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Products from Furans. 3.[1] Crystal and Molecular Structure, Proton Nuclear Magnetic Resonance, and Conformational Studies of 2-Aryl-Substituted 2-Methyl-6-hydroxy-2*H*-pyran-3(6*H*)-one Derivatives[2]

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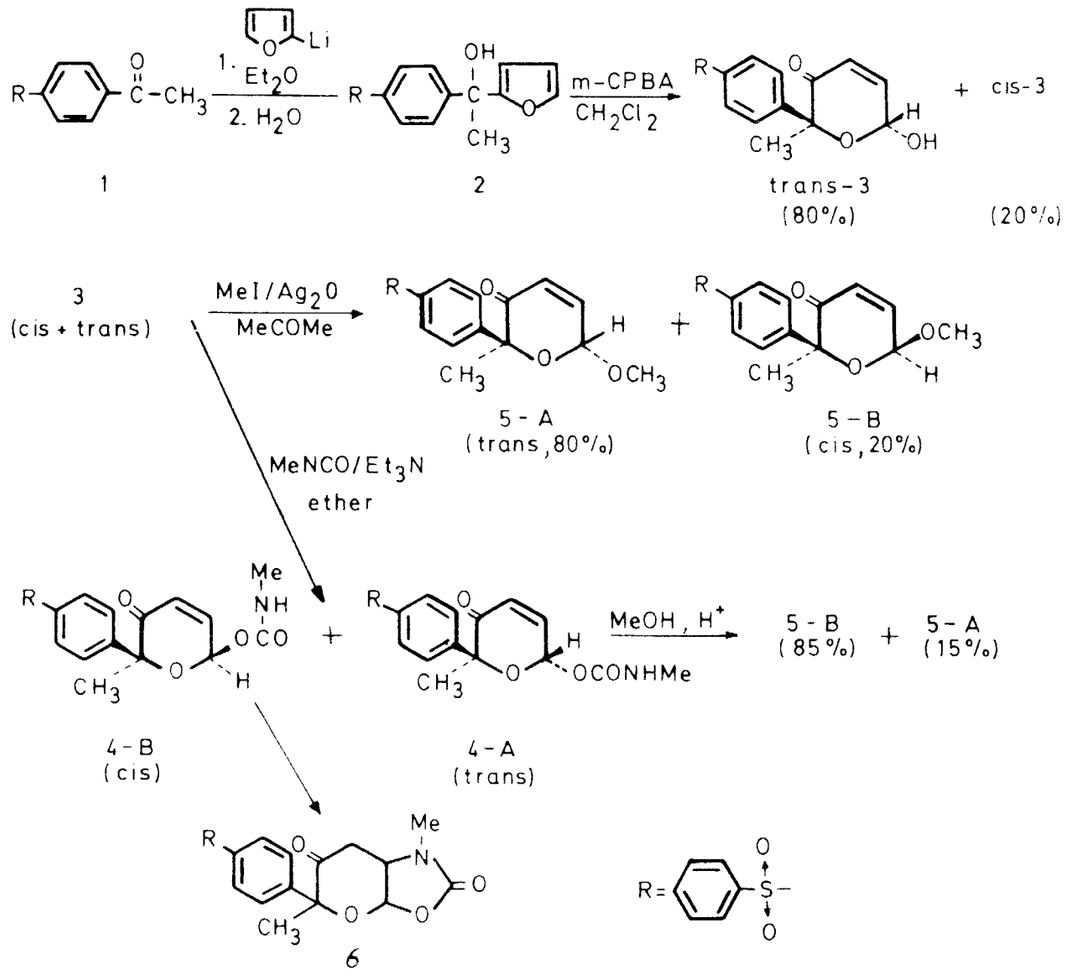
Crystallographic studies showed that the *p*-(benzenesulfonyl)phenyl substituent in 2-[*p*-(benzenesulfonyl)-phenyl]-2-methyl-6-methoxy-2*H*-pyran-3(6*H*)-one (**5-B**) and in 2-[*p*-(benzenesulfonyl)phenyl]-2-methyl-6-[[(methylamino)carbonyl]oxy]-2*H*-pyran-3(6*H*)-one (**4-A**) has a pseudoaxial orientation while the 6-substituent is cis in **5-B** and trans in **4-A** both in a sofa configuration. **5-B** crystallizes in space group P_{bca} with $Z = 8$ and the following lattice constants: $a = 14.784$ (3), $b = 28.713$ (5), $c = 8.229$ (1) Å. It refined to $R_1 = 0.037$ with 1769 independent reflections with $I > 2.5\sigma(I)$. **4-A** crystallizes in space group $P_{\bar{1}}$ with $Z = 2$ and the following lattice constants: $a = 9.472$ (2) Å, $b = 8.181$ (1) Å, $c = 13.972$ (2) Å, $\alpha = 97.30$ (1)°, $\beta = 95.27$ (1)°, $\gamma = 67.85$ (1)°. It refined to $R_1 = 0.046$ with 2246 independent reflections with $I > 2.0\sigma(I)$. ^{1}H NMR $J_{5,6}$ (vicinal) and $J_{4,6}$ (allylic) coupling constants of these and related compounds are correlated, and ambiguities in the use of ^{1}H NMR data for direct configurational assignment are clarified. A new equation of the Karplus–Garbisch type is also given which correlates the $J_{5,6}$ and $J_{4,6}$ with the dihedral angle between the vinyl and allylic hydrogen bonds. In addition, the conformational equilibria of the examined 2*H*-pyran-3(6*H*)-ones is discussed.

