Stereoselective Lateral Functionalization of Monosubstituted [2.2]Paracyclophanes by Directed *ortho*-Metalation−Homologous Anionic Fries Rearrangement[‡]

Thilo Focken,[a] Henning Hopf,*[a] Victor Snieckus,*[b] Ina Dix,[a] and Peter G. Jones*[c]

Keywords: Cyclophanes / Directed metalation / Fries rearrangement / Lateral functionalization / Stereoselective synthesis

Two efficient routes have been developed for the lateral functionalization of monosubstituted [2.2]paracyclophanes. After protection of the *ortho* site of an *O*-([2.2]paracyclophanyl) diisopropylcarbamate, an anionic Fries rearrangement resulted in a substitution of the benzylic position to give *syn*-4-hydroxy-*N*,*N*-diisopropyl-5-triethylsilyl-2-[2.2]paracyclophanecarboxamide (**4b**) with a *syn*/*anti* diastereoselectivity of more than 99:1. An alternate route consisted of the direct functionalization of the lateral position of *N*-*tert*-butyl-4-[2.2]paracyclophanecarboxamide (**9**) by directed metalation. The reaction was found to be highly stereoselective, with only the *syn* isomer **11** being formed.

Introduction

Although the functionalization of monosubstituted [2.2]paracyclophanes is well established for the *ortho*[2−4] and *pseudo-geminal*[5] positions, efficient derivatization of the ethano bridges in substituted [2.2]paracyclophanes has not been achieved.[6] Recently, Hou et al. reported the observation of lateral functionalization as a side reaction in the metalation of an oxazolinyl-[2.2]paracyclophane.[7]

Reinhoudt and Snieckus have described the lateral functionalization of calix[4]arenes by means of a homologous anionic *ortho* Fries rearrangement.[8] The application of a directed *ortho*-metalation-induced anionic Fries rearrangement to [2.2]paracyclophanes results in *ortho* functionalization, as shown in the synthesis of 5-formyl-4-hydroxy-[2.2]paracyclophane.[2,9] In contrast, Snieckus et al. showed that prior silicon protection of preferred *ortho*-metalation sites makes alternate ring remote deprotonation possible.[10,11] An application of this methodology is the synthesis of dibenzo[*bd*]pyranones from *O*-(*o*-biaryl) carbamates by a remote anionic Fries rearrangement.[11]

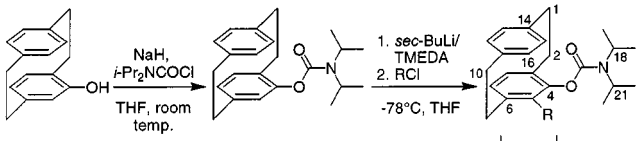
Here we report two methods for the stereoselective functionalization of one ethano bridge in monosubstituted [2.2]paracyclophanes. Firstly, we demonstrate lateral functionalization of *O*-([2.2]paracyclophanyl) diisopropylcarbamate (**2**) by the silicon protection−anionic Fries rearrangement approach. Furthermore, we announce the first preparatively efficient directed lateral metalation of *N*-*tert*-butyl-4-[2.2]paracyclophanecarboxamide (**9**).[12]

Results and Discussion

Rearrangement of *ortho*-Protected O-([2.2]Paracyclophanyl) Diisopropylcarbamates

Following the observation of the anionic Fries rearrangement of *O*-(4-[2.2]paracyclophanyl) diethylcarbamate to 5-formyl-4-hydroxy-[2.2]paracyclophane,[2,9] we considered that protection of the *ortho* position (C-5) might result in bridge (C-2) metalation and lateral migration of the carbamoyl group.[13]

We chose the *ortho*-protected *O*-(4-[2.2]paracyclophanyl) diisopropylcarbamates **3a** and **3b** for studies of this homologous anionic Fries rearrangement, since the trialkylsilyl groups are easily removable by fluoride sources.[10,14] Compounds **3a** and **3b** were readily prepared from 4-hydroxy-[2.2]paracyclophane[15] (**1**) by carbamoylation to **2** followed by standard directed *ortho*-metalation (DoM)[14] and silylation with TMSCl and TESCl, respectively (Scheme 1). The application of the DoM strategy to *O*-([2.2]paracyclo-



3	R	Yield, %
a	TMS	94
b	TES	73

Scheme 1. Synthesis of *ortho*-trialkylsilyl-substituted *O*-([2.2]paracyclophanyl) diisopropylcarbamates **3a** and **3b**

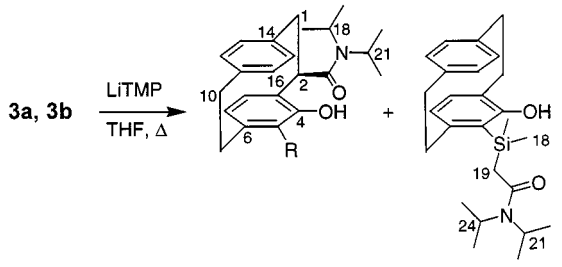
[‡] Cyclophanes, XLIX. − Part XLVIII: Ref.[1]

[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] Department of Chemistry, Queen's University,
Kingston, Ontario, K7L 3N6, Canada
E-mail: snieckus@chem.queensu.ca
[c] 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

  1434−193X/01/0612−2221 $ 17.50+.50/0

phanyl) carbamates was first developed by Hopf and Barrett.[2] The spectroscopic data for **2**, **3a**, and **3b** resemble those reported in the literature for diethylcarbamates.[2] In the proton NMR spectrum of **2**, the doublet at δ = 6.01, with a coupling constant of ^4J = 1.6 Hz, was assigned to the *ortho* proton (5-H), whereas the signal at lowest field (δ = 6.85) was assigned to the *pseudo-geminal* proton (15-H).

When the trimethylsilyl derivative **3a** was subjected to LDA treatment at room temperature, no reaction occurred and only starting material was isolated. However, when the reaction was carried out with LiTMP in refluxing THF, two products were formed (**4a**, **5**, Scheme 2). In contrast, treatment of the TES derivative **3b** with LiTMP under the same conditions exclusively resulted in compound **4b**. The formation of **4a** and **4b** may be explained by a homologous anionic Fries rearrangement mechanism, whereas **5** is the result of an α-methylsilyl deprotonation and subsequent migration, a reaction previously observed in the benzene and biaryl series.[11,16] On the basis of the previous observation,[11] it was possible to avoid this undesired rearrangement by using the more hindered and less acidic TES *ortho* protecting group.



4	R	Yield, %
a	TMS	18
b	TES	84

Scheme 2. Rearrangement of *O*-([2.2]paracyclophanyl) diisopropylcarbamates **3a** and **3b**

The structures of all rearranged products were assigned by NMR spectroscopic analysis. The proton NMR spectrum of **5** features, besides a low-field absorption of the hydroxy group at δ = 10.74, a characteristic pattern for the signals of the substituted TMS group. The two remaining methyl groups (17-H, 18-H) appear as singlets at δ = 0.24 and 0.43, whereas the methylene group (19-H) signal is split as an AB system, with doublets (^2J = 14.9 Hz) at δ = 2.17 and 2.33.

As expected, the NMR spectra of **4a** and **4b** are similar. They show signals for unsubstituted trialkylsilyl groups, with a singlet at δ = 0.36 for the TMS group and a multiplet at δ = 0.85−0.97 for the TES group. An indication of strong intramolecular hydrogen bonds is seen in the low-field resonance of the hydroxy groups, at δ = 12.60 (**4a**) and δ = 11.89 (**4b**). The substituted ethano bridge exhibits an easily interpreted signal splitting of the protons at C-1 and C-2. In the NMR spectrum of **4b**, one proton at C-1 (δ = 3.33) resonates as a double doublet ($^2J_{1,1}$ = 12.8 Hz, $^3J_{1,2}$ = 8.4 Hz), whereas the other proton signal is hidden under a multiplet originating from the second ethano bridge. As expected, the signal for 2-H is split as a double doublet ($^3J_{2,1}$ = 8.5 Hz, $^3J_{2,1}$ = 10.2 Hz).

