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SYNTHESIS, ABSOLUTE CONFIGURATION, OPTICAL PURITY AND SPECTRAL PROPERTIES OF OPTICALLY ACTIVE 3-METHYLCYCLOBUTENE

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Abstract—(+)-3-methylcyclobutene has been prepared from methylenecyclobutane and its absolute configuration and minimum optical purity have been determined. The UV and CD spectra of the cycloalkene are discussed and its optical activity compared with other cyclo-olefins.

Recent investigations on ORD and CD of chiral olefins[1-4] referred almost exclusively to steroidal olefins and *trans*-cycloalkenes. The Cotton effect sign associated with the principal $\pi \rightarrow \pi^*$ transition of these molecules has been related to stereochemistry.[1, 2]

We have begun a CD study of very simple aliphatic or alicyclic unsaturated molecules, whose conformational equilibrium allows a restricted number of low energy conformations. In a previous paper[5] we examined the influence of geometrical isomerism on the CD of aliphatic olefins having a 1,2-disubstituted double bond near an asymmetric C atom.

At present we are interested in small and medium ring 3-alkyl substituted cyclo-olefins, in order to obtain information on the effect of ring size on the magnitude and position of the Cotton effect near 200 mμ.

In this paper the synthesis of a simple optically active cycloalkene, (+)-3-methylcyclobutene,* and the determination of its absolute configuration and minimum optical purity are reported. Moreover, the UV and CD spectra of this cycloalkene are discussed and compared with other cyclo-olefins.

RESULTS AND DISCUSSION

The first approach to optically active 3-methylcyclobutene (I) was by the reaction between (−)-diisopinocampheylborane and excess (*R*)(*S*)-3-methylcyclobutene obtained by irradiation of a mixture of *cis*- and *trans*-1,3-pentadiene[7] (Chart 1). The olefin had α_D^{18} ($l = 1$) + 0·22°. Since this compound, as subsequently confirmed, had a very low optical purity, the preparation of optically active I was accomplished by a different route (Chart 1).

According to Brown *et al.*,[8] hydroboration of 1-methylcyclobutene (III), prepared

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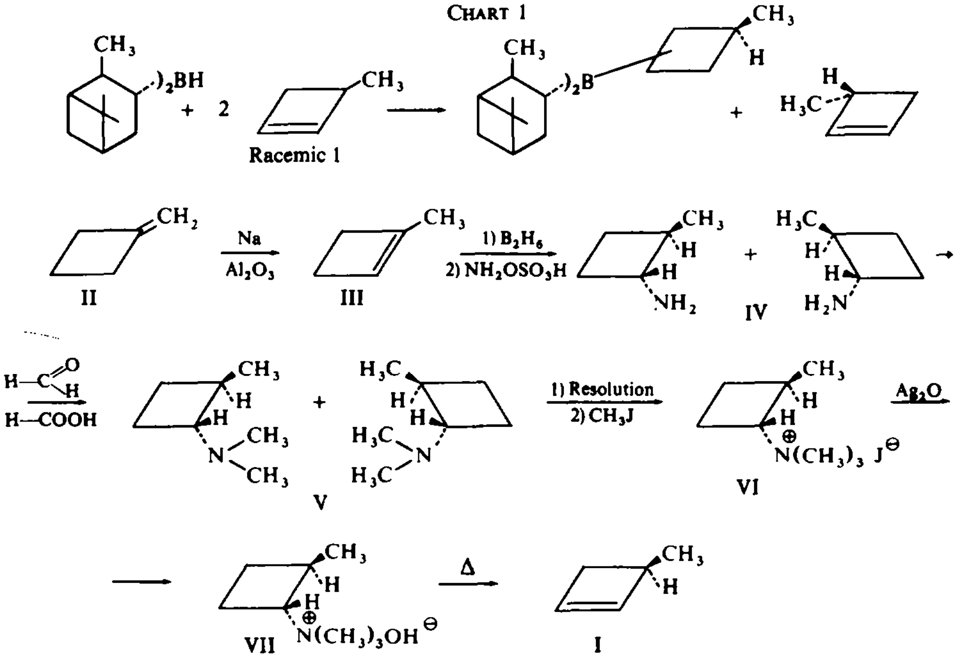
* See 6 for preliminary communication.

