Res Chem Intermed
DOI 10.1007/s11164-016-2688-3

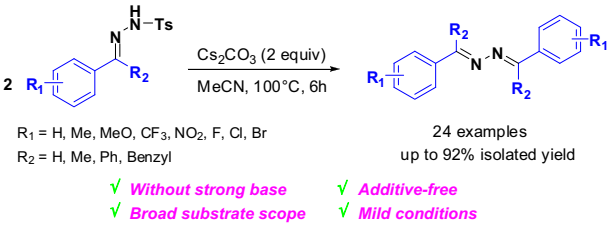
Cs_2CO_3-mediated decomposition of *N*-tosylhydrazones for the synthesis of azines under mild conditions

Zai-Gang Luo[1] · Peng Liu[2] · Yu-Yu Fang[1] · Xue-Mei Xu[1] · Cheng-Tao Feng[1] · Zhong Li[1] · Xiao-Mei Zhang[1] · Jie He[1]

Received: 26 May 2016 / Accepted: 1 August 2016

Abstract A facile, environmentally and efficient Cs_2CO_3-mediated decomposition of *N*-tosylhydrazones reaction has been developed for the synthesis of functionalized azines under mild conditions. This method offers broad substrate scope, occurs as additive-free, without strong base conditions, utilizes readily available reactants, and forms products in good to high yields.

Graphical Abstract



Electronic supplementary material The online version of this article (doi:10.1007/s11164-016-2688-3) contains supplementary material, which is available to authorized users.

✉ Zai-Gang Luo
luozi139@163.com

✉ Jie He
aust_jhe@163.com

[1] College of Chemical Engineering, Anhui University of Science and Technology, Huainan 232001, China

[2] Guang Zhou Institutes of Biomedicine and Health, Chinese Academy of Sciences, Guangzhou 510530, China

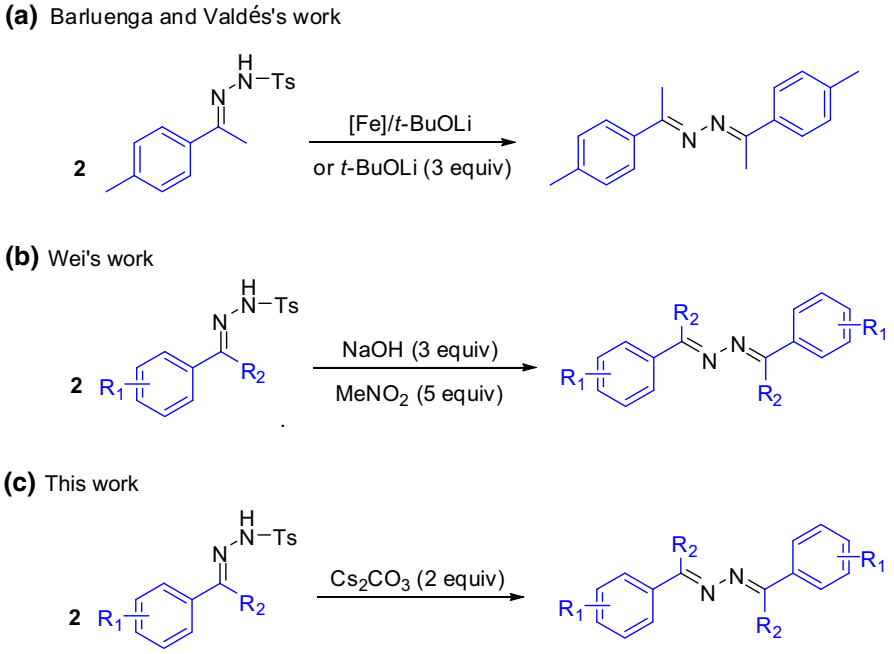
Published online: 10 August 2016

Keywords Decomposition · *N*-Tosylhydrazones · Cs_2CO_3 · Azines

Introduction

Azines, *N*–*N* linked diimines, which exhibit interesting biological [1–3], conductive [4–6], and optical [7–9] properties and are extensively used as synthetic intermediates [10–14], have received increasing attention in recent years. Generally, azines are prepared by the condensation of aldehydes or ketones with hydrazine hydrate in solution under refluxing conditions or with promoters such as iodine or acid [15–17]. These reactions proceed rapidly but often generate large amounts of unwanted byproducts. Very recently, Peltier et al. [18] reported the first examples of copper-catalyzed hydrohydrazination of terminal alkynes with hydrazine hydrate for the synthesis of symmetrical and unsymmetrical azines. However, hydrazine hydrate is a volatile liquid, which is extremely hazardous with risks of handling and transportation. In 2011, Lee et al. [19] demonstrated that the synthesized solid hydrazine can be a very valuable alternative for the toxic liquid hydrazine. Solid hydrazine is remarkably stable but is as reactive as liquid hydrazine even in the absence of solvents for the synthesis of azines. Although many of these methods provide an efficient route to azines they require toxic liquid hydrazine or synthesized solid hydrazine as a reactant, relatively harsh reaction conditions, and a tedious workup procedure. Thus, the development of a novel reaction system under mild reaction conditions is required.

