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Chinese Chemical Letters 22 (2011) 1143–1146
CHINESE CHEMICAL LETTERS
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Synthesis of the 1,3-oxathiolanes using asymmetrically oxiranes

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Received 24 February 2011
Available online 20 July 2011

Abstract

An efficient synthesis of 1,3-oxathiolane-2-imin derivatives is described *via* one-pot reaction between arylisothiocyanats, asymmetrically substituted oxiranes and catalytic amount of methanol. The mild reaction conditions and high yields of the products exhibit the good synthetic advantage of this method.
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Keywords: 1,3-Oxathiolane-2-imine; Oxirane; Methanol; One-pot reactions; Arylisothiocyanats

Because of the strain induced by the presence of a three membered ring (having a high thermodynamic driving force, usually greater than 20 kcal/mol) [1], epoxides are significantly more reactive than to other ethers. Thus, they become as useful building block compounds in organic synthesis. Synthetic procedures for epoxide ring opening can be based on nucleophilic or protic/Lewis acid-mediated electrophilic ring opening [2,3]. A number of procedures which feature the oxyphilic Lewis character of metal ions and non-metallic Lewis acids have been developed. Suitable epoxide opening catalysts include Lewis acids, Lewis bases, Bronsted acids, thioxanthenone-fused azacrown ethers, Schiff base and porphyrin complexes [3–14]. The regioselectivity has been found to be in many cases sensitive to the operating opening reactions, that is, if these were carried out under standard or chelating conditions [15–17]. Although, the use of chelating opening conditions affords a nice regioalternating process but the method is limited to the epoxides bearing chelate-forming substituents. Also, compounds containing an imine group are increasingly important in organic synthesis [18] and the mechanism of the *cis*/*trans* isomerization of imines is being studied in detail [19]. The 1,3-oxathiolane-2-imine structures include an exocyclic imine group and can be used in organic synthesis for the preparation of biologically active compounds. As part of our current studies on the development of new routes in heterocyclic synthesis, we report an efficient procedure for direct synthesis of 1,3-oxathiolan derivatives **3** from the reaction of epoxide **1** and arylisothiocyanate **2** in the presence of catalytic amount of methanol and NaH under solvent-free conditions at 50 °C in excellent yield (Scheme 1).

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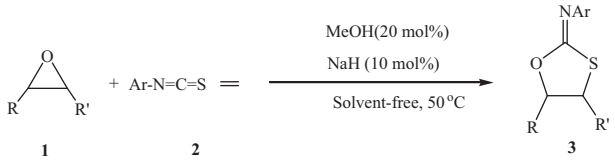
doi:10.1016/j.cclet.2011.05.021



Scheme 1. One-pot reaction of epoxide and arylisothiocyanate in the presence of catalytic amount of methanol.

Structures of compounds **3a–k** were assigned by IR, ^{1}H NMR, ^{13}C NMR and mass spectral data (Fig. 1) [20]. Due to the presence of a stereogenic center, the ^{1}H NMR spectrum of **3a** exhibited three multiplets at 3.50–3.58, 4.24–4.34 and 5.01–5.07 ppm arising from two CH_2 and CH protons, respectively. The ^{13}C NMR spectrum of **3a** appears 12 signals agreement with proposed structure. The mass spectrum of **3a** displayed the molecular ion peak at *m/z* 285. Although the mechanistic details of the reaction are not known, a plausible rationalization may be advanced to explain the product formation (Scheme 2). Presumably, the anionic intermediate A formed from the reaction of **2** with methoxide anion. After that by nucleophilic attacking of A to oxirane derivatives **1**, intermediate B was produced. Eventually the intermediate B can undergo cyclization under the employed reaction conditions to producing of intermediate C followed by losing of methoxy group, the product of **3** was generated.

