

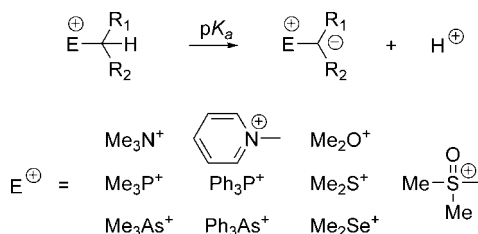
An Extensive Ylide Thermodynamic Stability Scale Predicted by First-Principle Calculations

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Thermodynamic stabilities of ylides are measured by the ease of the carbanion formation through the removal of a proton from their precursors. A full-spectrum scale of ylide thermodynamic stability is important to understand the reactivities and selectivities in ylide chemistry. In the present study is reported the first theoretical protocol for predicting the acidities of structurally unrelated ylide precursors in DMSO whose reliability has been tested against almost all the available experimental data. The ONIOM/G3B3//HF//CPCM/Bondi method is found to be the optimal protocol to handle the N-, P-, and S-containing ylides, whereas the B3LYP/6-311+G(3df,2p)//B3LYP/6-31G(d)//HF//CPCM/Bondi method can be used to deal with those systems for which the ONIOM/G3B3 method is not feasible. Extensive calculations on about 80 experimentally characterized ylide precursors show that this theoretical protocol can reliably predict the $\text{p}K_{\text{a}}$ values of diverse structurally unrelated ylide precursors in DMSO with an error bar of ca. 1.6–1.9 $\text{p}K_{\text{a}}$ units. With the authorized theoretical protocol in hand, we have developed an extensive scale of ylide thermodynamic stability that may find applications in synthetic organic chemistry.

1. Introduction

Carbanions neighboring a positively charged heteroatom (such as nitrogen, phosphorus, or sulfur) are referred to as “ylides”.¹ They are powerful and versatile reagents in organic chemistry, which undergo several important types of reaction such as olefination, cyclization to a three-membered ring, and rearrangement. Among these interesting compounds the phosphorus ylides have been studied the most intensively ever since the discovery of the Wittig reaction in the 1950s.² Furthermore, the past three decades have witnessed a dramatic expansion of

traditional ylide chemistry to include many other Group VB and VIB elements (such as N, As, S, and Se) both in their synthetic applications and in detailed structural and mechanistic considerations.³

The preparation of a ylide is often conducted through the deprotonation of its conjugate acid precursor named as an onium cation. The choice of bases has been one of the key considerations in ylide synthesis and is essentially relevant to the acidities of the onium cations. Furthermore, many previous investigations have implied that the ylide reactivities, reaction paths, and stereochemistry are inherently stability-dependent.^{4,5} This makes it important to quantitatively know the thermodynamic stability of ylides, which is again measured by the ease of the carbanion formation through the removal of a proton from the onium ion. Thus, an extensive scale of the acidities of ylide precursors is

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highly valuable for synthetic chemists who need to design the experiment involving ylides.

Early studies of the equilibrium acidities of ylide precursors dates back to as early as 1960s, but the use of different solvent systems in these studies makes it difficult to analyze the data.⁶ More recently Bordwell et al. established an “absolute” acidity scale in the DMSO (dimethyl sulfoxide) solution by using the overlapping indicator titration method.⁷ Afterward they reported the first scale of ylide precursor acidities for a number of Ph_3P^+ , R_3N^+ , and PyN^+ -containing onium salts in a *single* solvent, DMSO.⁸ In 1999 Cheng et al. extended this ylide stability scale to include Bu_3P^+ , Bu_2S^+ , Me_2S^+ , Bu_2Te^+ , Me_2Se^+ , and Ph_3As^+ -containing ylides by measuring the $\text{p}K_{\text{a}}$ values of their conjugate acids in DMSO.⁹ The pioneering studies of Bordwell’s and Cheng’s groups have led to the establishment of a fairly extensive scale of ylide stability and contributed considerably to the advance of ylide chemistry.

Nonetheless it should be noted that all of the ylides in Bordwell and Cheng’s scale are “stabilized” or “semi-stabilized” ylides containing strongly conjugating substituents (e.g., COOMe, CN, or aryl).^{8,9} Many “nonstabilized” ylides that bear electron-donating substituents have unfortunately not been examined (due to the limitation of overlapping indicator titration method), even though these compounds are synthetically important and enjoy the highest reactivity. Furthermore, the sophistication of the overlapping indicator titration method also limits the ability of many researchers to promptly estimate the thermodynamic stability of new ylides encountered in their experiments. At this point it is desirable to develop a theoretical method that can reliably predict the $\text{p}K_{\text{a}}$ values of various ylide precursors from the first principles of physics. This method, if available, will facilitate the mechanistic study and synthetic applications of ylides. Note that in the past several decades there have been a number of elegant studies reporting the theoretical calculation of gas-phase basicities of ylides.¹⁰ However, there has not been any study reporting the ab initio calculation of ylide precursor $\text{p}K_{\text{a}}$ values in the organic solvents.¹¹

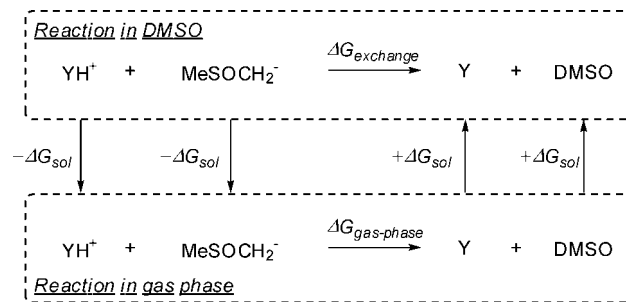
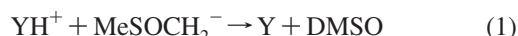


FIGURE 1. Thermodynamic cycle used for the $\text{p}K_{\text{a}}$ calculation.

