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Direct Transfer of the Sulfonylimino Group of Imino-λ^3-Bromane to *N*-Heterocycles and Trialkylamines: Synthesis of *N*-Iminoammonium Ylides under Metal-Free Conditions

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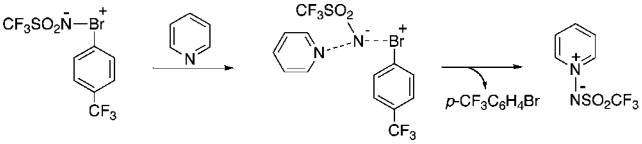
ABSTRACT



Exposure of *N*-heterocycles and aliphatic trialkylamines to trifluoromethanesulfonylimino-λ^3-bromane at room temperature results in direct transfer of the sulfonylimino group to the nitrogen atoms and affords a variety of iminoammonium ylides under transition-metal-free conditions. The imino-λ^3-bromane probably serves as an active nitrenoid species without any activation and produces the ammonium ylides via a bimolecular nucleophilic substitution process.

Hypervalent sulfonylimino-λ^3-iodanes PhI═NSO$_2$Ar enable a rich array of chemistry in modern organic synthesis.[1] They serve as excellent nitrenoid transfer agents either in the aziridination of alkenes or in the amidation of alkanes via C−H insertion using transition metal catalysts.[2,3] These reactions rely heavily on the hyper-leaving group ability of aryl-λ^3-iodanyl groups[4] and on the generation of active metal-nitrenoid species. Under thermal or catalytic conditions, they transfer the sulfonylimino groups to a wide range of heteroatom nucleophiles involving nitrogen heterocycles, sulfides, sulfoxides, selenides, phosphines, and arsines.[5−8] Thus, copper(II)-catalyzed reaction of PhI═NTs with excess amounts of pyridines at room temperature afforded the corresponding *p*-toluenesulfonyliminopyridinium ylides in good yields.[5a]

In 2007, we reported the first synthesis of the related group 17 sulfonylimino-λ^3-bromane **1**, which involves a facile ligand exchange of aryl(difluoro)-λ^3-bromane on the bromine(III) with trifluoromethanesulfonamide (TfNH$_2$) (Scheme 1).[9] The sulfonylimino-λ^3-bromane **1** functions as an efficient sulfonylimino group donor and directly undergoes aziridination of olefins at ambient temperature stereospecifically with retention of original stereochemistry. We report herein

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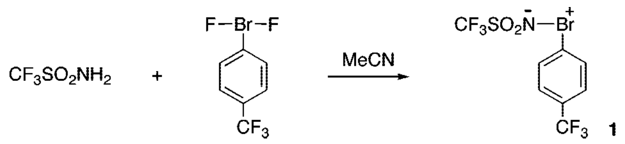
(1) Reviews: (a) Dauban, P.; Dodd, R. H. *Synlett* **2003**, 1571. (b) Muller, P.; Fruit, C. *Chem. Rev.* **2003**, *103*, 2905. (c) Zhdankin, V. V.; Stang, P. J. *Chem. Rev.* **2002**, *102*, 2523. (d) Varvoglis, A. *The Organic Chemistry of Polycoordinated Iodine*; VCH: New York, 1992. (e) *Hypervalent Iodine Chemistry*; Wirth, T., Ed.;Topics in Current Chemistry 224; Springer: Berlin, 2003. (f) Du Bois, J. *Chemtracts* **2005**, *18*, 1. (g) Zhdankin, V. V. *Sci. Synth.* **2007**, *31a* (Chapter 31.4.1), 161.

(2) For aziridination of olefins, see: (a) Mansuy, D.; Mahy, J.-P.; Dureault, A.; Bedi, G.; Battioni, P. *J. Chem. Soc., Chem. Commun.* **1984**, 1161. (b) Evans, D. A.; Faul, M. M.; Bilodeau, M. T. *J. Am. Chem. Soc.* **1994**, *116*, 2742. (c) Li, Z.; Quan, R. W.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1995**, *117*, 5889. (d) Au, S.-M.; Huang, J.-S.; Yu, W.-Y.; Fung, W.-H.; Che, C.-M. *J. Am. Chem. Soc.* **1999**, *121*, 9120. (e) Dauban, P.; Saniere, L.; Tarrade, A.; Dodd, R. H. *J. Am. Chem. Soc.* **2001**, *123*, 7707. (f) Guthikonda, K.; Du Bois, J. *J. Am. Chem. Soc.* **2002**, *124*, 13672. (g) Cui, Y.; He, C. *J. Am. Chem. Soc.* **2003**, *125*, 16202. (h) Leung, S. K.-Y.; Tsui, W.-M.; Huang, J.-S.; Che, C.-M.; Liang, J.-L.; Zhu, N. *J. Am. Chem. Soc.* **2005**, *127*, 16629.

