4,15-Diamino[2.2]paracyclophane, a Reusable Template for Topochemical Reaction Control in Solution[‡]

Holger Zitt,[a] Ina Dix,[a] Henning Hopf,*[a] and Peter G. Jones[b]

Keywords: Cyclophanes / Isocyanates / Photoadditions / Reusable spacers / Topochemical control

An efficient synthesis of [2.2]paracyclophane-4,15-dicarboxylic acid (**11**) from [2.2]paracyclophane (**8**) has been developed. The diacid was converted via the diazide **14** into the 4,15-diisocyanato[2.2]paracyclophane (**15**), a versatile intermediate that could be transformed into many new *pseudo*-geminally substituted derivatives of **8**. For example, treatment of **15** with alcohols provided the carbamates **16** and **17**. On treatment of **15** with diisopropylamine, the urea **18** was obtained, whereas reduction with lithium aluminium hydride afforded the cyclic urea **20**. Hydrolysis of **15** furnished the diamine **19**, which was used as a reusable spacer in a [2+2]photoaddition experiment. Thus, treatment of **19** with *trans*-cinnamoyl chloride (**25**) provided the bis(amide) **26**, which on irradiation in acetone ring-closed to give the cyclobutane **28**. Saponification of this yielded 3,4-diphenyl-1,2-cyclobutanedicarboxylic acid (**27**, β-truxinic acid) and returned the spacer system **19**, both in quantitative yield. The X-ray structures of **15** and **20** are reported.

Introduction

In a series of classical papers on the solid-state photochemical behavior of *trans*-cinnamic acid, Schmidt and coworkers demonstrated[2−4] a relationship between the orientation of the acid in the crystal lattice and the success and the stereochemical outcome of the photoprocess. Thus, the so-called α modification of *trans*-cinnamic acid underwent head-to-tail dimerization, yielding α-truxillic acid. In contrast, the β modification provided β-truxinic acid as the result of a head-to-head [2+2]cycloaddition. Finally, γ-*trans*-cinnamic acid did not undergo photodimerization at all. By X-ray crystallographic analysis, Schmidt determined the distance between the relevant moieties of the two reacting *trans*-cinnamic acid molecules as 3.6 Å in the first two cases, whereas it was over 4.7 Å in the γ case. There was thus a critical intermolecular threshold beyond which no product-forming interaction between the two molecules took place. This so-called "topochemical principle" has also been observed for the solid-state photochemical behavior of − inter alia[4] − various styryl derivatives,[5] quinones,[6] chalcones,[7] etc. Figuratively speaking, one can equate the limiting distance of ca 3.6 Å with the "length" of a p-orbital, and it is interesting to note that comparable dimensions have also been observed in other "layered structures" (graphite: 3.4 Å, distance between the paired bases in DNA: 3.4 Å). When the crystal structures of the *trans*-cinnamic acids are dismantled, by dissolution in an organic solvent, no [2+2]cycloaddition takes place on irradiation, and only *cis*/*trans*-photoisomerization is observed. Although in principle very attractive for stereoselective synthesis, topochemical reaction control has not become very important in this field, because its two main limitations could not be overcome. The crystal structure(s) of the starting material(s) often cannot be "adjusted" to one's needs (i.e., the critical distance cannot be chosen or tuned deliberately; it has to be "accepted"), and solid-state photochemical reactions, usually being surface processes, are often cumbersome to carry out and unsatisfactory in terms of yield.

In order to overcome these limitations, we suggested several years ago the use of the [2.2]paracyclophane system as a proxy for the crystal lattice:[1] it has a layered structure (intermolecular distance between the rings ca. 3 Å, below the critical distance of 3.6 Å), it can readily be functionalized,[8−10] and substituted cyclophanes and numerous derivatives are soluble in common organic solvents. Hence, topochemical reaction control should be possible in solution, avoiding the above pitfalls of the solid state.

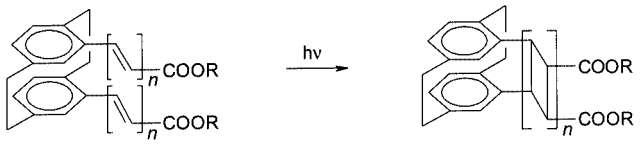
Results

To test the viability of these considerations, we prepared the cyclophane **1a** (R = CH_3), which very closely resembles

[‡] Topochemical Reaction Control in Solution, III. Part II: Ref.[1]

[a] Institut für Organische Chemie, Technische Universität Braunschweig,
Hagenring 30, 38106 Braunschweig, Germany
Fax: (internat.) +49−(0)531/391-5388
E-mail: h.hopf@tu-bs.de
[b] Institut für Anorganische und Analytische Chemie, Technische Universität Braunschweig,
Postfach 3329, 38023 Braunschweig, Germany
Fax: (internat.) +49−(0)531/391-5387
E-mail: jones@xray36.anchem.nat.tu-bs.de

Schmidt's β form of *trans*-cinnamic acid, the main difference being that the two phenyl rings are now clamped together tightly by ethano bridges. We were pleased to find that the intended intramolecular photoaddition not only yielded the cyclobutane derivative **2a** (R = CH_3) in 100% chemical yield in methanol, acetonitrile, cyclohexane, and other organic solvents, but also occurred stereospecifically and with the highest quantum yield of any cinnamic acid or ester dimerization ever studied (= 0.82 in acetonitrile at 0 °C, = 0.84 in methanol at −90 °C, Scheme 1). The free acid **1a** (R = H) and the ethyl ester (**1a**, R = C_2H_5) behaved similarly. Furthermore, on irradiation of the vinylogues of **1a**, **1b**, and **1c** (R = C_2H_5), respectively, the ladderanes **2b** and **2c** (R = C_2H_5) were produced in excellent yields (> 90% and 83%).[1,11,12] Clearly, the controlling effect of the cyclophane "lattice" extended beyond its immediate vicinity. On the other hand, irradiation of the tetraene **1d** did not afford a [7]ladderane derivative.[13]



1	n
a	1
b	2
c	3
d	4

R = H, CH_3, C_2H_5

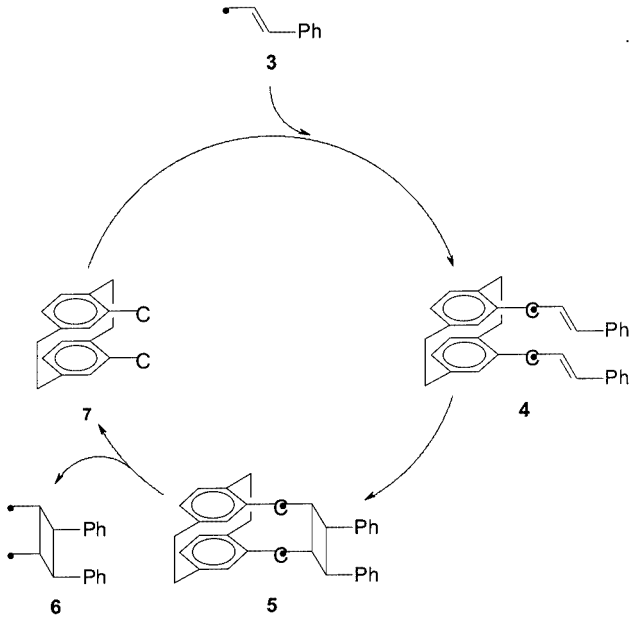
2	n	yield, %
a	1	100
b	2	> 90
c	3	83
d	4	0

Scheme 1. Photoaddition reactions in *pseudo*-geminal cinnamophanes

Although these experiments confirmed that, with a suitable scaffold, the result of solid-state photochemical reactions can be mimicked in solution,[14] they shared the common feature that the lattice (the cyclophane) and the part of the system in which the actual reaction takes place − the double bond(s) − were connected by carbon-carbon bonds, making application in synthesis impracticable,[15] since it would have to involve exclusive or preferential cleavage of the bond connecting the controlling/steering and the reacting parts of the whole system.

Any application of topochemical reaction control in solution with [2.2]cyclophanes as molecular "work-benches"[15] for preparative purposes would have to involve spacer systems with deliberately introduced breaking or detachment points. This is illustrated in symbolic form in Scheme 2 for a substrate molecule **3**, still showing some resemblance to *trans*-cinnamic acid.

In the first step, the lattice substitute **7**, bearing two reactive centers (open circles) in a *pseudo*-geminal relationship (i.e., directly opposite each other on the two benzene decks) interacts with the substrate **3** and forms the intermediate **4**. In principle, this interaction can be of any type: a covalent bond between functional groups, an ionic interaction (salt formation), a hydrogen bond, etc. With the substrate sections now in an alignment favorable for reaction, the process of interest, photoaddition in the case at hand, can take



Scheme 2. *pseudo*-Geminal [2.2]paracyclophanes as reusable spacers

place, yielding the intramolecular adduct **5**. Removal of the photoproduct **6** regenerates the spacer system **7**, ready to be used in a second cycle.

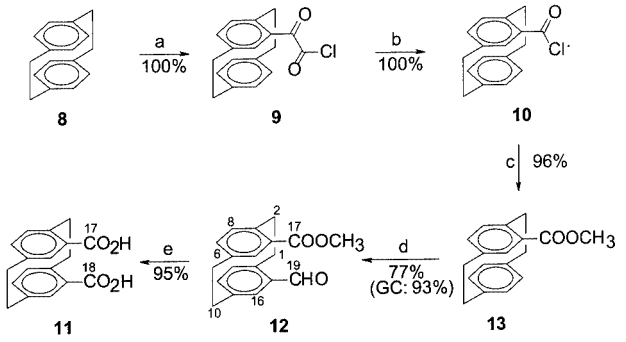
As far as functional groups are concerned, we are mostly interested in the *pseudo*-geminal diethynyl[16] and divinyl derivatives of [2.2]paracyclophane, the dicarboxylic acid, the bis(phenol),[17] and the diamine. Having prepared all of these during the last few years, we now describe in this paper the preparation, chemical properties, and the use of 4,15-diamino[2.2]paracyclophane in a cyclic process like the one described, thus for the first time demonstrating the feasibility of the above principle.

