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# Pyrido[1,2-*a*][1,2,4]triazol-3-ylidenes as a New Family of Stable Annulated *N*-Heterocyclic Carbenes: Synthesis, Reactivity, and Their Application in Coordination Chemistry and Organocatalysis

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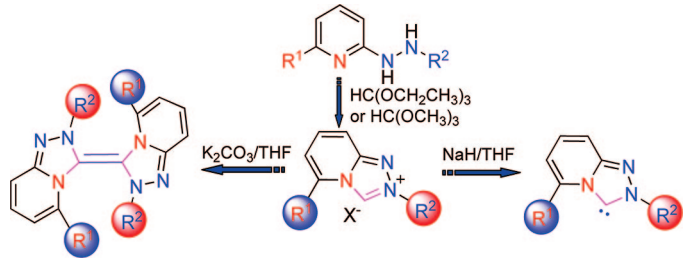


General synthetic avenues to the pyrido-annulated triazolium salts with different steric and electronic properties have been developed. This architecture can be readily altered with different *N*-alkyl or aryl substituents at the N2 position of the triazole ring and modifications to the pyridine backbone. Deprotonation of the triazolium salts **12** with NaH led to formation of stable carbenes **11** at room temperature as clearly demonstrated through ESI mass spectra and by observation of the characteristic $^{13}C$ NMR resonance for the carbene carbon at $\delta = 202-208$ ppm. In sharp contrast, treatment of these triazolium salts with $K_2CO_3$ led to dimerization of free carbenes **11**. The dimeric enetetramine $(\mathbf{11b})_2$ could react with elemental sulfur to deliver the corresponding thiourea **16** in toluene at 80 °C in good yield. A silver complex with the pyrido[1,2-*a*][1,2,4]triazol-3-ylidene is described, and the molecular structure of complex **17** was established by X-ray crystallography. The triazolium salts **12** turned out to be powerful catalysts in catalytic benzoin condensations and transesterifications at 25 °C. The catalytic activity was largely dependent on the steric and electronic nature of the $R^1$ and $R^2$ substituents of the triazolium salt. We rationalized that this type of triazolium-catalyzed benzoin condensations should undergo the "traditional" Breslow mechanism rather than the pathway of the dimer $(\mathbf{11})_2$ as the real catalytic species.

## Introduction

Since the first stable, crystalline imidazol-2-ylidene was prepared by Arduengo and co-workers in 1991,[1] *N*-heterocyclic carbenes (NHCs) have grown from being regarded as chemical curiosities to versatile ligands in transition metal mediated processes,[2,3] nucleophilic organic catalysts,[4] and reagents in organic reactions.[5] In the past ten years, imidazol-2-ylidenes **1**, saturated imidazolidin-2-ylidenes **2**, and 1,2,4-triazol-5-ylidenes **3** represent the typical architectures of stable nucleophilic singlet

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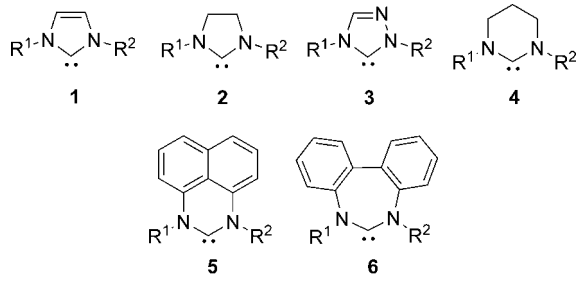
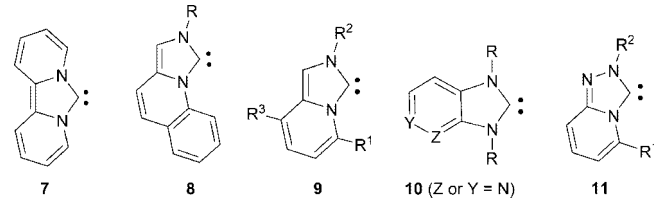
*N*-heterocyclic carbenes, and the chemistry of these compounds has been intensively studied.



The study of structure−reactivity relationships in diaminocarbenes is currently attracting intensive attention. It has been realized that several structural factors (e.g., the presence or absence of unsaturation at the C4−C5 bond in the imidazole/dihydroimidazole series, the steric bulkiness around the carbene carbon, and the presence of electron-withdrawing groups in the *N*-heterocyclic backbone or in *N*-aryl substituents, etc.) may have dramatic effects on the reactivity and stability of carbenes. Much work has therefore been devoted to the design and development of carbene compounds with novel structures to tune their steric and electronic properties by slight modification of the ring framework. Some new families of stable carbenes including those containing six-membered rings **4** and **5**,[6] seven-membered rings **6**,[7] and other cyclic/acyclic systems[8] have been described recently. In addition, the construction of annulated NHCs by carbo- or heterocycles is also an efficient strategy to modify the properties of Arduengo's "original" imidazol-2-ylidenes **1**.[9] In particular, recent investigations indicate that the pyrido-annulation significantly influences the stability and the $\sigma$-donor/$\pi$-acceptor ligand properties of carbenes and may be a tool for tuning their electronic properties, as was demonstrated in the bis(pyrido[*a*])-annulated imidazol-2-ylidene **7**,[10] the quinoline[*a*]-annulated imidazol-2-ylidenes **8**,[11] the pyrido[*a*]-annulated carbenes **9**[11] and their homologous pyrido[*b*]- and pyrido[*c*]-annulated NHCs **10**.[12] Although these pyrido-annulated NHCs fascinate chemists, only a few examples exist so far owing to the challenge posed by their synthesis.



The triazol-5-ylidenes **3** have turned out to be powerful organocatalysts since the convenient preparation of 1,3,4-triphenyl-4,5-dihydro-1*H*-1,2,4-triazol-5-ylidene in 1995.[13] Later, the triazolyl carbenes annulated by aliphatic cyclic skeleton have been described and exhibited highly catalytic activity in umpolung aldehyde chemistry.[14] Surprisingly, there is no information about the impact of the pyrido-annulation on the properties of triazol-5-ylidenes so far. We herein wish to report the highly efficient methods for the preparation of the pyrido-annulated triazolium salts **12a**−**g** in which $R^2$ may be both *N*-alkyl or aryl substituents, and describe for the first time the properties of the pyrido[1,2-*a*][1,2,4]triazol-3-ylidenes **11** as a new class of stable *N*-heterocyclic carbenes.

