Stereoselective synthesis of homoallylic alcohols of the [2.2]paracyclophane series and their use as auxiliaries in asymmetric allylboration of aldehydes

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Stereoselectivity of allylboration of 4-formyl[2.2]paracyclophane, 4-acetyl[2.2]paracyclophane, and 4-hydroxy-5-formyl[2.2]paracyclophane was studied and the relative configurations of the homoallylic alcohols obtained were established. Optically pure (*Sp,Sc*)-(+)-4-(1-hydroxy-1-methylbut-3-enyl)[2.2]paracyclophane and (*Rc,Sc*)-(+)-4-hydroxy-5-(1-hydroxybut-3-enyl)[2.2]paracyclophane were synthesized. The possibility of using (*Sp,Sc*)-(+)-4-(1-hydroxy-1-methylbut-3-enyl)[2.2]paracyclophane as a recoverable chiral auxiliary in asymmetric allylboration of aldehydes was demonstrated.

Key words: [2.2]paracyclophane, allylboration, stereoselectivity, optical activity, carbonyl derivatives, homoallylic alcohols, chiral auxiliaries of asymmetric synthesis.

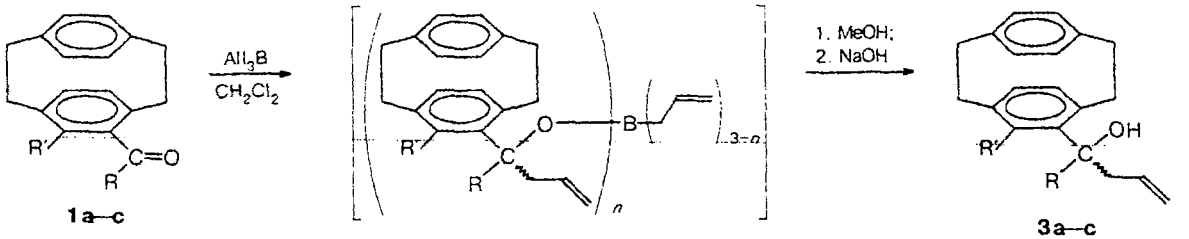
Monosubstituted and nonsymmetrical multisubstituted [2.2]paracyclophanes ([2.2]PC) are planar-chiral compounds. A number of optically active derivatives of [2.2]PC are used successfully as auxiliary reagents and ligands for the design of catalysts for asymmetric synthesis.[1] Therefore, the search and study of stereoselective reactions in the series of [2.2]PC[2] and the synthesis of new optically active derivatives based on this compound become highly important.[3]

In the framework of asymmetric synthesis, reactions of allylboron derivatives with carbonyl compounds are of considerable interest.[4] Allylboration is accompanied by 1,3-rearrangement *via* a rigid chair-like six-membered transition state. The use of optically active or sterically hindered allylboranes provides the possibility of enantio- and diastereoselective allylboration.[5]

The present study is devoted to the stereoselectivity of allylboration of a number of carbonyl derivatives of [2.2]PC possessing planar chirality, namely, 4-formyl-[2.2]PC (**1a**), 4-acetyl[2.2]PC (**1b**), and 4-hydroxy-5-formyl[2.2]PC (**1c**). It was found (for preliminary communication, see Ref. 6) that compounds **1a—c** react with triallylborane to give boron esters **2a—c**, whose alkaline hydrolysis yields the corresponding homoallylic alcohols **3a—c** (Scheme 1).

Alcohols **3a—c** have two elements of chirality, the planar-chiral paracyclophanyl fragment and the newly formed peripheral asymmetric center. Therefore, allylboration of racemic [2.2]PC carbonyl derivatives **1a—c** can yield two diastereomeric alcohols, namely, *rel*-(*Rp,Sc*) and *rel*-(*Rp,Rc*). It is shown in Scheme 2 that the chemical shifts of the protons located in the vicinity of the newly formed asymmetric center are substantially different for the two diastereomers. Thus the stereoselectivity of allylboration can be studied by analyzing the ^{1}H NMR spectra of the reaction mixtures.

Scheme 1



2a—c (n = 1—3)

a: R = R′ = H
b: R = Me, R′ = H
c: R = H, R′ = OH

Translated from *Izvestiya Akademii Nauk. Seriya Khimicheskaya*, No. 5, pp. 914—921, May, 2000.

It is known that one mole of triallylborane can react with one, two, or three moles of aldehyde, resulting in diallylborinates, allylboronates or borates $(RO)_3B$, respectively.[7] Allylboration of 4-formyl[2.2]PC **1a** follows a similar pattern (see Scheme 1, compound **2a**). At an equimolar ratio of reactants, allylboration proved to proceed nonstereoselectively giving after hydrolysis alcohol **3a** (Table 1). The ^1H NMR spectrum of the reaction mixture exhibited two sets of signals, corresponding to two diastereomers, in a ratio of 1 : 1.

Successive decrease in the All_3B : **1a** molar ratio increased the reaction stereoselectivity. When the All_3B : **1a** ratio was 1 : 2, the ratio of diastereomers amounted to 1.5 : 1.0 (*de* 20%). When the excess of the allylboryl groups relative to the carbonyl group was diminished to the equivalent ratio (All_3B : **1a** = 1 : 3), the ratio of diastereomers was 1.8 : 1.0 (*de* 29%). The concentrations of the reactants also influenced substantially the stereoselectivity of allylboration of aldehyde **1a**. Thus the diastereomer ratio obtained using a 0.01 *M* solution of All_3B in CH_2Cl_2 (All_3B : **1a** = 1 : 3) was 7 : 1 (*de* 75%).

