Stereoselective synthesis of *cis*-4,7-disubstituted 4,7-dihydroxy-4,7-dihydro[2.2]paracyclophanes

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The nucleophilic addition of butyllithium, phenyllithium, methyllithium, and triallylborane to [2.2]paracyclophane-4,7-quinone (**1**) proceeded regio- and stereospecifically to give the corresponding *cis*-4,7-disubstituted 4,7-dihydroxy-4,7-dihydro[2.2]paracyclophanes **2—5** with the *endo* orientation of the hydroxy groups. The structures of quinone **1** and diols **2**, **4**, and **5** were established by X-ray diffraction analysis.

Key words: [2.2]paracyclophanes, quinones, nucleophilic addition, organolithium compounds, organoboron compounds, allylboration, stereoselectivity, X-ray diffraction analysis.

The advantageous use of optically active compounds of the [2.2]paracyclophane ([2.2]PC) series in the asymmetric synthesis and catalysis[1—5] gave impetus to an extensive search for and investigation of stereoselective reactions of planar chiral [2.2]PC derivatives.[6—9]

Previously,[10] we have established that allylboration of monosubstituted carbonyl [2.2]PC derivatives proceeded stereoselectively, unlike the nonstereoselective nucleophilic addition of organolithium reagents at the C=O bond.[11]

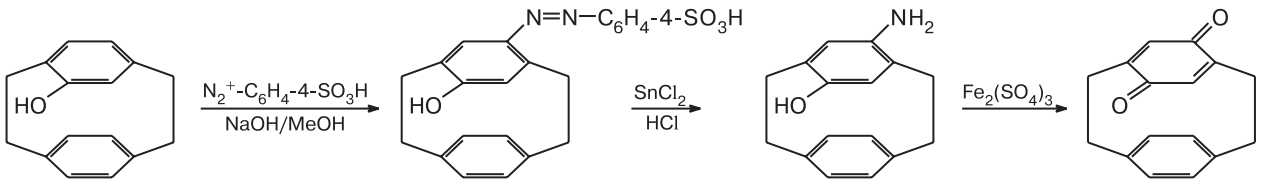
In the present study, we examined [2.2]PC-4,7-quinone (**1**). Although the synthesis of *para*-quinone **1** was described as early as 1966,[12] the chemical properties of compound **1**, as far as we know, remain virtually unstudied. Below, we report the results of investigation of the nucleophilic addition of triallylborane and organolithium reagents to quinone **1** (for preliminary communication, see Ref. 13).

Quinone **1** was synthesized from 4-OH-[2.2]PC according to a known procedure[12] with some modifications made by us (Scheme 1). Thus, the azo compound prepared *in situ* was reduced with tin dichloride instead of sodium hyposulfite used earlier. Oxidation of the resulting 4-OH-7-NH_2-[2.2]PC with iron(III) sulfate was carried out in hydrochloric rather than sulfuric acid. The procedure thus modified made it possible to obtain analytically pure quinone **1** in 74% yield.

The structure of compound **1** was established by X-ray diffraction analysis. In the crystal, a molecule of quinone **1** lies on a crystallographic center of symmetry as a result of which the O atoms are disordered and occupy identical positions in both rings of paracyclophane with occupancies of 0.5 (Fig. 1). In spite of the quinoid structure, the rings retain a boat-like conformation, though substantially flattened (the atoms of the ring are coplanar to within 0.076 Å), which is typical of paracyclophanes. The C(3), C(4), C(6), and C(7) atoms are most coplanar (the average deviation of the atoms from the plane through these atoms is 0.011 Å). The deviations of the C(2) and C(5) atoms bound to the CH_2CH_2 bridges are equal (0.171 Å). The folding of the ring along the C(3)...C(7) and C(4)...C(6) lines is characterized by equal angles (13.6°). The distance between the centroids of the rings is 2.939 Å.

The bond lengths are consistent with the quinoid structure. The bonds of the same type have close values.

Scheme 1



1 (74%)

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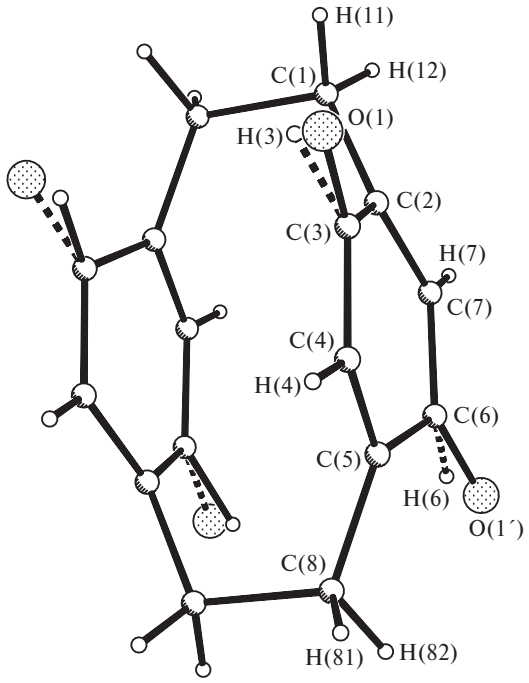


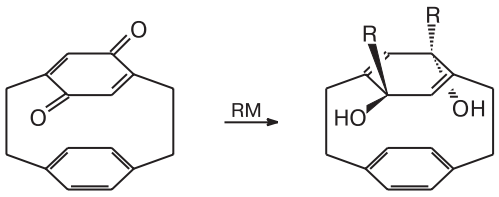
Fig. 1. Scheme of the superposition of the [2.2]paracyclophane-4,7-quinone molecules (**1**) according to the X-ray diffraction data.

Thus, C(2)—C(7) and C(4)—C(5) (C=C) are 1.368(3) and 1.367(3) Å, respectively; C(2)—C(3) and C(5)—C(6) (=C—C(=O)) are 1.450(3) and 1.443(3) Å, respectively; C(3)—C(4) and C(6)—C(7) (=CH—C(=O)) are 1.429(3) and 1.430(3) Å, respectively (the corresponding average values are 1.367, 1.447, and 1.430 Å). Apparently, the difference in the C=O bond lengths (O(1)—C(3), 1.209(3) Å; O(1´)—C(6), 1.252(3) Å) can be attributed to the difference in the strength of the O...H—C hydrogen bonds in which all H atoms of the ring (H(3), H(4), H(6), and H(7)) are involved. The O(1´) atom is involved in the shortest bond (H(3)*...O(1´), 2.40 Å). The remaining bonds are substantially weaker (H...O, 2.6—2.7 Å). The exocyclic C—CH_2 bond lengths (C(1)—C(2), 1.502(3) Å; C(5)—C(8), 1.509(3) Å) and the CH_2—CH_2 bond length (C(1)—C(8)*, 1.586(3) Å) have values typical of [2.2]PC derivatives.