## Results and Discussion

**Synthesis of the Pyrido-Annulated Triazolium Salts 12a−g.** Several approaches to triazolium salts are conceivable. For example, 1,4-disubstituted triazolium salts can be prepared by condensation of an alkyl or aryl hydrazine with *N*,*N*-diformylhydrazine,[15] followed by reaction with an amine. 3,4-Disubstituted 1-alkyl-4*H*-1,2,4-triazol-1-ium salts can be prepared from *N*-formylhydrazine and imidoyl chloride.[16] 1,3,4-Triphenyl-1,2,4-triazol-1-ium perchlorate can be synthesized via the cyclization of the *N*-phenylbenzamide phenylhydrazone with acetic anhydride and formic acid after treatment with perchloric acid.[17] In addition, triazolium salts can also be accessible via

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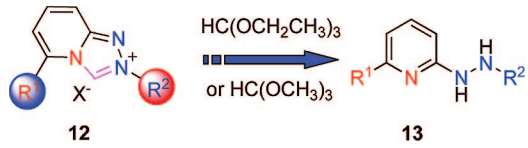


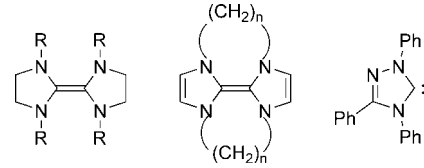

**FIGURE 1.** Design of the pyrido-annulated triazolium salts **12a**−**g**.

other routes such as those reported by Wanzlick[18] and Becker.[19] In this study, we take advantage of the cyclization of the pyridylhydrazine derivative **13** with trimethyl orthoformate or triethyl orthoformate to construct the pyrido[1,2-*a*][1,2,4]-triazolium skeleton **12** (Figure 1). Because the pyridylhydrazine derivatives **13** are prepared easily and are even commercially available, structural variations of the pyrido-annulated triazolium salts can be simply achieved through the choice of both the $R^1$ substituent of the pyridine ring and the $R^2$ group at the N2 position of the triazole ring. These compounds are easily synthesized from inexpensive starting materials and are isolated in analytically pure form as crystalline solids in good to excellent yields, depending on the nature of the $R^1$ and $R^2$ substituents. Furthermore, these ligands are stable enough in the air and can be stored with no special precautions. It is noteworthy that the preparation of the annulated triazolium salts has been performed without problems on 10-g scales.

**Method A.** As shown in Scheme 1, the synthesis of the bicyclic triazolium salt **12a** was a one-pot process from commercially available 1-(pyridin-2-yl)hydrazine **13a**, trimethyloxonium tetrafluoroborate, and triethyl orthoformate for the two-step conversion in 86% yield, which is proposed to involve the initial *N*-alkylation of **13a** with trimethyloxonium tetrafluoroborate to form the intermediate 1-methyl-2-(pyridin-2-yl)hydrazine, followed by the cyclization with triethyl orthoformate. Unfortunately, all attempts to isolate this intermediate were unsuccessful. While triethyloxonium tetrafluoroborate was used as an *N*-alkylating agent, 2-ethylpyrido[1,2-*a*][1,2,4]triazol-2-ium tetrafluoroborate **12b** was formed in 91% yield. Alternatively, the diethyl ether solution of $HBF_4$ could be used as the *N*-alkylating agent in place of triethyloxonium tetrafluoroborate. The structure of **12b** was confirmed by X-ray diffraction analysis (see Figure 1 in the Supporting Information). This protocol could also be extended to the synthesis of modified triazolium salts starting from 1-(substituted pyridin-2-yl)hydrazines, which are easily prepared from readily available pyridin-2-amine derivatives,[20] as illustrated in the synthesis of **12c** that contains a methyl group at the C6 of the pyridine ring.

**Method B.** Unfortunately, the protocols described above are limited to the synthesis of those bicyclic triazolium salts which bear the methyl or ethyl substituent at the N2 position of the triazole ring, and are inappropriate for the introduction of *N*-aryl substituents. To extend the possibilities of ligand tuning, we have developed another avenue to make the convenient introduction of aryl substituents at the N2 position of the triazole ring, as illustrated in the synthesis of **12d**−**g** via the condensation of hydrazines **13c**−**f** with triethyl orthoformate in the presence of ammonium hexafluorophosphate to afford the desired triazolium salts **12d**−**g** in 75%, 64%, 82%, and 77% yields, respectively (Scheme 2). Hydrazines **13c**−**f** were prepared by using the synthetic methods described previously for the three-step conversion, involving treatment of aniline derivatives with *m*-chloroperoxybenzoic acid to generate nitrosobenzenes, condensation of nitrosobenzenes with pyridin-2-amine derivatives to form diazenes, and reduction of diazenes with zinc and ammonium acetate.[21] The structure of **12d** was confirmed by X-ray diffraction analysis (see Figure 2 in the Supporting Information). In comparison with the first route, this route is more versatile and offers less restriction in the nature of the N2 $R^2$ group and involves more accessible starting materials.

**Synthesis, Characterization, Dimerization Behavior, and Reactivity of the Pyrido[1,2-*a*][1,2,4]triazol-3-ylidenes 11.** A distinguishing feature between unsaturated and saturated carbenes is their propensity to form enetetramines, the formal C=C dimers of the free carbenes.[1,22] *N*,*N*′-Substituted saturated diaminocarbenes of type **2** show a tendency to dimerize to the enetetramines $(\mathbf{2})_2$ if the *N*-substituents are sterically less crowded.[23] In sharp contrast, unsaturated diaminocarbenes of type **1** seldom form enetetramines except under very specific circumstances such as after suitable bridging **14**.[24] 1,2,4-Triazol−5-ylidene **15** is thermodynamically stable against dimerization to the enetetramine.[13] To the best of our knowledge, no example describing the dimerization of triazol-5-ylidenes has been clearly established so far. We herein present the synthesis, characterization, dimerization behavior, and reactivity of the first stable pyrido[1,2-*a*][1,2,4]triazol-3-ylidenes **11**.




Despite extensive application in organic catalysis,[3,4] the structures, properties, and stability of triazol-5-ylidenes have rarely been described. Deprotonation of appropriate cationic precursors by suitable bases is a widely applied, more convenient access to *N*-heterocyclic carbenes. In this study, our initial attempts focused on the direct deprotonation of the pyrido-annulated triazolium salts **12** in the presence of strong base (e.g., NaH, *t*-BuOK, $NaOCH_3$, etc.) at room temperature (Scheme 3). Perhaps the clearest spectroscopic evidence identifying **11** as an electron-rich NHCs is the appearance of a highly deshielded $^{13}C$ NMR (THF-$d_8$) signal for the $C_{carbene}$ at $\delta$ 202 to 208 ppm. The upfield shift of the pyrido-annulated NHCs **11** as compared to the nonannulated triazolylidene **15** ($\delta$ 214.6 ppm) reflects

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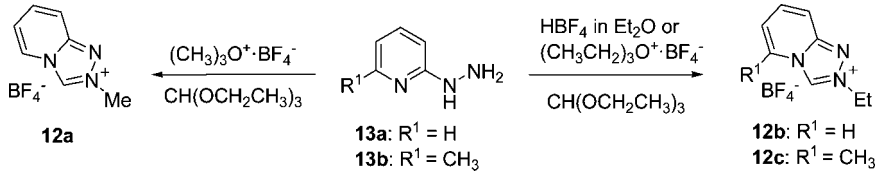
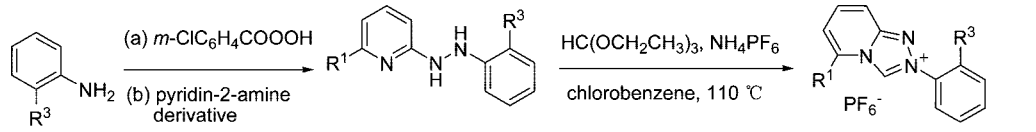
**SCHEME 1. Synthesis of the Pyrido-Annulated Triazolium Salts 12a−c**




