

referred to that of 2-nitroaniline as primary reference for reasons discussed previously. The pK_a of this base has been measured in several mineral acids, and the reported "best" value³⁴ of -0.29 was used. The primary reference pK_a for the tertiary anine series, namely for *N,N*-dimethyl-4-nitroaniline, was obtained by linear extrapolation of $(\log I - \log [HClO_4])$ vs. $[HClO_4]$ to $[HClO_4] = 0$ by the method of least squares. Subsequent pK values in each series were obtained by the usual stepwise procedure using consecutive indicators. Each pair of indicators gave several values for the pK of the second indicator, which were averaged.

The functions of H_0''' and H_A were calculated from the equations

$$H_0''' = pK_{B'''+H^+} - \log I_{B'''}$$

$$H_A = pK_{AH^+} - \log I_A$$

where B''' refers to a tertiary amine and A to an amide. The average value of the acidity in a given solution was determined from the pK and $\log I$ values of all indicators which had been studied in that solution.

Activity Coefficient Measurements. Solubilities in aqueous perchloric acids were measured in a thermostatically controlled ($25 \pm 0.1^\circ$) glove box to provide a measure of protection against possible explosion of the concentrated acid when saturated with organic substances. However no explosions occurred even with the most highly saturated solutions in the most concentrated perchloric acids used (ca. 80%). Activity coefficients were obtained from solubilities as described by Boyd.¹⁸ Solubilities of the neutral

bases were obtained from the absorbance of the free base peak in the ultraviolet spectrum, and for the salts the pentacyanopropenide peak at 412 nm was used. It was necessary to dilute the latter solutions, before measuring the spectra, using a perchloric acid solution of sufficient strength to prevent reversible deprotonation of the anilinium ions. Hence it was impossible to measure solubilities of some of the salts directly in water. The activity coefficients of these salts in the least concentrated acids possible for measurements were estimated from the Debye-Hückel theory, using the equation³⁵

$$-\log f_i = \frac{Z_i^2 \alpha \sqrt{\mu}}{1 + \beta r_i \sqrt{\mu}}$$

For water at 25° , $\alpha = 0.509$ and $\beta = 0.329 \times 10^8$;³⁵ r_i was taken as 5×10^{-8} cm and was calculated assuming complete dissociation of both the salt and perchloric acid in the solution.

The activity coefficients for one indicator (2,4-dinitroaniline) were checked using a distribution method. Methylene chloride was found to be a suitable solvent, and the distribution ratio between this solvent and perchloric acid was measured as a function of indicator concentration at different concentrations. The concentrations of 2,4-dinitroaniline in each phase were determined spectrophotometrically, after equilibration.

Acknowledgment. The continued financial support of the National Research Council of Canada is gratefully acknowledged.

(35) A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," 2nd ed, Wiley, New York, N. Y., 1963, p 150.

(34) M. A. Paul and F. A. Long, *Chem. Rev.*, **57**, 1 (1957).

Spiroaromaticity in Spiro[2.3]hexadienyl Anions. Kinetic Acidities in Highly Basic Media

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Abstract: Experimental tests for special stabilization (spiroaromaticity) in a spiro[2.3]hexadienyl anion compared with a series of spiro[2.3]hex-4-en-6-yl anions using polarography and kinetic acidity measurements reveal no significant stabilization. The kinetic acidity data were obtained by hydroxide ion catalyzed tritium exchange in dimethyl sulfoxide-water mixtures. The second-order rate constants were determined to be as follows: for **12**, 4.6×10^{-5} ; for **13**, 24.14×10^{-6} ; for **14**, 2.03×10^{-5} ; for **15** (mixture of isomers), 5.70×10^{-5} . Brønsted coefficients (β) of ca. 0.80 for proton abstraction from the spiro[2.3]hexadiene **12** and spiro[2.3]hex-4-ene **13** suggest that the transition states from both compounds resemble the carbanionic products.

Aromatic character was used originally to describe the special stability accruing to certain combinations of electrons in monocyclic systems with a continuous periphery of p atomic orbitals.¹ Other molecular geometries can also in principle allow for continuous overlap of the kind associated with classical aromaticity, and thus particular combinations of electrons in the overlapping orbitals can lead to stabilization of the ground state. In the candidates for such "nonclassical" aromaticity, smooth overlap of the cyclic arrays of p orbitals can be perturbed by the insertion of saturated carbon atoms and by nonplanar geometries. Homoaromaticity,² bicycloaromaticity,³

and spiroaromaticity⁴ have been suggested as three particular examples; general rules for the π -electron combinations which provide stabilization (and destabilization) have been formulated for these and other topologies.⁵

The effects of homoaromaticity have been observed in several instances, such as the difference of $10^{4.5}$ in the rate of exchange of the allylic protons in bicyclo[3.2.1]octa-2,6-diene compared with similar exchange in bicyclo[3.2.1]oct-2-ene. The diene undergoes exchange more rapidly, presumably *via* the homoaromatic anion **1**.⁶ Similarly, 3-methylbicyclo[3.2.2]nona-2,6,8-triene undergoes proton exchange 750 times faster than

(1) For discussion of aromaticity in modern terms, see (a) D. Ginsburg, Ed., "Non-benzenoid Aromatic Compounds," Interscience, New York, N. Y., 1959; (b) "Aromaticity," *Chem. Soc. Spec. Publ.*, No. 21 (1967); (c) G. M. Badger, "Aromatic Character and Aromatic Compounds," Cambridge University Press, London, 1969.

(2) (a) S. Winstein, *J. Amer. Chem. Soc.*, **81**, 6524 (1959); (b) R. J. Piccolini and S. Winstein, *Tetrahedron Suppl.*, **2**, 423 (1963).

(3) M. J. Goldstein, *J. Amer. Chem. Soc.*, **89**, 6357 (1967).

