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# Asymmetric Synthesis of *(R,S)*- and *(R,R)*-4-Hydroxy-5-(α-Substituted)-Hydroxymethyl[2.2]Paracyclophane and Derivatives by Stereoselective Addition to *(R)*-4-Hydroxy-5-Formyl[2.2]Paracyclophane and Derivatives

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**Abstract:** Highly diastereoselective nucleophilic addition reactions of organometallic reagents to formyl[2.2]paracyclophane derivatives which were ortho-substituted by hydroxy-, alkoxy- and trimethylsilyloxy-groups are reported. The absolute configuration of the newly formed secondary alcohols is assigned on the basis of the X-ray diffraction study as well as chemical correlation. The magnitude of the asymmetric induction and even the sense of chirality of the forming asymmetric carbon atoms of the alcohols depended on the nature of the ortho-substituents. 

## INTRODUCTION

The nucleophilic addition of organometallic reagents to the C=O double bonds of aldehydes and ketones is one of the most important and most explored reactions of asymmetric synthesis.[1] Recently, a number of such reactions have been investigated for planar chiral transition metal complexes, among which (arene)tricarbonylchromium complexes were most widely employed[2]. Addition of alkylmagnesium halides,[3] alkyllithium or hydrides[4] to the benzylic carbonyl group of the chiral complexes has been found to proceed in a highly stereoselective manner. It has also been shown that some of the resulting α-substituted benzyl alcohol tricarbonylchromium complexes were useful as chiral ligands in the catalytic asymmetric ethylation of benzaldehydes with diethylzinc and both planar and central chiralities are very important for the achievement of high enantioselectivity in these catalytic reactions[4].

However, another class of planar chiral compounds based on [2.2]paracyclophane derivatives has so far not been explored in these reactions and [2.2]paracyclophane, in general, has very rarely been used as a scaffolding unit for chiral auxiliaries in asymmetric synthesis.[5-7]

Recently we have elaborated two different approaches to racemic 4-formyl-5-hydroxy-[2.2]paracyclophane (FHPC)[6,7] and two effective resolution techniques[6,8] which allowed us to obtain enantiomers of FHPC in high enantiomeric purity (up to 98 % e.e.). It has also been shown that scalemic FHPC or its derivatives can be used as chiral auxiliaries for the asymmetric synthesis of β-hydroxy-α-amino acids and α-methyl-phenylalanine with e.e.s ranging mostly from 45 to 98%.

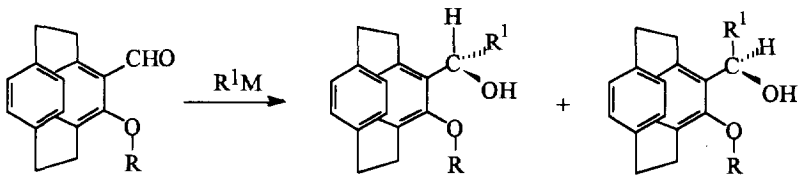
We report herein the nucleophilic addition of organomagnesium and organolithium reagents to the carbonyl group of FHPC and its derivatives, providing a new asymmetric center in the side chain of the molecule. In some cases diastereomeric carbinols having *(R)*- or *(S)*- configuration could be obtained with high diastereoselectivity. The compounds could be used in the future as prospective chiral ligands in catalytic asymmetric reactions, catalyzed by Lewis acids.

## RESULTS AND DISCUSSION

O-Alkylation of *(R)*-FHPC **1** with MeI and $^{i}$PrBr with formation of *(R)*-**2** and *(R)*-**3** respectively have been reported earlier[8]. *(R)*-5-trimethylsilyloxy[2.2]paracyclophane-4-carbaldehyde *(R)*-**4** has been obtained from *(R)*-FHPC and $Me_3SiCl$ in presence of $Et_3N$ in good yield, as described in the experimental section.

When *(R)*-FHPC is treated with either organomagnesium (EtMgI or *p*-TolMgBr) or organolithium (BuLi) reagents, exclusively one diastereoisomer in each of the reactions (**5, 6** or **7**, see Table 1, runs 1-3) is formed in high chemical yields. *(R)*-**4**, when reacted with EtMgI, produced one diastereoisomer as well (**12** see Table 1, run 8). On the other hand the addition of EtMgI and *p*-TolMgBr to the carbonyl groups of *(R)*-**2** and *(R)*-**3** resulted in a mixture of *(R,S)*- and *(R,R)*-diastereoisomers (**8, 9, 10** and **11**, see Table 1, runs 4-7).

**Table 1. Diastereoselective Nucleophilic Addition of Organometallic Reagents $R^1M$ to the Carbonyl Group of *(R)*-FHPC or its Derivatives.**