In the present study we attempt to bridge the gap by reporting the first theoretical protocol to accurately calculate the equilibrium acidities of various ylide precursors in DMSO. This work is a continuation of our efforts in studying the calculation of solution-phase organic chemistry *quantitatively*.¹² It is found that through the careful choice of theory combinations it is feasible to calculate the absolute $\text{p}K_{\text{a}}$ values of structurally unrelated ylide precursors within a precision of ca. 1.6 $\text{p}K_{\text{a}}$ units. With this useful method in hand we next develop an extensive thermodynamic stability scale of N-, P-, As-, O-, S-, and Se-ylides bearing a full spectrum of substituents. In particular, “non-stabilized” ylides carrying electron-donating substituents are now included in the present scale, which yields a great deal of new, quantitative information about the thermodynamic stability of ylides. The availability of this body of data allows us to examine a fundamental question of ylide chemistry: how do different Group VB and VIB elements and the substituents on these heteroatoms affect the ylide stability?

2. Results and Discussion

2.1. Evaluation of Different Theoretical Methods. To calculate the $\text{p}K_{\text{a}}$ value of a ylide precursor (YH^+) we consider the following proton-exchange reaction between YH^+ and a DMSO anion



If the free energy change of the above reaction in the DMSO solution is defined as $\Delta G_{\text{exchange}}$, the $\text{p}K_{\text{a}}$ value of YH^+ can be readily calculated by eq 2.¹²

$$\text{p}K_{\text{a}}(\text{YH}^+) = 35.0 + \frac{\Delta G_{\text{exchange}}}{2.303 \times RT} \quad (2)$$

To calculate $\Delta G_{\text{exchange}}$ we design a thermodynamic cycle as shown in Figure 1. The gas-phase part of the cycle can be handled by standard quantum chemical methods whereas the solvation free energies are calculated by using the polarized continuum solvation (PCM) model.¹³

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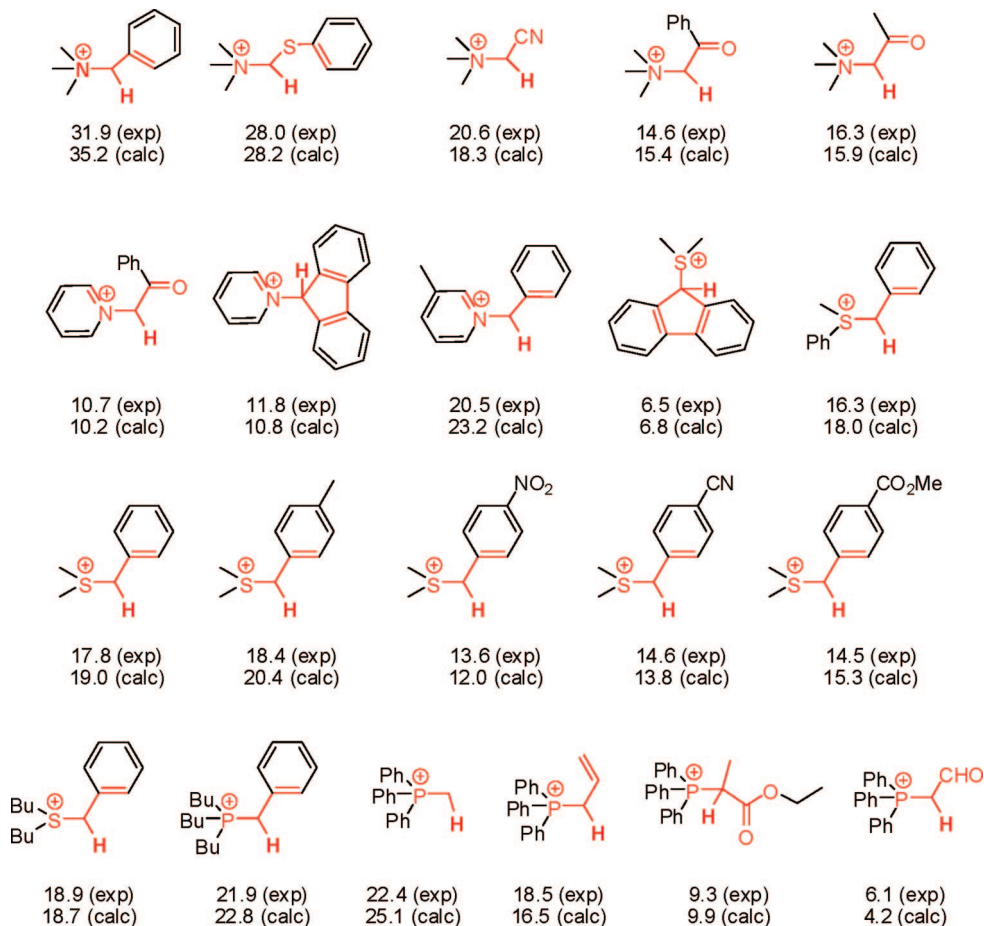


FIGURE 2. Twenty-one representative ylide precursors tested for the method development (core layer atoms are shown in red).