Derivatives of 2*H*-pyran-3(6*H*)-ones have been reported as antimicrobials and coccidiostatics[5–8] as well as intermediates in the synthesis of sugars,[9] disaccharides,[10] maltol,[11] and biological metabolites.[12] We have synthesized some 2*H*-pyran-3(6*H*)-ones having a 2-(para-substituted phenyl) substituent in an effort to produce compounds with increased antimicrobial and coccidiostatic activities and at the same time to investigate the configuration of this class of compounds which heretofore has not been examined. The significant biological activities[13] of the synthesized compounds together with the activities of other related compounds will be presented elsewhere.

A variety of methods have been reported for the synthesis of these pyranones from 2-furfuryl alcohol derivatives based either on an 1,4 halogen addition[11,14] to the furan ring and subsequent hydrolysis in mild acid followed by an immediate rearrangement to the six-membered 2*H*-pyran-3(6*H*)-one ring or on an oxidation procedure using *m*-chloroperbenzoic acid[5] (MCPBA) or pyridinium chlorochromate.[15] Other methods have also been reported.[16]

Scheme I



As shown in Scheme I, starting with *p*-(benzenesulfonyl)acetophenone (**1**), we synthesized α-methyl-α-*p*-[(benzenesulfonyl)phenyl]furfuryl alcohol (**2**), which on oxidation by MCPBA yields a cis and trans mixture of 2-methyl-2-[*p*-(benzenesulfonyl)phenyl]-6-hydroxy-2*H*-pyran-3(6*H*)-one (**3**) in which *trans*-**3** predominates. From this mixture, by a markedly stereoselective method,[6] we synthesized the isomeric methoxy compounds **5-A** and **5-B** and the carbamate **4-A**. We have not isolated **4-B** since under the reaction conditions it gave compound **6** by an intermolecular Michael reaction. Finally **4-A** upon

(1) For parts 1 and 2 see ref 7 and 8.
(2) This research was supported by the Hellenic National Research Foundation.
(3) Taken in part from the Ph.D. Thesis of E.A.C., Agricultural University of Athens, Department of Chemistry.
(4) Collaborator from the Physics Laboratory of the Agricultural University of Athens.
(5) Lefebvre, Y. *Tetrahedron Lett.* **1972**, 133–6.
(6) Laliberte, R. U.S. Patent 3 707 482; *Chem. Abstr.* **1973**, *79*, 524.
(7) Georgiadis, M. P. *J. Med. Chem.* **1976**, *19*, 346–9.
(8) Georgiadis, M. P.; Lefebvre, Y., submitted for publication.
(9) (a) Achmatowicz, O., Jr.; Grynkiewicz, G.; Szechner, B. *Tetrahedron* **1976** *32*, 1051–4. (b) Achmatowicz, O., Jr.; Srechner, B. *Carbohydr. Res.* **1976**, *50*, 23. (c) Achmatowicz, O., Jr.; Grynkiewicz, G. *Rocz. Chem.* **1976**, *50*, 719. (d) Achmatowicz, O., Jr.; Bielski, R.; Bukowski, P. *Ibid.* **1976**, *50*, 1535–43. (e) Achmatowicz, O., Jr.; Grynkiewicz, G. *Carbohydr. Res.* **1977**, *54*, 193. (f) Achmatowicz, O., Jr.; Bielski, R. *Ibid.* **1977**, *55*, 165.
(10) (a) Grynkievicz, G. *Synth. Commun.* **1978**, *8*, 491–6. (b) Grynkiewicz, G. *Synthesis* **1979**, 364–5.
(11) Weeks, P.; Brennan, T.; Brannegan, D.; Kuhla, D.; Elliott, M.; Watson, H.; Wlodecki, B.; Breitenbach, R. *J. Org. Chem.* **1980**, *45*, 1109–1113.
(12) Cavill, G.; Laing, O.; Williams, P. *Aust. J. Chem.* **1969**, *22*, 2145–70.
(13) Preliminary antimicrobial tests in vitro showed that these molecules and their derivatives have greater activity than ampicillin. Patent pending.
(14) Achmatowicz, O., Jr.; Bukowski, P.; Szechner, B.; Swierzchowska, Z.; Zamojski, A. *Tetrahedron* **1971**, 1973–96.
(15) Piancatelli, G.; Scettri, A.; D'Auria, M. *Tetrahedron Lett.* **1977**, 2199–2200.
(16) (a) Shoho, T.; Matsumura, Y. *Tetrahedron Lett.* **1976**, 1363–4. (b) Koga, K.; Yamada, S.; Yoh, M.; Mizoguchi, T. *Carbohydr. Res.* **1974**, *36* (2), C9–C11.

Table III. Observed Vinyl-Allylic Proton Spin Coupling Constants (in hertz) for 5-A, 5-B, and 4-A with Various Solvents and at Various Temperatures

solvent	temp, °C	dielectric const	5-A[a]			5-B			4-A		
			$J_{5,6}$	$J_{4,6}$	$J_{5,6}/J_{4,6}$	$J_{5,6}$	$J_{4,6}$	$J_{5,6}/J_{4,6}$	$J_{5,6}$	$J_{4,6}$	$J_{5,6}/J_{4,6}$
CD_3SOCD_3	25	46.7	2.2	1.3	1.7	2.4	1.2	2	2.2	1.6	1.4
CD_3CN[b]	25	37.5	2.1	1.4	1.5	2.5	1.2	2.1	2	1.6	1.3
$CDCl_3$	45	4.8	2	1.5	1.3	2.5	1.2	2.1			
$CDCl_3$	25	4.8	2	1.4	1.4	2.5	1.2	2.1	1.7	1.5	1.1
$CDCl_3$	−35	6.1	1.8	1.4	1.3	*c*					
CCl_4	25	2.2	1.9	1.6	1.2	*d*					

[a] Error in J of ±0.1 Hz. [b] Error in J of ±0.2 Hz. [c] Not soluble at low temperature. [d] Insoluble.

methanolysis yielded predominantly **5-B** through an inversion at C6.