**12a** **13a**: $R^1$ = H; **13b**: $R^1$ = $CH_3$ **12b**: $R^1$ = H; **12c**: $R^1$ = $CH_3$

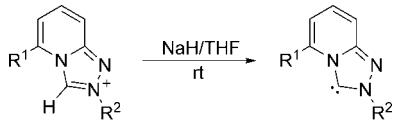
**SCHEME 2. Synthesis of the Pyrido-Annulated Triazolium Salts 12d−g**




**13c**: $R^1$ = H; $R^3$ = H
**13d**: $R^1$ = $CH_3$; $R^3$ = H
**13e**: $R^1$ = H; $R^3$ = $CH(CH_3)_2$
**13f**: $R^1$ = $CH_3$; $R^3$ = $CH(CH_3)_2$

**12d**: $R^1$ = H; $R^3$ = H
**12e**: $R^1$ = $CH_3$; $R^3$ = H
**12f**: $R^1$ = H; $R^3$ = $CH(CH_3)_2$
**12g**: $R^1$ = $CH_3$; $R^3$ = $CH(CH_3)_2$

**SCHEME 3. Preparation of the Pyrido[1,2-*a*][1,2,4]triazol-3-ylidenes 11**




**12** **11**

the influence of annulation on the divalent carbon.[13] The chemical shifts are reminiscent of the unsaturated carbenes of type **1**, which generally appear in the 205−220 ppm region.[2a−d] These values also fall in the range observed for the imidazo[1,5-*a*]pyridine skeleton carbenes **9** ($\delta$ 206−209 ppm).[11a] Thus, annulation is a particularly suitable tool for tuning the electronic properties of *N*-heterocyclic carbenes.

As shown in Figure 2, after treatment of the triazolium salt **12b** with 1.1 equiv of NaH in THF-$d_8$ in a sealed NMR tube at room temperature, a very clean reaction occurred immediately. The $^1$H NMR resonance signal for the NC*H*N proton at downfield chemical shift ($\delta$ 10.5 ppm) disappeared completely, suggesting the successful deprotonation of **12b** (Figure 2b). Concomitant with this observation was the appearance of a $^{13}$C NMR signal at $\delta$ 203.8 ppm (Figure 2c). There was no evidence for dimerization of carbene, as this signal did not change even after the THF-$d_8$ solution of **11b** ($R^1$ = H, $R^2$ = ethyl) was kept for several days at room temperature, thereby demonstrating the stability of the free carbene in solution. Further removal of the solvent afforded the free carbene as a pale yellow solid, which is also stable for a long period at room temperature. The ESI mass spectrum of a mixture of **12b** and NaH in a 1:1.1 ratio in THF showed the signal at *m*/*z* 148.9 assigned to the species **11b** ($[M + 2]^+$). In addition, treatment of the triazolium salts **12a**, **12c** and **12d−g** with NaH afforded the values of the $^{13}$C resonance for C3 at $\delta$ 203.8, 201.8, 204.2, 204.7, 207.4, and 206.1 ppm, respectively. Notably, the salts **12d−g** containing the aromatic $R^2$ substituents at the N2 position of the triazole rings gave rise to the slight downfield shifts (204.2−207.4 ppm) as compared to **12a−c** bearing the *N*-alkyl $R^2$ substituents (201.8−203.8 ppm). Unfortunately, all tries to obtain single crystals suitable for X-ray crystallography were unsuccessful.

More interestingly, deprotonation of the pyrido-annulated triazolium salt **12b** with $K_2CO_3$ did not lead to generation of the anticipated carbene **11b** but instead yielded the enetetramine **(11b)$_2$**, which has never previously been observed for triazol-5-ylidenes (Scheme 4). First, the ESI mass spectrum of a mixture of **12b** and $K_2CO_3$ in a 1:1.1 ratio in THF showed the signal at

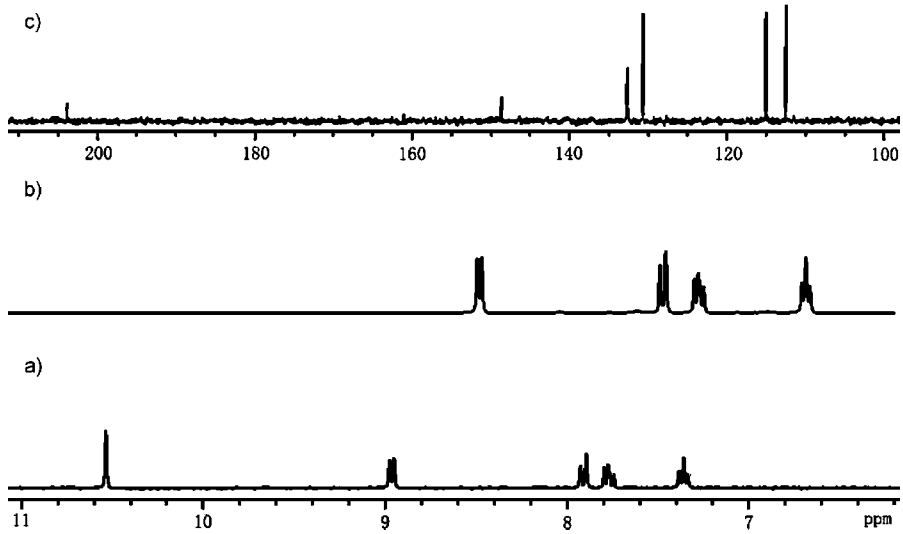
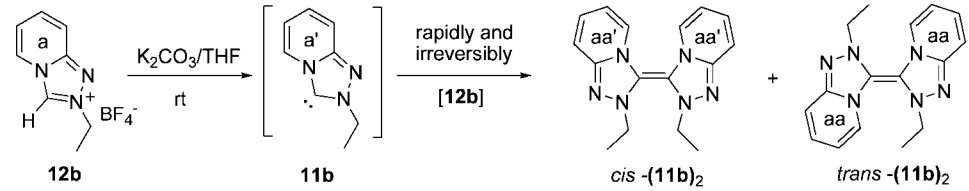



**FIGURE 2.** $^1$H NMR and $^{13}$C NMR spectra (THF-$d_8$) of **12b** in the presence of 1.1 equiv of NaH at 298 K: (a) the $^1$H NMR spectrum before addition of NaH; (b) the $^1$H NMR spectrum after treatment with NaH; and (c) the $^{13}$C NMR spectrum after treatment with NaH.

