DOI: 10.1002/cjoc.201400300

Ring Opening of *N*-Sulfonyl Aziridines by Amines in Silica-Water

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Ring opening reactions of *N*-sulfonyl aziridines by primary and secondary amines in silica gel (SG)-water system were achieved, which provided a mild, practical and environmentally benign method to synthesize mono- and bis-sulfonyl substituted amines. When primary and secondary amines were used in excess, they reacted with *N*-sulfonyl aziridines smoothly at room temperature, mainly affording 1∶1 ring opening products. Reactions of primary amines with 2 equiv. of aziridines produced 2∶1 ring opening products. Some 1∶1 products can be cyclized with CS_2 to synthesize *N*-sulfonyl cyclothioureas also in water.

Keywords aziridines, ring opening, amines, silica gel, reactions in water

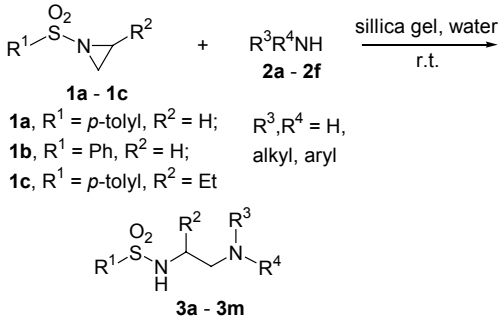
Introduction

According to the criteria of green chemistry, water is an ideal media for chemical reactions due to its low cost, safety and environmental compatibility. Although organic reactions in/on water have boosted in the past decades, water has not been commonly used as a solvent for organic reactions because of the poor solubility of most organic molecules in pure water.[1-7] To solve this problem, organic co-solvents and phase transfer catalysts (PTC) were introduced into aqueous reactions.[8-12]

Recently, Minakata and co-workers have developed the ring formation and opening reactions of aziridines in silica gel (SG)-water system.[13-16] SG accelerated the reactions like the function of PTC. Because SG is cheap, nontoxic, recyclable and environmentally benign, SG-water system provides a practical method to aqueous reactions. Moreover, other SG-promoted reactions have been reported in recent years.[17-27] SG was commonly thought to promote these reactions due to the moderate acidity and adsorptive nature of its surface. Inspired by these prominent works, we have proposed synthetic methods toward *N*-sulfonyl cyclothioureas from *N*-sulfonyl diamines and CS_2 in water, which could be promoted by SG.[28,29]

In organic synthesis, aziridine and its derivatives are important intermediates to prepare a variety of compounds, such as functionalized amines and nitrogen heterocyles.[30-33] Due to the ring strains, three-membered rings, such as aziridines, epoxides and cyclopropanes, are easily opened.[34-37] The ring opening reactions of aziridines are generally performed by Lewis acids or Brönsted acids catalysis in organic media.[38-40] In recent years, new approaches for the ring opening of aziridines, including microwave acceleration[41] as well as catalysis by trialkylphosphine,[42,43] *N*-heterocyclic carbene[44] and tetrabutylammonium bromide,[45] have been demonstrated. In most of the aforementioned literatures, the substrates are aziridines or *N*-sulfonyl aziridines with at least one group at carbon atoms of the ring. Moasser and co-workers reported the reactions of the *para*-substituted anilines with *N*-tosylaziridine in water, affording useful *N*-aryl-*N*′-tosylethylenediamines ligands.[46] However, most of the reactions were carried out at 50 ℃ to ensure the complete conversion of the anilines. Herein, we wish to report ring opening reactions of *N*-sulfonylaziridines by primary and secondary amines in SG-H_2O system at room temperature (Scheme 1).

Scheme 1 The 1∶1 reaction of aziridines and amines



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Received May 9, 2014; accepted August 16, 2014; published online October 8, 2014.
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/cjoc.201400300 or from the author.

Experimental

General

All reagents were purchased from commercial sources and used without any further purification. *N*-Sulfonyl aziridines were prepared according to the method reported in the literature.[47] The melting points were obtained on a Laboratory Devices X-4 melting apparatus and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ using TMS as an internal standard on a Bruker AVANCE III 400 (or 600) spectrometer at 400 (or 600) MHz and 100 (or 150) MHz respectively. HRMS data were obtained on a Bruker microOTOF-Q II (or Agilent Accurate-Mass-Q-TOF MS 6520) instrument.

General procedure for synthesis of compounds 3a—3m

SG (0.1 g, 40—60 mesh) was stirred to a dispersion of *N*-sulfonyl aziridines (1 mmol) and amines (2 mmol **2a**—**2e** or 1.5 mmol **2f**) in water (1 mL). The reaction mixture was stirred at room temperature for 12—14 h. After completion of the reaction (screened by TLC), ethyl acetate (10 mL) was added. The mixture was stirred for 10 min and centrifuged. The upper layer was separated and the lower layer was extracted with ethyl acetate (10 mL×2) repeatedly. The combined ethyl acetate layer was dried over anhydrous magnesium sulfate. Then the solvent was removed under reduced pressure and the residue was purified by flash column chromatography on SG using a mixture of ethyl acetate, petroleum ether and triethylamine as eluents to give the desired products.

General procedures for synthesis of compounds 4a—4f

SG (0.2 g, 40—60 mesh) was stirred to a dispersion of *N*-sulfonyl aziridines (2 mmol) and amines (1 mmol) in water (2 mL). The reaction mixture was stirred at room temperature or 40 ℃ for 9—14 h. After completion of the reaction (screened by TLC), compounds **4a**—**4f** were obtained by procedure similar to the preparation of **3a**—**3k**.

General procedure for synthesis of compounds 5a and 5b

To a stirred suspension of **3a** or **3b** (1.5 mmol) in water (10 mL) was added potassium hydroxide (3.0 mmol) and carbon disulfide (2.0 mmol) at 45 ℃. After the solid was dissolved, potassium chloroacetate (2.0 mmol) was added and the reaction mixture was stirred for 5 h at 45 ℃. Then the reaction mixture was extracted with ethyl acetate (10 mL×3). The combined organic layer was dried over anhydrous magnesium sulfate overnight. The solvent was removed under reduced pressure and the residue was purified by flash column chromatography on SG using a mixture of ethyl acetate, petroleum ether and triethylamine as eluents to give the desired products.

