

## Solvent Effects in NMR Spectroscopy

### I. Toluene-Induced Shifts in the Spectra of Non-Aromatic Heterocycles. A New Approach to Clarify the Origin of the Observed Solvent Shifts

KALEVI PIHLAJA and MIRJAMI ALA-TUORI

*Department of Chemistry, University of Turku, SF-20500 Turku 50, Finland*

The temperature dependent variations of the chemical shifts of the proton resonances of 1,3-dioxane (I), 2,2-dimethyl-1,3-dioxane (II), 2,2-*cis*-4,5,*trans*-6-pentamethyl-1,3-dioxane (III), 5,5-dimethyl-2-oxo-1,3-dioxane (IV), *trans*-4,6-dimethyl-2-oxo-1,3-dioxane (V), 5,5,6-trimethyl-4-oxo-1,3-dioxane (VI), *cis*-2,5,5,6-tetramethyl-4-oxo-1,3-dioxane (VII), and 1,4-dioxane (VIII) in toluene solutions have been determined.

The relation  $K = (B/T) - 1$  was found to best represent the dependence of the apparent equilibrium constant on temperature.  $B$  is a constant which expresses the "critical" temperature for the so-called collision complex equilibrium.

The apparent equilibrium constants, the enthalpy changes, the entropy changes, and the heat capacity changes at the normal probe temperature (33 K) were found to lie in the ranges 0.6–2.2 mol<sup>-1</sup>, 0.9–1.7 kcal/mol, 1.4–6.6 cal mol<sup>-1</sup> degree<sup>-1</sup>, and 4.4–15.0 cal mol<sup>-1</sup> degree<sup>-1</sup>, respectively.

However, all of the collected data indicate that no real one-to-one complex formation occurs. The observed chemical shifts are mainly due to solvation phenomena and the values of the thermodynamic quantities are merely indicative of a more or less extensive solvation.

The view that aromatic solvents may form stereospecific collision complexes with polar solutes has become surprisingly generally accepted.<sup>1-3</sup> Ledaal<sup>2</sup> proposed a common model in which the dipole axis of the solute molecule is located along the axis of symmetry of the aromatic solvent molecule with the positive end nearer, and the negative end farther from the latter. Moreover, almost all of the published papers include the assumption that one-to-one complexes are formed.<sup>1-8</sup>

Appreciable changes may occur in the chemical shifts of the different protons<sup>4</sup> of a polar molecule when it is transferred from an "inert" solvent to an aromatic one. Moreover, the aromatic solvent induced shift (ASIS)

usually depends on the relationship of the proton in question to the polar function of the solute molecule.<sup>4,5</sup> On the basis of this stereospecificity, solvent shifts are of great value in structure elucidation.

In view of the extensive use of solvent shifts in the empirical sense and the possibility of obtaining more information about weak molecular interactions, we undertook a study of the association of several six-membered saturated heterocycles with toluene. Our purpose was to determine the influence of different hetero atoms and ring conformations on the ASIS and to throw light on the actual course of complex formation and to clarify solvation effects.

### EXPERIMENTAL

All of the studied compounds except 1,4-dioxane had been prepared earlier.<sup>9-11</sup> 1,4-Dioxane was a commercial product (*p.a.*) from Merck.

The NMR spectra were recorded on a 60 MHz Perkin-Elmer R10 NMR spectrometer equipped with a variable temperature probe. Carbon tetrachloride was selected as the "inert" solvent owing to the low solubilities of the 2-oxo-1,3-dioxanes in hydrocarbon solvents. Toluene was used instead of benzene as the "active" solvent to permit the performance of measurements below 273 K. The solute concentrations were varied from 2 to 4 % (w/v) and the resonance positions (Hz) were measured from the signal of internally added tetramethylsilane (Tables 1-5). The NMR shifts in carbon tetrachloride were measured only at the normal probe temperature of 306.35 K (Tables 1-5). The chemical shifts of the different protons in 5,5,6-trimethyl-4-oxo-1,3-dioxane (VI) were measured also in a number of toluene carbon tetrachloride mixtures (Table 6 and Fig. 7).

Table 1. Chemical shifts of different protons in 1,3-dioxane (I) and 2,2-dimethyl-1,3-dioxane (II) in carbon tetrachloride at 33.2°C and in toluene at different temperatures.

Temp. °C	2-H		1,3-Dioxane <sup>a</sup>		5-H		2,2-Dimethyl-1,3-dioxane <sup>a</sup>		
	2-H	$\Delta_t$	4,6-H	$\Delta_t$	5-H	$\Delta_t$	2-Me	4,6-H	$\Delta_t$
33.2 (CCl <sub>4</sub> )	285.0	0	231.0	0	102.0	0	78.5	228.0	0
91.5	282.0	3.0	215.0	16.0	82.5	19.5	81.0	220.2	7.8
81.5	281.7	3.3	214.5	16.5	81.0	21.0	—	218.5	9.5
71.6	281.5	3.5	213.0	18.0	80.0	22.0	80.5	218.0	10.0
61.7	281.0	4.0	212.4	18.6	79.0	23.0	—	—	—
51.8	280.0	5.0	212.0	19.0	78.5	23.5	—	217.7	10.3
33.2	279.5	5.5	211.0	20.0	76.6	25.4	80.5	217.5	10.5
19.9	279.5	5.5	210.5	20.5	76.0	26.0	—	—	—
10.1	279.2	5.8	209.5	21.5	75.0	27.0	—	216.0	12.0
0.3	279.0	6.0	208.5	22.5	74.0	28.0	—	—	—
-9.5	278.0	7.0	207.6	23.4	73.0	29.0	—	214.0	14.0
-19.5	278.5	6.5	207.0	24.0	73.0	29.0	—	—	—
-29.5	278.5	6.5	207.0	24.0	72.5	29.5	80.5	213.0	15.0
-39.5 <sup>b</sup>	—	—	205.5	25.5	71.5	30.5	—	—	—
-49.5	—	—	205.0	26.0	71.0	31.0	—	211.7	16.3
-59.2	—	—	203.5	27.5	70.5	31.5	80.5	210.0	18.0

<sup>a</sup> Both compounds are mixtures of two equivalent conformations.