*(R)*- *(R, S)*- *(R,R)*-

R = H (**1**), $CH_3$ (**2**), $CH(CH_3)_2$ (**3**), $Si(CH_3)_3$ (**4**)

| run | OR | $R^1M$ | t, °C | Prod. | Yield, % | d.e, % | Abs. conf. of the side chain of maj. isomer |
|---|---|---|---|---|---|---|---|
| 1 | OH | n-BuLi | -78 | **5** | 85 | >98 | *(S)* |
| 2 | OH | EtMgI | -78 | **6** | 82 | >98 | *(S)* |
| 3 | OH | EtMgI | -23 | **6** | 96 | >98 | *(S)* |
| 4 | OH | EtMgI | +20 | **6** | 93 | >98 | *(S)* |
| 5 | OH | *p*-TolMgBr | -23 | **7** | 80 | >98 | *(S)* |
| 6 | OMe | EtMgI | -23 | **8** | 95 | 30 | *(S)* |
| 7 | OMe | EtMgI | +20 | **8** | 97 | 28 | *(S)* |
| 8 | OMe | *p*-TolMgBr | +20 | **9** | 71 | 34 | *(S)* |
| 9 | $OPr^i$ | EtMgI | -78 | **10** | 60 | 66 | *(R)* |
| 10 | $OPr^i$ | EtMgI | +20 | **10** | 98 | 72 | *(R)* |
| 11 | $OPr^i$ | *p*-TolMgBr | +20 | **11** | 86 | 70 | *(R)* |
| 12 | $OSiMe_3$ | EtMgI | -78 | **12** | 91 | >98 | *(R)* |

The ratios of the diastereoisomers of each of the compounds **8-11** were determined after work up of the reaction mixtures from their $^1$H NMR spectra before separation of the isomers. The isomers were subsequently separated by preparative chromatography on $SiO_2$. Surprisingly, in all the cases for which the temperature of the reaction was varied it was found to have a negligible effect on the d.e. of the reactions (see Table, runs. 2-4, 6-7, 9-10).

The single crystal X-ray diffraction study of the major diastereoisomeric carbinol **9** (Table 1, run 5) indicated the side chain asymmetric carbon atom to have *(S)*-configuration (Fig.1) by reference to the known *(R)*-absolute configuration of the chiral [2.2]paracyclophane moiety. The diastereoisomer **7**, obtained as the only isomer from **1**, was quantitatively converted[8] to the same *(R,S)*-**9** (Scheme 1) by a simple base induced O-alkylation. Since the reaction cannot possibly involve any change of the side chain or paracyclophane configurations, the absolute configuration of the initial **7** could safely be assigned as *(R,S)*. In turn, *(R,S)*-**7** was converted by O-alkylation with $^i$PrBr into *(R,S)*-**11** (see Scheme 1) which had been previously obtained as the minor diastereoisomer in the nucleophilic addition reaction of *p*-TolMgBr to *(R)*-**3** (Table 1, run 7).

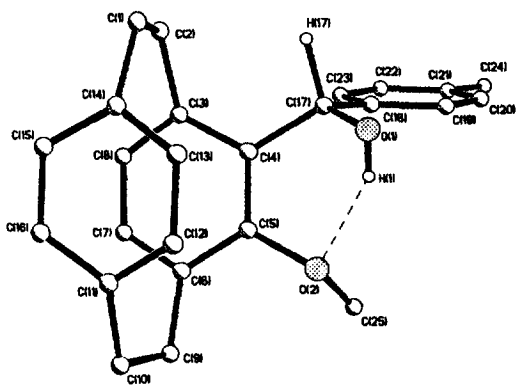
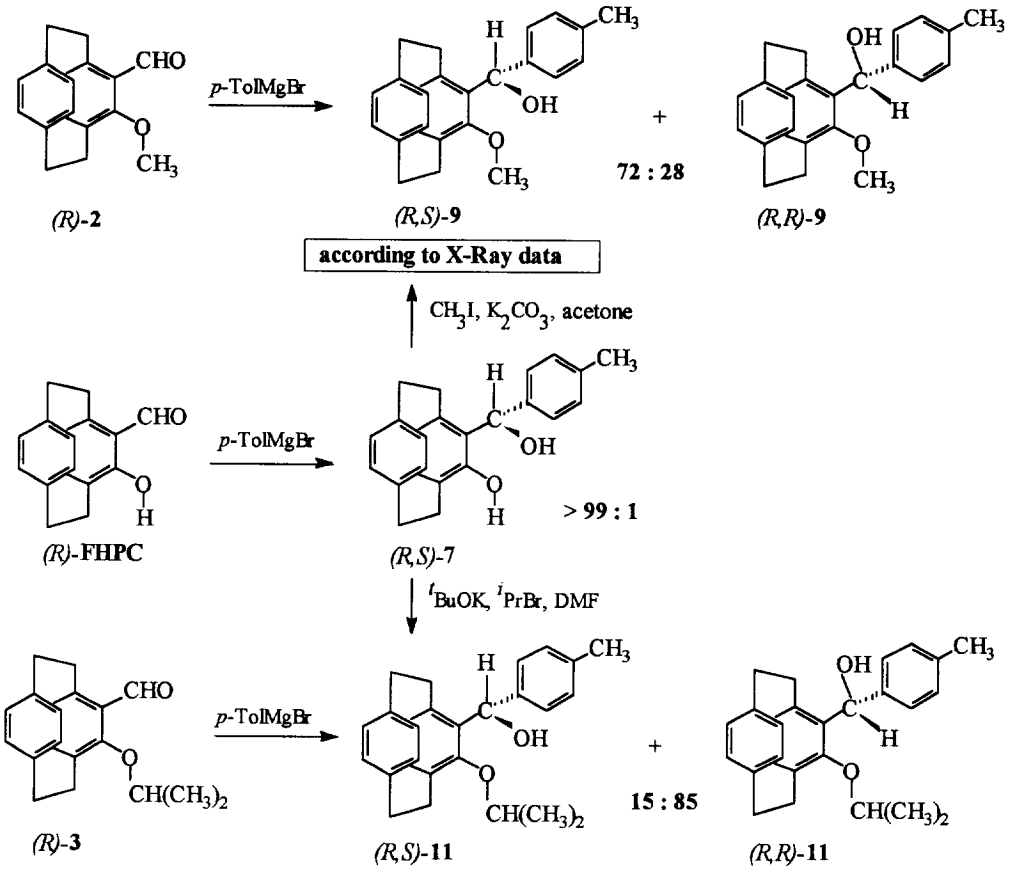


Fig. 1. Structure of the *(S)*-(4-methylphenyl)-[*(R)*-5-methoxy-[2.2]paracyclophane-4-yl]carbinol *(R,S)*-**9**.