The relative configuration at C-2 was established by X-ray crystallographic analysis of **4b** (Figure 1). Suitable crystals, in the form of prisms, were obtained by recrystallization from a mixture of ethanol and diethyl ether. Compound **4b** crystallizes with four independent molecules, in the chiral space group *P*1. Thanks to the presence of silicon, a third-row element, it was possible to determine the absolute configurations of the four molecules as two pairs of enantiomers of the same diastereomer (but this is only valid for the crystal actually measured). The molecules Si to C29 and Si′ to C29′ exhibit a (2*S*,p*R*) configuration, whereas the molecules Si′′ to C29′′ and Si* to C29* show the inverted configuration (2*R*,p*S*). Within the pairs Si to C29 and Si* to C29*, and Si′ to C29′ and Si′′to C29′′, the molecules are essentially inversion-symmetric to each other. The main difference between the pairs consists of different orientations of the TES and diisopropylamide groups.

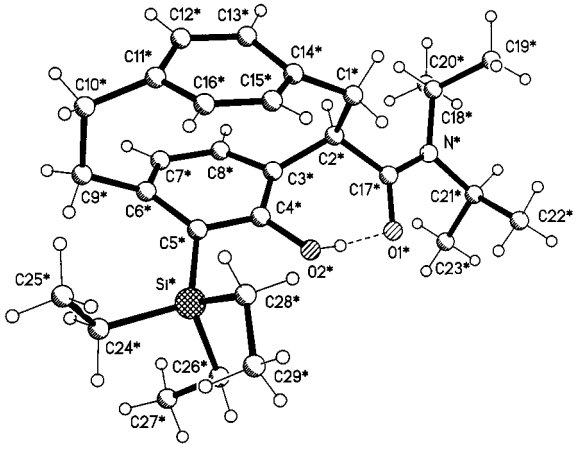


Figure 1. Structure of **4b** in the crystal (one independent molecule)

Some bond lengths in these molecules are noteworthy. The silicon−carbon bond Si−C5 is significantly elongated in all molecules, because of the sterically demanding geminal substitution pattern; it varies from 1.894(4) (C5′′−Si′′) to 1.923(5) Å (C5−Si), in contrast to the standard bond length of 1.868 Å for a C(sp^2_{ar})−SiX_3 bond.[17] A similar effect can be seen for the bond C2−C17, which is also elongated to 1.509(6) (C2′′−C17′′) to 1.532(6) Å (C2*−C17*); the standard length for a acyclic amide bond being 1.505 Å. In addition, the [2.2]paracyclophane skeleton shows ethano bridge bonds [C(sp^2_{ar})−C(sp^3) and C(sp^3)−C(sp^3)] appreciably longer than those in the unsubstituted parent compound, as a consequence of bridge substitution. As far as C(sp^2_{ar})−C(sp^3) bonds are concerned, only C1−C2, C2−C3, and C6−C9 are affected. The C(sp^2_{ar})−C(sp^3) bonds next to substituted positions are lengthened to 1.522(6) (C6′−C9′) to 1.533(5) Å (C2′−C3′), in comparison with 1.510 Å in the parent compound (except for C6*−C9*: 1.509(7) Å]. The C(sp^3)−C(sp^3) bonds C1−C2 are also slightly elongated, to 1.587(6) (C1′−C2′)

to 1.590(7) Å (C1−C2), as opposed to 1.571 Å in [2.2]paracyclophane [C1*−C2*: 1.577(8) Å is an exception]. Finally, the independent molecules form two types of hydrogen bonds: classical intramolecular hydrogen bonds with the hydroxy protons as hydrogen bond donors (D) and the amide oxygen O1 as acceptor (A), and nonclassical hydrogen bonds between methyl protons in the diisopropylamide groups and the amide oxygen atoms. These hydrogen bonds cause assembling of the molecules into double chains parallel to the *x* axis. The parameters are summarized in Table 1.

Table 1. Parameters of the hydrogen bonds in **4b**

H bond	H···A [Å]	D···A [Å]	D−H···A [°]
O2−H02···O1	1.74(5)	2.528(5)	154(4)
O2′−H02′···O1′	1.94(7)	2.558(4)	121(5)
O2′′−H02′′···O1′′	1.73(6)	2.561(4)	161(6)
O2*−H02*···O1	1.72(7)	2.537(5)	173(3)
C20*−H20L···O1	2.65	3.396(6)	133.2
C23*−H23L···O1′	2.47	3.268(6)	138.1
C23−H23A···O1′′	2.45	3.223(6)	135.9
C20−H20A···O1*	2.69	3.358(6)	125.5

In all isomers, the hydroxy groups and the diisopropylamide groups are *syn* to each other, so that the configurations of the enantiomers of **4b** are (2*R*,p*R*) and (2*S*,p*S*), respectively. We assume that the situation is analogous for **4a**, since its NMR spectra closely resemble those of **4b** (see above and Exp. Sect.).

The diastereomer with an *anti* arrangement of hydroxy and diisopropylamide groups was neither isolated nor found in the crystals. The only hints for the formation of the *anti* diastereomer are some very small signals in the NMR spectra of **4a** and **4b**, which could not be related to the respective starting materials **2** and **3**. Because of their low intensity, these signals could not be assigned. Comparison of appropriate integrals of **4b** with the integrals of these unassigned signals gives a diastereomeric ratio of > 99:1. That these residual absorptions are presumably caused by the *anti* isomer was shown after **4b** had been desilylated and the X-ray structure of the resulting amide **7** determined (see below).

The stereochemical outcome of the rearrangement, with its preference for the *syn* diastereomer, can be explained in terms of the formation of a five-membered cyclic tetrahedral intermediate **6** (Scheme 3). A *syn* deprotonation would be expected to be preferred because of the "Complex-Induced Proximity Effect" (CIPE),[18] in which *O*-carbamate−LiTMP coordination plays the role in conducting the base to the prochiral *syn*-C−H bond. Reinhoudt and Snieckus suggested a similar intermediate for the rearrangement of *O*,*O*′-(calix[4]arenediyl) dicarbamates.[8]

Of the various *ipso*-desilylation reagents (TFA, TBAF, or CsF[10,14]), TFA was chosen. It provided compound **7** in high yield (Scheme 3). Compound **7** was thus shown to be stable under strongly acidic conditions, rather than being transformed to a γ-lactone as has been observed in the benzene series.[13]

The structure of **7** was consistent with its ^{1}H and ^{13}C NMR spectra, which were similar to those of **4a** and **4b**. Thus, the signals of the protons at C-1 appeared as double doublets. The signal at δ = 3.36, with a coupling constant to 2-H of $^3J_{1,2}$ = 8.6 Hz, was assigned to *syn*-1-H, whereas the signal δ = 3.22, with the expected larger coupling constant to 2-H ($^3J_{1,2}$ = 9.7 Hz), was assigned to *anti*-1-H. As had been observed for compounds **4a** and **4b** (see above), the spectrum of **7** also showed very small signals which may belong to the *anti* diastereomer. As in the case of **4b**, comparison of the integrals implies a diastereomeric ratio of > 99:1. However, the existence of the *anti* diastereomer was implied by X-ray structural analysis (Figure 2). Suitable crystals were obtained by recrystallization from a mixture of ethanol and dichloromethane, and the *syn*/*anti* diastereomeric ratio was determined to be 96.5:3.5 by comparison of the occupancies of the disordered hydroxy group O(1) and O(1′). The significantly greater *anti*-diastereomeric component in this mixture, as compared to the NMR analysis in solution, might reflect enrichment during the recrystallization process.

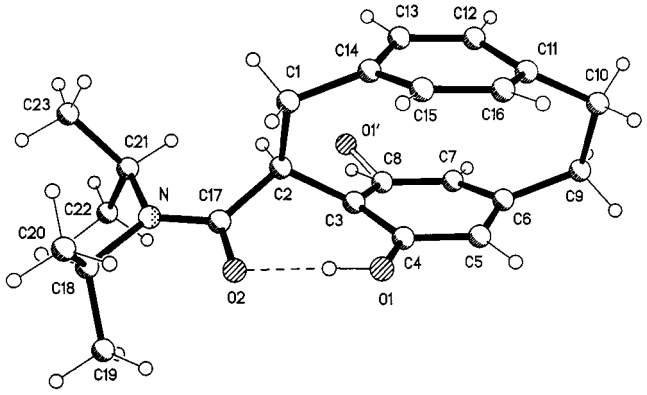
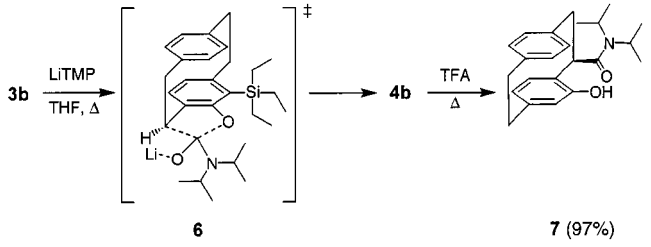


