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STERIC INHIBITION OF π-ELECTRON DELOCALIZATION IN 1,3-DIENES

CIRCULAR DICHROISM OF METHYLISOPULEGENE AND 3,8-*p*-MENTHADIENE[1]

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Abstract—The conjugated diene, "methylisopulegene" (**1**, 1-isopropenyl-2,4-dimethyl-1-cyclohexene), exhibits a CD Cotton effect (CE) with $\Delta\varepsilon_{217} = +1.77$ but no UV maximum down to 200 nm; whereas, the structurally related conjugated diene, 3,-8-*p*-menthadiene (**2**, 1-isopropenyl-4-methyl-1-cyclohexene), exhibits a more normal UV maximum at 232 nm ($\varepsilon = 17{,}300$) and a CE with $\Delta\varepsilon_{240} = +2.56$.

One of the more interesting spectroscopic properties of the 1,3-diene "methylisopulegene", first prepared by Grignard[2] nearly eighty years ago as the predominant (95 %) component of "methylpulegene", is its reported failure to show an absorption maximum above 210 nm in the UV spectrum.[3,4] The structure of "methylpulegene" was a subject of early controversy,[5] and its anomalous UV served to call into question the structural assignment(s)[5,6] in favor of a deconjugated diene.[3] However, Wolinsky and Chan[4] subsequently confirmed **1** as the structure of "methylisopulegene" using ozonolysis data and ^{1}H-NMR, and proposed that the anomalous UV spectrum could be explained by an inability of the component double bonds of the diene to achieve coplanarity, i.e. the diene has a large skew angle (50–90°), due to steric repulsions between the C-11 Me group and the C-8 CH_2 and C-9 CH_3 groups. They concluded that "π-orbital overlap and delocalization of electrons in the excited state is therefore prohibited."[4] Because "methylisopulegene" is optically active, it offers an excellent prospect for CD spectroscopy as a means of investigating the anomalous electronic transition. CD spectroscopy is often able to detect and resolve weak or otherwise masked UV absorbances. We therefore re-investigated methylisopulegene (**1**) and its des-Me analog, 3,8-*p*-menthadiene (**2**).[7]

Synthesis and stereochemistry

The starting material for the syntheses of **1** and **2** was (+)-pulegone, $[\alpha]_D^{20} + 22$ (neat). Methylisopulegene was prepared as previously described[4] by reaction of (+)-pulegone with methylmagnesium iodide in ether followed by acid-catalyzed dehydration. 3,8-*p*-menthadiene was prepared from the same bottle of (+)-pulegone as described[7] by reaction of its Z-tosylhydrazone with MeLi. Both dienes were purified to >99 % purity by gas chromatography on a

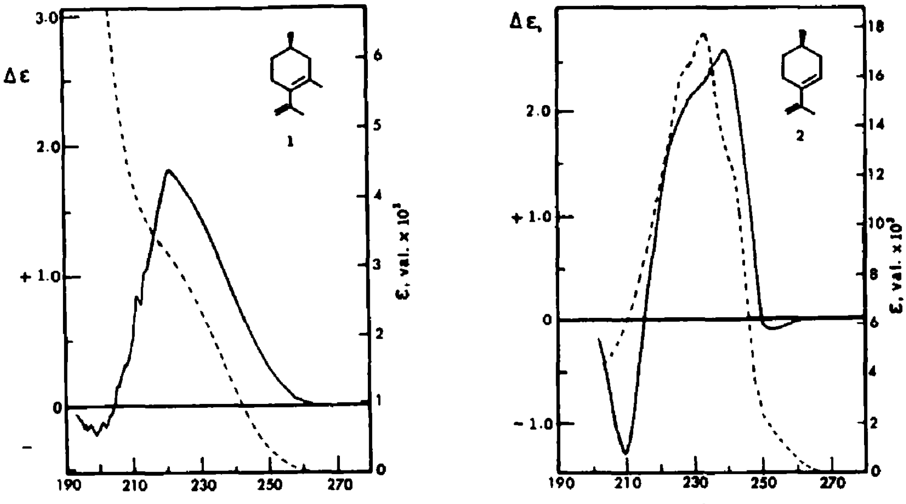
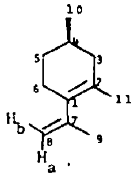
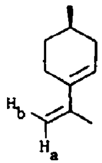


Fig. 1. CD (————) and UV (-----) spectral data for "methylisopulegene" (**1**) (left) and 3,8-*p*-menthadiene (**2**) in n-heptane in a 1.00 cm pathlength cell with concentrations *ca* 2 mg/100 mL.