For the major and minor diastereoisomers of **10** (Table 1, run 6) the absolute configurations of the new asymmetric centers were elucidated on the basis of $^1$H-$^1$H NOESY spectroscopy supported by results of AM1 calculations. Thus noticeable NOEs from α-H to isopropyl methyl group and from 2-H$^A$ to β-H were characteristic only for the major **10** diastereoisomer (Fig. 2, *a*) and were not found in the NOESY spectrum of the minor **10** diastereoisomer (Fig. 2, *b*). For the latter, however, pronounced NOEs from α-H to 1-H$^A$, 2-H$^A$ and H$^{13}$ and from the OH-group to H$^{12}$ and H$^{13}$ were observed whereas noticeable NOEs from the OH-group to bridge protons 1-H$^A$ and 2-H$^A$ were not found. The computer generated (AM1 calculated) structures reveal that for both diastereoisomers of **10** [*(R,S)* and *(R,R)*] the most stable conformation of the conformationally labile side chain is one with the ethyl-group turned away from the unsubstituted paracyclophane ring. Similar conformation of the side chain with the phenyl ring turned away from the unsubstituted paracyclophane ring can be observed in the solid-state structure of *(R,S)*-**9** (see Fig.1). Taken together the features of the NOESY spectra strongly support that the configuration of the minor isomer of **10** is *(R,S)* and the major isomer has *(R,R)*-configuration.




Scheme 1.

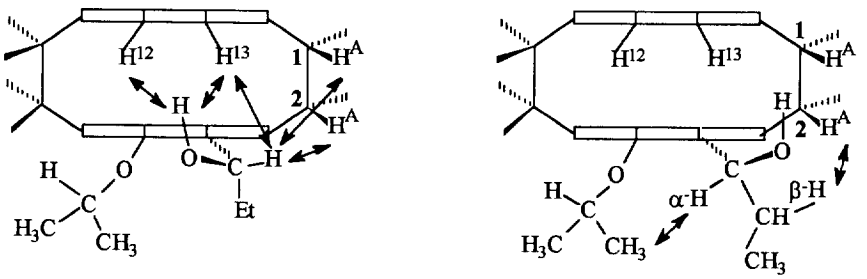
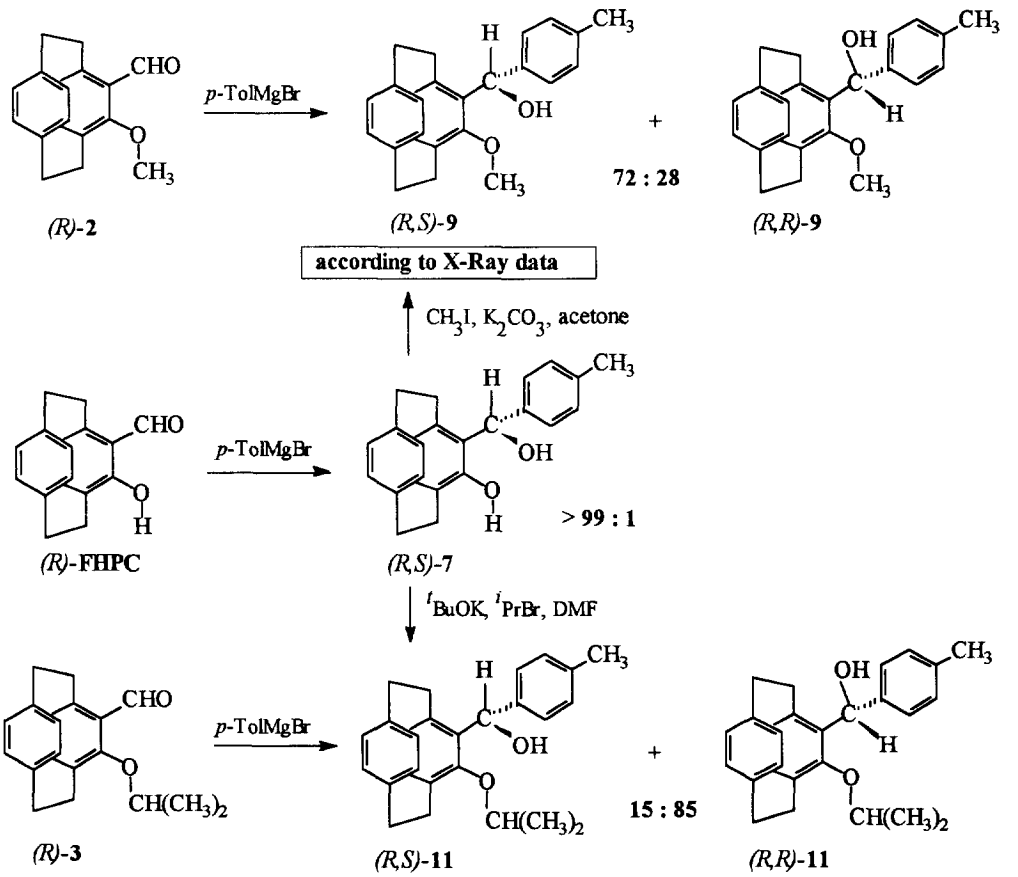



Fig. 2.

