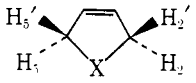
Interproton Spin–Spin Coupling across a Dual Path in 2,5-Dihydrofurans and Phthalans

M. Barfield,*[1a] R. J. Spear,[1b] and S. Sternhell*[1b]

Contribution from the Department of Chemistry, University of Arizona, Tucson, Arizona 85721, and the Department of Organic Chemistry, University of Sydney, N. S. W. 2006, Australia. Received December 17, 1974

Abstract: New NMR data for a series of two 2,5-dihydrofurans and six phthalans designed to produce predictable steric effects are presented. Calculations performed in terms of finite perturbation theory (FPT) in the semi-empirical INDO (intermediate neglect of differential overlap) approximation of the self-consistent-field molecular orbital theory (SCF-MO) give results for long-range coupling constants across a dual path in agreement with all known data for 2,5-dihydrofurans and phthalans. In particular, the effect of varying degrees of ring puckering was considered. Correlations between the magnitudes of these long-range coupling constants and stereoelectronic variables established here should be of utility in the determination of molecular structure.

In a previous communication,[2] we proposed a theoretical treatment for long-range coupling ($J_{2,5}$) in system **1** (X = O, NR, CR_2), which accounted for all major experimentally observed trends and, in particular, for the inequality of J_{trans} ($J_{2,5'}$) and J_{cis} ($J_{2,5}$) *even in planar systems.* Given the demonstrated sensitivity of both homoallylic coupling[3] and coupling across four single bonds[4-8] to conformational factors, it was expected that long-range coupling in system **1**, where both of these pathways are available, would vary with the conformation of the five-membered ring. To investigate the dependence of $J_{2,5}$ and $J_{2,5'}$ in **1** on conformation, we decided to synthesize a number of derivatives of 2,5-dihydrofuran (**1**, X = O) and phthalan **2** in which the *average* conformation of the five-membered ring was expected to vary because of steric factors and to compare the long-range coupling constants in these molecules with values calculated by the previously developed procedure[2] for various degrees of distortion from planarity.



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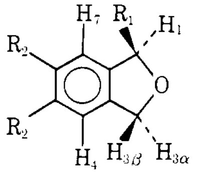
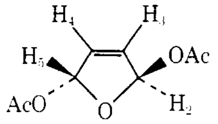


	R_2	R_1
2a,	H	H
b,	Ph	H
c,	Me	H
d,	*t*-Bu	H
e,	Ph	OMe
f,	*t*-Bu	OMe



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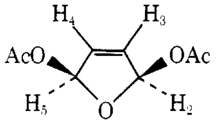
$J_{2,3} = +1.14$
$J_{2,4} = -1.14$
$J_{2,5} = +3.60$



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$J_{2,3} = +1.16$
$J_{2,4} = -0.91$
$J_{2,5} = +0.21$

The systems **1** (X = O) and **2** were chosen because they were relatively easy to manipulate synthetically and because any structural correlations developed (particularly the relation between $J_{2,5}$ and $J_{2,5'}$ with cis/trans stereochemistry) would be useful in the determination of stereochemistry in a wide range of substances.

At the time of commencement of this work, no information was available about the signs of the long-range coupling constants in 2,5-dihydrofuran derivatives, and accordingly we first investigated the NMR spectrum of methyl 2,5-dihydrofuroate[9] (**3**) and established (see Experimental Section and Table I) that both cis and trans H2,H5 coupling constants in this compound were positive, as predicted by us previously.[2] These signs were then assumed in the analysis of the NMR spectrum of 2,3-diphenyl-2,5-dihydrofuran[10] (**4**) (Table I).

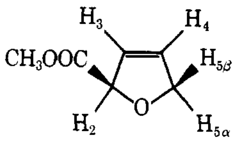
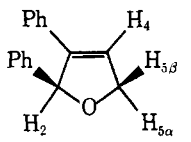
During the course of this work, three independent groups obtained the signs of analogous coupling constants and also found them to be positive. Jacobsen, Nielsen, and Schaumburg[11] reported data for *trans*- and *cis*-2,5-diacetoxy-2,5-dihydrofuran (**5** and **6**). Cole and Gilson[12] analyzed the NMR spectrum of 2,5-dihydrofuran in nematic phase and obtained the values of $J_{cis} = +4.19$ Hz and $J_{trans} = +6.66$ Hz, while Lozac'h and Braillon[13] analyzed the NMR spectra of 2,5-dihydrofuran, 2,5-dihydrothiophene, and butadiene sulfone and found all H2,H5 coupling constants to be positive. Their values, after allowing for the reversal of assignments,[13] for 2,5-dihydrofuran are $J_{cis} = +4.590$ Hz and $J_{trans} = +7.065$ Hz in fair agreement with the results of Cole and Gilson,[12] bearing in mind the different experimental conditions and entirely different spectral analyses. Our sign determinations (Table I) antedate the published results[11-13] and are, in fact, quoted as a private communication in the earliest of them.[11]

NMR Spectra and Average Conformation of Model Systems

The NMR parameters of the two 2,5-dihydrofuran derivatives investigated here are given in Table I, those for the six phthalan derivatives in Table II.

The relative assignments of $H_{5\alpha}$ and $H_{5\beta}$ in **3** and **4** were made on the basis of the relative magnitudes of the long-range coupling constants ($J_{2,5}$)[2,11-13] and could not be confirmed by either lanthanide induced shifts (LIS) or nuclear Overhauser experiments (NOE). The relative magnitudes of $J_{4,5\alpha}$ and $J_{4,5\beta}$ suggest that the ring is nearly planar but with a slight tendency for $H_{5\beta}$ to assume a pseudoaxial configuration. This is confirmed by the relative magnitudes of $J_{3,5\alpha}$ and $J_{3,5\beta}$.[4-6,8] Using the Karplus relation[14] and the conformational dependence of allylic coupling constants,[4-6,8] one can estimate[15] that the deviation of the dihedral angle between H_5 and H_4 from 60° is in the range of 0.5–3.0°, which corresponds to puckered angles in the range 1–5°. Clearly, this line of reasoning and the analogous cases developed below assume the existence of a single energetically favored conformation. For the present purpose, the as-

Table I. NMR Parameters for Methyl 2,5-Dihydro-2-furoate (3) and 2,3-Diphenyl-2,5-dihydrofuran (4)

Parameter[a]	 (3)			 (4)	
Solvent	CCl_4[b]	Benzene-d_6[c]	Me_2SO-d_6[d]	CCl_4[d]	Benzene-d_6[d]
Concn, %	9.2	10.5	7.5	13.5	13.5
$\delta H_{5\alpha}$	4.649	4.404	4.622	4.731	4.649
$\delta H_{5\beta}$	4.767	4.636	4.678	4.814	4.718
δH_2	5.116	5.184	5.235	5.956	5.949
δH_3	5.808	5.552	5.931		
δH_4	6.024	5.467	6.186	6.298	6.103
$J_{5\alpha,5\beta}$	−13.00	−13.14	−13.20	−13.81	−13.84
$J_{2,5\alpha}$	+3.22	+3.31	+3.40	+3.21	+3.32
$J_{3,5\alpha}$	−2.45	−2.38	−2.46		
$J_{4,5\alpha}$	+1.69	+1.71	+1.74	+2.04	+2.10
$J_{2,5\beta}$	+6.40	+6.45	+6.28	+5.87	+5.65
$J_{3,5\beta}$	−2.61	−2.61	−2.60		
$J_{4,5\beta}$	+1.58	+1.61	+1.58	+1.78	+1.66
$J_{2,3}$	+1.87	+1.86	+1.88		
$J_{2,4}$	−2.46	−2.50	−2.49	−1.85	−1.86
$J_{3,4}$	+6.19	+6.13	+6.22		