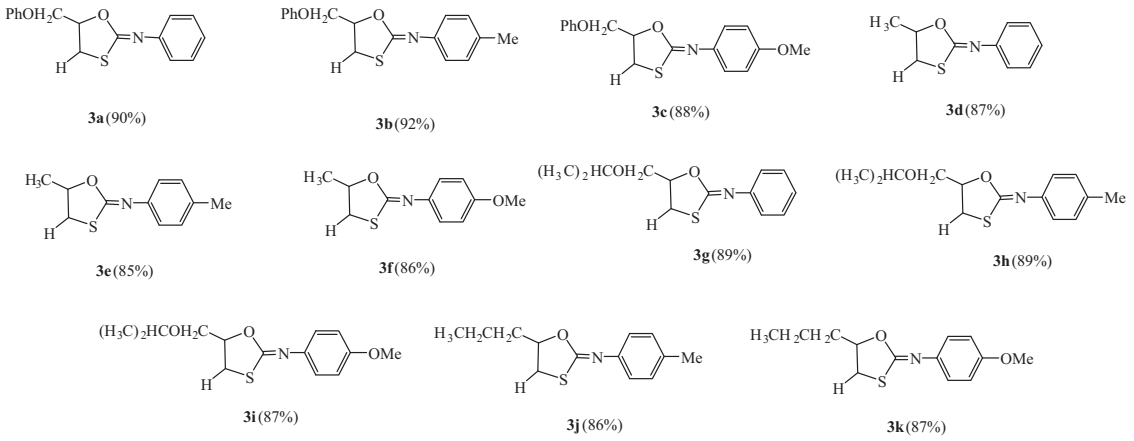
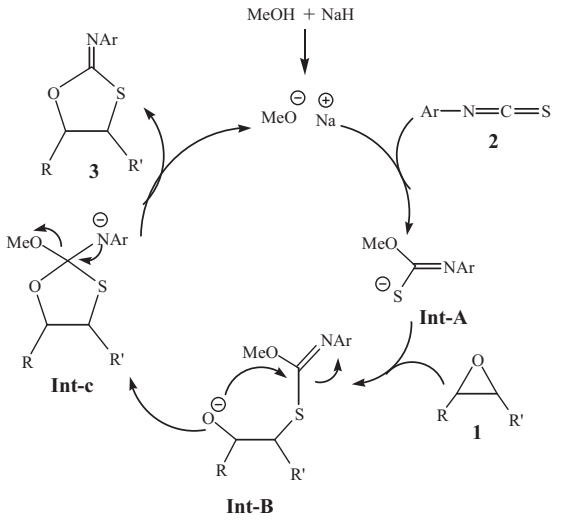


Fig. 1. Structures of compounds **3a–k**.



Scheme 2. Possible mechanism for the formation of products **3**.

In conclusion, we have developed the most useful and dependable procedure currently available for the synthesis of 1,3-oxathiolane-2-imine by using low cost and readily available starting materials in one-pot. This method represents a simple and green procedure, uses mild reaction conditions, and has general applicability. It avoids hazardous organic solvents and toxic catalysts and gives nearly quantitative yields without any by-products in most cases.

Acknowledgments

We gratefully acknowledge support of this research work by Islamic Azad University of Qaemshahr and the University of Gonbad Kavous.

