7. Substituent and Isotope Effects on the Hydrolysis Rates of 2-Aryl-2-diazocarboxylic Esters[1])

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Summary

The overall kinetic solvent isotope effects on the acid catalyzed hydrolysis of a series of 2-aryl-2-diazocarboxylic esters $ArCN_2COOCH_3$, and one 2-aryl-2-diazocarboxamide $C_6H_5CH_2CON(CH_3)_2$ vary inversely with the reactivity of the substrate, between limits of 3.14 and 1.46. A linear *Hammett* plot for the hydrolysis rates of the α-diazocarboxylic esters indicates that there is no mechanistic change for the hydronium-ion-catalyzed reaction. The relation between hydrolysis rate and buffer acid concentration deviates from linearity for high values of the latter. It is shown on the basis of the solvent isotope effects for the non-linear region that this deviation does not stem from a mechanistic change caused by the buffer base component. The specific salt effects on the general acid-catalyzed reaction are discussed.

Introduction. – The values of solvent kinetic isotope effects are often employed for the elucidation of hydrolysis mechanisms: a value of $k_{H_2O}/k_{D_2O} > 1$ normally implies a rate-determining protonation (AS_E2-mechanism), whereas $k_{H_2O}/k_{D_2O} < 0.5$ is consistent with a protonation equilibrium preceding a rate-determining substitution ($A2$- or $A1$-mechanism).

Application of this criterion to hydrolyses of aliphatic diazo compounds has led to mechanistic distinction according to the degree of substitution of the diazo C-atom. Deactivated primary diazoalkanes, *e.g.* diazoketones, are hydrolyzed by the $A2$-mechanism, whereas introduction of an alkyl or aryl substituent entails an AS_E2-mechanism [1][3]). Variation in the solvent isotope effect on hydrolysis of a series of diazo compounds, has been interpreted in terms of differences in transition state geometries for the proton transfer from the hydronium ion to the diazo substrate. In particular the AS_E2-hydrolyses of a series of aryl diazoalkanes

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[1]) Taken in part from the doctoral thesis of Mrs. *M.-H. Bui-Nguyen*, Lausanne 1976.

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[3]) Non-stabilised primary diazoalkanes, *e.g.* diazomethane [2] [3] and aryldiazomethanes [4], are hydrolyzed by H_3O^+ by an AS_E2-mechanism.

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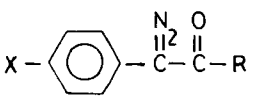
p-$NO_2C_6H_4CN_2X$ where X = H, CH_3, $COCH_3$, CO_2CH_3, displayed diminishing solvent isotope effects with decreasing reactivity, consistent with more 'product like' transition states for the protonation [5].

On the other hand *Jugelt* [6] has observed that for the two series of diazo compounds **1a–d** and **2a–c**, the solvent isotope effect diminishes with increasing substrate reactivity, and finally is reversed; for the least reactive **2a** he found $k_{H_2O}/k_{D_2O} = 1.45$, for **2c** $k_{H_2O}/k_{D_2O} = 0.58$. This variation was interpreted as indicating a mechanistic change from AS_E2 to $A2$.



1 R = C_6H_5
2 R = CH_3
3 R = OCH_3
4 R = $N(CH_3)_2$

a X = NO_2, **b** X = H, **c** X = CH_3, **d** X = OCH_3

We examine here the relation between the hydrolysis rates and the solvent isotope effect thereon, for a series of substituted aryl-diazocarboxylic esters **3a–3d** and the diazo-carboxamide **4b**. The substrates were prepared by standard methods [7] [8].

Hydrolyses. – *Products.* Hydrolysis of **3b**, **c**, **d** and **4b** in dioxane/water 60:40 (*v*/*v*), 0.5 M in perchloric acid, yielded only the corresponding mandelic esters and amide, respectively; the GC. yields were 100%, the yields of isolated products 90–95%. Under the same reaction conditions **3a** provided, in addition to the usual hydrolysis product, methyl p-nitrophenylglyoxylate **5a**, in 10% yield[4]).

Kinetics. The acid-catalyzed hydrolyses, followed by UV. spectroscopy, were first order for at least 90% reaction. The observed rate constants were accurately proportional to the concentrations of the acid catalyst (present in large excess); a typical plot is shown in *Figure 1.* The second-order rate constants k_{H_2O}, given by the slopes of such plots, are presented in *Tables 1–8.* The global solvent isotope effects k_{H_2O}/k_{D_2O} were found to be greater than 1, and so, although of varying magnitude, indicate a rate-determining protonation in all cases.

The second order rate constants for **3a–d** vary with ring substitution *(Tables 1–8);* this variation conforms well to the *Hammett* correlation where $\rho_{H_2O} = -1.89 \pm 0.06$ ($r = 0.999$), $\rho_{D_2O} = -1.79 \pm 0.07$ ($r = 0.998$), indicating that there is no mechanistic change. The large value found reveals a pronounced sensitivity of the protonation rates to the aryl substituents. This is no way surprising as the basic site – the π-electron rich diazo C-atom – is directly attached to the aromatic ring [10].

It is worthy of note, however, that the ^{13}C-chemical shifts of the diazo C-atoms of **3a–d** are very insensitive to substituents, and hence do not correlate with the basicity of the diazo C-atoms, in the manner previously described for diazo C-nucleophilicity [11]. As a further example, the diazo amide **4b** is protonated 250 times more rapidly than the corresponding methyl diazo-ester **3b**, despite very similar chemical shifts for both the diazo and carbonyl C-atoms of the two compounds.

