

2-Alkyl-2-methyl- and 2-Alkyl-2,4-dimethyl-1,3-dioxanes

IV. Hydrolytic Decomposition of 2-Alkyl-2-methyl-1,3-dioxanes. The Dependence of the Hydrolysis Rates on the Conformer Ratios

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Second-order rate coefficients of the acid-catalyzed hydrolysis of 2,2-dimethyl-, 2,2-diethyl-, 2-ethyl-2-methyl-, 2-propyl-2-methyl-, 2-isopropyl-2-methyl-, 2-butyl-2-methyl-, 2-*s*-butyl-2-methyl-, and 2-*t*-butyl-2-methyl-1,3-dioxanes in dilute perchloric acid solutions have been determined. The individual rates of both conformers were evaluated for the compounds with different alkyl substituents. A similar dependence of the rate coefficients on polar and steric effects prevails in the case of the studied compounds as found for 2-alkyl-2,4-dimethyl-1,3-dioxanes.

It has been shown earlier that 2-alkyl-2,4-dimethyl-1,3-dioxanes are hydrolyzed according to an A-1 mechanism.^{1,2} An NMR investigation revealed that the conformer ratios of 2-alkyl-2-methyl-1,3-dioxanes³ are in accordance with equilibration data for several stereoisomeric 2-alkyl-2,4-dimethyl-1,3-dioxanes.⁴ A study of the hydrolytic decomposition of 2-alkyl-2,4-dimethyl-1,3-dioxanes showed that separate Taft-Hammett plots are obtained for the *trans* and the *cis* series.² The aims of this study were to measure the hydrolysis rates, to determine the values of the free energy of activation for the individual conformers and to determine the dependence of the rates on polar and steric factors.

EXPERIMENTAL

The studied compounds were prepared earlier.³ The kinetic measurements were made spectrophotometrically as described previously.³ The values of the hydrolysis rates were determined at at least three temperatures for each compound (Table 1).

RESULTS AND DISCUSSION

The hydrolysis rates of the individual conformers of 2-alkyl-2-methyl-1,3-dioxanes can be estimated with the aid of the equations:

$$k_E/k_A = k(\text{trans-2,4-dimethyl-2-alkyl-1,3-dioxane})/k(\text{cis-2,4-dimethyl-2-alkyl-1,3-dioxane}) \quad (1)$$

$$k(\text{2-alkyl-2-methyl-1,3-dioxane}) = x_E k_E + (1 - x_E) k_A \quad (2)$$

where k_E is the rate of hydrolysis of the conformer with an equatorial alkyl group, k_A that of the conformer with an axial alkyl group, and x_E the mole fraction of the conformer with an equatorial alkyl group in the conformer mixture.

The second-order rate coefficients of the acid-catalyzed hydrolysis of *cis*- and *trans*-2,4-dimethyl-2-alkyl-1,3-dioxanes were measured or estimated in a previous paper² (Table 1). The mole fractions of the conformers of 2-alkyl-2-methyl-1,3-dioxanes were determined from NMR shifts of the methyl protons by Pihlaja and Äyräs.³

The values of the rate coefficients of the acid-catalyzed hydrolysis of the 2*e*-R, 2*a*-Me and 2*a*-R, 2*e*-Me forms of 2-alkyl-2-methyl-1,3-dioxanes estimated from eqns. (1) and (2) are presented in Table 3. The rates of hydrolysis of the conformers with axial alkyl groups differ only slightly from the rate of hydrolysis of "frozen" 2,2-dimethyl-1,3-dioxane. The rate of hydrolysis of 2*a*-isobutyl-2*e*-methyl-1,3-dioxane is, however, clearly higher, in agreement with

Table 1. Second-order rate coefficients of the acid-catalyzed hydrolysis of 2-alkyl-2-methyl- and 2-alkyl-2,4-dimethyl-1,3-dioxanes at different temperatures.

1,3-Dioxanes	12.1°C	20.0°C	25.0°C	$k_a, \text{M}^{-1}\text{s}^{-1}$		40.0°C	44.4°C
				30.0°C	35.0°C		
2,2-diMe			9.40		22.3		46.3
2,2-diEt			18.5		46.5		106.7
2-Me-2-Et			15.0		40.8		91.4
2-Me-2-Pr			14.15		34.7		80.75
2-Me-2-Bu			19.25		42.45		85.25
2-Me-2- <i>i</i> -Pr			24.2		55.0		125.8
2-Me-2- <i>i</i> -Bu			60.5	89.75	131.8		
2-Me-2- <i>s</i> -Bu			32.8	49.8		104.65	154.1
2-Me-2- <i>t</i> -Bu	60.4	118.2	172.5				
2,4-diMe-2- <i>i</i> -Bu (<i>cis</i>) ¹			15.9				
2,4-diMe-2- <i>i</i> -Bu (<i>trans</i>) ¹			40.9				
2,4-diMe-2- <i>i</i> -Pr (<i>cis</i>) ¹			4.26				
2,4-diMe-2- <i>i</i> -Pr (<i>trans</i>) ¹			34.0				
2,4-diMe-2- <i>s</i> -Bu (<i>cis</i>) ¹			5.1				
2,4-diMe-2- <i>s</i> -Bu (<i>trans</i>) ¹			51.1				
2,4-diMe-2- <i>t</i> -Bu (<i>cis</i>) ¹			5.35 ^a				
2,4-diMe-2- <i>t</i> -Bu (<i>trans</i>) ¹			177				
2,4-diMe-2-Et (<i>cis</i>) ¹			4.64				
2,4-diMe-2-Et (<i>trans</i>) ¹			14.0				
2,4-diMe-2-Pr (<i>cis</i>) ¹			6.0				
2,4-diMe-2-Pr (<i>trans</i>) ¹			20.8				
2,4-diMe-2-Bu (<i>cis</i>) ¹			7.1				
2,4-diMe-2-Bu (<i>trans</i>) ¹			29.4				

