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Selectivity and Isotope Effects in Hydronation of a Naked Aryl Anion

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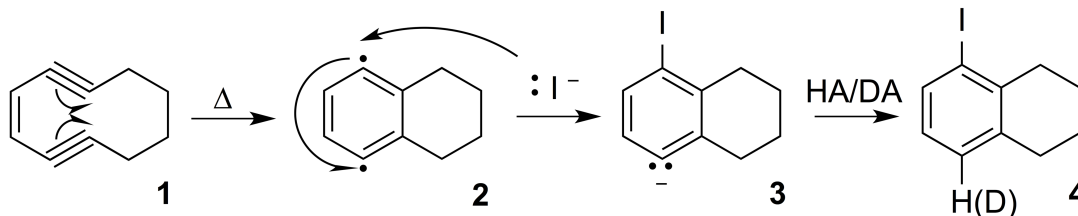
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Abstract An aryl anion is produced by rapid addition of iodide to the *p*-benzyne diradical formed by cycloaromatization of an enediyne. The aryl anion is then hydronated (protonated or deuterated) to form 1-iodotetrahydronaphthalene. Hydrons can be incorporated not only from water but also from such weak acids as DMSO and acetonitrile. The relative reactivity of each pair of hydron donors is evaluated from competition experiments. A low selectivity is observed and taken as evidence for a high basicity of the aryl anion. Moreover, the same relative reactivities are obtained with Bu₄NI as with LiI. Therefore the species undergoing hydronation is not an aryllithium but a naked aryl anion. These studies thus characterize the reactivity of a naked aryl anion in solution and contrast it with the reactivity of an aryllithium or an aryl Grignard.

Introduction

The chemistry of arynes has been studied extensively in recent years.¹ Nucleophilic addition is a newly discovered reaction of *p*-benzyne diradicals,² different from their usual atom abstraction.³ According to kinetic evidence, cyclodeca-1,5-diyne-3-ene (**1**) undergoes rate-limiting cycloaromatization to a *p*-benzyne (**2**), which rapidly adds iodide (or other nucleophile)⁴ to produce an aryl anion (**3**), which is then protonated by an acid HA to form 1-iodotetrahydronaphthalene (**4-h**) (Scheme 1). Alternatively, deuterium can be incorporated, even from such weak acids as dimethyl sulfoxide-*d*₆ (DMSO-*d*₆), to form **4-d**. We here

investigate more fully the hydronation of aryl anion **3** (where hydronation is attachment of a generic hydrogen cation, regardless of whether the hydrogen is protium or deuterium or tritium).⁵



Scheme 1. Mechanism for formation of iodoaromatic **4** via iodide addition to a *p*-benzyne diradical **2** derived from cyclodeca-1,5-diyne-3-ene (**1**), involving electron-pushing arrows for both two-electron and one-electron movements, followed by hydronation (protonation or deuteration) of **3**.

Deuterium incorporation represents a remarkable manifestation of a lack of selectivity in the reaction of **3**. The fact that DMSO-*d*₆ can compete with stronger acids demonstrates that the species generated by iodide addition to **2** is so strong a base that it is unselective toward hydronation. To provide more insight into the reactivity and selectivity of **3**, we have measured relative rates of its hydronation in binary mixtures of labeled and unlabeled DMSO, acetonitrile, RCOOH, and water, and we report relative kinetic acidities and H/D kinetic isotope effects (KIEs) on this hydronation step, evaluated by measuring the deuterium content of iodotetrahydronaphthalene **4**. That deuterium content is a permanent record of the quenching of **3**, and it can be analyzed by both ¹H NMR and mass spectrometry.

H/D KIEs of acetonitrile and DMSO can be evaluated from a direct competition experiment with a single solvent, but as a mixture of deuterated and undeuterated. The relative reactivity of two different acidic solvents can be evaluated from a direct competition experiment if one solvent is deuterated and the other is undeuterated. There are a total of six such pairs, chosen from water, acetonitrile, and DMSO. The relative reactivities of two

deuterated or two undeuterated solvents cannot be evaluated from the D content of product, because there is no way to ascertain which solvent is the source of D. However, those relative reactivities can be evaluated indirectly, by combining reactivities evaluated directly.

This is a particularly simple reaction, of some synthetic utility. Quenching of an aryl Grignard reagent in deuterated medium is a classical method for synthesis of deuterioaromatics,⁶ and with pedagogical value for illustrating the properties of Grignard reagents.⁷

The goal of this research is to compare the relative abilities of DMSO, CH₃CN, RCOOH, and H₂O to protonate aryl anion **3**, and to measure the associated KIEs. The number of suitable solvents is unfortunately quite limited, because most solvents quench the *p*-benzyne diradical by H-atom transfer faster than the diradical adds halide. We also investigate the ability of DMSO, CH₃CN, and H₂O to protonate a comparable aryllithium and aryl Grignard. We now report that anion **3** is remarkably unselective toward acids, and we interpret this as a characteristic of "naked" aryl anions.

