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STERIC EFFECTS IN SUBSTITUTED FIVE-MEMBERED RINGS. III[1].

cis- and trans-3-METHYLCYCLOPENTANOL

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It is known[2] that the configuration of the stereomeric 1,3-dimethylcyclopentanes as originally assigned had to be reversed and that they did not conform to the Auwers-Skita rule[3a]. The cis-isomer was found to have a lower heat content (so that the Conformational Rule[3] applies) and these results were retionalized[5] somewhat analogously to the 1,3-dimethylcyclohexanes.

Reduction of 3-methylcyclopentanone was reported by Godchot et al[6]. Configurations of the product alcohols were assigned on the bases of physical data, the reduction method employed and the saponification rates of the esters. The authors also stressed the point of the stereoisomer not conforming to the Auwers-Skita rule. In the light of present knowledge[2,3,7] the assignment was no more than tentative, nor was the purity of the alcohols sufficiently established, as actually pointed out later by one of the authors[8].

As part of a study of 1,3-substituted cyclopentanes, the title compounds were stereospecifically synthesized[1,9]. The lactone of cis-3-hydroxycyclopentanecarboxylic acid[10] was reduced with $LiAlH_4$ to cis-3-hydroxymethylcyclopentanol, which on selective monotosylation yielded exclusively the primary tosylate, in turn reduced with $LiAlH_4$ to cis-3-methylcyclopentanol (Table 1). The tosylate of the latter was passed through a column of activated basic alumina, whereby it underwent inversion and trans-3-methylcyclopentanol was obtained and purified through its p-nitrobenzoate.
This was found necessary as the inversion is not absolutely stereospecific, (Reinversion of the above crude trans-isomer by the same procedure gave the cis-alcohol contaminated with ca. 7% trans-alcohol).

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As can be seen from Table 1, the cis-alcohol reported was probably fairly pure, whereas the trans-alcohol was not. While the assignment of configuration had been correct, the physical properties of the alcohols were found slightly but significantly different from those reported.

Preparative quantities of the cis-and trans-3-methylcyclopentanol were obtained from 3-methylcyclopentanone, using catalytic- and Meerwein-Ponndorf-Verley reduction, respectively (Table 2). The impure alcohols were purified by fractional crystallization (12 times) of their p-nitrobenzoates and subsequent hydrolysis. The pysical constants of the alcohols are very close, precluding resolution of the mixtures even by v.p.c. on a variety of columns. This, and the close similarity of their spectral properties[1a], made analysis difficult as well.

TABLE 1

Properties of cis- and trans-3-Methylcyclopentanol and derivatives

Substituted Data/3-Methylcyclopentane	alcohols		acetates	
	cis	trans	cis	trans
b.p., C° (*)	149-150 (65/23mm)	149-151 (70/24mm)	157-159 (61.5/13mm)	159-160 (63/15mm)
n_D^t (*)	1.4465^{20} 1.4391^{40} (1.44374^{28})	1.4460^{20} 1.4386^{40} (1.44464^{28})	1.4282^{18} ($1.42695^{18.5}$)	1.4291^{18} ($1.42795^{20.5}$)
D_4^t (*)	0.9228^{20} (0.9119^{28})	0.9179^{20} (0.9129^{28})	0.9432^{18} ($0.9466^{18.5}$)	0.94595^{18} ($0.9480^{20.5}$)
k_2, oxid[1a] (l. mole^{-1} nim.$^{-1}$)	27.4	21.6		
	p - nitrobenzoates			
	cis	trans		
m.p., C° (*)	72-73.5 (71)	49-50 (44)		

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[*] Data in parenthesis are quoted from Reference 6.

Eventually quantitative IR analysis[11] was resorted to, using the peaks at 8.80µ and 10.33µ for the *cis-* and *trans*-isomers respectively. This yielded the product composition of various reductions as well as of equilibrium mixtures, (Results in Table 2). It is worth noting that, except for equilibrating conditions, all reductions lead to mixtures having the *cis*-isomer in excess, in contrast to what is recorded for reduction of 2-methylcyclopentanone[12]. The equilibration studies (isopropanol/aluminum isopropoxide at 84°) yield, for the isomerisation *cis*- $\rightleftarrows$ *trans*-3-methylcyclopentanol, a value of $\Delta F = -RT \ln K = -2 \times 357 \times 2.3 \times \log 1.32 = -0.2$ kcal/mole. The relation[13]: $\Delta F_{\text{oxid.}} = RT \ln k_{2,\ \text{stable}}/k_{2,\ \text{unstable}}$ applied to the oxidation rate data[1a] (Table 1) yields a similar value. The calculation of Ouannes, Ouannes and Jacques[14], lead to an energy difference which, although slightly in favour of the *cis*-isomer, contrary to our experimetal results, is still very close to the latter.

TABLE 2

Composition of mixtures of stereomeric 3-methylcyclopentanols

Origin of mixture	% cis-3-methylcyclopentanol*
Equilibrium (ex *trans*-isomer)	43
Equilibrium (ex *cis*-isomer)	43
Catalytic (Pt O_2/HOAc) reduction product	82
Catalytic (Ra-Ni/EtOH) reduction product	62
Chemical (Na/H_2O) reduction product	53
Chemical ($LiAlH_4$) reduction product+	60
Chemical ($NaBH_4$) reduction product+	65
Chemical (M - P - V) reduction product+ in equilibrating conditions	43

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* The estimated error is ± 2%.

\+ Evaluated only by visual comparison of IR spectra with those of known mixtures.

Incidentally, the density and refractive index of the *cis*-isomer are, contrary to the published data, the higher ones (though by a very small difference). In view of that and of the above stability order, the stereomeric 3-methylcyclopentanols are again seen to obey the Conformational Rule[3]. The stability order is in apparent contradiction with the situation in the case of 1,3-dimethylcyclopentane but this can be rationalized[14] on conformational grounds.

Another interesting fact is the reversal in the order of physical constants of the acetates compared with the parent alcohols. The Conformational Rule again indicates the *cis*-isomer as the more stable of the two, as in the case of the 1,2-dimethylcyclopentanes.

One may conclude that all the above reiterates[1a] the closeness in properties and chemical behaviour of 1,3-substituted cyclopentanes, especially of stereoisomers. This is in good agreement with results obtained by other investigators for solvolysis of tosylates[15,16] and oxidation rate studies[13b] of similar or even heavier 3-substituted cyclopentanols.

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