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The Preparation of Optically Active Trimethylcyclododecatriene by the Resolution of Racemic Oligomers and the Asymmetric Oligomerization

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Trimethylcyclododecatriene was prepared by the oligomerization of pentadiene, using the diethylaluminum chloride - titanium tetrabutoxide system as a catalyst. The resulting oligomer was fractionated by vapor-phase chromatography into geometrical (cis and trans) and structural (head-to-tail and head-to-head) isomers with respect to the pentadiene units involved. The structures of these isomers were proposed on the basis of infrared and NMR spectra of the oligomers and their hydrogenated products. The results of the oxidative degradation of the oligomers were compatible with the proposed structures. Further, the existence of stereoisomers was shown by resolution and asymmetric oligomerization. The resolution of *d*- and *l*-enantiomers was carried out through the asymmetric hydroboration of the oligomers, while the asymmetric oligomerization was achieved using the titanium menthoxide - diethylaluminum chloride system as a catalyst.

The cyclotrimers of butadiene[1] and pentadiene[2] have been known to be prepared by means of a transition metal catalyst. The geometrical isomers of the cyclotrimer of butadiene seem to be interesting in relation to the stereochemistry of oligomerization. Among possible isomers, *ttt*-, *ttc*-, and *tcc*-trimers have been reported by Wilke,[1] but little is known of the cyclotrimers of pentadiene-1, 3. In the latter there should exist stereoisomers as well as cis-trans and head-to-tail isomers, but no research has ever been undertaken on stereoisomers of this sort.[2] This paper will describe the separation of the geometrical isomers of the cyclotrimers of pentadiene-1, 3 by means of vapor-phase chromatography with a Gorey column, and the resolution of *d*- and *l*-enantiomers through asymmetric hydroboration. The asymmetric synthesis of optically active oligomers has also been successfully completed by using a titanium catalyst containing asymmetric component. The oligomers thus obtained are low in optical rotation and may, therefore, not be high in optical purity, but this report may have same value as the first one concerning the resolution of such oligomers and asymmetric oligomerization.

Trimethylcyclododecatriene was synthesized using titanium tetrabutoxide and diethylaluminum chloride as catalysts. The reaction was accompanied by the formation of a large amount of polymer of a low molecular weight, and the vacuum distillation afforded trimethylcyclododecatriene as a fraction with a boiling point of 80—100°C at 2 mmHg (whose yield was, however, as low as 15.7%). This compound showed the infrared absorptions for trans and cis unsaturations at 955 cm^{-1} and 735 cm^{-1} respectively. Its ultraviolet

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[1] G. Wilke, *J. Polymer Sci.*, **38**, 45 (1959); *Angew. Chem.*, **75**, 10 (1963); *Makromol. Chem.*, **69**, 18 (1963).
[2] G. Wilke, Japanese Pat. 263197; Brit. Pat. 860377.