N-Tosylhydrazones, derived from the corresponding aldehydes or ketones, have been extensively utilized as the precursors of diazo compounds or carbenes [20, 21]. In recent years, rapid progress has been made in tosylhydrazone-participated transition-metal-catalyzed or metal-free cross-coupling reactions [22–27]. For example, in the presence of PPh_3 and *t*-BuOLi, asymmetrical azines were formed in good yields by the metal-free cross-coupling reaction of tosylhydrazones with aldehydes [25]. In addition, these reactions reported in the literature were usually carried out in basic conditions. Decomposition of tosylhydrazones toward byproducts such as azines or *N*-substituted hydrazones usually took place [28–31]. Therefore, the transition-metal-catalyzed or metal-free decomposition of tosylhydrazones provides an attractive alternative to the reported methods for the synthesis of azines. In 2011, Fe-catalyzed or *t*-BuOLi-mediated decomposition of tosylhydrazone affording azine was reported by Barluenga et al. [30] (Scheme 1a). Recently, a similar transformation promoted by NaOH and CH_3NO_2 was reported by Sha and Wei [31] (Scheme 1b). The past developments are still far from being considered as environmentally benign since the use of a metal catalyst, strong base and toxic reagents restrict their applicability. Hence, the study of new procedures that are less hazardous to human health and the environment has received extensive attention. Considering the wide applications of azines, a mild base and solvent-controlled metal- and additive-free decomposition pathway toward azines using aldehyde tosylhydrazones and ketone tosylhydrazones as substrates is reported here (Scheme 1c).



Scheme 1 Synthesis of azines from *N*-tosylhydrazones

Experimental

Unless otherwise noted, all materials were obtained from commercial suppliers and dried and purified by standard procedures. The melting point was measured on a SGW X-4 monocular microscope melting point apparatus with thermometer unadjusted. ^{1}H NMR and ^{13}C NMR spectra were acquired on a Bruker Avance III 400 MHz spectrometer with $CDCl_3$ as the solvent and tetramethylsilane (TMS) as the internal standard. Mass spectra (MS) data were obtained using an Esquire 6000 Mass Spectrometer. Column chromatography was performed with silica gel (200 ~ 300 mesh; Qingdao Haiyang Chemical, China). Petroleum ether used for column-chromatography has a boiling range of 60–90 °C. Various *N*-tosylhydrazones **1a–x** were prepared according to the related literature [30, 31].

General procedure for the synthesis of azines 2a–x

A 25-mL Schlenk tube was charged with various *N*-tosylhydrazones (**1**) (0.5 mmol), Cs_2CO_3 (1 mmol) and CH_3CN (2 mL). The tube was sealed, and then the mixture was stirred under air at 100 °C for 6 h. The reaction mixture was then allowed to cool to ambient temperature. After concentration in vacuo, the crude product was purified by column chromatography on silica gel (petroleum ether:ethyl acetate = 10:1–6:1).

*1,2-bis(1-phenylethylidene)hydrazine (**2a**)* [11, 31] White solid, 54.3 mg, 92% yield. mp 123–125 °C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 7.93–7.90 (m, 4H),

7.43–7.42 (m, 6H), 2.32 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 157.8, 140.9, 131.6, 128.1, 124.0, 20.8. MS (ESI) m/z: 258.9 $[M + Na]^+$, 495.1 $[2M + Na]^+$.

1,2-bis(1-(p-tolyl)ethylidene)hydrazine (***2b***) [11, 12] White solid, 53.5 mg, 81 % yield. mp 152–154 °C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 7.86 (d, $J = 8.0$ Hz, 4H), 7.30 (d, $J = 8.0$ Hz, 4H), 2.45 (s, 6H), 2.35 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 157.7, 139.7, 129.1, 126.6, 21.4, 15.0. MS (ESI) m/z: 286.9 $[M + Na]^+$, 550.9 $[2M + Na]^+$.