Some difficulties may arise for the calculation of ylide pK_a values: (1) Although some studies have shown that the popular PCM models can reliably predict the solvation free energies of neutral and anionic organic species in the organic solvents,¹⁴ there has not been a comprehensive study demonstrating the reliability of PCM in handling organic cations in the nonaqueous solvents.¹⁵ Thus the present study on ylide pK_a values provides us a good opportunity to examine this problem. (2) Although a number of theoretical studies on the reactions involving various ylides have been reported,^{5,10} there has not been a comprehensive examination on the accuracy of the theoretical methods quantitatively against experimental data. To solve the problem we selected 21 representative ylide precursors (Figure 2) to compare the performance of different theoretical methods (Table 1).

The first theoretical method in the examination is B3LYP/6-311+G(3df,2p)//B3LYP/6-31G(d) in which the solvation free energy is handled by the IEFPCM-UA0 model (entry 1). This

method has been found to be sufficient to calculate the pK_a values of neutral organic acids in nonaqueous solvents.¹² However, it is found that the root-mean-square (rms) error of this method is as high as 3.0 pK_a units (or 4 kcal/mol). The maximum error of this method is also as high as 7.4 pK_a units (or 10 kcal/mol!). The use of the 6-31+(d) basis set in geometry optimization, which is sometimes necessary for phosphorus- and sulfur-containing compounds, does not diminish the rms error (entry 2). The use of other density functionals including B3P86, B3PW91, and BMK also gives large rms errors that are over 3 pK_a units (entries 3–5). These data suggest that a higher level of theoretical method should be used to handle organic ylides.

To compromise the accuracy and cost of the theoretical method we turn to the ONIOM-G3B3 method which was recently examined by us to have good performances for bulky organic systems.¹⁶ The atoms directly connected to the ylide carbon center are placed in the core layer and treated by the G3B3 method, whereas the remaining atoms are placed in the low layer and handled at the B3LYP/6-31G(d) level. It is satisfactory to find that the ONIOM method reduce the rms and maximum errors to ca. 2 and 4 pK_a units, respectively (entry 6). Change of the solvation model from IEFPCM to CPCM does not improve the calculation. However, the use of COSMO solvation model increases the rms error to 5.9 pK_a units (entry 8).¹⁷ Furthermore, replacement of the UA0 radii by the UFF

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TABLE 1. Performances of Different Theoretical Methods for the 21 Representative Ylide Precursors (unit: pK_a unit)

entry	method	basis set for geometry optimization	basis set for energy calculation	solvation model ^a	rms error	maximum error	r	mean error
1	B3LYP	6-31G(d)	6-311+G(3df,2p)	HF//IEFPCM/UA0	3.0	7.4	0.9510	-1.6
2	B3LYP	6-31+G(d)	6-311+G(3df,2p)	HF//IEFPCM/UA0	3.0	7.7	0.9550	-1.6
3	B3P86	6-31G(d)	6-311+G(3df,2p)	HF//IEFPCM/UA0	3.4	8.2	0.9536	-2.6
4	B3PW91	6-31G(d)	6-311+G(3df,2p)	HF//IEFPCM/UA0	3.3	8.0	0.9557	-2.5
5	BMK	6-31G(d)	6-311+G(3df,2p)	HF//IEFPCM/UA0	3.1	8.4	0.9462	-2.1
6	ONIOM-G3B3	6-31G(d)	6-31G(d)	HF//IEFPCM/UA0	2.1	4.3	0.9562	0.9
7	ONIOM-G3B3	6-31G(d)	6-31G(d)	HF//CPCM/UA0	2.1	4.3	0.9564	0.3
8	ONIOM-G3B3	6-31G(d)	6-31G(d)	HF//COSMO/UA0	5.9	8.2	0.9818	5.7
9	ONIOM-G3B3	6-31G(d)	6-31G(d)	HF//CPCM/UHF	3.8	6.2	0.9779	-3.4
10	ONIOM-G3B3	6-31G(d)	6-31G(d)	HF//CPCM/UAHF	10.1	16.4	0.9064	9.9
11	ONIOM-G3B3	6-31G(d)	6-31G(d)	HF//CPCM/Bondi(1.00)	4.8	7.8	0.9720	4.5
12	ONIOM-G3B3	6-31G(d)	6-31G(d)	HF//CPCM/Bondi(1.10)	2.9	5.2	0.9795	2.5
13	ONIOM-G3B3	6-31G(d)	6-31G(d)	HF//CPCM/Bondi(1.15)	2.1	4.0	0.9796	1.3
14	ONIOM-G3B3	6-31G(d)	6-31G(d)	HF//CPCM/Bondi(1.20)	1.6	3.3	0.9806	0.3
15	ONIOM-G3B3	6-31G(d)	6-31G(d)	HF//CPCM/Bondi(1.25)	1.7	3.3	0.9809	-0.7
16	ONIOM-G3B3	6-31G(d)	6-31G(d)	HF//CPCM/Bondi(1.30)	2.4	4.5	0.9804	-1.8
17	ONIOM-G3B3	6-31G(d)	6-31G(d)	HF//CPCM/Bondi(1.40)	4.3	6.9	0.9782	-3.9

