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STEREOISOMERS OF PERHYDROPHENANTHRENE. THE SYNTHESIS AND CRYSTAL STRUCTURE OF A DERIVATIVE OF THE *trans-syn-trans* ISOMER

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Abstract—The *trans-syn-trans* isomer of perhydrohenanthrene has the central ring in a boat conformation. A crystalline derivative (the dibenzoate of the *cis* 9,10-diol) was prepared, and the crystal structure was determined. The boat conformation is slightly twisted, as predicted by molecular mechanics.

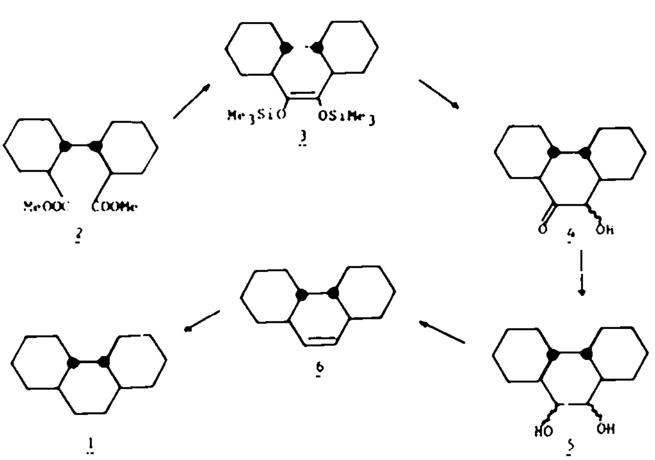
The conformational analysis of 6-membered rings in mono- and polycyclic systems has long been of interest, since such structures form the basic backbones for many natural products. The perhydrophenanthrenes are of particular interest because of their relationship to steroids, terpenes, and other natural products.[3,4] There are six possible stereoisomers of perhydrophenanthrene, and their relative energies have long been of interest. In 1953 Johnson estimated the relative energies of these isomers by simply counting the number of gauche butane interactions, and estimating other interactions.[5] Other calculations, including Hückel approaches,[6] and molecular mechanics calculations[7] have also been reported.

Only four of the six possible stereoisomers of perhydrophenanthrene have been isolated and described.[7] Direct hydrogenation of phenanthrene with Pt in acetic acid yields a mixture of *csc*(*cis-syn-cis*[7]) (60%) and *cst* isomers (40%). This mixture can be equilibrated over Pd and yields a mixture of approximately 85% *tat*, 5% *cat*, and 10% *cst*-perhydrophenanthrene.[7]

Hydrogenation of phenanthrene with Raney Ni at high pressure and temperature is reported[8] to give a mixture of all possible isomers. The assignments of the *cac*- and *tst*- isomers to the corresponding peaks in the gas phase chromatogram are still uncertain, because of the lack of authentic reference materials.

The results of the various theoretical approaches are all in qualitative agreement with each other and with the experimental data for the four most stable isomers, but some question still remains about the *tst* isomer (**1**) and the *cac* isomer. The major instability in **1** is brought about by the necessity of the central ring having a boat conformation. Such a conformation is known in some natural compounds and related derivatives.[9,10]

While we have seen **1** in a GLC chromatogram, we have not actually isolated the compound in the usual sense. Since it is probably a liquid, a crystalline derivative was wanted for structural studies. Several



Scheme 1.

syntheses were considered, and one was pursued sufficiently far as to give the diol **5**. The synthesis of **5**, and the proposed synthesis of **1** from **5** are outlined on the accompanying chart.