Figure 2. Structure of **7** in the crystal

Compound **7** crystallizes with one independent molecule in the centrosymmetric space group $P2_1/c$, allowing the relative configuration of the molecule to be determined. The crystals contain the *anti* diastereomer as the main component [O1: 0.965(3)] and the *syn* diastereomer [O1′: 0.035(3)] as determined by refinement of alternative disorder sites (see below). The relative configuration of the *anti* diastereomer is (2*S*,4*R*). As in compound **4b**, the C2−C17 bond in the amide is slightly elongated to 1.528(2) Å, as opposed to the corresponding standard bond length of 1.505 Å.[17] The

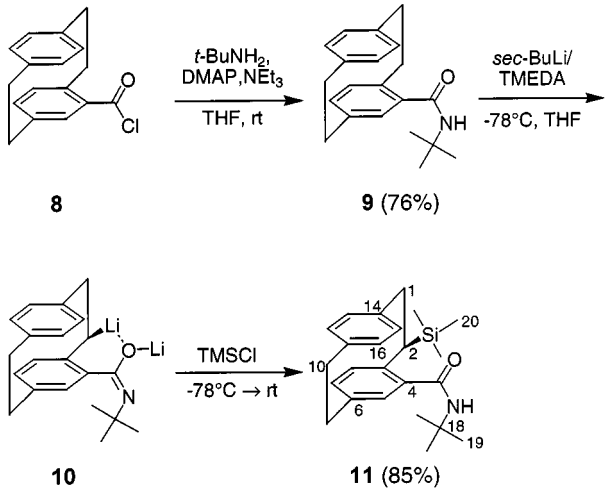


Scheme 3. Cyclic transition state and desilylation of **4b**

effects of the substitution in the [2.2]paracyclophane part are reflected in changes of the bond lengths of the ethano bridges: C1−C2 1.595(2) Å and C9−C10 1.588(2) Å for the $C(sp^3)-C(sp^3)$ bonds, C2−C3 1.531(2) Å for the $C(sp^2_{ar})-C(sp^3)$ bond. In contrast to triply substituted **4b**, compound **7** only shows elongation of the bridge bond at the substituted position. The substitution pattern of the hydroxy and amide groups results in one intramolecular hydrogen bond, O1−H01···O2 [1.65(2) Å, 2.547(1) Å, 173(2)°]. In addition, a nonclassical hydrogen bond is formed, C22−H22B···O2 [2.59 Å, 3.558(2) Å, 168.2°], giving rise to chains of molecules parallel to the *z* axis.

Lateral Deprotonation with N-*tert*-Butyl-4-[2.2]paracyclophanecarboxamide (9)

N-*tert*-Butyl-4-[2.2]paracyclophanecarboxamide (**9**) was prepared from the readily available [2.2]paracyclophane-4-carbonyl chloride[19] (**8**) and *tert*-butylamine, in 76% yield (Scheme 4). In its NMR spectrum, the signal of the *pseudo-geminal* proton (15-H) appears at lowest field (δ = 6.85) as a *pseudo*-doublet (^3J = 7.8 Hz), due to the deshielding effect of the carbonyl group. Metalation of **9** under optimized conditions (*s*BuLi/TMEDA/THF/−78 °C), followed by TMSCl quenching resulted in an 85% yield of the laterally silylated product **11**. The reaction is stereoselective, producing the *syn* diastereomer exclusively. This structure was established by NMR spectroscopy. The signal of the proton at C-2 appeared as a double doublet ($^3J_{2,1}$ = 8.0 Hz, $^3J_{2,1}$ = 10.5 Hz) at δ = 2.50, the larger coupling constant being assigned to coupling with *anti*-1-H. This proton was observed as a *pseudo*-triplet (^3J = 11.4 Hz) at δ = 3.54, whereas the signal of *syn*-1-H could not be resolved and was registered together with 9-H and 10-H as a multiplet at δ = 3.17.



Scheme 4. Synthesis of *syn*-*N*-*tert*-butyl-2-trimethylsilyl-4-[2.2]-paracyclophanecarboxamide (**11**)

Conclusive structural and stereochemical proof of the relative orientation of the two substituents in **11** was obtained by single-crystal X-ray analysis (Figure 3). Crystals, in the form of colorless prisms, were grown from a solution in methanol and dichloromethane. The Figure shows the proposed *syn* grouping of the silyl and amide substituents, thus establishing the relative configuration (2*R*,p*S*) or (2*S*,p*R*). Furthermore, the orientation of the carbonyl group towards the substituted ethano bridge is conspicuous.

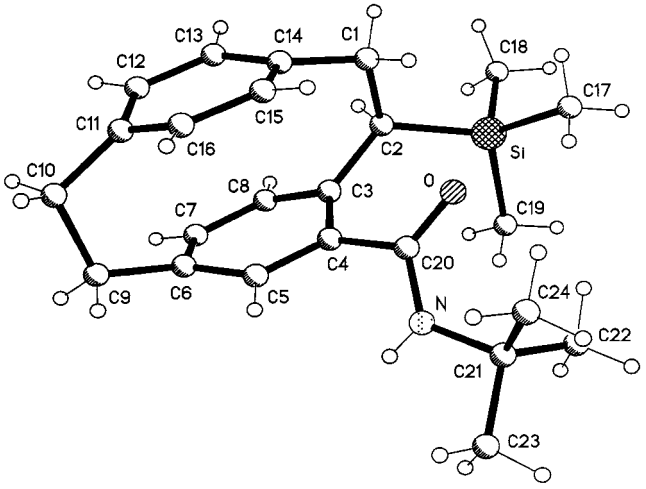


Figure 3. Structure of **11** in the crystal

Compound **11** crystallizes with one independent molecule in the centrosymmetric space group *C*2/*c* allowing the relative configuration of the molecule, established as (2*R*,4*S*), to be determined. The effects of the bulky substituents on the [2.2]paracyclophane skeleton are similar to those in the structure of compound **7**. The $C(sp^3)-C(sp^3)$ bonds [C1−C2 1.592(2) Å and C9−C10 1.585(2) Å] and the $C(sp^2_{ar})-C(sp^3)$ bond at the substituted position (C2−C3 1.528(2) Å] of the ethano bridges are lengthened. Furthermore, steric effects force the $C(sp^3)-Si$ bond [1.908(1) Å] to be significantly longer than the standard length.[17] The amide proton is not involved in hydrogen bonding, but a nonclassical intramolecular hydrogen bond is observed, C17−H17A···O [2.28 Å, 3.000(2) Å, 129.0°].

As for the metalation of **3a** and **3b**, we suggest that the operation of a CIPE[18] is responsible for the outcome of the metalation reaction on **9**. The orientation of the directing group is essential for the coordination of the base and deprotonation at C-2, as the C−H-*ortho* position is normally more acidic than the C−H bridge positions. The less acidic site is therefore preordained for deprotonation, because of the specific acid-base coordination. CIPE is also responsible for the *syn*-stereochemical outcome of the reaction since, in the dilithiated species (Scheme 4), *anti* deprotonation would necessitate involving a high-energy six-membered ring intermediate.

Summary and Conclusion

Two highly stereoselective methods for the functionalization of one bridge in monosubstituted [2.2]paracyclophanes have been developed. Reactions giving products **4b,**

7, and **11** proceed from readily available starting materials, are practically convenient, and give good to excellent yields.

The described homologous anionic Fries rearrangement, **3b** → **4b**, is an effective method for diastereoselective (*syn*/*anti* > 99:1) C-2 functionalization of [2.2]paracyclophanes. The directed lateral metalation, **8** → **11**, constitutes an alternate *syn*-diastereoselective method for C-2 functionalization of cyclophanes bearing a carbon-based substituent.

We hope to report on the use of these disubstituted cyclophanes as ligands in stereoselective synthesis in the near future.

