

Reactions and lifetime of the 6,6-dimethyl-3-phenylbenzenium ion in aqueous solution. Comparison with the 6-imino-3-phenylbenzenium ion (biphenyl-4-ylnitrenium ion)

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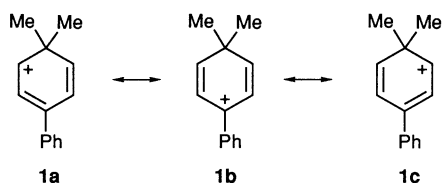
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The title cation (**1**) has been generated from three precursors in aqueous solution containing 20% acetonitrile; in the solvolysis of 6,6-dimethyl-3-phenylcyclohexa-2,4-dien-1-yl acetate (**9**) and from the isomeric alcohols 4,4-dimethyl-1-phenylcyclohexa-2,5-dien-1-ol (**7**) and 6,6-dimethyl-3-phenylcyclohexa-2,4-dien-1-ol (**8**) under acidic conditions. In addition, **8** reacts by way of **1** in weakly acidic solutions containing sodium azide to form an equilibrium mixture with an azide adduct, tentatively assigned as 6-azido-5,5-dimethyl-2-phenylcyclohexa-1,3-diene (**12**). This experiment provides a novel method for obtaining the $k_{az}:k_w$ ratio, which with the application of the azide clock method, supplies absolute rate constants. The overall analysis shows that **1** reacts in 20% acetonitrile forming **8** (90%, $k = 6.2 \times 10^6 \text{ s}^{-1}$), **7** (8%, $k = 5.5 \times 10^5 \text{ s}^{-1}$) plus a small amount of the rearrangement product 3,4-dimethylbiphenyl (**10**) (2%, $k = 1.6 \times 10^5 \text{ s}^{-1}$). The pK_R values are -5.3 for $\mathbf{1} \rightleftharpoons \mathbf{8} + \text{H}^+$ and -2.9 for $\mathbf{1} \rightleftharpoons \mathbf{7} + \text{H}^+$, and the equilibrium constant $\mathbf{7} \rightleftharpoons \mathbf{8}$ is 2.9×10^2 . The conjugated alcohol **8** is thus both the kinetic product and the thermodynamic product of the addition of water to **1**.

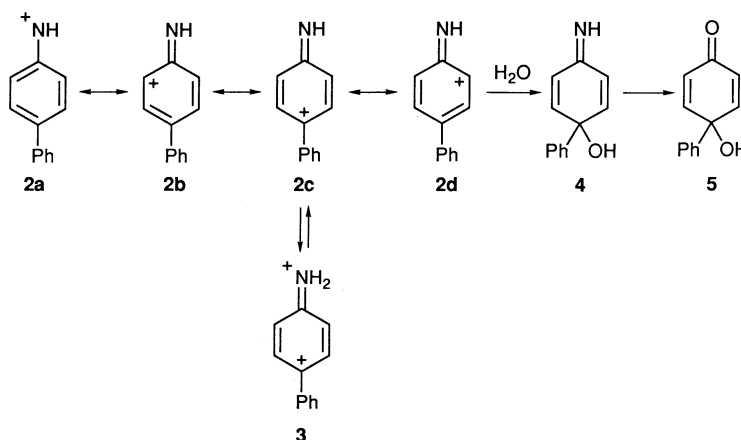
These results are compared with ones obtained previously for the biphenyl-4-ylnitrenium ion (**2**), a cation which can be regarded in terms of carbenium resonance contributors as the 6-imino-3-phenylbenzenium ion. The lifetimes in aqueous solution of the two cations are similar (*ca.* 150 ns for **1** and 300 ns for **2**), as is also the case for the rate constants for addition of water at the carbon that bears the phenyl group, the reaction that results in unconjugated alcohols. The difference is that the kinetic product with **2** is this unconjugated alcohol; an AM1 calculation suggests that the conjugated isomer would be the thermodynamic product, as is the case with **1**. It is suggested that the electronegative nitrogen of **2** results in a greater fraction of the positive charge being localized at the remote *para* carbon, so that is the site where water preferentially reacts.

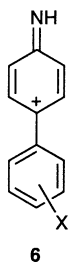
In this paper we explore the aqueous solution chemistry of the title carbocation **1**, as generated as a steady-state intermediate from several precursors.



The work was prompted by our findings with the biphenyl-4-ylnitrenium ion **2**, the reactive electrophile responsible for DNA

binding of the carcinogen 4-aminobiphenyl.¹⁻⁴ Although normally written as the structure **2a**, a nitrenium form, this cation is better regarded as an iminocyclohexadienyl ion; *i.e.* with carbenium forms **2b-d** as the major resonance contributors. Evidence for such an interpretation lies in the observation that the cation is protonated forming a dication **3** in 0.1–1.0 mol dm⁻³ HClO₄.⁵ The basicity is consistent with that of an imine which has a nearby positive charge. The cation **2** reacts with water exclusively at the position *para* to the nitrogen, forming the cyclohexadienone imine **4** (which slowly hydrolyses to the parent ketone **5**).⁶ Substituents in the phenyl ring attached at C4 have a pronounced effect on the rate constants for the reaction (Ren and McClelland, unpublished results). In quantitative terms, this ring appears to interact with the positive charge in





the same manner as the aryl ring in a benzylic-type cation, *i.e.* as if the structure of the nitrenium ion were **6**.

