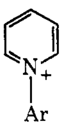
Formation of Phenylpyridinium Chloride from 5-Anilino-N-phenyl-2,4-pentadienylideniminium Chloride. Kinetics in Basic Media[1]

Elliot N. Marvell, Gerald Caple, and Iraj Shahidi

Contribution from the Department of Chemistry, Oregon State University, Corvallis, Oregon 97331. *Received January 27, 1970*

Abstract: In methanol solution 5-anilino-N-phenyl-2,4-pentadienylideniminium chloride (**2**) is converted quantitatively to N-phenylpyridinium chloride and aniline. The rate is not a simple function of substrate concentration in neutral solution. Addition of methoxide ion, triethylamine, or tri-*n*-butylamine converts **2** to 5-anilino-N-phenyl-2,4-pentadienylidenimine (**4**). Conversion of **4** to N-phenylpyridinium ion and aniline is faster than the reaction of **2** and is clearly first order in **4** (k_1 at 40° is 3.5×10^{-4} sec^{-1} with $\Delta H^{\ddagger} = 22.7$ kcal/mol and $\Delta S^{\ddagger} = 0.0$ eu). The reaction of **4** is not subject to general acid catalysis, and the rate is higher in dioxane or acetone than in methanol. A mechanism involving the electrocyclic ring closure of **4** as the rate-determining step is proposed.

Early in this century Zincke[3] discovered the first of a series of facile ring-opening reactions of pyridinium ions when he showed that 2,4-dinitrophenylpyridinium chloride (**1**) reacts (eq 1) with aniline to form a beautifully crystalline deep red salt, 5-anilino-N-phenyl-2,4-pentadienylideniminium chloride (**2**). Zincke presented evidence in support of his assignment of structure **2** to this salt and studied[4] a series of related products. Oddly enough König[5] found that these salts could be prepared conveniently *via* reaction of the pyridine–cyanogen bromide complex with the appropriate amine, and the salts are often called König's salts.



+ 2 $C_6H_5NH_2$ ⟶

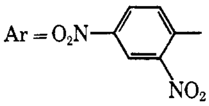
1

$[C_6H_5NH{=}CH{-}CH{=}CH{-}CH{=}CHNHC_6H_5]^+Cl$ (1)

2

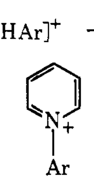
\+

$ArNH_2$



Zincke[3] called attention to the ring closure (eq 2) which salts (**2**) derived from primary amines will undergo, and this cleavage and reclosure process is the standard route to N-arylpyridinium salts which cannot be formed by direct reaction with pyridine. Closely related compounds have been utilized in an elegant synthesis of azulenes,[6] and the salts and the analogous bases are important intermediates in the synthesis of cyanine dyes.[7] Despite the general synthetic value of these ring-opening and ring-closure reactions, almost no work has been reported relative to the mechanisms of either process.

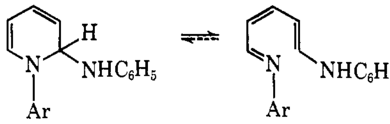
$[ArNH{=}CH{-}CH{=}CH{-}CH{=}CHNHAr]^+$ ⟶



\+ $ArNH_2$ (2)

3

In 1957 the first work on the mechanism of ring opening of **1** with aniline (eq 1) was reported by Van den Dunghen, Nasielski, and Van Laer.[8] The rate in 50% aqueous ethanol was first order in **1**, first order in aniline, and first order in hydroxide ion. No rate constant was reported, but a mechanism with a retro-electrocyclic reaction (eq 3) as the rate-determining step was proposed. Since we had shown[9] that substitution of an oxygen for the terminal carbon in a *cis*-hexatriene can increase the rate of electrocyclization by as much as 10^7, we were particularly interested in the influence of a nitrogen atom on the rate of this type of reaction.