<sup>b</sup> Owing to the broadening of this signal when approaching the coalescence temperature, its chemical shift was not employed in the calculation of the thermodynamic parameters of the collision complex equilibria. All values except those in the first line refer to solutions in toluene.

Table 2. Chemical shifts of different protons in 2,2,*cis*-4,5,*trans*-6-pentamethyl-1,3-dioxane (III) in carbon tetrachloride at 33.2°C and in toluene at different temperatures. All values except those in the first line refer to toluene solutions.

Temp. °C	2-CH <sub>3</sub> (both)	4-CH <sub>3</sub>	5-CH <sub>3</sub>	$\Delta_i$	6-CH <sub>3</sub>	4-H	$\Delta_i$	6-H	$\Delta_i$
33.2 (CCl <sub>4</sub> )	76.5	62.1	49.3	0	70.0	199.0	0	238.5	0
91.5	79.0	59.8	43.6	5.7	68.1	204.0	-5.0	241.0	-2.5
81.5			43.0	6.3		203.0	-4.0	241.2	-2.7
61.7	79.0	59.6	42.5	6.8	68.0	203.2	-4.2	240.5	-2.0
51.8			42.3	7.0		202.0	-3.0	240.0	-1.5
33.2			41.7	7.6		201.0	-2.0	239.5	-1.0
10.1			41.2	8.1		199.5	-0.5	239.0	-0.5
-9.5			39.4	9.9		197.8	+1.2	238.0	+0.5
-29.5	80.0	58.6	38.6	10.7	67.6	197.0	+2.0	237.7	+0.8
-49.5			37.0	12.3		196.0	+3.0	237.5	+1.0
-68.8	82.5	58.3	36.5	12.8	66.8	195.5	+3.5	237.0	+1.5
-78.4			36.0	13.3		195.0	+4.0	236.0	+2.5

Table 3. Chemical shifts of different protons in 5,5-dimethyl-2-oxo-1,3-dioxane (IV), *trans*-4,6-dimethyl-2-oxo-1,3-dioxane (V) and 1,4-dioxane (VIII) in carbon tetrachloride at 33.2°C and in toluene at different temperatures.

Temp. °C	5,5-Dimethyl-2-oxo-1,3-dioxane <sup>a</sup>				<i>trans</i> -4,6-Dimethyl-2-oxo-1,3-dioxane <sup>a</sup>				1,4-Dioxane <sup>a</sup>			
	5-Me	$\Delta_i$	4,6-H	$\Delta_i$	4,6-CH <sub>3</sub>	$\Delta_i$	5-H	$\Delta_i$	4,6-H	$\Delta_i$	2,3,5,6-H	$\Delta_i$
33.2 (CCl <sub>4</sub> )	67.0	0	241.5	0	87.3	0	115.5	0	280.5	0	217.0	0
91.5	32.5	34.5	203.5	38.0	57.8	29.5	72.5	43.0	245.0	35.5	206.0	11.0
81.5	31.0	36.0	202.0	39.5	57.3	30.0	72.0	43.5	244.2	36.3	205.0	12.0
71.6	30.0	37.0	201.5	40.0	57.0	30.3	71.8	43.7	244.5	36.0	—	—
61.7	29.0	38.0	200.0	41.5	—	—	—	—	—	—	205.0	12.0
51.8	—	—	—	—	56.0	31.3	70.3	45.2	242.0	38.5	204.0	13.0
33.2	26.5	40.5	198.0	43.5	54.0	33.3	69.0	46.5	240.0	40.5	203.0	14.0
24.7	—	—	—	—	—	—	—	—	—	—	202.5	14.5
19.9	25.5	41.5	198.0	43.5	—	—	—	—	—	—	—	—
15.0	—	—	—	—	—	—	—	—	—	—	202.0	15.0
10.1	—	—	—	—	51.3	36.0	65.6	49.9	238.7	41.8	—	—
0.3	24.0	43.0	196.5	45.0	—	—	—	—	—	—	—	—
-9.5	—	—	—	—	50.5	36.8	63.5	52.0	236.5	44.0	—	—
-19.5	22.5	44.5	195.0	46.5	—	—	—	—	—	—	—	—
-29.5	—	—	—	—	50.0	37.3	63.0	52.5	235.3	45.2	—	—
-39.5	21.0	46.0	194.5	47.0	—	—	—	—	—	—	—	—
-49.5	—	—	—	—	48.0	39.3	62.5	53.0	234.0	46.5	—	—
-68.8	—	—	—	—	47.5	39.8	61.7	53.8	232.5	48.0	—	—
-78.4	—	—	—	—	47.5	39.8	61.5	54.0	231.5	49.0	—	—

<sup>a</sup> All compounds are mixtures of two equivalent conformations. All values except those in the first line refer to toluene solutions.

Table 4. Chemical shifts of different protons in 5,5,6-trimethyl-4-oxo-1,3-dioxane (VI) in carbon tetrachloride at 33.2°C and in toluene at different temperatures. All values except those in the first line refer to toluene solutions. The equatorial 6-proton resonates at 229.0 cps in CCl<sub>4</sub> and at 194.0 cps in C<sub>6</sub>H<sub>6</sub>, but the signal is obscured by the spinning bands of the toluene methyl peak in toluene solution.

