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Experimental Studies of the ^{13}C NMR of Iodoalkynes in Lewis-Basic Solvents

Jeffrey A. Webb, Jaap E. Klijn, Philip Aru Hill, Jordan L. Bennett, and Nancy S. Goroff*

Department of Chemistry, State University of New York, Stony Brook, New York 11794-3400, and Department of Chemistry and Biochemistry, Denison University, Granville, Ohio 43023

nancy.goroff@sunysb.edu

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The ^{13}C NMR spectra of two different iodoalkynes, 1-iodo-1-hexyne (**1**) and diiodoethyne (**2**), exhibit a strong solvent dependence. Comparisons of the data with several common empirical models, including Gutmann's Donor numbers, Reichardt's E^N_T, and Taft and Kamlet's β and π^*, demonstrate that this solvent effect arises from a specific acid−base interaction. Solvent basicity measures such as Donor numbers and β values correlate well with the α-carbon chemical shift of **1**, but polarity measures such as E^N_T and π^* do not correlate. The similarity of the solvent effect for **1** and **2** suggests that carbon−carbon bond polarization may not play a role in the change in chemical shift, as previously hypothesized.

Introduction

We recently reported an unusual solvent effect in the ^{13}C NMR spectra of iodoalkynes.[1,2] Depending on the solvent, the chemical shift of the α-carbon can change by as much as 15 ppm. Because of the unusual magnitude and direction of this solvent effect, we have decided to study it both computationally and experimentally. Ab initio calculations, which have already been described, demonstrated that, in the gas phase, specific intermolecular interactions between the Lewis-acidic iodoalkyne and basic solvent (Figure 1) can explain this change.[2] Here we present experimental studies which probe the role of bulk solvent in the chemical shift change. These data describe the ^{13}C NMR of two iodoalkynes, 1-iodo-1-hexyne (**1**) and diiodoethyne (**2**), in a wide variety of solvents.

Laurence and co-workers have carried out extensive studies of iodoalkynes and their Lewis acidity.[3−8] They demonstrated that acid−base interactions can affect iodoalkyne vibrational spectra, in particular the carbon−iodine bond stretching frequency. Donation of electron density from the base into the C−I antibonding orbital weakens the C−I bond and lowers the frequency of vibration. In the presence of Lewis bases in nonpolar solvent, Laurence et al. observed separate C−I stretching modes corresponding to the free and complexed iodoalkyne.[4] They suggested that the difference in energy for these two stretching modes corresponds to the strength of the base.

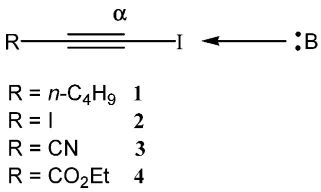

FIGURE 1. The interaction of a Lewis base (B) with an iodoalkyne.

Laurence and co-workers also examined the ^{13}C NMR spectra of different iodoalkynes. Iodine exerts a large magnetic influence on neighboring nuclei through the "heavy-atom effect" due to spin−orbit coupling of its valence electrons.[9−12] This relativistic effect lowers the chemical shift of the adjacent carbon atom by about 60 ppm. Laurence found that the chemical shift of the α-carbon in an iodoalkyne (*C*−I) is directly related to that of the analogous terminal alkyne (*C*−H),[8] with the iodoalkyne chemical shift approximately 70 ppm lower in frequency than the terminal alkyne value (i.e., around 0 ppm for an iodoalkyne in deuteriochloroform, CDCl$_3$). Interestingly, the two iodoalkynes that did not match Laurence's C−H/C−I correlation were those with Lewis-

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basic end groups, namely compounds **3** and **4**, each of which had a higher α-carbon chemical shift than predicted from the terminal-alkyne NMR.

Laurence et al. measured the NMR spectra of iodoalkynes only in $CDCl_3$. However, we have found that in DMSO or pyridine, the α-carbon chemical shifts of iodoalkynes move 10−15 ppm higher in frequency.[1] Here, we describe studies of the iodoalkyne chemical shift both in nonpolar solvents with dissolved base and in neat basic solvents. In both cases, the presence of a Lewis base has a measurable effect on the α-carbon chemical shift.