from methylenecyclobutane, and successive amination with hydroxylamine-O-sulfonic acid, gave stereoselectively *trans*-2-methyl-cyclobutylamine (IV; 43 % yield).*

The structure of IV was confirmed by NMR. The spectrum at 100 Mc shows a neat doublets at 1·00 ppm due to the Me group. This doublet is split in diastereoisomeric mixtures.[12] The low chemical shift of the methynic proton near the Me group (δ 2·05 ppm) was attributed to the $—NH_2$ in *cis* position.

As found in corresponding larger ring racemic homologs,[13] optically active 3-methylcyclobutene was formed in the Hofmann elimination of optically active *trans*-N,N,N-trimethyl-N-2-methylcyclobutyl-ammonium hydroxide (VII). This compound was obtained from the *trans*-amine (IV) via the corresponding N,N-dimethyl derivative (V), resolving V using (+)-tartaric acid and converting (−)V to the quaternary ammonium iodide (VI). Decomposition of the quaternary ammonium hydroxide (VII) at 125–135° afforded optically active I free from 1-methylcyclobutene. The only competing reaction appeared to be ring-opening leading to *trans*-1,3-pentadiene. This side reaction was reduced by operating at 115–120°, the yield of the diene dropping to less than 10%.

CHART 1



The NMR spectrum of (+)-I ($[\alpha]_D^{18}$ +116·24) shows, as reported in the literature,[14]

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* In addition to IV, this reaction produced other isomeric compounds (b.p. 82–86°), the amounts depending principally on the reaction temperature. The NMR spectrum of the reaction mixture showed a signal at 5·15 ppm due to olefinic protons. In addition to a band at 1605 cm^{-1} ($—NH_2$), a broader and less intense band, between 1620 and 1640 cm^{-1} was observed in the IR spectrum. Therefore, we believe that tris-(2-methylcyclobutyl)-borane, by analogy of cyclopropylmethyllithium,[9] cyclobutylmethyl organometallic compounds of sodium, lithium and magnesium[10] and diethylcyclopropylmethyl-borane,[11] can rearrange to isomeric acyclic compounds, probably through the intermediate tris-(cyclobutylmethyl)-borane.

a group of lines at 6·0 ppm (vinylic protons), a complex of lines between 1·9 and 2·9 ppm (allylic protons) and a doublet at 1·14 ppm (methylic protons).

Absolute configuration and minimum optical purity of (+)-I

An indication on the absolute configuration of (+)-3-methylcyclobutene (I) was obtained on the basis of the partial resolution of (*R*)(*S*)-3-methylcyclobutene by asymmetric hydroboration with (−)diisopinocamphenylborane.[15] Using Brown's original model[15] and according to that proposed by Varma and Caspi,[16] it was possible to predict the *R* configuration for (+)-3-methylcyclobutene (I) (Chart 1).

Confirmation of this was obtained from the asymmetric amination of 1-methylcyclobutene (III) with (−)diisopinocampheylborane and successively with hydroxylamine-O-sulfonic acid[5] (Chart 2). The optically active *trans*-2-methylcyclobutylamine