Preparation of 4,15-Diisocyanato[2.2]paracyclophane (15)

The "natural" precursor for 4,15-diamino[2.2]paracyclophane is the corresponding dinitro derivative. This was obtained in the late 1960s by Cram and Reich, by direct nitration of [2.2]paracyclophane (**8**), but the yields were so low (0.7%) that this approach had to be abandoned immediately.[18] The same authors also prepared the *pseudo*-geminal nitro-amino[2.2]paracyclophane from the parent hydrocarbon, but the yield of their five-step sequence was even worse (0.2%). Meanwhile, several amino[2.2]paracyclophanes have become available in far better yields by a novel method reported by Langer, Höcker, and co-workers,[19] but the 4,15-isomer required for this investigation was not obtained by them.

The route described here also started with the parent hydrocarbon **8**, a commercial product. This was first converted into the 4-methoxycarbonyl derivative **13**, by a procedure first described by Psiorz and Schmid,[20] which according to our experience is the best method for the functionalization of **8** known so far. As shown in Scheme 3, it

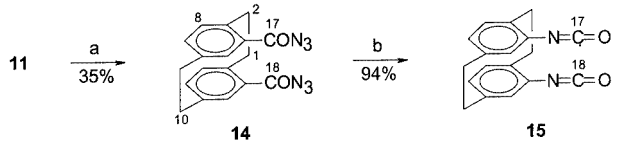
consisted first of the conversion of **8** into the keto acid chloride **9** with oxalyl chloride/aluminium trichloride.



Scheme 3. The preparation of [2.2]paracyclophane-4,15-dicarboxylic acid (**11**) from [2.2]paracyclophane (**8**); a) $(COCl)_2/AlCl_3$, −10 °C to −5 °C, 20 min; b) PhCl, Δ, 40 h; c) CH_3OH/CH_2Cl_2, Δ, 90 h; d) $TiCl_4/CH_3OCHCl_2$, $CHCl_2$, −10 ° C → room temp., 16 h; e) aq. KOH, refl., 22 h, then 35% H_2O_2, 10 °C, 20 min → 6 days, room temp.

Heating of **9** in refluxing chlorobenzene caused decarbonylation, and when the resulting acid chloride **10** was quenched with methanol, the ester **13** was obtained. The *pseudo*-geminal substitution pattern was generated by subjection of **13** to Rieche formylation with α,α-dichloromethyl methyl ether in the presence of titanium tetrachloride. Although the crude yield (as determined by GC analysis) of this step was also excellent, the *pseudo*-geminal formyl ester **12** was only isolated in 77% yield after chromatography/recrystallization. To oxidize **12** to [2.2]paracyclophane-4,15-dicarboxylic acid (**11**), various oxidation reagents were tried ($KMnO_4$, $AgNO_3$); the best yields were finally obtained with a large excess of hydrogen peroxide after **12** had been saponified to the free acid by potassium hydroxide treatment. The diacid is a known compound, having been prepared by Cram[21] and by us,[22] but by steps far less efficient than those reported here. Note that this derivative already belongs to the class of compounds discussed in general form in Scheme 2.

To introduce a nitrogen function into the ultimately required positions, **11** was next converted into the bis(keto azide) **14** by treatment first with thionyl chloride to yield the bis(acyl chloride) and then with sodium azide. The process could be interrupted at the stage of the acid chloride (a stable and isolable intermediate[13]), but could also be carried out as a one-step process as described in Scheme 4.



Scheme 4. The preparation of 4,15-diisocyanato[2.2]paracyclophane (**15**) from the diacid **11**; a) $SOCl_2$, DMF, refl., 2 h, then NaN_3, aq. acetone, 0 °C, 40 min; b) toluene, reflux, 30 min

Again, different substitution conditions were tried, and the result shown in the scheme is the optimized one. When **14** was heated in toluene it effortlessly underwent the desired double Curtius degradation, yielding 4,15-diisocyanato[2.2]paracyclophane (**15**) in practically quantitative yield. Again, this derivative was a stable solid, and single crystals of suitable quality for an X-ray structural study were obtained by sublimation (150 °C, $4\cdot10^{-3}$ Torr); the structure of **15** in the crystal is shown in Figure 1.

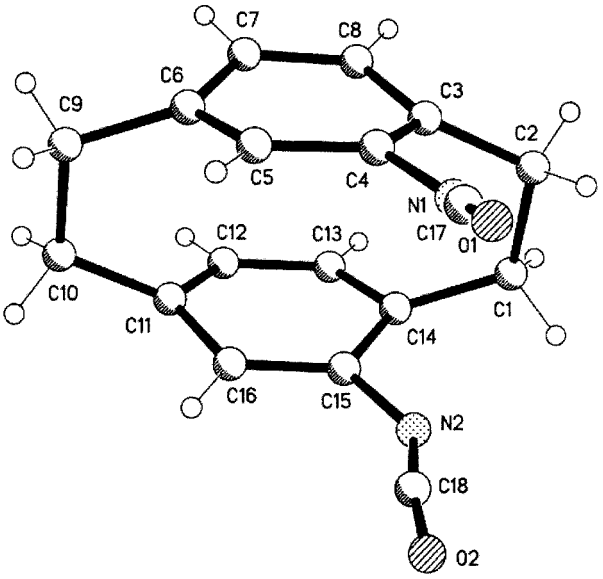


Figure 1. The molecule of compound **15** in the crystal; radii are arbitrary

The molecule displays no imposed symmetry. The cyclophane rings adopt the usual boat conformation. One isocyanate group is essentially coplanar with its ring, but the other is deflected out of plane towards the outside of the molecule (C17 by 0.55, O1 by 0.95 Å). The dimensions of the isocyanate groups, despite the risk of librational bond shortening, appear to be normal on comparison with the

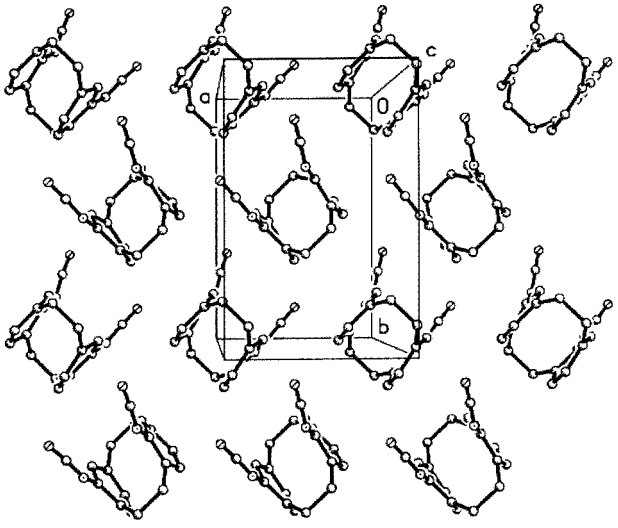


Figure 2. Packing of molecules of **15** in the crystal; H atoms are omitted for clarity; there are two such layers per *z* axis repeat

few other available data (Cambridge Database refcodes: BUBVEZ, HAMFIK, VAXRUH) for phenyl rings substituted with isocyanate: N−C 1.184, 1.196(5), C−O 1.169, 1.145(5) Å, N−C−O 170.6(5), 171.5(4)°. The crystal packing of **15** (Figure 2) involves layers of molecules with a herringbone pattern.

Several Reactions of 4,15-Diisocyanato[2.2]paracyclophane (15)

Since isocyanates display very rich preparative chemistry,[23] we thought it worthwhile to carry out some exploratory reactions with **15** before actually preparing the required diamine from it. The results of these transformations are illustrated in Scheme 5.

As expected, **15** reacted rapidly with ethanol to provide the bis(carbamate) **16** in good yield, and when the diisocyanate was treated under high dilution conditions with a diol − as a model compound we selected tetraethylene glycol − the expected intramolecular double addition took place to furnish the crown ether **17**. Since *pseudo*-geminally substituted [2.2]paracyclophanes can generally be rearranged into their *pseudo-meta* isomers, which are chiral, by heating, substrates such as **17** should in principle be usable to prepare novel chiral crown ethers. With excess diisopropylamine, **15** quantitatively provided the bis(urea) derivative **18**, again under very mild conditions (room temperature) and quickly (15 min). Since 4-isocyanato[2.2]paracyclophane had been reduced to the corresponding *N*-methylamino derivative[24] with lithium aluminium hydride, we assumed that the corresponding diamino derivative should also be preparable by hydride reduction of **15**. Surprisingly, this was not the case. As shown by its spectroscopic data (see Exp. Sect.) and X-ray crystallographic analysis (Figure 3), **15** was reduced to the cyclic urea **20** on treatment with lithium aluminium hydride in tetrahydrofuran.

