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SYNTHESIS AND ANTIMICROBIAL EVALUATION OF OXAZOLE-2(3*H*)-THIONE AND 2-ALKYLSULFANYL-1,3-OXAZOLE DERIVATIVES

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Dedicated to Prof. Victor Snieckus to celebrate his 77th birthday

Abstract – The preparation of oxazole-2(3*H*)-thiones (OXTs) by condensation of thiocyanic acid on α-hydroxycarbonyl substrates has been revisited. Extension to more complex scaffolds afforded chiral OXTs, whereas carbohydrate-fused 2-alkylsulfanyl-1,3-oxazolines led to original hemiaminal structures. A survey of the reactivity of OXTs with various electrophiles showed *S*- or *N*-chemoselectivity based on HSAB parameters. Antimicrobial evaluation of selected synthesized compounds was carried out, from which the hemiaminal **15** emerged as a promising antifungal agent.

INTRODUCTION

Treatment of infectious diseases still represents a topical challenge. The emergent infections as well as the increasing number of multi-drug resistant microbial pathogens - specially Gram-positive bacteria - have been a serious concern both in hospital and community settings.[1-3] Linezolid (**1**) (Zyvox™) (Figure 1) is a member of the oxazolidinone drugs active against most Gram-positive pathogens, namely *Staphylococcus aureus* (MRSA) and *Staphylococcus epidermis* (MRSE). Although it has been approved

for use in humans since 2000,[4-7] linezolid is not exempt from bacterial resistance and this has prompted the development of related classes of molecules, namely the thiazole-2(3*H*)thione (**2**), that has proven very active as antimicrobial agent.[8] The 2-iminothiazolidin-4-one (**3**)[9] and the thiazolamine (**4**)[8] have also exhibited high efficacy against Gram-positive bacteria.

The design of structurally-related candidates in view of identifying new, potent, selective and less toxic antimicrobial agents appeared as a particularly attractive target.

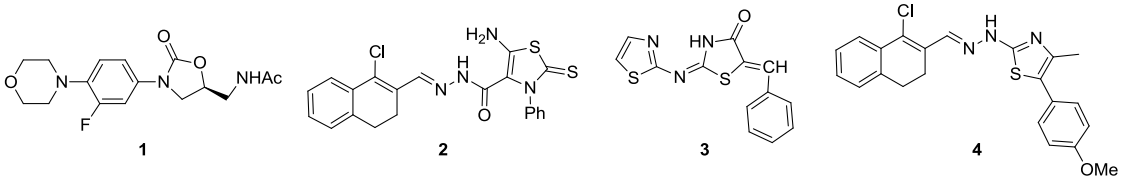
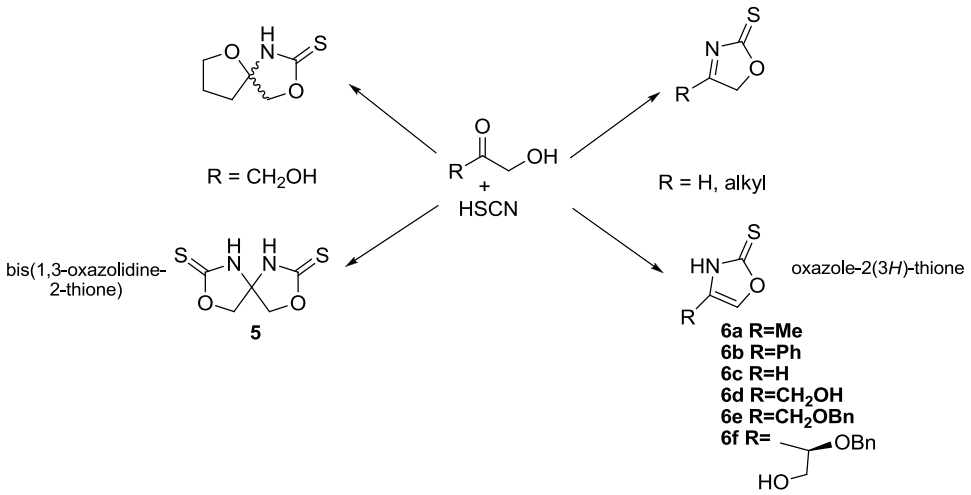


Figure 1. Examples of compounds with antibacterial activity

For more than a decade, we have explored the chemistry of cyclic thionocarbamates, particularly 1,3-oxazolidine-2-thiones (OZTs).[10] In sharp contrast with OZTs, their unsaturated counterparts 1,3-oxazoline-2-thiones (OXTs) have been scarcely studied, despite their broad chemical possibilities paired with a predictable bioactivity potential. Surprisingly for such a simple heterocyclic system, only a limited number of structures related to acetol were described.[11,12] Most syntheses of OXTs used either condensation of thiocyanic acid[13] or isothiocyanates[14,15] with an α-hydroxycarbonyl moiety, or reaction of an aminoketone with thiophosgene.[16]

Recently, we have introduced synthetic conditions for a better controlled condensation of α-hydroxyketones with thiocyanic acid towards the formation of bis(OZTs) **5** or OXTs **6** (Scheme 1).[17] The present paper revisits synthetic routes to OXTs and related 2-alkylsulfanyl-1,3-oxazoles and their biological evaluation as antimicrobial and antifungal agents.