CHART 2

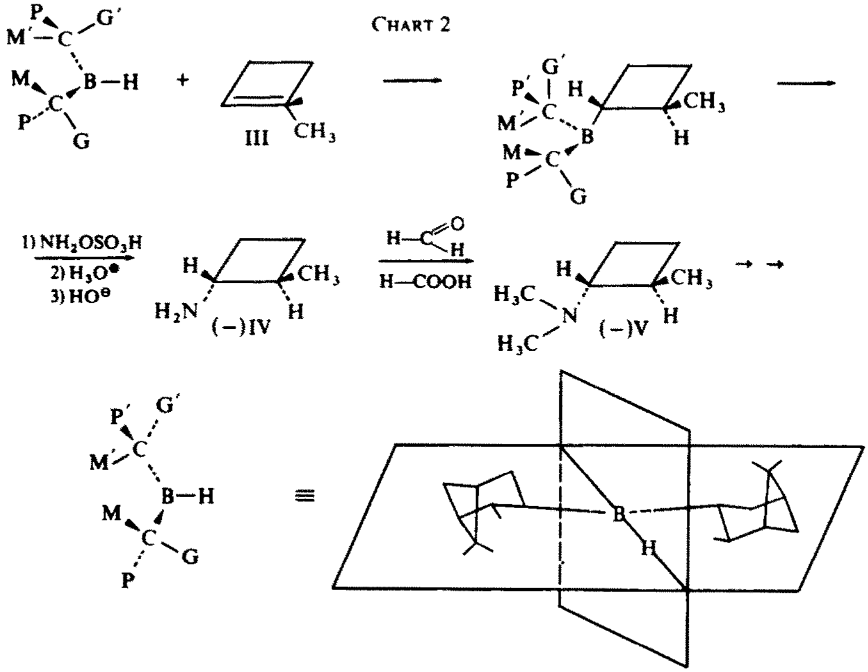
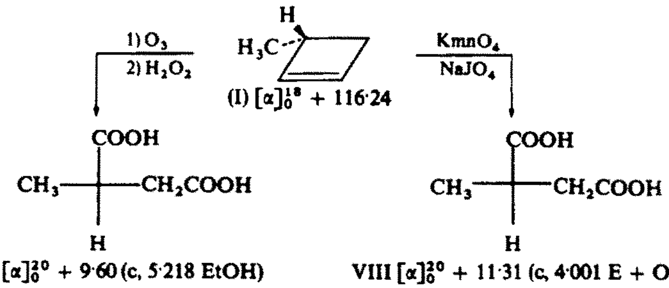


CHART 3



(IV) (α_D^{25} (l = 0·5)−0·60°), was then converted to the corresponding N,N-dimethyl derivative V [α_D^{25} (l = 1)−1·24°].

Inspection of models (Chart 2) indicates that 1-methylcyclobutene (III) could gain access to the (−)-reagent preferably along plane X and form a 4-membered transition state as indicated in Chart 2. On this basis it was possible to attribute the (1*R*:2*R*)-configuration to (−)-IV and (−)-V. Moreover, the *R* configuration was also attributed to (+)-3-methylcyclobutene (I) obtained from (−)-*trans*-N,N-dimethyl-2-methylcyclobutylamine (V).

The relationship between sign of the rotatory power and absolute configuration of (+)-I was determined by ozonization of (+)-I ($[\alpha]_D^{18}$ + 116·24) to (+)-methylsuccinic acid (VIII) [$[\alpha]_D^{20}$ + 9·60 (*c*, 5·219 EtOH)] (Chart 3).

As the relationship between sign of the rotatory power and absolute configuration is known for VIII,[17] (+)-3-methylcyclobutene has the *R*-configuration, as predicted by the asymmetric hydroboration reactions (Chart 1, 2).

The relationship between minimum optical purity and $[\alpha]_D$ of (+)-I could be established by attributing to (+)-I the same optical purity as (*R*)-methylsuccinic acid (VIII) from which it was obtained. In fact, recently the maximum value of the rotatory power of VIII has been established.[18]*

Nevertheless, since the ozonization of (+)-I to VIII can take place with considerable racemization, (+)-I [$[\alpha]_D^{18}$ + 116·24 (neat)] was converted to VIII [$[\alpha]_D^{20}$ + 11·31 (*c*, 4·001 EtOH)] (66·2% optical purity) by von Rudloff oxidant[19] (Chart 3). As in many cases this oxidation occurs with little racemization,[20] a 66·2% minimum optical purity was attributed to (*R*)-I [$[\alpha]_D^{18}$ + 116·24].