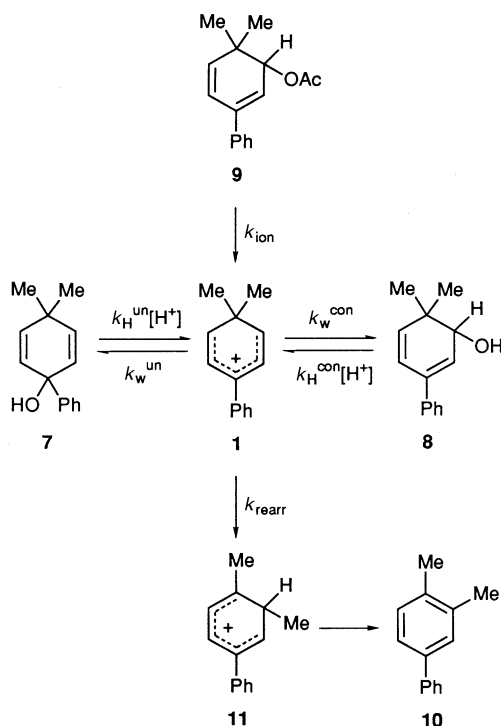
Williams and co-workers have also produced experimental evidence for the importance of carbocation resonance contributors though comparisons of rates of formation of the nitrenium ions.⁷ They found that *N*-alkyl substitution has little effect relative to the parent phenylnitrenium ion. Substitution at the *para* position however has a pronounced accelerating effect, indicating considerable stabilization of the cation.

The cation **1** provides a model for the carbenium forms of **2**, with the imine of the latter being replaced by two methyl groups. This grouping obviously is required to block immediate aromatization through loss of H⁺. We had anticipated on the basis of studies on similar systems⁸⁻¹⁴ that migration of one of the methyl groups would be a competing pathway. This does occur, but it is a minor process compared with solvent addition.

Results and discussion

Synthesis of compounds

Compounds **7-10** given in Scheme 1 were available as substrates



and products. The alcohol **7** was prepared from 4,4-dimethylcyclohexa-2,5-dien-1-one¹⁵ by reaction with phenyl lithium. The conjugated alcohol **8** is the more thermodynamically stable isomer (see later) and was prepared by isomerization of **7**. This reaction also results in formation of some of the biphenyl **10**; chromatographic separation of the mixture pro-

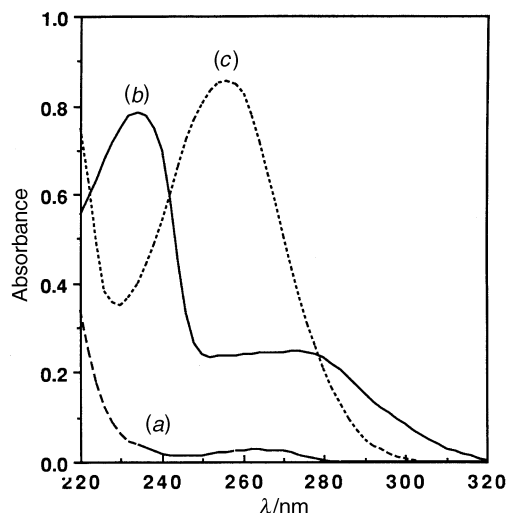


Fig. 1 UV spectra observed with 4,4-dimethyl-1-phenylcyclohexa-2,5-dien-1-ol (**7**) (8×10^{-5} mol dm⁻³) in acetic acid buffers (pH 5-6) in 20% acetonitrile. Curve (a) is the spectrum of the starting material, curve (b) is the spectrum after the initial kinetic phase and curve (c) is the final spectrum.

vides both products. An acetate ester could be formed by initially deprotonating the alcohol **10** with NaH, followed by the addition of acetic anhydride. The NMR spectrum of this material however showed that it was exclusively (>95%) the acetate **9** derived from the conjugated alcohol. Judging from the situation with the parent alcohols, **9** is likely to be thermodynamically more stable than the acetate derived from **7**, and isomerization to this more stable form could not be prevented.

Solvolysis of acetate **9**

The acetate **9** proved to be relatively reactive in aqueous acetonitrile solutions, solvolysing in 20% (by volume) acetonitrile with a rate constant k_{ion} of 1.34×10^{-3} s⁻¹. The reaction was sensitive to solvent polarity. Using data obtained in four acetonitrile-water mixtures (10, 20, 30 and 40% acetonitrile), a plot of $\log k_{\text{ion}}$ versus the solvent *Y* parameter¹⁶ was found to have a slope of 1.15. This obviously indicates that the solvolysis is proceeding in an S_N1 fashion, with the cation **1** as an intermediate.