(4) (a) R. Hoffmann, A. Imamura, and G. A. Zeiss, *ibid.*, **89**, 5215 (1967); *cf.* (b) H. E. Simmons and T. Fukunaga, *ibid.*, **89**, 5219 (1967); (c) R. Boschi, A. Dreiding and E. Heilbronner, *ibid.*, **92**, 123 (1970).

(5) M. J. Goldstein and R. Hoffmann, *J. Amer. Chem. Soc.*, **93**, 6193 (1971).

(6) (a) J. M. Brown and J. L. Occolowitz, *Chem. Commun.*, 376 (1965); (b) J. M. Nicholson, unpublished work cited by S. Winstein in ref 1b, p 34.

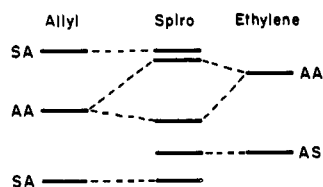
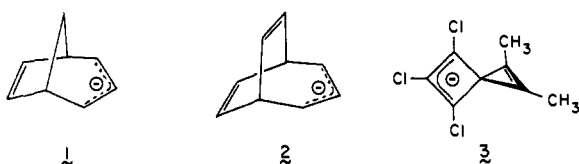


Figure 1. Interaction diagram for an allyl anion and an ethylene unit in spirogeometry.

3-methylbicyclo[3.2.2]nona-2,6-diene, which suggests bicycloaromatic stabilization for the anion **2**.⁷ No comparable tests for spiroaromaticity have been reported, perhaps owing to the lack of appropriate spirocycles where spiroaromaticity might be manifested. We recently uncovered a simple route⁸ to the first examples of the spiro[2.3]hexadiene and spiro[2.3]hex-4-ene ring systems and have undertaken to test for spiroaromaticity in the anion **3**.



Spiroaromaticity in Spiro[2.3]hexadien-6-yl Anions.⁹

Spiroconjugation can be viewed as a particular example of homoconjugation;¹⁰ two sets of p orbitals arranged in perpendicular rings joined by a common carbon atom of tetrahedral symmetry might interact in spite of the partially insulating effect of the saturated spiro atom. Detailed calculations of the extent and effects of such overlap have appeared,^{4b,11} and experiments have shown that spiroconjugation is important in the interpretation of electronic absorption spectra.^{4b,c,12}

When the spiro atom is the terminus for two continuous ribbons⁵ of p orbitals, ground state stabilization (spiroaromaticity) is predicted for certain combinations of π electrons.^{4a,5} In this work, we focus on the possibility of stabilization in the spirocycle composed of a cyclobutenyl fragment and a cyclopropene ring (e.g., **4**).



The spirocycle **4** can be viewed as an allyl system and an ethylene unit in perpendicular rings. From consideration of the symmetry of the molecular orbitals of the two components with respect to the plane of the three-membered ring and with respect to the plane of the four-membered ring (Figure 1), only the nonbonding (NBMO) allyl orbital and the antibonding ethylene orbital are seen to have the same symmetry properties, and thus it is only these that interact in the spiroge-

(7) (a) J. B. Grutzner and S. Winstein, *J. Amer. Chem. Soc.*, **90**, 6502 (1968); (b) S. W. Staley and D. W. Reichard, *ibid.*, **91**, 3998 (1969).

(8) Cf. (a) M. F. Semmelhack and R. J. DeFranco, *Tetrahedron Lett.*, 1061 (1971); (b) M. F. Semmelhack and R. J. DeFranco, *J. Amer. Chem. Soc.*, **94**, 2116 (1972).

(9) For a preliminary account of this work, see M. F. Semmelhack, R. J. DeFranco, Z. Margolin, and J. Stock, *J. Amer. Chem. Soc.*, **94**, 2115 (1972).

(10) S. Winstein, H. M. Walborsky, and K. Schreiber, *ibid.*, **72**, 5795 (1950).

(11) A. Tajiri and T. Nakajima, *Tetrahedron*, **27**, 6089 (1971).

(12) E. W. Garbisch, Jr., and R. F. Sprecher, *J. Amer. Chem. Soc.*, **88**, 3433, 3434 (1966).

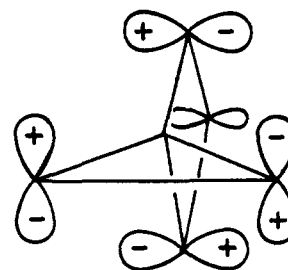
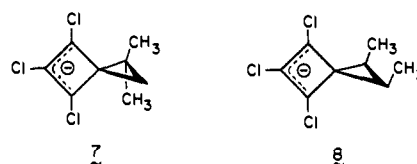


Figure 2. Spiro interaction of the NBMO of an allyl unit and the π^* orbital of an ethylene unit.

ometry. The interaction results in an array of five molecular orbitals (Figure 1) in which three are at bonding levels; *i.e.*, the NBMO has been stabilized. In the related spirocycle **5**, with a cyclopropane unit arranged in spiro geometry, no interaction of π orbitals across the spiro atom is possible, and the NBMO of the allyl system remains at the nonbonding level. A simple physical picture^{4a} of the spiroaromatic interaction is presented in Figure 2, showing the NBMO of the allyl system and the π^* orbital of the ethylene unit; the symmetry is such that smooth overlap is possible. The magnitude of the overlap, based on geometrical considerations,^{4a,b} is expected to be approximately 20% of that available to adjacent p orbitals in a benzene ring. Neither an experimental measure of per cent overlap nor a relationship to translate per cent overlap into kilocalories/mole of delocalization energy for spiroaromaticity is presently available. However, Heilbröner and coworkers have determined through photoelectron spectroscopy that for topologies which might show homoaromaticity, the interaction of π orbitals amounts to 30% of that for adjacent π bonds in benzene; in this case, a small delocalization energy of *ca.* 2.4 kcal/mol is calculated.¹³

