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ORIGINAL PAPER

Isocyanide-based multicomponent reaction for the formation of 1,3-oxathiolane-2-imine derivatives

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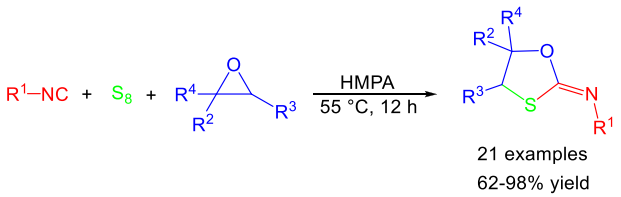
Abstract The adduct of isocyanide and elemental sulfur has been employed as the isothiocyanate source in reaction with oxirane to form 1,3-oxathiolane-2-imine derivatives. The optimum conditions are developed using HMPA at 55 °C for 12 h. Various isocyanides and oxiranes were tolerated under the optimum conditions.

Graphical abstract



Keywords Heterocycles · Oxirane · Isocyanide · Multi-component reaction · Elemental sulfur

Introduction

Organic synthesis relies on the transformation of functional groups or structural features exhibiting relatively high chemical reactivity. The ability to selectively form carbon-heteroatom bonds between organic fragments has been crucial to the development of synthetic organic chemistry. Complex molecules held together by carbon-heteroatom bonds can be synthesized through careful planning and execution of a series of chemical reactions that build up the desired structure step by step [1–6]. Besides the multistep synthesis, the desired products can also be produced through one-pot reactions of three or more starting compounds, the multicomponent reactions (MCRs). Many important heterocycles syntheses are MCRs [7, 8]. Isocyanides are among the most versatile substrates used in MCR for the syntheses of heterocyclic compounds. Since the pioneering work of Schollkopf [9], the MCRs of isocyanides have been well developed over the past decades. Regardless of the long history, these substrates still attract attention and new reports have been emerging constantly [10–14].

The 1,3-oxathiolane derivatives are highly valuable intermediates in organic synthesis and have been used as core structure for the development of herbicidal agents [15]. Many publications for the synthesis of 1,3-oxathiolanes have been reported, with ring opening of oxirane with heterocumulenes being among the most studied procedures [16–20]. Most of the methods proceeded in the presence of a catalyst, such as methoxide anion, oximes, nitromethan anion, and trialkyl phosphine using heterocumulenes and oxiranes as the starting materials. Although the reactions of three-membered heterocyclic compounds with heterocumulenes have well been studied, a relatively limited number of reports on the reaction of oxiranes with elemental sulfur have been reported [21–23].

In continue of our interest on heterocycles syntheses [24–27], we report an efficient and atom-economical route for the synthesis of 1,3-oxathiolan-2-imine derivatives from the reaction of isocyanides, elemental sulfur, and oxiranes.

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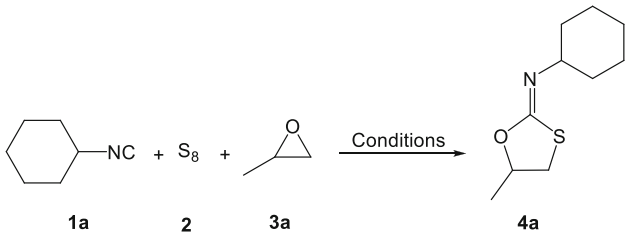
Results and discussion

Our study began by testing the reaction of cyclohexyl isocyanide (**1a**), elemental sulfur (**2**), and 2-methyloxirane (**3a**) in THF (Table 1). Stirring at reflux condition for 14 h, only afforded *N*-cyclohexyl-5-methyl-1,3-oxathiolan-2-imine (**4a**) in trace amounts.

To develop the reaction conditions, a variety of solvents and additives were examined (Table 1). The initial study demonstrated that the presence of additive was crucial to furnish the transformation in acceptable yield. Reaction conducted with KOAc formed the product in 31% yield (entry 2). Additive screen also showed that LiOAc, NaOAc, and $Mg(OAc)_2$ were not suitable in this transformation (entries 3–5). Reaction conducted with CsOAc proceeded in moderate conversion (entry 6). Among the phosphonium salts examined (entries 7–9), tetrabutylphosphonium acetate (TBPOAc) gave an excellent yield (entry 9). It is worth mentioning that organic ammonium salts completely inhibited the reaction probably due to the oxidizing the sulfide ion formed through the reaction progress. The study indicated that the reactivity is affected by both the cation and the anion of the salt; the tighter coordinating cation decreases the reactivity in appreciable manner. These finding encouraged us to examine the efficiency of HMPA both in the presence and in the absence of TBPOAc (entries 13 and 14). The desired product obtained in high yield when the reaction was conducted with HMPA (entry 14). We believed that the reaction proceeds through isocyanate intermediate (see Scheme 1) and additive anion reacts with the intermediate to form an anionic adduct which attacks on oxirane ring to form the desired product. In addition, when 1.1 mmol of cyclohexyl isothiocyanate was treated with **3a** (1.0 mmol) in HMPA, **4a** was achieved in 79% yield which supports the suggested mechanism pathway. Among the other polar

