Journal of Molecular Structure, 18 (1973) 421–428 © Elsevier Scientific Publishing Company, Amsterdam – Printed in The Netherlands

CONFORMATIONS OF HIGHLY HINDERED ARYL ETHERS

XXII. DIPOLE MOMENTS AND CONFORMATIONS OF 2,6-DISUB-STITUTED ARYL ETHERS*

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(Received 2 January 1973)

ABSTRACT

The dipole moments of the methyl, phenyl and 2,4-dinitrophenyl ethers of 2,6-R₂-4-methyl phenol (R = Me, Br, 1), of 2,4,6-trimethylphenyl benzyl ether and of 2-bromo-4,6-dinitrophenyl 2'-naphthyl ether have been measured. These values could be matched with those calculated using vector analysis and group moments by (a) considering twist conformations ($\theta = 60^{\circ}$ for methyl and $\theta = \theta' = 37^{\circ}$ for aryl ethers); (b) including appropriate mesomeric moments; (c) including an inductive moment of 0.35 D for the mesityl moiety; and (d) including an intramolecular charge-transfer moment of 1.0 D for the last-mentioned ether.

INTRODUCTION

In a previous part of this series¹ evidence was found from dipole moment measurements for the existence in diaryl ethers of an intramolecular charge-transfer moment (IMCTM) provided that appropriate electron donor and acceptor moieties are present. The present work was undertaken to explore this point further by varying the nature of the rings and their substituents. The compounds studied (Fig. 1) centre about 2,6-diiodo-4-methyldiphenyl ether **6** which represents the nucleus of the thyroid hormones, and for which the formation of an IMCTM has been postulated to be essential for biological activity².

On the one hand the iodine atoms were exchanged by bromine atoms and methyl groups in order to vary the acceptor moiety, and on the other the un-

^{*} Part XXI, submitted to Organic Mass Spectrometry.

^{**} Taken in part from the thesis presented by S.P.G.d.P. in partial fulfilment of the requirements for the degree of Master of Science in Physical Chemistry; presented at the VIII Mexican Congress of Chemistry, Querétaro, April 1973.









Fig. 1. Structures, conformations and dipole moments of the compounds studied; straight arrows represent inductive (IM), mesomeric (MM) and charge-transfer (CTM) moments present, curved arrows indicate degree of twisting about the ether links, and figures in parentheses are the dipole moments calculated as described in the text.

substituted ring was modified in order to reduce (2,4-dinitrophenyl) or enhance (2-naphthyl) its donor abilities. The anisoles (1-3) and the benzyl ether (10) were included so as to arrive at an estimate of any interaction moments between a given aryl substituent and the ether function, which have been shown to be of importance³⁻⁶.

EXPERIMENTAL

Materials

The synthesis and properties of the compounds studied are shown in Table 1. Known methods were used throughout. Details will be published elsewhere¹⁷ together with NMR data which confirmed product identity in all cases. Solid samples were extensively purified by recrystallization and their purity shown to be at least 99.90 mole % by differential scanning calorimetry as described previously³. Liquid samples were purified by repeated fractional distillation. Purities by differential scanning calorimetry were 99.91 % for 2 and 99.93 % for 10; the other liquids (1 and 3) could not be measured this way.

TABLE 1

No.	Method	Yield (%)	m.p./b.p. (°C)	Reference	Analysis			
					%C	%H	%N	%X
1	CH ₂ N ₂ /CH ₂ Cl ₂ ⁷	40	84 (2 torr)	B.p. 200–203 °C (760 torr) ⁸	<u> </u>			
2	CH ₂ N ₂ /CH ₂ Cl ₂	59	114 (2 torr)	B.p. 262–266 °C (760 torr) ⁹ ; see ref. 10				
3	CH ₂ N ₂ /CH ₂ Cl ₂	67	21-24	Lit. ¹¹ 25°C				
4	a		57-58	Lit.12 55-56 °C				
5	$(C_6H_5)_2I^+Br^{-13}$	35	85-86	Found	45.49	2.99		Br, 46.74
				$C_{13}H_{10}OBr_2$ req.	45.61	2.95		Br, 46.78
6	(C ₆ H ₅) ₂ I ⁺ Br ⁻	33	99~100	Found	35.87	2.26		I, 57.98
				$C_{13}H_{10}OI_2$ req.	35.77	2.29		I, 58.22
7	Ref. 14	35	152-153	Lit. ¹⁵ 153–154 °C				
8	Ref. 14	50	139140	Found	35.38	1.93	6.50	Br, 36.98
				$C_{13}H_8O_5N_2Br_2$ req.	35.77	1.84	6.42	Br, 36.69
9	Ref. 14	35	197198	Lit. ² 196–198 °C				
10	Ref. 16	51	109 (1.5 torr)					
11	Hems-Meltzer ¹⁷	44	133-134	Found	49.41	2.29	7.17	Br, 20.60
				C ₁₆ H ₉ N ₂ O ₅ Br req.	49.38	2.33	7.19	Br, 20.56

SYNTHESIS AND PROPERTIES OF COMPOUNDS STUDIED

^a Gift of Dr. Arnold Factor, General Electric Research and Development Center, Schenectady, New York.