^a For the hypothetical chair form.

Table 2. Corrected rate coefficients at 25°C and derived kinetic quantities for the hydronium ion-catalyzed hydrolysis of 2-alkyl-2-methyl-1,3-dioxanes.

1,3-Dioxane	E , kcal/mol	$\log A$	ΔS^\ddagger , e.u.	ΔG^\ddagger , kcal/mol	k_a^{25} , $M^{-1}s^{-1}$
2,2-diMe	15.47 ± 0.18	12.31 ± 0.13	-4.18 ± 0.60	16.13	9.45
2,2-diEt	16.99 ± 0.10	13.72 ± 0.07	+2.25 ± 0.33	15.73	18.45
2-Me-2-Et	17.54 ± 0.27	14.04 ± 0.19	+3.71 ± 0.88	15.84	15.2
2-Me-2-Pr	16.88 ± 0.30	13.52 ± 0.21	+1.84 ± 0.98	15.89	13.96
2-Me-2-Bu	14.43 ± 0.00	11.86 ± 0.00	-6.25 ± 0.01	15.70	19.25
2-Me-2- <i>i</i> -Pr	15.95 ± 0.62	13.07 ± 0.44	-0.74 ± 2.01	15.57	23.8
2-Me-2- <i>i</i> -Bu	14.21 ± 0.01	12.20 ± 0.02	-4.73 ± 0.11	15.03	60.50
2-Me-2- <i>s</i> -Bu	14.78 ± 0.36	12.35 ± 0.26	-4.01 ± 1.18	15.39	32.76
2-Me-2- <i>t</i> -Bu	13.78 ± 0.26	12.34 ± 0.20	-4.04 ± 0.90	14.40	173.7

 Table 3. Second-order rate coefficients of the acid-catalyzed hydrolysis of the conformational isomers of 2-alkyl-2-methyl-1,3-dioxanes and the mole fractions of the 2-*e*-R,2-*a*-Me conformers.³

Compound	x_E	k_{obs}	k_E/k_A	k_A	k_A/k_0	k_E	k_E/k_0
2,2-diMe	0.50	9.45	1	4.725	1	4.725	1
2,2-diEt	0.50	18.45	1	9.225	1.95	9.225	1.95
2-Me-2-Et	0.667	15.2	3.02	6.48	1.37	19.6	4.15
2-Me-2-Pr	0.625	13.96	3.47	5.49	1.16	19.0	4.03
2-Me-2-Bu	0.676	19.25	4.14	6.16	1.31	25.5	5.40
2-Me-2- <i>i</i> -Pr	0.737	23.8	7.98	3.87	0.82	30.9	6.55
2-Me-2- <i>i</i> -Bu	0.659	60.50	2.57	29.7	6.29	76.4	16.2
2-Me-2- <i>s</i> -Bu	0.691	32.76	10.0	4.54	0.96	45.4	9.62
2-Me-2- <i>t</i> -Bu	ca. 1	173.7	33.1	5.25 ^a	1.11	173.7	36.8

^a For the hypothetical chair form.

Table 4. Relative free energies of activation for the hydrolysis of the conformational isomers of 2-alkyl-2-methyl-1,3-dioxanes. The standard free energy differences between the ground states of the 2*a*-R,2*a*-Me and 2*a*-R,2*a*-Me forms of 2-alkyl-2-methyl-1,3-dioxanes and those between the transition states in the hydrolysis reactions. Values of the polar substituent constants and the quantity $\log(k/k_0)$ $-0.54(\Delta\pi)$ terms for the conformer pairs.