As shown in Figure 3, the additional bridge in **20** does not affect the overall boat conformation of the rings, but they are no longer parallel (interplanar angle 9°). The bridge angles at nitrogen are widened to C4−N1−C17 126.7° and C15−N2−C15 127.8(2)°. The molecules are

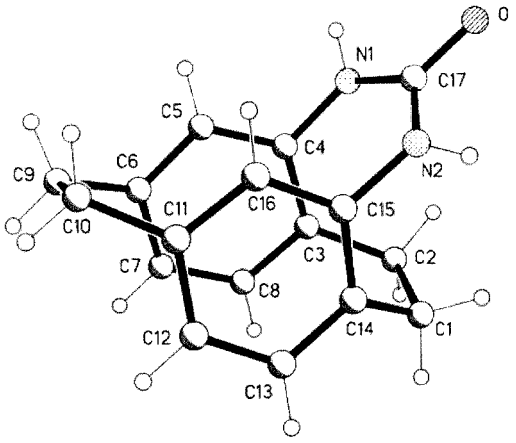
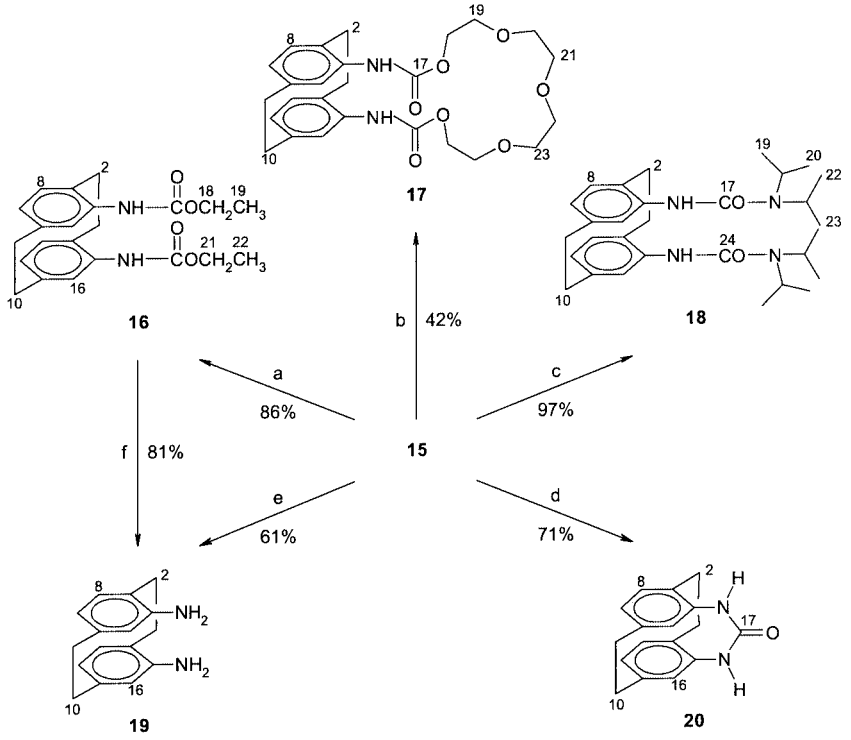


Figure 3. The molecule of compound **20** in the crystal; radii are arbitrary



Scheme 5. Various reactions of 4,15-diisocyanato[2.2]paracyclophane (**15**); a) C_2H_5OH, refl., 30 min; b) $HO(-CH_2CH_2O-)_4H$, toluene, refl., 7 days, high dilution; c) $HN(iPr)_2$, room temp., 15 min; d) $LiAlH_4$, THF, 90 min; e) toluene, HCl, refl., 2d, then KOH; f) C_2H_5OH, refl., 2 h, then aq. KOH, refl., 45 h

connected by classical hydrogen bonds N1−H01···O and N2−H02···O to form ribbons parallel to the *x* axis (Figure 4).

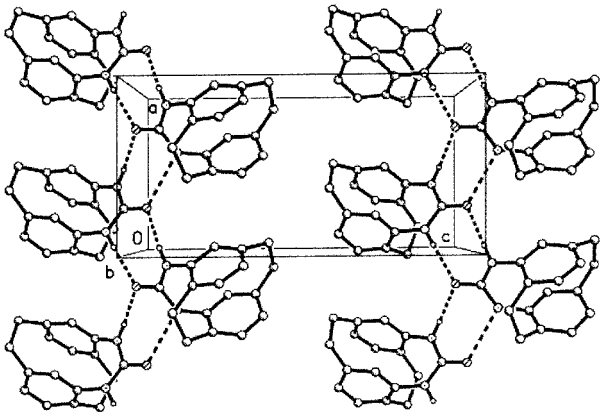
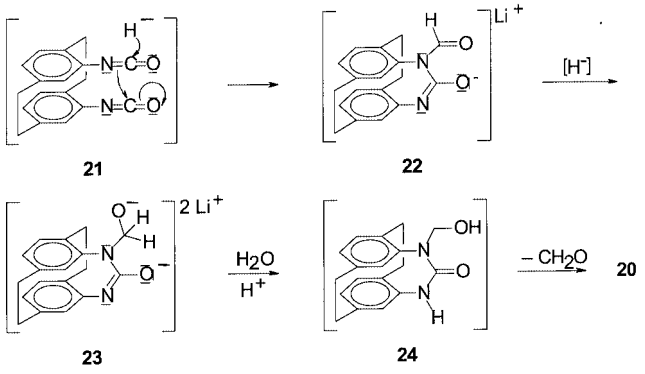


Figure 4. Packing of molecules of **20** in the crystal; H atoms (except those involved in hydrogen bonding) are omitted for clarity; hydrogen bonds are indicated by dashed lines

To explain the formation of **20**, we propose the neighboring group effect illustrated in Scheme 6. When hydride attacks the carbon center of one of the isocyanate substituents, bridging to the second NCO group occurs, resulting in the formation of the triply-bridged intermediate **22**.



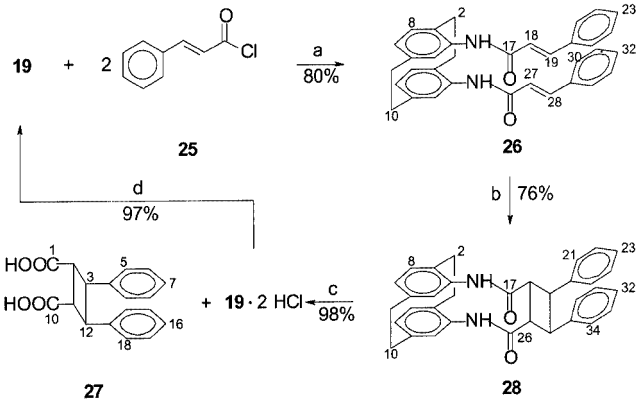
Scheme 6. The hydride reduction of **15** to the cyclic urea **20**

Further reduction provides **23**, which on hydrolysis (via the aminal **24**) and loss of formaldehyde (most probably reduced further by excess hydride reagent), yields the isolated bridged urea **20**.

Finally, the diamine **19** was obtained either by heating **15** in toluene under reflux in the presence of dilute hydrochloric acid and then liberating the free amine from the diammonium salt, or by hydrolysis of **16** with aqueous base, the bis(carbamic acid) presumably being produced as an intermediate (Scheme 5).

Use of 4,15-Diamino[2.2]paracyclophane (19) as a Reusable Template

The crucial experiment illustrating the feasibility of our general approach (Scheme 2) to employ *pseudo*-geminally functionalized [2.2]paracyclophanes as "lattice substitutes" is summarized in Scheme 7.



Scheme 7. Topochemical reaction control in solution: application of **19** as a reusable spacer for the synthesis of 3,4-diphenyl-1,2-cyclobutanedicarboxylic acid (**27**, β-truxinic acid): a) 1,4-dioxane, room temp., 24 h; b) *hν*, acetone, 7 h; c) concd. HCl, refl., 24 h; d) solid KOH

Treatment of **19** with cinnamoyl chloride (**25**) provided the unsaturated amide **26** in good yield (80%, not optimized). When this was irradiated in acetone with a 150 W medium-pressure mercury lamp, the ring-closed product **28** was produced, as confirmed spectroscopically (see Exp. Sect.), in 76% yield. The reaction was much slower than the photocyclization of the monoester **1a**. That the stereochemical information contained in **26** (both double bonds *E*-configured) was indeed not lost in the [2+2]cycloaddition step (i.e., that no *E*/*Z* photoisomerization had occurred) was finally proven by the saponification of **28** with concd. hydrochloric acid, which furnished β-truxinic acid (**27**) exclusively and in practically quantitative yield (98%). Furthermore, we were pleased to find that on neutralization of the acidic filtrate of the saponification experiment, the template molecule, 4,15-diamino[2.2]paracyclophane (**19**), was recovered in 97% yield.

Clearly, layered molecules of this type can successfully mimic the stereochemical control exerted by a crystal lattice.

Experimental Section

General Remarks: Melting points: Mel-Temp II apparatus, uncorrected. Analytical TLC: Macherey−Nagel Polygram Sil G/UV$_{254}$ and Polygram Alox N/UV$_{254}$. Column chromatography: Merck Kieselgel 60 (70−230 mesh). Analytical GC: Dani 86.10, OV-1 capillary column; 20 m. NMR: Bruker AC 200 F (^{1}H NMR: 200.1 MHz, ^{13}C NMR: 50.3 MHz) and Bruker AM 400 (^{1}H NMR: 400.1 MHz, ^{13}C NMR: 100.6 MHz). In the ^{1}H NMR spectra, the bridge protons (of the ethano bridge closer to the substituents) pointing away from the *pseudo*-geminal substituents are labeled "*a*" (anti), and "*s*" (syn) when they are oriented towards these substituents. In the ^{13}C NMR spectra the signals of the quaternary carbon atoms that could not be assigned are labeled "qC". MS: Finnigan MAT 8430 (EI, 70 eV). HRMS: by peak matching, resolution 10 000. GC/MS: Carlo Erba HRGC 5160 coupled to a Finnigan MAT

4515 (EI, 40 eV). IR: Nicolet 320 FT-IR spectrometer. UV/Vis: Hewlett Packard 8452 diode array. Elemental analyses: Institutes of Inorganic and Analytical and of Pharmaceutical Chemistry of the Technical University of Braunschweig.

