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

PROPERTIES OF SOME β-SUBSTITUTED CYCLOPENTANOLS.

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The conformation of five-membered rings was the subject of little systematic study up to the recent past. In the last few years rapid progress could be noted and the conformational analysis, geometry and energy calculation of cyclopentane itself[2,3,4], of rigid, fused five-membered rings[5], of flexible substituted cyclopentanes[2,5,6] and heterocyclic analogs[7] were studied.

The present study was initiated[1] in the hope that the investigation of steric effects in β-substituted cyclopentanols would lead to some information on interactions and conformation in the five-membered rings. β-substitution was chosen in order to avoid 1,2 interactions. Thus only distant substituents to the centre under scrutiny viz. the carbinol, affect the geometry and strains of the ring.

The synthesis of certain 3-and 3,4-substituted methylcylopentanols and their physical constants have been reported[1]. We wish to describe here an attempt to look into the steric effects which govern their behaviour using some spectroscopic and kinetic methods.

Following the techniques described by Huckel et al[9] and by Chiurdoglu et al[10], we studied the shift of the C-O stretching vibration in the 1000 cm^{-1} region by using solvents of different polarity or an HCl saturated carbon disulfide solution. The above mentioned groups report a definite trend for the C-O stretching vibration to shift to lower wave-number with increasing polarity of the solvent. This permits the identification of the C-O band, its position then indicating, in the cyclohexane series, if the OH-group is axial or equatorial[8]. In the cyclopentane series, some information on the

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conformation of a hydroxyl group should thus also be obtained[9].

Our results are summarized in Table 1. Shifts, in most cases, are small and rather erratic. We were repeatedly unable to duplicate the published data on cyclopentanol[9]. Thus in our hands this technique did not enable us to make unequivocal assignments of bands to the C–O vibration in the flexible cyclopentanols studied.

TABLE 1* .

$\nu_{max.}$ (C–O), cm^{-1}

Solute / Solvent	C_6H_{12}	CS_2	CHl_3	CS_2/HCl
Cyclopentanol	933–, 995+ 1065–	932–, 994+ 1035±, 1063±	938$^{b}_{-}$, 990+ 1035±, 1055+ 1069–	932–, 990+ 1032– 1065$^{b}_{-}$
trans-3-Methyl-		942–, 967± 1016+, 1063$^{b}_{-}$		942–, 964$^{b}_{-}$ 1016+, 1065$^{b}_{-}$
cis-3-Methyl-		947–, 1001+ 1075$^{b}_{-}$		947–, 997$^{b}_{-}$ 1004+, 1065$^{b}_{-}$
3,3-Dimethyl-		937–, 970– 1000±, 1062+		935=, 968$^{b}_{-}$ 998±, 1058+
trans-3,4-Dimethyl-		945–, 971– 1004+, 1060$^{b}_{-}$		940$^{b}_{-}$, 1000$^{b}_{+}$ 1055$^{b}_{=}$
3,3,4,4-Tetramethyl-	955$^{b}_{-}$, 1000+ 1023±	960–, 1004+ 1030+	962$^{b}_{-}$, 1004+ 1027+	960$^{b}_{-}$, 1003+ 1026+

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* b=broad, + and – refer to relative intensities.
The recorded values are of 0.2M solutions placed in 0.5 mm NaCl cells, using a Perkin Elmer 21 spectrophotometer. Every spectrum was calibrated using the polystyrene band at 11,035μ.

In the NMR spectra of the substituted cyclopentanols, the methylene-proton resonance region is complicated by the rather complex spin-spin interactions; analysis using techniques of decoupling will be reported in due course. On the other hand the chemical shifts of the methyl-hydrogens are of interest. According to various investigators[11], based on results from a great variety of rigid five-membered rings, the cis-1,3-hydroxyl-methyl interaction brings about a shift of the methyl resonance of more than 10 cps to lower field, as compared to the parent compound. A similar effect in 1,3-methyl-methyl substituted fused cyclopentanes was also described[12]. Table 2 presents the methyl resonances of the substituted cyclopentanols and the corresponding ketones.