10.1021/ol802383f CCC: $40.75

Scheme 1



a facile transfer of the sulfonylimino group of λ^3-bromane **1** to the nitrogen atom of *N*-heterocycles and aliphatic trialkylamines, which affords sulfonyliminoammonium ylides in excellent yields under metal-free, stoichiometric conditions at room temperature.[10]

Exposure of equimolar pyridine to the sulfonyimino-λ^3-bromane **1**[9] in acetonitrile at room temperature for 10 min under argon resulted in the facile transimination between Br(III) and N atoms, yielding *N*-triflyliminopyridinium ylide **2a**[11] quantitatively (Scheme 2). The transylidation probably involves the nucleophilic attack of pyridine to the ylidic nitrogen anion of the bromane **1** with concomitant reductive elimination of *p*-trifluoromethylphenyl bromide. It is noted that use of the corresponding sulfonylimino-λ^3-iodane *p*-$CF_3C_6H_4I{=}NSO_2CF_3$ instead of **1** showed no evidence for formation of the pyridinium ylide **2a** under the conditions, and a large amount of the hypervalent iminoiodane was recovered unchanged. These results indicate greater reactivity of the λ^3-bromane **1** toward pyridine compared to that of the imino-λ^3-iodane (compare Table 1, entries 1 and 2).

Scheme 2

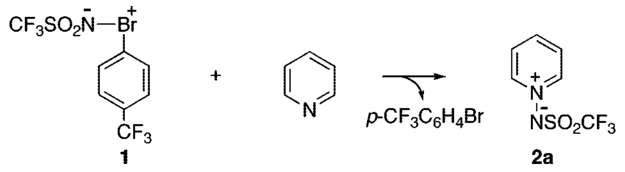
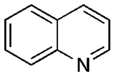
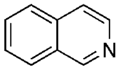
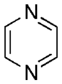


Table 1. Transylidation of Iminobromane **1** with *N*-Heterocycles[a]

entry	*N*-heterocycle	solvent	time	**2** yield (%)[b]	
1	pyridine	MeCN	10 min	**2a**	100
2[c]	pyridine	MeCN	10 min	**2a**	-
3	2-methylpyridine	MeCN	1 h	**2b**	50
4	2-methylpyridine[d]	MeCN	1 h	**2b**	76
5	2-methylpyridine	CH_2Cl_2	1 h	**2b**	79
6	3-methylpyridine	MeCN	10 min	**2c**	97
7	4-methylpyridine	MeCN	10 min	**2d**	96
8	3,5-dimethylpyridine	MeCN	10 min	**2e**	100
9	2,4,6-trimethylpyridine	MeCN	3 h	**2f**	trace
10	2,4,6-trimethylpyridine	CH_2Cl_2	4 h	**2f**	40
11	4-chloropyridine	MeCN	4 h	**2g**	92
12	4-chloropyridine	CH_2Cl_2	2 h[e]	**2g**	97
13	4-bromopyridine	MeCN	2 h	**2h**	74
14	4-cyanopyridine	MeCN	2 h	**2i**	48
15	4-cyanopyridine	CH_2Cl_2	1 h	**2i**	88
16		MeCN	3 h	**2j**	(86)
17		CH_2Cl_2	1 h	**2j**	87
18		MeCN	10 min	**2k**	92
19		MeCN	3 h	**2l**	52
20		CH_2Cl_2	1 h	**2l**	87

[a] Conditions: 1:1 *N*-heterocycle/bromane **1**, room temperature, Ar. [b] Isolated yields (^1H NMR yield). [c] Iodane *p*-$CF_3C_6H_4I{=}NSO_2CF_3$ was used. [d] 2-Methylpyridine (2.5 equiv) was used. [e] At 0 °C.