Table 1 Optimization of reaction conditions

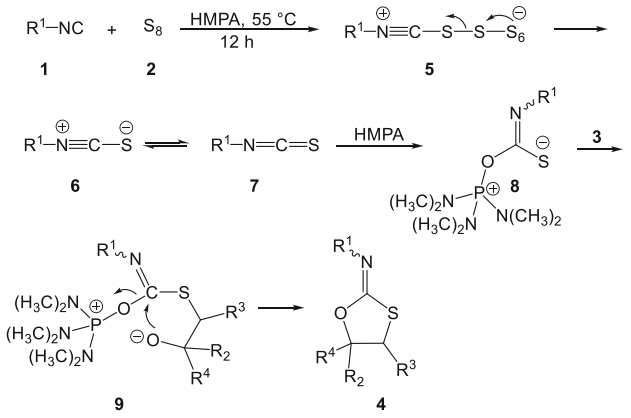


Entry	Additive	Solvent	Yield[a]/%
1	–	THF	Traces
2	KOAc	DMF	31
3	LiOAc	DMF	Traces
4	NaOAc	DMF	17
5	$Mg(OAc)_2$	DMF	Traces
6	CsOAc	DMF	59
7	TBPCl	DMF	31
8	TBPOH	DMF	42
9	TBPOAc	DMF	89
10	NH_4OAc	DMF	–
11	TBACl	DMF	–
12	TBAOAc	DMF	–
13	TBPOAc	HMPA	91
14	–	HMPA	89
15	–	DMF	Traces
16	–	DMA	Traces
17	–	NMP	Traces
18	–	DMSO	38
19	–	HMPA	51[b]

[a] Reaction conditions: **1a** (1.1 mmol), **2** (0.3 mmol), **3a** (1.0 mmol), and 5 cm^3 solvent were stirred at 55 °C for 12 h

[b] Reaction conducted at 50 °C

Scheme 1



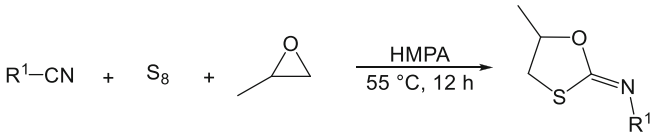
aprotic solvents examined, only DMSO afforded the product in moderate yield (entry 18).

The yield of **4a** remained almost the same upon increasing the reaction time and temperature (not shown in Table 1), but decreasing the reaction temperature adversely affected the yield of the product (entry 19). Our investigations for the reaction condition optimization demonstrated that **1a** (1.1 mmol), **2** (0.3 mmol), and **3a** (1.0 mmol) in 5 cm^3 HMPA at 55 °C for 12 h provided an improved condition for this transformation and the desired product was achieved in good yield.

After having defined the optimum reaction conditions, we sought to explore the scope of the reaction using a range of isocyanides (Table 2). Coupling of alkyl isocyanides proceeded with good yields (Table 2, entries 1 and 2). The reactions conducted with phenyl and naphtyl isocyanides (**1c**, **1d**) proceeded in high conversion (Table 2, entries 3 and 4). Benzyl isocyanide (**1e**) also afforded the desired product in acceptable yield (Table 2, entry 5). It should be noted that the reaction is completely chemo-selective, and no compound arising from the action of α-acidity of benzyl isocyanide (**1e**) is detected by crude GC–MS analysis. This reaction is not sensitive to steric effects on isocyanide structure as 2,6-dimethylphenyl isocyanide (**1f**) gave the desired product in excellent yield (Table 2, entry 6). Electron-rich isocyanide, such as **1g,** afforded the desired product in nearly quantative yield probably due to the greater nucleophilicity of the isocyanide (Table 2, entry 7).

The optimal reaction conditions were also proved to be effective in the preparation of a variety of 1,3-oxathiolane using substituted oxiranes (Table 3). The reactions conducted with alkyl-substituted oxiranes proceeded in good yields. A modest increase in yield occurred by enlarging the alkyl branch bound to the three-membered ring (entries 1, 2, 3, and 4). Acrylate and allylic moieties were also tolerated, and the desired products achieved in acceptable yield (entries 5 and 6). Epichlorohydrine (**3g**) gave the desired product in moderate yield (entry 7). Reaction conducted with cyclohexene oxide (**3h**) formed the product in excellent yield, while an epoxide derived from cycloheptene gave the desired product in moderate success (entries 8 and 9). No desired product was obtained using the oxirane derived from cyclopentene because of the high strain energy associated with the *trans* stereochemistry of the product (not shown in Table 3). In addition, no oxathiolane formation took place using cyclooctene oxide most likely due to the steric hindrance of the substrate (not shown in Table 3). 2-(Phenoxymethyl)oxirane (**3j**) reacted smoothly and gave the desired products in nearly quantative amount (entry 10). Note that, in the presence of alkyl-

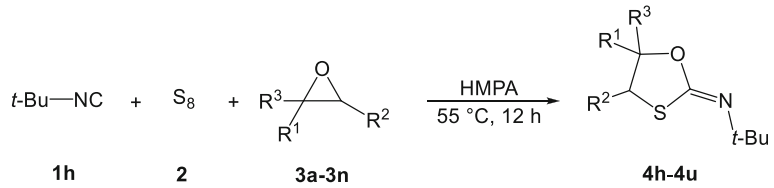
Table 2 Synthesis of 1,3-oxathiolane derivatives with various isocyanides