[a] Chemical shifts (δ) are in parts per million from Me_4Si, coupling constants (J) are in hertz. The signs of the vicinal coupling constants were assumed to be positive, and the geminal and allylic coupling constants were assumed to be negative.[4] [b] The signs of $J_{2,5\alpha}$ and $J_{2,5\beta}$ and the relative chemical shifts of H-3 and H-4 were determined by spin-tickling experiments (see Experimental Section). [c] The unique computational solution, confirmed by spin-tickling (see Experimental Section). [d] The signs of $J_{2,5\alpha}$ and $J_{2,5\beta}$ were assumed by analogy to the results for 3 in CCl_4 and benzene-d_6.

sumption about the existence of a single energy minimum is useful because it makes it convenient to compare experimental and calculated values. For empirical purposes, i.e., structural work by direct comparison of experimental data, this assumption need not, of course, be made.

The pucker angle θ_P is here taken as the angle between the plane formed by C_2-O-C_5 and the plane formed by C_2—C_3═C_4—C_5. This angle is depicted in Figure 1. It is also possible to define a dihedral angle ϕ_P between the planes formed by O—C_2—C_3 and C_2—C_3—C_4 and, to a good approximation, the two are related by $\phi_P = 0.585\theta_P$.

The system **4** was synthesized in the hope that the nonbonding interaction between the two phenyl groups would be relieved by ring puckering in the sense which would make the phenyl group at C_2 pseudo-axial. The relative magnitudes of $J_{4,5\alpha}$ and $J_{4,5\beta}$ listed in Table I indeed show that they are further apart (0.26-0.44 Hz) than in the case of **3** (0.10-0.16 Hz) and, hence, that the ring is on the average puckered to a greater extent. A quantitative comparison between the two systems is probably not strictly justified because the absolute values of the smaller of the two vicinal coupling constants show a significant increase as well but, by simple proportionality, it seems reasonable to suggest that a distortion of up to 10° in the dihedral angle between H_4 and H_5 is observed if **4** exists as a single conformer.

The relative assignments of $H_{3\alpha}$ and $H_{3\beta}$ in the phthalan derivatives **2** could be made unequivocally on the basis of NOE results (compare entries 9 and 14, Table II) in the case of the *tert*-butyl derivatives **2d** and **2f**. The assignments in the remainder of the series are based on analogy with these compounds.

Study of molecular models suggested that large groups at C_1 would tend to assume pseudo-axial configuration to relieve nonbonded interactions with H_7. Indeed, entries 13-16 in Table II show that, while **2e** is on the average planar by symmetry (the benzylic coupling constants[4,5,14] $J_{3\alpha,4}$ and $J_{3\beta,4}$ are identical), this no longer holds for the *tert*-butyl derivative **2f**. The difference in $J_{3\alpha,4}$ and $J_{3\beta,4}$ in **2f**, while small (0.08 Hz), is quite real as special care was taken with the determination of these coupling constants (see Experimental Section). Moreover, this difference represents a significant proportion of the total range of values assumed by ortho-benzylic coupling constants[16,17] and suggests a distortion of the order of 5° from the geometry where the bond

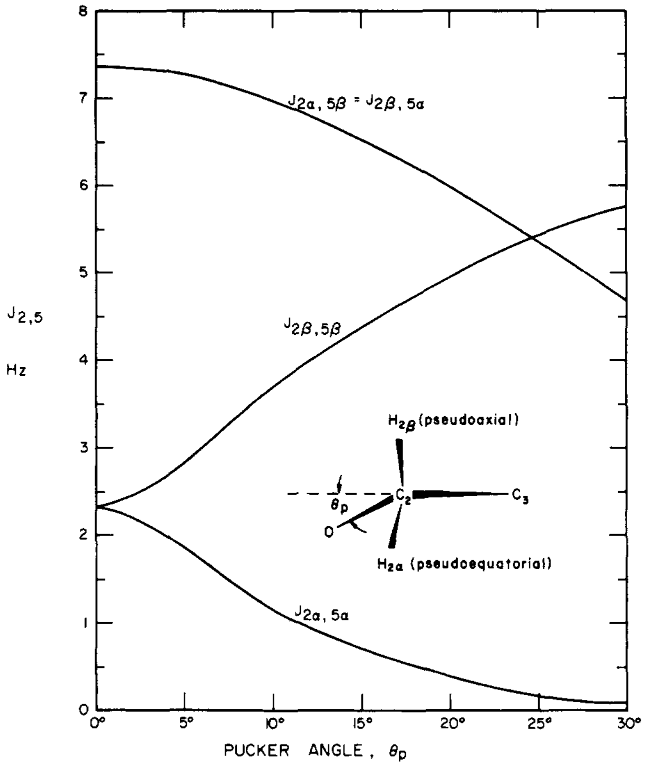


Figure 1. Plots of calculated values of $J_{2\alpha,5\beta} = J_{2\beta,5\alpha}$, $J_{2\alpha,5\alpha}$, and $J_{2\beta,5\beta}$ in 2,5-dihydrofuran (1, X = O) as functions of the pucker angle θ_P in the range 0-30°. The pucker angle and the H_α and H_β are defined schematically in the inset figure in which the C_2 and C_3 carbon atoms eclipse the C_5 and C_4 carbon atoms, respectively.

Table II. NMR Data for Phthalans

Entry	Compd	Solvent[a]	Concn w/v, %	Chemical shifts[b]						
				H_1	$H_{3\alpha}$	$H_{3\beta}$	H_4	H_7	OMe	Other
1	2a	$CDCl_3$	70.0	4.970	4.970	4.970	7.0–7.15 (m)			
2	2b	CCl_4	10.2	6.009	5.069	5.197	6.9–7.4 (m)			Ph, 7.21 (s)
3	2b	Benzene	9.8	6.068	4.969	5.102	6.5–7.5 (m)			Ph, 6.5–7.5 (m)
4	2b	$CDCl_3$	10.5	6.145	5.187	5.319	6.8–7.5 (m)			Ph, 7.30 (s)
5	2b	Acetone	10.3	6.105	5.114	5.282	6.9–7.5 (m)			Ph, 7.30 (s)
6	2b	Me_2SO	10.6	6.170	5.113	5.316	7.0–7.7 (m)			Ph, 7.34 (s)
7	2c	Benzene	11.5	5.188	4.849	4.956	6.7–7.2 (m)			Me, 1.367 (d)
8	2c	$CDCl_3$	10.2	5.304	5.018	5.111	7.0–7.3 (m)			Me, 1.487 (d)
9	2d	CCl_4	10.2	4.788	4.942	5.044	7.0–7.3 (m)			*t*-Bu, 0.94 (s)
10	2d	Benzene	9.6	4.890	4.883	4.970	6.75–7.15 (m)			*t*-Bu, 0.96 (s)
11	2d	$CDCl_3$	9.3	4.908	5.038	5.131	7.10–7.35 (m)			*t*-Bu, 0.96 (s)
12	2e	Benzene	9.3	6.163	5.046	5.172	6.389	6.413	3.21, 3.43	Ph, 7.0–7.5 (m)
13	2e	$CDCl_3$	11.5	6.105	5.141	5.278	6.783	6.503	3.76, 3.88	Ph, 7.31 (s)
14	2f	CCl_4	11.0	4.705	4.854	4.963	6.598	6.668	3.78	*t*-Bu, 0.93 (s)
15	2f	Benzene	12.5	4.929	4.925	5.008	6.361	6.704	3.44, 3.48	*t*-Bu, 1.04 (s)
16	2f	$CDCl_3$	11.0	4.856	4.984	5.080	6.719	6.783	3.88	*t*-Bu, 0.97 (s)