Scheme 1. Condensation of HSCN with α-hydroxycarbonyl compounds

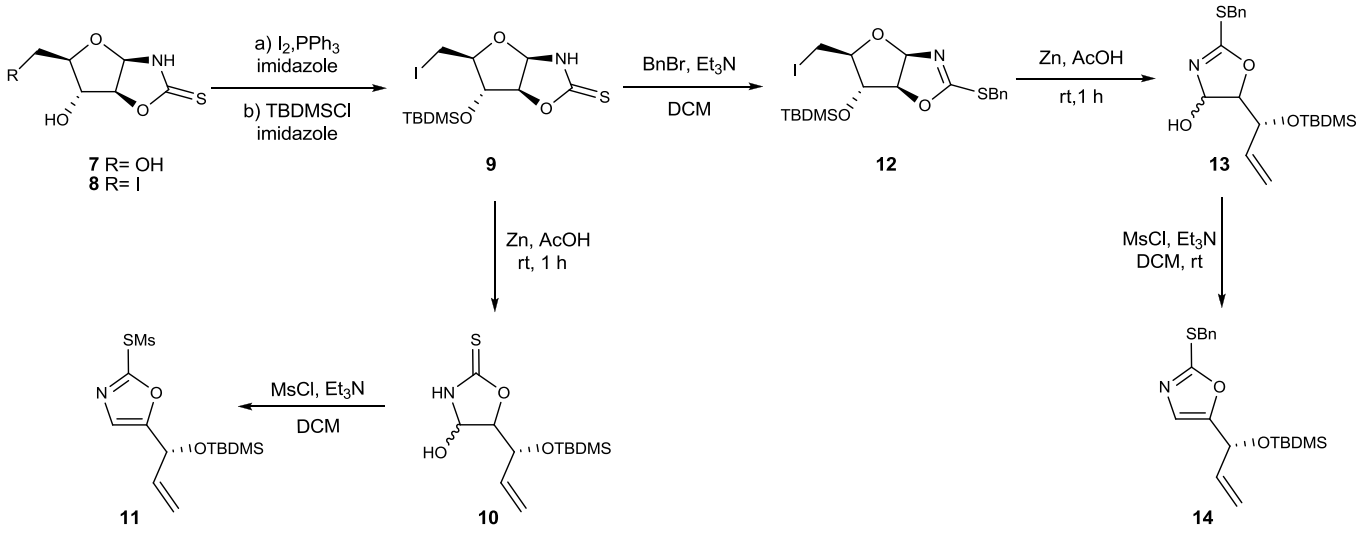
RESULTS AND DISCUSSION

1. CHEMISTRY

Looking back on the previous synthetic approaches to OXTs and aiming at a better knowledge of this uncommon heterocyclic pattern, the formation of OXTs based on the condensation of an α-hydroxycarbonyl precursor with thiocyanic acid was reconsidered and optimized. However the yields obtained are in perfect agreement with those previously reported by us[17] and compounds structure elucidation and characterization as biologically valuable molecular entities is now given for the first time. Their preparation was accomplished by reaction of ketones/aldehyde with 1.1 eq KSCN and amongst the acids used (HCl, TsOH and H_2SO_4 and the solvents tried (EtOH, water, THF), the most efficient system was HCl/EtOH for **6a** (R=Me), **6b** (R=Ph) and **6c** (R=H) (Scheme 1), yielding these compounds in 74%, 83% and 95% yield, respectively. However for **6a** also the system THF/HCl gave **6a** in 75%. These conditions led to poor yields when R=CH_2OH, and the most efficient system was water/HCl leading to the target compound only in 21% yield because this OXT is prone to undergo further reaction with HSCN to afford the spiro-bis(OZT) **5** (Scheme 1) previously described by Köll and coll.[18] Considering that (i) only a limited range of α-hydroxycarbonyl substrates is commercially available and (ii) most of them pose stability problems, we turn to using ketone masked compounds as ketals, which are easy to prepare and fairly stable. This was exemplified by reacting 2,2-dimethoxyethanol with thiocyanic acid in refluxing ethanol, to produce **6c** in 91% yield. From a general point of view, it can be stated that the EtOH/HCl system is very efficient to promote this reaction in good yields. Moreover, the presence of a free carbonyl group is not an essential requisite for the reaction: experiments involving 2,2-dimethoxyethanol indicate that ketals are appropriate substrates, the electrophilic center being restored *in situ* under acidic conditions. This was applied to prevent the competitive formation of a bis(OZT) in the case of 1,3-dihydroxyacetone, for which a selective protection sequence was set up. The carbonyl group was first protected to afford a dimethyl ketal with trimethyl orthoformate in CSA and methanol,[19] monobenzylation under classic conditions in the presence of NaH, BnBr and TBAI in THF gave the substrate that was transformed into **6e** (R=CH_2Bn) by reaction with KSCN in water/HCl in 60% yield. Synthesis of the chiral compound **6f** was achieved starting from a di-*O*-isopropylidene protected D-fructose,[20] which underwent selective 4,5-hydrolysis, oxidative cleavage and reduction with sodium borohydride[21] to give the starting material for the condensation with thiocyanic acid to afford **6f** in 60% yield.[17] This compound, bearing a well-defined stereogenic center, was prepared through a short reaction sequence involving simple and efficient steps.

An alternative strategy to access chiral OXTs could involve modification of a sugar-derived OZT with fused rings at the anomeric position[22-24] via a Vasella-type fragmentation[25] (Scheme 2). Starting with the

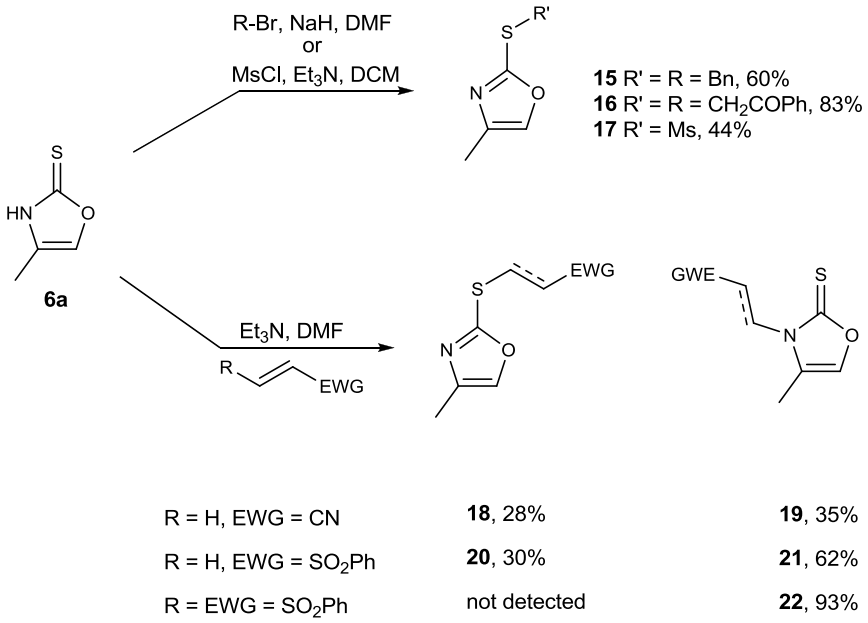
pre-formed OZT **7** fused on a D-*arabino* scaffold,[26] the iodinated precursor **8** was prepared in 96% yield applying Garegg's conditions,[27] then *O*-silylated (93% yield) to furnish **9**. This protected precursor underwent reductive fragmentation[25,28] in 86% yield to produce the chiral 4-hydroxy OZT **10**. Formation of this acyclic hydrated form of an OXT is unique as it is described only onto cyclic templates.[29] Furthermore and unexpectedly, only one diastereoisomer was detected by NMR, suggesting that no isomerisation occurred during the fragmentation process. Trying to form the related OXT through regioselective dehydration did not lead to the desired product. Reaction of the 4-hydroxy-OZT **10** with mesyl chloride solely afforded in 91% yield the unstable oxazole-derivative **11**. This transformation suggested, nonetheless, the 4,5-dehydration occurring prior to the *S*-mesylation.



Scheme 2. Synthesis of compounds **10** and **13**

Treatment of the OZT **9** with the benzyl bromide/Et_3N system[30] resulted in quantitative regioselective *S*-benzylation to afford the oxazoline **12**. Reductive fragmentation of this *S*-benzylated compound led to the chiral 2-benzylsulfanyl-1,3-oxazoline **13** in a single diastereoisomeric form in 86% yield. As expected, when submitted to mesylation conditions, dehydration of **13** took place to give the corresponding 1,3-oxazole **14** in 77% yield.

In contrast to the closely-related OZTs, which have been previously studied by us,[10,17,26,29-32] scarce data are available for OXTs. The ambident *N/S* nucleophilic system had to be investigated with regard to Pearson's HSAB theory,[33] and compound **6a** was used as the model substrate.[17] Application of standard alkylation conditions involving soft electrophiles e.g. benzyl bromide or bromoacetophenone resulted in the regioselective formation of 2-alkylsulfanyloxazoles **15** and **16**. This result indicates that the sulfur center in this system shows a soft character comparable to that observed in OZT systems.



