Dienone–Phenol Rearrangements of Bicyclic Cyclohexa-2,5-dien-1-ones; Kinetic Studies of the Importance of a Multistage Mechanism

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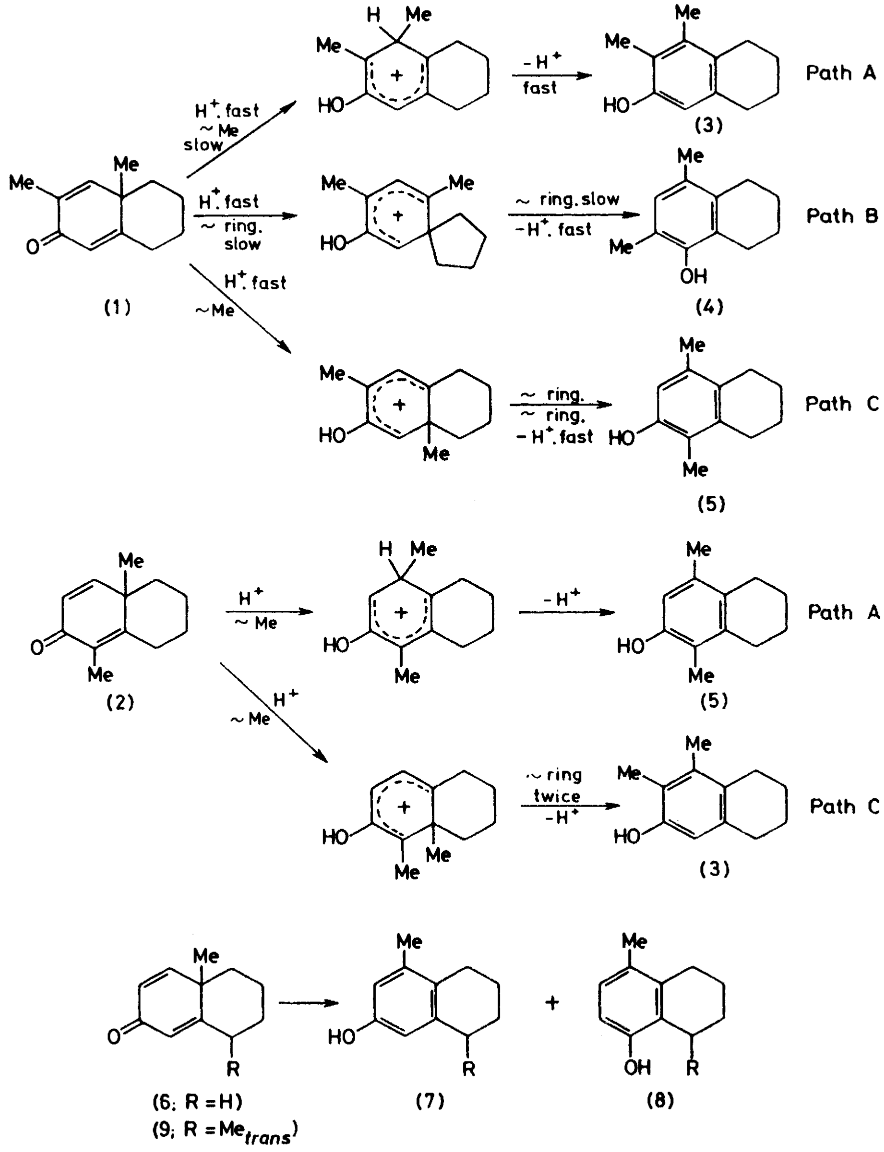
Kinetic measurements allow the relative importance of pathways for dienone–phenol rearrangements of two bicyclic cyclohexadienones to be assessed. For 3,4a-dimethyl-5,6,7,8-tetrahydronaphthalen-2(4a*H*)-one (1) the rearrangement rates in aqueous sulphuric acids were apportioned to three pathways. For the analogous 1,4a-dimethyltetrahydronaphthalenone (2) the rates were apportioned to two pathways, both of which allow the angular methyl group to migrate to sites *meta* to the oxygen function. The indirect path for this process, which involves three separate migration steps, is about as fast as the commonly accepted ' 1,2-migration ' of the methyl group. Comparisons are made with the analogous 4a-methyl-, and 4a,8-dimethyl-5,6,7,8-tetrahydronaphthalenones.