***N*-(2-(Cyclohexylamino)ethyl)-4-methylbenzenesulfonamide (3a)** Yield 66%; pale yellow solid; m.p. 60—61 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.96—1.78 (m, 10H, cyclohexane-H), 2.24 (m, 1H, cyclohexane-H), 2.45 (s, 3H, CH_3), 2.72 (t, J=5.4 Hz, 2H, cyclohexane-NHC**H$_2$**), 2.97 (t, J=5.7 Hz, 2H, SO_2NHCH_2), 7.33 (d, J=8.0 Hz, 2H, ArH), 7.77 (d, J=8.2 Hz, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.49, 24.93, 26.0, 33.7, 43.0, 44.8, 56.0, 127.2, 129.6, 137.0, 143.3; IR (KBr) ν_{max}: 3281, 1334, 1160 cm^{-1}; HRMS (ESI) *m*/*z*: (M+H$^+$) calcd for $C_{15}H_{24}N_2O_2SH^+$ 297.1637; found 297.1635.

***N*-(2-(Cyclohexylamino)ethyl)benzenesulfonamide (3b)** Yield 58%; pale yellow solid; m.p. 77—78 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.95—1.78 (m, 10H, cyclohexane-H), 2.23 (m, 1H, cyclohexane-H), 2.72 (t, J=5.7 Hz, 2H, cyclohexane-NHC**H$_2$**), 2.99 (t, J=5.6 Hz, 2H, SO_2NHCH_2), 7.54 (t, J=7.4 Hz, 2H, ArH), 7.60 (t, J=7.3 Hz, 1H, ArH), 7.90 (d, J=7.3 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 24.9, 26.0, 33.7, 43.0, 44.8, 56.0, 127.1, 129.0, 132.5, 139.9; IR (KBr) ν_{max}: 3280, 1328, 1157 cm^{-1}. HRMS (ESI) *m*/*z*: (M+H$^+$) calcd for $C_{14}H_{22}N_2O_2SH^+$ 283.1480; found 283.1477.

***N*-(2-(*tert*-Butylamino)ethyl)-4-methylbenzenesulfonamide (3c)** Yield 53%; white solid; m.p. 62—64 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.02 (s, 9H, $C(CH_3)_3$), 2.44 (s, 3H, PhC**H$_3$**), 2.63 (t, J=5.5 Hz, 2H, $C(CH_3)NHCH_2$), 2.96 (t, J=5.5 Hz, 2H, SO_2NHCH_2), 7.31 (d, J=7.8 Hz, 2H, ArH), 7.77 (d, J=8.0 Hz, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.5, 29.0, 41.0, 43.6, 50.3, 127.2, 129.6, 137.0, 143.2; IR (KBr) ν_{max}: 3427, 1336, 1161 cm^{-1}; HRMS (ESI) *m*/*z*: (M+H$^+$) calcd for $C_{13}H_{22}N_2O_2SH^+$ 271.1475; found 271.1481.

***N*-(2-(*tert*-Butylamino)ethyl)benzenesulfonamide (3d)** Yield 48%; white solid; m.p. 86—88 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.02 (s, 9H, $C(CH_3)_3$), 2.63 (t, J=5.6 Hz, 2H, $C(CH_3)NHCH_2$), 3.00 (t, J=5.6 Hz, 2H, SO_2NHCH_2), 7.53 (t, J=7.4 Hz, 2H, ArH), 7.59 (t, J=7.1 Hz, 1H, ArH), 7.90 (d, J=7.6 Hz, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 29.0, 41.0, 43.6, 50.3, 127.1, 129.1, 132.5, 140.0; IR (KBr) ν_{max}: 3449, 1321, 1163 cm^{-1}; HRMS (ESI) *m*/*z*: (M+H$^+$) calcd for $C_{12}H_{20}N_2O_2SH^+$ 257.1324; found 257.1321.

4-Methyl-*N*-(2-(octylamino)ethyl)benzenesulfonamide (3e) Yield 50%; Yellow viscous liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.88 (t, J=6.4 Hz, 3H, octane-H), 1.25 (s, 12H, octane-H), 1.32 (t, J=6.5 Hz, 2H, octane-H), 2.42 (s, 3H, PhC**H$_3$**), 2.44 (m, 2H, octane-H), 2.69 (t, J=6.0 Hz, 2H, octane-NHC**H$_2$**), 2.99 (t, J=6.0 Hz, 2H, SO_2NHCH_2), 7.30 (d, J=7.9 Hz, 2H, ArH), 7.75 (d, J=8.1 Hz, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.0, 21.5, 22.6, 27.2, 29.2, 29.4, 29.8, 31.8, 42.2, 47.9, 49.1, 127.12, 129.6, 137.0, 143.2; IR (KBr) ν_{max}: 3281, 1328, 1160 cm^{-1}; HRMS (ESI) *m*/*z*: (M+H$^+$) calcd for $C_{17}H_{30}N_2O_2SH^+$ 327.2106; found 327.2107.

4-Methyl-*N*-(2-(phenylamino)ethyl)benzenesul-

fonamide (3f)[42] Yield 80%; white solid; m.p. 89—90 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.43 (s, 3H, CH_3), 3.17 (s, 2H, PhNHC**H$_2$**), 3.26 (s, 2H, SO_2NHC**H$_2$**), 3.94 (s, 1H, PhN**H**), 5.20 (s, 1H, SO_2N**H**), 6.54 (d, J=7.2 Hz, 2H, ArH), 6.75 (d, J=6.5 Hz, 1H, ArH), 7.15 (t, J=6.7 Hz, 2H, ArH), 7.29 (d, J=6.9 Hz, 2H, ArH), 7.76 (d, J=7.3 Hz, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.5, 42.3, 43.4, 113.0, 118.0, 127.1, 129.3, 129.8, 136.7, 143.6, 147.4; IR (KBr) ν_{max}: 3056, 3310, 1319, 1154 cm^{-1}; HRMS (ESI) *m*/*z*: (M+H$^+$) calcd for $C_{15}H_{18}N_2O_2SNa^+$ 313.0987; found 313.0986.