Scheme 3. Reactivity of the ambident *N/S* nucleophilic system of compound **6a**

Depending on the type of electrophile involved under conditions formerly applied to OZTs,[30,31] a sharp contrast was observed in terms of regioselectivity. Reacting mesyl chloride with **6a** under standard conditions afforded a moderate yield (44%) of the *S*-mesylated compound **17**, and no *N*-reactivity could be detected, in contrast with previous reported results.[30] reaction with Michael acceptors led mixtures of *N*- and *S*-alkylated compounds. In the case of acrylonitrile, the *S*- and *N*-alkylated derivatives **18** and **19** were obtained in 28% and 35% yields respectively. Reacting phenyl vinyl sulfone afforded the *S*-alkylated product **20** in 30% yield, whereas the *N*-alkylated product **21** was isolated in 62% yield. The above results strongly diverge from the marked *N*-nucleophilicity and high chemo/regioselectivity reported on a simple OZT.[30] The observed reduced nucleophilicity of the nitrogen atom in **6a** (when compared to an OZT) might be explained by the delocalization of the *N*-lone pair into the "pro-aromatic" system. In fact, when applying the stronger electrophile (harder Michael acceptor) 1,2-bis(phenylsulfonyl)ethylene (BPSE), complete *N*-selectivity was observed in accordance with our previous findings,[31] affording **22** in 93% yield.

2. BIOLOGICAL TESTING

In our search for promising biomolecular entities, we have thus screened the synthesized compounds for their *in vitro* antibacterial and antifungal activities using the paper disk diffusion method.[34,35] The microorganisms used in the tests belong to the American Type Culture Collection (ATCC) and Centraalbureau voor Schimmelcultures (CBS) collections, from United States and The Netherlands, respectively. Regarding bacteria, tests were carried out with *Bacillus cereus (ATCC 11778), Bacillus subtilis (ATCC 6633)*, *Enterococcus faecalis (ATCC 29212), Escherichia coli (ATCC 8739), Listeria*

monocytogenes (ATCC 7644), Pseudomonas aeruginosa (ATCC 27853), Salmonella enteritidis (ATCC 13076) and *Staphylococcus aureus (ATCC25923).* With respect to fungi, the yeast *Candida albicans (ATCC 10231)* and the following filamentous fungi were used: *Alternaria alternata (CBS 108.41), Biscogniauxia mediterranea (CBS 101016), Botrytis* spp*., Byssochlamys fulva (CBS 146.48), Colletotrichum coffeanum (CBS 396.67), Fusarium culmorum (CBS 129.73), Pyricularia oryzae (CBS 433.70), Rhizopus* spp and *Stachybotrys chartarum* (*CBS 414.95*). The culture medium, incubation temperature and time used for bacteria growth was nutrient agar incubated at 37 ºC for 24 h, whereas for fungi potato dextrose agar was used, at 25 ºC for 48 h. Paper disks of 6.4 mm were placed on the agar and the solution of each substance (300 μg) in DMSO (15 μL) was applied on each disk. Chloramphenicol and actidione were used as antimicrobial controls for bacteria and fungi, respectively. After incubation, the nearest diameter of the inhibition zone was measured. At least three replicates were made. Eleven compounds, namely **6c**, **6d**, **6f**, **10**, **13**, **14**, **28**, **29**, **20**, **21** and **22**, presented some activity (see Table 1). The results are expressed in terms of the average diameter of inhibition (∅) in mm for the active compounds (300 μg). For comparison purposes, the inhibition diameter for control substances (chloramphenicol or actidione) are also shown for doses of 30 μg and 300 μg. Zones with inhibition diameter smaller than 10 mm and uniform growth in the disk were considered indicative of weak antimicrobial activity, from 10-15 mm, moderate activity, more than 15 mm, strong activity.

From the antimicrobial results obtained, compound **10** arises as the most promising one with a strong activity against the bacteria *B. cereus*, *B. subtilis*, *E. faecalis* and *S. aureus*, and also against most of the fungi tested. Remarkably, **10** possess a higher activity over *Candida albicans* and *Stachybotrys chartarum* than that of the control substances. In addition, compound **20** showed a strong activity against *B. subtilis* while **6d** was active against the fungi *B.* spp and **6f** showed a moderate activity against *Candida albicans* and *Colletotrichum coffeanum.*

Table 1. Inhibition zone (diameter in mm) as a criterion of antibacterial and antifungal activities of the OXTs and oxazole derivatives

Compound nr/Bacteria	**6c**	**6d**	**6f**	**10**	**20**	**22**	**Control**[a]	
							I	**II**
Bacillus cereus	12	<6.4	12	**19**	13	11	24	45
Bacillus subtilis	12	<6.4	<6.4	**28**	**20**	11	30	46
Enterococcus faecalis	12	<6.4	11	**16**	<6.4	<6.4	26	43
Escherichia coli	<6.4	8	<6.4	10	<6.4	<6.4	28	41
Listeria monocytogenes	nt	nt	nt	nt	<6.4	<6.4	31	45

Pseudomonas aeruginosa	<6.4	9	<6.4	8	<6.4	<6.4	<6.4	23
Salmonella enteritidis	nt	<6.4	nt	<6.4	nt	nt	36	46
Staphylococcus aureus	11	<6.4	11	**21**	<6.4	<6.4	27	41
Filamentous fungi							**Control**[b]	
							I	**II**
Alternaria alternata	<6.4	<6.4	<6.4	10	nt	nt	<6.4	<6.4
Biscogniauxia mediterranea	nt	<6.4	nt	12	nt	nt	52	70
Botrytis spp.	<6.4	**15**	<6.4	**15**	nt	nt	<6.4	20
Byssochlamys fulva	<6.4	<6.4	<6.4	**19**	nt	nt	18	45
Candida albicans	8	<6.4	12	**20**	nt	nt	<6.4	15
Colletotrichum coffeanum	10	8	12	**15**	nt	nt	16	24
Fusarium culmorum	nt	<6.4	nt	11	nt	nt	12	18
Pyricularia oryzae	<6.4	<6.4	<6.4	**18**	nt	nt	40	70
Rhizopus spp.	<6.4	<6.4	<6.4	**15**	nt	nt	11	19
Stachybotrys chartarum	nt	<6.4	nt	**10**	nt	nt	<6.4	<6.4

nt: not tested; diameter <6.4 means no microbial was not susceptible to compound, thus no antimicrobial activity; a) chloramphenicol was used as control for all bacteria and was tested in the quantities of I = 30 and II = 300 μg; b) control actidione was used for all the filamentous fungi whereas chloramphenicol was the control substance tested for *C. albicans*; inhibitions caused by I = 30 and II = 300 μg of control was assessed.