It can be remarked from *Table 1* that for compounds **3a–d** the less rapid protonations are associated with smaller solvent isotope effects. The same

[4]) The formation of oxidized side products, in variable yields, has also been observed in the hydrolysis of certain α-aryl-α-diazoketones [9].

correlation appears for the pair **2b**, **4b**. When the contrary trend was observed for diazoketones [6], it was interpreted as indicating a mechanistic change. For our compounds we have shown that the hydrolysis mechanism does not change with substituent. The most viable explanation is that the change in solvent isotope effect

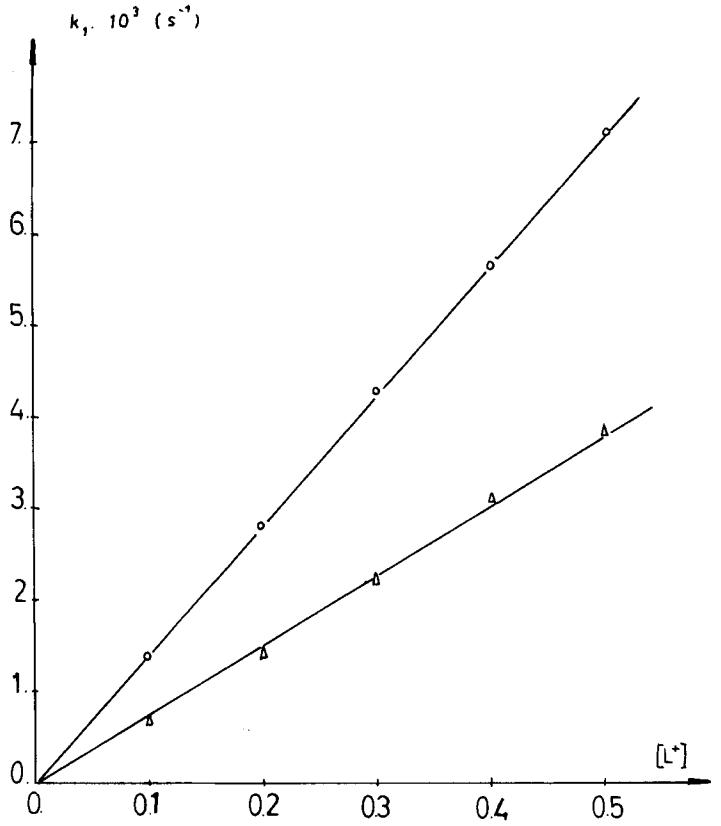


Fig. 1. *Hydrolysis of* **3c** *in dioxane/H_2O and dioxane/D_2O catalyzed by $HClO_4$ and $DClO_4$ respectively* ($\mu = 0.5$) (-○- dioxane/H_2O 60:40 (*v/v*); -△- dioxane/D_2O 60:40 (*v/v*))

Table 1. *Rate constants for hydronium-ion catalyzed hydrolysis of substituted aryl diazocarbonyl compounds*

Substrate	$10^4 \cdot k_{H_2O}$ [a][b] $M^{-1} s^{-1}$	$10^4 \cdot k_{D_2O}$ $M^{-1} s^{-1}$	$\frac{k_{H_2O}}{k_{D_2O}}$
3a	2.63 ± 0.07	1.80 ± 0.09	1.46
3b	83.9 ± 1.4	52.3 ± 1.4	1.60
3c	141 ± 1	80.4 ± 1.5	1.75
3d	266 ± 9	138 ± 2	1.93
4b	26000 ± 600	8280 ± 80	3.14

[a]) The errors quoted are standard deviations.
[b]) Solvent dioxane/water 60:40 (*v/v*); ionic strength maintained at 0.5M with $NaClO_4$.

reflects the variation in transition state structure for the proton transfer, as it becomes increasingly endoenergetic [12].

Curvature in general acid catalysis plots. General acid catalysis was observed for the hydrolysis of **3b** and **3d**, in buffered dichloroacetic acid solution, with the ionic strength maintained constant with $NaClO_4$. However, the linear relation between reaction velocity and general acid concentration shows downward curvature at higher buffer concentrations *(Fig. 2)*. Similar phenomena have been observed in the general acid catalyzed hydrolyses of acetals [13], a cyclic vinyl ether [14], aryldiazomethanes [4], 3-diazobutan-2-one and ethyl diazopropionate [15]; a variety of possible causes have been recognized [16]. The explanation that has previously been applied to the hydrolysis of the diazocarbonyl compounds is that, as the concentration of the conjugate base of the general acid catalyst increases (at constant buffer ratio), the deprotonation of the intermediate species becomes more significant, and finally more rapid than its decomposition.