The determination of the absolute configuration of the alcohols **6** and **8** has been carried out *via* series of chemical transformations (when the asymmetric center is not involved, see Scheme 2) performed just in the same manner as for carbinols **7**, **9** and **11** (Scheme 1). From $^1$H-NMR-spectral data some regular differences of chemical shifts in the diastereoisomeric pairs of **8** and **10** are revealed. Thus the $H^{12}$ and $H^{13}$ protons of the *(R,S)*-isomers resonate at a lower field than the same protons of *(R,R)*-isomers ($\Delta\delta$ = 0.2-0.4 for **8** and $\Delta\delta$ = 0.4-0.6 ppm for **10**). Also for *(R,R)*-isomers the bridge proton 2-$H^A$ absorbs at a higher field compared to the corresponding protons for *(R,S)*-isomers ($\Delta\delta$ = 0.6 ppm and 0.8 ppm, respectively). It should be mentioned that a correlation between the configuration of the asymmetric centers and the chemical shifts of the OH-group was also detected. When the formation of an intramolecular hydrogen bond is facile (*(R,S)*-isomers, see Fig.1[9]) the OH group is registrated at $\delta$ = 4.5-5.0 as a sharp doublet. Spin-spin coupling with $\alpha$-H in this case ($J^2$ = 6.2 Hz) indicated that there was no fast OH-proton exchange (on the NMR time scale). Apparently, a strong intramolecular hydrogen bond between the OH-group and the OR-substituent is formed here. In case of the *(R,R)*-isomers a significant steric congestion accompanies the formation of such a hydrogen bond and the OH-group proton resonates at $\delta$ = 1.5-1.7 (in $C_6D_6$) as a broad singlet.




Scheme 2.

Unfortunately, the attempts to convert *(R,S)*-**6** to **12** by O-trimethylsilylation with $Me_3SiCl/Et_3N$ gave, as the only detectable compound, a product with the trimethylsilyl-group at the carbinol oxygen atom. Nevertheless, the lowfield shift of 2-H$^{A}$ and the α-H signals and the upfield broad singlet of the OH-group in this case are suggesting the absolute configuration of **12** as *(R,R)*.

The $^1$H-NMR-spectrum of carbinol **5** is almost the same as that of *(R,S)*-**6** (apart from the signals of the two extra -$CH_2$-groups) so that both compounds presumably have the same absolute configuration.

Thus we found that the nucleophilic addition of the two types of organometallic reagents (BuLi and RMgX) to the carbonyl group of *(R)*-FHPC occurred with almost 100% diastereoselectivity. To account for the observation we assume that under the reaction conditions the organometallic reagents deprotonate the hydroxy-group of *(R)*-FHPC at the first stage of the reaction, producing a phenolate. The metal ion coordinates with both the ionized oxygen atom and the n-electrons of the C=O thereby activating the C=O bond towards nucleophilic attack and at the same time forming a rigid chelate (Fig. 3, path *a*). Examination of Dreiding models of the resulting chelate reveals that the *re*-face of the carbonyl group of FHPC is strongly sterically shielded by the unsubstituted aromatic ring of the paracyclophane moiety. Thus the second stage of the reaction, the nucleophilic attack itself, should predominantly occur from the sterically less hindered *si*-face of the carbonyl group, yielding a *(S)*-configuration of the newly formed asymmetric center (overall *(R,S)*-configuration of the predominant diastereoisomer) which was really observed (Table 1, runs 1-3).

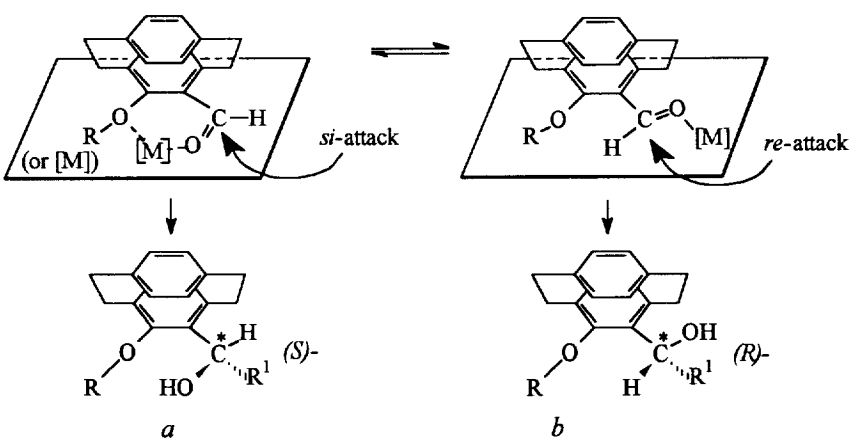



Fig. 3.