Diastereomeric alcohols **3a** were separated by preparative thin layer chromatography. The ^1H NMR spectrum of the major isomer (**3a′**) exhibited the signal for the bridge H_A proton of the [2.2]paracyclophanyl fragment in a higher field than that of the minor isomer (**3a″**) ($\Delta\delta = 0.35$), while the signal of the methine proton in the spectrum of **3a′** is located in a lower field than the corresponding signal in the spectrum of **3a″** ($\Delta\delta = 0.15$). Substantial $\Delta\delta$ values characterize also the displacement of all protons of the allyl fragment of **3a′** with respect to the corresponding protons of diastereomer **3a″** (see Scheme 2).

The increase in the stereoselectivity of allylboration following a decrease in the All_3B : **1a** molar ratio is due to the fact that, starting from the second equivalent of aldehyde **1a**, allylboronic and diallylborinic esters **2a**, formed in the reaction and containing a chiral paracyclophanyl fragment, act as the allylborating reagents instead of triallylborane All_3B.

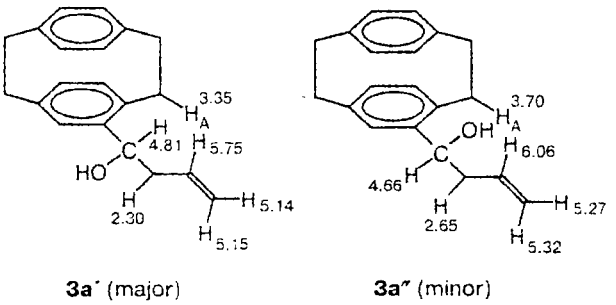
To determine the relative configurations of diastereomeric alcohols **3a′** and **3a″**, they were converted into the corresponding benzoates **4a′** and **4a″** (Scheme 3), which were studied by NMR using the ^1H NOESY technique (Scheme 4).

Table 1. The reaction of aldehyde **1a** with All_3B [a]

All_3B [b] : **1a**	Yield (%)	Isomer ratio[c] (*de* (%))	Configuration of the major isomer
1 : 1	98	1 : 1 (0)	—
1 : 2	93	1.5 : 1.0 (20)	*rel*-(*Rp,Rc*)
1 : 3	85	1.8 : 1.0 (29)	*rel*-(*Rp,Rc*)
1 : 3 [d]	60	7 : 1 (75)	*rel*-(*Rp,Rc*)

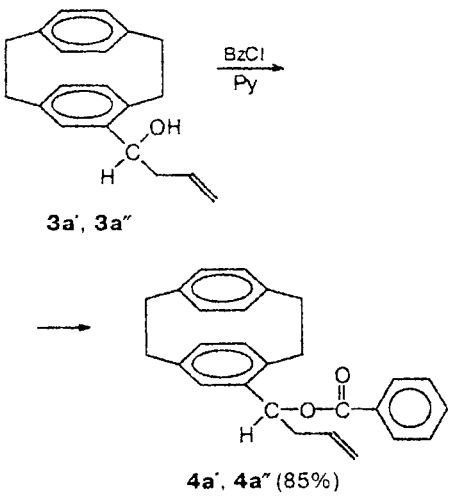
[a] Reaction conditions: solvent CH_2Cl_2, 0.08 mol L^{-1} **1a**, −78→20 °C, reaction duration 0.5 h.
[b] As a 0.3 *M* solution of All_3B in CH_2Cl_2.
[c] According to ^1H NMR spectroscopy.
[d] As a 0.01 *M* solution of All_3B; 38% of 4-formyl[2.2]PC was recovered.

Scheme 2



3a′ (major) **3a″** (minor)

Scheme 3

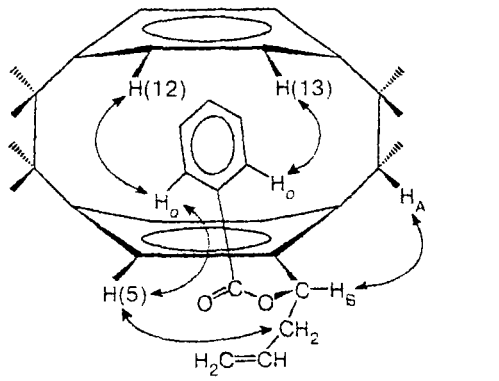


3a′, 3a″

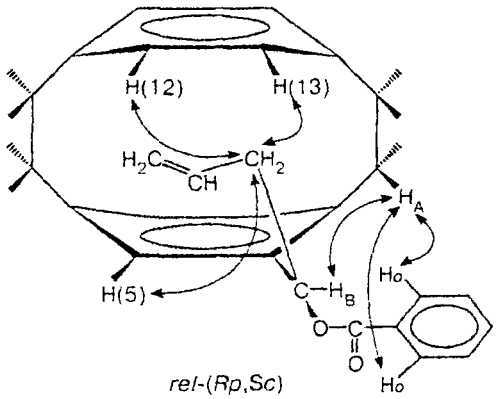
4a′, 4a″ (85%)

The spectrum of the major isomer **4a′**, like that of the minor isomer **4a″**, was found to display coupling between the methine H_B proton and the bridge H_A proton of the paracyclophanyl fragment. Whereas in the spectrum of benzoate **4a′**, the *ortho*-protons (H_o) of the phenyl group exhibit the nuclear Overhauser effect (NOE) with the H(5), H(12), and H(13) aromatic protons of the [2.2]PC rings, in the case of benzoate **4a″**, the NOE is observed only with the bridge H_A proton of [2.2]PC. In addition, the methylene protons of the $-CH_2-$ group of the allylic fragment in the spectrum of isomer **4a′** exhibit the NOE with H(5), whereas the same methylene protons in isomer **4a″** display clear-cut coupling both with H(5) and with the H(12) and H(13) aromatic protons of [2.2]PC. The presence of coupling detected in the spectra of benzoates **4a′** and **4a″** allow the relative configurations of the products to be identified as *rel*-(*Rp,Rc*) for the major isomer **4a′** and *rel*-(*Rp,Sc*) for the minor isomer **4a″**. Since esterification

Scheme 4*



rel-(*Rp*,*Rc*)
4a′ (major)



rel-(*Rp*,*Sc*)
4a″ (minor)

does not involve the asymmetric center of the initial alcohol, the major isomer of homoallylic alcohol **3a′** has the relative configuration *rel*-(*Rp*,*Rc*), while the minor product **3a″** is the *rel*-(*Rp*,*Sc*) isomer.