The C(3) and C(6) atoms have a planar configuration (the sums of the bond angles at these atoms are 360°). The unusually large O(1)—C(3)—C(4) (123.3(2)°), O(1´)—C(6)—C(7) (124.0(2)°),★ C(7)=C(2)—C(1) (122.14(19)°), and C(4)=C(5)—C(8) bond angles (122.06(19)°) are worthy of notice. Apparently, steric hindrances in this moiety are responsible for these distortions of the bond angles as well as for twisting of the O=C—C—CH_2 fragments (the O(1)C(3)C(2)C(1) and O(1´)C(6)C(5)C(8) torsion angles are 27.0 and 24.2°, respectively; the O(1)...C(1) and O(1´)...C(8) distances are 2.821 and 2.813 Å, respectively).

★ Generally, the CC(=O)C angle is the largest one in the carbonyl group.

Scheme 2



cis-endo

1 **2—5**

RM = All_3B, BuLi, MeLi, PhLi

R = All (**2**), Bu (**3**), Me (**4**), Ph (**5**)

We carried out a series of experiments on the addition of triallylborane and organolithium reagents to quinone **1**. The course of the reactions was monitored by ^{1}H NMR spectroscopy of the reaction mixtures.

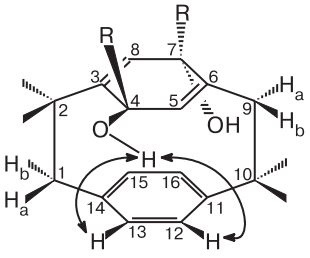
According to the published data,[14,15] the reactions of *para*-quinones with triallylborane proceeded as the 1,2-addition to give mixtures of *cis—trans* isomeric alcohols in 70—85% yields. The reaction of quinone **1** with two moles of All_3B in toluene at ~20 °C was completed in 0.5 h. After alkaline hydrolysis, individual *cis*-4,7-diallyl-4,7-dihydroxy-4,7-dihydro[2.2]paracyclophane (**2**) was obtained in quantitative yield (Scheme 2, Table 1, run *1*).

Table 1. Reactions of quinone **1** with organometallic compounds[a]

Run	Reagent	Ratio **1** : reagent	Time /h	Conversion[b] of **1** (%)	Product	Yield[c] (%)
1	All_3B	1 : 2	0.5	100	**2**	98
2	BuLi	1 : 2	2	50	**3**	44
3	BuLi	1 : 2	240	50	**3**	— [d]
4	BuLi	1 : 20	20	50	**3**	— [d]
5	BuLi	1 : 20	240	69	**3**	63
6 [e]	BuLi	1 : 2	5	75	**3**	52
7	MeLi	1 : 2	20	58	**4**	— [d]
8	MeLi	1 : 20	240	66	**4**	— [d]
9 [f]	MeLi	1 : 20	20	66	**4**	61
10	PhLi	1 : 2	2	50	**5**	— [d]
11	PhLi	1 : 20	2	50	**5**	— [d]
12	PhLi	1 : 20	240	75	**5**	71
13 [f]	PhLi	1 : 20	20	79	**5**	75

[a] Reaction conditions: +20 °C, the reagent was added to a 0.03 *M* solution of compound **1** in toluene.
[b] According to the data from ^{1}H NMR monitoring.
[c] The preparative yield is given.
[d] The product was not isolated preparatively.
[e] 20→110 °C.
[f] A 0.015 *M* solution of compound **1** was added to the reagent.

It should be noted that the 1,2-addition to quinone **1** can in principle afford three stereoisomers, *viz.*, *cis*-diol with the *endo* orientation of the OH groups, *cis*-diol with the *exo* orientation of the OH groups, and the *trans* isomer. The ^{1}H and ^{13}C NMR spectroscopic data provide unambiguous evidence for the *cis* structure of product **2**. With the aim of establishing the relative configuration of *cis*-diol **2**, we carried out NOE experiments. The ^{1}H NMR NOESY experiment showed substantial positive NOE between the proton of the OH group (δ 2.20) and the protons of the unsubstituted ring of paracyclophane (H(12), H(13), H(15), and H(16)). There are also interactions between the protons of the CH_2 group of the allyl fragment and the *ortho* H(5) and H(7) protons, whereas there are no interactions with the protons of the unsubstituted ring of paracyclophane. This is evidence for the *endo* orientation of the OH groups. The complete assignment of the signals in the ^{1}H NMR spectrum was made based on the NOESY data. The structure of diol **2** was also confirmed by X-ray diffraction analysis (Fig. 2, *a*).



cis-endo

2—5

It is known that the reactions of *para*-quinones with organolithium compounds generally proceed *via* the 1,2-addition to give mixtures of *cis—trans*-isomeric alcohols with the *cis* isomer predominating. The nucleophilic addition is accompanied by reduction of the starting quinone to hydroquinone.[16—18]

We found that the nucleophilic addition of organolithium reagents (BuLi, MeLi, or PhLi) to quinone **1** in toluene at ~20 °C proceeded regio- and stereospecifically to give the corresponding 1,2-addition products, *viz.*, *cis*-4,7-disubstituted 4,7-dihydroxy-4,7-dihydro[2.2]paracyclophanes **3—5** (see Scheme 2), regardless of the reagent ratio (2 : 1 or 20 : 1, see Table 1, runs *2—5*, *7*, *8*, and *10—12*).