Pyridines with a methyl group at the *meta* or *para* position as well as 3,5-dimethylpyridine rapidly afforded *N*-triflyliminopyridinium ylides **2c**−**e** in high yields under the metal-free conditions, while transfer of the sulfonylimino group to pyridines with electron-withdrawing *p*-chloro, *p*-bromo, and *p*-cyano groups slows down (2−4 h). In the transylidation of a sterically demanding pyridine with an *o*-methyl group, excess amounts (2.5 equiv) of the substrate were used to obtain a good yield (76%) of ylide **2b** (Table 1, entries 3 and 4). 2,4,6-Trimethylpyridine afforded only a trace amount of ylide **2f** under our conditions (Table 1, entry 9). *N*-Heterocycles such as quinoline, isoquinoline, and pyrazine produced the *N*-iminoammonium ylides **2j**−**l** smoothly.

Imination of 4,4′-bipyridyl with equimolar imino-λ^3-bromane **1** in acetonitrile gave a 72:28 mixture of monopyridinium ylide **3a** and bis(pyridinium ylide) **3b** quantitatively; however, use of excess amounts (3 equiv) of 4,4′-bipyridyl afforded a 96% yield of the monoylide **3a** selectively, and

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(3) For C-H insertion, see: (a) Breslow, R.; Gellman, S. H. *J. Am. Chem. Soc.* **1983**, *105*, 6728. (b) Espino, C. G.; Wehn, P. M.; Chow, J.; Du Bois, J. *J. Am. Chem. Soc.* **2001**, *123*, 6935. (c) Fructos, M. R.; Trofimenko, S.; Diaz-Requejo, M. M.; Perez, P. J. *J. Am. Chem. Soc.* **2006**, *128*, 11784. (d) Fiori, K. W.; Du Bois, J. *J. Am. Chem. Soc.* **2007**, *129*, 562. (e) Li, Z.; Capretto, D. A.; Rahaman, R.; He, C. *Angew. Chem., Int. Ed.* **2007**, *46*, 5184. (f) Li, Z.; Capretto, D. A.; Rahaman, R.; He, C. *J. Am. Chem. Soc.* **2007**, *129*, 12058.

(4) (a) Okuyama, T.; Takino, T.; Sueda, T.; Ochiai, M. *J. Am. Chem. Soc.* **1995**, *117*, 3360. (b) Ochiai, M. In *Chemistry of Hypervalent Compounds*; Akiba, K.-y., Ed.; Wiley-VCH: New York, 1999; p 359.

(5) *N*-Heterocycles: (a) Jain, S. L.; Sharma, V. B.; Sain, B. *Tetrahedron Lett.* **2003**, *44*, 4385. (b) He, L.; Chan, P. W. H.; Tsui, W.-M.; Yu, W.-Y.; Che, C.-M. *Org. Lett.* **2004**, *6*, 2405.

(6) Sulfides and sulfoxides: (a) Okamura, H.; Bolm, C. *Org. Lett.* **2004**, *6*, 1305. (b) Mancheno, O. G.; Bolm, C. *Org. Lett.* **2006**, *8*, 2349. (c) Muller, J. F. K.; Vogt, P. *Tetrahedron Lett.* **1998**, *39*, 4805. (d) Takada, H.; Nishibayashi, Y.; Ohe, K.; Uemura, S. *J. Org. Chem.* **1997**, *62*, 6512. (e) Leca, D.; Song, K.; Amatore, M.; Fensterbank, L.; Lacote, E.; Malacria, M. *Chem. Eur. J.* **2004**, *10*, 906. (f) Nishibayashi, Y.; Chiba, T.; Ohe, K.; Uemura, S. *J. Chem. Soc., Chem. Commun.* **1995**, 1243.

(7) Phosphines Yamada, Y.; Yamamoto, T.; Okawara, M. *Chem. Lett.* **1975**, 361.

(8) Arsines Ou, W.; Wang, Z.-G.; Chen, Z.-C. *Synth. Commun.* **1999**, *29*, 2301.

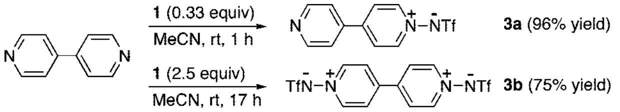
(9) Ochiai, M.; Kaneaki, T.; Tada, N.; Miyamoto, K.; Chuman, H.; Shiro, M.; Hayashi, S.; Nakanishi, W. *J. Am. Chem. Soc.* **2007**, *129*, 12938.

