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1,2,3-Triazoles: Gas Phase Properties

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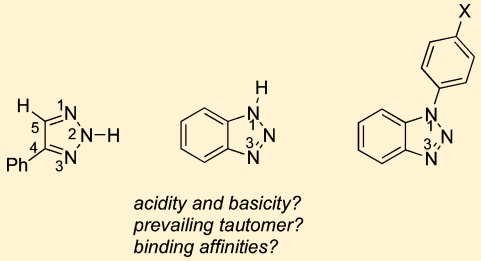
Supporting Information

ABSTRACT: 1,2,3-Triazoles have come to the forefront as compounds of import in a vast number of applications. The fundamental properties of these species, however, remain largely unknown. Herein, the gas phase properties of 4-phenyl-1,2,3-triazole, benzotriazole, and a series of 1-phenylbenzotriazoles are described. Proton affinity and acidity values are computed and measured. Furthermore, ion−molecule reactions and H/D exchange studies are used to ascertain tautomer prevalence for the 4-phenyl species.



INTRODUCTION

Since the discovery of "click chemistry" to synthesize substituted 1,2,3-triazoles via copper-catalyzed alkyne−azide 1,3-dipolar addition, these species have come to the forefront as important heterocycles in chemistry and biology.[1−26]

Click chemistry results in N1-substituted triazoles; we have in recent years developed a cascade reaction to make 4,5-disubstituted NH-1,2,3-triazoles, which gives us access to the regioselective synthesis of N2-substituted-1,2,3-triazoles.[27−29] We have also focused on the development of triazoles as effective ligands for organometallic catalysts, particularly as an alternative to *N*-heterocyclic carbenes.[30−37]

Fundamental studies on the properties of 1,2,3-triazoles are scarce.[38−41] In this paper, we describe our studies of 4-phenyl-1,2,3-triazole, benzotriazole, and a series of substituted 1-phenylbenzotriazoles. Such species are important precursors to functionalized triazoles, as well as novel ligands for gold catalysts.[27,28,30,32−37,42−46] Furthermore, the gas phase proton affinity of 4-phenyl-1,2,3-triazole had been previously studied, yielding some ambiguous results.[39] In this paper, we characterize the fundamental gas phase properties (acidity, basicity, and tautomer preference) of these triazoles.

RESULTS AND DISCUSSION

4-Phenyl-1,2,3-triazole (1). *i. Calculations: 4-Phenyl-1,2,3-triazole Tautomers, Acidity, Proton Affinity.* We first studied 4-phenyl-1,2,3-triazole (**1**), which had been the subject of a previous study, but with some ambiguous results (*vide supra*).[39] This particular compound is intriguing as there are eight possible tautomeric structures (five lowest are shown in Figure 1; three highest are in Supporting Information). In our experience DFT methods generally yield accurate values for thermochemical properties of heterocyclic rings, so we utilized B3LYP/6-31+G(d) to calculate the relative tautomeric stabilities, acidities (ΔH_{acid}), and proton affinities (PA).[47−52] Of the eight possible tautomeric structures, three are within 5 kcal mol^{-1} (**1a**, **1b**, **1c**).

The most stable tautomer "N2H" (**1a**) is calculated to be 3.9 kcal mol^{-1} more stable than the "N1H" tautomer **1b**. The "N3H" tautomer **1c** is 0.7 kcal mol^{-1} less stable than **1b**. We also calculated the acidities and basicities of the three most stable tautomers. The most acidic site of the N2H tautomer **1a** is predicted to be the N2−H (ΔH_{acid} = 337.1 kcal mol^{-1}). (We calculated just one C−H acidity on each ring to show that those sites will be less acidic than the N−H sites). The most acidic site of the N1H tautomer **1b** is the N1−H (ΔH_{acid} = 333.2 kcal mol^{-1}) and that of the N3H tautomer is the N3−H (ΔH_{acid} = 332.5 kcal mol^{-1}). Note that the differences in acidity among **1a**, **1b**, and **1c** are the same as the relative differences in tautomer stability, since the same anion structure is formed upon deprotonation of all three tautomers (*vide supra*). The most basic site of tautomer **1a** is the N3 (PA = 205.3 kcal mol^{-1}), though this site is only 3 kcal mol^{-1} more basic than the N1 site. For the N1H tautomer **1b**, the N3 is quite basic, with a calculated PA of 219.2 kcal mol^{-1}. When protonated, the N3H tautomer **1c** has the same structure as the protonated N1H tautomer **1b**; therefore, the PA of **1c** is 0.7 kcal mol^{-1} higher than that of **1b** (PA = 219.9 kcal mol^{-1}, at N1).

ii. Experiments: 4-Phenyl-1,2,3-triazole Acidity. We measured the acidity of 4-phenyl-1,2,3-triazole using acidity bracketing (details in the Experimental Section). The conjugate base of 4-phenyl-1,2,3-triazole deprotonates 2-chloropropionic acid (ΔH_{acid} = 337.0 ± 2.1 kcal mol^{-1}); however, the reaction in the opposite direction (2-chloropropionate with 4-phenyl-1,2,3-triazole) does not take place (Table 1). Deprotonated 4-phenyl-1,2,3-triazole is unable to deprotonate α,α,α-trifluoromethyl-*m*-cresol (ΔH_{acid} = 339.3 ± 2.1 kcal mol^{-1}) but the cresolate does deprotonate 4-phenyl-1,2,3-triazole. We there-

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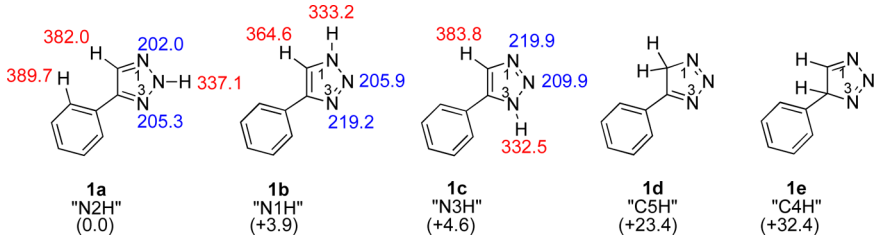

Figure 1. Possible tautomers of 4-phenyl-1,2,3-triazole (**1**). Gas phase acidities are in red; gas phase proton affinities are in blue. Relative stabilities are in parentheses. Calculations were conducted at B3LYP/6-31+G(d); reported values are ΔH (kcal mol^{-1}) at 298 K.