Entry	Coupling constants[c]									
	$J_{1,3\alpha}$	$J_{1,3\beta}$	$J_{1,4}$	$J_{1,7}$	$J_{3\alpha,3\beta}$	$J_{3\alpha,4}$	$J_{3\beta,4}$	$J_{3\alpha,7}$	$J_{3\beta,7}$	Additional
1	$\lvert J_{1,3\alpha} + J_{1,3\beta}\rvert = 4.3$									$J_{^{13}C-H_{benzylic}} = 147.1$
2	1.918	2.618			−12.16					
3	2.103	2.698			−12.24					
4	2.031[d]	2.662[d]			−12.24					
5	1.908	2.693			−12.35					
6	1.903	2.620			−12.48					
7	2.037	2.483			−12.16					$J_{CH_3,H_1} = 6.34$
8	1.962	2.413			−12.15					$J_{CH_3,H_1} = 6.41$
9	1.218[d]	3.094[d]			−12.21					NOE to *t*-Bu:$H_{3\alpha}$ + 2%; $H_{3\beta}$ + 10%; H_1 + 33%
10	1.209	3.047			−12.30					
11	1.090	3.050			−12.29					
12	2.114	2.987	*e*	*e*	−11.60	*e*	*e*	*e*	*e*	
13	2.208	3.044	0.45	−0.84	−11.60	−0.81	−0.80	0.45	0.45	
14	1.380	3.368	0.35	−0.68	−11.47	−0.69	−0.77	0.35	0.35	NOE to *t*-Bu:$H_{3\alpha}$ 0%; $H_{3\beta}$ + 38%; H_1 + 37%; H_7 + 18%
15	1.255	3.407	*f*	*f*	−11.51	*f*	*f*	*f*	*f*	
16	1.231	3.426	0.35	−0.71	−11.65	−0.71	−0.79	0.35	0.35	

[a] Benzene and Me_2SO refer to perdeuterio solvents. [b] In parts per million from Me_4Si, accurate to ±0.001 ppm; m, s, and d refer to multiplet, singlet, and doublet, respectively. All data are derived from 100-MHz spectra by iterative calculations (see Experimental Section). [c] In Hertz. Uncertainties are: $J_{1,3\alpha}$; $J_{1,3\beta}$; ±0.03 Hz; $J_{3\alpha,3\beta}$; $J_{1,4}$; $J_{3\alpha,7}$; $J_{3\beta,7}$; ±0.05 Hz; $J_{1,7}$; $J_{3\alpha,4}$; $J_{3\beta,4}$; ±0.01 Hz. [d] The signs of $J_{1,3\alpha}$ and $J_{1,3\beta}$ were shown by spin-tickling to be opposite in sign to $J_{3\alpha,3\beta}$ and thus presumably positive (see Experimental Section). [e] The proximity of the signals due to H_4 and H_7 did not permit determination of the benzylic coupling constants. [f] The complexity of the spectrum did not allow determination of the benzylic coupling constants.

C_4–H_4 bisects the methylene group at C_2. It is significant that $H_{3\alpha}$ is less strongly coupled to H_4 than $H_{3\beta}$ and is therefore pseudo-equatorial.[16,17] This makes the *tert*-butyl group on the average pseudo-axial as predicted on the basis of molecular models.

Calculation of Coupling Constants in 2,5-Dihydrofurans and Phthalans and Comparison with Experimental Results

Long-range H–H coupling constants $J_{2,5}$ in 2,5-dihydrofuran with varying degrees of ring puckering were calculated by means of the finite perturbation theory (FPT) formulation[18] for coupling constants in the semiempirical approximation of intermediate neglect of differential overlap (INDO). Standard molecular geometries[19] were used unless noted otherwise, in which case values were inferred from structurally similar molecules.[20] The H–C–H angle in 2,5-dihydrofuran was taken from the nematic liquid crystal results of Cole and Gilson.[12] It is interesting to note that this departure from tetrahedral does not have much effect on the calculated values as can be seen by comparing entries 1 and 2 in Table III. It should also be noted that the small differences between the result for planar geometry (item 2 in Table III) and that previously reported[2] are due to very small changes in the assumed geometry. The assumed bond lengths and bond angles are entered in footnote *a* of Table III. However, as the pucker angle was increased, it was necessary to decrease the C_2–O–C_5 and O–C–C bond angles to preserve the assumed bond lengths.

The calculated results for planar 2,5-dihydrofuran in Table III are in good agreement with the experimental results for the molecule[12,13] and for methyl 2,5-dihydrofuroate (Table I). The inherently larger trans $J_{2\alpha,5\beta}$ than cis $J_{2\alpha,5\alpha} = J_{2\beta,5\beta}$ H–H couplings were noted[3] in a detailed study of conformational effects on homoallylic coupling constants. This difference is greatly enhanced by substituent effects on the homoallylic couplings, especially in the case of coupling over a dual path.[2]

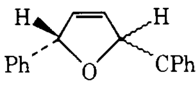
The effects of ring puckering on these long-range couplings are quite large as is indicated by the calculated results for entries 3–8 in Table III. These results are plotted

Table III. Calculated[a] Interproton Coupling Constants in 2,5-Dihydrofuran (1, X = O)

		Calculated long-range coupling constants, Hz				
Entry	Pucker angle, deg[b]	$J_{2\alpha,5\alpha}$	$J_{2\beta,5\beta}$	$J_{2\alpha,5\beta} = J_{2\beta,5\alpha}$	$J_{2\alpha,4} = J_{5\alpha,3}$	$J_{2\beta,4} = J_{5\beta,3}$
1	0	2.306	2.306	7.351	−1.595	−1.595
2[c]	0	2.368	2.368	7.562	−1.633	−1.633
3	5.002	1.801	2.846	7.275	−1.468	−1.717
4	5.478	1.742	2.913	7.257	−1.449	−1.734
5	10.051	1.119	3.703	6.957	−1.213	−1.947
6	15.027	0.689	4.368	6.521	−1.033	−2.100
7	19.999	0.375	4.951	5.955	−0.865	−2.227
8	29.95	0.057	5.774	4.650	−0.594	−2.411
9[d]	0	1.234		6.838	−0.511	
10[e]	0	1.361		6.994	−0.668	

[a] The molecular parameters used are: $r(C{=}C) = 1.337$, $r(C{-}C) = 1.54$, $r(C{-}O) = 1.43$, $r(C{-}H) = 1.09$, $r({=}C{-}H) = 1.08$ Å; $\angle C{=}C{-}C = 109$, $\angle C{-}O{-}C = 109.8$, $\angle H{-}C{-}H = 111.0°$. [b] The pucker angle is θ_p defined as the angle between the plane formed by $C_2{-}O{-}C_5$ and that of $C_2{-}C_3{=}C_4{-}C_5$ in 1. This is depicted schematically in Figure 1. Thus $H_{2\beta}$ and $H_{5\beta}$ tend to become pseudo-axial and $H_{2\alpha}$ and $H_{5\alpha}$ pseudo-equatorial. [c] $\angle H{-}C{-}H = 109.47°$. [d] 2β-hydroxy-2,5-dihydrofuran. The O—H bond is antiperiplanar to the C—O bond. [e] 2β-Hydroxy-2,5-dihydrofuran. The O—H bond is antiperiplanar to the $C_2{-}C_3$ bond.