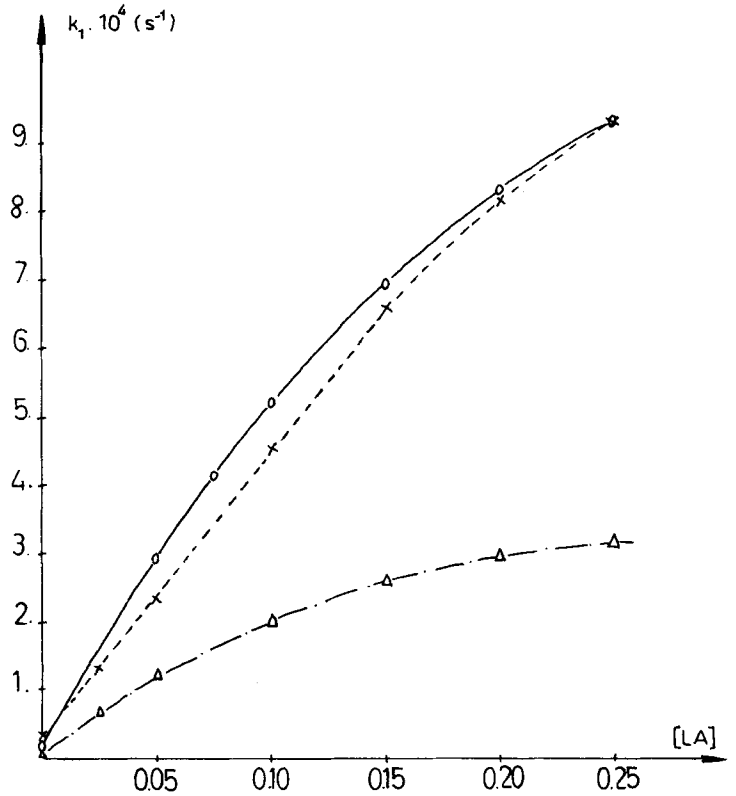


Fig. 2. *General acid catalysis of the hydrolysis of* **3d**
-O- Cl_2CHCO_2H/Cl_2CHCO_2Na 1:2 + $NaClO_4$ ($\mu = 0.5$) pH = 3.20 ± 0.02
-×- Cl_2CHCO_2H/Cl_2CHCO_2Na 1:2 + $NaNO_3$ ($\mu = 0.5$) pH = 3.11 ± 0.02
-△- Cl_2CHCO_2D/Cl_2CHCO_2Na 1:2 + $NaClO_4$ ($\mu = 0.5$) pD = 3.72 ± 0.02

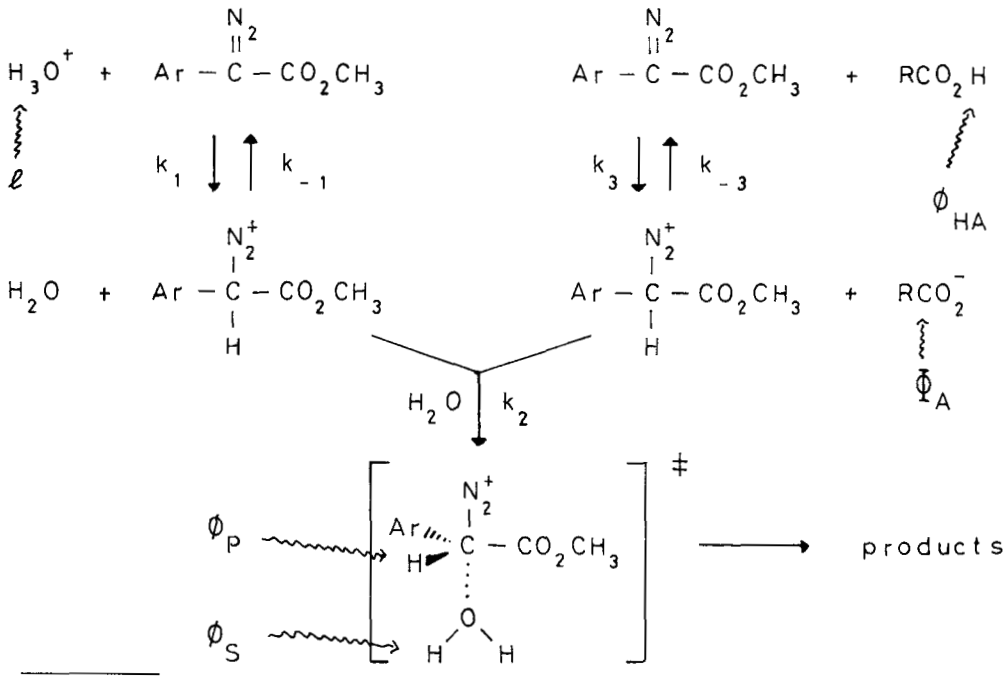
With reference to the *Scheme* the overall rate is given by

$$k_{obs.} = \frac{k_2 k_1 [H_3O^+] + k_3 [HA]}{k_2 + k_{-1} + k_{-3}[A^-]} \quad (1)$$

This expression fits the data for the hydrolyses of **3b** and **3d** in H_2O and D_2O extremely well[5]), when plotted as $1/(k_{obs.} - k_H[H_3O^+])$ against $1/[HA]$, where $k_H[H_3O^+]$ is the observed first order rate constant for the hydrolysis at the same acidity in the absence of buffer acid.

Another explanation of the observed curvature of the $k_{obs.}/[HA]$ plots would be the existence of specific salt effects [17], shown to be especially important in our reaction medium of dioxane/water 60:40 (*v/v*) at the high ionic strength of 0.5M [18]. In our experiments the downward curvature with decreasing added salt concentration is less for $NaNO_3$ than for $NaClO_4$. Hence $NaClO_4$ appears to accelerate the reaction more than $NaNO_3$. Such acceleration by ClO_4^- relative to NO_3^- of reactions involving organic substrates in dioxane/water, has already been observed by *Salomaa* for specific acid-catalyzed reactions [19]. This may, at first sight appear to contradict the recent result of *Jencks,* for specific salt effects on the general acid catalyzed hydrolysis of *N-p*-methoxybenzilidenepyrrolidinium ion in water [20]. There perchlorates (up to 1.0M) had, as in our case, the most marked

Scheme



5) In all cases $r > 0.997$.

effects, but retarded the reaction. In fact a reversal of the sign of the specific salt effect coefficient, on changing from aqueous to aqueous/dioxane solutions, is common. Whereas in aqueous solution an added salt may 'salt out' an organic solute, in the mixed solvent system the substrate will be 'salted into' a dioxane environment, with a consequent decrease in its activity [17]. The large diffusely charged perchlorate anion destabilizes organic substrates in dioxane/water by dissipating the protective dioxane-rich regions [21], and consequently accelerates their reactions. The observed curvature may therefore merely result from the differing specific salt coefficients of A^- and ClO_4^- (or NO_3^-).