Entry	Isocyanide	R^1	**4**, yield/%
1	**1a**	Cyclohexyl	**4a**, 89
2	**1b**	*n*-Propyl	**4b**, 87
3	**1c**	2-Naphthyl	**4c**, 95
4	**1d**	Phenyl	**4d**, 93
5	**1e**	Benzyl	**4e**, 80
6	**1f**	2,6-Dimethylphenyl	**4f**, 95
7	**1g**	4-Methoxyphenyl	**4g**, 98

For all entries except stated otherwise: **1** (1.1 mmol), **2** (0.3 mmol), and **3a** (1.0 mmol), in 5 cm^3 HMPA at 55 °C for 12 h

Table 3 Synthesis of 1,3-oxathiolane with various epoxides



1h **2** **3a-3n** **4h-4u**

Entry	Epoxide	R^1, R^2, R^3	**4**, yield/%
1	**3a**	Me, H, H	**4h**, 85
2	**3b**	Et, H, H	**4i**, 88
3	**3c**	*n*-Pr, H, CH_3	**4j**, 89
4	**3d**	$(CH_3)_2CHOCH_2$, H, H	**4k**, 93
5	**3e**	$CH_2CCH_3COOCH_2$, H, H	**4l**, 89
6	**3f**	$CH_2CHCH_2OCH_2$, H, H	**4m**, 83
7	**3g**	$ClCH_2$, H, H	**4n**, 73
8	**3h**	$-(CH_2)_4-$, H	**4o**, 95
9	**3i**	$-(CH_2)_5-$, H	**4p**, 62
10	**3j**	$PhOCH_2$, H	**4q**, 98
11	**3k**	H, Ph, H	**4r**, 83[a]
12	**3l**	Ph, Ph, H	**4s**, 79
13	**3m**	H, 4-MeO–C_6H_4, H	**4t**, 91[a,b]
14	**3n**	4-NO_2–C_6H_4, H, H	**4u**, 68

For all entries except stated otherwise: **1h** (1.1 mmol), **2** (0.3 mmol), and **3** (1.0 mmol), in 5 cm^3 HMPA at 55 °C for 12 h

[a] The yield of benzylic attacked product

[b] The mixture was stirred for 16 h

substituted oxiranes, the attack occurred exclusively at the terminal carbon of the ring. The difference in reactivity was reflected in the reaction of styrene oxide (**3k**), where the attack exclusively occurred at the benzylic position probably due to electronic effects (entry 11). Stilbene (**3l**) also formed the corresponding products in acceptable yield (entry 12). The product derived from stilbene showed no coupling constant between the two vicinal hydrogens. According to the Karplus curve, it could be deduced that the vicinal hydrogens have a dihedral angle of 90°. Electron-rich and electro-poor aryl oxiranes were also examined; in the presence of 2-(4-methoxyphenyl)oxirane (**3m**), the attack took place at the benzylic- position (entry 13), while 2-(4-nitrophenyl)oxirane (**3n**) gave the terminal-attacked product, exclusively (entry 14). Notably, the tolerance for nitro on the aromatic ring offers an opportunity for subsequent transformations.

Structures of compounds **4a**–**4u** were assigned by IR, ^{1}H NMR, ^{13}C NMR, and mass spectral data. The ^{1}H NMR spectrum of **4a** exhibited a characteristic (AB)X spin system for the CH_2–CH, together with a doublet for the methyl group. The ^{13}C NMR spectrum of **4a** shows eight signals in agreement with proposed structure. The mass spectrum of **4a** shows the molecular ion peak at *m*/*z* 199 (see Table 1, entry 1).

Although at this time, we cannot provide a definitive mechanism for the formation of 1,3-oxathiolanes **4**, a plausible rationalization is proposed in Scheme 1. Previous work proposed that isocyanides react with elemental sulfur to form isothiocyanate derivatives [28]. As shown in Scheme 1, the advanced mechanism starts with the formation of anionic adduct **5**, followed generation of **6.** The intermediate **6** tautomerized to isothiocyanate **7**. The reaction proceeds with the formation of anionic adduct **8** by the action of HMPA. This anionic adduct reacts with **3** to from ring-opened intermediate **9**. Cyclization of this intermediate and subsequent elimination of HMPA affords **4**.

In this report, we have attempted to demonstrate the importance of the reaction conditions to enable unique reactivity and selectivity in oxiranes ring opening. These reactions achieve good conversions and product yields and tolerate useful functional groups. The reactions proceeded in regioselective manner, and in all cases, only one regioisomer was detected by NMR analysis.

Experiment

Oxiranes, elemental sulfur, isocyanides, and catalyst were obtained from Merck and were used without further purification. Melting points were measured with Electrothermal-9100 apparatus. IR Spectra were recorded with Shimadzu IR-460 spectrometer. ^{1}H and ^{13}C NMR spectra were recorded with Bruker DRX-500 AVANCE instrument; in $CDCl_3$ at 500.1 and 125.7 MHz, resp; δ in ppm, J in Hz. Mass spectra were recorded with EI-MS (70 eV): Finnigan-MAT-8430 mass spectrometer. Elemental analyses (C, H, N) were performed with a Heraeus CHN-O-Rapid analyzer. The results agreed favorably with the calculated values. Column chromatography was performed using silica gel 60 (particle size 63–200 μm) (Merck, item number 7734-3). TLC was performed using silica gel 60 (Merck, item number 116835).