The use of the Garbisch[17] equation, which was effective for qualitative configurational assignments of 2*H*-pyran-3(6*H*)-one derivatives[9,14] based on their allylic and vicinal ^1H NMR coupling constants, could not give us a clear indication of the configuration of the synthesized products or any other 2*H*-pyran-3(6*H*)-one which is 2-aryl and 2-methyl disubstituted.[8]

In order to clarify the configuration of the **A** and **B** forms of this class of pyranones, we studied compounds **5-B** and **4-A** by crystallography. In addition, $J_{5,6}$ and $J_{4,6}$ for **5-A**, **5-B**, and **4-A** were measured at various temperatures and in a variety of solvents in order to elucidate the conformational equilibria of these compounds in solution.

Results and Discussion

Final atomic coordinates and thermal parameters for the X-ray structural analyses are presented in Tables I and II.[18] Bond distances and angles are reported in Figures 1 and 2.[18] The ranges of estimated standard deviations in the last significant digit given in Figures 1 and 2 are 5–6 in bond lengths involving C, N, and O atoms, 3–4 in bonds involving a hydrogen atom, 2–3 in bonds involving the sulfur atom, 2–3 in angles involving C, N, and O, 1–2 in angles involving one hydrogen atom, and 2–3 in angles involving two hydrogen atoms. Atoms C2, C3, C4, C5, C6, and O3 define a plane in **5-B** (largest deviation from the plane is 0.03 Å for C6) and a pseudoplane in **4-A** (largest deviation is 0.10 Å for C6). The ring oxygen is 0.50 Å from this plane in **5-B** and 0.56 Å from it in **4-A**. Thus, both molecules have the sofa[19] configuration.

It has been reported[14,19b] that when the substituent at C2 in the sofa ring of the 2-monosubstituted 2*H*-pyran-3(6*H*)-one is alkyl or phenyl, it is *pseudoequatorially* oriented. However, in compounds **3-5** there is a disubstitution (2-aryl and 2-methyl), and it can been seen in Figures 3 and 4 that the aryl group is *pseudoaxially* oriented in both **5-B** and **4-A**. This kind of preference of the aryl group has also been reported for molecules with chair conformation.[20,21]

In examining the preferred conformation of **5-B** and **5-A** in solution, we have incorporated the anomeric effect,[22] as it has been reported for 2*H*-pyran-3(6*H*)-one,[23] to calculate the approximate free-energy differences between the conformers. Such a rough calculation based on the additivity rule of energy differences between **5-B** and **5-A**

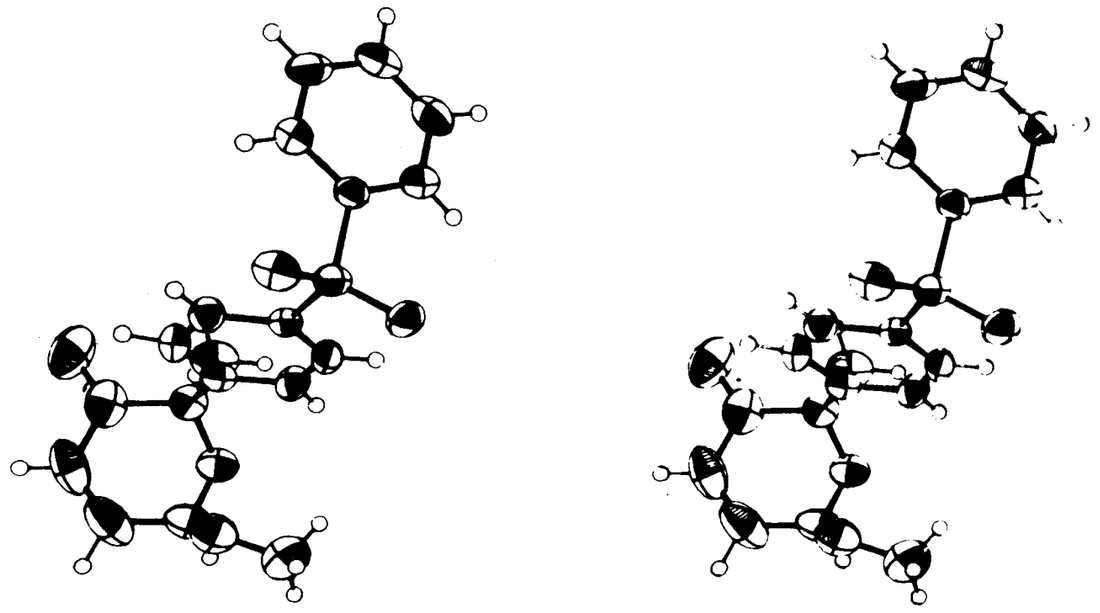
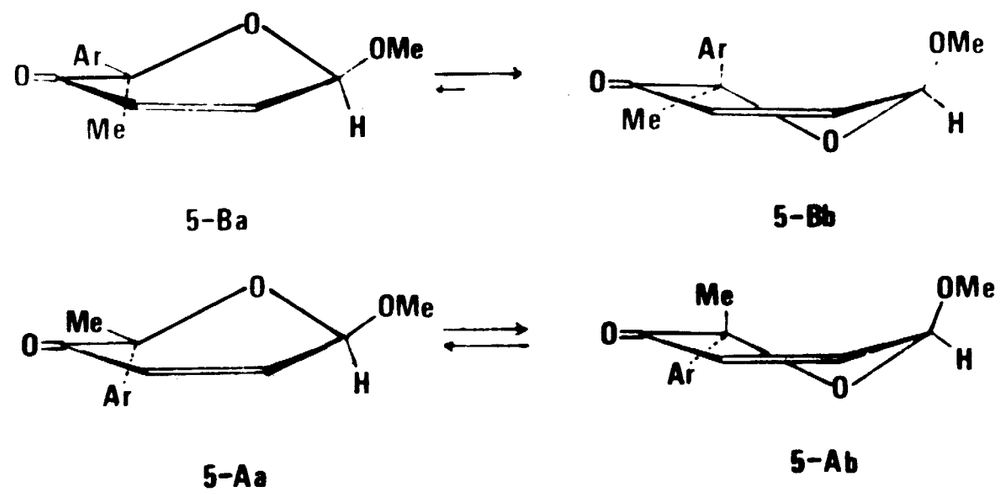


