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ROTATIONAL EQUILIBRIA IN 2-ARYL-*n*-PROPANOLS, 2-ARYL-*n*-PROPYL METHYL ETHERS AND 2-ARYL-*n*-PROPYL ACETATES. TRENDS CONSISTENT WITH A CH---O HYDROGEN BOND

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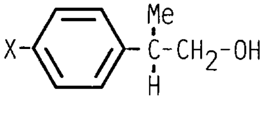
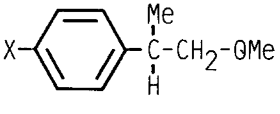
Summary: An ^{1}H-nmr study of rotational isomerism in the title compounds reveals an increasing population of gauche Aryl/OMe and gauche Aryl/OCOMe conformations as electron donor groups on the aromatic ring are replaced by electron withdrawing groups.

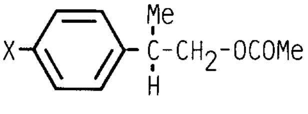
A detailed knowledge of intramolecular interactions is fundamental to a rationalization of conformational behaviour. For molecules containing both hydrogen bond donor and acceptor sites, intramolecular H-bonding can provide an attractive interaction which can influence significantly the conformational energy profile. Such an interaction is postulated to occur in compounds bearing hydroxyl and phenyl groups on adjacent carbon atoms, an OH---π H-bond stabilizing the gauche orientation of the two groups.[1] In the present note we report an investigation of the rotational isomerism within compounds of series (**1**), (**2**) and (**3**) using ^{1}H-nmr spectroscopy. The results provide evidence of a second interaction between a hydroxyl group and an aromatic ring, an interaction which involves the oxygen atom and which is also exhibited by ether and ester groups.



1 a X=OMe
b X=Et
c X=*t*-Bu
d X=H
e X=Cl
f X=I

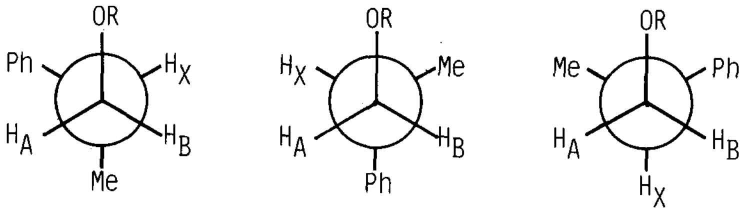


2 a X=NEt_2
b X=Et
c X=H
d X=OCOMe
e X=I
f X=COMe
g X=NO_2



3 a X=Et
b X=H
c X=OCOMe
d X=I
e X=COMe
f X=NO_2

Nmr signals for H_A and H_B, figure 1, in (**1**d) were distinguished on the basis of signal intensities in the corresponding spectrum of the mixture of



	I	II	III
Populations:	n_I	n_{II}	n_{III}
J_{AX}, J_{BX} :	J_t, J_g	J_g, J_t	$J_{g'}$, $J_{g'}$

Figure 1

diastereomeric alcohols $Ph\overset{*}{C}HMe.\overset{*}{C}HD.OH$ formed by reducing 2-phenylpropionaldehyde with lithium aluminium deuteride. The major product of the 55:45 mixture is assigned the RR/SS configuration on the basis of Cram's rule.[2] The proton in the -CHD- moiety of this isomer has the stereochemistry corresponding to H_B in figure 1 and appears to higher field than the analogous proton (H_A) in the minor product *viz* the RS/SR alcohol. The mixture of alcohols was methylated and acetylated and the products nitrated. As before, ^1H-nmr band intensities distinguished the signals for the RR/SS and RS/SR isomers and led to the unambiguous assignment of signals for H_A and H_B in **2c**, **2g**, **3b** and **3f**. In each one H_B is to higher field and we extrapolate this assignment to the other members of the series.[3]

Coupling constants J_{AX} and J_{BX} were calculated from high resolution 400 MHz spectra[4] of 5% solutions in the non-hydrogen bonding solvent cyclohexane-*d*$_{12}$, Table 1. Also listed in the Table are the rotamer populations n_I, n_{II} and n_{III}, figure 1, which were evaluated by solving the equations:[5]

$$\begin{aligned} J_{AX} &= n_I J_t + n_{II} J_g + n_{III} J_{g'} \\ J_{BX} &= n_I J_g + n_{II} J_t + n_{III} J_{g'} \\ 1 &= n_I + n_{II} + n_{III} \end{aligned}$$

The calculations were carried out using $J_t = 11.5$, $J_g = 4.5$ and $J_{g'} = 1.8$ Hz following Spassov and Stefanova[1c] who derived these values from data reported by Abraham and co-workers.[5,6]