(3)

Behavior of 2 in Methanol. Aside from the study by van den Dunghen, *et al.*, noted earlier,[8] Oda and Mita[10] have studied the kinetics of formation of **2** from **1**. They reported third-order kinetics first order in **1** and second order in aniline, a result not in complete agreement with the earlier study.[8] Preliminary studies using **1** and aniline in approximately stoichiometric ratio indicated that the kinetic behavior was complex. Thus, we were prompted to study the ring closure

---

(1) The authors are pleased to acknowledge the support of this work by the Public Health Service under Grant No. AM-07771 (CA-AM-10385). A preliminary report of this work has been published.[2]

(2) E. N. Marvell, G. Caple, and I. Shahidi, *Tetrahedron Lett.*, 277 (1967).

(3) Th. Zincke, *Justus Liebigs Ann. Chem.*, **330**, 361 (1903).

(4) Th. Zincke, *ibid.*, **333**, 296 (1904).

(5) W. König, *J. Prakt. Chem.*, **69**, 105 (1904).

(6) K. Hafner, *Justus Liebigs Ann. Chem.*, **606**, 79 (1957); K. Hafner, *Angew. Chem.*, 70, 419 (1958); K. Hafner and H. Kaiser, *Justus Liebigs Ann. Chem.*, **618**, 140 (1958); K. Hafner and K.-D. Asmus, *ibid.*, **671**, 31 (1964).

(7) F. Hamer, "Cyanine Dyes and Related Compounds," Interscience, New York, N. Y., 1964, pp 244–269.

(8) E. Van den Dunghen, J. Nasielski, and P. Van Laer, *Bull Soc. Chim. Belg.*, **66**, 661 (1957).

(9) E. N. Marvell, G. Caple, T. A. Gosink, and G. Zimmer, *J. Amer. Chem. Soc.*, **88**, 619 (1966).

(10) R. Oda and S. Mita, *Bull. Chem. Soc. Jap.*, **36**, 103 (1963).

reaction of **2** (eq 2) prior to investigating its formation from **1**.

Zincke[4] reported that N-phenylpyridium chloride and aniline are formed when **2** is heated either with ethanolic hydrogen chloride or with excess aniline (eq 2). Consonant with this report we found that **2** reacts to form the indicated products essentially quantitatively in methanol without added acid or base. In view of the color change during the reaction, ultraviolet spectroscopy seemed the analytical method of choice for a study of the kinetics. However **2** has two maxima, 407 and 485 nm, the relative intensities of which are concentration dependent. In acidic media only the uv max 485 (ϵ 115,000) appears while in basic solution the peak at 407 nm (ϵ 67,000) appears alone. These results agree well with the observations of Grigor'eva[11,12] for **2** in ethanol. The peaks are assigned to **2** (485 nm) and to the base **4** (407 nm) which results from dissociation of **2** (eq 4). The equilibrium constant for this dissociation in methanol is 3.8 × 10^{-9} mol/l. (see Experimental Section).

$$[C_6H_5NH(CH{=}CH)_2CH{=}NHC_6H_5]^+ \rightleftharpoons \underset{\mathbf{4}}{C_6H_5NH(CH{=}CH)_2CH{=}NC_6H_5} + H^+ \quad (4)$$

The rate of conversion of **2** to **3** (Ar = phenyl) and aniline in methanol was followed spectrophotometrically by converting all **2** and **4** to **2** with added hydrochloric acid prior to analysis. Though the rate data can be reasonably fitted to first-order kinetics,[2] careful studies of reactions carried to *ca.* 90% completion showed an inevitable upward drift in the rate constants. Analysis as a reaction half-order in **2** shows that the rate constants show a downward drift. In view of the complexity of the kinetics in neutral media and of the simpler situation pertaining in basic media, our main initial studies were confined to the latter medium and the results are reported in detail here.

Kinetics in Methanol with Added Base. In view of Zincke's report[4] of the formation of **3** (Ar = phenyl) from **2** in the presence of aniline, we studied the influence of bases on the rate. Interestingly, the addition of aniline has no measureable influence on the rate of the reaction. However, stronger bases do alter the rate in a very significant way. Addition of methoxide in amounts less than 1 equiv of **2** leads to an increase in the rate (Table I). When sufficient methoxide has been added to convert all **2** to **4**, the rate becomes independent of the methoxide concentration. Also when the rate plateau is reached the reaction is cleanly first order in **4**. In the presence of less than equivalent (in terms of **2**) concentrations of methoxide the rates are not of constant order in **2**, but approximate first-order reactions reasonably closely and all are listed as first-order rates in Table I.