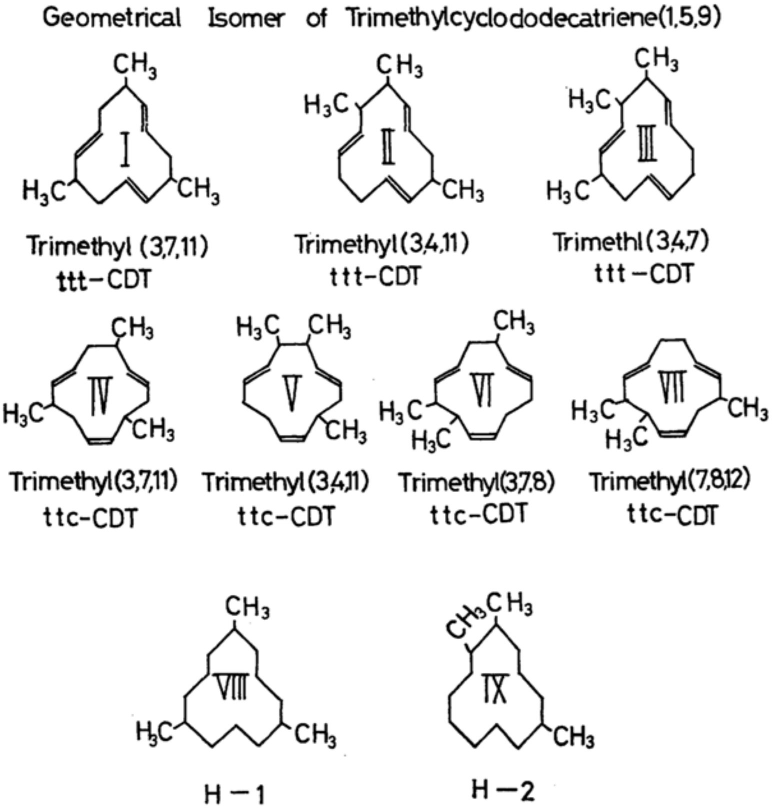

Fig. 1.

spectrum showed no absorption peak corresponding to the conjugated diene structure (at 230 mμ). Its NMR spectrum contained an olefinic proton absorption at τ=4.7—5.2, methine- and methylene-absorptions at τ=7.7—8.2, and a methyl absorption at τ=8.8—9.3, the intensity ratio being 6 : 9 : 9. In the hydrogenated product the ratio of methyl to methine and methylene was 9 : 21. These results accord with any of the cyclic structures, I—VII, in Fig. 1.

Of these, I and IV have all head-to-tail structures, while II, III, V, VI, and VII involve head-to-head and head-to-tail structures. Therefore, there should be two types of hydrogenated products. Hydrogenation with palladium black in ether yielded two products, which were then fractionated into two fractions (named H-1 and H-2) by vapor-phase chromatography using an Apiezone L column at 200°C. NMR study indicated that both H-1 and H-2 contained methyl and other protons in a ratio of 9 : 21, and that H-1 involved methyl absorption at 9.1 and 9.2, whereas H-2 involved such absorption at 9.15 and 9.25, together with that at 9.1 and 9.2. This fact may be accounted for by assuming that the H-1 fraction consists entirely of head-to-tail structures and involves three methyl groups located symmetrically to each other (structure VIII), while the H-2 fraction contains two types of methyl groups, resulting from both head-to-head and head-to-tail structures (structure IX).

Further fractionation by means of Gorey-column vapor-phase chromatography (Hitachi F6D-Q-45) at 180°C indicated that H-1 and H-2 consisted of two and three fractions respectively. This fact may be associated with the presence of cis and trans isomers of methyl groups.

The original trimethylcyclododecatriene was fractionated into five fractions, 1 through 5, forming 7, 13, 21, 15, and 44% of the total respectively. Their infrared spectra indicate that the fractions 1 and 2 correspond to the *ttt*-structure (I, II, or III), while the fractions 3, 4, and 5 correspond to the *ttc*-structure (IV, V, VI, or VII).

The hydrogenation of the fractions 1 and 3 gave H-1, whereas the fractions 2, 4, and 5 gave H-2. Furthermore, methylsuccinic acid was yielded exclusively from the fraction 1 by oxidative degradation with potassium permanganate, while the unfractionated oligomer gave a mixture of succinic, methylsuccinic, and α, α'-dimethylsuccinic acids. Thus, the fractions 1 and 3 must be symmetric in structure.

From these results we may conclude that the fractions 1, 2, and 3 correspond to the structures I, II (or III), and IV respectively. However, it still remains uncertain to which structure (V, VI, or VII) the fractions 4 and 5 correspond.

