Tetrahedron. Vol. 26, pp. 1839 to 1844. Pergamon Press 1970. Printed in Great Britain

STEREOCHEMISTRY OF PERHYDROTRIPHENYLENE—II

ABSOLUTE ROTATION AND CONFIGURATION OF OPTICALLY ACTIVE *ANTI-TRANS-ANTI-TRANS-ANTI-TRANS*-PERHYDROTRIPHENYLENE

M. Farina* and G. Audisio†

(*Received in the UK* 15 *November* 1969; *Accepted for publication* 15 *December* 1969)

Abstract—The resolution into antipodes of perhydrotriphenylene (I) (point group $\mathbf{D}_3$) through the thermal decomposition of the optically active t-butylperoxi-carbonyl derivative is described. The olefins Δ_1 and Δ_2-hexadecahydrotriphenylene were isolated as by-products. The optical purity of (−)I checked by the method of isotopic dilution reached 100%. ORD and CD of (+) perhydrotriphenylen-2-one—the synthesis of which is described—show a positive Cotton effect. By applying the octant rule, the *S*-configuration has been confirmed for (+)I, as foreseen by the Brewster semiempirical rule.

In the previous paper[1] we discussed the structure and reactivity of perhydrotriphenylene, and particularly its *anti-trans-anti-trans-anti-trans* stereoisomer (I), a highly symmetric chiral compound. We showed that by reaction with oxalyl chloride, I gives the perhydrotriphenylen-2-carboxylic acid (II) having the carboxylic group in equatorial position. Starting from this acid, I was obtained in optically active forms.[2] In this paper we wish to discuss this process and to describe the methods adopted for the determination of both optical purity and absolute configuration of the enantiomers of I.

Preparation of optically active perhydrotriphenylene

The chemical inactivity of I precludes the possibility of using direct methods of resolution, both classical and non classical. Even the formation of inclusion compounds of (±)I with optically active substances—profiting by the peculiar property of this compound[3, 4]—did not give appreciable results. Hence, we tried to prepare derivatives of I containing easily removable functional groups on which resolution could be performed. The key intermediate of this process is the perhydrotriphenylen-2-carboxylic acid (II), the synthesis and structural characterization of which were described in the previous paper.[1]

Acid II was resolved through its salt with dehydroabietylamine;[5, 6] the negative acid was obtained from the less soluble salt ($[\alpha]_D^{25} = -74{\cdot}5$ in benzene).

Among the various methods of decarboxylation tested, only the pyrolysis of t-butyl perester (III) in di-isopropylbenzene[7, 8] gave positive results.

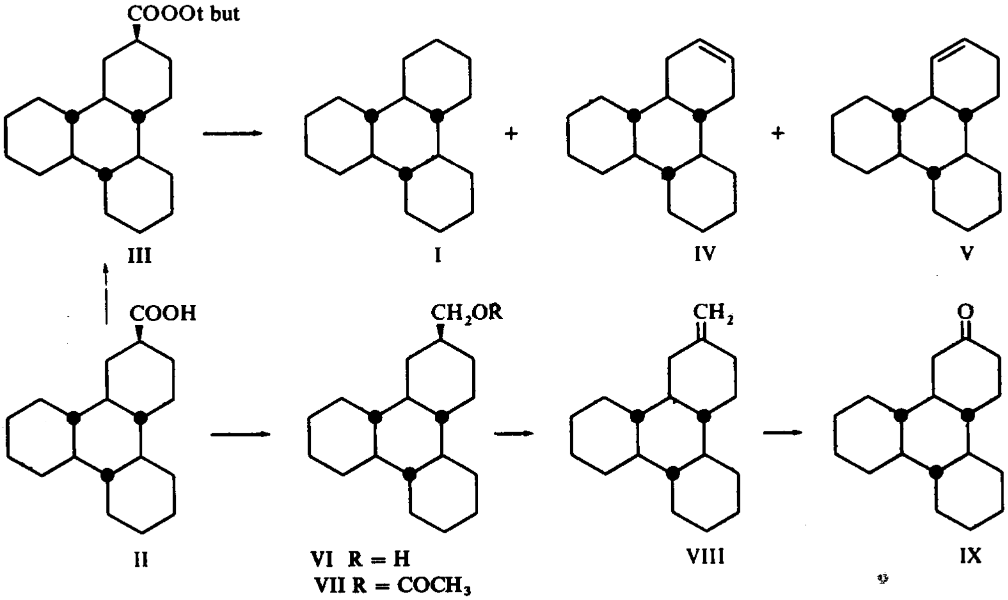
After sublimation and crystallization, the product had a rotatory power ranging between −96 and −100 (in methyl ethyl ketone) and a m.p. of 138–140°.[2] As revealed

---

* Istituto di Chimica Industriale del Politecnico, Milano, Italy.