Substituents	$\Delta G^\ddagger_{\text{rel}}(\text{ex-R})$ kcal/mol	$\Delta G^\ddagger_{\text{rel}}(\text{eq-R})$ kcal/mol	$\Delta G^\circ(\text{A-E})$ kcal/mol	$\Delta G_{\text{TS}}(\text{A-E})$ kcal/mol	$\log(k_{\Delta}/k_0)$ $-0.54(\Delta\pi)$	$\log(k_{\text{E}}/k_0)$ $-0.54(\Delta\pi)$	$\Sigma\sigma^*$
2,2-diMe	0	0	0	0	0.00	0.00	0.000
2,2-diEt	-0.40	-0.401	0	0	1.37	1.37	-0.200
2-Me-2-Et	-0.19	-0.84	0.41	1.06	0.68	1.16	-0.100
2-Me-2-Pr	-0.09	-0.82	0.30	1.03	0.60	1.145	-0.115
2-Me-2-Bu	-0.16	-1.00	0.44	1.28	0.66	1.27	-0.130
2-Me-2- <i>t</i> -Pr	+0.12	-1.11	0.61	1.84	0.99	1.90	-0.190
2-Me-2- <i>s</i> -Bu	-0.89	-1.65	0.40	1.16	1.34	1.75	-0.125
2-Me-2- <i>t</i> -Bu	+0.02	-1.34	0.48	1.84	1.06	2.06	-0.210
2-Me-2- <i>s</i> -Bu	-0.06	-2.14	^a	^a	1.665	3.13	-0.320

^a Unknown.

the strong interactions between the methyl groups of the isobutyl group and the equatorial 2-methyl substituent or the ring oxygen atoms.^{1,3} The rates of 2*e*-alkyl-2*a*-methyl-1,3-dioxanes increase appreciably in the order Me < Et ≈ Pr < Bu < *i*-Pr < *s*-Bu < *t*-Bu in accordance with the values of the polar substituent constants. Again, the isobutyl derivative is more reactive owing to additional interactions, which are similar to those in the other conformer, *i.e.* the ground state energies of 2-isobutyl-2-methyl-1,3-dioxanes are somewhat higher than those of the other compounds.

The free energies of activation of the conformational isomers of 2-alkyl-2-methyl-1,3-dioxanes and "frozen" 2,2-dimethyl-1,3-dioxane (Table 2; 16.13 + $RT \ln 2$ kcal/mol) are presented in Table 3 together with the standard free energy differences between the ground states of the 2*a*-R,2*e*-Me and 2*e*-R,2*a*-Me forms. These values show that the steric requirements of the axial alkyl groups increase the free energy of the transition state clearly more than those of the equatorial alkyl groups (Fig. 1). Branching at the α -position of the alkyl chain decreases appreciably the stability of the transition state of the 2*a*-R,2*e*-Me forms, whereas chain length has only a minor effect.

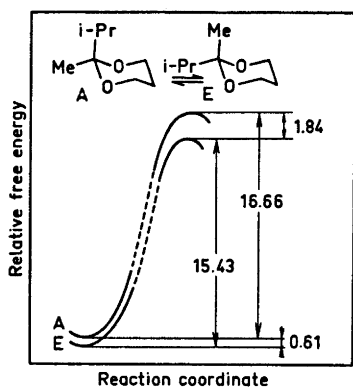


Fig. 1. The free energy profiles for the hydrolytic decomposition of the conformational isomers of 2-isopropyl-2-methyl-1,3-dioxane.

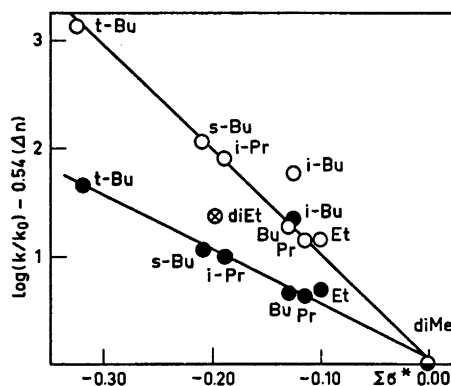


Fig. 2. The Taft-Hammett plots for the hydrolysis of the conformational isomers of 2-alkyl-2-methyl-1,3-dioxane. O, equatorial alkyl groups; ●, axial alkyl groups; ⊕, 2,2-diethyl-1,3-dioxane.

The dependence of the hydrolysis rates of the conformational isomers of 2-alkyl-2-methyl-1,3-dioxanes on polar factors is presented by Taft-Hammett plots (3) in Fig. 2:^{2,5}

$$\log(k/k_0) - (\Delta n) \times 0.54 = \sum \sigma^* \rho^* + b \quad (3)$$

where k is the rate coefficient of the conformer in question, k_0 that of "frozen" 2,2-dimethyl-1,3-dioxane, and Δn an integer which is the difference in the numbers of α -hydrogen atoms in the substituents of the reference acetal and

the compound in question. Good linear correlations are found for both series of conformers (Fig. 2), excluding again¹ the isobutyl derivatives, owing to the severe crowding of the substituents which increases the free energies of their ground states.

The derived Taft-Hammett equations

$$2a\text{-R-series: } (-5.041 \pm 0.278)\sigma^* + (0.041 \pm 0.050)$$

$$2e\text{-R-series: } (-9.645 \pm 0.289)\sigma^* + (0.056 \pm 0.052)$$

are in close agreement with those derived earlier for *cis*- and *trans*-2,4-dimethyl-2-alkyl-1,3-dioxanes:

$$cis\text{ series: } (-5.044 \pm 0.275)\sigma^* - (0.014 \pm 0.034)$$

$$trans\text{ series: } (-9.782 \pm 0.236)\sigma^* - (0.012 \pm 0.029)$$

This agreement confirms the value of NMR spectroscopy as a method for determining the relative amounts of conformers.

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