].

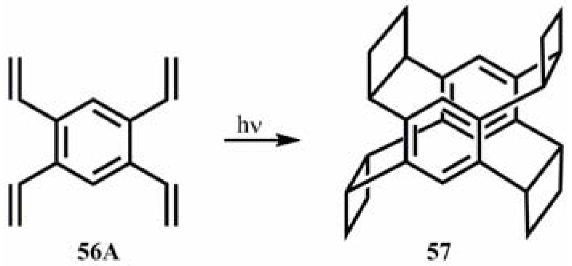
When a 2:1 mixture of **58a** and **58b** was irradiated, three [4.4.4](1,3,5)cylophanes were obtained: **59a**, **59b** and the mixed dimer **59a/b** (total yield 85%, ratio **59a**:**59b**:**59a/b** = 1:4:trace). Obviously, the



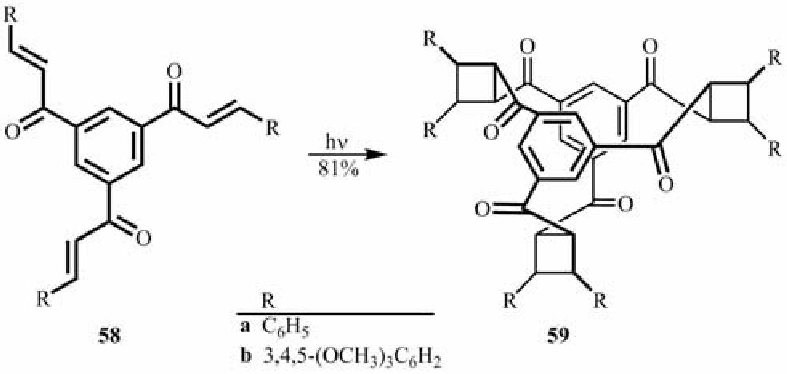
Scheme 18. Threefold photocycloaddition of (*E*,*E*,*E*)-1,3,5-tristyryl- and 1,3,5-trivinylbenzenes.



Scheme 19. Generation of pyrene derivative **55**.



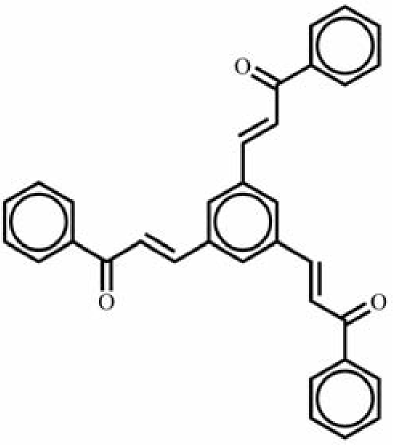
Scheme 20. Photodimerization of 1,2,4,5-tetraethenylbenzene **56** (conformer **A**).



Scheme 21. Threefold photocycloaddition of (*E*,*E*,*E*)-1,3,5-tricinnamoylbenzenes **58a**,**b**.

electron-rich compound **58b** has the higher reactivity in comparison to **58a** [54, 55].

Irradiation of **58a** in the crystalline state gave a head-to-tail-*cis* dimer with a single cyclobutane ring [54]. A related result was obtained for compound **60**, which has opposite enone functionalities [54]. Apart from oligomers, irradiation furnished a dimer with only one cyclobutane ring. A head-to-tail-*syn* adduct was obtained in the crystalline state and a head-to-head-*anti* adduct in solution [54]. In contrast to **58a**, isomer **60** is not capable to form cyclophanes.

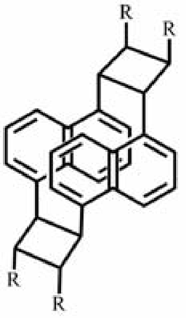


60

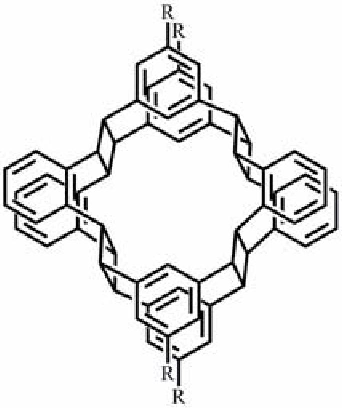
7. Conclusion and outlook

Multiple [2π+2π] 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.



