JOC Note

Unexpected Transfer of Tosyl Group of ArCH=NTs-Catalyzed by *N*-Heterocyclic Carbene

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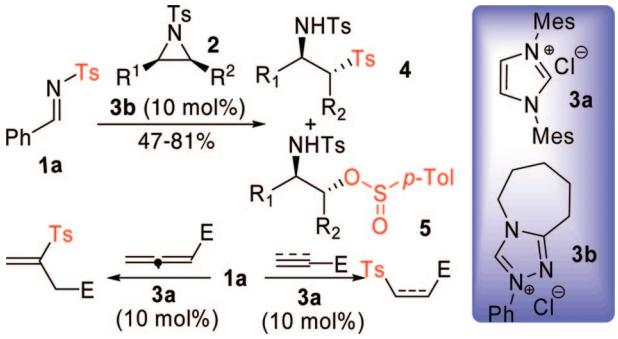
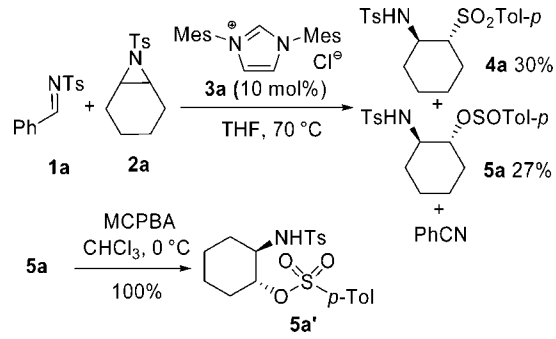
Received March 13, 2008



Reactions of *N*-tosylimines with aziridines and electron-deficient unsaturated compounds in the presence of catalytic amount of NHC afforded unexpected tosyl group transfer products in good to high yields, which represent a new reaction pattern for imines as well as for catalysis of NHC.

N-Heterocyclic carbenes (NHCs) are among the most efficient organocatalysts in organic synthesis.[1] Many types of reactions, such as benzoin condensation,[1i] the Stetter reaction,[1j] transesterification and acylation reactions,[1k,l] formation of homoenolates,[1m] ring-opening and ring-expansion reactions,[1m–p] and 1,2-addition reaction of carbonyls,[1q] can smoothly proceed using NHCs as catalyst.[1] A variety of chiral NHCs have also been developed and used in asymmetric catalysis successfully. In most cases, NHC served as nucleophilic species to initiate the reactions. There have also been reports that a hydrogen-bonded intermediate was formed between NHC and alcohol in the transesterification reaction.[2] In the course of studies on the transformations of imines[3] and aziridines,[4] we investigated the reaction of imines and aziridines in the presence of organocatalyst. To our surprise, unexpected tosyl-group transfer products were detected in the reaction of PhCH=NTs and aziridine in the presence of NHC·HCl.[5,6] Here, we disclose our results on the reaction of *N*-tosylimines with aziridines and electron-deficient unsaturated compounds using NHC as catalyst.

SCHEME 1. NHC-Catalyzed Reaction of Imines with Aziridines



We commenced our investigation by heating a solution of *N*-tosylaldimine **1a** with aziridine **2a** in the presence of 10 mol % of NHC·HCl **3a** in THF at 70 °C under argon (Scheme 1). Unexpectedly, ring-opening products of aziridine attacked by the O- and S- of the tosyl group were separated in 30% and 27% yields, respectively, accompanied a colorless oil product, which was determined as benzonitrile by GC−MS.[7] The ^{1}H NMR showed that the stereochemistry of the S-atom in **5a** was racemic. The antistereochemistry of product **5a** was confirmed by coupling constant of two hydrogens of its oxidation product **5a′** (J = 9 Hz). The structure of **4a** and its anti stereochemistry

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10.1021/jo800569g CCC: $40.75 © 2008 American Chemical Society
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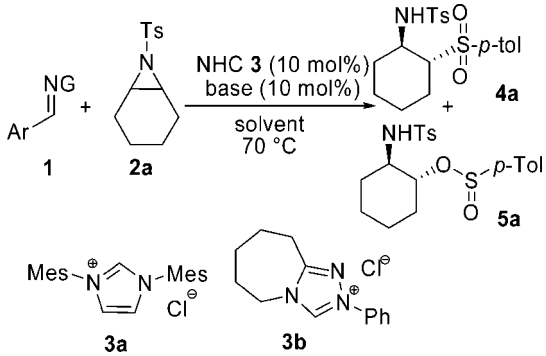
TABLE 1. Optimization of the Reaction of Imine 1 with Aziridine 2a Catalyzed by NHC·HCl 3a/Base[a]