in Figure 1 as functions of the pucker angle θ_p between 0 and 30°. The pucker angle is measured from the $C_2{-}O{-}C_5$ plane and the $C_2{-}C_3{=}C_4{-}C_5$ plane as depicted in Figure 1. From the figure, it is to be noted that the trans $J_{2\alpha,5\beta}$ coupling drops off as the H_α protons are moved pseudo-equatorially and the H_β protons become pseudoaxial. Furthermore, the cis coupling between the two pseudoaxial protons becomes greater and actually crosses that for the trans coupling near a pucker angle of 25°. The cis coupling associated with the pseudo-equatorial protons drops off rapidly to small values. The sense of the predicted change of $J_{2,5}$ with increased puckering is not inconsistent with that observed on comparing the data for compounds **3** and **4** in Table I, especially with regard to the decrease in $J_{2,5\beta}$. However, the changes are too small to consider them as a convincing verification of the calculated results—possibly the degree of puckering of **4** as compared with **3** is very slight (see above).



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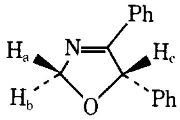

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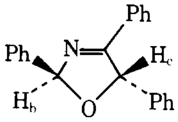
$J_{ac} = 3.20$

$J_{bc} = 5.59$



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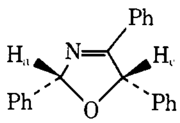
$J_{bc} = 5.5$



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$J_{ac} = 5.0$

Table IV. Calculated[a] Interproton Coupling Constants in Phthalan (2a)

	Calculated long-range coupling constants, Hz				
Pucker angle, deg[b]	$J_{1\alpha,3\alpha}$	$J_{1\beta,3\beta}$	$J_{1\alpha,3\beta} = J_{1\beta,3\alpha}$	$J_{1\alpha,4} = J_{3\alpha,4}$	$J_{1\beta,4} = J_{3\beta,4}$
0	0.524	0.524	4.284	−0.994	−0.994
5.002	0.276	0.812	4.232	−1.023	−0.964

[a] The molecular parameters used are: $r(C \overset{\cdots}{-} C) = 1.40$, $r(C{-}C) = 1.54$, $r(C{-}O) = 1.43$, $r(C{-}H) = 1.09$, $r({=}C{-}H) = 1.08$ Å; $\angle C{=}C{-}C = 107.3$; $\angle C{-}O{-}C = 109.8$, $\angle H{-}C{-}H = 111.0°$. [b] The pucker angle θ_p is defined as the angle between the plane formed by $C_1{-}O{-}C_3$ and the plane formed by the aromatic ring and the C_1 and the C_3 carbon atoms. Therefore, the situation is completely analogous to that depicted in Figure 1 for 2,5-dihydrofuran. As a consequence, $H_{1\beta}$ and $H_{3\beta}$ tend to become pseudo-axial and $H_{1\alpha}$ and $H_{3\alpha}$ pseudo-equatorial.

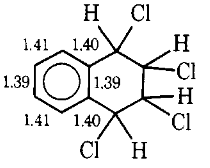
A much more convincing demonstration of the validity of the calculations listed in Table III can be found in the data for *cis*- and *trans*-2-phenyl-5-trityl-2,5-dihydrofurans (**7**), where $J_{2,5}$ in *both* isomers has been reported[21] to be 6.2 Hz. The value for the trans isomer is unexceptional, but that for the cis isomer is by far the largest cis $J_{2,5}$ coupling constant in any 2,5-dihydrofuran derivative. While the NMR data reported[21] are not in themselves detailed enough[22] to allow any deductions regarding the conformation of the cis isomer of **7**, inspection of molecular models shows that there is a severe crowding between the trityl and the phenyl groups. The latter are forced to take up pseudo-equatorial conformations leaving the protons at C_2 and C_5 pseudo-axial. This conformation corresponds to $J_{2\beta,5\beta}$ in Figure 1 for a high degree of puckering, and it can be seen that there is good agreement between the calculated and experimental values.

A similar trend can be observed in the recently reported data[23] for several series of 3-oxazolines, which are of course isoelectronic with 2,5-dihydrofurans. Results for compounds **8–10** are typical.[23] It can be seen that both values of $J_{2,5}$ in **8**, which should exist in an average conformation very similar to 2,3-diphenyl-2,5-dihydrofuran (**4**), are in fact almost identical with those shown in Table I, but $J_{2,5}$ in the cis isomer **10** where the steric repulsion between the *cis*-phenyl groups at C_2 and C_5 becomes severe is considerably elevated.

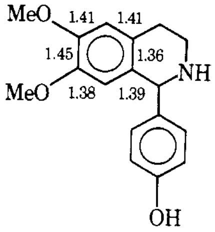
Where -OMe or -OAc groups are attached to C_2 and/or C_5 in derivatives of 2,5-dihydrofurans, the magnitudes of $J_{2,5}$ and $J_{2,5'}$ in **1** (X = O) become considerably reduced[2,11] with the cis ($J_{2,5}$) coupling becoming very small. It seems unlikely that this is primarily due to a severe steric distortion (e.g., the assumption of pseudo-diaxial conformation by the two acetoxy groups in **6** because the effect is almost identical for the cis and the trans isomers, taking either 2,5-dihydrofuran[12,13] or methyl 2,5-dihydrofuroate (Table I) as the base compound. It is much more probable that the effect is electronic in nature, and this was tested by performing calculations on the two most probable conformations of 2-hydroxy-2,5-dihydrofuran (Table III, entries 9 and 10). It can be seen that a very marked decrease of both long-range coupling constants is predicted and that it is essentially independent of the detailed conformation of the oxygen lone pairs. It therefore appears that the INDO-FPT treatment correctly predicts all so far observed steric and electronic effects on $J_{2,5}$ in 2,5-dihydrofurans.

Long-range interproton coupling constants in planar and 5° puckered phthalan calculated in the same manner as those for 2,5-dihydrofuran are shown in Table IV. The calculated values reproduce correctly the signs and relative magnitudes of $J_{1,3\alpha}$ and $J_{1,3\beta}$ in monosubstituted phthalans **2a–2f** (Table II), although the numerical agreement is somewhat inferior to that shown by 2,5-dihydrofurans. The experimental trends associated with the puckering of the ring, i.e., a decrease in $J_{1\alpha,3\alpha}$ and a somewhat smaller increase in $J_{1\alpha,3\beta}$ are only partially reproduced by the calculated values.

It is possible that this imperfect agreement is due to the expected[2] sensitivity of long-range coupling to the bond order (and hence bond length) of the aromatic bond. An experimental indication of this effect may be seen in the small, but significant, increases in the values of $J_{1,3\alpha}$ and $J_{1,3\beta}$ in **2** associated with the introduction of the two methoxyl groups at C_5 and C_6 (compare entries 3, 4, 12, 13, and 10, 11, 15, 16 in Table II). This cannot be due to an electronic effect of the substituent because, in a series of 6-substituted 1-phenylphthalans investigated by Fraser,[24] no such changes have been noted even though the substituents at C_6 span most of the usual Hammett range. On the other hand, one would expect that both steric and electronic repulsion between the two methoxyl groups would lead to a lengthening of the C_6–C_7 bond and a consequent shortening of the bond-forming part of the five-membered ring. Just such an effect of two vicinal groups on molecular geometry may be seen in a comparison of the lengths of aromatic bonds in a typical tetrahydronaphthalene derivative **11**[25] and the alkaloid coclaurine[26] **12**. Clearly, accurate diffraction data for compounds more closely related to phthalans would be desirable but appear to be unavailable.



