Preparations and Properties of Some Derivatives of Pseudo-Geminal Ketone of Tris[2.2.2]paraxylylene

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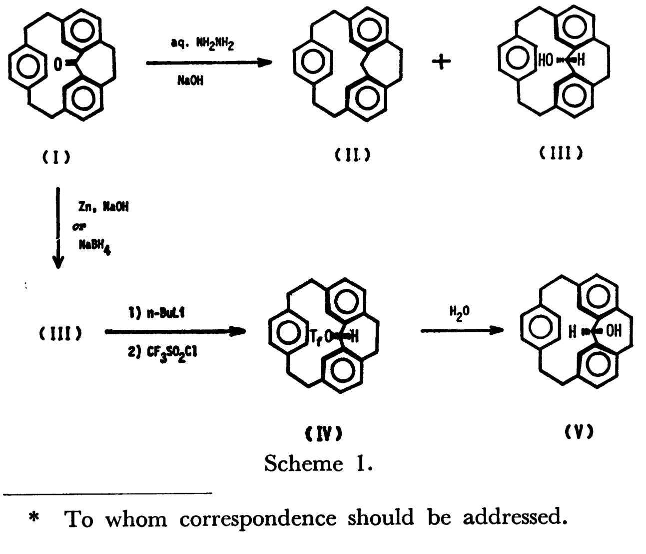
Some derivatives of pseudo-geminal ketone of tris[2.2.2]paraxylylene (I) were prepared and their spectral properties were investigated in connection with their structural characteristics. The stereochemistry of two isomers of pseudo-geminal carbinols of tris[2.2.2]paraxylylene (III and V) was determined on the basis of chemical shifts of benzhydryl protons and H_0 protons in NMR spectra and also of ν_{O-H} bands in IR spectra. The difference in chemical shifts of H_p protons of the two alcohols was explained in terms of the change in electron densities of *para* carbon atoms.

In the preceding paper,[1] the authors reported the high yield preparation of pseudo-geminal ketone of tris[2.2.2]paraxylylene (I) and its spectral properties in connection with its structure. The remarkable high frequency shift of $\nu_{C=O}$ band in the IR spectrum and the large hypochromic effect of intramolecular charge-transfer absorption on the electronic spectrum of I compared with the corresponding spectral characteristics of 5*H*-10,11-dihydrodibenzo[*a*,*d*]cyclohepten-5-one [VI] indicate the lack of coplanarity between carbonyl and benzene planes, and the presence of angle strain about the carbonyl.

Taking these characteristics into consideration, some derivatives of I were prepared in order to elucidate relationships between structures and spectral properties. In this paper, the authors describe some interesting NMR spectral characteristics in the pseudo-geminal tris[2.2.2]paraxylylene derivatives.

Results and Discussion

Preparation. Pseudo-geminal ketone (I) was prepared from tris[2.2.2]paraxylylene by acetylation, bromoform reaction and intramolecular Friedel-Crafts acylation.[1] Reduction of I with sodium tetrahydroborate(—1) in dioxane or with zinc powder in alkaline aqueous ethanol gave 92% or 71% yield, respectively, of "equatorial" alcohol (III), mp 181.0 °C, exclusively. The Wolff-Kishner reduction of I with aqueous hydrazine and sodium hydroxide at 195 °C yielded 44% of pseudo-geminal methanotris[2.2.2]paraxylylene (II) and 46% of III. III was converted into the corresponding trifluoromethanesulfonate (IV) on treatment with butyllithium and trifluoromethanesulfonyl chloride in ether. IV was hydrolyzed in aqueous dioxane to give the stereoisomeric "axial" alcohol (V), mp>300 °C, in quantitative yield.



Scheme 1.