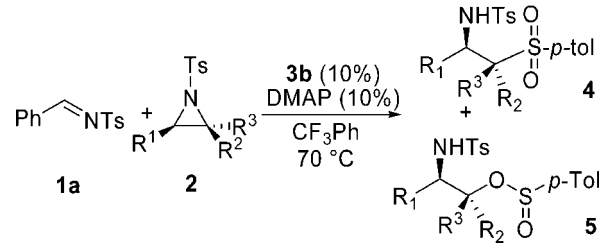
entry	1, Ar, G	base/solvents	yield%[b]	4/5[c]
1	**a**, Ph, Ts	−/THF	57	1.1/1
2	**a**, Ph, Ts	−/toluene	72	1.3/1
3	**a**, Ph, Ts	DBU/toluene	81	1.7/1
4	**a**, Ph, Ts	DBU/NO_2Ph	67	2.7/1
5	**a**, Ph, Ts	DBU/FPh	81	2.2/1
6	**a**, Ph, Ts	DBU/MeOPh	67	3.4/1
7	**a**, Ph, Ts	DBU/CF_3Ph	86	2.6/1
8	**a**, Ph, Ts	DMAP/ CF_3Ph	77	4.4/1
9	**a**, Ph, Ts	^{i}Pr$_2$NEt/ CF_3Ph	97	2.2/1
10	**a**, Ph, Ts	DMAP/ CF_3Ph[d]	72	4.5/1
11	**a**, Ph, Ts	DMAP/ CF_3Ph[e]	NR[f]	
12	**b**, 4-$NO_2C_6H_4$, Ts	DBU/toluene	20	1/0
13	**c**, 4-$MeOC_6H_4$, Ts	DBU/toluene	73	2.3/1
14	**d**, 4-BrC_6H_4, Ts	DBU/toluene	87	2.0/1
15	**e**, 2,4-diClC_6H_3, Ts	DBU/toluene	73	2.0/1
16	**f**, 1-Naphthyl, Ts	DBU/toluene	73	1.6/1
17	**g**, 4-ClC_6H_4, Ph	DBU/toluene	NR	
18	**h**, Ph, S(O)Bu^t	DBU/toluene	NR	
19	**i**, 4-MeC_6H_4, P(O)Ph_2	DBU/toluene	NR	
20	**j**, Ph, SO_2CH_3	DBU/toluene	NR	

[a] All reactions were performed on a 0.5 mmol scale in 2.5 mL of solvent at 70 °C in 24 h. [b] Isolated yield of **4** and **5**. [c] Determined by ^{1}H NMR. [d] NHC·HCl **3b** was used. [e] No NHC was added. [f] NR = no reaction.

were determined by comparison of its ^{1}H NMR with that of product obtained from the reaction of **2a** with PhSH followed by oxidation using *m*-CPBA.[8]

The influences of bases and solvents on the reaction using NHC·HCl **3** were investigated (Table 1). The yields of **4a** and **5a** were 30% and 27%, respectively, when the reaction proceeded in THF using 10 mol % of NHC·HCl **3a** (entry 1), which increased to 41% and 31%, respectively, if toluene was solvent (entry 2). It increased further to 51% and 30% if 10 mol% of DBU was added (entry 3). The yields of both **4a** and **5a** were unchanged when the reaction was run under aerobic conditions. An increase of catalyst loading to 20 mol % did not increase the yields of products but shortened the reaction time. A screen of common solvents showed that no products were separated when the reaction proceeded in EtOH, CH_2Cl_2, MeCN, and hexane, while complex products were provided using DMF as solvent (not showed in Table 1); however, the yield and selectivity were improved using other aromatic solvents combined with the change of bases (entries 4−9). Among them, the best yields (97%) of **4a** and **5a** with a ratio of 2.2:1 were provided when using ^{i}Pr$_2$NEt as base and CF_3Ph as solvent (entry 9), while the better selectivity (the ratio of 4.4:1 for **4a** and **5a**) was realized in CF_3Ph using DMAP as base (entry 8). Almost the same selectivity was given when the NHC·HCl **3b**[9] was used in DMAP/CF_3Ph (entry 10 vs entry 8). Control experiments showed that no tosyl-transfer product was detected when the reaction proceeded in the absence of NHC (entry 11).