11



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Conclusions

The combination of empirical and theoretical data presented above should enable the structural chemist to use the magnitudes of long-range coupling constants across a double path in 2,5-dihydrofurans and phthalans to obtain information about their stereochemistry, but no simple universally applicable correlations emerge. Clearly, as with many applications of the Karplus relationship, either the configuration or the conformation must be derived from independent data or analysis.

The temptation to extend the trends observed here for **1** (X = O) (and its benzo analog, phthalan) to systems where the second path is *not* via oxygen should be resisted. We have noted previously[2] that not only the magnitudes of the long-range coupling constants but also the predictive value of our calculations may alter with the nature of X. Since then, a number of results[13,27,28] confirmed the need for separate studies of each system as the nature of the group X changes.

On the other hand, the data for oxazolines,[21,29] where an sp^2 hybridized nitrogen atom has been substituted for one of the sp^2 hybridized carbons in a 2,5-dihydrofuran, suggest that these systems are very closely analogous. However, Joseph-Nathan, Garcia, and Diaz[30] report that the substitution of an $-N{=}N-$ moiety for the $-C{=}C-$ moiety in a rigid cyclopentane derivative[2] causes sign inversion of the long-range coupling constants. Besides the values for long-range coupling constants across the dual path, Tables III and IV also list the values for allylic and benzylic coupling constants, respectively. The magnitudes and steric dependence[8] of the allylic coupling constants in 2,5-dihydrofuran are of the right order of magnitude but appear to be somewhat underestimated. It seems unlikely than an improvement on the INDO–FPT scheme, such as the one described in ref 8, would be of help in this case. Comparison of entry 1 with entries 9 and 10 in Table III clearly shows that the effect of an additional electronegative substituent is of the same type as that observed experimentally. For example, compare the data for 2,5-diacetoxy-2,5-dihydrofurans[11] **5** and **6** with those for 2,5-dihydrofuran itself[13] or with those for methyl 2,5-dihydrofuroate (**3**).

The calculated values for *o*-benzylic coupling in phthalan in Table IV are consistent with a π-electron mechanism for this type of coupling in toluene based on the valence bond[31,32] method ($^4J^{\pi}{}_{HH'} = -1.45 \sin^2 \phi$, where ϕ is the angle measured from the plane of aromatic ring), an LCAO–MO treatment[33] with configuration interaction in the triplet manifold, and with the all-valence electron INDO–FPT description.[17] The calculated *o*-benzylic coupling constants are in good agreement with the experimental results for items 13, 14, and 16 in Table II.

Experimental Section

Analysis of NMR Spectra. Light petroleum refers to fraction bp 55–65°. Melting points were determined on a Koffler block and are uncorrected. Infrared and ultraviolet spectra were recorded on a Perkin-Elmer 221 and Perkin-Elmer 4000A spectrophotometers and mass spectra on an AEI-MS-9 spectrometer. Proton NMR spectra were recorded on a Varian Associates HA-100D or XL-100 spectrometers. Unless otherwise stated, NMR data were obtained by first-order analysis in cases where all $\Delta\nu/J$ ratios were larger than 6 or by iterative computer analysis using LAOCN3[34] or LAME[35] programs executed on an IBM 7040 computer. Unless otherwise stated, the parameters listed are believed to be significant to better than ±3 in the last place quoted. Chemical shifts (δ) are given in parts per million from internal Me_4Si and coupling constants (J) in hertz.

Microanalyses were performed by the Australian Microanalytical Service, Melbourne.

Analytical gas–liquid chromatography (GLC) was carried out either on a Hewlett-Packard F & M 400 or F & M 402 instrument using 1.75 m × 3 mm i.d. columns packed as indicated and helium as the carrier gas. Preparative GLC was performed either on a Hewlett-Packard Prepmaster Jr. 776 or an instrument constructed in these laboratories employing a gas-density detector. The columns used were 20 or 25 mm i.d. and 1.2 or 2.4 m long. Nitrogen was used as the carrier gas.

General Procedure for Determination of Signs in Multispin Systems. Spin-tickling was chosen as the method of determining the relative signs[36] of coupling constants in compounds whose NMR spectra were analyzed in the course of this work. The principles of the method has been fully described,[36] but the great majority of sign determinations described in the literature refers to lightly coupled three-spin systems, and no general procedure for determinations of signs in systems of four or five nuclei is available. Since spin-tickling was used in a number of analyses described in this work, including four and five-spin systems, it may be useful to describe briefly a general method of arriving at computational solutions which are unique with respect to relative signs of coupling constants with the aid of spin-tickling. Complete analyses of the spectra were achieved using the following steps.

(i) In the noniterative part of the LAOCN3 or LAME analysis,[34,35] the signs of geminal, vicinal, allylic, etc., coupling constants which are well documented[3-5,14] are inserted, and the signs of all other coupling constants are varied in all possible combinations. Thus the number of noniterative analyses performed is generally equal to the number of possible combinations of signs of coupling constants being investigated although, for more strongly coupled systems, some combinations of signs can, of course, be excluded at this stage.

(ii) For each combination, the transitions are assigned, and the iterative portion of the program is carried out in the usual manner.[34,35] At this stage, it was often found that some combinations of signs lead to divergence (failure to iterate) or unreasonably large rms errors which could not be reduced by changing the absolute magnitudes of the initial parameters. It must be noted that the criterion for failure in such cases is not an arbitrary limit (say >0.2 Hz) set on the rms error but rather the observation of a significant number of errors in line positions which are clearly beyond the experimental error of measurement.

(iii) The remaining solutions, which typically do not differ significantly either in rms errors or in the absolute magnitudes of the NMR parameters, are then tabulated separately listing the calculated frequency and transition number for each transition. It is almost always found that all transitions in all solutions can be matched (and, of course, can be matched to the experimental spectrum), but that the transition numbers assigned to them in the various solutions differ.

(iv) The transition numbers available from the output of the LAOCN3 or LAME[34,35] correspond in a simple fashion to a convenient representation of the energy-level diagram, which permits the identification of unconnected, regressively connected, and progressively connected transitions by inspection.[37]

(v) Pairs of connected transitions can then be identified[36] by tickling experiments, care being taken to irradiate a single transition, i.e., one as well removed as possible from its neighbors. This can be clearly done using several transitions in turn and leads to an unequivocal choice of a unique solution in all but a few cases, generally those where some coupling constants are vanishingly small.

A convenient method involved listing the transition numbers for all permissible solutions directly under the experimental spectrum and marking out suitable pairs of connected nuclei before commencing spin-tickling.

Phthalan (2a) was prepared by a previously described procedure[38] as a colorless fluorescent oil, bp 105° (50 mm) [lit.[38] bp 85° (20 mm)]. The ^{13}C satellite spectrum of the signal assigned to the benzylic protons (Table II, entry 1), obtained with decoupling of aromatic protons, consisted of a pair of triplets of total width 4.3 ± 0.1 Hz each. The analysis of this type of spectrum has been extensively discussed[39] and, if one assumes that $J_{1,3\alpha}$ and $J_{1,3\beta}$ are both positive by analogy with the remaining phthalan derivatives studied in this series (see Table II and below), this spacing corresponds to the sum of the two coupling constants. Unfortunately, the difference between them, which should correspond to the spacing between the strong outer lines of the inner group,[39] could not be determined accurately. Judging by the width of the middle component of the triplet compared with the natural width of lines in this spectrum, the difference between the two coupling constants is about 0.6 Hz, which leads to the not unreasonable values of approximately 1.85 and 2.45 Hz.