**SCHEME 4. Dimerization Behavior of the Pyrido[1,2-*a*][1,2,4]triazol-3-ylidenes 11b**




*m*/*z* 293 assigned to the species **(11b)$_2$** ([M − 1]$^+$). The dimerization behavior of the pyrido-annulated triazol-3-ylidene **11b** was then clearly demonstrated by its time-resolved $^1$H NMR and $^{13}$C NMR spectra by mixing a sample of **12b** and $K_2CO_3$ (1.1 equiv) in a sealed NMR tube in THF-$d_8$ at room temperature (Figure 3). The first $^1$H NMR spectrum exhibited the signals derived from the triazolium salt **12b** (Figure 3a). Figure 3b indicated the formation of enetetramine **(11b)$_2$**, but was still dominated by the resonance signals of **12b** after 15 min. With time, the intensities of **(11b)$_2$** resonance signals increased and those of **12b** decreased. After 24 h, the $^1$H NMR resonance signal arising from the starting material **12b** nearly disappeared (Figure 3c). Furthermore, the $^1$H NMR and $^{13}$C NMR spectra did not display any additional changes over several weeks at room temperature (Figure 3d,e). The $^1$H NMR and $^{13}$C NMR spectra gave two sets of resonance signals with different intensities, which reveals the presence of both cis and trans isomers of the enetetramine **(11b)$_2$** in an approximate 1:10 ratio. We assume that the trans dimer is the major product due to steric hindrance, but all attempts to isolate individual cis and trans isomers failed at this stage.[6e,25] It is notable that in these $^1$H NMR spectra the broad signals marked as H ($\delta$ 8.11 to 8.24 ppm) are possibly assigned to the released C3 protons of triazolium ring after deprotonation with $K_2CO_3$ (Figure 3b−d). Furthermore, the $^{13}$C NMR resonance signal at $\delta$ 203.8 ppm was not detected over the period monitored, demonstrating the rapid dimerization of the most likely intermediate carbene **11b**. For comparison, the rapid dimerization of carbene is typical for saturated *N*-heterocyclic carbenes of the imidazolidin-2-ylidene type **2**. Therefore, the pyrido-annulated triazol-3-ylidenes **11** feature the spectroscopic properties of unsaturated *N*-heterocyclic carbenes of type **1** but the dimerization of saturated derivatives **2**. We rationalize that the dimer **(11b)$_2$** should be generated from the indirect proton-catalyzed carbene dimerization pathway.[26] In the presence of $K_2CO_3$, the deprotonation of the triazolium salt **12b** is slow so that relatively large quantities of unreacted triazolium salt still remain in the reaction system, which can serve as a protic catalyst for the dimerzation of the free carbene to the olefin **(11b)$_2$**. To clarify the mechanism of dimerization proposed, the triazolium salt **12b** was added to a

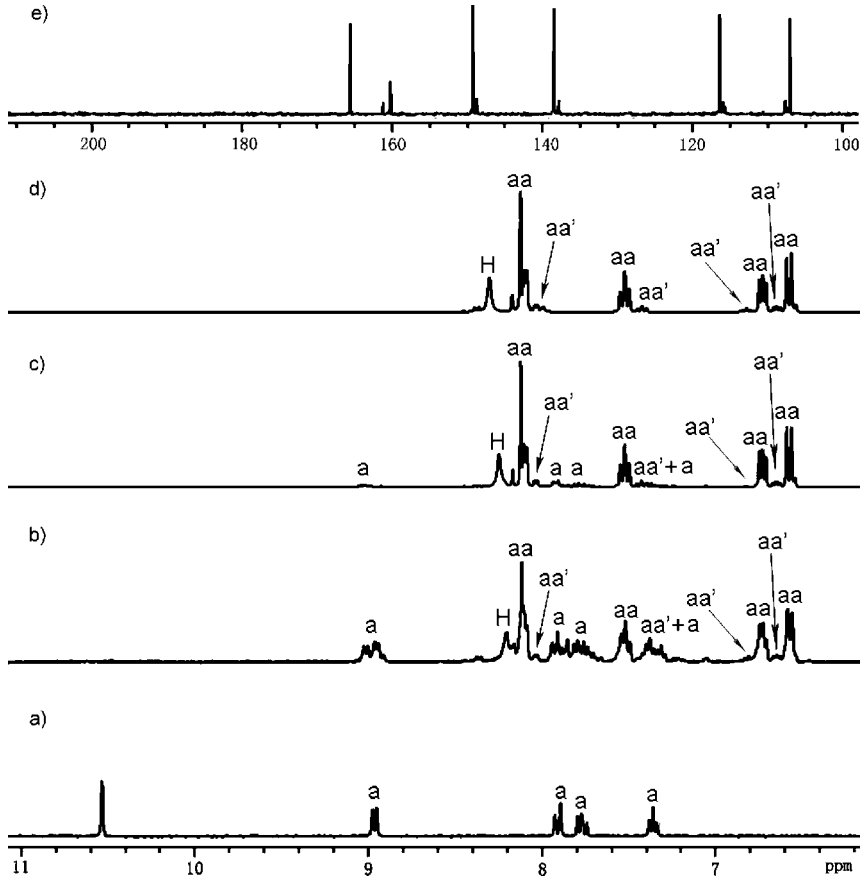
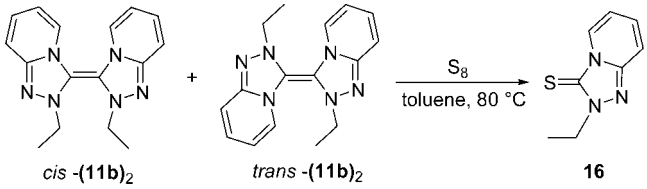
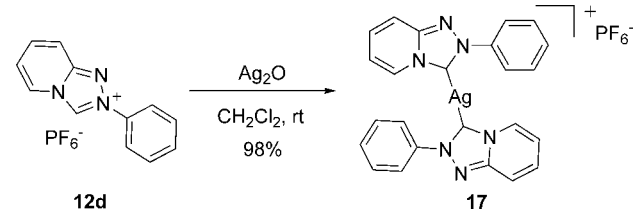



**FIGURE 3.** Time-resolved $^1$H NMR and $^{13}$C NMR spectra (THF-$d_8$) of **12b** in the presence of 1.1 equiv of $K_2CO_3$ at 298 K: (a) the $^1$H NMR spectrum prior to addition of $K_2CO_3$; (b) the $^1$H NMR spectrum after 15 min; (c) the $^1$H NMR spectrum after 24 h; (d) the $^1$H NMR spectrum after several weeks; and (e) the $^{13}$C NMR spectrum after several weeks.

**SCHEME 5. Preparation of the Thiourea 16**




**SCHEME 6. Synthesis of the Pyrido-Annulated Triazol-3-ylidene-Silver(I) Hexafluorophosphate Complex 17**




solution of the isolated carbene **11b** in THF-$d_8$. The $^{13}$C NMR resonance at $\delta$ 203.8 ppm disappeared but instead gave rise to the signals assigned to the enetetramine **(11b)$_2$**. Thus, these results showed that addition of triazolium salt could efficiently catalyze its dimerization, clearly demonstrating the indirect proton-catalyzed pathway of carbene dimerization.

The dimer **(11b)$_2$** was found to be stable in air at room temperature. While the isolated sample **(11b)$_2$** was further heated to 80 °C in toluene-$d_8$ in a sealed NMR tube for 24 h, we observed no evidence for an equilibrium between the NHC and its dimer in solution. However, it should be known that the C−C double bond of type **(2)$_2$** can be cleaved in reactions with electrophiles with the liberation of **2**.[2a−d,6e] In this study, we found that the dimer **(11b)$_2$** could also react with elemental sulfur to deliver the thiourea **16** in toluene at 80 °C in 96% yield (Scheme 5). The thiourea **16** was characterized by X-ray structure analysis (see Figure 3 in the Supporting Information).