TABLE 2[*]

Methyl proton magnetic resonances, τ.

Substituted cyclopentane	ketone		alcohol			acetate		
	Signal	Chem. shift	Signal	Chem. shift	Average	Signal	Chem. shift	Average
cis-3-Methyl	8.82 8.92	8.87	8.88 8.97	8.93	8.97	8.89 8.98	8.93	8.96
trans-3-Methyl			8.95 9.04	9.00		8.93 9.03	8.98	
3,3-Dimethyl	8.92	8.92	8.89 9.04	8.89 9.04	8.96			
trans-3,4-Dimethyl	8.83 8.93	8.88	8.94 8.99 9.07	8.97 9.03	9.00			
3,3,4,4-Tetramethyl	8.95	8.95	9.03 9.17	9.03 9.17	9.10			

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[*] The spectra were obtained on a Varian A-60 instrument using approx. 10% $^{w}/_{v}$ solutions in $CDCl_3$ with TMS as internal standard. Preliminary measurements were performed on a DP-60 instrument with the help of Dr. A. Loewenstein, to whom our grateful thanks are extended.

As can be seen no such shift can be observed and rather the opposite happens to a certain extent i.e. a shift of about 0.1 ppm to higher field is observed. Even in the 3,3,4,4-tetramethylcyclopentanol, where one *cis*-methyl is to be assumed in a pseudo-axial position this is the case. Also in *both* acetates of the stereomeric 3-methylcyclopentanols , the methyl resonance appears at the same field as that of the corresponding alcohol and is not shifted to higher field,as recorded for compounds which *cis*-1,3 pseudo-diaxial substitution[11] All that is taken as indication of very weak, if any, *cis*-1,3 interaction in flexible β-substituted cyclopentanes. In the analogous rigid systems[11], the interference found is forcefully imposed and should be regarded as specific to such structures. Whether the observed shift to higher field is relevant has to be seen; attention is drawn to the fact that shifts become larger as 3,4-substitution increases.

As a further method for obtaining information on steric interactions, the oxidation rates of the above alcohols were measured[13]. The results are tabulated in Table 3.

TABLE 3*

Oxidation Rates of Substituted Cyclopentanols

Compound	k_2, l.mole^{-1} min.$^{-1}$	Rel. Rate
Cyclopentanol	14.9	1
trans-3-Methyl-	21.6	1.4
cis-3-Methyl-	27.4	1.8
trans-3,4-Dimethyl -	30.8	2.0
3,3-Dimethyl-	34.2	2.2
3,3,4,4-Tetramethyl -	93.0	6.2

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* Rates were measured at 25°, in 90% $^{v}/_{v}$ acetic acid, following spectrophotometrically the disappearance of Cr^{VI}; all data are average of at least 3 runs.[13]

A definite trend is observed, viz. increased substitution leads to higher rate. On the other hand, the differences are so small that they might be due to several minor effects and may possibly not be accounted for by current theories[14,15,16]. However, the steady increase in oxidation rate with increasing substitution calls for some rationalisation.

Calculations have shown[2] that cyclopentanol prefers the C_s (envelope)[5] conformation (although the pseudo-rotation is inhibited only to a small extent) and cyclopentanone the C_2 (half chair)[5] conformation (stabilized by a large inhibition to pseudorotation). It appears[6], however, that as β-substituents enter into cyclopentanone, the C_s (envelope) conformation, or a closely related one[4,6], becomes preferred. At the same time an obvious increase in the barrier of pseudorotation is to be considered[2,4,6]. The factors leading to the small but regular oxidation rate increase could thus be: (i) the strain relief in going to the ketone, rises with the number of substituents; (ii) the increasing inhibition to pseudorotation facilitates the reaction, which is known to have a large negative entropy of activation[16].

Further studies are in progress and it is hoped that they will shed more light on this problem.

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