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Fe(II)-Catalyzed Isomerization of 4-Vinylisoxazoles into Pyrroles

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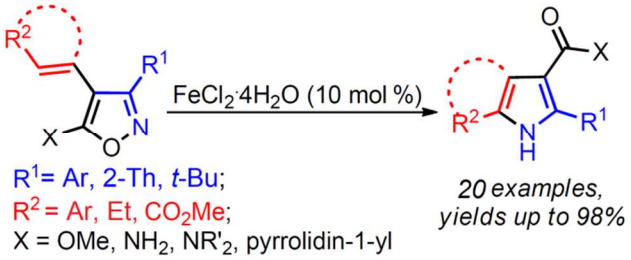
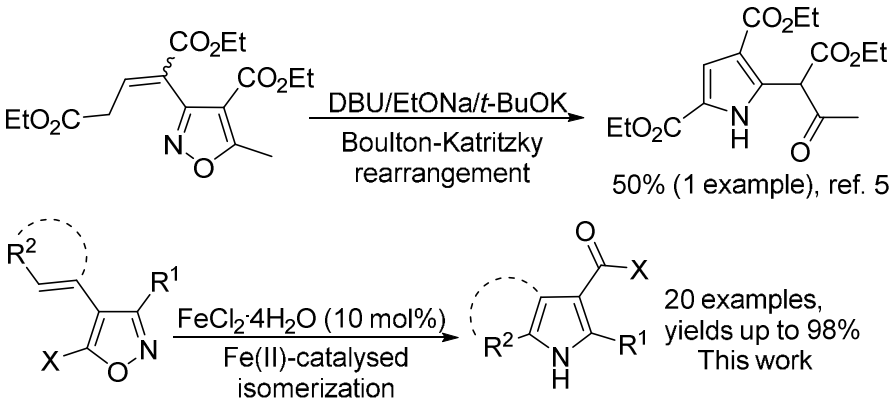


ABSTRACT: The first synthesis of pyrroles by Fe(II)-catalyzed isomerization of 4-vinylisoxazoles is reported. 5-Alkoxy, amino and *N*,*N*-dialkylamino-3-aryl/alkyl-4-(2-R-vinyl)isoxazoles afford 2-aryl/alkyl-5-aryl/alkyl/methoxycarbonyl-1*H*-pyrrol-3-carboxylic acid derivatives typically under mild conditions with cheap and available $FeCl_2 \cdot 4H_2O$ as a catalyst. The isomerization of 5-alkoxy/amino-3-arylisoxazoles, bearing unsaturated carbo and heterocyclic substituents at the position 4, gives the corresponding fused pyrrolecarboxylic acid derivatives in high yields. DFT calculations were used to elucidate a probable mechanism of the isomerization and explain the influence of steric congestion of the vinyl moiety on the isomerization pathway.

INTRODUCTION

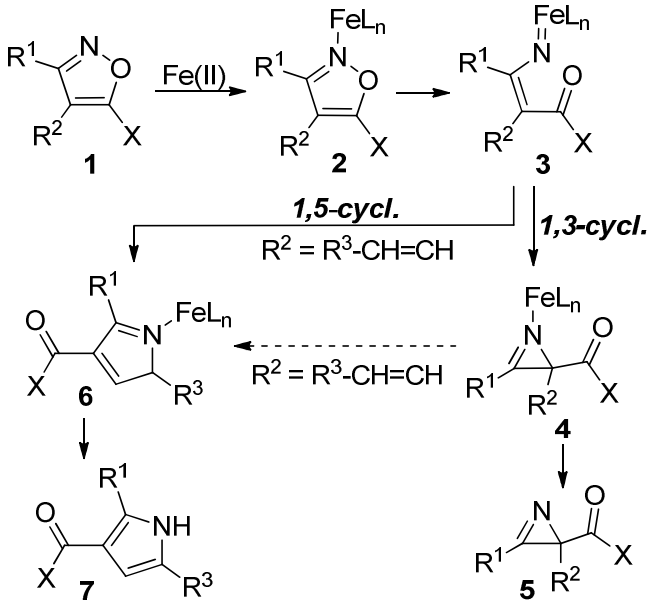
Pyrrole moieties are widely present in natural compounds, pharmaceuticals and new materials.[1, 2] Accordingly, the development of the synthesis of pyrrole containing compounds is a very active area of research. While a plethora of preparative methods for the synthesis of this five-membered ring structure have been developed[2] there still remains a great need to find new, efficient, and practical methodologies for the preparation of functionalized pyrroles from inexpensive and available starting materials. Although ring-to-ring intramolecular isomerization is a 100% atom economical reaction,[3]

the use of this type of processes for the preparation of pyrrole derivatives is quite rare. The dehydrative rearrangement of aryl and alkyl substituted isoxazolines gives the corresponding pyrroles in 32-75% yields.[4] To the best of our knowledge, only a single example of an isoxazole-pyrrole isomerization was published.[5] It involved the Boulton-Katritzky rearrangement[6] of diethyl 2-(4-(ethoxycarbonyl)-5-methylisoxazol-3-yl)pent-2-enedioate to diethyl 5-(1-ethoxy-1,3-dioxobutan-2-yl)-1*H*-pyrrole-2,4-dicarboxylate induced by a base (Scheme 1).



Scheme 1. Pyrrole synthesis via isomerization of 4-vinylizoxazoles

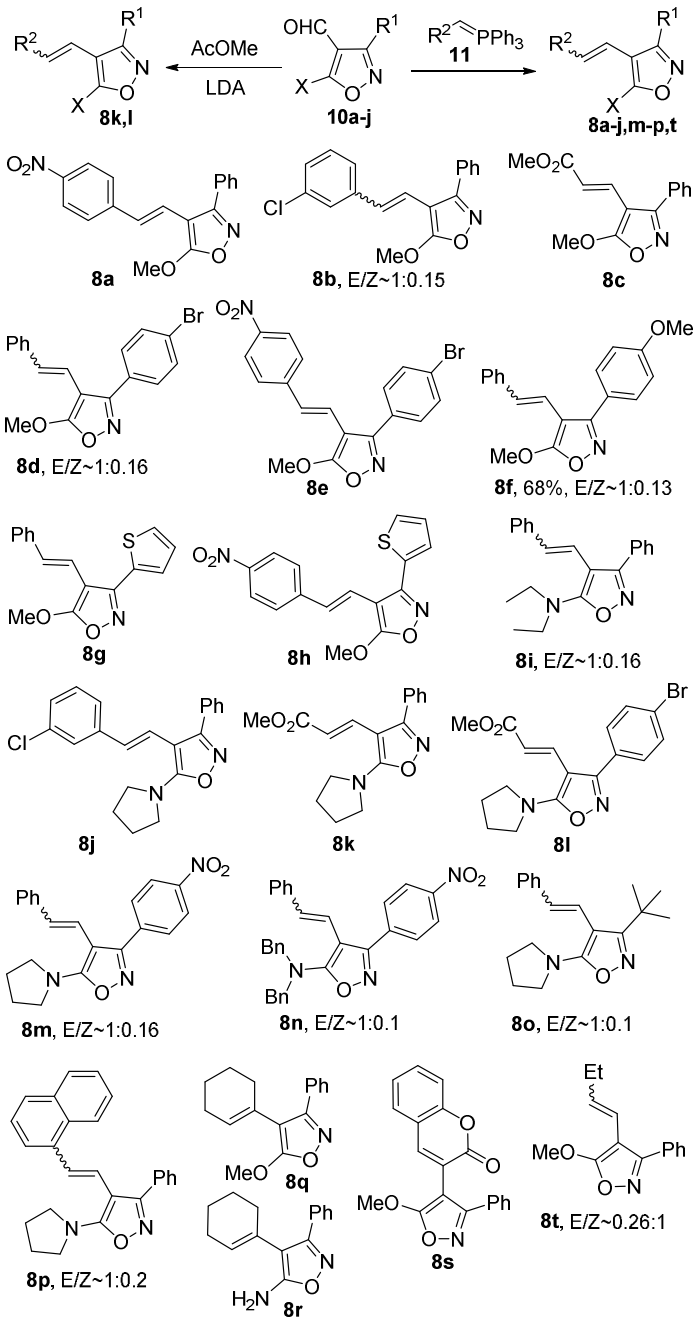
5-Heterosubstituted isoxazoles can be transformed into the corresponding 2*H*-azirines by reactions with metal salts or complexes.[7] Iron(II) salts are the most effective catalysts for this isomerization.[7, 8] It was assumed that the transformation proceeds via the formation of the isoxazole Fe-complex **2**, which facilitates the cleavage of the N-O bond, and the subsequent 1,3-cyclization of the iron vinyl nitrene complex **3**, leading to 2*H*-azirine **5** (Scheme 2).[7, 8] We argued that, if the starting isoxazole **1** will contain the vinyl-substituent at the position 4, the corresponding iron vinyl nitrene complex **3** can, along with the 1,3-cyclization into complex **4**, undergo the 1,5-cyclization into complex **6** to form pyrrole derivatives **7**.



Scheme 2. Possible pathways of Fe(II)-catalyzed transformations of 4-vinylizoxazoles

RESULTS AND DISCUSSION

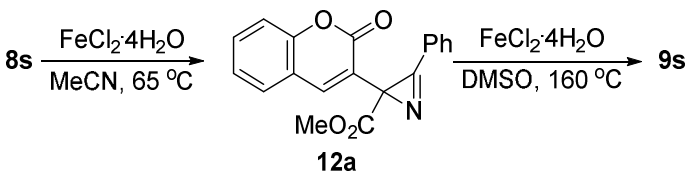
To start with, we heated an acetonitrile solution of isoxazole **8a** in the presence of 10 mol % of $FeCl_2 \cdot 4H_2O$ at 65 °C. The starting material was completely consumed in 6 h giving pyrrole **9a** as the only product (Table 1). It was isolated by column chromatography in 97% yield. To evaluate the scope of the reaction we synthesized a series of 4-vinylisoxazoles **8a-o,t** with different substituents at the C3 and C5 positions of the ring and at position C2 of the alkenyl moiety (Scheme 3). Isoxazoles **8a-j,m-p,t** were prepared by the Wittig reaction of isoxazole-4-carbaldehydes **10a-j** with the ylides **11a-g**. Compounds **8k,l** with $R^2 = CO_2Me$ and X = pyrrolidin-1-yl were prepared by condensation of the corresponding isoxazole-4-carbaldehydes **10f,g** with methyl acetate. Isoxazoles **8a,c,e,g,h,j-l** are obtained as pure *E*-isomers, while isoxazoles **8b,d,f,i,m-p** are *E*/*Z*-mixtures containing less than 17% of the *Z*-isomer. Only compound **8t** contained the *Z*-isomer as the major isomer (1:0.26 ratio). Isoxazoles **8q-s**, bearing unsaturated cyclic substituents with the appropriate C=C bond, (Scheme 3) were additionally synthesized to check whether the reaction could be used for the preparation of fused pyrrole derivatives.



Scheme 3. Synthesis of vinylisoxazoles **8**

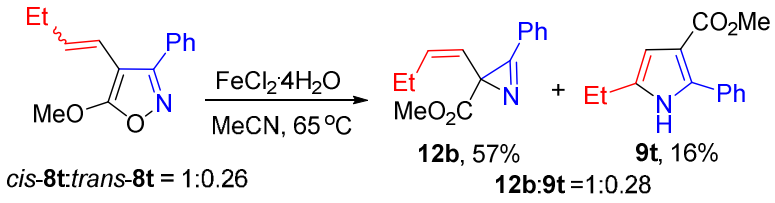
The results of Fe(II)-catalytic isomerization of 4-vinylisoxazoles **8a-t** are depicted in Table 1. Aryl groups with halogen, nitro or methoxy substituents, thien-2-yl, methoxycarbonyl, amino and *N*-substituted amino groups tolerate the reaction conditions, providing good yields of pyrroles **9a-t**. All the new compounds were characterized by ^{1}H and ^{13}C NMR and mass spectrometry. The structure

of compound **9e** was also established by single crystal X-ray diffraction (see the Supporting Information). Pyrroles **9a-m, p-r** were obtained by heating the corresponding 4-vinylisoxazoles with a catalytic amount of $FeCl_2 \cdot 4H_2O$ in MeCN at 65 °C for 4-6 h. For the isomerization of isoxazoles **8n**, **o** to pyrroles **9n**, **o** within a reasonable time, a higher temperature, 80 °C, was required. When the reaction of isoxazole **8s** was carried out under the standard reaction conditions (10 mol % of $FeCl_2 \cdot 4H_2O$, MeCN, 65 °C), the only product was azirine **12a** (88%). The use of harsher isomerization conditions (DMSO, 160 °C) resulted in the expected pyrrole **9s** (80%) formation. It is worth noting that heating azirine **12a** at 160 °C in DMSO in the absence of $FeCl_2 \cdot 4H_2O$ did not give even traces of pyrrole **9s**. At the same time, heating azirine **12a** with $FeCl_2 \cdot 4H_2O$ at 160 °C in DMSO led to a quantitative transformation of the azirine into pyrrole **9s** (Scheme 4).



Scheme 4. The reaction of isoxazole **8r**

Unexpectedly, when a mixture of the *cis*- and *trans*-isomers of propenylisoxazole *cis*- and *trans*-**8t**, in the ratio 1:0.26, was reacted with a catalytic amount of $FeCl_2 \cdot 4H_2O$ in MeCN at 65 °C, azirine **12b** and pyrrole **9t** were isolated in practically the same ratio (1:0.28) (Scheme 5).

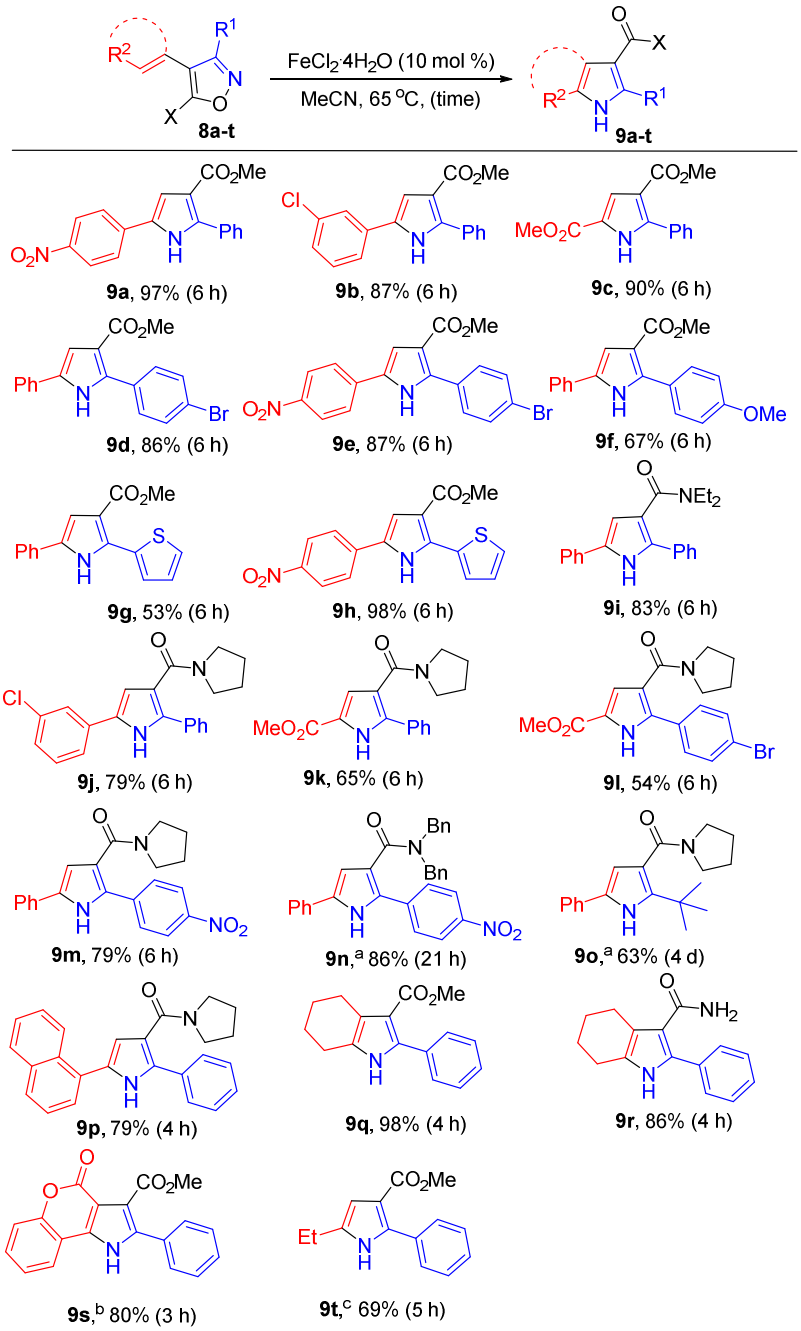


Scheme 5. The reaction of isoxazoles *cis*- and *trans*-**8t**

This, together with the results presented above, suggests that azirine **12b** and pyrrole **9t** are formed from *cis*- and *trans*-**8t**, respectively. Therefore, this reaction is a good candidate for checking the

reaction mechanism by quantum-chemical calculations to determine factors that affect the isomerization pathway.