Temp. °C	2-H (eq.)	$\Delta_t$	2-H (ax.)	$\Delta_t$	6-CH <sub>3</sub> (eq.)	$\Delta_t$	5-CH <sub>3</sub> (eq.)	$\Delta_t$	5-CH <sub>3</sub> (ax.)	$\Delta_t$
33.2 (CCl <sub>4</sub> )	318.0	0	320.0	0	73.0	0	70.9	0	73.5	0
91.5	288.0	30.0	298.0	22.0	53.0	20.0	59.1	11.8	63.5	10.0
71.6	286.0	32.0	296.0	24.0	51.2	21.8	58.4	12.5	62.8	10.7
51.8	285.0	33.0	295.0	25.0	49.6	23.4	57.0	13.9	62.3	11.2
33.2	282.5	35.5	294.0	26.0	48.3	24.7	56.6	14.3	62.1	11.4
10.1	280.5	37.5	292.0	28.0	46.5	26.5	56.0	14.9	61.9	11.6
- 9.5	279.0	39.0	290.0	30.0	44.2	28.8	54.8	16.1	61.6	11.9
-29.5	276.0	42.0	288.0	32.0	43.0	30.0	54.2	16.7	61.2	12.3
-49.5	274.0	44.0	286.5	33.5	41.9	31.1	54.0	16.9	61.2	12.3
-59.2	273.0	45.0	286.0	34.0	40.4	32.6	53.4	17.5	61.1	12.4
-68.8	272.5	45.5	285.0	35.0	38.9	34.1	52.2	18.7	60.8	12.7
-78.4	271.5	46.5	284.0	36.0	38.2	34.8	52.3	18.6	60.5	13.0
-88.1	271.0	47.0	283.5	36.5	36.9	36.1	51.8	19.1	60.5	13.0

Table 5. Chemical shifts of different protons in *cis*-2,5,5,6-tetramethyl-4-oxo-1,3-dioxane (VII) in carbon tetrachloride and toluene at different temperatures. All values except those in the first three lines refer to toluene solutions.

Temp. °C	2-H (ax.)	$\Delta_t$	2-CH <sub>3</sub> (eq.)	$\Delta_t$	6-H (ax.)	$\Delta_t$	6-CH <sub>3</sub> (eq.)	$\Delta_t$	5-CH <sub>3</sub> (eq.)	$\Delta_t$	5-CH <sub>3</sub> (ax.)	$\Delta_t$
33.2 (CCl <sub>4</sub> )	319.0	0	87.3	0	226.0	0	71.0	0	69.0	0	71.6	0
91.5 (CCl <sub>4</sub> )	—	—	88.0	-0.7	—	—	71.2	-0.2	69.0	0.0	71.0	+0.6
0.3 (CCl <sub>4</sub> )	—	—	86.5	0.8	—	—	70.5	+0.5	68.5	+0.5	71.0	+0.6
91.5	300.0	19.0	73.7	13.6	188.0	38.0	54.3	16.7	60.2	8.8	65.0	6.6
71.6	299.0	20.0	73.1	14.2	—	—	53.6	17.4	60.0	9.0	64.5	7.1
51.8	297.0	22.0	72.6	14.7	—	—	52.0	19.0	59.7	9.3	63.8	7.8
33.2	295.5	23.5	72.0	15.3	188.0	38.0	50.7	20.3	58.5	10.5	62.8	8.8
10.1	293.6	25.4	71.1	16.2	—	—	48.6	22.4	57.8	11.2	62.2	9.4
- 9.5	292.0	27.0	70.8	16.5	—	—	47.1	23.9	56.8	12.2	61.3	10.3
-29.5	291.0	28.0	70.7	16.6	—	—	45.4	25.6	56.8	12.2	61.7	9.9
-49.5	289.0	30.0	70.0	17.3	—	—	44.3	26.7	56.6	12.4	61.0	10.6
-68.8	286.8	32.2	69.8	17.5	187.0	39.0	42.1	28.9	56.2	12.8	61.5	10.1

## RESULTS

Generally, the equilibrium constant for collision complex formation is expressed by the equation<sup>1,12</sup>

$$K = p/(1-p) \quad (1)$$

where  $p$  is the fraction of the solute present in complex form. The quantity  $p$  can be calculated from the expression

$$p = (\Delta_t' - \Delta_0)/(\Delta_c' - \Delta_0) \quad (2)$$

Table 6. The dependence of the proton chemical shifts of 5,5,6-trimethyl-4-oxo-1,3-dioxane on the mol fraction of toluene in toluene-CCl<sub>4</sub> mixtures. The parameters of the linear equation  $\Delta_{\text{obs}} = mx_{\text{tol}} + b$ <sup>a</sup> are given. See also Fig. 7.

$x_{\text{tol}}$	$\Delta(6\text{-Me})$	$\Delta(5e\text{-Me})$	$\Delta(5a\text{-Me})$	$\Delta(2e\text{-H})$	$\Delta(2a\text{-H})$	$\Delta(6a\text{-H})$
0	0	0	0	0	0	0
0.15	4.0	2.5	1.5	6.0	6.0	5.0
0.20	6.0	(4.5)	3.5	7.0	7.0	(6.0)
0.25	6.5	4.0	3.5	9.5	10.0	12.0
0.35	10.0	6.5	4.5	14.0	12.5	15.0
0.40	11.5	7.0	6.0	15.0	15.0	18.0
0.50	13.5	8.5	6.5	18.0	18.0	21.0
0.60	16.5	10.5	7.5	20.0	21.0	25.5
0.70	18.5	12.0	9.5	24.0	23.0	27.0
0.80	21.0	13.5	10.5	27.5	25.0	31.5
$m$ , Hz	25.96	17.06	12.84	32.60	30.27	38.44
$b$ , Hz	0.55	0.07	0.25	1.36	1.99	1.35
$\sigma_m$ , Hz	0.67	0.46	0.76	1.13	1.36	2.24
$\sigma_b$ , Hz	0.33	0.24	0.37	0.55	0.66	1.15
$r$	0.898	0.915	0.898	0.898	0.898	0.898

<sup>a</sup> The deviation of this parameter from zero shows that toluene exerts even in extreme dilution a small effect on the chemical shifts.