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[20] *General procedure for preparation of compounds **3a–k***: A mixture of methanol (20 mol%) and NaH (10 mol%) was stirred for 10 min. Then, arylisothiocyanate derivatives **2** (2 mmol) was gently added and warmed at about 50 °C for 2 h. Then, after addition of oxirane derivatives **1** (2 mmol) the reaction mixture was stirred for 4 h. After completion of the reaction (monitored by TLC), the mixture of reaction was purified by column chromatography (SiO_2; *n*-hexane/AcOEt 9:1) to afford pure title compounds. *N-(5-Methyl-1,3-oxathiolan-2-ylidene)benzenamine* **(3a)**: Yellow powder, yield: 0.51 g (90%). IR (KBr) (ν_{max}/cm^{-1}): 2928, 1735, 1644, 1483, 1234 and 1072. ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.50–3.59 (m, 2 H, CH_2), 4.24–4.35 (m, 2 H, CH_2), 5.01–5.05 (m, 1 H, CH), 6.96–7.38 (m, 10 H, 10 CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 33.5 (CH_2), 66.9 (CH_2), 78.9 (CH), 114.6 (2 CH), 121.2 (2 CH), 121.7 (CH), 124.4 (CH), 129.1 (2 CH), 129.6 (3 CH), 148.9 (C), 158.0 (C), 162.9 (C). Anal. Calcd. for $C_{16}H_{15}NO_2S$ (285.36): C, 67.35, H, 5.30, N, 4.91. Found: C, 67.23, H, 5.21, N, 4.85. *4-Methyl-N-(5-methyl-1,3-oxathiolan-2-ylidene)benzenamine* **(3b)**: Yellow powder, yield: 0.55 g (92%). IR (KBr) (ν_{max}/cm^{-1}). 2972, 1652, 1593, 1481, 1373 and 1266. ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.36 (s, 3 H, Me), 3.49–3.58 (m, 2 H, CH_2), 4.25–4.28 (m, 1 H, CH), 4.32–4.34 (m, 1 H, CH), 4.99–5.04 (m, 1 H, CH), 6.91 (d, 2 H, ^3J = 8.2 Hz, 2 CH), 6.96 (d, 2 H, ^3J = 8.3 Hz, 2 CH), 7.02 (t, 1 H, ^3J = 7.3 Hz, CH), 7.16 (d, 2 H, ^3J = 8.2, 2 CH), 7.33 (t, 2 H, ^3J = 7.9 Hz, 2 CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 20.9 (Me), 33.5 (CH_2), 66.9 (CH_2), 78.9 (CH), 114.7 (2 CH), 121.0 (2 CH), 121.7 (CH), 129.6 (2 CH), 129.7 (2 CH), 133.9 (C), 146.4 (C), 158.1 (C), 162.6 (C). Anal. Calcd. for $C_{17}H_{17}NO_2S$ (299.39): C, 68.20, H, 5.72, N, 4.68. Found: C, 68.25, H, 5.83, N, 4.75. *4-Methoxy-N-(5-methyl-1,3-oxathiolan-2-ylidene)benzenamine* **(3c)**: Pale yellow powder, yield: 0.45 g (89%). IR (KBr) (ν_{max}/cm^{-1}): 2974, 1642, 1590, 1481, 1373 and 1118. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.22 (d, 6 H, ^3J = 6.2, 2 Me), 3.34–3.42 (m, 2 H, CH_2), 3.62–3.70 (m, 3 H, 3 CH), 4.76–4.77 (m, 1 H, CH), 6.98 (d, 2 H, ^3J = 7.6, 2 CH), 7.12 (t, 1 H, ^3J = 7.4, CH), 7.33 (t, 2 H, ^3J = 7.4, 2 CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 22.3 (2 Me), 33.9 (CH_2), 67.3 (CH_2), 73.7 (CH), 80.4 (CH), 121.3 (2 CH), 126.8 (CH), 128.9 (2 CH), 149.0 (C), 163.5 (C). Anal. Calcd. for $C_{17}H_{17}NO_3S$ (315.36): C, 64.74, H, 5.43, N, 4.44. Found: C, 64.65, H, 5.38, N, 4.35. *4-Methyl-N-(5-propyl-1,3-oxathiolan-2-ylidene)benzenamine* **(3d)**: Yellow powder, yield: 0.47 g (89%). IR (KBr) (ν_{max}/cm^{-1}): 1762, 1642, 1590, 1481, 1373 and 1118. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.15 (d, 6 H, ^3J = 6.5, 2 Me), 2.33 (s, 3 H, Me), 3.31–3.38 (m, 2 H, CH_2), 3.59–3.73 (m, 3 H, 3 CH), 4.71–4.73 (m, 1 H, CH), 7.06 (d, 2 H, ^3J = 7.8, 2 CH), 7.25 (d, 2 H, ^3J = 7.6, 2 CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 21.9 (Me), 22.1 (2 Me), 33.4 (CH_2), 67.2 (CH_2), 72.7 (CH), 80.3 (CH), 121.1 (2 CH), 129.7 (2 CH), 133.6 (C), 146.5 (C), 163.3 (C). Anal. Calcd. for $C_{10}H_{11}NOS$ (193.26): C, 62.15, H, 5.74, N, 7.25. Found: C, 61.98, H, 5.62, N, 7.14. *4-Methoxy-N-(5-propyl-1,3-oxathiolan-2-ylidene)benzenamine* **(3e)**: Pale yellow powder, yield: 0.34 g (87%). IR (KBr) (ν_{max}/cm^{-1}): 1762, 1642, 1590, 1481, 1373 and 1118. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.52 (d, 3 H, ^3J = 6.2, Me), 3.01–3.05 (m, 1 H, CH), 3.33–3.37 (m, 1 H, CH), 4.71–4.75 (m, 1 H, CH), 6.97 (d, 2 H, ^3J = 7.3, 2 CH), 7.10 (t, 1 H, ^3J = 7.2, CH), 7.30 (t, 2 H, ^3J = 7.2, 2 CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 19.4 (Me), 37.1 (CH_2), 78.7 (CH), 119.5 (2 CH), 125.2 (CH), 129.1 (2 CH), 137.1 (C), 149.1 (C), 151.1 (C), 163.6 (C). Anal. Calcd. for $C_{11}H_{13}NOS$ (207.29): C, 63.74, H, 6.32, N, 6.76. Found: C, 63.67, H,

