

Rates of Protonation of Aromatic Radical Anions in Dimethyl Sulfoxide

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The electrochemical behavior of aromatic hydrocarbons has been the subject of a large number of investigations.¹ In aprotic solvents, two polarographic waves are observed, associated with initial reduction of the hydrocarbon to the corresponding radical anion and subsequent reduction of this to the dianion, at potentials E_1 and E_2 , respectively. When increasing amounts of a proton source, *e.g.*, phenol, are added, the first wave grows at the expense of the second, the total height remaining constant, until a point is reached where one merely observes a single two-electron wave. It is now generally accepted that this response to added proton donors is associated with the fact that protonation of the initially formed radical anion ($\text{ArH}\cdot^-$) forms a neutral radical ($\text{ArH}_2\cdot$) which is *easier* to reduce than the starting hydrocarbon, and hence immediately accepts a second electron.¹ These features are summarized in Scheme I, where E_3 is positive of E_1 . Although some exceptions have been noted, *e.g.*, where $\text{ArH}_2\cdot$ dimerizes at a rate competitive with its reduction, or where the dihydroaromatic ArH_3 is itself reducible, this so-called "ECE" behavior is exhibited by a surprisingly large number of aromatic hydrocarbons.¹ A model for studies of this type is the behavior of 9,10-diphenylanthracene (1e) in dimethylformamide (DMF), reported by Santhanam and Bard.² Figure 1 illustrates the observed behavior. The solid and dotted lines represent the polarographic behavior of 1e before and after addition of a 50-fold excess of phenol.

The solvents most often employed in such studies have been DMF, acetonitrile, and 96% dioxane. Dimethyl sulfoxide (DMSO) seems, however, to have been used only infrequently.³ In the course of experiments designed to explore the electrochemical behavior of *trans*-15,16-dimethyldihydropyrene⁴ and cyclooctatetraene⁵ in DMSO, we had occasion to examine the polarographic response of 1e to proton donors in DMSO. We were surprised to observe that addition of 30-fold excess of 2,4,5-trimethylphenol (TMP)⁶ to the solution resulted in a negligible increase (<2%) in the height of the first wave of 1, in contrast to the marked increase noted in DMF.² Anthracene (1a), on the other hand, behaved much as expected, although the first wave did not appear to grow as rapidly as has been

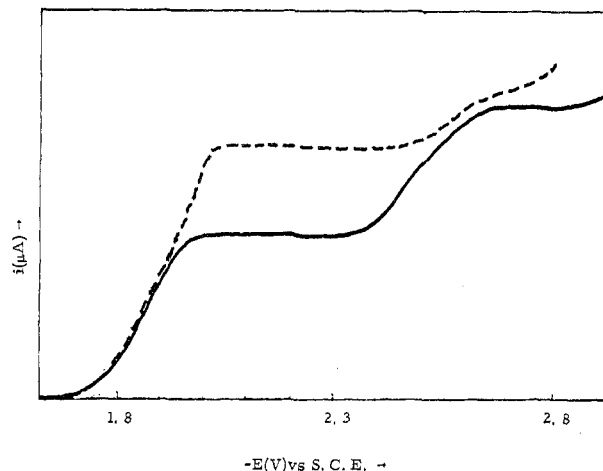
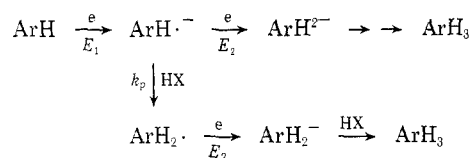
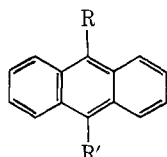


Figure 1. Solid line: polarographic behavior of 9,10-diphenylanthracene (1 mM) in dimethylformamide containing tetrabutylammonium iodide (0.1 M). Dashed line: same, with 50 mM phenol added. From K. S. V. Santhanam and A. J. Bard, *J. Amer. Chem. Soc.*, 88, 2669 (1966).