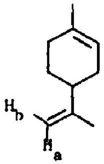
Table 1. ^{13}C and ^{1}H NMR Chemical Shifts and Assignments[a]



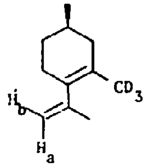
1



2



limonene



	1		2		limonene			
	^{13}C	^{1}H	^{13}C	^{1}H	^{13}C[b]	^{1}H	^{13}C	^{1}H
1	125.7(s)[c]	-	136.3(s)	-	41.2(d)	1.28(br.s)	125.6(s)[c]	-
2	133.7(s)[c]	-	124.4(d)	5.85	30.9(t)[c]	1.99(br.s)	133.8(s)[c]	-
3	40.2(t)	2.02(br)	34.6(t)	2.30(br.s)	120.7(d)	5.39(br)	40.1(t)	2.02(br)
4	29.1(d)	1.2(br.m)[d]	28.4(d)	1.28(br.m)[d]	133.5(s)	-	29.5(d)	1.2(br.m)
5	31.5(t)	[e]	31.4(t)	1.73(br.s)	30.7(t)[c]	1.99(br.s)	31.5(t)	1.67
6	29.6(t)	2.02(br.s)	25.7(t)	2.30(br.s)	28.0(t)	[f]	29.1(t)	2.02(br)
7	147.2(s)	-	143.5(s)	-	149.9(s)	-	147.2(s)	-
8	112.0(t)	a 4.87(br.m)[g] b 4.58(br.m)[g]	109.6(t)	a 4.92(br.m) b 4.89(br.m)	108.4(t)	a 4.703[c] b 4.698[c]	112.1(t)	a 4.86(br.m b 4.59(br.m
9	22.2(q)	1.75(s)	20.2(q)	1.84(s)	20.7(q)	1.64(s)[h]	22.1(q)	1.75(dd)[i]
10	21.8(q)	0.94(d,5.6Hz)	21.8(q)	0.94(5.9Hz)	23.4(q)	1.72(s)[h]	21.8(q)	0.94(d, 4.9Hz)
11	20.2(q)	1.61(s)	-	-	-	-	- (CD$_3$)	-

[a] Chemical shifts in δ ppm from tetramethylsilane measured in CDCl$_3$ on a JEOL FX-100 nmr spectrometer; splitting: s=singlet, d=doublet, t=triplet, q=quarter, m=multiplet, br=broad.

[b] Assignments from spectrum 400 in L.F. Johnson and W.C. Jankowski, "Carbon-13 NMR Spectra", J. Wiley, New York 1972.

[c] Suggested assignments but may be reversed.

[d] When this signal is irradiated, the ^{13}C-4 signal becomes a singlet.

[e] Buried under the 1.75 δ CH$_3$ signal.

[f] Buried under the 1.64, 1.72 and 1.99 δ signals.

[g] When the allylic hydrogens are irradiated, this signal becomes d, J=3 Hz.

[h] The CH$_3$(s) signal of 1-methylcyclohexene appear at 1.65 δ; the CH$_3$(s) signal of 2-methyl-1-pentene appears at 1.73 δ: C.J. Pouchert and R.J. Campbell, "The Aldrich Library of NMR Spectra", Aldrich Chemical Co., Milwaukee, 1974, spectra nos. 1,39C and 1,238 respectively.

[i] J= 1.0, 1.5 Hz.

