Intramolecular Catalysis. Part 6.[1] The Intramolecular Cannizzaro Reaction and Hydration of Phenanthrene-4,5-dicarbaldehyde and [α,α'-$^2H_2$]Phenanthrene-4,5-dicarbaldehyde

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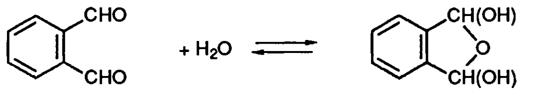
Phenanthrene-4,5-dicarbaldehyde has been shown to form a bridged (cyclic) hydrate in aqueous solution, as a *cis–trans* mixture. The rate coefficients for the uncatalysed hydration has been measured at two temperatures and the activation parameters evaluated. The dialdehyde, as well as the α,α'-dideuterio isomer, has been shown to undergo a Cannizzaro reaction in 70% (v/v) dioxane–water. The reaction has been shown to be intramolecular and of the second order, *i.e.* first order in the monoanion of the hydrate and in base. The rate coefficients have been measured at several temperatures and activation parameters evaluated. The kinetic isotope effect, k_H/k_D, was found to be *ca.* 1.7 and the kinetic solvent isotope effect, k_{H_2O}/k_{D_2O}, *ca.* 0.59. The alkaline hydrolysis of the corresponding lactone of 5-(hydroxymethyl)phenanthrene-4-carboxylic acid was studied under the same conditions. As an intermediate in the intramolecular Cannizzaro reaction, the lactone can be excluded as it cannot be detected directly under conditions where it is relatively long-lived. The evidence for the Cannizzaro reaction indicates a mechanistic pathway involving rate-determining hydride transfer from the chain tautomer of the dianion of the hydrate.

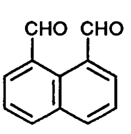
The hydration of aldehydes has been reviewed comprehensively.[2] However, although the hydration of aromatic aldehydes is normally not significant,[3] unless powerful electron-withdrawing groups are present,[3–5] a number of aromatic dialdehydes, where the two groups are proximate, are extensively hydrated. The latter hydrates appear to be cyclic. Thus, the hydration of *o*-phthalaldehyde (**1**) has been investigated and the hydrate (**2**) shown to be cyclic.[6,7] The value of K_H for Scheme 1 is defined by the relationship eqn. (1) below and has been measured at a range of temperatures, as have the kinetics of hydration.[6,7] The dialdehydes, naphthalene-1,8-dicarbaldehyde (**3**) and phenanthrene-4,5-dicarbaldehyde (**4**), form hydrates.[8,9] The structure of the hydrate of the former dialdehyde appears to be cyclic,[8] as shown in **5**.



1 **2**

Scheme 1.

$$K_H = [\text{Hydrate}][\text{Aldehyde}] \qquad (1)$$



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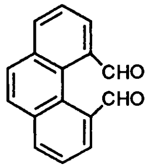

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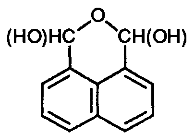

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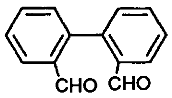
Both the aromatic dialdehydes, *o*-phthalaldehyde (**1**) and biphenyl-2,2'-dicarbaldehyde (**6**), have been shown to undergo intramolecular Cannizzaro reactions in base solution and their mechanisms of reaction have been investigated.[1,10,11] The extensively hydrated *o*-phthalaldehyde forms a mono-anion in base which rearranges both directly and by a reaction catalysed by base.[10] The unhydrated biphenyl-2,2'-dicarbaldehyde rearranges by a reaction which is second-order in base.[1] Both thus react *via* the mono-anion of a hydrate. Naphthalene-1,8-dicarbaldehyde also undergoes a Cannizzaro reaction,[8] which gives a product expected from an intramolecular reaction.



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The hydration and Cannizzaro reaction of 4,5-phenanthrenedicarbaldehyde, as well as that of the α,α'-dideuterio compound, has been investigated in this study. The structure of the hydrate has been determined, as well as the extent and rates of hydration. The rates of the Cannizzaro reaction, activation parameters, kinetic solvent isotope and isotope effects, isotope labelling, and studies of possible intermediates are reported.