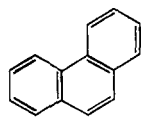
Scheme I



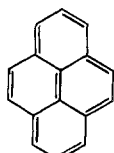
reported for anthracene in DMF.⁷ In order to understand this phenomenon better, the response of the polarographic behavior of a number of hydrocarbons to added proton donors in DMSO was then examined. Most hydrocarbons were examined in the presence of TMP; with others, phenol, resorcinol, or 9-phenylfluorene were also used as proton donors. 9-Phenylfluorene (9-PF) was selected because its pK_a in DMSO (16.4) is exactly the same as that of phenol,⁸ thus permitting comparison of the relative effectiveness of a carbon acid *vs.* oxygen acid in protonation of aromatic radical anions. Comparisons of the relative efficiency of various radical anions by the same proton donor, or of a given radical anion by different proton donors, were made using measured values of k_p , the bimolecular rate constant for protonation (Scheme I). Values of k_p were estimated using polarographic theory for the ECE process as developed by Nicholson and coworkers.⁹ Values of k_p could also be calculated by the method of Mark and Janata,¹⁰ but these values were generally two or more orders of magnitude higher than those computed by the Nicholson procedure. This is presumably because of certain approximations involved in the computational method, based upon reaction-layer theory, used by Mark.¹⁰ It is now recognized that numerical procedures, such as that used by Nicholson,⁹ are more valid than reaction-layer theory for such calculations¹¹ and indeed more recent work by Mark has been based upon the Nicholson procedure.⁸ Table I tabulates values of (a) i_k/i_d , the ratio of currents for the first polarographic curve in the presence and absence of added proton donors, respectively; (b) protonation rate constants, k_p , calculated using measured polarographic drop times, the concentration of added proton donor, and a working curve constructed from data computed by Nicholson and coworkers,⁹ and (c) for some hydrocarbons, electron densities at the carbon of highest electron density in the radical anion, as computed by simple Hückel MO theory. Some data for DMF taken from the literature are shown in Table II for comparison purposes. Because some measurements were made at the ends of the working curve, the data must be regarded as



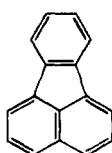
- 1a, R = R' = H
b, R = CH₃; R' = H
c, R = C₆H₅; R' = H
d, R = R' = CH₃
e, R = R' = C₆H₅



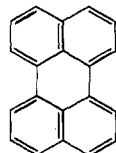
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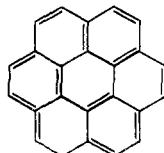
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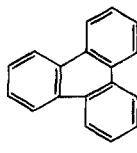
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Table I
Polarographic Response of Hydrocarbons to Added Proton Donors

Hydrocarbon ^a	Proton donor ^b	i_k/i_d^c	$k_p, M^{-1} \text{ sec}^{-1}$	Electron density ^d
COT ^d	TMP	1.7	~3000	0.125
2	TMP	1.5	~900	0.17
3	TMP	1.2	130	0.14
1a	TMP	1.1	75	0.19
4	TMP	1.0 ^e	≤1	0.12
5	TMP	1.0 ^e	≤1	0.11
6	TMP	1.3	400	0.06
7	TMP	1.4	630	0.06
1b	TMP	1.1	80	
1c	TMP	1.1	75	
1d	TMP	1.2	125	
1e	TMP	1.0 ^e	≤1	
1a	Resorcinol ^f	1.4	250	
1a	9-PF	1.03	22	
3	9-PF	1.03	23	

^a Proton donor concentrations 1 mM; hydrocarbon concentration 0.5–1 mM. ^b 1 mM; TMP = 2,4,5-trimethylphenol; 9-PF = 9-phenylfluorene. ^c Defined as in ref 9. ^d COT = cyclooctatetraene. ^e $i_k = (0.97 \pm 0.02)i_d$ for these compounds. This may be an electrocapillary effect of phenol. ^f 2.8 mM. ^g A. Streitwieser and J. Brauman, "Supplemental Tables of Molecular Orbital Calculations," Pergamon Press, Oxford, 1965.