The replacement of the hydroxy group with a more bulky alkoxy one is playing a crucial role in the stereochemical outcome of the reaction. As the size of the alkoxy-group is increasing, *re*-attack of the nucleophiles starts to compete with the *si*-attack and greater proportions of the *(R,R)*-diastereoisomers are detected in the reaction mixture (Table 1, runs 4-7) until the introduction of trimethylsilyloxy-group brought about the preponderance of the *re*-attack with no *(R,S)*-diastereoisomer detectable for the EtMgI addition to *(R)*-**4** (Table 1, run 8). Two explanations can be put forward to rationalize these results:

a) The chelation of the metal ion by the carbonyl and alkoxy-groups is still present in the transition state of the addition but the *si*-attack of the nucleophiles becomes sterically hindered by the bulky O-alkyl substituent and, eventually, the bulky trimethylsilyloxy-substituent blocks the *si*-attack entirely

b) In addition to the chelated structures, another unchelated complex, existing in an equilibrium with the chelated structure, might be a reactive intermediate in the addition reaction (Fig.3, path *b*). The steric shielding by the unsubstituted phenylene ring of the paracyclophane makes the *si*-attack sterically unfavorable in this complex. As the size of the O-alkyl substituent increases, greater proportions of the conformation exist in the solution until the bulky O-trimethylsilyloxy-substituent shifts the equilibrium completely to the right with the concomitant predominance of the *re*-attack and the formation of *(R,R)*-**12** as the only diastereoisomer in the solution.

## CONCLUSION

A highly diasteroselective preparation of chiral secondary alcohols, having a chiral paracyclophane moiety attached to its benzylic carbon atom, has been developed. The synthetic protocol allows to obtain alcohols with opposite absolute configurations, starting with FHPC or its derivative of the same absolute configurations. The diastereoisomeric α-substituted benzylic alcohols contain extra *ortho*-paracyclophane substituents which are capable of metal ion coordination. The newly synthesized compounds could be expected to find applications as useful chiral ligands in asymmetric Lewis acid metal promoted reactions in the same way but, hopefully, more efficient than other chiral diols and diphenols[10].

**Acknowledgments**.

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## EXPERIMENTAL SECTION

*General.* - $^1$H NMR spectra were obtained on a Bruker AMX-400 instrument at 400.13 MHz with $C_6H_6$ (δ = 7.27) as an internal standard. Optical rotations were measured with a Perkin-Elmer-241 polarimeter in a thermostated cell at 25°C. TLC-analysis and chromatographic resolution of the diastereomers were performed on silica-gel precoated plates "Silufol UV-254 (Chemapol). Benzene was dried over molecular sieves 3Å and was used without further purification. $Et_2O$ was distilled from benzophenone ketyl under argon immediately before use. $Me_3SiCl$ was distilled from anhydrous $K_2CO_3$ before use. *Chemical calculations.* - The geometry optimization for *(R,S)*-**10** and *(R,R)*-**10** was performed on IBM-compatible 5x86-processor computer, using semi-empirical AM1 approach. *X-ray diffraction study.* - $C_{25}H_{26}O_2$ (M = 358.46) tetragonal, space group $P4_12_12$, at 293° $a$ = 9.341(2), $c$ = 5.191 (8)Å, $V$ = 3934Å$^3$, $Z$ = 8, $D_c$ = 1.208 g cm$^{-3}$. X-ray diffraction experiment was carried out with a Siemens P3/PC diffractometer (T = 293 K, graphite-monochromated Mo-Kα-radiation, λ = 0.71073Å, Θ/2Θ - scan technique, no absorption correction was applied, μ(MoKα) = 0.75 cm$^{-1}$, Θ = 2-22°). The structure was solved by direct methods and refined by full-matrix least-squares technique in the anisotropic approximation. All H atoms were located in the difference Fourier synthesis and included in the refinement in the isotropic approximation. Final discrepancy factors are: $R1$ = 0.0528 (on $F$ for 955 reflections with $I>2\sigma(I)$), $wR2$ = 0.0948 (on $F^2$ for all 1515 reflections used in the refinement of 348 parameters). All calculations were carried out on IBM PC with the help of SHELXTL PLUS 5 (gamma version) program.

*(R)-5-trimethylsilyloxy[2.2]paracyclophane-4-carbaldehyde (R)*-**4**. - To a solution of *(R)*-FHPC (0.067 g, 0.27 mmol) in 3 ml of benzene were added $Me_3SiCl$ (0.05 ml, 0.044 g, 0.4 mmol) and $Et_3N$ (0.056 ml, 0.04 g, 0.4 mmol). The mixture was stirred under reflux for 2.5 h. The insoluble precipitate was removed by filtration, the filtrate was evaporated *in vacuo*, yielding 0.084 g (97 %) of **4** as a colourless oil. $^1$H NMR

($C_6D_6$, δ, ppm, J, Hz): 0.17 (s, 9H, $Si(CH_3)_3$); 2.35-3.28 (m, 7H, $-CH_2-CH_2-$), 4.48 (m, 1H, $-CH_2-CH_2-$); 6.20 (d, 1H, 7- or 8-*H*, $J_o$ = 7.5 Hz), 6.34 (d.d, 1H, 15- or 16-*H*, $J_o$ = 7.9 Hz, $J_m$ = 1.6 Hz), 6.37 (d, 1H, 7- or 8-*H*, $J_o$ = 7.5 Hz), 6.53 (d.d, 1H, 15- or 16-*H*, $J_o$ = 7.9 Hz, $J_m$ = 1.6 Hz), 6.62 (d.d, 1H, 12-*H*, $J_o$ = 7.9 Hz, $J_m$ = 1.6 Hz), 7.03 (d.d, 1H, 13-*H*, $J_o$ = 7.9 Hz, $J_m$ = 1.6 Hz), 10.4 (s, 1H, C*H*O).

*Synthesis of the Grignard reagents.* - Ethylmagnesium iodide and *p*-tolylmagnesium bromide were obtained by treatment of activated ($I_2$) magnesium strips (10.5 mmol) with ethyliodide or *p*-tolylbromide (10 mmol) respectively in $Et_2O$ (10 ml).