TABLE 2. Tosyl-Transfer Reaction from Imine 1a to Aziridines 2 Catalyzed by NHC·HCl 3b/DMAP[a]



entry	2, R^1, R^2, R^3	yield%[b]	4/5[c]
1	**e**, ^{n}Bu, H, H	79	2.8/1
2	**e**, ^{n}Bu, H, H	68[d]	2.3/1
3	**a**, $-(CH_2)_4-$, H	72	4.5/1
4	**f**, ^{n}hexyl, H, H	69	2.6/1
5	**g**, $C_{16}H_{33}$, H, H	67	3.3/1
6	**h**, H, Ph, H	51	1/0
7	**i**, Me, H, Ph	85	1/0
8	**k**, H, H, H	73	2.9/1

[a] Run at 70 °C using 10 mol % of **3b** and DMAP on a 0.5 mmol scale in 2.5 mL of CF_3Ph in 24 h. [b] Isolated yield of **4** and **5**. [c] Determined by ^{1}H NMR. [d] 10 mol % of **3a** was used.

The effect of different aldimines to this tosyl-transfer reaction was also examined using **3a**/DBU as catalyst in toluene (Table 1, entries 11−19). As expected, all *N*-tosyl aromatic aldimines reacted with aziridine **2a** successfully (entries 12−15) except **1b** with nitro group as substituent on the phenyl ring, which gave only 20% yield of *S*-attacked product (entry 11). However, other aldimines with sulfinyl, phosphinoyl, phenyl, and mesyl as substituent on nitrogen gave no products (entries 16−19). These results may reflect the importance of electronic effect of imine in the reaction.

With the optimized conditions, the scope of the reaction was investigated and the results were compiled in Table 2. Compared to the reaction of aziridine **2e** using **3a**/DMAP as catalyst, that use of **3b**/DMAP provided better results either in yield or selectivity (entry 1 vs entry 2). Thus, NHC·HCl **3b** was used in all reactions.

All reactions delivered products **4** and **5** in good yields except that using aziridine **2h** derived from styrene, which gave **4h** in 51% yield (entry 6). The ratio of **4** and **5** was between 2.6−4.5. However, aziridines **2h** and **2i** with Ph as substituent afforded *S*-attacked product only (entries 6 and 7). The reactions provided terminal attacked products when monosubstituted aziridines were used (entries 1−5) while that of phenyl-substituted aziridines preferred to produce benzylic attacked products (entries 6 and 7). Reaction of aziridine **2b** derived from cyclopetene gave only 10% yield of products, while that of **2c**,**d** derived from cycloheptene and cyclooctene and that of disubstituted aziridine **2j** derived from oct-2-ene provided no product (not showed in Table 2).

Surprisingly, propargyl ester **7**, allenyl ester **9**, and α,β-unsaturated ester **11** are suitable acceptors of the tosyl group of imines. Reactions of them with *N*-tosyl imine **1a** afforded tosyl-

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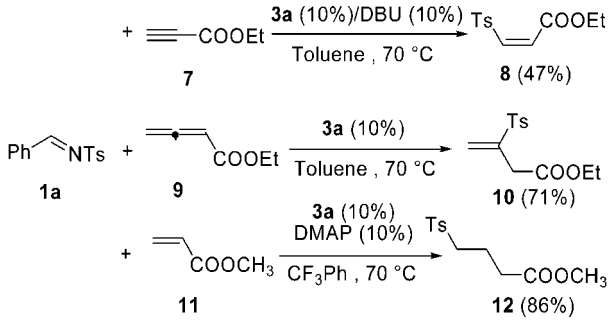
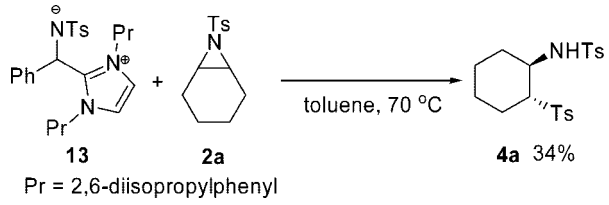
SCHEME 2. Tosyl-Transfer Reactions of Imines with Unsaturated Substrates