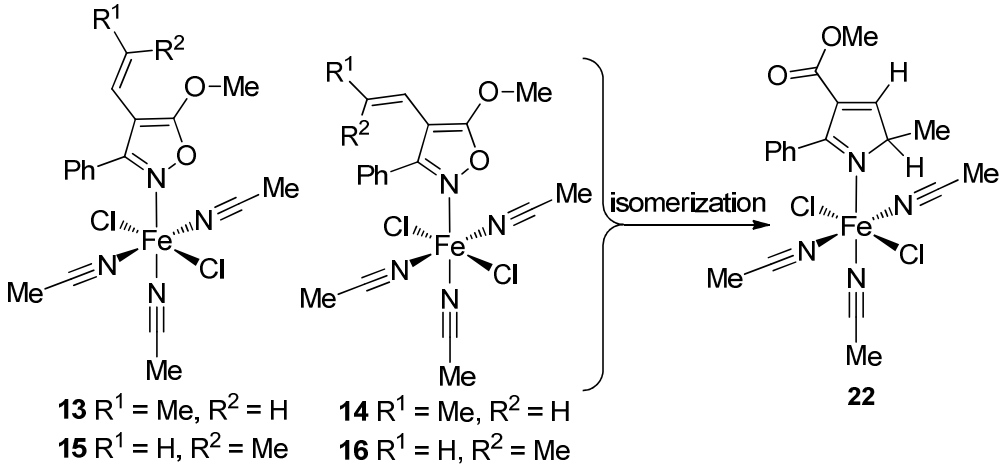
Table 1. Synthesis of substituted pyrroles **9**



[a] 80 °C; [b] DMSO, 160 °C; [c] 110 °C

Taking into account (a) the crystal structure of $FeCl_2 \cdot 4H_2O$,[9] (b) the same results on Fe(II)-catalyzed reactions of isoxazoles **8**, in which anhydrous $FeCl_2$ was used instead of the tetrahydrate, (c) the use of MeCN as the reaction media, as well as (d) the ability of MeCN to displace water in $FeCl_2 \cdot 4H_2O$

with the formation of $Fe(MeCN)_4Cl_2$,[10] we chose complexes **13-16** as the starting model compounds for calculations (Scheme 6). Fe-pyrrole complex **22**, the most probable precursor of the 1*H*-pyrrole of type **9**, was computed as the final isomerization product of complexes **13-16**.



Scheme 6. Model complexes **13-16, 22** for calculations

For a formally d^6 Fe(II) complex four spin states are possible: singlet, triplet, quintet, and sextet. The quintet state is usually the thermodynamically most stable in solution.[11] Calculations of iron complexes **13**, **14**, **22** and **TS**$^{21\text{-}22}$ were performed (Table 2, Figs. 1, 2, Schemes S1, S2 in the Supporting Information) and it was found that the singlet, triplet and sextet states are much higher in energy than the quintet states for complexes **13**, **14**, **22** and **TS**$^{21\text{-}22}$.

Table 2 Relative Gibbs free energies (in kcal mol^{-1}, 298 K, PCM model for MeCN) of different spin states for iron complexes **13**, **14**, **22** and **TS**$^{21\text{-}22}$ computed at the DFT B3LYP/6-31G(d){CHNOCl}/SDD{Fe} level.

Complex	Singlet	Triplet	Quintet	Septet
13	31.6	25.8	0.0	59.8
14	31.0	25.4	0.0	60.2
22	31.7	25.4	0.0	54.7
TS$^{21\text{-}22}$	36.6	21.7	0.0	21.7

This suggested a single-state reactivity of the complexes under consideration and, therefore, the transformation pathways of complexes **13**-**16**, leading to the pyrrole and azirine products were computed in the quintet state.

According to the calculations (Fig. 1, Scheme S1 in the Supporting Information), there are two possible reaction pathways for the formation of pyrrole **22** from isoxazole complex **13**.

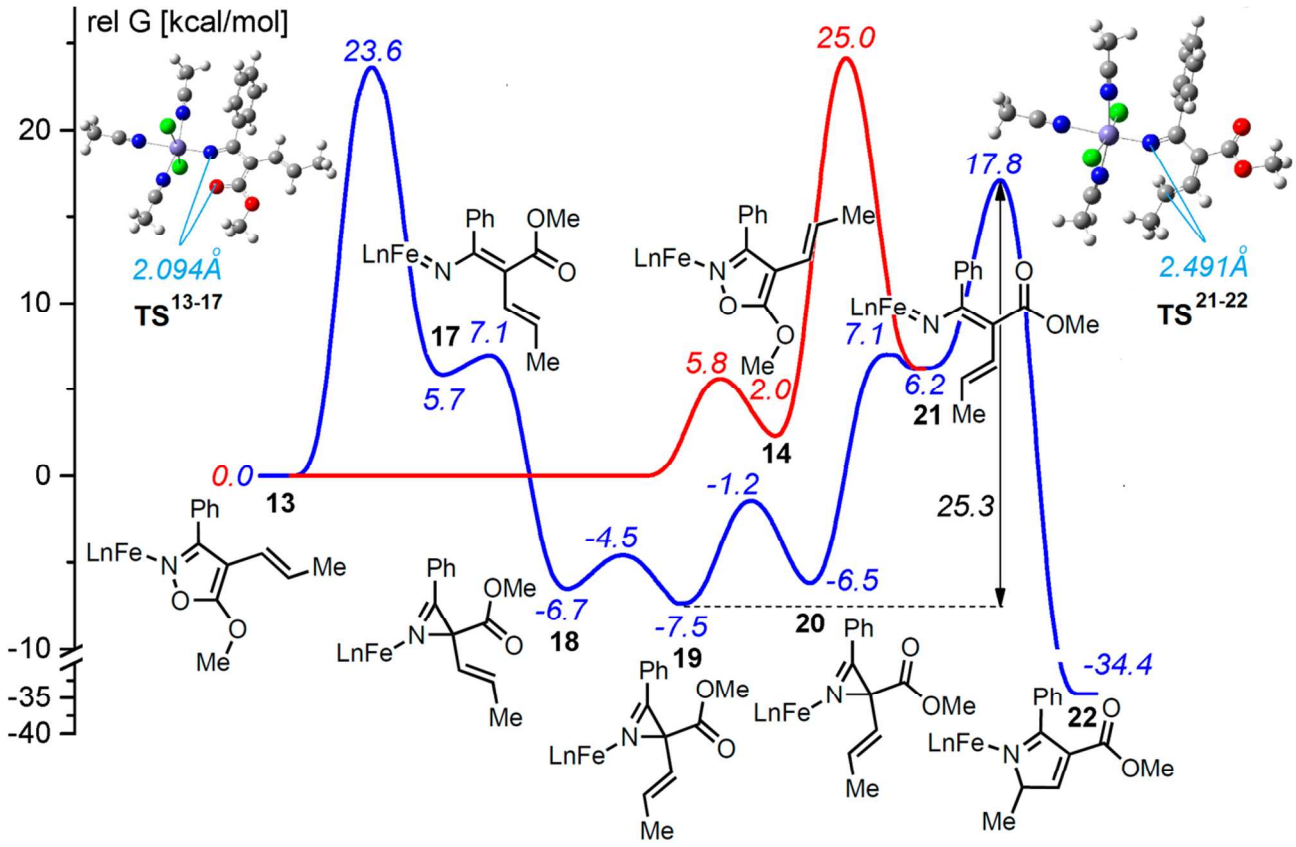


Figure 1. Energy profiles for the transformations of complexes **13**, **14**. Relative Gibbs free energies (in kcal mol^{-1}, 298 K, PCM model for MeCN) computed at the DFT B3LYP/6-31G(d){CHNOCl}/SDD{Fe} level.

The first pathway (blue) involves the isoxazole ring opening in **13** with the formation of Fe-nitrene complex **17**, the cyclization of **17** into Fe-azirine complex **18**, and the low-barrier conformational transformations of the latter to conformer **20**, which can undergo the azirine ring opening to give Fe-

nitrene complex **21** in a conformation appropriate for cyclization. This then cyclizes irreversibly into pyrrole **22**. The second pathway (red) involves the low barrier rotation of the propenyl group of isoxazole complex **13** around the C-C bond to form conformer **14**, followed by the isoxazole ring opening, leading directly to Fe-nitrene complex **21** (precursor of pyrrole **22**). Complex **21**, however, has a very low barrier for the cyclization into azirine **20**. The free energy barrier for the transformation of the lowest energy azirine complex **19** into pyrrole **22** is about 25 kcal mol^{-1}.

The change of the conformation of the C=C double bond from *trans* to *cis* alters the isomerization pathway of complex **15** compared with complex **13** due to additional steric hindrance (Fig. 2, Scheme S2 in the Supporting Information).

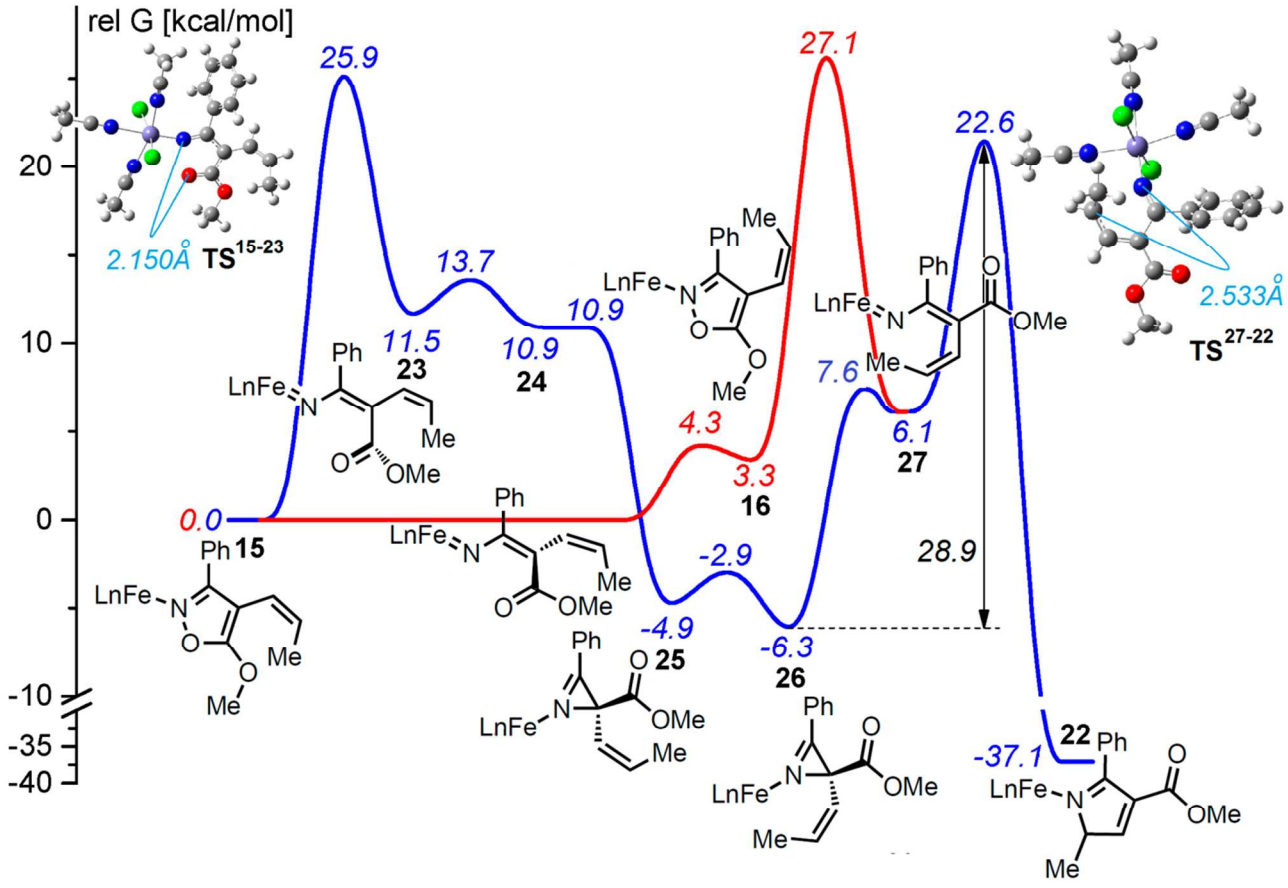


Figure 2. Energy profiles for the transformations of complexes **15**, **16**. Relative Gibbs free energies (in kcal mol^{-1}, 298 K, PCM model for MeCN) computed at the DFT B3LYP/6-31G(d){CHNOCl}/SDD{Fe} level.

According to the calculations the isoxazole ring opening in **15** leads to Fe-nitrene complex **23**, which transforms into conformer **24**. The latter undergoes an almost barrierless cyclization into Fe-azirine complex **25**, which, via a low barrier, gives a more stable conformer **26**. The latter can undergo the azirine ring opening to give Fe-nitrene complex **27**, which can cyclize into pyrrole **22**. The second pathway (red) involves the low barrier rotation of the propenyl group of isoxazole complex **15** around the C-C bond to form conformer **16**, followed by the isoxazole ring opening in **16**, leading directly to Fe-nitrene complex **27**, which has a very low barrier for the cyclization into azirine **26**. The free energy barrier for the transformation of the lowest energy azirine complex **26** into pyrrole **22** is about 29 kcal mol^{-1}, i.e. by 4 kcal mol^{-1} higher than for the transformation **19→22**.

The change from the Me-group in the model compounds to Et, like in **8s**, will further increase the difference in the barriers for cyclization of the Et-analogs of nitrene complexes **21** and **27**. Therefore we can conclude that the formation of azirine **12b** and pyrrole **9t** from *cis*- and *trans*-**8t**, respectively, under Fe(II)-catalysis in MeCN at 65 °C is due to a much higher barrier for the transformation of the corresponding Fe-(*cis*-R-vinyl)azirine complex into the pyrrole complex compared with the *trans*-isomer due to a higher steric crowding of the vinyl moiety. The exclusive formation of only pyrrole **9t** (69%) from the mixture of *cis*- and *trans*-isomers of propenylisoxazole *cis*- and *trans*-**8t** at a higher temperature (110 °C) is in full agreement with the calculations .

Thus, according to the calculations and experimental results the increase of steric congestion in isoxazole hinders the transformation of the transient Fe-azirine complex into the corresponding pyrrole derivative, thereby requiring a higher temperature for isomerization.