CONCLUSION

Synthetic pathways to oxazole-2(3*H*)-thiones (OXTs) **6a-f** and closely related 2-alkylsulfanyl-1,3-oxazole structures were revisited. Additionally, a method was devised employing a carbohydrate-fused 1,3-oxazolidine-2-thione scaffold to produce original hemiaminal derivatives **10** and **13**. The reactivity of OXTs with electrophiles was surveyed in terms of *S*/*N*-chemoselectivity and a marked difference in behaviour was observed, compared to that of formerly studied 1,3-oxazolidine-2-thiones.

Antimicrobial testing on bacteria and filamentous fungi was performed on six of the prepared compounds, among which the hemiaminal **10** overhangs as showing the broadest activity range, being even superior to the respective controls in the case of *Candida albicans* and *Stachybotrys chartarum*. Compound **10** could therefore be seen as a lead candidate for future exploration of this family of heterocycles.

EXPERIMENTAL

General: Anhydrous reactions were carried out under argon atmosphere in pre-dried flasks, using anhydrous solvents. TLC on precoated aluminum-back plates (Merck Kieselgel $60F_{254}$) were visualized by UV light (254 nm) and by charring after exposure to a 10% H_2SO_4 solution in methanol or to a 5%

solution of phosphomolybdic acid in ethanol. Flash column chromatography was carried out using Kieselgel Si60, 40-63μm (E. Merck). Melting points (°C) were obtained using a Büchi 510 capillary apparatus. Optical rotations were measured at 20 °C with a Perkin Elmer 341 polarimeter with a path length of 1 dm. ^{1}H and ^{13}C NMR spectra were recorded on a 250 MHz Bruker Avance DPX250 spectrometer or a 400 MHz Bruker Avance 2 spectrometer. Chemical shifts are expressed in parts per million (ppm) downfield from TMS internal standard and coupling constants are given in Hz. IR absorption frequencies (Thermo-Nicolet AVATAR 320 spectrometer) are given in cm^{-1}. Mass spectra were recorded on a Perkin Elmer Sciex API 300 spectrometer for negative (ISN) and positive (ISP) electrospray ionization. High resolution mass spectra (HRMS) were recorded with a MicrOTOF-QII spectrometer in the electrospray ionisation (ESI) mode or in chemical ionisation (CI) mode.

4-Phenyloxazole-2(3*H*)-thione (6b): α-Hydroxyacetophenone (1.00 g, 7.34 mmol) and KSCN (1.07 g, 11.01 mmol) were dissolved in EtOH (30 mL). After cooling at –5 °C, 12M aq HCl (1.10 mL, 13.2 mmol) was carefully added and the mixture was stirred under reflux for 24 h, then cooled by treating with crushed ice. After extraction with EtOAc (3 x 25 mL), the combined organic phase was successively washed with saturated aq $NaHCO_3$, water, brine, and finally dried over $MgSO_4$. After filtration and concentration under reduced pressure, the residue was subjected to flash chromatography on silica gel (PE/EtOAc 9:1) to afford compound **6b** (1.09 g, 84%) as a reddish oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.37-7.43 (m, 2H, Ph), 7.44-7.45 (m, 1H, Ph) 7.48-7.52 (m, 2H, Ph), 7.54 (s, 1H, H-5), 12.50 (brs, 1H, N-H). ^{13}C NMR (62.89 MHz, $CDCl_3$): δ 125.3 (CH-Ph), 128.7 (C-4), 129.4, 129.7 (CH-Ph), 131.9 (C-5), 134.7 (C_{IV}-Ph), 179.3 (C=S). IR (NaCl) 3280 (NH), 1635 (C=C), 1495, 1054 (N-CS-O), 1455, 1451 (Ph). HRMS: calcd. for C_9H_8NOS $[M+H]^+$ 178.0327, found 178.0325.

Oxazole-2(3*H*)-thione (6c): 2,2-Dimethoxyethanol (0.80 g, 7.5 mmol) and KSCN (1.10 g, 11.3 mmol) were dissolved in EtOH (30 mL). After cooling at –5 °C, 12M aq HCl (1.13 mL, 13.6 mmol) was carefully added and the mixture was stirred under reflux for 24 h, then cooled by treating with crushed ice. After extraction with EtOAc (3x25 mL), the combined organic phase was successively washed, with saturated aqueous $NaHCO_3$, water, brine, and finally dried over anhydrous $MgSO_4$. After filtration and concentration under reduced pressure, the residue was purified by column chromatography (PE/EtOAc 6:4) to afford the OXT **6c** (0.69 g, 91% yield) as white crystals; mp 147-8 °C (Lit.[11] mp 147 °C). ^{1}H NMR (250 MHz, MeOH-d_4): δ 7.14 (s, 1H, H-4), 7.54 (s, 1H, H-5). ^{13}C NMR (62.89 MHz, MeOH-d_4): δ 116.9 (C-4), 137.7 (C-5), 181.1 (C=S). HRMS: calcd. for C_3H_4NOS $[M+H]^+$ 102.0014, found 102.0017.[36]

4-(Hydroxymethyl)oxazole-2(3*H*)-thione (6d): 1,3-Dihydroxyacetone dimer (1.00 g, 11.1 mmol monomer) and KSCN (0.54 g, 5.55 mmol) were dissolved in H_2O (30 mL). After cooling at –5 °C, 12M aq HCl (0.83 mL, 10 mmol) was carefully added and the mixture was stirred at 65 ºC for 24 h, then cooled by treating with crushed ice. After extraction with EtOAc (3 x 25 mL), the combined organic

phase was successively washed with saturated aq $NaHCO_3$, water, brine, and finally dried over anhydrous $MgSO_4$. After filtration and concentration under reduced pressure, the residue was subjected to flash chromatography on silica gel (PE/EtOAc 1:1, v/v) to afford compound **6d** as a yellow oil (0.15 g, 21%). ^{1}H NMR (250 MHz, DMSO-d_6): δ 4.24 (s, 2H, CH_2O), 5.35 (brs, 1H, OH), 7.60 (s, 1H, H-5), 12.87 (brs, 1H, NH). ^{13}C NMR (62.89 MHz, DMSO-d_6): δ 52.1 (CH_2), 131.5 (C-4), 133.7 (C-5), 178.6 (C=S). IR (NaCl) 3500 (OH), 3276 (NH), 3142, 2926, 2889, 2853, 1659 (C=C), 1502, 1463, 1414, 1061 (N-CS-O). HRMS: calcd. for $C_4H_6NO_2S$ $[M+H]^+$ 132.0119, found 132.0123.

3-Benzyloxy-2,2-dimethoxypropan-1-ol (8): A suspension of NaH (60% dispersion in mineral oil, 147 mg, 3.67 mmol) in THF (15 mL) was treated at 0 ºC with a solution of the diol **7** (500 mg, 3.67 mmol)[19] in THF (15 mL). After stirring 30 min, a catalytic amount of Bu_4NI (42 mg, 0.11 mmol) and benzyl bromide (0.44 mL, 3.67 mmol) were added and the mixture stirred during 8 h. After quenching with crushed ice and extraction with EtOAc (3x20 mL), the combined organic phase was washed with water, brine, then dried over anhydrous $MgSO_4$. After filtration and concentration under reduced pressure, the residue was subjected to flash chromatography on silica gel (PE/EtOAc 8:2) to deliver the alcohol **8** (531 mg, 64%) as a colourless oil.[19] ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.39 (t, 1H, J_{vic}=5.5, O*H*), 3.24 (s, 6H, OMe), 3.53 (s, 2H, CH_2OBn), 3.68 (d, 2H, CH_2OH), 4.56 (s, 2H, CH_2Ph), 7.27-7.34 (m, 5H, Ph). ^{13}C NMR (62.89 MHz, $CDCl_3$) δ 48.2 (O*Me*), 60.2 (CH_2OH), 67.9 (CH_2OBn), 76.4 (CH_2Ph), 99.8 (C-2), 127.2, 127.7, 128.2 (CH-Ph), 137.4 (C_{IV}-Ph). HRMS: calcd. for $C_{12}H_{18}O_4Na$ $[M+Na]^+$ 249.1103, found 249.1099.