6 ft × 3/8 in. diam. aluminum column of 3 % Apiezon L on Chromosorb W, AW-DMCS. Since the dienes are prepared from the same (+)-pulegone, they consequently have the same absolute configuration (4*R*) and, presumably, the same enantiomeric excess.

RESULTS AND DISCUSSION

The CD and UV data for **1** and **2** are presented in the Fig, in which it can be clearly seen that **1** exhibits a moderately intense CD CE, with reduced rotatory strength $[R]_{217} = +5.58$ but only a slight inflection in the UV at 217 nm. Thus, there is indeed an electronic transition for **1** in the vicinity of 220 nm, but one considerably weaker in intensity ($\varepsilon_{217}^{\text{infl}} = 3300$) than that expected for a 1,3-diene of its structure (the Woodward–Fieser Rules[8] predict a maximum at 234 nm for **1**). These data may be contrasted with those found for the des-Me diene (**2**): a UV maximum at 232 nm with $\varepsilon = 17{,}300$ and a CD CE with $[R]_{240} = +6.13$. A shorter wavelength electronic transition is also observed in the CD of **2** with $[R]_{210} = -1.5$. The origin of that transition is not entirely clear but may be of the σ-π^* type, as has been concluded for other 1,3-dienes.[9]

The near identity of the [R] values associated with the intense long wavelength transitions suggests that the largest contributions to the CD CE emanate from similarly juxtaposed extrachromophoric perturbers as opposed to contributions mainly from an inherently chiral diene chromophore.[9,10] The relative unimportance of a possibly skewed diene for the CD CE follows from the deduction, based on the π-π^* λ_{max} differences, that the diene chromophore of **1** is significantly more skewed than that of **2**; yet, the [R] values are closely similar. As has been suggested earlier,[4] and is clear from space-filled molecular models,[11] diene **1** is sterically crowded in such a way as to restrain the C=C units from approaching near co-planarity. Certainly, the addition of a methyl group to C-2 of **2** is the important steric restraint found in **1**. Steric inhibition to effective conjugation has been observed in other diene systems[12] where steric inhibition of diene co-planarity results in hypsochromically shifted, less strongly allowed electronic transitions.[13,14]

Further evidence for ineffective conjugation of the diene of **1** may be found in its NMR spectra (Table 1), which also confirm its structure assignment. Comparison of the ^{13}C-7 chemical shifts of **1**, **2** and limonene finds the resonance of **1** appearing between those of conjugated diene **2** and the deconjugated diene limonene (even after correcting for the expected influence of the added C-2 Me group on ^{13}C-7), i.e. **1** is not as effectively conjugated as is **2**. The varying relative chemical shifts for the other olefinic carbons of **1** and **2** are less easily interpreted in connection with conjugation because the observed changes also reflect sensitivity toward Me substitution at C-2 as well as spatial orientation effects. Comparison of the ^{1}H-NMR spectra of **1**, **2** and limonene also lead to the conclusion that the diene of **1** is severely skewed: the more shielded H_b signal of the $=CH_2$ group of **2** moves even farther upfield ($4.89\,\delta$ to $4.58\,\delta$) in **1** reflecting its further entry into the shielding cone of the endocyclic C=C. Similarly, the isopropenyl Me signal at $1.84\,\delta$ in **2** is shielded and moves to $1.75\,\delta$ in **1**. These two observations are consistent with the isopropenyl group being twisted about the C_1–C_7 bond from near co-planarity in **2** to substantially skewed in **1**.