Table 7. The values of  $m$  and  $\Delta_c$  for the different protons in the studied compounds derived by least squares fit of the equation  $\Delta_i = mT + \Delta_c$ <sup>a</sup>

Compound	Protons	$m$ , cps/K	$\sigma_m$ , cps/K	$\Delta_c$ , cps	$\sigma(\Delta_c)$ , cps	$\sigma(m, \Delta_c)$
I	4,6-H	0.0712	0.0022	-42.01	0.64	-0.0014
I	5-H	0.0776	0.0024	-48.69	0.71	-0.0017
II	4,6-H	0.0591	0.0044	-29.61	1.32	-0.0057
III	4-H	0.0553	0.0024	-15.11	0.67	-0.0016
III	6-H	0.0285	0.0014	-7.68	0.40	-0.0006
III	5-Me	0.0456	0.0024	-21.98	0.69	-0.0016
IV	4,6-H	0.0672	0.0042	-63.33	1.32	-0.0055
IV	5-Me	0.0852	0.0027	-66.25	0.83	-0.0022
V	4,6-H	0.0818	0.0027	-64.97	0.78	-0.0021
V	5-H	0.0718	0.0049	-69.12	1.43	-0.0069
V	4,6-Me	0.0663	0.0034	-53.58	0.97	-0.0032
VI	2e-H	0.0986	0.0020	-65.65	0.55	-0.0011
VI	2a-H	0.0819	0.0016	-51.67	0.44	-0.0007
VI	5e-Me	0.0394	0.0016	-26.26	0.42	-0.0006
VI	5a-Me	0.0148	0.0009	-15.78	0.24	-0.0002
VI	6e-Me	0.0865	0.0022	-51.37	0.58	-0.0012
VII	2a-H	0.0812	0.0021	-48.33	0.60	-0.0012
VII	2e-Me	0.0247	0.0014	-22.80	0.42	-0.0006
VII	5e-Me	0.0279	0.0025	-18.86	0.73	-0.0018
VII	5a-Me	0.0250	0.0034	-16.06	1.00	-0.0034
VII	6e-Me	0.0748	0.0025	-43.71	0.72	-0.0017
VIII	2,3,5,6-H	0.0504	0.0046	-29.44	1.49	-0.0068

<sup>a</sup> Also the standard errors and the covariances of the parameters are shown.

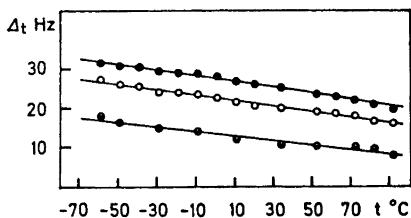


Fig. 1. Temperature-dependent solvent shifts  $\Delta(C_6H_5CH_3-CCl_4)$  of 1,3-dioxane (○ 4,6-H; ● 5-H) and 2,2-dimethyl-1,3-dioxane (● 4,6-H).

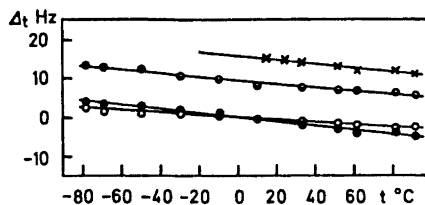


Fig. 2. Temperature-dependent solvent shifts  $\Delta(C_6H_5CH_3-CCl_4)$  of 2,2,*cis*-4,5,*trans*-6-pentamethyl-1,3-dioxane (○ 4-H; ● 6-H; ● 5-Me) and 1,4-dioxane (2,3,5,6-H ×).

where  $\Delta'_c$  is the chemical shift of a solute proton in the complex,  $\Delta_0$  the corresponding chemical shift in an "inert" solvent ( $CCl_4$ ) and  $\Delta'_i$  the observed shift in an "active" solvent ( $C_6H_5CH_3$ ) at temperature  $t$ .

By changing the notation, we may write

$$p = \Delta_i / \Delta_c \quad (3) \quad K = \Delta_i / (\Delta_c - \Delta_i) \quad (4)$$

$\Delta_c$  can be estimated by extrapolation of a plot of  $\Delta_i$  versus temperature to 0 K. The plots in Figs. 1–5 and the data in Table 7 show that a good linear dependence prevails between  $\Delta_i$  and temperature.\* Hence

$$\Delta_i = mT + \Delta_c \quad (5)$$

When eqn. (5) is substituted in eqn. (4), the relation

$$K = (-\Delta_c/m)(1/T) - 1 = (B/T) - 1 \quad (6)$$

where  $B$  is a constant which defines the "critical" temperature for the complex formation, is obtained. This equation implies that the apparent equilibrium constant is a linear function of reciprocal temperature. Therefore a plot of  $\log K$  against reciprocal temperature is not linear but has a curvature which depends on the magnitude of the change in the heat capacity.

The following equations may hence be derived for the calculation of the enthalpy, entropy, and heat capacity changes at different temperatures:

$$\Delta H = -RT(K+1)/K \pm (R/K^2)\sigma_B \quad (7)$$

$$\Delta S = (\Delta H/T + R \ln K) \pm (K+1)[\sigma(\Delta H)/T] \quad (8)$$

$$\Delta C_p = (-1/R)(\Delta H/T)^2 \pm [2\sigma(\Delta S)/K] \quad (9)$$

The standard error of the critical temperature  $B$  may be estimated from the expression

\* In this connection it is worth mentioning that the ASIS is also an approximately linear function of the density of toluene at various temperatures. In other words, when the temperature is lowered, the solvation shells become more tightly bound and the attractive forces between the solute and solvent molecules predominate. Correspondingly, a higher temperature increases the disorder of the solution, and above the "critical" temperature, repulsive forces predominate, *i.e.* the ASIS changes sign.<sup>18</sup>

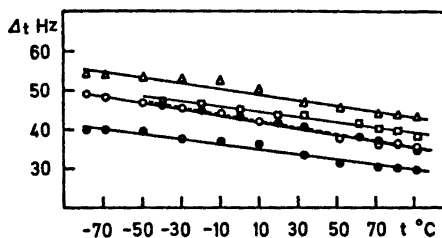


Fig. 3. Temperature-dependent solvent shifts  $\Delta(C_6H_9CH_3 - CCl_4)$  of 5,5-dimethyl-2-oxo-1,3-dioxane ( $\square$  4,6-H;  $\bullet$  5-Me) and *trans*-4,6-dimethyl-2-oxo-1,3-dioxane ( $\circ$  4,6-H;  $\bullet$  4,6-Me;  $\triangle$  5-H).