General procedure for the preparation of compounds 4

To a stirred solution of oxirane (1.0 mmol) and elemental sulfur (0.3 mmol) in 5 cm^3, HMPA as a solvent were added isocyanide (1.1 mmol). The mixture was stirred for 12 h at 55 °C. After completion of the reaction, it was diluted by 5 cm^3 EtOAc and 5 cm^3 saturated NH_4Cl solution. The mixture stirred for additional 30 min and two layers were separated. The aqueous layer was then extracted with EtOAc (3 × 4 cm^3). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by chromatography (silica gel, hexane:EtOAc) to give the desired product.

N-Cyclohexyl-5-methyl-1,3-oxathiolan-2-imine
(**4a**, $C_{10}H_{17}NOS$)
The crude product was purified by column chromatography (SiO_2; hexane/EtOAc 4/1; $R_f = 0.39$) affording 0.18 g (89%) **3a**. Pale yellow solid; m.p.: 79–81 °C; IR (KBr): $\bar{\nu} = 3017$, 2987, 1629, 1309, 1148 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 1.18$–1.32 (6*H*, m, 3 CH_2), 1.37 (3*H*, d, $^{3}J = 6.7$ Hz, Me), 1.66–1.77 (2*H*, m, CH_2), 2.01–2.05 (2*H*, m, CH_2), 3.50–3.59 (2*H*, m, CH_2), 3.67–3.71 (1*H*, m, CH), 4.76–4.82 (1*H*, m, CH) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 19.1$ (Me), 24.9 (CH_2), 25.6 (2 CH_2), 34.2 (2 CH_2), 36.0 (CH_2), 47.5 (CH), 70.1 (CH), 166.2 (C) ppm; EI-MS (70 eV): *m/z* (%) = 199 (M^+, 3), 184 (13), 116 (86), 104 (44), 98 (18), 83 (100).

5-Methyl-N-propyl-1,3-oxathiolan-2-imine
(**4b**, $C_7H_{13}NOS$)
The crude product was purified by column chromatography (SiO_2; hexane/EtOAc 4/1; $R_f = 0.32$) affording 0.14 g (87%) **4b**. Yellow oil; IR (KBr): $\bar{\nu} = 3014$, 2965, 1621, 1334, 1142 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 1.11$ (3*H*, t, $^{3}J = 6.7$ Hz, Me), 1.28 (3*H*, d, $^{3}J = 6.4$ Hz, Me), 1.86–1.91 (2*H*, m, CH_2), 2.73–2.78 (2*H*, m, CH_2), 3.11–3.16 (1*H*, m, CH), 3.32–3.37 (1*H*, m, CH), 4.61–4.66 (1*H*, m, CH) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 14.1$ (Me), 24.2 (Me), 26.5 (CH_2), 36.9 (CH_2), 47.9 (CH_2), 72.1 (CH), 163.1 (C) ppm; EI-MS (70 eV): *m/z* (%) = 159 (M^+, 2), 104 (100), 102 (34), 86 (67), 57 (47).

5-Methyl-N-(naphthalen-2-yl)-1,3-oxathiolan-2-imine
(**4c**, $C_{14}H_{13}NOS$)
The crude product was purified by column chromatography (SiO_2; hexane/EtOAc 6/1; $R_f = 0.37$) affording 0.23 g (95%) **4c**. Pale yellow solid; m.p.: 130–133 °C; IR (KBr): $\bar{\nu} = 3019$, 2967, 1650, 1314, 1124 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 1.33$ (3*H*, d, $^{3}J = 6.8$ Hz, Me), 3.31–3.45 (2*H*, m, 2 CH), 4.67–4.74 (1*H*, m, CH), 7.33 (1*H*, d, $^{3}J = 7.2$ Hz, CH), 7.53–7.60 (2*H*, m, 2 CH), 7.89 (1*H*, s, CH), 7.96–8.16 (3*H*, m, 3 CH) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 19.1$ (Me), 35.6 (CH_2), 73.0 (CH), 122.6 (CH), 123.1 (CH), 127.3 (CH), 127.6 (CH), 128.1 (CH), 128.6 (CH), 129.3 (CH), 131.1 (C), 131.4 (C), 144.7 (C), 168.3 (C) ppm; EI-MS (70 eV): *m/z* (%) = 243 (M^+, 6), 182 (34), 149 (78), 133 (57), 127 (100), 93 (35).

5-Methyl-N-phenyl-1,3-oxathiolan-2-imine
(**4d**, $C_{10}H_{11}NOS$)
The crude product was purified by column chromatography (SiO_2; hexane/EtOAc 5/1; $R_f = 0.41$) affording 0.18 g (93%) **4d**. Pale yellow solid; m.p.: 75–77 °C; IR (KBr): $\bar{\nu} = 3011$, 2988, 1641, 1325, 1114 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 1.31$ (3*H*, d, $^{3}J = 6.4$ Hz, Me), 3.26–3.33 (1*H*, m, CH), 3.44–3.49 (1*H*, m, CH), 4.75–4.84 (1*H*, m, CH), 6.91 (2*H*, d, $^{3}J = 7.8$ Hz, 2 CH), 7.3–7.28 (3*H*, m, 3 CH) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 20.3$ (Me), 38.4 (CH_2), 70.3 (CH), 117.1 (2CH), 120.1 (CH), 125.7 (2CH), 141.6 (C), 160.1 (C) ppm; EI-MS (70 eV): *m/z* (%) = 193 (M^+, 1), 136 (81), 77 (100), 59 (53), 57 (78), 41 (31), 18 (22).