Methyl [2.2]Paracyclophane-4-carboxylate (13): was prepared according to the procedure of Psiorz and Schmid.[20]

Methyl 15-Formyl[2.2]paracyclophane-4-carboxylate (12): Compound **13** (24.18 g, 0.091 mol) was placed in a three-necked 4 L flask, equipped with internal thermometer, dropping funnel, and nitrogen inlet tube, and the apparatus was flushed with nitrogen. After 1.2 L of dichloromethane had been added, the solution was cooled to −10 °C with an ice-salt bath. Over 10 min, titanium(IV) chloride (37 mL, 64.01 g, 0.337 mol) was added (formation of a brown color), followed over 5 min by α,α-dichloromethyl methyl ether (30 mL, 38.70 g, 0.338 mol). During the addition of the reagents the internal temperature was kept at −5 to −10 °C. The mixture was stirred for 16 h while the temperature was allowed to rise to room temp. After decomposition with 400 g of ice in a separating funnel, the organic phase was removed and the aqueous phase was washed with dichloromethane (2 × 200 mL). The combined organic phases were washed with sodium bicarbonate solution, water, and brine, and dried with magnesium sulfate. The solution was concentrated to ca. 100 mL and filtered through a silica gel column. After complete solvent removal, 25.30 g of an amorphous solid was obtained. According to GC analysis, this consisted of 93% of the desired **12** and three of its isomers produced as trace components. Recrystallization from cyclohexane (900 mL) yielded 19.11 g of pure crystalline **12** (needles); 1.50 g of additional product (total yield 20.61 g, 77%) was isolated from the mother liquor. Analytically pure material was obtained by high-vacuum sublimation (160 °C, $4\cdot10^{-3}$ mbar). m.p. 169 °C (cyclohexane). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 2.98−3.17 (m, 6 H, 1*a*-H, 2*a*-H, 9-H, 10-H), 3.82 (s, 3 H, 18-H), 4.08−4.20 (m, 2 H, 1*s*-H, 2*s*-H), 6.61 (d, $^3J_{8\text{-H},7\text{-H or }13\text{-H},12\text{-H}}$ = 7.8 Hz, 1 H, 8-H or 13-H), 6.64 (d, $^3J_{8\text{-H},7\text{-H or }13\text{-H},12\text{-H}}$ = 7.8 Hz, 1 H, 8-H or 13-H), 6.69 (dd, $^3J_{7\text{-H},8\text{-H or }12\text{-H},13\text{-H}}$ = 7.8, $^4J_{7\text{-H},5\text{-H or }12\text{-H},16\text{-H}}$ = 2.0 Hz, 1 H, 7-H or 12-H), 6.71 (dd, $^3J_{7\text{-H},8\text{-H or }12\text{-H},13\text{-H}}$ = 7.8, $^4J_{7\text{-H},5\text{-H or }12\text{-H},16\text{-H}}$ = 2.0 Hz, 1 H, 7-H or 12-H), 7.07 (d, $^4J_{5\text{-H},7\text{-H or }16\text{-H},12\text{-H}}$ = 2.0 Hz, 1 H, 5-H or 16-H), 7.08 (d, $^4J_{5\text{-H},7\text{-H or }16\text{-H},\ 12\text{-H}}$ = 2.0 Hz, 1 H, 5-H or 16-H), 9.92 (s, 1 H, 19-H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 31.1, 35.0 (C-1, C-2), 34.6, 34.7 (C-9, C-10), 51.9 (C-18), 130.8 (qC), 133.7, 134.4 (C-5, C-16), 135.7, 136.1 (C-8, C-13), 136.0, 138.1 (C-7, C-12), 136.5 (qC), 139.7 (qC), 140.1 (qC), 142.1 (qC), 143.5 (qC), 167.0 (C-17), 190.6 (C-19) ppm. IR (KBr): $\tilde{\nu}$ = 3475 cm^{-1} (w), 3454 (w), 3026 (w), 2943 (m), 2936 (m), 1711 (vs), 1683 (s), 1433 (m), 1290 (m), 1274 (s), 1199 (m), 1074 (s), 983 (w). UV/Vis (MeCN): λ_{max} (lg ε) = 252 nm (4.10), 310 (3.40). MS (EI, 70 eV)**:** *m*/*z* (%) = 294 (100) [M^+], 267 (11), 266 (56), 263 (10), 236 (12), 163 (10), 162 (72), 147 (25), 133 (42), 132 (33), 119 (22), 105 (10), 104 (39), 103 (20), 78 (10), 77 (15). $C_{19}H_{18}O_3$ (294.33): calcd. C 77.53, H 6.16; found C 77.48, H 6.27.

[2.2]Paracyclophane-4,15-dicarboxylic Acid (11): A suspension of **12** (15.00 g, 51 mmol) in potassium hydroxide solution (1 M, 1.5 L) was heated under reflux for 22 h. After the mixture had been cooled to 10 °C, a H_2O_2 solution (35%, 200 g, 2.05 mol) was added over 20 min, and the mixture was kept at room temp. for 6 days. It was cooled again (ice-water bath) and acidified with concd. hydrochloric acid. The precipitate was removed by filtration, washed with water, and dried at 100 °C in a drying oven, to give 14.36 g (95%) of an amorphous, colorless solid. m.p. 336−342 °C (ref.: 335−340 °C[21]). ^{1}H NMR (400.1 MHz, [D$_6$]DMSO): δ = 2.92−2.96 (m, 2 H, 1*a*-H, 2*a*-H), 3.02−3.05 (m, 4 H, 9-H, 10-H), 4.04−4.08 (m, 2 H, 1*s*-H, 2*s*-H), 6.65 (d, $^3J_{8\text{-H},7\text{-H}}$ = $^3J_{13\text{-H},12\text{-H}}$ = 7.7 Hz, 2 H, 8-H, 13-H), 6.70 (dd,$^3J_{7\text{-H},8\text{-H}}$ = $^3J_{12\text{-H},13\text{-H}}$ = 7.7, $^4J_{7\text{-H},5\text{-H}}$ = $^4J_{12\text{-H},16\text{-H}}$ = 1.8 Hz, 2 H, 7-H, 12-H), 7.03 (d, $^4J_{5\text{-H},7\text{-H}}$ = $^4J_{16\text{-H},12\text{-H}}$ = 1.8 Hz, 2 H, 5-H, 16-H), 12.19 (br. s, COOH) ppm. ^{13}C NMR (100.6 MHz, [D$_6$]DMSO): δ = 34.0 (C-1, C-2), 34.2 (C-9, C-10), 131.0 (qC), 133.8, 135.9, 136.3 (C-5, C-16, C-7, C-12, C-8, C-13), 139.3 (qC), 142.2 (qC), 167.5 (C-17, C-18) ppm. IR (KBr): $\tilde{\nu}$ = 3435 cm^{-1} (m), 3429 (m), 3148 (m), 3135 (m), 3127 (m), 3048 (m), 3018 (m), 3011 (m), 2967 (m), 2879 (m), 2870 (m), 2857 (m), 1688 (vs), 1649 (m), 1639 (m), 1594 (m), 1558 (m), 1489 (m), 1435 (m), 1419 (m), 1401 (m), 1310 (s), 1297 (s), 1277 (s), 1212 (m), 931 (m), 909 (m). UV/Vis (MeCN): λ_{max} (lg ε) = 240 nm (4.05), 306 (3.20). MS (EI, 70 eV): *m*/*z* (%) = 296 (5) [M^+], 279 (21), 278 (100), 149 (20), 148 (40), 131 (44), 105 (13), 104 (12), 91 (11). $C_{18}H_{16}O_4$ (296.31): calcd. C 72.96, H 5.44; found C 72.82, H 5.46.

[2.2]Paracyclophane-4,15-dicarbonyl Diazide (14): A solution of sodium azide (11.12 g, 0.171 mol) in 85 mL of water was added over 45 min to a suspension of [2.2]paracyclophane-4,15-dicarbonyl dichloride (5.70 g, 0.017 mol) in acetone (100 mL), prepared from **11** and thionyl chloride according to ref.[13] After the mixture had been stirred for 1 h, ice water (500 mL) was added, and the precipitate was removed by filtration through a glass frit. The pale yellow solid was washed with water and dried in a desiccator over phosphorus pentoxide: 5.71 g (96%) of **14** as pale yellow microcrystals. m.p. 102 °C (decomp). ^{1}H NMR (400.1 MHz, [D$_6$]DMSO): δ = 3.08−3.12 (m, 6 H, 1*a*-H, 2*a*-H, 9-H, 10-H), 3.99−4.11 (m, 2 H, 1*s*-H, 2*s*-H), 6.79 (d, $^3J_{8\text{-H},7\text{-H}}$ = $^3J_{13\text{-H},12\text{-H}}$ = 7.8 Hz, 2 H, 8-H, 13-H), 6.87 (dd, $^3J_{7\text{-H},8\text{-H}}$ = $^3J_{12\text{-H},13\text{-H}}$ = 7.8, $^4J_{7\text{-H},5\text{-H}}$ = $^4J_{12\text{-H},16\text{-H}}$ = 1.8 Hz, 2 H, 7-H, 12-H), 7.10 (d, $^4J_{5\text{-H},7\text{-H}}$ = $^4J_{16\text{-H},12\text{-H}}$ = 1.8 Hz, 2 H, 5-H, 16-H) ppm. ^{13}C NMR (100.6 MHz, [D$_6$]DMSO): δ = 33.4, 33.9 (C-1, C-2, C-9, C-10), 129.9 (qC), 133.7, 136.7, 138.3 (C-5, C-16, C-7, C-12, C-8, C-13), 140.2 (qC), 142.7 (qC), 172.2 (C-17, C-18) ppm. IR (KBr): $\tilde{\nu}$ = 3457 cm^{-1} (w), 3444 (w), 3424 (w), 3147 (w), 2941 (m), 2858 (w), 2271 (m), 2141 (vs), 1686 (s), 1671 (s), 1260 (s), 1191 (vs), 1158 (s), 1135 (m), 997 (s), 917 (m). UV/Vis (MeCN): λ_{max} (lg ε) = 308 nm (3.44), 268 (4.16), 216 (4.52), 192 (4.43). MS (EI, 70 eV): *m*/*z* (%) = 346 (2) [M^+], 290 (9), 263 (11), 144 (15), 145 (100), 131 (25), 116 (12), 90 (13). HR-MS ($M^+ - N_2$): calcd. 311.1117; found 311.1117±2 ppm.