† Istituto di Chimica delle Macromolecole del Consiglio Nazionale delle Richerche, Milano, Italy.

by IR and NMR analyses, the product consisted essentially of (−)I, but hydrocarbon impurities were present in appreciable amounts. The UV spectrum shows intense absorptions around 280 nm, which may be attributed to aromatic compounds, such as di-isopropylbenzene or its dimer. The presence of such impurities may be explained by considering that crystalline I easily forms inclusion compounds with a number of substances. Aromatic impurities were removed by chromatography on silica-gel; however, the eluted product still contained olefinic impurities, as shown by UV absorptions at about 200 nm.



Pure I was obtained by further chromatography on $AgNO_3$-SiO_2; I shows the following physical properties: $[\alpha]_D^{25} = -93°$ (in MEK), m.p. 144°, no absorption in the UV up to 190 nm, IR and NMR spectra identical with those of (±)I, and only one peak in the gaschromatographic analysis.

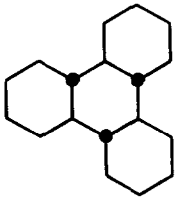
The unsaturated fraction obtained by $AgNO_3$-SiO_2 chromatography had m.p. 116° and $[\alpha]_D^{25} = -142$; the elemental analysis corresponds to the formula $C_{18}H_{28}$, i.e., to a hexadecahydrotriphenylene. Its NMR spectrum at high field is similar to that of I, whereas at low field, a complex signal appears at about 5·60 δ (olefinic protons), which, after decoupling from the signals at 2·20 δ (protons on saturated carbons adjacent to the double bond), changes into a singlet. In this way, the equivalence of the two protons on the double bond is demonstrated; as a consequence, formula IV or Δ_2-hexadecahydrotriphenylene (point group C_2) must be attributed to the product.

A second olefin is also present (in the ratio 1:2); its NMR spectrum shows downfield signals (at about 5·70 δ) and most probably is Δ_1-hexadecahydrotriphenylene (V). The presence of these two olefins is due to α-hydrogen abstraction during the decarboxylation of perester. Their high rotatory power explains the higher optical activity of crude perhydrotriphenylene in comparison with that of the pure one.

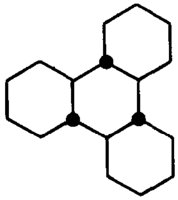
The optical purity of (−)I obtained by this process reaches practically 100%. We checked this value with the method of isotopic dilution,[9] by mixing a sample of (−)I with a sample of ^{14}C-labelled (±)I and by repeated crystallizations of the mixture. By using the Gerlach's formula,[10] we obtained an absolute rotation of −92 ± 2 practically coincident with the highest value found by us.

Absolute configuration of perhydrotriphenylene enantiomers

Some problems connected with the particular type of asymmetric C atoms present in I as well as with their nomenclature have been discussed previously.[11, 13] Here, we apply the rule for equivalent centres of the recent nomenclature by Cahn *et al.*,[14] according to which Ia has configuration *S* and Ib *R*.



Ia (+) S

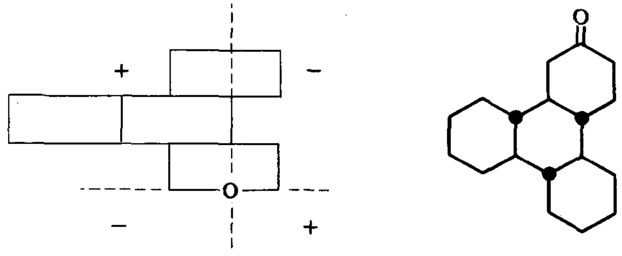


Ib (−) R

The absolute configuration was determined experimentally starting from the partially resolved acid II ($[\alpha]^{25}_{D}$ = +30, optical purity 40%). By reduction with LAH, (+)II was converted into (+) 2-perhydrotriphenylenylcarbinol (VI) and into the corresponding (+) acetate (VII). Pyrolysis of (+)VII at about 560° yielded a mixture of products from which (+) 2-methylenperhydrotriphenylene (VIII) was obtained. (+)VIII was converted into (+) perhydrotriphenylen-2-one (IX) both by ozonolysis and by the Lemieux reaction.[15]