In our previous paper[1] we reported studies of the products of dienone–phenol rearrangements of the two bicyclic cyclohexadienones (1) and (2). We established that (1) rearranges by three routes, giving a ' *meta*-methylphenol ' product (3) by Path A, a ' *para*-methylphenol ' (4) by Path B, and a different ' *meta*-methylphenol ' (5) by an indirect Path C which involves a 1,2-methyl shift followed by a rearrangement *via* a spiran



SCHEME 1

intermediate. Reaction of dienone (2), whose substitution pattern excludes Path B as a route to phenols,* gives two '*meta*-methylphenols' (3) and (5), by Paths C and A, respectively. This work has potential implications for all dienone–phenol rearrangements, and other cationic rearrangements, of compounds related to (1) and (2). One simple case is the parent bicyclic dienone (6), which rearranges to (7) and (8) in varying proportions in a variety of acidic media.[2] Clearly, (7) might form by Paths A and/or C. Although most discussions have considered Path A alone,[3-5] one study has suggested that Path C is the major route to this product.[6] We now report kinetic studies of the rearrangements of dienones (1) and (2) in aqueous sulphuric acids, in order to gain reliable measures of the rates of Paths A—C. These are compared with other rates, including those reported for the analogues (6) and (9) which lack the methyl groups we use to distinguish between Paths A and C. We find that these methyl groups do not greatly affect the rates, and deduce that both Paths A and C are involved about equally in the formation of (7) from (6).

EXPERIMENTAL

The cyclohexadienones (1) and (2) were analytically pure samples whose preparation and properties are given in the previous paper.[1] U.v. spectra were obtained using a Unicam SP 8-100 grating spectrophotometer system in which the cell temperatures were maintained at 25.0 ± 0.1 °C by water circulating through a hollow cell block from a thermostat circulator and monitored by a small platinum resistance thermometer fitted into one cell. Basicity studies on (1) (see Table 1) and kinetic measurements on (1) and (2) were performed using solutions in aqueous sulphuric acid, by the u.v. and acidity function methods, and use equations (1) and (2) as before.[2,7,8] All the kinetic measurements on (1) used acids which gave complete (>99.9%) protonation and represent rates of reaction of the monocation. For (2), almost the same range of acids was used and all the acidic solutions had identical spectra and intensities at, or within a minute or two of, the time of mixing. These spectra were very different from the spectrum in water, and were ascribed to the monocation: ^{1}H n.m.r. studies confirmed this. Rate constants were calculated using Swinbourne's method [9] or a computer program. The program took the experimentally determined absorbance at 'infinite time', D_∞, calculated the rate constant, then varied D_∞ by an iterative technique to minimise the sum of squares of deviations of all the experimental points from a first-order kinetic line. The optimised value of D_∞ was always close to the experimental value, but the latter could not be relied upon entirely because colour developed in the most concentrated acid solutions at long reaction times and, in some cases (see Tables) the absorbance due to dienone cation fell and then, after a few half-lives, slowly increased again. This effect may be due to sulphonation or oxidation of the phenolic products. The rate constants are presented in Tables 2 and 3: nearly all kinetic runs showed clean first-order reaction over at least four half-lives, using the experimental D_∞ values. In the most concentrated acids (>74%) dienone (2) did not show a clean kinetic pattern: at first it reacted relatively quickly but then slowed to about one-half the rate, to an apparently clean first-order process (see Table 3). There are a number of possible explanations, but the most likely seems to be that, in the necessarily complex overall kinetic scheme, no one step is always rate-determining and it may take some hours before equilibrium kinetics are achieved. One possibility we considered was that the 'dead-end' spiran intermediate involved in an abortive Path B process, or one of the intermediates in Path C could accumulate in the early stages of reaction. However, when the reaction was followed by ^{1}H n.m.r. spectroscopy the only detectable species were the dienone's cation and the phenolic products [almost entirely (5)] which were consumed and formed at equal rates (see Table 4).

RESULTS AND DISCUSSION

The basicity measurements on dienone (1) (see Table 1) show that its protonation follows Hammett's acidity function H_0, and that its thermodynamic pK is (−2.18 ± 0.11). This value is in excellent agreement with a correlation equation given previously [2] (see footnote *d* of Table 1).