4-(Benzyloxymethyl)oxazole-2(3*H*)-thione (6e): A solution of 3-(benzyloxy)-2,2-dimethoxypropan-1-ol[17] (80 mg, 0.35 mmol) and KSCN (34 mg, 0.35 mmol) in H_2O (10 mL) was cooled at –5 °C, then 12M aq HCl (60 μL, 0.72 mmol) was added and the mixture was stirred at 60 ºC for 24 h. After cooling with crushed ice and extraction with EtOAc (3x15 mL), the combined organic phase was successively washed with saturated aq $NaHCO_3$, water, brine, and finally dried over anhydrous $MgSO_4$. After filtration and concentration under reduced pressure, the residue was subjected to flash chromatography (PE/EtOAc 1:1) to afford compound **6e** as an orange oil (31 mg, 40%). ^{1}H NMR (250 MHz, $CDCl_3$): δ 4.33 (s, 2H, CH_2OBn), 4.56 (s, 2H, OCH_2Ph), 7.20 (s, 1H, H-5), 7.26-7.36 (m, 5H, Ph), 11.38 (brs, 1H, NH).^{13}C NMR (62.89 MHz, $CDCl_3$): δ 59.8 (CH_2OBn), 72.9 (CH_2Ph), 127.8 (C-4), 128.2, 128.5, 128.8 (CH-Ph), 134.2 (C-5), 136.6 (C_{IV}-Ph), 179.6 (C=S). IR (NaCl) 3239 (NH), 2926, 2902 (CH), 1650 (C=C), 1518, 1350, 1049 (N-CS-O), 1466, 1464 (Ph). MS (IS) *m/z*=222.5 $[M+H]^+$, 239.0 $[M+NH_4]^+$. HRMS: calcd. for $C_{11}H_{11}NO_2SNa$ $[M+Na]^+$ 244.0408, found 244.0410.

(1,2,5-Trideoxy-5-iodo-β-D-arabinofuranoso)[2,1-*d*]oxazolidine-2-thione (13): The D-*arabino*-OZT derivative **12** (2.18 g, 11.4 mmol),[26] triphenylphosphine (5.97 g, 22.8 mmol) and imidazole (1.55 g, 22.8 mmol) were dissolved in dry THF (30 mL). After cooling the solution at 0 ºC, iodine (3.48 g, 13.7 mmol)

was added gradually. The coloration faded and the mixture was stirred at rt overnight. The solvent was removed under reduced pressure and the residue was purified by column chromatography (PE/EtOAc 1:1) to afford the iodide **8** (3.30 g, 96%) as a white solid; mp 168-170 °C; $[\alpha]_D^{20}$ - 24 (*c* 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.09-3.22 (m, 2H, H-5a, H-5b), 4.04 (td, 1H, $J_{3\text{-}4}$=1.7, $J_{4\text{-}5a}$=$J_{4\text{-}5b}$=7.1, H-4), 4.25 (brs, 1H, H-3), 5.11 (d, 1H, $J_{1\text{-}2}$=5.6, H-2), 5.88 (d, 1H, $J_{1\text{-}2}$=5.6, H-1), 5.97 (d, 1H, $J_{3\text{-}OH}$=4.2, O*H*), 11.00 (brs, 1H, NH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 6.2 (C-5), 76.3 (C-3), 85.4 (C-4), 89.5 (C-1), 91.1 (C-2), 188.0 (C=S). IR (NaCl) 3500 (OH), 3155 (NH), 2950, 2925, 2858 (CH), 1480, 1311, 1027 (N-CS-O), 609 (C-I). HRMS: calcd. for $C_6H_9INO_3S$ $[M+H]^+$ 301.9348, found 301.9349.

(3-*O*-*tert*-Butyldimethylsilyl-1,2,5-trideoxy-5-iodo-β-D-arabinofuranoso)[2,1-*d*]-1,3-oxazolidine-2-thione (9): To the solution of compound **8** (114.4 mg, 0.38 mmol) in dry DMF (10 mL) cooled to 0 ºC, imidazole (51.7 mg, 0.76 mmol) and *tert*-butyldimethylchlorosilane (85.8 mg, 0.57 mmol) were added. The mixture was stirred 5 h at rt, then cooled with crushed ice and extracted with EtOAc (3x20 mL). The combined organic phase was washed with water, brine, then dried over $MgSO_4$. After filtration and concentration under reduced pressure, the residue was subjected to flash chromatography (PE/EtOAc 9:1) to afford compound **9** (146.8 mg, 93%) as a white solid; mp 112-113 °C; $[\alpha]_D^{20}$ - 53 (*c* 0.7, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.17 (s, 6H, *Me*$_2$Si), 0.89 (s, 9H, *t-Bu*Si), 3.09 (t, 1H, $J_{5a\text{-}5b}$=$J_{4\text{-}5b}$=10.0, H-5b), 3.22 (dd, 1H, $J_{4\text{-}5a}$=5.6, H-5a), 4.24 (dd, 1H, H-4), 4.58 (s, 1H, H-3), 5.03 (d, 1H, $J_{1\text{-}2}$=5.3, H-2), 5.93 (d, 1H, H-1), 8.10 (brs, 1H, NH). ^{13}C NMR (100 MHz, $CDCl_3$): δ -4.6, -4.4 (*Me*$_2$Si), 4.1 (C-5), 18.0 (C_{IV}-*t*-Bu), 25.7 (*Me*$_3$C), 77.7 (C-3), 87.6 (C-4), 89.8 (C-1), 92.6 (C-2), 188.7 (C=S). IR (NaCl) 3224 (NH), 2980, 2956, 2920 (CH), 1479, 1319, 1024 (N-CS-O), 1220 ($SiMe_2$), 609 (C-I). HRMS: calcd. for $C_{12}H_{22}INO_3SSiNa$ $[M+Na]^+$ 438.0032, found 438.0029.