Experimental Section

1-Iodo-1-hexyne (1).[13] Several synthetic routes have been used to prepare **1**. The following procedure is preferred because it provides **1** in good yields and high purity. Under argon atmosphere, 1-hexyne (1.64 g, 20 mmol), $AgNO_3$ (0.84 g, 5 mmol), and *N*-iodosuccinimide (9.89 g, 44 mmol) were added to 200 mL of acetone. The reaction mixture was stirred at room temperature for approximately 3 h. Cold water (100 mL) was added to quench the reaction. Hexanes (100 mL) was added, and the resulting organic layer was washed with water and brine (∼250 mL each), and finally with 0.05 M $Na_2S_2O_3$, to remove I_2, until the organic layer had no color. The organic layer was dried with $MgSO_4$ and concentrated in vacuo to yield a brown liquid (2.50 g, 60%). A slight pink color is an indication of the presence of I_2 in the product. ^{13}C NMR (62 MHz, $CDCl_3$) δ −7.7, 13.5, 20.5, 21.8, 30.5, 94.8.

Diiodoethyne (2). A typical synthetic procedure (modified from Dehn[14]) is as follows: Acetylene gas was bubbled into a mechanically stirred solution of KI (25.54 g, 154 mmol) in 50 mL of water. NaOCl solution (10−13% available chlorine) was added dropwise to the solution at such a rate that the yellow color of OI^- anion would quickly disappear. Addition of NaOCl solution and bubbling of acetylene gas were stopped when no color change was observed upon addition of the NaOCl solution. The reaction was cooled in an ice bath. The precipitate was filtered and washed with cold water. The product was dissolved in 75 mL of petroleum ether and dried with calcium chloride. Recrystallization of the product from the decanted petroleum ether yielded **2** (9.497 g, 44.5% based on KI). ^{13}C NMR (75 MHz, $CDCl_3$) δ 0.62, mp 78−79 °C (lit. mp 79 °C).

NMR Experiments. Solvents were used as purchased without further purification. For dilute experiments, samples were prepared by dissolving a 1:1 mixture of **1** and the base of interest (for example, 0.1 mmol of each) in hexanes, and diluting the sample to 1 mL in a volumetric flask. The concentrations of **1** and base ranged from 0.010 to 0.50 M. NMR spectra were obtained at 25 °C, using a Varian Inova 600 operating at 150.8 MHz for ^{13}C. For neat solvent experiments, samples were prepared by dissolving **1 (**0.062 g, 0.30 mmol) or **2** (0.083 g, 0.30 mmol) in the solvent of interest and diluting the sample to 1 mL in a volumetric flask. NMR spectra of **1** in neat solvents were obtained at 25 °C, using a Varian Inova 600 operating at 150.8 MHz for ^{13}C. NMR spectra of **2** in neat solvents were obtained at 25 °C, using a Bruker AC-300, interfaced to a Techmagnetics Tecmag MacSpect 3 controller, operating at 75 MHz. For all experiments an external lock signal was produced by using a sealed glass capillary containing either cyclohexane-d_{12} (for experiments with **1**) or acetone-d_6 (for experiments with **2**).

Results and Discussion

Iodoalkynes in the Presence of Dilute Base. Initial experiments indicated that basic solvents such as pyridine can have a significant effect on the chemical shift of the α-carbon of an iodoalkyne. To explore whether this solvent effect comes from bulk or molecular properties, we measured the chemical shift of **1** in the presence of dilute base. For these experiments, hexanes was used as a nonpolar, noninteracting solvent. We chose compound **1** as the substrate for these studies because it is easily prepared, because the α-carbon chemical shift appears far from other peaks in the NMR spectrum (−8.1 ppm at 0.1 M in hexanes), and because **1** lacks other functional groups that might complicate the interactions with solvent. In each case, a 1:1 mixture of **1** and the appropriate base was dissolved in hexanes, and the α-carbon chemical shift was measured.