Product analysis was carried out for the solvolysis in 20% acetonitrile. The solvent also contained 0.010 mol dm⁻³ Na₂HPO₄-0.002 mol dm⁻³ NaH₂PO₄, to provide a pH that was sufficiently basic to prevent further reactions. Three products were observed, with the conjugated alcohol **8** the major product at $89.8 \pm 0.5\%$, the unconjugated alcohol **7** at $7.9 \pm 0.4\%$ and $2.3 \pm 0.4\%$ of the rearranged **10**. Since **7** and **8** are stable under these conditions, the rate constant ratios of eqns. (1)-(3) describe the partitioning of **1** into the three products. The assumption is made that methyl migration is rate-determining in the rearrangement reaction. That is, once the cation **11** forms it rapidly aromatizes by loss of a proton.

$$\frac{k_w^{\text{un}}}{k_w^{\text{un}} + k_w^{\text{con}} + k_{\text{rearr}}} = 0.079 \quad (1)$$

$$\frac{k_w^{\text{con}}}{k_w^{\text{un}} + k_w^{\text{con}} + k_{\text{rearr}}} = 0.898 \quad (2)$$

$$\frac{k_{\text{rearr}}}{k_w^{\text{un}} + k_w^{\text{con}} + k_{\text{rearr}}} = 0.023 \quad (3)$$

Acid-catalysed reactions of unconjugated alcohol **7**

Solutions of this alcohol are unstable in weakly acidic solutions. Initial experiments involved UV spectroscopy, and the

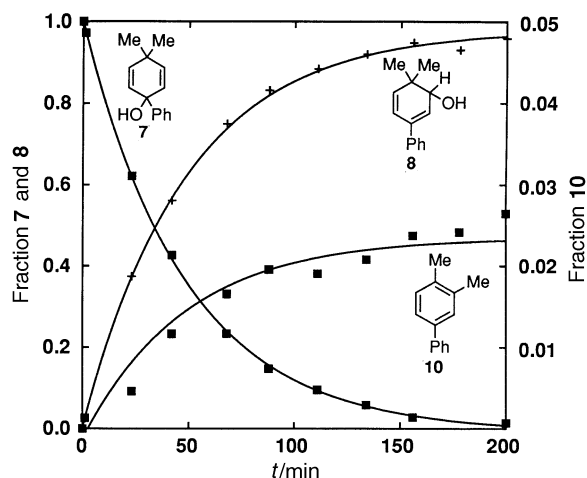


Fig. 2 Fraction of starting material **7**, and the two products **8** and **10** for a solution of 4,4-dimethyl-1-phenylcyclohexa-2,5-dien-1-ol (**7**) (initially $2 \times 10^{-4} \text{ mol dm}^{-3}$) in acetic acid buffer (pH 6.2, $[\text{NaOAc}] = 0.02 \text{ mol dm}^{-3}$, $[\text{HOAc}] = 0.002 \text{ mol dm}^{-3}$) in 20% acetonitrile

pertinent spectra are given in Fig. 1. At wavelengths above 230 nm, $ca. 10^{-4} \text{ mol dm}^{-3}$ solutions of **7** are only weakly absorbing, as shown in curve (a). Addition of acid results in an absorbance increase, resulting eventually in a spectrum [curve (b)] that closely resembles that of **8**. Further changes then occur, resulting ultimately in a spectrum corresponding closely to that of **10** [curve (c)]. The two changes are separated by three orders of magnitude in rate, and thus each can be analysed in terms of single exponential kinetics. Both follow the same kinetic pattern, a first-order dependence on H^+ concentration. Experiments in acetate buffers show no dependence on the concentration of the buffer. The first-order dependence in $[\text{H}^+]$ holds to solutions of pH $ca. 7$, where the rates become too slow to measure conveniently. Values of k_{H^+} , the catalytic coefficient in H^+ , are given in eqns. (4) and (5).

$$k_{\text{H}^+}(\text{A} \rightarrow \text{B}) = k_{\text{H}^+}^{\text{un}} \left(\frac{k_{\text{w}}^{\text{con}} + k_{\text{rearr}}}{k_{\text{w}}^{\text{un}} + k_{\text{w}}^{\text{con}} + k_{\text{rearr}}} \right) = (6.8 \pm 0.4) \times 10^2 \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1} \quad (4)$$

$$k_{\text{H}^+}(\text{B} \rightarrow \text{C}) = k_{\text{H}^+}^{\text{con}} \left(\frac{k_{\text{rearr}}}{k_{\text{w}}^{\text{con}} + k_{\text{rearr}}} \right) = (7.1 \pm 0.3) \times 10^{-1} \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1} \quad (5)$$

To understand better the chemistry behind these changes, the reaction was followed with HPLC. Fig. 2 illustrates results for times representing the faster reaction. The starting alcohol **7** decreases in a first-order reaction, with a rate constant that is within experimental error the same as that obtained from the UV changes in the same solution. Two products appear, the isomeric alcohol **8** and the rearrangement product **10** in a ratio $[\mathbf{8}]:[\mathbf{10}] = 43 \pm 4$. The HPLC peak for **7** does not completely disappear even at times corresponding to 20 half-lives of the faster kinetic process. The ratio $[\mathbf{7}]:[\mathbf{8}]$ is approximately 0.003 at this stage, but there is considerable uncertainty in this number. This is due to the small amount of **7** that is present, coupled with its HPLC sensitivity being only $ca. 1/3$ that of **8** at the monitoring wavelength. At much longer times, the alcohol **8** disappears along with the small amount of **7**. The rate constant for this process is identical to that obtained for the slow kinetic phase observed spectrally. At times corresponding to 10 half-lives of this kinetic stage, the only substance present is the biphenyl **10**.