Experimental Section

General: ^{1}H and ^{13}C NMR: Bruker AC 200 (200.1 MHz), Bruker Avance 300 (300.1 MHz and 75.5 MHz) or Bruker Avance DRX 400 (400.1 MHz and 100.6 MHz) in $CDCl_3$. Chemical shifts are reported relative to tetramethylsilane as internal standard or $CDCl_3$ (δ_C = 77.05), respectively. ^{13}C NMR spectra were proton-decoupled. Assignments of protons and carbon atoms are based on ^{13}C DEPT, ^{13}C J-MOD, H-COSY, HMQC, and HMBC experiments. − IR: Nicolet 320 FT-IR spectrometer, KBr pellet. − UV/Vis: HP 8452 A Diode Array Spectrophotometer in acetonitrile. − MS (EI) and HRMS: Finnigan MAT 8400 MSS I or Finnigan 8460 at 70 eV. − Melting points: Fisher-Scientific hot-stage or Reichert hot-stage; values are not corrected. − Flash chromatography: Merck silica gel 60 (230−400 mesh). − All reactions were carried out under argon in oven-dried glassware, using syringe-septum cap techniques. THF was distilled from sodium/benzophenone ketyl prior to use. Diisopropylamine, *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA), triethylsilyl chloride (TESCl), trimethylsilyl chloride (TMSCl), and dichloromethane were dried and distilled from CaH_2. All other reagents were used without further purification. The phrase "workup in the usual manner" refers to extraction of the reaction mixture with dichloromethane, drying of the combined organic extracts with Na_2SO_4 or $MgSO_4$, and evaporation of the solvent under reduced pressure. − 4-Hydroxy-[2.2]paracyclophane (**1**)[15] and 4-[2.2]paracyclophanecarbonyl chloride (**8**)[19] were synthesized according to literature procedures.

***O*-(4-[2.2]Paracyclophanyl) Diisopropylcarbamate (2):** 4-Hydroxy-[2.2]paracyclophane (**1**) (1.5 g, 6.7 mmol) was added at 0 °C to a suspension of NaH (300 mg, 12.5 mmol) in THF (60 mL). After the mixture had been stirred for 15 min at room temp., diisopropylcarbamoyl chloride (1.3 g, 7.9 mmol) was added. The mixture was stirred for 12 h at room temp. and hydrolyzed with cooling. Workup in the usual manner and purification of the crude product by flash chromatography (dichloromethane) afforded 2.23 g (94%) of **2** as a colorless solid. Recrystallization from ethanol gave colorless needles, m.p. 183−184 °C. − IR: $\tilde{\nu}$ = 3008 cm^{-1} (w), 2990 (m), 2963 (s), 2929 (s), 2854 (w), 1712 (vs), 1595 (w), 1560 (w), 1497 (m), 1467 (m), 1432 (s), 1412 (s), 1373 (s), 1311 (vs), 1234 (vs), 1139 (vs), 1044 (vs), 1009 (s), 897 (m), 876 (m), 797 (m), 753 (m), 717 (m), 656 (m). − ^{1}H NMR (300.1 MHz): δ = 1.30 (br. s, 6 H, 19-H, 20-H), 1.46 (br. s, 6 H, 22-H, 23-H), 2.73 (m, 1 H, 1-H, 2-H, 9-H or 10-H), 2.92−3.23 (m, 7 H, 1-H, 2-H, 9-H, 10-H), 3.93 (br. s, 1 H, 18-H), 4.25 (br. s, 1 H, 21-H), 6.01 (d, $^4J_{5,7}$ = 1.6 Hz, 1 H, 5-H), 6.39−6.48 (m, 4 H, 7-H, 8-H, 12-H, 16-H), 6.54 (dd, 1 H, $^3J_{13,12}$ = 7.8 Hz, $^4J_{13,15}$ = 1.8 Hz, 13-H), 6.85 (dd, 1 H, $^3J_{15,16}$ = 7.8 Hz, $^4J_{15,13}$ = 1.8 Hz, 15-H). − ^{13}C NMR (75.5 MHz): δ = 21.5, 20.4 (C-19, C-20, C-22, C-23), 31.4, 34.5, 34.7, 35.2 (C-1, C-2, C-9, C-10), 46.4 (C-18, C-21), 128.1 (C-5), 129.5, 129.6, 132.2, 132.9, 133.3, 135.1 (C-7, C-8, C-12, C-13, C-15, C-16), 131.3, 139.2, 139.4, 141.2, (C-3, C-6, C-11, C-14), 149.3 (C-4), 152.9 (C-17). − UV/Vis: λ_{max} (lg ε) = 194 nm (4.65), 224 (4.26). − MS: *m*/*z* (%) = 352 (28), 351 (100) [M$^+$], 128 (25) [$C_7H_{14}NO^+$], 120 (21) [$C_8H_8O^+$], 104 (21) [$C_4H_8^+$], 103 (15), 91 (17), 86 (55) [$C_4H_8NO^+$], 78 (12) [C_6H_6]. − HRMS ($C_{23}H_{29}NO_2$): calcd. 351.2198; found 351.2180. − Calcd. C 78.59, H 8.32, N 3.99; found C 78.52, H 8.34, N 3.80.

***O*-(5-Trimethylsilyl-4-[2.2]paracyclophanyl) Diisopropylcarbamate (3a):** A solution of *O*-(4-[2.2]paracyclophanyl) diisopropylcarbamate (**2**) (352 mg, 0.001 mol) in THF (15 mL) was added dropwise to a solution of TMEDA (0.18 mL, 1.2 mmol) and *s*BuLi (1.2 mmol) in THF (5 mL) at − 78 °C. After stirring for 10 min at − 78 °C, the reaction mixture was treated with TMSCl (0.38 mL, 2.99 mmol). The resulting solution was allowed to warm to room temp., whereupon saturated aqueous NH_4Cl (10 mL) was added. After usual workup, 400 mg (94%) of **3a** was obtained as a colorless oil, which slowly crystallized. Recrystallization from ethanol gave colorless needles, m.p. 159−160 °C. − IR: $\tilde{\nu}$ = 2995 cm^{-1} (m), 2965 (m), 2932 (m), 2899 (w), 2860 (w), 1714 (vs), 1455 (w), 1431 (s), 1374 (m), 1314 (vs), 1262 (m), 1245 (m), 1218 (m), 1170 (m), 1156 (m), 1142 (s), 1129 (m), 1040 (s), 1014 (m), 903 (w), 892 (w), 859 (m), 836 (s), 753 (m). − ^{1}H NMR (300.1 MHz): δ = 0.30 (s, 9 H, 24-H), 1.33 (d, 3 H, $^3J_{22/23,21}$ = 6.8 Hz, 22-H or 23-H), 1.34 (d, 3 H, $^3J_{19/20,18}$ = 6.8 Hz, 19-H or 20-H), 1.40 (d, 3 H, $^3J_{22/23,21}$ = 6.8 Hz, 22-H or 23-H), 1.44 (d, 3 H, $^3J_{19/20,18}$ = 6.7 Hz, 19-H or 20-H), 2.73 (m, 1 H, 1-H, 2-H, 9-H or 10-H), 2.87−3.09 (m, 6 H, 1-H, 2-H, 9-H or 10-H), 3.23 (m, 1 H, 1-H, 2-H, 9-H or 10-H), 3.52 (sept, 1 H, $^3J_{18,19/20}$ = 6.8 Hz, 18-H), 4.82 (sept, 1 H, $^3J_{21,22/23}$ = 6.8 Hz, 21-H), 6.36 (d, 1 H, $^3J_{7/8,8/7}$ = 7.7 Hz, 7-H or 8-H), 6.40 (dd, 1 H, ^3J = 7.9, ^4J = 1.8 Hz, 12-H, 13-H, 15-H or 16-H), 6.45 (d, 1 H, $^3J_{7/8,8/7}$ = 7.7 Hz, 7-H or 8-H), 6.55 (dd, 1 H, ^3J = 7.8, ^4J = 1.6 Hz, 12-H, 13-H, 15-H or 16-H), 6.64 (m, 2 H, 12-H, 13-H, 15-H or 16-H). − ^{13}C NMR (75.5 MHz): δ = 1.5 (C-24), 20.2, 20.6, 20.9, 21.6 (C-19, C-20, C-22, C-23), 31.5, 34.6, 35.8, 36.1 (C-1, C-2, C-9, C-10), 45.1 (C-18), 47.9 (C-21), 129.3, 131.2, 132.2, 132.7, 132.8, 137.0 (C-7, C-8, C-12, C-13, C-15, C-16), 130.1, 131.8, 139.0, 139.5, (C-3, C-5, C-11, C-14), 148.2 (C-6), 151.8, 154.6 (C-4, C-17). − UV/Vis: λ_{max} (lg ε) = 196 nm (4.77), 228 (4.21). − MS: *m*/*z* (%) = 424 (45), 423 (100) [M$^+$], 176 (17), 128 (42) [$C_7H_{14}NO^+$], 86 (64) [$C_4H_8NO^+$]. − HRMS ($C_{26}H_{37}NO_2Si$): calcd. 423.2594; found 423.2593. − Calcd. C 73.31, H 8.80, N 3.31; found C 73.81, H 8.81, N 3.18.