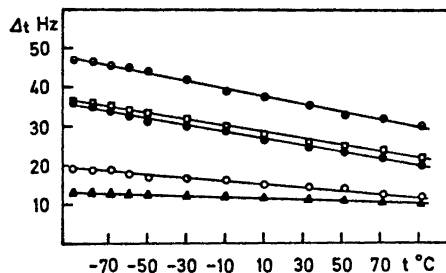


Fig. 4. Temperature-dependent solvent shifts  $\Delta(C_6H_9CH_3 - CCl_4)$  of 5,5,6-trimethyl-4-oxo-1,3-dioxane ( $\circ$  5-Me;  $\bullet$  2e-H;  $\bullet$  6e-Me;  $\square$  2a-Me;  $\triangle$  5a-Me).

$$\sigma_B = \frac{\sqrt{(\sigma(\Delta_c))^2 + (B\sigma_m)^2 + 2B\sigma(m, \Delta_c)}}{m} \quad (10)$$

where  $\sigma(\Delta_c)$  is the standard error of  $\Delta_c$ ,  $\sigma_m$  the standard error of  $m$ , and  $\sigma(m, \Delta_c)$  the covariance of  $m$  and  $\Delta_c$  (Table 7).

## DISCUSSION

In earlier reports<sup>1,14,15</sup> it has been assumed that  $\log K$  varies linearly as reciprocal temperature. However, our results show that ASIS for the studied compounds is a linear function of temperature (Figs. 1–5). Of course, the conclusion that the apparent equilibrium constant is linearly dependent on reciprocal temperature is directly supported only when eqn. (5) is fulfilled. The relatively great number of experiments carried out in this study led us to conclude that a change in heat capacity is very probable also in the case of collision complex equilibria or solvation phenomena reported by other workers.<sup>1–8</sup> For this reason we replotted both the values of  $K$  and the values of  $\log K$  for the shift of the 12- $\alpha$ -hydrogen of 5 $\alpha$ -androstan-11-one against reciprocal temperature since Laszlo and Williams<sup>1</sup> reported a nonlinear relation between  $\Delta_t$  and  $T$  in this case. The resulting curves show that a good linear correlation exists between  $K$  and  $1/T$  (Fig. 6):

$$K = (157.8 \pm 4.6)/T - (0.131 \pm 0.018) \quad (11)$$

Consequently, the values  $-0.78 \pm 0.01$  kcal/mol,  $-4.5 \pm 0.1$  cal mol<sup>-1</sup> degree<sup>-1</sup> and  $-3.5 \pm 0.1$  cal mol<sup>-1</sup> degree<sup>-1</sup> are obtained for the enthalpy, entropy, and heat capacity changes, respectively. Laszlo and Williams<sup>1</sup> reported the value  $-0.65 \pm 0.15$  kcal/mol for the enthalpy change and assumed the heat capacity change to be zero.

Fort and Lindstrom<sup>13</sup> evaluated  $\Delta_c$  for *t*-butyl and adamantyl halides by linear extrapolation but nevertheless presented  $\log K$  as a linear function of reciprocal temperature. This is, strictly speaking, inconsistent since it means that both  $K$  and  $\log K$  should be linear functions of  $1/T$  (cf. eqns. (5) and (6)).

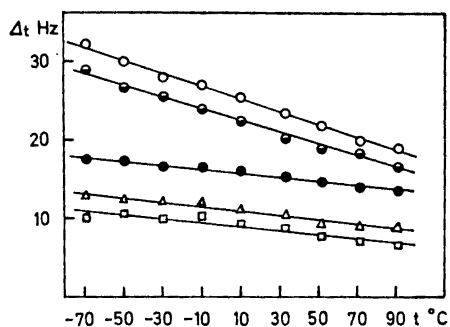


Fig. 5. Temperature-dependent solvent shifts  $\Delta t$  ( $C_6H_5CH_3-CCl_4$ ) of *cis*-2,5,5,6-tetramethyl-4-oxo-1,3-dioxane (○ 2a-H; ● 6e-Me; ● 2e-Me; △ 5e-Me; □ 5a-Me).

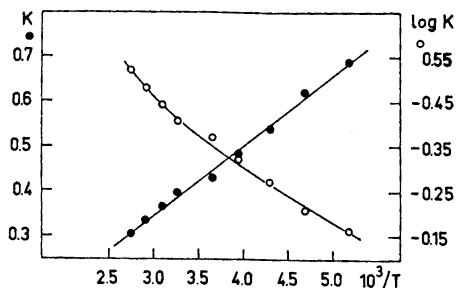


Fig. 6. Apparent equilibrium constant ( $K$ ) and its logarithm as function of reciprocal temperature for the 12- $\alpha$ -H of 5 $\alpha$ -androstan-11-one.

Table 8 shows the values of the critical temperature (eqn. (6)) and the values of  $\Delta H$ ,  $\Delta S$ , and  $\Delta C_p$  calculated from eqns. (7)–(9) and those of  $\Delta H$  and  $\Delta S$  presented by Fort and Lindstrom.<sup>13</sup>

Table 8. Thermodynamic parameters for the collision complex equilibria of *t*-butyl and adamantyl halides in several aromatic solvents. The values calculated in this work from the results of Fort and Lindstrom at 25°C are compared with the results of these authors.