These results point to a mechanism whereby **7** undergoes an H^+ -catalysed ionization to the cation **1**, which then converts to the isomer **8** and a small amount of **10**. The ratio $[\mathbf{8}]:[\mathbf{10}] = 43$

is within experimental error the same as the ratio of 39 obtained in the solvolysis of the acetate precursor **9**. This demonstrates that a common cationic intermediate **1** is involved in both reactions. At the completion of the fast kinetic process, the two alcohols have achieved equilibrium. The equilibrium concentration **7** ($ca. 0.3\%$) is however sufficiently small that it can be ignored in the kinetic analysis. Therefore, with the assumption of a steady-state in **1**, the observed rate constant for the fast kinetic process is given by the term containing the microscopic rate constants in eqn. (4) above. The ratio in brackets in this expression is the fraction of **1** that reacts to form **8** and **10**. This fraction is calculated as 0.92 from the product analysis involving the acetate **9** [add eqn. (2) and (3) above]. Thus, $k_{\text{H}^+}^{\text{un}}$ is obtained as $7.4 \times 10^2 \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$. This number is slightly larger than the observed value of k_{H^+} because of the 8% of **1** that returns to this alcohol.

At the completion of the fast kinetic phase, the solution contains $ca. 98\%$ of **8**. This explains the similarity in the UV spectrum at this stage to that of this material. An H^+ -catalysed ionization of **8** to form **1** does occur, and eventually **10** forms as the only species present. The observed rate constant for this process is given by the expression containing the microscopic rate constants in eqn. (5). The term in brackets in this equation represents the fraction of **1** that undergoes methyl migration in competition with the addition of water to form **8**. Values of this fraction are available from two independent product analyses; 0.025 from the experiments with **9** and 0.023 from the experiments with **7**. Using the average, $k_{\text{H}^+}^{\text{con}}$ is calculated as $29 \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$. This number is much larger than the observed rate constant for the disappearance of **8**, since with this alcohol cation formation is largely reversible.

The equilibrium constant relating the two alcohols is given by a ratio of rate constants [eqn. (6)]. This can now be calculated,

$$\frac{[\mathbf{8}]}{[\mathbf{7}]} = \frac{k_{\text{w}}^{\text{con}} k_{\text{H}^+}^{\text{un}}}{k_{\text{w}}^{\text{un}} k_{\text{H}^+}^{\text{con}}} \quad (6)$$

since the absolute values for $k_{\text{H}^+}^{\text{con}}$ and $k_{\text{H}^+}^{\text{un}}$ have been determined as outlined above, and the ratio $k_{\text{w}}^{\text{un}}:k_{\text{w}}^{\text{con}}$ is available from the products obtained with **9**. The value of $[\mathbf{8}]:[\mathbf{7}]$ is thus obtained as 2.9×10^2 . This is clearly consistent with the HPLC analysis that shows that there is only a small amount of **7** at equilibrium.

Reaction in the presence of sodium azide

In order to obtain absolute values for the k_{w} terms, we initially sought to detect **1** using flash photolysis, employing the acetate **9** as precursor.¹⁷ These experiments proved unsuccessful, since irradiation of **9** in 20% acetonitrile failed to give either a transient in flash photolysis experiments or products on steady-state irradiation that were consistent with a cation intermediate. We turned therefore to the azide-clock method,¹⁸⁻²⁰ and after some experimentation discovered what appears to be a novel method to obtain the required $k_{\text{w}}:k_{\text{az}}$ ratio. As illustrated in Fig. 3, the experiment involves the alcohol **8** as the precursor, being added to weakly acidic solutions (pH 5-6) containing sodium azide. This results in a decrease in the area of the peak for **8** in the HPLC, with an eventual levelling at some intermediate value. As discussed above, **8** reacts in acidic solutions to form **10**. That process, however, is not the one being observed, since at pH 5.7 it has a half-life of $5 \times 10^5 \text{ s}$. Indeed very little **10** is formed even at the longest times shown in this figure. The HPLC traces do reveal a new peak growing in at the same rate as **8** decays. As shown in Fig. 3, this peak forms to a greater extent when the decrease of **8** is greater.

Our interpretation is that the new peak represents an azide-substituted adduct, and what is being observed is an approach to equilibrium involving **8** and this azide. As shown in equilibrium (7), the position of this equilibrium depends on both

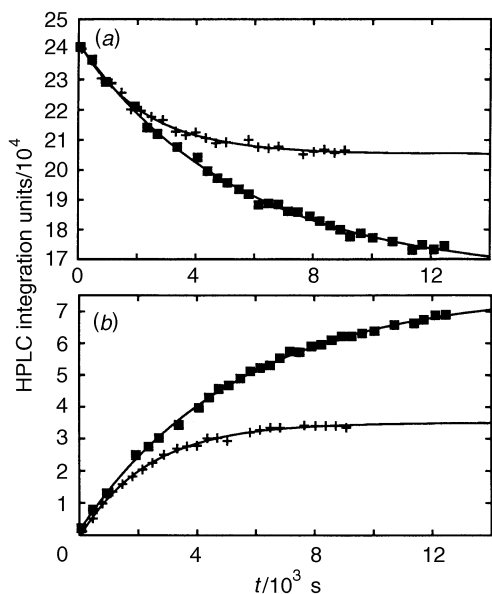
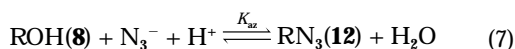