In order to decide between the possible causes of curvature of the $k_{obs.}$/[HA] plot, one might use the solvent isotope effects. If deprotonation of the diazonium ion by the buffer base in high concentration were responsible for the curvature, by changing the rate-determining step, then the solvent isotope effect should diminish in consequence. In an $A2$-hydrolysis where deprotonation by water is more rapid than substitution, the solvent isotope effect is given by

$$k_{H2O}/k_{D2O} = l^3/\phi_p(\phi_s)^2 \tag{2}$$

where l, ϕ_p, and ϕ_s are the fractionation factors [22] [23] for the protons indicated in the *Scheme* (it is assumed that the transfer activity coefficients of the substrate and transition state are both close to unity [24]). This expression is dominated by the l^3 term, and the isotope effect typically has values around 0.3.

In the presence of the buffer components, the situation is more complex: though the D_3O^+ present in D_2O will form more of the substrate conjugate acid than will H_3O^+ in H_2O, the concentration of D_3O^+ for a given concentration of buffer in D_2O will be correspondingly less than that of H_3O^+ in H_2O. The isotope effect would then be given by,

$$k_{H_2O}/k_{D_2O} = \phi_{HA}/\Phi_A\phi_p(\phi_s)^2. \tag{3}$$

Here Φ_A is the product of the fractionation factors of the solvation shell of A^- (*i.e.* the transfer activity coefficient of A^- from H_2O to D_2O [25]), and ϕ_{HA} is for the acid proton indicated in the *Scheme*. The values of Φ_A and ϕ_{HA} are known to be 0.90 and 0.96 [26] respectively for acetic acid, and should be very similar for dichloroacetic acid. *Albery* has determined the values of ϕ_p and ϕ_s, for the transition state of the second step in the hydrolysis of ethyl diazoacetate, to be 1.00 and 0.95 respectively [27], and these should be good estimates for those in the *Scheme*. Insertion of these values into equation (3) generates a value of 1.2 for the solvent isotope effect, in the limit of completely reversible protonation by the buffer system in water. The corresponding value in dioxane/water 24:76 (*mol/mol*), should not be substantially different, as the fractionation factors vary only slightly up to dioxane/water 45:55 (*mol/mol*) [23]. Thus according to the *Scheme* at high buffer concentrations the overall solvent isotope effect should tend to 1.2.

As can readily be seen from *Figure 2*, the observed isotope effect in the region of pronounced curvature is large, precisely $k_{H_2O}/k_{D_2O} = 2.9$ for a 0.25 M solution of

buffered acid. On this basis we can exclude deprotonation of the diazonium ion intermediate by the buffer base component as the cause of curvature.

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Experimental Part

General Remarks. Melting points (m.p.) were measured on a *Büchi-Tottoli* apparatus. Elemental analyses were performed by Mr. *E. Thommen,* Organic Chemistry Institute of the University of Basel. Spectra and analytical measures were performed on the following instruments. – IR.: *Beckmann* IR-20A (data given in cm^{-1}). – UV.: *Carl Zeiss* RPQ 20A (data λ_{max}(nm.), $\varepsilon(M^{-1}cm^{-1})$). – ^{1}H-NMR.: *Varian* A60-A, *Bruker* WP-60 (FT) (chemical shifts (δ) in ppm from TMS in $CDCl_3$; coupling constants (J) in Hz; s = Singlet, d = Doublet, t = Triplet, qa = Quadruplet, m = Multiplet, br. = broad). – ^{13}C-NMR.: *Bruker* HX-90 (22.6 MHz) (δ in ppm relative to TMS in $CDCl_3$; C_o, C_m, C_p = ortho, meta and para carbon atoms, resp.). – MS.: *Bell and Howell* CEC 21-190, (70 eV; data given as fragment mass (intensity as % of base peak)). – GLC.: *Hewlett Packard* 5750; Titrations: *Metrohm* Dosimat; pH determinations: *Radiometer* PHM 25 SE meter with combined glass-calomel electrode; Kinetics: *Pye Unicam* SP 1800, with sample holder thermostatted to $\pm 0.1°$ by water circulation around the sample cells. RT. = room temperature.

Methyl-p-*nitrophenyldiazoacetate* (**3a**) was prepared according to [7], recrystallized from ethyl acetate, m.p. 153–155° (dec.) (lit. [7] 149–150° dec.). – ^{13}C-NMR.: 52.6 (OCH_3); 64.6 (CN_2); 122.8 (C_o); 123.9 (C_p); 133.5 (C_m); 144.7 (CCN_2); 163.1 (CO).

Methyl phenyldiazoacetate (**3b**) was prepared according to [8]. B.p. 68–70°/0.05 Torr (lit. [8] 62–64°/0.0003 Torr. – ^{13}C-NMR. ($CDCl_3$): 51.9 (OCH_3); 62.7 (CN_2); 123.6 (C_o); 125.1 (C_p); 125.5 (CCN_2); 128.6 (C_m); 165.1 (CO).