**Synthesis of the Pyrido-Annulated Triazol-3-ylidene-Silver(I) Hexafluorophosphate Complex 17.** To further get structural information about carbenes **11**, the triazolium salts **12** were expected to be coordinated to a silver unit to give the air-stable silver(I) complexes.[3e,27] In this study, the silver(I) bis-carbene complex **17** was obtained by reaction of silver oxide with 2 equiv of **12d** in dichloromethane (Scheme 6). After workup, complex **17** was isolated as highly thermally stable single crystals (mp 293−294 °C).

Single-crystal X-ray diffraction analysis confirmed the silver(I) bis-carbene complex **17** with $PF_6^-$ as the noncoordinating counterion and showed a two-coordinate Ag(I) atom in a close linear environment with a C6−Ag−C18 angle of 174.8° (Figure 4). In addition to the two-coordinate environment for the Ag(I) atom, several features of this structure, including the planar geometry around the nitrogen atoms and the Ag−$C_{carbene}$ bond distances (2.085 and 2.102 Å for C6−Ag and C18−Ag, respectively) and the N−$C_{carbene}$ bond lengths (average 1.354 Å), are in agreement with those of other silver(I) bis- or monocarbene complexes previously reported.[3e,9f,g,27d,28] A series of $\pi-\pi$ packing interactions which exist among the benzene ring, pyridine ring, and triazole ring with the centroid distances in the range of 3.534 to 3.842 Å play an important part in the connection of two adjacent molecules. Recently, Nolan et al. described that the 2,5,6,7-tetrahydro-2-phenyl-3*H*-pyrrolo[2,1-*c*][1,2,4]triazol-3-ylidene-silver(I) complex displays a $^{13}$C NMR signal at 176.9 ppm, illustrating an average donating ability similar to that of the previously discussed unsaturated silver(I) NHC complexes.[29] However, in this study, the $^{13}$C NMR spectrum of the pyrido-annulated triazol-3-ylidene-silver(I) complex **17** does not exhibit any signal between 160 and 200 ppm. A similar observation for imidazol-2-ylidene was also made recently by Nolan.[29]

**Catalytic Benzoin Condensation.** It is well-established that carbenes are versatile nucleophilic organic catalysts for a number of important transformations.[4] The benzoin condensation is of much interest as a convenient method of carbon−carbon bond formation, which affords an atom-economic approach to α-hydroxy ketones serving as important intermediates in organic synthesis. Debate over the mechanism of the carbene-catalyzed benzoin condensation has led to several different mechanistic models.[4a,d,e] Of the well-established mechanisms, both monomer- and dimer-catalyzed pathways have been proposed. One based on the mechanistic proposal by Breslow has a thiazol-2-ylidene as the catalytically active species.[30] Another model has been based on the formation of carbene dimers presented by Lemal et al.[31]

In this study, we were fortunate to obtain both of the carbenes **11** and the enetetramines **(11)$_2$**, and more importantly, there is no equilibrium observed between the NHCs and their dimers in solution at room temperature. We thereby felt that this was a chance to find evidence of the mechanism of the carbene-catalyzed benzoin condensation. By the NMR signals we observed the formation of free carbene arising from the deprotonation of the pyrido-annulated triazolium salt **12b** in the presence of strong base at room temperature. After screening a variety of bases (i.e., NaH, DBU, $Et_3N$, DIPEA, and *t*BuOK), we found that *t*BuOK was clearly the best choice in terms of yield. Thus, a typical benzoin condensation was carried out by treatment of benzaldehyde in the presence of 2 mol % of **12b** and 2 mol % of *t*-BuOK in THF at 25 °C for 15 h. We were delighted to find that our catalytic system could afford excellent yields up to 93%. In sharp contrast, the isolated carbene dimer **(11b)$_2$** could not prompt the benzoin condensation at 25 °C. Therefore we rationalized that this type of triazolium-catalyzed benzoin condensation should undergo the "traditional" Breslow

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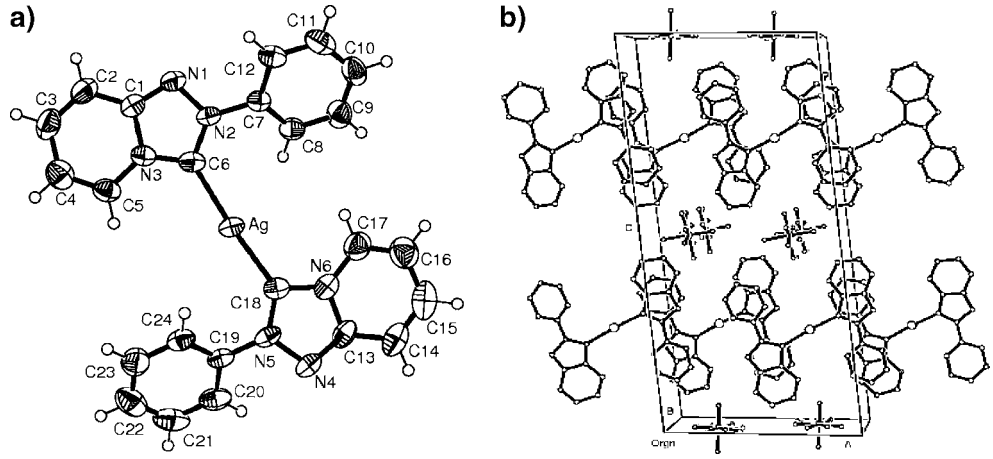



**FIGURE 4.** (a) ORTEP drawing of the molecular structure of **17**, with $PF_6^-$ anions omitted for clarity. Thermal ellipsoids are set at the 30% probability level. (b) The unit cell packing diagram viewed down the *b* axis.

**SCHEME 7. Two Possible Mechanisms of the Triazolium-Catalyzed Benzoin Condensation**

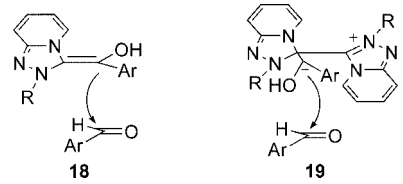
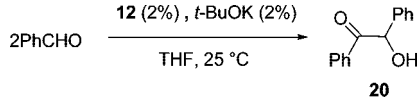



**TABLE 1. Screening of Ligand 12 for the Benzoin Condensation**[a]

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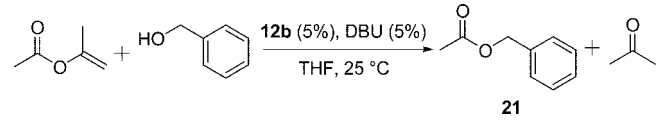
| entry | ligand | yield (%)[b] |
|---|---|---|
| 1 | **12a** | 88 |
| 2 | **12b** | 93 |
| 3 | **12c** | |
| 4 | **12d** | 47 |
| 5 | **12e** | |
| 6 | **12f** | 36 |
| 7 | **12g** | |

[a] Reactions were performed on a 2.0 mmol scale with 2 mol % of ligand **12** and 2 mol % of *t*-BuOK in 2.0 mL of THF under $N_2$ atmosphere at 25 °C for 15 h. [b] Yield of isolated product based on benzaldehyde after chromatographic purification.

mechanism **18** rather than the pathway of the bis(triazol-3-ylidene) dimer as the real catalytic species **19** (Scheme 7).