Fig. 3 HPLC integration units as a function of time for the reaction of 6,6-dimethyl-1-phenylcyclohexa-2,4-dien-1-ol (**8**) (initially 2×10^{-4} mol dm $^{-3}$) in acetic acid buffer (pH 5.7, [NaOAc] = 0.03 mol dm $^{-3}$, [HOAc] = 0.009 mol dm $^{-3}$) in 20% acetonitrile. (a) **8**; (b) azide product. [NaN $_3$] = 0.0195 (■) and 0.0065 mol dm $^{-3}$ (+).



the concentration of azide ion and the pH (in solutions where azide is not protonated). Indeed, increasing the concentration of azide ion at constant pH or increasing the acidity at constant azide concentration leads to a greater shift of the equilibrium away from **8**. The new product proved to be too unstable to isolate for structural characterization. We believe that it has the structure **12**. This is based on the observation that a UV spectrum recorded as the compound elutes from the HPLC is essentially the same as that of **8**. This is also seen in the quantitative HPLC analyses, which show that at any given time, the area of the new product is within experimental error the same as the area of **8** which has been lost.

Detailed quantitative experiments were carried out under the conditions of Fig. 3, varying the azide concentration at a pH of 5.7. An equilibrium constant K_{az} can be defined for solutions of constant pH using eqn. (8). This constant is experimentally

$$K_{\text{az}}' = [\text{H}^+]K_{\text{az}} = \frac{[\text{RN}_3]}{[\text{ROH}][\text{N}_3^-]} = \frac{k_{\text{H}}^{\text{con}}[\text{H}^+]k_{\text{az}}}{k_{\text{w}}^{\text{con}}k_{\text{ion}}} \quad (8)$$

determined according to eqn. (9), where Area $\mathbf{8}_{\text{nit}}$ and Area $\mathbf{8}_{\text{eq}}$

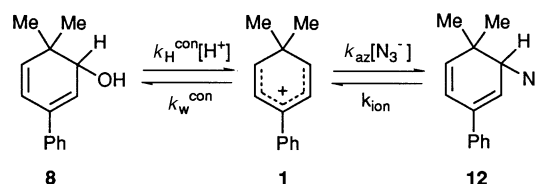
$$K_{\text{az}}' = \left(\frac{\text{Area}\mathbf{8}_{\text{nit}} - \text{Area}\mathbf{8}_{\text{eq}}}{\text{Area}\mathbf{8}_{\text{eq}}} \right) \frac{1}{[\text{N}_3^-]} \quad (9)$$

are the HPLC peak areas for **8** at the beginning of the reaction and after equilibrium has been reached. Values of K_{az}' determined in this way for a number of concentrations of azide ion are given in Table 1. As is required by the equilibrium model, the numbers are constant within experimental uncertainty. The average value of K_{az}' (pH = 5.7) is 23 ± 1.2 dm 3 mol $^{-1}$. The value of K_{az} ($[\text{RN}_3]:[\text{ROH}][\text{N}_3^-][\text{H}^+]$) is 1.2×10^7 dm 6 mol $^{-2}$.

The equilibration occurs by way of the cation **1**, as shown in Scheme 2. First-order rate constants determined by fitting the changes in the HPLC peak areas to an exponential equation refer to an approach to equilibrium. With a steady-state assumption in **1**, these are given by eqn. (10). With the recog-

Table 1 Calculated equilibrium constant and observed rate constant for the interconversion of 6,6-dimethyl-1-phenylcyclohexa-2,4-dien-1-ol (**8**) and azide adduct in acetic acid buffer (pH 5.7, [NaOAc] = 0.03 mol dm $^{-3}$; [HOAc] = 0.009 mol dm $^{-3}$) in 20% acetonitrile at 25 °C

[NaN $_3$]/10 $^{-3}$ mol dm $^{-3}$	$K_{\text{az}}'/\text{dm}^3$ mol $^{-1}$	$k_{\text{eq}}/10^{-4}$ s $^{-1}$
3.30	24.4	6.97
3.72	23.8	6.17
4.13	23.0	5.84
4.89	23.7	5.13
6.49	26.5	4.23
8.07	24.2	3.51
9.63	22.8	3.09
9.64	22.4	3.28
11.95	22.5	2.95
15.7	23.8	2.32
19.5	23.6	1.83
40.0	24.1	1.32
65.0	23.2	1.068



Scheme 2

$$k_{\text{eq}} = \frac{k_{\text{H}}^{\text{con}}[\text{H}^+]k_{\text{az}}[\text{N}_3^-] + k_{\text{w}}^{\text{con}}k_{\text{ion}}}{k_{\text{w}}^{\text{con}} + k_{\text{az}}[\text{N}_3^-]} \quad (10)$$

nition of the relation between K_{az}' and the rate constants [eqn. (8)], this can be rearranged to give eqn. (11). This equation was

$$k_{\text{eq}} = \frac{k_{\text{ion}}K_{\text{az}}'[\text{N}_3^-] + k_{\text{ion}}}{1 + \left(\frac{k_{\text{az}}}{k_{\text{w}}^{\text{con}}} \right) [\text{N}_3^-]} \quad (11)$$

fitted to the experimental data of Table 1 to provide the three parameters, k_{ion} as 2.3×10^{-3} s $^{-1}$, the ratio $k_{\text{az}}:k_{\text{w}}^{\text{con}}$ as 8.1×10^2 dm 3 mol $^{-1}$, and K_{az}' as 21.0 dm 3 mol $^{-1}$. The satisfactory agreement of the last number with the value determined from the HPLC peak areas (23.7) is one aspect of consistency in the analysis. A second is provided by $k_{\text{H}}^{\text{con}}$, which is calculated from the three fitted parameters, as in eqn. (12). The number so

$$k_{\text{H}}^{\text{con}} = \frac{K_{\text{az}}'k_{\text{ion}}}{\left(\frac{k_{\text{az}}}{k_{\text{w}}^{\text{con}}} \right) [\text{H}^+]} \quad (12)$$

obtained is 30 dm 3 mol $^{-1}$ s $^{-1}$, in excellent agreement with the value of 29 obtained in a completely independent fashion as described above.