1,2-bis(1-(4-methoxyphenyl)ethylidene)hydrazine (***2c***) [11] White solid, 65.9 mg, 89% yield. mp 169–171 °C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 7.93 (d, $J = 4.0$ Hz, 4H), 6.99 (d, $J = 4.0$ Hz, 4H), 3.90 (s, 6H), 2.37 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 160.9, 157.8, 131.4, 128.1, 113.7, 55.4, 14.8. MS (ESI) m/z: 319.0 $[M + Na]^+$, 615.1 $[2M + Na]^+$.

1,2-bis(1-(3-methoxyphenyl)ethylidene)hydrazine (***2d***) [11] White solid, 66.6 mg, 90% yield. mp 163–165 °C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 7.80–7.77 (m, 4H), 7.52–7.50 (m, 2H), 7.04–7.01 (m, 2H), 3.96 (s, 6H), 2.66 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 158.9, 133.6, 130.4, 128.4, 120.6, 111.6, 55.5, 31.8. MS (ESI) m/z: 319.1 $[M + Na]^+$, 615.1 $[2M + Na]^+$.

1,2-bis(1-(2-methoxyphenyl)ethylidene)hydrazine (***2e***) [12] White solid, 64.4 mg, 87% yield. mp 155–157°C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 7.78 (d, $J = 4.0$ Hz, 2H), 7.52 (t, $J = 6.0$ Hz, 2H), 7.06–7.01 (m, 4H), 3.96 (s, 6H), 2.66 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 158.9, 133.6, 130.4, 128.4, 120.6, 111.6, 55.5, 31.8. MS (ESI) m/z: 319.1 $[M + Na]^+$, 615.2 $[M + Na]^+$.

4,4′-hydrazine-1,2-diylidenebis(ethan-1-yl-1-ylidene))dianiline (***2f***) [9] White solid, 59.2 mg, 89% yield. mp 162–164 °C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 8.21 (d, $J = 8.0$ Hz, 4H), 7.42 (d, $J = 4.0$ Hz, 4H), 4.79 (s, 4H), 2.51 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 147.9, 131.6, 130.4, 129.4, 123.2, 22.1. MS (ESI) m/z: 265.0 $[M - H]^-$.

1,2-bis(1-(4-(trifluoromethyl)phenyl)ethylidene)hydrazine (***2g***) [32] White solid, 84.6 mg, 91% yield. mp 134–136 °C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 8.07 (d, $J = 4.0$ Hz, 4H), 7.74 (d, $J = 4.0$ Hz, 4H), 2.38 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 156.9, 141.4, 131.7, 131.4, 127.0, 125.42, 125.39, 125.36, 125.33, 122.98, 15.1. MS (ESI) m/z: 372.8 $[M + H]^+$.

1,2-bis(1-(4-nitrophenyl)ethylidene)hydrazine (***2h***) [31] Yellow solid, 75.8 mg, 93% yield. mp 165–167 °C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 7.86 (d, $J = 8.0$ Hz, 4H), 7.29 (d, $J = 8.0$ Hz, 4H), 2.45 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 145.9, 134.0, 130.1, 128.6, 21.8. MS (ESI) m/z: 325.6 $[M - H]^-$.

1,2-bis(1-(3-nitrophenyl)ethylidene)hydrazine (***2i***) [19] Yellow solid, 73.4 mg, 90% yield. mp 161–163 °C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 8.81–8.80 (m, 2H), 8.35–8.32 (m, 4H), 7.69–7.66 (m, 2H) 2.45 (s, 6H). ^{13}C NMR (100 MHz,

$CDCl_3$, ppm) δ: 145.9, 140.0, 130.5, 130.1, 128.6, 124.0, 21.8. MS (ESI) m/z: 325.4 $[M - H]^-$.

1,2-bis(1-(2-nitrophenyl)ethylidene)hydrazine ***(2j)*** [33] Yellow solid, 71.7 mg, 88% yield. mp 155–157 °C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 8.15 (d, $J = 8.0$ Hz, 2H), 7.78–7.75 (m, 2H), 7.66–7.63 (m, 2H), 7.49–7.47 (m, 2H), 2.60 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 152.9, 128.6, 128.5, 123.3, 115.4, 115.2, 15.0. MS (ESI) m/z: 325.4 $[M - H]^-$.

1,2-bis(1-(4-fluorophenyl)ethylidene)hydrazine ***(2k)*** [11, 12] White solid, 53.0 mg, 78% yield. mp 158–160 °C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 7.93–7.90 (m, 4H), 7.43–7.42 (m, 4H), 2.32 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 145.6, 128.9, 128.2, 123.9, 123.4, 18.3. MS (ESI) m/z: 294.9 $[M + Na]^+$, 567.0 $[2M + Na]^+$.