Determination of Stereochemistry of Pseudo-Geminal Carbinols of Tris[2.2.2]*paraxylylene.* Based on molecular model (Dreiding and CPK), the pseudo-geminal bridged tris[2.2.2]paraxylylenes are regarded to have appreciably rigid structures, where conformation change between "equatorial" and "axial" positions about pseudo-geminal bridge carbon seems to be difficult and environments of these positions seem to differ remarkably. The stereochemistry of the two isomeric

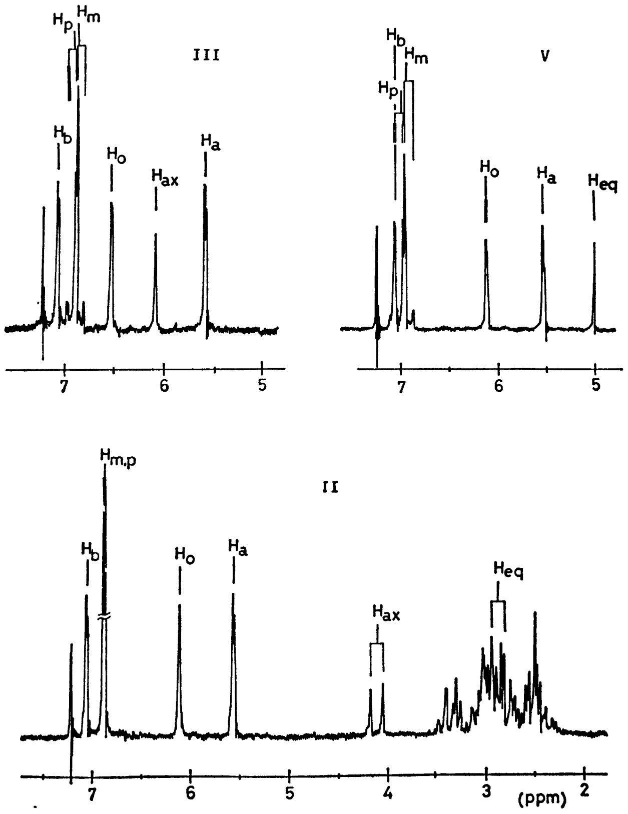


Fig 1. Aromatic and benzhydryl regions of NMR spectra of II, III and V.

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Table 1. The NMR chemical shifts of pseudo-geminal bridged tris[2.2.2]paraxylylenes and related compounds in $CDCl_3$ at 31.5° (δ from internal TMS).

Compound	H_o	H_m	H_p	H_a	H_b	H_{ax}	H_{eq}	$-CH_2-$	OH
I[a]	6.21	7.00	7.16	5.51	7.03			2.3—3.4	
II	6.12	6.88	5.57	5.57	7.07	4.12	2.88	2.4—3.5	
III	6.52	6.87	6.91	5.56	7.07	6.07		2.3—3.4	1.60
V	6.11	6.94	6.97	5.52	7.05		5.01	2.3—3.2 3.7—3.9	2.00
VI[a]	8.0	7.1—7.4						3.10	
VII		7.09					4.10	3.16	
VIII		7.0—7.5					5.91	2.9—3.4	2.22

a) Ref. 1.

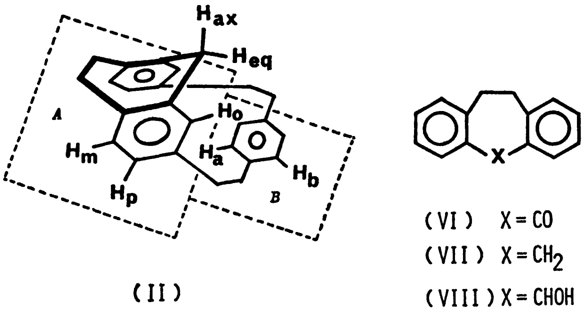

Fig. 2

alcohols (III and V) was investigated mostly by means of NMR spectra. The NMR spectral data of the two alcohols are given in Table 1 along with those of the related compounds. Absorptions of the aromatic and benzhydryl protons are shown in Fig. 1.

The seven membered ring of II (bold line, Fig. 2) is forced to be in a boat conformation due to the remarkably large barrier to the expected conformation change, as shown by the NMR spectra of II in hexachlorobutadiene which shows no substantial temperature dependence up to 180 °C. Irradiation at δ 2.88 caused increase in area intensity of the H_o signal (δ 6.12) of II by 22±1%, while only a very small increase (2.7±0.1%) was observed upon irradiation at δ 4.12. From this nuclear Overhauser effect[2] the higher field signal (δ 2.88) was determined to be H_{eq}, "equatorial" about pseudo-geminal carbon, and the lower (δ 4.12) to be H_{ax}, "axial". Since the chemical shift of a proton α to hydroxyl was reported to be not remarkably affected by the change in stereochemistry of the group,[3] assignments of stereochemistry of the present carbinols are made as shown in Fig. 1. Deshielding of the H_o protons of III (by 0.41 ppm lower field than those of V) is, thus, mainly attributed to anisotropic effect of the "equatorial" oxygen atom in a close proximity.