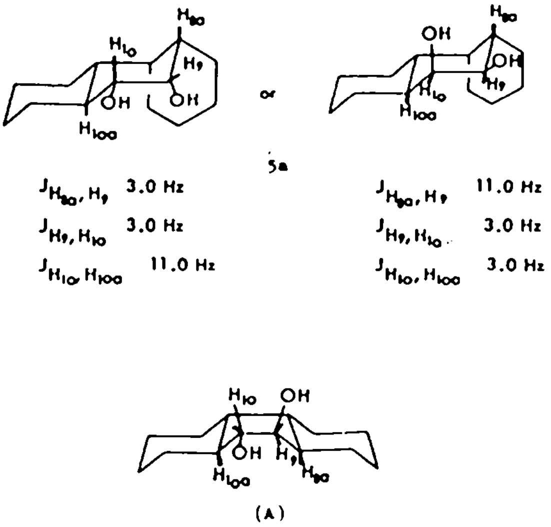
Compound **2** has long been known, and is available from the procedure of Linstead and Doering.[11]

The catalytic hydrogenation of diphenic acid with Pt in acetic acid was reproduced according to the reported procedure,[11] except that the starting mixture was carefully degassed before applying hydrogen. In constrast with the previous results[11] this made additional catalyst unnecessary after a prolonged reaction time. Esterification of *csc*-perhydrodiphenic acid was accomplished in 89% yield using methanol/sulfuric acid, the by-product being 9% of the mono-methyl ester. The equilibration of the dimethyl ester with sodium methoxide to yield **2** was carried out, although a prolonged reaction time and a more concentrated solution were found necessary to give good results. Under these conditions, **2** was obtained in 68% yield. This procedure is much more practical than the inversion on the acid directly, followed by reesterification using diazomethane.[13]

Of the possible methods for forming a CC bond between the carboxylate carbons, we found that the acyloin condensation gave a reasonable yield, following Ruhlmann.[12] One had to be concerned, however, that the reduction of the acyloin **4** to the isomeric diols, **5**, might occur with isomerization at an adjacent ring juncture. To avoid this problem, the acyloin condensation to **3**, cleavage in refluxing methanol to **4** and the reduction of the latter with sodium borohydride rather than with lithium aluminum hydride to give **5** was done without isolation (i.e. distillation) of the intermediate products. In contrast to the previous results, a mixture of three stereoisomeric dials **5a**, **5b**, **5c** was obtained in reasonable yield (60%), with **5a** and **5c** being the major components. The latter compound was not found in the diol mixture which resulted from the reduction of **4** with lithium aluminum hydride. It was easy to isolate **5a** and **5c** in pure form by a fractional crystallization.

The three diols (**5a**, **5b**, and **5c**) are believed to be the 3 possible stereoisomers of *tst*-perhydrophenanthrene-9,10-diol. All gave the proper C-H analysis. The proton NMR spectrum of the dimesylate of **5a** showed coupling constants of 3.0, 3.0 and 11.0 Hz. The large value for the one constant, and the small values of the other two suggested that **5a** was the *trans* diol (A). This finding was in agreement with the failure we noted of the compound to form a cyclic thiocarbonate, but the chromatographic behavior of the 3 diols (R_f values respectively **5a**, 0.35; **5b**, 0.25; **5c**, 0.15) suggested that **5a** was forming an intramolecular H- bond, which would be only possible in a *cis* diol. H-bonding studies by IR spectroscopy in 0.005 M solutions in CCl_4 were carried out, and they showed from the respective shifts of the OH adsorptions compared with those for free secondary hydroxyls[13] that **5a** was indeed a *cis* diol, and **5b** and **5c** were *trans* diols. A combination of these facts indicates that **5a** must not have the carbon skeleton desired, but must instead be a *cst*-perhydrophenanthrene-9,10-diol. This was confirmed, after several unsuccessful attempts due to the insolubility of **5a** in many solvents, by an oxidative cleavage of the vicinal diol **5a** with purple benzene[14] to *cst*-perhydrodiphenic acid, a known[11] compound.

By the same procedure, **5c** was converted to the known[11] *tst*-perhydrodiphenic acid. Combining this fact with the results of the NMR and H bonding studies on **5c**, the structure shown below (A) is proposed for the latter:



Scheme 2.