TABLE 1

Basicity data for 3,4a-dimethyl-5,6,7,8-tetrahydronaphthalen-2(4a*H*)-one (1) [a,b]

λ/nm	$(H_0)_{\frac{1}{2}}$ [c]	m_0 [c]	Medium effect
252	−2.18 ± 0.10	1.05 ± 0.10	Strong
272	−2.10 ± 0.05	1.00	Unimportant
315	−2.26 ± 0.12	1.01 ± 0.08	Small
Weighted mean [d]	−2.18 ± 0.11	1.02 ± 0.10	

[a] Free dienone, $\lambda_{max.}$(H_2O) 251 nm (ε 15 710); cation, $\lambda_{max.}$ (83.8% H_2SO_4) 272 and 316 nm (ε 13 950 and 5 980). [b] Measured at 25.0 °C in aqueous sulphuric acid. Values of Hammett's acidity function, H_0, are taken from ref. 11. [c] Quantities are defined in the basicity equation (1). [d] The value (−2.18 ± 0.11) is taken to be the thermodynamic pK of (1), whose protonation follows the Hammett acidity function. The calculated (predicted) value, using equation (9) of ref. 2 is −2.17 ± 0.12.

TABLE 2

Kinetics for rearrangement of (1) in aqueous sulphuric acid at 25 °C; u.v. measurements at 270 or 269 nm [a]

Wt. % acid	H_0	10^6k_1/s^{-1}	$-\log_{10}k_1$
66.8	−5.33	2.77	5.56
71.3	−6.04	4.22	5.37
76.5	−6.89	2.95	5.53
79.0	−7.31	3.78	5.42
79.0	−7.31	4.22	5.37
82.1	−7.81	3.60	5.44
83.6	−8.07	3.80	5.42
83.9	−8.12	5.53	5.26

[a] These results were obtained partly by J. W. P. and partly by J. H. Z., using different samples; J. W. P. used a Unicam SP 1800 u.v. spectrometer as in ref. 2.

The rate constants given in Tables 2 and 3 show that increasing acidity causes the cations of the dienones (1) and (2) to rearrange more rapidly. Plots of $\log_{10}k_1$ against Hammett's acidity function H_0 are linear, fitting equations (3) and (4).

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* These paths assume that the non-dienone ring is not cleaved. Our experiments have shown no evidence of such cleavage.

TABLE 3

Kinetics for rearrangement of (2) in aqueous sulphuric acid at 25 °C; u.v. measurements at 269 or 260 nm

Wt. % acid	H_0	$10^6k_1/s^{-1}$	$-\log_{10}k_1$
63.5	−4.84	11.0	−4.96
66.8	−5.33	12.9	−4.89
68.8	−5.65	14.9	−4.83
70.5	−5.88	16.7	−4.78
71.3	−6.04	17.3	−4.76
74.3	−6.52	21.7	−4.66
76.2	−6.84	13.6	−4.87 [a]
77.8	−7.11	9.65	−5.01 [a]
79.3	−7.35	6.17	−5.21 [a]
82.5	−7.90	3.08	−5.51 [a]
83.9	−8.12	17.6	−4.76 [a,b]
	−8.12	4.14— 7.50	−5.38 to −5.12 [a,c]

[a] These values are omitted from the correlation by equation (4). [b] Over first 11 h reaction. [c] Over first 96 h.

$$\underset{[B]}{\text{Dienone}} \underset{K_A}{\overset{H^+,\ \text{fast}}{\rightleftharpoons}} \underset{[BH^+]}{\text{Cation}} \xrightarrow[\text{Slow}]{k_1} \text{Products}$$

$$\log_{10}[BH^+]/[B] = m_0\,[(H_0)_{\frac{1}{2}} - H_0] \qquad (1)$$
$$= (\varepsilon - \varepsilon_B)/(\varepsilon_{BH^+} - \varepsilon)$$

Under our conditions of complete protonation of the dienone, equation (2) applies.

$$d[\text{Products}]/dt = -d[\text{stoicheiometric dienone}]/dt = -d[BH^+]/dt = k_1[BH^+] \qquad (2)$$

$$\text{For (1): } \log_{10}k_1 = -5.81 \pm 0.23 - H_0\,(0.05 \pm 0.03) \qquad (3)$$

$$\text{For (2): } \log_{10}k_1 = -5.84 \pm 0.04 - H_0\,(0.18 \pm 0.01) \qquad (4)$$

Similar behaviour has been found for the other dienones we have studied before [2,8,10] and, in particular, for the bicyclic analogues (6) and (9).[2] The near parallelism of the plots for (1), (2), (6), and (9) allows one to discuss quantitatively the relative reactivities of the various compounds. The kinetically controlled product ratios reported in the previous paper [1] allow the total rates to be dissected into rate constants for each reaction path. We previously compared rates at a common acidity, $H_0 - 5.80$ (corresponding [11] to *ca.* 70% w/w sulphuric acid), and do the same here (see Table 5). At this stage we see that all the reaction paths followed by the methylated dienones (1) and (2) have rates very similar to those found for the analogues (6) and (9).* More detailed analysis is possible.