Methyl p-*tolylglyoxylate* (**5c**). To 8.1 g (66 mmol) methyl chloroglyoxylate [28] and 6.1 g (66 mmol) toluene in 50 ml nitrobenzene were added 13.2 g (90 mmol) aluminium chloride at $-10°$, in portions during 90 min. A vacuum of 20 Torr was applied to the resultant red solution, until the evolution of gas ceased, after which 50 g ice were added. The organic phase was separated, washed with 20 ml 5% hydrochloric acid, 20 ml 5% $NaHCO_3$-solution and dried over $MgSO_4$. The solvent was eliminated and the resultant oil distilled: 7.3 g (62%) b.p. 131–132°/11 Torr. – IR. (CCl_4): 2970, 1700. – ^{1}H-NMR.: 2.40 (*s*, 3 H, ArCH_3); 3.89 (*s*, 3 H, OCH_3); 7.23 and 7.82 (*AB*-system, J_{AB} = 8 Hz, 4 H, ArH). – MS.: 178 (2, M^+), 119 (100), 91 (46), 65 (16), 40 (14).

$C_{10}H_{10}O_3$ (178.1) Calc. C 67.47 H 5.65% Found C 67.65 H 5.63%

Methyl-p-*tolylglyoxylate hydrazone* (*syn*- and *anti*-isomers). Hydrazine hydrate (3.7 ml, 76 mmol) in CH_3COOH/H_2O 1:1 (12 ml) was added at 5° to a solution of **5c** (6.6 g, 37 mmol) in methanol (20 ml), then stirred at RT. for 65 h. The solution was concentrated *in vacuo,* 40 ml water and 40 ml CH_2Cl_2 were added, the organic layer was washed with 20 ml 5% hydrochloric acid, 20 ml 5% $NaHCO_3$-solution, and 20 ml sat. NaCl-solution, and dried over $MgSO_4$. Evaporation of the solvent yielded 5.8 g (83% crude yield) of a viscous liquid. The crude product (2 g) was chromatographed on a column of silica (100 g, *Fluka* type 60). Elution with CCl_4/ether 3:2 yielded the *syn*-isomer: 1.1 g, m.p. 63–64.5°. – UV. (ethanol): 302 (9,000), 235 (11,900). – IR. (KBr): 3360–3240, 1700; (CCl_4): 3370–3240, 1700 (no change on dilution). – ^{1}H-NMR.: 2.41 (*s*, 3 H, ArCH_3); 3.78 (*s*, 3 H, OCH_3); 7.00–7.51 (*m*, 4 H, ArH); 8.31 (br. *s*, 2 H, NH_2). – MS.: 192 (68, M^+), 159 (13), 133 (100), 91 (88), 65 (15).

$C_{10}H_{12}N_2O_2$ (192.2) Calc. C 62.50 H 6.28 N 14.57% Found C 62.48 H 6.50 N 14.31%

Further elution with $CHCl_3/CH_3OH$ 9:1 yielded the *anti*-isomer: 0.8 g, m.p. 80–81°. – UV. (ethanol): 273 (9600), 217 sh. (9,400). – IR. (KBr): 3370–3320, 1670. – IR. (CCl_4): 3450–3240, 1670 (on dilution the band at 3450 cm^{-1} becomes more intense relative to the band at 3240 cm^{-1}). – ^{1}H-NMR.: 2.38 (*s*, 3 H, ArCH_3); 3.70 (*s*, 3 H, OCH_3); 6.35 (br. *s*, 2 H, NH_2); 6.95–7.36 (*m*, 4 H, ArH). – MS.: 192 (65), 133 (96), 91 (100), 73 (42), 61 (63), 45 (86), 43 (65).

$C_{10}H_{12}N_2O_2$ (192.2) Calc. C 62.50 H 6.28 N 14.57% Found C 62.53 H 6.24 N 14.70%

Methyl p-*tolyldiazoacetate* (**3c**). Lead tetraacetate (1.04 g, heated for 30 min at 40°/0.1 Torr to remove acetic acid) and the mixture of *syn*- and *anti*-isomers of methyl *p*-tolylglyoxylate hydrazone (2.9 g, 15 mmol) were stirred 10 min at 0° in 75 ml CH_2Cl_2. After adding 10 g *Celite* and 23 ml water and waiting for a further 5 min the suspension was filtered and the solid washed with 2×20 ml CH_2Cl_2. The CH_2Cl_2 solution was washed with 50 ml water, 30 ml sat. NaCl-solution, and dried over $MgSO_4$. The solvent was evaporated and the orange liquid residue was distilled: 1.6 g (55%) of **3c**, b.p. 84–85°/ 0.1 Torr. – UV. (cyclohexane): 440 (100), 305 sh. (4,900), 276 (9,300), 243 sh. (14,100), 230 (16,200). – IR. (CCl_4): 2080, 1700. – ^{1}H-NMR.: 2.33 (*s*, 3 H, ArCH_3); 3.85 (*s*, 3 H, OCH_3); 7.16, 7.39 (*AB*-system, J_{AB}=9 Hz, 4 H, ArH). – ^{13}C-NMR.: 20.9 (ArCH_3); 51.7 (OCH_3); 62.7 (CN_2); 121.8 (C_p); 123.8 (C_o); 129.2 (C_m); 135.2 (CCN_2); 165.2 (CO).