Experimental

Materials.—4,5-Phenanthrenedicarbaldehyde was prepared from pyrene monozonide by the method of Van Duuren *et al.*[12] The product was purified by preparative HPLC using a silica column and dichloromethane as the eluant. The second fraction, on evaporation, gave the product as a pale yellow crystalline solid. This was dissolved in dry ethyl acetate and reisolated by evaporation, m.p. 173–175 °C (lit.,[12] 169–171 °C). It has been reported[12] that the dialdehyde could be recrystallised from methylene chloride/hexane; but this could not be reproduced. The hydrate apparently forms readily.[9] [α,α'-$^2H_2$]Phenanthrene-4,5-dicarbaldehyde was prepared by the reduction of pyrene-4,5-dione with $LiAlD_4$, followed by oxidation of the diol by sodium periodate, using methods similar to those of Harvey *et al.*[13] The purification and physical characteristics were as for the ordinary dialdehyde described above (purity >95% by ^1H NMR spectroscopy). The lactone of 5-(hydroxymethyl)phenanthrene-4-carboxylic acid was prepared by a crossed-Cannizzaro

Table 1. Rate coefficient (k_{obs}) for the uncatalysed hydration of phenanthrene-4,5-dicarbaldehyde in water at constant ionic strength (μ = 0.1 mol dm^{-3}) at 19.5 and 30.4 °C.[a]

T/°C	$k_{obs}/10^{-3}$ s^{-1}
19.5	1.34
30.4	2.24

[a] The rate coefficients were reproducible to ±3%.

Table 2. Rate coefficients (k_2) for the intramolecular Cannizzaro reaction of phenanthrene-4,5-dicarbaldehyde and alkaline hydrolysis of the lactone of 5-(hydroxymethyl)phenanthrene-4-carboxylic acid at constant ionic strength (μ = 0.1 mol dm^{-3}) at different temperatures.[a]

	k_2/dm^3 mol^{-1} s^{-1}			
	30.0 °C	40.0 °C	50.0 °C	60.0 °C
Cannizzaro reaction	0.864 (1.47)[b] (0.510)[c]	1.78	3.20	6.40
Alkaline hydrolysis	0.0310	0.0590	0.115	0.222

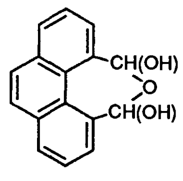
[a] The rate coefficients were reproducible to ±3%. [b] k_2 for the Cannizzaro reaction in 70% (v/v) dioxane–deuterium oxide. [c] k_2 for the Cannizzaro reaction of [α,α'-$^2H_2$]phenanthrene-4,5-dicarbaldehyde.

reaction of 5-formyl-4-phenanthroic acid[14] and formalin as described by Barton *et al.*[15] to give a fawn-coloured crystalline solid, recrystallised from ethanol, m.p. 177–178 °C (lit.,[15] 177–178 °C).

Solvents were purified as described previously.[16]

Measurements.—The ^{1}H NMR spectra were measured using Bruker WP80SY and Anaspect EM360 spectrometers. Tetramethylsilane was used as an internal standard, except in aqueous solutions where it was used externally. The ^{1}H NMR spectra of phenanthrene-4,5-dicarbaldehyde in carbon tetrachloride indicated the expected structure with formyl [δ 10.0 (s, 2 H)] and aromatic [δ 7.8–8.4 (m, 8 H)] protons. A similar result was observed in deuteriated dimethyl sulphoxide. In deuteriated dimethyl sulphoxide–deuterium oxide, no formyl proton could be observed and two new signals (δ 6.0 and 6.1) in a ratio of *ca.* 2.5 (low δ/high δ) were observed. This behaviour is very similar to that observed for *o*-phthalaldehyde.[6] The hydrate is a bridged (cyclic) monohydrate **7** which occurs as a *cis–trans* mixture. Faye *et al.*[17] have shown that a general relation exists for such stereochemically related systems. The hemiacetal protons of the *cis*-isomer are predicted to appear at 0.2–0.3 ppm towards low field relative to those of the *trans*-isomer. Thus, the *cis*-isomer appears predominate. The ^{13}C NMR spectra of the dialdehyde in dioxane showed the aromatic (multiplet) and formyl carbons (singlet, 191.2 ppm). Addition of water gave two new absorptions (singlets; 99.5 and 100.2 ppm). These results confirm the formation of the bridged (cyclic) monohydrate **7** from the dialdehyde.