CONCLUSION

The first syntheses of pyrrole derivatives by Fe(II)-catalyzed intramolecular isomerization of isoxazoles are developed. 5-Alkoxy, amino or *N*,*N*-dialkylamino-3-aryl/alkyl-4-(2-R-

vinyl)isoxazoles afford 2-aryl/alkyl-5-aryl/alkyl/methoxycarbonyl-1*H*-pyrrol-3-carboxylic acid derivatives typically under mild reaction condition with a cheap and available $FeCl_2 \cdot 4H_2O$ as a catalyst. The isomerization of 5-alkoxy/amino-3-arylisoxazoles, bearing cyclic substituents with the appropriate C=C bond at the position 4, affords the corresponding fused pyrroles. The DFT calculations suggest a single-state quintet reactivity of the Fe(II)-complexes of the heterocycles under consideration and Fe(II)-nitrene complexes. According to the calculations, the isomerization involves isoxazole ring opening of the Fe(II)-isoxazole complex to form a Fe(II)-nitrene complex. The latter undergoes a low-barrier cyclization into the Fe(II)-complex of 2-(2-R-vinyl)-2*H*-azirine. The *trans*-isomer of the azirine complex can give a Fe(II)-(*trans*-2-R-vinyl)-substituted nitrene complex, which has the appropriate conformation to undergo a 1,5-cyclization into the 2*H*-pyrrole derivative. The free energy barrier for the transformation of the Fe(II)-complex of 2-(*cis*-2-R-vinyl)-2*H*-azirine into the pyrrole is much higher and this prevents the formation of the pyrrole derivative under mild conditions due to higher steric crowding of the alkenyl moiety, so that in this case the final isomerization product is 2-(*cis*-2-R-vinyl)-2*H*-azirine. Since increase of steric congestion at the vinyl moiety hinders the transformation of an intermediate Fe-azirine complex into the corresponding pyrrole, such isoxazoles require the use of harsher reaction conditions for isomerization to pyrroles.

EXPERIMENTAL SECTION

General Information and Methods

Melting points were determined on a capillary melting point apparatus using unsealed capillary. ^1H (400 MHz) and ^{13}C (100 MHz) NMR spectra were recorded in $CDCl_3$ and DMSO-d_6 with NMR-spectrometer. Chemical shifts (δ) are reported in parts per million downfield from tetramethylsilane (TMS δ 0.00). ^1H NMR spectra were calibrated according to the residual peak of $CDCl_3$ (7.26 ppm) or DMSO-d_6 (2.50 ppm). For new compounds $^{13}C\{^1H\}$ and ^{13}C DEPT135 were recorded and

calibrated according to the peak of $CDCl_3$ (77.00 ppm) or DMSO-d_6 (39.51 ppm). For all new final pyrroles, initial isoxazoles and for the most of undescribed intermediate substances $^{13}C\{^1H\}$ and ^{13}C DEPT135 were recorded and calibrated according to the peak of $CDCl_3$ (77.00 ppm). Mass spectra were recorded on a HRMS-ESI-QTOF mass-analyzer, electrospray ionization, positive mode. Thin-layer chromatography (TLC) was conducted on aluminium sheets with 0.2 mm silica gel with fluorescent indicator, silica 60 M was used for column chromatography. The known compounds were prepared by published procedures: 5-chloro-3-phenylisoxazole-4-cabaldehyde **29a**,[12] 5-chloro-3-(4-nitrophenyl)isoxazole-4-cabaldehyde **29c**,[13] 3-(*tert*-butyl)-5-chloroisoxazole-4-carbaldehyde **29d**,[13] 5-methoxy-3-phenylisoxazole-4-carbaldehyde **10a**[12] and phosphonium salts **11**.[14-16] Compounds **28a,b** were synthesized by a slightly modified literature procedure.[17] Compounds **10c**,**d** and **10e-j** were synthesized by slightly modified literature procedures.[8c]

Synthesis of Starting Materials

*3-(4-Bromophenyl)-5-methoxyisoxazole-4-carbaldehyde (**10b**)*. *N,N*-Dimethylformamide (DMF) (6.0 mL, 78 mmol) was added dropwise to phosphorus oxychloride (15.4 mL, 165 mmol) under stirring and ice-cooling. The solution was stirred for 15 min, put in freezer (-18 °C) and held there until a colorless precipitate was formed. 3-(4-Bromophenyl)isoxazol-5(4*H*)-one (2.33 g, 9.7 mmol) was added to the preheated to 75 °C the reaction mixture and stirred for 3 h. The reaction mixture was cooled and poured onto crushed ice. The precipitate formed was filtered off, washed with water and dried in vacuum to give 1.93 g (70%) of 3-(4-bromophenyl)-5-chloroisoxazole-4-carbaldehyde (**29b**) as a yellowish solid, mp 55-56 °C (water). ^1H NMR ($CDCl_3$): δ = 7.64-7.66 (m, 2H), 7.69-7.72 (m, 2H), 9.96 (s, 1H). ^{13}C NMR ($CDCl_3$): δ = 113.2 (C), 125.2 (C), 126.0 (C), 130.6 (CH), 132.1 (CH), 162.1 (C), 163.4 (C), 181.5 (CH). Aldehyde **29b** was used without further purification. To a suspension of aldehyde **29b** (715 mg, 2.5 mmol) in absolute methanol (10 mL) a solution of sodium methoxide, prepared from sodium (230 mg, 10.0 mmol) and absolute methanol (5 mL), was added dropwise. The reaction mixture was stirred for 30 min, poured into cold water and acidified

with acetic acid. The precipitate was filtered off, washed with water and dried on air to give 557 mg (79%) of pure product as a yellowish solid, mp 105-106 °C (water/MeOH). ^{1}H NMR ($CDCl_3$): δ = 4.35 (s, 3H), 7.61-7.63 (m, 2H), 7.71-7.73 (m, 2H), 9.74 (s, 1H). ^{13}C NMR ($CDCl_3$): δ = 59.0 (CH_3), 96.0 (C), 125.5 (C), 126.4 (C), 130.4 (CH), 131.9 (CH), 162.9 (C), 175.8 (C), 181.0 (CH). HRMS (ESI-TOF) (m/z): $[M+H]^+$ Calcd. for $C_{11}H_9BrNO_3^+$ 281.9760; Found 281.9790.

*5-Methoxy-3-(4-methoxyphenyl)isoxazole-4-carbaldehyde (**10c**).* A mixture of 3-(4-methoxyphenyl)isoxazol-5(4*H*)-one (1.68 g, 8.79 mmol) and triethyl orthoformate (6 g) was heated at 100-110 °C for 1 h. The volatiles were evaporated in vacuum and the residue was suspended in 2% aq. H_2SO_4 and stirred for 1 h. Water was evaporated and the residue was stirred with a mixture of diethyl ether/hexane (1:1, 10 mL). The precipitate formed was filtered off, washed with cold ethanol and dried on air to give 3-(4-methoxyphenyl)-5-oxo-4,5-dihydroisoxazole-4-carbaldehyde (**28a**) (1.26 g, 65%), as an orange solid, mp 149-150 °C (dec.). ^{1}H NMR spectrum of **28a** consisted of very wide signals due to the tautomeric equilibrium. HRMS (ESI-TOF) (m/z): 220.0604 Calcd. for $C_{11}H_{10}NO_4^+$ $[M+H]^+$; Found 220.0596. Aldehyde **28a** was used without further purification. To a suspension of aldehyde **28a** (1.00 g, 4.56 mmol) in THF (10 mL) a solution of diazomethane, prepared from *N*-nitroso-*N*-methylurea (1.41 g, 13.6 mmol), 40% aq KOH (3.45 g, 61.2 mmol) and ether(10 mL), was slowly added under stirring and ice-cooling. The reaction mixture was stirred for 1 h at room temperature, the excess of diazomethane was quenched with acetic acid and the solvents were removed in vacuum. The residue was filtered through a pad of silica, eluting with light petroleum/ethyl acetate (3:1) to give, after evaporation of the solvents, washing of the precipitate with pentane and drying on air, aldehyde to give 153 mg (14%) of aldehyde **10c** as a colorless solid, mp 112-113 °C (ethyl acetate/light petroleum). ^{1}H NMR ($CDCl_3$): δ = 3.86 (s, 3H), 4.33 (s, 3H), 7.00 (d, J = 8.9 Hz, 2H), 7.78 (d, J = 8.9 Hz, 2H), 9.74 (s, 1H). ^{13}C NMR ($CDCl_3$): δ = 55.4 (CH_3), 58.8 (CH_3), 96.1 (C), 114.1 (CH), 119.7 (C), 130.4 (CH), 161.6 (C), 163.6 (C), 175.4 (C), 181.5 (CH). HRMS (ESI-TOF) (m/z): $[M+H]^+$ Calcd. for $C_{12}H_{12}NO_4^+$ 234.0761; Found 234.0742.

*5-Methoxy-3-(thiophen-2-yl)isoxazole-4-carbaldehyde (**10d**).* A mixture of 3-(thiophen-2-yl)isoxazol-5(4*H*)-one (1.52 g, 9.10 mmol) and triethyl orthoformate (6 g) was heated at 100-110 °C for 1 h. The volatiles were evaporated in vacuum and the residue was suspended in 2% aq. H_2SO_4 and stirred for 1 h. Water was evaporated and a mixture of diethyl ether/hexane (1:1, 10 mL) was added to the residue. The precipitate formed was filtered off, washed with cool ethanol and dried on air to give 5-oxo-3-(thiophen-2-yl)-4,5-dihydroisoxazole-4-carbaldehyde (**28b**) (1.23 g, 69%), as an orange solid, mp 145-146 °C (dec.), ^{1}H NMR spectrum of **28b** consisted of very wide signals due to the tautomeric equilibrium. Aldehyde **28b** was used without further purification. To a suspension of aldehyde **28b** (1.09 g, 5.56 mmol) in THF (10 mL) a solution of diazomethane, obtained from *N*-nitroso-*N*-methylurea (1.55 g, 15.0 mmol), 40% aq KOH (3.45 g, 61.2 mmol) and ether (10 mL), was slowly added under stirring and ice-cooling. The reaction mixture was stirred for 1 h at rt, the excess of diazomethane quenched with acetic acid and the solvents were removed in vacuum. The residue was filtered through a pad of silica, eluting with light petroleum/ethyl acetate (3:1) to give, after evaporation of the solvents, washing of the precipitate with pentane and drying on air, aldehyde **10d** as a colorless solid, mp 95-96 °C (ethyl acetate/light petroleum), yield 351 mg (30 %). ^{1}H NMR ($CDCl_3$): δ = 4.33 (s, 3H), 7.16 (dd, *J* = 3.8, 1.1 Hz, 1H), 7.49 (dd, *J* = 5.0, 1.1 Hz, 1Hz), 8.19 (dd, *J* = 5.0, 3.8 Hz, 1H), 9.82 (s, 3H). ^{13}C NMR ($CDCl_3$): δ = 58.9 (CH_3), 95.8 (C), 127.8 (CH), 128.2 (C), 129.1 (CH), 132.3 (CH), 157.9 (C), 176.1 (C), 180.7 (CH). HRMS (ESI-TOF) (m/z): $[M+Na]^+$ Calcd. for $C_9H_7NNaO_3S^+$ 232.0039; Found 232.0038.

General procedure (A) for the synthesis of 5-amino-3-substituted isoxazole-4-carbaldehydes 10e-j. An excess of an appropriate amine (2 mmol) and potassium carbonate (1.5 mmole) was added to a solution of 5-chloroisoxazole-4-carbaldehyde **29** (1 mmol) in a minimum volume of dry DMF. The mixture was stirred at room temperature until the reaction completion (monitored by TLC). Water was added to the reaction mixture and the precipitate formed was filtered off, washed with water and dried on air, then washed with ether and dried again to give pure product. If the product

wasn't crystallized, it was extracted with ether and the ether solution was washed with brine and dried over sodium sulfate. Ether was evaporated and the residue was purified by filtration through a pad of silica. After evaporation of solvents, the residue was washed with hexane, dried on air to give pure compound.

*5-(N,N-Diethylamino)-3-phenylisoxazole-4-carbaldehyde (**10e**).* Compound **10e** was prepared from 5-chloro-3-phenylisoxazole-4-carbaldehyde **29a** (518 mg, 2.5 mmol), diethylamine (366 mg, 5.0 mmol) and potassium carbonate (525 mg, 3.8 mmol) for 1 week according to the general procedure A. The product was purified by filtration through a pad of silica (light petroleum/ethyl acetate, 8:1) to give a yellow solid (380 mg, 62%), mp 87-88 °C (light petroleum/EtOAc). ^{1}H NMR ($CDCl_3$): δ = 1.30 (t, *J* = 7.1 Hz, 6H), 3.82 (q, *J* = 7.1 Hz, 4H), 7.46-7.50 (m, 3H), 7.55-7.57 (m, 2H), 9.32 (s, 1H). ^{13}C NMR ($CDCl_3$): δ = 13.7 (CH_3), 45.6 (CH_2), 96.5 (C), 128.1 (C), 128.7 (CH), 129.3 (CH), 130.0 (CH), 166.6 (C), 167.8 (C), 181.5 (CH). HRMS (ESI-TOF) (m/z): $[M+H]^+$ Calcd. for $C_{14}H_{17}N_2O_2^+$ 245.1285; Found 245.1286.

*3-Phenyl-5-(pyrrolidin-1-yl)isoxazole-4-carbaldehyde (**10f**)*. Compound **10f** was prepared from 5-chloro-3-phenylisoxazole-4-carbaldehyde **29a** (882 mg, 4.25 mmol), pyrrolidine (604 mg, 8.50 mmol) and potassium carbonate (880mg, 6.38 mmol) for 0.5 h according to the general procedure A. A colorless solid, mp 120-121 °C (DMF/water), yield 735 mg (71%). ^{1}H NMR ($CDCl_3$): δ = 2.03-2.06 (m, 4H), 3.84-3.88 (m, 4H), 7.46-7.50 (m, 3H), 7.59-7.62 (m, 2H), 9.45 (s, 1H). ^{13}C NMR ($CDCl_3$): δ = 25.4 (CH_2), 50.1 (CH_2), 97.1 (C), 128.2 (C), 128.6 (CH), 129.2 (CH), 130.1 (CH), 165.3 (C), 167.3 (C), 181.6 (CH). HRMS (ESI-TOF) (m/z): $[M+H]^+$ Calcd. for $C_{14}H_{15}N_2O_2^+$ 243.1128; Found 243.1126.

*3-(4-Bromophenyl)-5-(pyrrolidin-1-yl)isoxazole-4-carbaldehyde (**10g**)*. Compound **10g** was prepared from 3-(4-bromophenyl)-5-chloroisoxazole-4-carbaldehyde **29b** (551 mg, 1.92 mmol), pyrrolidine (273 mg, 3.85 mmol) and potassium carbonate (398 mg, 2.88 mmol) for 0.5 h according to the general procedure A. A colorless solid, mp 137-138 °C (DMF/water), yield 467 mg (76%). ^{1}H

NMR ($CDCl_3$): δ = 2.04-2.07 (m, 4H), 3.82-3.86 (m, 4H), 7.49-7.51 (m, 2H), 7.60-7.61 (m, 2H), 9.48 (s, 1H). ^{13}C NMR ($CDCl_3$): δ = 25.4 (CH_2), 50.1 (CH_2), 97.1 (C), 124.6 (C), 127.2 (C), 130.7 (CH), 131.8 (CH), 164.1 (C), 167.2 (C), 180.9 (CH). HRMS (ESI-TOF) (m/z): $[M+H]^+$ 321.0233 Calcd. for $C_{14}H_{14}BrN_2O_2^+$; Found 321.0224.