Ketones, unlike aldehydes, are known to react only with two allyl groups of All_3B.[7] It was found that the stereochemical outcome of allylboration of ketone **1b** depends neither on the ratio nor on the concentrations of the reactants. Even with a twofold molar excess of All_3B, the reaction proceeds stereospecifically with *de* > 99% (Table 2).

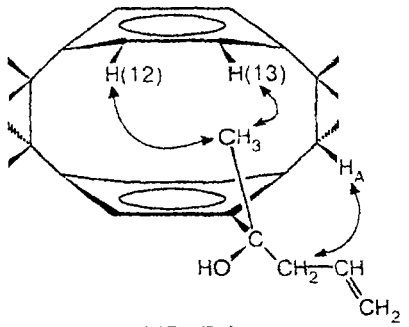
In order to determine the relative configuration of alcohol **3b**, we carried out a ^{1}H NOESY experiment. The characteristic couplings for alcohol **3b** are those between the $-CH_2-$ methylene protons of the allyl group and the H_A proton, whose signal occurs in a lower field (3.85—3.95 ppm) than the signals of other protons of the bridge (2.75—3.15 ppm), and also the NOE between the protons of the methyl group and the H(12) and H(13) aromatic protons. The presence of these interactions suggests that the relative configuration of alcohol **3b** is *rel*-(*Rp*,*Rc*).

* Hereinafter, only the *Sp*,*Sc*-isomer is shown for the enantiomeric pair *rel*-(*Rp*,*Rc*) and only the *Sp*,*Rc*-isomer is shown for the *rel*-(*Rp*,*Sc*) pair.

Table 2. Reaction of ketone **1b** with All_3B [a]

All_3B : **1b**	Concentration of **1b**, /mmol mL^{-1}	Yield (%)	Configuration of alcohol **3b** [b]
1 : 2 [c]	0.08	75	*rel*-(*Rp*,*Rc*)
1 : 1	0.08	93	*rel*-(*Rp*,*Rc*)
1 : 1	0.04	90	*rel*-(*Rp*,*Rc*)
2 : 1	0.04	95	*rel*-(*Rp*,*Rc*)

[a] Reaction conditions: solvent CH_2Cl_2, +40 °C, reaction duration 5 h.
[b] In all cases, *de* was >99% (^{1}H NMR data).
[c] 15% of 4-acetyl[2.2]PC was recovered.



rel-(*Rp*,*Rc*)
3b

Thus, allylboration provided the possibility of performing the first stereoselective nucleophilic addition to the C=O bond in monosubstituted carbonyl derivatives of [2.2]PC. The reactions of 4-acetyl- and 4-benzoyl[2.2]PC with organic compounds of Mg and Li are known to be nonstereoselective.[8]

The reaction of *ortho*-disubstituted 4-hydroxy-5-formyl[2.2]PC **1c** with triallylborane was carried out at an equimolar ratio of the reactants and with excess All_3B (Table 3).

It should be noted that the molecule of **1c** contains a hydroxy group, able to protolyze one B—All bond. The *ortho*-arrangement of the formyl and hydroxy groups creates conditions for the formation of the chelate structure of allylboronic ester. The ^{11}B NMR spectrum (in CH_2Cl_2) of this ester contains only one signal at 34 ppm, which points unambiguously to the formation of $AllB(OR)_2$.[9] Note that this allylboronic ester is hydro-

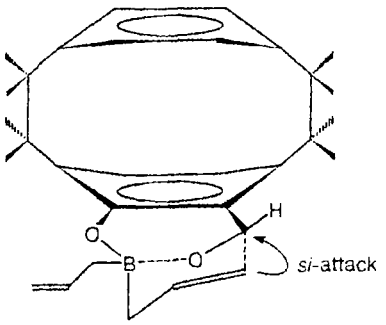
Table 3. Reaction of hydroxy aldehyde **1c** with All_3B [a]

All_3B : **1c**	Yield (%)	Configuration of alcohol **3c** [b]
1 : 1	85	*rel*-(*Rp*,*Sc*)
2 : 1	87	*rel*-(*Rp*,*Sc*)

[a] Reaction conditions: solvent CH_2Cl_2, 0.08 mol L^{-1} of **1c**, −78→+20 °C, reaction duration 0.5 h.
[b] In all cases, *de* was >99% (^{1}H NMR data).

lyzed under substantially more severe conditions (heating with an aqueous solution of NaOH at 50 °C for 6 h) than allylboron esters **2a,b** derived from monosubstituted [2.2]PC. The formation of only allylboronic ester in the reaction of hydroxy aldehyde **1c** even with excess All_3B is consistent with the assumption that this ester has a chelate structure.

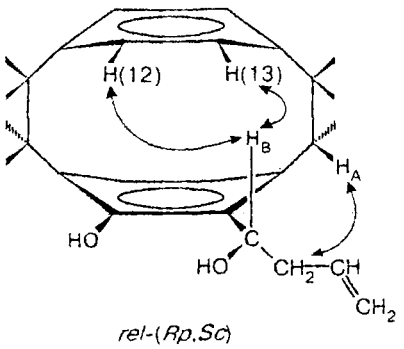
The chelate formation in the transition state (structure **A**), together with the fact that nucleophilic attack from the side nonshielded by the second [2.2]PC ring is preferred, predetermine the *si*-attack for (*R*)-**1c** (or *re*-attack for (*S*)-**1c**), which should yield a pair of enantiomers with the *rel*-(*Rp,Sc*) configuration.