TABLE 4

Kinetics for rearrangement of (2) in 86.5% aqueous sulphuric acid at 35 °C, determined by ^1H n.m.r. spectroscopy [a]

Peaks used (δ values)	$10^5k_1/s^{-1}$
8.12, 7.12 [b]	8.7 ± 0.4
2.40 [c]	9.3 ± 0.3
2.20 [b]	8.2 ± 0.3

[a] The dienone cation has δ 8.12 (1 H, d, *J* 9 Hz, 4-H), 7.12 (1 H, d, *J* 9 Hz, 3-H), 2.20 (3 H, s, 1-Me), and 1.43 (3 H, s, 4a-Me). The chemical shifts agree excellently with those reported for other analogous cations (K. L. Cook, M. J. Hughes, and A. J. Waring, *J. Chem. Soc., Perkin Trans. 2*, 1972, 1506). [b] Due to unchanged dienone cation. [c] Due to phenolic product.

TABLE 5

Dissected rate constants for rearrangement processes, at 25 °C, in aqueous H_2SO_4 at $H_0 - 5.80$ [a]

Compound		$10^7k_1/s^{-1}$
Path A	(1)	(5.5 ± 2.0)
Path B	(1)	(12 ± 2)
Path C	(1)	(15 ± 2.8)
Path A	(2)	(147 ± 4)
Path C	(2)	(11 ± 1.5)
Path B	(6)	(3.3 ± 0.4)
Paths (A + C)	(6)	(12 ± 1.3)
Path B	(9)	(10.2 ± 1.5)
Paths (A + C)	(9)	(14.5 ± 2.0)

[a] H_0 taken from the scale of ref. 11.

TABLE 6

Arrhenius activation energy differences, in kJ mol^{-1}

	Temp. (°C)	Acidity, $\%H_2SO_4$		
Compound (1)	25	72.7	$E_A - E_C$	2.5 ± 0.6
			$E_A - E_B$	1.9 ± 0.6
	100	50	$E_A - E_C$	1.2 ± 0.3
			$E_A - E_B$	1.5 ± 0.3
Compound (2)	25	79.1	$E_C - E_A$	6.0 ± 0.6
	100	50	$E_C - E_A$	4.7 ± 0.2

In discussing the rearrangement rates an earlier result is useful. Methyl migrations from C-4 of 2,4,4-trimethylcyclohexa-2,5-dienone to C-5 and to C-3 are respectively 4.2 and 1.8 times faster than that in the 4,4-dimethyldienone.† These factors are assumed to reflect the electronic influence of the 2-methyl group, which accelerates migration to either C-5 or C-3 by 4.2 times, and a superimposed steric retardation by a factor of 0.4 on the cation preceding the 2,3,4-trimethylphenol product which has four buttressing adjacent substituents.[2]

The rate of Path B for the α-methylated bicyclic dienone (1) studied here is faster than those for (6) and (9) by factors of *ca.* 3.6 and 1.2, respectively, which compare well with the factors just mentioned. Turning to the rates of the direct methyl-shift reaction (Path A) we see that (2) reacts *ca.* 27 ± 7 times faster than (1). Both compounds have a methyl group α to the carbonyl, but their steric interactions and those in the cations immediately preceding the products are significantly different, and we have no satisfactory analogues for comparison. For (6) and (9) we do not know the rate of Path A, but only of Paths A and C together: these are *ca.* 0.08 as fast as Path A for (2) and *ca.* 2.0 as fast as Path A for (1). For Path C alone the rates of (1) and (2) are very close, differing by a factor of only 1.3 ± 0.4, and the sum of Paths A and C for (6) falls between them. The sums of rates for Paths A and C for (1), (2), (6), and (9) are $(2.0 \pm 0.2) \times 10^{-6}$, 15.8×10^{-6}, $(1.2 \pm 0.1) \times$