*3-(4-Nitrophenyl)-5-(pyrrolidin-1-yl)isoxazole-4-carbaldehyde (**10h**).* Compound **10h** was prepared from 5-chloro-3-(4-nitrophenylisoxazole)-4-carbaldehyde **29c** (907 mg, 3.59 mmol), pyrrolidine (512 mg, 7.20 mmol) and potassium carbonate (745 mg, 5.40 mmol) for 0.5 h according to the general procedure A. A colorless solid, mp 166-167 °C (DMF/water), yield 942 mg (91%). ^1H NMR (DMSO-d_6): δ = 1.99-2.02 (m, 4H), 3.72-3.75 (m, 4H), 7.87-7.90 (m, 2H), 8.31-8.33 (m, 2H), 9.60 (s, 1H). ^{13}C NMR (DMSO-d_6): δ = 24.9 (CH_2), 49.6 (CH_2), 96.8 (C), 123.3 (CH), 130.4 (CH), 135.0 (C), 148.9 (C), 161.7 (C), 168.1 (C), 180.3 (CH). HRMS (ESI-TOF) (m/z): $[M+H]^+$ Calcd. for $C_{14}H_{14}N_3O_4^+$ 288.0979; Found 288.0972.

*5-(Dibenzylamino)-3-(4-nitrophenyl)isoxazole-4-carbaldehyde (**10i**).* Compound **10i** was prepared from 5-chloro-3-(4-nitrophenylisoxazole)-4-carbaldehyde **29c** (233 mg, 0.92 mmol), dibenzylamine (364 mg, 1.85 mg) and potassium carbonate (192 mg, 1.38 mmol) for 2 h at 40 °C according to the general procedure A. A colorless solid, mp 160-161 °C (DMF/water), yield 371 mg (90%). ^1H NMR ($CDCl_3$): δ = 4.97 (s, 4H), 7.26-7.28 (m, 4H), 7.33-7.41 (m, 6H), 7.83 (d, J = 8.7 Hz, 2H), 8.36 (d, J = 8.7 Hz, 2H), 9.41 (s, 1H). ^{13}C NMR ($CDCl_3$): δ = 53.3 (CH_2), 96.9 (C), 123.8 (CH), 128.0 (CH), 128.3 (CH), 129.0 (CH), 130.4 (CH), 134.4 (C), 135.1 (C), 149.0 (C), 164.6 (C), 169.3 (C), 180.6 (C). HRMS (ESI-TOF) (m/z): $[M+Na]^+$ Calcd. for $C_{24}H_{19}N_3NaO_4^+$ 436.1268; Found 436.1286.

*3-(tert-Butyl)-5-(pyrrolidin-1-yl)isoxazole-4-carbaldehyde (**10j**).* Compound **10j** was prepared from 3-(*tert*-butyl)-5-chloroisoxazole-4-carbaldehyde **29d** (350 mg, 1.87 mmol), pyrrolidine (266 mg, 3.74 mmol) and potassium carbonate (387 mg, 2.80 mmol) for 0.5 h according to the general procedure A. A colorless solid, mp 128-129 °C (DMF/water), yield 375 mg (91%). ^1H NMR (DMSO-d_6): δ = 1.32 (s, 9H), 1.94-1.97 (m, 4H), 3.61-3.65 (m, 4H), 9.69 (s, 1H). ^{13}C NMR

(DMSO-d_6): δ = 24.8 (CH_2), 27.5 (CH_3), 33.3 (C), 49.6 (CH_2), 97.6 (C), 169.4 (C), 169.8 (C), 180.0 (CH). HRMS (ESI-TOF) (m/z): 245.1260 Calcd. for $C_{12}H_{18}N_2NaO_2^+$ $[M+Na]^+$; Found 245.1263.

General procedure B for the synthesis of 4-alkenylisoxazoles 8 by Wittig reaction. Compounds **8a-j,m-o,s** were synthesized by a slightly modified literature procedure.[18] Potassium *tert*-butoxide was added to a suspension of alkyltriphenylphosphonium salt **11** (1.5-1.6 mmol) in dry THF. The mixture was stirred for 0.5 h at rt, and then aldehyde **10** (1.0 mmol) was added. The reaction mixture was refluxed until full conversion of starting aldehyde. If decomposition of phosphonium ylide was proceeded faster, than the reaction ended (bleaching of reaction mixture), freshly prepared ylide in dry THF was added. After full conversion of aldehyde, the reaction mixture was filtered, the solvent was evaporated, and the residue purified by column chromatography, using a mixture of light petroleum ether and ethyl acetate as eluent. The solid obtained after evaporation of the solvents was washed with pentane.

*(E)-5-Methoxy-4-(4-nitrostyryl)-3-phenylisoxazole (**8a**).* Compound **8a** was prepared from (4-nitrobenzyl)triphenylphosphonium bromide **11a** (406 mg, 0.85 mmol), potassium *tert*-butoxide (95 mg, 0.85 mmol) and 5-methoxy-3-phenylisoxazole-4-carbaldehyde **10a** (109 mg, 0.54 mmol) in THF (12 mL) for 2 h according to the general procedure B. The product was purified by column chromatography (light petroleum/ethyl acetate, 4:1-2:1). An orange solid, mp 145-146 °C (light petroleum/ethyl acetate), yield 124 mg (72%). ^{1}H NMR ($CDCl_3$): 4.32 (s. 3H), 6.84 (d, J = 16.5 Hz, 1H), 7.00 (d, J = 16.5 Hz, 1H), 7.45-7.47 (m, 2H), 7.52-7.54 (m, 3H), 7.60-7.63 (m, 2H), 8.15-8.16 (m, 2H). ^{13}C NMR ($CDCl_3$): 58.3 (CH_3), 91.2 (C), 119.9 (CH), 124.1 (CH), 126.2 (CH), 126.2 (CH), 128.6 (CH), 128.99 (CH), 129.01 (C), 130.1 (CH), 144.3 (C), 146.4 (C), 164.3 (C), 169.7 (C). HRMS (ESI-TOF) (m/z): $[M+H]^+$ Calcd. for $C_{18}H_{15}N_2O_4^+$ 323.1032; Found 323.1026.

*(E/Z)-4-(3-Chlorostyryl)-5-methoxy-3-phenylisoxazole (**8b**).* Compound **8b** was prepared from (3-chlorobenzyl)triphenylphosphonium chloride **11b** (511 mg, 1.20 mmol), potassium *tert*-butoxide (135 mg, 1.20 mmol) and 5-methoxy-3-phenylisoxazole-4-carbaldehyde **10a** (163 mg, 0.80 mmol)

in THF (8 mL) for 3 h according to the general procedure B. The product was purified by column chromatography (light petroleum/ethyl acetate, 8:1). A light yellow solid, mp 88-89 °C (light petroleum/ethyl acetate), yield 199 mg (80%), (*E*/*Z*)-mixture (~1:0.15). ^{1}H NMR ($CDCl_3$): for (*E*)-isomer δ = 4.29 (m, 3H), 6.67 (d, *J* = 16.5 Hz, 1H), 6.89 (d, *J* = 16.5 Hz, 1H), 7.15-7.27 (m, 3H), 7.34 (s, 1H), 7.61-7.63 (m, 2H), 7.51-7.52 (m, 3H); for (*Z*)-isomer 3.92 (s, 3H), 6.17 (d, *J* = 11.8 Hz, 1H), 6.54 (d, *J* = 11.8 Hz, 1H), 7.12-7.23 (m, 4H), 7.40-7.42 (m, 2H), 7.65-7.67 (m, 2H). ^{13}C NMR ($CDCl_3$): for (*E*)-isomer δ = 58.1 (CH_3), 91.3 (C), 116.6 (CH), 124.1 (CH), 125.8 (CH), 127.1 (CH), 127.5 (CH), 128.5 (CH), 128.9 (CH), 129.8 (CH), 129.8 (C), 129.9 (CH), 134.6 (C), 139.6 (C), 164.2 (C), 169.3 (C). HRMS (ESI-TOF) (m/z): $[M+H]^+$ Calcd. for $C_{18}H_{15}ClNO_2^+$ 312.0786; Found 312.0790.

*(E)-Methyl 3-(5-methoxy-3-phenylisoxazole-4-yl)acrylate (**8c**).* Compound **8c** was prepared from (2-methoxy-2-oxoethyl)triphenylphosphonium bromide **11c** (477 mg, 1.15 mmol), potassium *tert*-butoxide (129 mg, 1.15 mmol) and 5-methoxy-3-phenylisoxazole-4-carbaldehyde **10a** (145 mg, 0.71 mmol) in THF (8 mL)for 4 h according to the general procedure B. The product was purified by column chromatography (light petroleum/ethyl acetate, 5:1). A colorless solid, mp 115-116 °C (light petroleum/ethyl acetate), yield 81 mg (44%). ^{1}H NMR ($CDCl_3$): δ = 3.74 (s, 3H), 4.29 (s, 3H), 6.31 (d, *J* = 16.0 Hz, 1H), 7.37 (d, *J* = 16.0 Hz, 1H), 7.48-7.51 (m, 3H), 7.55-7.57 (m, 2H). ^{13}C NMR ($CDCl_3$): δ = 51.5 (CH_3), 58.4 (CH_3), 90.2 (C), 116.8 (CH), 128.4 (C), 128.5 (CH), 129.0 (CH), 130.2 (CH), 131.8 (CH), 164.6 (C), 167.7 (C), 170.9 (C). HRMS (ESI-TOF) (m/z): $[M+H]^+$ Calcd. for $C_{14}H_{14}NO_4^+$ 260.0917; Found 260.0918.

*(E/Z)-3-(4-Bromophenyl)-5-methoxy-4-styrylisoxazole (**8d**).* Compound **8d** was prepared from benzyltriphenylphosphonium bromide **11d** (433 mg, 1.00 mmol), potassium *tert*-butoxide (113 mg, 1.00 mmol) and 3-(4-bromophenyl)-5-methoxyisoxazole-4-carbaldehyde **10b** (169 mg, 0.60 mmol) in THF (10 mL)for 0.17 h according to the general procedure B. The product was purified by column chromatography (light petroleum/ethyl acetate, 5:1). A colorless solid, mp 65-69 °C (light

petroleum/ethyl acetate), yield 50 mg (23%), (*E*/*Z*)-mixture (~1:0.16). ^{1}H NMR ($CDCl_3$): for (*E*)-isomer δ = 4.28 (s, 3H), 6.61 (d, *J* = 16.5 Hz, 1H), 6.95 (d, *J* = 16.5 Hz, 1H), 7.20-7.24 (m, 1H), 7.29-7.33 (m. 2H), 7.36-7.38 (m, 2H), 7.52 (d, *J* = 8.4 Hz, 2H), 7.64 (d, *J* = 8.4 Hz, 2H); for (*Z*)-isomer δ = 3.88 (s, 3H), 6.10 (d, *J* = 11.7 Hz, 1H), 6.66 (d, *J* = 11.7 Hz, 1H), 7.20-7.24 (m, 3H), 7.29-7.38 (m, 2H), 7.51 (d, *J* = 8.6 Hz, 2H), 7.56 (d, *J* = 8.6 Hz, 2H). ^{13}C NMR ($CDCl_3$): for (*E*)-isomer δ = 58.1 (CH_3), 91.5 (C), 114.6 (CH), 124.3 (C), 125.9 (CH), 127.4 (CH), 128.4 (C), 128.6 (CH), 129.5 (CH), 130.1 (CH), 132.1 (CH), 137.5 (C), 163.2 (C), 169.3 (C); for (Z)-isomer δ = 57.8 (CH_3), 128.0 (CH), 128.1 (CH), 129.2 (CH), 131.8 (CH), 133.4 (CH). HRMS (ESI-TOF) (m/z): $[M+H]^+$ Calcd. for $C_{18}H_{15}BrNO_2^+$ 356.0281; Found 356.0273.

*(E)-3-(4-Bromophenyl)-5-methoxy-4-(4-nitrostyryl)isoxazole (**8e**)*. Compound **8e** was prepared from (4-nitrobenzyl)triphenylphosphonium bromide **11a** (478 mg, 1.00 mmol), potassium *tert*-butoxide (113 mg, 1.00 mmol) and 3-(4-bromophenyl)-5-methoxyisoxazole-4-carbaldehyde **10b** (169 mg, 0.60 mmol) in THF (12 mL) for 1 h according to the general procedure B. The product was purified by column chromatography (light petroleum/ethyl acetate, 5:1-2:1). An orange solid, mp 160-161 °C (light petroleum/ethyl acetate), yield 111 mg (46%). ^{1}H NMR (DMSO-d_6): δ = 4.31 (s, 3H), 6.95 (d, *J* = 16.4 Hz, 1H), 7.03 (d, *J* = 16.4 Hz, 1H), 7.60 (d, *J* = 8.4 Hz, 2H), 7.73 (d, *J* = 8.8 Hz, 2H), 7.79 (d, *J* = 8.4 Hz, 2H), 8.15 (d, *J* = 8.8 Hz, 2H). ^{13}C NMR (DMSO-d_6): δ = 59.0 (CH_3), 90.6 (C), 119.7 (CH), 123.9 (CH), 126.4 (CH), 126.8 (CH), 127.7 (C), 128.0 (C), 130.4 (CH), 132.2 (CH), 143.9 (C), 145.9 (C), 162.5 (C), 169.7 (C). HRMS (ESI-TOF) (m/z): $[M+Na]^+$ Calcd. for $C_{18}H_{13}BrN_2NaO_4^+$ 422.9951; Found 422.9968.

*(E/Z)-5-Methoxy-3-(4-methoxyphenyl)-4-styrylisoxazole (**8f**)*. Compound **8f** was prepared from benzyltriphenylphosphonium bromide **11d** (315 mg, 0.73 mmol), potassium *tert*-butoxide (82 mg, 0.73 mmol) and 5-methoxy-3-(4-methoxyphenyl)isoxazole-4-carbaldehyde **10c** (106 mg, 0.45 mmol) in THF (9 mL) for 1.5 h according to the general procedure B. The product was purified by column chromatography (light petroleum/ethyl acetate, 8:1-5:1). A colorless solid, mp 81-83 °C

(hexane), yield 95 mg (68%), (*E*/*Z*)-mixture (~1:0.13). ^{1}H NMR ($CDCl_3$): for (*E*)-isomer δ = 3.88 (s, 3H), 4.27 (s, 3H), 6.68 (d, *J* = 16.5 Hz, 1H), 6.98 (d, *J* = 16.5 Hz, 1H), 7.02 (d, *J* = 8.7 Hz, 2H), 7.18-7.24 (m, 1H), 7.29-7.33 (m, 2H), 7.37-7.39 (m, 2H), 7.58 (d, *J* = 8.7 Hz, 2H); for (*Z*)-isomer δ = 3.83 (s, 3H), 3.84 (s, 3H), 6.13 (d, *J* = 11.6 Hz, 1H), 6.65 (d, *J* = 11.6 Hz, 1H), 6.94 (d, *J* = 8.5 Hz, 2H), 7.18-7.24 (m, 3H), 7.29-7.33 (m, 2H), 7.69 (d, *J* = 8.5 Hz, 2H). ^{13}C NMR ($CDCl_3$): for (*E*)-isomer δ = 55.4 (CH_3), 58.0 (CH_3), 91.4 (C), 114.3 (CH), 115.3 (CH), 121.8 (C), 125.9 (CH), 127.2 (CH), 128.6 (CH), 129.0 (CH), 129.9 (CH), 137.8 (C), 160.9 (C), 163.9 (C), 169.0 (C); for (*Z*)-isomer 57.6 (CH_3), 114.0 (CH), 116.2 (CH), 127.2 (CH), 128.0 (CH), 128.1 (CH), 129.1 (CH), 132.8 (CH). HRMS (ESI-TOF) (m/z): $[M+H]^+$ Calcd. for $C_{19}H_{18}NO_3^+$ 308.1281; Found 308.1274.