***O*-(5-Triethylsilyl-4-[2.2]paracyclophanyl) Diisopropylcarbamate (3b):** As described for **3a**, a mixture of *O*-(4-[2.2]paracyclophanyl) diisopropylcarbamate (**2**) (450 mg, 1.28 mmol), *s*BuLi (1.54 mmol), and TMEDA (0.23 mL, 1.52 mmol) in THF (30 mL) was treated with TESCl (0.5 mL, 2.98 mmol) at − 78 °C. After the reaction mixture had warmed to room temp., saturated aqueous NH_4Cl (10 mL) was added and the mixture was worked up in the usual manner. The crude product was purified by flash chromatography (Et_2O/hexane, 1:6 to 2:3) to afford two fractions: 58 mg (13%) of starting material **2** and 432 mg (73%) of **3b** as a white solid, m.p. 138−139 °C. − IR: $\tilde{\nu}$ = 2997 cm^{-1} (w), 2963 (s), 2931 (m), 2875 (m), 1712 (vs), 1459 (w), 1429 (m), 1372 (m), 1313 (s), 1241 (w), 1217 (w), 1143 (m), 1043 (s), 1020 (m), 798 (w), 755 (w), 735 (w), 721 (m). − ^{1}H NMR (300.1 MHz): δ = 0.82−0.98 (m, 15 H, 24-H, 25-H), 1.33 (d, 3 H, $^3J_{22/23,21}$ = 6.8 Hz, 22-H or 23-H), 1.34 (d, 3 H, $^3J_{19/20,18}$ = 6.7 Hz, 19-H or 20-H), 1.39 (d, 3 H, $^3J_{22/23,21}$ = 6.8 Hz, 22-H or 23-H), 1.45 (d, 3 H, $^3J_{19/20,18}$ = 6.7 Hz, 19-H or 20-H), 2.75 (m, 1 H, 1-H, 2-H, 9-H or 10-H), 2.85−3.18 (m, 7 H, 1-H, 2-H, 9-H, 10-H), 3.49 (sept, 1 H, $^3J_{18,19/20}$ = 6.8 Hz, 18-H), 4.83 (sept, 1 H, $^3J_{21,22/23}$ = 6.8 Hz, 21-H), 6.33 (d, 1 H, $^3J_{7/8,8/7}$ =

7.6 Hz, 7-H or 8-H), 6.35 (dd, 1 H, ^3J = 7.9, ^4J = 1.6 Hz, 12-H, 13-H, 15-H or 16-H), 6.41 (d, 1 H, $^3J_{7/8,8/7}$ = 7.7 Hz, 7-H or 8-H), 6.59 (m, 3 H, 12-H, 13-H, 15-H or 16-H). − ^{13}C NMR (75.5 MHz): δ = 5.3 (C-24), 7.8 (C-25), 20.2, 20.6, 20.9, 21.6 (C-19, C-20, C-22, C-23), 31.7, 34.6, 35.9, 36.1 (C-1, C-2, C-9, C-10), 45.0 (C-18), 48.0 (C-21), 129.6, 130.8, 131.8, 132.8, 133.0, 137.4 (C-7, C-8, C-12, C-13, C-15, C-16), 129.1, 129.9, 139.0, 139.6 (C-3, C-5, C-11, C-14), 148.9 (C-6), 151.7, 155.2 (C-4, C-17). − UV/Vis: λ_{max} (lg ε) = 198 nm (4.70), 230 (4.20). − MS: *m*/*z* (%) = 467 (11), 466 (29) [M$^+$], 128 (39) [$C_7H_{14}NO^+$], 127 (36), 86 (100) [$C_4H_8NO^+$]. − HRMS ($C_{29}H_{43}NO_2Si$): calcd. 465.3063; found 465.3367. − Calcd. C 74.79, H 9.31, N 3.01; found C 74.82, H 9.46, N 2.89.

Rearrangement of *O*-(5-Trimethylsilyl-4-[2.2]paracyclophanyl) Diisopropylcarbamate (3a): *n*BuLi (2.0 mmol) was added at 0 °C to a solution of 2,2,6,6-tetramethylpiperidine (0.34 mL, 2.00 mmol) in THF (5 mL). After the mixture had been stirred for 5 min at room temp., a solution of **3a** (212 mg, 0.500 mmol) in 10 mL of THF was added. The reaction mixture was refluxed for 5 h, treated with saturated aqueous NH_4Cl (5 mL), and the mixture worked up in the usual manner. Flash chromatography (Et_2O/hexane, 2:3) gave two fractions. The first fraction consisted of *syn*-4-hydroxy-*N*,*N*-diisopropyl-5-trimethylsilyl-2-[2.2]paracyclophanecarboxamide (**4a**) (39 mg, 18%). Recrystallization from ethanol afforded colorless prisms, m.p. 166−167 °C. − IR: $\tilde{\nu}$ = 3025 cm^{-1} (w), 2986 (s), 2937 (s), 2920 (s), 2896 (m), 2854 (m), 2788 (m), 2714 (m), 1599 (m), 1566 (vs), 1549 (s), 1478 (m), 1429 (s), 1379 (s), 1354 (s), 1305 (m), 1247 (s), 1206 (w), 1148 (m), 1091 (w), 945 (w), 854 (vs), 830 (s), 805 (m), 764 (m), 714 (w). − ^{1}H NMR (300.1 MHz): δ = 0.36 (s, 9 H, 24-H), 1.43 (m, 12 H, 19-H, 20-H, 22-H, 23-H), 3.00 (m, 3 H, 9-H, 10-H), 3.21 (m, 2 H, 1-H, 9-H, 10-H), 3.38 (dd, $^2J_{1,1}$ = 12.8, $^3J_{1,2}$ = 8.4 Hz, 1 H, 1-H), 3.81 (br. s, 1 H, 18-H or 21-H), 3.98 (ps-t, 1 H, $^3J_{2,1}$ = 8.9, $^3J_{2,1}$ = 9.6 Hz, 2-H), 4.29 (br. s, 1 H, 18-H or 21-H), 6.19 (d, $^3J_{7,8}$ = 7.7 Hz, 1 H, 7-H), 6.27 (d, $^3J_{8,7}$ = 7.7 Hz, 1 H, 8-H), 6.48 (d, 1 H, $^3J_{12/13,13/12}$ = 7.6 Hz, 12-H or 13-H), 6.56 (d, 1 H, $^3J_{16,15}$ = 7.7 Hz, 16-H), 6.62 (d, 1 H, $^3J_{12/13,13/12}$ = 7.8 Hz, 12-H or 13-H), 7.11 (d, 1 H, $^3J_{15,16}$ = 7.6 Hz, 15-H), 12.60 (s, 1 H, OH). − ^{13}C NMR (75.5 MHz): δ = 1.2 (C-24), 19.9, 20.0, 21.3 (C-19, C-20, C-22, C-23), 35.0 (C-9, C-10), 37.9 (C-1), 46.3 (C-18, C-21), 53.1 (C-2), 118.7 (C-3), 123.9 (C-7), 128.9 (C-15), 129.1 (C-5), 131.1, 132.2, 132.3 (C-12, C-13, C-16), 136.1, 138.7 (C-11, C-14), 137.2 (C-8), 150.7 (C-6), 161.9 (C-4), 175.7 (C-17). − UV/Vis: λ_{max} (lg ε) = 202 nm (4.70), 230 (4.22) (sh), 330 (2.233). − MS: *m*/*z* (%) = 424 (33), 423 (100) [M$^+$], 408 (14) [M$^+$ − CH_3], 380 (13) [M$^+$ − C_3H_7], 322 (11), 319 (39) [M$^+$ − C_8H_8], 304 (10), 203 (42), 176 (12), 105 (10), 104 (99) [$C_8H_8^+$], 100 (47), 86 (54) [$C_4H_8NO^+$]. − HRMS ($C_{26}H_{37}NO_2Si$): calcd. 423.2594; found 423.2582. − The second fraction consisted of α-[(4-hydroxy-5-[2.2]paracyclophanyl)dimethylsilyl]-*N*,*N*-diisopropylacetamide (**5**) (92 mg, 44%). Recrystallization from ethanol gave yellow needles, m.p. 141−142 °C. − IR: $\tilde{\nu}$ = 3047 cm^{-1} (w), 2968 (m), 2929 (m), 2863 (w), 1594 (vs), 1547 (m), 1484 (m), 1453 (s), 1374 (m), 1342 (s), 1268 (m), 1245 (m), 1227 (m), 1158 (w), 1130 (m), 1095 (m), 1047 (w), 863 (m), 839 (m), 816 (m), 776 (w), 768 (w). − ^{1}H NMR (200.1 MHz): δ = 0.24 (s, 3 H, 17-H or 18-H), 0.43 (s, 3 H, 17-H or 18-H), 1.29 (d, 6 H, $^3J_{22/23,21}$ = 6.8 Hz, 22-H, 23-H), 1.42 (ps-t, 6 H, $^3J_{25/26,24}$ = 6.6 Hz, 25-H, 26-H), 2.17 (d, 1 H, $^2J_{19,19}$ = 14.9 Hz, 19-H), 2.33 (d, 1 H, $^2J_{19,19}$ = 14.9 Hz, 19-H), 2.53 (m, 1 H, 1-H, 2-H, 9-H or 10-H), 2.96−3.29 (m, 6 H, 1-H, 2-H, 9-H or 10-H), 3.49 (m, 1 H, 1-H, 2-H, 9-H or 10-H), 3.85 (br. s, 1 H, 24-H), 4.08 (m, 1 H, 21-H), 6.16 (d, $^3J_{7,8}$ = 7.5 Hz, 1 H, 7-H), 6.28 (dd, 1 H, $^3J_{16,15}$ = 7.8 Hz, $^4J_{16,12}$ = 1.8 Hz, 16-H), 6.38 (d, $^3J_{8,7}$ = 7.5 Hz, 1 H, 8-H), 6.50 (dd, 1 H, $^3J_{12/13,13/12}$ = 7.8 Hz, $^4J_{12/13,16/15}$ = 1.7 Hz, 12-H or 13-H), 6.60 (dd, 1 H, $^3J_{12/13,13/12}$ = 7.8 Hz, $^4J_{13/13,16/15}$ = 1.9 Hz, 12-H or 13-H), 7.01 (dd, 1 H, $^3J_{15,16}$ = 7.8 Hz, $^4J_{15,13}$ = 1.8 Hz, 15-H), 10.74 (br. s, 1 H, OH). − ^{13}C NMR (75.5 MHz): δ = −0.5 (C-17 or C-18), −0.2 (C-17 or C-18), 19.2, 19.8 (C-22, C-23, C-25, C-26), 24.4 (C-19), 29.7, 32.7, 34.1, 34.8 (C-1, C-2, C-9, C-10), 44.8 (C-21, C-24), 117.7, 122.3, 126.1 (C-3, C-6, C-11 or C-14), 124.6, 127.3, 130.8, 131.1, 131.2, 136.3 (C-7, C-8, C-12, C-13, C-15, C-16), 139.3, 147.6 (C-3, C-6, C-11 or C-14), 159.6 (C-4), 172.6 (C-20). − UV/Vis: λ_{max} (lg ε) = 200 nm (4.68), 224 (4.26) (sh), 332 (3.08). − MS: *m*/*z* (%) = 424 (10), 423 (31) [M$^+$], 280 (19), 201 (16), 200 (100), 177 (10), 176 (32), 104 (14) [$C_8H_8^+$]. − HRMS ($C_{26}H_{37}NO_2Si$): calcd. 423.2594; found 423.2582.