***N*-(2-(Phenylamino)ethyl)benzenesulfonamide (3g)** Yield 74%; white solid; m.p. 72—73 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.22 (t, J=5.7 Hz, 2H, PhNHC**H$_2$**), 3.30 (t, J=5.6 Hz, 2H, SO_2NHC**H$_2$**), 3.86 (s, 1H, PhN**H**), 4.92 (s, 1H, SO_2N**H**), 6.57 (d, J=8.0 Hz, 2H, ArH), 6.76 (t, J=7.3 Hz, 1H, ArH), 7.17 (t, J=7.7 Hz, 2H, ArH), 7.53 (t, J=7.6 Hz, 2H, ArH), 7.61 (t, J=7.3 Hz, 1H, ArH), 7.87 (d, J=7.8 Hz, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 42.4, 43.5, 113.1, 118.2, 127.0, 129.2, 129.4, 132.8, 139.8, 147.3; IR (KBr) ν_{max}: 3028, 3390, 1317, 1162 cm^{-1}; HRMS (ESI) *m*/*z*: (M+H$^+$) calcd for $C_{14}H_{16}N_2O_2SH^+$ 277.1011; found 277.1010.

***N*-(2-((4-Methoxyphenyl)amino)ethyl)-4-methylbenzenesulfonamide (3h)**[42] Yield 78%; white solid; m.p. 99—100 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.42 (s, 3H, PhC**H$_3$**), 3.15 (t, J=5.7 Hz, 2H, PhNHC**H$_2$**), 3.22 (t, J=4.8 Hz, 2H, SO_2NHC**H$_2$**), 3.51 (s, 1H, PhN**H**), 3.74 (s, 3H, OCH_3), 4.79 (s, 1H, SO_2N**H**), 6.51 (d, J=8.9 Hz, 2H, ArH), 6.75 (d, J=8.8 Hz, 2H, ArH), 7.29 (d, J=8.0 Hz, 2H, ArH), 7.73 (d, J=8.2 Hz, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.5, 42.4, 44.4, 55.8, 114.6, 114.9, 127.1, 129.8, 136.7, 141.5, 143.6, 152.6; IR (KBr) ν_{max}: 3285, 1516, 1158 cm^{-1}.

***N*-(2-((4-Methoxyphenyl)amino)ethyl)benzenesulfonamide (3i)** Yield 68%; white solid; m.p. 79—80 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.18 (t, J=5.6 Hz, 2H, PhNHC**H$_2$**); 3.23 (t, J=5.2 Hz, 2H, SO_2NHC**H$_2$**), 3.50 (s, 1H, PhN**H**), 3.74 (s, 3H, —OCH_3), 4.81 (s, 1H, SO_2N**H**), 6.52 (d, J=8.8 Hz, 2H, ArH), 6.75 (d, J=8.8 Hz, 2H, ArH), 7.51 (t, J=7.5 Hz, 2H, ArH), 7.59 (t, J=7.3 Hz, 1H, ArH), 7.86 (d, J=7.3 Hz, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 42.4, 44.4, 55.8, 114.6, 114.9, 127.0, 129.2, 132.75, 139.7, 141.5, 152.6; IR (KBr) ν_{max}: 3057, 3254, 1313, 1158 cm^{-1}; HRMS (ESI) *m*/*z*: (M+H$^+$) calcd for $C_{15}H_{18}N_2O_3SH^+$ 307.1116; found 307.1115.

***N*-(2-(Diethylamino)ethyl)-4-methylbenzenesulfonamide (3j)** Yield 56%; light yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.91 (t, J=7.1 Hz, 6H, CH_2C**H$_3$**), 2.38 (q, J=7.2 Hz, 4H, C**H$_2$**CH_3); 2.45 (s, PhC**H$_3$**, 3H), 2.49 (t, J=5.8 Hz, 2H, NC**H$_2$**), 2.95 (t, J=5.8 Hz, 2H, SO_2NHC**H$_2$**), 7.33 (d, J=8.0 Hz, 2H, ArH), 7.78 (d, J=8.2 Hz, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 11.6, 21.5, 40.2, 46.2, 51.0, 127.1, 129.6, 136.8, 143.2; IR (KBr) ν_{max}: 3289, 1331, 1162 cm^{-1}; HRMS (ESI) *m*/*z*: (M+H$^+$) calcd for $C_{13}H_{22}N_2O_2SH^+$ 271.1475; found 271.1478.

***N*-(2-(Diethylamino)ethyl)benzenesulfonamide (3k)** Yield 60%; yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.90 (t, J=7.1 Hz, 6H, CH_2C**H$_3$**), 2.39 (q, J=7.0 Hz, 4H, C**H$_2$**CH_3), 2.48 (t, J=5.8 Hz, 2H, NC**H$_2$**), 2.97 (t, J=5.8 Hz, 2H, SO_2NHC**H$_2$**), 7.54 (t, J=7.4 Hz, 2H, ArH), 7.60 (t, J=7.3 Hz, 1H, ArH), 7.90 (d, J=7.3 Hz, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 11.6, 40.2, 46.2, 50.9, 127.1, 129.0, 132.5, 139.7; IR (KBr) ν_{max}: 3295, 1330, 1163 cm^{-1}; HRMS (ESI) *m*/*z*: (M+H$^+$) calcd for $C_{12}H_{20}N_2O_2SH^+$ 257.1318; found 257.1320.

***N*-(1-((4-Methoxyphenyl)amino)butan-2-yl)-4-methylbenzenesulfonamide (3l)** Yield 65%; white solid; m.p. 109—110 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 0.79 (t, J=7.4 Hz, 3H, CH_2C**H$_3$**), 1.42—1.47 (m, 1H, C**H$_2$**CH_3), 1.52—1.58 (m, 1H, C**H$_2$**CH_3), 2.42 (s, 3H, PhC**H$_3$**), 2.98 (dd, J=12.8, 7.2 Hz, 1H, PhNHC**H$_2$**), 3.09 (dd, J=12.7, 4.6 Hz, 1H, PhNHC**H$_2$**), 3.29—3.34 (m, 1H, SO_2NHC**H**), 3.52 (s, 1H, PhN**H**), 3.74 (s, 3H, OCH_3), 4.69 (s, 1H, SO_2N**H**), 6.42 (d, J=8.8 Hz, 2H, ArH), 6.72 (d, J=8.8 Hz, 2H, ArH), 7.26 (d, J=8.6 Hz, 2H, ArH), 7.75 (d, J=8.1 Hz, 2H, ArH); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 9.8, 21.5, 26.4, 48.5, 54.8, 55.8, 114.3, 114.8, 127.1, 129.6, 137.7, 141.8, 143.4, 152.4; IR (KBr) ν_{max}: 3260, 1316, 1159 cm^{-1}; HRMS (ESI) *m*/*z*: (M+H$^+$) calcd for $C_{18}H_{24}N_2O_3SH^+$ 349.1580; found 349.1576.