Table 1. Summary of Results for Acidity Bracketing of 4-Phenyl-1,2,3-triazole (1)

		proton transfer[b]	
reference compound	ΔH_{acid}[a]	ref. acid	conj. base
methylcyanoacetate	340.80 ± 0.60	−	+
α,α,-trifluoromethyl-*m*-cresol	339.3 ± 2.1	−	+
2-chloropropionic acid	337.0 ± 2.1	+	−
malononitrile	335.8 ± 2.1	+	−
per-fluoro-tert-butanol	331.6 ± 2.2	+	−

[a]Acidities are in kcal mol^{-1}.[53,54] [b]"+" indicates the occurrence and "−" indicates the absence of proton transfer.

fore bracket the ΔH_{acid} of 4-phenyl-1,2,3-triazole as 338 ± 3 kcal mol^{-1}.

iii. Experiments: 4-Phenyl-1,2,3-triazole Proton Affinity. We find that 3-bromopyridine (PA = 217.5 ± 2.0 kcal mol^{-1}) deprotonates protonated 4-phenyl-1,2,3-triazole; the opposite reaction (4-phenyl-1,2,3-triazole deprotonating protonated 3-bromopyridine) does not occur (Table 2). With 3-fluoropyr-

Table 2. Summary of Results for Proton Affinity Bracketing of 4-Phenyl-1,2,3-triazole (1)

		proton transfer[b]	
reference compound	PA[a]	ref. base	conj. acid
pyridine	222.3 ± 2.0	+	−
butylamine	220.2 ± 2.0	+	−
3-bromopyridine	217.5 ± 2.0	+	−
3-fluoropyridine	215.6 ± 2.0	−	+
2-chloropyridine	215.3 ± 2.0	−	+
o-toluidine	212.9 ± 2.0	−	+
aniline	210.9 ± 2.0	−	+
2,4-pentadione	208.8 ± 2.0	−	+

[a]PAs are in kcal mol^{-1}.[53] [b]"+" indicates the occurrence and "−" indicates the absence of proton transfer.

idine (PA = 215.6 ± 2.0 kcal mol^{-1}), the reference base does not deprotonate protonated 4-phenyl-1,2,3-triazole, but 4-phenyl-1,2,3-triazole does deprotonate protonated 3-fluoropyridine, putting the PA at 217 ± 3 kcal mol^{-1}.

An examination of the computational versus experimental results indicates some discrepancies (Table 3). The most stable tautomer **1a** has a predicted acidity of 337.1 kcal mol^{-1}, which is consistent with the experimentally bracketed value (338 kcal mol^{-1}). In contrast, the calculated PA value for the more stable tautomer **1a**, 205.3 kcal mol^{-1} does not agree with the bracketed PA (217 kcal mol^{-1}). Instead, the measured PA corresponds to the less stable tautomer (**1b** or **1c**). These results seem to imply that, in our acidity studies, tautomer **1a** predominates, whereas in our PA studies, tautomer **1b**

Table 3. Calculated (B3LYP/6-31+G(d); 298 K) and Experimental Acidity and Proton Affinity Data for 4-Phenyl-1,2,3-triazole (1)

substrate	relative tautomer stability[a]	calculated value	experimental value[b]
ΔH_{acid}[a]			
4-phenyl-1,2,3-triazole (**1**)			338
"N2H" tautomer (**1a**)	0.0	337.1	
"N1H" tautomer (**1b**)	3.9	333.2	
"N3H" tautomer (**1c**)	4.6	332.5	
PA[a]			
4-phenyl-1,2,3-triazole (**1**)			217
"N2H" tautomer (**1a**)	0.0	205.3	
"N1H" tautomer (**1b**)	3.9	219.2	
"N3H" tautomer (**1c**)	4.6	219.9	

[a]Values are in kcal mol^{-1}. [b]Experimental value is from bracketing measurement; error is ±3 kcal mol^{-1}.

predominates (or maybe even **1c**, though calculations indicate that **1c** should be even less stable than **1b**).

The PA of **1** was measured previously by Abboud and coworkers, who obtained a value similar to ours (216 kcal mol^{-1}, using the equilibrium method in an FTMS).[39] The authors were unable to explain why the measured PA corresponded to the less stable tautomer **1b** so they made the assumption that "the phenomenon is a thermodynamic one and involves the most stable neutral tautomer or isomer and the most stable cation, even if these are not directly linked...".[39] This explanation seems unsatisfactory to us; all proton transfers must occur within ion−molecule complexes and reactants and products must in fact be "directly linked". We therefore must explain why the measured acidity points to the predominance of tautomer **1a** yet the proton affinity to the less stable tautomer **1b**.

We first considered the possibility that the calculations are inaccurate. To test the accuracy of the calculations, we examined the methylated derivatives 1-methyl-4-phenyl-1,2,3-triazole and 2-methyl-4-phenyl-1,2,3-triazole (Figure 2). These methylated derivatives cannot tautomerize, so we can compare calculated and experimentally measured PA values without the complicating factor of tautomer ambiguity.

Calculations predict that the most basic site of 1-methyl-4-phenyl-1,2,3-triazole is the N3, with a PA of 224.3 kcal mol^{-1}. The bracketing reaction of 1-methyl-4-phenyl-1,2,3-triazole with 3-picoline proceeds in both directions, placing the PA at 226 ± 3 kcal mol^{-1} (Table in SI).

The most basic site of 2-methyl-4-phenyl-1,2,3-triazole is predicted to be the N3, with a calculated PA of 210.8 kcal mol^{-1}. Bracketing experiments indicate a "crossover" point

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Figure 2. Computed proton affinities for 1-methyl- and 2-methyl-4-phenyl-1,2,3-triazole. Calculations were conducted at B3LYP/6-31+G(d); reported values are ΔH (kcal mol^{-1}) at 298 K.

between 210.9 and 212.4 kcal mol^{-1} (Table in SI). *N*-Methylacetamide is able to deprotonate protonated 2-methyl-4-phenyl-1,2,3-triazole, but 2-methyl-4-phenyl-1,2,3-triazole cannot deprotonate protonated *N*-methylacetamide. Aniline does not deprotonate protonated 2-methyl-4-phenyl-1,2,3-triazole, but the opposite reaction does occur. We therefore bracket the PA of 2-methyl-4-phenyl-1,2,3-triazole as 212 ± 3 kcal mol^{-1}.

The studies with the methylated derivatives indicate that our DFT calculations should be quite accurate (for 1-methyl-4-phenyl-1,2,3-triazole, the computed versus experimental PA is 224 versus 226 kcal mol^{-1}; for the 2-methyl derivative, it is 211 versus 212 kcal mol^{-1}).

If we trust our calculations, we still have a mystery. The acidity measurement is consistent with structure **1a**: our experimental ΔH_{acid} of 338 kcal mol^{-1} is closer to that calculated for **1a** (337 kcal mol^{-1}) than that for **1b** (333 kcal mol^{-1}, Table 3). However, the experimental PA is consistent with **1b**: the measured PA is 217 kcal mol^{-1}, which is much closer to the calculated PA for **1b** (219.2 kcal mol^{-1}) than for **1a** (205.3 kcal mol^{-1}, Table 3).

First, let us consider proton affinity. In the bracketing experiment, two reactions are conducted: protonated reference base (BH$^+$) with the triazole, and protonated triazole with the neutral reference base (B).