The low field absorption of the "axial" proton in the present system is consistent with those reported for the 3,4-homotropylidenes,[4] dihydropleiadenes[5] or dihydroanthracenes.[6]

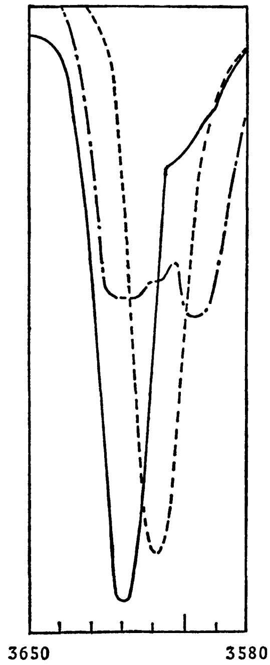

Fig. 3. ν_{O-H} absorptions of III (——), V (- - -) and VIII (— — —) in CCl_4. Concentration 5×10^{-4} M, cell thickness 2.5 cm.

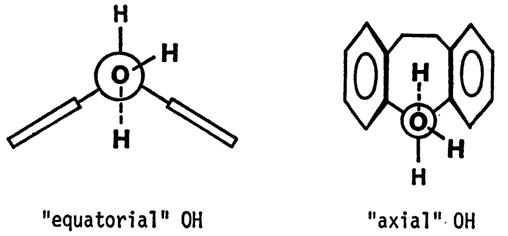

Fig. 4.

A marked difference between observed ν_{O-H} of these two isomeric alcohols in also in line with the present stereochemistry. The ν_{O-H} values of III, V and VIII (dilute solutions in carbon tetrachloride) are shown in Fig. 3. The "axial" hydroxyl group is expected to interact with a phenyl group (Fig. 4), known as the π-hydrogen bonding,[7] shifting the ν_{O-H} of V to a relatively low frequency, 3608 cm^{-1}. On the other hand, the ν_{O-H} of III appears at relatively high frequency, 3619 cm^{-1}, again in line with the sterochemistry, where the "equatorial" hydroxyl group does not seem to interact with phenyl group. The above consideration is supported by IR spectra of structurally related compounds, 9-fluorenol (3591 cm^{-1}, only the "axial" conformation is allowed) and VIII (3620, 3609^{sh} and 3597 cm^{-1}, more than two conformations are allowed due to its flexible structure). The stereochemistry of the alcohols (III and V), therefore, suggests highly stereoselective attacks (*anti* to the *B* benzene ring) of nucleophiles such as hydride or hydroxide, toward the carbonyl carbon.

Chemical Shift of Pseudo-Geminal Bridged Tris[2.2.2]-*paraxylylene.* A remarkable characteristic appearing in the NMR chemical shifts (Table 1) of the pseudo-geminal bridged tris[2.2.2]paraxylylenes is the absorption of H_o and H_a protons at a considerably high field. All of the H_a protons of the four derivatives (I, II, III and V) are observed by 1.5 ppm upfield (δ from 5.51 to 5.57) than *p*-xylene. We come across a similar situation in the aromatic protons of 4,5 : 7,8-dibenzo[2.2]paracyclophane (IX, Fig. 5)[8] showing absorption at δ 5.50, which is located just above (*ca.* 3.0 Å) the aromatic ring. Thus, for the H_a protons of our present compounds, considered to be located just above (3.1 Å) the "face"[1] benzene rings (*A*) judging from molecular models, the observed high field shifts are attributed to a transannular shielding effect of the *A* rings (see II).

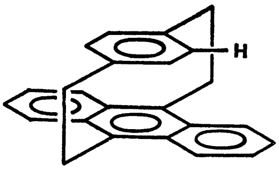

Fig. 5.