Methods

The dipole moments were determined as described previously¹⁻⁶ by the method of Halverstadt and Kumler¹⁸ using a WTW Dipolemeter and a specially designed pycnometer¹⁹. Calculations were carried out by machine computation using a recently devised program²⁰, and the error limits quoted are based on a 90 % level of confidence. All figures reported are in Debye units.

RESULTS

The dipole moments determined from measurements of relative permittivity and density for dilute solutions of ethers 1–11 in benzene at $25.00\pm0.02^{\circ}$ are shown in Table 2. Between 6 and 8 points were used to obtain the final values; the raw data will be published elsewhere¹⁷.

The dipole moments calculated for any given conformation were obtained by vector addition incorporating the bond angles, group and mesomeric moment values described previously¹⁻⁶. The sensitivity of the calculated dipole moment to small changes in molecular dimensions varies with the compounds studied and depends, in general, upon the orientations of the various group moments with respect to the bond angles. In these compounds, the sensitivity varied from zero to approximately 0.15 D per ten degree rotational change about the C_{ar}-O bond.

The measured and calculated (in parenthesis) dipole moments are compared (Fig. 1) for the conformation indicated, together with their interaction moments.

DISCUSSION

2,4,6-Trimethylanisole (1)

The measured moment can be explained only by the inclusion of an interaction moment of 0.35 D acting along the C_{ar} -O bond as shown. Since oxygen cannot expand its octet, this cannot have a mesomeric origin and it would seem that the trimethylphenyl moiety exerts an additional moment transmitted by the sigma bond to the ether linkage, and can be appropriately termed an inductive moment. Space-filling molecular models show that the closest approach to coplanarity (required for resonance interaction) results in a twist angle of 60°. On account of symmetry, however, it is not possible on the basis of the present results, to distinguish between this conformation and any others. Furthermore, the inductive moment, unlike the mesomer moment, is not a function of the twist angle³.

2,6-Dimethyldiphenyl ether (4)

This compound was studied in place of the mesitol derivative which could not be obtained in sufficient amount and purity despite numerous trials¹⁷. Satis-

factory agreement between measured and calculated dipole moments could only be obtained by including the aforementioned inductive moment. Symmetry again precludes assignment of a preferred conformation although on the basis of other studies^{1,4} (and further evidence presented below) a twist arrangement seems probable.

2,4,6-Trimethylphenyl 2',4'-dinitrophenyl ether (7)

Inclusion of the inductive moment for the mesitol moiety and the previously determined mesomeric moment for the 2,4-dinitrophenoxy moiety leads to good agreement only for the twist conformation.

2,4,6-Trimethylphenyl benzyl ether (10)

Molecular models and NMR studies¹⁶ show that in this ether rotation about the C_{ar} -O bond is even more hindered than in 4 and that a skew conformation (Fig. 1) is preferred. Although the present result sheds no light on conformational aspects, it does confirm again the presence and magnitude of the quoted inductive moment.

2,6-Dibromo-4-methylanisole (2)

Good agreement in this case could be obtained by including a mesomeric moment of 0.80 D (coplanar maximum) into the aromatic moiety and assuming the same conformation as in 1 and similar hindered anisoles³. This value is approximate since the dipole moment is rather insensitive to its magnitude. The value quoted is one consistent with considerations and results for the following two compounds.

2,6-Dibromo-4-methyldiphenyl ether (5)

Excellent agreement could be obtained for this ether by inclusion of a mesomeric moment of $0.51 (0.80 \cos^2 37^\circ)$, and by considering twist angles of 37° about each C–O bond.

2,6-Dibromo-4-methylphenyl 2',4'-dinitrophenyl ether (8)

The same considerations as above lead to a calculated dipole moment of 6.43 which is 9% too low. Use of a smaller mesomeric moment into the dibromo ring, which may well be the case, leads to concordance within the experimental error.

2,6-Diiodo-4-methylanisole (3)

From the measured dipole moment a mesomeric moment of 0.56 D (coplanar maximum) can be deduced for this aryl moiety provided that, as before, the

methoxyl group is twisted 60° out of coplanarity. It is similar (and may be equal) to that in the corresponding dibromo analogue.

2,6-Diiodo-4-methyldiphenyl ether (6)

Inclusion of this mesomeric moment, corrected for the twist conformation, leads to excellent agreement.

