Tetrahedron Letters 50 (2009) 5351–5353

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Iodine-catalyzed intermolecular hydroamination of vinyl arenes

J. S. Yadav *, B. V. Subba Reddy, T. Srinivasa Rao, B. Bala M. Krishna

Division of Organic Chemistry, Indian Institute of Chemical Technology, Hyderabad 500 007, India

ARTICLE INFO

Article history:
Received 22 May 2009
Revised 30 June 2009
Accepted 3 July 2009
Available online 9 July 2009

Keywords:
Hydroamination
Vinyl arenes
Molecular iodine
Sulfonamides

ABSTRACT

The vinyl arenes undergo smooth hydroamination with sulfonamides in the presence of 10 mol % of iodine to furnish tosyl and mesyl-protected secondary amines in excellent yields in short reaction times. The use of inexpensive and readily available molecular iodine makes this method quite simple, more convenient, and practical.

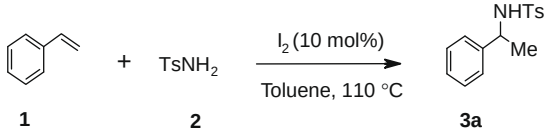
The intermolecular hydroamination of alkenes is one of the direct and most efficient approaches for the production of amines.[1,2] Consequently; there have been some reports on intermolecular hydroamination of olefins with amides using $Ph_3PAuOTf$, $Cu(OTf)_2$/BINAP, $(COD)Pt(OTf)_2$, $Bi(OTf)_3$/$[Cu(CH_3CN)_4]PF_6$, $FeCl_3$, TfOH, $InBr_3$, silicotungstic acid, and $[(PhO)_3P]AuCl$/AgOTf.[3–5] Uncatalyzed hydroamination is prohibited by a large activation energy barrier under ambient conditions, especially with electronically neutral alkenes. However, few intermolecular additions of amines to olefins have been reported with $Pd(O_2CCF_3)_2$/DPPF/TfOH, $[Rh(COD)(DPEphos)]BF_4$, and $Ph_3CB(C_6F_5)_4$.[6,7] Since amines and their derivatives have become increasingly useful and important in the field of drugs and pharmaceuticals, the hydroamination of alkenes remains an important and challenging strategy.

Recently, molecular iodine has received considerable attention in organic synthesis because of its low cost and ready availability. The mild Lewis acidity associated with iodine has enhanced its use in organic synthesis to perform several organic transformations using stoichiometric levels to catalytic amounts.[8]

Following our interest in the catalytic uses of molecular iodine,[9] we herein report an efficient method for the hydroamination of vinyl arenes with sulfonamides using molecular iodine. Initially, we attempted an intermolecular hydroamination of a readily available styrene **1** (3 equiv) with *p*-toluenesulfonamide **2** (1 equiv) in the presence of 10 mol % of I_2. The reaction proceeded well in toluene at 110 °C and the desired product, α-phenylethyl amide (**3a**) was isolated in 92% yield (Scheme 1).

This result provided the incentive for further study of reactions with various olefins and sulfonamides. Interestingly, various vinyl arenes such as *p*-methyl-, *p*-*t*-butyl-, *p*-chloro-, *p*-methoxy-, and α-methylstyrenes underwent smooth hydroamination with *p*-toluenesulfonamide under identical conditions (Table 1, entries **b**–**k**). The reactions proceeded smoothly by 10 mol % of iodine in refluxing toluene under neutral conditions to afford the α-amido derivatives in excellent yields. In case of styrenes, the products were formed by the selective addition of $TsNH_2$ at benzylic position (Table 1, entries **a**–**k**). Furthermore, cyclic olefins such as 1,2-dihydronaphthalene and indene also participated well in this reaction to give the corresponding 1-amido derivatives in good yields (Table 1, entries **l**–**o**, Scheme 2).

Next, we have investigated the reactions of alkenes with different sulfonamides such as benzenesulfonamide, methanesulfonamide, and saccharin (Table 1). Interestingly, α-methylstyrene also underwent smooth addition with $TsNH_2$ under similar conditions (Table 1, entry **k**). Furthermore, saccharin also underwent smooth hydroamination with *p*-methylstyrene to produce the corresponding amido derivative (Table 1, entry **e**). The yields were generally high and the reactions went to completion in short times (Table 1, entries **a**–**o**). In general, the hydroamination was clean and no



Scheme 1.