Spectral properties

The UV spectrum of I, in the vapour phase at room temperature, shows the beginning of a strong and broad absorption band at about 189 mμ; and, three shoulders of lower intensity at about 192, 195 and 208 mμ respectively were observed. The spectrum of I, in n-heptane solution, shows two shoulders at about 192 mμ (log ε 3·73) and 195 mμ (log ε 3·58) respectively.

These results are in accord with what has been observed in the UV spectrum of cyclobutene.[21] Worthy of mention is the fact that 4-methyl-*cis*-2-pentene, comparable to 3-methylcyclobutene as to number of C atoms and distribution with respect to the

TABLE 1. SPECTRAL PROPERTIES OF (*R*)-3-METHYLCYCLOBUTENE

$[\phi]_D^{18}$	Circular dichroism[a]			
	λ (mμ)	Δε[b]	[θ] × 10^{-3c}	Predicted Cotton effect
+120 (neat)	191	−6·84	−22·5	Negative
	193[d]	−5·00	−16·5	

[a] At 27° (*c*, 0·735 g/l; n-heptane).

[b] Values calculated for a 66% optical purity.

[c] Molecular ellipticity, calculated as [θ] = 3300 × Δε.

[d] Shoulder.

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* It is to be noted that this value [$[\alpha]_D^{20}$ + 17·09 (*c*, 4·421 EtOH)] refers to the optically pure (*S*)-2-methyl-1-butanol [$[\alpha]_D^{25}$ − 5·82].[18]

double bond, shows in the vapour phase two steps-out at 192 and 197 mμ respectively.[22]

The CD of (*R*)-3-methylcyclobutene, in n-heptane solution, resulted in a curve with a negative maximum of strong intensity at 191 mμ and a shoulder at 193 mμ (Table 1).

The wavelength of the CD maximum corresponds almost exactly to that of a shoulder observed in the UV spectrum of I. On this basis and from a comparison of the CD and UV data with those of some olefins and *trans*-cyclo-octene (which, as recently reported,[1] should not be treated as a special case for spectroscopic calculations), it is possible to assign the absorption at 191 mμ to a $\pi_x \rightarrow \pi_x^*$ transition.[23,24,*]

The sign of the Cotton effect of I corresponds to that predicted on the basis of the octant diagrams developed for steroidal olefins and *trans*-cycloalkenes.[2]

In the light of this, a negative Cotton effect could be anticipated for (*R*)-3-methylcyclopentene supposing that the Cotton effect is due mainly to the position of the Me group in the octants and only secondarily to deformation of the ring system. Indeed, this compound presented a strong negative Cotton effect at 188 mμ.[25,†]

The CD maximum of (*R*)-I appears at shorter wavelengths than that of many other chiral six-membered cyclo-olefins.[2,26] This fact, probably related to the considerable strain in I, is in agreement with the difference observed between the UV spectrum of cyclobutene[21] and that cyclohexene:[27] the spectrum of cyclobutene is weaker and shifted to shorter wavelengths.

Finally, from the above results, it is possible to conclude that the Octant Rule[2] is useful to relate the chirality of 3-methyl substituted 4 or 5-membered cycloalkenes to their $\pi_x \rightarrow \pi_x^*$ CD maxima.

EXPERIMENTAL

All m.ps and b.ps are uncorrected. Rotatory powers were taken on a Schmidt-Haensch polarimeter. IR spectra were obtained using a Perkin–Elmer 225 spectrophotometer. NMR spectra were measured with a Varian Model HA-100 spectrometer. UV spectra were measured with a Cary Model 14 spectrophotometer. CD curves were obtained with a Jouan-Roussel CD 185 dichrograph. GC was obtained using a Perkin–Elmer gas-chromatograph Model 810. Analyses were carried out by Dr. A. Bernhardt, Mulheim, Germany. Photolises were conducted with a Hanau 30 watt low pressure mercury arc used without filters.

(R)(S)-3-*Methylcyclobutene*. Irradiation of a mixture of *trans*- and *cis*-1,3-pentadiene in cyclohexane gave rise to (*R*)(*S*)-3-methylcyclobutene,[7] b.p. 27–28°, n_D^{20} 1·3968 (lit.[7] b.p. 29·9°).