As in the case of allyl derivative **2**, the cross-peaks in the ^{1}H NMR NOESY spectra of diols **3** and **4** are indicative of the *endo* orientation of the OH groups (see above). Diol **5** also has an analogous configuration as evidenced by positive NOE (5%) on the H(13) proton of the aromatic ring in the *pseudo-gem* position (δ 7.22) and NOE (4%) on the adjacent H(5) proton (δ 5.60) upon irradiation of the hydroxy proton (δ 2.21). At the same time,

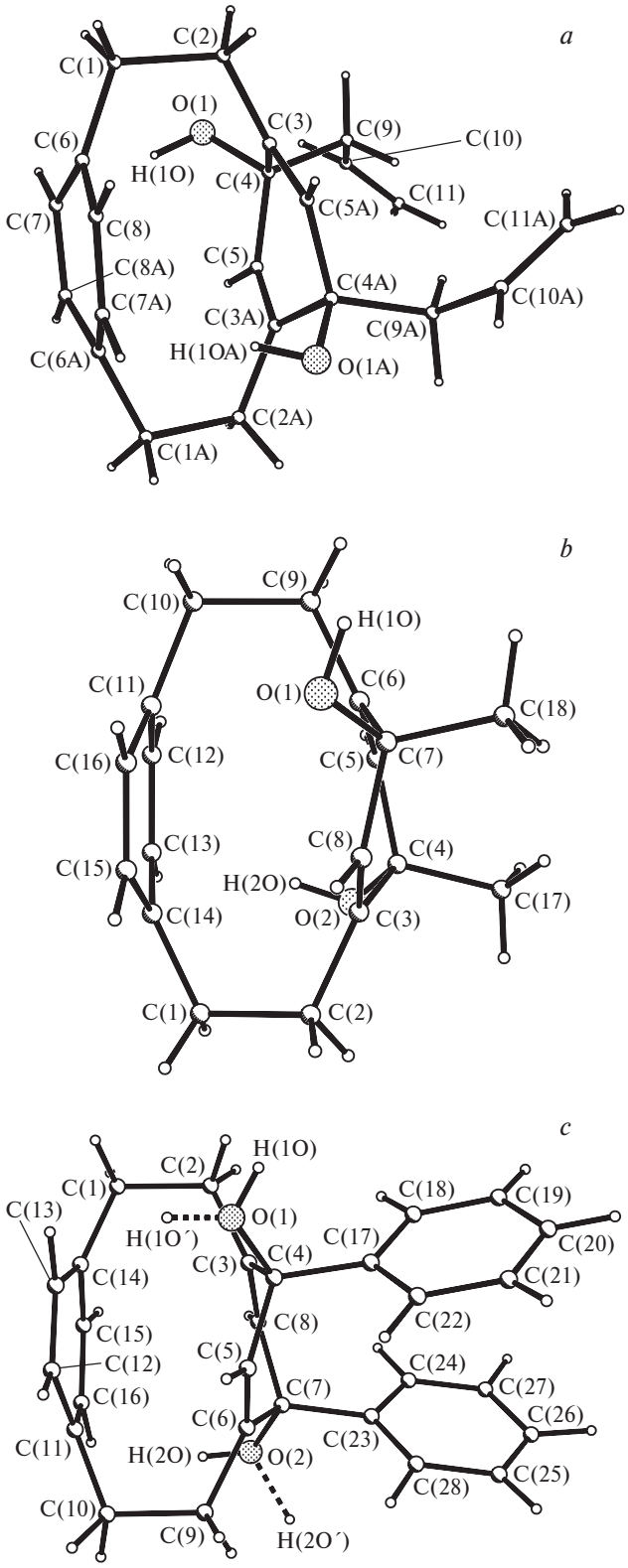


Fig. 2. Molecular structures of *cis*-4,7-diallyl-4,7-dihydroxy-4,7-dihydro[2.2]paracyclophane (**2**) (*a*), *cis*-4,7-dimethyl-4,7-dihydroxy-4,7-dihydro[2.2]paracyclophane (**4**) (*b*), and *cis*-4,7-diphenyl-4,7-dihydroxy-4,7-dihydro[2.2]paracyclophane (**5**) (*c*) according to the X-ray diffraction data.

there is NOE between the protons of the unsubstituted ring of paracyclophane and the phenyl group. The data from the NOESY experiments for methyl derivative **4** also allowed us to make the complete assignment of the signals in its ^{1}H NMR spectrum. The complete assignment of the signals for the protons in the ^{1}H NMR spectrum of butyl derivative **3** is hampered by their substantial overlapping. Interestingly, the overall pattern and the chemical shifts of the signals for the protons of the paracyclophane core in the ^{1}H NMR spectra of these three alcohols are virtually independent of the substituent R. The structures of diols **4** and **5** were established also by X-ray diffraction analysis (see Fig. 2, *b*, *c*).

Unlike the reaction of quinone **1** with All_3B, which was completed in 30 min, the reaction of **1** with two moles of an organolithium reagent was only half completed at ~20 °C even after 2 h (see Table 1, runs *2* and *10*). An increase in the reaction time to 240 h has no effect on the conversion of quinone **1** (see Table 1, run *3*). The reaction mixture always contained unconsumed quinone **1**, and even traces of the monoaddition product of the organolithium reagent were not detected. Neither the use of a 10-fold excess (with respect to each carbonyl group of quinone **1**) of the reagent (see Table 1, run *11*) nor an increase in the reaction time to 20 h (see Table 1, runs *4* and *7*) have a substantial effect on the conversion of the starting quinone.

An attempt to increase the yield of diol **3** by raising the temperature of the reaction of quinone **1** with BuLi to 110 °C led to an increase in the conversion of **1** to 75% (5 h) but afforded a series of unidentified by-products. As a result, no essential increase in the yield of compound **3** was achieved (see Table 1, run *6*).

However, to judge the stereoselectivity of the process, it is necessary to achieve a high conversion. An essential increase in the conversion of quinone **1** was attained either by increasing the reaction time to 240 h with the simultaneous use of a 20-fold excess of the reagent (see Table 1, runs *5*, *8*, and *12*) or by changing the order in which the reagents were added, *i.e.*, by the slow addition of a solution of quinone **1** to the organolithium reagent (see Table 1, runs *9* and *13*). An increase in the conversion of quinone **1** did not change the selectivity of the reactions, which afforded exclusively *cis*-diols **3—5** as before.