1-Phenylphthalan (2b). Reduction of *o*-benzoylbenzoic acid with lithium aluminum hydride[40] gave α-phenyl-*o*-xylene-α,α'-diol as colorless crystals: mp 73-75° (lit.[40] mp 76°); NMR ($CDCl_3$, 10% w/v) δ 4.1 (2 H, broad, exchange with D_2O, 2 × OH), 4.30, 4.41 (2 H, AB quartet, $J_{AB} = -12.5$ Hz, $-CH_2-$), 5.87 (1 H, s, methine), 7.1-7.4 (9 H, m, HAr). Treatment of this material (10 g) with orthophosphoric acid (50%, 100 ml) for 2 hr at 100° followed by distillation gave 1-phenylphthalan (**2b**) as a colorless oil (5.4 g), bp 122-123° (1.1 mm), which crystallized on cooling to a solid, mp ~25° [lit.[40] mp 35° (bp 164° (15 mm)]. The portion of the NMR spectrum of **2b** in $CDCl_3$ (Table II, entry 4) assigned to H_1, $H_{3\alpha}$, and $H_{3\beta}$ formed a clear 12-line pattern after irradiation of the aromatic protons. The fit of the iterative analysis[34] of this spectrum was independent (rms error in each case was 0.009 Hz) of the signs of the two long-range coupling constants; i.e., taking $J_{3\alpha,3\beta}$ as negative,[4,14] all four possible sign combinations for $J_{1,3\alpha}$ and $J_{1,3\beta}$ (++, −−, +−, and −+) gave acceptable solutions with very similar sets of absolute values for all output parameters. Tickling experiments (see above—triple irradiation was involved as decoupling of the aromatic protons had to be maintained) readily eliminated all but the first possibility, to give the results listed in Table II, entry 4. The NMR spectra of **2b** in other solvents (Table II, entries 2, 3, 5, and 6) were analyzed by the iterative procedures,[34] the signs of long-range coupling constants being taken as positive.

1-Methylphthalan (2c). Reduction of *o*-acetylbenzoic acid with lithium aluminum hydride[38] gave α-methyl-*o*-xylene-α,α'-diol as colorless crystals: mp 64-66° (lit.[38] mp 66-67°); NMR ($CDCl_3$, 10% w/v) δ 1.42 (3 H, d, $J_{Me,H} = 6.5$ Hz, -Me), 4.1 (2 H, broad, exchange with D_2O, 2 × OH), 4.46, 4.57 (2 H, AB quartet, $J_{AB} = -12.5$ Hz, $-CH_2-$), 4.98 (1 H, q, $J_{Me,H} = 6.5$ Hz, methine), 7.1-7.6 (4 H, m, HAr). Treatment of this material (10 g) with orthophosphoric acid (50%, 100 ml) for 2 hr at 100° followed by distillation gave 1-methylphthalan (**2c**) as a colorless fluorescent oil, bp 94-95° (25 mm) [lit.[38] bp 82-83° (13 mm)].

The NMR spectra of **2c** in deuteriobenzene and deuteriochloroform with decoupling of aromatic protons (Table II, entries 7 and 8) were analyzed as $ABCD_3$ systems by the iterative procedure,[34] the signs of the long-range coupling constants ($J_{1,3\alpha}$ and $J_{1,3\beta}$) being taken to be positive.

1-*tert*-Butylphthalan (2d). Phthalic anhydride (20 g) was added in small portions to a solution of *tert*-butylmagnesium chloride [from magnesium (12 g) and *tert*-butyl chloride (55 ml)] in ether. After the addition was completed, the mixture was refluxed for 4 hr then stirred overnight. After acidification, the ether layer was separated and extracted with aqueous sodium carbonate solution which was then acidified and extracted with ether. Removal of the ether yielded *o*-pivaloylbenzoic acid (17 g) as white crystals, mp 116-118° (lit.[41] mp 118°). This material (17 g) in dry tetrahydrofuran (250 ml) was added dropwise, with stirring, to lithium aluminum hydride (9.0 g) in dry tetrahydrofuran (500 ml). The mixture was refluxed for 2 hr then stirred overnight. Work-up gave α-*tert*-butyl-*o*-xylene-α,α'-diol as an oil (15 g) which was not further purified: NMR ($CDCl_3$, 10% w/v) δ 0.87 (9 H, s, CMe_3), 3.7 (2 H, broad, exchange with D_2O, 2 × OH), 4.50 (1 H, s, methine), 4.55, 4.70 (2 H, AB quartet, $J_{AB} = -13$ Hz, $-CH_2-$), 7.0-7.5 (4 H, m, HAr). The purity, determined by NMR, was >90%.

This material (13 g) was heated on a steam bath with orthophosphoric acid (50%, 140 ml) for 2 hr with occasional shaking. The mixture was cooled and worked up to yield a red oil. Distillation afforded a fraction (5.4 g), bp 138-142° (28 mm), of a colorless fluorescent oil which consisted (by GLC, W-98, 92°) of a 3:1 mixture of two compounds, retention times 6.5 and 7.5 min, respectively. The components were separated by preparative GLC (W-98, 103°). The major component, a colorless oil, was identified as 1-*tert*-butylphthalan (**2d**): ν_{max} (CCl_4) 1480, 1460, 1397, 1366, 1055, 1035 cm^{-1}; λ_{max} (hexane) 259.5 nm (ϵ 520), 262 (555), 264 (680), 266 (700), 269.5 (500), 272.5 (740), 277.5 (94).

Anal. Calcd for $C_{12}H_{16}O$: C, 81.8; H, 9.2. Found: C, 81.7; H, 9.3.

The minor component, a colorless liquid, was identified as 3,3,4-trimethylisochroman: ν_{max} (CCl_4) 1490, 1455, 1445, 1385, 1375 cm^{-1}; λ_{max} (hexane) 258.5 nm (ϵ 355), 260.5 (360), 263.5 (375), 265 (415), 272 (430); NMR ($CDCl_3$, 5% w/v) δ 1.24, 1.30 (2 × 3 H, s, 2 × C-3 CH_3), 1.28 (3 H, d, $J_{CH_3,H_4} = 7.0$ Hz, C-4, CH_3), 2.69 (1 H, q, $J_{CH_3H_4} = 7.0$ Hz, H4), 5.85 (2 H, s, CH_2), 6.85-7.45 (4 H, m, HAr).

Anal. Calcd for $C_{12}H_{16}O$: C, 81.8; H, 9.2. Found: C, 81.4; H, 9.3.

The NMR spectrum of 1-*tert*-butylphthalan (**2d**) in CCl_4 (10.2% w/v) was analyzed as a three-spin system (after decoupling of aromatic protons) by the procedure outlined above. Three acceptable solutions were found for the combinations of signs of $J_{1,3\alpha}$ and $J_{1,3\beta}$ (++, −−, +−), the fourth possible solution (−+) being incompatible with the experimental spectrum. Spin-tickling (see above) readily identified the first solution as the only correct one and the relative assignments of $H_{3\alpha}$ and $H_{3\beta}$ were made on the basis of a very significant positive nuclear Overhauser effect (entry 9, Table II). The NMR spectra of **2d** in deuteriobenzene and deuteriochloroform (entry 10 and 11, Table II) were analyzed by the iterative procedure[34] with decoupling of aromatic protons, the signs of long-range coupling constants being assumed to be positive by analogy.