The ORD curve of IX shows a positive Cotton effect (peak at 308 nm, trough at 272 nm) in the region characteristic of ketones. CD measurements show that the CO group is the only asymmetric chromophore in the region 330–200 nm. The ORD curve is not perfectly symmetric. This effect may be due to the contribution of the highly asymmetric carbon skeleton; however, considerable asymmetry has been observed in other simple ketones, such as (*S*)-4-methyl-hexan-3-one.[16]

The octant rule applied to our disubstituted cyclohexanone clearly indicates that (+)IX has the absolute configuration shown in the scheme; consequently (+)I has configuration *S*. This assignment coincides with that previously made,[2] based on the Brewster semiempirical rule.[17]



(+) IX

CONCLUSIONS

Among all optically active organic compounds, *anti-trans-anti-trans-anti-trans* perhydrotriphenylene (I) possesses the highest degree of symmetry (point group $\mathbf{D}_3$). Incidentally, we would like to point out that the same $\mathbf{D}_3$ symmetry is also the highest symmetry found in optically active inorganic compounds reported hitherto, such as $[\mathrm{Fe^{II}}(1{,}10\ \mathrm{phenantroline})_3]^{2+}$.[18] Because of its high rigidity and symmetry, I is a very useful element for the determination of the relationships between molecular structure and optical activity of the compounds which do not show absorptions in the near UV. Actually, its rotatory power is only 27% higher than that calculated by the Brewster method.[17] The rotatory power of (−)I increases slightly with temperature (only 7% from 20° to 70°) and obeys a one-term Drude equation, with $\lambda_0 = 178$ nm.

Obtaining optically active I brought to light some additional features of the crystal structures formed by this versatile molecule.

(−)I forms a series of inclusion compounds having a slightly different structure from that of the racemic compound.[19] The space group of the adduct (−)I-n-heptane is $P6_3$ (instead of $P6_3/m$); the presence of only one enantiomer prevents the existence of intermolecular mirror symmetry elements. Similarly to the racemic compound,[3, 4] the adducts of (−)I with n-hydrocarbons longer than C_{12} show a congruent melting at a higher temperature than pure (−)I; the included component being the same, the m.p. is much higher for the optically active adduct than for the racemic one. For example, the (−)I-hexadecane adduct melts at 162–163°, whereas the racemic one melts at 145° (pure (−)I and (±)I melt at 144° and 128° respectively).

By γ-irradiation of the inclusion compound of (−)I with *trans*-1,3-pentadiene an isotactic polymer was obtained, which showed a detectable optical activity;[19] in this way, the first example of an asymmetric polymerization in the solid state was obtained.

A more detailed study of the properties of optically active I, in particular the radiation polymerization of included monomers and the behaviour on melting of (−)I, (±)I and of their inclusion compounds, will be dealt with in further communications. Investigations are in progress on the configurational stability of I and on the possibility of obtaining other stereoisomers of perhydrotriphenylene in optically active forms.

EXPERIMENTAL

The IR spectra were recorded on a Perkin–Elmer 137 spectrophotometer, the UV spectra on a Cary 15 instrument and the NMR spectra on a Varian HA 100. The chemical shifts are given in δ units. A photoelectric polarimeter Perkin–Elmer 141 was used to determine the rotatory power, usually at 25°. The ORD was recorded on a JASCO spectropolarimeter, model ORD/UV-5. The CD measurements were carried out using a Roussel–Jouan Dicrograph II. Mass spectra were obtained from a Hitachi–Perkin Elmer RMV6D single focus spectrometer, equipped with an all glass heated system, ionization potential 70 ev. The radiochemical data were detected by a Beckmann CPM-100 instrument at liquid scintillation system. M.ps were determined by a hot stage polarizing microscope and are uncorrected. As to partially resolved samples, the m.ps can be used for diagnostic purposes. The m.ps of (−)I and of its inclusion compound with n-hexadecane were registered by a Mettler MP 1 apparatus connected with a potentiometric recorder.