$C_{10}H_{10}N_2O_2$ (190.2) Calc. C 63.16 H 5.29 N 14.72% Found C 63.07 H 5.23 N 14.83%

Methyl p-*methoxyphenyldiazoacetate* (**3d**) was prepared according to [8], m.p. 47–48° (lit. [8] 50.5–51.5°). – ^{13}C-NMR.: 51.7 (CO_2CH_3); 55.1 (ArOCH_3); 62.1 (CN_2); 114.2 (C_o); 116.5 (C_p); 125.5 (C_m); 157.6 (CCN_2); 165.2 (CO).

syn-N,N-*Dimethylphenylglyoxylamide hydrazone*. *N,N*-Dimethylphenylglyoxylamide [29] (2.6 g, 25 mmol) was reacted with hydrazine hydrate (1.8 ml, 38 mmol) as described above for the preparation of **3c**. The resultant solid was recrystallized twice from ether: white crystals (1.7 g, 63%); m.p. 108–109°. – UV. (ethanol): 281 (11,800), 258 sh. (9,900), 218 (13,700). – IR. (KBr): 3420–3200, 2940, 1620. – IR. (CCl_4): 3420–3200, 2930, 1650 (no change on dilution). – ^{1}H-NMR.: 2.87 (*s*, 3 H, NCH_3); 3.12 (*s*, 3 H, NCH_3); 5.82 (*s*, 2 H, NH_2); 7.27–7.69 (*m*, 5 H, ArH). – MS.: 191 (33, M^+), 190 (27), 119 (100), 77 (67), 44 (27).

$C_{10}H_{13}N_3O$ (191.2) Calc. C 62.80 H 6.85 N 21.94% Found C 62.62 H 6.80 N 22.06%

N,N-*Dimethylphenyldiazoacetamide* (**4b**). Activated manganese dioxide (1.5 g, 13 mmol, *Merck*) was stirred for 40 min at room temperature with a solution of **6e** (1 g, 5 mmol) in $CHCl_3$ (15 ml). After filtration, the solvent was evaporated and the residue distilled: orange liquid **4b** (0.8 g, 80%), b.p. 72–74°/0.05 Torr. – UV. (cyclohexane). 440 (110), 302 (3,900), 280 (12,800), 261 (16,200). – IR. (film): 2920, 2060, 1620 (CCl_4): 2940, 2070 (doublet), 1640. – ^{1}H-NMR.: 2.95 (*s*, 6 H, $N(CH_3)_2$); 7.12–7.44 (*m*, 5 H, ArH). – ^{13}C-NMR.: 37.6 ($N(CH_3)_2$); 62.1 (CN_2); 124.0 (C_o); 125.2 (C_p); 127.3 (CCN_2); 128.4 (C_m); 165.0 (CO). – MS.: 189 (14, M^+), 161 (5), 132 (36), 105 (100), 90 (28), 77 (43), 72 (24).

Triphenylphosphine adduct, prepared according to [30], m.p. 149–150.5° (from ether-petrol).

$C_{28}H_{26}N_3OP$ (451.5) Calc. C 74.48 H 5.89 N 9.30% Found C 74.76 H 6.01 N 9.27%

Methyl p-*nitrophenylglyoxylate* (**5a**). *p*-Nitrophenylglyoxylic acid [31] was methylated with one equivalent of diazomethane in ether to yield **5a**, recrystallized from methanol, m.p. 98–99°. – IR. (KBr): 1750, 1700. – ^{1}H-NMR.: 4.02 (*s*, 3 H, OCH_3); 8.21 and 8.40 (*AB*-System, J_{AB}=8.4 Hz, 4 H, ArH). – MS.: 181 (3, M^+-28), 150 (100), 104 (50).

$C_9H_7NO_5$ (209.2) Calc. C 51.68 H 3.37 N 6.70% Found C 51.52 H 3.55 N 6.65%

Hydrolyses. Generally the diazo compound (100 mg) was added to a solution of $HClO_4$ 0.5M in dioxane/water 6:4 (30 ml). After 10 half lives of reaction the medium was neutralized with 5 ml $NaHCO_3$-solution, and extracted with CH_2Cl_2 (5×20 ml). The extract was dried over $MgSO_4$ and the solvent was removed *in vacuo*. The products so obtained from the hydrolyses of **3b**, **3c**, **3d** and **4b** were identical chromatographically (GC., TLC.), spectroscopically (IR., NMR., MS.) and in m.p. (for **3c**, **4b**) with the authentic mandelic esters [32] [33], and mandelamide [34] respectively. Hydrolysis of **3a** as above gave a mixture of 2 products in the ratio of 1:4 (GC. column OV 17 3%, temp. 190°, $t_{ret.}$ 120 and 168 s.). These were separated by preparative TLC. (*Merck*, silica type GF_{254}) with CH_2Cl_2 as eluent. Comparison with authentic samples showed them to be **5a** and methyl *p*-nitromandelate [35] respectively.

Kinetics. Dioxane was rid of acetals by treatment with acid, then distilled from sodium under nitrogen. Water was distilled twice from alkaline permanganate solution. Deuterated water contained 99.8% deuterium, no correction was made to 100%. Dioxane/water mixtures were prepared by weight. Perchloric acid solutions were prepared by dilution to 0.5N of the concentrated acid (*Fluka, puriss.* grade – titrated as 67.89%) with dioxane/water, after addition of dioxane to compensate for the water included in the acid. The acidity of the solutions obtained was controlled by titration with NaOH-solution. The stock solution of dichloroacetic acid buffer was obtained by partial neutralization of a known quantity

of acid (*Fluka, puriss.*) with 2.0N NaOH, addition of the appropriate quantity of dioxane and dilution to 0.5N. Sodium deuteroxide (*Merck*, 40%) was diluted with deuterium oxide to 0.1N, and titrated with hydrochloric acid 1.0N. This solution was used to prepare buffered dichloroacetic acid in dioxane/deuterium oxide. The hydrolysis solutions were prepared by dilution of the stock solutions with solutions of sodium perchlorate or sodium nitrate 0.5M in dioxane/water.