Figure 3. ORTEP drawing for **5-B**.

Scheme II



(see Scheme II) gives $\Delta G°_{5\text{-B}} - \Delta G°_{5\text{-A}} > 10$ kJ/mol, where $\Delta G°_{5\text{-B}} = \Delta G°_{5\text{-Ba}} - \Delta G°_{5\text{-Bb}}$ and $\Delta G°_{5\text{-A}} = \Delta G°_{5\text{-Aa}} - \Delta G°_{5\text{-Ab}}$.[24] Thus, we can assume that compound **5-B** in solution is more than 99% in the conformation given by crystallography (Scheme II, **5-Bb**). On the other hand, in the trans diastereoisomer **5-A**, as well as in **4-A**, the energy difference between conformers **5-Aa** and **5-Ab** (Scheme II) is small, because there is a rivalry between the trans subsituents for possession of the favorable pseudoaxial position. Therefore, the contributions of both **5-Aa** and **5-Ab** in the conformation equilibrium in solution must be significant, and the same behavior is expected for **4-A**. A small variation in the ^1H NMR coupling constants of **5-A** as a function of temperature in $CDCl_3$ (Table III) was observed, while the same coupling constants for the cis diastereoisomer **5-B** remain unaltered.

To strengthen this evidence, we have also studied the variations of the ^1H NMR coupling constant as a function of dielectric constants. Since the energy difference in the case of the conformers of **5-A** and **4-A** is small, the solvent as well as the anomeric effect may play an important role in determining the favorable conformation in solution. We have observed (see Table III) a dependence of the ^1H NMR coupling constants of **5-A** and **4-A** on the polarity of the

(17) Garbisch, E. *J. Am. Chem. Soc.* **1964**, *86*, 5561–5.
(18) See paragraph at end of paper regarding supplementary material.
(19) (a) Toromanoff, E. *Top. Stereochem.* **1967**, *2*, 157. (b) Achmatovicz, O., Jr.; Burrynska, M. *Pol. J. Chem.* **1979**, *53*, 265–76.
(20) Shapiro, B.; Gattuso, M.; Hepfinger, N.; Shone, R.; White, W. *Tetrahedron Lett.* **1971**, 219–22.
(21) Allinger, N.; Tribble, M. *Tetrahedron Lett.* **1971**, 3259–62.
(22) Eliel, E. L.; Allinger, N. L.; Angyall, A. A.; Morrison, J. J. *Org. Chem.* (*NY*) **1971**, *21*, 375.
(23) The free energy values were taken from 19b and references therin.
(24) Note that by taking the difference between the conformational energy differences, $\Delta G°_{5\text{-B}}$ and $\Delta G°_{5\text{-A}}$, unknown factors are eliminated and a rough calculation based on literature data is possible.