*(E)-5-Methoxy-4-styryl-3-(thiophen-2-yl)isoxazole (**8g**).* Compound **8g** was prepared from benzyltriphenylphosphonium bromide **11d** (303 mg, 0.70 mmol), potassium *tert*-butoxide (79 mg, 0.70 mmol) and 5-methoxy-3-(thiophen-2-yl)isoxazole-4-carbaldehyde **10d** (88 mg, 0.42 mmol) in THF (11 mL) for 1 h according to the general procedure B. The product was purified by column chromatography (light petroleum/ethyl acetate, 8:1). A colorless solid, mp 95-96 °C (light petroleum/ethyl acetate), yield 76 mg (64%). ^{1}H NMR ($CDCl_3$): δ = 4.27 (s, 3H), 6.85 (d, *J* = 16.4 Hz, 1H), 7.03 (d, *J* = 16.4 Hz, 1H), 7.18-7.20 (m, 1H), 7.22-7.26 (m, 1H), 7.32-7.36 (m, 2H), 7.42-7.44 (m, 2H), 7.49-7.50 (m, 2H). ^{13}C NMR ($CDCl_3$): δ = 58.1 (CH_3), 91.5 (C), 114.7 (CH), 126.0 (CH), 127.4 (CH), 127.7 (CH), 127.8 (CH), 128.2 (CH), 128.6 (CH), 129.9 (CH), 130.1 (C), 137.6 (C), 158.5 (C), 169.3 (C). HRMS (ESI-TOF) (m/z): $[M+H]^+$ Calcd. for $C_{16}H_{14}NO_2S^+$ 284.0740; Found 284.0734.

*(E)-5-Methoxy-4-(4-nitrostyryl)-3-(thiophen-2-yl)isoxazole (**8h**).* Compound **8h** was prepared from (4-nitrobenzyl)triphenylphosphonium bromide **11a** (383 mg, 0.80 mmol), potassium *tert*-butoxide (90 mg, 0.80 mmol) and 5-methoxy-3-(thiophen-2-yl)isoxazole-4-carbaldehyde **10d** (97 mg, 0.46 mmol) in THF (13 mL) for 3 h according to the general procedure B. The product was purified by column chromatography (light petroleum/ethyl acetate, 5:1 + 1% of CH_2Cl_2). An orange solid, mp

170-172 °C (light petroleum/ethyl acetate), yield 85 mg (56%). ^{1}H NMR (DMSO-d_6): δ = 4.31 (s, 3H), 7.10 (d, *J* = 16.4 Hz, 1H), 7.18 (d, *J* = 16.4 Hz, 1H), 7.30 (dd, *J* = 4.8, 3.9 Hz, 1H), 7.70-7.71 (m, 1H), 7.79 (d, *J* = 8.8 Hz, 2H), 7.83-7.85 (m, 1H), 8.19 (d, *J* = 8.8 Hz, 2H). ^{13}C NMR (DMSO-d_6): δ = 59.0 (CH_3), 90.4 (C), 119.6 (CH), 124.0 (CH), 126.8 (CH), 126.8 (CH), 128.5 (CH), 128.6 (C), 129.0 (CH), 129.3 (CH), 143.9 (C), 146.0 (C), 157.7 (C), 169.8 (C). HRMS (ESI-TOF) (m/z): $[M+Na]^+$ Calcd. for $C_{16}H_{12}N_2NaO_4S^+$ 351.0410; Found 351.0415.

*(E/Z)-N,N-Diethyl-3-phenyl-4-styrylisoxazole-5-amine (**8i**).* Compound **8i** was prepared from benzyltriphenylphosphonium bromide **11d** (766 mg, 1.77 mmol), potassium *tert*-butoxide (199 mg, 1.77 mmol), 5-(diethylamino)-3-phenylisoxazole-4-carbaldehyde **10e** (288 mg, 1.18 mmol) in THF (11 mL) and additional ylide from benzyltriphenylphosphonium bromide **11d** (156 mg, 0.36 mmol) and potassium *tert*-butoxide (41 mg, 0.36 mmol) in 5mL of THF for 2.5 h according to the general procedure B. The product was purified by column chromatography (light petroleum/ethyl acetate, 8:1). A yellow solid, mp 80-82 °C (pentane), yield 302 mg (82%), (*E*/*Z*)-mixture (~1:0.16). ^{1}H NMR ($CDCl_3$): for (*E*)-isomer δ = 1.29 (td, J = 7.0, 0.7 Hz, 6H), 3.52 (qd, J = 7.0, 0.7 Hz, 4H), 6.36 (dd, *J* = 16.3, 1.5 Hz, 1H), 6.84 (dd, *J* = 16.3, 1.5 Hz, 1H), 7.21-7.24 (m, 1H), 7.29-7.34 (m, 4H), 7.44-7.47 (m, 3H), 7.63-7.66 (m, 2H); for (*Z*)-isomer δ = 1.10 (td, J = 7.1, 0.9 Hz, 6H), 3.37 (qd, J = 7.1, 0.9 Hz, 4H), 6.38 (dd, *J* = 11.6, 1.3 Hz, 1H), 6.59 (dd, *J* = 11.6, 1.3 Hz, 1H), 7.15-7.24 (m, 3H), 7.29-7.34 (m, 2H), 7.44-7.47 (m, 3H), 7.59-7.62 (m, 2H). ^{13}C NMR ($CDCl_3$): for (*E*)-isomer δ = 13.7 (CH_3), 43.9 (CH_2), 92.0 (C), 117.1 (CH), 125.7 (CH), 127.1 (CH), 128.1 (CH), 128.4 (CH), 128.8 (CH), 129.1 (C), 130.4 (C), 130.7 (CH), 137.1 (C), 163.4 (C), 166.8 (C); for (*Z*)-isomer δ = 13.8 (CH_3), 43.0 (CH_2), 88.0 (C), 119.0 (CH), 125.7 (CH), 127.2 (CH), 128.0 (CH), 128.5 (CH), 128.9 (CH), 129.2 (CH), 130.4 (CH), 131.2 (C), 133.4 (CH), 163.3 (C), 165.1 (C). HRMS (ESI-TOF) (m/z): $[M+H]^+$ Calcd. for $C_{21}H_{23}N_2O^+$ 319.1805; Found 319.1807.

*(E)-4-(3-Chlorostyryl)-3-phenyl-5-(pyrrolidin-1-yl)isoxazole (**8j**).* Compound **8j** was prepared from (3-chlorobenzyl)triphenylphosphonium chloride **11b** (511 mg, 1.20 mmol), potassium *tert*-butoxide

(135 mg, 1.20 mmol), 3-phenyl-5-(pyrrolidin-1-yl)isoxazole-4-carbaldehyde **10f** (194 mg, 0.80 mmol) in THF (7 mL) and additional ylide from (3-chlorobenzyl)triphenylphosphonium bromide **11b** (191 mg, 0.45 mmol) and potassium *tert*-butoxide (51 mg, 0.45 mmol) in THF (8 mL) for 6 h according to the general procedure B. The product was purified by column chromatography (light petroleum/ethyl acetate, 4:1). A colorless solid, mp 133-134 °C (light petroleum/ethyl acetate), yield 198 mg (71%). ^{1}H NMR ($CDCl_3$): δ = 2.00-2.03 (m, 4H), 3.63-3.66 (m, 4H), 6.10 (d, *J* = 16.2 Hz, 1H), 6.92 (d, *J* = 16.2 Hz, 1H), 7.06-7.08 (m, 1H), 7.12-7.14 (m, 1H), 7.17-7.18 (m, 1H), 7.21-7.22 (m, 1H), 7.43-7.46 (m, 3H), 7.57-7.61 (m, 2H). ^{13}C NMR ($CDCl_3$): δ = 25.5 (CH_2), 48.8 (CH_2), 90.5 (C), 118.5 (CH), 123.8 (CH), 125.3 (CH), 126.6 (CH), 127.3 (CH), 128.5 (CH), 128.7 (CH), 129.3 (CH), 129.7 (CH), 130.5 (C), 134.5(C), 139.9 (C), 163.2 (C), 165.7 (C). HRMS (ESI-TOF) (m/z): $[M+H]^+$ Calcd. for $C_{21}H_{20}ClN_2O^+$ 351.1259; Found 351.1255.

*(E/Z)-3-(4-Nitrophenyl)-5-(pyrrolidin-1-yl)-4-styrylisoxazole (**8m**)*. Compound **8a** was prepared from benzyltriphenylphosphonium bromide **11d** (520 mg, 1.20 mmol), potassium *tert*-butoxide (135 mg, 1.20 mmol) and 3-(4-nitrophenyl)-5-(pyrrolidin-1-yl)isoxazole-4-carbaldehyde **10h** (230 mg, 0.80 mmol) in THF (14 mL) for 2 h according to the general procedure B. The product was purified by column chromatography (light petroleum/ethyl acetate, 5:1-4:1). A red solid, mp 144-145 °C (light petroleum/ethyl acetate), yield 274 mg (70%), (*E*/*Z*)-mixture (~1:0.05). ^{1}H NMR ($CDCl_3$): for (*E*)-isomer δ = 2.00-2.03 (m, 4H), 3.64-3.67 (m, 4H), 6.20 (d, *J* = 16.2 Hz, 1H), 6.90 (d, *J* = 16.2 Hz, 1H), 7.20-7.32 (m, 5H), 7.82-7.85 (m, 2H), 8.26-8.29 (m, 2H); for (*Z*)-isomer 1.84-1.88 (m, 4H), 3.51-3.54 (m, 4H), 6.41 (d, *J* = 11.6 Hz, 1H), 6.55 (d, *J* = 11.6 Hz, 1H), 7.20-7.32 (m, 5H), 7.68 (d, *J* = 8.9 Hz, 2H), 8.10 (d, *J* = 8.9 Hz, 2H). ^{13}C NMR ($CDCl_3$): for (*E*)-isomer δ = 25.5 (CH_2), 48.7 (CH_2), 90.3 (C), 116.2 (CH), 123.7 (CH), 125.7 (CH), 127.3 (CH), 128.7 (CH), 129.6 (CH), 131.1 (CH), 137.2 (C), 137.3 (C), 148.2 (C), 161.1 (C), 165.9 (C). HRMS (ESI-TOF) (m/z): $[M+H]^+$ Calcd. for $C_{21}H_{20}N_3O_3^+$ 362.1499; Found 362.1497.

*(E/Z)-N,N-Dibenzyl-3-(4-nitrophenyl)-4-styrylisoxazole-5-amine (**8n**).* Compound **8n** was prepared from benzyltriphenylphosphonium bromide **11d** (433 mg, 1.00 mmol), potassium *tert*-butoxide (113 mg, 1.00 mmol) and 5-(dibenzylamino)-3-(4-nitrophenyl)isoxazole-4-carbaldehyde **10i** (180 mg, 0.44 mmol) in THF (11 mL) for 4 h according to the general procedure B. The product was purified by column chromatography (light petroleum/ethyl acetate, 8:1). A yellow oil, yield 186 mg (88%), (*E*/*Z*)-mixture (~1:0.1). ^{1}H NMR ($CDCl_3$): for (*E*)-isomer δ = 4.65 (s, 4H), 6.28 (d, *J* = 16.3 Hz, 1H), 6.66 (d, *J* = 16.3 Hz, 1H), 7.03-7.05 (m, 2H), 7.17-7.25 (m, 3H), 7.29-7.42 (m, 10H), 7.83-7.86 (m, 2H), 8.27-8.30 (m, 2H); for (*Z*)-isomer 4.60 (s, 4H), 6.26 (d, *J* = 11.5 Hz, 1H), 6.54 (d, *J* = 11.5 Hz, 1H), 7.05-7.07 (m, 2H), 7.17-7.25 (m, 3H), 7.29-7.42 (m, 10H), 7.66-7.68 (m, 2H), 8.08-8.10 (m, 2H). ^{13}C NMR ($CDCl_3$): for (*E*)-isomer δ = 52.5 (CH_2), 92.3 (C), 115.8 (CH), 123.7 (CH), 125.8 (CH), 127.6 (CH), 127.6 (CH), 127.8 (CH), 128.6 (CH), 128.9 (CH), 129.7 (CH), 132.9 (CH), 136.6 (C), 136.7 (C), 136.8 (C), 148.3 (C), 161.7 (C), 167.4 (C). HRMS (ESI-TOF) (m/z): $[M+Na]^+$ Calcd. for $C_{31}H_{25}N_3NaO_3^+$ 510.1788; Found 510.1785.

*(E/Z)-3-(tert-Butyl)-5-(pyrrolidin-1-yl)-4-styrylisoxazole (**8o**).* Compound **8o** was prepared from benzyltriphenylphosphonium bromide **11d** (476 mg, 1.10 mmol), potassium *tert*-butoxide (124 mg, 1.10 mmol), 3-(*tert*-butyl)-5-(pyrrolidin-1-yl)isoxazole-4-carbaldehyde **10j** (150 mg, 0.67 mmol) in THF (10 mL) and additional ylide from benzyltriphenylphosphonium bromide **11d** (200 mg, 0.46 mmol) and potassium *tert*-butoxide (53 mg, 0.47 mmol) in 7 mL of THF for 20 h according to the general procedure B. The product was purified by column chromatography (light petroleum/ethyl acetate, 8:1). A colorless solid, mp 112-113 °C (light petroleum/ethyl acetate), yield 100 mg (52%), (*E*/*Z*)-mixture (~1:0.1). ^{1}H NMR ($CDCl_3$): for (*E*)-isomer δ = 1.37 (s, 9H), 1.87-1.93 (m, 4H), 3.40-3.44 (m, 4H), 6.35 (d, *J* = 15.9 Hz, 1H), 6.88 (d, *J* = 15.9 Hz, 1H), 7.21-7.27 (m, 1H), 7.33-7.37 (m, 2H), 7.41-7.43 (m, 2H); for (*Z*)-isomer 1.34 (s, 9H), 1.95-1.99 (m, 4H), 3.35-3.39 (m, 4H), 6.42 (d, *J* = 11.7 Hz, 1H), 6.53 (d, *J* = 11.7 Hz, 1H). ^{13}C NMR ($CDCl_3$): for (*E*)-isomer δ = 25.5 (CH_2), 28.8 (CH_3), 33.3 (C), 48.6 (CH_2), 86.8 (C), 118.5 (CH), 125.9 (CH), 127.2 (CH), 128.7 (CH), 132.3

(CH), 137.6 (C), 165.8 (C), 170.8 (C). HRMS (ESI-TOF) (m/z): $[M+H]^+$ Calcd. for $C_{19}H_{25}N_2O^+$ 297.1961; Found 297.1957.