A UV spectrophotometric method was used to study the hydration and Cannizzaro reaction of the dialdehyde. The spectrophotometer used was a Unicam SP8-100 and the cell temperature was controlled to ±0.05 °C by means of a Churchill thermocirculator. The technique used was essentially that previously described.[1,6] The substrate concentration was *ca.* 5 × 10^{-5} mol dm^{-3}. In water, the dialdehyde spontaneously hydrated, apparently independent of pH at *ca.* pH 7, and the first-order rate coefficient, k_{obs}, could be determined. For hydration, the reaction was followed at 257 nm, which was λ_{max} for the hydrate. The dialdehyde had very much less intense absorptions with λ_{max} at 250 and 295 nm. Measurements of the spectra of the dialdehyde in dioxane and extrapolation back to zero time in water gave almost identical results. In 70% (v/v) dioxane–water, the spectra of the dialdehyde did not change and was almost identical with that in dioxane. However, on addition of a trace of acid or base, a rapid change occurred to the spectrum finally in water. Both the ^{1}H NMR and UV spectral studies indicated that the dialdehyde was completely hydrated in water and 70% (v/v) dioxane–water at equilibrium. The rate coefficient for hydration in water, k_{obs}, was measured at 19.5 and 30.4 °C, as shown in Table 1, and is equal to k_H for the hydration (*cf.* ref. 6). The α,α'-dideuterio dialdehyde also gave complete hydration. The pK_a for the hydrate could not be measured by UV spectroscopy as no change was observed on apparent ionisation, and a rapid rearrangement occurs in base. Other methods were precluded by the low solubility of the dialdehyde and its hydrate. The pK_a value can be confidently estimated from that of the bridged monohydrate of phthalaldehyde[6] to be about 11.8 at 30 °C in water. At the base concentrations studied here (see below), the hydrate can be assumed to be in the form of the mono-anion.



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The product of the Cannizzaro reaction was shown to be quantitatively the anion of 5-(hydroxymethyl)phenanthrene-4-carboxylic acid by isolation as the lactone and UV spectral comparison with the product of hydrolysis of the lactone. The substrate concentrations for both the reactions were about 5 × 10^{-5} mol dm^{-3} and the base concentrations 2 × 10^{-3}–5 × 10^{-2} mol dm^{-3}. The ionic strength was held constant (μ = 0.1 mol dm^{-3}) with sodium chloride. The reactions were found to be strictly first-order in substrates. The final absorbances were assumed to be those measured after ten half-lives and gave linear plots to about 80% reaction. There was no evidence of any relatively stable intermediate formation in the Cannizzaro reaction, *i.e.* good isosbestic points were found. The base was in at least a tenfold excess and the reactions were both found to be of first-order in base over the concentrations studied (*n.b.* the mono-anion of the hydrate is the 'real' substrate in the Cannizzaro reaction). The rate coefficients for the Cannizzaro reaction are shown in Table 2, as are those for alkaline hydrolysis of the corresponding lactone. The rate coefficient for the Cannizzaro reaction in 70% (v/v) dioxane–deuterium oxide was also measured and is shown in Table 2. The lactone products of the Cannizzaro reaction of the α,α'-dideuterio substrate in water and the ordinary substrate in D_2O showed no significant incorporation of the solvent isotope in the product.