***syn*-4-Hydroxy-*N*,*N*-diisopropyl-5-triethylsilyl-2-[2.2]paracyclophanecarboxamide (4b):** As described for **4a**, a mixture of 2,2,6,6-tetramethylpiperidine (0.25 mL, 1.48 mmol), *n*BuLi (1.47 mmol), and *O*-(5-triethylsilyl-4-[2.2]paracyclophanyl) diisopropylcarbamate (233 mg, 0.500 mmol) (**3b**) was refluxed in THF (15 mL) for 6 h. After treatment with saturated aqueous NH_4Cl (5 mL) and workup in the usual manner, purification of the crude product by flash chromatography (Et_2O/hexane, 1:6) yielded 196 mg (84%) of **4b** as a colorless solid, m.p. 107−108 °C. − IR: $\tilde{\nu}$ = 3005 cm^{-1} (m), 2951 (vs), 2934 (s), 2911 (s), 2873 (s), 2809 (w), 2771 (w), 2719 (m), 2673 (br. m), 1600 (vs), 1568 (vs), 1544 (m), 1476 (m), 1463 (s), 1428 (s), 1381 (m), 1366 (vs), 1347 (s), 1322 (m), 1250 (m), 1205 (w), 1160 (w), 1135 (w), 1043 (m), 1005 (m), 974 (w), 935 (w), 872 (w), 800 (m), 757 (m), 722 (s), 665 (m), 618 (m). − ^{1}H NMR (300.1 MHz): δ = 0.85−0.97 (m, 15 H, 24-H, 25-H), 1.34−1.43 (m, 12 H, 19-H, 20-H, 22-H, 23-H), 2.89 (m, 1 H, 9-H, 10-H), 3.06−3.21 (m, 4 H, 1-H, 9-H, 10-H), 3.33 (dd, $^2J_{1,1}$ = 12.8, $^3J_{1,2}$ = 8.4 Hz, 1 H, 1-H), 3.75 (br. s, 1 H, 18-H or 21-H), 3.92 (dd, 1 H, $^3J_{2,1}$ = 8.5 Hz, $^3J_{2\text{-H},1\text{-H}}$ = 10.2 Hz, 2-H), 4.26 (br. s, 1 H, 18-H or 21-H), 6.13 (d, $^3J_{7,8}$ = 7.7 Hz, 1 H, 7-H), 6.21 (d, $^3J_{8,7}$ = 7.8 Hz, 1 H, 8-H), 6.49 (m, 2 H, 12-H or 13-H, 16-H), 6.61 (dd, 1 H, $^3J_{12/13,13/12}$ = 7.97 Hz, $^4J_{12/13,16/15}$ = 1.8 Hz, 12-H or 13-H), 7.07 (dd, 1 H, $^3J_{15,16}$ = 8 Hz, $^4J_{15,13}$ = 1.8 Hz, 15-H), 11.89 (s, 1 H, OH). − ^{13}C NMR (75.5 MHz): δ = 5.5 (C-24), 8.1 (C-25), 20.4, 21.7 (C-19, C-20, C-22, C-23), 35.6, 35.8 (C-9, C-10), 38.4 (C-1), 46.8 (C-18, C-21), 53.8 (C-2), 119.0 (C-3), 124.0 (C-7), 127.4 (C-5), 129.7 (C-15), 131.2, 132.9, 133.0 (C-12, C-13, C-16), 136.7, 139.2 (C-11, C-14), 137.9 (C-8), 152.3 (C-6), 162.7 (C-4), 176.2 (C-17). − UV/Vis: λ_{max} (lg ε) = 202 nm (4.66), 230 (4.20, sh), 332 (3.24). − MS: *m*/*z* (%) = 466 (34), 465 (100) [M$^+$], 437 (10), 436 (29) [M$^+$ − Et], 422 (11), 361 (33) [M$^+$ − C_8H_8], 332 (24), 308 (17), 262 (16), 233 (15), 232 (17), 231 (53), 205 (11), 206 (14), 203 (17), 131 (11), 128 (15), 113 (17), 105 (12), 104 (79) [$C_8H_8^+$], 100 (37) [$C_5H_{10}NO^+$], 91 (36), 86 (26) [$C_4H_8NO^+$], 83 (12), 71 (15), 70 (12), 69(15). − HRMS ($C_{29}H_{43}NO_2Si$): calcd. 465.3063; found 465.3052. − Calcd. C 74.79, H 9.31, N 3.01; found C 74.80, H 9.57, N 2.80.