1,2-bis(1-(4-bromophenyl)ethylidene)hydrazine ***(2l)*** [12] White solid, 76.8 mg, 78% yield. mp 153–155 °C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 7.27 (d, $J = 4.0$ Hz, 4H), 6.86 (d, $J = 4.0$ Hz, 4H) 2.16 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 139.2, 132.0, 130.7, 129.4, 126.9, 30.7. MS (ESI) m/z: 394.9 $[M + H]^+$.

1,2-bis(1-(3-chlorophenyl)ethylidene)hydrazine ***(2m)*** [11] White solid, 61.8 mg, 81% yield. mp 158–160 °C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 7.79–7.77 (m, 2H), 7.53–7.49 (m, 2H), 7.06–7.01 (m, 4H), 2.66 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 158.9, 133.6, 130.4, 128.4, 125.8, 120.6, 111.6, 21.2. MS (ESI): $m/z = 304.1$ $[M + H]^+$.

1,2-bis(1-(naphthalen-2-yl)ethylidene)hydrazine ***(2n)*** [34] Yellow solid, 73.9 mg, 88% yield. mp 189–191°C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 8.52 (s, 1H), 8.10–8.08 (m, 1H), 8.03–8.01 (m, 1H) 7.95 -7.92 (m, 2H), 7.67–7.59 (m, 2H), 2.78 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 136.6, 133.6, 131.4, 129.4, 128.8, 127.9, 127.6, 26.8. MS (ESI) m/z: 358.9 $[M + Na]^+$, 695.0 $[2M + Na]^+$.

1,2-dibenzylidenehydrazine ***(2o)*** [31] White solid, 44.2 mg, 85% yield. mp 125–127°C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 8.72 (s, 2H), 7.90–7.89 (m, 4H), 7.51–7.50 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 162.1, 131.2, 128.8, 128.6, 128.0. MS (ESI) m/z: 231.8 $[M + Na]^+$, 440.9 $[2M + Na]^+$.

1,2-bis(2-methoxybenzylidene)hydrazine ***(2p)*** [35] White solid, 54.3 mg, 81% yield. mp 234–236°C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 8.20 (s, 2H), 7.86 (d, $J = 8.0$ Hz, 2H), 7.38–7.34 (m, 2H), 6.98–6.95 (m, 2H), 6.89 (d, $J = 8.0$ Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 158.0, 133.2, 131.9, 129.0, 128.0, 120.9, 111.0, 55.6. MS (ESI) m/z: 292.9 $[M + Na]^+$, 563.0 $[2M + Na]^+$.

1,2-bis(4-nitrobenzylidene)hydrazine ***(2q)*** [16, 19] Yellow solid, 66.3 mg, 89% yield. mp 260–262 °C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 10.19 (s, 2H), 8.43 (d, $J = 8.0$ Hz, 4H), 8.11 (d, $J = 8.0$ Hz, 4H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 156.6, 148.2, 140.5, 129.4, 128.7, 128.0. MS (ESI) m/z: 319.0 $[M + Na]^+$, 615.1 $[2M + Na]^+$.

*1,2-bis(3-nitrobenzylidene)hydrazine (**2r**)* [16, 19] Yellow solid, 63.3 mg, 85% yield. mp 248–250°C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 10.16 (s, 2H), 8.21 (d, J = 8.0 Hz, 2H), 7.98–7.94 (m, 2H), 7.60–7.57 (m, 2H), 7.48–7.46 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 148.2, 146.9, 136.0, 134.2, 129.4, 127.9, 123.9. MS (ESI) m/z: 323.0 $[M + Na]^+$, 623.1 $[2M + Na]^+$.

*Dimethyl 4,4′-(hydrazine-1,2-diylidenebis(methanylylidene))dibenzoate (**2s**)* [36] White solid, 68.0 mg, 84% yield. mp 200–202°C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 10.12 (s, 2H), 7.99 (d, J = 8.0 Hz, 4H), 7.59 (d, J = 8.0 Hz, 4H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 166.5, 164.4, 136.4, 133.9, 131.5, 129.7, 52.2. MS (ESI) m/z: 347.0 $[M + Na]^+$, 671.1 $[2M + Na]^+$.

*1,2-bis(4-chlorobenzylidene)hydrazine (**2t**)* [16, 19] White solid, 56.8 mg, 82% yield. mp 145–147°C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 8.21 (s, 2H), 8.06–8.03 (m, 4H), 7.60–7.57 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 143.8, 133.4, 131.4, 129.8, 129.1, 128.0. MS (ESI) m/z: 300.9 $[M + Na]^+$, 579.1 $[2M + Na]^+$.