The original trimethylcyclododecatriene was resolved by asymmetric hydroboration with diisopinocampheyl borane,[3] which had itself been prepared from BF_3 etherate, sodium borohydride and α-pinene $[\alpha]_D^{20}=+43.8°$, followed by hydroxylation with hydrogen peroxide. From the reaction product, the *ttt*- and *ttc*-oligomers remaining unreacted were fractionated by vapor-phase chromatography, these oligomers showed optical rotations of $-8.0°$ and $-15.7°$ respectively. The other products were hydroxylated products of the oligomer, $[\alpha]_D^{20}=-11.4°$, and isopinocampheol, $[\alpha]_D^{20}=-28.3°$. The optical rotations of unreacted and reacted oligomers are not high, but the resolution may take place to a significant extent.

Finally, we tried to synthesize the optically active oligomer by means of asymmetric oligomerization, using titanium tetramenthoxide or tetraamyloxide and diethylaluminum monochloride as catalysts. The fractions with boiling points of 80—100°C/2 mmHg (yield 10%) and of 100—120°C/2 mmHg (yield 4%) distilled from the reaction product were treated with triethylaluminum and phenylisocyanate in order to remove the menthol. The two fractions thus obtained, which were confirmed by vapor-phase chromatography and IR to contain no menthol, had optical rotations, $[\alpha]_D^{15}$, of $-8.6°$ and $-4.4°$. The distillation residue had $[\alpha]_D^{15}=-2.0°$.

In the case of the titanium tetraamyloxide-diethylaluminum chloride catalyst also, the optically active oligomer was obtained by the same method. The optical rotations were as follows: fraction 80—100°C/2 mmHg, $[\alpha]_D^{15}=-0.9°$ (yield 12%), and the distillation residue, $[\alpha]_D^{15}=-0.5°$.

In conclusion, we have succeeded in the resolution and asymmetric synthesis of trimethylcyclododecatriene.

Our success in the fractionation of geometrical isomers and in the resolution of the enantiomer shows the existence of such isomers. The success in asymmetric oligomerization suggests the possibility that the asymmetric ligand, if present, in titanium catalyst has an asymmetric steric effect on the formation of trimethylcyclododecatriene.

Experimental

Preparation of Trimethylcyclododecatriene. In a 50 m*l* test tube there were placed 10 m*l* (0.1 mol) of purified pentadiene-1, 3, 10 m*l* of purified benzene, and 1 mmol of purified titanium tetra-*n*-butoxide under a nitrogen atmosphere. After 6 mmol of diethylaluminum monochloride had then been added, the test tube was sealed and subjected to a reaction. After the reaction had continued for 48 hr at 40°C, the reaction product was treated with 2 m*l* of methanol and washed with diluted sulfuric acid. After drying with calcium chloride, fractional distillation under a vacuum yielded 1.2 g (15.7%) of trimethylcyclododecatriene (80—100°C/2 mmHg), together with a liquid polymer. The trimethylcyclododecatriene had a boiling point of 256—261°C/760 mmHg and a refractive index, n_D^{20}, of 1.4918.

Found: C, 87.97; H, 11.69%; mol wt (cryoscopic method), 204. Calcd for $C_{15}H_{24}$; C, 88.16; H, 11.84%; mol wt, 204.

The infrared spectrum showed trans- and cis-unsaturations at 955 cm^{-1} and 735 cm^{-1} respectively, but no vinyl unsaturation. The ultraviolet spectrum showed no peak at 230 mμ corresponding to that of the conjugated double bond. NMR study confirmed the presence of methine, methylene, and methyl groups in a 6 : 9 : 9 ratio.

Hydrogenation of Trimethylcyclododecatriene. Two hundred milligrams of purified trimethylcyclododecatriene were hydrogenated in 2 m*l* of ether with 200 mg of a Pd-black catalyst at 25°C under H_2-pressure (300 mmH_2O). The product was trimethylcyclododecane, which was a mixture of H-1 and H-2.