* Corresponding author. Tel.: +91 40 27193434; fax: +91 40 27160512.
E-mail address: yadav@iict.res.in (J.S. Yadav).

0040-4039/$ - see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2009.07.010

Table 1
Iodine-catalyzed intermolecular hydroamination of vinyl arenes

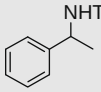
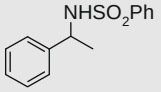
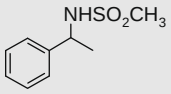
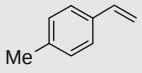
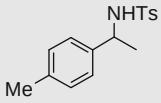
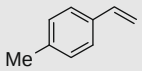
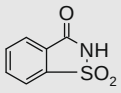
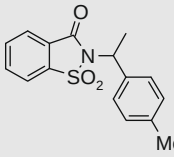
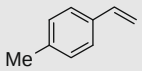
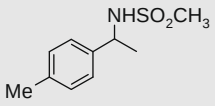
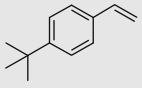
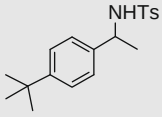
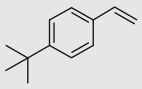
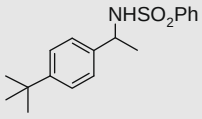
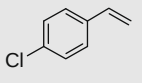
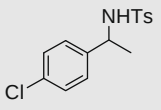
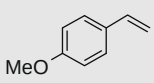
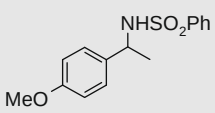
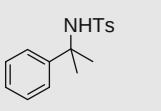
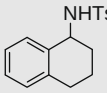
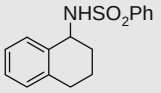
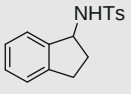
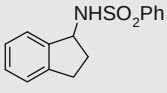
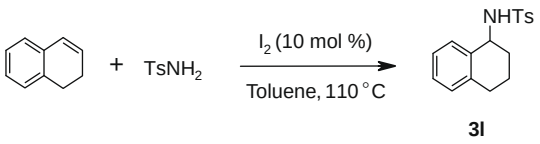
Entry	Alkene (3 equiv)	Nucleophile (1 equiv)	Product[a]	Time (h)	Yield[b] (%)
a		$TsNH_2$		2.0	92
b		$PhSO_2NH_2$		2.5	90
c		$CH_3SO_2NH_2$		4.0	86
d		$TsNH_2$		2.0	90
e				2.0	78
f		$CH_3SO_2NH_2$		4.0	78
g		$TsNH_2$		2.5	85
h		$PhSO_2NH_2$		2.5	86
i		$TsNH_2$		3.0	80
j		$PhSO_2NH_2$		1.5	75
k		$TsNH_2$		3.0	76

Table 1 (*continued*)

Entry	Alkene (3 equiv)	Nucleophile (1 equiv)	Product[a]	Time (h)	Yield[b] (%)
l		$TsNH_2$		2.5	86
m		$PhSO_2NH_2$		3.0	80
n		$TsNH_2$		3.0	84
o		$PhSO_2NH_2$		3.5	80

[a] The products were characterized by NMR, IR, and mass spectrometry.
[b] Yield refers to pure products after chromatography.



Scheme 2.

by-products such as iodo adducts were detected under these conditions.

The effects of various solvents such as dichloroethane, THF, acetonitrile 1,4-dioxane, and toluene were studied in the hydroamination of styrene with $TsNH_2$. Low yields (10–50%) were obtained when styrene was reacted with $TsNH_2$ using 10 mol % of iodine in dichloroethane, THF, acetonitrile, and 1,4-dioxane. Of these, toluene appeared to give the best results. In the absence of catalyst, the reactions did not proceed even after long reaction times (10–24 h). There was no significant improvement in reaction rate and yields when the reaction was performed using stoichiometric amounts of iodine. However, long reaction times (36–48 h) are required when 5 mol % of iodine was used. Therefore, the use of 10 mol % of iodine is ideal to achieve the best conversion. The use of excess of olefin (3 equiv) was also crucial to obtain high conversion. This method does not require the use of expensive or corrosive reagents and no precautions need to be taken to exclude moisture from the reaction medium. The scope and generality of this process is illustrated with respect to various olefins and sulfonamides and the results are presented in Table 1.[10] Mechanistically, iodine may initially react with sulfonamide to furnish a catalytic amount of HI, which subsequently may react with olefin. The resulting iodide may undergo a nucleophilic substitution by the amine to furnish the desired product.