Table II
Solvent and Proton Donor Effects upon Protonation Rates

Hydrocarbon	Proton donor	$-k_p, M^{-1} \text{ sec}^{-1}$	
		DMSO	DMF
1a	2,4,5-Trimethylphenol	75	
	Phenol		390 ^a
	Resorcinol	250	1300 ^b
	9-Phenylfluorene	22	
1e	2,4,5-Trimethylphenol	<1	
	Phenol		30 ^c
3	2,4,5-Trimethylphenol	130	
	9-Phenylfluorene	23	

^a Computed from data in ref 1c, p 137. ^b Reference 10. ^c Reference 2.

approximate, but the trends evident in the data are clear enough for qualitative interpretations to be made.

Several comments may be made upon the data in Table I. With the exception of coronene (6) and triphenylene (7), there is a rough correlation between the protonation rate and the electron density at the position of highest electron density (presumably the site of protonation) in the radical anion. The correlation is qualitatively reasonable, but in view of the simplified nature of the MO calculations employed, and the neglect of steric and other factors, one would probably not expect agreement any better than that observed. The qualitative correlation between protonation rates and electron densities revealed by the data is probably real and not fortuitous, however. A similar correlation has in fact been observed between reaction rates of aromatic radical cations and the extent of charge dispersal in the radical cation.¹² In that study it was noted that two types of radical cations tend to react relatively slowly toward nucleophiles: (a) those with highly dispersed charge and (b) those in which the reactive sites of a ring system with a substantial degree of charge localization happen to bear blocking groups. Thus, the anthracene (1a) radical cation is very reactive toward nucleophiles, since the positive charge is localized largely on atoms 9 and 10, while the perylene (5) radical cation is much less reactive because the charge is spread rather evenly over the whole system. The radical cation of 1e is

also relatively stable because of the presence of the two phenyl groups.¹² The same generalizations seem to be true for the radical anions listed in Table I. The low reactivity of 1e is apparently associated with an electronic effect (rather than steric) since 1a–d all react rather rapidly with added proton donors. It appears that the radical anions of COT, 6, and 7 are protonated at rates considerably higher than would have been anticipated from electron densities. This could be because the apparent correlation for the other compounds is not real, or because the two compounds may be deviating because of some other effect. In this connection, it may be noted that in all three substances the unpaired electron in the radical anion enters either of a pair of degenerate molecular orbitals. A number of such species, including in fact the radical anions of 6 and 7, have been found previously to exhibit a range of anomalous properties.¹³

Mark and coworkers have examined the polarographic behavior of 4 in DMF.¹⁴ They reported that the first wave does not increase in height upon addition of proton donors, but that the wave does shift toward more positive potentials. They concluded that the radical anion is protonated under these conditions, and that the resulting radical undergoes a rapid following chemical reaction rather than reduction. This cannot be true for 4 in DMSO. The half-wave potential, height, and log-plot slope of the first wave are all unchanged upon addition of TMP (the second wave does grow and move to more positive potentials), and furthermore, the reversible couple observed for 4 by cyclic voltammetry (100 mV/sec) at a platinum electrode is unchanged upon addition of TMP. In DMSO, therefore, the radical anion of 4 is not protonated on the voltammetric time scale.

Rates of protonation by the carbon acid 9-phenylfluorene (9-PF) can be seen to be slower than by the oxygen acids of similar pK_a (phenols). The data also demonstrate a difference between kinetic and thermodynamic acidities for several substances. For example, 2,4,5-trimethylphenol must have a higher pK_a than 9-PF in DMSO;¹⁵ yet it protonates the radical anions of 1a and 3 faster than does the latter. A similar contrast may be noted between data taken in DMF vs. that in DMSO. Most acids,¹⁶ including phenol,¹⁷ have smaller pK_a 's in DMSO than in DMF, yet proton transfers to radical anions can be seen (Table II) to be higher in DMF than in DMSO.