Since the absorption of the H_o protons of II appears at δ 6.12, a field higher than the corresponding noncyclic VII by 0.97 ppm, the transannular shielding of the *B* ring is estimated to be 0.82 ppm assuming a 0.15 ppm[9] upfield shift due to the inductive effect of the *meta* methylene bridges. This reduced transannular shielding is responsible for deviation (1.6 Å by the model) of location of the H_o proton from the center of the *B* ring.

The H_p protons of II appear at a field only 0.21 ppm higher than VII. This relatively small shift is mostly attributable to the *meta* methylene bridges. Only a negligibly small transannular shielding seems to be present at this position.

An interesting difference (0.06 ppm) between the chemical shifts of the H_p protons is seen for V as compared with III.[10] Since the distance between the H_p hydrogen and the hydroxyl oxygen atoms is estimated to be 6.0—6.1 Å, at most a 0.2 ppm difference is responsible for the change in the chemical shift due to anisotropic shielding and electrostatic field effect.[11,12] The main part of the difference is, therefore, interpreted in terms of the change in electron densities of the *para* carbon atoms. Linear correlations of chemical shifts of aromatic protons with electron densities of ring carbon atoms have been well established.[13] The CNDO/2[14] calculations were carried out for two conformations, where the hydroxyl was perpendicular or coplanar to the phenyl plane, of benzyl alcohol taken as a model compound. The calculated electron density of the *para* carbon was lower (by 0.003 *e*, which caused by 0.04 ppm down field shift according to the equation[13b]) for the perpendicular form. This is clearly in line with the observed lower chemical shift in V.

Experimental

Measurements and Calculations. All the melting points were uncorrected. NMR spectra were recorded with a Varian HA-100 or a Varian EM-360 spectrometer. The former was also employed for the variable-temperature and the nuclear Overhauser experiments. The sample for the latter experiment was degassed. Mass spectra were determined with a Hitachi RMU-6C mass spectrometer with ionization current 70 eV. Electronic spectra were measured with a Hitachi EPS-3T recording spectrophotometer, the IR spectra being taken on a Hitachi EPI-G3 grating infrared spectrophotometer. Theoretical calculations were carried out by use of the FACOM 230-75 computer at the Data Processing Center of Kyoto University.

Pseudo-Geminal "Equatorial" Carbinol of Tris[2.2.2]*paraxylylene (III). a) Zinc Reduction*: To a hot solution of 520 mg of I in 70 ml of ethanol was added a mixture of 7 g of zinc powder, 7 g of sodium hydroxide and 10 ml of water. The mixture was refluxed for 2 hr and concentrated to half volume. After being cooled to room temperature, the mixture was filtered. The filtrate was extracted six times with ether. The combined ether extract was washed with saturated aqueous sodium chloride, dried over anhydrous magnesium sulfate, and the solvent was evaporated. The residual solids were recrystallized with benzene-dichloromethane (6/1 vol/vol) to give 370 mg (71%) of III as colorless prisms; mp 181.0 °C. MS *m/e* (rel intensity): 340 (M$^+$, 88), 322 (36), 311 (54), 218 (100), 205 (31), 193 (32), 133 (47), and 104 (36). IR (KBr): 3470, 3000, 2930, 2840, 1495, 1440, 1155, 1045, 1040, 805, 620, and 455 cm^{-1}. UV (cyclohexane) λ_{max}: 279^{sh} (ε 800), 265 (900), 272^{sh} (930), 274 (1000), and 281 nm (910). Found: C, 88.48; H, 7.05%. Calcd for $C_{25}H_{24}O$: C, 88.19; H, 7.11%.

b) Sodium Tetrahydroborate (−1) Reduction: To a stirred solution of 430 mg (1.27 mmol) of I and 0.5 ml of 0.1 M aqueous sodium hydroxide in 10 ml of dioxane was added 242 mg (6.35 mmol) of sodium tetrahydroborate (−1) at room temperature, stirring being continued for 3 hr. Excess tetrahydroborate (−1) was removed by boiling the solution for 5 min. The solution was then cooled and extracted three times with chloroform. The combined chloroform extract was washed with saturated aqueous sodium chloride and dried over anhydrous sodium sulfate, the solvent being evaporated. The residual solids were chromatographed on a silica gel column with benzene to give 397 mg (92%) of III.