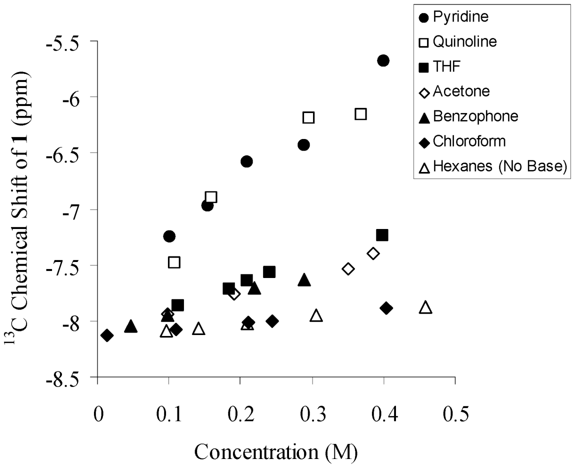

FIGURE 2. Dilute solution studies of **1** complexed with several bases in hexanes. Concentration of base and **1** kept approximately equal.

The dilute solution experiments (Figure 2) provide qualitative evidence for the importance of specific molecular interactions and Lewis basicity to the observed solvent effect, consistent with computational results. As shown in Figure 2, even without added base, the chemical shift changes slightly with increased concentration (−7.9 ppm at 0.4 M in hexanes), perhaps because of self-aggregation of the iodoalkyne. But adding a Lewis base to the solution affects the chemical shifts even more. Pyridine and quinoline, the two strongest bases, cause the biggest change in α-carbon chemical shift; for example, the α-carbon of **1** produces a shift of −5.7 ppm in a 0.4 M solution of pyridine.

Nonetheless, in each case, the effect of dilute amounts of base is much smaller than that of the corresponding bulk solvent. For instance, in pure pyridine, the chemical shift of **1** is +3.85 ppm. The relatively small changes in chemical shift in these dilute solutions make it impossible to calculate a reliable association constant for **1** with any of the bases examined. These experiments also raise the question of whether other bulk properties, in particular solvent polarity, might be significant contributors to the observed solvent effect.

Iodoalkynes in Neat Basic Solvents. To examine the role of bulk solvent properties in the observed NMR shifts, we carried out studies in neat solvents of varying basicity and polarity, including halogenated hydrocarbons, aromatic solvents, amines, and ethers. The observed α-carbon chemical shift for **1**, δ(**1**), spans a range

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TABLE 1. Neat Solvent NMR Data and Selected Solvent Parameters

solvent	$\delta(1)^b$	$\delta(2)^c$	DN^d	$E^N_T{}^e$	β^f	$\pi^{*\,f}$	$B_{soft}{}^g$	$\delta(CHCl_3)^h$
hexanes	−7.95	−1.45		0.009	0.00	−0.08		
$CDCl_3$	−7.96	0.62		0.256				
$CHCl_3{}^a$	−7.10	0.61		0.259	0.00	0.58	1.0	0.20
dichloroethane	−6.89	1.34		0.327				
CCl_4	−6.29	0.47		0.052			0.0	
benzene	−6.10	1.27	0.1	0.111	0.10	0.59	10.0	
ethyl acetate	−4.53	3.47	17.1	0.228	0.45	0.55		
diethyl ether	−4.40		19.2	0.117	0.47	0.27	20.5	0.74
acetonitrile	−3.62	5.26	14.1	0.460	0.31	0.75	17.0	0.56
tetrahydrofuran	−3.33	4.67	20.0	0.207	0.55	0.58	25.0	0.79
acetone	−2.72	5.80	17.0	0.355	0.48	0.71	18.0	0.92
dimethyl sulfide	−1.56	7.31		0.065				
dimethylformamide	0.27	8.68	26.6	0.404	0.69	0.88	30.0	1.30
triethylamine	2.78		31.7	0.043	0.71	0.14		1.22
dimethyl sulfoxide	3.55	12.36	29.8	0.444	0.76	1.00	32.0	1.32
quinoline	3.75	13.67		0.269			50.0	
pyridine	3.85	13.03	33.1	0.302	0.64	0.87	57.5	1.56
HMPA	5.09	11.65	38.8	0.315				2.06
diethylamine	7.10			0.145				
N-methylimidazole	7.17	16.40						