A

Indeed, allylboration of hydroxy aldehyde **1c** proceeds stereospecifically to give alcohol **3c** (*de* > 99%). The ^1H NMR spectrum of the reaction mixture exhibits signals for only one diastereomer of homolallylic alcohol **3c**.

The relative configuration of alcohol **3c** was established from the data of a ^1H NOESY experiment. The NOE observed between the $-CH_2-$ methylene protons of the allyl fragment and the bridge H_A proton of [2.2]PC and between the methine H_B proton and the protons H(12) and H(13) of the unsubstituted ring provides evidence for the relative configuration of alcohol **3c** to be identified unambiguously as *rel*-(*Rp,Sc*).



rel-(*Rp,Sc*)
3c

These results are consistent with the data obtained previously on the addition of Mg and Li organic derivatives to the carbonyl group of the (*R*)-enantiomer **1c**, which yields the (*Rp,Sc*)-diastereomer with *de* > 99%.[10] Thus, nucleophilic addition to hydroxy aldehyde **1c** is stereoselective irrespective of the nature of the organometallic reagent (Li, Mg, B).

To summarize the data on the relative configurations of homoallylic alcohols **3a—c**, it should be noted that the major isomers of alcohol **3a** and alcohols **3b** and **3c** are characterized by identical relative configurations of the newly formed asymmetric center (the inversion in the designation of the configuration of the paracyclophanyl fragment in alcohol **3c**, prepared from hydroxy aldehyde **1c**, is due to the seniority of the OH group over the C(OH) group according to the nomenclature rules). This may suggest that the *si*-attack is preferred for carbonyl derivatives of [2.2]PC having the (*S*)-configuration and the *re*-attack is more favorable for the derivatives having the (*R*)-configuration. Elucidation of the factors that account for this regularity requires additional study.

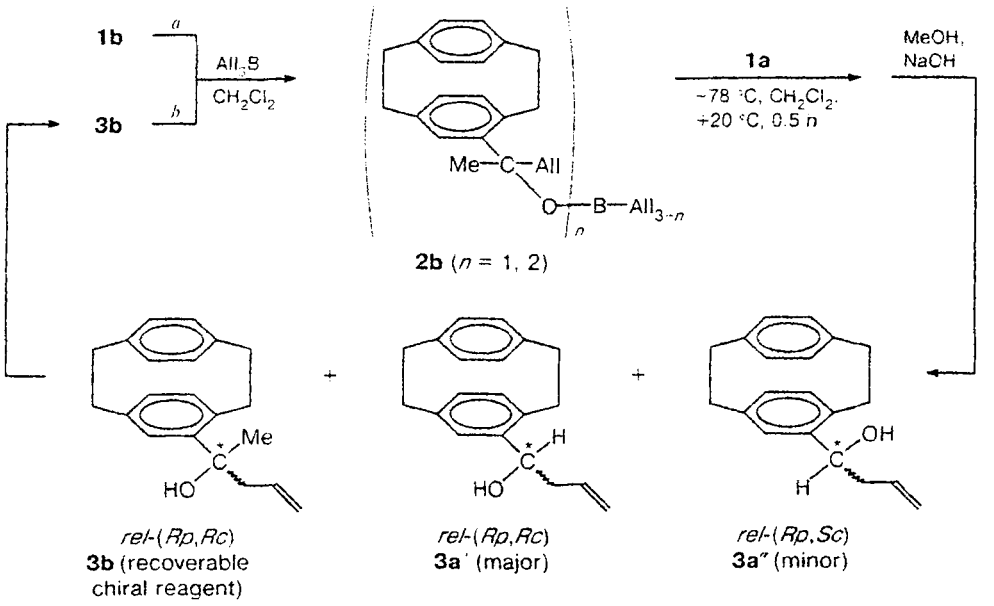
Since the allylboration of ketone **1b** and hydroxy aldehyde **1c** is stereospecific and the resulting esters **2b** and **2c** contain reactive allylboryl groups, we attempted to use the planar-chiral paracyclophanyl allylboron esters as reagents for asymmetric allylboration.

The reaction of 4-formyl[2.2]PC **1a** with allylboron esters **2b** was used as the model reaction. This particular aldehyde was chosen due to the opportunity to study the process stereoselectivity by ^1H NMR spectroscopy using racemic esters **2b** (n = 1, 2; the composition was not determined). One equivalent of aldehyde **1a** was added to allylboron esters **2b**, prepared *in situ* by the reaction of ketone **1b** with All_3B (All_3B : **1b** = 1 : 1) (Scheme 5, pathway *a*). After alkaline hydrolysis, alcohols **3a** were isolated in 92% yield; the **3a″** : **3a′** diastereomer ratio was 1 : 3, *i.e.*, *de* reached 50% (see Experimental, entry *1*).

It should be emphasized that the chiral inductor is recovered almost quantitatively as alcohol **3b** and can be used repeatedly. Thus the reaction of alcohol **3b** with 1 mol-equiv. of All_3B gave allylborating reagent **2b**, which was used subsequently in the reaction with aldehydes **1a** (see Scheme 3, pathway *b*). After alkaline hydrolysis, 91% of alcohol **3b** was recovered. The products, alcohols **3a′** and **3a″**, were isolated in 90% yield. The **3a″** : **3a′** ratio of isomers amounted to 1.0 : 2.1, *i.e.*, *de* is equal to 35% (see Experimental, entry *2*). Thus, we demonstrated that paracyclophanyl alcohols possessing planar chirality can be used, in principle, as recoverable auxiliaries in the asymmetric allylboration of carbonyl compounds.