***N*-(1-(Cyclohexylamino)butan-2-yl)-4-methylbenzenesulfonamide (3m)** Yield 67%; Yellow viscous liquid; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 0.81 (t, J=7.4 Hz, 3H, CH_2C**H$_3$**), 0.86—0.92 (m, 2H, cyclohexane-H), 1.11—1.19 (m, 3H, cyclohexane-H), 1.46—1.53 (m, 2H, C**H$_2$**CH_3), 1.56—1.76 (m, 5H, cyclohexane-H), 2.10—2.15 (m, 1H, cyclohexane-H), 2.42 (s, 3H, $PhCH_3$), 2.46—2.54 (m, 2H, cyclohexane-NHC**H$_2$**), 3.03—3.07 (m, 1H, SO_2NHC**H**), 7.28 (d, J=8.1 Hz, 2H, ArH), 7.75 (d, J=8.1 Hz, 2H, ArH); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 9.8, 21.5, 24.9 (2C), 26.0, 26.3, 33.4 (2C), 48.6, 54.8, 56.0. 127.1, 129.3, 137.9, 143.0; IR (KBr) ν_{max}: 3283, 2929, 1327, 1159 cm^{-1}; HRMS (ESI) *m*/*z*: (M+H$^+$) calcd for $C_{17}H_{28}N_2O_2SH^+$ 325.1944; found 325.1943.

***N*,*N*'-((Cyclohexylazanediyl)bis(ethane-2,1-diyl))-bis(4-methylbenzenesulfonamide) (4a)** Yield 55%; white solid; m.p. 95—96 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.05—1.71 (m, 10H, cyclohexane-H), 2.11 (s, 1H, cyclohexane-H), 2.45 (s, 6H, CH_3), 2.51 (t, J=5.8 Hz, 4H, NC**H$_2$**), 2.86 (t, J=5.1 Hz, 4H, SO_2NHC**H$_2$**), 5.00 (s, 2H, NH), 7.35 (d, J=8.0 Hz, 4H, ArH), 7.80 (d, J=8.0 Hz, 4H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.5, 25.9, 26.0, 28.7, 41.5, 49.6, 59.2, 127.2, 129.8, 137.0, 143.4; IR (KBr) ν_{max}: 3266, 2935, 1335, 1165 cm^{-1}; HRMS (ESI) *m*/*z*: (M+H$^+$) calcd for $C_{24}H_{35}N_3O_4S_2H^+$ 494.2147; found 494.2161.

***N*,*N*'-((*tert*-Butylazanediyl)bis(ethane-2,1-diyl))-dibenzenesulfonamide (4b)** Yield 53%; white sticky solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.98 (s, 9H, $C(CH_3)_3$), 2.57 (t, J=6.2 Hz, 4H, NC**H$_2$**), 2.86 (t, J=

6.0 Hz, 4H, $SO_2NHC\mathbf{H_2}$), 4.97 (s, 2H, NH), 7.54 (t, J= 7.2 Hz, 4H, ArH), 7.59 (t, J=7.3 Hz, 4H, ArH), 7.89 (d, J=8.1 Hz, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 27.0, 43.3, 50.5, 55.2, 127.0, 129.1, 132.6, 140.1; IR (KBr) ν_{max}: 3444, 1321, 1160 cm^{-1}; HRMS (ESI) m/z: (M+H$^+$) calcd for $C_{20}H_{29}N_3O_4S_2H^+$ 440.1678; found 440.1675.

***N*,*N*′-((Benzylazanediyl)bis(ethane-2,1-diyl))bis(4-methylbenzenesulfonamide) (4c)** Yield 63%; white sticky solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.43 (s, 6H, PhC$\mathbf{H_3}$), 2.53 (t, J=5.6 Hz, 4H, NC$\mathbf{H_2}$CH$_2$), 2.94 (d, J=5.4 Hz, 4H, $SO_2NHC\mathbf{H_2}$), 3.44 (s, 2H, PhC$\mathbf{H_2}$), 5.08 (s, 2H, NH), 7.15 (d, J=6.2 Hz, 2H, ArH), 7.30 (t, J= 7.3 Hz, 7H, ArH), 7.74 (d, J=8.0 Hz, 4H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.5, 40.7, 53.2, 58.5, 127.2, 127.4, 128.6, 128.9, 129.8, 136.7, 137.8, 143.4; IR (KBr) ν_{max}: 3446, 1325, 1159 cm^{-1}; HRMS (ESI) m/z: (M+H$^+$) calcd for $C_{25}H_{31}N_3O_4S_2H^+$ 502.1829; found 502.1832.

***N*,*N*′-((Benzylazanediyl)bis(ethane-2,1-diyl))dibenzenesulfonamide (4d)** Yield 70%; white sticky solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.53 (t, J=5.7 Hz, 4H, NC$\mathbf{H_2}$CH$_2$), 2.95 (q, J=5.4 Hz, 4H, $SO_2NHC\mathbf{H_2}$), 3.45 (s, 2H, PhC$\mathbf{H_2}$), 5.18 (s, 2H, NH), 7.16 (d, J=7.2 Hz, 2H, ArH), 7.28 (d, J=7.2 Hz, 3H, ArH), 7.51 (t, J=7.6 Hz, 4H, ArH), 7.58 (t, J=7.2 Hz, 2H, ArH), 7.87 (d, J=7.8 Hz, 4H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 40.7, 53.3, 58.5, 127.1, 127.5, 128.6, 128.9, 129.2, 132.6, 137.7, 139.7; IR (KBr) ν_{max}: 3445, 1316, 1160 cm^{-1}; HRMS (ESI) m/z: (M+H$^+$) calcd for $C_{23}H_{27}N_3O_4S_2H^+$ 474.1516; found 474.1522.

***N*,*N*′-(((2-Hydroxyethyl)azanediyl)bis(ethane-2,1-diyl))bis(4-methylbenzenesulfonamide) (4e)** Yield 47%; white solid; m.p. 78−79 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.44 (s, 6H, CH_3), 2.55 (m, 6H, NCH_2), 2.97 (t, J=4.8 Hz, 4H, $SO_2NHC\mathbf{H_2}$), 3.70 (t, J=4.7 Hz, 2H, C$\mathbf{H_2}$OH), 6.24 (s, 2H, NH), 7.36 (d, J=8.0 Hz, 4H, ArH), 7.82 (d, J=8.2 Hz, 4H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.5, 40.9, 54.0, 55.6, 59.6, 127.1, 129.8, 136.9, 143.3; IR (KBr) ν_{max}: 3431, 3284, 1325, 1159 cm^{-1}; HRMS (ESI) m/z: (M+H$^+$) calcd for $C_{20}H_{29}N_3O_5S_2H^+$ 456.1621; found 456.1626.