(10) For reviews on *N*-heterocyclic ammonium ylides, see: (a) Tamura, Y.; Ikeda, M. *Adv. Heterocycl. Chem.* **1981**, *29*, 71. (b) Timpe, H.-J. *Adv. Heterocycl. Chem.* **1974**, *17*, 213.

(11) The pyridinium ylide **2a** has been prepared by thermal reaction (80 °C) of triflyl azide in pyridine in the presence of Cu catalyst in a moderate yield (47%). See: Xu, Y.; Zhu, S. *Tetrahedron* **1999**, *55*, 13725.

the bis-ylide **3b** was produced predominantly by using 2.5 equiv of the iminobromane **1** (Scheme 3).

Scheme 3



Changing a solvent from acetonitrile to dichloromethane increases reactivity of the imino-λ^3-bromane **1** toward *N*-heterocycles and accelerates their iminations. Thus, the reaction of 2-methylpyridine in dichloromethane afforded a higher yield (79%) of the ylide **2b** than that in acetonitrile (Table 1, entries 3 and 5). To our delight, the ylide **2f** with two *o*-methyl groups was produced in 40% yield in dichloromethane. Transylidation to weak nucleophiles such as 4-cyanopyridine and pyrazine was greatly improved in the solvent, and more than 85% yields of the ylides **2i** and **2l** were produced. It seems reasonable to assume that, in a coordinating solvent such as acetonitrile, solvent coordination to the positively charged bromine(III) atom of **1** probably takes place and increases its stability. Experimental evidence for the solvent coordination to the bromine(III) in acetonitrile solution was obtained by the detailed analysis of the ESI mass spectrum of the iminobromane **1**, which revealed the prominent ion peaks of [**1**·MeCN·Na]$^+$ at *m*/*z* 435 and [**1**·MeCN·H_2O·Na]$^+$ at *m*/*z* 453, in addition to the peaks of the dimer (*m*/*z* 767) and the trimer (*m*/*z* 1138) (Figure 1). Coordination of a solvent molecule will decrease the leaving group ability of the aryl-λ^3-bromanyl group,[12] which in turn decreases the reactivity of the imino-λ^3-bromane **1** toward *N*-heterocycles.

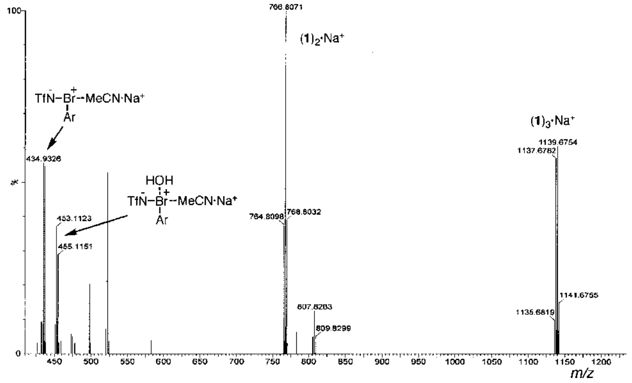


Figure 1. ESI mass spectrum of the imino-λ^3-bromane **1** in MeCN (5×10^{-3} M). Ar = *p*-$CF_3C_6H_4$.

The molecular structures of the sulfonyliminoammonium ylides **2c** and **2k** were determined unambiguously by X-ray crystal analysis (Figure 2).[13] The N1–N2 bond distances (1.4228 Å for **2c** and 1.4208 Å for **2k**) are in a good agreement with the mean value 1.401–1.454 Å reported for N–N single bonds,[14] indicating little double-bond character for the ylidic bonds.[11,15]

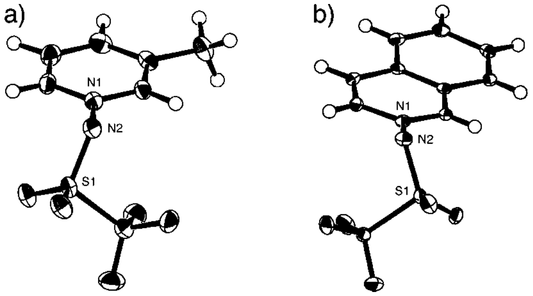


Figure 2. ORTEP drawing of nitrogen ylides: (a) **2c** and (b) **2k**. Selected bond lengths (Å) and angles (deg): N1–N2 1.4228(9), S1–N2 1.5809(8), N1–N2–S1 112.65(5) for **2c**; N1–N2 1.4208(13), S1–N2 1.5776(11), N1–N2–S1 115.39(7) for **2k**.