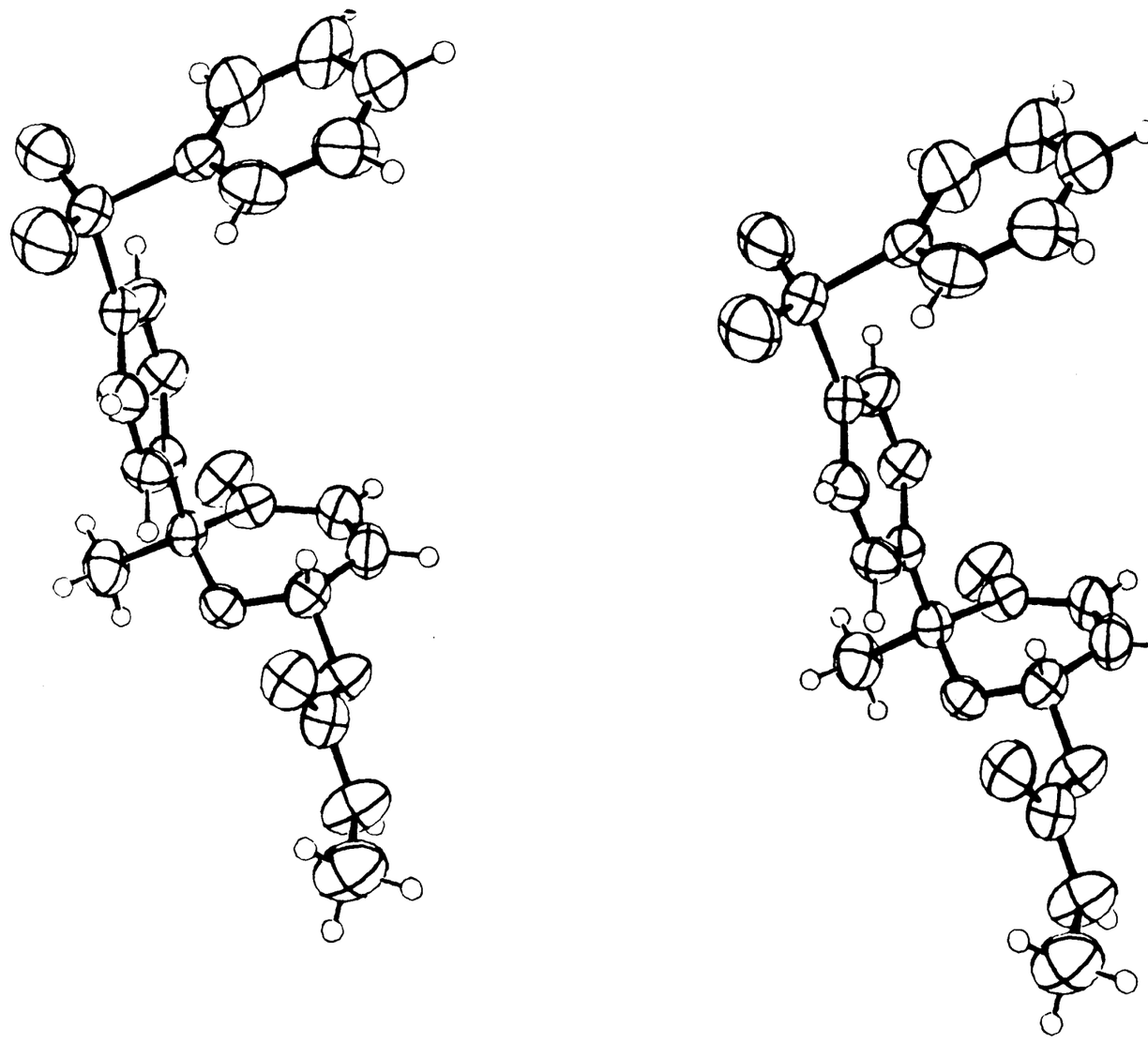
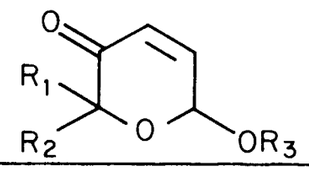
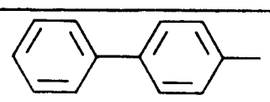
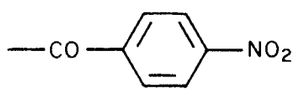
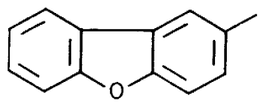
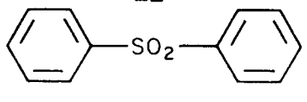


Figure 4. ORTEP drawing for **4-A**.

Table IV. Observed Vinyl–Allylic Proton Spin Couplings (in hertz) of Several Derivatives of 2H-Pyran-3(6*H*)-one



no.	R_1	R_2	R_3	conformer	$J_{5,6}$ [a]	$J_{4,6}$	$J_{5,6}/J_{4,6}$
7	 I [b]	Me	Me	cis	2.5	1.0	2.5
8	I [b]	Me	Me	trans	1.5	1.5	1
9	I [b]	Me	$CH(Me)_2$	cis	3.0	1.5	2
10	I [b]	Me	$CH(Me)_2$	trans	1.5	1.5	1
11	I [b]	Me		trans [d]	1.5	1.5	1
12	 II [c]	Me	H	trans [d]	1.5	1.5	1
13	II [c]	Me	CONHMe	trans	1.5	1.5	1
14	II [c]	H	H	trans [d]	3.5	0	
3	 III	Me	H	trans [d]	1.6	1.6	1
4-A	III	Me	CONHMe	trans	1.7	1.5	1.1
5-B	III	Me	Me	cis	2.5	1.2	2.1
5-A	III	Me	Me	trans	2.0	1.4	1.4

[a] Error in J of ±0.2 Hz. [b] Private communication with Y. Lefevre and R. Lalibrete. [c] See ref 8. [d] Predominant conformer.

solvent used. However, in the case of the cis diastereomer **5-B**, there is a relatively great energy difference between **5-Ba** and **5-Bb** which cannot be overcome by the weak solvent effect; such a dependence was not expected, and it was not observed.

The well-known Garbisch equation[17] correlates the *vicinal* and *allylic* ^1H NMR coupling constants with the dihedral angle in a CH=CH—CH system. This equation can be used satisfactorily for qualitative configurational estimations of 2*H*-pyran-3(6*H*)-ones, even though it gives slightly higher values for $J_{5,6}$ and $J_{4,6}$ than the observed ones.[14] This small discrepancy of the Garbisch equation may be due to the two electronegative heteroatoms adjacent to C6 (O1 and O6). The observed changes in the values of $J_{5,6}$ and $J_{4,6}$ with different substituents at C6 confirm this assumption (Table IV, compounds **7**, **9** and **4-A** and **5-A**).

However, when there is 2-aryl-2-methyl disubstitution, as in our case, the Garbisch equation cannot be applied satisfactorily for qualitative estimation of dihedral angles from the observed proton coupling constants or vice-versa, and this must be due to the axial orientation of the phenyl ring (compare **12** vs. **14** in Table IV). For example, inserting in the Garbisch equation the crystallographic values

for the dihedral angle of $\varphi_1 = 48°$ for **5-B** and $\varphi_2 = 110°$ for **4-A**, both defined by the planes C6, C5, and H5 and C5, C6, H6,[25] we find $J_{5,6} = 4.5$ Hz and $J_{4,6} = -0.8$ Hz for **5-B** and $J_{5,6} = 3.6$ Hz and $J_{4,6} = -2.3$ Hz for **4-A**, which are quite different from the observed values. Conversely, when the experimentally found $J_{5,6}$ and $J_{4,6}$ coupling constants[26] of **5-B** and **4-A** were used in the Garbisch equation, the calculated angles φ_1 and φ_2 were 70° and 49°, respectively, and this would lead to an erroneous configurational assignment.