***N*,*N*′-(((2-Hydroxyethyl)azanediyl)bis(ethane-2,1-diyl))dibenzenesulfonamide (4f)** Yield 60%; white sticky solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.54 (t, J= 4.9 Hz, 6H, NC$\mathbf{H_2}$), 2.99 (t, J=4.8 Hz, 4H, $SO_2NHC\mathbf{H_2}$), 3.70 (d, J=4.1 Hz, 2H, C$\mathbf{H_2}$OH), 7.57 (m, 6H, ArH), 7.94 (d, J=7.0 Hz, 4H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 40.9, 53.9, 55.6, 59.6, 127.1, 129.2, 132.6, 139.9; IR (KBr) ν_{max}: 3436, 1331, 1160 cm^{-1}; HRMS (ESI) m/z: (M+H$^+$) calcd for $C_{18}H_{25}N_3O_5S_2Na^+$ 450.1133; found 450.1132.

1-Cyclohexyl-3-tosylimidazolidine-2-thione (5a) Yield 51%; white solid; m.p. 193−194 ℃; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.09−1.77 (m, 10H, cyclohexane-H), 2.42 (s, 3H, CH_3), 3.56 (t, J=8.6 Hz, 2H, cyclohexane-NC$\mathbf{H_2}$), 4.12 (t, J=8.6 Hz, 1H, $SO_2NC\mathbf{H_2}$), 4.36 (m, J=11.8 Hz, 1H, cyclohexane-H), 7.31 (d, J= 8.0 Hz, 2H, ArH), 7.79 (d, J=8.2 Hz, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.7, 25.2, 25.3, 29.2, 42.1, 46.0, 55.3, 129.0, 129.2, 135.0, 144.8, 176.6; IR (KBr) ν_{max}: 3441, 2935, 1361, 1171 cm^{-1}; HRMS (ESI) m/z: (M+H$^+$) calcd for $C_{16}H_{22}N_2O_2S_2Na^+$ 361.1020; found 361.1035.

1-Cyclohexyl-3-(phenylsulfonyl)imidazolidine-2-thione (5b) Yield 71%; white solid; m.p. 190−191 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.05−1.56 (m, 10H, cyclohexane-H), 3.57 (t, J=8.6 Hz, 2H, cyclohexane-NC$\mathbf{H_2}$), 4.14 (t, J=8.6 Hz, 2H, $SO_2NC\mathbf{H_2}$), 4.35 (m, 1H, cyclohexane-H), 7.52 (t, J=7.7 Hz, 2H, ArH), 7.62 (d, J=7.4 Hz, 1H, ArH), 8.11 (d, J=7.6 Hz, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 25.2, 25.3, 29.2, 42.1, 45.9, 55.4, 128.9, 129.0, 133.8, 138.0, 176.6; IR (KBr) ν_{max}: 3663, 2938, 1354, 1170 cm^{-1}; HRMS (ESI) m/z: (M+H$^+$) calcd for $C_{15}H_{20}N_2O_2S_2Na^+$ 347.0864; found 347.0854.

Crystal structure determinations

X-ray crystallographic analysis of **4a** was performed at 113 K by using a Brucker Smart 1000 CCD-X diffractometer with Mo Kα radiation (λ=0.71073 Å) and a graphite monochromator. Crystal system: triclinic, P1. Crystal dimensions: 0.26 mm×0.20 mm×0.18 mm. Crystal data: Z=4, a=12.060 (2) Å, b=15.661 (3) Å, c=16.751 (3) Å, α=102.60 (3)°, β=108.34 (3)°, γ= 92.74(3)°, V=2907.5(10) Å^3. ρ_{calcd}=1.033 g/cm^3, μ= 0.219 mm^{-1}, 26600 total reflections ($2\theta_{max}$=50.0°), 10187 unique reflections (R_{int}=0.044), R_1=0.0633 [I>2(I)], wR_2 (all data)=0.2312, GOF =1.081 (744 parameters) (CCDC-991013).

Results and Discussion

Initially we chose ring opening of *N*-tosylaziridine (**1a**) by cyclohexylamine (**2a**) as model reaction. When the solvent was selected from ethyl ether, THF, acetonitrile and ethanol, TLC analysis showed a variety of by-products emerged at ambient temperature although **1a** was poorly converted. Notably, **1a** was so easy to polymerize in an organic solvent at raised temperature that the reaction generated complicated products under reflux in the abovementioned solvents. Then water was employed as the reaction media. However, **1a** was dissolved in water so poorly that it reacted with the amine slowly; sometimes the reaction mixture became viscous and caused stirring trouble. Then SG was incorporated into the reaction mixture and the ring opening in SG-H_2O system was achieved satisfactorily. We found that the reaction was affected by the amount of SG. A total of 1 g SG for 1 mmol **1a** was too much to cause the increase of 2∶1 ring opening product and other by-products. Further experiments indicated that the type of SG, either 40−60 mesh or 200−300 mesh for column chromatography is not critical, which is somewhat different from the literature.[23] SG (40−60 mesh) was preferred in this reaction because it facilitated the fol-

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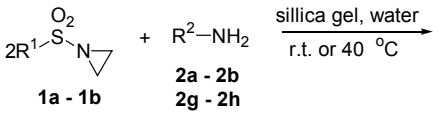
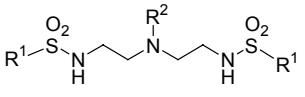
lowing filtration. Without water, the stirring was difficult and the reaction was not complete in 24 h. Grinding the mixture in a mortar could accelerate the reaction and **1a** was entirely consumed in 1 h. However, even with large excess of cyclohexylamine the selectivity of the reaction was not good and complicated products were observed by TLC. Finally the optimum reaction conditions were found as follows: 0.1 g SG (40—60 mesh) for 1 mmol aziridine, 1∶2 ratio of *N*-sulfonyl aziridines to amine, and room temperature.