Experimental Section

Materials. Cyclodeca-1,5-diyne-3-ene (**1**) was synthesized by a standard procedure.⁸ ¹H NMR (500 MHz, CD₃CN), δ 5.81 (2H, s, CH=CH), 2.34 (4H, m, CH₂), 1.86 (4H, m, CH₂CH₂). Deuterated solvents (CD₃CN and DMSO-*d*₆, 99.96% D) were purchased from Cambridge Isotope Labs or Aldrich. Authentic 1-iodotetrahydronaphthalene (**4**) was prepared from 5,6,7,8-tetrahydro-1-naphthylamine + *p*-TsOH + NaNO₂ + KI in CH₃CN. 1-Naphthylmagnesium bromide (**5**) was purchased from Aldrich. 1-Naphthyllithium (**6**) was freshly prepared from 1-bromonaphthalene + 2.2 equiv. *t*-butyllithium in pentane with 1% THF (*Caution*: Pyrophoric!) at 0 °C.⁹ Unlabeled solvents, iodide salts, and 1,3,5-

trichlorobenzene (internal standard) were purchased from Aldrich and used without further purification.

Sample Preparation. Stock solutions containing ~ 5 mM cyclodeca-1,5-diyne-3-ene (**1**) and 500 mM lithium or tetrabutylammonium iodide were prepared in binary mixtures of CH₃CN, CD₃CN, DMSO, and/or DMSO-*d*₆ in a flame-dried flask. Iodide (I⁻) was selected as the nucleophile because it affords higher yields and competes more effectively for *p*-benzyne **2** than does Br⁻ or Cl⁻.^{2,4} For some experiments a known amount of H₂O, D₂O, acetic acid (CH₃COOH/D), or methanol (CH₃OH/D) was added. An aliquot of the stock solution was transferred to a flame-dried NMR tube and sealed. An initial NMR spectrum was taken, and the tube was immersed in a 55±1 °C oil bath for 10 hours. According to measured rate constants,² this time is sufficient for > 97% completion, which was confirmed by NMR analysis.

Instrumentation. GC-mass spectra were obtained on a Thermo-Finnigan Trace GC/MS Plus with a Restek RTX-5MS GC column, operated under split mode with a split ratio of 50 and with electron-impact ionization. ¹H NMR spectra were obtained on a JEOL 500-MHz ECA spectrometer. Karl-Fischer titrations were performed with a Mettler-Toledo DL39 Karl-Fischer Titrator and C30 Compact Karl-Fischer Coulometer.

Determination of water content. Organic solvents were dried over molecular sieves. Residual H₂O in a protio solvent was assumed to be the same as in the corresponding deuterated solvent, inasmuch as the same drying protocol was used for both. This was confirmed by Karl-Fischer titration of each solvent, and the H₂O content was found to be ≤ 200 ppm, or 0.01 M. This is sufficiently low that it does not contribute significantly to protonation of the aryl anion.

However, water content in reaction mixtures exceeded that in dried solvent, because additional water was introduced with substrate. Attempts to dry the sample over molecular

sieves caused decomposition of the enediyne. However, dry solvent is not necessary, because water must be added to some samples in order to set up a competition. Therefore the concentration of residual H₂O in reaction mixtures was evaluated using three different methods: 1) by ¹H NMR integration relative to internal standard, leading to [H₂O] = 0.24 M in CD₃CN and 0.107 M in DMSO-*d*₆, 2) by Karl-Fischer titration of a DMSO–DMSO-*d*₆ reaction mixture, leading to [H₂O] = 0.098 M, and 3) by measuring how the D content of product depends on the concentration of added H₂O and using the Solver routine of Excel to find the value of residual [H₂O] that minimizes the relative standard deviation of $k_{\text{H}_2\text{O}}/k_{\text{CD}_3\text{CN}}$ or $k_{\text{H}_2\text{O}}/k_{\text{DMSO-}d_6}$, as presented in Tables 3 and 4, leading to [H₂O] = 0.238 M in CD₃CN and 0.083 M in DMSO-*d*₆. Deviations in H₂O content measured by any of these methods were no greater than ±0.03 M, which leads to a deviation in the measured relative kinetic acidities of no more than ±10 %.

Evaluation of relative reactivities. Equations S1 to S8 express direct evaluations of relative kinetic acidities derived from experimentally measured D content, %D, and from %H = 100 - %D. Note that all rate constants are phenomenological rate constants, without statistical corrections, on a per-molecule basis, not per-hydron.

For eq S1 and S2 [H₂O] was evaluated as the sum of the added water and the residual water. Eq S3 to S8 represent direct measurements of the relative kinetic acidity of protio and deuterio solvents, also derived from experimentally measured D content. The contribution of residual H₂O, as evaluated in Table 3 or 4, was subtracted as expressed in the equations.