5-[(1*R*)-1-*tert*-Butyldimethylsilyloxyprop-2-en-1-yl]-4-hydroxy-1,3-oxazolidine-2-thione (10): Activated zinc dust (169.4 mg, 2.59 mmol) was added to a solution of compound **9** (153.7 mg, 0.37 mmol) in acetic acid (5 mL). The mixture was stirred 1 h at rt, then filtered through a cotton pad to discard the metal. The solution was co-evaporated with toluene (3x) then concentrated under reduced pressure. Purification of the residue by flash chromatography (PE/EtOAc 9:1) afforded compound **10** (92.1 mg, 86%) as a yellow oil; $[\alpha]_D^{20}$ - 30 (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 0.10 (s, 6H, *Me*$_2$Si), 0.90 (s, 9H, *t-Bu*Si), 3.49 (brs, 1H, OH), 4.42-4.44 (m, 1H, *CH*OSi), 4.59 (dd, 1H, $J_{4\text{-}5}$=2.3, $J_{5\text{-}6}$=4.6, H-5), 5.30 (dt, 1H, J_{gem}=1.3, J_{vic}=10.7, =C*H*$_2$-Z), 5.34 (d, 1H, H-4), 5.42 (dt, 1H, J_{vic}=17.2, $^4J_{allylic}$=1.3, =C*H*$_2$-E), 5.82 (ddd, 1H, $^3J_{CHOSi}$=5.6, =C*H*), 7.75 (brs, 1H, NH). ^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ -4.9, -4.3 (*Me*$_2$Si), 18.2 (C_{IV}-*t*-Bu), 25.8 (*Me*$_3$C), 71.7 (*CH*OSi), 80.9 (C-4), 92.1 (C-5), 119.0 (=*CH*$_2$), 134.1 (=*CH*), 189.4 (C=S). IR (NaCl) 3488 (OH), 3224 (NH), 2950, 2925, 2853 (CH), 1640 (C=C), 1480, 1345, 1030 (N-CS-O), 1220 ($SiMe_2$). HRMS: calcd. for $C_{12}H_{24}NO_3SSi$ $[M+H]^+$

290.1246, found 290.1255.

5-[(1*R*)-*tert*-Butyldimethylsilyloxyprop-2-en-1-yl]-2-mesylsulfanyl-1,3-oxazole (11): To a solution of **10** (503.7 mg, 1.74 mmol) in dry CH_2Cl_2 (5 mL), triethylamine (1 mL, 7.2 mmol) and methanesulfonyl chloride (0.4 mL, 5.2 mmol) were successively added and the mixture was stirred during 45 min at rt, then quenched by treating with crushed ice. After extraction with CH_2Cl_2 (3x25 mL), the combined organic phase was washed with water, brine, then dried over $MgSO_4$. After filtration and concentration under reduced pressure, the residue was purified by column chromatography (PE/EtOAc 8:2) to afford the unstable methanethiosulfonate **16** (553.5 mg, 91%) as a yellow oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.10 (s, 6H, *Me*$_2$Si), 0.92 (s, 9H, *t-Bu*Si), 3.54 (s, 3H, *Me*SO_2), 5.29 (d, 1H, J_{vic}=5.6, *CH*OSi), 5.31 (dt, 1H, J_{gem}=1.4, J_{vic}=9.6, =C*H*$_2$-Z), 5.45 (dt, 1H, , J_{vic}=16.8, $^4J_{allylic}$=1.4, =C*H*$_2$-E), 5.98 (ddd, 1H, $^3J_{CHOSi}$=5.6, =C*H*), 7.16 (brs, 1H, H-4). ^{13}C NMR (62.89 MHz, $CDCl_3$): δ -4.9, -4.3 (*Me*$_2$Si), 18.4 (C_{IV}-*t*-Bu), 25.8 (*Me*$_3$C), 49.8 (*Me*SO_2), 62.2 (*CH*OSi), 117.4 (=*CH*$_2$), 127.2 (C-4), 136.1 (=*CH*), 151.0 (C-2), 159.2 (C-5). MS (IS): *m/z*=350.5 $[M+H]^+$, 367.5 $[M+NH_4]^+$, 372.5 $[M+Na]^+$.

2-Benzylsulfanyl-4,5-dihydro-3-*O*-*tert*-butyldimethylsilyl-1,2,5-trideoxy-5-iodo-β-D-arabinofuranoso)-[2,1-*d*]-1,3-oxazole (12): To a solution of **9** (300 mg, 0.72 mmol) in dry CH_2Cl_2 (10 mL), were added triethylamine (0.15 mL, 1.08 mmol) and benzyl bromide (0.13 mL, 1.09 mmol). The reaction was stirred during 3 h at rt, then cooled by treating with crushed ice. After extraction with CH_2Cl_2 (3x25 mL), the combined organic phase was washed with water, brine, then dried over $MgSO_4$. After filtration and concentration under reduced pressure, the residue was purified by column chromatography (PE/EtOAc 95:5) to afford compound **12** (360.3 mg, 99%) as a colourless oil. $[\alpha]_D^{20}$ - 59 (*c* 0.9, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.10 (s, 6H, *Me*$_2$Si), 0.74 (s, 9H, *t-Bu*Si), 2.73 (dd, 1H, $J_{4\text{-}5b}$=9.4, $J_{5a\text{-}5b}$=10.3, H-5b), 2.91 (dd, 1H, $J_{4\text{-}5b}$=4.9, H-5a), 3.88 (ddd, 1H, $J_{3\text{-}4}$=2.6, H-4), 4.01 and 4.14 (2d, AB system, 2H, J_{gem}=13.3, S*CH*$_2$Ph), 4.17 (brs, 1H, H-3), 4.60 (dd, 1H, $J_{1\text{-}2}$=5.9, $J_{2\text{-}3}$= 1.1, H-2), 5.96 (d, 1H, H-1), 7.10-7.23 (m, 5H, Ph). ^{13}C NMR (62.89 MHz, $CDCl_3$): δ -4.6, -4.5 (*Me*$_2$Si), 5.2 (C-5), 18.0 (C_{IV}-*t*-Bu), 25.8 (*Me*$_3$C), 36.6 (S*CH*$_2$Ph), 79.4 (C-3), 85.7 (C-4), 90.8 (C-2), 101.1 (C-1), 127.9, 128.8, 129.2 (CH-Ph), 136.4 (C_{IV}-Ph), 169.9 (=*C*-SBn). IR (NaCl) 2961, 2925, 2848 (CH), 1594, 1037 (-N=CS-O), 1461, 1458 (Ph), 1251 ($SiMe_2$), 698 (C-I). HRMS: calcd. for $C_{19}H_{29}INO_3SSi$ $[M+H]^+$ 506.0682, found 506.0695.