The interaction of π orbitals in derivatives of **4** ought to be particularly evident in the stability of the allyl anion (e.g., **3**) where the bonding orbitals are filled. A comparison of the stability of **3** (related to the known spiro[2.3]hexadiene **6**) and the anions **7** and **8** (related to



the spiro[2.3]hex-4-enes **9–11**) would provide a direct test for spiroaromaticity. However, the determination of the thermodynamic stability is complicated by the kinetic instability of the anions, apparently due to α elimination of chloride anion and irreversible reaction (s) of the resulting carbene. We have directed our efforts toward the determination of relative rates of formation of the anions, with the assumption that the rates reflect the stability of the anions. Two approaches have been investigated: polarographic half-wave potentials and base-catalyzed proton exchange rates.

Polarographic Evidence. Electrolytic reduction of organic halides involves a two-electron transfer, result-

(13) P. Bischof, R. Gleiter, and E. Heilbröner, *Helv. Chem. Acta*, **53**, 1425 (1970).

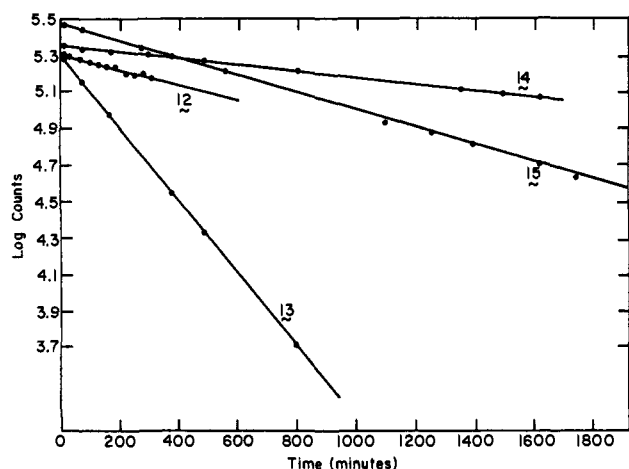
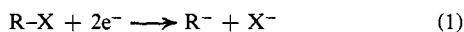


Figure 3. Illustrative plots for exchange kinetics on the tritium-labeled spirocycles 12-15.

ing in the carbanion (eq 1).¹⁴ The polarographic re-



duction half-wave potentials have been suggested to reflect the carbanionic nature of the transition state—less negative reduction potentials imply a more stable carbanionic product.¹⁵ Assuming significant spiroaromaticity in **3**, the half-wave potential for reduction of **6** should be a less negative value than the corresponding half-wave potentials of **9**, **10**, and **11** for which spiroaromatic stabilization of the transition state is not possible. In fact, the polarographic half-wave potentials (ref 8b) for **9**, **10**, and **11** are all *less negative* than that for **6** (Table I). Thus spiroaromaticity of **3** is not

Table I. Polarographic Half-Wave Potentials

	Spirocycle	$E_{1/2}$ (vs. sce), V
6		-1.68 ± 0.03
9		-1.58 ± 0.02
10		-1.63 ± 0.02
11		-1.61 ± 0.02

a significant factor in the rate of electroreduction of **6**; the polarographic results suggest that anion **3** is *less* easily formed than anions **7** and **8**.

(14) I. M. Kolthoff and J. J. Lingane, "Polarography," Vol. 2, 2nd ed, Interscience, New York, N. Y., 1952, p 647.

(15) (a) P. Zuman, *Collect. Czech. Chem. Commun.*, **25**, 3225 (1960); (b) A. Streitwieser and C. Perrin, *J. Amer. Chem. Soc.*, **86**, 4938 (1964); (c) F. L. Lambert, *J. Org. Chem.*, **31**, 4184 (1966).

It may be argued that the half-wave potentials do not reflect the stability of the anions, especially in light of reports that electroreduction of benzylic halides^{15b} and vinyl halides¹⁶ involves substantial radical character at the carbon atom undergoing reduction. However, the simple orbital interaction diagram (Figure 1) shows that a radical intermediate from **6**, with five π electrons, might also be specially stabilized owing to interaction between the rings. The effect on the half-wave potentials might be smaller for a radical-like transition state, but it would be in the same direction. In summary, polarographic results reveal no special stabilization for the reduction product from **6**.

Kinetic Acidity Evidence. Another approach to the anions **3**, **7**, and **8** involved proton abstraction from C-6 of the trichlorospirocycles **12-15**, which are obtained by electroreduction of the corresponding tetrachlorospirocycles (**6**, **9**, **10**).¹⁷ A direct test for spiroaromatic stabilization of the anion **3** is measurement of K_a , the acid dissociation equilibrium constant for **12**; however, this technique was not pursued owing to the kinetic instability of anion **3**. Many examples are available for carbon acids¹⁸ and other acidic species¹⁹ which indicate that for a series of molecules of similar structure, plots of $\log k$ (where k is the rate constant for proton abstraction) against $\text{p}K_a$ are linear, and Streitwieser provides evidence that $\log k$ for arylmethanes is related to the π -electron delocalization energy difference between the carbanion and the parent hydrocarbon.²⁰ In order to gain information about the stability of anions **3**, **7**, and **8**, the kinetic acidities of the corresponding spirocycles **12-15** were studied.

In practice, a simple and accurate procedure involves measurement of the rate of tritium loss from the carbon of interest in the presence of base.²¹ For these experiments, the spirocycles **12-15** with tracer levels of tritium at C-6 were prepared by electrolytic reduction of the spirocycles **6**, **9**, and **10** in the presence of tritium-enriched water. All were obtained with high specific activity, $>10^6$ cpm/mg (Packard Model 314DC Tri-Carb scintillation spectrometer). The epimers **15a** and **15b** have not been separated and were studied as a mixture. Attempts to introduce tritium by base-catalyzed exchange using a large excess of tritium-enriched water in dimethyl sulfoxide containing sodium hydroxide was unsatisfactory owing to low incorporation of tritium over short (10-24 hr) periods and thermal decomposition of the spirocycles over longer periods.