Compound	Solvent	Fort and Lindstrom			$B, K$	This work		
		$K$	$-\Delta H,$ kcal/mol	$-\Delta S,$ e.u.		$-\Delta H,$ kcal/mol	$-\Delta S,$ e.u.	$-\Delta C_p,$ cal/mol degree
<i>t</i> -BuCl	$C_6H_6$	1.11	1.19	3.8	629	1.13	3.6	7.2
	PhF	1.69	0.86	1.8	802	0.94	2.1	5.0
	PhCl	1.51	0.93	2.3	748	0.98	2.5	5.5
	PhBr	0.92	1.19	2.7	572	1.24	4.3	8.6
	PhI	1.68	1.12	2.8	799	0.94	2.1	5.1
<i>t</i> -BuBr	$C_6H_6$	1.15	1.23	3.8	641	1.11	3.4	7.0
	PhF	1.51	0.90	2.2	748	0.98	2.5	5.5
	PhCl	1.77	0.83	1.6	826	0.93	2.0	4.9
	PhBr	1.54	0.99	0.3	757	0.98	2.4	5.4
<i>t</i> -BuI	$C_6H_6$	1.39	1.00	2.7	713	1.02	2.8	5.9
	PhF	1.82	0.88	1.8	841	0.92	1.9	4.8
	PhCl	1.57	0.84	1.9	766	0.97	2.4	5.3
$C_{10}H_{15}Cl$	$C_6H_6$	1.18	1.09	3.3	650	1.09	3.3	6.8
	PhF	0.77	1.07	4.1	528	1.36	5.1	10.5
	PhCl	0.89	1.08	3.8	564	1.26	4.4	9.0
	PhI	1.51	1.07	2.3	748	0.98	2.5	5.5
$C_{10}H_{15}Br$	$C_6H_6$	1.24	0.82	2.3	668	1.07	3.2	6.5
	PhF	1.00	0.96	3.2	596	1.18	4.0	7.9
	PhCl	1.03	1.00	3.3	605	1.17	3.9	7.7
	PhI	1.72	1.03	1.6	811	0.94	2.1	5.0
$C_{10}H_{15}I$	$C_6H_6$	1.24	0.92	2.6	668	1.07	3.2	6.5
	PhF	1.05	1.01	3.3	611	1.16	3.8	7.6
	PhCl	1.15	1.03	3.2	641	1.11	3.4	6.9
	PhI	1.59	1.04	2.3	772	0.96	2.3	5.3



Comparison of the results in Table 8 reveals that marked differences exist between the values of  $\Delta H$  and  $\Delta S$  reported by Fort and Lindstrom and those calculated from their data using eqns. (7) and (8). The values of  $\Delta C_p$  vary between  $-5$  and  $-10$  cal mol $^{-1}$  degree $^{-1}$ . However, the differences between the thermodynamic parameters of the various complexes are still very small and for this reason we agree with the conclusion of Fort and Lindstrom<sup>13</sup> that the calculated equilibrium constants and energy quantities have no very clear-cut meaning, but perhaps indicate the orders of magnitude of the weak interactions which in our opinion are largely due to solvation and not to complex formation. In this connection we refer to the following discussion and the results presented in the second paper of this series.<sup>15a</sup>

Bowie *et al.*<sup>14</sup> investigated the dependence of the resonance positions of the methoxyl protons of anisole, *p*-nitroanisole and *p*-*N,N*-dimethylaminoanisole on temperature and plotted the values of  $\log K$  against  $1/T$ . We reviewed their results and computed the values of  $\Delta H$ ,  $\Delta S$ , and  $\Delta C_p$  at 25°C on an IBM 1130 computer at the Computer Center of our University. The

Table 9. Values of thermodynamic quantities for anisole, *p*-nitroanisole, *p*-*N,N*-dimethylaminoanisole, and *p*-nitrobenzaldehyde.

Compound	$-\Delta H$ , kcal/mol	$-\Delta S$ , cal/mol degree	$-\Delta C_p$ , cal/mol degree	Reference
Anisole	$1.08 \pm 0.03$	$5.57 \pm 0.10$	$3.4 \pm 1.1$	This work, 25°C
	$1.01 \pm 0.04$	$5.38 \pm 0.13$	0 (assumed)	14, 20°C
<i>p</i> -Nitroanisole	$0.94 \pm 0.03$	$3.97 \pm 0.08$	$4.45 \pm 0.9$	This work, 25°C
	$0.85 \pm 0.04$	$3.74 \pm 0.15$	0 (assumed)	14, 20°C
<i>p</i> - <i>N,N</i> -Dimethylaminoanisole	$1.17 \pm 0.03$	$6.34 \pm 0.09$	$2.8 \pm 0.9$	This work, 25°C
	$1.11 \pm 0.03$	$6.19 \pm 0.11$	0 (assumed)	14, 20°C
<i>p</i> -Nitrobenzaldehyde	$0.58 \pm 0.02$	$3.12 \pm 0.06$	$0.6 \pm 0.4$	This work, 25°C
	$0.56 \pm 0.01$	$3.07 \pm 0.04$	0 (assumed)	16, 25°C

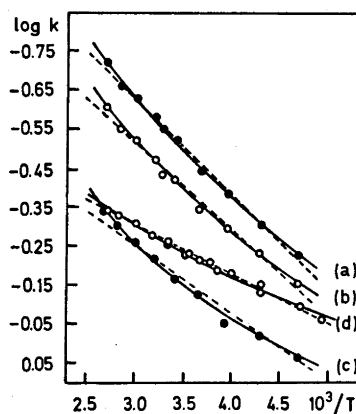


Fig. 7. Dependence of the logarithms of the apparent equilibrium constants on reciprocal temperature for the methoxyl protons of anisole (b), *p*-nitroanisole (c), *p*-*N,N*-dimethylaminoanisole (a), and those for the *meta* protons of *p*-nitrobenzaldehyde (d).

results are shown in Table 9 together with the values at 20°C reported by Bowie *et al.*<sup>14</sup> Also the data of Klinck and Stothers<sup>16</sup> for the *meta* protons of *p*-nitrobenzaldehyde are included (Fig. 7). In all cases the curvilinear plots gave a better fit to the experimental values although the change in heat capacity for *p*-nitrobenzaldehyde differs only slightly from zero.