61 (R=H, C_6H_5)



62 (R=$C(CH_3)_3$)

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**→**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

1. Selected books: a) Gleiter, R. and Hopf, H. 2004, Modern Cyclophane Chemistry, Wiley-VCH, Weinheim; b) Vögtle, F. 1993, Cyclophane Chemistry: Synthesis, Structures and Reactions, Wiley, Chichester; c) Diederich, F. 1991, Cyclophanes, The Royal Society of Chemistry, London; d) Keehn, P. 1983, Cyclophanes I and II, Elsevier, Amsterdam.
2. Selection of review articles since 2006: a) Kotha, S., Shirbhate, M. E. and Waghule, G. T. 2015, Beilstein J. Org. Chem., 11, 1274-1331; b) Elacqua, E., Friscic, T. and MacGillivray, L. R. 2012, Israel J. Chem., 52, 53-59; c) David, O. R. P. 2012, Tetrahedron, 68, 8977-8993;

d) Paradies, J. 2011, Synthesis, 23, 3749-3766; e) Mori, T. and Inoue, Y. 2011, Topics in Current Chemistry, 298, 99-128; f) Morisaki, Y. and Chujo, Y. 2011, Polymer Chemistry, 2, 1249-1257; g) Elacqua, E. and MacGillivray, L. R. 2010, Eur. J. Org. Chem., 6883-6894; h) Ramaiah, D., Neelakandan, P. P., Nair, A. K. and Avirah, R. R. 2010, Chem. Soc. Rev., 39, 4158-4168; i) Takamura, H. 2009, Current Organic Chemistry, 13, 1633-1653; j) Bogdan, N. D. and Grosu, I. 2009, Current Organic Chemistry, 13, 502-531; k) Aly, A. A. and Brown, A. B. 2009, Tetrahedron, 65, 8055-8089; l) Morisaki, Y. and Chujo, Y. 2009, Bl. Chem. Soc. Jap., 82, 1070-1082; Morisaki, Y. and Chujo, Y. 2008, Progr. Polym. Sci., 33, 346-384; m) Rowlands, G. J. 2008, Org. Biomol. Chem., 6, 1527-1534; n) Campos, J., Conejo-Garcia, A., Entrena, A., Gallo, M. A. and Espinosa, A. 2007, Targets in Heterocycl. Chem., 11, 431-448; o) Brase, S. 2007, Asymmetric Synthesis, 62-66; p) Campbell, K. and Tykwinski, R. R. 2006, Carbon Rich Compounds: From Molecules to Materials, M. M. Haley, R. R. Tykwinski (Eds.), Wiley-VCH, Weinheim, 229-294; q) Gleiter, R., Hellbach, B., Gath, S. and Schaller, R. J. 2006, Pure and Appl. Chem., 78, 699-706; r) Ernst, L. 2006, Annual Reports on NMR Spectroscopy, 60, 77-143; s) Morisaki, Y. and Chujo, Y. 2006, Angew. Chem. Int. Ed., 45, 6430-6437.