^a The basis set for the solvation free energy calculation is 6-31+G(d,p).

and UAHF radii also increases the rms error to 3.8 and 10.1 pK_a units, respectively (entries 9–10). This observation indicates that the choice of atomic radii may also affect the calculation.

Previous studies showed that scaled atomic radii often can improve the calculation of solvation free energies in nonaqueous solvents.^{12,18} The rationale for the reparameterization method is that the solvation cavity in an organic solvent may have a different size as compared to the cavity created by the same solute in water. Using this strategy we have examined different scaling factors for the Bondi radii ranging from 1.00 to 1.40 (entries 11–17). Our results show that the minimum rms error can be obtained when the scaling factor equals 1.20. Thus, we conclude that the optimal method should be a combination of ONIOM/G3B3 for the gas-phase energy calculation and HF/6-31+G(d,p)//CPCM/Bondi(1.20) for the solvation energy calculation. The rms error of this method is 1.6 pK_a units for the 21 ylide precursors.

2.2. More Experimental pK_a Values for Ylide Precursors.

Having optimized a theoretical protocol that can handle 21 ylide precursors, we next examine whether the same method can be applied to all the other ylide precursors whose pK_a values have been experimentally measured. To this end we have systematically calculated the cesium ion-pair acidities for 78 structurally unrelated ylide precursors. The ONIOM/G3B3//HF//CPCM/Bondi(1.20) method is used for all the N-, P-, and S-containing ylides. As to the As-, Se-, and Te-containing ylides, the ONIOM/G3B3 method is not feasible and we have to go back to the B3LYP/6-311+G(3df,2p)//B3LYP/6-31G(d)//HF//CPCM/Bondi(1.20) method. Note that for the Te-containing ylides, the basis set for Te is LanL2dz.

Our calculation results are listed in Table 2. It is found that the newly developed theoretical protocol can successfully predict the pK_a values for almost all the N-, P-, and S-containing ylide precursors whose pK_a values range from about 5 to 45 (Figure 3). The correlation coefficient between the experimental and theoretical pK_a values is as high as 0.9834, and the rms error is 1.6 pK_a units. Note that we find six ylide precursors whose

experimental pK_a values differ from the theoretical predictions by over 3.5 pK_a units. These compounds are Pyr⁺-CH₂-COMe, (EtO)₂PO-CH₂Cl, (MeO)₂PO-NH₂, Et₃N⁺-CH₂-C₆H₄COOMe, Ph₃P⁺-NH-C₆H₄Me, and Ph₃P⁺-CHMe₂. Further examinations are needed to clarify the disagreement between theory and experiment. However, it is important to point out that some of the ylides (such as Ph₃P⁺-CHMe₂) are unstable so that only one-point (instead of three-point) titrations are possible in their pK_a measurements.^{8f}

Furthermore, it can be easily seen that the theoretical predictions for the As-, Se-, and Te-containing ylide precursors are less accurate (Figure 3), presumably due to the use of a lower level theory for these heavy atoms. Nonetheless, when all the experimental data including N, P, S, As, Se, and Te ylides are considered, the correlation coefficient between the experimental and theoretical pK_a values is 0.9670 (for 93 compounds) and the rms error is only slightly increased to 1.9 kcal/mol.

2.3. An Extensive Ylide Thermodynamic Stability Scale.

A reliable as well as extensive scale of ylide thermodynamic stability is fundamental to the study and application of ylide derivatives in organic chemistry. Despite the great efforts of several groups,^{6,8,9} the solution-phase acidities of many important ylide precursors have not been successfully measured. In the above study we show that by using state-of-the-art methods in computational chemistry, a carefully calibrated theoretical protocol can reliably predict the pK_a values of structurally unrelated ylide precursors in DMSO with an error bar of ca. 1.6–1.9 pK_a units. This theoretical protocol provides an opportunity to obtain the *first*, extensive scale of ylide thermodynamic stability.

