TABLE I

DATA FOR *cis*- AND *trans*-1-CHLORO-1,3-BUTADIENE

Chloride	$n^{20}D$	Ultraviolet[a] λ_{max}, mμ (ε)	Retention times,[b] min	Bp, °C	Yield, %
cis-1-Chloro-1,3-butadiene[c]	1.4707	233 (26,900)	136	66.5–68	72
trans-1-Chloro-1,3-butadiene[d]	1.4696	228 (18,700)	141	66–67.5	52

[a] The solvent was cyclohexane. [b] The flow rate (He) was 213 ml/min. [c] Contained 10% *trans* isomer. [d] Contained 15% *cis* isomer.

On the other hand, in the elimination with *cis*-1,4-dichloro-2-butene, hydrogen–chlorine bonding, leading to *cis*-diene, would be impossible since the extended π bonding in this transition state would prevent rotation of the 2,3-carbon bond. Steric hindrance between the chlorine atoms in the transition state would cause these atoms to lie away from each other and, hence, elimination would lead to the *trans* diene.

Experimental Section[10]

Reaction of *cis*- and *trans*-1,4-Dichloro-2-butene with Sodium Amide.—To a 500-ml, five-neck, round-bottom flask, equipped with a dropping funnel, fritted-glass nitrogen inlet, thermometer, mechanical stirrer, and outlet to a Dry Ice trap, and containing 20 g (0.51 mol) of sodium amide in 250 ml of mineral oil at 80°, was added, dropwise, 25 g (0.20 mol) of the dichloride in 135 ml of mineral oil. When the addition was complete, the trap was removed from the Dry Ice bath, and the ammonia was allowed to evaporate. The remaining liquid was distilled.

Identification and Analysis of the Products.—*cis*-1-Chloro-1,3-butadiene was confirmed as the principal product from *trans*-1,4-dichloro-2-butene on the basis of its boiling point, and infrared, ultraviolet, and nmr spectra. These spectra were all essentially identical with those of commercial 1-chloro-1,3-butadiene, obtained from Aldrich Chemical Co., Inc. Vpc analysis indicated that the commercial 1-chloro-1,3-butadiene contained approximately 85% *cis* isomer and 15% *trans* isomer.

trans-1-Chloro-1,3-butadiene was confirmed as the principal product from *cis*-1,4-dichloro-2-butene on the basis of the following observations: its nmr spectra showed only vinyl hydrogen absorption, the boiling point and the nmr, infrared, and ultraviolet spectra were very similar to those of *cis*-1-chloro-1,3-butadiene, and *trans*-1-chloro-1,3-butadiene rearranged with iodine to a *cis*–*trans* mixture, as described by Viehe.[6,11]

The 1-chloro-1,3-butadienes were analyzed by vpc according to the procedure of Viehe.[6] Peak enhancement studies confirmed that the products from *cis*- and *trans*-1,4-dichloro-2-butene were composed of the same compounds, but in different quantities.

Preparations and Purities of *cis*- and *trans*-1,4-Dichloro-2-butene.—*cis*-1,4-Dichloro-2-butene was synthesized according to the procedure of Babbit, Amundsen, and Steiner.[12] *trans*-1,4-Dichloro-2-butene was obtained from Eastman Organic Chemicals Department. Vpc analysis showed that the *cis* isomer was contaminated with approximately 5% of an unknown impurity, and a trace of the *trans* isomer. *trans*-1,4-Dichloro-2-butene contained only a trace of the *cis* isomer and no other impurities. The conditions for analysis on an Aerograph 90 P-3 chromatograph were as follows: flow rate (He), 323 ml/min; column length and diameter, 6 ft × 0.25 in.; column temperature, 29°; column composition, 2.5% SE-30 on 60–80 mesh DMCS Chromosorb W. Under these conditions the retention times of *cis*- and *trans*-1,4-dichloro-2-butene, are, respectively, 3.2 and 4.0 min.