It should be noted that the complete conversion of quinone **1** was not achieved even with the use of a large excess of the organolithium reagent and by increasing the reaction time to 240 h. The ^{1}H NMR spectra of the reaction mixtures have signals for the protons of only two compounds, *viz.*, of the corresponding diol **3—5** and the starting quinone **1**. Hence, it can be stated that the spectra have no signals for the protons of 4,7-dihydroxy[2.2]paracyclophane (**6**), which is a probable product of reduction of quinone **1** under the action of RLi. Hydroquinone **6**, which was synthesized by reduction of quinone **1** with an excess of hydrazine hydrate and isolated with an impurity of the starting compound **1** (10%), appeared to be very unstable and was oxidized in air (particularly in solution) to form quinone **1**. We also attempted to detect the possible formation of hydroquinone **6** in the reactions under consideration by the *in situ* transformation of **6** into the known dimethyl ether.[19] For this purpose, an excess of MeI was added to the reaction mixture, which was obtained by keeping quinone **1** with a 10-fold excess of BuLi for 20 h. The reaction mixture was stirred at ~20 °C for 25 h and then decomposed with NH_4Cl. However, we did not detect methylated derivatives of hydroquinone **6** and diol **3** among the reaction products. The ^{1}H NMR spectrum of the reaction mixture has only signals of the starting quinone **1** and diol **3** in a ratio of 1 : 1.5 (the conversion of **1** was 60%). It should be noted that ^{1}H NMR spectroscopy showed the formation of hydroquinone **6** and diol **3** (in a ratio of 1 : 2) in the reaction of quinone **1** with a 10-fold excess of BuLi in THF performed at −78 °C for 2 h (this reaction also afforded 10% of an unidentified by-product).

In our opinion, the low conversion of quinone **1** in its reactions with organolithium reagents can be attributed, in particular, to steric hindrances resulted from the formation of molecular complexes of the starting quinone **1** with lithium alkoxides of diols **3—5**.

A comparative analysis of the results of X-ray diffraction study of alcohols **2**, **4**, and **5** revealed the structural features characteristic of a new class of [2.2]PC derivatives, *viz.*, *cis*-4,7-disubstituted 4,7-dihydroxy-4,7-dihydro[2.2]paracyclophanes with the *endo* orientation of the OH groups (see Figs. 2, *a—c*).

The crystal structures of alcohols **2**, **4**, and **5** are centrosymmetrical and contain racemic mixtures of enantiomeric molecules. All molecules (**2**, **4**, and **5**) have similar structures and are the *cis* stereoisomers with the OH groups in the *endo* orientation. Molecule **2** is located on a crystallographic twofold axis. In the crystal, the molecules are linked in chains along the *b* axis through the weak intermolecular O(1)—H(1O)...O(1′) hydrogen bonds involving the hydroxy groups (O...O, 2.918(2) Å; H(1O)...O(1′), 2.60(2) Å). Molecules **4** and **5** have no symmetry elements. In the crystal structure of **4**, the H(1O) and H(2O) atoms, unlike those in molecule **2**, are in *trans* orientations and the molecules are linked in chains along the *c* axis through the O(2)...H(1O)—O(1) hydrogen bonds (O...O, 2.816(2) Å; H...O, 1.93(2) Å). The H of the second OH group (H(2O)) is not involved in hydrogen bonding. In the crystal structure of **5**, the H atoms of both OH groups are disordered over two positions. Molecules **5** are linked in chains along the [011] direction through the H(1O) and H(2O′) atoms involved in the intermolecular O(1)—H(1O)...O(1′) hydrogen bond (H(1)...O(1′) 2.09(5), Å; O(1)...O(1′), 2.974(5) Å)

and a stronger symmetrical O(2)—H(2O′)...O(2′) hydrogen bond (O(2)...O(2′), 2.804(4) Å; H(2O)...O(2) and H(2O′)...O(2′) are 1.40(2) Å).

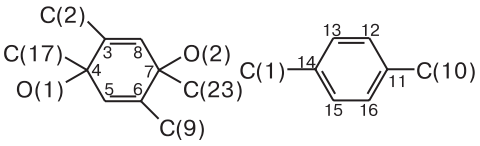
In all molecules, the substituted ring is strongly distorted (the average deviations of the atoms from the planes are ±0.18, 0.19, and 0.20 Å in **2**, **4**, and **5**, respectively) and adopts a boat conformation. The substituents are located in axial positions and the O atoms are in pseudoequatorial positions. In molecule **2**, the O(1) (O(1A)) atoms deviate from the mean plane of the ring by 0.460(2) Å. In compounds **4** and **5**, the O(1) and O(2) atoms deviate from the mean plane of the ring by 0.464(2), 0.487(2) Å (**4**) and 0.277(4), 0.311(4) Å (**5**), respectively. The base of the boat is formed by the atoms deprived of substituents, *viz.*, C(3), C(5), C(3A), C(5A) (**2**) and C(3), C(5), C(6), C(8) (**4** and **5**), *i.e.*, the introduction of substituents at positions 4 and 7 of the ring (All, Me, or Ph) leads (irrespective of the effective volumes of the substituents) to the inversion of the C(3),C(6)-boat conformation typical of the paracyclophane rings. The boat conformations in molecules **2**, **4**, and **5** have close geometric characteristics. Thus, the folding angle along the C(4)...C(5A) line (and along the C(4A)...C(5) line) for the C(4),C(4A)-boat in **2** is 24.2°, whereas the folding angles along the C(3)...C(5) and C(6)...C(8) lines for the C(4),C(7)-boat in **4** and **5** are 24.0(1) and 26.6(1)° (**4**), 30.9(2) and 30.3(2)° (**5**), respectively.

In compounds **2**, **4**, and **5**, the unsubstituted ring adopts a boat-like conformation typical of unsubstituted rings in paracyclophanes (the base of the boat is formed by the unsubstituted CH groups). In molecule **2**, four atoms (C(7), C(8), C(7A), and C(8A)) are coplanar (to within 0.03 Å), the C(6) and C(6A) atoms deviate by 0.170 Å, and the folding angle along the C(7)...C(8) line is 13.5°. In molecules **4** and **5**, the deviations of the C(11) and C(14) atoms from the C(12)C(13)C(15)C(16) plane are 0.159 and 0.170 Å in **4** and 0.158(4) and 0.144(4) Å in **5**, the folding angles along the C(12)...C(16) and C(13)...C(15) lines are 12.6(1) and 13.5(1)° in **4** and 12.2 and 11.3° in **5**, respectively. The distance between the centroids of the rings are 3.126 Å (**2**), 3.106 Å (**4**), and 3.109 Å (**5**).