Results and Discussion

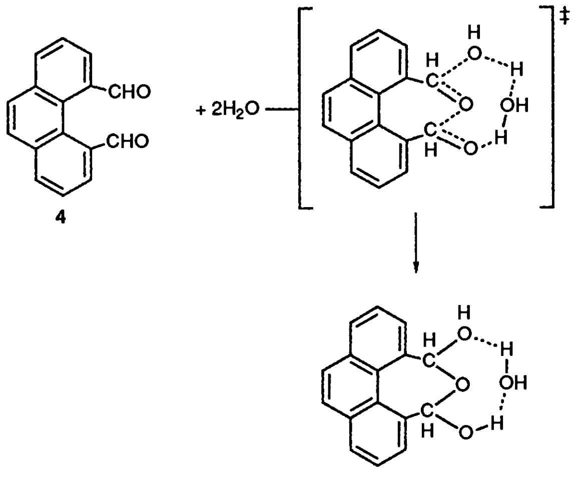
Hydration of Phenanthrene-4,5-dicarbaldehyde.—The hydrate is the bridged structure **7**, as a *cis/trans* mixture. The kinetics of the uncatalysed hydration indicate a very rapid reaction as was observed for *o*-phthalaldehyde (7.83 × 10^{-3} s^{-1} at 30 °C).[6] The activation parameters at 30.0 °C for the reaction are shown in Table 3. The very large negative $\Delta S^\ddagger$ value for hydration and small $\Delta H^\ddagger$ value are comparable to those observed for *o*-phthalaldehyde.[6] A pathway was suggested for the hydration of that dialdehyde[6] which also fits the evidence for the present substrate. This is shown for phenanthrene-4,5-dicarbaldehyde

Table 3. Activation parameters, at constant ionic strength (μ = 0.1 mol dm^{-3}), for the uncatalysed hydration in water and intramolecular Cannizzaro reaction in 70% (v/v) dioxane–water of 4,5-phenanthrenedicarbaldehyde at 30.0 °C[a]

	$\Delta H^{\ddagger}$/kcal mol^{-1} [c]	$\Delta S^{\ddagger}$/cal mol^{-1} K^{-1}
Hydration	7.7	−45
Cannizzaro reaction	12.8	−17
[Alkaline hydrolysis of lactone	12.6	−24][b]

[a] Values of $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ are considered accurate to within ±300 cal mol^{-1} and ±1 cal mol^{-1} K^{-1}, respectively. [b] Alkaline hydrolysis of lactone of 5-(hydroxymethyl)phenanthrene-4-carboxylic acid in 70% (v/v) dioxane–water. [c] 1 cal = 4.184 J.

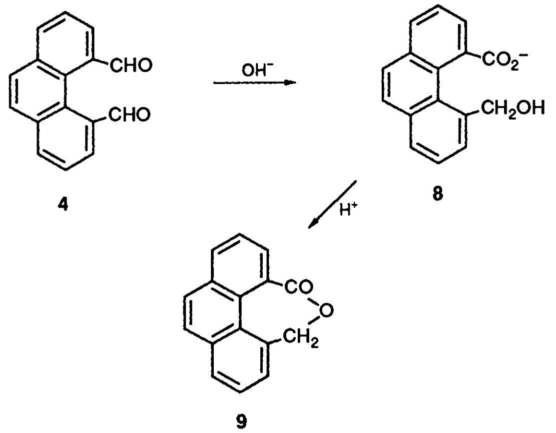
below in Scheme 2. This is shown as a concerted reaction involving the dialdehyde and two water molecules (neglecting further solvation). One water molecule attacks the first carbonyl group, which then attacks the second carbonyl group intramolecularly. The nucleophilic process is assisted by a second water molecule acting as a general acid–base in transferring a proton. Such a process agrees with both a rapid rate and the $\Delta S^{\ddagger}$ value, as well as related mechanisms.[6,4,18]



Scheme 2.

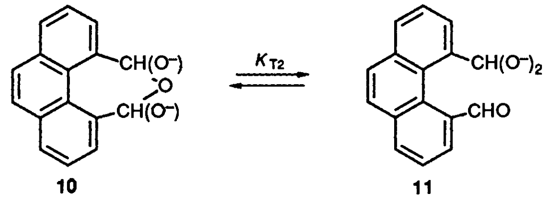
Hydration of Dialdehydes.—Some general considerations can now be made relating to the hydration of aryl dialdehydes, **1**, **3** and **4**. The reasons for the formation of cyclic monohydrates of aryl dialdehydes with proximate formyl groups are the relief of unfavourable stereoelectronic effects. Both repulsive dipole–dipole and steric 'bulk' interactions are relieved on forming the hydrates. These steric effects already cause extensive or complete deconjugation between the formyl and aryl groups in such systems, *cf.* ref. 19. The reason why no such relatively stable hydrate occurs for biphenyl-2,2′-dicarbaldehyde[10] is that coaxial twisting relieves such interactions and this also allows conjugation between the formyl and phenyl groups.