SCHEME 3. Formation of Imine−NHC Adduct and Tosyl-Transfer Reaction

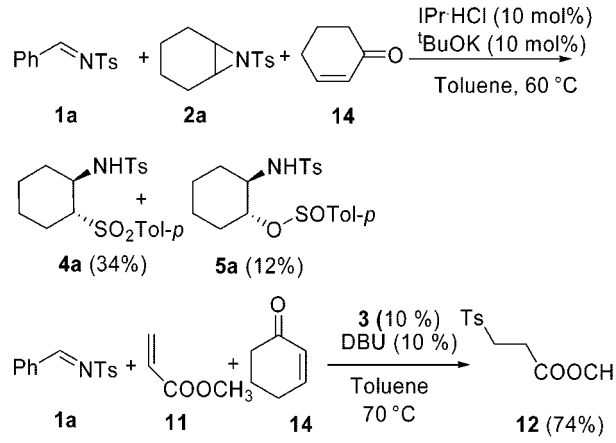


transfer products **8**, **10**, and **12** in moderate to good yields, respectively (Scheme 2).[10] It was worth noting that in these cases only *S*-attacked products were detected. It has well been documented that aza-Morita−Baylis−Hillman products or cycloaddition products are provided in the reaction of electron-deficient unsaturated esters with imines catalyzed by amines or organophosphines.[11,12] However, no such products were detected under our reaction conditions.

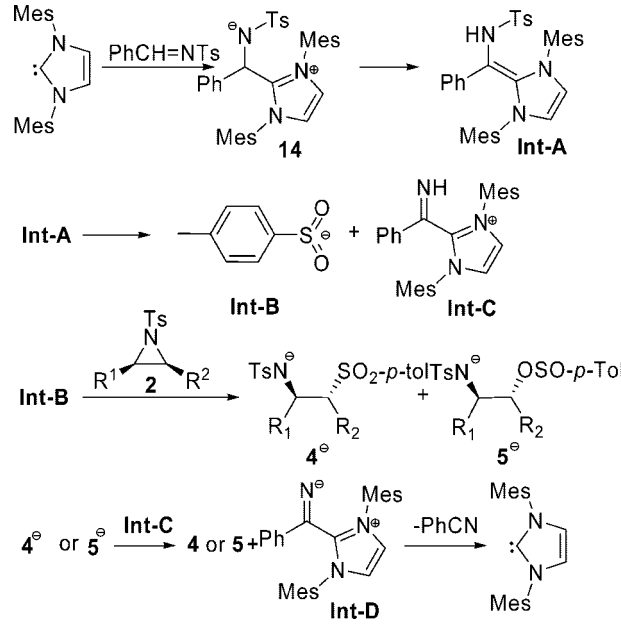
Bode has reported the formation of the stable *N*-tosylimine−NHC adduct, which inhibited the further catalytic process in the reaction of *N*-tosylimine and enals in the presence of NHC.[5b] Ye recently reported the aza-Morita−Baylis−Hillman reaction of *N*-tosylimine with cyclic enones catalyzed by NHC.[5c] However, when we treated the aziridine **2a** with imine−NHC adduct **13** prepared from *N*-tosylimine **1a** and IPr·HCl,[5c] tosyl-transfer product **4a** was separated in 34% yield (Scheme 3). Also, in the cross-over reaction of **1a**, **2a** and cyclohexenone **14** in the presence of IPr·HCl and base, no aza-Morita−Baylis−Hillman product was detected; instead, tosyl-transfer products **4a** and **5a** in a ratio of 3:1 were obtained in 46% yield. The reaction of **1a**, **11**, and cyclohexenone **14** using NHC·HCl as catalyst also gave no aza-Morita−Baylis−Hillman product, but tosyl-transfer product (Scheme 4). These results indicated that *N*-tosylimine−NHC adduct should be an active intermediate.

According to the clues we have found, a plausible reaction path can be proposed (Scheme 5). The reaction of imine **1** with NHC forms the adduct **14**,[5] and then proton transfer of which provides **int-A** and decomposition of **int-A** gives **int-B** and **int-C**. Attack of **int-B** to aziridine **2** gives rise to $\mathbf{4}^-$ and $\mathbf{5}^-$ and

SCHEME 4. Cross-over Reactions of Imine, Aziridine, or Acrylate and Cyclohexenone in the Presence of NHC



SCHEME 5. Plausible Mechanism of Tosyl-Transfer Reaction



attraction of proton from **int-C** by $\mathbf{4}^-$ and $\mathbf{5}^-$ affords final products **4** and **5** and **int-D**, which deliveres PhCN and NHC to complete the catalytic cycle.[13]

In conclusion, an unexpected tosyl-transfer was discovered from the reaction of *N*-tosylimines with aziridines and α,β-unsaturated esters catalyzed by NHC, which represents a new reaction patent for imine as well as for catalysis of NHC. Controlled experiments showed that *N*-tosylimine-NHC adduct should be an active species. Further investigations on the detailed mechanism and extension of the reaction are in progress.