For the reaction of the protonated B (BH$^+$) with **1** (column with header "conj. acid" in Table 2 (fourth column)), 4-phenyl-1,2,3-triazole can deprotonate protonated 3-fluoropyridine (PA = 215.6 kcal mol^{-1}) and any protonated base with a PA lower than 215 kcal mol^{-1}. This result would appear to be consistent with the presence of at least some **1b**, because **1a** should not be basic enough to deprotonate protonated reference bases with PA values higher than 205 kcal mol^{-1}. However, as depicted in Figure 3, there is actually a possibility that **1a** could ultimately undergo proton transfer reactions with bases with PAs over 205 kcal mol^{-1}. In Figure 3, the protonated reference base BH$^+$ first forms an ion–molecule complex with triazole **1a**, which is roughly 20 kcal mol^{-1} exothermic (to form ***A***).[55,56] Proton transfer between the most basic site of **1a** (N3, calculated PA = 205 kcal mol^{-1}) and BH$^+$ is endothermic (to form complex ***B***), but allowed energetically, since the complex is still less than the total energy of the system (indicated by the dotted line).[56] Now the reference base B can access the N2–H proton (exothermic by 5 kcal mol^{-1}) to form the **1c** tautomer of the triazole (complex ***C***). The N1 of **1c** is basic enough to deprotonate the protonated BH$^+$ (to form complex ***D***), which can then lead to the observable products, B and protonated triazole, in an overall thermoneutral reaction. The structure of the protonated triazole would not be that of **1aH**$^+$ but, instead, that of **1bH**$^+$ (or **1cH**$^+$ - these have the same structure). By mass spectrometry, however, one only tracks the *m*/*z* ratio, so the presence of any protonated triazole yields the "+" in Table 2. Computationally, the path in Figure 3 would be predicted to be accessible for any base with a PA of about 215 kcal mol^{-1} or lower, which is what we observe experimentally (Table 2).

Thus, from the results for the proton transfer in this direction, we can only conclude that we may have **1a**, **1b**, or a mixture; any combination of these species could result in the observed proton transfers shown in Table 2.

What about the opposite direction? When B is allowed to react with protonated **1**, we find that reference bases with PAs below that of 3-bromopyridine (PA = 217.5 kcal mol^{-1}) do not appear to deprotonate protonated triazole (Table 2, third column). This would imply that only **1bH**$^+$ (which has the same structure as **1cH**$^+$) is present. However, does this mean that the initial vaporized triazole was only structure **1b**?

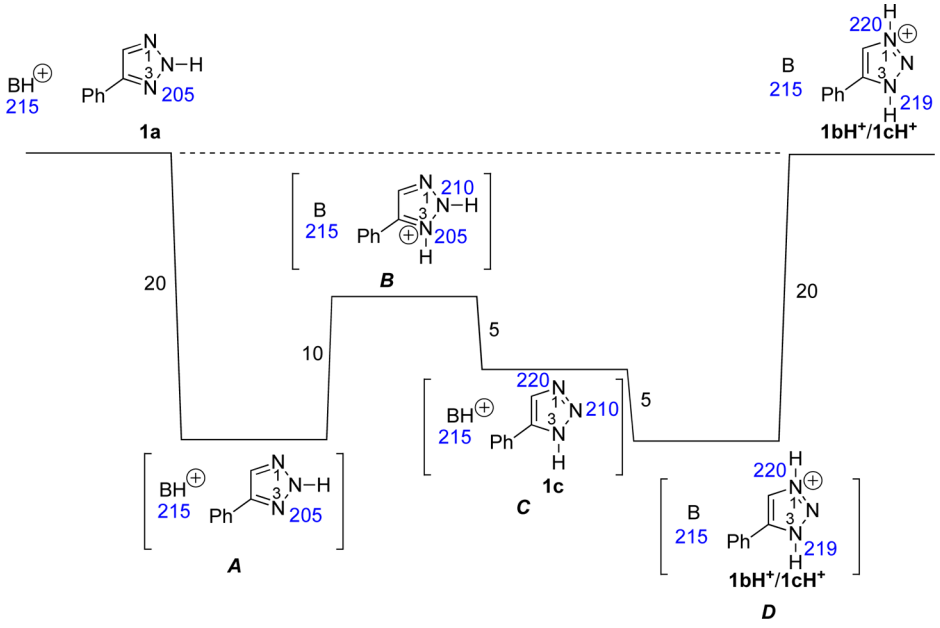

Figure 3. Pathway by which a protonated reference base BH$^+$ could react with the N2H tautomer of 4-phenyl-1,2,3-triazole (**1a**). Values are in kcal mol^{-1}. Blue values are PAs; for the triazole, values are calculated at B3LYP/6-31+G(d)(ΔH).

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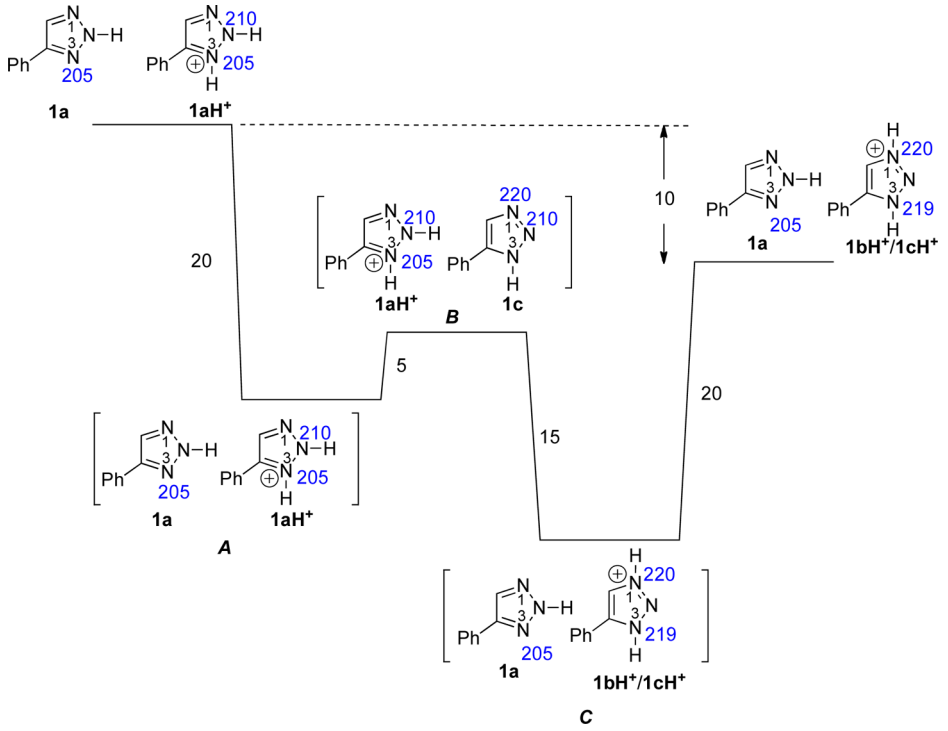

Figure 4. Pathway for reaction of neutral and protonated forms of the N2H tautomer of 4-phenyl-1,2,3-triazole (**1a** with **1aH**$^+$). Values are in kcal mol^{-1}. Blue values are PAs; for the triazole, values are calculated at B3LYP/6-31+G(d) (ΔH).