[a] Chloroform used as purchased, including 1% ethanol as stabilizing agent. [b] ^{13}C chemical shift of the α-carbon of **1**, relative to external cyclohexane-d_{12} lock. [c] ^{13}C chemical shift of the α-carbon of **2**, relative to external acetone-d_6 lock. [d] Gutmann's donor number, from ref 15. [e] Reichardt's E^N_T values, from ref 16. [f] Taft and Kamlet's β and π^* parameters, from refs 17−20. [g] Laurence's B_{soft}, from ref 4. [h] ^1H chemical shift of chloroform, as reported in ref 26.

of more than 15 ppm, from −7.9 ppm in hexanes to +7.2 ppm in *N*-methyl imidazole (Table 1). Interestingly, even nonpolar solvents such as CCl_4 exert a noticeable effect on the chemical shift. Qualitatively, the more basic solvents produced larger changes in $\delta(\mathbf{1})$.

To help understand these data, we turned to several common empirical models of solvent behavior. These models include Gutmann's donor number system for Lewis bases,[15] Reichardt's polarity measure, E^N_T,[16] and Taft and Kamlet's β and π^* solvent model.[17−20] In addition, we compared our data with Laurence's proposed measure of soft basicity, B_{soft}.[4] Analysis with additional empirical solvent models is described in the Supporting Information.

For a given Lewis base, Gutmann has defined the donor number (DN) as the negative enthalpy of formation of a 1:1 complex of that base with the Lewis acid antimony(V) chloride, $SbCl_5$, in dilute solution, typically in dichloroethane.[15] The DN parameter reflects only the molecular behavior of the solvent, not bulk properties.[21,22] Nonetheless, a linear regression demonstrates that the ^{13}C NMR data for **1** correlate very well with DN values (Figure 3, $R^2 = 0.873$). This analysis yields eq 1, describing the chemical shift (in ppm) of the α-carbon, $\delta(\mathbf{1})$, as a function of the donor number of the solvent used.

$$\delta(\mathbf{1}) = -7.99 + 0.32(\mathrm{DN}) \qquad (1)$$

In contrast, Reichardt's E^N_T parameters, which act as an empirical measure of bulk solvent polarity, do not correlate significantly with the data in Table 1 (Figure 4, $R^2 = 0.0495$). The E^N_T values are based on the solvatochromic shift in the absorption maximum of a betaine dye.[16] This dye is not Lewis acidic, and its absorption maximum is a good measure of nonspecific solvent polarity effects.[23,24]

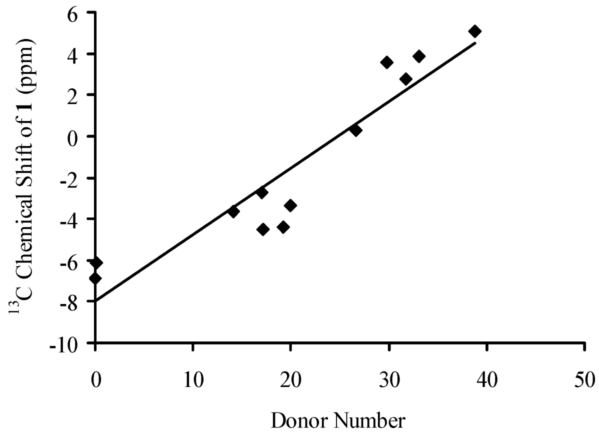

FIGURE 3. The α-carbon ^{13}C NMR shift of **1** as a function of Gutmann's donor numbers.[15]