Table I. Influence of Bases on the Rate of Formation of **3**[a]

Run no.	Temp, °C	Base added	Concentration $[M] \times 10^5$	$k_1 \times 10^4$, sec^{-1}
1	40.0	MeO^-	0.4	0.31
2	40.0	MeO^-	1.0	1.96
3	40.0	MeO^-	2.0	3.24
4	39.2	MeO^-	12.0	3.04
5	39.2	MeO^-	24.0	3.04
6	39.2	MeO^-	240.0	3.06
7	40.0	Et_3N	0.4	0.33
8	40.0	Et_3N	1.0	1.80
9	40.0	Et_3N	5.9	2.96
10	39.2	Et_3N	2.0	2.68
11	39.2	Et_3N	11.7	3.08
12	39.2	Et_3N	100.0	3.47
13	40.0	Bu_3N	0.4	0.27
14	40.0	Bu_3N	1.0	1.50
15	40.0	Bu_3N	2.0	2.58
16	39.2	Bu_3N	10.9	3.05
17	39.2	Bu_3N	11.8	3.08

[a] The initial concentration of **2** is 2.0 × 10^{-5} *M*.

This special behavior, *i.e.*, an initial rate increase with added base leading to a plateau where the rate is independent of the base concentration and the reaction is first order in **4** is not dependent on the structure of the base. Thus both triethylamine and tri-*n*-butylamine show the same behavior (Table I) as methoxide ion, although in keeping with their relative basicities the latter are less effective than is methoxide. A series of runs in methanol containing excess triethylamine was used to obtain the activation parameters, $\Delta H^{\ddagger} = 22.7$ kcal/mol and $\Delta S^{\ddagger} = 0.0$ eu, which were calculated in the usual manner.[13]

Salt and Solvent Influence. In the presence of excess base the reactive entity is **4**. The rate of its reaction is not altered by the addition of lithium perchlorate (Table II, runs 1 and 2). However change from a solvent of higher to lower ionizing power causes a small but measurable increase in the rate (Table II). This solvent change does not induce any alteration in the nature of the reaction since only phenylpyridinium chloride and aniline were isolated from a preparative run in 80% dioxane–20% methanol.

Table II. Influence of Lithium Perchlorate and of Solvent on the Rate of Reaction of **4**

Run no.	Solvent[a]	$[LiClO_4]$, $[M] \times 10^4$	[**2**], $[M] \times 10^4$	$[Et_3N]$, $[M] \times 10^4$	$k_1 \times 10^4$ sec^{-1}	Temp, °C
1	Methanol	0.00	0.199	10.0	3.48	40
2	Methanol	20.0	0.199	10.0	3.53	40
3	Methanol		3.24	5.15	0.96	30
4	80 MeOH–20 dioxane		3.24	5.15	1.26	30
5	60 MeOH–40 dioxane		3.24	5.15	1.72	30
6	40 MeOH–60 dioxane		3.24	5.15	2.56	30
7	20 MeOH–80 dioxane		3.24	5.15	4.60	30
8	Dioxane[b]		1.00	2.20	15.0	30
9	Acetone[b]		3.10	6.50	5.8	30

[a] Mixed solvent compositions are vol/vol per cent. [b] Contains a small but unknown amount of methanol.

General Acid Catalysis. The reaction of **4** to form **3** (Ar = phenyl) and aniline requires an additional proton. In methanol containing methoxide ion, the sole source of the proton is the solvent while in the presence of triethylamine or tri-*n*-butylamine the tertiary ammonium ion provides an additional source. Since the same rate for reaction of **4** is found in either case (Table I), it appears that the reaction of **4** is not general acid catalyzed. The assumption of a lack of general acid

---

[11] N. E. Grigor'eva, I. K. Gintse, and A. P. Severina, *Zh. Obshch. Khim.*, **26**, 3447 (1956).

[12] N. E. Grigor'eva, L. P. Kruglyak, and L. I. Shcherbakova, *ibid.*, **31**, 2425 (1961).

[13] A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," 2nd ed, Wiley, New York, N. Y., 1961, pp 99–101.