3. Juriew, J., Merkuschew, E., Skorochodowa, T., Winter, W. and Meier, H. 1981, Angew. Chem., 93, 285-286; Angew. Chem. Int. Ed. Engl., 20, 269-270.
4. Jiang, X.-K., Ji, G.-Z. and Wang, D, Z.-R. 1996, J. Fluorine Chem., 79, 173-178.
5. a) Caldwell, R. A. 1980, J. Am. Chem. Soc. 102, 4004-4007; b) Meier, H. 1992, Angew. Chem., 104, 1425-1446; Angew. Chem. Int. Ed. Engl., 31, 1399-1420 and references therein.
6. Winter, W., Langjahr, U., Meier, H., Merkuschev, E. B. and Juriew, Y. G. 1984, Chem. Ber., 117, 2452-2463.
7. Tobe, Y. and Takeda, T. 2010, Science for Synthesis, 45b, 1311-1348.
8. Meier, H. 1992, Recent Trends in Photochemistry 177-207, T. S. Akasheh (Ed.), University Press, Yarmouk, Jordan.
9. Meier, H., Zertani, R., Noller, K., Oelkrug, D. and Krabichler, G. 1986, Chem. Ber., 119, 1716-1724.
10. Turro, N. J., Ramamurthy, V. and Scaiano, J. 2010, Modern Molecular Photochemistry of Organic Molecules, University Science Books, Sausalito/California.
11. Schmidt, M. J. 1971, Pure Appl. Chem., 27, 647-678.
12. Yang, S.-Y., Deng, X.-L., Jin, R.-F., Naumov, P., Panda, M. K., Huang, R.-B., Zheng, L.-S. and Teo, B. K. 2014, J. Am. Chem. Soc., 136, 558-561.
13. Hasegawa, M., Maekawa, Y., Kato, S. and Saigo, K. 1987, Chem. Lett., 16, 907-910.
14. Chung, C., Nakamura, F., Hashimoto, Y. and Hasegawa, M. 1991, Chem. Lett., 20, 779-782.
15. Maekawa, Y., Kato, S. and Hasegawa, M. 1991, J. Am. Chem. Soc., 113, 3867-3872.
16. Chung, C. M., Kunita, A., Hayashi, K., Nakamura, F., Saigo, K. and Hasegawa, M. 1991, J. Am. Chem. Soc., 113, 7316-7322.
17. Kato, S., Nakatani, M., Harashina, H., Saigo, K., Hasegawa, M. and Sato, S. 1986, Chem. Lett., 15, 847-850.
18. MacGillivray, L. R., Reid, J. L. and Ripmeester, J. A. 2000, J. Am. Chem. Soc., 122, 7817-7818.
19. Friscic, T. and MacGillivray, L. R. 2003, Chem. Commun., 1306-1307.
20. Papaefstathiou, G. S., Friscic, T. and MacGillivray, L. R. 2005, J. Am. Chem. Soc., 127, 14160-14161.
21. Friscic, T. and MacGillivray, L. R. 2006, Austr. J. Chem., 59, 613-616.
22. Elacqua, E., Bucar, D.-K., Skvortsova, Y., Baltrusaitis, J., Geng, M. L. and MacGillivray, L. R. 2009, Organic Letters, 11, 5106-5109.
23. Elacqua, E., Jurgens, P. T., Baltrusaitis, J. and MacGillivray, L. R. 2012, Cryst. Eng. Comm., 14, 7567-7571.
24. Stojakovic, J., Farris, B. S. and MacGillivray, L. R. 2014, Faraday Discussions (Mechanochemistry), 170, 35-40.
25. Liu, D., Ren, Z.-G., Li, H.-X., Lang, J.-P., Li, N.-Y. and Abrahams, B. F. 2010, Angew. Chem. Int. Ed. Engl., 49, 4767-4770.
26. Feeder, N. and Nakanishi, F. 1996, Mol. Cryst. Liq. Cryst. A, 276/277, 177-187.