*(E/Z)-4-(2-(Naphthalen-1-yl)vinyl)-3-phenyl-5-(pyrrolidin-1-yl)isoxazole (**8p**)*. Compound **8p** was prepared from (naphthalene-1-ylmethyl)triphenylphosphonium bromide **11e** (482 mg, 1.00 mmol), potassium *tert*-butoxide (112 mg, 1.00 mmol), 3-phenyl-5-(pyrrolidin-1-yl)isoxazol-4-carbaldehyde **10f** (170 mg, 0.70 mmol) in THF (10 mL) and additional ylide from (naphthalene-1-ylmethyl)triphenylphosphonium bromide **11e** (375 mg, 0.78 mmol) and potassium *tert*-butoxide (87 mg, 0.78 mmol) in THF (7 mL) for 17 h according to the general procedure B. The product was purified by column chromatography (light petroleum/ethyl acetate, 8:1). A yellowish solid, mp 128-131 °C, yield 227 mg (88%), (*E*/*Z*)-mixture (~1:0.21). ^{1}H NMR ($CDCl_3$): for (*E*)-isomer δ = 2.00-2.03 (m, 4H), 3.68-3.71 (m, 4H), 6.93 (d, *J* = 15.9 Hz, 1H), 7.00 (d, *J* = 15.9 Hz, 1H), 7.33-7.48 (m, 6H), 7.54-7.56 (m, 1H), 7.67-7.74 (m, 4H), 7.81-7.83 (m, 1H); for (*Z*)-isomer δ = 1.67-1.70 (m, 4H), 3.41-3.49 (m, 4H), 6.69 (d, *J* = 11.6 Hz, 1H), 7.01-7.08 (m, 3H), 7.21-7.25 (m, 1H), 7.33-7.50 (m, 6H), 7.59-7.61 (m, 1H), 7.69-7.73 (m, 1H), 7.81-7.85 (m, 1H). ^{13}C NMR ($CDCl_3$): for (*E*)-isomer δ = 25.5 (CH_2), 48.7 (CH_2), 91.2 (C), 119.7 (CH), 122.3 (CH), 123.7 (CH), 125.6 (CH), 125.68 (CH), 125.73 (CH), 126.1 (CH), 127.2 (CH), 128.4 (CH), 128.6 (CH), 128.9 (CH), 129.1 (CH), 130.8 (C), 131.0 (C), 133.6 (C), 135.6 (C), 163.4 (C), 165.5 (C); for (*Z*)-isomer δ = 25.1 (CH_2), 47.8 (CH_2), 88.5 (C), 120.1 (CH), 123.9 (CH), 125.1 (CH), 125.3 (CH), 125.4 (CH), 126.1 (CH), 127.3 (CH), 127.5 (CH), 127.8 (CH), 128.2 (CH), 128.3 (CH), 128.9 (CH), 130.0 (C), 131.3 (C), 133.4 (C), 133.9 (C), 163.5 (C), 165.1 (C). HRMS (ESI-TOF) (m/z): $[M+H]^+$ Calcd. for $C_{25}H_{23}N_2O^+$ 367.1805; Found 367.1808.

*(E/Z)-4-(But-1-en-1-yl)-5-methoxy-3-phenylisoxazole (**8t**)*. Compound **8t** was prepared from was prepared by using the general procedure from triphenyl(propyl)phosphonium bromide **11g** (1079 mg, 2.80 mmol), potassium *tert*-butoxide (314 mg, 2.80 mmol), 5-methoxy-3-phenylisoxazole-4-carbaldehyde **10a** (379 mg, 1.87 mmol) in THF (26 mL) and additional ylide from

triphenyl(propyl)phosphonium bromide **11g** (269 mg, 0.70 mmol) and potassium *tert*-butoxide (78 mg, 0.70 mmol) in THF (5 mL) for 5 h according to the general procedure B. The product was purified by column chromatography (light petroleum/ethyl acetate, 8:1). A yellow oil, yield 342 mg (80%), (*E*/*Z*)-mixture (~0.26:1). ^{1}H NMR ($CDCl_3$): for (*E*)-isomer δ = 1.08 (t, *J* = 7.5 Hz, 3H), 2.10-2.18 (m, 2H), 4.20 (s, 3H), 5.94 (dt, *J* = 16.1, 1.4 Hz, 1H), 6.08 (dt, *J* = 16.1, 6.4 Hz, 1H), 7.45-7.47 (m, 3H), 7.59-7.61 (m, 2H); for (*Z*)-isomer δ = 0.96 (t, *J* = 7.5 Hz, 3H), 2.03 (pd, *J* = 7.5, 1.5 Hz, 2H), 4.15 (s, 3H), 5.70 (dt, *J* = 10.9, 7.2 Hz, 1H), 5.85 (dt, *J* = 10.9, 1.5 Hz, 1H), 7.45-7.44 (m, 3H), 7.67-7.72 (m, 2H). ^{13}C NMR ($CDCl_3$): for (*E*)-isomer δ = 13.7 (CH_3), 26.5 (CH_2), 57.8 (CH_3), 114.8 (CH), 128.4 (CH), 128.6 (CH), 129.6 (C), 133.8 (CH); for (*Z*)-isomer δ = 13.6 (CH_3), 22.7(CH_2), 57.9 (CH_3), 89.7 (C), 114.3 (CH), 127.9 (CH), 128.5 (CH), 129.6 (CH), 130.0 (C), 137.7 (CH), 163.9 (C), 168.3 (C). HRMS (ESI-TOF) (m/z): $[M+H]^+$ Calcd. for $C_{15}H_{18}NO_3^+$ 260.1276; Found 260.1274.

General procedure C for the synthesis of (5-aminoisoxazole-4-yl)acrylates 8k,l. Compounds **8k,l** were synthesized by a slightly modified literature procedure.[8b] A solution of *N,N*-diisopropylamine (DIPA) (2 mmol) in dry THF was cooled down to -78°C and solution of butyl lithium in hexane (2 mmol) was added under stirring. Methyl acetate (2 mmol) was added in 10 min and then a solution of isoxazol-4-carbaldehyde **10** (1 mmol) in dry THF was added in 10 min. The mixture was stirred for 20 min and then quenched with saturated aq NH_4Cl. The product was extracted with ethyl acetate, washed with brine and dried over sodium sulfate. The solvents were evaporated, the residue was dissolved in benzene and *p*-toluenesulphonic acid (5 mg) was added to the solution. The mixture was refluxed for 2 h with Dean-Stark trap. The solvent was evaporated and the residue was purified by column chromatography. The corresponding 5-amino-4-unsubstituted-isoxazole was eluted first, followed by the target product as pure (*E*)-isomer.

*(E)-Methyl 3-(3-phenyl-5-(pyrrolidin-1-yl)isoxazole-4-yl)acrylate (**8k**)*. Compound **8k** as a colorless solid, mp 188-189 °C (light petroleum/ethyl acetate), yield 199 mg (71%), and *3-phenyl-5-*

*(pyrrolidin-1-yl)isoxazole (**30a**)*, as a colorless solid, mp 105-107 °C (light petroleum/ethyl acetate), yield 47 mg (23%), were obtained from DIPA (202 mg, 2.00 mmol), *n*-BuLi (2.5 M, 1 mL, 2.00 mmol), methyl acetate (149 mg, 2.00 mmol) and 3-phenyl-5-(pyrrolidin-1-yl)isoxazole-4-carbaldehyde **10f** (230 mg, 0.95 mmol) in THF (14 mL) according to the general procedure C. The products were purified by column chromatography (light petroleum/ethyl acetate 4:1). **30a:** ^{1}H NMR ($CDCl_3$): 2.00-2.04 (m, 4H), 3.44-3.47 (m, 4H), 5.14 (s, 1H), 7.39-7.43 (m, 3H), 7.74-7.77 (m, 2H). The spectral data are in agreement with previously reported values.[8e] **8k**: ^{1}H NMR ($CDCl_3$): 2.03-2.07 (m, 4H), 3.65 (s, 2H), 3.70-3.73 (m, 4H), 5.37 (d, J = 15.7 Hz, 1H), 7.45-7.51 (m, 5H), 7.71 (d, J = 15.7 Hz, 1H). ^{13}C NMR ($CDCl_3$): 25.4 (CH_2), 49.0 (CH_2), 51.2 (CH_3), 89.9 (C), 112.0 (CH), 128.69 (CH), 128.73 (CH), 129.6 (CH), 129.8 (C), 134.0 (CH), 163.5 (C), 166.5 (C), 168.3 (C). HRMS (ESI-TOF) (m/z): $[M+H]^+$ Calcd. for $C_{17}H_{19}N_2O_3^+$ 299.1390; Found 299.1388.

*(E)-Methyl 3-(3-(4-bromophenyl)-5-(pyrrolidin-1-yl)isoxazole-4-yl)acrylate (**8l**)*. Compound **8l** as a light yellow solid, mp 184-185 °C (light petroleum/ethyl acetate), yield 100 mg (44%), and *3-(4-bromophenyl)-5-(pyrrolidin-1-yl)isoxazole (**30b**)*, as a colorless solid, mp 115-116 °C (light petroleum/ethyl acetate), yield 74 mg (45%), were obtained from DIPA (122 mg, 1.20 mmol), *n*-BuLi (2.5 M, 0.5 mL, 1.25 mmol), methyl acetate (89 mg, 1.20 mmol) and 3-(4-bromophenyl)-5-(pyrrolidin-1-yl)isoxazole-4-carbaldehyde **10g** (180 mg, 0.56 mmol) in THF (11 mL) according to the general procedure C. The products were purified by column chromatography (light petroleum/ethyl acetate 6:1-4:1). **30b**: ^{1}H NMR ($CDCl_3$): δ = 2.00-2.04 (m, 4H), 3.43-3.47 (m, 4H), 5.10 (s, 1H), 7.53-7.56 (m, 2H), 7.61-7.64 (m, 2H). ^{13}C NMR ($CDCl_3$): 25.6 (CH_2), 47.8 (CH_2), 74.0 (CH), 123.6 (C), 128.1 (CH), 129.3 (CH), 131.8 (C), 162.6 (C), 169.3 (C). HRMS (ESI-TOF) (m/z): 293.0284 Calcd. for $C_{13}H_{14}BrN_2O$ $[M+H]^+$; Found 293.0272. **8l**: ^{1}H NMR ($CDCl_3$): δ = 2.03-2.06 (m, 4H), 3.67 (s, 3H), 3.69-3.71 (m, 4H), 5.39 (d, J = 15.7 Hz, 1H), 7.38 (d, J = 8.4 Hz, 2H), 7.59 (d, J = 8.4 Hz, 2H), 7.69 (d, J = 15.7, 1H). ^{13}C NMR ($CDCl_3$): 25.4 (CH_2), 49.0 (CH_2), 51.3 (CH_3), 89.7 (C), 112.5 (CH), 124.1 (C), 128.8 (C), 130.4 (CH), 132.0 (CH), 133.8 (CH), 162.5 (C), 166.6

(C), 168.2 (C). HRMS (ESI-TOF) (m/z): $[M+H]^+$ Calcd. for $C_{17}H_{18}BrN_2O_3^+$ 377.0495; Found 377.0483.

*4-(Cyclohex-1-en-1-yl)-5-methoxy-3-phenylisoxazole (**8q**).* A suspension of morpholinium 4-(cyclohex-1-enyl)-3-phenylisoxazol-5-olate[19] (129 mg, 0.393 mmol) in THF (15 mL) was cooled to 0 °C and the ether solution of diazomethane, obtained from *N*-nitrozo-*N*-methylurea (412 mg, 4 mmol), was slowly added. The mixture was stirred at rt for 2 hours, quenched by AcOH and the solvents were removed in vacuo. The residue was purified by column chromatography, using a mixture of light petroleum ether and ethyl acetate (8:1) as eluent to give pure product as colorless oil, yield 55 mg (55%). ^{1}H NMR ($CDCl_3$): δ = 1.62-1.93 (m, 4H), 2.02-2.03 (m, 2H), 2.10-2.11 (m, 2H), 4.12 (s, 3H), 5.69-5.70 (m, 1H), 7.40-7.43 (m, 3H), 7.62-7.64 (m, 2H). ^{13}C NMR ($CDCl_3$): δ = 21.9 (CH_2), 22.8 (CH_2), 25.5 (CH_2), 28.7 (CH_2), 57.9 (CH_3), 95.7 (C), 126.0 (C), 127.9 (CH), 128.4 (CH), 129.3 (CH), 129.4 (CH), 130.4 (C), 163.4 (C), 168.5 (C). HRMS (ESI-TOF) (m/z): $[M+H]^+$ Calcd. for $C_{16}H_{18}NO_2^+$ 256.1332; Found 256.1335.

*4-(5-Methoxy-3-phenylisoxazol-4-yl)-2H-chromen-2-one (**8s**).* A solution of $HN(SiMe_3)_2$ (1.06 mL, 5.1 mmol) in dry THF (5mL) was cooled down to -78 °C under Ar. A solution of *n*-BuLi (2.5 M in hexane, 2.05 mL, 5.1 mmol) was added and the mixture was stirred for 10 min. A solution of methyl 2-(2-oxo-2*H*-chromen-4-yl)acetate (923 mg, 4.2 mmol) in THF (16 mL) was added to the reaction mixture for 3 minutes and the mixture was stirred for 15 min, the solution of benzoyl chloride (682 mg, 4.9 mmol) in THF (5 mL) was then added in one portion, and the mixture was stirred for 15 min at -78 °C and 2 days at rt. The reaction mixture was quenched by aq saturated NH_4Cl, extracted with EtOAc, the organic layer was washed with brine and dried over Na_2SO_4. The solvents were evaporated to give light yellow solid (1.67 g). The mixture of this solid and $NH_2OH{\cdot}HCl$ (1.34 g, 19.3 mmol) was refluxed in MeOH (15 mL) for 24 h. Water was added, precipitate formed was filtered of, washed with water, ether and dried on air to give 4-(2-oxo-2*H*-chromen-4-yl)-3-phenylisoxazol-5(4*H*)-one **32** as colorless solid, mp 183-184 °C (dec., MeOH/H_2O), yield 1027 mg

(79% on 2 steps). ^{1}H NMR (DMSO-d_6): δ = 7.26-7.42 (m, 2H), 7.45-7.53 (m, 5H), 7.59-7.64 (m, 1H), 7.76-7.78 (m, 1H), 8.17 (s, 1H). ^{13}C NMR (DMSO-d_6): δ = 89.9 (C), 116.0 (CH), 117.9 (C), 119.1 (C), 124.7 (CH), 127.1 (CH), 128.1 (C), 128.4 (CH), 129.0 (CH), 130.9 (CH), 131.8 (CH), 142.9 (CH), 152.9 (C), 158.7 (C), 161.6 (C), 170.3 (C). HRMS (ESI-TOF) (m/z): $[M+Na]^+$ Calcd. for $C_{18}H_{11}NNaO_4^+$ 328.0580; Found 328.0573. A suspension of 4-(2-oxo-2*H*-chromen-4-yl)-3-phenylisoxazol-5(4*H*)-one **32** (455 mg, 1.42 mmol) in THF (13 mL) was cooled to 0 °C and an ether solution of diazomethane, obtained from *N*-nitrozo-*N*-methylurea (440 mg, 4.27 mmol), was slowly added. The mixture was stirred at rt for 1 h, quenched by AcOH and the solvents were removed in vacuo. The residue was purified by column chromatography, using DCM as eluent to give pure product. A colorless solid, mp 162-163 °C (DCM), yield 336 mg (74%). ^{1}H NMR ($CDCl_3$): δ = 4.19 (s, 3H), 7.24-7.28 (m, 1H), 7.32-7.43 (m, 5H), 7.49-7.55 (m, 3H), 7.59 (s, 1H). ^{13}C NMR ($CDCl_3$): δ = 58.2 (CH_3), 87.8 (C), 116.6 (CH), 117.9 (C), 119.0 (C), 124.5 (CH), 127.6 (CH), 127.8 (CH), 128.7 (CH), 129.5 (C), 129.7 (CH), 131.6 (CH), 142.9 (CH), 153.6 (C), 159.5 (C), 163.9 (C), 170.0 (C). HRMS (ESI-TOF) (m/z): $[M+Na]^+$ Calcd. for $C_{19}H_{13}NNaO_4^+$ 342.0737; Found 342.0733.

General procedure D for the synthesis of pyrroles 9 from 4-vinylisoxazoles 8. A mixture of isoxazole **8** (1 mmol) and $FeCl_2 \cdot 4H_2O$ (0.1 mmol) was stirred at 65°C in acetonitrile for 6 h, unless otherwise specified. The solvents were evaporated and the residue was dissolved in CH_2Cl_2 or $CHCl_3$ and filtered through a pad of silica. The solvents were evaporated and solid compounds were washed with pentane, dried on air to give pure products.