Taft and Kamlet have developed a solvatochromic comparison method that includes parameters for both basicity (β) and polarity (π^*) effects.[17−20] The β values come from the solvatochromic shift in the absorption spectrum of 4-nitroaniline. Unlike Gutmann's donor numbers, the β values therefore reflect bulk solvent basicity, and in particular solvent hydrogen-bond acceptor ability. The π^* parameters, similar to Reichardt's E^N_T values, were determined via solvatochromic shifts in the absorption spectra of several nitroaromatics, including

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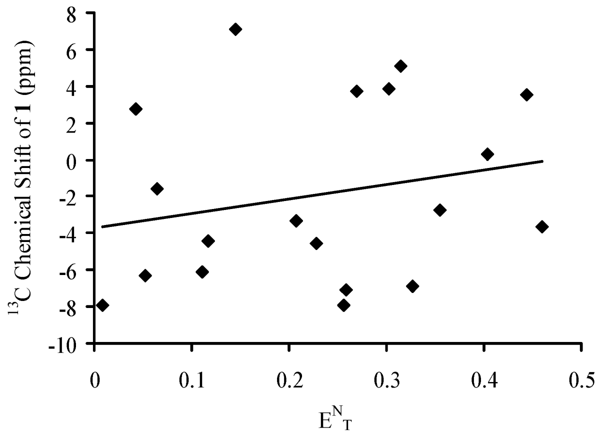

FIGURE 4. The α-carbon ^{13}C NMR shift of **1** as a function of Reichardt's normalized $E^N{}_T$ polarity model.[16]

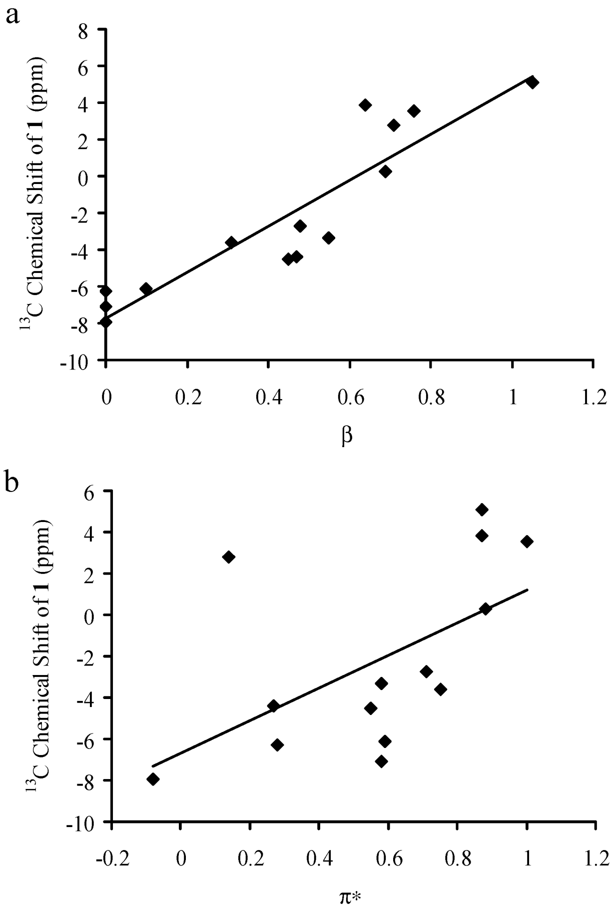

FIGURE 5. The α-carbon ^{13}C NMR shift of **1** as a function of Taft and Kamlet's solvatochromatic parameters: (a) β and (b) π^*.[17-20]

4-nitroanisole, and *N*,*N*-diethyl-3-nitroaniline. Linear regression analysis shows that the NMR data for **1** correlate well with β alone (Figure 5a, $R^2 = 0.838$), but not with π^* (Figure 5b, $R^2 = 0.316$). In addition, linear analysis with both parameters offers no significant improvement over using β alone ($R^2 = 0.845$). This analysis indicates that although β is not perfectly correlated with the NMR data, π^* cannot explain the