In Table 3 we list the pK_a values of a number of synthetically relevant N-, P-, As-, O-, S-, and Se-ylide precursors. “Stabilized”

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TABLE 2. Experimental and Theoretical pK_a Values for Various Ylide Precursors in DMSO^a

Entry	structure	pK_a in DMSO		Entry	structure	pK_a in DMSO	
		Exp	Theor			Exp	Theor
1		42.0 ^{19a}	41.9	40		17.9 ^{19j}	17.8
2		16.5 ^{19b}	16.3	41		17.5 ^{19j}	19.1
3		19.4 ^{19c}	19.4	42		18.9 ^{19j}	18.5
4		20.2 ^{19a}	20.6	43		15.6 ^{19j}	16.6
5		24.9 ^{19d}	25.2	44		30.8 ^{19k}	34.0
6		11.8 ^{19b}	(7.6)	45		27.5 ^{19k}	29.4
7		14.1 ^{19b}	14.3	46		18.8 ^{19k}	18.4
8		24.9 ^{19d}	23.1	47		6.5 ^{19k}	6.3
9		17.7 ^{19b}	18.4	48		17.6 ^{19k}	17.7
10		17.8 ^{19a}	18.2	49		18.0 ^{19k}	19.0
11		21.0 ^{19a}	(26.4)	50		14.6 ^{19k}	14.5
12		29.9 ^{19e}	31.4	51		14.2 ^{19k}	14.2
13		20.2 ^{19e}	23.4	52		11.4 ^{19k}	11.1
14		13.0 ^{19f}	12.5	53		29.2 ^{19k}	31.0
15		18.8 ^{19f}	19.6	54		28.0 ^{19k}	30.0

TABLE 2. Continued

Entry	structure	p <i>K</i> _a in DMSO		Entry	structure	p <i>K</i> _a in DMSO	
		Exp	Theor			Exp	Theor
16		6.0 ^{19a}	5.4	55		23.6 ^{19k}	25.3
17		15.6 ^{19f}	15.5	56		27.6 ^{19k}	(32.0)
18		27.6 ^{19g}	29.3	57		27.1 ^{19k}	30.1
19		16.4 ^{19g}	15.7	58		8.4 ^{19k}	8.0
20		18.6 ^{19g}	17.9	59		22.7 ^{19k}	19.4
21		26.2 ^{19g}	(31.0)	60		23.8 ^{19k}	20.7
22		28.7 ^{19g}	30.3	61		18.4 ^{19k}	16.6
23		23.2 ^{19g}	(18.9)	62		18.2 ^{19k}	16.3
24 ^c		24.9 ^{19g}	22.5	63		17.0 ^{19k}	15.1
25		18.3 ^{19g}	16.7	64		16.1 ^{19k}	14.0
26		24.9 ^{19g}	25.5	65		9.8 ^{19k}	7.4
27 ^c		16.3 ^{19g}	16.1	66		8.6 ^{19k}	11.9
28		19.3 ^{19g}	17.1	67		23.1 ^{19k}	23.2

TABLE 2. Continued

Entry	structure	pK _a in DMSO		Entry	structure	pK _a in DMSO	
		Exp	Theor			Exp	Theor
29		18.2 ^{19g}	15.0	68		23.6 ^{19k}	25.0
30		8.5 ^{19g}	10.1	69		19.5 ^{19k}	20.1
31		13.2 ^{19h}	11.0	70		19.2 ^{19k}	19.0
32		12.9 ^{19h}	10.8	71		11.1 ^{19k}	9.5
33		11.6 ^{19h}	8.7	72		24.2 ^{19k}	20.9
34		7.6 ^{19h}	(4.0)	73		19.6 ^{19k}	16.3
35		6.9 ^{19h}	4.1	74		18.7 ^{19k}	14.6
36		6.4 ^{19h}	3.1	75		18.5 ^{19k}	13.8
37		10.6 ¹⁹ⁱ	11.9	76		16.4 ^{19k}	11.7
38		10.7 ¹⁹ⁱ	8.8	77		23.7 ^{19k}	21.5
39		23.1 ^{19j}	21.8	78		11.2 ^{19k}	11.0



^a Core layer atoms are shown in red.

(i.e., E⁺-CH₂COMe and E⁺-CH₂SO₂Me), “semi-stabilized” (i.e., E⁺-CH₂CH=CH₂, E⁺-CH₂Ph, and E⁺-CH₂SMe), and

“non-stabilized” (i.e., E⁺-CH₃, E⁺-CH₂CH₃, and E⁺-CHMe₂) ylides are all considered. To compare the effect of different

TABLE 3. An Extensive Ylide Thermodynamic Stability Scale (Estimated Error Bar ≈ 1.6 – 1.9 p*K*_a units)^a

$$E^+ - \begin{array}{c} R_1 \\ | \\ C - H \\ | \\ R_2 \end{array} \xrightarrow{pK_a} E^+ - \begin{array}{c} R_1 \\ | \\ C^- \\ | \\ R_2 \end{array} + H^+$$