We have come to the conclusion that it is preferable to use the quotient $J_{5,6}/J_{4,6}$ for configurational estimations of various 2*H*-pyran-3(6*H*)-ones instead of using their individual values because in configurationally similar molecules the coupling constants $J_{5,6}$ and $J_{4,6}$ may vary while their quotient remains the same (compare **13** vs. **3** and **9** vs. **5-B** in Table IV). Thus, when the value of the quotient $J_{5,6}/J_{4,6}$ is approximately 1 it indicates the trans configuration, and when it is approximately 2 it indicates the cis one. Therefore, a direct configurational assignment is possible by using the value of the quotient $J_{5,6}/J_{4,6}$. For a quantitative determination of the dihedral angle we propose a Garbisch-type equation with parameters modified in accordance with our experimental results.

$$J_{5,6} = 3.6 \cos^2 \varphi + 1.6 \sin^2 \varphi$$

$$J_{4,5} = 4.7 \cos^2 \varphi - 1.6 \sin^2 \varphi$$

$$0° \leq \varphi \leq 90° \text{ (cis isomer)}$$

$$J_{5,6} = 2.5 \cos^2 \varphi + 1.6 \sin^2 \varphi$$

$$J_{4,6} = -1.6 \sin^2 \varphi$$

$$90° \leq \varphi \leq 180° \text{ (trans isomer)}$$

In the above equations the parameters have been calculated by using the observed coupling constants and the crystallographic dihedral angles of **5-B** and **4-A**.

It should be mentioned that the calculated angle for the trans isomer represents the weighted average of the two conformers.

Conclusions

We note that the nature and the number of substituents at C2 determine the configuration of the predominant diastereoisomer and that the Garbisch equation cannot be applied to this type of molecules because of the axially oriented aryl group. Finally, a direct configurational assignment is possible from the quotient $J_{5,6}/J_{4,6}$ of vicinal to allylic coupling constants.

Experimental Section

General Methods. All melting points were determined on a Thomas-Hoover apparatus and are uncorrected. NMR spectra at room temperature were determined on a Varian 60-MHz spectrophotometer (Model 360 EM) with Me_4Si as an internal reference (δ 0.00); those at other temperatures were determined on a Varian 60-MHz instrument (Model A-60) with methanol for temperature calibration. The coupling constants are given in hertz. IR spectra were recorded on a Perkin-Elmer Model 283B infrared spectrophotometer. Gas chromatographs were obtained on a Perkin-Elmer Model Sigma 3 chromatograph provided with a Sigma 10 data microprocessor. Elemental analyses were performed at the University of Thessaloniki.

Materials. Commercial anhydrous ether (Carlo Erba) was used without further purification. *n*-BuLi was purchased from Merck as a solution in *n*-hexane (15% m/v) and MCPBA (80%) from EGA-CHIMIE. The starting material, *p*-(benzenesulfonyl)-acetophenone, was prepared from diphenyl sulfide according to the Szmant and Palopoli method.[27] Diphenyl sulfide was prepared from benzene and S_2Cl_2.[28]

α-Methyl-α-[*p*-(benzenesulfonyl)phenyl]furfuryl Alcohol (2). In a solution of freshly distilled furan (70 mL) in anhydrous THF (100 mL) was added *n*-BuLi in hexane (15%, 135 mL) dropwise under N_2 with the temperature maintained below −5 °C. After being stirred for 1.5 h at 20 °C, the mixture was cooled to 0 °C, and *p*-acetophenyl phenyl sulfone (18 g, 0.069 mol) was added portionwise. The reaction was allowed to proceed at room temperature overnight. After hydrolysis and workup of the mixture in the conventional manner, evaporation gave a red liquor of crude **2** (29 g) which was used without further purification: IR 3407 (OH), 1012, 1028, 882, 740 (furan), 1325, 1112 (SO_2) cm^{-1}; NMR ($CDCl_3$) δ 7.75 (m, 5 H aromatic), 7.35 (m, 4 H aromatic), 7.1 (q, 1 H furan), 6.15 (q, 2 H furan), 3.0 (br s, disappeared on addition of D_2O, OH), 1.8 (s, 3 H, angular methyl).