The ligand survey for the catalytic benzoin condensation of benzaldehyde was carried out in the presence of 2 mol % of **12** and 2 mol % of *t*-BuOK in THF at 25 °C for 15 h, and the results are summarized in Table 1. We found that the yields of the benzoin condensations were largely dependent on the steric and electronic natures of the $R^1$ and $R^2$ substituents of the triazolium salts **12a**−**g**. For example, the yields would decrease dramatically as the $R^2$ substituent of the N2 position of the triazole ring varied from the *N*-alkyl group to the *N*-aryl group (compare entries 1, 2, 4, and 6). In particular, the presence of one methyl group at the C6 position of the pyridine ring would result in loss of catalytic activity (e.g., **12c**, **12e**, and **12g**) possibly due to the steric hindrance created by the methyl group (entries 3, 5, and 7). The triazolium salt **12b** thus turned out to be a particularly effective ligand, affording as high as 93% isolated yield (entry 2).

**SCHEME 8. Catalytic Transesterification Reaction of Benzyl Alcohol with Isopropenyl Acetate by 12b**

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**Catalytic Transesterification Reaction.** The importance of esters in organic synthesis has encouraged the development of a variety of methods for their preparation, involving reaction of alcohol with carboxylic acid, ester interchange, and transesterification. In the past few years, the research groups of Nolan[32] and Hedrick[33] simultaneously reported the first use of various alkyl- or aryl-substituted imidazol-2-ylidenes as efficient transesterification catalysts in 2002.[4] In this study, we were pleased to find that the transesterification of benzyl alcohol with isopropenyl acetate was able to proceed smoothly in the presence of the pyrido-annulated trazolium salt **12b**. Under optimal conditions (5 mol % of **12b**, 5 mol % of DBU, THF, 3 h), our catalytic system could afford the desired product **21** in 93% isolated yield at 25 °C (Scheme 8).

## Conclusion

In summary, the pyrido-annulated triazolium salts **12a**−**g** have been readily synthesized in a straightforward fashion from inexpensive starting materials in good yields. Novel stable pyrido[1,2-*a*][1,2,4]triazol-3-ylidenes **11** have been prepared by deprotonation of triazolium salts **12**. The triazolium salts can be modified by changing the $R^1$ substituent on pyridine and the $R^2$ group on the N2 position of the triazole to tune the electronic and steric nature of the derived carbenes. These carbenes exhibit the spectroscopic properties of unsaturated *N*-heterocyclic carbenes but undergo dimerizations reminiscent of saturated derivatives. The dimeric enetetramine **(11b)$_2$** could react with elemental sulfur to deliver the corresponding thiourea **16** in toluene at 80 °C in good yield. The pyrido-annulated triazolium salt **12d** could react with $Ag_2O$ to form the silver(I) bis-carbene complex **17** with a two-coordinate Ag(I) atom in a close linear environment. The triazolium salts **12** turned out to be powerful

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catalysts in catalytic benzoin condensation and transesterification at 25 °C. The catalytic activity was largely dependent on the steric and electronic nature of the $R^1$ and $R^2$ substituent of the triazolium salt. The triazolium-catalyzed benzoin condensations are proposed to undergo the "traditional" Breslow mechanism rather than the dimer pathway. Further investigations into other versions of organocatalysis, organometallic catalysis, as well as the related reaction mechanisms are currently underway and will be reported in due course.

## Experimental Section

**General Remarks.** $^1$H NMR spectra were obtained with a Bruker AV-300, a Varian Inova-400, or a Varian Inova-600 spectrometer, while $^{13}$C NMR spectra were recorded with a Bruker AV-300, a Varian Inova-400, or a Varian Inova-600. The $^1$H chemical shifts were measured relative to tetramethylsilane as the internal reference, while the $^{13}$C NMR chemical shifts were recorded with THF-$d_8$, $CDCl_3$, or $CD_3OD$ as the internal standard. Elemental analyses were performed with a CARLO ERBA1106 instrument. The mass spectra (ESI) were obtained by using a Finnigan-LCQDECA spectrometer, and the GC-MS spectra were recorded with an Agilent 6890-5973 machine.

**Materials.** Unless otherwise noted, all reagents were obtained from commercial suppliers and used without further purification. Benzaldehyde, benzyl alcohol, and isopropenyl acetate were freshly distilled under reduced pressure prior to use. Solvents were dried by refluxing for at least 24 h over $CaH_2$ ($CH_2Cl_2$) and sodium/benzophenone (THF or diethyl ether), and freshly distilled prior to use. Unless otherwise indicated, all syntheses and manipulations were carried out under dry $N_2$ atmosphere. The pyridylhydrazine **13a** and **13b** were synthesized according to the procedure reported by Lien et al.[20] The pyridylhydrazine derivates **13c**, **13d**, **13e**, and **13f** were prepared by the literature procedure.[21]

**General Procedure for the Preparation of the Pyrido[1,2-*a*][1,2,4]triazol-2-ium salts 12a−c. 2-Methylpyrido[1,2-*a*][1,2,4]-triazol-2-ium tetrafluoroborate (12a):** A flame-dried round-bottomed flask equipped with a reflux condenser was charged with trimethyloxonium tetrafluoroborate (1.78 g, 12 mmol), 1-(pyridin-2-yl)hydrazine **13a** (1.09 g, 10 mmol), and chlorobenzene (30 mL). The mixture was then stirred for 30 min, followed by addition of trimethyl orthoformate (2.2 mL, 20 mmol). After being heated at 110 °C for 10 h, the reaction mixture was concentrated in vacuo. The resulting residue was recrystallized from acetone to give the triazolium salt **12a** as colorless crystals in 86% yield. Mp 171−173 °C. $^1$H NMR (600 MHz, $CD_3OD$) $\delta$ 4.41 (s, 3 H), 7.43 (t, $J$ = 7.2 Hz, 1 H), 7.85−7.87 (m, 1 H), 7.98 (d, $J$ = 9.6 Hz, 1 H), 8.73 (d, $J$ = 7.8 Hz, 1 H). $^{13}$C NMR (150 MHz, $CD_3OD$) $\delta$ 40.5, 116.4, 119.6, 127.1, 134.9, 149.2. MS (ESI$^+$) $m/z$ 133 [M − $BF_4$ − H]$^+$. Anal. Calcd for $C_7H_8BF_4N_3$: C, 38.05; H, 3.65; N, 19.02. Found: C, 37.96; H, 3.53; N, 19.29.