Registry No.—*cis*-1,4-Dichloro-2-butene, 1476-11-5: *trans*-1,4-dichloro-2-butene, 110-57-6; sodium amide, 12125-45-0; *cis*-1-chloro-1,3-butadiene, 10033-99-5; *trans*-1-chloro-1,3-butadiene, 16503-25-6.

Acknowledgment.—Acknowledgment is made to the Research Corporation for support of this research. We are indebted to Mr. Gerald Oliver of the Jet Propulsion Laboratory, Pasadena, Calif., for the nmr spectra.

---

[10] Boiling points are uncorrected.

[11] Viehe reports that heating a mixture of *cis*-1-chloro-1,3-butadiene and a solution of 1% iodine in benzene at 100° gives an equilibrium mixture of 70 ± 5% *cis* isomer and 30 ± 5% *trans* isomer. We confirmed this using the *cis*-1-chloro-1,3-butadiene from *trans*-1,4-dichloro-2-butene. Heating the *trans*-1-chloro-1,3-butadiene with iodine–benzene solution gave a mixture of 60% *cis* isomer and 40% *trans* isomer. The rearrangment undoubtedly would have gone to equilibrium if the decomposition products had been removed and the iodine replenished. We found that disappearance of iodine was rapid, and if more iodine was added, the rearrangement continued.

[12] J. Babbit, L. Amundsen, and R. Steiner, *J. Org. Chem.*, **25**, 2231 (1960).

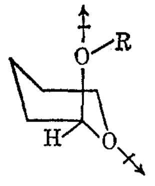
A Conformational Analysis of Some 2-Alkoxytetrahydropyrans

GARY O. PIERSON AND OLAF A. RUNQUIST

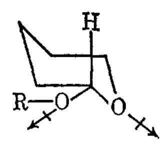
Hamline University, St. Paul, Minnesota

Received January 11, 1968

Oxane rings substituted in the 2 position by electronegative groups are generally more stable with the 2 substituent in an axial conformation. The interactions which cause the observed destabilization of the equatorial conformation in these compounds are commonly referred to as the anomeric effect, a term first used by Lemieux and Chu.[1] Examples of the anomeric effect are to be found in certain 1-substituted D-glucopyranosides,[2] 2-substituted tetrahydropyrans,[3,4] and substituted dioxanes.[5] Edward[6] has explained the anomeric effect in terms of a dipole–dipole interaction between the lone electron pairs of the ring oxygen and the substituent bond. Because of the angles between the dipoles, this interaction would be much smaller for an axial substituent (A) than for an equatorial substituent (B).



A



B

As would be expected in a dipole–dipole interaction, the magnitude of the anomeric effect is dependent on the dielectric constant of the solvent. A solvent of high

---

[1] R. U. Lemieux and N. J. Chu, Abstracts, 133rd National Meeting of the American Chemical Society, San Francisco, Calif., April 1958, p 31N.

[2] For examples, see E. L. Eliel, N. J. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," John Wiley and Sons, Inc., New York, N. Y., 1965, pp 375–377.

[3] G. E. Booth and R. J. Ouelette, *J. Org. Chem.*, **31**, 544 (1966).

[4] C. B. Anderson and D. T. Sepp, *Chem. Ind.* (London), 2054 (1964).

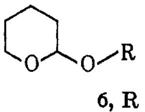
[5] C. Altona, C. Romers, and E. Havinga, *Tetrahedron Lett.*, No. 10, 16 (1959).

[6] J. T. Edward, *Chem. Ind.* (London), 1102 (1955).

dielectric constant would be expected to stabilize the equatorial conformer by reducing the strength of the dipole interaction. The actual strength observed for the anomeric effect varies considerably with changing solvent polarity. For example, Rowley and Bailey[7] have obtained values for the anomeric effect in glucose of 0.35 kcal/mol in water and 0.90 kcal/mol in methanol, while Levene and Hill[8] obtained a value for mannose of 1.15 kcal/mol in pyridine. Booth and Ouellette[3] have estimated the value for the anomeric effect in 2-halotetrahydropyrans to be greater than 2.3 kcal/mol in a series of nonpolar and slightly polar solvents.