In our experiment, we sublime the neutral triazole into the gas phase via the solids probe. Hydronium ion (H_3O^+) is then used to protonate the triazole. Because crystal structures of the neutral triazole indicate that **1a** is the most stable structure in the solid state, we would expect the initially vaporized neutral triazole to be the more stable structure **1a**.[39] However, after protonation to form **1aH**$^+$, further reaction with neutral **1a** can take place to form the thermodynamically more stable protonated structure **1bH**$^+$ (Figure 4). Essentially, by the time we form protonated **1** and transfer it to the second cell for reaction (see Experimental Section for details), the **1H**$^+$ ions are predominantly **1bH**$^+$.

Thus, in the direction where we bracket protonated triazole with reference bases B, we probably have only **1bH**$^+$ (although we may have started under our gas phase conditions with some amount of, if not all, **1a**). To probe this possibility and our theory that **1aH**$^+$ could be isomerizing to **1bH**$^+$, we performed the protonation of **1** under conditions that would minimize isomerization: we remove the protonated **1** from the neutral **1** environment as quickly as possible. First, we vaporize **1** into the gas phase via a heated solids probe. Second, we allow hydronium to protonate **1** and form **1H**$^+$. At this point, we transfer protonated triazole out of the neutral triazole environment, to the second adjoining cell of our FTMS, to allow it to react with reference bases. We varied the time that we waited after protonation and before transfer out of the neutral triazole environment. We then measured the efficiency of proton transfer between the protonated triazole and aniline, which has a PA of 211 kcal mol^{-1}. With a PA of 211, aniline will only be protonated if **1aH**$^+$ is present. As can be seen from Table 4, as the time before transfer decreases, the efficiency of the reaction by which aniline deprotonates protonated triazole increases. That is, when the protonated triazole is taken out of the neutral triazole environment more quickly, we see more proton transfer with aniline. This implies that more **1aH**$^+$ is present. We therefore believe that, under our normal conditions (4 s before transfer), isomerization from **1aH**$^+$ to **1bH**$^+$ occurs. Thus, by the time we add the reference base, we are only seeing results with **1bH**$^+$.

Table 4. Efficiencies of Reactions between Protonated 4-Phenyl-1,2,3-triazole (1H$^+$) and Aniline as a Function of Time before Transferring Protonated 4-Phenyl-1,2,3-triazole from Neutral Triazole Environment

time before transfer (seconds)	efficiency of proton transfer from **1H**$^+$ to aniline (PA = 211 kcal mol^{-1})
4	1.2%
0.2	7.0%
0.05	11.4%

Another way to test this theory is through the use of an appropriately chosen deuterated reference base. Ethylene glycol-O-d_2 has a PA of 195 kcal mol^{-1}. If allowed to react with **1aH**$^+$, we would expect exchange of a proton for a deuteron, resulting in a unit increase in the mass-to-charge ratio (m/z 146 to m/z 147, Figure 5). This reaction should be thermoneutral.[57,58]

In contrast, because of its higher PA, **1bH**$^+$ should not be able to exchange its proton (Figure 6).

Again, we varied the time in which the protonated triazole remained in the neutral triazole environment (before transfer to the second cell for reaction with deuterated ethylene glycol). The longer we wait after the protonation step (and before transfer out of the neutral triazole environment), the more neutral-triazole-catalyzed isomerization should occur (to transform **1aH**$^+$ to **1bH**$^+$). We find that at shorter times before transfer (1 and 2 s), we do in fact see m/z 147, indicating that H/D exchange takes place. For 4 s and higher, we no longer see an appreciable amount of m/z 147. This would indicate that at shorter times before transfer, we have **1aH**$^+$, which is capable of

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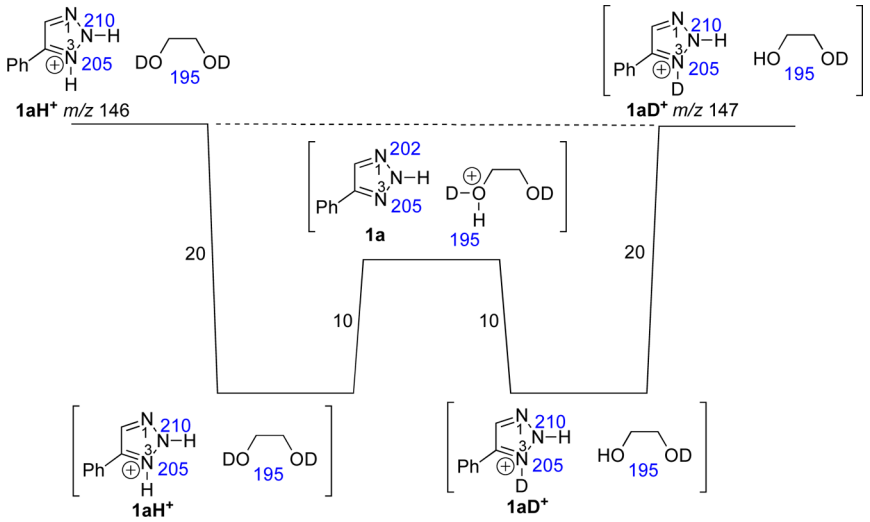


Figure 5. Pathway for reaction of protonated N2H tautomer of 4-phenyl-1,2,3-triazole (**1aH**$^+$) with ethylene glycol-O-d_2. Values are in kcal mol^{-1}. Blue values are PAs; for the triazole, values are calculated at B3LYP/6-31+G(d)(ΔH).

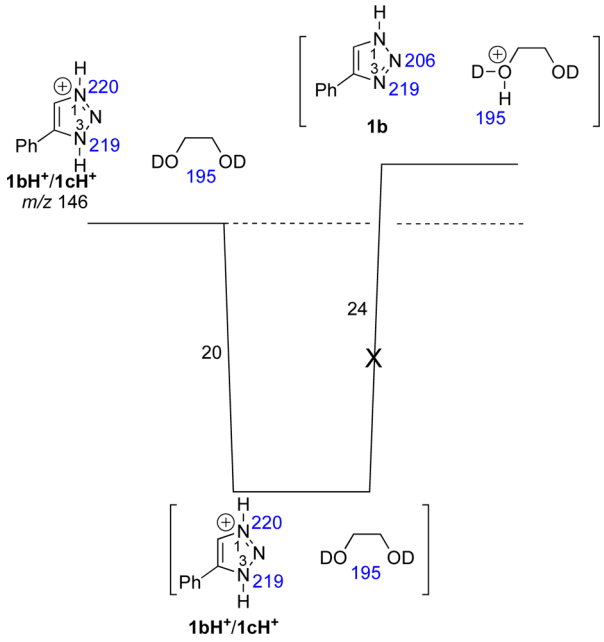
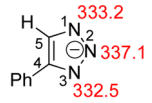