In summary, we have described a simple and efficient protocol for the intermolecular hydroamination of vinyl arenes with sulfonamides using iodine as the novel reagent under neutral conditions. The notable features of this procedure are high conversions, short reaction times, operational simplicity, and ready availability of reagents at low cost which make it a useful and attractive strategy

for the preparation of α-phenylethyl amine, 1-aminodihydroindane, and 1-aminotetrahydronaphthalene derivatives.

Acknowledgment

T.S.R. and B.M.K. thank the CSIR, New Delhi, for the award of fellowships.

References and notes

1. (a) Hong, S.; Marks, T. *Acc. Chem. Res.* **2004**, *37*, 673; (b) Bellor, M.; Seayad, J.; Tillack, A.; Jiao, H. *Angew. Chem., Int. Ed.* **2004**, *43*, 3368; (c) Molander, G. A.; Romero, A. C. *Chem. Rev.* **2002**, *102*, 2161.
2. (a) Senn, H. M.; Blochl, P. E.; Tongi, A. *J. Am. Chem. Soc.* **2000**, *122*, 4098; (b) Muller, T. E.; Beller, M. *Chem. Rev.* **1998**, *98*, 675.
3. (a) Zhang, J. L.; Yang, C.-G.; He, C. *J. Am. Chem. Soc.* **2006**, *128*, 1798; (b) Taylor, J. G.; Whittall, N.; Hii, K. K. *Org. Lett.* **2006**, *8*, 3561.
4. (a) Karshtedt, D.; Bell, A. T.; Tilley, T. D. *J. Am. Chem. Soc.* **2005**, *127*, 12640; (b) Qin, H.; Yamagiwa, N.; Matsunaga, S.; Shibasaki, M. *Chem. Asian J.* **2007**, *2*, 150; (c) Michaux, J.; Vincent, T.; Marque, S.; Wehbe, J.; Prim, D.; Campagne, J.-M. *Eur. J. Org. Chem.* **2007**, 2601.
5. (a) Li, Z.; Zhang, J.; Brouwer, C.; Yang, C.-G.; Reich, N. W.; He, C. *Org. Lett.* **2006**, *8*, 4175; (b) Huang, J.-M.; Wong, C.-M.; Xub, F.-X.; Loh, T.-P. *Tetrahedron Lett.* **2007**, *48*, 3375; (c) Yang, L.; Xu, L.-W.; Xia, C.-G. *Tetrahedron Lett.* **2008**, *49*, 2882; (d) Giner, X.; Najera, C. *Org. Lett.* **2008**, *10*, 2919.
6. (a) Utsunomiya, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2003**, *125*, 14286; (b) Utsunomiya, M.; Kuwano, R.; Kawatsura, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2003**, *125*, 5608.
7. (a) Kawatsura, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2000**, *122*, 9546; (b) Anderson, L. L.; Arnold, J.; Bergman, R. G. *J. Am. Chem. Soc.* **2005**, *127*, 14542; (c) Ryu, J.-S.; Li, G. Y.; Marks, T. J. *J. Am. Chem. Soc.* **2003**, *125*, 12584.
8. (a) Togo, H.; Iida, S. *Synlett* **2006**, 2159; (b) Lin, X.-F.; Cui, S.-L.; Wang, Y. G. *Tetrahedron Lett.* **2006**, *47*, 4509; (c) Chen, W.-Y.; Lu, J. *Synlett* **2005**, 1337; (d) Royer, L.; De, S. K.; Gibbs, R. A. *Tetrahedron Lett.* **2005**, *46*, 4595; (e) Banik, B. K.; Fernandez, M.; Alvarez, C. *Tetrahedron Lett.* **2005**, *46*, 2479; (f) Wang, S.-Y. *Synlett* **2004**, 2642; (g) Ko, S.; Sastry, M. N. V.; Lin, C.; Yao, C.-F. *Tetrahedron Lett.* **2005**, *46*, 5771; (h) Pukan, P. *Synth. Commun.* **2004**, *34*, 1065; (i) Chu, C.-M.; Yao, C.-F.; Huang, W. J.; Liu, J. T. *Tetrahedron Lett.* **2007**, *48*, 6881.