2-Benzylsulfanyl-5-[(1*R*)-1-*tert*-butyldimethylsilyloxyprop-2-en-1-yl]-4,5-dihydro-4-hydroxy-1,3-oxazole (13): Activated zinc dust (169.4 mg, 2.59 mmol) was added to a solution of compound **12** (187 mg, 0.37 mmol) in acetic acid (5 mL). The mixture was stirred 1 h at rt, then filtered through a cotton pad to discard the metal. The solution was co-evaporated with toluene (3x) then concentrated under reduced pressure. Purification of the residue by flash chromatography (PE/EtOAc 9:1) afforded compound **13** (121 mg, 86%) as a yellow oil; $[\alpha]_D^{20}$ - 52 (*c* 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 0.08 (s, 6H,

Me$_2$Si), 0.89 (s, 9H, *t-Bu*Si), 4.23 (s, 2H, S*CH*$_2$Ph), 4.25-4.28 (m, 1H, *CH*OSi), 4.33 (dd, 1H, $J_{4\text{-}5}$=3.5, $J_{5\text{-}6}$=4.6, H-5), 5.20 (dt, 1H, J_{gem}=1.4, J_{vic}=10.4, =C*H*$_2$-Z), 5.31 (dt, 1H, J_{vic}=17.2, $^4J_{allylic}$=1.3, =C*H*$_2$-E), 5.53 (d, 1H, H-4), 5.76 (ddd, 1H, $^3J_{CHOSi}$=6.3, =C*H*), 7.26-7.37 (m, 5H, Ph). ^{13}C NMR (100 MHz, DMSO-d_6): δ -4.9, -4.3 (*Me*$_2$Si), 18.3 (C_{IV}-*t*-Bu), 25.8 (*Me*$_3$C), 36.3 (S*CH*$_2$Ph), 73.1 (*CH*OSi), 90.2 (C-5), 91.0 (C-4), 117.8 (=*CH*$_2$), 127.8, 128.8, 129.2 (CH-Ph), 135.7 (=*CH*), 135.9 (C_{IV}-Ph), 170.0 (C-2). IR (NaCl) 3488 (OH), 2950, 2925, 2853 (CH), 1635 (C=C), 1584, 1030, 697 (-N=CS-O), 1468, 1466 (Ph), 1220 (SiMe$_2$). HRMS: calcd. for $C_{19}H_{30}NO_3SSi$ $[M+H]^+$ 380.1716, found 380.1719.

2-Benzylsulfanyl-5-[(1*R*)-1-*tert*-butyldimethylsilyloxy-prop-2-en-1-yl]-1,3-oxazole (14): To a solution of **13** (660.5 mg, 1.74 mmol) in dry CH_2Cl_2 (8 mL), triethylamine (1 mL, 7.2 mmol) and methanesulfonyl chloride (0.4 mL, 5.2 mmol) were successively added and the mixture was stirred during 45 min at rt, then quenched by treating with crushed ice. After extraction with CH_2Cl_2 (3x25 mL), the combined organic phase was washed with water, brine, then dried over $MgSO_4$. After filtration and concentration under reduced pressure, the residue was purified by column chromatography (PE/EtOAc 19:1) to afford compound **14** (485 mg, 77%) as a yellow oil; $[\alpha]_D^{20}$ - 67 (*c* 1.1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.10 (s, 6H, *Me*$_2$Si), 0.84 (s, 9H, *t-Bu*Si), 4.29 (s, 2H, S*CH*$_2$Ph), 5.13 (m, 1H, *CH*OSi), 5.17 (dt, 1H, J_{gem}=1.4, J_{vic}=10.3, =C*H*$_2$-Z), 5.35 (dt, 1H, J_{vic}=17.1, $^4J_{allylic}$=1.4, =C*H*$_2$-E), 5.90 (ddd, 1H, $^3J_{CHOSi}$=5.4, =C*H*), 6.79 (d, 1H, $^4J_{allylic}$=0.6, H-4), 7.18-7.31 (m, 5H, Ph). ^{13}C NMR (100 MHz, $CDCl_3$): δ -4.8, -4.7 (*Me*$_2$Si), 18.4 (C_{IV}-*t*-Bu), 25.8 (*Me*$_3$C), 37.0 (S*CH*$_2$Ph), 67.8 (*CH*OSi), 116.4 (=*CH*$_2$), 124.7 (C-4), 127.8, 128.7, 129.0 (CH-Ph), 136.6 (C_{IV}-Ph), 136.7 (=*CH*), 154.5 (C-5), 159.6 (C-2). IR (NaCl) 2950, 2930, 2884 (CH), 1671, 1638 (C=C), 1580, 1027, 696 (-N=CS-O), 1456, 1454 (Ph), 1230 (SiMe$_2$). HRMS: calcd. for $C_{19}H_{28}NO_2SSi$ $[M+H]+$ 362.1610, found 362.1611.

2-Benzylsulfanyl-4-methyl-1,3-oxazole (15): NaH (60% dispersion in mineral oil; 0.26 g, 6.5 mmol) was carefully added to a stirred solution of **6a** (0.50 g, 4.34 mmol) in dry DMF (20 mL) cooled at -5 ºC. After 15 min, benzyl bromide (0.57 mL, 4.8 mmol) was added and stirring continued 2.5 h at rt. After quenching with crushed ice and extraction with EtOAc (3x20 mL), the combined organic phase was washed with water, brine, then dried over anhydrous $MgSO_4$. After filtration and concentration under reduced pressure, the residue was purified by column chromatography (PE/EtOAc 19:1) to afford compound **15** (0.54 g, 60%) as a colourless oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.14 (s, 3H, Me), 4.37 (s, 2H, S*CH*$_2$Ph), 7.24-7.38 (m, 6H, H-5, Ph). ^{13}C NMR (62.89 MHz, $CDCl_3$): δ 11.7 (Me), 37.0 (S*CH*$_2$Ph), 127.8, 128.7, 129.0 (CH-Ph), 135.8 (C-5), 136.4 (C_{IV}-Ph), 137.9 (C-4), 159.3 (C-2). IR (NaCl) 3180, 2976, 2885 (CH), 1649 (C=C), 1616, 1021 (N=CS-O), 1463, 1459, 1454 (Ph). HRMS: calcd. for $C_{11}H_{12}NOS$ $[M+H]^+$ 206.0640, found 206.0648.

2-(Benzoylmethyl)sulfanyl-4-methyl-1,3-oxazole (16): NaH (60% dispersion in mineral oil; 40 mg, 1 mmol) was carefully added to a stirred solution of the OXT **6a** (100 mg, 0.87 mmol) in dry DMF (4 mL)

cooled at -5 ºC. After 15 min, 2-bromoacetophenone (191 mg, 0.96 mmol) was added and stirring continued for 1 h at rt. After quenching with crushed ice and extraction with EtOAc (3x15 mL), the combined organic phase was washed with water, brine, then dried over anhydrous $MgSO_4$. After filtration and concentration under reduced pressure, the residue was purified by column chromatography (PE/EtOAc 6:4) to afford compound **16** (186 mg, 83%) as a yellow oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.13 (s, 3H, Me), 4.76 (s, 2H, S*CH*$_2$CO), 7.36 (s, 1H, H-5), 7.47-7.53 (m, 2H, *meta*-CH-Ph), 7.59-7.65 (m, 1H, *para*-CH-Ph), 8.01-8.04 (m, 2H, *ortho*-CH-Ph). ^{13}C NMR (62.89 MHz, $CDCl_3$): δ 11.6 (Me), 40.9 (S*C*H$_2$CO), 128.6, 128.9, 133.9 (CH-Ph), 135.3 (C_{IV}-Ph), 136.1 (C-5), 137.9 (C-4), 158.7 (C-2), 192.9 (CO). IR (NaCl) 3020, 2966, 2884 (CH), 1675, 1630, 1080 (N=CS-O), 1696 (C=O), 1625 (C=C), 1424, 1449, 1398 (Ph), 1050, 929. HRMS: calcd. for $C_{12}H_{12}NO_2S$ $[M+H]^+$ 234.0589, found 234.0581.