It is possible to show that also in several other cases<sup>7,17-21</sup>  $\log K$  is a non-linear function of temperature and that  $K$  often is a linear function of reciprocal temperature (eqns. (5) and (6)).

Of the compounds studied in this work, all but 2,2-*cis*-4,5-*trans*-6-pentamethyl-1,3-dioxane (III) exist in a chair form or a slightly deformed chair form. III has the twist conformation.<sup>22-24</sup>

The solvent shifts  $\Delta(C_6H_5CH_3 - CCl_4)$  are always upfield except those for the 2-methyl group protons of 2,2-dimethyl-1,3-dioxane (II), which are slightly deshielded (2 Hz) and the protons of III for which the solvent shifts are very small and very specific owing to the twist conformation. 1,3-Dioxane (I), II, and 1,4-dioxane (VIII) show similar toluene induced shifts at the normal probe temperature (Tables 1 and 3), in agreement of the similarity of their conformations and polar functions. A 2-oxo group increases appreciably the polar functions of 1,3-dioxanes and hence the toluene-induced shifts of 2-oxo-1,3-dioxanes are at least twice those of the corresponding 1,3-dioxanes (Tables 1 and 3).<sup>24</sup> Similarly, a 4-oxo group tends to increase the toluene-induced shifts greatly, although the influence is somewhat less marked than in 2-oxo-1,3-dioxanes owing to the lesser symmetry of the polar function for 4-oxo-1,3-dioxanes (Tables 3-5).<sup>25</sup>

It is not easy to construct a special collision complex for all of the above compounds, but the toluene-induced shifts are best explainable with the aid of structural parameters on one hand and with the aid of more or less effective solvation on the other. For instance, the spectrum of III shows features which are clearly indicative of the twist conformation and of very loose solvation. All methyl groups except the 5-methyl group of III as well as the 4- and 6-protons are almost unaffected by toluene. An additional feature of this compound is the appreciable crossover effect of the resonances of the protons in positions 4 and 6, the critical temperature being only about 270 K for these protons. Moreover, the shifts of the 2-, 4-, and 6-methyl group protons are almost independent of temperature (Table 2).

Usually, as can be seen from Table 10, different protons in the same compound yield nearly equal values for the thermodynamic parameters. The values for the different compounds lie in very narrow ranges, but show also some differences which are obviously mainly structural indicators. For instance, both the 2-oxo-1,3-dioxanes IV and V gave exactly the same values for the thermodynamic quantities as did also 1,3-dioxane and the 4-oxo-1,3-dioxanes (I, VI, VII). This may be an indication that 2-oxo-1,3-dioxanes are ester-type compounds, whereas 4-oxo-1,3-dioxanes resemble the normal acetal 1,3-dioxane more.<sup>26</sup> As to the magnitude of the toluene-induced shifts in these compounds, it is very likely that 2-oxo-1,3-dioxanes are most effectively solvated and also the structural effect of the polar function on each position is very similar. In the case of 4-oxo-1,3-dioxane, structural factors are clearly different in the 2, 5, and 6 positions, in agreement with the observed shifts.

Table 10. Values of the "critical" temperatures, equilibrium constants, and thermodynamic parameters at the reference temperature 306.35 K.

Compound	Location of proton	B K	K	$-\Delta H$ kcal/mol	$-\Delta S$ e.u.	$-\Delta G$ kcal/mol	$-\Delta C_p$ cal/degree mol
I	4,6-H	590 ± 10	0.925	1.27 ± 0.02	4.29 ± 0.14	-0.05	8.61 ± 0.30
I	5-H	628 ± 11	1.05	1.19 ± 0.02	3.79 ± 0.14	0.03	7.58 ± 0.25
I	Average			1.23	4.0	-0.01	8.1
II	4,6-H	501 ± 16	0.64	1.565 ± 0.08	6.01 ± 0.42	-0.28	13.1 ± 1.3
III	5-CH <sub>3</sub>	482 ± 11	0.57	1.67 ± 0.07	6.56 ± 0.32	-0.34	15.0 ± 1.2
III	4-H <sup>a</sup>	274 ± 3	0.08	7.0 ± 0.9	32.5 ± 3.8	-1.3	378 ± 99
III	6-H <sup>a</sup>	269 ± 3	0.06	8.7 ± 1.2	39.8 ± 5.0	-1.4	592 ± 162
IV	4,6-H	942 ± 40	2.08	0.90 ± 0.02	1.49 ± 0.19	0.45	4.36 ± 0.13
IV	5-CH <sub>3</sub>	777 ± 15	1.54	1.005 ± 0.012	2.45 ± 0.10	0.26	5.42 ± 0.18
IV	Average			0.95	2.0	0.36	4.9
V	4,6-H	794 ± 17	1.59	0.99 ± 0.01	2.31 ± 0.11	0.28	5.27 ± 0.14
V	4,6-CH <sub>3</sub>	808 ± 27	1.64	0.98 ± 0.02	2.22 ± 0.17	0.30	5.15 ± 0.21
V	5-H	962 ± 47	2.14	0.89 ± 0.02	1.40 ± 0.21	0.46	4.28 ± 0.19
V	Average			0.95	2.0	0.35	4.9
VI	2a-H	630 ± 8	1.06	1.18 ± 0.01	3.74 ± 0.09	0.04	7.50 ± 0.17
VI	2e-H	666 ± 8	1.17	1.13 ± 0.01	3.36 ± 0.09	0.10	6.81 ± 0.15
VI	5e-CH <sub>3</sub>	667 ± 16	1.18	1.125 ± 0.02	3.35 ± 0.16	0.10	6.79 ± 0.28
VI	6e-CH <sub>3</sub>	594 ± 8	0.94	1.26 ± 0.02	4.23 ± 0.12	-0.04	8.48 ± 0.26
VI <sup>b</sup>	Average			1.17	3.7	0.05	7.4
VII	2a-H	595 ± 8	0.94	1.26 ± 0.02	4.21 ± 0.11	-0.03	8.44 ± 0.24
VII	5e-CH <sub>3</sub>	677 ± 36	1.21	1.11 ± 0.05	3.26 ± 0.35	0.11	6.64 ± 0.59
VII	5a-CH <sub>3</sub>	643 ± 50	1.10	1.16 ± 0.08	3.61 ± 0.56	0.06	7.26 ± 1.02
VII	6e-CH <sub>3</sub>	584 ± 10	0.91	1.28 ± 0.03	4.37 ± 0.15	-0.05	8.79 ± 0.34
VII <sup>c</sup>	Average			1.20	3.9	0.02	7.8
VIII	2,3,5,6-H	584 ± 61	0.91	1.28 ± 0.15	4.38 ± 0.92	-0.06	8.80 ± 2.02