4,15-Diisocyanato[2.2]paracyclophane (15): A solution of **14** (4.23 g, 0.012 mol) in 150 mL of anhydrous toluene was heated at reflux for 30 min under nitrogen. At ca. 95 °C, gas evolution set in. After the solvent had been removed in vacuo, 3.32 g (94%) of an ochre-colored solid was obtained. An analytically pure sample (colorless needles) was obtained by high-vacuum sublimation (150 °C, $4\cdot10^{-3}$ mbar); m.p. 153 °C. ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 2.89−2.97 (m, 2 H, 1*a*-H, 2*a*-H), 2.99−3.08 (m, 4 H, 9-H, 10-H), 3.50−3.54 (m, 2 H, 1*s*-H, 2*s*-H), 6.26 (d, $^4J_{5\text{-H},7\text{-H}}$ = $^4J_{16\text{-H},12\text{-H}}$ = 1.6 Hz, 2 H, 5-H, 16-H), 6.43 (dd, $^3J_{7\text{-H},8\text{-H}}$ = $^3J_{12\text{-H},13\text{-H}}$ = 7.9, $^4J_{7\text{-H},5\text{-H}}$ = $^4J_{12\text{-H},16\text{-H}}$ = 1.6 Hz, 2 H, 7-H, 12-H), 6.48 (d, $^3J_{8\text{-H},7\text{-H}}$ = $^3J_{13\text{-H},12\text{-H}}$ = 7.9 Hz, 2 H, 8-H, 13-H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 31.0 (C-1, C-2), 34.7 (C-9, C-10), 130.1 (C-5, C-16), 130.8 (C-7, C-12), 132.4 (qC), 133.6 (qC), 135.1 (C-8, C-13), 141.1 (qC) ppm; the carbon atoms of NCO groups were unresolved. IR (KBr): $\tilde{\nu}$ = 3452 cm^{-1} (w), 2856 (w), 2358 (w), 2283 (vs), 1591 (w), 1560 (w), 1070 (w), 882 (w). UV/Vis (MeCN): λ_{max} (lg ε) = 236 nm (4.19), 204 (4.69). MS (EI, 70 eV): *m*/*z* (%) = 290 (32) [M^+], 146 (10), 145 (100), 90 (8), 89 (4). $C_{18}H_{14}N_2O_2$ (290.31): calcd. C 74.47, H 4.86, N 9.65; found C 74.31, H 4.91, N 9.32.

Bis(carbamate) 16: A suspension of **15** (0.150 g, 0.52 mmol) in 25 mL of ethanol was heated under reflux for 30 min. The clear solution was cooled to room temp. and the solvent was removed in

vacuo. The resulting solid was purified by column chromatography on silica gel (dichloromethane/ethyl acetate = 1:1) to give 0.17 g (86%) of **16** as a colorless, amorphous solid. m.p. 178 °C. ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 1.32 (t, $^3J_{19\text{-H},18\text{-H}} = {}^3J_{22\text{-H},21\text{-H}}$ = 7.2 Hz, 6 H, 19-H, 22-H), 2.85−2.90 (m, 2 H, 1*a*-H, 2*a*-H), 2.97−3.03 (m, 4 H, 9-H, 10-H), 3.29−3.34 (m, 2 H, 1*s*-H, 2*s*-H), 4.23 (q, $^3J_{18\text{-H},19\text{-H}} = {}^3J_{21\text{-H},22\text{-H}}$ = 7.2 Hz, 4 H, 18-H, 21-H), 6.42 (dd, $^3J_{7\text{-H},8\text{-H}} = {}^3J_{12\text{-H},13\text{-H}}$ = 7.8, $^4J_{7\text{-H},5\text{-H}} = {}^4J_{12\text{-H},16\text{-H}}$ = 1.8 Hz, 2 H, 7-H, 12-H), 6.51 (d, $^3J_{8\text{-H},7\text{-H}} = {}^3J_{13\text{-H},12\text{-H}}$ = 7.8 Hz, 2 H, 8-H, 13-H), 6.59 (ps-s, 2 H, 5-H, 16-H), 6.88 (br. s, 2 H, NH) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 14.6 (C-19, C-22), 31.5 (C-1, C-2), 34.7 (C-9, C-10), 61.2 (C-18, C-21), 125.4 (C-5, C-16), 130.0 (C-7, C-12), 131.6 (qC), 134.0 (qC), 135.2 (C-8, C-13), 140.0 (qC), 154.7 (C-17, C-20) ppm. IR (KBr): $\tilde{\nu}$ = 3304 cm^{-1} (s), 3057 (w), 3039 (w), 2931 (m), 1727 (vs), 1687 (vs), 1532 (m), 1493 (s), 1423 (m), 1382 (m), 1337 (s), 1226 (s), 1066 (s), 897 (w). UV/Vis (EtOH): λ_{max} (lg ε) = 236 nm (4.19), 208 (4.67). MS (EI, 70 eV): *m*/*z* (%) = 382 (44) [M$^+$], 337 (5), 336 (14), 307 (10), 192 (15), 191 (62), 174 (9), 163 (20), 146 (26), 145 (100), 119 (19), 91 (18). $C_{22}H_{26}N_2O_4$ (382.45): calcd. 69.09, H 6.85, N 7.33; found C 69.05, H 6.89, N 7.14.

Crown Ether 17: A solution of **15** (0.200 g, 0.69 mmol) in 100 mL of anhydrous toluene was placed in a 250-mL flask equipped with a reflux condenser and a septum. The mixture was heated to reflux, and tetraethylene glycol (0.140 g, 0.72 mmol) in 42 mL of toluene was added by motor-driven syringe at 1.5 mL·h^{-1}. When addition was complete, the mixture was heated at reflux for 7 days. After the mixture had cooled to room temp., the solvent was removed in vacuo, and the remaining light-brown oil, dissolved in a few mL of ethyl acetate, was purified by column chromatography on silica gel with ethyl acetate to give 0.140 g (42%) of **17** as a colorless solid. m.p. 119−120 °C. ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 2.84−2.89 (m, 2 H, 1*a*-H, 2*a*-H), 2.93−3.03 (m, 4 H, 9-H, 10-H), 3.26−3.31 (m, 2 H, 1*s*-H, 2*s*-H), 3.67−3.76 (m, 8 H, 20-H, 21-H, 22-H, 23-H), 3.79−3.81 (m, 4 H, 19-H, 24-H), 4.28−4.36 (m, 4 H, 18-H, 25-H), 6.39 (dd, $^3J_{7\text{-H},8\text{-H}} = {}^3J_{12\text{-H},13\text{-H}}$ = 7.8, $^4J_{7\text{-H},5\text{-H}} = {}^4J_{12\text{-H},16\text{-H}}$ = 1.6 Hz, 2 H, 7-H, 12-H), 6.49 (d, $^3J_{7\text{-H},8\text{-H}} = {}^3J_{12\text{-H},13\text{-H}}$ = 7.8 Hz, 2 H, 5-H, 16-H), 6.55 (d, $^4J_{7\text{-H},5\text{-H}} = {}^4J_{12\text{-H},16\text{-H}}$ = 1.6 Hz, 2 H, 7-H, 12-H), 6.99 (br. s, 2 H, NH) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 31.4 (C-1, C-2), 34.8 (C-9, C-10), 64.7 (C-18, C-25), 69.6 (C-19, C-24), 70.8 (C-20, C-23), 70.9 (C-21, C-22), 125.5 (C-5, C-16), 130.1 (C-7, C-12), 131.4 (qC), 135.2 (C-8, C-13), 140.0 (qC), 154.5 (C-17, C-26) ppm; one quaternary carbon atom was unresolved. IR (KBr): $\tilde{\nu}$ = 3434 cm^{-1} (s), 3429 (s), 2928 (s), 2900 (s), 2894 (s), 2858 (s), 1732 (vs), 1702 (s), 1637 (m), 1617 (m), 1600 (s), 1572 (s), 1533 (vs), 1492 (s), 1456 (s), 1439 (m), 1422 (m),1289 (s), 1229 (vs), 1189 (w), 1129 (s), 1102 (s), 1072 (s). UV/Vis (MeCN): λ_{max} (lg ε) = 236 nm (4.18, sh), 272 (3.35). MS (EI, 70 eV): *m*/*z* (%) = 484 (100) [M$^+$], 469 (6), 397 (6), 396 (21), 352 (22), 308 (13), 290 (13), 280 (14), 191 (22), 190 (87), 189 (19), 147 (10), 146 (79), 145 (80), 120 (22), 119 (38), 117 (10), 91 (22), 89 (26), 45 (42). $C_{26}H_{32}N_2O_7$ (484.45): calcd. C 64.45, H 6.66, N 5.78; found C 64.51, H 6.80, N 5.53.