It was noted at the outset that while Scheme I accounts for the polarographic behavior of a large number of hydrocarbons, occasional exceptions are encountered. Two such cases were observed in this study. The first wave for phenanthrene (2) does increase in height with added TMP, but simultaneously a new wave appears between the original two. As has been pointed out previously, this behavior appears to be associated with dimerization of the radical $\text{ArH}_2\cdot$ (Scheme I) at a rate competitive with reduction, followed by reduction of the dimer.^{1a,b} The reduced dimer has in fact been obtained from a preparative-scale electrolytic reduction of phenanthrene in DMF.¹⁹ The behavior of 9,10-dimethylanthracene (1d) is harder to explain. All of the other anthracenes studied exhibited the usual increase in height of the first wave, at the expense of the second, with added TMP; even 1e exhibited this behavior in the presence of the stronger acid, benzoic acid, or of large excesses of TMP. In contrast, both waves of 1d increased with added proton donor. This may be because (unlike anthracene itself) the radical anion of 1d is protonated partly at positions other than 9 or 10 as a consequence of the electronic and steric effects of the two methyl groups. If this occurred, the resulting material, a 2,3-dihydroanthracene, would be expected to be reducible further.

Experimental Section

Polarographic and cyclic voltammetric measurements were carried out with the aid of a Princeton Applied Research Model 170 electrochemical instrument. Polarograms were measured in the conventional manner before and after addition of known amounts of proton donor.

Cyclooctatetraene was purified by vacuum distillation under nitrogen. Purity of the other hydrocarbons was assessed by thin layer chromatography. If more than one spot was observed, the hydrocarbon was purified by column chromatography, sublimation, and/or recrystallization. Dimethyl sulfoxide (Matheson Coleman and Bell) was used as received. Tetrabutylammonium perchlorate (Southwestern Analytical Labs), the supporting electrolyte, was dried in an Abderhalden drying pistol.

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Registry No.—1a, 120-12-7; 1b, 779-02-2; 1c, 602-55-1; 1d, 781-43-1; 1e, 1499-10-1; 2, 85-01-8; 3, 129-00-0; 4, 206-44-0; 5, 198-55-0; 6, 191-07-1; 7, 217-59-4; COT, 629-20-9.

References and Notes

- (a) M. E. Peover, *Electroanal. Chem.*, **2**, 1 (1967); (b) G. J. Hoijtink, *Advan. Electrochem. Electrochem. Eng.*, **7**, 221 (1970); (c) A. J. Fry, "Synthetic Organic Electrochemistry," Harper and Row, New York, N. Y., 1972, p 258 ff.
- K. S. V. Santhanam and A. J. Bard, *J. Amer. Chem. Soc.*, **88**, 2669 (1966).
- However, see J. R. Jezorek and H. B. Mark, Jr., *J. Phys. Chem.*, **74**, 1627 (1970).
- A. J. Fry, L. L. Chung, and V. Boekelheide, *Tetrahedron Lett.*, **445**, 1354 (1974).
- A. J. Fry, C. S. Hutchins, and L. L. Chung, submitted for publication.
- TMP was used because it is less hydroscopic and more easily purified (sublimation) than phenol.
- Reference 1c, p 137.
- (a) 9-Phenylfluorene: C. D. Ritchie and R. E. Uschold, *J. Amer. Chem. Soc.*, **90**, 2821 (1968). (b) Phenol: L. M. Kolthoff, M. K. Chamtoon, Jr., and S. Bhowmik, *ibid.*, **90**, 23 (1968).
- R. S. Nicholson, J. M. Wilson, and M. L. Olmstead, *Anal. Chem.*, **38**, 542 (1966).
- J. Janata and H. B. Mark, Jr., *J. Phys. Chem.*, **72**, 3616 (1968).
- S. W. Feldberg, *Electroanal. Chem.*, **3**, 199 (1969).
- (a) L. S. Marcoux, J. M. Fritsch, and R. N. Adams, *J. Amer. Chem. Soc.*, **89**, 5766 (1967); (b) R. N. Adams, *Accounts Chem. Res.*, **2**, 175 (1969).
- (a) R. D. Rataiczak and M. T. Jones, *J. Chem. Phys.*, **56**, 3898 (1972); (b) M. G. Townsend and S. I. Weissman, *ibid.*, **32**, 309 (1960); (c) H. M. McConnell and A. D. McLachlan, *ibid.*, **34**, 1 (1961); (d) R. E. Jesse, P. Biloen, R. Prins, J. D. W. v. Voorst, and G. J. Hoijtink, *Mol. Phys.*, **6**, 633 (1963).
- J. R. Jezorek, A. Lagu, T. M. Seigel, and H. B. Mark, Jr., *J. Org. Chem.*, **38**, 788 (1973).
- Phenol has the same pK_a as 9-phenylfluorene;^a with three methyl groups, TMP must be less acidic than phenol.
- R. L. Benoit and C. Buisson, *Electrochim. Acta*, **18**, 105 (1973).
- The pK_a of phenol in DMF has not been measured, but *p*-chloro- and *m*-chlorophenol have $pK_a = 16.8$ and 16.3, respectively, in DMF.¹⁸ The parent compound should therefore have $pK_a \gg 17$ in DMF; it is 16.4 in DMSO.^{8b}
- C. D. Ritchie and G. H. Megerle, *J. Amer. Chem. Soc.*, **89**, 1447 (1967).
- S. Wawzonek and D. Wearing, *J. Amer. Chem. Soc.*, **81**, 2067 (1959).