N-Benzyl-5-methyl-1,3-oxathiolan-2-imine
(**4e**, $C_{11}H_{13}NOS$)
The crude product was purified by column chromatography (SiO_2; hexane/EtOAc 3/1; $R_f = 0.43$) affording 0.17 g (82%) **4e**. Colorless solid; m.p.: 71–73 °C; IR (KBr): $\bar{\nu} = 3023$, 2956, 1633, 1314, 1121 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$):): $\delta = 1.27$ (3*H*, d, $^{3}J = 6.8$ Hz, Me), 2.81–2.89 (2*H*, m, 2 CH), 3.36–3.53 (2*H*, m, 2 CH), 7.14 (1*H*, t, $^{3}J = 6.5$ Hz, CH), 7.27–7.43 (4*H*, m, 4 CH) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 21.3$ (Me), 34.7 (CH_2), 49.7 (CH_2), 72.1 (CH), 123.7 (2 CH), 125.1 (CH), 128.9 (2 CH), 139.6 (C), 165.3 (C) ppm; EI-MS (70 eV):

m/z (%) = 207 (M^+, 1), 134 (46), 91 (100), 59 (51), 57 (23).

N-(2,6-Dimethylphenyl)-5-methyl-1,3-oxathiolan-2-imine (**4f**, $C_{11}H_{13}NO_2S$)

The crude product was purified by column chromatography (SiO_2; hexane/EtOAc 5/1; $R_f = 0.38$) affording 0.21 g (95%) **4f**. Pale yellow solid; m.p.: 111–113 °C; IR (KBr): $\bar{\nu} = 3012$, 2965, 1632, 1326, 1108 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 1.23$ (3*H*, d, $^3J = 6.7$ Hz, Me), 2.27 (3*H*, s, Me), 2.29 (3*H*, s, Me), 3.46–3.59 (2*H*, m, 2 CH), 4.71–4.76 (1*H*, m, CH), 7.19 (1*H*, d, $^3J = 6.9$ Hz, CH), 7.23 (1*H*, d, $^3J = 7.1$ Hz, CH), 7.37 (1*H*, d, $^3J = 7.5$ Hz, CH) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 19.3$ (Me), 19.6 (Me), 22.5 (Me), 36.9 (CH_2), 71.1 (CH), 125.1 (CH), 127.6 (C), 127.8 (C), 130.2 (CH), 131.1 (CH), 147.5 (C), 165.2 (C) ppm; EI-MS (70 eV): *m/z* (%) = 221 (M^+, 6), 163 (42), 148 (61), 116 (23), 105 (100).

N-(4-Methoxyphenyl)-5-methyl-1,3-oxathiolan-2-imine (**4g**, $C_{11}H_{13}NO_2S$)

The crude product was purified by column chromatography (SiO_2; hexane/EtOAc 3/1; $R_f = 0.53$) affording 0.22 g (98%) **4g**. Yellow oil; IR (KBr): $\bar{\nu} = 3015$, 2988, 1643, 1321, 1122 cm^{-1}; ^1H NMR (500.1 MHz, $CDCl_3$): $\delta = 1.35$ (3*H*, d, $^3J = 6.1$ Hz, Me), 3.53–3.62 (2*H*, m, 2 CH), 3.71 (3*H*, s, OMe), 4.72–4.78 (1*H*, m, CH), 6.93 (2*H*, d, $^3J = 6.9$ Hz, 2 CH), 7.28 (2*H*, d, $^3J = 6.9$ Hz, 2 CH) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 20.9$ (Me), 36.3 (CH_2), 53.7 (OMe), 71.9 (CH), 115.3 (2 CH), 125.1 (C), 126.1 (2 CH), 151.3 (C), 167.2 (C) ppm; EI-MS (70 eV): *m/z* (%) = 223 (M^+, 5), 150 (58), 107 (100), 116 (24), 59 (37).

N-(tert-Butyl)-5-methyl-1,3-oxathiolan-2-imine (**4h**, $C_8H_{15}NOS$)

The crude product was purified by column chromatography (SiO_2; hexane/EtOAc 7/1; $R_f = 0.42$) affording 0.15 g (85%) **4h**. Yellow oil; IR (KBr): $\bar{\nu} = 3031$, 2973, 1652, 1341, 1142 cm^{-1}; ^1H NMR (500.1 MHz, $CDCl_3$): $\delta = 1.17$ (3*H*, d, $^3J = 6.7$ Hz, Me), 1.37 (9*H*, s, 3 Me), 3.25–3.41 (2*H*, m, 2 CH), 4.64–4.71 (1*H*, m, CH) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 21.1$ (Me), 28.3 (3 Me), 37.4 (CH_2), 57.1 (C), 79.3 (CH), 165.2 (C) ppm; EI-MS (70 eV): *m/z* (%) = 173 (M^+, 7), 116 (20), 100 (36), 83 (56), 57 (100).