The rates of tritium loss were determined with the labeled spirocycles **12-15** at *ca.* 3×10^{-4} M in homogeneous aqueous solution containing sodium hydroxide at 0.2 M and 38 mol % dimethyl sulfoxide. Initial plots of \log cpm *vs.* time (Figure 3) yielded approximate parameters which were subjected to least-squares

(16) A. J. Fry and M. A. Mitnick, *J. Amer. Chem. Soc.*, **91**, 6207 (1969).

(17) M. F. Semmelhack, R. J. DeFranco, and J. Stock, *Tetrahedron Lett.*, 1371 (1972).

(18) (a) R. E. Dessy, Y. Okuzumi, and A. Chen, *J. Amer. Chem. Soc.*, **84**, 2899 (1962); (b) A. I. Shatenshtein, *Advan. Phys. Org. Chem.*, **1**, 161 (1963); (c) D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press, New York, N. Y., 1963, p 14 ff.

(19) Cf. J. E. Leffler and E. Grunwald, "Rates and Equilibria of Organic Reactions," Wiley, New York, N. Y., 1963, p 235.

(20) (a) A. Streitwieser, Jr., and W. C. Langworthy, *J. Amer. Chem. Soc.*, **85**, 1757 (1963); (b) A. Streitwieser, Jr., W. C. Langworthy, and J. I. Brauman, *ibid.*, **85**, 1761 (1963).

(21) E. Halevi and F. A. Long, *J. Amer. Chem. Soc.*, **83**, 2809 (1961).

analysis²² using the following equation

$$\ln [(a_0 - a_\infty)/(a_t - a_\infty)] = k_1 t$$

where a_t is counts per minute for an aliquot after time t . The quantity a_∞ was determined for spirocycle **13** as the cpm after more than 7 half-lives; it was approximately 2% of a_0 . For spirocycle **12**, the value of a_∞ could not be determined with confidence since thermal isomerization of **12** becomes important at long reaction times; therefore, a_∞ was estimated at ca. 2% of a_0 . No significant effect on the value of k_1 was found when a_∞ was varied over the range 1–5% of a_0 . The quantity a_0 and the pseudo-first-order rate constants, k_1 , are treated as adjustable parameters; values are calculated which best fit the experimental data. The pseudo-first-order rate constants were converted to the second-order rate constants, k_2 , which are displayed in Table II. The first-order dependence on hydroxide ion concentration has been verified for tritium exchange of spirocycle **13** at 25° and 63 mol % dimethyl sulfoxide in water. For sodium hydroxide concentrations of 0.10, 0.05, and 0.03 *M* (constant ionic strength), rates (k_2) of 0.028, 0.021, and 0.029 l/(mol sec), respectively, were obtained.

Spirocycles **12** and **15** have been recovered (80–85%) from the basic medium (25°) after periods of 4 and 30 hr, respectively, showing that the loss of tritium in the kinetic runs is due to simple proton exchange and not as the result of an undesired reaction such as base-catalyzed hydrolysis (Figure 3).

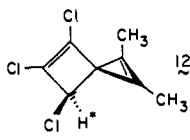
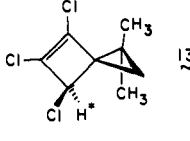
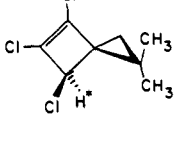
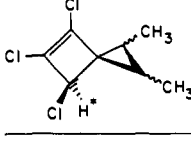
The spiro[2.3]hex-4-enes **13–15**, where spiroaromaticity is not possible, were studied to provide comparison with **12** and as probes of the steric effect of substitution on the cyclopropyl ring. The data show that the rate constants are relatively insensitive to steric factors. The largest difference, surprisingly between the epimers **13** and **14**, is a factor of only 12. This difference is counter to the simple intuitive expectation that the more crowded spirocycle, **14**, should lead more rapidly to the anion, a less crowded species; at present we have no explanation.

Activation parameters for tritium exchange in spirocycles **12–14** were determined from second-order rate constants at 25 and 13° using 63.0 mol % dimethyl sulfoxide and 0.1 *M* sodium hydroxide in water. The values of E_a and ΔS^\ddagger are presented in Table II.

The data make clear that there is no significant difference in kinetic acidity for the spiro[2.3]hexadiene **12** compared with **13**, **14**, and **15**. Among the possible explanations are the following: (1) the chlorine substituents interact strongly by an inductive effect to stabilize the highest filled orbital of anion **3**, thereby drastically reducing the interaction with the ethylene π^* orbital; (2) anion **3** is not planar (sp^3 hybridization at C-6) so that the spiro interaction is minimized; (3) the transition state leading to anion **3** closely resembles the starting material **12**, where no spiroaromaticity is possible; (4) the transition state leading to **3** differs from the transition states leading to the comparison anions (for example, in terms of more or less C–H bond breaking), in which case similar rates need not mean similar anion stability;^{18c} and (5) overlap of π -orbital

(22) A nonlinear least-squares program (MAXLIK) prepared by R. Williamson and modified by M. J. Goldstein was generously provided by Professor Goldstein. We are indebted to Professor Goldstein for his assistance with the calculations.