Resolution of perhydrotriphenylen-2-carboxylic acid (II)

(a) *Salt with amine D.* An ethereal soln (0·23 N) of amine D (160 ml) obtained[5, 6] from commercial amine D (Hercules Powder Co) was added to a soln of acid II (10 g) in ether (1 l); 10 g of salt precipitated, its rotatory power after 6 crystallizations from EtOH reached the constant value of −23·2 ($\mathrm{CHCl_3}$, 25°, Na-light). The highest rotatory power of the positive salt was +54.

(b) *Hydrolysis of the salt.* 20 g of salt ($[\alpha]_D^{25}$ = 23·2) wetted with a few drops of EtOH and 400 ml 5% KOH were heated in water bath for 20 hr. After ether extraction of the amine, it was acidified with 35 ml conc HCl. The ppt was recrystallized from 1:1 acetone–toluene: 8·9 g, yield 89·5% $[\alpha]_D^{25}$ = −74·5 (benzene), m.p. 232°. From a positive salt with $[\alpha]_D^{25}$ = +49·5, an acid with $[\alpha]_D^{25}$ = +40 was obtained.

Optically active perhydrotriphenylene (I)

(a) *Chloride of acid* II. 3·3 g of acid II (0·0114 moles) with $[\alpha]_D^{25}$ = −74·5 were mixed with 2·8 g PCl_5 in N_2 atm. After 30 min, toluene (10 ml) was added, and the soln was heated to 70–80° for ½ hr. Then the solvent and $POCl_3$ were removed under reduced press.

(b) *Perester and its decomposition.* t-butylhydroperoxide (1·34 ml) in 1,4-diisopropylbenzene (5 ml) was added dropwise at 0–5° to a soln of acid chloride in diisopropylbenzene (15 ml) and pyridine (1·1 ml). The mixture was stirred at room temp for 4 hr. The soln was washed with 10% H_2SO_4 and with H_2O several times. After drying it was heated to 150° for 4 hr. Diisopropylbenzene was distilled at reduced press, and from the residue a crystalline product was obtained (1·3 g from EtOH, yield 46%) consisting of (−)I (90%) and of (−)IV and (−)V (10%). Pure (−)I was obtained by chromatography on silica gel imbedded with $AgNO_3$ (n-heptane eluent). M.p. 144° $[\alpha]_D^{25}$ = −93.

The mixture of IV and V had m.p. 116° and $[\alpha]_D^{25}$ = 142. (Found: C, 88·34; H, 11·6; $C_{18}H_{28}$ requires: C, 88·45; H, 11·55%).

Optical purity of I

Two runs accomplished on samples initially having a quite different optical purity are reported.

$[\alpha]_D^{25i}$	$[\alpha]_D^{25f}$	C	S_i	S_f	Q	Absolute rotation D line, 25°
−80·2	−88·3	1·10	823	567	1·45	−92
−40·4	−79·1	1·96	634	487	1·30	−92

We used the formula $A = \alpha_i\sqrt{\left(\frac{QC-1}{Q-1}\right)}$ derived from,[10] where $Q = S_i/S_f$, S being the specific activity value in n curie/g; $C = \frac{[\alpha]_f}{[\alpha]_i}$, and indexes i and f mean initial and final. The error was evaluated to be ±2°. The ^{14}C labelled compound was prepared by Dr. Pedretti, its preparation will be described in a further paper.

2-Perhydrotriphenylenylcarbinol-acetate (VII). 2 g of VI ($[\alpha]_D^{25}$ = +46) (obtained from (+)II ([α] + 40) in Ac_2O (10 ml) were refluxed for 4 hr. After addition of MeOH (40 ml) heating was continued for 1 hr. VII precipitated on cooling: 2·2 g, yield 90%, m.p. 126–128°, $[\alpha]_D^{25}$ = −40·5 (heptane). The NMR spectrum is consistent with the formula: it shows a doublet centred at 3·73 δ ($—CH_2O—$) and a singlet at 2·00 δ ($CH_3—COO$).