N-(tert-Butyl)-5-ethyl-1,3-oxathiolan-2-imine (**4i**, $C_{14}H_{19}NO_3S$)

The crude product was purified by column chromatography (SiO_2; hexane/EtOAc 7/1; $R_f = 0.40$) affording 0.17 g (88%) **4i**. Yellow oil; IR (KBr): $\bar{\nu} = 3009$, 2967, 1631, 1311, 1130 cm^{-1}; ^1H NMR (500.1 MHz, $CDCl_3$): $\delta = 1.03$ (3*H*, t, $^3J = 6.9$ Hz, Me), 1.32 (9*H*, s, 3 Me), 1.62 (2*H*, m, CH_2), 3.28–3.36 (2*H*, m, 2 CH), 4.71–4.76 (1*H*, m, CH) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 11.3$ (Me), 22.1 (Me), 29.1 (3 Me), 35.1 (CH_2), 56.1 (C), 79.8 (CH), 165.5 (C) ppm; EI-MS (70 eV): *m/z* (%) = 187 (M^+, 5), 116 (34), 100 (48), 83 (41), 57 (100).

N-(tert-Butyl)-5-methyl-5-propyl-1,3-oxathiolan-2-imine (**4j**, $C_{11}H_{21}NOS$)

The crude product was purified by column chromatography (SiO_2; hexane/EtOAc 8/1; $R_f = 0.39$) affording 0.20 g (94%) **4j**. Yellow oil; IR (KBr): $\bar{\nu} = 3020$, 2964, 1645, 1313, 1121 cm^{-1}; ^1H NMR (500.1 MHz, $CDCl_3$): $\delta = 1.11$ (3*H*, t, $^3J = 6.7$ Hz, Me), 1.24 (3*H*, s, Me), 1.41 (9*H*, s, 3 Me), 1.72–1.90 (4*H*, m, 2 CH_2), 3.31–3.40 (2*H*, m, 2 CH) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 11.7$ (Me), 22.6 (CH_2), 22.9 (Me), 27.9 (3 Me), 32.1 (CH_2), 38.1 (CH_2), 57.1 (C), 85.1 (C), 165.7 (C) ppm; EI-MS (70 eV): *m/z* (%) = 215 (M^+, 7), 116 (52), 100 (67), 83 (40), 57 (100).

N-(tert-Butyl)-5-(isopropoxymethyl)-1,3-oxathiolan-2-imine (**4k**, $C_{11}H_{21}NO_2S$)

The crude product was purified by column chromatography (SiO_2; hexane/EtOAc 6/1; $R_f = 0.40$) affording 0.21 g (93%) **4k**. Colorless oil; IR (KBr): $\bar{\nu} = 3025$, 2977, 1631, 1341, 1122 cm^{-1}; ^1H NMR (500.1 MHz, $CDCl_3$): $\delta = 1.21$ (6*H*, d, $^3J = 6.3$ Hz, 2 Me), 1.45 (9*H*, s, 3 Me), 3.32–3.50 (2*H*, m, 2 CH), 3.78–3.89 (3*H*, m, 3 CH), 4.73–4.79 (1*H*, m, CH) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 22.3$ (2 Me), 29.1 (3 Me), 33.4 (CH_2), 55.1 (C), 68.1 (CH_2), 71.3 (CH), 79.2 (CH), 165.9 (C) ppm; EI-MS (70 eV): *m/z* (%) = 231 (M^+, 5), 165 (100), 107 (40), 86 (78), 59 (60), 57 (54), 54 (26).

[2-(tert-Butylimino)-1,3-oxathiolan-5-yl]methyl methacrylate (**4l**, $C_{12}H_{19}NO_3S$)

The crude product was purified by column chromatography (SiO_2; hexane/EtOAc 3/1; $R_f = 0.57$) affording 0.23 g (89%) **4l**. Yellow oil; IR (KBr): $\bar{\nu} = 3011$, 2967, 1731, 1633, 1345, 1122 cm^{-1}; ^1H NMR (500.1 MHz, $CDCl_3$): $\delta = 1.46$ (9*H*, s, 3 Me), 1.90 (3*H*, s, Me), 3.31–3.44 (2*H*, m, 2 CH), 4.25–4.32 (2*H*, m, 2 CH), 4.90–4.96 (1*H*, m, CH), 6.71–6.80 (2*H*, m, 2 CH) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 19.4$ (Me), 29.7 (3 Me), 35.1 (CH_2), 57.1 (C), 70.3 (2 CH), 79.2 (CH), 125.3 (CH_2), 134.1 (C), 166.2 (C), 167.3 (C) ppm; EI-MS (70 eV): *m/z* (%) = 257 (M^+, 5), 142 (76), 135 (80), 85 (65), 77 (100), 59 (51), 54 (32).