**2-Ethyl pyrido[1,2-*a*][1,2,4]triazol-2-ium tetrafluoroborate (12b):** This compound was prepared following the same procedure as described above for **12a**, using **13a** as the starting material and triethyloxonium tetrafluoroborate as the *N*-alkylating agent. Compound **12b** was obtained as colorless crystals in 91% yield after crystallization from acetone. Mp 112−114 °C. $^1$H NMR (600 MHz, $CD_3OD$) $\delta$ 1.70 (t, $J$ = 7.2 Hz, 3 H), 4.71 (q, $J$ = 7.2 Hz, 2 H), 7.43 (t, $J$ = 6.6 Hz, 1 H), 7.84−7.87 (m, 1 H), 8.00 (d, $J$ = 10.2 Hz, 1 H), 8.70 (d, $J$ = 7.8 Hz, 1 H). $^{13}$C NMR (150 MHz, $CD_3OD$) $\delta$ 14.4, 50.2, 116.4, 119.6, 127.2, 134.9, 149.3. MS (ESI$^+$) $m/z$ 147 [M − $BF_4$ − H]$^+$. Anal. Calcd for $C_8H_{10}BF_4N_3$: C, 40.89; H, 4.29; N, 17.88. Found: C, 40.65; H, 4.08; N, 17.71.

**2-Ethyl-5-methylpyrido[1,2-*a*][1,2,4]triazol-2-ium tetrafluoroborate (12c):** This compound was prepared following the same procedure as described above for **12a**, using **13b** as the starting material and triethyloxonium tetrafluoroborate as the *N*-alkylating agent. Compound **12c** was obtained as colorless crystals in 65% yield after crystallization from acetone. Mp 185−187 °C.$^1$H NMR (600 MHz, $CD_3OD$) $\delta$ 1.72 (t, $J$ = 7.2 Hz, 3 H), 2.81 (s, 1 H), 4.70 (q, $J$ = 7.8 Hz, 2 H), 7.25 (d, $J$ = 6.6 Hz, 1 H), 7.77−7.80 (m, 1 H), 7.84 (d, $J$ = 9.0 Hz, 1 H). $^{13}$C NMR (150 MHz, $CD_3OD$) $\delta$ 14.4, 17.8, 50.2, 113.7, 118.1, 135.1, 137.6, 139.1, 149.8. MS (ESI$^+$) $m/z$ 161 [M − $BF_4$ − H]$^+$. Anal. Calcd for $C_9H_{12}BF_4N_3$: C, 43.41; H, 4.86; N, 16.87. Found: C, 43.26; H, 4.52; N, 16.44.

**The Alternative Preparation of the Pyrido[1,2-*a*][1,2,4]triazol-2-ium salts 12b,c.** Compounds **12b** and **12c** were prepared following the same procedure as described above for **12a**, using **13a** and **13b** as the starting materials, respectively. Tetrafluoroborate acid (50% in diethyl ether) was used as the *N*-alkylating agent in place of triethyloxonium tetrafluoroborate. Compounds **12b** and **12c** were obtained in 86% and 81% yields, respectively.

**General Procedure for the Preparation of the Pyrido[1,2-*a*][1,2,4]triazol-2-ium salts 12d−g. 2-Phenylpyrido[1,2-*a*][1,2,4]-triazol-2-ium hexafluorophosphate (12d):** A dry, argon-flushed Schlenk tube equipped with a reflux condenser was charged with 1-(pyridin-2-yl)-2-phenylhydrazine **13c** (3.7 g, 20 mmol), ammonium hexafluorophosphate (3.26 g, 20 mmol), trimethyl orthoformate (4.4 mL, 40 mmol), and dry THF (30 mL). After being heated at 80 °C for 10 h, the mixture was cooled to room temperature and concentrated in vacuo. The resulting residue was recrystallized from acetone to give the triazolium salt **12d** as colorless crystals in 75% yield. Mp 203−205 °C. $^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$ 7.52 (t, $J$ = 7.2 Hz, 1 H), 7.71 (t, $J$ = 7.8 Hz, 1 H), 7.77 (t, $J$ = 8.4 Hz, 2 H), 7.94−7.96 (m, 1 H), 8.09 (d, $J$ = 7.8 Hz, 2 H), 8.21 (d, $J$ = 9.0 Hz, 1 H), 8.87 (d, $J$ = 7.2 Hz, 1 H), 11.46 (s, 1 H). $^{13}$C NMR (150 MHz, DMSO-$d_6$) $\delta$ 115.2, 118.8, 121.7, 126.6, 130.4, 131.4, 134.5, 135.2, 135.3, 147.3. MS (ESI$^+$) $m/z$ 195 [M − $PF_6$ − H]$^+$. Anal. Calcd for $C_{12}H_{10}F_6N_3P$: C, 42.24; H, 2.95; N, 12.32. Found: C, 42.56; H, 3.01; N, 12.29.

**5-Methyl-2-phenylpyrido[1,2-*a*][1,2,4]triazol-2-ium hexafluorophosphate (12e):** This compound was prepared following the same procedure as described above for **12d**, using **13d** as the starting material. Compound **12e** was obtained as a white solid in 64% yield after crystallization from acetone. Mp 274−276 °C. $^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$ 2.83 (s, 3 H), 7.39 (d, $J$ = 6.6 Hz, 1 H), 7.72 (t, $J$ = 7.2 Hz, 1 H), 7.79 (t, $J$ = 8.4 Hz, 2 H), 7.89−7.92 (m, 1 H), 8.08 (d, $J$ = 9.0 Hz, 1 H), 8.17 (d, $J$ = 7.8 Hz, 2 H), 11.56 (s, 1 H). $^{13}$C NMR (150 MHz, DMSO-$d_6$) $\delta$ 17.7, 112.5, 117.1, 121.5, 130.4, 131.3, 134.8, 135.4, 136.4, 147.6. MS (ESI$^+$) $m/z$ 209 [M − $PF_6$ − H]$^+$. Anal. Calcd for $C_{13}H_{12}F_6N_3P$: C, 43.96; H, 3.41; N, 11.83. Found: C, 44.30; H, 3.66; N, 11.85.

**2-(2-Isopropylphenyl)pyrido[1,2-*a*][1,2,4]triazol-2-ium hexafluorophosphate (12f):** This compound was prepared following the same procedure as described above for **12d**, using **13e** as the starting material. Compound **12f** was obtained as colorless crystals in 82% yield after crystallization from acetone. Mp 214−215 °C. $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 1.20(d, $J$ = 6.8 Hz, 6 H), 2.86−2.93 (m, 1 H), 7.52−7.58 (m, 2 H), 7.61 (d, $J$ = 8.0 Hz, 1 H), 7.75 (d, $J$ = 3.6 Hz, 2 H), 7.94−7.98 (m, 1 H), 8.19 (d, $J$ = 9.2 Hz, 1 H), 8.88 (d, $J$ = 6.8 Hz, 1 H), 11.33 (s, 1 H). $^{13}$C NMR (100 MHz, DMSO-$d_6$) $\delta$ 24.1, 27.6, 115.6, 119.0, 127.1, 127.4, 127.5, 128.0, 132.8, 133.8, 134.8, 137.8, 145.2, 147.7. MS (ESI$^+$) $m/z$ 238 [M − $PF_6$]$^+$. Anal. Calcd for $C_{15}H_{16}F_6N_3P$: C, 47.01; H, 4.21; N, 10.96. Found: C, 46.71; H, 4.41; N, 11.24.