It was not possible to obtain suitable crystals for X-ray analysis from the parent diol itself. Thus, several derivatives were synthesized including the diacetate, dibenzoate, bis-3,5-dinitrobenzoate and the bis-*p*-bromobenzoate. Of these, the dibenzoate crystals looked to be the most suitable for X-ray analysis, and they proved to be adequate. The fractional atomic coordinates obtained are given in Table 1.

A plot of the molecule as determined by crystallography is shown in Fig. 1. The stereochemistry is clearly evident. The numbering system is shown in Fig. 1, and the pertinent geometric data are given in Table 2. The molecular packing is shown in Fig. 2.

The structure of the parent hydrocarbon has been calculated by the MM2 force field program,[15] and it can be compared with the experimental structure. According to MM2, the C_2 form (twist) of cyclohexane is more stable than the C_{2v} form (boat) by 1.10 kcal/mol. But the fusion of the other rings onto the cyclohexane to give the perhydrophenanthrene system prevents the center ring in the latter molecule from easily achieving a C_2 conformation. The C_{2v} is not very stable in this molecule either, and the calculations show that the energy minimum is somewhere in between these two conformational extremes. If the central ring is forced to have a C_{2v} conformation (so that the overall conformation of the molecule is C_s), the energy is 0.55 kcal/mol above the slightly twisted (C_1) form which is obtained when the energy is allowed to minimize. The calculated angle of twist about the 21–22 bond (arbitrary X-ray numbering, Fig. 1) is found to be 18.4°, and this may be compared with the experimental value found from the crystal structure, which is 19.1(.9)°. It would appear that the presence of the benzoate groups and the crystal packing forces change this angle very little from its calculated (gas phase) value in this case.

Table 1. Fractional unit cell atomic coordinates

Atom	x/a	y/b	z/c
O(1)	0.1959(5)	0.3459(5)	0.5233(4)
O(2)	0.3750(6)	0.3035(8)	0.5338(7)
O(3)	0.3176(5)	0.3360(5)	0.2395(4)
O(4)	0.2761(6)	0.1076(5)	0.1603(6)
C(1)	0.2644(7)	0.2939(8)	0.5579(7)
C(2)	0.1836(8)	0.2184(7)	0.6336(6)
C(3)	0.0443(9)	0.1826(9)	0.6372(8)
C(4)	-0.0253(9)	0.115(1)	0.7107(8)
C(5)	0.046(1)	0.0876(9)	0.7762(8)
C(6)	0.186(1)	0.1210(1)	0.7719(9)
C(7)	0.2549(9)	0.1852(9)	0.6980(8)
C(8)	0.3374(7)	0.2226(7)	0.1660(6)
C(9)	0.4482(7)	0.2610(7)	0.0891(6)
C(10)	0.5209(8)	0.3988(8)	0.1025(7)
C(11)	0.6167(9)	0.4286(9)	0.0233(8)
C(12)	0.6415(8)	0.319(1)	-0.0637(8)
C(13)	0.5711(8)	0.1825(9)	-0.0757(7)
C(14)	0.4732(8)	0.1532(8)	0.0025(7)
C(15)	0.2645(7)	0.4212(7)	0.4493(6)
C(16)	0.2410(7)	0.5508(7)	0.4965(6)
C(17)	0.3380(8)	0.6668(8)	0.6271(7)
C(18)	0.3365(9)	0.8109(8)	0.6733(7)
C(19)	0.385(1)	0.8663(8)	0.5754(8)
C(20)	0.2808(9)	0.7542(8)	0.4499(7)
C(21)	0.2724(7)	0.6071(7)	0.3977(6)
C(22)	0.1684(7)	0.4918(7)	0.2684(6)
C(23)	0.0531(8)	0.5183(8)	0.2352(7)
C(24)	-0.0289(8)	0.4078(9)	0.1007(7)
C(25)	-0.0939(8)	0.2528(9)	0.0818(7)
C(26)	0.0176(8)	0.2236(8)	0.1215(7)
C(27)	0.0976(7)	0.3392(7)	0.2575(6)
C(28)	0.2010(7)	0.3129(7)	0.3078(6)