5-[(Allyloxy)methyl]-N-(tert-butyl)-1,3-oxathiolan-2-imine (**4m**, $C_{11}H_{19}NO_2S$)

The crude product was purified by column chromatography (SiO_2; hexane/EtOAc 5/1; $R_f = 0.46$) affording 0.19 g (85%) **4m**. Yellow oil; IR (KBr): $\bar{\nu} = 3010$, 2977, 1734, 1644, 1340, 1143 cm^{-1}; ^1H NMR (500.1 MHz, $CDCl_3$):

$\delta = 1.56$ (9*H*, s, 3 Me), 3.42–4.17 (6*H*, m, 6 CH), 4.91–5.39 (3*H*, m, 3 CH), 5.73–5.81 (1*H*, m, CH) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 30.2$ (3 Me), 35.7 (CH_2), 58.1 (C), 73.2 (CH_2), 79.6 (CH_2), 81.1 (CH), 119.7(CH_2), 136.1(CH), 164.8 (C) ppm; EI-MS (70 eV): *m/z* (%) = 229 (M^+, 5), 206 (51), 149 (100), 142 (67), 91 (72), 59 (60), 57 (56), 54 (27).

N-(tert-Butyl)-5-(chloromethyl)-1,3-oxathiolan-2-imine (**4n**, $C_8H_{14}ClNOS$)

The crude product was purified by column chromatography (SiO_2; hexane/EtOAc 3/1; $R_f = 0.52$) affording 0.15 g (71%) **4n**. Yellow oil; IR (KBr): $\bar{\nu} = 3024$, 2970, 1641, 1340, 1136 cm^{-1}; ^{1}H NMR (500.1 MHz, $CDCl_3$): $\delta = 1.47$ (9*H*, s, 3 Me), 3.61–3.92 (4*H*, m, 4 CH), 4.88–4.94 (1*H*, m, CH) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 29.4$ (3 Me), 37.1 (CH_2), 45.8 (CH_2), 56.1 (C), 83.5 (CH), 165.1 (C) ppm; EI-MS (70 eV): *m/z* (%) = 207 (M^+, 4), 135 (100), 70 (54), 59 (60), 54 (20).

N-(tert-Butyl)hexahydrobenzo[d][1,3]oxathiol-2-imine (**4o**, $C_{11}H_{19}NOS$)

The crude product was purified by column chromatography (SiO_2; hexane/EtOAc 8/1; $R_f = 0.27$) affording 0.20 g (95%) **4o**; IR (KBr): $\bar{\nu} = 3028$, 2976, 1633, 1323, 1109 cm^{-1}; ^{1}H NMR (500.1 MHz, $CDCl_3$): $\delta = 1.53$ (9*H*, s, 3 Me), 1.44–2.11 (8*H*, m, 4 CH_2), 3.70–3.75 (1*H*, m, CH), 5.11–5.15 (1*H*, m, CH) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 25.1$ (CH_2), 25.7 (CH_2), 29.1 (CH_2), 31.6 (CH_2), 32.9 (3 Me), 40.1 (CH), 57.3 (C), 83.2 (CH), 169.2 (C) ppm; EI-MS (70 eV): *m/z* (%) = 213 (M^+, 5), 149 (100), 98 (75), 91 (63), 71 (55), 59 (48), 54 (26).

N-(tert-Butyl)hexahydro-4H-cyclohepta[d][1, 3]oxathiol-2-imine (**4p**, $C_{12}H_{21}NOS$)

The crude product was purified by column chromatography (SiO_2; hexane/EtOAc 7/1; $R_f = 0.37$) affording 0.13 g (58%) **4p**. m.p.: 181–183 °C; IR (KBr): $\bar{\nu} = 3051$, 2917, 1631, 1312, 1123 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 1.41$–148 (2*H*, m, CH_2), 1.54 (9*H*, s, 3 Me), 1.68–2.27 (8*H*, m, 4 CH_2), 3.72–3.76 (1*H*, m, CH), 5.04–5.11 (1*H*, m, CH) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 23.1$ (CH_2), 24.6 (CH_2), 29.3 (CH_2), 32.2 (3 Me), 32.7 (CH_2), 35.1 (CH_2), 43.5 (CH), 56.1 (C), 86.3 (CH), 165.2 (C) ppm; EI-MS (70 eV): *m/z* (%) = 227 (M^+, 4), 135 (100), 98 (67), 77 (85), 70 (54), 59 (60), 54 (20).

N-(tert-Butyl)-5-(phenoxymethyl)-1,3-oxathiolan-2-imine (**4q**, $C_{14}H_{19}NO_2S$)

The crude product was purified by column chromatography (SiO_2; hexane/EtOAc 5/1; $R_f = 0.48$) affording 0.26 g (98%) **4q**. m.p.: 65–67 °C; IR (KBr): $\bar{\nu} = 3037$, 2922, 1632, 1324, 1136 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 1.51$ (9*H*, s, 3 Me), 3.51–3.59 (2*H*, m, 2 CH), 4.23–4.31 (2*H*, m, 2 CH), 4.87–4.92 (1*H*, m, CH), 6.83 (1*H*, t, $^3J = 7.1$ Hz, CH), 7.06 (2*H*, d, $^3J = 7.1$ Hz, 2 CH), 7.21 (2*H*, t, $^3J = 7.1$ Hz, 2 CH) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 30.1$ (3 Me), 34.7 (CH_2), 55.1 (C), 67.1 (CH_2), 78.9 (CH), 114.3 (2 CH), 121.9 (CH), 129.2 (2 CH), 159.6 (C), 165.2 (C) ppm; EI-MS (70 eV): *m/z* (%) = 265 (M^+, 4), 98 (67), 77 (100), 70 (54), 59 (60), 54 (20).