Next, the reactions of different amines were investigated. As summarized in Table 1, aliphatic and alicyclic primary amines (**2a**—**2c**) reacted with *N*-tosylaziridine and *N*-phenylsulfonylaziridine steadily to give ring opening products **3a**—**3e** in moderate yields (Entries 1—5). However, aniline and *p*-methoxyaniline underwent similar reactions to afford the corresponding products in good yields (Entries 6—9). Secondary amine such as diethylamine afforded the corresponding products **3j** and **3k** in moderate yields (Entries 10, 11). Interestingly, the regioselectivities of the ring opening reactions of 2-ethyl-*N*-tosylaziridine with *p*-methoxyaniline and cyclohexylamine were satisfactory, and the yields of the corresponding products **3l** and **3m** were 65% and 67%, respectively (Entries 12, 13). Moreover, 2∶1 ring opening reactions in SG-H_2O was investigated by treatment of amines with 2 equiv. of aziridines (Scheme 2). As shown in Table 2, cyclohexylamine, *t*-butylamine, benzylamine and aminoethanol reacted with *N*-sulfonyl aziridines at different temperatures to give desired disulfonyl triamines in moderate yields. It is worthy to note that the reaction of aminoethanol with *N*-sulfonyl aziridines generated complicated products without SG and the target products were hard to isolate. Unlike 1∶1 ring opening products, most of the 2∶1 products were isolated as white viscous oils and became solids gradually in a refrigerator. However, **4a** was obtained as a white solid. Its structure was revealed by single-crystal X-ray diffraction study (Figure 1) in addition to IR, ^{1}H NMR, ^{13}C NMR and HRMS analysis.

Scheme 2 The 2∶1 reaction of aziridines and primary amines





Enlightened by the role of silica gel and water established by Minakata and co-workers,[16] we proposed a plausible pathway for this reaction (Scheme 3). Most of the amines employed are soluble in water. Silica gel can absorb them from water *via* hydrogen bonds and accumulate them on the surface of SG. The sulfonylaziridine is insoluble in water, and most of its molecules are absorbed on the SG surface due to the hydrophobic effect. Therefore, on the surface of SG an interface will generate, in which the concentrations of both sulfonylaziridine and amine are high enough to let the reaction between them take place readily. When amine was in excess, the firstly formed monosulfonyl diamine was pushed out of SG surface by amine molecules, so it scarcely contacted with sulfonylaziridine and the formation of 2∶1 product was inhibited. On the contrary, the 2∶1 product was yielded dominantly when sulfonylaziridine was in excess.

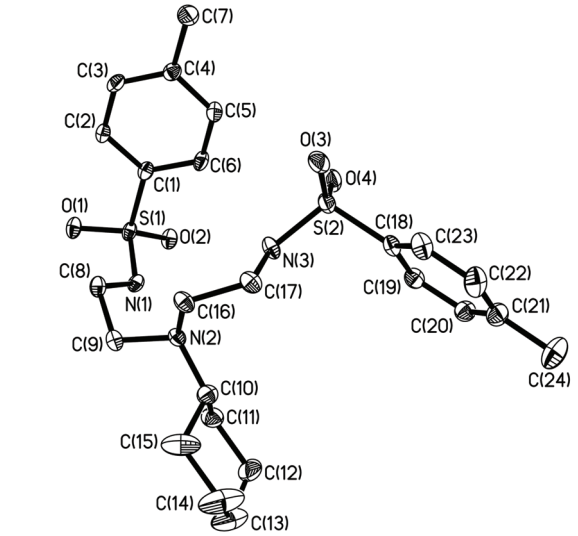
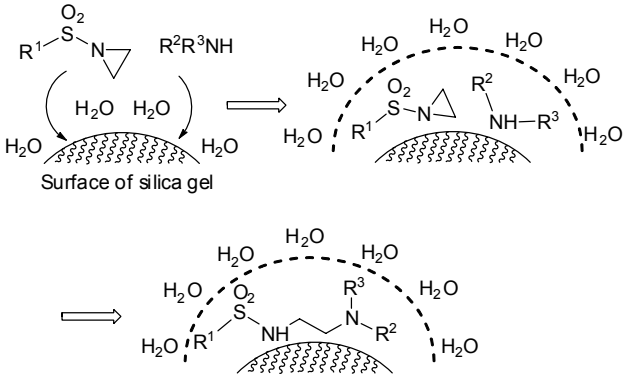


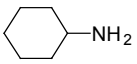
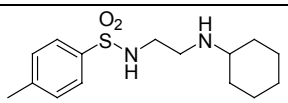
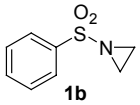
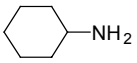
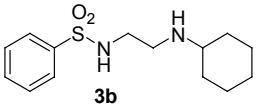
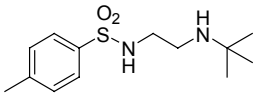
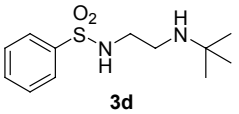
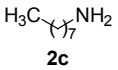
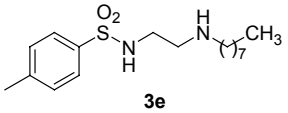
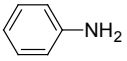
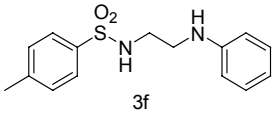
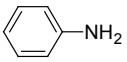
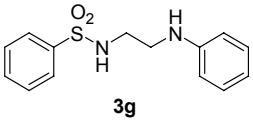
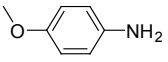
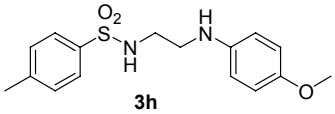
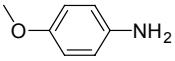
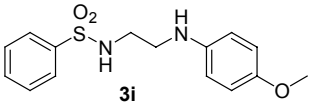
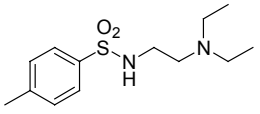
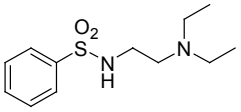
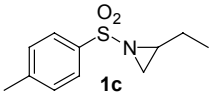
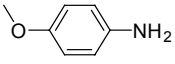
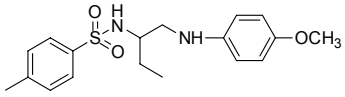
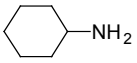
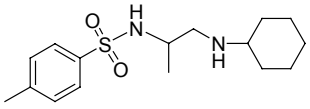
Figure 1 Crystal structure of **4a** (H atoms were omitted for clarity).