Table II. Rates of Base-Catalyzed Tritium Exchange

Spirocycle	Second-order rate constant ^c (no. of detn)	ΔS^\ddagger , eu	E_a , kcal/mol
 12	4.6 ± 0.2^a (6)	+11	+25
 13	24.14 ± 0.05 (2)	–6	+18
 14	2.03 ± 0.04 (2)	–9	+19
 15	5.70 ± 0.05^b (4) H* is enriched in tritium		

^a Data were collected for only 300 min (15% exchange) owing to the known [M. F. Semmelhack and R. J. DeFranco, *J. Amer. Chem. Soc.*, **94**, 2116 (1972)] thermal instability of **12**. ^b This entry represents an experiment using a mixture of the two *cis*-1,2-dimethyl isomers (75% **15a** and 25% **15b**). ^c The units are l/(mol sec) ($\times 10$).

ribbons on spiro[2.3]hexadienyl anions is not significant—there is no spiroaromaticity.

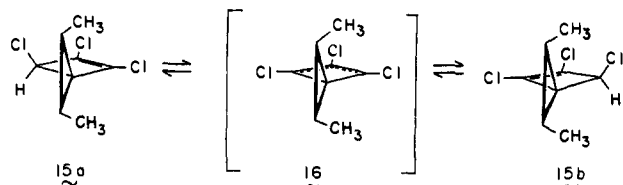
It is not now possible to provide definitive evidence concerning the effect of chlorine substituents in minimizing spiroaromatic stabilization in **3**. However, anion **3** is not a highly stabilized species; the pK_a of **12** is ~ 32 .²³ For comparison, various estimates for the pK_a of the methyl protons in propene are known, including a low value of $pK_a \sim 35$.²⁴ Propene is not a geometrically ideal prototype for anions such as **3**, but no better model seems to be available. Thus, as a crude estimate, the three chlorine substituents may stabilize the spirohexadienyl anions so as to lower the pK_a by as little as 3–4 pK_a units. It is likely that the chlorines are acting to reduce any spiroaromatic stabilization, but we feel that this could not be a large enough effect to explain the observation of no rate acceleration for **12** compared with **13–15**.

(23) This value is an approximate upper limit. Unpublished results of F. A. Long and Z. Margolin indicate that the rate constant for deprotonation of chloroform is greater than that for **12** by a factor of 10^8 , in the same medium. If protonation of the anions approaches diffusion control, the pK_a 's must also differ by a factor of 8. More likely, because of the allylic delocalization effects in the anion from **12**, the actual rate of protonation is not diffusion controlled and the ΔpK_a is somewhat less than 8. The same workers estimate the pK_a for chloroform at ~ 24 , so the pK_a of **12** must be somewhat less than 32.

(24) D. J. Cram estimates a pK_a of 35 for propene (ref 18c, p 19) while other estimates range as high as 40 (from E. M. Kosower, "Physical Organic Chemistry," Wiley, New York, N. Y., 1968, p 27; this reference was pointed out by one of the referees). Generally, pK_a determinations in dimethyl sulfoxide media give lower values (pK_a for diphenylmethane is reported as 28.6 in DMSO, 33.1 in cyclohexylamine, and 35 in benzene²⁵) than in the nonpolar solvents usually used to determine the acidity of very weak acids such as propene.

(25) A. Streitwieser and J. H. Hammons, *Progr. Phys. Org. Chem.*, **3**, 55 (1965).

The following experiment lends strong support to the supposition that the anions in these systems are indeed planar. A mixture of 40% **15a** and 60% **15b** was sub-



jected to a basic medium (0.2 M sodium hydroxide, 38 mol % dimethyl sulfoxide in water) identical with that used in the kinetic runs, for 30 hr at 25°. The spirocycles were recovered in a combined yield of 83% with the composition 75% **15a** and 25% **15b**; the isomers thus interconvert during exchange, which requires an intermediate with the symmetry of anion **16**.

The nature of the transition state for proton transfer in the spirocycles has been explored by measuring the effect on the rates of exchange of changing the basicity of the medium. For the reaction



the relation between the second-order rate constant k_2 and the acid dissociation constant K_a (for the conjugate acid of the base, B) was expressed by Brønsted and Pedersen²⁶ as

$$\log k_2 = \beta pK_a + \text{constant}$$

For proton transfer from N-H and O-H units²⁷ as well as from a variety of weak carbon acids²⁸ (e.g., chloro carbons and cyano carbons) the coefficient β has values between zero and unity, depending on the extent of proton transfer in the transition state.²⁹ A value of β equal to unity is compatible with a product-like transition state. Identical values for β in proton abstraction from different acids is compelling evidence for an identical degree of proton transfer in the different transition states.³⁰

(26) J. N. Brønsted and K. J. Pedersen, *Z. Phys. Chem.*, **108**, 185 (1924).

(27) M. Eigen, *Angew. Chem., Int. Ed. Engl.*, **3**, 1 (1964).

(28) (a) Z. Margolin and F. A. Long, *J. Amer. Chem. Soc.*, **94**, 5108 (1972); (b) E. A. Walters and F. A. Long, *ibid.*, **91**, 3733 (1969); (c) F. Hibbert, E. A. Walters, and F. A. Long, *ibid.*, **93**, 2829 (1971); (d) F. Hibbert and F. A. Long, *ibid.*, **93**, 2836 (1971).

(29) (a) R. P. Bell, "The Proton in Chemistry," Cornell University Press, Ithaca, N. Y., 1959, Chapter 10; (b) R. A. Marcus, *J. Phys. Chem.*, **72**, 891 (1968); (c) ref 19, p 238; (d) K. J. Pedersen, *J. Phys. Chem.*, **38**, 581 (1934).