5,6-Dimethoxy-1-phenylphthalan (2e). Veratric acid (32 g) was heated for 7 hr at 60-70° with formaldehyde solution (30%, 230 ml) which had previously been saturated with hydrogen chloride at ~15°. The mixture was then stirred overnight, concentrated in vacuo, and then water (100 ml) was added. The resulting mixture was neutralized with aqueous ammonia and 5,6-dimethoxyphthalide precipitated out as white crystals, mp 157-158° (lit.[42] mp 154-156°): NMR ($CDCl_3$, 9.5% w/v) δ 3.94, 3.99 (2 × 3 H, s, 2 × OCH_3), 5.22 (2 H, s, CH_2), 6.94 (1 H, s, H_4), 7.28 (1 H, s, H_7).

This material (37 g) was treated with a solution of potassium permanganate (30 g) and sodium carbonate (18 g) in water (900 ml). When the purple color had disappeared, the solution was filtered and the filtrate acidified and concentrated to give 4,5-dimethoxyphthalic acid (30.6 g) as white crystals, mp 200-202° (lit.[42] 206°).

This material (19 g) was heated for 1 hr with acetic anhydride. The acetic anhydride was distilled to yield 4,5-dimethoxyphthalic anhydride (15 g) as long needles, mp 181-182° (sublimes at ~170°) (lit.[42] mp 175-177°).

Phenylmagnesium bromide [from bromobenzene (12.5 g) and magnesium (3.3 g)] in ether, was added dropwise, with stirring, to a solution of 4,5-dimethoxyphthalic anhydride (13.25 g) in refluxing anhydrous benzene. A precipitate formed immediately and, after the addition was completed, the mixture was refluxed for 2 hr, cooled, and worked up. The combined organic layers were extracted with aqueous sodium carbonate solution which, upon acidification, yielded 2-benzoyl-4,5-dimethoxybenzoic acid as colorless needles (8.9 g): mp 203-204° (benzene); ν_{max} ($CHCl_3$) 3600-2400 (broad), 1722, 1688, 1598, 1580, 1515, 1460, 1445, 1355, 1285, 1180 cm^{-1}; λ_{max} (EtOH) 249.5 nm (ϵ 22,200), 255 (21,700), 288 (6000); NMR ($CDCl_3$; 10% w/v) δ 3.87, 3.94 (2 × 3 H, s, 2 × OCH_3), 6.83 (1H, s, H3), 7.53 (1H, s, H6), 7.2-7.8 (5H, m, phenyl).

Anal. Calcd for $C_{16}H_{14}O_5$: C, 67.1; H, 4.9. Found: C, 67.4; H, 5.0.

2-Benzoyl-4,5-dimethoxybenzoic acid (8.9 g) in tetrahydrofuran (250 ml) was added dropwise, with stirring, to lithium aluminum hydride (2.5 g) in anhydrous tetrahydrofuran (150 ml). After the addition was complete, the mixture was refluxed for 2 hr and then stirred overnight. Work-up gave 4,5-dimethoxy-α-phenyl-1,2-xylene-α,α'-diol (9.0 g) as white crystals: mp 90-91°; ν_{max} ($CHCl_3$) 3610, 3450 (broad), 1610, 1519, 1464, 1452, 1280, 1100, 1013 cm^{-1}; λ_{max} (EtOH) 216 nm (ϵ 31,200); 236 (10,800), 279 (2830), 282 (2920), 285.5 (2750); NMR ($CDCl_3$, 10% w/v) δ 3.69, 3.78 (2 × 3 H, s, 2 × OCH_3), 3.8 (2 H, broad, exchanges in D_2O, 2 × OH), 4.33, 4.48 (2 H, AB quartet, $J_{AB} = -12.5$ Hz, -CH_2-), 5.87 (1 H, s, methine), 6.72, 6.80 (2 × 1 H, s, H_3 and H_6), 7.27 (5 H, s, phenyl).

Anal. Calcd for $C_{16}H_{18}O_4$: C, 70.1; H, 6.6. Found: C, 70.2; H, 7.0.

This material (3 g) was heated on a steam bath with orthophosphoric acid (50%, 20 ml) for 2 hr, with occasional shaking, cooled, and worked up to give a red oil. Chromatography on alumina eluted 5,6-dimethoxy-1-phenylphthalan (**2e**) in benzene as colorless crystals (1.1 g): mp 50-51° (pentane-ether); ν_{max} ($CHCl_3$) 1614, 1504, 1463, 1453, 1337, 1290, 1104, 1040, 1027 cm^{-1}; λ_{max} (cyclohexane) 276 nm (ϵ 2240), 281.5 (2960), 285 (3340), 291 (3180), 296 (2160).

Anal. Calcd for $C_{16}H_{16}O_3$: C, 75.0; H, 6.3. Found: C, 75.3; H, 6.4.

The NMR spectra of 5,6-dimethoxy-1-phenylphthalan (**2e**) in deuteriobenzene and deuteriochloroform (entries 12 and 13, Table II) were analyzed by the iterative procedure[34] with either (i) decoupling of the phenyl resonance, (ii) the phenyl resonance and that assigned to H_4, and (iii) the phenyl resonance and that assigned to H_7. No sign determinations were carried out, it being assumed by analogy that $J_{1,3\alpha}$ and $J_{1,3\beta}$ were positive, ortho-benzylic coupling constants negative, and meta-benzylic coupling constants positive.[4,5,14,16,17]

1-*tert*-Butyl-5,6-dimethoxyphthalan (2f). *tert*-Butylmagnesium chloride [from magnesium (6 g) and *tert*-butyl chloride (27 ml)] in ether was added dropwise, with stirring, to a solution of 4,5-dimethoxyphthalic anhydride (see above) (14 g) in refluxing anhydrous benzene. After the addition was completed, the mixture was stirred overnight at room temperature and then worked up. The combined organic layers were extracted with aqueous sodium carbonate solution which, upon acidification, yielded 2-pivaloyl-4,5-dimethoxybenzoic acid (9.5 g) as colorless crystals: mp 75-77° (benzene-light petroleum); ν_{max} ($CHCl_3$) 3580, 3450 (broad), 1755, 1660, 1497, 1468, 1460, 1310, 1153, 1110, 1075, 1027 cm^{-1}; λ_{max} (EtOH) 223.5 nm (ϵ 13,000), 261.5 (4000), 295 (2820), 300.0 (2700); NMR ($CDCl_3$, 10% w/v) δ 1.09 (9 H, s, CMe_3), 3.91, 3.98 (2 × 3 H, s, 2 × OCH_3), 6.99 (1 H, s, H_7), 7.16 (1 H, s, H_4).

Anal. Calcd for $C_{14}H_{18}O_5$: C, 63.1; H, 6.8. Found: C, 63.1; H, 6.6.

The organic layer remaining after extraction with sodium carbonate solution was dried and the solvent removed to yield a yellow oil which crystallized on standing. This product was identified as 3-*tert*-butyl-5,6-dimethoxyphthalide, colorless needles (3.9 g): mp 140-141° (methanol); ν_{max} ($CHCl_3$) 1750, 1602, 1503, 1468, 1333, 1287, 1135, 1070, 1034, 989 cm^{-1}; λ_{max} (EtOH) 224 nm (ϵ 30,200), 259 (9200), 295 (6850), 299.5 (6650); NMR ($CDCl_3$, 10% w/v) δ 1.00 (9 H, s, CMe_3), 3.91, 3.96 (2 × 3 H, s, 2 × OCH_3), 5.02 (1 H, s, H_3), 6.90 (1 H, s, H_4), 7.27 (1 H, s, H_7).