Preparation of Some Thio vulpinic Acids

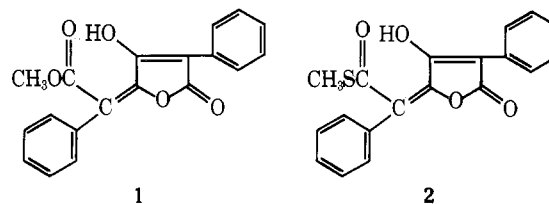
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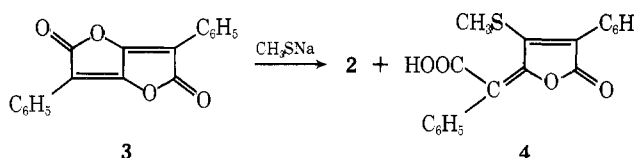
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Recent findings of anti-inflammatory activity in the vulpinic acid series¹ prompted us to undertake the investigation of some thio analogs of this interesting series of

lichen metabolites.² One thio analog of vulpinic acid (1) is the thiol ester 2. Since the dilactone 3 is converted to 1 by



reaction with sodium methoxide,² the reaction of 3 with the sodium salt of methyl mercaptan was studied. Two products were isolated from this reaction in about 50% yield each, both of which analyzed for the expected product.



The structure of 2 was established by comparison of its nmr and mass spectra with that of 1. Both 1 and 2 have very similar characteristic aromatic proton peaks at δ 7.4 (8 protons) and 8.2 (2 protons) and enolic protons at δ 13.8 and 13.65, respectively. The latter indicate chelate-type hydrogen bonding between the enol and the ester carbonyl, and provide strong evidence for the stereochemistry about the exocyclic double bond. The mass spectra of both 1 and 2 show molecular ion peaks, and also strong peaks at m/e 290 corresponding to the m/e for 3 formed by the primary elimination of the elements of methanol and methyl mercaptan, respectively.³ The nmr of 4 showed a one-proton peak at δ 10.90 characteristic of a carboxylic acid, and the mass spectrum, in addition to the molecular ion peak, showed a strong peak at m/e 294 which is consistent with the loss of CO_2 from the molecular ion. Only a weak peak at m/e 290 was present.

Another thio vulpinic acid is 5, in which the lactone is replaced by a thiolactone. Since, as shown above, sulfur anions can displace the ring oxygen of 3, we attempted to prepare 6, which could conceivably be converted to 5 via the monothiodilactone 7 by processes analogous to those used for the preparation of 1. However, although reaction of 3 with hydrogen sulfide in the presence of sodium methoxide gave a base-soluble product, on attempted recrystallization from methanol of the crude product obtained by acidification of the basic solution, only 3 was isolated. This suggested that 3 was opened to give the