*General method of the nucleophilic addition reaction.* -To a solution of 0.054 g (0.21 mmol) of *(R)*-FHPC in 1 ml abs. $Et_2O$ at -23° C were added 0.47 ml of 1N EtMgI solution in $Et_2O$ (0.47 mmol) under stirring and the reaction mixture was kept at this temperature for 1 h.[11] Then the mixture was allowed to warm up to room temp., quenched with saturated aqueous $NH_4Cl$ solution, washed twice with $H_2O$. The residue after evaporation of the solvent *in vacuo* was analyzed by $^1H$ NMR spectroscopy. The individual diastereomers were separated by preparative chromatography ($SiO_2$, plate 20x20 cm, benzene-$Et_2O$=4:1). In some cases the amount of the minor isomer was too small to obtain well resolved $^1H$ NMR spectrum or satisfactory optical rotation measurement.

*(S)-Butyl-[(R)-5-hydroxy[2.2]paracyclophane-4-yl]carbinol* ***(R,S)-5*** was obtained as an yellowish oil. - $^1H$ NMR ($C_6D_6$): δ = 0.82 (t, 3H, $CH_2(CH_2)_2CH_3$), 0.97-1.18 (m, 4H, $CH_2(CH_2)_2CH_3$), 1.32-1.54 (m, 2H, $CH_2(CH_2)_2CH_3$), 1.72 (d, 1H, CH(Bu)(O*H*)), 2.53-3.37 (m, 7H, $-CH_2-CH_2-$), 3.82 (m, 1H, $-CH$H-$CH_2$), 4.50 (m, 1H, C*H*(Bu)(OH)), 6.17 (d, 1H, 7-or 8-*H*, $J_o$ = 7.8 Hz), 6.40 (d, 1H, 7-or 8-*H*, $J_o$ = 7.8 Hz), 6.46 (d.d, 1H, 16-*H*, $J_o$ = 7.8 Hz, $J_m$ = 1.6 Hz), 6.58 (m, 2H, 12-, 15-*H*), 7.19 (d.d, 1H, 13-*H*, $J_o$ = 7.8 Hz, $J_m$ = 1.6 Hz), 9.1 (s, 1H, O*H*). - EI-MS m/z 310 ($M^+$) - $[\alpha]_D^{25}$ = +76.03 (c = 0.44,benzene).

*(S)-Ethyl-[(R)-5-hydroxy[2.2]paracyclophane-4-yl]carbinol* ***(R,S)-6.*** - M.p. 113-115 ° C. - $^1H$ NMR ($C_6D_6$): δ = 0.68 (t, 3H, $CH_2CH_3$), 1.35-1.45 (m, 2H, $CH_2CH_3$), 1.57 (d, 1H, CH(Et)(O*H*)), 2.50-3.36 (m, 7H, $-CH_2-CH_2-$), 3.80 (m, 1H, $-CH$H-$CH_2$), 4.35 (m, 1H, C*H*(Et)(OH)), 6.16 (d, 1H, 7- or 8-H, $J_o$ = 7.6 Hz), 6.40 (d, 1H, 7- or 8-H, $J_o$ = 7.6 Hz), 6.45 (d.d, 1H, 16-*H*, $J_o$ = 7.9 Hz, $J_m$ = 2.0 Hz), 6.59 (d.d, 1H, 12-*H*, $J_o$ = 7.9 Hz, $J_m$ = 2.0 Hz), 6.53 (d.d, 1H, 15-*H*, $J_o$ = 7.9 Hz, $J_m$ = 2.0 Hz), 7.18 (d.d, 1H, 13-*H*, $J_o$ = 7.9 Hz, $J_m$ = 2.0 Hz), 9.02 (s, 1H, O*H*). - $[\alpha]_D^{25}$ = +130.5 (c = 0.57, benzene). - Found: C, 80.86; H, 8.07%. $C_{19}H_{22}O_2$ requires C, 80.81; H, 7.86%.

*(S)-(4-Methylphenyl)-[(R)-5-hydroxy[2.2]paracyclophane-4-yl]carbinol* ***(R,S)-7.*** - M. p. > 250 ° C. - $^1H$ NMR ($C_6D_6$): δ = 2.30 (s, 3H, $PhCH_3$), 2.55-2.75 (m, 2H, $-CH_2-CH_2-$), 2.70 (d, 1H, CH(Et)(O*H*)), 3.00-3.30 (m, 5H, $-CH_2-CH_2-$), 3.45 (m, 1H, $-CH$H-$CH_2$), 5.87 (d, 1H, C*H*(Et)(OH), J = 1.9 Hz), 6.14 (d, 1H, 7- or 8-H, $J_o$ = 7.8 Hz), 6.40 (d, 1H, 7- or 8-H, $J_o$ = 7.8 Hz), 6.48 (d.d, 1H, 15-*H*, $J_o$ = 8.0 Hz, $J_m$ = 1.9 Hz), 6.61 (d.d, 1H, 16-*H*, $J_o$ = 8.0 Hz, $J_m$ = 1.9 Hz), 6.80 (d.d, 1H, 12-*H*, $J_o$ = 7.8 Hz, $J_m$ = 1.9 Hz), 7.07 (d.d, 1H, 13-*H*, $J_o$ 7.8 Hz, $J_m$ = 1.9 Hz), 7.08 (d, 2H, $C_4H_6$-$CH_3$, J = 8.3 Hz), 7.15 (d, 2H, $C_4H_6$-$CH_3$, J = 8.3 Hz), 9.22 (s, 1H, O*H*). - $[\alpha]_D^{25}$ = +201.4 (c = 0.35, benzene). - Found: C, 83.58; H, 7.44%. $C_{24}H_{24}O_2$ requires C, 83.69; H, 7.02%.