The conformational equilibrium of compounds exhibiting the anomeric effect would be expected to be altered by both the polar and steric nature of the substituent groups. Increasing the substituent polarity would increase the strength of the substituent dipole. Such an increase in dipole strength would greatly increase the interaction in the equatorial conformer (B) where the dipoles are nearly parallel. The same increase in dipole strength would be expected to have a much smaller effect on the axial conformer (A) where the dipoles are at widely divergent angles. Thus increasing the polarity of the substituent would be expected to shift the equilibrium toward the axial conformation by increasing the magnitude of the dipole interaction. The steric requirement of a substituent should also have an effect on the conformational equilibrium. Since the axial conformer is more stericly crowded due to diaxial interactions, an increase in substituent size would be expected to favor the equatorial conformer.

This paper describes a conformational study of several 2-alkoxytetrahydropyrans (**1**–**10**) in which the steric and polar nature of the substituents vary over a fairly wide range. The particular compounds were chosen in an attempt to discern the dependency of the conformational equilibrium upon the steric and polar requirements of the alkoxy substituent. The conformational equilibrium was determined *via* nmr techniques. Since the spin–spin coupling constants are related to the dihedral angle between the C–H bonds by a $\cos^2 \theta$ function, it is often possible to determine conformational equilibria from the magnitude of these coupling constants.[3,9] To obtain reasonably quantitative results, the coupling constants for the reference proton in both of its conformations must be known. These coupling constants can be obtained from suitably chosen model compounds which are conformationally homogeneous and closely analogous to the system being studied. In the study of the 2-alkoxytetrahydropyran system the C-2 proton resonance was observed. The model compound used to obtain the coupling constant for a totally axial substituent was methyl 2-deoxy-α-D-glucopyranoside. This compound is assumed to be a completely axial conformer because of the two separate 1,3 diaxial interactions which would occur in the equatorial conformer. The model compound used to obtain the coupling constants for the equatorial conformer was *cis*-4-methyl-2-methoxytetrahydropyran;[4] this compound is believed to exist entirely as the equatorial conformer because of the strong 1,3 diaxial interactions between the methyl and methoxy groups which would occur in the axial conformer.



1, R = H
2, R = CH_3
3, R = C_2H_5
4, R = $(CH_2)_2Cl$
5, R = CH_2CHCl_2
6, R = CH_2CF_3
7, R = CH_2CCl_3
8, R = $CH(CH_3)_2$
9, R = $C(CH_3)_3$
10, R = C_6H_5

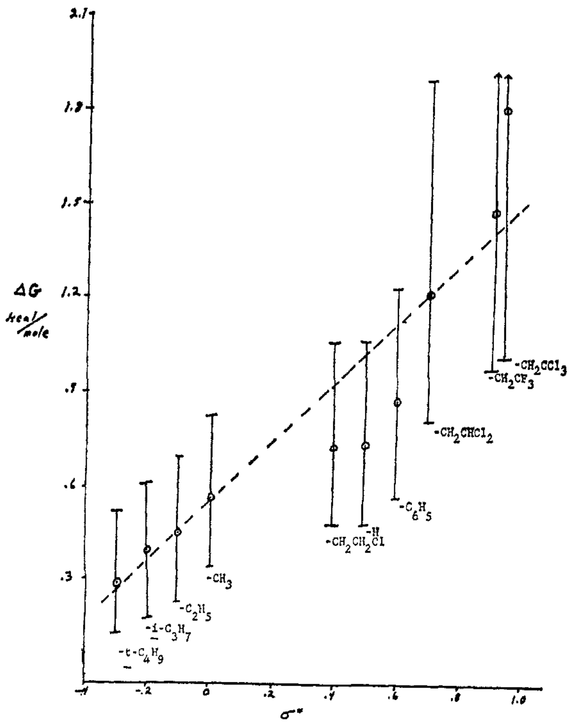
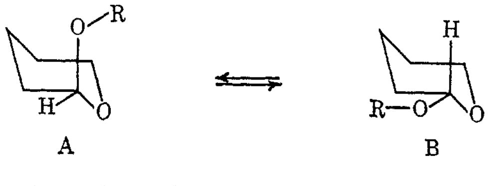