<sup>a</sup> Reference temperature 253.65 K.

<sup>b</sup> 6a-H and 5a-CH<sub>3</sub> not included, see text.

<sup>c</sup> 6a-H and 2e-CH<sub>3</sub> not included, see text.

However, the contribution of the solvent is still very great, although slightly less than in 2-oxo-1,3-dioxanes because of the somewhat different polar functions.

If our approach to explain the "collision complex equilibria" as the sum of structural factors and solvation phenomena is correct, geminal methyl groupings at position 2 of 1,3-dioxane should retard somewhat the formation of the solvent shell. This conclusion is in accordance with the observed shifts and the fact that II has a greater tendency than that of I to be "uncomplexed" in toluene (Table 10). The dependence of the solvation on steric factors is still more evident in the case of III. The chemical shifts of all groups in III and especially those of 4- and 6-protons are typical indicators of the twist conformation and hence the value  $-\Delta H_{4,6}(\text{III}) + \Delta H(\text{I}) = 7.85 - 1.23 = 6.6$  kcal/mol is very strong evidence for the different ring conformation and reflects more or less the enthalpy difference between the chair and twist forms of 1,3-dioxane (7.2 - 8.5 kcal/mol<sup>23,27,28</sup>).

If we now accept that the parameters given in Table 10 are the best indicators of ring structure, conformation, and extent of solvation, the parameters for 1,4-dioxane (VIII) should be nearly equal to those for 1,3-dioxane. This conclusion is justified by the data in Table 10 and by the fact that the toluene-induced shift in VIII is nearly equal to the average of the different chemical shifts in I (Tables 1 and 3).

For the existence of the previously postulated one-to-one complexes, it is necessary that the solvent shift is a linear function of the mol fraction of toluene in its mixtures with the inactive solvent carbon tetrachloride, although this is not a direct confirmation of the complex formation. To test the possibility of complex formation with the studied compounds, we recorded the spectra of 5,5,6-trimethyl-4-oxo-1,3-dioxane in toluene- $\text{CCl}_4$  mixtures. The curves plotting the observed solvent shifts against the mol fraction of toluene are in all cases reasonably linear (Table 6, Fig. 8).

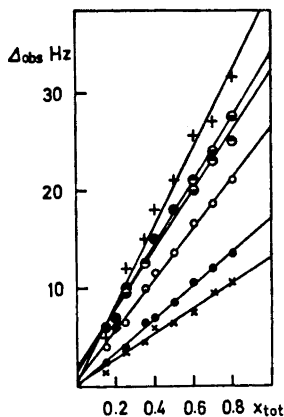


Fig. 8. Dependence of the proton chemical shifts of 5,5,6-trimethyl-4-oxo-1,3-dioxane on the mol fraction of toluene in toluene-carbon tetrachloride mixtures + 6-H;  $\circ$  2e-H;  $\bullet$  2a-H;  $\square$  6e-Me;  $\bullet$  5e-Me;  $\times$  5a-Me.

Another fact that may influence the results is the small "nonideality" of carbon tetrachloride. We could not, however, use any inactive hydrocarbon as solvent because of low solute solubility. We therefore recorded the NMR spectrum of *cis*-2,5,5,6-tetramethyl-4-oxo-1,3-dioxane in carbon tetrachloride over a range of temperatures. Except those for the 2-methyl group, the results (Table 5) indicate that the change in resonance positions is random and well within the error limits.

As to the structures of the collision complexes, our approach was based on the assumption of one-to-one complexes. However, the calculated apparent equilibrium constants and thermodynamic parameters represent average values for the actual situation. In reality, toluene undergoes self-association<sup>13</sup> and forms solvation shells around the solute molecules.<sup>15,29</sup> The limited variation of the entropy changes suggests that the solvation is similar for most of the studied polar compounds.

Solvation and toluene-induced chemical shifts seem to depend mainly on two factors, namely on the distance from the solute proton to the polar center

of the molecule and on the steric crowding around the solute molecule, *i.e.* the stability of the solvation shell.\*

We are collecting more data to confirm that it is not at all suitable to speak of definite complexes excluding charge-transfer and hydrogen-bonded complexes. The results of this work will be published in the near future.<sup>15b</sup>

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\* After this paper was written, Laszlo and Engler (*J. Am. Chem. Soc.* **93** (1971) 1317) proposed a time-averaged cluster of solvent molecules around the solute, in close agreement with our opinion.