2-Methylenperhydrotriphenylene (VIII). By pyrolysis of VII (1 g) at 560° in slow N_2 stream and after chromatography on silica gel (20 g) in CCl_4, 300 mg of VIII were obtained, yield 30%. $[\alpha]_D^{25}$ = +63 ($CHCl_3$), m.p. 107–109°.

The IR spectrum shows the characteristic peaks of the $C{=}CH_2$ group at 1650 and 888 cm^{-1}. The NMR spectrum shows a signal at about 4·44 δ (vinylidenic protons).

Perhydrotriphenylen-2-one (IX)

(a) Compound VIII (60 mg) in $CHCl_3$ (5 ml) was treated with excess of O_3 at 0°. After removal of the solvent, it was heated in the presence of 3% H_2O_2 for 5 hr on the water bath. After addition of KOH and ether extraction, IX was crystallized from acetone–water.

(b) A soln of VIII (101 mg) in dioxan (50 ml) was added to a soln of KIO_4 (830 mg), $KMnO_4$ (30 mg) K_2CO_3 (10 mg) in H_2O (50 ml). The mixture was stirred at room temp for 200 hr, then it was diluted with water and extracted with ether, 40 mg from acetone–H_2O, m.p. 98–101°. $[\alpha]_D$ = +51 (EtOH).

Carbonyl absorption at 1720 cm^{-1}, Mass spectrum with molecular peak at 260 *m/e*.

A small amount of impurities with different mol. wts were revealed by mass and UV spectra.

Acknowledgements—We are much indebted to the Laboratory Virus e Biosintesi Vegetali of CNR, Milano, Italy, for determining ORD and radiochemical data, and to Dr. R. Capellini for his valid experimental work.

REFERENCES

[1] M. Farina and G. Audisio, *Tetrahedron* **26**, 1827 (1970).
[2] M. Farina and G. Audisio, *Tetrahedron Letters* 1285 (1967).
[3] M. Farina, G. Allegra and G. Natta, *J. Am. Chem. Soc.* **86**, 516 (1964).
[4] G. Allegra, M. Farina, A. Immirzi, A. Colombo, U. Rossi, R. Broggi and G. Natta, *J. Chem. Soc.* B, 1020 (1967).
[5] B. Sjöberg and S. Sjöberg, *Ark. Kemi* **22**, 447 (1964).
[6] W. J. Gottstein and L. C. Cheney, *J. Org. Chem.* **30**, 2072 (1965).
[7] K. B. Wiberg, B. R. Lowry and T. M. Colby, *J. Am. Chem. Soc.* **83**, 3998 (1961).
[8] C. Rückardt, *Fortschr. Chem. Forsch.* **6**, 251 (1966).
[9] M. Raban and K. Mislow, *Topics in Stereochemistry* **2**, 199 (1967).
[10] H. Gerlach, *Helv. Chim. Acta* **49**, 2481 (1966).
[11] G. Natta and M. Farina, *Tetrahedron Letters* 703 (1963).
[12] M. Farina, *Ibid.* 2097 (1963).
[13] M. Farina, M. Peraldo and G. Natta, *Angew. Chemie* **77**, 149 (1965); Int. Ed. **4**, 107 (1965).
[14] R. S. Cahn, C. K. Ingold and V. Prelog, *Experientia* **12**, 81 (1956).
[15] R. U. Lemieux and E. Von Rudloff, *Canad. J. Chem.* **33** (II) 1710 (1955).
[16] L. Lardicci, P. Salvadori, C. Botteghi and P. Pino, *Chem. Comm.* **7**, 381 (1968).
[17] J. H. Brewster, *J. Am. Chem. Soc.* **81**, 5475, 5483 (1959).
[18] F. P. Dwyer and E. C. Gyarfas, *J. Proc. Roy. Soc. N.S. Wales* **83**, 263 (1950); see also: F. Woldbye, *Optical Rotatory Dispersion and Circular Dichroism in Organic Chemistry* (Edited by G. Snatzke), Chapt. 6. Heyden, London (1967).
[19] M. Farina, G. Audisio and G. Natta, *J. Am. Chem. Soc.* **89**, 5071 (1967).