Cannizzaro Reaction.—The product of the Cannizzaro reaction of phenanthrene-4,5-dicarbaldehyde (**4**) is the anion of 5-(hydroxymethyl)phenanthrene-4-carboxylic acid (**8**) as shown in Scheme 3 below. The reaction is completely intramolecular as shown by conducting the Cannizzaro reaction of the dialdehyde in D_2O or the dideuteriodialdehyde in water; both of which gave no significant incorporation of the solvent isotope in the product.



Scheme 3.

Kinetics of the Cannizzaro Reaction.—The intramolecular reaction is first order in the substrate (the anion of the hydrate) and first order in hydroxide anion. This clearly suggests the importance of the ring dianion **10** or its chain tautomer **11** (Scheme 4). The reaction is about 1.7 times faster in D_2O than H_2O. This is close to the value observed in our previous study[10] of an intramolecular Cannizzaro reaction, as well as that for an intermolecular reaction.[20] It does clearly indicate that the greater basicity or nucleophilicity of deuteroxide in D_2O, than of hydroxide in H_2O, is involved[21] and that the rate-determining step does not involve the ionisation process itself. The latter would be expected to give rise to a primary isotope effect in the opposite direction.



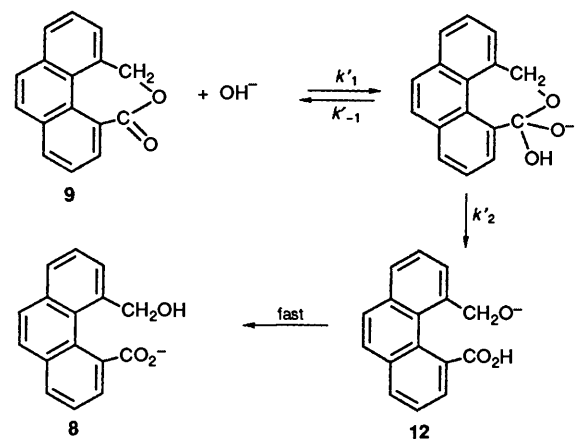
Scheme 4.

Kinetic Isotope Effect.—A small, but definite, primary isotope effect, k_H/k_D, equal to *ca.* 1.7 is observed. This is very close to the value observed in other intramolecular[10] and intermolecular[22,23] Cannizzaro reactions. If corrected, as before,[10] for the reverse secondary isotope effect, k_H/k_D would be *ca.* 2.3. While this value is still small, it is comparable to those found in other hydride transfer reactions.[24] Hydride transfer certainly occurs in the rate-determining step for the reaction under study.