**2-(2-Isopropylphenyl)-5-methylpyrido[1,2-*a*][1,2,4]triazol-2-ium hexafluorophosphate (12g):** This compound was prepared following the same procedure as described above for **12d**, using **13f** as the starting material. Compound **12g** was obtained as a white solid in 77% yield after crystallization from acetone. Mp 296−297 °C. $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 1.21 (d, $J$ = 7.2 Hz, 6 H), 2.81 (s, 3 H), 2.89−2.93 (m, 1 H), 7.39 (d, $J$ = 6.8 Hz, 1 H), 7.52−7.57 (m, 1 H), 7.63 (d, $J$ = 8.0 Hz, 1 H), 7.76 (d, $J$ = 4.0 Hz, 2 H), 7.89−7.93 (m, 1 H), 8.05 (d, $J$ = 9.2 Hz, 1 H), 11.33 (s, 1 H). $^{13}$C NMR (100 MHz, DMSO-$d_6$) $\delta$ 18.1, 24.1, 27.7, 112.9, 117.4, 127.5, 127.6, 128.0, 132.9, 133.9, 135.1, 135.8, 137.0, 145.3, 148.1. MS (ESI$^+$) $m/z$ 252 [M − $PF_6$]$^+$. Anal. Calcd for

$C_{16}H_{18}F_6N_3P$: C, 48.37; H, 4.57; N, 10.58. Found: C, 48.57; H, 4.66; N, 10.85.

**Procedure for the Preparation of 2-Ethylpyrido[1,2-*a*][1,2,4]triazol-3-thione 16.** The mixture of **12b** (117.5 mg, 0.5 mmol) and $K_2CO_3$ (75.9 mg, 0.55 mmol) in THF (5.0 mL) was stirred under $N_2$ atmosphere at room temperature for 24 h, and then filtered through a celite plug. The filtrate was evaporated under vacuum, and the resulting residue was purified by crystallization from hexane to give the enetetramine **(11b)$_2$** as a white solid. The enetetramine **(11b)$_2$** further reacted with $S_8$ (9.6 mg, 0.3 mmol) in toluene (10 mL) at 80 °C for 6 h. The mixture was then cooled to room temperature and concentrated in vacuo. The resulting residue was recrystallized from hexane to afford the thiourea **16** as colorless crystals in 92% yield. Mp 59−60 °C. $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.43 (t, $J$ = 7.2 Hz, 3 H), 4.40 (q, $J$ = 7.2 Hz, 2 H), 6.74 (t, $J$ = 6.5 Hz, 1 H), 7.20−7.35 (m, 2 H), 8.28 (d, $J$ = 7.1 Hz, 1 H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 13.3, 44.9, 113.0, 115.1, 126.2, 130.7, 145.3, 158.5. MS (ESI$^+$) $m/z$ 181 [M + H]$^+$. Anal. Calcd for $C_8H_9N_3S$: C, 53.61; H, 5.06; N, 23.44; S, 17.89. Found: C, 53.46; H, 5.23; N, 22.23; S, 17.70.

**Procedure for the Preparation of 2-Phenylpyrido[1,2-*a*][1,2,4]triazol-3-ylidene-Silver(I) Hexafluorophosphate Complex (17).** 2-Phenylpyrido[1,2-*a*][1,2,4]triazol-2-ium hexafluorophosphate **12d** (412 mg, 1.2 mmol) and silver oxide (139 mg, 0.6 mmol) were added to $CH_2Cl_2$ (15 mL). The suspension became clear after stirring for 6 h at room temperature and the mixture was filtered through celite. The solvent was removed in vacuo at room temperature to give a white solid, which was recrystallized from $CH_2Cl_2$ to afford the colorless crystalline product **17** in 98% yield. Mp 293−294 °C. $^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 7.36 (t, $J$ = 6.6 Hz, 1 H), 7.40−7.68 (m, 3 H), 7.80−7.86 (m, 1 H), 8.05−8.11 (m, 3 H), 9.23 (d, $J$ = 7.0 Hz, 1 H). $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$ 115.2, 116.3, 124.2, 130.2, 130.4, 131.1, 133.7, 140.1, 148.7. Anal. Calcd for $C_{24}H_{18}AgF_6N_6P$: C, 44.81; H, 2.82; N, 13.06. Found: C, 44.65; H, 2.92; N, 12.87.

**General Procedure for the Catalytic Benzoin Condensation by the Pyrido-Annulated Triazolium Salts 12.** A flame-dried Schlenk tube with a magnetic stirring bar was charged with the triazolium salt **12** (0.04 mmol) and dry THF (2 mL) at 25 °C, followed by addition of a THF solution of *t*-BuOK (0.4 M, 100 $\mu$L, 0.04 mmol). After the mixture was stirred for 10 min, benzaldehyde (202 $\mu$L, 2 mmol) was added. The reaction mixture was then stirred at the same temperature for 15 h, poured into water, and extracted twice with dichloromethane. The combined organic layers were evaporated and the resulting residue was purified by column chromatography on silica gel eluting with ethyl acetate/petroleum ether (1/9) to provide 2-hydroxy-1,2-diphenylethanone (**20**): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.54 (br s, 1 H), 5.96 (s, 1 H), 7.26−7.34 (m, 5 H), 7.38−7.54 (m, 3 H), 7.91−7.93 (m, 2 H). $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 76.2, 127.8, 128.5, 128.7, 129.1, 133.6, 133.8, 139.0, 199.0. GC-MS (EI$^+$) $m/z$ 211 [M − H]$^+$.

**Procedure for the Catalytic Transesterification Reaction.** A flame-dried Schlenk tube with a magnetic stirring bar was charged with **12b** (23.6 mg, 0.1 mmol), DBU (15 $\mu$L, 0.1 mmol), and THF (1.0 mL) under $N_2$ atmosphere at 25 °C. After the mixture was stirred for 10 min, benzyl alcohol (208 $\mu$L, 2 mmol) and isopropenyl acetate (262 $\mu$L, 2.4 mmol) were added. After the reaction mixture was stirred at the same temperature for 3 h, the volatiles were removed and the resulting residue was purified by column chromatography on silica gel eluting with ethyl acetate/petroleum ether (1/12) to give the benzyl acetate (**21**) as a viscous oil in 93% yield. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 2.10 (s, 3 H), 5.11 (s, 2 H), 7.35−7.37 (m, 5 H). $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 20.9, 38.3, 66.2, 128.2, 128.5, 135.9, 170.8. GC-MS (EI$^+$) $m/z$ 149 [M − H]$^+$.

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**Supporting Information Available:** Copies of $^1$H and $^{13}$C NMR spectra for compounds **12a**−**g**, **(11b)$_2$**, **16**, **17**, **20**, and **21**, ORTEP drawings of **12b**, **12d**, and **16**, and X-ray crystallographic data in CIF format for **12b**, **12d**, **16**, and **17.** This material is available free of charge via the Internet at http://pubs.acs.org.

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