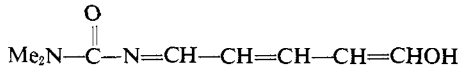
Table III. Rate of Reaction of **4** in Methanol Containing Benzoic Acid–Sodium Benzoate Buffer[a]

Benzoic acid, $M \times 10^5$	Sodium benzoate, $M \times 10^4$	$LiClO_4$, $M \times 10^4$	$k_1 \times 10^4$ sec^{-1}
			2.73
0.21	0.20		2.73
1.06	1.01		2.81
1.60	1.52		2.75
2.13	2.03		2.73
		2.03	2.75
0.21	0.20	1.83	2.72
1.06	1.01	1.01	2.78
1.60	1.52	0.51	2.77

[a] At 39.2°. Initial concentration of **2** is 2.13×10^{-5} M and of triethylamine is 2.21×10^{-4} M.

catalysis is supported by the data of Table III. All the runs were made under conditions which ensure that **4** remains the substrate. Relative magnitudes of the K_a's show that the main acid moiety present is triethylammonium ion, but clearly the amount of available acid in the two forms varies markedly without change in the rate. The same result obtains whether the reaction was carried out at constant ionic strength or not. A series of runs in acetone containing varying amounts of added benzoic acid showed that a 20-fold change in the concentration of the acid produced less than 3% change in rate (see Experimental Section).

Discussion of Mechanism. Dianils of glutacondialdehyde such as **4** contain a complex array of functionalities including amine, enamine, imino carbonyl, and polyene entities. Both intra- and intermolecular reactions are possible and reactions with acids, bases, and nucleophiles are clearly likely. Even a brief *a priori* consideration of mechanistic possibilities for the reaction of eq 2 will reveal a bewildering array which might include for the significant ring-closure step internal nucleophilic addition, addition–elimination sequences, and electrocyclization. The single mechanistic study of this type of reaction extant[14] found that the ring closure of **5** to give pyridine and dimethylamine is not subject to general catalysis. The pH–rate profile has a maximum at 11.8, and the rate is first order in **5** and a complex function of the hydroxide ion concentration. The authors proposed a mechanism which involves an internal nucleophilic addition to a carbonyl. The hydrolysis of **5** to glutacondialdehyde is a competing process.

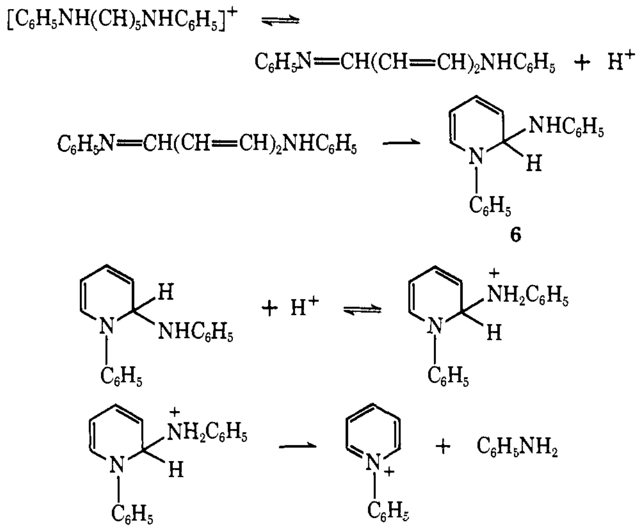


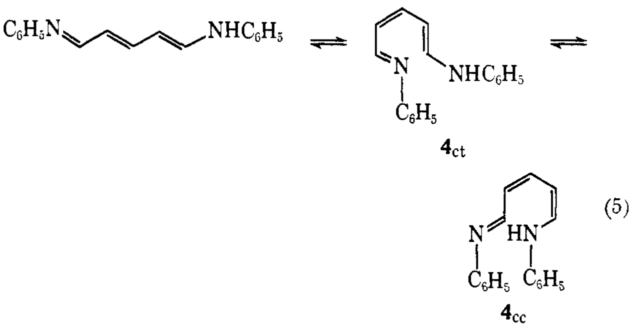
$$Me_2N{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}N{=}CH{-}CH{=}CH{-}CH{=}CHOH$$