Figure 6. Pathway for reaction of protonated N1H tautomer of 4-phenyl-1,2,3-triazole (**1bH**$^+$) with ethylene glycol-O-d_2. Values are in kcal mol^{-1}. Blue values are PAs; for the triazole, values are calculated at B3LYP/6-31+G(d)(ΔH).

undergoing H/D exchange. At longer times before transfer, the ion population has isomerized to **1bH**$^+$ and reaction with deuterated ethylene glycol does not effect H/D exchange. This lends further evidence to our theory that our vaporized triazole definitely has **1a** present, which when protonated forms **1aH**$^+$, which, given enough time in a neutral triazole environment, will isomerize to **1bH**$^+$. Although we know that **1a** must be present, we cannot know whether **1b** is or is not present.[59]

Can our acidity experiments shed more light on this puzzle? The bracketed value of 338 kcal mol^{-1} is consistent with the calculated acidity value of **1a** (337 kcal mol^{-1}). Does this indicate the presence of **1a** only? First, let us consider the reaction of deprotonated triazole with reference acids (third column in Table 1). Whether we have **1a** or **1b** present, deprotonation results in the same structure (deprotonated **1**), so in this direction one brackets the most basic site, which is the N2.



deprotonated **1**

In the opposite direction, conjugate bases of reference acids are allowed to react with **1** (Table 1, rightmost column). If **1b** (ΔH_{acid} (calculated) = 333 kcal mol^{-1}, Figure 1) were present, one would expect the conjugate bases of 2-chloropropionic acid (ΔH_{acid} = 337.0 kcal mol^{-1}) and malononitrile (ΔH_{acid} = 335.8 kcal mol^{-1}) to effect proton transfer, but they do not ("–" in rightmost column of Table 1). This result certainly implies that little to no **1b** is present. There is always the possibility that a base with PA higher than the acidity of **1b** follows the path shown in Figure 7, though it seems unlikely that ion–molecule complex B would *never* decomplex to give deprotonated triazole (indicating proton transfer). Because of this possible path, however, we cannot fully discount the presence of **1b** though we consider it unlikely.

Thus, our results indicate the certain presence of **1a**, with a possibility of some **1b**, under our gas phase conditions. This is consistent with the calculations, which indicate that **1a** is the most stable structure.[60]

Benzotriazoles: Parent and 1-Phenyl-Substituted. *Benzotriazole (Parent, 2). i. Calculations: Benzotriazole Tautomers, Acidity, Proton Affinity.* Benzotriazole has two possible tautomeric structures (Figure 8). The most stable tautomer "N1H" (**2a**) is calculated to be only 0.2 kcal mol^{-1} more stable than the "N2H" tautomer **2b**. We also calculated the acidities and basicities of both tautomers. The most acidic site of **2a** is predicted to be the N1–H (ΔH_{acid} = 334.0 kcal mol^{-1}). (One C–H acidity was calculated to show that those sites will be less acidic than the N–H sites). For the N2H tautomer **2b**, the N–H has a ΔH_{acid} of 333.8 kcal mol^{-1} (0.2 kcal mol^{-1} less acidic than **2a**, which also reflects the relative tautomer stability). The most basic site of tautomer **2a** is the N3 (PA = 217.5 kcal mol^{-1}). For **2b**, the N1 and N3 are equivalent and have a calculated PA of 205.0 kcal mol^{-1}.

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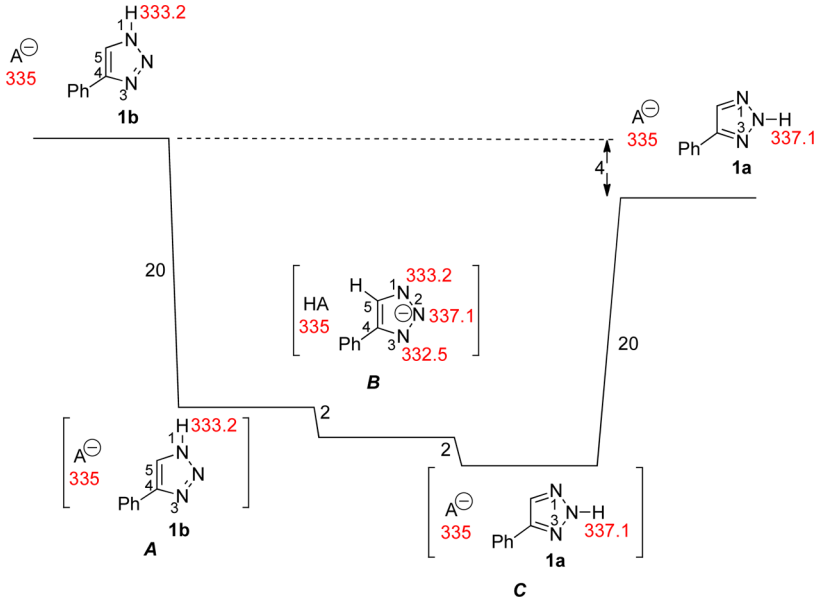

Figure 7. Pathway by which conjugate bases of reference acids could react with **1b**. Values are in kcal mol^{-1}. Red values are ΔH_{acid} values; for the triazole, values are calculated at B3LYP/6-31+G(d)(ΔH).

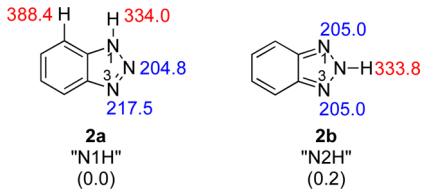

Figure 8. Two possible tautomeric structures of benzotriazole (**2**). Gas phase acidities are in red; gas phase proton affinities are in blue. Relative stabilities are in parentheses. Calculations were conducted at B3LYP/6-31+G(d); reported values are ΔH (kcal mol^{-1}) at 298 K.

ii. Experiments: Benzotriazole Acidity. We measured the acidity of benzotriazole using acidity bracketing (Table 5). The conjugate base of benzotriazole deprotonates 2-chloropropionic acid (ΔH_{acid} = 337.0 ± 2.1 kcal mol^{-1}); the reaction in the opposite direction (2-chloropropionate with benzotriazole) also occurs (Table 5). We therefore bracket the ΔH_{acid} of benzotriazole as 337 ± 3 kcal mol^{-1}.