Bis(amide) 18: A sample of **15** (0.154 g, 0.53 mmol) was stirred at room temp. with freshly distilled diisopropylamine. As shown by TLC analysis, the reaction was over after 15 min. Removal of excess amine in vacuo (first by rotary evaporation, then under high vacuum) yielded 0.252 g (97%) of **18** as a colorless, amorphous solid. Column chromatography on silica gel with dichloromethane/ethyl acetate (10:1) provided analytically pure material. m.p. 126 °C. ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 1.24 (d, $^3J_{19\text{-H or 20-H},18\text{-H}} = {}^3J_{22\text{-H or 23-H},21\text{-H}} = {}^3J_{26\text{-H or 27-H},25\text{-H}} = {}^3J_{29\text{-H or 30-H},28\text{-H}}$ = 6.8 Hz, 12 H, 19-H, 22-H, 26-H, 29-H or 20-H, 23-H, 27-H, 30-H), 1.33 (d, $^3J_{20\text{-H or 19-H},18\text{-H}} = {}^3J_{23\text{-H or 22-H},21\text{-H}} = {}^3J_{27\text{-H or 26-H},25\text{-H}} = {}^3J_{30\text{-H or 29-H},28\text{-H}}$ = 6.8 Hz, 12 H, 20-H, 23-H, 27-H, 30-H or 19-H, 22-H, 26-H, 29-H), 2.85−2.90 (m, 2 H, 1*a*-H, 2*a*-H), 2.95−3.00 (m, 4 H, 9-H, 10-H), 3.35−3.40 (m, 2 H, 1*s*-H, 2*s*-H), 3.93 (sept, $^3J_{18\text{-H},19\text{-H},20\text{-H}} = {}^3J_{21\text{-H},22\text{-H},23\text{-H}} = {}^3J_{25\text{-H},26\text{-H},27\text{-H}} = {}^3J_{28\text{-H},29\text{-H},30\text{-H}}$ = 6.2 Hz, 4 H, 18-H, 21-H, 25-H, 28-H), 6.37 (dd, $^3J_{7\text{-H},8\text{-H}} = {}^3J_{12\text{-H},13\text{-H}}$ = 7.7, $^4J_{7\text{-H},5\text{-H}} = {}^4J_{12\text{-H},16\text{-H}}$ = 1.8 Hz, 2 H, 7-H, 12-H), 6.46 (d, $^4J_{7\text{-H},5\text{-H}} = {}^4J_{12\text{-H},16\text{-H}}$ = 1.8 Hz, 2 H, 8-H, 13-H), 6.51 (d, $^3J_{7\text{-H},8\text{-H}} = {}^3J_{12\text{-H},13\text{-H}}$ = 7.7 Hz, 2 H, 5-H, 16-H), 6.74 (br. s, 2 H, NH) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 21.2, 22.1 (C-20, C-23, C-27, C-30, C-19, C-22, C-26, C-29), 32.1 (C-1, C-2), 34.7 (C-9, C-10), 45.5 (C-18, C-21, C-25, C-28), 125.9 (C-5, C-16), 129.5 (C-7, C-12), 133.1 (qC), 134.9 (C-8, C-13), 137.0 (qC), 139.6 (qC), 156.2 (C-17, C-24) ppm. IR (KBr): $\tilde{\nu}$ = 3568 cm^{-1} (w), 3530 (w), 3502 (m), 3474 (m), 3465 (m), 3448 (m), 3442 (m), 3434 (m), 3427 (m), 3413 (m), 1677 (vs), 1665 (s), 1614 (vs), 1576 (m), 1448 (s), 1326 (m), 1031 (vs), 1017 (vs), 998 (s), 974 (m), 884 (m), 767 (s), 754 (s), 719 (m), 691 (s). UV/Vis (MeCN): λ_{max} (lg ε) = 274 nm (3.55, sh), 246 (4.20), 216 (4.56), 192 (4.51). MS (EI, 70 eV): *m*/*z* (%) = 492 (68) [M$^+$], 450 (9), 449 (26), 393 (11), 391 (41), 348 (61), 291 (12), 265 (10), 246 (30), 204 (14), 146 (24), 145 (30), 128 (27), 120 (14), 119 (41), 100 (38), 91 (15), 86 (88), 58 (19), 44 (30), 43 (100). $C_{30}H_{44}N_4O_2$ (492.69): calcd. C 73.13, H 9.00, N 11.37; found C 73.14, H 8.93, N 11.29.

[2.2]Paracyclophane-4,15-diamine (19). Variant A: Concd. hydrochloric acid (50 mL) was added to a suspension of **15** (1.06 g, 3.7 mmol) in 50 mL of toluene, and the mixture was heated under reflux with vigorous stirring for 48 h. After the two-phase mixture had cooled to room temp., the aqueous phase was separated and the organic phase was extracted three times with 100 mL portions of concd. hydrochloric acid. The combined aqueous phases were cooled in a ice-water bath, after which potassium hydroxide solution was added until the mixture was basic. The precipitated brown material was removed by filtration, washed with water, and dried under vacuum in a desiccator over phosphorus pentoxide: 0.54 g (61%) of the ochre-colored **19**. m.p. 205 °C.

Variant B: A sample of **15** (7.11 g, 0.025 mol) was suspended in 400 mL of ethanol, and the mixture was heated under reflux for 2 h. Aqueous potassium hydroxide solution (20%, 40 mL) was added, and the brown suspension was heated under reflux for 45 h. The cooled reaction mixture was poured into 600 mL of ice-cold potassium hydroxide solution (20%), and the precipitated light brown solid was filtered off through a glass frit. The filtrate was concentrated in a rotary evaporator, yielding additional product. The combined precipitates were washed with water and dried in a desiccator over phosphorus pentoxide to provide 4.73 g (81%) of **19**.

An analytically pure sample was obtained by recrystallization from ethanol, colorless needles, m.p. 203 °C (EtOH). ^{1}H NMR (400.1 MHz, [D$_6$]DMSO): δ = 2.65−2.69 (m, 2 H, 1*a*-H, 2*a*-H), 2.74−2.84 (m, 4 H, 9-H, 10-H), 3.33−3.37 (m, 2 H, 1*s*-H, 2*s*-H), 4.53 (br. s, 4 H, NH_2; exchangeable with D_2O), 5.81 (dd, $^3J_{7\text{-H},8\text{-H}} = {}^3J_{12\text{-H},13\text{-H}}$ = 7.5, $^4J_{7\text{-H},5\text{-H}} = {}^4J_{12\text{-H},16\text{-H}}$ = 1.7 Hz, 2 H, 7-H, 12-H), 5.84 (d, $^4J_{5\text{-H},7\text{-H}} = {}^4J_{16\text{-H},12\text{-H}}$ = 1.7 Hz, 2 H, 5-H, 16-H), 6.16 (d, $^3J_{8\text{-H},7\text{-H}} = {}^3J_{13\text{-H},12\text{-H}}$ = 7.5 Hz, 2 H, 8-H, 13-H) ppm. ^{13}C NMR (100.6 MHz, [D$_6$]DMSO): δ = 29.8 (C-1, C-2), 35.0 (C-9, C-10), 121.7 (C-7, C-12), 123.1 (C-3, C-14), 123.4 (C-5, C-16), 134.7 (C-8, C-13), 139.5 (C-6, C-11), 147.6 (C-4, C-15) ppm. IR (KBr): $\tilde{\nu}$ = 3456 cm^{-1} (s), 3450 (s), 3442 (s), 3406 (s), 3399 (s), 3375 (s), 3350 (s), 3336 (s), 3218 (m), 2926 (vs), 2852 (m), 1715 (w), 1654 (s), 1624 (vs), 1597 (s), 1566 (s), 1542 (m), 1499 (s), 1456 (m),

1427 (vs), 1287 (m), 879 (m), 773 (m), 755 (m). UV/Vis (MeCN): λ_{max} (lg ε) = 248 nm (3.88), 312 (3.28). MS (EI, 70 eV): *m/z* (%) = 238 (45) [M^+], 120 (10), 119 (100), 92 (6), 91 (8). $C_{16}H_{18}N_2$ (238.32): calcd. C 80.63, H 7.61, N 11.75; found C 80.13, H 7.52, N 11.63.

1,3-Diaza-[3.2.2](1,2,5)(1,2,5)cyclophan-2-one (20): A suspension of **15** (0.500 g, 1.7 mmol) in 100 mL of THF was added over 15 min, at reflux temperature and under nitrogen, to a suspension of lithium aluminium hydride (0.270 g, 7.1 mmol) in 50 mL of anhydrous THF. The reaction mixture was heated for an additional 80 min and then allowed to cool to room temp., and the excess hydride reagent was destroyed by addition of water (20 mL). The precipitated inorganic salts were brought into solution by addition of 10 mL of 2 M sulfuric acid, 200 mL of dichloromethane was added, and after phase separation, the inorganic phase was washed thoroughly with dichloromethane. The combined organic phases were washed with bicarbonate solution, water, and brine, and dried with magnesium sulfate. After solvent removal in a rotary evaporator, the remaining solid was dried under high vacuum to provide 0.32 g (71%) of **20**, amorphous, off-white solid that did not melt below 200 °C. ^{1}H NMR (200.1 MHz, [D$_6$]DMSO): δ = 2.74−2.88 (m, 2 H, 1*a*-H, 2*a*-H), 2.88−3.12 (m, 4 H, 9-H, 10-H), 3.33−3.45 (m, 2 H, 1*s*-H, 2*s*-H), 6.31 (dd, $^3J_{7\text{-H},8\text{-H}} = {}^3J_{12\text{-H},13\text{-H}} = 7.9$, $^4J_{7\text{-H},5\text{-H}} = {}^4J_{12\text{-H},16\text{-H}} = 1.7$ Hz, 2 H, 7-H, 12-H), 6.43 (d, $^3J_{8\text{-H},7\text{-H}} = {}^3J_{13\text{-H},12\text{-H}} = 7.9$ Hz, 2 H, 8-H, 13-H), 6.50 (d, $^4J_{5\text{-H},7\text{-H}} = {}^4J_{16\text{-H},12\text{-H}} = 1.7$ Hz, 2 H, 5-H, 16-H), 7.81 (br. s, 2 H, NH) ppm. ^{13}C NMR (50.3 MHz, [D$_6$]DMSO): δ = 31.4 (C-1, C-2), 35.0 (C-9, C-10), 131.6, 133.8, 137.9 (C-5, C-16, C-7, C-12, C-8, C-13), 138.4 (qC), 138.5 (qC), 141.1 (qC), 154.2 (C-17) ppm. IR (KBr): $\tilde{\nu}$ = 3427 cm^{-1} (m), 3422 (m), 3326 (m), 3281 (m), 3271 (m), 3223 (m), 3055 (m), 2935 (m), 2361 (m), 2343 (m), 2333 (m), 1654 (vs, C=O), 1598 (m), 1560 (m), 1486 (m), 1471 (m), 1452 (m), 1439 (m), 1257 (m), 1231 (m), 1159 (m), 1095 (m), 790 (m), 755 (m). MS (EI, 70 eV): *m/z* (%) = 264 (100) [M^+], 263 (20), 249 (31), 247 (13), 234 (9), 145 (9), 119 (37), 92 (5), 91 (11). $C_{17}H_{16}N_2O$ (264.34): calcd. C 77.25, H 6.10, N 10.60; found C 77.27, H 6.11, N 10.82.