Table 2. The most important bond distances and bond angles (pm,°) as determined by crystallography

C(1) - O(1)	132(1)	C(8) - O(3)	134(1)
C(1) - O(2)	118(1)	C(8) - O(4)	118(1)
C(1) - C(2)	152(1)	C(8) - C(9)	150(1)
O(1) - C(15)	147(1)	O(3) - C(28)	146(1)
C(15) - C(16)	151(1)	C(27) - C(28)	149(1)
C(16) - C(17)	155(1)	C(26) - C(27)	154(1)
C(17) - C(18)	154(2)	C(25) - C(26)	153(2)
C(18) - C(19)	155(2)	C(24) - C(25)	154(1)
C(19) - C(20)	153(1)	C(23) - C(24)	153(1)
C(20) - C(21)	152(1)	C(22) - C(23)	152(1)
C(16) - C(21)	155(1)	C(22) - C(27)	154(1)
C(21) - C(22)	156(1)	C(15) - C(28)	155(1)
O(1) - C(1) - O(2)	125(1)	O(3) - C(8) - O(4)	125.3(7)
C(2) - C(1) - O(1)	111.9(7)	C(9) - C(8) - O(3)	110.9(6)
C(2) - C(1) - O(2)	123(1)	C(9) - C(8) - O(4)	123.8(7)
C(1) - O(1) - C(15)	116.6(6)	C(8) - O(3) - C(28)	118.3(6)
C(16) - C(15) - C(28)	114.1(8)	C(15) - C(28) - C(27)	111.5(7)
O(1) - C(15) - C(28)	108.1(5)	O(3) - C(28) - C(15)	107.2(5)
C(16) - C(15) - O(1)	107.0(6)	C(27) - C(28) - O(3)	107.9(7)
C(15) - C(16) - C(17)	109.1(7)	C(26) - C(27) - C(28)	113.9(7)
C(17) - C(16) - C(21)	112.0(6)	C(22) - C(27) - C(26)	110.7(7)
C(15) - C(16) - C(21)	108.4(6)	C(22) - C(27) - C(28)	111.4(5)
C(16) - C(21) - C(20)	111.4(6)	C(23) - C(22) - C(27)	108.0(6)
C(16) - C(21) - C(22)	111.5(5)	C(21) - C(22) - C(27)	111.4(7)
C(20) - C(21) - C(22)	114.4(8)	C(21) - C(22) - C(23)	116.9(6)
C(16) - C(21) - C(22) - C(27)	19.1(9)		
C(28) - O(3) - C(8) - C(9)	172.0(6)		
C(15) - O(1) - C(1) - C(2)	179.9(4)		
O(3) - C(8) - C(9) - C(10)	3(1)		
O(3) - C(8) - C(9) - C(14)	-175.5(7)		
O(1) - C(1) - C(2) - C(3)	13.8(8)		
O(1) - C(1) - C(2) - C(7)	-166.9(6)		

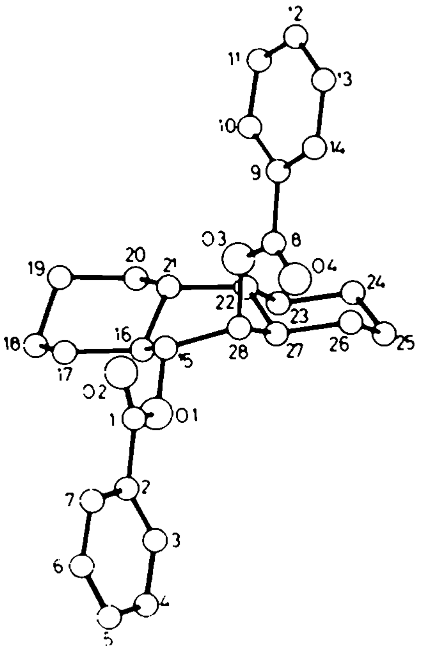


Fig. 1. The crystal structure of *tst*-perhydrophenanthrene-9,10-diol dibenzoate.