Ratios $k_{\text{CH}_3\text{CN}}/k_{\text{DMSO}}$, $k_{\text{CD}_3\text{CN}}/k_{\text{DMSO}d_6}$, $k_{\text{H}_2\text{O}}/k_{\text{CH}_3\text{CN}}$, $k_{\text{H}_2\text{O}}/k_{\text{DMSO}}$, $k_{\text{D}_2\text{O}}/k_{\text{CD}_3\text{CN}}$, and $k_{\text{D}_2\text{O}}/k_{\text{DMSO}d_6}$ could not be measured directly, because these represent competition between two proton donors or two deuterium donors. Nor could the ratio $k_{\text{H}_2\text{O}}/k_{\text{D}_2\text{O}}$ be measured directly, because the reaction of **1** is not possible in a purely

aqueous medium. Instead these relative reactivities were calculated indirectly by combining already determined relative reactivities, according to eq S9 to S30.

Results

Source of H. Table 1 presents the deuterium content of product **4** from hydronation of aryl anion **3** in mixtures containing added acetic acid, acetic acid-*d*, or methanol-*d*₄, evaluated by both NMR and mass-spectrometry. The two methods agree, within experimental error. Clearly CH₃COOD does not compete with CH₃CN for hydronation of **3**. Increased [CH₃COOD] in DMSO increases %D, but not in proportion to concentration, and the small increase observed can be attributed to conversion of trace H₂O to D₂O. Likewise, incomplete deuteration in CD₃CN with added CH₃COOH is due to trace H₂O. Finally, increased [CH₃COOH] in DMSO-*d*₆ does not decrease %D beyond a small experimental error, and certainly not in proportion to the increase in [CH₃COOH]. Likewise, addition of CD₃OD does not affect the extent of deuteration. Therefore the dominant H-donor is neither RCOOH nor methanol, but residual H₂O.

Table 1. Deuterium content of product in the hydronation of aryl anion **3** in mixtures containing acetic acid or methanol-*d*₄.

Acid	[Acid], mM	Solvent	%D _{NMR}	%D _{MS}
CH ₃ COOD	50	CH ₃ CN	0	0
CH ₃ COOD	50	DMSO	9	8
CH ₃ COOD	125	DMSO	12	11
CH ₃ COOH	50	CD ₃ CN	90	86
CH ₃ COOH	50	DMSO- <i>d</i> ₆	63	60
CH ₃ COOH	125	DMSO- <i>d</i> ₆	60	60
CD ₃ OD	150	CH ₃ CN	0	0
CD ₃ OD	150	DMSO	0	0

Counterion dependence. Table 2 summarizes the deuterium content of product **4** from hydronation of aryl anion **3** in four different binary solvent mixtures, evaluated from both NMR spectra and mass-spectrometric analysis. Again the two methods agree, within experimental error. In CD₃CN the extent of D incorporation is more extensive than in DMSO-*d*₆. A key result is that the same D content is obtained with Bu₄N⁺I⁻ as with Li⁺I⁻.

Table 2. %D in **4** on hydronation of **3** in binary solvent mixtures.

Solvent Mixture	Li ⁺ I ⁻ ^a	Li ⁺ I ⁻ ^b	Bu ₄ N ⁺ I ⁻ ^a	Bu ₄ N ⁺ I ⁻ ^b
CD ₃ CN/CH ₃ CN (2:1)	41 %	41 %	45 %	40 %
DMSO- <i>d</i> ₆ /DMSO (2:1)	27 %	23 %	29 %	27 %
CD ₃ CN/DMSO (1:1)	69 %	70 %	72 %	67 %
DMSO- <i>d</i> ₆ /CH ₃ CN (6:1)	10 %	8 %	13 %	9 %

^aBy NMR. ^bBy mass-spec.

Relative kinetic acidities and KIEs. Relative kinetic acidities were measured by a competitive method based on % D in **4**, and taking into account the concentration of solvents: H₂O, D₂O, CH₃CN, CD₃CN, DMSO, and DMSO-*d*₆. Ordinarily LiI was used to produce **4**, but the results in Table 2 show that the same D content is observed with Bu₄NI. Tables 3 to 10 summarize the experimentally measured D content in product **4** from eight direct comparisons of one deuterated and one undeuterated solvent, along with the relative kinetic acidities derived therefrom, corrected as necessary for water content using eq S1-8. These were then combined using eq S9-30 to evaluate indirectly the relative kinetic acidities of two deuterated or two undeuterated solvents, where it is impossible to distinguish the source of H or D in product.

Table 3. Deuterium content in the product from the hydronation of aryl anion **3** in mixtures of 1.00 mL CD₃CN and volume $V_{\text{H}_2\text{O}}$ of added H₂O, measured by both ¹H NMR and mass spectrometry. Also included are relative kinetic acidities, calculated according to eq S1.

$V_{\text{H}_2\text{O}}$, μL	[H ₂ O], ^a M	[CD ₃ CN],M	%D _{NMR}	%D _{MS}	$k_{\text{H}_2\text{O}}/k_{\text{CD}_3\text{CN}}^{\text{c}}$
0	0.238 ^b	19.06	92	90	7.92
25	1.59	18.59	60	57	8.32
50	2.87	18.15	45	45	7.73
75	4.09	17.73	35	36	7.87
100	5.26	17.33	29	30	7.87

^aIncluding residual. ^bResidual, to minimize the relative standard deviation of $k_{\text{H}_2\text{O}}/k_{\text{CD}_3\text{CN}}$.