5

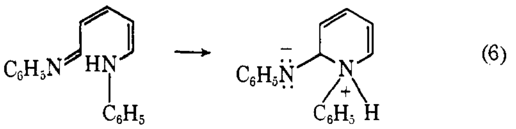
The data obtained in the present study clearly establish that **4** undergoes conversion to products in a reaction not subject to either acid or base catalysis. A general mechanism compatible with the experimental observations is shown in Scheme I. The rate-determining step must be the ring closure from **4** to **6**. It is assumed by analogy with 1,5-(N,N-dipyrrolidyl)pentamethine perchlorate[15] that **2** is predominantly in an all *trans* form. Presumably then **4** must also exist predominantly in a form with both carbon–carbon double bonds *trans*. Some *cis–trans* interconversion process is clearly required prior to the ring-closure step. It has been shown[16] that irradiation of salts such as **2** causes formation of at least a mono-*cis* isomer which reverts rapidly in a dark reaction to the all *trans* form. The barrier to rotation about a carbon–carbon bond in the symmetrical resonance hybrid was measured as 6 ± 2 kcal/mol.[17] Even if this barrier were not that small the equilibrium of eq 4 would permit any carbon–carbon bond to be converted to a single bond in **4** so a series of protonation and deprotonation steps would allow the equilibria of eq 5 to be established with such rapidity that these apparent *cis–trans* interconversions are not likely to become rate determining.

Scheme I





The ring closure step **4** → **6** can be visualized as an electrocyclic process $\mathbf{4}_{ct}$ → **6** or alternatively as the intramolecular addition of an amine to an imino carbonyl, $\mathbf{4}_{cc}$ → **6**. Though the difference between these is relatively subtle there exists one important operational distinction. Nucleophilic addition (eq 6) converts a neutral molecule to a dipolar species, while the electrocyclic process (eq 3, Ar = phenyl) interconverts two neutral molecules. Three experimental ob-



---

(14) S. L. Johnson and K. L. Rumon, *Tetrahedron Lett.*, 1721 (1966).

(15) W. Hoppe and F. Baumgartner, *Z. Kristallogr. Kristallgeometrie, Kristallphys. Kristallchem.*, **108**, 323 (1957).

(16) F. Dorn, J. Kotschy, and H. Kausen, *Ber. Bunsenges. Phys. Chem.*, **69**, 11 (1965).

(17) F. Baumgartner, E. Gunther, and G. Scheibe, *Z. Elektrochem.*, **60**, 570 (1956).

servations suggest that the ring closure occurs *via* an electrocyclic reaction and not nucleophilic addition. These are the response of rate to solvent changes and to added salts and the magnitude of the entropy of activation.

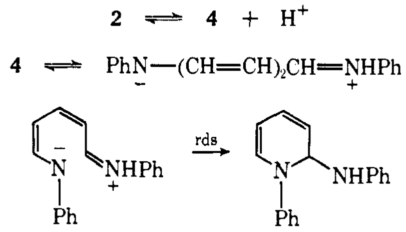
In general a reaction which converts a neutral molecule to a nonpolar activated complex will vary only slightly in rate with solvent change, while the rate of a reaction converting a neutral molecule to a dipolar transition state will be directly related to the ability of the solvent to stabilize ionic species.[18] The order and relative magnitude of solvent ionizing power can be estimated from the E_T (30) values;[19] methanol 55.5, acetone 42.2, and dioxane 36.0. Our rate constants show an inverse relationship with this measure of solvent ionizing power. The *ca.* fivefold change observed in the present case is of the expected magnitude for an electrocyclic reaction, but is precisely in the converse direction to that expected of the nucleophilic addition.

The acceleration produced by ionic salts of the reaction of a neutral molecule which proceeds *via* a dipolar transition state is well documented.[20] Frequently the magnitude of the acceleration is larger in poorly ionizing solvents,[21] and may be very large. For the reaction of **4** addition of lithium perchlorate does not alter the rate. Thus once again the results are in accord with predictions based on a nonpolar transition state.