Scheme 3 Possible function of silica gel-water system



For developing the application of the reaction, we used **3a** and **3b** as the substrates for cyclizations with CS_2 in water.[29,48] Nucleophilic additions of **3a** and **3b** with CS_2 generated dithiocarbamates, which were subsequently treated with chloroacetic acid to yield substituted *N*-sulfonylcyclothioureas **5a** and **5b**, respectively (Scheme 4). As such, aqueous one-pot synthetic method to *N*-sulfonylcyclothioureas can be achieved via ring opening of sulfonylaziridines with primary amines and the following cyclizations with CS_2 in the presence of

Table 1 The 1∶1 reaction products of aziridines and amines[a]

Entry	Aziridine	Amine	Product	*t*/h	Yield[b]/%
1	 **1a**	 **2a**	 **3a**	14	66
2	 **1b**	 **2a**	 **3b**	12	58
3	**1a**	 **2b**	 **3c**	14	53
4	**1b**	 **2b**	 **3d**	12	48
5	**1a**	 **2c**	 **3e**	12	50
6	**1a**	 **2d**	 3f	14	80
7	**1b**	 **2d**	 **3g**	12	74
8	**1a**	 **2e**	 **3h**	12	78
9	**1b**	 **2e**	 **3i**	12	68
10	**1a**	 **2f**	 **3j**	14	56
11	**1b**	 **2f**	 **3k**	12	60
12	 **1c**	 **2e**		12	65
13	**1c**	 **2a**		12	67

[a] Reaction conditions: *N*-sulfonyl aziridine (1 mmol), amine (2 mmol **2a**—**2e**, 1.5 mmol **2f**), SG (0.1 g, 40—60 mesh), 1 mL H_2O, room temperature. [b] Isolated yield.

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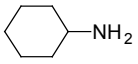
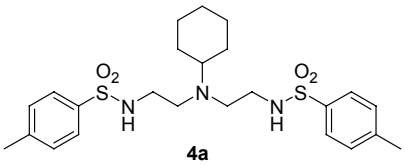
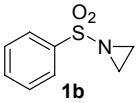
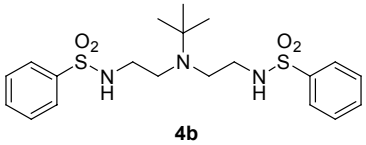
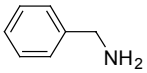
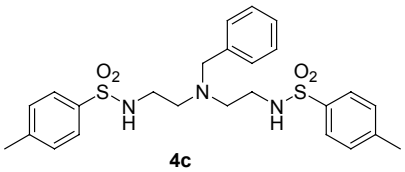
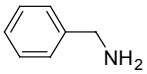
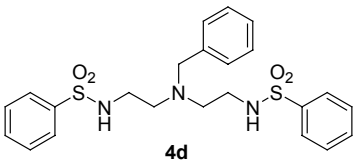
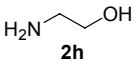
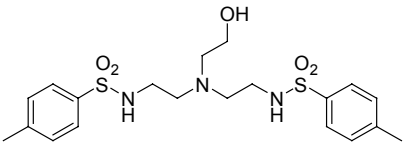
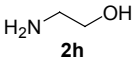
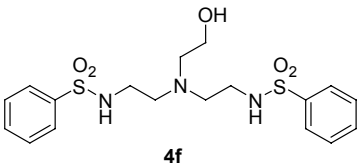
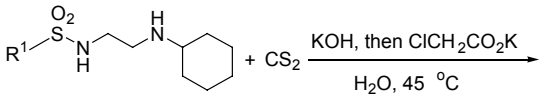
Table 2 The 2∶1 reaction products of aziridines and amines[a]

Entry	Aziridine	Amine	Product	*t*/h	*T*/℃	Yield[b]/%
1	 **1a**	 **2a**	 **4a**	9	40	55
2	 **1b**	 **2b**	 **4b**	9	40	53
3	**1a**	 **2g**	 **4c**	9	40	63
4	**1b**	 **2g**	 **4d**	9	40	70
5	**1a**	 **2h**	 **4e**	14	r.t.	47
6	**1b**	 **2h**	 **4f**	14	r.t.	60

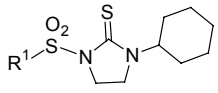
[a] Reaction conditions: *N*-sulfonyl aziridine (2 mmol), amine (1 mmol), SG (0.2 g, 40—60 mesh), 2 mL H_2O, room temperature or 40 ℃. [b] Isolated yield.

$ClCH_2CO_2K$.

Scheme 4 The synthesis of *N*-sulfonylcyclothioureas



3a, 3b



5a, R^1 = *p*-tolyl
5b, R^1 = Ph

Conclusions

The ring opening of *N*-tosylaziridine and *N*-phenylsufonylaziridine by primary and secondary amines took place smoothly in silica gel-H_2O system at room temperature to give the corresponding 1∶1 ring opening products in moderate to good yields. Furthermore, reactions of primary amines with 2 equiv. of aziridines afforded 2∶1 ring opening products in moderate yields. The 1∶1 products of primary amines and aziridines can be further transformed to *N*-sulfonylcyclothioureas by CS_2 and chloroacetic acid in water. In summary, we described a mild, practical method to produce mono- and bis-sulfonyl substituted amines in an environmentally benign SG-H_2O system.

Acknowledgement

We appreciate the financial support from the National Natural Science Foundation of China (No. 20802049).

References

[1] Gawande, M. B.; Bonifácio, V. D. B.; Luque, R.; Branco, P. S.; Varma, R. S. *Chem. Soc. Rev.* **2013**, *42*, 5522.
[2] Simon, M.-O.; Li, C.-J. *Chem. Soc. Rev.* **2012**, *41*, 1415.