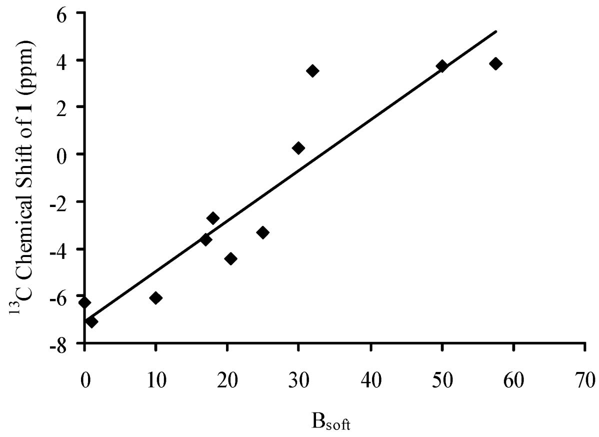

FIGURE 6. The α-carbon ^{13}C NMR shift of **1** as a function of Laurence's B_{soft} values.[4]

remaining deviations. The linear relation between $\delta(\mathbf{1})$ and β is shown in eq 2.

$$\delta(\mathbf{1}) = -7.72 + 12.50(\beta) \qquad (2)$$

In addition to the models described above, we also compared our data with B_{soft}, a parameter developed by Laurence and co-workers to quantify "soft" basicity.[4] Like iodoalkynes, Laurence et al. found that iodine cyanide (ICN) gives two distinct IR peaks for the C−I stretch when in the presence of dilute solutions of various Lewis bases. They defined B_{soft} as the difference in the C−I stretching frequency of ICN, free vs complexed, and offered it as a general measure of "soft" basicity. The chemical similarity between Laurence's system and the one described here suggests that there should be a strong correlation between B_{soft} and our experimental ^{13}C NMR shift. Yet B_{soft} reflects a snapshot on the IR time scale of the vibrational properties of separate free and complexed ICN, without regard to the equilibrium constant for complexation. It should act as a measure of the enthalpy, but not the entropy, of complexation. The $\delta(\mathbf{1})$ values, on the other hand, represent a weighted average of all iodohexyne molecules present in the solution, necessarily incorporating both enthalpy and entropy effects. The two data sets may therefore diverge if entropy plays a more significant role in complexation for some solvents than others. In fact, the NMR data correlate about as well with the B_{soft} values (Figure 6, $R^2 = 0.857$) as with DN or β, suggesting that there are no major changes in the entropy of interaction as the solvent changes. The lack of entropy effects implies that steric interactions are not significant for this system, understandable given the linear geometry of the iodoalkyne.

These comparisons with empirical models demonstrate that the observed solvent effect results from specific solute−solvent interactions. They also suggest a strong similarity between the interactions of solvent with **1** and with hydrogen-bond donating solutes. For example, solvent effects on the NMR spectra of dissolved $CHCl_3$ have been extensively studied, and its ^{13}C NMR chemical shift has been shown to depend on the basicity of the solvent used.[18,25-27] Two groups have correlated these data with Taft and Kamlet's β values, with one study suggesting that solvent polarity also plays a role.[18,27] A further confirmation of the similarity in the two systems

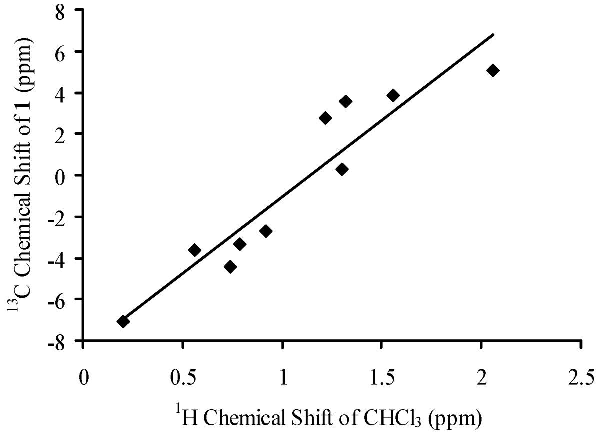

FIGURE 7. The α-carbon ^{13}C NMR shift of **1** as a function of ^{1}H NMR shifts of CHCl$_3$.[22]