*1,2-bis(3-chlorobenzylidene)hydrazine (**2u**)* [1] White solid, 55.4 mg, 80% yield. mp 146–148°C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 8.21 (s, 2H), 7.97–7.95 (m, 2H), 7.67–7.64 (m, 2H), 7.59–7.31 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 154.6, 135.3, 134.2, 129.1, 128.6, 123.5. MS (ESI) m/z: 276.4 $[M - H]^-$.

*1,2-bis(naphthalen-1-ylmethylene)hydrazine (**2v**)* [37] Blown solid, 70.1 mg, 91% yield. mp 232–234°C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 10.46 (s, 2H), 9.31 (d, J = 4.0 Hz, 2H), 8.17 (d, J = 8.0 Hz, 2H) 8.06 (d, J = 4.0 Hz, 2H), 7.99 (d, J = 8.0 Hz, 2H) 7.77–7.73 (m, 2H), 7.69–7.31 (m,4H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 147.8, 134.5, 131.7, 131.5, 129.7, 128.7, 128.1, 126.4, 125.9, 124.5. MS (ESI) m/z: 332.8 $[M + Na]^+$, 642.9 $[2M + Na]^+$.

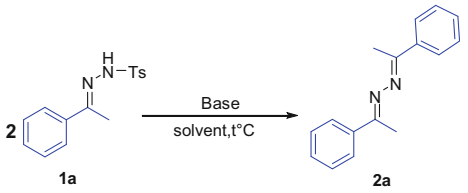
*1,2-bis(1,2-diphenylethylidene)hydrazine (**2w**)* [38] Brown oil, 74.7 mg, 77% yield. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 7.56–7.54 (m, 8H), 7.36–7.33 (m, 8H), 7.31–7.27 (m, 4H), 3.16 (s, 4H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 136.3, 135.4, 131.5, 131.3, 129.8, 129.7, 128.9, 45.8. MS (ESI) m/z: 411.0 $[M + Na]^+$, 799.1 $[2M + Na]^+$.

*1,2-bis(diphenylmethylene)hydrazine (**2x**)* [11] White solid, 65.7 mg, 73% yield. mp 220–222°C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 8.14–8.12 (m, 8H), 7.73–7.70 (m, 4H), 7.58–7.55 (m, 8H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 163.1, 134.3, 129.8, 128.9, 125.7. MS (ESI) m/z: 382.9 $[M + Na]^+$, 743.0 $[2M + Na]^+$.

Results and discussion

We initiated the present study with *N*-tosylhydrazone **1a** as the model substrate for optimizing the reaction conditions, and various bases, solvents, and temperatures were then screened (Table 1). First, we chose Li_2CO_3 (2 equiv) as the base in CH_3CN at 100 °C for 6 h, and the desired product **2a** was obtained in 46 % yield (Table 1, entry 1). Next, a range of bases such as Na_2CO_3, K_2CO_3, Cs_2CO_3,

Table 1 Optimization of the reaction conditions



Entry	Base (eq)	Solvent	T (°C)	Time (h)	Yield (%)[a]
1	Li_2CO_3 (2)	MeCN	100	6	46
2	Na_2CO_3 (2)	MeCN	100	6	45
3	K_2CO_3 (2)	MeCN	100	6	67
4	**Cs_2CO_3 (2)**	**MeCN**	**100**	**6**	**92**
5	$NaHCO_3$ (2)	MeCN	100	6	35
6	KH_2PO_3 (2)	MeCN	100	6	33
7	NaOH (2)	MeCN	100	6	47
8	KOH (2)	MeCN	100	6	49
9	*t*-BuOK (2)	MeCN	100	6	58
10	Cs_2CO_3 (1)	MeCN	100	6	75
11	Cs_2CO_3 (3)	MeCN	100	6	79
12	Cs_2CO_3 (2)	DMF	100	6	80
13	Cs_2CO_3 (2)	DMSO	100	6	79
14	Cs_2CO_3 (2)	CH_3OH	100	6	26
15	Cs_2CO_3 (2)	$CHCl_3$	100	6	40
16	Cs_2CO_3 (2)	DMA	100	6	52
17	Cs_2CO_3 (2)	Acetone	100	6	29
18	Cs_2CO_3 (2)	DCE	100	6	42
19	Cs_2CO_3 (2)	H_2O	100	6	n.d.
20	Cs_2CO_3 (2)	MeCN	90	6	77
21	Cs_2CO_3 (2)	MeCN	110	6	82