Anal. Calcd for $C_{14}H_{18}O_4$: C, 67.2; H, 7.3. Found: C, 67.3; H, 7.4.

A solution of 2-pivaloyl-4,5-dimethoxybenzoic acid (9.5 g) and 3-*tert*-butyl-5,6-dimethoxyphthalide (3.9 g) in tetrahydrofuran (300 ml) was added dropwise, with stirring, to a suspension of lithium aluminum hydride (4.0 g) in tetrahydrofuran (300 ml). After the addition was complete, the mixture was refluxed for 2 hr and then stirred overnight. Work-up gave α-*tert*-butyl-4,5-dimethoxy-1,2-xylene-α,α'-diol as colorless crystals (9.0 g): mp 118.5-119.5°; ν_{max} ($CHCl_3$) 3615, 3470 (broad), 1610, 1512, 1460, 1265, 1100, 1094 cm^{-1}; λ_{max} (EtOH) 234.5 nm (ϵ 10,000), 278.5 (2650), 282 (2720), 286 (2570). NMR ($CDCl_3$, 10% w/v) δ 0.90 (9 H, s, CMe_3), 3.05 (2 H, broad, exchange with D_2O, 2 × OH), 3.84 (6 H, s, 2 × OCH_3), 4.39, 4.66 (2 H, AB quartet, $J_{AB} = -12$ Hz, -CH_2-), 4.59 (1 H, s, methine), 6.85, 6.99 (2 × 1 H, s, H_3 and H_6).

Anal. Calcd for $C_{14}H_{22}O_4$: C, 66.1; H, 8.7. Found: C, 66.3; H, 8.8.

The material (9 g) was heated, on a steam bath, with orthophosphoric acid (50%, 60 ml) for 2 hr, shaking occasionally. After cooling, work-up yielded a red oil. Chromatography on alumina gave 1-*tert*-butyl-5,6-dimethoxyphthalan (**2f**), eluted with benzene-light petroleum (1:1) as a colorless oil (3.5 g) which could not be crystallized: ν_{max} ($CHCl_3$) 1609, 1500, 1459, 1348, 1275, 1100, 1056 cm^{-1}; λ_{max} (EtOH) 232.5 nm (ϵ 2350), 278 (3130), 283 (3820), 287 (4100), 291 (3820), 296 (2350). The NMR spectra of 1-*tert*-butyl-5,6-dimethoxyphthalan (entries 14-16, Table II) were analyzed in a manner analogous to that used for 1-phenyl-5,6-dimethoxyphthalan.

Anal. Calcd for $C_{14}H_{20}O_3$: C, 71.2; H, 8.5. Found: C, 69.9; H, 8.5.

Methyl 2,5-Dihydro-2-furoate (3). A sample of 2,5-dihydro-2-furoic acid kept under refrigeration since the original investigation[9] (300 mg) in ether (10 ml) was treated dropwise with an ethereal solution of diazomethane until the yellow color just persisted. The ether was washed with water, dried, and removed in vacuo to yield methyl 2,5-dihydro-2-furoate (**3**) as a yellow oil which was better than 95% pure by NMR and whose NMR spectrum was identical with that previously obtained.[9]

The NMR spectrum of **3** in CCl_4 (9.2% w/v) consisted of a singlet (δ 3.68, 3 H intensity, -OMe) and a five-spin multiplet for the ring protons. The analysis of this spectrum involved not only the determination of the relative signs of $J_{2,5\alpha}$ and $J_{2,5\beta}$ but also the relative assignments of H_3 and H_4. The known[14] relative signs of allylic (negative) and vicinal (positive) coupling constants were used to distinguish between the last two possibilities which thus increased the number of initial analyses to eight. However, all solutions with $J_{2,5\alpha}$ and $J_{2,5\beta}$ of different signs ($+-$ or $-+$) failed to converge, and spin-tickling experiments clearly differentiated between the four remaining solutions to give the results quoted in Table I.

The analysis of the NMR spectrum of **3** in deuteriobenzene utilized the thus obtained knowledge of the relative magnitudes of allylic and vicinal coupling constants (for example, that the absolute magnitude of $J_{2,4}$ is larger than that of $J_{2,3}$) and, of course, the known signs of vicinal, geminal, and allylic coupling constants. It was found that only the solution with $J_{2,5\alpha}$ and $J_{2,5\beta}$ positive converged in the iterative step, and this result was further confirmed by tickling experiments.

The analysis of the NMR spectrum of **3** in Me_2SO-d_6 was carried out utilizing the results for sign determinations in the other solvents (see footnote *d*, Table I).

2,3-Diphenyl-2,5-dihydrofuran (4) was prepared by a previously reported procedure[10] as colorless crystals, mp 78-79° (lit.[10] mp 79-80°). The NMR spectra in CCl_4 and benzene-d_6 (Table I) were analyzed using LAOCN3,[34] the signs of $J_{2,5\alpha}$ and $J_{2,5\beta}$ being assumed to be positive by analogy with methyl 2,5-dihydro-2-furoate.

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Conformational Analysis. CVIII. The Calculation of the Structures and Energies of Alkanethiols and Thiaalkanes by the Molecular Mechanics Method[1,2]

Norman L. Allinger* and Mary James Hickey

Contribution from the Departments of Chemistry, University of Georgia, Athens, Georgia 30602, and Wayne State University, Detroit, Michigan 48202.

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Abstract: The molecular mechanics method has been extended to include thiols and thioethers. Compounds studied include simple alkane derivatives, cyclic compounds, and bicyclic compounds, including rather strained ones. Bond lengths, bond angles, dihedral angles, rotational barriers, and heats of formation are all calculated and, in general, the agreement with the available experimental evidence is good.

The molecular mechanics or force field method is a semiempirical method for use in the calculation of geometries and energies of molecules.[3,4] The method has been shown to be a very fast, efficient way of determining these quantities, usually with good accuracy. It has been extensively applied by us in a consistent way to hydrocarbons[5,6] and less extensively to a few other classes of compounds including alkenes,[7] ketones,[8] silanes,[9] and conjugated systems.[10] The present work is an extension to simple sulfur compounds.

The force field developed herein is that described earlier,[5] with appropriate additions to deal with the sulfur atom. The necessary constants are given in Table IX. A few points are worth further discussion here.

As was discussed earlier with hydrocarbons,[5] it was advantageous to parameterize the force field so that rotational barriers calculated by minimization of the energies at both the minimum and maximum points on the rotational curve come out to be slightly lower than the experimental values. This is because the normal coordinate corresponding to the rotation which is measured experimentally does not allow for bond stretching and angle bending, which will occur when the energy is minimized. The stretching and bending force constants used were initially taken from the literature. In order to fit available structural information, it was necessary to reduce the bending constant by about 50%, for reasons previously described.

On the whole, the C–X stretching constants are about ¾ as large as the corresponding S–X constants, while the bending constants involving sulfur are somewhat larger than those corresponding ones in hydrocarbons. The sulfur compounds therefore tend to stretch more and bend less than do the corresponding hydrocarbons.

The van der Waals properties used for sulfur require comment. Since there are lone pairs of electrons on sulfur,