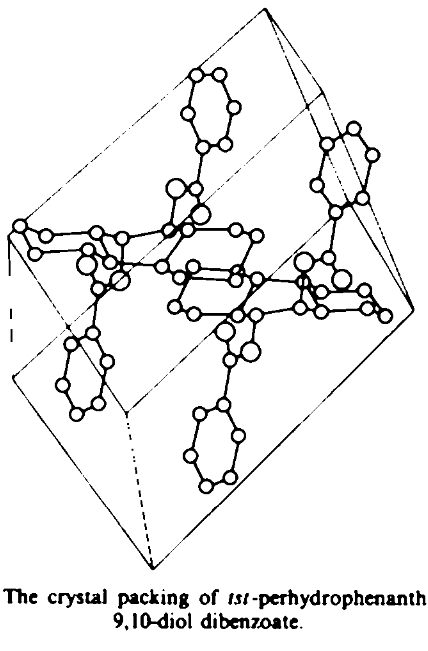


Fig. 2. The crystal packing of *tst*-perhydrophenanthrene-9,10-diol dibenzoate.

EXPERIMENTAL

General methods. Proton NMR spectra were taken on a Varian T 60, HA 100 or Hitachi R 20 spectrometer, ^{13}C NMR spectra with a Jeolco FT 100 spectrometer, IR spectra with Perkin Elmer spectrometers, models 621 and 257. The C, H analyses were carried out by Atlanta Microlabs, Atlanta, Ga. TLC was performed on silica gel H (Merck) or silufol (Applied Science) with 50% H_2SO_4 (A), Iodine (B) or anisaldehyde soln (C) as the detecting agent. The eluting solvent was benzene/MeOH (19/1) unless otherwise stated. Analytical VPC was performed on a Perkin Elmer F 11 chromatograph with flame ionization detector and a 50 ft/0.02" support coated capillary column (Perkin-Elmer) with Carbowax 20M as the stationary phase. Preparative VPC was done on a Varian Aerograph 700 with a 30 ft/3/8" column, with 10% carbowax 20M on chromosorb W 60/80 as the stationary phase. Hydrogenations at atmospheric pressure were done by simply stirring the soln under a measured H_2 atmosphere until the theoretical uptake was reached. Hydrogenations up to 60 psi were performed on the Parr apparatus. Hydrogenations or Diels Alder reactions at high pressure and elevated temp were done with a Magne Dash autoclave, Autoclave Engineers, Erie, Pennsylvania.

Special procedures

csc-*Perhydrodiphenic acid.* Prepared according to Ref. 11. Yield: 59%, m.p. 286 286° (Lit.[11]: 56-63%, m.p. 282–284°).

csc-*Perhydrodiphenic acid dimethylester.* Prepared from the acid according to Ref. 11. Yield: 88.5%, m.p. 72 74° (lit.[11]: 95%, m.p. 67–72°) by products: 9.3% monoester, m.p. 124-126° (lit.[11]: 2.5%, m.p. 124–126°).

tst-*Perhydrodiphenic acid dimethylester* (**2**). Prepared according to Ref. 11, but with changes in procedure. The concentration of the NaOMe was increased 10 times, and the reaction time was increased to 3 hr. Yield: 67%, m.p. 49 54° (lit.[11]: 58%, m.p. 47–56°). By product: 15.1% monoester, m.p. 114–116° (lit.[11], m.p.: 117°).