[a] Reaction conditions: **1a** (0.5 mmol), solvent (2 mL), 90–110 °C, 6 h

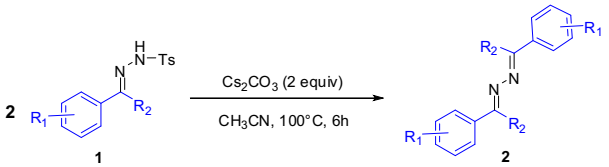
[b] Isolated yield

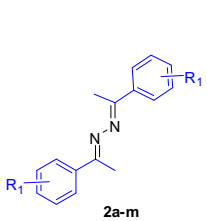
Bold values indicate the optimal reaction conditions

$NaHCO_3$, KH_2PO_4, NaOH, KOH and *t*-BuOK were then screened, and Cs_2CO_3 was found to be the most suitable base (Table 1, entries 2–9). Raising or decreasing the loading of Cs_2CO_3 did not deliver an improvement in the yield of product **2a** (Table 1, entry 10–11). Then, various solvents were screened and evaluated. The identical reaction performed in DMF, DMSO, CH_3OH, $CHCl_3$, *N*,*N*-dimethylacetamide (DMA), acetone and 1,2-dichloroethane (DCE) lowered the yield of the product **2a** (Table 1, entries 12–18), while no target compound **2a** was detected when H_2O was used as the solvent (Table 1, entry 19). Finally, a diminished chemical yield was observed when the reaction temperature was dropped to 90 °C or elevated to 110 °C (Table 1, entries 20–21). Therefore, the optimal reaction conditions were selected as shown in entry 4.

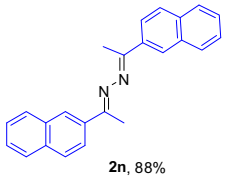
With these optimized conditions in hand, the scope of both aldehyde tosylhydrazones and ketone tosylhydrazones were established and the results are presented in

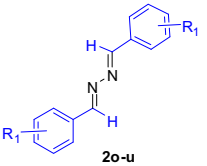
Table 2 Cs_2CO_3-mediated synthesis of azines



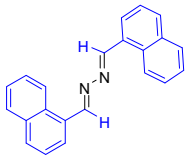


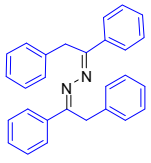
R_1 = H, **2a**, 92%
R_1 = 4-Me, **2b**, 81%
R_1 = 4-MeO, **2c**, 89%
R_1 = 3-MeO, **2d**, 90%
R_1 = 2-MeO, **2e**, 87%
R_1 = 4-NH_2, **2f**, 89%
R_1 = 4-CF_3, **2g**, 91%
R_1 = 4-NO_2, **2h**, 93%
R_1 = 3-NO_2, **2i**, 90%
R_1 = 2-NO_2, **2j**, 88%
R_1 = 4-F, **2k**, 78%
R_1 = 4-Br, **2l**, 78%
R_1 = 3-Cl, **2m**, 81%

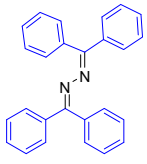




R_1 = H, **2o**, 85%
R_1 = 2-MeO, **2p**, 81%
R_1 = 4-NO_2, **2q**, 89%
R_1 = 3-NO_2, **2r**, 85%
R_1 = 4-MeOCO, **2s**, 84%
R_1 = 4-Cl, **2t**, 82%
R_1 = 3-Cl, **2u**, 80%