Finally the entropy of activation supports the same conclusion. Ionization of a neutral molecule brings about a notable decrease in entropy which results from ordering of solvent molecules in the solvation shells of the ions.[22] A similar decrease in the entropy of activation is observed for reaction of neutral molecules *via* a dipolar transition state. Values of $\Delta S^{\ddagger}$ between -7 and -26 eu have been observed for ionization of carbon acids.[22] For a reaction more nearly comparable with the nucleophilic addition process under consideration here, values of $\Delta S^{\ddagger}$ between -10 and -15 eu were observed.[23] The above data pertain to aqueous solutions and it is known[24] that the values generally are larger in less polar solvents. Had the reaction of **4** been of the nucleophilic addition type a $\Delta S^{\ddagger}$ of -15 to -20 eu might well have been expected. The $\Delta S^{\ddagger} = 0$ eu does not support that mechanism. However it may be suggested that the $\Delta S^{\ddagger}$ is not in agreement with the value normally expected (-5 to -10 eu) of an electrocyclic ring closure process.[25] The slightly more positive value observed may be the result of a small decrease in polarity in passing from the ground state (C=N moiety) to the transition state (C—N—C group).

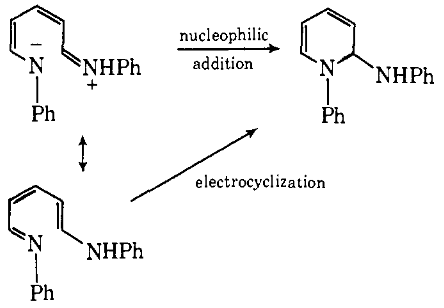
While the interpretation of the rate-determining ring closure as an electrocyclic process provides a better interpretation of our data, there are certain similarities between the present results and those found for the hydrolysis of imines[26,27] which deserve inspection. Thus, both benzylidene-1,1-dimethylethylamine[26] and **2** show a pH-independent reaction in the basic region, and both show a rate depression as the acidity of the medium is increased. Cordes and Jencks[26] have shown that the rate-determining step in the hydrolysis in the basic region is the attack of hydroxide ion on the protonated imine, and the rate decreases in more acidic media as water replaces hydroxide as the nucleophile. An analogous expression for the reaction of **2** can be written (Scheme II). This scheme will account for the pH-independent behavior in the basic region and for the reduction in rate with increasing acidity. The rate reduction would be attributed to protonation of the aminoid nitrogen to give **2** which reacts more slowly since it is effectively stabilized as a symmetrical resonance hybrid. However this scheme is really exactly the process we have termed an electrocyclic process. Whether it is to be called a nucleophilic addition or an electrocyclization depends purely and simply on the resonance contributing form one chooses to write for the reactant. Consequently the similarities between the imine hydrolysis and the present process support the interpretation made here.

Scheme II



$$\mathbf{2} \rightleftharpoons \mathbf{4} + H^+$$

$$\mathbf{4} \rightleftharpoons \underset{-}{PhN}\text{—}(CH{=}CH)_2CH{=}\underset{+}{N}HPh$$



In view of our conclusion that the rate-determining step for cyclization of **4** is an electrocyclic process, it is interesting to compare the rates for **4** (3.0×10^{-4} sec^{-1} at 40° in methanol) and for *cis*-β-ionone (2.3×10^{-3} sec^{-1} at 40° in carbon tetrachloride).[9] The difference in solvents probably plays only a minor role in accounting for the rate difference, since the rate for *cis*-β-ionone changes only 40% when pyridine is used as solvent.[28] Unfortunately a direct comparison of the rates for the two compounds is not possible. The rate constant given above for reaction of **4** includes an equilibrium constant for the $\mathbf{4}_{tt} \rightleftharpoons \mathbf{4}_{ct}$ process. Since this equilibrium constant must be small, the intrinsic rate constant for the $\mathbf{4}_{ct} \rightarrow \mathbf{6}$ reaction

---

[18] For a thorough discussion of these generalizations see K. B. Wiberg, "Physical Organic Chemistry," Wiley, New York, N. Y., 1964, pp 379–388.

[19] K. Dimroth, C. Reichart, T. Siepman, and F. Bohlmann, *Justus Liebigs Ann. Chem.*, **661**, 1 (1963).

[20] *Cf.* ref 14, pp 153–155.

[21] S. Winstein, S. Smith, and D. Darwish, *J. Amer. Chem. Soc.*, 81, 5511 (1959).