6-Hydroxy-2-[*p*-(benzenesulfonyl)phenyl]-2-methyl-2*H*-pyran-3(6*H*)-one (3). MCPBA (83%, 40 g, 0.281 mol) was added by portions in a cold solution of **2** (27 g, 0.082 mol) in $CHCl_3$ (150 mL) at a temperature between 10 and 15 °C. After the mixture was stirred for 3 h, the reaction was over (TLC). The mixture was cooled, and the precipitated solid (*m*-chlorobenzoic acid) was filtered off. The filtrate was washed successively with 20% KI, 30% $Na_2S_2O_3$, concentrated $NaHCO_3$, and H_2O, dried over $MgSO_4$, and evaporated to a yellowish liquor which was chromatographed on silica gel (800 g). Elution with ether–hexane (80:20) and evaporation of the pure fractions gave 2.5 g of *p*-acetophenyl phenyl sufone and 13 g of the title product (**3**). Two recrystallization from EtOAc–hexane gave 11 g of analytically pure material: 50% total yield for two steps; mp 130–131 °C. The product from reaction of a sample of **3** with $(CH_3)_3SiCl$ and Et_3N gave upon GC two peaks in the ratio 75:25 (3-cis and 3-trans, respectively): IR, (KBr) 3460, 3360 (OH), 1685 (conj C=O), 1310, 1110 (SO_2) cm^{-1}; NMR ($CDCl_3$) δ 7.75 (m, 4 H aromatic), 7.40 (m, 5 H aromatic), 6.65 (dd, 1 H double bond, $J_{db} = 10$, $J_{vic} = 1.6$), 6.0 (dd, 1 H, double bond, $J_{db} = 10$, $J_{allylic} = 1.6$), 5.3 (d, 1 H, allylic, $J_{H-OH} = 7.5$), 3.6 (d, 1 H, $J_{H-OH} = 7.5$, disappeared on addition of D_2O, OH), 1.6 (s, 3 H, angular methyl). Anal. Calcd for $C_{18}H_{16}O_5S$: C, 62.78; H, 4.68. Found: C, 62.83; H, 4.80.

6-Methoxy-2-[*p*-(benzenesulfonyl)phenyl]-2-methyl-2*H*-pyran-3(6*H*)-one (5-A). To a solution of **3** (0.95 g, 0.0027 mol) and MeI (3 mL) in Me_2CO (20 mL) was added powdered Ag_2O (2.7 g) portionwise. The mixture was stirred overnight, refluxed with Norite, and filtered on Celite, and the filtrate was evaporated. The residue (two spots on TLC) was chromatographed on silica gel (120 g) with ether–hexane (40:60) as the eluant. Fractions with the higher R_f value were evaporated, yielding **5-A** as a yellowish oil (0.7 g, 70.8% yield), and fractions with the lower R_f value gave **5-B** (1.8 g, 20% yield): IR 2940 (CH_3), 1693 (conj C=O), 1315, 1160 (SO_2) cm^{-1}; NMR ($CDCl_3$) δ 7.7 (m, 4 H, aromatic), 7.35 (m, 5 H, aromatic), 6.65 (dd, 1 H, double bond, $J_{db} = 10$, $J_{vic} = 2.0$), 5.96 (dd, 1 H, double bond, $J_{db} = 10$, $J_{allylic} = 1.4$), 5.03 (t, 1 H, allylic), 3.45 (s, 3 H, OCH_3), 1.7 (s, 3 H, angular methyl).

2-[*p*-(Benzenesulfonyl)phenyl]-2-methyl-6-[[(methylamino)carbonyl]oxy]-2*H*-pyran-3(6*H*)-one (4). In a solution of **3** (6.89 g, 0.02 mol) and MeNCO (16 mL) in anhydrous ether (300 mL) and CH_2Cl_2 (50 mL) was added Et_3N (8.5 mL) portionwise. The mixture was stirred for 2 h at room temperature and kept at 5 °C for 20 h (TLC). Afterward it was washed with H_2O to neutrality, dried over $MgSO_4$ and evaporated under reduced pressure. The residue was chromatographed on silica gel (1:25) and eluted with ether–EtOAc (9:1) to yield, after evaporation of the solvent, 7.2 g of **4-A**. Recrystallization from acetone–hexane gave analytically pure material: 6.8 g (yield 84.7%); mp 150 °C.

Another fraction gave 0.3 g of a yellow solid which NMR and IR showed to be **6**: IR (KBr) 3440 (NHCO), 1765, 1695 (NHCO), 1300, 1160 (SO_2) cm^{-1}; NMR ($CDCl_3$) δ 7.5 (m, 9 H aromatic), 6.75 (dd, 1 H, double bond, $J_{db} = 10$, $J_{vic} = 1.7$), 6.35 (t, 1 H, allylic), 6.15 (dd, 1 H, double bond, $J_{db} = 10$, $J_{allylic} = 1.5$), 5.45 (t, 1 H, NH, $J = 4.2$), 2.8 (d, 3 H, CH_3, $J = 4.2$), 1.65 (s, 3 H, angular methyl).

(25) The Dreiding model gives dihedral angles 40° and 100°, respectively.

(26) It is clear from the ^1H NMR data (see Experimental Section) that the H4, H5 and H6 protons belong to an AMX system, and therefore second-order effects can be neglected.

(27) Szmant, H.; Palopoli, F. *J. Am. Chem. Soc.* **1950**, *72*, 1757–60.

(28) Hartman, W.; Smith, L.; Dickey, J. *Org. Synth.* **1934**, *14*, 36–38.

Table V. Experimental Data for the X-ray Diffraction Studies

parameter	5-B	4-A
	Crystal Parameters[a]	
crystal system	orthorhombic	triclinic
space group	P_{bca}	$P\bar{1}$
a, Å	14.784 (3)	9.472 (2)
b, Å	28.713 (5)	8.181 (1)
c, Å	8.229 (1)	13.972 (2)
α, β, γ, deg		97.30 (1), 95.27 (1), 67.85 (1)
V, Å^3	3493 (1)	993.5 (4)
Z	8	2
mol wt	358.4	401.4
D(calcd), g cm^{-3}	1.364	1.341
D(measd), g cm^{-3}	1.35	1.33
	Measurement of Data	
radiations	Mo Kα ($\bar{\lambda}$ = 0.7107 Å)	
filter	Zr	
reflcns measd	$+h,+k,+l$	$\pm h,-k,\pm l$
2θ range, deg	3–45.0	
scan type	ω	
scan speed	variable with 1°/min for weak reflcns	
scan range, deg	0.9	
reflcns collected	2275 independent	2802 total, 2585 independent
reflcns considered obsd	$I > 2.5\sigma(I)$, 1769	$I > 2.0\sigma(I)$, 2246
abs coef, cm^{-1}	2.1	2.0

[a] Unit-cell parameters were derived from a least-squares fit to the setting angles of 15 high-order reflections.