E ⁺	-CHR ₁ R ₂							
	CHMe ₂	CH ₂ CH ₃	CH ₃	CH ₂ SCH ₃	CH ₂ Ph	CH ₂ CH=CH ₂	CH ₂ SO ₂ Me	CH ₂ COMe
H	57.8	56.0	52.5 (56.0 ^b)	43.4 (45.0 ^{19g})	43.2 (43.0 ^{19l})	41.7 (44.0 ^{19g})	32.1 (31.1 ^{19g})	26.6 (26.5 ^{19g})
Me ₃ N ⁺	42.5	41.4	41.9 (42.0 ^{19a})	36.5	35.2 (31.9 ^{19a})	31.9	19.5	15.9 (16.3 ^{19a})
	26.6	25.5	26.0	21.2	21.0 (20.5 ^{19b})	18.7	14.2	7.6 (11.8 ^{19b})
Me ₃ P ⁺	32.1	29.5	26.2	19.4	20.2	19.5	9.3	9.7
Ph ₃ P ⁺	26.4	25.9	25.2 (22.4 ^{19a})	18.0	17.7 (17.4 ^{19k})	16.5 (18.5 ^{19f})	5.9	6.4 (7.1 ^{19a})
Me ₃ As ⁺	35.2	33.3	32.0	23.6	26.0	24.0	12.9	11.6
Ph ₃ As ⁺	32.5	29.1	29.3	19.3	19.4 (22.7 ^{19k})	21.1	9.7	6.7
Me ₂ O ⁺	36.3	38.0	34.8	- ^c	30.1	30.0	15.7	15.3
Me ₂ S ⁺	28.7	27.8	24.5	17.5	19.0 (17.8 ^{19k})	16.3	6.3	8.5
	19.9	17.3	15.0 (18.2 ^{19g})	10.7	11.0	11.1	2.3	3.3
Me ₂ Se ⁺	33.0	33.2	30.5	22.1	23.2 (23.1 ^{19k})	22.0	10.8	7.9

^a The ONIOM/G3B3//HF//CPCM/Bondi(1.20) method is used for all the N-, P-, O-, and S-containing ylides, whereas the B3LYP/6-311+G(3df,2p)//B3LYP/6-31G(d)//HF//CPCM/Bondi(1.20) method is used for the As- and Se-ylides. ^b An estimated value, see ref 19g. ^c Geometry optimization of this particular compound fails.

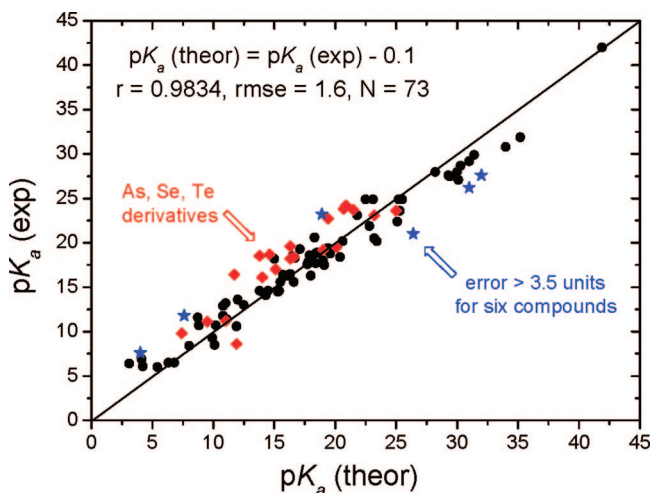


FIGURE 3. Correlation between the experimental and theoretical p*K*_a values for structurally unrelated ylide precursors.

positively charged heteroatoms on the acidity of ylide precursors, we also provide the theoretical p*K*_a values for the corresponding methane derivatives where E⁺ = H. Note that the available experimental data are also shown in Table 3. Comparing the experimental and theoretical data one can easily conclude that (1) the theoretical predictions are fairly accurate for almost all the compounds and (2) the acidities of many synthetically important ylide precursors remain unknown experimentally, but the current theoretical approach can partly solve the problem.

2.4. Discussion. 2.4.1. Effects of Different Adjacent Onium Cations on Ylide Stability. Several previous studies have compared the acidifying effects of different adjacent onium cations.^{8,9} Here we can generate more conclusions on the basis of a larger sample of data. First, we compare the acidifying

effects of Me₃N⁺, Me₃P⁺, Me₃As⁺, Me₂O⁺, Me₂S⁺, and Me₂Se⁺ (Figure 4). It is found that Me₃N⁺ has the lowest acidifying effect whose ylide-stabilizing effect is only ca. 14–20 kcal/mol (i.e., Δp*K*_a = 10–15 p*K*_a units). This value is in good agreement with Bordwell's and Cheng's values which were reported to be about 10–12 p*K*_a units.^{8e,9a} Compared to Me₃N⁺, Me₃P⁺ exhibits a significantly stronger acidifying effect that amounts to ca. 25 p*K*_a units. This observation is understandable because Me₃N⁺ shows a lack of resonance stabilization effect and nitrogen is less polarizable than phosphorus.²⁰ Interestingly, although Me₃As⁺ (Δp*K*_a ≈ 20 p*K*_a units) also shows a stronger acidifying effect than Me₃N⁺, this effect is less strong as compared to that of Me₃P⁺. Because the polarization and inductive effects for P are both smaller than those of As (polarization parameters are 24.5 versus 29.1;²¹ the field parameters are 0.97 versus 1.05²²), the stronger acidifying effect of Me₃P⁺ than Me₃As⁺ can only be interpreted by the 2p(C)–σ*(P–C) interaction being more efficient than the 2p(C)–σ*(As–C) interaction. Note that the dπ–p interaction is usually not considered as a driving force to stabilize the ylide because various theoretical studies have shown that the 3d or 4d orbitals are too high in energy for efficient overlap with the lone pair orbital at the carbanion center.²³