^cAverage = 7.94±0.2.

Table 4. % Deuterium content of product in the hydronation of aryl anion **3** in mixtures of 1.00 mL DMSO-*d*₆ and volume $V_{\text{H}_2\text{O}}$ of added H₂O, measured by both ¹H NMR and mass spectrometry. Also included are relative kinetic acidities, calculated according to eq S2.

$V_{\text{H}_2\text{O}}$, μL	[H ₂ O], ^a M	[DMSO <i>d</i> ₆],M	%D _{NMR}	%D _{MS}	$k_{\text{H}_2\text{O}}/k_{\text{DMSO}d_6}^{\text{c}}$
0	0.083 ^b	14.07	87	84	28.75
2	0.19	14.04	63	63	42.59
5	0.36	14.00	50	47	41.44
8	0.52	13.96	42	39	39.22
10	0.63	13.93	34	32	47.77

^aIncluding residual. ^bResidual, to minimize the relative standard deviation of $k_{\text{H}_2\text{O}}/k_{\text{DMSO}-d_6}$. ^cAverage = 42±2 (omitting inaccurate ratio at low %H).

Table 5. % Deuterium content of product and kinetic isotope effect (KIE) for acetonitrile in the hydronation of aryl anion **3** in binary mixtures of CD₃CN and CH₃CN, measured by both ¹H NMR and mass spectrometry. Also included are relative kinetic acidities, calculated according to eq S3.

$V_{\text{CD}_3\text{CN}}$,mL	$V_{\text{CH}_3\text{CN}}$,mL	[CD ₃ CN],M	[CH ₃ CN],M	%D _{NMR}	%D _{MS}	$k_{\text{CH}_3\text{CN}}/k_{\text{CD}_3\text{CN}}^{\text{b}}$
1.00	0.00	19.06	0.00	100	96	-

0.50	0.50	9.53	9.53	29	31	2.14
0.67	0.33	12.77	6.29	46	45	2.13
0.67	0.33 ^a	12.77	6.29	46	44	2.18
0.80	0.20	15.25	3.81	59	56	2.45

^aWith 5 μ L added water. ^bAverage= 2.22 \pm 0.15.

Table 6. % Deuterium content of product and relative kinetic acidities in the hydronation of aryl anion **3** in binary mixtures of CD₃CN and DMSO, measured by both ¹H NMR and mass spectrometry. Also included are relative kinetic acidities, calculated according to eq S4.

$V_{\text{CD}_3\text{CN},\text{mL}}$	$V_{\text{DMSO},\text{mL}}$	$[\text{CD}_3\text{CN}],\text{M}$	$[\text{DMSO}],\text{M}$	%D _{NMR}	%D _{MS}	$k_{\text{CD}_3\text{CN}}/k_{\text{DMSO}}^{\text{a}}$
0.50	0.50	9.53	7.03	69	67	2.19
0.33	0.67	6.29	9.43	55	53	2.20
0.20	0.80	3.81	11.26	37	38	2.07

^aAverage = 2.15 \pm 0.07.

Table 7. % Deuterium content of product and KIE for DMSO in the hydronation of aryl anion **3** in binary mixtures of DMSO-*d*₆ and DMSO, measured by both ¹H NMR and mass spectrometry. Also included are relative kinetic acidities, calculated according to eq S5.

$V_{\text{DMSO}d_6},\text{mL}$	$V_{\text{DMSO},\text{mL}}$	$[\text{DMSO}d_6],\text{M}$	$[\text{DMSO}],\text{M}$	%D _{NMR}	%D _{MS}	$k_{\text{DMSO}}/k_{\text{DMSO}d_6}^{\text{a}}$
1.00	0.00	14.07	0.00	79	76	-
0.95	0.05	13.36	0.70	70	68	2.71
0.90	0.10	12.66	1.41	62	60	2.84
0.85	0.15	11.96	2.11	57	56	2.42
0.80	0.20	11.25	2.81	53	49	2.95
0.75	0.25	10.55	3.52	39	41	3.33

^aAverage = 2.7 \pm 0.4.

Table 8. % Deuterium content of product and relative kinetic acidities in the hydronation of aryl anion **3** in binary mixtures of CH₃CN and DMSO-*d*₆, measured by both ¹H NMR and mass spectrometry. Also included are relative kinetic acidities, calculated according to eq S6.

$V_{\text{CH}_3\text{CN},\text{mL}}$	$V_{\text{DMSO}d_6,\text{mL}}$	$[\text{CH}_3\text{CN}],\text{M}$	$[\text{DMSO}d_6],\text{M}$	%D _{NMR}	%D _{MS}	$k_{\text{CH}_3\text{CN}}/k_{\text{DMSO}d_6}$ ^a
0.10	0.90	1.91	12.66	32	29	12.97
0.08	0.92	1.52	12.94	45	41	8.63
0.05	0.95	0.95	13.37	50	49	10.31
0.03	0.97	0.57	13.65	61	57	10.15
0.01	1.00	0.19	13.93	71	67	14.16

^aAverage = 11.2±2.3.

