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STERIC REQUIREMENTS OF $^{4}J_{H-C-C-O-H}$- AND $^{4}J_{H-C-C-S-H}$-COUPLINGS

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Hydroxyl protons in saturated systems H-C-C-O-H show $^{4}J_{H,H}$-couplings if the protons and the connecting atoms are in a coplanar arrangement (Fig.1: $\varphi = 180^{\circ}$ or 0°, $\vartheta = 180^{\circ}$ or 0°) (1,2).

Thus, not only the conformation of the hydroxyl group but also that of the hydroxyl proton is important, and a trans arrangement of a proton and a vicinal hydroxyl group alone is not a sufficient condition for OH-long-range coupling.

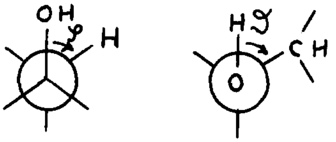

FIG.1.: Definition of the dihedral angles φ and ϑ .

However, for pyranoses it has been shown 2) that the position of the hydroxyl proton of an axial anomeric hydroxyl group gauche to the ring oxygen and outside the ring has considerable statistical weight. Thus, if the C-atom adjacent to the anomeric center bears an axial proton a $^{4}J_{H-C-C-O-H}$-coupling should always be observable. This has been used in determining the configuration and conformation of many pyranoses 1,2).

These considerations should also apply to other six membered cyclic hemiacetals. Thus, the proton resonance spectra a) of the dimers of acetoin,

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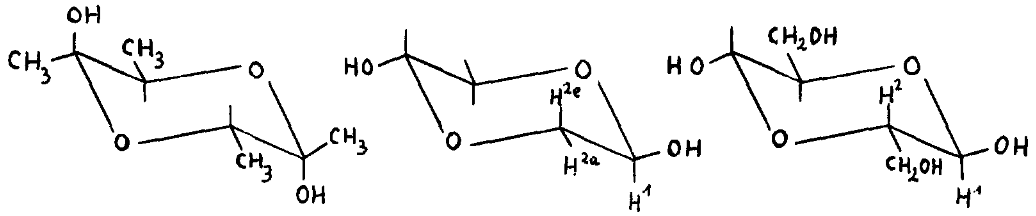
a) The spectra were recorded with a Varian HA-100 spectrometer.



glycolaldehyde and glyceraldehyde, which form from the monomers on standing [3] are only consistent with structures I – III.

The dimeric acetoin (I) gives rise to only one hydroxyl resonance (5.54 ppm) [b] split into a doublet by a long range coupling to the methine proton (3.85 ppm). The methine proton is further coupled to a methyl group (0.98 ppm), ($^{3}J_{CH3,H}$ = 6.6 c/s). Another methyl group appears as a singlet at 1.15 ppm. The $^{4}J_{H-C-C-O-H}$coupling indicates the trans-diaxial arrangement of the hydroxyl group and the methine proton and the symmetry of the molecule follows from the number of different proton resonances in the spectrum.

Similar considerations lead to formulas II and III for dimeric glycolaldehyde and the dimer of glyceraldehyde. No OH-long-range coupling can be found, and the conclusion that the hemiacetal hydroxyl groups are equatorially oriented is further supported by the coupling of the ring protons (II: [b] $J_{H^1,H^{2e}}$ = 2.4 c/s, $J_{H^1,H^{2a}}$ = 7.0 c/s. III: [b] J_{H^1,H^2} = 7.5 c/s).

If by special steric requirements a hydroxyl group and a trans standing vicinal proton are forced into a plane, OH-long-range couplings may also be observable in five-membered rings. Thus, in the polycyclic alcohol phorbol [c] (IV) the hydroxyl group in 4-position (5.39 ppm [d]) shows a long-range coupling of 1.0 c/s to H^{10} (3.04 ppm).

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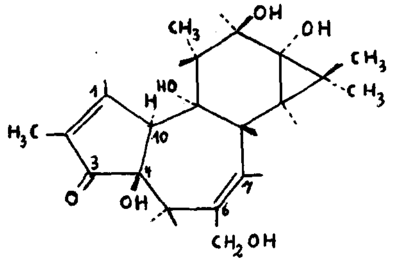
b) In dimethylsulfoxide-d_6 with tetramethylsilane as internal standard.

c) We thank Prof. Dr. E. Hecker and Dr. H.W.Thielmann [4] for a sample of this substance.

d) In dimethylsulfoxide-d_6 : acetone-d_6 = 1 : 3 with tetramethylsilane as internal reference.



IV

The trans position of OH^4 and H^{10}, which could not be proved by chemical means $^{4)}$, as well as the considerable distortion of the five membered ring has been demonstrated by x-ray analysis $^{5)}$. Moreover, the proton OH^4 is very probably fixed in a nearly coplanar arrangement with C^4, C^{10} and H^{10} by a hydrogen bond to the carbonyl oxygen C^3=O. On removing the double bond C^6=C^7 - e.g. by hydroxylation - the long-range coupling $^4J_{OH^4,H^{10}}$ becomes small and could only be observed by the sharpening of the OH^4 signal on decoupling from H^{10}. Apparently, the double bond C^6=C^7 has some influence on the angle φ (Fig. 1) between OH^4 and H^{10}. No other hydroxyl group in phorbol (IV) shows longe-range couplings.