The stability of the Group VIB ylides can be understood in a similar manner. Me₂O⁺ is the weakest stabilization group with an acidifying effect of ca. 15 p*K*_a units. Me₂S⁺ is the strongest stabilization group with an acidifying effect of ca. 25 p*K*_a units. Me₂Se⁺ is positioned in the middle with an acidifying effect of

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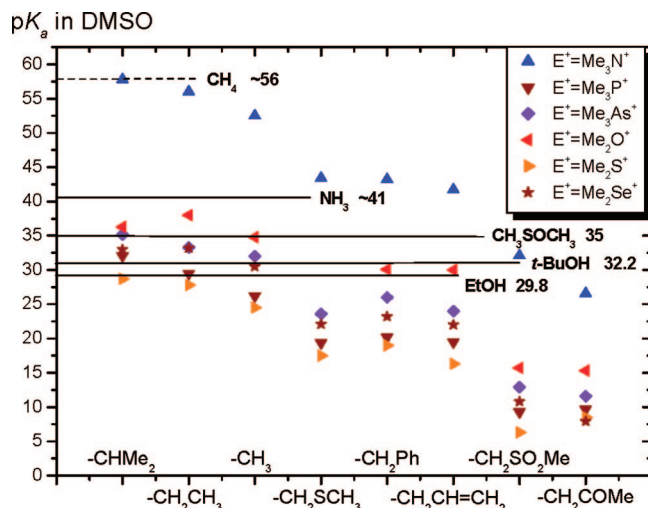


FIGURE 4. Compare the acidifying effects of different adjacent onium cations.

ca. 20 pK_a units. These observations are in good agreement with Cheng's experiments.⁹ They can be explained in terms of the polarizability of the onium cations and the energy level of the $\sigma^*(E^+-C)$ orbital. It is interesting to see that the Group VB ylides are always less stable than the Group VIB ylides in the same row when the remaining substituents on the ylides are the same. For instance, the pK_a values for $Me_3N^+-CH_3$ and $Me_2O^+-CH_3$ are 41.9 and 34.8. The pK_a values for $Me_3P^+-CH_3$ and $Me_2S^+-CH_3$ are 26.2 and 24.5. The pK_a values for $Me_3As^+-CH_3$ and $Me_2Se^+-CH_3$ are 32.0 and 30.5. These observations were previously explained by the fact that the E^+-C bond lengths in Group VIB ylides are shorter than those in the Group VB ylides.⁹ Thus, the Group VIB ylides are expected to exhibit a stronger σ^*-p interaction than the Group VB ylides.

Compared to Me_3N^+ , the pyridinium cation (Pyr^+) shows a much stronger acidifying effect which amounts to 20–30 pK_a units. This result is in agreement with Bordwell's study^{8e} and can be explained by the delocalization of the negative charge on the carbon atom of the ylide into the pyridinium ring. On the other hand, Ph_3P^+ and Ph_3As^+ are stronger ylide stabilizing groups than Me_3P^+ and Me_3As^+ due to obvious reasons. Finally, dimethyloxosulfonium (Me_2SO^+) is a much stronger ylide stabilizing group than Me_2S^+ whose acidifying effect amounts to ca. 30 pK_a units. Thus dimethyloxosulfonium ylides are thermodynamically the most stable ylides in Table 3.

2.4.2. Correlation between the Acidities of $E^+-CHR_1R_2$ and $H-CHR_1R_2$. Bordwell and co-workers reported the pK_a

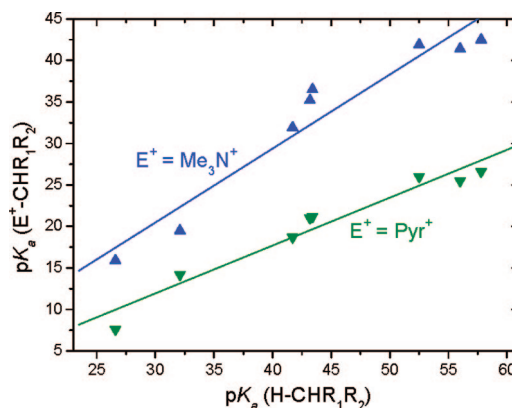


FIGURE 5. Correlation between the acidities of $E^+-CHR_1R_2$ and $H-CHR_1R_2$.

values of a large number of carbon acids with a formula of $H-CHR_1R_2$.⁷ If there is a correlation between the acidities of $E^+-CHR_1R_2$ and $H-CHR_1R_2$, one can readily estimate the acidity of many ylide precursors from Bordwell's existing data. However, due to the limitation of experimental data for ylides, this question has not been examined in the previous studies.

Here we plot the acidities of different $E^+-CHR_1R_2$ against those of $H-CHR_1R_2$. Figure 5 shows the example plots for Me_3N^+ - and Pyr^+ -containing ylides. It is found from Figure 5 and Table 4 that the correlations are generally good between the acidities of $E^+-CHR_1R_2$ against those of $H-CHR_1R_2$. The correlation coefficients range from 0.9643 to 0.9933. Therefore, one can use the equations described in Table 4 to rapidly estimate the acidities of many more ylide precursors from Bordwell's existing data⁷ for various mono- and disubstituted methanes.