Bis(amide) 26: A solution of *trans*-cinnamoyl chloride (0.427 g, 2.6 mmol) in 5 mL of dioxane was added under nitrogen to a suspension of **19** (0.310 g, 1.3 mmol) in 30 mL of anhydrous dioxane. The mixture was stirred for 24 h at room temp, the solvent was removed in vacuo, and the residue was dissolved in 50 mL of dichloromethane. The resulting green suspension was filtered through a glass frit, and the precipitate was washed with 50 mL of dichloromethane and then dried under high vacuum to provide 0.104 g of a grayish solid. The solvent was removed from the filtrate in vacuo, and the residue was taken up in hot ethanol (5 mL). After the solution had cooled to room temp., pentane was added, and the precipitate thus formed was removed by filtration and dried, yielding an additional 0.262 g of **26**. Finally, when the solvent from the mother liquor of this last purification step was removed and the resulting residue purified by chromatography on silica gel (dichloromethane/diethyl ether = 10:1), an additional 0.150 g of product resulted, providing a total yield of 0.516 g (80%) of **26**. An analytically pure sample was obtained by recrystallization (colorless plates) from acetone. m.p. 142 °C (decomp.). ^{1}H NMR (400.1 MHz, [D$_6$]acetone): δ = 2.77−2.88 (m, 2 H, 1*a*-H, 2*a*-H), 3.00−3.11 (m, 4 H, 9-H, 10-H), 3.32−3.43 (m, 2 H, 1*s*-H, 2*s*-H), 6.50 (dd, $^3J_{7\text{-H},8\text{-H}} = {}^3J_{12\text{-H},13\text{-H}} = 7.9$, $^4J_{7\text{-H},5\text{-H}} = {}^3J_{12\text{-H},16\text{-H}} = 1.8$ Hz, 2 H, 7-H, 12-H), 6.57 (d, $^3J_{8\text{-H},7\text{-H}} = {}^3J_{13\text{-H},12\text{-H}} = 7.9$ Hz, 2 H, 8-H, 13-H), 6.74 (d, $^4J_{5\text{-H},7\text{-H}} = {}^3J_{16\text{-H},12\text{-H}} = 1.8$ Hz, 2 H, 5-H, 16-H), 6.85 (d, $^3J_{18\text{-H},19\text{-H}} = {}^3J_{27\text{-H},28\text{-H}} = 15.5$ Hz, 2 H, 18-H, 27-H), 7.19−7.22 (m, 4 H, 22-H, 24-H, 31-H, 33-H), 7.28−7.33 (m, 2 H, 23-H, 32-H), 7.52−7.54 (m, 4 H, 21-H, 25-H, 30-H, 34-H), 7.81 (d, $^3J_{19\text{-H},18\text{-H}} = {}^3J_{28\text{-H},27\text{-H}} = 15.5$ Hz, 2 H, 19-H, 28-H) ppm. ^{13}C NMR (100.6 MHz, [D$_6$]acetone): δ = 32.1 (C-1, C-2), 34.7 (C-9, C-10), 120.7 (C-18, C-27), 127.0 (C-5, C-16), 128.1 (qC), 128.7 (C-7, C-12), 129.8, 130.8 (C-21, C-22, C-24, C-25, C-30, C-31, C-33, C-34), 133.2 (C-23, C-32), 134.4 (C-8, C-13), 134.7 (qC), 135.5 (qC), 139.9 (qC), 142.4 (C-19, C-28), 164.9 (C-17, C-26) ppm. IR (KBr): $\tilde{\nu}$ = 3433 cm^{-1} (m), 3423 (m), 3239 (s), 3059 (m), 3028 (m), 2972 (m), 2956 (m), 2929 (s), 2853 (m), 1670 (vs), 1658 (vs), 1628 (vs), 1612 (vs), 1600 (s), 1577 (m), 1564 (s), 1535 (vs), 1490 (s), 1448 (s), 1439 (m), 1417 (s), 1340 (vs), 1205 (s), 1197 (s), 1165 (m), 989 (m), 981 (m), 969 (m), 889 (m), 862 (m), 792 (m), 758 (s). UV/Vis (MeCN): λ_{max} (lg ε) = 220 nm (4.63, sh), 276 (4.66), 300 (4.51, sh). UV/Vis (MeOH): λ_{max} (lg ε) = 208 nm (4.67), 220 (4.62), 280 (4.68), 290 (4.65, sh). MS (EI, 70 eV): *m/z* (%) = 498 (63) [M^+], 469 (8), 408 (9), 407 (32), 368 (20), 367 (24), 251 (8), 249 (19), 248 (35), 220 (18), 158 (16), 145 (13), 130 (11), 131 (100), 120 (14), 119 (17), 103 (48), 91 (22), 77 (15). $C_{34}H_{30}N_2O_2$): (498.60): calcd. C 81.90, H 6.06, N 5.62; found C 81.95, H 6.08, N 5.49.

Cyclobutane Derivative 28: In a photoreactor, acetone (200 mL) was purged of oxygen by a rapid stream of nitrogen. After 15 min, **26** (0.45 g, 0.9 mmol) was added under nitrogen. The solution was irradiated for 7 h, through a Pyrex filter, and after completion of the photoaddition the solvent was removed in vacuo. The residue was purified by column chromatography on silica gel (dichloromethane/diethyl ether = 10:1) to provide 0.34 g (76%) of a colorless, amorphous solid. Analytically pure **28** was obtained by recrystallization from methanol/methyl isobutyl ketone = 9:1 (colorless plates). m.p. 230 °C (decomp.). ^{1}H NMR (400.1 MHz, [D$_6$]acetone): δ = 2.95−3.07 (m, 6 H, 1*a*-H, 2*a*-H, 9-H, 10-H), 3.68−3.72 (m, 2 H, 1*s*-H, 2*s*-H), 4.36−4.38 (m, 2 H, 18-H, 27-H), 4.66−4.67 (m, 2 H, 19-H, 28-H), 6.34 (dd, $^3J_{7\text{-H},8\text{-H}} = {}^3J_{12\text{-H},13\text{-H}} = 7.8$, $^4J_{7\text{-H},5\text{-H}} = {}^3J_{12\text{-H},16\text{-H}} = 1.8$ Hz, 2 H, 7-H, 12-H), 6.48 (d, $^3J_{8\text{-H},7\text{-H}} = {}^3J_{13\text{-H},12\text{-H}} = 7.8$ Hz, 2 H, 8-H, 13-H), 6.98−7.12 (m, 10 H, 21-H, 22-H, 23-H, 24-H, 25-H, 30-H, 31-H, 32-H, 33-H, 34-H), 7.86 (d, $^4J_{5\text{-H},7\text{-H}} = {}^3J_{16\text{-H},12\text{-H}} = 1.8$ Hz, 2 H, 5-H, 16-H), 8.18 (br. s, 2 H, NH). ^{1}H NMR (400.1 MHz, [D$_4$]methanol): δ = 2.95−3.00 (m, 2 H, 1*a*-H, 2*a*-H), 3.01−3.06 (m, 4 H, 9-H, 10-H), 3.59−3.63 (m, 2 H, 1*s*-H, 2*s*-H), 4.32−4.33 (m, 2 H, 18-H, 27-H), 4.62−4.63 (m, 2 H, 19-H, 28-H), 6.37 (dd, $^3J_{7\text{-H},8\text{-H}} = {}^3J_{12\text{-H},13\text{-H}} = 7.8$, $^4J_{7\text{-H},5\text{-H}} = {}^3J_{12\text{-H},16\text{-H}} = 1.8$ Hz, 2 H, 7-H, 12-H), 6.50 (d, $^3J_{8\text{-H},7\text{-H}} = {}^3J_{13\text{-H},12\text{-H}} = 7.8$ Hz, 2 H, 8-H, 13-H), 7.00−7.13 (m, 10 H, 21-H, 22-H, 23-H, 24-H, 25-H, 30-H, 31-H, 32-H, 33-H, 34-H), 7.72 (d, $^4J_{5\text{-H},7\text{-H}} = {}^3J_{16\text{-H},12\text{-H}} = 1.8$ Hz, 2 H, 5-H, 16-H) ppm. ^{13}C NMR (100.6 MHz, [D$_6$]acetone): δ = 30.4 (C-1, C-2), 36.0 (C-9, C-10), 42.6 (C-18, C-27), 47.9 (C-19, C-28), 123.3 (C-5, C-16), 126.4 (qC), 126.5 (C-23, C-32), 128.6, 128.9 (C-21, C-22, C-24, C-25, C-30, C-31, C-33, C-34), 129.0 (C-7, C-12), 135.7 (C-8, C-13), 139.6 (qC), 141.5 (qC), 141.9 (qC), 170.3 (C-17, C-26) ppm. ^{13}C NMR (100.6 MHz, [D$_4$]methanol): δ = 30.8 (C-1, C-2), 36.3 (C-9, C-10), 43.2 (C-18, C-27), 49.3 (C-19, C-28), 124.0 (C-5, C-16), 127.0 (C-23, C-32), 127.6 (qC), 128.9, 129.3 (C-21, C-22, C-24, C-25, C-30, C-31, C-33, C-34), 129.8 (C-7, C-12), 136.0 (C-8, C-13), 139.5 (qC), 141.4 (qC), 143.3 (qC), 172.1 (C-17, C-26) ppm. IR (KBr): $\tilde{\nu}$ = 3400 cm^{-1} (s), 3348 (s), 3085 (m), 3058 (m), 3027 (m), 2853 (m), 1693 (s), 1648 (s), 1602 (m), 1573 (vs), 1530 (vs), 1496 (s), 1480 (m), 1473 (m), 1455 (s), 1420 (vs), 1385 (m), 1363 (m), 1334 (m), 1321 (m), 1303 (m), 1290 (s), 1262 (m), 1238 (m), 1199 (m), 1190 (m), 1155 (m), 1114 (m), 1103 (m), 747 (m). UV/Vis (MeCN): λ_{max} (lg ε) = 250 nm (4.33), 258 (4.30, sh). MS (EI, 70 eV): *m/z* (%) = 498 (55) [M^+], 482 (22), 480 (58), 479 (11), 349 (12), 350 (20), 318 (15), 300 (23), 232 (13), 205 (14), 131 (34), 121

(19), 119 (100), 103 (37), 91 (21), 77 (22). $C_{34}H_{30}N_2O_2$ (498.64): calcd. C 81.90, H 6.06, N 5.62; found C 81.72, H 6.03, N 5.57.