As seen in Table 1, the values of k_{eq} decrease with increasing azide concentration. This may seem surprising, but it is a consequence of the relative values of the rate constants in eqn. (10), and a change in a rate-determining step as the concentration of azide is varied. At low azide concentrations, $k_{\text{w}}^{\text{con}} > k_{\text{az}}[\text{N}_3^-]$ so that the interconversion of **12** and **1** is rate-determining. Thus, ionization is the rate-determining step for **12**→**8**, and capture of **1** by the azide ion is rate-determining for **8**→**12**. At higher concentrations, however, $k_{\text{w}}^{\text{con}} < k_{\text{az}}[\text{N}_3^-]$. Now, the rate-determining step for **12**→**8** is the hydration of **1**, while the H $^+$ -catalysed formation of **1** is rate-determining for **8**→**12**.

Also surprising is the high thermodynamic affinity of azide compared with water. This is better seen by recasting the equi-

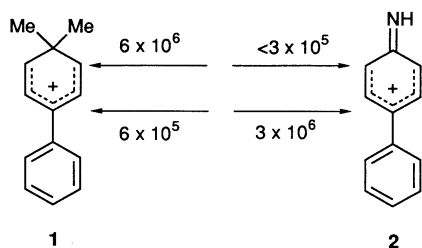


Fig. 4 Comparison of rate constants (s^{-1} , 20–25 °C) for the addition of water to cyclohexadienyl cations. The rate constant $3 \times 10^6 \text{ s}^{-1}$ for reaction of **2** is directly measured by flash photolysis.⁵ The upper limit for reaction at the other position is based on the absence of the product that would form for such a reaction.⁶

Table 2 Absolute rate constants and equilibrium constants

Constant	Value
$k_w^{\text{un}}/\text{s}^{-1}$	5.5×10^5 ^a
$k_{\text{H}}^{\text{un}}/\text{dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$	7.4×10^2
$\text{p}K_{\text{R}}(\mathbf{1} \rightleftharpoons \mathbf{7})$	-2.9 ^b
$k_w^{\text{con}}/\text{s}^{-1}$	6.2×10^6 ^c
$k_{\text{H}}^{\text{con}}/\text{dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$	2.9×10^1
$\text{p}K_{\text{R}}(\mathbf{1} \rightleftharpoons \mathbf{8})$	-5.3 ^b
$[\mathbf{8}]_{\text{eq}} : [\mathbf{7}]_{\text{eq}}$	2.9×10^2
$k_{\text{rearr}}/\text{s}^{-1}$	1.6×10^5 ^d

^a Calculated from the value of k_w^{con} with $k_w^{\text{un}} : k_w^{\text{con}} = 0.088$. ^b Calculated as $-\log(k_w : k_{\text{H}})$. ^c Calculated from $k_{\text{az}} : k_w^{\text{con}} = 8.1 \times 10^2$, with $k_{\text{az}} = 5 \times 10^9 \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$. ^d Calculated from the value of k_w^{con} with $k_{\text{rearr}} : k_w^{\text{con}} = 0.025$.

librium in the form of equilibrium (13). The equilibrium



constant for this system, explicitly including the concentration of water, is given by eqn. (14) where $K_{\text{a}}(\text{HN}_3)$ is the acid dissoci-

$$K_{\text{Haz}} = \frac{[\text{RN}_3][\text{H}_2\text{O}]}{[\text{ROH}][\text{HN}_3]} = K_{\text{az}}K_{\text{a}}(\text{HN}_3)[\text{H}_2\text{O}] \quad (14)$$

ation of HN_3 . Using a value of $10^{-4.46}$ measured by pH titration in 20% acetonitrile, K_{Haz} is 1.8×10^4 . Azide ion has a long history showing a high kinetic affinity for C^+ centres. The present experiments show that it also has a relatively high thermodynamic affinity.

The absolute value for k_w^{con} is obtained from the ratio ($k_{\text{az}} : k_w^{\text{con}}$) with the assumption that $k_{\text{az}} = 5 \times 10^9 \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$.^{18–20} Since the ratio $k_w^{\text{un}} : k_w^{\text{con}}$ and $k_{\text{rearr}} : k_w^{\text{con}}$ are known [eqns. (1)–(3)], the absolute values for k_w^{un} and k_{rearr} can also be calculated. These constants are summarized in Table 2. Also included in this Table are the $\text{p}K_{\text{R}}$ values for the equilibrium hydration of the cation **1** to form the two alcohols **6** and **7**, calculated as the ratio of rate constants.