Kinetic runs were initiated by injection of 20 µl of diazo compound (approx. 0.01M in dioxane/water), into 3 ml of hydrolysis solution previously thermostatted in the spectrometer cells for at least 30 min. The kinetics of the hydrolyses were followed at the maximum of the diazo absorption band. The results were fitted to a first order equation (followed for over 90% reaction) by linear regression on an IBM 7040 computer. For slow reactions the data were analysed by *Guggenheim*'s method [36].

Kinetic Results. All rate constants are for hydrolyses in dioxane/water 60:40 (*v/v*) 25°, $\mu = 0.5$.

Table 2. *Hydrolysis of* **3a** (perchloric acid catalysis)

In dioxane/H_2O				In dioxane/D_2O			
Run no.	$[HClO_4]$	$[NaClO_4]$	$k_{obs} \cdot 10^4 s^{-1}$	Run no.	$[DClO_4]$	$[NaClO_4]$	$k_{obs} \cdot 10^4 s^{-1}$
170.1	0.099	0.4	2.58	190.1	0.103	0.4	1.71
170.2			2.60	190.2			1.66
170.3			2.59	190.3			1.68
171.1	0.199	0.3	5.34	191.1	0.203	0.3	3.38
171.2			5.36	191.2			3.26
171.3			5.42	191.3			3.48
172.1	0.300	0.2	7.53	192.1	0.299	0.2	4.96
172.2			7.50	192.2			4.90
172.3			7.54	192.3			4.87
173.1	0.401	0.1	10.73	193.1	0.403	0.1	7.19
173.2			10.49	193.2			7.16
173.3			10.60	193.3			7.13
174.1	0.502	-	13.23				
174.2			13.17				
174.3			13.31				

Table 3. *Hydrolysis of* **3b** (perchloric acid catalysis)

In dioxane/H_2O				In dioxane/D_2O			
Run no.	$[HClO_4]$	$[NaClO_4]$	$k_{obs} \cdot 10^4 s^{-1}$	Run no.	$[DClO_4]$	$[NaClO_4]$	$k_{obs} \cdot 10^4 s^{-1}$
240.1	0.100	0.4	8.73	251.1	0.103	0.4	4.47
240.2			8.76	251.2			4.44
240.3			8.75	251.3			4.53
241.1	0.197	0.3	17.72	252.1	0.203	0.3	9.12
241.2			17.67	252.2			9.17
241.3			17.70	252.3			9.13
242.1	0.401	0.1	34.17	253.1	0.403	0.1	20.33
242.2			34.74	253.2			20.76
242.3			34.43	253.3			20.55
243.1	0.500	-	42.47	254.1	0.503	-	25.16
243.2			42.77	254.2			25.39
243.3			42.20	254.3			25.26

Table 4. *Hydrolysis of* **3c** (perchloric acid catalysis)

In dioxane/H_2O				In dioxane/D_2O			
Run no.	$[HClO_4]$	$[NaClO_4]$	$k_{obs} \cdot 10^3 s^{-1}$	Run no.	$[DClO_4]$	$[NaClO_4]$	$k_{obs} \cdot 10^3 s^{-1}$
311.1	0.099	0.4	1.37	321.1	0.101	0.4	0.69
311.2			1.39	321.2			0.69
311.3			1.38	321.3			0.69
312.1	0.201	0.3	2.82	322.1	0.202	0.3	1.42
312.2			2.81	322.2			1.42
312.3			2.81	322.3			1.41
313.1	0.300	0.2	4.29	323.1	0.300	0.2	2.21
313.2			4.26	323.2			2.23
313.3			4.24	323.3			2.23
314.1	0.402	0.1	5.60	324.1	0.402	0.1	3.11
314.2			5.69	324.2			3.12
314.3			5.62	324.3			3.11
315.1	0.503	–	7.00	325.1	0.501	–	3.83
315.2			6.93	325.2			3.89
315.3			7.09	325.3			3.85

Table 5. *Hydrolysis of* **3d** (perchloric acid catalysis)

In dioxane/H_2O				In dioxane/D_2O			
Run no.	$[HClO_4]$	$[NaClO_4]$	$k_{obs} \cdot 10^3 s^{-1}$	Run no.	$[DClO_4]$	$[NaClO_4]$	$k_{obs} \cdot 10^3 s^{-1}$
470.1	0.099	0.4	2.53	477.1	0.103	0.4	1.41
470.2			2.54	477.2			1.40
470.3			2.59	477.3			1.39
471.1	0.201	0.3	5.69	478.1	0.203	0.3	2.76
471.2			5.76	478.2			2.78
471.3			5.71	478.3			2.83
472.1	0.300	0.2	7.76	479.1	0.304	0.2	4.04
472.2			7.92	479.2			4.07
472.3			7.71	479.3			4.08
473.1	0.401	0.1	10.32				
473.2			10.39				
473.3			10.61				
474.1	0.502	–	13.58				
474.2			13.54				
474.3			13.57				

