Substituent Effects in the Acid-Catalyzed Hydrolysis of Cyclic Acetals of Benzophenones

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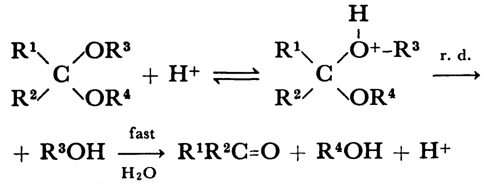
Synopsis. Eight 2,2-diaryl-1,3-dioxanes were prepared and the kinetic substituent effects regarding acid-catalyzed hydrolysis were studied in 80% dioxane–water(v/v) at 30 °C. The log *k* were well correlated with the Yukawa-Tsuno equation; $\log k/k_0 = -2.92(\sigma^0 + 0.385\Delta\bar{\sigma}_R{}^+)(r = 0.999)$.

There have been numerous investigations on the acid-catalyzed hydrolysis of acetals from a mechanistic point of view.[1–3] It is generally accepted that the acetals hydrolyze by an **Al** mechanism; pre-equilibrium protonation, rate-determining oxocarbenium ion formation, and fast degradation into carbonyl compound and alcohol (Scheme 1). As one part of the experimental evidence that supports the mechanism, a number of data have been collected related to kinetic substituent effects for the hydrolysis of a variety of acetals.[2] However, little is known about the cyclic acetals of benzophenones, especially with six-membered and higher ring sizes,[4] probably because of difficulties in a synthesis by traditional methods.[5]

Recently, we have discovered a facile synthetic method for cyclic and acyclic acetals of benzophenone using a redox reaction of diphenyldiazomethane(DDM) with 2,3-dichlore-5,6-dicyanobenzoquinone(DDQ) in the presence of suitable alcohols.[6–8] This discovery prompted us to synthesize cyclic acetals of benzophenones with a series of substituents and to obtain further information concerning the structure-reactivity relationship regarding the hydrolysis of acetals.



Scheme 1.

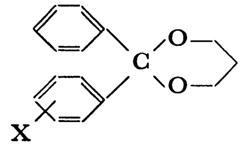
Table 1. Preparation and Hydrolysis of 2,2-Diaryl-1,3-dioxanes (**1a**—**h**)

Acetals	Substituents	Yields/%[a)]	Mp θ_m/°C	$10^4 k_{obsd}$ (s^{-1})[b)]
1a	*p*-OCH_3	62	52—53	51.0
1b	*p*-CH_3	52	76—78	17.1
1c	*m*-CH_3	61	67—69	6.96
1d	*p*-Ph	46	154—156	4.99
1e	H	84	113—115	1.36
1f	*p*-Cl	55	60—61	1.13
1g	*m*-Cl	56	75—77	0.311
1h	*m*-NO_2	58	oil	0.0396

a) Isolated yields by column chromatography(Al_2O_3).
b) All rates were measured in 80% dioxane-water at 30 °C under the constant HCl concentration(0.2 mol dm^{-3}).

Results and Discussion

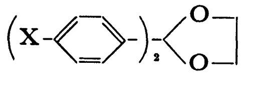
The eight *m*- and *p*-substituted 2,2-diaryl-1,3-dioxanes (**1a**—**h**) were prepared and the rates of acid-catalyzed hydrolyses of these six-membered cyclic acetals were determined in 80% dioxane-water (by volume) at 30 °C (Table 1). When various values of log *k* were correlated with the standard Hammett σ and the Brown σ⁺, the σ substituent constants gave a better result ($\rho=-3.10$, $r=0.997$) than σ⁺, ($\rho=-2.19$, $r=0.974$). It can be corroborated, however, that the resonance substituent effects moderately contribute to the stabilization of the transition state as evaluated from the value of the resonance reaction constant ($R=0.385$) in the satisfactory Yukawa-Tsuno equation.[9]



X=		X=
1a; *p*-OCH_3		**1e**; H
1b; *p*-CH_3		**1f**; *p*-Cl
1c; *m*-CH_3		**1g**; *m*-Cl
1d; *p*-Ph		**1h**; *m*-NO_2

$$\log k/k_0 = -2.92(\sigma^0 + 0.385\Delta\bar{\sigma}_{R^+}) - 0.05 \quad (n=8,\ r=0.999)$$

In Table 2, the Hammett parameters have been collected for the hydrolysis of **1** and related cyclic acetals. The hydrolysis of **1** provided a larger negative ρ value, accompanied by increased resonance effects than that of the corresponding five-membered cyclic acetals, 2,2-diaryl-1,3-dioxolanes(**2**),[10] though a straightforward comparison is somewhat ambiguous because of the change in the solvent composition. Whereas, monoaryl substituted 1,3-dioxolanes(**3**) were more subject to both polar and resonance effects than **1**.[11]



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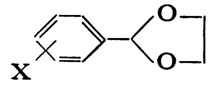

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Table 2. Hammett Parameters for Hydrolysis of **1**, **2**, and **3**

Substrates	ρ	R	No. of substituents	Solvent	r	T/C°	Ref.
1	-2.92	0.385	8	80% Dioxane	0.999	30	This work
2[a)]	-2.08[b)]	0.240[b)]	4	20% Dioxane	0.998	25	10
3	-3.28[b)]	0.457[b)]	5	50% Dioxane	0.999	30	11

a) The σ^+ and σ^0 values used are the sums of the values for the two substituents. b) Original data were treated according to Yukawa-Tsuno equation.

Experimental

Materials. 1,4-Dioxane was refluxed over metal sodium and fractionated. The substituted diphenyldiazomethanes(DDMs) were synthesized by the oxidation of the corresponding benzophenone hydrazones with yellow mercury oxide as has been described.[12] Also, solid DDMs were purified by recrystallization from petroleum ether or ether. The melting points of these DDMs have been reported elsewhere.[13] The m-NO_2 substituted DDMs had a mp of 53—54 °C (lit,[14]; oil). The acetals (**1a**—**h**) were produced by a reaction of DDMs with DDQ in the presence of 1,3-propanediol according to our previous methods.[8] The structures of **1a**—**h** were confirmed by IR, NMR, and elemental analyses. The yields and mp are collected in Table 1.

Kinetic Measurements. The rates of hydrolysis of **1a**—**h** were measured in 80% dioxane-water(v/v) at a constant acid(HCl) concentration(0.200 mol dm^{-3}). The rates were measured spectrophotometrically with a JASCO UVIDEC 505 spectrophotometer by following the increase in absorption due to the benzophenone at constant temperature maintained by circulating water from a Haake constant temperature circulating bath. Pseudo-first-order rate constants (k_{obsd}) were determined from logarithmic plots of (A_∞—A_t) against time. These were linear over 3 half-times.

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