Direct transfer of the trifluoromethanesulfonylimino group of the imino-λ^3-bromane **1** to aliphatic trialkylamines proceeds smoothly even at 0 °C under metal-free conditions and results in the formation of the corresponding ammonium ylides **4** selectively in high yields. Thus, stoichiometric reactions of *N*-methylpiperidine, quinuclidine, and 4-diazabicyclo[2.2.2]octane (DABCO) with the bromane **1** in dichloromethane at 0 °C afforded high yields (87%, 94%, and 89%) of the iminoammonium ylides **4b**–**d**, respectively (Table 2, entries 2–4). Exposure of DABCO to 2.5 equiv of the bromane **1** in dichloromethane produced the bis-ylide **4e** (87% yield) selectively.

Reaction mechanisms involving a unimolecular decomposition of the imino-λ^3-bromane **1** (path a: nitrene mechanism) and a bimolecular nucleophilic substitution on the nitrogen atom (path b: nitrenoid mechanism) are shown in Scheme 4. Nucleophilic pyridine probably coordinates to the positively charged bromine(III) atom of the bromane **1** and produces tricoordinated λ^3-bromane **5** with a T-shaped structure; however, this process does not seem to be productive and the λ^3-bromane **5** will be equilibrated with the uncoordinated and/or solvent-coordinated imino-λ^3-bromane.[16] Path a involves generation of highly reactive free nitrene **6** via unimolecular decomposition of **1**, because of

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[12] Ochiai, M.; Suefuji, T.; Miyamoto, K.; Shiro, M. *Org. Lett.* **2005**, *7*, 2893.

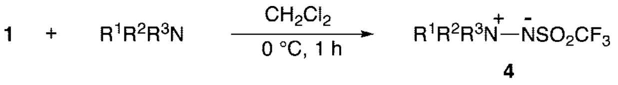
[13] See Supporting Information, CCDC-705152 for **2c**, and CCDC-705153 for **2k**.

[14] Allen, F. H.; Kennard, O.; Watson, D. G.; Brammer, L.; Orpen, A. G.; Taylor, R. *J. Chem. Soc., Perkin Trans. 2* **1978**, S1.

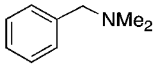
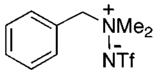
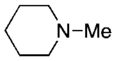
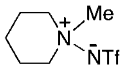
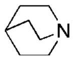
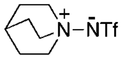
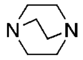
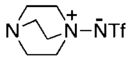
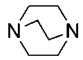
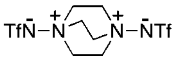
[15] For solid-state structures of iminoammonium ylides, see: (a) Legault, C.; Charette, A. B. *J. Am. Chem. Soc.* **2003**, *125*, 6360. (b) Poe, R.; Schnapp, K.; Young, M. J. T.; Grayzar, J.; Platz, M. S. *J. Am. Chem. Soc.* **1992**, *114*, 5054. (c) Morris, D. G.; Muir, K. W.; Chii, C. O. W. *Polyhedron* **2003**, *22*, 3345. (d) Cameron, A. F.; Duncanson, F. D.; Morris, D. G. *Acta Crystallogr.* **1976**, *B32*, 1987.

[16] As pointed out by one of the reviewers, ligand coupling pathway on bromine(III) of the λ^3-bromane **5**, yielding directly the pyridinium ylide **2a**, cannot be rigorously ruled out.

Table 2. Transylidation of Iminobromane **1** with *tert*-Amines[a]



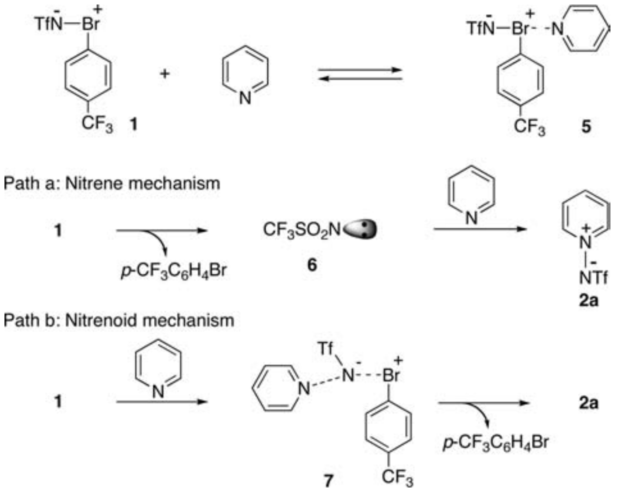
$1 + R^1R^2R^3N \xrightarrow[0\ °C,\ 1\ h]{CH_2Cl_2} R^1R^2R^3\overset{+}{N}-\overset{-}{N}SO_2CF_3$ **4**

entry	*tert*-amine	product	**4**	yield (%)[b]
1[c]			**4a**	88
2			**4b**	87
3			**4c**	94
4			**4d**	89
5[d]			**4e**	87