Figure 1.—The relationship between substituent Taft constant and conformational free-energy difference of 2-alkoxytetrahydropyrans.

Results and Discussion

The observed coupling constant of a rapidly equilibrating system is a time average of the components of the system. The equilibrium constant between conformers A and B of the 2-alkoxytetrahydropyran system can be estimated from the distance between the two outside peaks of the C-2 proton resonance provided $J_{2,3a}$ and $J_{2,3e}$ are known for both conformers. The C-2 proton resonance is a part of an ABX system with the C-2 absorption well downfield of the C-3 protons. If weak transition states are ignored, the distance between the two outside peaks of the C-2 absorption can be approximated as equal to $J_{2,3a} + J_{2,3e}$. This sum shall be referred to as J_A and J_B for conformers A and B, respectively. The observed distance between the two outside peaks, J^0, is equal to $J_A N_A + J_B N_B$ where N_A and N_B are the percentages of the two conformers. Values for J_A (4.7 cps) and J_B (10.5 cps) were obtained



---

[7] H. H. Rowley and S. D. Bailey, *J. Amer. Chem. Soc.*, **62**, 2562, (1940).

[8] P. A. Levene and D. W. Hill, *J. Biol. Chem.*, **102**, 536 (1933).

[9] Edgar W. Garbish, Jr., *J. Amer. Chem. Soc.*, **86**, 1780 (1964).

TABLE I

COUPLING CONSTANTS OF SOME SUBSTITUTED TETRAHYDROPYRANS

No.	Compounds	Source	$J_{1,2}$, cps			
			$J_{a,a}$	$J_{a,e}$	$J_{e,e}$	$J_{e,a}$
1	*cis*-4-Methyl-2-methoxytetrahydropyran	*a*	8.3	2.2		
2	*cis*-4-Methyl-2-butoxytetrahydropyran	*a*	8.5	2.0		
3	Methyl 2-deoxy-2-D-glucose	*b*			3.5	1.2
4	Acetylated sugars	*c*	5–8 (av 6.9)	2–6.2 (av 3.3)	3.0	
5	α-D-Glucopyranosides	*d*		3.0–3.5		
6	α-D-Manopyranosides	*d*			1.0–1.5	
7	Acetylated mannose derivatives	*e*	6.5–8.7 (av 7.5)		1.0	

[a] C. B. Anderson and D. T. Sepp, *Chem. Ind.* (London), 2054 (1964). [b] This paper. [c] R. U. Lemieux, R. K. Kullnig, H. J. Bernstein, and W. C. Schneider, *J. Amer. Chem. Soc.*, **80**, 6098 (1958). [d] R. U. Lemieux and B. Fraser-Reid, *Can. J. Chem.*, **42**, 532 (1964). [e] K. Onedera, S. Hirano, F. Masuda, and N. Kashimura, *J. Org. Chem.*, **31**, 2403 (1966).