N-(tert-Butyl)-4-phenyl-1,3-oxathiolan-2-imine (**4r**, $C_{13}H_{17}NOS$)

The crude product was purified by column chromatography (SiO_2; hexane/EtOAc 5/1; $R_f = 0.61$) affording 0.19 g (83%) **4r**. m.p.: 76–78 °C; IR (KBr): $\bar{\nu} = 3040$, 2970, 1634, 1310, 1130 cm^{-1}: ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 1.60$ (9*H*, s, 3 Me), 4.81 (1*H*, dd, $^2J = 10.1$ Hz, $^3J = 5.6$ Hz, CH), 5.12 (1*H*, dd, $^2J = 10.1$ Hz, $^3J = 6.9$ Hz, CH), 5.32 (1*H*, m, CH), 7.17–7.42 (5*H*, m, 5 CH) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 30.1$ (3 Me), 51.4 (CH_2), 56.2 (C), 80.3 (CH), 127.1 (2 CH), 128.5 (CH), 129.7 (2 CH), 136.1 (C), 166.8 (C) ppm; EI-MS (70 eV): *m/z* (%) = 235 (M^+, 4), 98 (67), 77 (100), 70 (54), 59 (60).

N-(tert-Butyl)-4,5-diphenyl-1,3-oxathiolan-2-imine (**4s**, $C_{19}H_{21}NOS$)

The crude product was purified by column chromatography (SiO_2; hexane/EtOAc 3/1; $R_f = 0.51$) affording 0.25 g (79%) **4s**. m.p.: 101–103 °C; IR (KBr): $\bar{\nu} = 3041$, 2938, 2231, 1634, 1318, 1134 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 1.46$ (9*H*, s, 3 Me), 4.11 (1*H*, s, CH), 5.67 (1*H*, s, CH), 7.14–7.32 (10*H*, m, 10 CH) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 29.6$ (3 Me), 46.3 (CH), 57.1 (C), 72.2 (CH), 120.1 (C), 126.7 (CH), 127.9 (CH), 128.1 (2 CH), 128.4 (2 CH), 128.5 (2 CH), 129.1 (2 CH), 134.2 (C), 1383.0 (C), 167.2 (C) ppm; EI-MS: *m/z* (%) = 311 (M^+, 4), 162 (21), 146 (34), 135 (74), 119 (80), 102 (58), 77 (100), 43 (32).

N-(tert-Butyl)-4-(4-methoxyphenyl)-1,3-oxathiolan-2-imine (**4t**, $C_{14}H_{19}NO_2S$)

The crude product was purified by column chromatography (SiO_2; hexane/EtOAc 4/1; $R_f = 0.58$) affording 0.24 g (91%) **4t**. m.p.: 141–143 °C; IR (KBr): $\bar{\nu} = 3025$, 2961, 1648, 1305, 1128 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 1.42$ (9*H*, s, 3 Me), 3.27 (1*H*, dd, $^2J = 11.1$ Hz, $^3J = 5.6$ Hz, CH), 3.71 (1*H*, dd, $^2J = 11.1$ Hz, $^3J = 4.2$ Hz, CH), 3.80 (3*H*, s, OMe), 4.70 (1*H*, m, CH), 6.78 (2*H*, d, $^3J = 7.1$ Hz, 2 CH), 6.90 (2*H*, d, $^3J = 7.1$ Hz, 2 CH) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 29.7$ (3 Me), 49.1 (CH), 55.2 (OMe), 57.0 (C), 76.2 (CH_2), 115.1 (2 CH), 128.6 (2 CH), 137.1 (C), 159.2 (C), 167.3 (C) ppm; EI-MS: *m/z* (%) = 265 (M^+, 4), 162 (21), 146 (34), 135 (74), 107 (100), 102 (58), 43 (32).

N-(tert-Butyl)-5-(4-nitrophenyl)-1,3-oxathiolan-2-imine (**4u**, $C_{13}H_{16}N_2O_3S$)

The crude product was purified by column chromatography (SiO_2; hexane/EtOAc 2/1; $R_f = 0.28$) affording 0.17 g (62%) **4u**. m.p.: 192–194 °C; IR (KBr): $\bar{\nu} = 3030$, 2938, 1634, 1547, 1360, 1134 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 1.43$ (9*H*, s, 3 Me), 3.40–3.56 (2*H*, m, 2 CH), 5.11–5.16 (1*H*, m, CH), 7.69 (2*H*, d, $^3J = 7.3$ Hz, 2 CH), 8.08 (2*H*, d, $^3J = 8.1$ Hz, 2 CH) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 29.6$ (3 Me), 41.1 (CH_2), 57.2 (C), 89.1 (CH), 126.2 (2 CH), 129.0 (2 CH), 147.1 (C), 149.4 (C), 166.3 (C) ppm; EI-MS: *m/z* (%) = 280 (M^+, 4), 162 (21), 146 (34), 135 (74), 119 (80), 102 (100), 77 (34), 43 (32).

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