Now we present the tentative results of the use of optically active paracyclophanyl allylboron esters as reagents for asymmetric allylboration of benzaldehyde. For this purpose, enantiomerically pure homoallyl alcohols **3b** and **3c** were synthesized from optically pure (+)-(*S*)-4-acetyl[2.2]PC **1b** [12,16] and (+)-(*R*)-4-hydroxy-5-formyl[2.2]PC **1c**,[11] respectively. Ketone (+)-(*S*)-**1b** was prepared from (+)-(*S*)-4-carboxy[2.2]PC ((*S*)-**6**).[12] Racemic acid **6** was synthesized by oxidation of 4-formyl[2.2]PC with potassium permanganate. Acid **6** was resolved into enantiomers by a previously described procedure.[13]

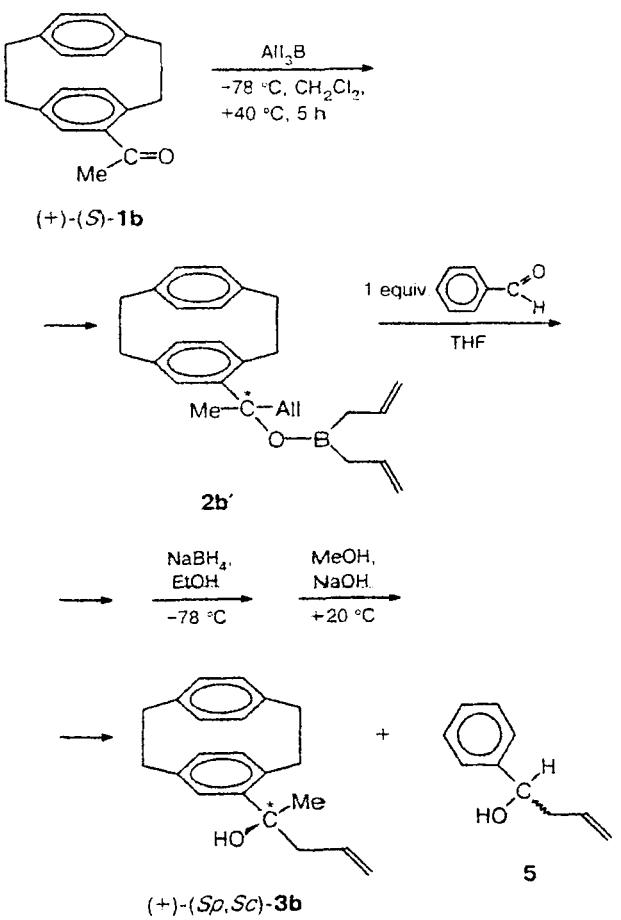
Scheme 5



Alcohol (+)-(*Sp*,*Sc*)-**3b** was prepared in 97% yield, $[\alpha]_D^{25}$ +39.34° (*c* 0.966, benzene). Alcohol (+)-(*Rp*,*Sc*)-**3c** was isolated in 85% yield, $[\alpha]_D^{25}$ +90.66° (*c* 0.364, benzene). The reaction of ketone (+)-(*S*)-**1b** with excess All_3B in CH_2Cl_2 gave diallylborinic ester **2b′** (Scheme 6). An excess of All_3B was taken in order to rule out the possibility of formation of allylboronic ester. After compound **2b′** had been freed from the solvent and excess All_3B by vacuum evaporation, the ^{11}B NMR spectrum contained only one signal at 53 ppm, corresponding to the ester All_2BOR (**2b′**).[9] One equivalent of benzaldehyde was added to the diallylborinic ester **2b′** thus obtained. Alcohols (+)-(*Sp*,*Sc*)-**3b′** and **5** resulting from hydrolysis were separated by chromatography and isolated quantitatively (see Experimental, entry *3*).

The enantiomeric excess for allyl(phenyl)carbinol (**5**) was determined by ^1H NMR spectroscopy using a chiral shift reagent, *viz.*, tris(heptafluorobutyroyl-D-camphorato)europium(III) (Eu(hfc)$_3$). The ^1H NMR spectra of the complexes prepared by the reaction of racemic alcohol **5** with either an equimolar amount or a 1.5-fold excess of optically active Eu(hfc)$_3$ were found to exhibit signals for the methine protons of the —CH(OH) groups in 1 : 1 ratio. This provided grounds for using this method for determination of the enantiomeric purity of alcohol **5**, prepared in the reaction of optically active diallylborinic ester **2b′** with 1 equiv. of benzaldehyde. In the spectrum of the complex of alcohol **5**, the ratio of the signals for the above-indicated protons was 1.00 : 1.45, which corresponds to an enantiomeric excess (*ee*) of 18%. It is noteworthy that the stereoselectivity observed in the asymmetric allylboration of benzaldehyde even by sterically hindered monoallylboronic esters is among the lowest.[14]

Scheme 6



Thus, we demonstrated that allylboration makes it possible to perform stereoselectively the nucleophilic addition to the C=O bond in both di- and monosubstituted carbonyl derivatives of [2.2]PC. New enantiomerically pure [2.2]PC derivatives containing two elements of chirality in the structure, namely, the paracyclophanyl fragment with planar chirality and the newly formed peripheral asymmetric center in the side chain, were synthesized. The possibility of using optically active alcohols of the [2.2]PC series possessing planar chirality as recoverable auxiliaries in asymmetric allylboration was demonstrated. It appears of interest to study the possibility of asymmetric allylboration by reagents based on compounds with planar chirality in which allylboryl groups are located in the close vicinity of the symmetry plane, in particular, allylboron esters of phenols of the [2.2]paracyclophane series.