6-Methoxy-2-*p*-[(benzenesulfonyl)phenyl]-2-methyl-2*H*-pyran-3(6*H*)-one (5-B). $HClO_4$ (70%, 2.5 mL) was added by portions in a suspension of **4** (4.4 g, 0.0106 mol) in absolute MeOH (120 mL). After the mixture was stirred for 15 min, it turned into a clear solution, and subsequently white crystals of **5-B** precipitated. After additional stirring for 1 h and cooling to −10 °C, filtration afforded 2.5 g of pure **5-B** (cis isomer only). An additional amount of 0.4 g of **5-B** was received from the filtrate after neutralization, chromatography, and several recrystallizations from ethanol (total yield for cis isomer **5-B** was 2.9 g, 76.3%): mp 144–145 °C; IR (KBr) 1685 (conj C=O), 1310, 1160 (SO_2) cm^{-1}; NMR ($CDCl_3$) δ 7.7 (m, 4 H aromatic), 7.4 (m, 5 H aromatic), 6.6 (dd, 1 H, double bond, J_{db} = 10, J_{vic} = 2.5), 6.03 (dd, 1 H, double bond, J_{db} = 10, $J_{allylic}$ = 1.2), 5.2 (q, 1 H, allylic), 3.25 (s, 3 H, OCH_3), 1.63 (s, 3 H, angular methyl). Anal. Calcd for $C_{19}H_{18}O_5S$: C, 63.67; H, 5.07. Found: C, 63.57; H, 5.10.

Crystallographic Analyses. Single crystals, suitable for X-ray work, were obtained by slow evaporation of an acetone solution. Crystals of dimensions 0.3 × 0.4 × 0.5 mm for **5-B** and 0.3 × 0.3 × 0.5 mm for **4-A** were chosen for the structure determinations. Photographic investigations indicated the space groups (Table V). Measurements were made on a Syntex $P2_1$ diffractometer. A variable scanning rate was used, with 1°/min for the weak reflections. Each 0.9° scan was divided into 15 equal (time) intervals and the 13 contiguous intervals which had the highest single accumulated count at their midpoint were used to calculate the scanning intensity. Background counts, each lasting for half the total time used for the net scan ($^{13}/_{15}$th of the total scan time), were measured at ω settings 0.9° above and below the calculated K$\bar{\alpha}$ value for each reflection.

A plot of the intensities of three monitor reflections, measured periodically, showed a 10% deterioration of the crystal of **5-B** during data collection. A correction for this was applied during data reduction, but one was not applied for absorption or secondary extinction for either structure. The nonhydrogen atoms were located by using direct methods (MULTAN). All chemically anticipated hydrogen atoms were located from a difference Fourier synthesis calculated from the block-diagonal least-squares refined structural model (R_1 = 0.062[29] for **5-B** and R_1 = 0.076 for **4-A**) which included unit weights and anisotropic thermal parameters. An anomalous dispersion correction was used for the sulfur atom only. The final block-diagonal least-squares cycle used weights calculated by the formula $1/w = \sigma^2(F_0) + (kF_0)^2$, where k is 0.02 for **5-B** and 0.005 for **4-A**, included isotropic thermal parameters for the hydrogen atoms and anisotropic for the rest and converged to R_1 = 0.037, R_2 = 0.045, and GOF = 1.77[29] for **5-B** and to R_1 = 0.046, R_2 = 0.052, and GOF = 4.12 for **4-A**. Difference maps calculated at these points revealed no unusual features. Some of the nonhydrogen atoms had rather high (≥7) isotropic thermal parameters. For **5-B**: O3, 7.5; C4, 7.0; C5, 7.8; C20, 7.0. For **4-A**: C17, 7.0; C18, 7.5 (Tables I and II[18] and Figures 3 and 4). This may be due to the fact that we did not apply a secondary extinction correction. The programs of the XTL system of the Syntex $P2_1$ diffractometer were used for all the calculations.

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Registry No. **1**, 65085-83-8; **2**, 81830-82-2; *cis*-**3**, 81830-83-3; *trans*-**3**, 81830-84-4; **4A**, 81830-88-8; **5A**, 81830-85-5; **5B**, 81830-86-6; **6**, 81830-87-7; **7**, 50768-33-7; **8**, 50768-34-8; **9**, 50768-36-0; **10**, 50768-37-1; **11**, 81830-89-9; **12**, 81830-90-2; **13**, 81830-91-3; **14**, 81830-92-4; furan, 110-00-9.

Supplementary Material Available: Listings of fractional and anisotropic thermal parameters for nonhydrogen atoms of both **5-B** and **4-A** (Table I) and of fractional and isotropic thermal parameters for hydrogen atoms of **5-B** and **4-A** (Table II), bond distances and angles for **5-B** (Figure 1) and **4-A** (Figure 2), and an ORTEP stereopacking diagram for **5-B** (9 pages). Ordering information is given on any current masthead page. A listing of observed and calculated structure factor amplitudes from the final cycles of least-squares refinement for both structures may be obtained from A.T.

(29) $R_1 = \sum||F_o| - |F_c||/\sum|F_o|$, $R_2 = [|\sum w(|F_o| - |F_c|)^2/\sum w|F_o|^2]^{1/2}$, and GOF = $[\sum w(F_o - F_c)^2/(N_{ref} - N_{var})]^{1/2}$.