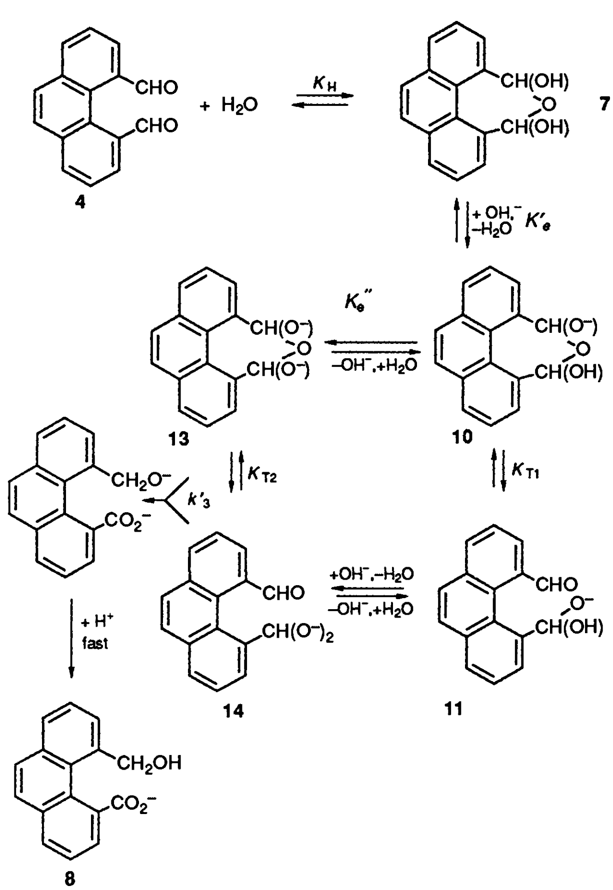
Activation Parameters for the Cannizzaro Reaction.—The entropy and enthalpy of activation for the intramolecular Cannizzaro reaction, shown in Table 3, are typical for a bimolecular reaction. As such it can only be compared with the same reaction of *o*-phthalaldehyde for which the enthalpy and entropy of activation are significantly greater and less negative, respectively. It would appear that the transition state for the 4,5-phenanthrene system requires more orientation and ordering, but it is energetically more favourable than that of the 1,2-benzene system. The first has a seven-membered ring transition state and the second a five-membered ring. It is difficult to compare the 4,5-phenanthrene with the 2,2′-biphenyl system. The latter has an initial state consisting of a dialdehyde and two hydroxide anions, while the former consists of the monoanion of the hydrate and one hydroxide anion.

Lactone Hydrolysis.—The rate coefficients for alkaline hydrolysis of the lactone of 5-(hydroxymethyl)phenanthrene-4-carboxylic acid (**9**) at various temperatures are shown in Table

2, with the activation parameters shown in Table 3. The rate of hydrolysis of the lactone in this study is only slightly slower than that of the closely related lactone of 2′-(hydroxymethyl)biphenyl-2-carboxylic acid previously studied.[10] The rate ratio of the phenanthrene to the biphenyl lactone is *ca.* 0.84 at 40 °C, when corrected for the change of solvent.[25] The activation parameters for both seven-membered lactones are comparable; although $\Delta H^{\ddagger}$ for the hydrolysis of the phenanthrene lactone is somewhat larger. These effects probably arise from the greater molecular rigidity of the phenanthrene lactone. Scheme 5 shows the suggested mechanistic pathway for the alkaline hydrolysis for these lactones, with k_1 as the rate-determining step. However, an important conclusion from this study is that the hydrolysis of the phenanthrene lactone is *ca.* 13 times *slower* than the Cannizzaro reaction. If the lactone was an intermediate in the latter reaction, it would be expected to be observed to form and then disappear by UV spectroscopy. As the lactone is not observed, it cannot be an intermediate in the intramolecular Cannizzaro reaction under study.

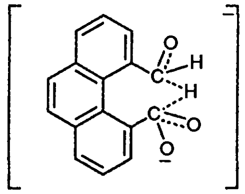


Scheme 5.



Scheme 6.

Proposed Mechanism for the Intramolecular Reaction.—The suggested mechanistic pathway for the intramolecular Cannizzaro reaction of phenanthrene-4,5-dicarbaldehyde is shown in Scheme 6. The more likely path is that *via* the chain dianionic tautomer **13**, the formation of which would precede the rate-determining step. The transition state would then be **15**; the drive for reaction being hydride transfer to the electrophilic centre of the carbonyl group. The seven-membered ring in **15** would be either buckled or strained, or possibly both.



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It is now possible to compare the intramolecular Cannizzaro reactions of *o*-phthalaldehyde[1] and phenanthrene-4,5-dicarbaldehyde for identical kinetic paths. Thus, at 60 °C, the 4,5-phenanthrene system is about 7×10^2 more reactive than the 1,2-benzene system. The factors responsible for this large effect must be that the stereochemical and steric bulk effects are more favourable in the 4,5-phenanthrene system. In our previous studies[26] of ring-chain tautomerism in phthalaldehydic and 5-formyl-4-phenanthroic acids, a similar result was observed with a ratio of equilibria of 4×10^2. The relief of compressional steric bulk interactions and ring-size factors, in the main, contribute to this effect.

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Paper 0/01356K
Received 29*th March* 1990
Accepted 15*th August* 1990