27. Moorthy, J. N. and Venkatakrishnan, P. 2007, Cryst. Growth and Design, 7, 713-718.
28. Hasegawa, M., Saigo, K., Mori, T., Uno, H., Nohara, M. and Nakanishi, H. 1985, J. Am. Chem. Soc., 107, 2788-2793.
29. Nishimura, J., Horikoshi, Y., Wada, Y., Takahashi, H. and Sato, M. 1991, J. Am. Chem. Soc., 113, 3485-3489.
30. Nishimura, J., Horikoshi, Y., Wada, Y., Takahashi, H., Machino, S. and Oku, A. 1989, Tetrahedron Lett., 30, 5439-5442.
31 Wada, Y., Tago, T., Sugata, K. and Nishimura, J. 1992, J. Org. Chem., 57, 5955-5959.
32 Zertani, R. and Meier, H. 1986, Chem. Ber., 119, 1704-1715.
33 Meier, H. Praß, E. and Noller, K. 1988, Chem. Ber., 121, 1637-1641.
34 Shim, S. C., Lee, S. S. and Choi, S. J. 1990, Photochem. Photobiol. Sci., 51, 1-7.
35 Kim, J. H. and Sohn, S. H. 1995, J. Photoscience, 2, 99-101.
36 Müller, E., Meier, H. and Sauerbier, M. 1970, Chem. Ber., 103, 1356-1363.
37 Nakamura, Y., Hagashida, Y., Wada, Y. and Nishimura, J. 1997, Tetrahedron, 53, 4593-4600.
38 Skoric, I., Basaric, N., Marinic, Z., Visnjevac, A., Kojic-Prodic, B. and Sindler-Kulyk, M. 2005, Chem. Eur. J., 11, 543-551.
39 Vuk, D., Marinic, Z., Molcanov, K., Kojic-Prodic, B. and Sindler-Kulyk, M. 2012, Tetrahedron, 68, 6873-6880.
40. Kaupp, G., Frey, H. and Behmann, G. 1988, Chem. Ber., 121, 2135-2145.
41. Kinder, M. A. and Margaretha, P. 2000, Org. Lett., 2, 4253-4255.
42. Kinder, M. A. and Margaretha, P. 2003, Photochem. Photobiol. Sci., 2, 1220-1224.
43. Collin, P. J., Roberts, D. B., Sugowdz, G., Wells, D. and Sasse, W. H. F. 1972, Tetrahedron Lett., 13, 321-324.
44. Cheng, S. F., Chen, B., Yang, X.-J., Luo, L., Zhang, L.-P., Wu, L.-Z. and Tung, C.-H. 2014, Photochem. and Photobiol. Sci., 13, 261-265.
45. Xu, H.-X., Cheng, S.-F., Yang, X.-J., Chen, B., Chen, Y., Zhang, L.-P., Wu, L.-Z., Fang, W., Tung, C.-H. and Weiss, R. G. 2012, J. Org. Chem., 77, 1685-1692.
46. Xu, H.-X., Chen, B., Zhang, L.-P., Wu, L.-Z. and Tung, C.-H. 2011, Tetrahedron Lett., 52, 2946-2949.
47. Luo, L., Cheng, S.-F., Chen, B., Tung, C.-H. and Wu, L.-Z. 2010, Langmuir, 26, 782-785.
48. Xu, H.-X., Chen, B., Zhang, L.-P., Wu, L.-Z. and Tung, C.-H. 2009, Tetrahedron Lett., 50, 4965-4968.
49. Luo, L., Liao, G. H., Wu, X.-L., Lei, L., Tung, C.-H. and Wu, L.-Z. 2009, J. Org. Chem., 74, 3506-3515.
50. Liao, G. H., Luo, L., Xu, H.-X., Wu, X.-L., Lei, L., Tung, C.-H. and Wu, L.-Z. 2008, J. Org. Chem., 73, 7345-7348.
51. Lei, L., Luo, L., Wu, X.-L., Liao, G. H., Wu, L.-Z. and Tung, C.-H. 2008, Tetrahedron Lett., 49, 1502-1505.
52. Petermann, R., Schnorpfeil, C., Lehmann, M., Fetten, M. and Meier, H. 2000, J. Inf. Recording, 25, 259-264.
53. Wada, Y., Ishimura, T. and Nishimura, J. 1992, Chem. Ber., 125, 2155-2157..
54. Karpuk, E., Schollmeyer, D. and Meier, H. 2007, Eur. J. Org. Chem., 1983-1990.
55. Meier, H. and Karpuk, E. 2004, Tetrahedron Lett., 45, 4477-4480.
56. a) Meier, H., Prass, E., Zertani, R. and Eckes, H.-L. 1989, Chem. Ber., 122, 2139-2147; b) Takeuchi, M., Tuihiji, T. and Nishimura, J. 1993, J. Org. Chem., 58, 7388-7392.
57. a) Schnorpfeil, C., Meier, H. and Irie, M. 2001, Helv. Chim. Acta, 84, 2467-2475; b) Petermann, R., Schnorpfeil, C., Lehmann, M., Fetten, M. and Meier, H. 2000, J. Int. Record., 25, 259-264; c) Yu, R., Yakimansky, A., Voigt-Martin, I. G., Fetten, M., Schnorpfeil, C., Schollmayer, D. and Meier, H. 1999, J. Chem. Soc. Perkin Trans., 2, 1881-1890; d) Meier, H., Fetten, M., Schnorpfeil, C., Yakimansky, A. V. and Voigt-Martin, I. G. 1999, Tetrahedron Lett., 40, 4791-4794; e) Müller, K., Meier, H., Bou as-Laurent, H. and Desvergne, J. P. 1996, J. Org. Chem., 61, 5474-5480; f) Meier, H., Müller, K. and Fetten, M. 1996, J. Inform. Record. Mat., 22, 421-427; g) Meier, H. and Müller, K. 1995, Angew. Chem. Int. Ed., 34, 1437-1439.