2,6-Diiodo-4-methylphenyl 2',4'-dinitrophenyl ether (9)

This compound, previously reported² is included here to complete the series. Excellent agreement (+1%) was obtained for the twist conformation without inclusion of a mesomeric moment into the diiodo-moiety (calcd. dipole moment = 6.64); this may be present but barely detectable (calcd. dipole moment with 0.56 mesomeric moment = 6.36).

2-Bromo-4,6-dinitrophenyl 2'-naphthyl ether (11)

In this ether four different twist conformations are possible. The two in which the bromo substituent is endo are unlikely to be preferred because in the analogous α -naphthyl ether X-ray crystallographic structural analysis has shown²³ that it is exo and the ortho nitro group is endo, being twisted and accommodated over the other ring. Thus the preferred conformation of 11 is either 11a or 11b.



The dipole moment calculated for 11 in either of these conformations with inclusion of the appropriate mesomeric moment for the substituted aryl moiety (2.30^1) is 2.55, compared to the measured value of 3.52 ± 0.25 . Inclusion of an IMCTM (as shown in 11a) of 1.0 directed as before¹ from the inner ring of the naphthalene moiety to the closest nitro group, leads to perfect agreement (calcd. 3.54; an IMCTM of 1.5 gives a resultant of 4.05). The smaller IMCTM in the β compared to the nitro group; in the α -ether it is the Cl'-C2' bond (p = 0.725) and in the β ether, in conformation 11b, it is the C2'-C3' bond (p = 0.603)²⁴. NMR evidence, to be presented elsewhere²⁵, indicates, however that conformation 11a is preferred.

TABLE 2

No.	ε ₁	<i>V</i> ₁	αª	βª	$P_{2\infty}$	M _R ^b	μ (D) ^c
1	2.271	1.14514	1.60	-0.181	88.22	46.57	1.43 ± 0.07
2	2.266	1.14527	2.74	-0.642	186.68	54.00	2.55 ± 0.23
3	2.270	1.14533	2.10	-0.734	193.38	63.14	2.52 ± 0.28
4	2.264	1.14559	1.20	-0.278	96.11	61.42	1.30 ± 0.17
5	2.271	1.14526	1.80	-0.483	182.69	72.20	2.33 ± 0.25
6	2.265	1.14545	1.38	-0.691	172.58	86.64	2.10 ± 0.18
7	2.270	1.14544	10.85	0.420	683.22	77.41	5.44 ± 0.21
8	2.269	1.14531	12.63	-0.603	1098.31	83.54	7.05 ± 0.23
9ª	2.275	1.14499	9.13	-0.707	971.56	93.98	6.55±0.19
10	2.269	1.14577	1.05	-0.592	81.85	40.54	1.42±0.25
11	2.265	1.14547	3.71	-0.613	340.99	87.98	3.52 <u>+</u> 0.25

DIPOLE MOMENT RESULTS

 α and β are the slopes of the relative permittivity (dielectric constant) and specific volume, respectively, vs. weight fraction.

^b The molar refraction (M_R) is the sum of the bond refractions for the sodium D-line given by Vogel et al.²¹.

^c 1 D equals 3.33564×10^{-30} Cm in the SI system²².

^d Values taken from ref. 2.

Calculations were carried out¹⁷ on other conformations previously considered probable⁴. In general agreement with measured values was poor except for the twist conformations described above.

Only in ether 11 was an IMCTM detected. Thus it would seem that the other diaryl ethers examined do not bear appropriate combinations of electron donating and accepting moieties.

DISCUSSION

The question of conformational preference(s) in diaryl ethers and related compounds continues to be studied actively^{*}, and no generalized picture has yet emerged. This is due in part to the fact that a great variety of conformational influences are present (steric hindrance, conjugative tendency, dipolar repulsion, intramolecular complex formation, etc.), whose relative importance depends on the nature and number of substituents.

The present work adduces additional evidence in favor of: (1) our earlier suggestion that conjugative tendencies when present are an important barrier to rotation about single ether bonds²⁷; (2) that they lead to the preferential adoption of twist conformations in many ethers; and (3) that attractive (e.g. complex formation) interactions between appropriate substituents on different rings can be present, and can affect conformational preference.

^{*} Earlier work on this problem has been reviewed briefly in refs. 1 and 4. In addition to our own recent work^{2.6}, other recent studies involving dipole moments are given in ref. 26.

ACKNOWLEDGEMENTS

It is a pleasure to acknowledge here the excellent technical assistance of Q. F. B. Arturo Ramírez M. We wish to thank Dr. Arnold Factor for a generous gift of one of the compounds measured, and Prof. W. D. Kumler for his helpful comments.

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