Finally $^4J_{H-C-C-O-H}$-couplings should be observable in all systems where rotation around the C-C-bond is possible as in ethanols CH_3 - C - O - H. The magnitude of the long-range coupling will be the weighed mean of the coupling constants of all possible conformations. The barrier to rotation around the C-C-bond in ethanes CH_3-C- is about 3 kcal./mole and in consequence at room temperature nearly all molecules have staggered conformation [$\varphi \approx 60$, 180 and 300° (Fig. 1)]. As we know from cyclohexanols $^{2)}$ no OH-long-range coupling can be observed for $\varphi = 60$ or 300°. The statistical weight of molecules with a C-H proton properly oriented ($\varphi \approx 180^\circ$) for a long-range coupling in thus $\frac{1}{3}$.

On the other hand the barrier to rotation around the C-O bond is only about 1 kcal./mole $^{6)}$, and in consequence the distribution of the OH proton around the C-O bond is much more continuous than the distribution of the C-H proton around the C-C bond in ethanes. However, assuming that the $^4J_{H-C-C-O-H}$-coupling can be approximated $^{7)}$ by equation (1):

$$(1) \quad {}^4J_{H-C-C-O-H} = a \cdot \cos^2\varphi \cdot \cos^2\vartheta - b$$

it can be shown with the same arguments that have been given for ethanes $^{8)}$, that in molecules with the C-O bond as a three fold axis of symmetry, as in <u>tert</u>.-butanol, the OH-long-range coupling is independent of the barrier to rotation of the hydroxyl proton. In this case the mean coupling constant is given by

$$(2) \qquad {}^{4}\bar{J}_{CH_3,OH} = \frac{1}{3}\left(\frac{a}{2} - b\right)$$

Introducing a-b = J_{MAX} and taking into consideration the fact[2)] that the OH-long-range coupling is zero for φ = 60° and ϑ = 180°, it follows from equations (1) and (2):

$$(3) \qquad {}^{4}\bar{J}_{CH_3,OH} = \frac{1}{9}\, J_{MAX} \; .$$

From our previous work [2)] we estimate J_{MAX} = 2 c/s ± 50 %, leading to values $a = \frac{8}{3}$ and $b = \frac{2}{3}$ (± 50 %), and thus expect an OH-long-range coupling of 0.1 - 0.2 c/s for tert.-butanol and similar coupling constants for iso-propanol and ethanol.

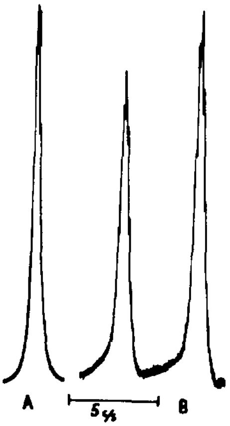


FIG. 2. A: 100-Mc proton resonance of the methyl groups of tert.-butanol,
and B: of the OH-proton of iso-propanol [e)].

Figure 2 A shows the methyl resonance (1.143 ppm[e)]) of tert.-butanol. The two lines are separated by 0.09 ± 0.01 c/s. On decoupling from the hydroxyl signal (3.968 ppm) the splitting disappears.

Figure 2 B shows the OH-resonance (-3.120 ppm[f)]) of iso-propanol. Of the expected septet five lines can be distinguished. We find a line separation of 0.10 ± 0.01 c/s. and ${}^{3}J_{OH,H}$ = 4.20 ± 0.03 c/s. On selective spin decoupling of the low field line (-6.214 ppm) of the methyl doublet, the low field septet of the hydroxyl resonance (-3.099 ppm) collapses. On the other hand, irradiating the high field line (-6.275 ppm) of the methyl doublet results in sharpening of the high field hydroxyl septet (-3.141 ppm), thus indicating a positive ${}^{3}J_{H,OH}$-coupling.

A long-range coupling of about 0.1 c/s is also found between the hydroxyl-

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e) In 0.2 ccm dimethylsulfoxide-d_6 + 0.2 ccm acetone-d_6 + 0.1 ccm tetramethylsilane as internal standard. The solution was degassed.

f) In 0.2 ccm dimethylsulfoxid-d_6 + 0.2 ccm acetone-d_6 + 0.1 ccm benzene as internal standard. The solution was degassed.

proton and the methyl group in ethanol. Selective spin decoupling of the outer lines (-6.161 and -6.301 ppm [g]) of the methyl triplet sharpens the corresponding outer lines (-2.871 and -2.966 ppm) of the hydroxyl resonance, again indicating the same signs for the $^3J_{CH,H}$- and the $^3J_{OH,H}$- proton coupling.

The main problem in resolving these small couplings is suppressing intermolecular proton exchanges. Assuming a transversal relaxation time $T_2 \approx 5$ s, the mean lifetime of the O-H-bond should be at least about 100 s in order to resolve a doublet with splitting of 0.1 c/s and coupling of 0.2 c/s [9]. The observed splittings may thus be smaller than the coupling constants owing to slow proton exchange reactions and partial overlap of lines.