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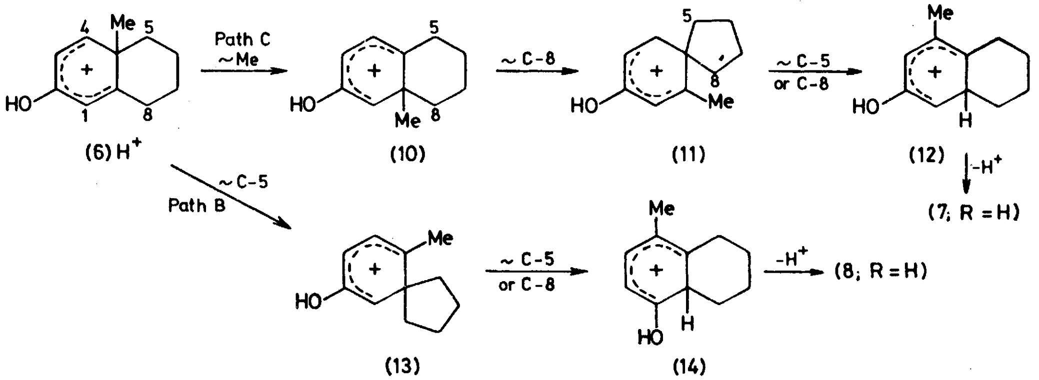
* The product ratios were not measured at exactly $H_0 - 5.80$, but they should not change much with acidity. The satisfactory accordance with the Arrhenius equation of the ratios found in 50% H_2SO_4 at 100 °C and those in 72—79% H_2SO_4 at 25 °C confirms this view.

† The statistical factor of 0.5 is applied to the total rate for 4,4-dimethylcyclohexa-2,5-dienone.

10^{-6}, and (1.45 ± 0.2) × 10^{-6} s^{-1}, respectively, at H_0 − 5.80 and 25 °C. It is clear from these comparisons that the rates of the complex Path C are perfectly normal and that, if anything, the ' odd ' result is the high rate of Path A in compound (2).

Implications.—The results obtained should allow us to estimate the relative contributions of Paths A and C to the formation of the ' *meta*-methylphenol ' (7; R = H) from the simple bicyclic dienone (6). In one approach we use a comparison with the results of our study[8] which showed the rate constants for methyl migration in 2,4,4,5-tetramethylcyclohexa-2,5-dienone (to C-3) and its 3,4,4-trimethyl analogue (to C-5) to be virtually identical [k_1 = (1.33 ± 0.04) × 10^{-5} and (1.26 ± 0.03) × 10^{-5} s^{-1}, respectively, in H_2SO_4 of H_0 − 5.80 at 25 °C]. If we accept these migrations to be satisfactory analogues of the Path A migrations in (1) and (6) the latter should both have about equal rates, *i.e. ca.* 5.5 × 10^{-7} s^{-1} as found for (1). Thus Paths A and C are estimated to contribute about equally to the formation of (7; R = H) from (6), and (7; R = Me) from (9). An obvious check of this prediction would be available from rearrangement of a sample of (6) labelled suitably in the dienone ring with ^{13}C.



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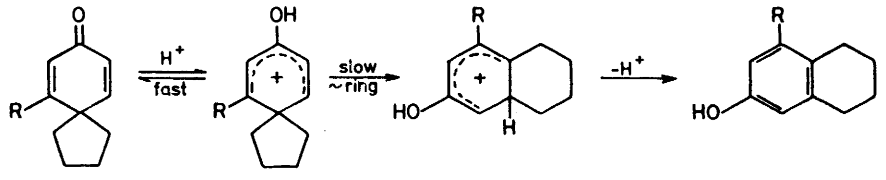

(15; R = Me)
(16; R = H)

The Kinetic Details of Paths B and C.—The steps of Paths B and C are shown in Scheme 2. For simplicity, the prototype dienone (6) is shown, but the same arguments apply to dienones (1) and (2), apart from minor kinetic factors due to their extra methyl groups and the fact that for (2) Path B cannot proceed beyond the intermediate of type (13) or (14).