*Methyl 5-(4-nitrophenyl)-2-phenyl-1H-pyrrole-3-carboxylate (**9a**).* Compound **9a** was obtained from (*E*)-5-methoxy-4-(4-nitrostyryl)-3-phenylisoxazole **8a** (64 mg, 0.20 mmol) and $FeCl_2 \cdot 4H_2O$ (4 mg, 0.02 mmol) in MeCN (3 mL) according to the general procedure D. The product was purified by filtration through a pad of silica (CH_2Cl_2/MeOH 1:0-20:1). An orange solid, mp 245-247 °C (CH_2Cl_2/MeOH), yield 62 mg (97%). ^{1}H NMR (DMSO-d_6): δ = 3.67 (s, 3H), 7.31 (d, *J* = 2.4 Hz, 1H), 7.43-7.49 (m, 3H), 7.64-7.66 (m, 2H), 8.07 (d, *J* = 8.8 Hz, 2H), 8.22 (d, *J* = 8.8 Hz, 2H), 12.19

(s, 1H). ^{13}C NMR (DMSO-d_6): δ = 50.8 (CH_3), 112.3 (CH), 113.2 (C), 124.2 (CH), 124.5 (CH), 127.7 (CH), 128.4 (CH), 129.6 (CH), 129.7 (C), 131.1 (C), 137.8 (C), 140.0 (C), 145.1 (C), 164.0 (C). HRMS (ESI-TOF) (m/z): $[M+H]^+$ Calcd. for $C_{18}H_{15}N_2O_4^+$ 323.1026; Found 323.1026.

*Methyl 5-(3-chlorophenyl)-2-phenyl-1H-pyrrole-3-carboxylate (**9b**).* Compound **9b** was obtained from (*E*/*Z*)-4-(3-chlorostyryl)-5-methoxy-3-phenylisoxazole **8b** (99 mg, 0.32 mmol) and $FeCl_2 \cdot 4H_2O$ (7 mg, 0.035 mmol) in MeCN (3 mL) according to the general procedure D. The product was purified by filtration through a pad of silica (light petroleum/ethyl acetate 4:1). A light yellow solid, mp 58-60 °C (light petroleum/ethyl acetate), yield 88 mg (87%). ^{1}H NMR ($CDCl_3$): δ = 3.77 (s, 3H), 7.02 (d, *J* = 3.0 Hz, 1H), 7.22-7.24 (m, 1H), 7.30-7.34 (m, 1H), 7.36-7.45 (m, 4H), 7.49-7.50 (m, 1H), 7.62-7.64 (m, 2H), 8.65 (br.s., 1H). ^{3}C NMR ($CDCl_3$): δ = 51.1 (CH_3), 110.1 (CH), 113.6 (C), 122.0 (CH), 124.0(CH), 127.0 (CH), 128.3 (CH), 128.6 (CH), 128.9 (CH), 130.29 (CH), 130.33 (C), 131.5 (C), 133.2 (C), 135.1 (C), 138.4 (C), 165.0 (C). HRMS (ESI-TOF) (m/z): $[M+H]^+$ Calcd. for $C_{18}H_{15}ClNO_2^+$ 312.0786; Found 312.0786.

*Dimethyl 5-phenyl-1H-pyrrole-2,4-dicarboxylate (**9c**).* Compound **9c** was obtained from **(***E*)-methyl 3-(5-methoxy-3-phenylisoxazole)acrylate **8c** (49 mg, 0.19 mmol) and $FeCl_2 \cdot 4H_2O$ (4 mg, 0.02 mmol) in MeCN (4 mL) for 18 h according to the general procedure D. The product was purified by filtration through a pad of silica (ethyl acetate). A colorless solid, mp 150-152 °C (ethyl acetate), yield 44 mg (90%). ^{1}H NMR ($CDCl_3$): δ = 3.76 (s, 3H), 3.82 (s, 3H), 7.39 (d, *J* = 2.8 Hz, 1H), 7.41-7.46 (m, 3H), 7.61-7.64 (m, 2H), 9.57 (br.s., 1H). ^{13}C NMR ($CDCl_3$): δ = 51.2 (CH_3), 51.8 (CH_3), 113.8 (C), 118.5 (CH), 122.0 (C), 128.2 (CH), 129.1 (CH), 129.2 (CH), 130.7 (C), 140.8 (C), 161.3 (C), 164.4 (C). HRMS (ESI-TOF) (m/z): $[M+H]^+$ Calcd. for $C_{14}H_{14}NO_4^+$ 260.0917; Found 260.0910.

*Methyl 2-(4-bromophenyl)-5-phenyl-1H-pyrrole-3-carboxylate (**9d**).* Compound **9d** was obtained from (*E*/*Z*)-3-(4-bromophenyl)-5-methoxy-4-styrylisoxazole **8d** (37 mg, 0.10 mmol) and $FeCl_2 \cdot 4H_2O$ (2 mg, 0.01 mmol) in MeCN (3 mL) according to the general procedure D. The product was purified by filtration through a pad of silica (light petroleum/ethyl acetate 3:1). A colorless

solid, mp 190-191 °C (light petroleum/ethyl acetate), yield 32 mg (86%). ^{1}H NMR (DMSO-d_6): δ = 3.67 (s, 3H), 6.99 (s, 1H), 7.23-7.27 (m, 1H), 7.37-7.41 (m, 2H), 7.59-7.61 (m, 2H), 7.63-7.65 (m, 2H), 7.77-7.79 (m, 2H), 11.89 (s, 1H). ^{13}C NMR (DMSO-d_6): δ = 50.7 (CH_3), 108.7 (CH), 112.5 (C), 121.2 (C), 124.3 (CH), 126.7 (CH), 128.7 (CH), 130.5 (CH), 130.7 (C), 131.3 (C), 131.6 (CH), 132.2 (C), 136.4 (C), 164.3 (C). HRMS (ESI-TOF) (m/z): $[M+H]^+$ Calcd. for $C_{18}H_{15}BrNO_2^+$ 356.0281; Found 356.0276.

*Methyl 2-(4-bromophenyl)-5-(4-nitrophenyl)-1H-pyrrole-3-carboxylate (**9e**).* Compound **9e** was obtained from (*E*)-3-(4-bromophenyl)-5-methoxy-4-(4-nitrostyryl)isoxazole **8e** (38 mg, 0.095 mmol) and $FeCl_2 \cdot 4H_2O$ (2 mg, 0.01 mmol) in MeCN (3 mL) according to the general procedure D. The product was purified by filtration through a pad of silica ($CHCl_3$). A yellow solid, mp 258-259 °C ($CHCl_3$), yield 33 mg (87%). ^{1}H NMR (DMSO-d_6): δ = 3.68 (s, 3H), 7.31 (s, 1H), 7.60-7.62 (m, 2H), 7.66-7.68 (m, 2H), 8.06 (d, *J* = 8.8 Hz, 2H), 8.23 (d, *J* = 8.8 Hz, 2H), 12.23 (s, 1H). ^{13}C NMR (DMSO-d_6): δ = 50.9 (CH_3), 112.4 (CH), 113.5 (C), 121.7 (C), 124.2 (CH), 124.6 (CH), 130.0 (C), 130.2 (C), 130.6 (CH), 131.7 (CH), 137.6 (C), 138.5 (C), 145.2 (C), 164.0 (C). HRMS (ESI-TOF) (m/z): $[M+Na]^+$ Calcd. for $C_{18}H_{13}BrN_2NaO_4^+$ 422.9951; Found 422.9953.

*Methyl 2-(4-methoxyphenyl)-5-phenyl-1H-pyrrole-3-carboxylate (**9f**).* Compound **9f** was obtained from (*E*/*Z*)-5-methoxy-3-(4-methoxyphenyl)-4-styrylisoxazole **8f** (49 mg, 0.16 mmol) and $FeCl_2 \cdot 4H_2O$ (4 mg, 0.02 mmol) in MeCN (3 mL) according to the general procedure D. The product was purified by filtration through a pad of silica (light petroleum/ethyl acetate 4:1). A colorless solid, mp 130-131 °C (light petroleum/ethyl acetate), yield 33 mg (67%). ^{1}H NMR ($CDCl_3$): δ = 3.77 (s, 3H), 3.84 (s, 3H), 6.96 (d, *J* = 8.6 Hz, 2H), 6.98 (d, *J* = 2.7 Hz, 1H), 7.25-7.28 (m, 1H), 7.38-7.41 (m, 2H), 7.50-7.52 (m, 2H), 7.57-7.59 (d, *J* = 8.6 Hz, 2H), 8.59 (br.s., 1H). ^{13}C NMR ($CDCl_3$): δ = 51.0 (CH_3), 55.3 (CH_3), 108.9 (CH), 112.8 (C), 113.7 (CH), 123.9 (CH), 124.2 (C), 127.0 (CH), 129.0 (CH), 130.2 (CH), 131.3 (C), 131.5 (C), 138.0 (C), 159.8 (C), 165.3 (C). HRMS (ESI-TOF) (m/z): $[M+H]^+$ Calcd. for $C_{19}H_{18}NO_3^+$ 308.1281; Found 308.1283.

*Methyl 5-phenyl-2-(thiopen-2-yl)-1H-pyrrole-3-carboxylate (**9g**).* Compound **9g** was obtained from (*E*)-5-methoxy-4-styryl-3-(thiophen-2-yl)isoxazole **8g** (51 mg, 0.18 mmol) and $FeCl_2 \cdot 4H_2O$ (4 mg, 0.02 mmol) in 4 mL of MeCN according to the general procedure D. The product was purified by filtration through a pad of silica (light petroleum/ethyl acetate 5:1). A viscous light-yellow oil, yield 27 mg (53%). ^{1}H NMR ($CDCl_3$): δ = 3.83 (s, 3H), 6.98 (d, *J* = 3.0 Hz, 1H), 7.10 (dd, *J* = 5.1, 3.7 Hz, 1H), 7.26-7.30 (m, 1H), 7.36 (dd, *J* = 5.1, 1.1 Hz, 1H), 7.36-7.42 (m, 2H), 7.51-7.53 (m, 2H), 7.58 (dd, *J* = 3.7, 1.1 Hz, 1H) ^{13}C NMR ($CDCl_3$): δ = 51.1 (CH_3), 109.3 (CH), 113.7 (C), 124.1 (CH), 126.2 (CH), 127.26 (CH), 127.32 (CH), 127.5 (CH), 129.0 (CH), 130.9 (C), 131.1 (C), 131.9 (C), 132.8 (C), 165.0 (C). HRMS (ESI-TOF) (m/z): $[M+Na]^+$ Calcd. for $C_{16}H_{13}NNaO_2S^+$ 306.0559; Found 306.0550.

*Methyl 5-(4-nitrophenyl)-2-(thiophen-2-yl)-1H-pyrrole-3-carboxylate (**9h**).* Compound **9h** was obtained from (*E*)-5-methoxy-4-(4-nitrostyryl)-3-(thiophen-2-yl)isoxazole **9h** (42 mg, 0.13 mmol) and $FeCl_2 \cdot 4H_2O$ (3 mg, 0.02 mmol) in MeCN (3 mL) according to the general procedure D. The product was purified by filtration through a pad of silica (light petroleum/ethyl acetate 3:1). An orange solid, mp 210-212 °C (light petroleum/ethyl acetate), yield 41 mg (98%). ^{1}H NMR (DMSO-d_6): δ = 3.74 (s, 3H), 7.18 (dd, *J* = 5.0, 3.7 Hz, 1H), 7.30 (s, 1H), 7.66 (dd, *J* = 3.7, 1.1 Hz, 1H), 7.69 (dd, *J* = 5.0, 1.1 Hz, 1H), 8.08 (d, *J* = 8.8 Hz, 2H), 8.23 (d, *J* = 8.8 Hz, 2H), 12.13 (br.s., 1H). ^{13}C NMR (DMSO-d_6): δ = 50.9 (CH_3), 112.5 (CH), 113.4 (C), 124.1 (CH), 124.8 (CH), 126.7 (CH), 127.9 (CH), 128.7 (CH), 130.0 (C), 131.7 (C), 132.8 (C), 137.4 (C), 145.3 (C), 163.8 (C). HRMS (ESI-TOF) (m/z): $[M+Na]^+$ Calcd. for $C_{16}H_{12}N_2NaO_4S^+$ 351.0410; Found 351.0404.

*N,N-Diethyl-2,5-diphenyl-1H-pyrrole-3-carboxamide (**9i**).* Compound **9i** was obtained from (*E*/*Z*)-*N,N*-diethyl-3-phenyl-4-styrylisoxazole-5-amine **8i** (120 mg, 0.38 mmol) and $FeCl_2 \cdot 4H_2O$ (8 mg, 0.04 mmol) in MeCN (3 mL) according to the general procedure D. The product was purified by filtration through a pad of silica (CH_2Cl_2/MeOH 1:0-50:1). A yellowish solid, mp 183-184 °C (CH_2Cl_2/MeOH), yield 99 mg (83%). ^{1}H NMR ($CDCl_3$): δ = 0.81 (br.s., 2H), 1.16 (br.s., 2H), 3.13

(br.s., 2H), 3.51 (br.s., 2H), 6.44 (d, *J* = 2.6 Hz, 1H), 7.18-7.28 (m, 4H), 7.33-7.40 (m, 4H), 7.46-7.47 (m, 2H), 9.32 (br.s., 1H). ^{13}C NMR ($CDCl_3$): δ = 12.5 (br.s., CH_2), 13.7 (br.s., CH_2), 38.9 (br.s., CH_2), 43.0 (br.s., CH_2), 107.3 (CH), 118.4 (C), 124.2 (CH), 126.1 (CH), 126.5 (CH), 126.9 (CH), 128.65 (CH), 128.73 (CH), 130.0 (C), 131.9 (C), 132.0 (C), 132.6 (C), 168.7 (C). HRMS (ESI-TOF) (m/z): $[M+H]^+$ Calcd. for $C_{21}H_{23}N_2O^+$ 319.1805; Found 319.1803.

*(5-(3-Chlorophenyl)-2-phenyl-1H-pyrrole-3-yl)(pyrrolidine-1-yl)methanone (**9j**).* Compound **9j** was obtained from (*E*)-4-(3-chlorostyryl)-3-phenyl-5-(pyrrolidin-1-yl)isoxazole **8j** (62 mg, 0.18 mmol) and $FeCl_2 \cdot 4H_2O$ (4 mg, 0.02 mmol) in MeCN (3 mL) according to the general procedure D. The product was purified by filtration through a pad of silica (ethyl acetate). A colorless solid, mp 205-206 °C (ethyl acetate), yield 49 mg (79%). ^{1}H NMR ($CDCl_3$): δ = 1.55-1.58 (m, 2H), 1.72-1.76 (m, 2H), 2.83-2.86 (m, 2H), 3.54-3.57 (m, 2H), 6.29 (d, *J* = 2.2 Hz, 1H), 7.15-7.28 (m, 8H), 7.38 (s, 1H), 10.33 (br.s., 1H). ^{13}C NMR ($CDCl_3$): δ = 24.4 (CH_2), 25.7 (CH_2), 45.8 (CH_2), 48.0 (CH_2), 108.4 (CH), 118.5 (C), 122.6 (CH), 124.3 (CH), 126.1(CH), 126.5 (CH), 127.1 (CH), 128.6 (CH), 129.9 (CH), 131.0 (C), 132.0 (C), 132.1 (C), 133.9 (C), 134.5 (C), 167.6 (C). HRMS (ESI-TOF) (m/z): $[M+H]^+$ Calcd. for $C_{21}H_{20}ClN_2O^+$ 351.1259; Found 351.1269.