It is interesting to compare the OH-long-range couplings of tert.-butanol, iso-propanol and ethanol with the SH-long-range couplings of the corresponding thiols, which have already been published by Rousselot [10]. While the ^4J-OH-couplings all have approximately the same value of 0.1 c/s, tert.-butylmercaptan shows [f] a long-range coupling $^4J_{SH,H} = 0.57 \pm 0.02$ c/s, and for iso-propylmercaptan we find [f] $^4J_{SH,H} = + 0.37 \pm 0.01$ c/s. The SH-long-range coupling in ethylmercaptan is very small ($^4J_{SH,H} \approx 0.05 \pm 0.03$ c/s) and is only visible in a sharpening of the SH-signals on selective decoupling of the methyl lines. The spectrum of iso-propylmercaptan was compared with a calculated spectrum[h]. The much larger dependence on substitution of the SH-long-range coupling compared with the OH-long-range coupling suggests a direct interaction of the methyl protons with the sulfur orbitals.

The $^4J_{H-C-C-S-H}$-coupling is positive, as was shown for iso-propylmercaptan. Selective spin decoupling of the low field line (-6.037 ppm [f]) of the methyl resonance results in collapsing of the low field SH-septet (-5.214 ppm) and vice versa, indicating a positive $^3J_{SH,H}$-coupling (provided that the $^3J_{CH,H}$-coupling is positive). "Spin tickling" [11] of lines of the methine proton resonance results in splitting of lines in the SH-septet, demonstrating a

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[g] In 0.5 ccm dimethylsulfoxide-d_6 + 0.1 ccm benzene as internal standard. The solution was degassed.

[h] We thank Dr. H. Günther, university of Cologne, for the calculation with aid of the program Laokoon II.

positive $^{4}J_{H-C-C-S-H}$-coupling relative to the positive $^{3}J_{H-C-C-H}$-coupling.

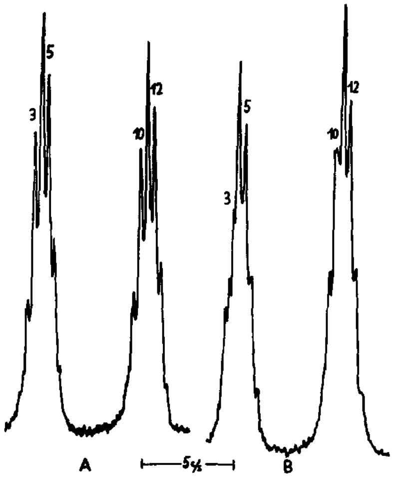

FIG. 3. A: 100-Mc-proton resonance of the SH proton of *iso*-propylmercaptan $^{f)}$.

B: As A, when the line of the methine proton resonance with spin state (SH: $+\frac{1}{2}$, CH_3: +1) was irradiated.

Figure 3 shows the regressive splitting of line 3 and progressive splitting of line 10 of the SH resonance on irradiating that line (-4.158 ppm $^{f)}$) of the methine proton resonance corresponding to the transition with spin state SH $+\frac{1}{2}$ and methyl protons +1. If the SH-long-range coupling were negative then line 5 would be split regressively and line 12 progressively.

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REFERENCES

1. J.C.Jochims, G.Taigel, A.Seeliger, P.Lutz and H.E.Driesen, *Tetrahedron Letters* 4363 (**1967**).
2. J.C.Jochims, W.Otting, A.Seeliger and G.Taigel, *Chem. Ber.* in press.
3. Houben-Weyl, *Methoden der Organischen Chemie*, Vol. VI/4, p. 410. 4. edition, Georg Thieme Verlag, Stuttgart (1966).
4. E.Hecker, H.Bartsch, H.Bresch, M.Gschwendt, E.Härle, G.Kreibich, H.Kubinyi, H.U.Schairer, Ch.v.Szczepanski and H.W.Thielmann, *Tetrahedron Letters* 3165 (**1967**).
5. W.Hoppe, F.Brandl, J.Strell, M.Röhrl, J.Gassmann, E.Hecker, H.Bartsch, G.Kreibich and Ch.v.Szczepanski, *Angew. Chemie* **79**, 824 (1967).
6. E.V.Ivash and D.M.Dennison, *J.Chem.Phys.* **21**, 1804 (1953).
7. V.F.Bystrov and A.U.Stepanyants, *J.Mol.Spectroscopy* **21**, 241 (1966).
8. J.C.Schug, P.E.McMahon and H.S.Gutowsky, *J.Chem.Phys.* **33**, 843 (1960).
9. M. Takeda and E.O.Stejskal, *J.Amer.chem.Soc.* **82**, 25 (1960).
10. M-M.Rousselot, *Compt.Rend.Acad.Sc.[Paris]*, **262 C**, 26 (1966).
11. R.Freeman and W.A.Anderson, *J.Chem.Phys.* **37**, 2053 (1962).