Experimental

NMR spectra were recorded on a Bruker AMX-400 instrument (400.13 MHz) in $CDCl_3$ and DMSO-d_6. The residual signals of the solvent protons with the chemical shifts δ 7.27 and 2.50 ppm, respectively, were used as the internal standards. Mass spectra were run on a Kratos MS 90 mass spectrometer, an energy of ionizing electrons of 70 eV and temperatures of 200 or 250 °C. TLC analysis was performed on Silufol UV-254 plates (Chemapol); chromatographic purification and separation of diastereomers were carried out on silica gel Kieselgel 60 (Merck) and Kieselgel 60 F_{254} plates (Merck). The specific optical rotation was determined on a EPO-1 instrument.

All the reactions were carried out in anhydrous solvents in an atmosphere of dry argon.

4-(1-Hydroxybut-3-enyl)[2.2]paracyclophane (3a). A solution of aldehyde **1a** (0.1 g, 0.424 mmol) in 5 mL of CH_2Cl_2 was cooled to −70 °C and All_3B (0.08 mL, 0.445 mmol) was added with stirring. The reaction mixture was stirred for 30 min at room temperature and 3 mL of methanol and 2 mL of a 10% aqueous solution of NaOH were added successively. The organic layer was washed with water and dried with Na_2SO_4. The product was isolated by column chromatography (elution with benzene). Yield 0.115 g (97%). MS, *m/z* (I_{rel} (%)): 278 $[M]^+$ (1.4), 260 $[M - H_2O]^+$ (44), 237 $[M - C_3H_5]^+$ (3), 155 (100). **Major isomer (3a').** M.p. 63 °C. ^1H NMR ($CDCl_3$), δ: 1.95 (d, 1 H, −CH(OH), ^3J = 3.3 Hz); 2.15–2.45 (m, 2 H, $-CH_2-CH=$); 2.80–3.25 (m, 8 H, $-CH_2-CH_2-$); 4.81 (m, −CH(OH)); 5.14 (br.d, 1 H, *cis*-CHH=CH−, ^3J = 11.6 Hz); 5.15 (br.d, 1 H, *trans*-CHH=CH−, ^3J = 16.0 Hz); 5.60–5.70 (m, 1 H, $-CH=CH_2$); 6.40–6.65 (m, 7 H, H arom.). **Minor isomer (3a").** Oil. ^1H NMR ($CDCl_3$), δ: 1.70 (br.s, 1 H, −CH(OH)); 2.50–2.80 (m, 2 H, $-CH_2-CH=$); 2.90–3.30 (m, 7 H, $-CH_2-CH_2-$); 3.60–3.75 (m, 1 H, −CHH−CH_2−); 4.66 (dd, −CH(OH), ^3J = 7.8 Hz, ^3J = 1.6 Hz); 5.27 (br.d, 1 H, *cis*-CHH=CH−, ^3J = 10.2 Hz); 5.32 (br.d, 1 H, *trans*-CHH=CH−, ^3J = 17.2 Hz); 6.06 (m, 1 H, $-CH=CH_2$); 6.35–6.60 (m, 7 H, H arom.).

4-(1-Benzoyloxybut-3-enyl)[2.2]paracyclophane (4a). Benzoyl chloride (0.1 mL, 0.86 mmol) was added to a solution of alcohol **3a** (60 mg, 0.215 mmol) in 2 mL of freshly distilled pyridine. The reaction mixture was stirred for 2 h at 100 °C, cooled to room temperature, and neutralized with 2 *N* HCl, the products were extracted with ether, and the extract was twice washed with water and dried with Na_2SO_4. The product was purified by column chromatography (elution with benzene). Yield 80%. Found (%): C, 85.06; H, 7.44. $C_{27}H_{22}O_2$. Calculated (%): C, 84.78; H, 6.85. MS, *m/z* (I_{rel} (%)): 382 $[M]^+$ (3), 261 $[M - BzO]^+$ (38), 260 $[M - BzOH]^+$ (78). **Major isomer (4a').** Oil. ^1H NMR (DMSO), δ: 2.41 (t, 2 H, $-CH_2-CH=$, ^3J = 6.7 Hz); 2.88–3.15 (m, 7 H, $-CH_2-CH_2-$); 3.36–3.48 (m, 1 H, −CHH−CH_2−); 4.93 (dd, 1 H, *cis*-CHH=CH−, ^3J = 10.8 Hz, ^2J = 1.8 Hz); 4.97 (dd, 1 H, *trans*-CHH=CH−, ^3J = 17.3 Hz, ^2J = 1.8 Hz); 5.55–5.67 (m, 1 H, $-CH=CH_2$); 6.08, 6.31 (d, H(12), H(13), ^3J = 7.8 Hz); 6.35 (t, 1 H, −CH(O−), ^3J = 6.1 Hz); 6.47 (d, 1 H, H(8), ^3J = 7.7 Hz); 6.50 (dd, 1 H, H(7), ^3J = 7.7 Hz, ^4J = 1.7 Hz); 6.53 (br.s, 2 H, H(15), H(16)); 6.70 (d, 1 H, H(5), ^4J = 1.7 Hz); 7.65 (t, 2 H, H_m, ^3J = 8.1 Hz); 7.75 (tt, 1 H, H_p, ^3J = 8.1 Hz, ^4J = 1.2 Hz); 8.24 (dd, 2 H, H_o, ^3J = 7.5 Hz, ^4J = 1.2 Hz). **Minor isomer (4a").** M.p. 118–119.5 °C. ^1H NMR (DMSO), δ: 2.83 (t, 2 H, $CH_2-CH=$, ^2J = 6.7 Hz); 2.85–3.15 (m, 7 H, $-CH_2-CH_2-$); 3.40–3.50 (m, 1 H, −CHH−CH_2−); 5.06 (dd, 1 H, *cis*-CHH=CH−, ^3J = 10.1 Hz, ^2J = 1.8 Hz); 5.18 (dd, 1 H, *trans*-CHH=CH−, ^3J = 17.1 Hz, ^2J = 1.8 Hz); 5.83–6.10 (m, 1 H, $-CH=CH_2$); 6.13 (t, 1 H, −CH(O−), ^3J = 6.8 Hz); 6.35–6.44 (m, 2 H, H(12), H(13)); 6.47 (d, 1 H, H(8), ^3J = 7.6 Hz); 6.51 (dd, 1 H, H(7), ^3J = 7.6 Hz, ^4J = 1.8 Hz); 6.53–6.58 (m, 2 H, H(15), H(16)); 6.59 (d, 1 H, H(5), ^4J = 1.8 Hz); 7.50 (t, 2 H, H_m, ^3J = 7.9 Hz); 7.63 (t, 1 H, H_p, ^3J = 7.9 Hz); 7.94 (d, 2 H, H_o, ^3J = 7.9 Hz).