Table 6. *Hydrolysis of* **3b** (buffered dichloroacetic acid catalysis, $[LA]/[A^-] = 1$)

In dioxane/H_2O					In dioxane/D_2O				
Run no.	[HA]	$[NaClO_4]$	pH ± 0.02	$k_{obs} \cdot 10^4 s^{-1}$	Run no.	[HA]	$[NaClO_4]$	pD ± 0.02	$k_{obs} \cdot 10^4 s^{-1}$
270.1	0.05	0.45	2.78	0.68	280.1	0.1	0.4	3.16	0.412
270.2				0.69	280.2				0.398
270.3				0.68	280.3				0.409

Table 6 (continued)

In dioxane/H_2O					In dioxane/D_2O				
Run no.	[HA]	[$NaClO_4$]	pH ± 0.02	$k_{obs} \cdot 10^4 s^{-1}$	Run no.	[HA]	[$NaClO_4$]	pD ± 0.02	$k_{obs} \cdot 10^4 s^{-1}$
271.1	0.1	0.4	2.79	1.12	281.1	0.2	0.3	3.16	0.710
271.2				1.12	281.2				0.707
271.3				1.12	281.3				0.695
272.1	0.2	0.3	2.80	1.85	282.1	0.3	0.2	3.16	0.92
272.2				1.82	282.2				0.91
272.3				1.84	282.3				0.91
273.1	0.3	0.2	2.81	2.35	283.1	0.4	0.1	3.18	1.04
273.2				2.38	283.2				1.03
273.3				2.36	283.3				1.04
274.1	0.5	–	2.83	2.84	284.1	0.5	–	3.18	1.12
274.2				2.78	284.2				1.11
274.3				2.78	284.3				1.13

Table 7. *Hydrolysis of* **3d** (buffered dichloroacetic acid catalysis, $[LA]/[A^-] = 0.5$)

In dioxane/H_2O					
Run no.	[HA]	salt	[salt]	pH ± 0.02	$k_1 \cdot 10^4 s^{-1}$
480.1	0.05	$NaClO_4$	0.4	3.17	2.97
480.2					3.03
480.3					2.82
481.1	0.075		0.35	3.19	4.19
481.2					4.17
481.3					4.15
482.1	0.1		0.3	3.20	5.22
482.2					5.34
482.3					5.12
483.1	0.15		0.2	3.22	6.94
483.2					6.95
483.3					6.99
484.1	0.2		0.1	3.21	8.41
484.2					8.27
484.3					8.35
485.1	0.25		–	3.21	9.40
485.2					9.45
485.3					9.22
486.1	0.025	$NaNO_3$	0.45	3.09	1.28
486.2					1.29
486.3					1.27
487.1	0.05		0.4	3.13	2.39
487.2					2.23
487.3					2.33
488.1	0.1		0.3	3.12	4.60
488.2					4.60
488.3					4.51

Table 7 (continued)

In dioxane/H_2O					
Run no.	[HA]	salt	[salt]	pH ± 0.02	$k_1 \cdot 10^4 s^{-1}$
489.1	0.15		0.35	3.12	6.61
489.2					6.65
489.3					6.62
490.1	0.2		0.1	3.18	8.10
490.2					8.22
490.3					8.14
491.1	0.25		–	3.21	9.37
491.2					9.35
491.3					9.30
492.1	$HClO_4$		0.5	2.20	1.73
492.2	0.006				1.77
492.3					1.71

In dioxane/D_2O					
Run no.	[DA]	salt	[salt]	pD ± 0.02	$k_1 \cdot 10^4 s^{-1}$
493.1	0.025	$NaClO_4$	0.45	3.30	0.647
493.2					0.651
493.3					0.647
494.1	0.05		0.4	3.31	1.20
494.2					1.21
494.3					1.23
495.1	0.1		0.3	3.32	2.03
495.2					2.07
495.3					2.04
496.1	0.15		0.2	3.32	2.62
496.2					2.60
496.3					2.64
497.1	0.20		0.1	3.33	2.99
497.2					2.99
497.3					2.95
498.1	0.25		–	3.34	3.21
498.2					3.23
498.3					3.11

Table 8. *Hydrolysis of* **4b** (perchloric acid catalysis)

In dioxane/H_2O				In dioxane/D_2O			
Run no.	[$HClO_4$]	[$NaClO_4$]	$k_{obs} \cdot 10^1 s^{-1}$	Run no.	[$DClO_4$]	[$NaClO_4$]	$k_{obs} \cdot 10^1 s^{-1}$
519.1	0.04	0.46	0.784	522.1	0.04	0.46	0.311
519.2			0.782	522.2			0.306
519.3			0.782	522.3			0.308
520.1	0.06	0.44	1.21	523.1	0.075	0.425	0.557
520.2			1.50	523.2			0.562
520.3			1.30	523.3			0.560

Table 8 (continued)

In dioxane/H_2O				In dioxane/D_2O			
Run no.	$[HClO_4]$	$[NaClO_4]$	$k_{obs} \cdot 10^1 s^{-1}$	Run no.	$[DClO_4]$	$[NaClO_4]$	$k_{obs} \cdot 10^1 s^{-1}$
521.1	0.1	0.4	2.43	524.1	0.1	0.4	0.792
521.2			2.39	524.2			0.792
521.3			2.23	524.3			0.815
				525.1	0.2	0.3	1.53
				525.2			1.63
				525.3			1.67
				526.1	0.3	0.2	2.54
				525.2			2.39
				526.3			2.43

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