Table 5. Summary of Results for Acidity Bracketing of Benzotriazole (2)

		proton transfer[b]	
reference compound	ΔH_{acid}[a]	ref. acid	conj. base
2,4-pentadione	343.8 ± 2.1	−	+
methylcyanoacetate	340.8 ± 2.1	−	+
α,α,α-trifluoromethyl-*m*-cresol	339.3 ± 2.1	−	+
2-chloropropionic acid	337.0 ± 2.1	+	+
malononitrile	335.8 ± 2.1	+	−
pyruvic acid	333.5 ± 2.9	+	−
per-fluoro-tert-butanol	331.6 ± 2.2	+	−
difluoroacetic acid	331.0 ± 2.2	+	−
1,1,1-trifluoro-2,4-pentadione	328.3 ± 2.9	+	−

[a]Acidities are in kcal mol^{-1}.[53,54] [b]"+" indicates the occurrence and "−" indicates the absence of proton transfer.

iii. Experiments: Benzotriazole Proton Affinity. In bracketing the PA of benzotriazole, we find that 3-chloropyridine (PA = 215.9 ± 2.0 kcal mol^{-1}) deprotonates protonated benzotriazole; the opposite reaction (benzotriazole deprotonating protonated 3-chloropyridine) also occurs (Table 6). We therefore bracket the PA of benzotriazole to be 216 ± 3 kcal mol^{-1}.

Table 6. Summary of Results for Proton Affinity Bracketing of Benzotriazole (2)

		proton transfer[b]	
reference compound	PA[a]	ref. base	conj. acid
pyridine	222.3 ± 2.0	+	−
propylamine	219.4 ± 2.0	+	−
dimethylacetamide	217.0 ± 2.0	+	−
3-chloropyridine	215.9 ± 2.0	+	+
methylamine	214.9 ± 2.0	−	+
m-toluidine	214.1 ± 2.0	−	+
aniline	210.9 ± 2.0	−	+
2,4-pentadione	208.8 ± 2.0	−	+

[a]PAs are in kcal mol^{-1}.[53] [b]"+" indicates the occurrence and "−" indicates the absence of proton transfer.

We also examined the "locked" tautomer 1-methylbenzotriazole (**3**, Figure 9), to assess the accuracy of the calculations (since there is no tautomer ambiguity for this compound). We bracket a gas phase acidity of 379 ± 3 kcal mol^{-1} (calculated value is 379.1 kcal mol^{-1}) and a gas phase proton affinity of 223

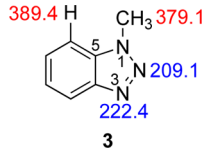

Figure 9. Calculated properties of 1-methylbenzotriazole (**3**). Gas phase acidities are in red; gas phase proton affinities are in blue. Calculations were conducted at B3LYP/6-31+G(d); reported values are ΔH (kcal mol^{-1}) at 298 K.

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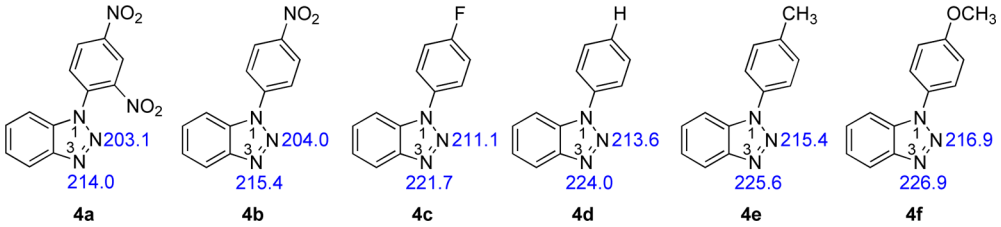

Figure 10. Calculated proton affinities of 1-phenylbenzotriazoles studied herein. Calculations were conducted at B3LYP/6-31+G(d); reported values are ΔH (kcal mol^{-1}) at 298 K.

± 3 kcal mol^{-1} (calculated value is 222.4 kcal mol^{-1}), indicating that the calculations do appear to be accurate.[61]

Thus, the experimental acidity of the *parent* benzotriazole **1** is measured to be 337 ± 3 kcal mol^{-1}. This value is consistent with an earlier measurement by Taft and co-workers (338 ± 2 kcal mol^{-1}).[62] Because the calculated acidity of the N1H and N2H tautomers is roughly the same (334 kcal mol^{-1}, where the deprotonated structures for both tautomers is the same), the experimental acidity value cannot be used to differentiate which structure(s) exist in the gas phase under our conditions. The experimental proton affinity is 216 ± 3 kcal mol^{-1}. This value is consistent with the N1H tautomer **2a** (calculated PA = 217.5 kcal mol^{-1}) but not the N2H tautomer **2b** (PA = 205.0 kcal mol^{-1}). Because the calculations predict that **2b** should be only minimally less stable (0.2 kcal mol^{-1}) than **2a**, one might expect experimental evidence for the presence of **2b**. However, this system would have the same caveats that the 4-phenyl-1,2,3-triazole system has, wherein protonated bases can cause tautomerization, and so we cannot be sure of the structures present under our conditions: it could be **2a**, **2b**, or some mixture thereof. Previous gas phase studies (UV, FTIR) give conflicting results as to which tautomer predominates, although solid state and aqueous studies point to the N1H tautomer **2a**.[63−74]

*1-Phenylbenzotriazoles (**4**).* Having characterized the parent benzotriazole, we moved on to a system that might be useful synthetically, the 1-phenylbenzoatriazoles (Figure 10). We have been utilizing benzotriazoles as ligands for gold catalysts, and have found that triazole ligands can effect a reversal in selectivity for reactions catalyzed by gold catalysts with triazole versus a more traditional (such as triphenylphosphine) ligand.[30,32−37] We were therefore interested in characterizing a series of phenylbenzotriazoles with varying substitution, to assess the effect of that substitution on proton affinity. Also, we were interested in whether substrate proton affinity and binding to gold would be related, in which case the proton affinity could be used as a guide for designing effective ligands for gold catalysts.

*1-Phenylbenzotriazole (**4d**). i. Calculations: 1-Phenylbenzotriazole (**4d**) Proton Affinity.* The most basic site of 1-phenylbenzotriazole (**4d**, Figure 10) is the N3, which has a calculated PA of 224.0 kcal mol^{-1}. The N2 position is about 10 kcal mol^{-1} less basic (Figure 10).

*ii. Experiments: 1-Phenylbenzotriazole (**4d**) Proton Affinity.* The PA of 1-phenylbenzotriazole was experimentally bracketed (bracketing tables for all phenylbenzotriazoles are in the Supporting Information). The reaction of protonated 1-phenylbenzotriazole with cyclohexylamine proceeds, as does the reaction of protonated cyclohexylamine with 1-phenylbenzotriazole. Therefore, we bracket the PA of 1-phenylbenzotriazole to be 223 ± 3 kcal mol^{-1}.

*2′,4′-Dinitro-1-phenylbenzotriazole (**4a**). i. Calculations: 2′,4′-Dinitro-1-phenylbenzotriazole (**4a**) Proton Affinity.* 2′,4′-Dinitro-1-phenylbenzotriazole (**4a**) has a calculated PA of 214.0 kcal mol^{-1}, at the N3 site (Figure 10). The N2 site is less basic, with a PA of 203.1 kcal mol^{-1}.