In conclusion, the evidence points to a sterically induced, severely twisted and consequently deconjugated chromophore in **1**, yet one still capable of exhibiting an hypsochromically-shifted, hypochromic long wavelength electronic transition as seen in the CD spectra. Nevertheless, even the now obvious steric inhibition arguments ascribed to the Me group at C-2 do not always carry over to apparently similar situations. For, as has been observed earlier,[15] 1-isopropenyl-2,3-dimethyl-1-cyclopentene exhibits a UV spectrum ($\varepsilon_{243}^{\text{max}} = 9850$, $\varepsilon_{237}^{\text{max}} = 10{,}130$)[15] more like **2** than **1**.[16]

EXPERIMENTAL

CD spectra were recorded on a JASCO J-40 instrument equipped with a photoelastic modulator, UV spectra were recorded on a Cary 219 spectrophotometer, and sodium D-line rotations were determined on a Perkin–Elmer model 141 polarimeter. NMR spectra were determined on a JEOL FX-100 instrument at 100 MHz (^{1}H) and 25 MHz (^{13}C), and infrared spectra were recorded on a Perkin–Elmer 599 spectrophotometer. Analytical gas chromatography was performed on a Varian 2400 instrument on a 6 ft × 1/8 in. diam. column packed with 5 % SE-30 on Chromosorb W, AW-DMCS. Preparative gas chromatography was performed on a Varian-Aerograph 1700 instrument using a 6 ft × 3/8 in. diam. column packed with 3 % Apiezon L or 5 % SE-30 on Chromosorb W, AW-DMCS. Spectral data were obtained using spectral grade solvents (Matheson). (+)-Pulegone was from Aldrich.

"*Methylisopulegene*", (4R)-1-*isopropenyl*-2,4-*dimethyl*-1-*cyclohexene* (**1**).[4] This diene was prepared according to the procedure of Wolinsky and Chan[4] from (+)-pulegone, $[\alpha]_D^{20} = +22°$ (neat) by reaction with MeMgI followed by acid-catalyzed dehydration. It was isolated from the olefin-containing distillation fraction ("methylpulegene") by preparative gas chromatography to >99 % purity. It had $\varepsilon_{217}^{\text{infl}} = 3300$, $\Delta\varepsilon_{217} = +1.77$ and $[R] = +5.58$ in n-heptane (Figure), and ir (film): 1635 cm^{-1}. The ^{1}H and ^{13}C-NMR are found in the Table.

Trideuteriomethylisopulegene, (4R)-1-*isopropenyl*-2-*methyl*-4-*trideuteriomethyl*-1-*cyclohexene*. This diene was prepared and isolated as above starting with (+)-pulegone from the same bottle and CD_3MgI. It had $\varepsilon_{217}^{\text{infl}} = 3700$, $\Delta\varepsilon_{222} = +1.75$ and $[R] = +5.79$ in n-heptane; ^{1}H and ^{13}C-NMR are found in the Table.

3,8-p-*Menthadiene*, (4R)-1-*isopropenyl*-4-*methyl*-1-*cyclohexene* (**2**). This diene was prepared from (+)-pulegone (from the same bottle as above) via its Z-p-toluenesulfonylhydrazone by reaction with MeLi (Alfa) as described by Dauben *et al.*[7] It was purified to >99 % purity by preparative gas chromatography and had $\varepsilon_{232}^{\text{max}} = 17{,}300$, $\Delta\varepsilon_{240} = +2.56$ and $[R] = +6.13$ in n-heptane (Fig. 1), and ir (film): 1610, 1635 cm^{-1}. Its ^{1}H and ^{13}C-NMR are found in the Table.

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[14] The CD and UV data for the trideuteriomethyl analog of **1**, prepared by reaction of (+)-pulegone with CD_3MgI, are closely similar to those of **1**, as expected. Yet, there are small differences $\{[R]_{222} = +5.79$ vs $[R]_{217} = +5.58$ for **1**, and $\varepsilon_{217}^{\text{infl}} = 3700$ vs $\varepsilon_{217}^{\text{infl}} = 3300$ in **1**$\}$ which suggest that the trideuteriomethyl analog may have a slightly smaller diene skew angle, i.e. be better conjugated, than **1** because of the relatively smaller steric size of CD_3 *vs* Me at C-2.

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[16] Additional data supporting differences in conjugation may be found in the C=C stretching region in the IR: ν (film) = 1635 cm^{-1} for **1**, 1610, 1635 cm^{-1} for **2**, 1650 cm^{-1} for limonene and 1618 cm^{-1} (Ref. 15) for this diene.