*(S)-Ethyl-[(R)-5-methoxy[2.2]paracyclophane-4-yl]carbinol* ***(R,S)-8 (major).*** M.p. 135.5-137 ° C. $R_f$ 0.67 (benzene). $^1H$ NMR ($C_6D_6$): δ = 1.08 (t, 3H, $CH_2CH_3$), 1.54-1.95 (m, 2H, $CH_2CH_3$), 2.48-3.26 (m, 8H, $-CH_2-CH_2-$), 3.35 (s, 3H, $OCH_3$), 4.59-473 (m, 2H, CH(Et)(O*H*) and C*H*(Et)(OH)), 6.18 (d, 1H, 7- or 8-*H*, $J_o$ = 8.0 Hz), 6.26 (d, 1H, 7- or 8-*H*, $J_o$ = 8.0 Hz), 6.48 (d.d, 1H, 16-*H*, $J_o$ = 8.0 Hz, $J_m$ = 1.8 Hz), 6.57 (d.d, 1H, 15-*H*, $J_o$ = 8.0 Hz, $J_m$ = 1.8 Hz), 7.00 (d.d, 1H, 12-*H*, $J_o$ = 8.0 Hz, $J_m$ = 1.8 Hz), 7.35 (d.d, 1H, 13-*H*, $J_o$

= 8.0 Hz, $J_m$ = 1.8 Hz). - $[\alpha]_D^{25}$ = +186.9 (c = 0.23, benzene). - Found: C, 81.08; H, 8.29%. $C_{20}H_{24}O_2$ requires C, 81.04; H, 8.16%.

*(R)-Ethyl-[(R)-5-methoxy[2.2]paracyclophane-4-yl]carbinol* ***(R,R)-8*** *(minor).* - $R_f$ 0.54 (benzene). - $^1$H NMR ($C_6D_6$): δ = 0.93 (t, 3H, $CH_2CH_3$), 1.55-2.02 (m, 2H, $CH_2CH_3$), 2.61-3.34 (m, 7H, -$CH_2$-$CH_2$-), 3.43 (s, 3H, $OCH_3$), 3.81 (m, 1H, -CHH-$CH_2$), 4.95 (m, 1H, CH(Et)(OH)), 6.26 (d, 1H, 7- or 8-H, $J_o$ = 7.5 Hz), 6.32 (d, 1H, 7- or 8-H, $J_o$ = 7.5 Hz), 6.59 (d.d, 1H, 15- or 16-H, $J_o$ = 7.5 Hz, $J_m$ = 1.1 Hz), 6.66 (d.d, 1H, 15- or 16-H, $J_o$ = 7.5 Hz, $J_m$ = 1.1 Hz), 6.82 (d.d, 1H, 12-H, $J_o$ = 7.5 Hz, $J_m$ = 1.1 Hz), 6.98 (d.d, 1H, 13-H, $J_o$ = 7.5 Hz, $J_m$ = 1.1 Hz).

*(S)-(4-Methylphenyl)-[(R)-5-methoxy[2.2]paracyclophane-4-yl]carbinol* ***(R,S)-9*** *(major).* - $R_f$ 0.55 (benzene). - M. p. 168-169 ° C. - $^1$H NMR ($C_6D_6$): δ = 2.02 c (3H, $C_6H_4CH_3$), 2.44-3.31 (m, 8H, -$CH_2$-$CH_2$-,), 2.91 (s, 3H, $OCH_3$), 4.77 (m, 1H, CH($C_6H_4CH_3$)(OH)), 5.95 (d, 1H, CH($C_6H_4CH_3$)(OH)), 6.27 (d.d., 2H, 7-, 8-H, J = 7.8), 6.53 (d.d, 1H, 15- or 16-H, J = 7.8, J = 1.8), 6.62 (d.d, 1H, 15- or 16-H, J = 7.8, J = 1.8), 6.98 (d.d, 1H, 12-H, J = 7.8, J = 1.7), 7.08 (d, 2H, $C_6H_4CH_3$, J = 8.2), 7.38 (d, 2H, $C_6H_4CH_3$, J = 8.2), 7.42 (d.d, 1H, 12-H, J = 7.8, J = 1.7). - $[\alpha]_D$ = + 70.91 (c = 0.33, benzene). Found: C, 84.08; H, 7.34%. $C_{25}H_{26}O_2$ requires C, 83.76; H, 7.31%.