Table 9. % Deuterium content of product and relative kinetic acidities in the hydronation of aryl anion **3** in binary mixtures of CH₃CN and D₂O, measured by both ¹H NMR and mass spectrometry. Also included are relative kinetic acidities, calculated according to eq S7.

$V_{\text{D}_2\text{O},\text{mL}}$	$V_{\text{CH}_3\text{CN},\text{mL}}$	$[\text{D}_2\text{O}],\text{M}$	$[\text{CH}_3\text{CN}],\text{M}$	%D _{NMR}	%D _{MS}	$k_{\text{D}_2\text{O}}/k_{\text{CH}_3\text{CN}}$ ^a
200	0.80	11.05	15.25	71	67	3.24
150	0.85	8.29	16.20	62	57	3.02
100	0.90	5.53	17.15	53	49	3.39
75	0.93	4.15	17.63	40	41	3.03

^aAverage = 3.2±0.2.

Table 10. % Deuterium content of product and relative kinetic acidities in the hydronation of aryl anion **3** in binary mixtures of 1.00 mL DMSO and D₂O, measured by both ¹H NMR and mass spectrometry. Also included are relative kinetic acidities, calculated according to eq S8.

$V_{\text{D}_2\text{O},\text{mL}}$	$[\text{D}_2\text{O}],\text{M}$	$[\text{DMSO}],\text{M}$	%D _{NMR}	%D _{MS}	$k_{\text{D}_2\text{O}}/k_{\text{DMSO}}$ ^a
10	0.55	13.93	29	25	10.51
20	1.08	13.79	51	49	14.22
30	1.61	13.66	57	57	12.58

50	2.63	13.40	64	67	10.84
75	3.86	13.08	72	74	10.31

^aAverage = 11.7±1.7.

Summary. Table 11 presents a compilation of all possible relative kinetic acidities and KIEs. There are a total of 15 different ratios. Each ratio was evaluated twice, by two different equations, which correspond to two different sets of reactions. The direct comparisons were obtained from a series of binary mixtures. The indirect comparisons were obtained by combining ratios from two or three series of binary mixtures. Values from the two different methods are the same, within a small but not negligible experimental error, regardless of whether they were measured directly or indirectly, or even indirectly by two different equations.

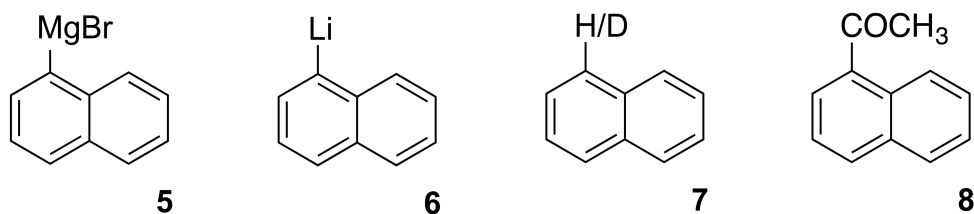
Table 11. Relative kinetic acidities $k_{\text{Solvent}}/k_{\text{Solvent}}$ in the hydration of aryl anion **3**. Values determined directly from pairwise comparison, according to eq S1-8, are indicated in boldface.

Solvent	CH ₃ CN	DMSO	D ₂ O	CD ₃ CN	DMSO- <i>d</i> ₆
H₂O	3.57±0.26 ^l	15.3±1.4 ^k	1.12±0.10 ^u	7.9±0.2	42±2
	3.7±0.8 ^j	17.1±0.8 ^l	1.32±0.27 ^v	8.3±1.8 ^a	47±7 ^b
CH₃CN	≡1	4.8±0.4 ^q		2.22±0.15	11.2±2.3
		4.3±0.5 ^r		2.13±0.45 ^c	11.8±1.1 ^f
DMSO		≡1			2.7±0.4
					2.5±0.2 ^e
D₂O	3.2±0.2	11.7±1.7		7.1±0.6 ^m	32±6 ^o
	2.4±0.4 ^g	13±3 ^h	≡1	5.4±0.8 ⁿ	36±7 ^p
CD₃CN		2.15±0.07			5.3±0.3 ^s
		1.93±0.30 ^d		≡1	5.9±0.9 ^t

^aeq S9. ^beq S10. ^ceq S11. ^deq S12. ^eeq S13. ^feq S14. ^geq S15. ^heq S16. ⁱeq S17. ^jeq S18. ^keq S19. ^leq S20. ^meq S21. ⁿeq S22. ^oeq S23. ^peq S24. ^qeq S25. ^req S26. ^seq S27. ^teq S28. ^ueq S29. ^veq S30.