[3] Mojet, B. L.; Ebbesen, S. D.; Lefferts, L. *Chem. Soc. Rev.* **2010**, *39*, 4643.
[4] Butler, R. N.; Coyne, A. G. *Chem. Rev.* **2010**, *110*, 6302.
[5] Chanda, A.; Fokin, V. V. *Chem. Rev.* **2009**, *109*, 725.
[6] Panchadhayee, R.; Misra, A. K. *ARKIVOC* **2009**, (ii), 298.
[7] Bai, L.; Zhang, X.; Ma, N. *Chin. J. Chem.* **2014**, *32*, DOI: 10.1002/cjoc.201300253.
[8] Shirakawa, S.; Maruoka, K. *Angew. Chem., Int. Ed.* **2013**, *52*, 4312.
[9] Li, C. J.; Chen, L. *Chem. Soc. Rev.* **2006**, *35*, 68.
[10] Lindström, U. M. *Chem. Rev.* **2002**, *102*, 2751.
[11] Hashimoto, T.; Maruoka, K. *Asymmetric Phase Transfer Catalysis*, Ed.: Maruoka, K., Wiley-VCH, Weinheim, **2008**, pp. 1—9.
[12] Dehmlow, E. V.; Dehmlow, S. S. *Phase Transfer Catalysis*, Verlag Chemie, Weinheim, **1980**, pp. 9—22.
[13] Minakata, S.; Komatsu, M. *Chem. Rev.* **2009**, *109*, 711.
[14] Minakata, S.; Takeda, Y.; Murakami, Y.; Ikeda, Y. *Asian J. Org. Chem.* **2012**, *1*, 226.
[15] Minakata, S.; Murakami, Y.; Takeda, Y. *J. Org. Chem.* **2011**, *76*, 6277.
[16] Minakata, S.; Kano, D.; Oderaotoshi, Y.; Komatsu, M. *Angew. Chem., Int. Ed.* **2004**, *43*, 79.
[17] Reddy, B. M.; Kumar, V. V. R.; Reddy, N. C. G.; Rao, S. M. *Chin. Chem. Lett.* **2014**, *25*, 179.
[18] Agarwal, S.; Aware, U.; Patil, A.; Rohera, V.; Ghate, M.; Jain, M.; Patel, P. *Bull. Korean Chem. Soc.* **2012**, *33*, 377.
[19] Nandi, G. C.; Samai, S.; Kumar, R.; Singh, M. S. *Synth. Commun.* **2011**, *41*, 417.
[20] Wu, H.; Lin, W.; Wan, Y.; Xin, H. Q.; Shi, D. Q.; Shi, Y. H.; Yuan, R.; Bo, R. C.; Yin, W. *J. Comb. Chem.* **2010**, *12*, 31.
[21] Ding, Q.; Cao, B.; Zong, Z.; Peng, Y. *J. Comb. Chem.* **2010**, *12*, 370.
[22] Yang, X. D.; Zeng, X. H.; Zhao, Y. H.; Wang, X. Q.; Pan, Z. Q.; Li, L.; Zhang, H. B. *J. Comb. Chem.* **2010**, *12*, 307.
[23] Basu, B.; Paul, S.; Nanda, A. K. *Green Chem.* **2009**, *11*, 1115.
[24] Okamura, H.; Iiji, H.; Hamada, T.; Iwagawa, T.; Furuno, H. *Tetrahedron* **2009**, *65*, 10709.
[25] Zhang, E.; Tu, Y. Q.; Fan, C. A.; Zhao, X.; Jiang, Y. J.; Zhang, S. Y. *Org. Lett.* **2008**, *10*, 4943.
[26] You, L.; Feng, S.; An, R.; Wang, X.; Bai, D. *Tetrahedron Lett.* **2008**, *49*, 5147.
[27] Mangu, N.; Kaiser, H. M.; Kar, A.; Spannenberg, A.; Beller, M.; Tse, M. K. *Tetrahedron* **2008**, *64*, 7171.
[28] Wan, G. X.; Xu, L.; Ma, X. S.; Ma, N. *Tetrahedron Lett.* **2011**, *52*, 6250.
[29] Wan, G. X.; Xu, L.; Ma, X. S.; Zhang, Y.; Wang, J.; Zhang, J.; Ma, N. *Chin. J. Chem.* **2011**, *29*, 2081.
[30] Padwa, A. In *Comprehensive Heterocyclic Chemistry*, Eds.: Katritzky, A. R.; Ramsden, C. A.; Scriven, E. F. V.; Taylor, R. J. K., Elsevier, Oxford, **2008**, Vol. 1, pp. 1—104.
[31] Florio, S.; Luisi, R. *Chem. Rev.* **2010**, *110*, 5128.
[32] Sweeney, J. *Eur. J. Org. Chem.* **2009**, 4911.
[33] Dauban, P.; Malik, G. *Angew. Chem., Int. Ed.* **2009**, *48*, 9026.
[34] Zhang, J.; Meng, L.; Li, C.; Xiao, G. *Chin. J. Chem.* **2013**, *31*, 1508.
[35] Bao, H.; Wang, Z.; You, T.; Ding, K. *Chin. J. Chem.* **2012**, *30*, 67.
[36] Han, Y.; Fu, Q.; Tang, W.; Yan, C. *Chin. J. Chem.* **2012**, *30*, 1867.
[37] Kang, Q.; Wang, L.; Zheng, Z.; Li, J.; Tang, Y. *Chin. J. Chem.* **2014**, *32*, DOI: 10.1002/cjoc.201400053.
[38] Stanković, S.; D'hooghe, M.; Catak, S.; Eum, H.; Waroquier, M.; Van Speybroeck, V.; De Kimpe, N.; Ha, H. J. *Chem. Soc. Rev.* **2012**, *41*, 643.
[39] Yang, T.-P.; Li, Q.; Lin, J.-H.; Xiao, J.-C. *Chem. Commun.* **2014**, *50*, 1077.
[40] Rajabi, N. A.; Atashgah, M. J.; BabaAhmadi, R.; Hyland, C.; Ariafard, A. *J. Org. Chem.* **2013**, *78*, 9553.
[41] Nadir, U. K.; Singh, A. *Tetrahedron Lett.* **2005**, *46*, 2083.
[42] Fan, R.-H.; Hou, X.-L. *J. Org. Chem.* **2003**, *68*, 726.
[43] Wu, J.-Y.; Luo, Z.-B.; Dai, L.-X.; Hou, X.-L. *J. Org. Chem.* **2008**, *73*, 9137.
[44] Wu, J.; Sun, X. Y.; Ye, S. Q. *Tetrahedron Lett.* **2006**, *47*, 4813.
[45] Li, X.; Li, G.; Chang, H. H.; Zhang, Y.; Wei, W. L. *RSC Adv.* **2014**, *4*, 649.
[46] Zhu, M. P.; Moasser, B. *Tetrahedron Lett*. **2012**, *53*, 2288.
[47] Bieber, L. W.; de Araújo, M. C. F. *Molecules* **2002**, *7*, 902.
[48] Ding, C.; Zhang, M.; Geng, L.; Li, R. *ARKIVOC* **2010**, (xi), 49.

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