***syn*-4-Hydroxy-*N*,*N*-diisopropyl-2-[2.2]paracyclophanecarboxamide (7):** A sample of **4b** (0.168 g, 0.36 mmol) was refluxed in TFA (10 mL) for 2 h. The reaction mixture was neutralized with 2 M NaOH with ice-cooling. The usual workup gave a crude product, which was purified by flash chromatography (Et_2O/hexane, 1:6 to 2:3) to give 124 mg (97%) of **7** as a pale yellow solid, m.p. 212−213 °C. − IR: $\tilde{\nu}$ = 3016 cm^{-1} (w), 2976 (m), 2928 (s), 2865 (w), 2698 (m), 2635 (m), 1611 (w), 1563 (vs), 1508 (m), 1460 (m), 1444 (m), 1397 (m), 1336 (s), 1286 (w), 1254 (w), 1206 (w), 1159 (w), 1127 (w), 1111 (w), 1048 (w), 889 (w), 873 (w), 714 (w). − ^{1}H NMR (300.1 MHz): δ = 1.37 (d, 6 H, ^3J = 6.7 Hz, 19-H, 20-H, 22-H or 23-H), 1.43 (d, 6 H, ^3J = 6.7 Hz, 19-H, 20-H, 22-H or 23-H), 2.81−3.13 (m, 4 H, 9-H, 10-H), 3.22 (dd, $^2J_{1,1}$ = 13.1, $^3J_{1,2}$ = 9.7 Hz, 1 H, 1-H), 3.36 (dd, $^2J_{1,1}$ = 13.1, $^3J_{1,2}$ = 8.6 Hz, 1 H, 1-

H), 3.83 (br. s, 1 H, 18-H or 21-H), 4.00 (ps-t, 1 H, $^3J_{2,1}$ = 9.1 Hz, 2-H), 4.25 (br. s, 1 H, 18-H or 21-H), 5.63 (d, $^4J_{5,7}$ = 1.8 Hz, 1 H, 5-H), 6.17 (dd, $^3J_{7,8}$ = 7.9, $^4J_{7,5}$ = 1.8 Hz, 1 H, 7-H), 6.26 (d, $^3J_{8,7}$ = 7.9 Hz, 1 H, 8-H), 6.36 (dd, 1 H, $^3J_{13,12}$ = 7.9 Hz, $^4J_{13,15}$ = 1.7 Hz, 13-H), 6.51 (dd, 1 H, $^3J_{12,13}$ = 7.9 Hz, $^4J_{12,16}$ = 1.9 Hz, 12-H), 6.58 (dd, 1 H, $^3J_{16,15}$ = 7.8 Hz, $^4J_{16,12}$ = 1.8 Hz, 16-H), 7.24 (dd, 1 H, $^4J_{15,13}$ = 1.9 Hz, 15-H), 11.92 (s, 1 H, OH). − ^{13}C NMR (75.5 MHz): δ = 20.4, 21.9 (C-19, C-20, C-22, C-23), 34.7 (C-9), 35.1 (C-10), 38.4 (C-1), 46.8 (C-18, C-21), 53.3(C-2), 120.8 (C-3), 122.4 (C-7), 124.9 (C-5), 129.4 (C-15), 131.8 (C-16), 132.6 (C-12, C-13), 135.5 (C-8), 136.6 (C-14), 139.4 (C-11), 143.7 (C-6), 157.4 (C-4), 176.2 (C-17). − UV/Vis: λ_{max} (lg ε) = 198 nm (4.65), 226 (4.23). − MS: *m*/*z* (%) = 352 (19), 351 (72) [M$^+$], 247 (31) [M$^+$ − C_8H_8], 147 (26), 120 (15), 105 (10), 104 (72) [C_8H_8], 100 (100) [$C_5H_{10}NO^+$], 91 (10), 86 (30) [$C_4H_8NO^+$]. − HRMS ($C_{23}H_{29}NO_2$): calcd. 351.2198; found 351.2189.

***N-tert*-Butyl-4-[2.2]paracyclophanecarboxamide (9):** 4-Dimethylaminopyridine (0.06 g, 0.5 mmol), triethylamine (0.84 mL, 6.0 mmol), and *tert*-butylamine (0.63 mL, 6.0 mmol) were added to a solution of 4-[2.2]paracyclophanecarbonyl chloride (**8**) (1.35 g, 5.00 mmol) in THF (50 mL). A white precipitate was formed. The reaction mixture was stirred for 16 h at room temp. and subsequently treated with saturated aqueous $NaHCO_3$. After the usual workup and purification of the crude product by flash chromatography (Et_2O/hexane, 1:6 to 2:3), 1.2 g (76%) of **9** was obtained as a pale yellow solid, m.p. 114−118 °C. − IR (KBr): $\tilde{\nu}$ = 3326 cm^{-1} (s), 3010 (w), 2972 (m), 2958 (m), 2930 (m), 2890 (w), 2850 (w), 1643 (vs), 1524 (vs), 1502 (m), 1478 (w), 1450 (m), 1391 (w), 1366 (w), 1360 (w), 1305 (m), 1238 (w), 1224 (m), 902 (w), 819 (w), 728 (w). − ^{1}H NMR (300.1 MHz): δ = 1.45 (s, 9 H, 19-H), 2.90−3.17 (m) and 3.62 (m, 8 H, 1-H, 2-H, 9-H, 10-H), 5.41 (s, 1 H, NH), 6.42−6.53 (m, 5 H, 7-H, 8-H, 12-H, 13-H, or 16-H), 6.62 (ps-s, 1 H, 5-H), 6.85 (ps-d, 1 H, $^3J_{15\text{-H},13\text{-H}}$ = 7.8 Hz, 15-H). − ^{13}C NMR (75.5 MHz): δ = 28.6 (C-19), 34.5, 34.8, 35.0, 35.2 (C-1, C-2, C-9, C-10), 51.1 (C-18), 131.5, 131.7, 132.2, 132.3, 134.2, 135.5 (C-5, C-7, C-8, C-12, C-13, C-15, C-16), 136.2, 137.9, 138.9, 139. 2, 139.8 (C-3, C-4, C-6, C-11, C-14), 168.3 (C-17). − UV/Vis (MeCN): λ_{max} (lg ε) = 198 nm (4.58), 228 (4.22). − MS: *m*/*z* (%) = 307 (9) [M$^+$], 251 (7) [M$^+$ − C_4H_8], 147 (100) [$C_9H_9NO^+$], 131 (11) [$C_9H_7O^+$], 130 (14), 105 (9), 104 (14) [$C_8H_8^+$], 103 (38). − HRMS ($C_{21}H_{25}NO$): calcd. 307.1936; found 307.1908. − Calcd. C 82.04, H 8.20, N 4.56; found C 82.01, H 8.21, N 4.33.

***syn*-*N*-*tert*-Butyl-2-trimethylsilyl-4-[2.2]paracyclophanecarboxamide (11):** A solution of *N*-*tert*-butyl-4-[2.2]paracyclophanecarboxamide (**9**) (308 mg, 1.0 mmol) in THF (15 mL) was added dropwise to a mixture of TMEDA (0.49 mL, 3.25 mmol) and *s*BuLi (3.21 mmol) in THF (5 mL) at −78 °C. The resulting deep brown reaction mixture was stirred for 2 h at −78 °C and subsequently treated with TMSCl (0.60 mL, 4.73 mmol). After warming up to room temp. over a period of 5 h, the resulting colorless solution was quenched with saturated aqueous NH_4Cl (10 mL). The usual workup and purification of the crude product by flash chromatography (Et_2O/hexane, 1:6) afforded 321 mg (85%) of **10** as a white solid, m.p. 98−100 °C. − IR: $\tilde{\nu}$ = 3444 cm^{-1} (w), 3423 (m), 2975 (m), 2944 (m), 2900 (m), 2855 (w), 1666 (vs), 1656 (s), 1591 (w), 1551 (w), 1504 (vs), 1475 (m), 1449 (s), 1391 (w), 1365 (m), 1296 (m), 1281 (m), 1243 (s), 1214 (m), 1197 (w), 1170 (w), 964 (w), 896 (w), 878 (s), 838 (s), 751 (w), 716 (m). − ^{1}H NMR (300.1 MHz): δ = 0.19

Table 2. Summary of the crystal data, data collection, and refinement parameters for the three crystal structures reported in this paper

Compound	**4b**	**7**	**11**
Empirical formula	$C_{29}H_{43}NO_2Si$	$C_{23}H_{29}NO_2$	$C_{24}H_{33}NOSi$
M_r	465.73	350.46	379.60
Crystal habit	colorless prism	colorless tablet	colorless tablet
Crystal size [mm]	0.45 × 0.38 × 0.25	0.39 × 0.36 × 0.14	0.43 × 0.31 × 0.15
Crystal system	triclinic	monoclinic	monoclinic
Space group	*P*1	$P2_1/c$	*C*2/*c*
Cell constants:			
a [Å]	11.5061(14)	21.5534(16)	29.763(2)
b [Å]	13.3836(16)	7.9485(8)	12.1577(10)
c [Å]	18.888(2)	11.2564(10)	12.3734(10)
α [°]	70.061(4)	90	90
β [°]	78.839(4)	100.674(3)	102.428(3)
γ [°]	89.888(4)	90	90
V [Å^3]	2676.1	1895.0	4372.4
Z	4	4	8
D_x [Mg m^{-3}]	1.156	1.228	1.153
μ [mm^{-1}]	0.113	0.077	0.121
Transmissions			
F(000)	1016	756	1648
T [°C]	−130	−130	−130
$2\theta_{max}$	56	56	56
No. of reflections:			
measured	36066	36056	15766
unique	21198	4803	5430
R_{int}	0.098	0.054	0.041
Parameters	1233	248	254
Restraints	1091	1	0
$wR(F^2$, all refl.)	0.221	0.136	0.117
$R[F, > 4\sigma(F)]$	0.082	0.046	0.042
S	1.03	1.05	1.06
max. Δρ [e Å^{-3}]	0.58	0.42	0.34