9. (a) Yadav, J. S.; Reddy, B. V. S.; Hashim, S. R. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3025; (b) Yadav, J. S.; Reddy, B. V. S.; Premalatha, K.; Swam, T. *Tetrahedron Lett.* **2005**, *46*, 2687; (c) Yadav, J. S.; Reddy, B. V. S.; Sabitha, G.; Reddy, G. S. K. K. *Synthesis* **2000**, 1532; (d) Yadav, J. S.; Reddy, B. V. S.; Rao, C. V.; Chand, P. K.; Prasad, A. R. *Synlett* **2001**, 1638; (e) Yadav, J. S.; Reddy, B. V. S.; Reddy, M. S.; Prasad, A. R. *Tetrahedron Lett.* **2002**, *43*, 9703.
10. *Experimental procedure*: A mixture of olefin (3 mmol), sulfonamide (1 mmol), and iodine (10 mol %) was stirred in toluene (5 mL) at 110 °C for a specified time to complete the reaction indicated by TLC (Table 1). After completion of the reaction, reaction mixture was cooled to room temperature and then washed with saturated sodium thiosulfate aqueous solution, and the solution was extracted with ethyl acetate (2 × 10 mL). The combined organic layers were dried over anhydrous Na_2SO_4, concentrated in vacuo, and purified by column chromatography. The products were characterized by IR, ^{1}H NMR, ^{13}C NMR, and mass spectrometry.*N-[1-(4-Methylphenyl)ethyl]-p-toluenesulfonamide (entry* **3d**): Light green solid, mp 114–116 °C, IR (KBr): *ν* 3252, 2920, 1646, 1513, 1324, 1158, 1083, 958, 810, 666 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): *δ* 7.63 (d, *J* = 7.5 Hz, 2H), 7.18 (d, *J* = 8.3 Hz, 2H), 6.98 (s, 4H), 5.16 (d, *J* = 6.8 Hz, 1H), 4.45–4.36 (m, 1H), 2.43 (s, 3H), 2.30 (s, 3H), 1.43 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): *δ* 20.89, 21.35, 23.39, 53.32, 125.96, 127.01, 128.99, 129.26, 136.89, 137.65, 139.11, 142.85. ESI-MS (*m*/*z*): (M+Na): 312. HRMS *m*/*z*: calcd for $C_{16}H_{19}NO_2NaS$ $[M+Na]^+$: 312.1034, found, 312.1044.*N-[1-[4-(tert-Butyl)phenyl]ethyl]-benzenesulfonamide (entry* **3h**): IR (neat): *ν* 3276, 3061, 2962, 2868, 1512, 1447, 1323, 1165, 1091, 962, 833, 721 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): *δ* 7.71–7.66 (m, 2H), 7.38–7.23 (m, 3H), 7.11–6.94 (m, 4H), 5.89 (d, *J* = 7.3 Hz, 1H), 4.51–4.3 (m, 1H), 1.41 (d, *J* = 7.3 Hz, 3H), 1.24 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): *δ* 23.3, 31.15, 34.24, 53.38, 125.15, 125.73, 126.92, 128.55, 131.96, 138.69, 140.68, 150.05. ESI-MS: *m*/*z*: (M+Na): 340. HRMS *m*/*z*: calcd for $C_{18}H_{23}NO_2NaS$ $[M+Na]^+$: 340.1347, found, 340.1351.*N-(2,3-Dihydro-1H-1-indenyl)-p-toluenesulfonamide (entry* **3n**): White solid, mp 139–141 °C, IR (KBr): *ν* 3261, 3064, 2924, 2854, 1596, 1457, 1422, 1317, 1159, 1092, 917, 668 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): *δ* 7.87 (d, *J* = 8.0 Hz, 2H), 7.39–7.13 (m, 6H), 4.89–4.69 (m, 2H), 3.03–2.7 (m, 2H), 2.52 (s, 3H), 2.44–2.30 (m, 1H), 1.90–1.71 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): *δ* 21.49, 29.90, 34.59, 58.67, 124.04, 124.74, 126.78, 127.10, 128.21, 129.72, 138.21, 141.96, 142.78, 143.36. ESI-MS (*m*/*z*): (M+Na): 310. HRMS *m*/*z*: calcd for $C_{16}H_{17}NO_2NaS$ $[M+Na]^+$: 310.0877, found, 310.0881.