*ii. Experiments: 2′,4′-Dinitro-1-phenylbenzotriazole (**4a**) Proton Affinity.* Bracketing experiments with 2′,4′-dinitro-1-phenylbenzotriazole were carried out (Table in SI). While *m*-toluidine (PA = 214.1 ± 2.0 kcal mol^{-1}) can deprotonate protonated 2′,4′-dinitro-1-phenylbenzotriazole, the opposite reaction does not occur (2′,4′-dinitro-1-phenylbenzotriazole cannot deprotonate protonated toluidine). *N*-Methylacetamide (PA = 212.4 ± 2.0 kcal mol^{-1}) is unable to deprotonate 2′,4′-dinitro-1-phenylbenzotriazole, but the opposite reaction occurs. We therefore bracket the PA of 2′,4′-dinitro-1-phenylbenzotriazole to be 213 ± 3 kcal mol^{-1}.

*4′-Nitro-1-phenylbenzotriazole (**4b**). i. Calculations: 4′-Nitro-1-phenylbenzotriazole (**4b**) Proton Affinity.* 4′-Nitro-1-phenylbenzotriazole (**4b**) has a calculated PA of 215.4 kcal mol^{-1}, at the N3 site (Figure 10). The N2 site has a lower PA of 204.0 kcal mol^{-1}.

*ii. Experiments: 4′-Nitro-1-phenylbenzotriazole (**4b**) Proton Affinity.* The reaction between 4′-nitro-1-phenylbenzotriazole and 3-chloropyridine (PA = 215.9 ± 2.0 kcal mol^{-1}) proceeds in both directions; we therefore bracket the PA as 216 ± 3 kcal mol^{-1} (Table in SI).

*4′-Fluoro-1-phenylbenzotriazole (**4c**). i. Calculations: 4′-Fluoro-1-phenylbenzotriazole (**4c**) Proton Affinity.* 4′-Fluoro-1-phenylbenzotriazole (**4c**) has a calculated PA of 221.7 kcal mol^{-1}, at the N3 site (Figure 9). The less basic N2 site has a calculated PA of 211.1 kcal mol^{-1}.

*ii. Experiments: 4′-Fluoro-1-phenylbenzotriazole (**4c**) Proton Affinity.* We bracketed the PA of 4′-fluoro-1-phenylbenzotriazole (Table in SI). Pyridine (PA = 222.3 ± 2.0 kcal mol^{-1}) can deprotonate protonated 4′-fluoro-1-phenylbenzotriazole, but isobutylamine (PA = 221.0 ± 2.0 kcal mol^{-1}). In the opposite direction, 4′-fluoro-1-phenylbenzotriazole can deprotonate protonated isobutylamine, but not protonated pyridine. We therefore bracket the PA of 4′-fluoro-1-phenylbenzotriazole as 222 ± 3 kcal mol^{-1}.

*4′-Methyl-1-phenylbenzotriazole (**4e**). i. Calculations: 4′-Methyl-1-phenylbenzotriazole (**4e**) Proton Affinity.* The most basic site of 4′-methyl-1-phenylbenzotriazole (**4e**) has a calculated PA of 225.6 kcal mol^{-1}, at the N3 site (Figure 10). The N2 site is less basic and has a PA of 215.4 kcal mol^{-1}.

*ii. Experiments: 4′-Methyl-1-phenylbenzotriazole (**4e**) Proton Affinity.* We bracketed the PA of 4′-methyl-1-phenylbenzotriazole (Table in SI). The reaction with 3-picoline (PA = 225.5 ± 2.0 kcal mol^{-1}) proceeds in both directions: 3-picoline can deprotonate protonated 4′-methyl-1-phenylbenzotriazole, and 4′-methyl-1-phenybenzotriazole can deprotonate

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protonated picoline. The PA of 4′-methyl-1-phenylbenzotriazole is therefore 226 ± 3 kcal mol^{-1}.

*4′-Methoxy-1-phenylbenzotriazole (**4f**). i. Calculations: 4′-Methoxy-1-phenylbenzotriazole (**4f**) Proton Affinity.* The calculated PA of the most basic site of 4′-methoxy-1-phenylbenzotriazole (**4f**) is 226.9 kcal mol^{-1}, at N3; the N2 has a PA of 216.9 kcal mol^{-1}.

*ii. Experiments: 4′-Methoxy-1-phenylbenzotriazole (**4f**) Proton Affinity.* 3-Picoline (PA = 225.5 ± 2.0 kcal mol^{-1}) is unable to deprotonate protonated **4f**, but 4-picoline (PA = 226.4 ± 2.0 kcal mol^{-1}) can. In the opposite direction, **4f** can deprotonate protonated 3-picoline, but cannot deprotonate protonated 4-picoline. These results place the PA of 4′-methoxy-1-phenylbenzotriazole (**4f**) at 226 ± 3 kcal mol^{-1} (Table in SI).

Proton Affinity of 1-Phenylbenzotriazoles, Summary. A summary of the calculated and experimental values for the proton affinities of the 1-phenylbenzotriazoles studied herein are shown in Table 7. The experimental and computational values correlate, indicating the accuracy of the computational method for these species. As would be expected, more electron donating substituents correlate to an increase in the PA.

Table 7. Calculated (B3LYP/6-31+G(d); 298 K) and Experimental Proton Affinity Data for 1-Phenylbenzotriazoles (4), in kcal mol^{-1}

substrate	calculated value	experimental value[a]
2′,4′-dinitro-1-phenylbenzotriazole (**4a**)	214.0	213
4′-nitro-1-phenylbenzotriazole (**4b**)	215.4	216
4′-fluoro-1-phenylbenzotriazole (**4c**)	221.7	222
1-phenylbenzotriazole (**4d**)	224.0	223
4′-methyl-1-phenylbenzotriazole (**4e**)	225.6	226
4′-methoxy-1-phenylbenzotriazole (**4f**)	226.9	226

[a]Experimental value is obtained by bracketing; error is ±3 kcal mol^{-1}.

1-Phenylbenzotriazoles as Ligands. One of our primary interests is in the utility of triazoles as ligands for transition metal catalysis. We have recently reported the application of triazole ligands for tuning the reactivity of cationic gold(I) catalysts.[30,32−37] As a first step toward understanding the correlation (if any) between ligand basicity and catalyst efficacy, we conducted a study comparing our PA data with triazole binding affinity data.[30] Specifically, we measured the ^{31}P NMR shift for the binding of the 1-phenylbenzotriazoles to AuPPh$_3$ cation in chloroform (Figure 11).[75] The Au(I) complexes are generally two-coordination linear complexes. The X-ray crystallographic structures from our previous studies have confirmed this conformation for the triazole-gold complexes.[30,33,35,36] Therefore, ^{31}P NMR should provide a direct measurement of the binding ability of various triazoles toward gold cations.[76] A strong correlation between the triazole PA and the ^{31}P NMR shift was observed: as PA increases, so too does the chemical shift. This is due to the deshielding effects (toward the P-ligand) provided by the strong coordination of triazole to the opposite side of the gold cation. As a result, there is an increase of the induced magnetic field and one sees ^{31}P downfield shifts with the more strongly coordinating 1,2,3-triazole ligands (those with electron donating substituents, such as **4f**). These results show that gas phase proton affinity can be used as a predictor of ligand binding, which is useful for ligand design. The NMR experiments are not nearly as simple to carry out as a gas phase PA calculation, so this correlation, while perhaps not completely surprising, is potentially quite useful.