As can be seen from Table 2, which gives selected bond lengths, the paracyclophane cores in molecules **2**, **4**, and **5** have identical geometric parameters. It should be noted that the C(4)—C(17) and C(7)—C(23) bonds at which the All (**2**) and Ph (**5**) substituents are located have equal lengths (the average value is 1.546 Å) in spite of the different nature of the atoms (C_{sp^3} and C_{sp^2}) in the substituents. These bond lengths are larger even than the standard C_{sp^3}—C_{sp^3} bond length (1.53 Å). By contrast, these bond lengths in molecule **4** (the average value is 1.533 Å) are equal to the standard value.[20] The substantially elongated bonds in the ethylene bridge CH_2CH_2 (the average value is 1.587 Å) are typical of paracyclophanes.

Hence, we demonstrated that the nucleophilic addition of BuLi, PhLi, MeLi, and All_3B to quinone **1** proceeded regio- and stereospecifically to give the corresponding *cis*-diols **2—5** with the OH groups in the *endo* orientations. The stereospecificity observed in the reactions of quinone **1** with organometallic reagents is attributed to the shielding effect of the unsubstituted ring of [2.2]PC, which hinders the attack of the nucleophile on the inside of the quinoid ring.

Table 2. Selected bond lengths (*d*) in molecules **2**, **4**, and **5**



Bond	*d*/Å		
	2	**4**	**5**
C(4)—O(1), C(7)—O(2)	1.441(2)	1.448(2), 1.436(2)	1.445(3), 1.440(3)
C(3)—C(8), C(5)—C(6)	1.326(2)	1.327(2), 1.330(2)	1.324(4), 1.323(4)
C(3)—C(4), C(6)—C(7)	1.526(2)	1.528(2), 1.525(2)	1.526(4), 1.537(4)
C(4)—C(5), C(7)—C(8)	1.521(2)	1.515(2), 1.508(2)	1.520(4), 1.521(4)
C(4)—C(17), C(7)—C(23)	1.549(2)	1.528(2), 1.537(2)	1.546(4), 1.543(4)
C(2)—C(3), C(6)—C(9)	1.517(2)	1.514(2), 1.510(2)	1.509(4), 1.519(4)
C(1)—C(2), C(9)—C(10)	1.591(2)	1.586(2), 1.584(2)	1.578(4), 1.593(4)
C(14)—C(15), C(13)—C(14)	1.398(2), 1.392(2)	1.391(2), 1.395(3)	1.397(5), 1.402(4)
C(11)—C(12), C(11)—C(16)	1.392(2), 1.398(2)	1.392(2), 1.390(2)	1.396(4), 1.385(4)
C(12)—C(13), C(15)—C(16)	1.391(2)	1.386(2), 1.389(2)	1.384(4), 1.387(4)
C(10)—C(11), C(1)—C(14)	1.508(2)	1.509(2), 1.511(2)	1.501(4), 1.503(4)

Experimental

The ^1H and ^{13}C NMR spectra were recorded on a Bruker AMX-400 instrument (400.13 and 100.61 MHz, respectively) in $CDCl_3$ and DMSO-d_6 with the use of the residual signals for the protons of the solvents at δ 7.27 and 2.50, respectively, as the internal standards. Since the signals of the paracyclophane core in the ^1H NMR spectra are substantially overlapped, the chemical shifts are given in reference to the centers of the cross-peaks in the 2D experiments.

The mass spectra (EI) were measured on a Kratos MS-90 mass spectrometer at 200 or 250 °C; the energy of ionizing electrons was 70 eV. The IR spectra were recorded on a Specord M-82 instrument.

The TLC analysis was carried out on Sorbfil PTSKh-AF-A-UF (Sorbpolimer Joint-Stock Company, Krasnodar, Russia) and Silufol UV-254 (Chemapol) plates. Chromatographic purification and separation of the diastereomers were performed on silica gel Kieselgel 60 (Merck) and Kieselgel 60 F_{254} (Merck) plates.

4-Hydroxy[2.2]paracyclophane was synthesized according to a known procedure.[21]

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

[2.2]Paracyclophane-4,7-quinone (1). Sodium nitrite (0.490 g, 7.1 mmol) was added to a solution of sulfanilic acid (1.12 g, 6.47 mmol) and (0.342 g, 3.23 mmol) Na_2CO_3 in H_2O (30 mL) cooled to +15 °C. The reaction mixture was stirred for 30 min and poured into a mixture of ice (30 g) and concentrated HCl (0.71 mL, 8.52 mmol). A yellow solution of the diazonium salt was stirred at 0 °C for 30 min. A solution of 4-hydroxy[2.2]paracyclophane (0.962 g, 4.29 mmol) in MeOH (150 mL) was mixed with a solution of NaOH (0.945 g, 23.62 mmol) in H_2O (20 mL) and the reaction mixture was cooled to +5 °C. Then a solution of the diazonium salt was added with vigorous stirring, the temperature being maintained at no higher than +5 °C. The dark-claret solution of the azo compound was stirred at +5 °C for 1 h and then at ~20 °C for 5 h. Then the solution was kept for ~8 h. Concentrated HCl (20 mL) and a solution of $SnCl_2 \cdot 2H_2O$ (6.7 g, 29.7 mmol) in concentrated HCl (10 mL) were successively added to the solution of the azo compound and the mixture was refluxed for 1 h. Then $Fe_2(SO_4)_3$ (42 g, 105 mmol) was added and the mixture was refluxed with srirring for 8 h. Quinone **1** was extracted with $CHCl_3$, dried with Na_2SO_4, concentrated *in vacuo*, and chromatographed on silica gel ($CHCl_3$ as the eluent). Analytically pure quinone **1** was obtained in a yield of 0.758 g (74%), t.decomp. 210—238 °C (*cf.* lit. data[12]: t.decomp. 150 °C). Found (%): C, 80.39; H, 6.11. $C_{16}H_{14}O_2$. Calculated (%): C, 80.65; H, 5.92. IR (KBr), ν/cm^{-1}: 1650 (C=O) (*cf.* lit. data[12]: 1656 (C=O) (CH_2Cl_2)).