2-Methanesulfonylsulfanyl-4-methyl-1,3-oxazole (**17**)**:** To a solution of **6a** (200 mg, 1.74 mmol) in dry CH_2Cl_2 (5 mL), triethylamine (0.38 mL, 2.61 mmol) and methanesulfonyl chloride (0.2 mL, 2.6 mmol) were successively added at 0 °C and the mixture was stirred during 2 h at rt, then quenched by treating with crushed ice. After extraction with CH_2Cl_2 (3x20 mL), the combined organic phase was washed with water, brine, then dried over $MgSO_4$. After filtration and concentration under reduced pressure, the residue was purified by column chromatography (PE/EtOAc 8:2) to afford compound **17** (144 mg, 0.75 mmol, 44%) as an unstable yellow oil: ^{1}H NMR (250 MHz, $CDCl_3$) δ 2.27 (s, 3H, Me), 3.56 (s, 3H, $MeSO_2$), 7.67 (s, 1H, H-5); ^{13}C NMR (62.89 MHz, CDCl3) δ 11.8 (C-6), 49.9 (CH_3SO_2), 140.5 (C-5), 140.8 (C-4), 150.7 (C-2). MS (IS): m/z = 194.5 [M+H]+, 216.0 [M+Na]+

Reaction of acrylonitrile with 6a: Acrylonitrile (87 µL, 1.33 mmol) and triethylamine (3 mL, 22 mmol) were added to a solution of **6a** (100 mg, 0.87 mmol) in dry DMF (3 mL) and stirring was maintained 24 h at rt. After quenching with crushed ice and extraction with EtOAc (3x15 mL), the combined organic phase was washed with water, brine, then dried over $MgSO_4$. After filtration and concentration under reduced pressure, the residue was purified by column chromatography (PE/EtOAc 1:1) to afford successively:

2-(2-Cyanoethyl)sulfanyl-4-methyl-1,3-oxazole (**18**)**:** yellow oil (41 mg, 28%). ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.15 (s, 3H, Me), 2.95 (t, 2H, J_{vic}=7.0, *CH*$_2$CN), 3.37 (t, 2H, *CH*$_2$S), 7.40 (s, 1H, H-5). ^{13}C NMR (62.89 MHz, $CDCl_3$): δ 11.7 (Me), 18.8 (*CH*$_2$CN), 28.0 (*CH*$_2$S), 117.9 (C≡N), 136.4 (C-5), 138.1 (C-4), 158.8 (C-2). IR (NaCl) 3150, 3020, 2982 (CH), 2255 (CN), 1625 (C=C), 1640 (-N=CS-O). HRMS: calcd. for $C_7H_8N_2OSNa$ $[M+Na]^+$ 191.0255, found 191.0259.

3-(2-Cyanoethyl)-4-methyloxazole-2(3*H*)-thione (**19**)**:** yellow solid (51 mg, 36%); mp 43-45 °C. 1H NMR (250 MHz, CDCl3): δ 2.25 (s, 3H, Me), 3.06 (t, 2H, J_{vic}=6.0, *CH*$_2$CN), 4.17 (t, 2H, *CH*$_2$N), 7.11 (s, 1H, H-5). 13C NMR (62.89 MHz, $CDCl_3$): δ 8.7 (Me), 15.7 (*CH*$_2$CN), 41.2 (*CH*$_2$N), 117.2 (C≡N), 127.3

(C-4), 132.0 (C-5), 178.9 (C=S). IR (NaCl) 3140, 3020, 2977 (CH), 2255 (CN), 1627 (C=C), 1050 (N-CS-O). HRMS: calcd. for $C_7H_8N_2OSNa$ $[M+Na]^+$ 191.0255, found 191.0248.

Reaction of phenyl vinyl sulfone with 6a: Phenyl vinyl sulfone (221 mg, 1.31 mmol) and triethylamine (3 mL, 22 mmol) were added to a solution of **6a** (100 mg, 0.87 mmol) in dry DMF (3 mL) and stirring was maintained 24 h at rt. After quenching with crushed ice and extraction with EtOAc (3x15 mL), the combined organic phase was washed with water, brine, then dried over $MgSO_4$. After filtration and concentration under reduced pressure, the residue was purified by column chromatography (PE/EtOAc 1:1) to afford:

2-[(2-Phenylsulfonyl)ethyl]sulfanyl-4-methyl-1,3-oxazole (**20**): colorless oil (74 mg, 30%). ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.08 (s, 3H, Me), 3.32-3.39 (m, 2H, *CH*$_2$S), 3.60-3.66 (m, 2H, *CH*$_2$SO$_2$), 7.34 (s, 1H, H-5), 7.57-7.63 (m, 2H, *meta*-CH-Ph), 7.67-7.70 (m, 1H, *para*-CH-Ph), 7.93-7.96 (m, 2H, *ortho*-CH-Ph). ^{13}C NMR (62.89 MHz, $CDCl_3$): δ 11.6 (Me), 25.1 (*C*H$_2$S), 55.9 (*C*H$_2$SO$_2$), 128.3, 129.5 (CH-Ph), 134.1 (*para*-CH-Ph), 136.3 (C-5), 138.1, 138.7 (C-4, C_{IV}-Ph), 157.7 (C-2). IR (NaCl) 3145, 3020, 2982 (CH), 1630 (C=C), 1640, 1511 (-N=CS-O), 1419, 1481 (Ph), 1370 (SO_2), 1040, 933. HRMS: calcd. for $C_{12}H_{14}NO_3S_2$ $[M+H]^+$ 284.0415, found 284.0425.

4-Methyl-3-[(2-phenylsulfonyl)ethyl]oxazole-2(3*H*)-thione (**21**): white solid (153 mg, 62%); mp 128-129 °C; ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.24 (s, 3H, Me), 3.76 (t, 2H, J_{vic}=6.4, *CH*$_2$SO$_2$), 4.30 (t, 2H, *CH*$_2$N), 7.02 (s, 1H, H-5), 7.56-7.62 (m, 2H, *meta*-CH-Ph), 7.66-7.72 (m, 1H, *para*-CH-Ph), 7.88-7.91 (m, 2H, *ortho*-CH-Ph). ^{13}C NMR (62.89 MHz, $CDCl_3$): δ 8.6 (Me), 38.8 (*C*H$_2$N), 51.7 (*C*H$_2$SO$_2$), 127.9 (C-4), 127.8, 129.6, 131.7 (*C*H-Ph), 134.4 (C-5), 138.7 (C_{IV}-Ph), 178.5 (C=S). IR (NaCl) 3140, 3020, 2977 (CH), 1625 (C=C), 1511, 1143 (N-CS-O), 1420, 1481 (Ph), 1390 (SO_2) 1045, 917. HRMS: calcd. for $C_{12}H_{14}NO_3S_2$ $[M+H]^+$ 284.0415, found 284.0418.

Preparation of 4-Methyl-3-[(2-phenylsulfonyl)vinyl]oxazole-2(3*H*)-thione (22): Prepared in 93% yield according to ref. 17.

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