[a] Conditions: 1:1 amine/bromane **1**, CH_2Cl_2, 0 °C, 1 h, Ar. [b] Isolated yields. [c] MeCN, room temperature. [d] Iminobromane **1** (2.5 equiv) was used.

the hyper-leaving group ability of aryl-λ^3-bromanyl groups. Leaving group ability of aryl-λ^3-bromanyl groups is greater than that of aryl-λ^3-iodanyl groups.[17] Nucleophilic attack of pyridine to the electron-deficient nitrene **6** with a highly electron-withdrawing triflyl group ($\sigma_p = 0.96$)[18] produces the pyridinium ylide **2a**. Alternatively, in path b, nucleophilic pyridine directly attacks the negatively charged nitrogen atom of **1**, because its σ* N−Br orbital is a low-lying LUMO.[9] Here, the bromane **1** acts as a nitrenoid species and affords **2a** via S_N2 type transition state **7**.

Scheme 4



It should be possible to distinguish between these two processes by evaluating the time course for the formation of the ylides **2**. If generation of the nitrene **6** is involved (path a), one might expect that the rate of pyridinium ylide formation should be almost independent of pyridine concentration, while that in a bimolecular concerted process path b seems to depend on the concentration. Rate-determining attack of pyridine on the free nitrene **6** seems to be unlikely. Figure 3 clearly indicates that transylidation between the imino-λ^3-bromane **1** and 4-bromopyridine at 23 °C does not involve the intermediacy of the nitrene **6**, since the rate of formation of the pyridinium ylide **2h** in MeCN-d_3 obviously depends on the concentration of the pyridine.[19] As a result, reaction of the bromane **1** with 4-bromopyridine seems to produce the ylide **2h** via a concerted S_N2-type transition state such as **7**. This mechanism well explains the observed decrease in the rates of transylidation of sterically demanding pyridines, shown in Table 1. A similar concerted process is discussed in the aziridination of olefins with the bromane **1**.[9]

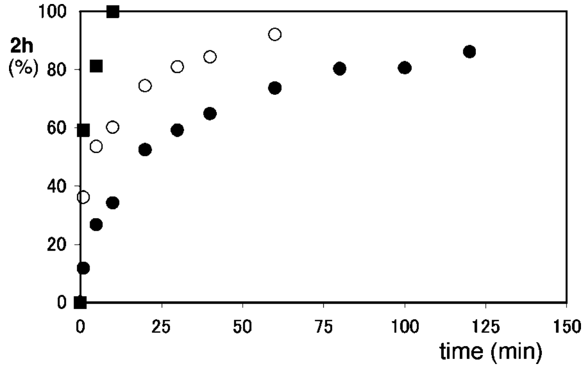


Figure 3. Time courses for transylidation between the imino-λ^3-bromane **1** (0.05 M) and 4-bromopyridine in MeCN-d_3 at 23 °C under argon: yields of the ylide **2h** were determined by ^{1}H NMR. Concentration of 4-bromopyridine: (■) 0.25 M, (○) 0.1 M, (●) 0.05 M.

In conclusion, direct transfer of the sulfonylimino group of the imino-λ^3-bromane **1** to the nitrogen atoms of *N*-heterocycles and aliphatic trialkylamines provides a useful tool for the synthesis of a variety of iminoammonium ylides under metal-free conditions at ambient temperature. The imino-λ^3-bromane **1** probably acts as a reactive nitrenoid species without any external activation and affords the ylides via a bimolecular nucleophilic substitution process.

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Supporting Information Available: Experimental details and X-ray crystallographic data in CIF format for **2c** and **2k**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(19) Addition of excess *p*-(trifluoromethyl)bromobenzene (0.5 M) did not decrease the rate of formation of **2h** to a discernible extent.