For purposes of discussion and comparison a weighted average of each pair of values in Table 11 will be used. For example, H₂O reacts 7.9 times as fast as CD₃CN and 42 times as fast as DMSO-*d*₆, and H₂O reacts 3.6 times as fast as CH₃CN and 16 times as fast as DMSO. Also CH₃CN reacts 4.6 times as fast as DMSO. These last three values could not be measured directly because each compares two protioacids. The greater kinetic acidity of acetonitrile over DMSO is consistent with the results in Table 2, which show more D incorporation in CD₃CN than in DMSO-*d*₆. The three ratios $k_{\text{H}_2\text{O}}/k_{\text{D}_2\text{O}}$, $k_{\text{CH}_3\text{CN}}/k_{\text{CD}_3\text{CN}}$, and $k_{\text{DMSO}}/k_{\text{DMSO-}d_6}$ represent the KIEs for the three solvents. The values are 1.2, 2.2, and 2.5, respectively.

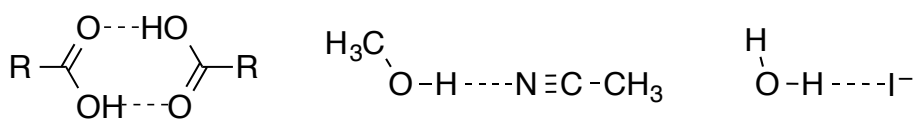
Reaction of two organometallics. Neutralizations of 1-naphthylmagnesium bromide (**5**) and 1-naphthyllithium (**6**) show that these are quite different from aryl anion **3**. Tables S1-2 present the experimentally measured D content in **7** from hydronation of **5** or **6** in binary mixtures of water and acetonitrile or DMSO. There is no variation with solvent ratio, so the incomplete but constant deuterium incorporation with variable amounts of D₂O must be due to contamination of commercial **5** and of **6** with naphthalene-*h*. (We considered attempting to prepare pure **5**, but concluded that the impurity in no way confounds the product analysis. This evidence for the presence of impurity may be informative to readers.) Therefore water (H₂O or D₂O) is the only H/D-donor, and neither acetonitrile nor DMSO is capable. This is a selectivity not manifested by the aryl anion **3**.



A complication is that aryllithium **6** also undergoes addition to acetonitrile, to afford, after hydrolytic workup, a small amount of 1-acetylnaphthalene (**8**), identified by GC-MS. No such product was detected from **3** because the addition requires metal coordination at C≡N.¹⁰ In aqueous CD₃CN, D₂O from base-catalyzed exchange of **8-d**₃ is presumed to be the source of the trace *7-d*.

Discussion

Source of H. According to Table 1, neither acetic acid nor methanol is effective at hydronating **3**. This result forces us to reject the earlier assumption that it is a carboxylic acid that competes with DMSO for quenching the anion.² The ineffectiveness of such a strong base to deprotonate acetic acid or methanol may be surprising, but that is the conclusion required by the data. We rationalize this relative unreactivity to hydrogen bonding of a carboxylic acid or methanol to itself, to solvent, or to I⁻, as suggested in Scheme 2. In contrast, a hydrogen-bonded water has a second hydrogen available, as also suggested in Scheme 2, and the first hydrogen bond may make that hydrogen less electron-poor and thus less strongly hydrogen-bonded than the first. Thus the only acids effective at hydronating **3** are water, acetonitrile, and DMSO, not acetic acid or methanol.



Scheme 2. Reduction of the kinetic acidity of a carboxylic acid or of methanol by hydrogen bonding, whereas hydrogen bonding of water can leave one H available.

Selectivity. The data in Table 11 show that water, acetonitrile, and DMSO all compete for **3**, which is rather unselective among these hydrogen donors. Figure 1 shows a Brønsted plot of the relative reactivities of water, acetonitrile, and DMSO vs the pK_a of those acids, corrected for statistics.¹¹ It should be noted that the pK_a of 31.3 for CH_3CN and of 35.1 for DMSO are for DMSO as solvent,¹² whereas the pK_a of 18.38 for H_2O is for 20% H_2O in DMSO,¹³ which is the closest available model for the oligomeric water of our kinetic studies. The slope is therefore questionable, but it corresponds to an exceptionally low Brønsted α of only 0.04 ± 0.01 , suggesting an early transition state. Although water is the strongest acid, the organic solvent can dominate when it is in excess over water.