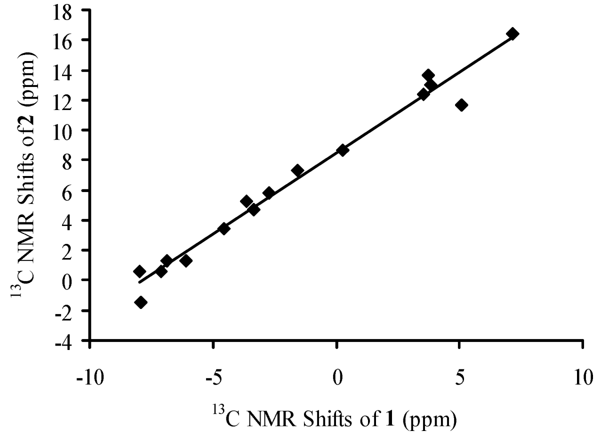

FIGURE 8. The α-carbon ^{13}C NMR shift of **2** as a function of the α-carbon ^{13}C NMR shift of **1**.[26]

comes from comparing the ^{13}C NMR data for **1** to the ^{1}H NMR data for CHCl$_3$ (Figure 7, $R^2 = 0.885$).

In addition, the direction of the solvent effect is the same for both chloroform and compound **1**. For example, the ^{13}C chemical shift of chloroform in HMPA is 4.2 ppm higher than that in cyclohexane.[26] Nonetheless, it is noteworthy that the observed ^{13}C chemical shift range for **1** is significantly larger than that for chloroform. Iodoalkynes have a unique sensitivity to solvent basicity in their NMR spectra.

Diiodoethyne. Calculations have suggested that carbon−carbon bond polarization is an important component of the mechanism for this solvent effect.[2] To examine the role of bond polarization in the NMR of iodoalkyne, we turned to studies of diiodoethyne (**2**). While iodohexyne (**1**) is a monodentate iodoalkyne with no competing functional groups, compound **2** contains two Lewis-acidic iodine atoms, each bonded to one of the carbon atoms of the lone triple bond. Because the triple bond cannot be polarized in both directions at once, the symmetry of **2** might lead to a lessening of the NMR solvent effect, compared to that of **1**.

Figure 8 shows a plot of the α-carbon chemical shift of **1** vs the carbon chemical shift of **2** in the same solvent. As can be seen, the solvent effect is virtually the same in **1** and **2** ($R^2 = 0.977$), but the NMR signal of **2** is slightly *more* sensitive to solvent (slope = 1.10). These data suggest that either bond polarization is not a significant component of the solvent effect or that, on the NMR time scale, many of the diiodoethyne molecules are complexed to only one Lewis base. We are currently addressing these two possibilities via computer modeling.

Conclusions

The experimental studies described here have demonstrated the generality of the solvent effect previously observed in the NMR signal of iodoalkynes. Correlations with various empirical models of solvent basicity, including Gutmann's donor numbers and Taft and Kamlet's β values, indicate that acid−base interactions are responsible for the observed change in chemical shift. Solvent polarity does not appear to play a role, as demonstrated by the poor correlation to Reichardt's E^{N}_{T} and Taft and Kamlet's π^* parameter.

Nonetheless, there is still more to learn about the mechanism by which the solvent−solute interactions lead to an increase in chemical shift. Calculations indicate that polarization of the carbon−carbon triple bond plays a role. But experiments on the symmetric substrate diiodoethyne (**2**) suggest that the situation may be more complicated than originally proposed.

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Supporting Information Available: Details of each linear regression analysis. This material is available free of charge via the Internet at http://pubs.acs.org.

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