For comparison purposes, the triphenylmethyl cation has $\text{p}K_{\text{R}} = -6.5$ and $k_w = 1.7 \times 10^5 \text{ s}^{-1}$.²¹ Thus, the cyclohexadienyl cation **1** is somewhat more stable thermodynamically, and somewhat less stable kinetically. This contrasting behaviour is consistent with trends observed in plots of $\log k_w$ versus $\text{p}K_{\text{R}}$,¹⁷ which suggest that for cations with the same $\text{p}K_{\text{R}}$, the kinetic barrier for water addition increases with increasing steric congestion at the C^+ centre.

Comparison of nitrenium and carbenium ions

A comparison of rate constants for water addition to **1** and the nitrenium ion **2** is shown in Fig. 4. The lifetimes of these two cations in water are remarkably similar, *ca.* 150 ns for **1** and 300 ns for **2**. Also similar are the rate constants for water addition at the carbon bearing the phenyl group, a factor of just five distinguishing the two reactions. This comparison therefore pro-

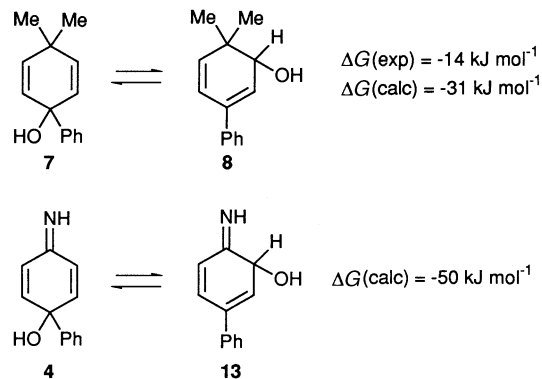


Fig. 5 Free energy changes for the isomerization of cyclohexadienols. Calculated values are based on the AM1 semi-empirical method.

vides good support for the representation of the nitrenium ion as an iminocyclohexadienyl cation.

Where the comparison breaks down is for the reaction at the carbon adjacent to the nitrogen and *gem*-dimethyl group. In the latter case, this is the kinetically preferred site, favoured by about an order of magnitude over the reaction at the position *para* to the methyl groups. This site has also been shown experimentally to be thermodynamically favoured. With the nitrenium ion however, the *para* position is kinetically favoured, sufficiently so that no product derived from water addition at the *ortho* site is obtained.

With the imino system, the thermodynamic preference is not experimentally known. To probe this situation, AM1 calculations were performed for the pairs of isomeric alcohols that are formed in each system (Fig. 5). While the absolute numbers are debatable because of the semi-empirical nature of the method, the calculations do reproduce the thermodynamic preference for **8** over **7**, in fact within a factor of two of the experimental value. With the imino system the calculations show an even greater preference for the conjugated adduct (**13**). This suggests that this is the thermodynamic product in this system as well.

The behaviour of the biphenyl-4-yl nitrenium ion is not unusual, since other aryl nitrenium ions, including the parent cation, show a kinetic preference for reaction with water at the carbon *para* to the nitrogen.²² One simple explanation is that the electronegative nitrogen causes the positive charge to localize at the most distant *para* carbon. In other words the resonance contributor **2c** in the nitrenium system is more important than the contributors **2b** and **2d** where the positive charge is on the carbon adjacent to the electronegative atom. Precedence for such an interpretation can be found in the chemistry of benzylic-type carbocations bearing CF_3 groups at the benzylic carbon. These cations have the unusual feature of reacting at least partly at the *para* carbon.^{23–26} Arguments have been advanced that the electronegative fluorines result in the positive charge being localized to a significant extent at this carbon, directing incoming nucleophiles to react at this site.

Experimental

4,4-Dimethyl-1-phenylcyclohexa-2,5-dien-1-ol (7). 4,4-Dimethylcyclohexa-2,5-dione¹⁵ (1.22 g, 10.0 mmol) in 10 cm^3 of dry tetrahydrofuran (THF) was added dropwise at -78 °C to phenyllithium (10.1 mmol) in hexanes under an Argon atmosphere. After stirring at -78 °C for 30 min, the flask was allowed to warm to room temperature, at which point it was stirred for a further hour. Aqueous K_2CO_3 was then added, the organic layer was separated and dried over MgSO_4 . After removal of the solvent, chromatography on silica gel with 15% ethyl acetate–85% hexane gave 1.32 g of product as a viscous oil, which solidifies to a waxy solid on complete removal of solvent. $\delta_{\text{H}}(\text{CDCl}_3, 200 \text{ MHz})$ 1.16 (s, 3 H), 1.18 (s, 3 H), 5.76 (d, 2 H,

$J = 8$ Hz), 5.82 (d, 2 H, $J = 8$ Hz), 7.2–7.4 (mult., 3 H) and 7.45–7.55 (mult., 2 H); HRMS (EI, 70 eV): m/z , 200.1200. $C_{14}H_{16}O$ requires 200.1201.

6,6-Dimethyl-3-phenylcyclohexa-2,4-dien-1-ol (8) and 3,4-dimethylbiphenyl (10). When 4,4-Dimethyl-1-phenylcyclohexa-2,5-dien-1-ol (7) contains trace amounts of solvents (hexane and/or ethyl acetate) it slowly isomerizes to **8** and loses water to form **10**. Thus, after standing for several days a mixture of the three compounds was obtained. These could be separated by chromatography on silica gel with 15% ethyl acetate–85% hexanes; **10** elutes first as a colourless liquid, then **7** and then **8** elutes as a sticky oil.