4-(1-Hydroxy-1-methylbut-3-enyl)[2.2]paracyclophane (3b). A solution of ketone **1b** (0.1 g, 0.4 mmol) in 5 mL of CH_2Cl_2 was cooled to −70 °C and All_3B (0.07 mL, 0.4 mmol) was added with stirring. The reaction mixture was refluxed for 5 h and 3 mL of methanol and 2 mL of a 10% aqueous solution of NaOH were added successively. The organic layer was washed with water and dried with Na_2SO_4. The product was isolated by column chromatography (elution with benzene) followed by recrystallization from hexane. Yield 0.11 g (93%). M.p. 51 °C. Found (%): C, 86.40; H, 8.27. $C_{21}H_{24}O$. Calculated (%): C, 86.25; H, 8.27. MS, *m/z* (I_{rel} (%)): 292 $[M]^+$ (2), 274 $[M - H_2O]^+$ (28), 251 $[M - C_3H_5]^+$ (47), 169 (100). ^1H NMR (DMSO), δ: 1.51 (s, 3 H, CH_3); 2.28 (d, 2 H, $-CH_2-CH$, ^3J = 6.5 Hz); 2.75–3.15 (m, 7 H, $-CH_2-CH_2-$); 3.85–3.95 (m, 1 H, −CHH−CH_2−); 4.7 (br.s, 1 H, −OH); 4.81 (br.d, 1 H, *cis*-CHH=CH−, ^3J = 10.1 Hz); 4.83 (br.d, 1 H, *trans*-CHH=CH−, ^3J = 19.1 Hz); 5.27–5.40 (m, 1 H, $-CH=CH_2$); 6.27 (dd, 1 H, H(7), ^3J = 7.8 Hz, ^4J = 1.8 Hz); 6.30 (d, 1 H, H(8), ^3J = 7.8 Hz); 6.35 (d, 1 H, H(5), ^4J = 1.8 Hz); 6.53 (br.s, 2 H, H(15), H(16)); 6.30, 6.65 (dd, H(12), H(13), ^3J = 7.9 Hz, ^4J = 1.8 Hz).

4-Hydroxy-5-(1-hydroxybut-3-enyl)[2.2]paracyclophane (3c). A solution of 4-hydroxy-5-formyl[2.2]PC (0.1 g, 0.4 mmol) in 5 mL of CH_2Cl_2 was cooled to −70 °C and All_3B (0.07 mL, 0.4 mmol) was added with stirring. The reaction mixture was stirred for 30 min at room temperature, 3 mL of methanol and 2 mL of a 30% aqueous solution of NaOH were added successively, and the mixture was stirred for 6 h at 50 °C. The organic layer was washed with water and dried with Na_2SO_4. The product was isolated by column chromatography (elution with benzene) followed by recrystallization from hexane. Yield 0.098 g (85%). M.p. 158 °C. Found (%): C, 81.52; H, 7.66. $C_{21}H_{22}O_2$. Calculated (%): C, 81.59; H, 7.54. MS, *m/z* (I_{rel} (%)): 294 $[M]^+$ (3), 276 $[M - H_2O]^+$ (13), 260 (17), 169 (100). ^1H NMR (DMSO), δ: 2.05–2.30 (m, 2 H, $-CH_2-CH=$); 2.40–2.70 (m, 2 H, $-CH_2-CH_2-$); 2.80–3.25 (m, 6 H, $-CH_2-CH_2-$); 4.79 (br.s, 1 H, −CH(O−)); 4.96 (dd, 1 H, *cis*-CHH=CH−, ^3J = 10.4 Hz); 4.98 (dd, 1 H, *trans*-CHH=CH−, ^3J = 17.1 Hz); 5.60–5.70 (m, 1 H, $-CH=CH_2$); 6.03, 6.23 (both d, 2 H, H(7), H(8), ^3J = 7.7 Hz, ^4J = 1.9 Hz); 6.37, 6.52 (both d, 2 H,

H(15), H(16), ^3J = 7.7 Hz, ^4J = 1.9 Hz); 6.72, 6.81 (both dd, 2 H, H(12), H(13), ^3J = 7.7 Hz, ^4J = 1.9 Hz); 6.8 (br.s, 1 H, —CO<u>H</u>); 9.95 (br.s, 1 H, —O<u>H</u>).