Oxidative Degradation of Trimethylcyclododecatriene. Trimethylcyclododecatriene was oxidized by the drop-by-drop addition of a potassium permanganate solution for 4 hr at 5°C. After the oxidation, sulfur dioxide was passed through until the solution became clear. After the product had then been extracted with ether, the ether was evaporated off and the residue esterified in a mixture of benzene and ethanol by the azeotropic method. The distillates (bp 104—110°C/18 mmHg) were identified as the ethyl esters of succinic, methylsuccinic, and α, α'-dimethylsuccinic acid by vapor-phase chromatography.

Resolution of Trimethylcyclododecatriene. 0.90 g of sodium borohydride was dissolved in 25 m*l* of the diethylene glycol dimethylester (diglyme) and then admixed with 9.8 g of α-pinene $[\alpha]_D^{20}=+43.8°$.

A solution of boron trifluoride-etherate (3.9 g in 5 m*l* of diglyme) was added, drop by drop, over a 15 min period at 0—5°C, after which the mixture was stirred for 4 hr. Furthermore, 4.2 g of trimethylcyclododecatriene were added, drop by drop, over a 15 min period, after which the reaction mixture was subjected to the reaction for 4 hr while being stirred under cooling with ice. One milliliter of water was added to decompose the residual hydride. The reaction mixture was then separated into two layers; the lower layer involved diglyme and water, while the upper layer contained organo-borane, coming from trimethylcyclododecatriene, and unreacted trimethylcyclododecatriene. The upper layer was treated with 30 m*l* of a 3 N sodium hydroxide solution and 30 m*l* of 30% hydrogen peroxide at room temperature and with stirring for one hour. The vacuum distillation of the reaction product yielded 7.2 g of the fraction of 80—100°C/2 mmHg, together with a solid residue. The former fraction contained trimethylcyclododecatriene (optically active), isopinocampheol, and a trace of α-pinene; the latter solid was a mixture of hydroxylated trimethylcyclododecatriene, a solid residue, and a trace of isopinocampheol. They were further fractionated by fractional vapor-phase

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[3] H. C. Brown, N. R. Ayyangar, G. Zweifel and T. Munekata, *J. Am. Chem. Soc.*, **86**, 397, 1071, 1076 (1964).

chromatography. Their optical rotations were as follows: *ttt*-trimethylcyclododecatriene, $[\alpha]_D^{20}=-8.0°$, *ttc*-trimethylcyclododecatriene, $[\alpha]_D^{20}=-15.7°$, isopinocampheol, $[\alpha]_D^{20}=-28.3°$ (literature[3] $-32.4°$), and hydroxylated trimethylcyclododecatriene, $[\alpha]_D^{20}=-11.4°$.

Asymmetric Synthesis of Optically Active Trimethylcyclododecatriene. Optically active trimethylcyclododecatriene was synthesized in a manner similar to that adopted for the optically inactive one, except for the use of an asymmetric titanium alkoxide catalyst, which was prepared in a way to be described later. In order to remove the menthol, 5 m*l* of the product oligomer was treated with 1.5 m*l* of triethylaluminum and 1.5 m*l* of phenyl isocyanate. In the oligomer thus treated, no trace of menthol was found by vapor-phase chromatography or by IR.

Preparation of Titanium Tetraamyloxide. One mol of titanium tetrachloride, purified by refluxing it in the presence of copper powder under nitrogen, was reacted with 5 mol of purified amylalcohol ($[\alpha]_D^{15}=-4.9°$) in *n*-hexane solution at room temperature for 4 hr under dehydrated ammonia vapor. The reaction product was then filtered and subjected to distillation; boiling point 150—152°C/1 mmHg (literature 154°C/0.5 mmHg[4]). The vapor-phase chromatography of the decomposition product obtained with methanol-water showed the presence of tetraamylalcoxide.

Preparation of Titanium Tetramenthoxide. Titanium tetramenthoxide (white powder, melting point over 200°C) was prepared from titanium tetrachloride and menthol ($[\alpha]_D^{15}=-48°$) by the same method.

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4) D. C. Bradley, R. C. Mehrotra and W. Wardlew, *J. Chem. Soc.*, **1952**, 2027.