6.26, N, 6.67. *N-(5-(Phenoxymethyl)-1,3-oxathiolan-2-ylidene)benzenamine* **(3f)**: Pale yellow powder, yield: 0.35 g (85%). IR (KBr) (ν_{max}/cm^{-1}): 1762, 1642, 1590, 1481, 1373 and 1118. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.52 (d, 3 H, ^3J = 6.2, Me), 2.29 (s, 3 H, Me), 3.03–3.08 (m, 1 H, CH), 3.36–3.39 (m, 1 H, CH), 4.73–4.76 (m, 1 H, CH), 7.22 (d, 2 H, ^3J = 8.5, 2 CH), 7.27 (d, 2 H, ^3J = 8.5, CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 19.5 (Me), 20.7 (Me), 37.8 (CH_2), 78.5 (CH), 119.1 (2 CH), 129.6 (2 CH), 134.6 (C), 137.0 (C), 146.5 (C), 163.3 (C). Anal. Calcd. for $C_{11}H_{13}NO_2S$ (223.29): C, 59.17, H, 5.87, N, 6.27. Found: C, 59.25, H, 5.92, N, 6.34. *4-Methyl-N-(5-(phenoxymethyl)-1,3-oxathiolan-2-ylidene)benzenamine* **(3g)**: Pale yellow powders, yield: 0.45 g (89%). IR (KBr) (ν_{max}/cm^{-1}): 2925, 1652, 1593, 1491, 1100, 912 and 744. ^{1}H NMR (500.1 MHz, $CDCl_3$): δ 1.22 (d, 6 H, ^3J = 6.2, 2 Me), 3.34–3.42 (m, 2 H, CH_2), 3.62–3.70 (m, 3 H, 3 CH), 4.76–4.77 (m, 1 H, CH), 6.98 (d, 2 H, ^3J = 7.6, 2 CH), 7.12 (t, 1 H, ^3J = 7.4, CH), 7.33 (t, 2 H, ^3J = 7.4, 2 CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 22.3 (2 Me), 33.9 (CH_2), 67.3 (CH_2), 73.7 (CH), 80.4 (CH), 121.3 (2 CH), 126.8 (CH), 128.9 (2 CH), 149.0 (C), 163.5 (C). Anal. Calcd. for $C_{13}H_{17}NO_2S$ (251.34): C, 62.12, H, 6.82, N, 5.57. Found: C, 61.97, H, 6.78, N, 5.48. *4-Methoxy-N-(5-(phenoxymethyl)-1,3-oxathiolan-2-ylidene)benzenamine* **(3h)**: Yellow powders, yield: 0.47 g (89%). IR (KBr) (ν_{max}/cm^{-1}): 2925, 1692, 1543, 1491, 1100, 912 and 780. ^{1}H NMR (500.1 MHz, $CDCl_3$): δ 1.15 (d, 6 H, ^3J = 6.5, 2 Me), 2.33 (s, 3 H, Me), 3.31–3.38 (m, 2 H, CH_2), 3.59–3.73 (m, 3 H, 3 CH), 4.71–4.73 (m, 1 H, CH), 7.06 (d, 2 H, ^3J = 7.8, 2 CH), 7.25 (d, 2 H, ^3J = 7.6, 2 CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 21.9 (Me), 22.1 (2 Me), 33.4 (CH_2), 67.2 (CH_2), 72.7 (CH), 80.3 (CH), 121.1 (2 CH), 129.7 (2 CH), 133.6 (C), 146.5 (C), 163.3 (C). Anal. Calcd. for $C_{14}H_{19}NO_2S$ (265.37): C, 63.37, H, 7.22, N, 5.28. Found: C, 63.32, H, 7.18, N, 5.20. *N-(5-Isopropoxymethyl-1,3-oxathiolan-2-ylidene)benzenamine* **(3i)**: Pale yellow powders, yield: 0.49 g (87%). IR (KBr) (ν_{max}/cm^{-1}): 2925, 1692, 1543, 1491, 1100, 912 and 780. ^{1}H NMR (500.1 MHz, $CDCl_3$): δ 1.17 (d, 6 H, ^3J = 6.5, 2 Me), 3.32–3.40 (m, 2 H, CH_2), 3.64–3.71 (m, 2 H, CH_2), 3.72–3.75 (m, 1 H, CH), 3.78 (s, 3 H, MeO), 4.69–4.74 (m, 1 H, CH), 6.84 (d, 2 H, ^3J = 8.8, 2 CH), 6.91 (d, 2 H, ^3J = 8.8, 2 CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 22.0 (2 Me), 33.5 (CH_2), 55.4 (MeO), 67.3 (CH_2), 72.7 (CH), 80.2 (CH), 114.3 (2 CH), 122.3 (2 CH), 142.3 (C), 156.5 (C), 163.3 (C). Anal. Calcd. for $C_{14}H_{19}NO_3S$ (281.37): C, 59.76, H, 6.81, N, 4.98. Found: C, 59.65, H, 6.74, N, 4.87. *N-(5-Isopropoxymethyl-1,3-oxathiolan-2-ylidene)-4-methylbenzenamine* **(3j)**: Pale yellow powders, yield: 0.40 g (86%). IR (KBr) (ν_{max}/cm^{-1}): 1762, 1642, 1590, 1481, 1373 and 1118. ^{1}H NMR (500.1 MHz, $CDCl_3$): δ 1.10 (t, 2 H, ^3J = 7.4, Me), 1.77–1.82 (m, 2 H, CH_2), 1.93–1.99 (m, 2 H, CH_2), 2.32 (s, 3 H, Me), 3.07–3.11 (m, 1 H, CH), 3.33–3.37 (m, 1 H, CH), 4.52–4.56 (m, 1 H, CH), 6.88 (d, 2 H, ^3J = 8.2, 2 CH), 7.12 (d, 2 H, ^3J = 8.2, 2 CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 10.9 (Me), 21.6 (CH_2), 21.9 (Me), 27.8 (CH_2), 36.8 (CH_2), 84.5 (CH), 121.7 (2 CH), 129.4 (2 CH), 134.5 (C), 147.4 (C), 164.3 (C). Anal. Calcd. for $C_{13}H_{17}NOS$ (235.34): C, 66.35, H, 7.28, N, 5.95. Found: C, 66.28, H, 7.19, N, 5.87. *N-(5-Isopropoxymethyl-1,3-oxathiolan-2-ylidene)-4-methoxybenzenamine* **(3k)**: Pale yellow powders, yield: 0.44 g (87%). IR (KBr) (ν_{max}/cm^{-1}): 1762, 1642, 1590, 1481, 1373 and 1118. ^{1}H NMR (500.1 MHz, $CDCl_3$): δ 1.10 (t, 2 H, ^3J = 7.4, Me), 1.77–1.82 (m, 2 H, CH_2), 1.93–1.99 (m, 2 H, CH_2), 3.08–3.12 (m, 1 H, CH), 3.34–3.37 (m, 1 H, CH), 3.81 (s, 3 H, MeO), 4.52–4.55 (m, 1 H, CH), 6.85 (d, 2 H, ^3J = 8.2, 2 CH), 6.92 (d, 2 H, ^3J = 8.2, 2 CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 10.8 (Me), 28.1 (CH_2), 30.4 (CH_2), 36.9 (CH_2), 56.4 (MeO), 84.5 (CH), 115.2 (2 CH), 123.6 (2 CH), 143.3 (C), 157.3 (C), 164.3 (C). Anal. Calcd. for $C_{13}H_{17}NO_2S$ (251.34): C, 62.12, H, 6.82, N, 5.57. Found: C, 61.97, H, 6.73, N, 5.48.