***cis*-4,7-Diallyl-4,7-dihydroxy-4,7-dihydro[2.2]paracyclophane (2).** Triallylborane (0.1 mL, 0.57 mmol) was added with stirring to a solution of quinone **1** (0.06 g, 0.25 mmol) in toluene (6 mL). The yellow solution of the quinone immediately turned colorless. The reaction mixture was stirred at ~20 °C for 0.5 h and hydrolyzed by the successive addition of MeOH (3 mL) and a 10% aqueous solution of NaOH (10 mL). The organic layer was washed with H_2O, dried with Na_2SO_4, and concentrated *in vacuo*. Compound **2** was obtained in a yield of 0.081 g (99.8%), m.p. 101—101.5 °C (from heptane). Found (%): C, 81.83; H, 8.00. $C_{22}H_{26}O_2$. Calculated (%): C, 81.95; H, 8.13. MS, *m/z* (I_{rel} (%)): 304 $[M - H_2O]^+$ (1.3); 281 $[M - All]^+$ (38.3); 263 $[M - H_2O - All]^+$ (3.7); 240 $[M - 2\,All]^+$ (14.2); 104 (100). ^1H NMR ($CDCl_3$), δ: 1.97—2.20 (m, 4 H, 2 CH_2); 2.20 (s, 2 H, 2 OH); 2.20 (m, 2 H, $H(2)_a$, $H(9)_a$); 2.99 (m, 2 H, $H(1)_a$, $H(10)_a$); 2.65 (m, 2 H, $H(2)_b$, $H(9)_b$); 2.87 (m, 2 H, $H(1)_b$, $H(10)_b$); 4.83 (s, 2 H, H(5), H(8)); 5.03 (d, 2 H, 2 *trans*-H_2C=, ^3J = 24.1 Hz); 5.10 (d, 2 H, 2 *cis*-H_2C=, ^3J = 9.7 Hz); 5.76 (m, 2 H, 2 CH=); 6.93 (d, 2 H, H(12), H(15), ^3J = 7.8 Hz); 7.06 (d, 2 H, H(13), H(16), ^3J = 7.8 Hz). ^{13}C NMR, δ: 32.13, 33.83 (C(1), C(2), C(9), C(10)); 47.05 (CH_2); 73.80 (C(4), C(7)); 118.29 (=CH_2); 129.23, 131.79, 134.15, 134.98 (CH=, C(12), C(13), C(15), C(16), C(5), C(8)); 139.26, 142.79 (C(3), C(6), C(14), C(11)).

***cis*-4,7-Dibutyl-4,7-dihydroxy-4,7-dihydro[2.2]paracyclophane (3).** A 2.005 *M* BuLi solution in hexane (0.2 mL, 0.4 mmol) was added with stirring to a solution of quinone **1** (0.03 g, 0.13 mmol) in toluene (5 mL). The reaction mixture was stirred at ~20 °C for 5 h and decomposed with a saturated solution of NH_4Cl. The organic layer was washed with H_2O, dried with Na_2SO_4, and concentrated *in vacuo*. The residue was chromatographed on Kieselgel 60 F254 plates (a 10 : 1 benzene—AcOEt mixture as the eluent). Unconsumed quinone **1** was isolated in a yield of 0.01 g (35%). Alcohol **2** was obtained in a yield of 0.02 g (44.8% with respect to a total amount of **1** or 89.7% with respect to consumed **1**), m.p. 119.5—120 °C (from heptane). Found (%): C, 81.31; H, 9.74. $C_{24}H_{34}O_2$. Calculated (%): C, 81.56; H, 9.67. MS, *m/z* (I_{rel} (%)): 354 $[M]^+$ (0.80); 336 $[M - H_2O]^+$ (7.31); 297 $[M - Bu]^+$ (13.61); 104 (100). ^1H NMR ($CDCl_3$), δ: 0.83 (t, 6 H, 2 Me, ^3J = 7.2 Hz); 1.05—1.50 (m, 12 H, 2 $(CH_2)_3$); 1.60 (s, 2 H, 2 OH); 2.28 (m, 2 H, $H(2)_a$, $H(9)_a$); 2.70 (m, 2 H, $H(2)_b$, $H(9)_b$); 2.89 (m, 2 H, $H(1)_b$, $H(10)_b$); 3.02 (m, 2 H, $H(1)_a$, $H(10)_a$); 4.87 (s, 2 H, H(5), H(8)); 6.95 (dd, 2 H, H(12), H(15), ^3J = 7.8 Hz, ^4J = 1.8 Hz); 7.03 (dd, 2 H, H(13), H(16), ^3J = 7.8 Hz, ^4J = 1.8 Hz).

***cis*-4,7-Dihydroxy-4,7-dihydro-4,7-dimethyl[2.2]paracyclophane (4).** A solution of quinone **1** (0.30 g, 1.26 mmol) in anhydrous toluene (78 mL) was added to a 0.41 *M* MeLi solution (60 mL) in Et_2O (24.6 mmol) for 7 h. The reaction mixture was stirred for 1.5 h and decomposed with a saturated solution of NH_4Cl. The organic layer was washed with H_2O, dried with Na_2SO_4, and concentrated *in vacuo*. The residue was chromatographed on a column with SiO_2 (a 5 : 1 benzene—AcOEt mixture as the eluent). Unconsumed quinone **1** was isolated in a yield of 0.080 g (26.7%). Diol **4** was obtained in a yield of 0.207 g (61% with respect to a total amount of **1** or 92.2% with respect to consumed quinone **1**), m.p. 104—104.5 °C. Found (%): C, 80.28; H, 8.17. $C_{18}H_{22}O_2$. Calculated (%): C, 79.96; H, 8.20. MS, *m/z* (I_{rel} (%)): 270 $[M]^+$ (9); 252 $[M - H_2O]^+$ (23); 224 $[M - H_2O - CO]^+$ (1.6); 237 $[M - H_2O - Me]^+$ (2.37); 209 $[M - H_2O - Me - CO]^+$ (9.3); 165 $[M - 104]^+$ (6.6); 148 $[M - H_2O - 104]^+$ (15); 135 $[M - 2\,H - CO - 105]^+$ (10.6); 117 $[M - H_2O - 2\,H - CO - 105]^+$ (21.4); 104 (100). ^1H NMR ($CDCl_3$), δ: 1.09 (s, 6 H, 2 Me); 2.09 (br.s, 2 H, 2 OH); 2.21 (m, 2 H, $H(2)_a$, $H(9)_a$); 2.71 (m, 2 H, $H(2)_b$, $H(9)_b$); 2.62—3.14 (m, 6 H, bridging CH_2); 2.89 (m, 2 H, $H(1)_b$, $H(10)_b$); 3.03 (m, 2 H, $H(1)_a$, $H(10)_a$); 4.92 (s, 2 H, H(5), H(8)); 6.97 (d, 2 H, H(12), H(15), ^3J = 7.8 Hz); 7.04 (d, 2 H, H(13), H(16), ^3J = 7.8 Hz).