*(R)-Ethyl-[(R)-5-(prop-2-yloxy)[2.2]paracyclophane-4-yl]carbinol* ***(R,R)-10*** *(major)* - $R_f$ 0.66 (benzene). - M. p. 63.5-65° C. - $^1$H NMR ($C_6D_6$): δ = 0.98 (d, 3H, OCH($CH_3$)$_2$), 1.07 (t, 3H, $CH_2CH_3$), 1.37 (d, 3H, OCH($CH_3$)$_2$), 1.48-2.05 (m, 2H, $CH_2CH_3$), 3.25 (d, 1H, CH(Et)(OH)), 2.64-3.39 (m, 7H, -$CH_2$-$CH_2$-), 3.82 (m, 1H, -CHH-$CH_2$), 3.94 (sept, 1H, OCH($CH_3$)$_2$), 5.10 (d.d, 1H, CH(Et)(OH)), 6.23 (d, 1H, 7- or 8-H, $J_o$ = 7.5 Hz), 6.31 (d, 1H, 7- or 8-H, $J_o$ = 7.5 Hz), 6.65 (d.d, 1H, 16-H, $J_o$ = 7.8 Hz, $J_m$ = 1.8 Hz), 6.70 (d.d, 1H, 15-H, $J_o$ = 7.8 Hz, $J_m$ = 1.8 Hz), 6.83 (d.d, 1H, 12-H, $J_o$ = 7.8 Hz, $J_m$ = 1.8 Hz), 6.96 (d.d, 1H, 13-H, $J_o$ = 7.8 Hz, $J_m$ = 1.8 Hz). - $[\alpha]_D$ = + 118.06 (c = 0.43, benzene). Found: C, 81.65; H, 8.68%. $C_{22}H_{28}O_2$ requires C, 81.44; H, 8.70%.

*(S)-Ethyl-[(R)-5-(prop-2-yloxy)[2.2]paracyclophane-4-yl]carbinol* ***(R,S)-10*** *(minor).* - $R_f$ 0.77 (benzene). - $^1$H NMR ($C_6D_6$): δ = 0.95 (d, 3H, OCH($CH_3$)$_2$), 1.19-1.27 (m, 6H, OCH($CH_3$)$_2$ and $CH_2CH_3$), 1.67-2.02 (m, 2H, $CH_2CH_3$), 2.45-3.89 (m, 8H, -$CH_2$-$CH_2$-), 4.09 (sept, 1H, OCH($CH_3$)$_2$), 4.76 (m, 1H, CH(Et)(OH)), 5.31 (d, 1H, CH(Et)(OH)), 6.19 (d, 1H, 7- or 8-H, $J_o$ = 8.0 Hz), 6.29 (d, 1H, 7- or 8-H, $J_o$ = 8.0 Hz), 6.53 (d.d, 1H, 16-H, $J_o$ = 8.0 Hz, $J_m$ = 2.0 Hz), 6.60 (d.d, 1H, 15-H, $J_o$ = 8.0 Hz, $J_m$ = 2.0 Hz), 7.07 (d.d, 1H, 12-H, $J_o$ = 8.0 Hz, $J_m$ = 2.0 Hz), 7.34 (d.d, 1H, 13-H, $J_o$ = 8.0 Hz, $J_m$ = 2.0 Hz).

*(R)-(4-methylphenyl)-[(R)-5-(prop-2-yloxy)[2.2]paracyclophane-4-yl]carbinol* ***(R,R)-11***. *(major).* - colourless oil - $R_f$ 0.40 (benzene). - $^1$H NMR ($C_6D_6$): δ = 0.90 (d, 3H, OCH($CH_3$)$_2$), 1.33 (d, 3H, OCH($CH_3$)$_2$), 2.22 c (3H, $C_6H_4CH_3$), 2.51-3.25 (m, 8H, -$CH_2$-$CH_2$-), 4.01 (sept, 1H, OCH($CH_3$)$_2$), 6.22 (d, 1H, 7- or 8-H, $J_o$ = 7.8 Hz), 6.36 (d, 1H, 7- or 8-H, $J_o$ = 7.8 Hz), 6.44 (m, 1H, CH(Et)(OH)), 6.65 (m, 15-, 16-H, 2H), 6.92 (d.d, 1H, 12- or 13-H, $J_o$ = 7.8 Hz), 7.00 (d, 1H, 12- or 13-H, $J_o$ = 7.8 Hz), 7.12 (d, 2H, $C_6H_4CH_3$, $J_o$ = 8.2 Hz), 7.50 (d, 2H, $C_6H_4CH_3$, $J_o$ = 8.2 Hz). - EI-MS m/z 386 ($M^+$) - $[\alpha]_D$ = + 157.8 (c = 0.4, benzene).

*(R)-Ethyl-[(R)-5-trimethylsilyloxy[2.2]paracyclophane-4-yl]carbinol* ***(R,R)-12*** was obtained as a colourless oil. - $^1$H NMR ($C_6D_6$): δ = 0.26 (s, 9H, OSi($CH_3$)$_3$), 1.03 (t, 3H, $CH_2CH_3$), 1.49-1.88 (m, 2H, $CH_2CH_3$), 1.70 (d, 1H, CH(Et)(OH)), 2.48-3.38 (m, 7H, -$CH_2$-$CH_2$-), 3.85 (m, 1H, -CHH-$CH_2$), 4.97 (d, 1H, CH(Et)(OH)), 6.20 (d, 1H, 7- or 8-H, $J_o$ = 7.9 Hz), 6.29 (d, 1H, 7- or 8-H, $J_o$ = 7.9 Hz), 6.60 (d.d, 1H, 16-H, $J_o$ = 7.9 Hz,

$J_m$ = 1.3 Hz), 6.71 (d.d, 1H, 15-***H***, $J_o$ = 7.9 Hz, $J_m$ = 1.3 Hz), 6.86 (d.d, 1H, 12-***H***, $J_o$ = 7.9 Hz, $J_m$ = 1.2 Hz), 7.01 (d.d, 1H, 13-***H***, $J_o$ = 7.9 Hz, $J_m$ = 1.2 Hz). - EI-MS m/z 354 ($M^+$) - $[\alpha]_D^{25}$ = +78.1 (c = 0.29, benzene).

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