Pseudo-Geminal Methanotris[2.2.2]*paraxylylene (II).* A mixture of 50 mg of I, 200 mg of sodium hydroxide, 10 drops of hydrazine hydrate (abt. 80%) and 4 ml of diethylene glycol was refluxed for 40 min. After being cooled, the mixture was extracted with ether. The extract was washed with aqueous sodium chloride and dried over anhydrous magnesium sulfate. The solvent was evaporated and the residue was chromatographed on a silica gel column with hexane-dichloromethane (1 : 1) and then dichloromethane. The first fraction gave 21 mg (44%) of II, and the second fraction gave 23 mg (46%) of III which was identified with an authentic III by NMR and IR spectra. Recrystallization of II from hexane-chloroform gave colorless plates; mp 189.5—190.5 °C. MS *m/e* (rel intensity): 324 (M$^+$, 100), 220

(26), 219 (40), 205 (61), 129 (26), 104 (21), and 83 (28). IR (KBr): 3000, 2930, 2850, 1500, 1440, 1100, 810, 590, and 460 cm^{-1}. UV (cyclohexane) λ_{max}: 258^{sh} (ε 650), 261^{sh} (690), 266 (860), 274 (1060), 279 (830), and 282 nm (1070). Found: C, 92.42; H, 7.48%. Calcd for $C_{25}H_{24}$: C, 92.54; H, 7.46%.

The Trifluoromethanesulfonate of III (IV). To a stirred solution of 190 mg of III in 5 ml of dry ether was added 0.3 ml of abt. 20% butyllithium in hexane at room temperature, stirring being continued for 10 min. A few drops of trifluoromethanesulfonyl chloride were then added, and stirring was continued for 10 min at room temperature. The solvent was removed under reduced pressure and the residue was chromatographed on a silica gel column with benzene. The crystals from the major fraction were recrystallized from petroleum ether to give 180 mg (68%) of IV as colorless needles; mp 158.5—159.0 °C (dec). IR (KBr): 2930, 1415, 1250, 1215, 1200, 950, 890, 805, 635, 605, 580, 515, and 460 cm^{-1}. NMR ($CDCl_3$): δ 2.0—3.5 (m, 12H, $-CH_2-$), 5.56 (m, 2H, H_a), 6.39 (m, 2H, H_0), 6.93 (d, 2H, J=8.0 Hz, H_m), 7.00 (s, 1H, H_{ax}), 7.01 (dd, 2H, J=8.0 Hz, J=1.5 Hz, H_p), and 7.12 (m, 2H, H_b). Found: C, 66.18; H, 5.19%. Calcd for $C_{26}H_{23}F_3O_3S$: C, 66.09; H, 4.91%.

Pseudo-Geminal "Axial" Carbinol of Tris[2.2.2]paraxylylene (V). A solution of 52 mg of IV in 9 ml of dioxane and 6 ml of water in a sealed tube was placed in a bath kept at 110.6±0.1 °C for 23 hr. After being cooled, the reaction mixture was diluted with water and extracted with ether–benzene (1 : 1). The ether–benzene extract was washed with aqueous sodium hydrogencarbonate and then with saturated aqueous sodium chloride, and dried over anhydrous sodium sulfate. The solvent was evaporated to yield 39 mg (100 %) of colorless crystals of V, which was recrystallized from benzene to give colorless needles; mp> 300 °C. MS m/e (rel intensity): 340 (M^+, 6), 322 (45), 218 (46), 202 (19), 104 (100), 103 (27), and 78 (32). IR (KBr): 3430, 3000, 2930, 2840, 1500, 1440, 1045, 1030, 810, 630, 580, and 460 cm^{-1}. UV (cyclohexane) λ_{max}: 244^{sh} (ε 4940), 265^{sh} (1240), 274 (1320), and 284 nm (1110). Found: C, 88.42; H, 7.26%. Calcd for $C_{25}H_{24}O$: C, 88.19; H, 7.11%.

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