3,4-Diphenyl-1,2-cyclobutanedicarboxylic Acid (β-Truxinic Acid, 27): The photoproduct **28** (0.12 g, 0.24 mmol) was suspended in 10 mL of concd. hydrochloric acid, and the mixture was heated under reflux for 24 h. The mixture was poured into 10 mL of water, and the precipitate was removed by filtration. After drying in a desiccator over phosphorus pentoxide, 0.070 g (98%) of a colorless solid was obtained, and identified as **27** by its spectroscopic data (see below). The filtrate was made basic by addition of potassium hydroxide, and the solid formed was removed by filtration. After drying in a desiccator over phosphorus pentoxide, 0.55 g (97%) of **19** was isolated, identified by comparison with an authentic sample (see above).

β-Truxinic Acid (27): m.p. 209−212 °C (ref.: 210 °C[25]). ^{1}H NMR (400.1 MHz, [D$_6$]DMSO): δ = 3.79−3.80 (m, 2 H, 2-H, 11-H), 4.19−4.21 (m, 2 H, 3-H, 12-H), 6.95−7.10 (m, 10 H, 5-H, 6-H, 7-H, 8-H, 9-H, 14-H, 15-H, 16-H, 17-H, 18-H), 12.40 (br. s, 2 H, COOH) ppm. ^{13}C NMR (100.6 MHz, [D$_6$]DMSO): δ = 42.6 (C-2, C-11), 44.5 (C-3, C-12), 125.9 (C-7, C-16), 127.7 (C-5, C-9, C-14, C-18); 127.9 (C-6, C-8, C-15, C-17), 139.3 (C-4, C-13), 174.0 (C-1, C-10) ppm. IR (KBr): $\tilde{\nu}$ = 3433 cm^{-1} (m), 3080 (m), 3065 (m), 3047 (m), 3031 (m), 2937 (m), 1704 (vs), 1415 (m), 1281 (m), 1256 (m), 1234 (m), 771 (w). MS (EI, 70 eV): *m/z* (%) = 278 (9) [M$^+$ − H$_2$O], 264 (21), 250 (65), 205 (34), 179 (21), 178 (15), 162 (96), 148 (100), 147 (80), 131 (64), 120 (20), 103 (24), 91 (25), 77 (12).

X-ray Structure Determinations: Details are presented in Table 1. Data collection and reduction: Crystals were mounted in inert oil on glass fibers and transferred to the cold gas stream of the diffractometer (**15**: Stoe STADI-4; **20**: Siemens P4, both with Siemens LT-2 low-temperature attachments). Measurements were performed with monochromated Mo-K_α radiation. Cell constants were refined from ±ω-angles (Stoe) or setting angles (Siemens) of ca. 60 reflections to 2θ 25°. Structure solution and refinement: The structures were solved with direct methods and refined anisotropically against F^2 (program SHELXL-97, G.M. Sheldrick, University of Göttingen). The NH hydrogens of **20** were refined freely; other H atoms were included with a riding model or with rigid methyl groups. For compound **20**, the absolute structure could not be determined and Friedel opposite reflections were therefore merged. To improve the stability of refinement, a system of restraints to displacement factor components was employed for both structures.

CCDC-176589 (**15**) and 176590 (**20**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: (internat.) +44−1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

Table 1. Details of X-ray structure analyses of **15** and **20**

Compound	**15**	**20**
Empirical formula	$C_{18}H_{14}N_2O_2$	$C_{17}H_{16}N_2O$
Formula mass	290.31	264.32
Habit	colorless rhomb	pale brown prism
Crystal size/mm	0.3×0.23×0.15	0.48×0.3×0.14
Crystal system	monoclinic	orthorhombic
Space group	$P2_1/n$	$P2_12_12_1$
Cell constants:		
a [Å]	7.369(2)	7.3116(8)
b [Å]	11.331(3)	11.6991(16)
c [Å]	16.570(4)	14.9534(16)
β [°]	94.36(3)	90
V [Å^3]	1379.5	1279.1
Z	4	4
D_x [Mg·m^{-3}]	1.398	1.373
μ [mm^{-1}]	0.09	0.09
F(000)	608	560
T [°C]	−130	−100
$2\theta_{max}$	50	55
No. of reflections:		
measured	2675	3265
independent	2420	1705
R_{int}	0.046	0.030
Parameters	199	189
Restraints	200	194
wR (F^2, all refl.)	0.171	0.078
R [F, >4σ(F)]	0.069	0.037
S	1.02	0.89
Max. Δρ [e·Å^{-3}]	0.23	0.19

[1] H. Hopf, H. Greiving, P. G. Jones, P. Bubenitschek, *Angew. Chem.* **1995**, *107*, 742−744; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 685−687.

[2] M. D. Cohen, G. M. J. Schmidt, *J. Chem. Soc.* **1964**, 1996−2000.

[3] G. M. J. Schmidt, *J. Chem. Soc.* **1964**, 2014−2021; cf.: J. Bregman, K. Osaki, G. M. J. Schmidt, F. I. Sonntag, *J. Chem. Soc.* **1964**, 2021−2030.

[4] For a collection of papers by G. M. J. Schmidt and his collaborators see: *Solid State Photochemistry* (Ed.: D. Ginsburg), Verlag Chemie, Weinheim, **1976**.

[5] B. S. Green, L. Heller, *J. Org. Chem.* **1974**, *39*, 196−201.

[6] R. C. Cookson, D. A. Cox, J. Hudec, *J. Chem. Soc.* **1961**, 4499−4506; cf.: D. Rabinovich, G. M. J. Schmidt, *J. Chem. Soc. (B)* **1967**, 144−149.

[7] D. Rabinovich, G. M. J. Schmidt, *J. Chem. Soc. (B)* **1970**, 6−10 and refs. cited therein.

[8] P. M. Keehn, S. M. Rosenfeld (Eds.), *Cyclophanes I, II*, Academic Press, New York, N. Y., **1983**.

[9] F. Vögtle, *Cyclophane Chemistry*, J. Wiley & Sons, Chichester, **1993**.

[10] H. Hopf, *Classics in Hydrocarbon Chemistry*, Wiley-VCH, Weinheim, **2000**, Chapter 12.3, pp. 337−368.

[11] H. Greiving, H. Hopf, P. G. Jones, J.-P. Desvergne, H. Bouas-Laurent, *J. Chem. Soc., Chem. Commun.* **1994**, 1075−1076.

[12] H. Hopf, H. Greiving, P. G. Jones, P. Bubenitschek, H. Bouas-Laurent, J.-P. Desvergne, *Liebigs Ann.* **1995**, 1949−1956; cf.: H. Hopf, U. Meyer, N. Lahrahar, P. Marsau, H. Greiving, J.-P. Desvergne, H. Bouas-Laurent, *Liebigs Ann. Chem.* **1997**, 381−384.

[13] Chr. Beck, Ph. D. Dissertation, Braunschweig, **1999**.

[14] B. S. Green, *Nature* **1994**, *371*, 320; cf.: S. A. Fleming, C. L. Bradford, J. J. Gao, in: *Molecular and Supramolecular Photochemistry, Vol. 1: Organic Photochemistry* (Eds.: V. Ramamurthy, K. S. Schanze), Marcel Dekker, Inc., New York, N. Y., **1997**, pp. 210−212 and refs. quoted.

[15] For the construction and use of chemical work-benches, see: J. Mulzer, K. Schein, J.-W. Bats, J. Buschmannn, P. Luger, *Angew. Chem.* **1998**, *110*, 1625−1628; *Angew. Chem. Int. Ed.* **1998**, *37*, 15666−1569; cf.: J. Mulzer, I. Böhm, J.-W. Bats, *Tetrahedron Lett.* **1998**, *39*, 9643−9646.

[16] I. Dix, Ph. D. Dissertation, Braunschweig, **2001**, cf.: A. J. Boydston, M. Haley, H. Hopf, I. Dix, L. Bondarenko, T. Weakly,

Angew. Chem. **2001**, *113*, 3074−3077; *Angew. Chem. Int. Ed.* **2001**, *40*, 2986−2989.

[17] J. Hillmer, Ph. D. Dissertation, Braunschweig, **1991**.

[18] H. J. Reich, D. J. Cram, *J. Am. Chem. Soc.* **1968**, *91*, 3527−3533; cf. H. Allgeier, M. G. Siegel, R. C. Helgeson, E. Schmidt, D. J. Cram, *J. Am. Chem. Soc.* **1974**, *97*, 3782−3789.

[19] J. Lahann, H. Höcker, R. Langer, *Angew. Chem.* **2001**, *113*, 746−749; *Angew. Chem. Int. Ed.* **2001**, *40*,

[20] M. Psiorz, R. Schmid, *Chem. Ber.* **1987**, *120*, 1825−1828.

[21] E. A. Truesdale, D. J. Cram, *J. Org. Chem.* **1979**, *45*, 3974−3981.

[22] A. F. Mourad, H. Hopf, *Chem. Ber.* **1980**, *113*, 2358−2371.

[23] R. Richter, H. Ulrich, in: *The Chemistry of Functional Groups* (Ed.: S. Patai), *The Chemistry of Cyanates and Their Thio Derivatives*, J. Wiley and Sons, Chichester, **1977**, Part 2, Chapter 17, pp. 619−818.

[24] H. Hopf, W. Grahn, D. G. Barrett, A. Gerdes, J. Hillmer, J. Hucker, Y. Okamoto, Y. Kaida, *Chem. Ber.* **1990**, *123*, 841−845.

[25] G. Kaupp, *Angew. Chem.* **1992**, *104*, 606−609; *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 592−595.

Received February 1, 2002
[O02059]