(30) Recently Bordwell and coworkers³¹ have shown that for certain carbon acids, in particular the nitroalkanes, the coefficient β does not seem to be directly related to the degree of proton transfer, and they bring into question the general interpretation of the magnitude of β for carbon acids. Strong carbon acids such as the nitroalkanes and carbonyl compounds generally have highly delocalized conjugate bases with the negative charge concentrated on an oxygen atom. The activation energy for proton abstraction must reflect the process of detaching a proton from the carbon of interest and the process of changing the molecular geometry to allow delocalization. Our interpretation of the data of Bordwell³¹ is that for processes where a proton is removed from an sp³ carbon to give a highly delocalized, oxygen-stabilized anion, the geometry change is the dominant factor in the overall activation energy, so that changes in the nature of the base used to abstract the proton have little effect on the rate of proton removal; i.e., β is approximately constant.

In other examples of carbon acids, where the charge is localized on the carbon, but stabilized via inductive effects of cyano and halo substituents, accurate β values have been determined which correlate well with variations in the transition state;²⁸ in several of these cases, primary hydrogen isotope effects are known which give additional evidence for the nature of the transition state. The spirocycles are clearly much more like the weak acids of Long and coworkers,²⁸ having no opportunity for extensive delocalization including an oxygen, and thus

The value of β is usually determined as the slope of a plot of $\log k$ as a function of pK_a or as a function of ΔpK_a .²⁷ The conventional methods of obtaining β involve a study of the rates of proton transfer using a series of different bases in aqueous solution. For weak acids with $pK_a > 28$, such as the spirocycles **12**–**15**, the rates of exchange in water are much too slow to be measured conveniently. In recent reports,³² Bell and Cox pointed out that varying the dimethyl sulfoxide concentration provides a reliable method of changing the basicity for determination of the Brønsted coefficient β in highly basic media. In this case, the quantity ΔpK_a is derived as follows³²

$$\Delta pK_a = pK_{RH} - pK_{H_2O}$$

$$\Delta pK_a = pK_{RH}^0 - (H_- + \log [H_2O]/[OH^-])$$

where pK_{RH} refers to the acid dissociation constant of the carbon acid (spirocycle) in the medium of interest, pK_{H_2O} is the corresponding quantity for water (the conjugate acid of the base catalyst), pK_{RH}^0 refers to the carbon acid in pure water, and H_- is an acidity function for the dimethyl sulfoxide–water–hydroxide ion system.³³ The values of pK_{RH} for the spirocycles **12**–**15** are not known with certainty, but the slope β does not depend on the precise value of pK_{RH} and can be obtained from a plot of

$$\log k \text{ vs. } (H_- + \log [H_2O]/[OH^-])$$

The rates of loss of tritium from spiro[2.3]hexadiene **12** and spiro[2.3]hex-4-ene **13** were determined in duplicate at five different concentrations of dimethyl sulfoxide with 0.1 M sodium hydroxide at 25°. Derivation of the second-order rate constants (k_2) as before led to the values displayed in Table III.

Table III. Dependence of Rate Constant^a on Dimethyl Sulfoxide Concentration

Mol % DMSO	$10^6 k_2(\mathbf{12})$, l./.(mol sec)	$10^6 k_2(\mathbf{13})$, l./.(mol sec)	$(H_- + \log [H_2O]/[OH^-])^b$
46.0	12.2	101	20.45
50.4	26.6	299	20.93
53.6	52.3	491	21.27
59.0	130.0	1430	21.85
63.0	332.0	2800	22.23

^a Each rate constant is the result of two parallel runs following the first 15% of exchange or more; the uncertainty is $\pm 4\%$ or less.

^b Calculated from the data of Bowden and Cockerill.³⁵

Two H_- acidity functions,^{34,35} derived in dimethyl sulfoxide–water media, were used to obtain values for β . The H_- acidity function based on deprotonation of amine indicator acids³⁴ led to β values of 1.40 for both **12** and **13**. Using the H_- acidity function based on fluorene derivatives as indicator acids,³⁵ β values of 0.79 for **12** and 0.80 for **13** were obtained (Figure 4). The second set of values seems more reliable because

we feel the magnitude of β should be useful in estimating the extent of proton transfer in the transition state.

(31) F. G. Bordwell and W. J. Boyle, Jr., *J. Amer. Chem. Soc.*, **94**, 3907 (1972), and references therein.

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(1) the spirocycles are more similar to the fluorene indicator acids than to the amines and (2) the amine scale was derived with hydroxide ion at 0.011 *M*, whereas the fluorene scale was obtained with hydroxide ion at 0.047 *M*, much closer to the value of 0.1 *M* used in this work. The difference in β using the different H_- functions was unexpected, because Bell and Cox report much closer agreement in values of β from the same two H_- functions over the range 40–50 mol % dimethyl sulfoxide in water.^{32b} However, our experiments are over a wider and higher range of dimethyl sulfoxide concentrations (46–63 mol %) where the difference in the two H_- functions is apparently more significant.

The most important fact is that with either H_- acidity function, the values of β are nearly identical for spirocycles **12** and **13**, indicating nearly identical transition states for proton transfer. The relatively high values for β , near to unity, indicate that the transition states resemble the carbanion products, and the rate constants should reflect any special stabilization in the anions.³⁶ From these results, we conclude that spiroaromaticity is *not* a significant stabilizing factor in the ground state of spiro[2.3]hexadienyl anions.

Experimental Section

General. All solvents used were ACS Reagent Grade and were not further purified unless otherwise noted. Preparative glpc was performed on a Varian Aerograph Model A90-P3 gas chromatograph. The Health Model EUA-19-4 polarograph was used for determination of half-wave potentials; all preparative electrochemical reactions were done using a Wenking Model 68-FR-0.5 potentiostat, and a three-electrode cell as described before.^{8,17} Anhydrous magnesium sulfate was used to dry all organic extracts. The tritium-enriched water (International Chemical and Nuclear Corp.) was 100 mCi/ml in activity.