[22] *Cf.* ref 14, pp 132–142.

[23] P. Salomaa and K. Sallinen, *Acta Chem. Scand.*, **19**, 1054 (1965).

[24] R. G. Pearson, *J. Chem. Phys.*, **20**, 1478 (1952).

[25] E. N. Marvell, G. Caple, and B. Schatz, *Tetrahedron Lett.*, 385 (1965).

[26] See E. H. Cordes and W. P. Jencks, *J. Amer. Chem. Soc.*, **85**, 2843 (1963), and references to previous studies listed therein.

[27] K. Koehler, W. Sandstrom, and E. H. Cordes, *ibid.*, **86**, 2413 (1964).

[28] T. Chadwick, Oregon State University, unpublished information.

must be much larger than the value given, but the factor is not at present measurable. Also *cis*-β-ionone has a methyl group on the terminal carbon of the dienone system which has a *cis* relationship with the dienone chain. A methyl similarly placed in a triene reduces the electrocyclization rate by a factor of 100.[25] Thus the best that can be said at present is that the electrocyclization rates for dienylidenimines are nearer to those of the *cis*-dienones than to those of simple trienes (5.1×10^{-5} sec^{-1} in the vapor phase at 132°).[29]

Experimental Section

5-Anilino-N-phenyl-2,4-pentadienylideniminium Chloride (2). The salt was prepared according to the procedure of Zincke.[3,4] A solution containing 8.00 g (86 mmol) of aniline in 100 ml of 80% aqueous ethanol was added slowly to a solution of 12.09 g (39 mmol) of 2,4-dinitrophenylpyridinium chloride in 100 ml of the same solvent. After a few minutes crystals start to form, and these were removed at 10-min intervals until crystals of 2,4-dinitroaniline begin to appear. The combined crops of **2** were recrystallized from methanol, washed with anhydrous ether, and dried *in vacuo* to constant weight: mp 146–147°, λ_{max} (MeOH) 485 nm (ϵ 115,000) [lit. mp 142–143°,[4] λ_{max} (EtOH) 485 nm (ϵ 127,000)[11]].

5-Anilino-N-phenyl-2,4-pentadienylidenimine (4). This substance was prepared by the method of Zincke.[4] A dilute aqueous solution of sodium hydroxide was added to a solution of **2** in methanol until no further change in color was observed. The crystals of **4** were isolated by filtration and were dried *in vacuo*, mp 84–85°, λ_{max} (CH_3OH) 407 nm (ϵ 67,000) [lit.[12] mp 85–86°, λ_{max} (EtOH) 406 nm (ϵ 65,000)].

Product Isolation Experiments. A solution containing *ca.* 5 mmol of **2** in the appropriate solvent was mixed with *ca.* 30 mmol of triethylamine and the solution was allowed to stand at room temperature for 24 hr. After removal of the solvent by evaporation, repeated trituration of the residue with anhydrous ether left an insoluble salt. The salt was recrystallized from ethanol–ethyl acetate giving white needles, mp 104° [lit.[4] mp 105°]. Aniline was isolated from the ether solution and was identified by ir and uv spectra as well as by formation of benzanilide, mp 163° (lit.[30] mp 160°). Reaction in methanol gave 105% recovery of phenylpyridinium chloride and 94% of aniline. In 80% dioxane–20% methanol reaction gave 110% of the salt and 93% of aniline.

Equilibrium Constant for Dissociation of 2. Methanol was dried by the method of Lund and Bjerrum,[31] after which it was distilled from sulfanilic acid using a 3-ft Fenske column. Standard solutions of salicylic acid and sodium methoxide were prepared in methanol and the concentrations checked by titration. Buffer solutions containing known concentrations of salicylic acid and its sodium salt were prepared by mixing the acid and methoxide solutions, and these were thermostated at 40.0°. A weighed amount of **2** was dissolved rapidly in a known volume of methanol at 40°, and an aliquot of this was mixed immediately with a known volume of the buffer solution. The absorbance of the solution at 485 nm and 407 nm was measured at 3-min intervals using a Cary 15 with a cell compartment thermostated at 40°. The time of mixing the solutions was used as zero time and a plot of log *A* *vs.* time was extrapolated to zero time to obtain the concentrations of both **2** and **4** in the solution. Buffer concentrations were adjusted so that absorbance at 485 and 407 nm was approximately equal. The K_a at 40° in methanol was then calculated according to the procedure of Kolthoff and Guss.[32] An average value for K_a from five runs at differing buffer concentrations and ratios was 3.7×10^{-9} mol/l. At the concentrations involved K_a was independent of the ionic strength.