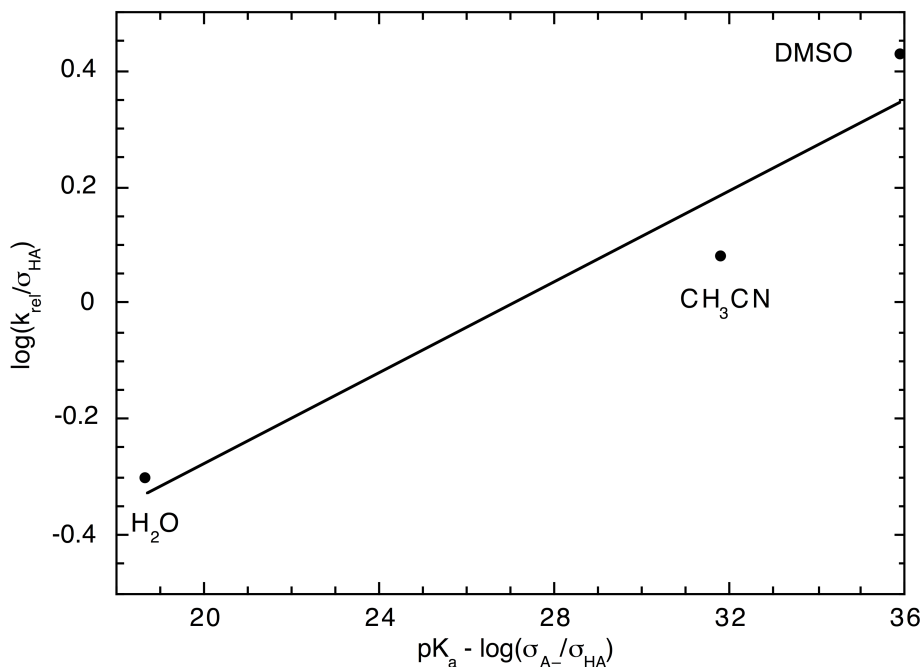


Figure 1. Statistically corrected Brønsted plot of relative kinetic acidity vs. pK_a .

This small slope provides a graphic contrast between the kinetic and thermodynamic acidities of these acids. It is considerably smaller than the slopes of 0.25, 0.30, and 0.36 for the substituent effects on the basicities of *o*, *m*, and *p* substituted aryllithiums, compared to the gas-phase basicities of the corresponding aryl anions,¹⁴ or the 0.7 for the correlation between calculated gas-phase basicities of alkyl lithiums and alkyl anions.¹⁵ The H/D KIEs are all small, 1.1 for water, 2.2 for acetonitrile, and 2.5 for DMSO. The KIEs for the organic solvents are substantially lower than the 6-7 expected for loss of the zero-point energy of a C-H bond.¹⁶ An even lower KIE, near unity, is reasonable for water, which can deliver its hydron merely upon approach by the base. A low H/D KIE was previously seen for neutralization of RLi and RMgX by methanol.¹⁷ Such studies were complicated by the inability to disperse the reactant into the solution before it reacts. The remarkable feature of this reaction is that **3** is generated "suddenly", in homogenous solution, so that its intrinsic reactivity can be recognized.

Lifetime of intermediates. The suddenness of the generation of aryl anion **3** is a consequence of the short lifetime of *p*-benzyne **2**. That is too reactive for its lifetime to be measured experimentally. One estimate of its lifetime can be based on the calculated barrier of ~ 5 kcal/mol to chloride addition to a *p*-benzyne, arising from the need to desolvate Cl^- .⁴ Another estimate can be based on the calculated barrier of 1.4 kcal/mol for hydrogen transfer from 1,4-cyclohexadiene to *p*-benzyne.¹⁸ Then because Γ^- is 24 times as reactive as Br^- and Br^- is 20 times as reactive as Cl^- ,^{2,4} while H transfer from 1,4-cyclohexadiene is 2.5 times as fast as Br^- addition,² the activation barrier for Γ^- addition must be nearly zero, corresponding to a lifetime of the *p*-benzyne diradical of $< 10^{-9}$ sec.

The lifetime of the aryl anion is also very short, by comparison with the rate constant of 10^{10} to 10^{11} s^{-1} for protonation of cyanocarbanions by H_2O , which is limited by the rate of

solvent reorganization.¹⁹ This explains why there is insufficient time for Li⁺ to combine at carbon.

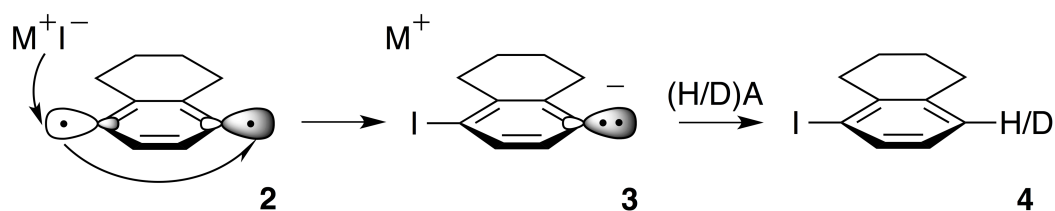
Amplification of basicity. The lack of selectivity among water, acetonitrile, and DMSO demonstrates that **3** is an exceedingly strong base. Indeed, the p*K*_a of benzene is +43,²⁰ so that its conjugate base, an aryl anion, is expected to be sufficiently basic to deprotonate any of these acids. In contrast, the I⁻ reactant is a very weak base, whose conjugate acid HI has a p*K*_a ~ 0 (p*K*_a of HCl and HBr in DMSO are 1.8 and 0.9, respectively).²⁰ Therefore the reaction of weak base I⁻ with the *p*-benzyne produces the strongly basic aryl anion and thereby amplifies basicity by > 40 powers of 10.

Comparison with organometallics. According to Tables S1-2, only water is capable of hydronating 1-naphthylmagnesium bromide (**5**) or 1-naphthyllithium (**6**), in contrast to aryl anion **3**, which reacts also with DMSO and acetonitrile. Although the D content of product **4** might suggest that DMSO-*d*₆ and CD₃CN had reacted with **5** and **6**, there is no variation with solvent ratio. Therefore the presence of **4-d** is due to contamination of commercial **5** or **6** with naphthalene-*h*, and water (H₂O or D₂O) is the only H/D-donor, while neither acetonitrile nor DMSO is effective. This is a selectivity not manifested by the aryl anion **3**.