Radioactivity measurements were done with a Packard Tri-Carb Liquid Scintillation Counting System Model 314DC at *ca.* -4° , using 20-ml vials (low-potassium glass) holding 5 ml of the scintillation fluid (5.0 g of 2,5-diphenyloxazole and 0.3 g of 1,4-bis[2-(5-phenyloxazolyl)]benzene/l. of toluene) and 10 ml of toluene (which contained the sample). Background readings were *ca.* 35 cpm.

Preparation of the Tritium-Enriched Spirocycles 12–15. As described earlier, each of the tetrachlorospirocycles (2–3 mmol samples of **6**, **9**, and **10**) was subjected to controlled potential electrolysis in dimethylformamide containing lithium perchlorate, and 150 μ l (8.33 mmol, 100 mc/ml) of tritium-enriched water was added to the cathode solution. After the initial current of 200 mA (at a potential of -2.05 V) dropped to a constant reading of 5 mA (*ca.* 3 hr), the brown solution in the cathode compartment was added to 120 ml of water and washed four times with 40-ml portions of *n*-pentane. The colorless organic extract was washed with water, dried, and concentrated at aspirator pressure to afford a colorless oil. Short-path distillation gave material of >99% purity (glpc and nmr spectral analysis). Final purification of isomers **13** and **14** was achieved by preparative glpc as described earlier.^{8,17} Each sample showed more than 10^6 cpm/mg under the counting conditions specified above.

General Kinetic Procedures. A mixture of 10.0 ml of water and 20.0 ml of 1.000 *M* aqueous sodium hydroxide solution was diluted to 100 ml with dimethyl sulfoxide (73 ml) at 25° . The resulting solution (0.2 *M* sodium hydroxide and 38 mol % dimethyl sulfoxide) was allowed to equilibrate in a water bath at $25.07 \pm 0.02^\circ$ for 30 min. Then 5.0 μ l (*ca.* 7 mg, 30 μ mol) of the tritium-labeled spirocycle was injected *via* syringe; the mixture was shaken vigorously and returned to the constant-temperature bath. Aliquots (5.00 ml)

(36) However, the accuracy of the value for β (0.80) depends on the validity of two assumptions: (1) that the spirocycles **12** and **13** behave similarly to the fluorene indicator acids which were used to determine the H_- function, and (2) that the activation energy for proton transfer from the spirocycles is sensitive to changes in the extent of carbon–hydrogen bond breaking, unlike the nitroalkanes studied by Bordwell.³⁰ Greater confidence in the accuracy of the magnitude of β must await more systematic studies of weak carbon acids in order to establish the reliability of the H_- function.

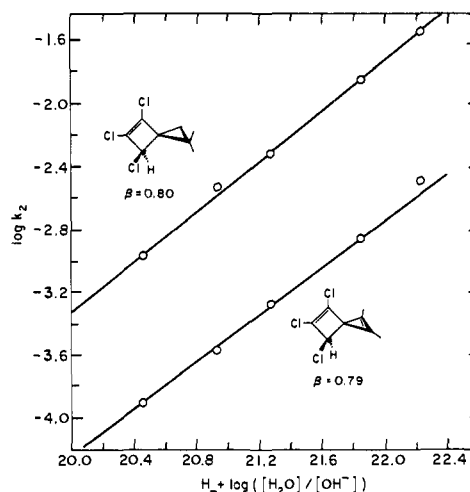


Figure 4. Determination of the Brønsted slope β for the spirocycles **12** and **13**.

of the solution were taken at various times and added to a separatory funnel containing a heterogeneous mixture of hydrochloric acid (0.10 *M*, 10 ml) and toluene (15.00 ml). The funnel was shaken for 30 sec to neutralize the base and extract the spirocycle into the toluene layer. A 10-ml aliquot of the upper layer was combined with 5 ml of the scintillation fluid, stored for at least 1 hr in the freezer (-5°) of the scintillation counter, and then counted. The counting period was chosen to accumulate 10,000 or more counts, generally 1 to 3 min, in order to reduce the statistical counting error. In this way, the rate of loss of tritium from each of the labeled spirocycles was determined and the second-order rate constants were calculated (see Table II).

Determination of the Dependence of the Rate Constant on Hydroxide Ion Concentration. According to the general procedure, three separate base solutions were prepared at 63 mol % dimethyl sulfoxide and 0.1 *M* ionic strength by varying the sodium hydroxide and sodium chloride concentrations. The results of tritium exchange from spiro[2.3]hex-4-ene (**13**) in each of the base solutions are presented above; each rate constant is the average of duplicate runs.

Base-Catalyzed Equilibration of the Spirocycles 15a and 15b. A mixture of **15a** (40%) and **15b** (60%)^{8,17} (103 mg, 0.48 mmol) was dissolved in 500 ml of an aqueous solution containing 38 mol % dimethyl sulfoxide and 0.20 *M* in sodium hydroxide. The homogeneous solution was allowed to stand at 23° for 30 hr, then it was poured into 350 ml of water, and the resulting mixture was washed with six 50-ml portions of *n*-pentane; the combined organic solution was washed with three 100-ml portions of water, dried, and concentrated at aspirator pressure. The clear liquid residue (86 mg, 83% recovery) was shown by ¹H nmr and glpc analysis to consist of **15a** (75%) and **15b** (25%) in greater than 95% purity.

Table IV

Spiro- cycle	Temp, $^\circ\text{C}$	Second- order rate constant, l. mol ⁻¹	E_{a} , kcal/mol	ΔS^\ddagger , eu
		sec ⁻¹ $\times 10^4$		
12	13.11	5.84	+25	+11
	25.07	33.2		
13	13.11	77.0	+18	-6
	25.07	280		
14	13.11	7.80	+19	-9
	25.07	29.7		

The Stability of Spiro[2.3]hexadiene 12 in Aqueous Base. Exactly as above for the equilibration of isomers **15a** and **15b**, a sample of spiro[2.3]hexadiene **12** (100 mg, 0.48 mmol) was dissolved in 500 ml of 0.2 *M* aqueous sodium hydroxide containing 38 mol % dimethyl sulfoxide and allowed to stir for 4 hr. Isolation as before gave 88 mg (88% recovery) of the starting spirocycle in greater than 98% purity by ¹H nmr analysis.