Asymmetric hydroboration of (R)(S)-3-*methylcyclobutene*. To a suspension of (−)-diidopinocampheylborane (0·031 mole; prepared from (+)-α-pinene, $[\alpha]_D^{25}$ + 40·0) in diglyme at −15°, was added racemic 3-methylcyclobutene (4·21 g, 0·062 mole). The reaction mixture was stirred for 4 hr at 0°. Water (1 ml) was added to decompose any residual hydride. The unreacted olefin was recovered from the reaction mixture by distillation at 0–10° at reduced press (20 mm). The olefin was collected in a cold trap (−78°) and dried. Fractional distillation afforded (+)-3-methyl-cyclobutene (1·9 g, 44% yield) b.p. 27–28°, α_D^{18} (l = 1) + 0·22° (neat).

1-*Methylcyclobutene* (III). Base-catalyzed isomerization of II[28] gave rise to III, b.p. 38°, n_D^{20} 1·4089 (lit.[29] b.p. 750 mm 37·1°, n_D^{18} 1·4088).

Racemic trans-2-*methylcyclobutylamine* (IV). A soln of $NaBH_4$ (4·2 g, 0·11 mole) in diglyme (35 ml) was added to a soln of III (18·7 g, 0·27 mole) in diglyme (10 ml). This mixture was treated dropwise during 2 hr at 0° with $BF_3 \cdot Et_2O$ (19·1 ml) and after 4 hr at room temp with a soln of hydroxylamine-O-sulfonic

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[*] Considering 3-methylcyclobutene as a disubstituted ethylene, it is possible to define as "z" the C—C sigma axis, "y" in the plane of the C—H bonds perpendicular to "z" and the "x" axis perpendicular to the "yz" plane passing through the centre of the double bond.

[†] On the basis of the regional chirality rule,[26] it is also possible to predict a negative Cotton effect for (*R*)-3-methylcyclopentene.

acid (35·0 g, 0·30 mole) in diglyme (135 ml). After cooling, the mixture was treated with conc HCl (100 ml) and water (2 l) and extracted with ether. The acid soln was made alkaline with NaOH aq and continuously extracted with ether. The Et_2O extract was dried and distilled to give IV (10·0 g, 42·9% yield), b.p. 95–95°, n_D^{25} 1·4290. (Found: C, 70·71; H, 13·05; N, 16·25. $C_5H_{11}N$ requires: C, 70·53; H, 13·02; N, 16·45%).

Racemic and optically active trans-N,N-*dimethyl-2-methylcyclobutylamine* (V). Amine IV (8·67 g, 0·1 mole) was added dropwise to a 99% soln of formic acid (23·45 g, 0·5 mole). To the resulting mixture a 40% soln of formaldehyde (20·7 ml) was added and the reaction flask heated on a water bath until vigorous evolution of gas started. The flask was removed to allow the reaction to subside (30 min) and then heated again at 95° for 8 hr. Dilute HCl (50 ml) was added to the product and the soln evaporated to dryness at 25 mm. The crystalline residue was dissolved in water and the amine liberated by the addition of NaOH aq and then extracted with ether. After removing the solvent, the residue was distilled to give V (7·95 g, 94% yield), b.p. 114–115°, n_D^{25} 1·4215. (Found: C, 74·26; H, 13·12; N, 12·20. $C_7H_{15}N$ requires: C, 74·27; H, 13·26; N, 12·37%).

The amine V (12·3 g, 0·108 mole) and (+)-tartaric acid (14·5 g, 0·12 mole) in EtOH (50 ml) gave 20 g of a salt, which was crystallized 6 times from EtOH–n-pentane to give 10 g of (−)-V (+)tartrate, m.p. 69°, $[\alpha]_D^{25}$ −2·45 (*c*, 1·63 water); the base obtained from this salt had α_D^{25} (l = 1) −38·76° (neat).