TABLE II

CONFORMATIONAL PERCENTAGES AND FREE ENERGIES OF 2-ALKOXYTETRAHYDROPYRANS

R	Shift	J^0, cps	N_A, %	ΔG, kcal mol
H	5.1	6.0	77	0.75 ± 0.3
CH_3	5.6	6.3	72	0.58 ± 0.3
C_2H_5	5.45	6.5	68	0.47 ± 0.3
$(CH_2)_2Cl$	5.3	6.0	77	0.75 ± 0.3
CH_2CHCl_2	5.4	5.5	88	1.2 ± 0.6
CH_2CF_3	5.2	5.2	92	1.5
CH_2CCl_3	5.05	5.0	95	1.8
$CH(CH_3)_2$	5.35	6.7	66	0.42 ± 0.3
$C(CH_3)_3$	5.2	6.9	62	0.31 ± 0.3
C_6H_5	4.8	5.8	81	0.90 ± 0.4

from coupling constants observed for methyl 2-deoxy-α-D-glucopyranoside and *cis*-4-methyl-2-methoxytetrahydropyran, respectively. Coupling constants observed for several carbohydrate derivatives of known configuration (see Table I) are consistent with the values chosen for J_A and J_B. The value of N_A can be calculated from the equation

$$N_A = \frac{J_B - J^0}{J_B - J_A}$$

The free-energy difference between the two conformers can be obtained from

$$\Delta G = RT \ln \frac{N_A}{1 - N_A}$$

Table II lists the J^0 values and chemical shifts observed for the compounds studied. The values calculated for N_A and ΔG are also included. Since the J^0 values could only be estimated to ±0.5 cps the values given for N_A and ΔG are subject to considerable error. The relationship between the observed free-energy difference and the Taft polar constants for the R groups is given in Figure 1. The slope of the line given in Figure 1 is consistent with the expected increase in dipole interaction with increasing substituent polarity (higher Taft values). The linearity of the graph seems to indicate that the steric size of the substituent has little or no effect on the conformational free energy.

A value for the anomeric effect which can be compared to values previously reported may be obtained by adding 0.9–1.0 kcal/mol[10] to the free energies listed in Table II to account for diaxial interactions. Thus, the anomeric effect for this series of 2-alkoxytetrahydropyrans varies from 1.3 to 2.8 kcal/mol. Since these results were obtained in nonpolar solvents, the values are consistent with those of earlier workers.[3,7,8]

TABLE III

PHYSICAL CONSTANTS AND ANALYTICAL DATA FOR 2-ALKOXYTETRAHYDROPYRANS NOT PREVIOUSLY REPORTED

R	Bp, °C (mm)	$n^{20}D$	Calcd, %		Found, %	
			C	H	C	H
$CH(CH_3)_2$	159–160	1.4242	66.63	11.18	66.80	11.39
$C(CH_3)_3$	169–170	1.4290	68.31	11.47	68.40	11.75
CH_2CHCl_2	84–86 (10)	1.4724	42.23	6.08	44.17[a]	6.08
CH_2CF_3	141–143	1.3784	45.65	6.02	46.10	5.48
CH_2CCl_3	88–89 (10)	1.4796	36.00	4.75	37.56[a]	4.86

[a] These compounds were purified by chromatography only since they tended to decompose on distillation. The infrared and nmr spectra were in complete agreement with the proposed structures.

Experimental Section

All compounds, with the two exceptions noted below, were prepared according to the procedure of Woods and Kramer[11] and purified by distillation. Physical constants and analytic data for compounds not previously reported in the literature are listed in Table III. The 2-hydroxytetrahydropyran was prepared by the procedure of Schniep and Geller,[12] and the 2-(2-chloroethoxy)tetrahydropyran was purchased from Aldrich Chemicals. All spectra were run as neat samples on a Varian A-60A spectrometer operating at 38°. Coupling constants were reproducible to 0.5 cps.

Registry No.—**1,** 694-54-2; **2,** 931-60-2; **3,** 4819-83-4; **4,** 5631-96-9; **5,** 16408-82-5; **6,** 16408-83-6; **7,** 16408-84-7; **8,** 1927-70-4; **9,** 1927-69-1; **10,** 4203-50-3.

---

(10) E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p 236.

(11) G. F. Woods and D. N. Kramer, *J. Amer. Chem. Soc.*, **69**, 2246 (1947).

(12) L. E. Schniep and H. H. Geller, *ibid.*, **68**, 1646 (1946).