8: δ_H (CDCl₃, 200 MHz) 1.11 (s, 3 H), 1.19 (s, 3 H), 1.7 (d, 1 H, $J = 7$ Hz, OH), 4.08 (dd, 1 H, $J = 7$ Hz and $J' = 3$ Hz), 5.82 (d, 1 H, $J' = 8$ Hz), 6.24 (dd, 1 H, $J' = 3$ Hz and $J'' = 1$ Hz), 6.52 ($J' = 8$ Hz and $J'' = 1$ Hz) and 7.3–7.5 (mult., 5 H); HRMS (EI, 70 eV): m/z , 200.1205. $C_{14}H_{16}O$ requires 200.1201.

10: δ_H (CDCl₃, 200 MHz) 2.13 (s, 3 H), 2.15 (s, 3 H) and 7.2–7.6 (mult., 8 H); HRMS (EI, 70 eV): m/z , 182.1902. $C_{14}H_{14}$ requires 182.1096.

6,6-Dimethyl-3-phenylcyclohexa-2,4-dien-1-yl acetate (9). Sodium hydride (0.4 g of 60% dispersion in oil, 10.5 mmol) was washed three times with dry hexanes, and after evaporation of the hexanes, 2 cm³ of dry THF was added. 4,4-Dimethyl-1-phenylcyclohexa-2,5-dien-1-ol (7 (10.0 mmol) in 10 cm³ of dry THF was then slowly added. After stirring at 40 °C for 2 h, the mixture was cooled to –78 °C and acetic anhydride (10.6 mmol) in 5 cm³ of THF was slowly added. After warming to room temperature, aqueous K₂CO₃ was added, and the mixture extracted with diethyl ether. After drying over CaCl₂ and removal of the solvents, chromatography on silica gel with 20% ethyl acetate–80% hexanes afforded 1.24 g of **9** as a colourless oil.

δ_H (CDCl₃, 200 MHz) 1.13 (s, 3 H), 1.19 (s, 3 H), 5.32 (d, 1 H, $J = 3$ Hz), 5.84 (d, 1 H, $J' = 8$ Hz), 6.05 (dd, 1 H, $J = 3$ Hz and $J' = 1$ Hz), 6.32 ($J' = 8$ Hz and $J' = 1$ Hz) and 7.3–7.5 (mult., 5 H). HRMS (EI, 70 eV): m/z , 242.1309. $C_{16}H_{18}O_2$ requires 242.1307.

UV spectroscopic studies

These were performed with a Cary 2200 spectrometer thermostatted at 25 °C by injecting 0.003 cm³ of a stock solution of the substrate in acetonitrile into 3 cm³ of an appropriate solution in a UV cuvette. The final concentration of the substrate was 1×10^{-4} mol dm³. The data from the spectrometer were transferred directly to a computer, where first-order rate constants were calculated by fitting the exponential equation to the traces of absorbance *versus* time.

HPLC

These experiments were performed with a Waters 600E system with UV detector. Conditions: 1 × 10 cm C18 column, flow rate = 2 cm³ min⁻¹, isocratic 30:70 methanol:water for 6 min followed by a linear gradient from 6–9 min to 15:85 methanol:water followed by isocratic 15:85 methanol:water from 9–16 min, detector wavelength at 220 nm for 0–6 min followed by 235 nm from 6–16 min. Retention times: 4.8 min (**7**), 5.2 min (**8**), 10.5 (**9**), 13.8 min (**12**) and 14.5 min (**10**). Peak areas were converted into absolute quantities by use of response factors determined by injecting known amounts of the authentic samples of **7–10**. Solutions of substrates of concentration $1–2 \times 10^{-4}$ mol dm³ were placed in a constant temperature bath at 25 °C. At appropriate times 0.080 cm³ were removed and injected directly to the HPLC.

Acid dissociation constants in 20% acetonitrile

These were determined by measuring the pH with a combination electrode for solutions containing known amounts of CH₃COOH:CH₃COONa or HN₃:NaN₃ in 20% acetonitrile, with the ionic strength at 0.1 mol dm³ maintained where neces-

sary with NaCl. The measured pH was corrected by the subtraction of 0.08. This factor was based on the measured pH of 1.92 for a solution of 0.01 mol dm³ HCl–0.09 mol dm³ NaCl in 20% acetonitrile. The pK_a was then calculated using the Henderson–Hasselbach equation; 5.20 for CH₃COOH and 4.46 for HN₃.

Computations

Semi-empirical calculations were carried out using the MOPAC 93 suite of programs²⁷ on a Hewlett-Packard work station running the Unix operating system. Geometry optimizations, force calculations and thermodynamic calculations were accomplished using the AM1 semi-empirical Hamiltonian.²⁸ The geometry was initially optimized using high levels of precision (precise, GNORM = 0.0 and SCFCRT = 1D-15) to obtain enthalpies of formation. The optimized structure was then submitted to a force calculation and thermodynamical calculation to obtain thermodynamic parameters necessary for the change in Gibbs' energy.

Acknowledgements

The continued financial support of the Natural Sciences and Engineering Research Council of Canada is gratefully acknowledged.

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Paper 6/06786G

Received 3rd October 1996

Accepted 5th November 1996