Determination of the Energy of Activation and Entropy of Activa-

tion for the Spirocycles **12**, **13**, and **14**. Using a mixture of 0.1 *M* aqueous sodium hydroxide containing 63 mol % dimethyl sulfoxide tritium exchange from spirocycles **12**, **13**, and **14** was studied at 25.07 and 13.11°. The results are displayed in Table IV. Each entry is the average of duplicate runs.

Dependence of the Rate Constant on Mol % Dimethyl Sulfoxide. According to the general procedure, tritium exchange from spiro[2.3]hexadiene **12** and spiro[2.3]hex-4-ene **13** was followed in aqueous solutions of 0.10 *M* sodium hydroxide containing 46.0, 50.4, 59.0, and 63.0 mol % dimethyl sulfoxide in separate determinations. The second-order rate constants were calculated and are presented in

Table II. Duplicate runs were carried out at each different concentration of dimethyl sulfoxide.

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Base-Catalyzed Hydrolysis of *N*-Acylpyrroles. A Measurable Acidity of a Steady-State Tetrahedral Intermediate

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Abstract: The basic hydrolysis of *N*-acetylpyrrole is second order in hydroxide ion at low base concentrations while first order in hydroxide ion at high base concentrations. There is an inverse solvent isotope effect and no general base catalysis. On the other hand, the hydrolysis of *N*-*p*-nitrobenzoylpyrrole is first-order in hydroxide ion and is subject to general base catalysis. The mechanisms of the two hydrolyses (involving a change in the rate-determining step in the acetyl system) and the source of their differences are analyzed in detail. We also describe a unique sigmoid pH-rate profile for *N*-salicylpyrrole. Its flex point lies 1.4 pH units above the pK_a of the substrate. Moreover, the rate is independent of the pH for all pH values above 11. These results are interpreted in terms of a kinetically important ionization of a steady-state intermediate, the first example of its kind. Both formation and collapse of the intermediate involve intramolecular participation.

The mechanisms for the base-catalyzed hydrolysis of a variety of acetamides, acetanilides, and acylimidazoles have been explored in detail.²⁻⁴ We report here an investigation of the basic hydrolysis of yet another type of amide, the *N*-acylpyrrole. Since *N*-acylpyrroles are interesting from an electronic standpoint,⁵ we were curious about their hydrolytic behavior which had previously never been studied. We also had a specific reason for carrying out this work: Pollack and Bender⁶ maintained that the basic hydrolysis of *p*-nitroacetanilide involves an anionic intermediate that collapses *via* a preequilibrium ionization rather than by a general base mechanism. They based their conclusion solely on the presence of an inverse solvent isotope effect, recognizing that this is not always a decisive piece of evidence. We found that *N*-acetylpyrrole displays kinetics very similar to those of *p*-nitroacetanilide (including an inverse solvent isotope effect). However, *N*-acylpyrroles react somewhat faster than anilides, thereby enabling us to operate at a pH range where general base catalysis can be observed. Thus, we could test the validity of the solvent isotope effect as a mechanistic criterion.

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Experimental Section

Synthesis. We used two methods to prepare the *N*-acylpyrroles. The first, direct acylation of pyrrole, was successful only with *N*-acetylpyrrole. The second method, reaction of an amide with 2,5-dimethoxytetrahydrofuran,⁷ provided the other substrates.

***N*-Acetylpyrrole.** Triethylamine (30 g, 0.30 mol) was added to a mixture of pyrrole (22 g, 0.33 mol) and acetic anhydride (36 g, 0.35 mol). The solution was boiled under reflux for 16 hr, cooled, diluted with 100 ml of ether, and washed with water and saturated aqueous sodium chloride. A tar-like precipitate formed during the sodium chloride wash. After filtering the ether layer through anhydrous sodium sulfate, we removed the ether with the aid of a rotary evaporator to secure a thick brown oil. The oil was distilled through a 6-in. Vigreux column to give 18 g (50%) of *N*-acetylpyrrole, bp 178° (lit.⁸ 179-181°). After purification of the product by two distillations through a spinning band column, we obtained material which was greater than 99% pure (glc). The ir spectrum (carbonyl at 1719 cm⁻¹) and nmr (AA'BB' sextet) were consistent with acetylation on the nitrogen.

Anal. Calcd for C₈H₇NO: C, 66.03; H, 6.47; N, 12.84. Found: C, 65.96; H, 6.58; N, 12.71.

***N*-Benzoylpyrrole.**⁷ 2,5-Dimethoxytetrahydrofuran (8.5 g, 0.064 mol) and benzamide (6.0 g, 0.050 mol) in 50 ml of glacial acetic acid were boiled under reflux for 48 hr. The mixture was cooled, poured onto ice, neutralized with sodium bicarbonate, and extracted with ether. Removal of the solvent from the ether extract left a thick brown oil which was purified first by steam distillation and then by vacuum distillation, bp 125° (1.8 mm). The colorless product (4.0 g, 47%) possessed a carbonyl stretching band at 1698 cm⁻¹ and a characteristic nmr sextet (triplets at δ 6.0 and 7.1). Glc analysis proved that the product was greater than 95% pure.

***N*-*p*-Nitrobenzoylpyrrole.** Equimolar amounts of *p*-nitrobenzamide (16.6 g) and 2,5-dimethoxytetrahydrofuran (13.2 g) were dissolved in 100 ml of glacial acetic acid, and the mixture was heated

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