Note that the slopes of the correlation equations are always less than unity. They decrease in the order Me_3N^+ (0.89) > Me_2Se^+ (0.86) > Ph_3As^+ (0.83) > Me_3As^+ (0.79) > Me_2O^+ (0.76) > Me_3P^+ (0.74) > Me_2S^+ (0.73) > Ph_3P^+ (0.72) > Pyr^+ (0.58) > Me_2SO^+ (0.55). Thus, for strongly ylide-stabilizing onium cations (such as Pyr^+ and Me_2SO^+), the acidifying effect of additional substituents on the ylide is relatively small.

3. Summary

Thermodynamic acidities of ylide precursors in nonaqueous solvents are fundamental to synthetic organic chemistry. Although the acidities of some ylide precursors have been experimentally measured, it is important to develop a theoretical method that can reliably predict these quantities from the first principles because not all the ylides are amenable to experi-

TABLE 4. Correlation between the Acidities of $E^+-CHR_1R_2$ and $H-CHR_1R_2$

Entry	E^+	Correlation equation	Correlation coefficient
1	Me_3N^+	$pK_a(E^+-CHR_1R_2) = 0.89 pK_a(H-CHR_1R_2) - 6.3$	0.9643
2	Pyridinium^+	$pK_a(E^+-CHR_1R_2) = 0.58 pK_a(H-CHR_1R_2) - 5.4$	0.9725
3	Me_3P^+	$pK_a(E^+-CHR_1R_2) = 0.74 pK_a(H-CHR_1R_2) - 12.3$	0.9865
4	Ph_3P^+	$pK_a(E^+-CHR_1R_2) = 0.72 pK_a(H-CHR_1R_2) - 14.3$	0.9821
5	Me_3As^+	$pK_a(E^+-CHR_1R_2) = 0.79 pK_a(H-CHR_1R_2) - 10.2$	0.9883
6	Ph_3As^+	$pK_a(E^+-CHR_1R_2) = 0.83 pK_a(H-CHR_1R_2) - 15.8$	0.9892
7	Me_2O^+	$pK_a(E^+-CHR_1R_2) = 0.76 pK_a(H-CHR_1R_2) - 5.1$	0.9649
8	Me_2S^+	$pK_a(E^+-CHR_1R_2) = 0.73 pK_a(H-CHR_1R_2) - 13.8$	0.9772
9	Me_2SO^+	$pK_a(E^+-CHR_1R_2) = 0.55 pK_a(H-CHR_1R_2) - 13.1$	0.9889
10	Me_2Se^+	$pK_a(E^+-CHR_1R_2) = 0.86 pK_a(H-CHR_1R_2) - 15.0$	0.9933

mental characterization. Here we show that by using state-of-the-art methods in computational chemistry, a carefully calibrated theoretical protocol can reliably predict the pK_a values of structurally unrelated ylide precursors in DMSO with an error bar of ca. 1.6–1.9 pK_a units. Importantly, this theoretical approach is essentially an *ab initio* one, with almost no recourse to experimental data. With the authorized theoretical protocol in hand, we develop the *first*, extensive scale of ylide thermodynamic stability that is expected to find applications in synthetic organic chemistry. The good agreement between calculated and available experimental results (both quantitatively and qualitatively) confirms that the theoretical approach described here can be employed to obtain useful chemical results of relatively high accuracy.

4. Computational Methodologies

All the calculations were performed with the Gaussian03 programs,²⁴ using a HP Superdome Sever (32 × 1.5 GHz Itanium 2 Madison CPU). Geometry optimizations were conducted with the B3LYP/6-31G(d) and B3LYP/6-31+G(d) methods. Each optimized structure was confirmed by the frequency calculation at the same level to be the real minimum without any imaginary vibration frequency. For compounds that had multiple conformations, efforts were made to find the lowest energy conformation by comparing the structures optimized from different starting geometries.

Harmonic vibrational frequencies were calculated by using the B3LYP/6-31G(d) method from the optimized geometries. Zero-point vibrational energy (ZPE) corrections were obtained by using unscaled frequencies. Single-point electronic energies were then calculated at the B3LYP/6-311+G(3df,2p) or ONIOM/G3B3 methods. The free energy change was then obtained after correction with ZPE, thermal corrections (0→298 K), and the entropy terms. It is worth noting that all the calculated gas-phase free energies correspond to the reference state of 1 atm, 298 K.

To calculate solvation energies, we used the CPCM model of Barone and Cossi²⁵ at the HF/6-31+G(d,p) level¹¹ (Solution method = Matrix Inversion, Polarization charges = Total charges, Cavity = GePol (RMin = 0.200, OFac = 0.890)). The default sphere list was used, where NSphG = 18, radii = Bondi. The gas-phase geometry was used for all of the solution-phase calculations, as it has been demonstrated that the change of geometry by the solvation effect is usually not significant for relatively rigid organic molecules.¹² Furthermore, geometry optimization in solution often fails to converge^{11,14b} making this approach less user-friendly. All the solution-phase free energies reported in the paper correspond to the reference state of 1 mol/L, 298 K.

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Supporting Information Available: Cartesian coordinates of optimized structures and Detailed thermodynamic data. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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