(s, 9 H, 20-H), 1.44 (s, 9 H, 19-H), 2.50 (dd, $^3J_{2,1}$ = 8.0, $^3J_{2,1}$ = 10.5 Hz, 1 H, 2-H), 2.90 (m, 2 H, 9-H, 10-H), 3.17 (m, 3 H, 1-H, 9-H, 10-H), 3.54 (t, $^3J_{1,2}$ = 11.4 Hz, 1 H, 1-H), 5.29 (s, 1 H, NH), 6.37−6.48 (m, 4 H, 7-H, 8-H, 12-H, 13-H or 16-H), 6.58 (m, 2 H, 5-H, 7-H, 8-H, 12-H o. 13-H), 6.86 (ps-d, 1 H, $^3J_{15,13}$ = 7.8 Hz, 15-H). − ^{13}C NMR (75.5 MHz): δ = 0.2 (C-20), 29.0 (C-19), 34.7, 34.9, 37.7 (C-1, C-9, C-10), 45.6 (C-2), 51.1 (C-18), 131.0, 131.1, 132.1, 132.5, 133.1, 133.4, 138.1 (C-5, C-7, C-8, C-12, C-13, C-15, C-16), 134.5, 138.0, 141.9, 144.4 (C-3, C-4, C-6, C-11, C-14), 169.1 (C-17). − UV/Vis: λ_{max} (lg ε) = 200 nm (4.63), 230 (4.23). − MS: *m/z* (%) = 380 (33), 379 (100) [M^+], 365 (28), 364 (84) [$M^+ - CH_3$], 323 (15), 322 (13), 275 (10), 261 (11), 260 (39) [$M^+ - C_8H_8$, $-CH_3$], 220 (13), 219 (69) [$C_{12}H_{17}NOSi^+$], 218 (20), 205 (19), 204 (60) [$C_{16}H_{12}^+$], 186 (18), 146 (16), 104 (21), 74 (11), 73 (44). − HRMS ($C_{24}H_{33}NOSi$): calcd. 379.2331; found 379.2323. − Calcd. C 75.93, H 8.76, N 3.69; found C 76.31, H 8.85, N 3.45.

X-ray Crystallography: A summary of the crystal data, data collection, and refinement parameters for the three crystal structures reported in this paper is given in Table 2. − Structure Determination of **4b**, **7**, and **11**: A cut prism (**4b**) or a cut tablet (**7** and **11**) was mounted on a glass fiber in inert oil and transferred to the cold gas stream of a Bruker SMART 1000 CCD diffractometer fitted with a Siemens LT-3 low-temperature attachment. Data were collected with ω-scan and ϕ-scan methods (**4b** and **7**) or the ω-scan method (**11**) using graphite-monochromated Mo-K_α radiation (λ = 0.71073 Å). All unique data were used for calculations (program SHELXL-97, G. M. Sheldrick, University of Göttingen). The structures **7** and **11** were solved by direct methods, and all structures were refined anisotropically by full-matrix, least squares on F^2. Because of the very large number of atoms in the structure, **4b** was solved using the novel direct method program SHELXD (G. M. Sheldrick, private communication). The hydroxy and amide hydrogen atoms were refined freely. The remaining hydrogen atoms were refined with a riding model or as rigid methyl groups. The Flack parameter for the absolute structure of **4b** is −0.17(12). The hydroxy group in compound **7** is disordered over two positions, with occupancies of 0.965(3) for O1 and 0.035(3) for O1′, implying the presence of a small amount of an alternative isomer (see Discussion). Crystallographic data for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-155004 (**4b**), -155005 (**7**), and -155006 (**11**). Copies of the data can be obtained free of charge on applicaton to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

Acknowledgments

T. F. would like to thank the "Förderverein der Freunde des Instituts für Organische Chemie an der Technischen Universität Braunschweig e.V." for financial support. V. S. is grateful to NSERC Canada for financial assistance through the RG program and we also thank the Fonds der Chemischen Industrie for continuous support of our studies.

[1] V. V. Kane, A. Gerdes, W. Grahn, L. Ernst, I. Dix, P. G. Jones, H. Hopf, *Tetrahedron Lett.* **2001**, 373−376.
[2] H. Hopf, D. G. Barrett, *Liebigs Ann.* **1995**, 449−451; D. G. Barrett, Diploma Thesis, Technische Universität Braunschweig, **1988**.
[3] A. Cipiciani, F. Fringuelli, V. Mancini, O. Piermatti, F. Pizzo, *J. Org. Chem.* **1997**, *62*, 3744−3747.
[4] V. Rozenberg, V. Kharitonov, D. Antonov, E. Sergeeva, A. Aleshkin, N. Ikonnikov, S. Orlova, Y. Belokon′, *Angew. Chem.* **1994**, *106*, 106−108; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 91−93.
[5] H. J. Reich, D. J. Cram, *J. Am. Chem. Soc.* **1969**, *91*, 3505−3516; H. J. Reich, D. J. Cram, *J. Am. Chem. Soc.* **1968**, *90*, 1365−1367; E. A. Truesdale, D. J. Cram, *J. Org. Chem.* **1980**, *45*, 3974−3981; H. Zitt, Dissertation, Technische Universität Braunschweig, **1999**; C. Beck, Dissertation, Technische Universität Braunschweig, **1998**.
[6] The formation of laterally substituted tertiary [2.2]paracyclophanecarboxamides was reported as a side reaction in the diploma thesis of D. G. Barrett.[2] However, the process was not optimized at that time.
[7] X.-L. Hou, X.-W. Wu, L.-X. Dai, B.-X. Cao, J. Sun, *Chem. Commun.* **2000**, 1195−1196. For an alternate route to 4-oxazolinyl-[2.2]paracyclophane see Chr. Schulz, Dissertation, Technische Universität Braunschweig, **2000**.
[8] O. Middel, Z. Greff, N. J. Taylor, W. Verboom, D. N. Reinhoudt, V. Snieckus, *J. Org. Chem.* **2000**, *65*, 667−675.
[9] D. Pamperin, C. Schulz, H. Hopf, C. Syldatk, M. Pietzsch, *Eur. J. Org. Chem.* **1998**, 1441−1445.
[10] R. J. Mills, N. J. Taylor, V. Snieckus, *J. Org. Chem.* **1989**, *54*, 4372−4385.
[11] W. Wang, V. Snieckus, *J. Org. Chem.* **1992**, *57*, 424−426.
[12] Lateral metalation is a well-established reaction in *ortho*-alkyl-substituted aromatics: R. D. Clark, R. Jahangir, *Org. React.* **1995**, *47*, 1−314.
[13] For a study of simple *O*-(*o*-tolyl) carbamates producing benzofuranones by this type of reaction, see: M. A. J. Miah, S. Chattopadhyay, M. Tsukazaki, M. Wicki, T. Nguyen, M. Kerr, A. Kalinin, V. Snieckus, *Synlett* **1997**, 839−841.
[14] V. Snieckus, *Chem. Rev.* **1990**, *90*, 879−933 and references therein.
[15] K. Krohn, H. Rieger, H. Hopf, D. Barrett, P. G. Jones, D. Döring, *Chem. Ber.* **1990**, *123*, 1729−1732.
[16] J. E. MacDonald, G. S. Poindexter, *Tetrahedron Lett.* **1987**, *28*, 1851−1852.
[17] F. H. Allen, O. Kennard, D. G. Watson, L. Brammer, A. G. Orpen, R. Taylor, *J. Chem. Soc., Perkin Trans. 2* **1987**, S1−S19.
[18] P. Beak, A. I. Meyers, *Acc. Chem. Res.* **1986**, *19*, 353−356.
[19] M. Psiorz, R. Schmid, *Chem. Ber.* **1987**, *120*, 1825−1828.

Received December 27, 2000
[O00659]