Study of the reaction stereoselectivity

Entry *1*. A solution of ketone **1b** (0.1 g, 0.4 mmol) in 5 mL of CH_2Cl_2 was cooled to −70 °C and All_3B (0.07 mL, 0.4 mmol) was added with stirring. The reaction mixture was refluxed for 5 h and excess All_3B and the solvent were evaporated *in vacuo*. The residue (allylboron ester **2b**) was dissolved in 2 mL CH_2Cl_2, the resulting solution was cooled to −70 °C, and a solution of aldehyde **1a** (0.09 g, 0.38 mmol) was added. The reaction mixture was stirred for 30 min at room temperature and 3 mL of methanol and 2 mL of a 10% aqueous solution of NaOH were added successively. The organic layer was washed with water and dried with Na_2SO_4. The products were isolated by column chromatography (elution with benzene). The yield of alcohol **3b** was 0.112 g (96%) and the yield of alcohol **3a** was 0.097 g (92%).

Entry *2*. A solution of alcohol **3b** (0.1 g, 0.4 mmol) in 5 mL of CH_2Cl_2 was cooled to −70 °C and All_3B (0.07 mL, 0.4 mmol) was added with stirring. The reaction mixture was stirred at room temperature for 30 min and excess All_3B and the solvent were evaporated *in vacuo*. The residue (**2b**) was dissolved in 2 mL of CH_2Cl_2, a solution of aldehyde **1a** (0.09 g, 0.38 mol) was added with stirring to this solution cooled to −70 °C, and the mixture was subsequently worked-up as in entry *1*. The yield of alcohol **3b** was 0.106 g (91%) and the yields of alcohol **3a** was 0.095 g (90%).

Entry *3*. A solution of ketone (*S*)-(+)-**1b** with $[\alpha]_D^{25}$ +63.4° (*c* 0.44, $CHCl_3$) (Ref. 16: $[\alpha]_D^{25}$ +65° (*c* 0.5, $CHCl_3$)) (0.140 g, 0.56 mmol) in 5 mL of CH_2Cl_2 was cooled to −70 °C and All_3B (0.12 mL, 0.69 mmol) was added with stirring. The reaction mixture was refluxed for 5 h and excess All_3B and the solvent were evaporated *in vacuo*. ^{11}B NMR (CH_2Cl_2), δ: 53. Freshly distilled benzaldehyde (0.06 mL, 0.56 mmol) was added with stirring to a solution of the diallylborinic ester synthesized in 3.5 mL of THF cooled to −70 °C. After 17 h, the reaction mixture was treated with a solution of $NaBH_4$ (0.15 g) in 8 mL of EtOH and stirred for 1 h. The reaction mixture was allowed to warm up to room temperature and 3 mL of MeOH and a solution of NaOH (0.36 g) in 7 mL of H_2O were successively added. The mixture was stirred for 30 min and concentrated and the residue was extracted with ether (3×25 mL), washed with H_2O, and dried with Na_2SO_4. The products were isolated by column chromatography (elution with benzene). The yield of alcohol (*Sp,Sc*)-**3b** was 0.127 g (86%). The yield of alcohol **5** was 0.065 mg (97%), *ee* 18%.

4-Carboxy[2.2]paracyclophane (6). A solution of $KMnO_4$ (3.4 g, 21.5 mmol) in 80 mL of H_2O and 30 mL of pyridine was added dropwise at −3 °C over a period of 2 h to a solution of aldehyde **1a** (10 g, 42.4 mmol) in 70 mL of pyridine. The reaction mixture was allowed to warm up to room temperature (stirring for 3 h). An excess of aqueous NaOH was added and the precipitate of MnO_2 was filtered off and washed with H_2O. The aqueous-pyridine fraction was concentrated *in vacuo* at a temperature not higher than 40 °C. Acid **6** was reprecipitated twice: first it was dissolved in an excess of aqueous NaOH and filtered, the precipitate was washed with water, and the filtrate was acidified with HCl to pH 1. The precipitate of acid **6** was filtered off and washed with distilled water. The yield of acid **6** was 5.7 g (54%). M.p. 224 °C (Ref. 15: m.p. 224 °C).

(*Sp,Sc*)-(+)-4-(1-Hydroxy-1-methylbut-3-enyl)[2.2]paracyclophane ((*Sp,Sc*)-3b) was prepared similarly to racemic **3b** from (*S*)-(+)-4-acetyl[2.2]PC with $[\alpha]_D^{25}$ +63.4° (*c* 0.44, $CHCl_3$) (Ref. 16: $[\alpha]_D^{25}$ +65° (*c* 0.5, $CHCl_3$)). The yield of alcohol (*Sp,Sc*)-(+)-**3b** was 96%. Oil. Found (%): C, 86.87; H, 8.89. $C_{21}H_{24}O$. Calculated (%): C, 86.25; H, 8.27. $[\alpha]_D^{25}$ +39.34° (*c* 0.966, benzene).

(*Rp,Sc*)-(+)-4-Hydroxy-5-(1-hydroxybut-3-enyl)[2.2]paracyclophane ((*Rp,Sc*)-3c) was prepared by the procedure described for the synthesis of racemic **3c** from (*R*)-(+)-4-hydroxy-5-formyl[2.2]PC with $[\alpha]_D^{25}$ +575.8° (Ref. 11: $[\alpha]_D^{25}$ +572.9° (*c* 0.55, benzene)). The yield of (*Rp,Sc*)-(+)-**3c** was 82%. An analytically pure sample was prepared by recrystallization from pentane. M.p. 95.5—96 °C. Found (%): C, 81.80; H, 7.36. $C_{21}H_{22}O_2$. Calculated (%): C, 81.59; H, 7.54. $[\alpha]_D^{25}$ +90.66° (*c* 0.364, benzene).

This work was financially supported by the Russian Foundation for Basic Research (Project Nos. 97-03-32972a and 96-15-97289). The work by N. V. Vorontsova was supported by the Educational Scientific Center on the Chemistry of Organometallic Compounds (the Federal Target Program "Integration," Grant 234).

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Received July 9, 1999;
in revised form December 27, 1999