Table 1 ^{1}H-Nmr Data and Rotamer Populations in C_6D_{12} solution at 293 K

Series	No.	Aryl subst.	H_A ppm	H_B ppm	H_X ppm	J_{AX} Hz	J_{BX} Hz	n_I	n_{II}	n_{III}
Alcohols	**1a**	OMe	3.45	3.42	2.71	7.09	6.39	0.45	0.35	0.20
	1b	Et	3.48	3.43	2.73	6.98	6.50	0.43	0.36	0.21
	1c	*t*-Bu	3.50	3.46	2.76	7.05	6.39	0.44	0.35	0.21
	1d	H	3.54	3.51	2.80	7.06	6.19	0.45	0.33	0.22
	1e	Cl	3.43	3.40	2.71	7.16	6.14	0.46	0.32	0.22
	1f	I	3.43	3.41	2.69	7.28	6.02	0.48	0.30	0.22
Ethers	**2a**	NEt_2	3.34	3.21	2.80	5.27	8.65	0.18	0.66	0.16
	2b	Et	3.36	3.26	2.88	5.51	8.04	0.22	0.58	0.20
	2c	H	3.37	3.28	2.91	5.56	7.87	0.23	0.56	0.21
	2d	OCOMe	3.36	3.28	2.91	5.76	7.55	0.26	0.52	0.22
	2e	I	3.34	3.27	2.85	5.96	7.08	0.30	0.46	0.24
	2f	COMe	3.39	3.33	2.97	6.11	7.01	0.32	0.45	0.23
	2g	NO_2	3.40	3.38	3.03	6.64	6.01	0.41	0.32	0.27
Esters	**3a**	Et	4.10	3.97	2.97	6.28	8.09	0.31	0.56	0.13
	3b	H	4.12	3.99	2.99	6.47	7.86	0.33	0.53	0.14
	3c	OCOMe	4.09	3.97	2.99	6.56	7.69	0.35	0.51	0.14
	3d	I	4.09	3.97	2.96	6.83	7.36	0.39	0.46	0.15
	3e	COMe	4.11	3.96	3.06	6.88	7.24	0.40	0.45	0.15
	3f	No_2	4.12	4.01	3.14	7.25	6.68	0.46	0.38	0.16

The strength of an intramolecular OH---π H-bond increases with increasing π electron density on the aromatic ring.[7] However, the rotamer populations of the series of alcohols (**1**) show only small variations with substituents and the discernible trend is, in fact, contrary to that expected for OH---π hydrogen bonding. Thus rotamers I and III are populated the most in the compounds bearing electron withdrawing halide groups. This suggests that a further interaction is operating, a conclusion supported by the data for the series (**2**) and (**3**). The rotational equilibria in these series are strongly dependent upon aryl ring substituents. They show an increasing preference for the OMe and OCOMe groups to orientate gauche to the aryl ring as electron donor groups at the *para* position are replaced by electron withdrawing groups. This offers unambiguous evidence that intramolecular interactions other than simple steric effects are involved. These will be discussed elsewhere. Here we note only that one possible interaction consistent with the trends is an intramolecular *ortho* CH---O hydrogen bond. Electron withdrawing groups at the *para* position polarize the C-H bond which should enhance the interaction whereas with electron donor substituents the polarizing field is expected to be reduced or even reversed. In the esters (3) there are two H-bond acceptor sites. However, the singly bonded oxygen rather than the carbonyl oxygen seems the more likely participant because the latter would involve an eight membered chelate ring.

A similar interaction may well be present in series (1), at least within the fraction of rotamers I and III in which the OH group is favourably orientated. Clearly this would not include forms where the OH is participating in an OH---π hydrogen bond. The apparent relative insensitivity of the rotamer populations to aryl substituents in this series might then arise because the substituent dependence of the newly identified interaction is in the opposite sense to that of an OH---π H-bond and the two more or less cancel.

In conclusion, we have demonstrated the existence of an interaction between an oxygen atom and an aromatic ring by varying the electronic properties of the latter and monitoring the effect on the conformational behaviour of the system. The use of p-substituted derivatives has the merit of keeping steric factors essentially constant which simplifies interpretation. We believe that this approach is a useful probe for distinguishing between steric and non-steric interactions involving a phenyl ring.

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References and notes

1. a) H.S. Aaron, 'Topics in Stereochemistry' ed N.L. Allinger and E.L.Eliel vol 11, p.1 1979; b) P. von R. Schleyer, C. Wintner, D.S. Trifan and R. Bacskai, Tetrahedron Lett., 1 (1959); c) S.L. Spassov and R. Stefanova, J. Mol. Structure, 42, 109 (1977).
2. D.J. Cram and F.D. Greene, J. Am. Chem. Soc., 75, 6005 (1953).
3. The assignments confirm those reported in ref 1c.
4. Digital resolution was better than 0.09 Hz per point. Simulated spectra (UEANMR programme) were in satisfactory agreement with experimental ones.
5. R.J. Abraham, P. Loftus and W.A. Thomas, Tetrahedron, 33, 1227 (1977).
6. R.J. Abraham and G. Gatti, J. Chem. Soc. B, 961 (1969).
7. eg. M. Oki and H. Iwamura, Bull. Chem. Soc. Jpn., 32, 1135 (1959).

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