tst-*Perhydrophenanthrene*-9,10-*diols* (trans-**5c**, *and* cis-**5a**). The soln of **3** (26 g) obtained from **2** (20 g) according to Ref. 12 was freed from xylene on the rotavap, and the residue was dissolved in MeOH (300 ml). AcOH (1 ml) was added, and the soln was stirred with portions of $NaBH_4$ (total 10 g) while maintaining the pH at 6 to 7 with the aid of 5% AcOH in MeOH. After 2 hr of stirring, charcoal was added, and the soln was filtered. The filtrate was evaporated and the residue was stirred for 10 min in hot water (200 ml, 80°). The residue was collected by filtration and recrystallized from MeOH, yield of **5c**, 58%, m.p. 179–181°. By fractional crystallization from the mother liquor it was possible to obtain **5a** in pure form (by TLC), yields of **5a**, 10%, m.p. 183 185°. Diol **5b** was not obtained pure. (Found: Diol **5a**: C, 74.71; H, 10.75; R_f 0.35; Diol **5c**: C, 74.96; H, 10.80, R_f 0.15. Diol **5b**, R_f 0.25. Calc for $C_{14}H_{24}O_2$: C, 74.95; H, 10.78%). Derivatives of diol **5c** were prepared in the usual ways.

Dimesylate. Yield 95%, m.p. 143.5°(d). Found: C, 50.46, H, 7.45. Calc. for $C_{16}H_{28}O_6S_2$: C, 50.50; H, 7.42%.

Diacetate. Yield 96%, m.p. 73.5–75°. Found: C, 69.94; H, 9.13. Calc. for $C_{18}H_{28}O_4$: C, 70.10; H, 9.15%.

Dibenzoate: Yield 82%, m.p. 121–122°. Found: C, 77.77; H, 7.46. Calc. for $C_{28}H_{32}O_4$: C, 77.75; H, 7.46%.

Bis-p-bromobenzoate: Yield 91%, m.p. 178-179°. Found: C, 56.95; H, 5.16. Calc. for $C_{28}H_{30}Br_2O_4$: C, 56.97; H. 5.12%.

Diol cleavage of **5a** *and* **5c**. A soln of the respective diol (**5a**), 112 mg, together with finely powdered $KMnO_4$ (211 mg) and 10 ml of a soln of dicyclohexyl-18-crown-6 in benzene (1 g/500 ml) was stirred for 3 hr, filtered, and the ppt was stirred in 5% NaOHaq (10 ml) for 10 min. The soln was filtered and the filtrate was acidified with HCl (10%). After one day the soln deposited crystals, 46 mg (36%), m.p. 167 174° (m.p. *cst*-perhydrodiphenic acid: 174°[11]).

The same procedure was applied to **5c**, and yielded 50 mg (41%) of crystals, m.p. 216–220° (m.p. *tst*-perhydrodiphenic acid: 223°[11]).

The IR spectra of the acids obtained are identical to those of authentic samples.

IR measurements of intramolecular hydrogen bonding in diols **5a** *and* **5c**. The spectrum of a 0.005 molar soln of the respective diol in CCl_4 was measured in a 20 mm cell. The region from 3500 to 3800 cm^{-1} was expanded and calibrated with *cis*-cyclohexanediol (3626 and 3587 cm^{-1}). **5a**: $\Delta v = 61\ cm^{-1}$ (*cis* diol). Standard value for free secondary. **5c**: $\Delta v = 1\ cm^{-1}$ (*trans* diol). OH groups: 3626 cm^{-1}.[13]

Crystallography. The data were collected on a Syntex-P3 diffractometer at −30°C. Of 5213 measured reflections, 1925 were regarded as significant (I > 3). The space group found was P$\bar{1}$. The density of the crystal was 1.2 g cm^{-3}, and there were two molecules in the unit cell. The unit cell showed the following dimensions (angstroms and degrees): a. 10.77 (1), b. 11.73 (2); c. 12.00 (2); alpha 115.97 (9); beta 87.50 (9); gamma 116.66 (9). The structure was solved by direct methods using the program SHELXTL. The R_1 value was 7.43% and R_2 was 8.39%. The geometric data are summarized in Table 1. The structural data have been submitted to the Cambridge Crystallographic Data Center.

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