CONCLUSIONS

We have measured the proton affinity and acidity of 4-phenyl-1,2,3-triazole; the acidity has not heretofore been measured. Together with H/D exchange data, we can establish that under our gas phase conditions, the N2H tautomer **1a** is definitively present. Tautomer **1b** may be present, though it seems unlikely. The parent and 1-phenylbenzotriazoles have also been characterized, with previously unknown acidity and proton affinity values being assessed. A correlation between gas phase proton affinity and binding to Au(I) in solution (as measured by ^{31}P NMR shifts) is established, showing that PA can be used as an indicator of the binding ability of 1,2,3-triazoles to metal cations. These studies are thus useful for the design of catalysts containing this interesting new class of ligands.

EXPERIMENTAL SECTION

Bracketing Method. Acidity and proton affinity bracketing measurements were conducted using a Fourier Transform Ion Cyclotron Resonance Mass Spectrometer (FTMS) with a dual cell setup, which has been described previously.[47,49,50,77−79] In our FTMS, two adjoining 2-in. cubic cells are positioned collinearly with the magnetic field produced by a 3.3 T superconducting magnet. The pressure of the dual cell is pumped down to less than 1 × 10^{-9} Torr. Solid triazoles are introduced into the cell via a heatable solids probe. Hydroxide or hydronium ions are generated from water pulsed into

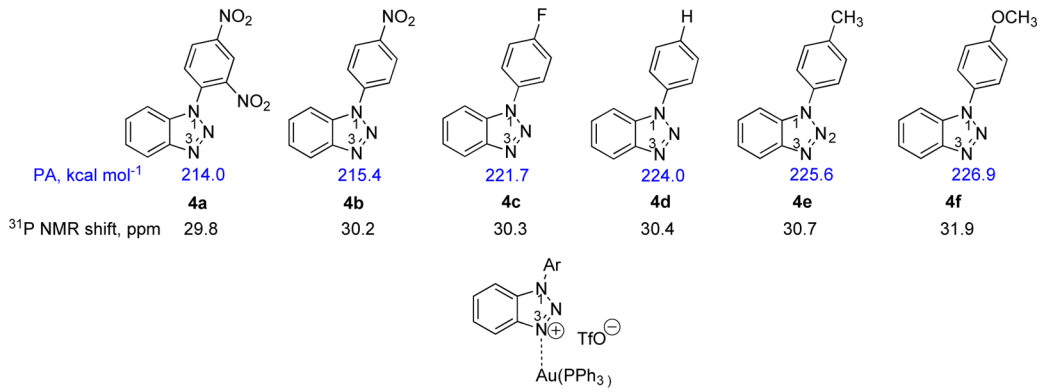

Figure 11. Calculated (B3LYP/6-31+G(d), Δ*H*, kcal mol^{-1}) PAs for a series of 1-phenylbenzotriazoles and experimental ^{31}P NMR shifts in ppm for those triazoles bound to AuPPh$_3$ cation, in CDCl$_3$.

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the cell, and ionized by an electron beam (typically 8 eV (for HO^-), or 20 eV (for H_3O^+) and 6 μA, ionization time 0.5 s). Liquid reference acids or bases are introduced via a batch inlet system or a leak valve, and allowed to react with either hydroxide (for acidity measurement) or hydronium ions (for proton affinity (PA) measurement).

The typical protocol for bracketing experiments has been described previously by us.[47,49,50,77−79] Briefly, ions are generated from a reference compound (acid or base) or the substrate whose acidity or PA is unknown (in our case, a triazole), selected, transferred to an adjoining cell via a 2-mm hole in the center of the central trapping plate, cooled by a pulse of argon (that raises the cell pressure to 10^{-5} Torr), and allowed to react with a neutral (either a reference compound or triazole). Proton transfer reactions are conducted in both directions. The occurrence of proton transfer is regarded as evidence that the reaction is exothermic ("+" in the tables).

We run bracketing reactions under pseudofirst order conditions, where the amount of the neutral substrate is in excess relative to the reactant ions. Reading the pressure from an ion gauge is often unreliable, both because of the gauge's remote location as well as varying sensitivity for different substrates.[80,81] We therefore "back out" the neutral pressure from a control reaction (described previously).[49,77,82−84]

For the ^{31}P NMR experiments, the samples were prepared with a fixed concentration of 0.05 M PPh_3Au(triazole)OTf in $CDCl_3$. The complexes were prepared and purified (through recrystallization) as previously reported.[30] To ensure accurate chemical shift measurement, 85% H_3PO_4 was used as an internal standard (0 ppm) in a sealed capillary. The NMR experiments were conducted at room temperature. Based on our previous work, we expect the complexes to be extremely stable, with no dissociation on the NMR time scale, such that the chemical shift differences should reflect the electronic effects of the phenyl ring substituents.[30]

Calculations. For all reported calculated values, B3LYP/6-31+G(d)[85−87] (using Gaussian03[88] and Gaussian09[89]) was used. Geometries were fully optimized and frequencies were calculated. No scaling factor was applied. All the acidity, proton affinity and relative stability values reported are ΔH at 298 K.

■ ASSOCIATED CONTENT

Supporting Information

Cartesian coordinates for all calculated species and full citations for references with greater than 16 authors are available. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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(58) There are other pathways by which **1aH**$^+$ can exchange its proton (including isomerization to form **1bD**$^+$) but the key point is that reaction between **1aH**$^+$ and deuterated ethylene glycol should result in a unit increase in m/z ratio.
(59) One other possibility that we should mention involves the less basic site of **1b** (N2, calculated PA = 205.9 kcal mol^{-1}). It is possible that when we shorten the time between protonation of **1** by hydronium and transfer of **1H**$^+$ to the second cell, we could get a mixture of ions resulting from the protonation of **1b** at N2 as well as N3. **1b** protonated at N2 would undergo proton transfer with aniline and exchange with deuterated ethylene glycol. However, because **1a** is calculated to be more stable and because our acidity bracketing results point toward the presence of **1a** and the absence of **1b** (*vide supra*), we think this scenario is unlikely and that some amount of **1a** must be present.
(60) Protonated **1b** and **1c** are the same structure and deprotonated **1a**, **1b**, and **1c** are also the same structure. Calculations indicate less than a 1 kcal mol^{-1} difference between the stabilities of **1b** and **1c**, so arguments that apply to the possible presence of **1b** apply to **1c** as well; that is, either and/or both could be present.
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