***cis*-4,7-Dihydroxy-4,7-dihydro-4,7-diphenyl[2.2]paracyclophane (5).** A solution of quinone **1** (0.159 g, 0.67 mmol) in anhydrous toluene (42 mL) was added to a 0.44 *M* PhLi solution (30 mL) in Et_2O (13.2 mmol) during 4.5 h. The reaction mixture was stirred for 1.5 h and decomposed with a saturated solution of NH_4Cl. The organic layer was washed with H_2O, dried with Na_2SO_4, and concentrated *in vacuo*. The residue was chromatographed on a column with SiO_2 (a 7 : 1 benzene—AcOEt mixture as the eluent). Unconsumed quinone **1** was isolated in a yield of 0.022 g (14%). Diol **5** was obtained in a yield of 0.197 g (75% with respect to a total amount of **1** or 94.7% with respect to consumed quinone **1**), t.decomp. 236—244 °C. Found (%): C, 84.85; H, 6.33. $C_{28}H_{26}O_2$. Calculated (%): C, 85.24; H, 6.64. MS, *m*/*z* (I_{rel} (%)): 394 $[M]^+$ (2.4); 376 $[M - H_2O]^+$ (34); 348 $[M - H_2O - CO]^+$ (4.0); $[M - H_2O - Ph]^+$ (3.70); 271 $[M - H_2O - 105]^+$ (44.4); 259 $[M - 2\,H - CO - 105]^+$ (41.9); 243 $[M - 2\,Ph]^+$; $[M - H_2O - CO - 105]^+$ (16.7); 105 (100). ^1H NMR ($CDCl_3$), δ: 2.21 (s, 2 H, 2 OH); 2.46—2.62 (m, 2 H, bridging CH_2); 2.76—3.21 (m, 6 H, bridging CH_2); 5.60 (s, 2 H, H(5), H(8)); 6.68—6.81 (m, 8 H, 2 Ph); 6.82—6.92 (m, 2 H, 2 Ph); 7.11 and 7.22 (both d, 2 H each, H(12), H(13), H(15), H(16), ^3J = 7.8 Hz). ^{13}C NMR ($CDCl_3$), δ: 33.17 (C(1), C(10)); 34.25 (C(2), C(9)); 77.22 (C(4), C(7)); 126.23 (C(19), C(21), C(25), C(27)); 126.69 (C(22), C(24)); 127.37 (C(12), C(13), C(15), C(16)); 129.72 (C(18), C(28)); 131.96 (C(20), C(26)); 137.89 (C(5), C(8)); 139.36 (C(17), C(23)); 139.74 (C(11), C(14)); 142.61 (C(3), C(6)).

Synthesis of 4,7-dihydroxy[2.2]paracyclophane (6). Hydrazine hydrate (0.02 mL, 0.42 mmol) was added to a solution of quinone **1** (50 mg, 0.21 mmol) in anhydrous EtOH (15 mL). The reaction mixture was refluxed for 2 h, the solvent and an

Table 3. Crystallographic data and details of the structure refinement of compounds **1**, **2**, **4**, and **5**

Parameter	Compound			
	1	**2**	**4**	**5**
Molecular formula	$C_{16}H_{14}O_2$	$C_{22}H_{26}O_2$	$C_{18}H_{22}O_2$	$C_{28}H_{26}O_2$
M	238.27	322.43	270.36	394.49
Crystal system	Monoclinic	Orthorhombic	Monoclinic	Triclinic
Space group	*C*2/*c*	*Pbca*	$P2_1/n$	$P\bar{1}$
T/K	163	153	140	110
a/Å	12.533(7)	12.418(5)	6.773(2)	6.593(5)
b/Å	7.867(2)	9.632(3)	27.892(7)	11.651(8)
c/Å	11.749(5)	14.781(5)	7.660(2)	14.605(10)
α/deg	—	—	—	110.43(2)
β/deg	97.83(4)	—	100.121(6)	92.64(2)
γ/deg	—	—	—	105.23(2)
V/Å^3	1147.6(9)	1768(1)	1424.5(6)	1003(2)
Z	4	4	4	2
d_{calc}/g cm^{-3}	1.379	1.211	1.261	1.307
Color, crystal habitus	Colorless prism	Colorless platelet		Colorless needle
Dimensions/mm	0.40×0.20×0.20	0.30×0.20×0.15	0.10×0.30×0.40	0.04×0.08×0.24
Diffractometer	«Syntex $P2_1$»		«Bruker SMART»	
Radiation	Mo-Kα (λ = 0.71073 Å)			
μ/cm^{-1}	0.90	0.76	0.80	0.80
Scan mode	θ/2θ		ϕ/ω	
$2\theta_{max}$/deg	60	50.06	60	50.02
Total number of reflections	3577	1860	16779	8256
Number of independent reflections (R_{int})	1509 (0.0191)	1568 (0.0189)	4161 (0.0598)	5764 (0.0800)
R_1 (based on *F* for reflections with $I > 2\sigma(I)$)	0.0626 (953)	0.0433 (1246)	0.0678 (2848)	0.0533 (3761)
WR_2 (based on F^2 for all reflections)	0.1507	0.1408	0.1740	0.1536
Number of parameters in refinement	116	161	269	391
Weighting scheme	$w^{-1} = \sigma^2(F_o^2) + (aP)^2 + bP\ (P = 1/3(F_o^2 + 2F_c^2)$			
a	0.0739	0.1000		0.0767
b	0.3333	0.0000		0.0000
GOF	0.987	1.030	1.057	0.773
F(000)	504	696	584	420

excess of hydrazine hydrate were distilled off *in vacuo*, and the flask was filled with argon. Weakly colored crystals were obtained in a yield of 50 mg. According to the ^{1}H NMR spectroscopic data, the crystals contained 90% of hydroquinone **6** and 10% of the starting quinone **1**. ^{1}H NMR ($CDCl_3$), δ: 2.45—2.60 (m, 2 H, CH_2); 2.99—3.20 (m, 4 H, 2 CH_2); 3.20—3.34 (m, 2 H, 2 CH_2); 4.25 (br.s, 2 H, 2 OH); 5.59 (s, 2 H, H(5), H(8)); 6.44 and 7.01 (both d, 2 H each, H(12), H(13), H(15), H(16), ^3J = 7.8 Hz, ^4J = 1.8 Hz).