Kinetic Studies. Kinetic runs were made under two sets of conditions.

(a) In the presence of sufficient added base to convert all **2** to **4**, solutions of **4** in methanol, purified as described under equilibrium studies, and of the proper base in methanol were brought to the desired temperature and mixed. The reaction mixture was placed in a uv cell and the absorbance measured as a function of time using a Cary 15 spectrometer equipped with a thermostated cell holder. The temperature was maintained within ±0.1°.

(b) Kinetic studies in solutions containing insufficient base to convert all **2** to **4** were carried out in a flask immersed in a thermostated bath. The reaction solution was maintained under nitrogen and protected from direct light. Aliquots were removed at appropriate intervals and sufficient methanolic hydrogen chloride was added to ensure that all unreacted substrate was converted to **2**. Analysis was made immediately after mixing by determination of the absorbance at 485 nm using a Cary 15 spectrophotometer.

Results

The kinetic results in basic solution in methanol are listed in Table I–III. The behavior of a typical kinetic run in neutral methanol is shown in Table IV where the data are calculated as both half order and first order to show the drifts generally observed. A typical run in basic methanol is shown in Table V.

Table IV. Typical Kinetic Results for **2** in Methanol[a]

Time (sec × 10^3)	A_t	$k_1 \times 10^6$ (sec^{-1})	$k_{1/2} \times 10^8$ ($M^{-1/2}$ sec^{-1})
0.00	1.952		
14.4	1.807	5.36	2.92
50.4	1.494	5.32	2.72
75.6	1.285	5.52	2.75
104.4	1.078	5.68	2.80
147.6	0.830	5.80	2.59
172.8	0.707	5.88	2.53
201.6	0.586	5.97	2.46
237.6	0.460	6.08	2.38
410.4	0.125	6.68	2.00

[a] Temp = 40.0°; [**2**] = 5×10^{-4} *M*; A_∞ = 0.0.

Table V. Typical Kinetic Run for **2** in Basic Methanol[a]

Time (sec × 10^3)	A_t	$k_1 \times 10^5$ (sec^{-1})
0	1.523	
3.6	1.128	8.38
7.2	0.833	8.39
10.8	0.617	8.38
14.4	0.457	8.36
18.0	0.340	8.33
21.6	0.251	8.34
25.2	0.185	8.38
28.8	0.140	8.29

[a] Temp = 30.0°; [**2**] = $2.77 + 10^{-5}$ *M*; [Et_3N] = 6.56×10^{-4} *M*; A_∞ = 0.0.

Table VI. First-Order Rate Constants for **2** in Acetone Containing Varying Amounts of Triethylamine and Benzoic Acid[a]

Benzoic acid concn, [*M*] × 10^4	k_1 (sec^{-1})
0.00	5.79
0.31	6.19
0.61	6.32
0.92	6.40
3.07	6.37
6.14	6.35

[a] Temp = 30.0°; [**2**] = 3.1×10^{-5} *M*; and [Et_3N] = 6.5×10^{-4} *M*.

The activation parameters were determined from the following data: temperature in °C, $k_1 \times 10^5$ sec^{-1}; 20°, 2.59; 30°, 8.36; 40°, 30.7. In Table VI are listed the rates for a series of runs made in acetone solution containing varying amounts of triethylamine and benzoic acid.

---

(29) K. E. Lewis and H. Steiner, *J. Chem. Soc.*, 3080 (1964).

(30) R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "Systematic Identification of Organic Compounds," 5th ed, Wiley, New York, N. Y., 1964, p 326.

(31) H. Lund and J. Bjerrum, *Ber.*, **64**, 210 (1931).

(32) I. M. Kolthoff and L. S. Guss, *J. Amer. Chem. Soc.*, **60**, 2516 (1938).