We wish to identify the rate-determining step for Path C, and draw on data for Path B also.* First we argue that the spiran intermediate (11) in Path C rearranges rapidly to the cation (12) and thence, rapidly, to the phenol (7). The spiran (11) is actually the cation of the bicyclic dienone (15), whose rearrangement in dilute aqueous methanolic sulphuric acid has been studied over a short acidity range by Hemetsberger. More data are available for the analogue (16), which rearranges just twice as fast.[12] Even at low acidities (15) and (16) rearrange rapidly.† At H_0 0, the observed pseudo-first-order rate constant for (15) at 25 °C is *ca.* 1.6 × 10^{-4} s^{-1}. This refers to reaction of the small amount of cation present, which will be of the order of 1—2%, so must be multiplied by *ca.* 50 or 100 (to *ca.* 1.0—1.6 × 10^{-2} s^{-1}) to be compared with the rate constants we found for Path C for the *cations* of (1), (2), (6), and (9).‡ These are of the order of 1 × 10^{-7} s^{-1}, when extrapolated to H_0 0. Thus the rearrangement of the spiran intermediate (11) to the phenol (7; R = H) is *ca.* 10^5 faster than the actual rate constants for Path C.

We will next argue that the step in which the spiran intermediate (11) is formed from (10) is not rate-determining in Path C, but this requires a prior discussion of Path B. If the formation of the spiran intermediate (13) of

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* These discussions apply to the standard conditions, H_0 − 5.80 at 25 °C in aqueous H_2SO_4. They will apply equally at lower acidity, but not at the higher acidities for (2) whose kinetics become irregular (see earlier).

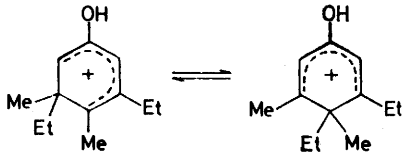
† The data of ref. 12 for (16) at 30 °C are correlated by equation (5). Correction to 25 °C, using isolated data at this temperature, gives equation (6).

$$\log_{10}k_{\text{obs.}} \doteq -1.18H_0 - 3.56 \text{ at } 30\ °\text{C} \quad (5)$$

$$\doteq -1.18H_0 - 3.78 \text{ at } 25\ °\text{C} \quad (6)$$

‡ This assumes (16) to have similar basicity properties to 4,4-dimethyl-, 4-ethyl-4-methyl-, and 4-methyl-4-n-propyl-cyclohexadienones.[10]

Path B is rate determining, and the subsequent migration of C-5 or C-8 [for dienone (6)] or of C-8 [for (9)] is fast, then this path should have about equal rates in (6) and (9). In contrast, if the second stage, (13)→(14), is rate determining (9) should rearrange by Path B much faster than does (6). This is because the migrating group (C-8) for (9) resembles the s-butyl group which we know [13] to migrate *ca.* 350 times faster than the ethyl or n-propyl groups which act as models for the migrating group in (6). In fact Path B in (9) has a rate constant three times larger than in (6) (3.3×10^{-7} and 1.0×10^{-6} s^{-1} respectively), which is consistent with the view that the formation of the spiran of type (13) is the slow step. We now return to Path C, and will show that formation of the spiran intermediate (11) should be much faster than those just discussed. The rearrangement of (10) to (11) involves migration of the ring, C-8, from the *meta*- to the *para*-position relative to the hydroxy-group.



(17) (18)

This is closely analogous to the rearrangement of (17) to (18) which we have studied before.[8] In contrast, the spiran formation in Path B involves migration of the ring from the *para*- to the *meta*-position, and is analogous to the process (18)→(17). We showed [8] that the equilibrium (17)⇌(18) lies heavily towards (18), in the ratio of at least 97 : 3. This is, of course, in accordance with the known stability of analogous Wheland intermediates. Thus, the spiran intermediate of type (11) in Path C should form from (10) at least 32 times faster than the spiran (13) in Path B forms from (6), *i.e.* with a rate constant of at least 1.0×10^{-5} s^{-1}. This is faster than the overall rate for path C, although only by a minimum factor of 7—9. The methyl migration step in Path C remains most likely to be rate determining. Estimates of rate constants for analogous methyl migrations to alkyl-substituted carbon atoms in other dienone–phenol rearrangements are [8,10] at least 3×10^{-7} s^{-1} and at least 1.7×10^{-7} s^{-1}. These agree closely with the values appropriate to Path C for (1) (3.5×10^{-7} s^{-1}) * or for (2) (6×10^{-7} s^{-1}).†

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* The rate-constant for Path C in (1), divided by 4.2 to allow for the electronic effect of the 3-methyl group.

† Half of the rate-constant for Path C in (2), to allow for the effect of the 1-methyl group (see earlier).

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