A tetralyllithium or tetralyl Grignard would be a closer comparison to our tetralyl anion, but we are convinced that the aromatic second ring in the model 1-naphthyl organometallics is not so different from a tetrahydro ring as to warrant exploration. The differences are very minor, as can be seen by comparing structure **3** with structures **5** and **6**. Perhaps the more pertinent model would be one that includes a halogen, such as a 4-halotetralyl-lithium or -Grignard. Such a model might be prompted by the results with 4-halotetralyl anion, where the deuterium content of the halotetralin product increases from X = I to Br to Cl.² Although this appeared to be a remote substituent effect on the basicity and

H/D selectivity of the aryl anion, it was concluded that the variations arise indirectly, through hydrogen bonding of X^- to the carboxylic acid (or to water), whose reactivity is reduced, relative to that of solvent. Because hydrogen bonding increases from I^- to Br^- to Cl^- , the relative effectiveness of solvent also increases in this order. Therefore it is also not necessary to explore a 4-halotetraaryl lithium or Grignard.

Naked aryl anion. Table 2 displays the remarkable result that the same relative reactivities are obtained with $Bu_4N^+I^-$ as with Li^+I^- . In principle, an aryllithium $ArLi$ might be produced from reaction of **2** with Li^+I^- , but certainly not with $Bu_4N^+I^-$, which can form only a $Bu_4N^+Ar^-$ ion pair. However, it is highly unlikely that $ArLi$ and a $Bu_4N^+Ar^-$ ion pair would show the same relative reactivities toward hydronation, as is confirmed by comparison with Table S2. Therefore neither with $Bu_4N^+I^-$ nor with Li^+I^- is $ArLi$ formed. Instead aryl anion **3** is so reactive that it is quenched by hydronation more rapidly than the Li^+ can migrate to the *para* carbon to form $ArLi$, as suggested in Scheme 3. The species whose reactivity and extreme unselectivity are here studied is thus a naked aryl anion, Ar^- .



Scheme 3. Formation and hydronation of a naked aryl anion, with $M = Li$ or Bu_4N .

Although aryl anions have been studied extensively in the gas phase,²¹ such an unambiguous example of a naked aryl anion in solution is rare. Even if an aryl anion is not coordinated to a metal, it is usually not free in solution but is ion-paired with a metal cation. Examples include electron-poor arenes undergoing hydrogen exchange catalyzed by strong bases containing Li^+ ,²² K^+ ,²³ or Cs^+ ,²⁴ reaction of sodium methoxide with arylsilanes,²⁵ and

dinitrobenzoates undergoing decarboxylation.²⁶ One notable exception is the proposed aryl anion from two-electron reduction of an aryl halide, which adds intramolecularly to an ester,²⁷ but where the addition might be concerted with the second electron transfer. Competition experiments, as in these studies, might provide evidence for the intermediacy of a naked aryl anion.

Naked anions are well established, especially in the context of cyanide and fluoride anions of high nucleophilicity.²⁸ They are not necessarily solvent-free or counterion-free, but they are neither hydrogen-bonded nor covalently bonded to a metal. These results show that a naked aryl anion is quite different from an aryllithium or an aryl Grignard. Nevertheless, according to SciFinder[®], many researchers continue to refer to these organometallic reagents, and others, as aryl anions,²⁹ even though this is well recognized as an oversimplification.³⁰ The conflation of organometallics and carbanions is an example of a rhetorical device known as synecdoche.³¹

Conclusions

Iodide addition to the *p*-benzyne diradical **2** obtained from enediyne **1** produces a highly basic aryl anion, **3**, thereby amplifying basicity by >40 powers of 10. Aryl anion **3** is then hydronated by DMSO, acetonitrile, or water, to form 1-iodotetrahydronaphthalene **4**. All fifteen relative reactivities of these three acids and their deuterated isotopologues were measured by assaying the deuterium content of **4** from competition experiments using one deuterated acid and one undeuterated. The fact that **3** is generated "suddenly", in homogenous solution, permits measurement of its intrinsic reactivity, without the interference of mixing control. The data show that **3** is unselective among these weak acids, with a Brønsted α of only 0.04 and with low H/D KIEs. Because the same relative reactivities are obtained with Bu₄Ni as with LiI we conclude that the species undergoing hydronation is not an aryllithium

but a naked aryl anion, whose lifetime is too short to allow formation of an aryllithium. This may represent the first authenticated example of a metal-free aryl anion in solution.

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ASSOCIATED CONTENT

Supporting Information. Additional experimental details; Figures S1-S2; eq S1-S8 for direct evaluation of relative reactivities; eq S9-S30 for indirect evaluation of relative reactivities; Tables S1-S2 reporting D content. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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[31] The part for the whole, as in "All hands on deck." (hands for sailors). Also, the whole for the part, as in "Boston wins World Series." (city for Red Sox players).

TOC Graphic