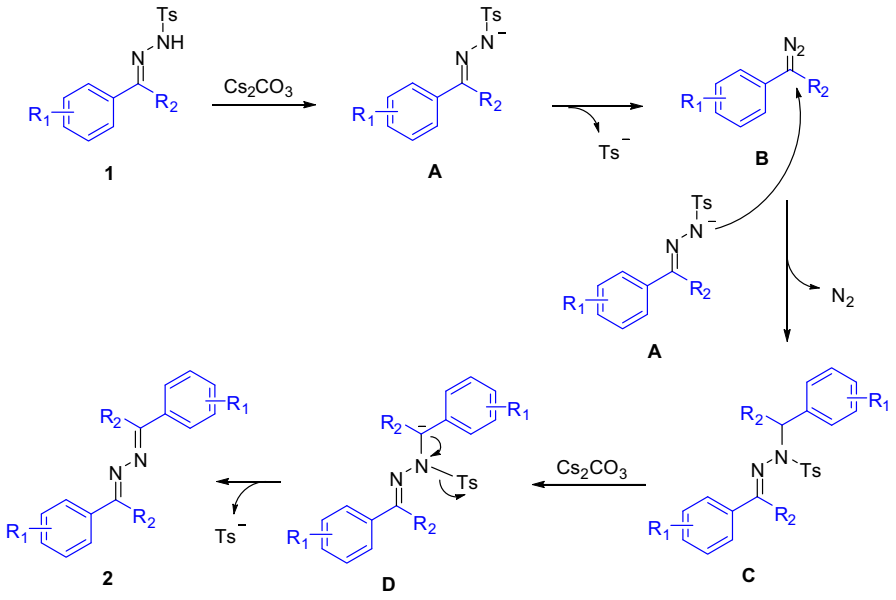






Reaction conditions: *N*-tosylhydrazones **1** (0.5 mmol), CH_3CN (2 ml). Isolated yield

Table 2. First, when R_2 was the methyl group and the phenyl ring with electron-withdrawing substituents (*p*-CF_3, *p*-NO_2, *m*-NO_2, *o*-NO_2,) or electron-donating substituents (*p*-Me, *p*-MeO, *m*-MeO, *o*-MeO, *p*-NH_2), as well as the para-, ortho- and meta-substituted groups, all of the substrates **1a–j** gave the desired products in good to excellent yields (**2a**–**j**), showing no obvious electronic effect in this transformation. The para- and meta-substituted halogen atoms such as fluorine, bromine and chlorine were well tolerated, affording the corresponding products in good yields (**2k**–**m**). Notably, 2-acetonaphthone tosylhydrazone **1n** was also a suitable substrate for this reaction, which reacted smoothly to give the expected products in good yields (**2n**, 88 %). Similarly, when R_2 was a hydrogen atom, the substrates **1o–u** bearing different kinds of functional groups on the phenyl ring, such as methoxyl, nitro, methoxycarbonyl and chloro groups, all reacted smoothly to afford the desired azines in good



Scheme 2 Proposed reaction mechanism

yields (**2o**–**2u**). It was observed that 1-naphthaldehyde tosylhydrazone **1v** converted to azine **2v** in excellent yields (91%). Next, the reaction efficiency affected by steric effects was also considered. Gratifyingly, under the standard conditions, when R_2 was a benzyl or phenyl group, *N*-tosylhydrazones **1w** and **1x** could be smoothly transformed into azines **2w** and **2x** in 77 and 73 % yields, respectively. Obviously, the above results indicate that the reaction was insensitive to the sterically hindered substrates. In addition, we tried to synthesize the asymmetrical azines from the two different *N*-tosylhydrazones, such as **1a** and **1c**; however, the reaction system was messy and no main products could be isolated and obtained.

In the light of the nature of *N*-tosylhydrazones and based on previous reports [27, 31], a plausible mechanism is proposed (Scheme 2). Initially, the intermediate anion **A** was formed in the presence of the base via removal of a proton on the nitrogen of tosylhydrazones **1**. Subsequently, intermediate **A** is converted in situ to the corresponding diazo compound **B** with concomitant elimination of the Ts group [27]. Next, decomposition of **B** by interaction with **A** afforded the intermediate **C**. Eventually, symmetrical azines **2** were then obtained by base-catalyzed elimination of TsH from intermediate **C**.

Conclusions

In conclusion, we have developed a simple, mild, and efficient protocol for the synthesis of symmetrical azines from *N*-tosylhydrazones in the Cs_2CO_3 and CH_3CN reaction system. The method offers broad substrate scope, occurs as additive-free,

without strong base conditions, utilizing readily available reactants, and forms products in good to high yields, which represents an environmentally and efficient access to the C–N bond construction.

Acknowledgments The authors gratefully acknowledge the financial support from the National Natural Science Foundation of China (21102003) and the Natural Science Foundation of Anhui Province (1608085MB38).