Experimental Section

Representative Procedure for the Tosyl-Transfer Reaction of Aziridines and *N*-Tosylimines. To a solution of *N*-tosylphenylimine **1a** (130 mg, 0.5 mmol) in 2.5 mL of trifluoromethylbenzene was added aziridine **2a** (125 mg, 0.5 mmol) under argon, followed by addition of NHC salt **3b** (12 mg, 0.05 mmol) and DMAP (6 mg, 0.05 mmol). The resulting solution was allowed to

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(13) The transfer of sulfonyl radical to alkene was reported: (a) Nair, V.; Augustine, A.; Suja, T. D. *Synthesis* **2002**, 2259.

stir at 70 °C and monitored by TLC. The reaction mixture was directly onto a silica gel column. The products **4a** and **5a** were isolated by flash column chromatography (petroleum ether/ethyl acetate, 10:1 to 5:1 to 3:1).

4-Methyl-*N*-(2-tosylcyclohexyl)benzenesulfonamide (4a): colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.10−1.40 (m, 4H), 1.51−1.62 (m, 1H), 1.67−1.76 (m, 1H), 1.81−1.91 (m, 1H), 2.40−2.46 (m, 1H), 2.46 (s, 6H), 3.01 (td, J = 3.6 Hz, 10.5 Hz, 1H), 3.28−3.38 (m, 1H), 6.32 (s, 1H), 7.30−7.36 (m, 4H), 7.61 (d, J = 8.1 Hz, 2H), 7.78 (d, J = 8.1 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.46, 21.55, 22.50, 23.25, 25.29, 51.44, 64.56, 127.25, 128.85, 129.50, 129.73, 133.32, 136.99, 143.37, 145.12; ESI-MS 430.2 (M + Na^+); EI-MS *m*/*z* 407 (M^+, 0.37), 252 (100), 187 (23), 155 (38), 91 (77); IR (cm^{-1}) 3256, 2939, 2865, 1597, 1452, 1335, 1314, 1303, 1288, 1160, 1143. Anal. Calcd for $C_{20}H_{25}NO_4S_2$: C, 58.94; H, 6.18; N, 3.44. Found: C, 59.20; H, 6.37; N, 3.15.

2-(4-Methylphenylsulfonamido)cyclohexyl 4-Methylbenzenesulfinate (5a). The compound was isolated as an inseparable mixture of two diastereoisomers (1:1), whose NMR peaks were hard to distinguish: colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.00−1.40 (m, 8H), 1.40−1.60 (m, 3H), 1.60−1.80 (m, 2H), 2.08−2.22 (m, 2H), 2.27−2.40 (m, 1H), 2.29 (s, 3H), 2.42 (s, 3H), 2.44 (s, 3H), 2.46 (s, 3H), 2.81−3.00 (m, 2H), 3.70−3.82 (m, 1H), 3.95−4.05 (td, J = 4.2, 9.9 Hz, 1H), 5.55 (d, J = 3 Hz, 1H), 5.92 (d, J = 5.2 Hz, 1H), 7.03 (d, J = 8.4 Hz, 2H), 7.25−7.38 (m, 6H), 7.47 (d, J = 7.8, 2H), 7.57 (d, J = 8.1 Hz, 2H), 7.69 (d, J = 8.1 Hz, 2H), 7.82 (d, J = 8.1 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.36, 21.49, 23.56, 23.76, 23.88, 26.59, 32.54, 32.60, 32.90, 32.55, 55.96, 56.26, 75.83, 79.98, 124.93, 125.40, 127.20, 127.46, 136.92, 137.33, 139.93, 141.44, 142.65, 142.90, 143.03, 143.25; ESI-MS 408.2 (M + H^+), 430.2 (M + Na^+); IR (cm^{-1}) 3248, 2941, 2864, 1598, 1453, 1335, 1164, 1093. Anal. Calcd for $C_{20}H_{25}NO_4S_2$: C, 58.94; H, 6.18; N, 3.44. Found: C, 58.74; H, 6.31; N, 3.27.

Acknowledgment. Financial support from National Natural Science Foundation of China, the Major Basic Research Development Program (2006CB806100), the Chinese Academy of Sciences and Science, and the Technology Commission of Shanghai Municipality are acknowledged.

Supporting Information Available: Experimental procedures and characterization data for products **4a**,**e**−**i**,**k**, **5a**,**e**−**g**,**k**, **5a′**,**f′**, **10**, and **12**, synthetic procedure and analysis data for NHC **3b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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