Evaporation of the combined mother liquors from the initial mixture and from the first recrystallization gave 10·5 g of (+)-V (+)-tartrate; the amine obtained from this salt (4·1 g) had α_D^{25} (l = 1) + 18·80° (neat).

trans-N,N,N-*Trimethyl*-N-2-*methylcyclobutylammonium iodide* (VI). Methyl iodide (18·0 g, 0·11 mole) was added dropwise to a soln of V (7·95 g, 0·07 mole) in ether (20 ml). The mixture was evaporated at 0·5 mm and 40° to give VI (17·8 g, 100% yield), m.p. 230–232. (Found: N, 5·14. $C_8H_{18}NJ$ requires: N, 5·49%).

Racemic and optically active 3-*methylcyclobutene* (I). Compound VI (15·9 g, 0·061 mole) was added to a slurry of Ag_2O in water [prepared from $AgNO_3$ (68 g), water (1160 ml) and NaOH (16 g)]. The mixture was stirred at 20° for 6 hr and filtered. The filtrate was concentrated at 35–40° at 20 mm Hg and the residue was transferred to a round-bottomed flask connected to a series of two traps, the first cooled with Dry Ice–acetone and the second with liquid air. The temp w as raised gradually to 115° at which point slow decomposition of VII takes place.

The liquid condensed in the traps was washed several times with cold 5% HCl, then ice-cold water and finally dried on molecular sieves. Distillation of the product gave I (2·44 g, 60% yield), b.p. 28°, n_D^{20} 1·3968.

The IR spectrum agrees well with that reported for an authentic sample of (*R*)(*S*)-3-methylcyclobutene.[30] GC showed only one peak.

Compound VI (17·9 g, 0·11 mole), obtained from (−)-V gave in the same manner (+)-I (2·90 g, 64% yield), b.p. 28°, n_D^{20} 1·3967, $[\alpha]_D^{18}$ +116·24 (neat).

Similarly (+)-V afforded (−)-I, $[\alpha]_D^{18}$ 56·24 (neat).

Oxidation of (+)-3-*methylcyclobutene*: (R)-*methylsuccinic acid* (VIII)

(a) Compound (+)-I [$[\alpha]_D^{18}$ +116·24 (neat)] (0·68 g, 0·01 mole), dissolved in $CH_2C\!-_2$ (20 ml) was cooled to −80° and treated with a stream of O_3 until the soln was faintly blue. The solvent was evaporated under reduced press and the residue in 3% H_2O_2 (50 ml) was heated until a reaction began and again for 30 min after it had ceased. The mixture was evaporated under reduced press and the residual solid (0·34 g, 26% yield) was crystallized from benzene–n-heptane, m.p. 106–108°, $[\alpha]_D^{20}$ +9·60 (*c*, 5·218 EtOH).

(b) Compound I [$[\alpha]_D^{18}$ +116·24] (0·68 g, 0·01 mole) was oxidized with $KMnO_4/NaIO_4$ as described for racemic I.[14] The resulting acid VIII (0·50 g, 38% yield) had m.p. 107–108°, $[\alpha]_D^{20}$ +11·31 (*c*, 4·001 EtOH) (lit.[31] m.p. 115°, $[\alpha]_D^{20}$ +16·59 (*c*, 4·136 EtOH).

Asymmetric hydroboration of III. To a suspension of (−)-diisopinocampheylborane (0·204 mole) in diglyme at 0° was added dropwise compound III (13·85 g, 0·203 mole). The mixture was stirred for 4 hr at 0° and 12 hr at room temp. Hydroxylamine-O-sulfonic zcid (71·07 g) in diglyme (286 ml) was added and the soln heated to 60° for 3 hr. The soln was cooled and worked up as described for the preparation of IV. The Et_2O extract was distilled to give (−)-*trans*- IV (2·1 g, 11·8% yield), b.p. 95°, n_D^{25} 1·4288, α_D^{25} (l = 0·5)–0·6° (neat). (−)-IV was then converted in the corresponding N,N-dimethyl-derivative (−)-V, b.p. 114–115, n_D^{25} 1·4216, α_D^{25} (l = 1)–1·24° (neat).

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