X-ray diffraction study of compounds 1, 2, 4, and 5. Single crystals of alcohol **2** were prepared by crystallization from heptane. Single crystals of alcohols **4** and **5** and quinone **1** were obtained by crystallization from benzene. The principal characteristics of the crystals, experimental data, and details of the structure refinements are given in Table 3. The X-ray diffraction data sets were collected on a Bruker SMART CCD Area Detector diffractometer at 110—140 K (**4**, **5**) equipped with a low-temperature Oxford Cryosystems Cryostream Cooler attachment. The X-ray data were processed using the SAINT[22] and SADABS programs.[23] The X-ray data sets for compounds **1** and **2** were collected on a Syntex $P2_1$ diffractometer at 163 K. The experimental data were processed and the equivalent reflections were merged using the SHELXTL program package.[24] All structures were solved by direct methods. The nonhydrogen atoms were revealed from difference electron density syntheses and refined anisotropically based on F^2_{hkl}. The positions of the H atoms were also located from the difference electron density synthesis and refined isotropically. All calculations were carried out with the use of the SHELXTL PLUS 5 program package.[25]

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References

1. R. Yanada, M. Higashikava, Y. Miwa, T. Taga, and F. YonEda, *Tetrahedron Asymmetry*, 1992, **3**, 1387.
2. V. Rozenberg, V. Kharitonov, D. Antonov, E. Sergeeva, A. Aleshkin, N. Ikonnikov, S. Orlova, and Yu. Belokon´, *Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 91.
3. A. Pelter, R. A. N. C. Crump, and H. Kidwell, *Tetrahedron Lett.*, 1996, **37**, 1273.
4. Yu. Belokon´, M. Moskalenko, N. Ikonninov, L. Yashkina, D. Antonov, E. Vorontsov, and V. Rozenberg, *Tetrahedron Asymmetry*, 1997, **8**, 3245.
5. P. J. Pye, K. Rossen, R. A. Reamer, N. N. Tsou, R. P. Volante, and P. J. Reider, *J. Am. Chem. Soc.*, 1997, **119**, 6207.
6. D. J. Cram and F. L. Harris, Jr., *J. Am. Chem. Soc.*, 1967, **89**, 4642.
7. A. Pelter, H. Kidwell, and R. A. N. C. Crump, *J. Chem. Soc., Perkin Trans. 1*, 1997, 3137.
8. H. J. Reich and K. E. Yelm, *J. Org. Chem.*, 1991, **56**, 5672.
9. E. V. Sergeeva, V. I. Rozenberg, E. V. Vorontsov, T. I. Danilova, Z. A. Starikova, A. I. Yanovsky, and Yu. N. Belokon´, *Tetrahedron Asymmetry*, 1996, **7**, 3445.
10. N. V. Vorontsova, V. I. Rozenberg, E. V. Vorontsov, O. L. Tok, and Yu. N. Bubnov, *Izv. Akad. Nauk, Ser. Khim.*, 2000, 914 [*Russ. Chem. Bull., Int. Ed.*, 2000, **49**, 912].
11. D. J. Cram and H. P. Fisher, *J. Org. Chem.*, 1965, **30**, 1815.
12. D. J. Cram and A. C. Day, *J. Org. Chem.*, 1966, **31**, 1227.
13. N. V. Vorontsova, V. I. Rozenberg, E. V. Vorontsov, D. Yu. Antonov, and Yu. N. Bubnov, *Izv. Akad. Nauk, Ser. Khim.*, 2000, 568 [*Russ. Chem. Bull., Int. Ed.*, 2000, **49**, 572].
14. B. M. Mikhailov, G. S. Ter-Sarkisyan, and N. A. Nikolaeva, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1968, 541 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1968, 547 (Engl. Transl.)].
15. G. S. Ter-Sarkisyan, N. A. Nikolaeva, V. G. Kiselev, and B. M. Mikhailov, *Zh. Obshch. Khim.*, 1971, **41**, 152 [*J. Gen. Chem. USSR*, 1971, **41** (Engl. Transl.)].
16. J. McKinley, A. Aponick, J. C. Raber, Ch. Fritz, D. Montgomery, and C. T. Wigal, *J. Org. Chem.*, 1997, **62**, 4874.
17. D. Liotta, M. Saindane, and C. Barnum, *J. Org. Chem.*, 1997, **81**, 3369.
18. F. Alonso and M. Yus, *Tetrahedron*, 1991, **47**, 7471.
19. M. Takeshita, H. Tsuzuki, and M. Tashiro, *Bull. Chem. Soc. Jpn.*, 1992, **65**, 2076.
20. *Structure Correlation*, Eds. H.-B. Burgi and J. D. Dunitz, VCH, Weinheim—New York, 1994, **2**, 768.
21. K. Krohn, H. Reiger, H. Hopf, D. Barrett, P. G. Jones, and D. Döring, *Chem. Ber.*, 1990, **123**, 1729.
22. *SMART V5.051 and SAINT V5.00, Area Detector Control and Integration Software*, Bruker AXS Inc., Madison (WI-53719, USA), 1998.
23. G. M. Sheldrick, *SADABS*, Bruker AXS Inc., Madison (WI-53719, USA), 1997.
24. G. M. Sheldrick, *SHELXTL Ver.5.0. Software Reference Manual*, Siemens Industrial Automation, Inc., Madison, 1995.
25. G. M. Sheldrick, *SHELXTL-97, Version 5.10*, Bruker AXS Inc., Madison (WI-53719, USA), 1997.

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