References

1. V.B. Kurteva, S.P. Simeonov, M. Stoilova-Disheva, Pharmacol. Pharm. **2**, 1 (2011)
2. L. Gäinä, A. Csámpai, G. Túrós, T. Lovász, V. Zsoldos-Mády, I.A. Silberg, P. Sohár, Org. Biomol. Chem. **4**, 4375 (2006)
3. Y.A. Kuznetsova, V.B. Romakh, Appl. Biochem. Biotechnol. **61**, 205 (1996)
4. I. Cianga, M. Ivanoiu, Eur. Polym. J. **42**, 1922 (2006)
5. W.B. Euler, M. Cheng, C. Zhao, Chem. Mater. **11**, 3702 (1999)
6. E.C. Kesslen, W.B. Euler, Chem. Mater. **11**, 336 (1999)
7. W. Tang, Y. Xiang, A. Tong, J. Org. Chem. **74**, 2163 (2009)
8. N. Rajendiran, T. Balasubramanian, Spectrochim. Acta, Part A **68**, 894 (2007)
9. M. Lewis, R. Glaser, J. Org. Chem. **67**, 1441 (2002)
10. J. Wen, A. Wu, Y. Miao, J. Zhu, Tetrahedron Lett. **56**, 5512 (2015)
11. J. Wen, A. Wu, M. Wang, J. Zhu, J. Org. Chem. **80**, 10457 (2015)
12. W. Han, G. Zhang, G. Li, H. Huang, Org. Lett. **16**, 3532 (2014)
13. R. Cohen, B. Rybtchinski, M. Gandelman, L.J.W. Shimon, J.M.L. Martin, D. Milstein, Angew. Chem. Int. Ed. **42**, 1949 (2003)
14. G.S. Chen, M. Anthamatten, C.L. Barnes, R. Glaser, J. Org. Chem. **59**, 4336 (1994)
15. J. Safari, S. Gandomi-Ravandi, Synth. Commun. **41**, 645 (2011)
16. H.M. Nanjundaswamy, M.A. Pasha, Synth. Commun. **37**, 3417 (2007)
17. H.M. Nanjundaswamy, Synth. Commun. **36**, 3161 (2006)
18. J.L. Peltier, R. Jazzar, M. Melaimi, G. Bertrand, Chem. Commun. **52**, 2733 (2016)
19. B. Lee, K.H. Lee, J. Cho, W. Nam, N.H. Hur, Org. Lett. **13**, 6386 (2011)
20. Z. Shao, H. Zhang, Chem. Soc. Rev. **41**, 560 (2012)
21. Q. Xiao, Y. Zhang, J. Wang, Acc. Chem. Res. **46**, 236 (2013)
22. X. Li, X. Liu, H. Chen, W. Wu, C. Qi, H. Jiang, Angew. Chem. Int. Ed. **53**, 14485 (2014)
23. Z. Liu, H. Tan, L. Wang, T. Fu, Y. Xia, Y. Zhang, J. Wang, Angew. Chem. Int. Ed. **54**, 3056 (2015)
24. W. Xiong, C. Qi, H. He, L. Ouyang, M. Zhang, H. Jiang, Angew. Chem. Int. Ed. **54**, 1 (2015)
25. Q. Sha, Y. Ling, W. Wang, Y. Wei, Adv. Synth. Catal. **355**, 2145 (2013)
26. M. Ohashi, T. Kambara, T. Hatanaka, H. Saijo, R. Doi, S. Ogoshi, J. Am. Chem. Soc. **133**, 3256 (2011)
27. T. Yao, K. Hirano, T. Satoh, M. Miura, Angew. Chem. Int. Ed. **51**, 775 (2012)
28. V.K. Aggarwal, J. de Vicente, R.V. Bonnert, J. Org. Chem. **68**, 5381 (2003)
29. A. Hamze, B. Tréguier, J.D. Brion, M. Alami, Org. Biomol. Chem. **9**, 6200 (2011)
30. J. Barluenga, M. Tomás-Gamasa, F. Aznar, C. Valdés, Eur. J. Org. Chem. **1520**, 7486 (2011)
31. Q. Sha, Y. Wei, Tetrahedron **69**, 3829 (2013)
32. D.R. Tolentino, L. Jin, M. Melaimi, G. Bertrand, Chem.-Asian J. **10**, 2139 (2015)
33. L.Y. Hsu, C.E. Nordman, D.H. Kenny, Acta Crystallogr. C **C49**, 394 (1993)
34. M.N. Zhao, H. Liang, Z.H. Ren, Z.H. Guan, Synthesis **44**, 1501 (2012)
35. B. Lee, S.H. Kang, D. Kang, K.H. Lee, J. Cho, W. Nam, O.H. Hancd, N.H. Hur, Chem. Commun. **47**, 11219 (2011)
36. M. Giurg, S.B. Said, S. Syper, J. Mlochowski, Synth. Commun. **31**, 3151 (2001)
37. M.R. Mahmoud, E.A.A. El-Bordany, N.F. Hassan, F.S.M. Abu El-Azm, Phosphorus Sulfur **182**, 2507 (2007)
38. P. Yates, E.M. Levi, B.L. Shapiro, Can. J. Chem. **52**, 3343 (1974)