*Methyl 5-phenyl-4-(pyrrolidine-1-carbonyl)-1H-pyrrole-2-carboxylate (**9k**).* Compound **9k** was obtained from (*E*)-methyl 3-(3-phenyl-5-(pyrrolidin-1-yl)isoxazole-4-yl)acrylate **8k** (75 mg, 0.25 mmol) and $FeCl_2 \cdot 4H_2O$ (5 mg, 0.025 mmol) in 3 mL of MeCN according to the general procedure D. The product was purified by filtration through a pad of silica (ethyl acetate). A colorless solid, mp 195-197 °C (ethyl acetate), yield 49 mg (65%). ^{1}H NMR ($CDCl_3$): δ = 1.66-1.73 (m, 2H), 1.79-1.86 (m, 2H), 3.05-3.09 (m, 2H), 3.56-3.59 (m, 2H), 3.86 (s, 3H), 7.04 (d, *J* = 2.6 Hz, 1H), 7.33-7.42 (m, 3H), 7.54-7.56 (m, 2H), 9.39 (br.s., 1H). ^{13}C NMR ($CDCl_3$): δ = 24.4 (CH_2), 25.9 (CH_2), 45.7 (CH_2), 48.3 (CH_2), 51.7 (CH_3), 115.9 (CH), 119.9 (C), 122.3 (C), 126.7 (CH), 128.6 (CH), 129.0 (CH), 131.0 (C), 134.5 (C), 161.4 (C), 165.7 (C). HRMS (ESI-TOF) (m/z): $[M+H]^+$ Calcd. for $C_{17}H_{19}N_2O_3^+$ 299.1390; Found 299.1394.

*Methyl 5-(4-bromophenyl)-4-(pyrrolidine-1-carbonyl)-1H-pyrrole-2-carboxylate (**9l**)*. Compound **9l** was obtained from (*E*)-methyl 3-(3-(4-bromophenyl)-5-(pyrrolidin-1-yl)isoxazole-4-yl)acrylate **8l** (50 mg, 0.14 mmol) and $FeCl_2 \cdot 4H_2O$ (3 mg, 0.015 mmol) in MeCN (3 mL) according to the general procedure D. The product was purified by filtration through a pad of silica (ethyl acetate). A colorless solid, mp 177-179 °C (ethyl acetate), yield 26 mg (54%), ^{1}H NMR ($CDCl_3$): δ = 1.72-1.78 (m, 2H), 1.82-1.89 (m, 2H), 3.11-3.14 (m, 2H), 3.55-3.59 (m, 2H), 3.85 (s, 3H), 7.00 (d, J = 2.5 Hz, 1H), 7.43 (d, J = 8.5 Hz, 2H), 7.51 (d, J = 8.5 Hz, 2H), 9.54 (br.s.. 1H). ^{13}C NMR ($CDCl_3$): δ = 24.4 (CH_2), 25.9 (CH_2), 45.8 (CH_2), 48.5 (CH_2), 51.8 (CH_3), 115.9 (CH), 120.0 (C), 122.5 (C), 122.7 (C), 128.4 (CH), 129.9 (C), 132.1 (CH), 133.6 (C), 161.3 (C), 165.5 (C). HRMS (ESI-TOF) (m/z): $[M+H]^+$ Calcd. for $C_{17}H_{18}BrN_2O_3^+$ 377.0495; Found 377.0499.

*(2-(4-Nitrophenyl)-5-phenyl-1H-pyrrole-3-yl)(pyrrolidin-1-yl)methanone (**9m**)*. Compound **9m** was obtained from (*E*/*Z*)-3-(4-nitrophenyl)-5-(pyrrolidin-1-yl)-4-styrylisoxazole **8m** (52 mg, 0.14 mmol) and $FeCl_2 \cdot 4H_2O$ (3 mg, 0.015 mmol) in MeCN (3 mL) according to the general procedure D. The product was purified by filtration through a pad of silica ($CHCl_3$). A yellow solid, mp 268-269 °C ($CHCl_3$), yield 41 mg (79%). ^{1}H NMR (DMSO-d_6): δ = 1.70-1.76 (m, 2H), 1.79-1.86 (m, 2H), 3.19-3.22 (m, 2H), 3.46-3.49 (m, 2H), 6.80 (d, J = 2.5 Hz, 1H), 7.26-7.29 (m, 1H), 7.40-7.44 (m, 2H), 7.82-7.86 (m, 4H), 8.25-8.27 (m, 2H), 11.74 (s, 1H). ^{13}C NMR (DMSO-d_6): δ = 24.0 (CH_2), 25.5 (CH_2), 45.4 (CH_2), 48.0 (CH_2), 107.8 (CH), 122.4 (C), 123.8 (CH), 124.7 (CH), 126.4 (CH), 127.0 (CH), 128.0 (C), 128.7 (CH), 131.3 (C), 134.3 (C), 138.2 (C), 145.2 (C), 165.5 (C). HRMS (ESI-TOF) (m/z): $[M+H]^+$ Calcd. for $C_{21}H_{20}N_3O_3^+$ 362.1499; Found 362.1504.

*N,N-Dibenzyl-2-(4-nitrophenyl)-5-phenyl-1H-pyrrole-3-carboxamide (**9n**)*. Compound **9n** was obtained from (*E*/*Z*)-*N,N*-dibenzyl-3-(4-nitrophenyl)-4-styrylisoxazole-5-amine **8n** (133 mg, 0.27 mmol) and $FeCl_2 \cdot 4H_2O$ (5 mg, 0.025 mmol) in in MeCN (3 mL) at 80 °C for 21 h according to the general procedure D. The product was purified by filtration through a pad of silica (ethyl acetate/CH_2Cl_2 1:0-2:1). orange solid, mp 251-252 °C (ethyl acetate/CH_2Cl_2), yield 115 mg (86 %).

^{1}H NMR (DMSO-d_6): δ = 4.37 (s, 2H), 4.57 (s, 2H), 6.80 (s, 1H)m 7.08-7.10 (m, 2H), 7.24-7.43 (m, 11H), 7.75 (d, *J* = 8.8 Hz, 2H), 7.77-7.79 (m, 2H), 8.11 (d, *J* = 8.8 Hz, 2H), 11.82 (s, 1H). ^{13}C NMR (DMSO-d_6): δ = 46.8 (CH_2), 51.1 (CH_2), 107.7 (CH), 120.7 (C), 123.7 (CH), 124.7 (CH), 126.3 (CH), 127.1 (CH), 127.3 (CH), 127.8 (C), 128.5 (CH), 128.7 (CH), 131.1 (C), 145.1 (C), 168.1 (C). HRMS (ESI-TOF) (m/z): $[M+H]^+$ Calcd. for $C_{31}H_{26}N_3O_3^+$ 488.1969; Found 488.1990.

*(2-(tert-Buthyl)-5-phenyl-1H-pyrrole-3-yl)(pyrrolidin-1-yl)methanone (**9o**).* Compound **9o** was obtained from (*E*/*Z*)-3-(*tert*-butyl)-5-(pyrrolidin-1-yl)-4-styrylisoxazole **8o** (60 mg, 0.2 mmol) and $FeCl_2 \cdot 4H_2O$ (4 mg, 0.02 mmol) in 4 mL of MeCN at 80 °C for 4 d according to the general procedure D. The product was purified by filtration through a pad of silica (light petroleum/ethyl acetate 1:1-0:1). A light yellow solid, mp 240-241 °C (light petroleum/ethyl acetate), yield 38 mg (63%). ^{1}H NMR ($CDCl_3$): δ = 1.40 (s, 9H), 1.83-1.95 (m, 4H), 3.38-3.41 (m, 2H), 3.58-3.61 (m, 2H), 6. 36 (d, *J* = 2.8 Hz, 1H), 7.17-7.21 (m, 1H), 7.32-7.36 (m, 2H), 7.41-7.43 (m, 2H), 8.24 (br.s., 1H). ^{13}C NMR ($CDCl_3$): δ = 24.7 (CH_2), 26.0 (CH_2), 30.0 (CH_3), 32.6 (C), 45.5 (CH_2), 49.1 (CH_2), 105.7 (CH), 117.5 (C), 123.6 (CH), 126.1 (CH), 128.78 (C), 128.84 (CH), 132.4 (C), 138.9 (C), 168.4 (C). HRMS (ESI-TOF) (m/z): $[M+H]^+$ Calcd. for $C_{19}H_{25}N_2O^+$ 297.1961; Found 297.1973.

*(5-(Naphthalen-1-yl)2-phenyl-1H-pyrrol-3-yl)(pyrrolidin-1-yl)methanone (**9p**).* Compound **9p** was obtained from *(E/Z)*-4-(2-(naphthalen-1-yl)vinyl)-3-phenyl-5-(pyrrolidin-1-yl)isoxazole **8p** (112 mg, 0.31 mmol) and $FeCl_2 \cdot 4H_2O$ (7 mg, 0.035 mmol) in 9 mL of MeCN for 4 h according to the general procedure D. The product was purified by filtration through a pad of silica (light petroleum/ethyl acetate 4:1-1:1). A colorless solid, mp 250-251 °C (light petroleum/ethyl acetate), yield 89 mg (79%). ^{1}H NMR (DMSO-d_6): δ = 1.68-1.73 (m, 2H), 1.76-1.82 (m, 2H), 3.21-3.24 (m, 2H), 3.44-3.47 (m, 2H), 6.51 (d, J = 2.5 Hz, 1H), 7.25-7.29 (m, 1H), 7.38-7.42 (m, 2H), 7.54-7.68 (m, 6H), 7.91-7.936 (m, 1H), 7.98-8.00 (m, 1H), 8.29-8.31 (m, 1H), 11.70 (s, 1H). ^{13}C NMR (DMSO-d_6): δ = 24.0 (CH_2), 25.5 (CH_2), 45.3 (CH_2), 47.9 (CH_2), 110.2 (CH), 118.8 (C), 125.43 (CH), 125.47 (CH), 126.0 (CH), 126.2 (CH), 126.5 (CH), 126.6 (CH), 126.8 (CH), 127.4 (CH), 128.3 (CH), 128.4 (CH),

130.22 (C), 130.25 (C), 130.32 (C), 130.8 (C), 132.2 (C), 133.5 (C), 166.2 (C). HRMS (ESI-TOF) (m/z): $[M+H]^+$ Calcd. for $C_{25}H_{23}N_2O^+$ 367.1805; Found 367.1811.

*Methyl 2-phenyl-4,5,6,7-tetrahydro-1H-indole-3-carboxylate (**9q**).* Compound **9q** was obtained from 4-(cyclohex-1-en-1-yl)-5-methoxy-3-phenylisoxazole **8q** (40 mg, 0.16 mmol) and $FeCl_2 \cdot 4H_2O$ (4 mg, 0.02 mmol) in MeCN (3 mL) 4 h according to the general procedure D. The product was purified by filtration through a pad of silica (light petroleum/ethyl acetate 3:1). A colorless solid, mp 131-132 °C (light petroleum/ethyl acetate), yield 39 mg (98%). ^{1}H NMR ($CDCl_3$): δ = 1.78-1.84 (m, 4H), 2.55-2.58 (m, 2H), 2.75-2.78 (m, 2H), 3.69 (s, 3H), 7.30-7.39 (m, 3H), 7.49-7.53 (m, 2H), 8.01 (ws, 1H). ^{13}C NMR ($CDCl_3$): δ = 22.5 (CH_2), 22.8 (CH_2), 23.3 (CH_2), 23.4 (CH_2), 50.5 (CH_3), 109.9 (C), 120.2 (C), 127.7 (CH), 127.8 (C), 128.0 (CH), 128.9 (CH), 133.0 (C), 135.8 (C), 166.1 (C). HRMS (ESI-TOF) (m/z): $[M+H]^+$ Calcd. for $C_{16}H_{18}NO_2^+$ 256.1332; Found 256.1342.

*2-Phenyl-4,5,6,7-tetrahydro-1H-indole-3-carbamide (**9r**).* Compound **9r** was obtained from 4-(cyclohex-1-en-1-yl)-phenylisoxazol-5-amine **8r**[20] (99 mg, 0.41 mmol) and $FeCl_2 \cdot 4H_2O$ (9 mg, 0.045 mmol) in MeCN (5 mL) for 4 h according to the general procedure D. The product was purified by filtration through a pad of Al_2O_3 (ethyl acetate). A light yellow solid, mp 209-210 °C (ethyl acetate), yield 85 mg (86%). ^{1}H NMR (DMSO-d_6): δ = 1.69-1.74 (m, 4H), 2.51-2.54 (m, 4H), 6.70 (ws, 1H), 6.89 (ws, 1H), 7.18-7.22 (m, 1H), 7.31-7.35 (m, 2H), 7.51-7.53 (m, 2H), 10.81 (s, 1H). ^{13}C NMR (DMSO-d_6): δ = 22.1 (CH_2), 22.2 (CH_2), 22.7 (CH_2), 23.2 (CH_2), 115.8 (C), 116.7 (C), 126.0 (CH), 126.9 (CH), 127.2 (C), 128.0 (CH), 128.7 (C), 133.1 (C), 168.3 (C). HRMS (ESI-TOF) (m/z): $[M+H]^+$ Calcd. for $C_{15}H_{16}N_2O^+$ 241.1335; Found 241.1343.

*Methyl 2-(2-oxo-2H-chromene-3-yl)-3-phenyl-2H-azirine-2-carboxylate (**12a**).* Compound **12a** was obtained from 4-(5-methoxy-3-phenylisoxazol-4-yl)-2*H*-chromen-2-one **8s** (168 mg, 0.52 mmol) and $FeCl_2 \cdot 4H_2O$ (11 mg, 0.055 mmol) in MeCN (4 mL) for 3 h according to the general procedure D. The product was purified by filtration through a pad of silica (DCM). A colorless solid, mp 129-130 °C (DCM), yield 147 mg (88%). ^{1}H NMR ($CDCl_3$): δ = 3.75 (s, 3H), 7.24-7.28 (m, 1H), 7.32-

7.34 (m, 1H), 7.45-7.53 (m, 2H), 7.56-7.60 (m, 2H), 7.63-7.66 (m, 1H), 7.85 (s, 1H), 8.10-8.12 (m, 2H). ^{13}C NMR ($CDCl_3$): δ = 37.9 (C), 52.9 (CH_3), 116.6 (CH), 118.8 (C), 121.2 (C), 124.5 (CH), 125.7 (C), 127.9 (CH), 129.4 (CH), 131.2 (CH), 131.7 (CH), 134.3 (CH), 140.7 (CH), 153.6 (C), 161.1 (C), 163.7 (C), 170.7 (C). HRMS (ESI-TOF) (m/z): $[M+Na]^+$ Calcd. for $C_{19}H_{13}NNaO_4^+$ 342.0737; Found 342.0746.

*Methyl 4-oxo-2-phenyl-1,4-dihydrochromeno[4,3-b]pyrrole-3-carboxylate (**9s**).* Compound **9s** was obtained from 4-(5-methoxy-3-phenylisoxazol-4-yl)-2*H*-chromen-2-one **8s** (101 mg, 0.32 mmol) and $FeCl_2 \cdot 4H_2O$ (7 mg, 0.035 mmol) in DMSO (2 mL) at 160 °C for 3 h according to the general procedure D. The product was purified by filtration through a pad of Al_2O_3 (ethyl acetate). A colorless solid, mp 243-244 °C (ethyl acetate), yield 81 mg (80%). ^{1}H NMR (DMSO-d_6): δ = 3.76 (s, 3H), 7.38-7.42 (m, 1H), 7.45-7.56 (m, 5H), 7.63-7.66 (m, 2H), 8.23-8.25 (m, 1H), 13.04 (s, 1H). ^{13}C NMR (DMSO-d_6): δ = 51.9 (CH_3), 107.0 (C), 111.6 (C), 112.9 (C), 116.8 (CH), 122.0 (CH), 124.2 (CH), 128.1 (CH), 128.6 (CH), 128.9 (CH), 129.5 (CH), 130.0 (C), 135.8 (C), 137.6 (C), 151.6 (C), 156.2 (C), 164.8 (C). HRMS (ESI-TOF) (m/z): $[M+Na]^+$ Calcd. for $C_{19}H_{13}NNaO_4^+$ 342.0737; Found 342.0729.

*(Z)-Methyl 2-(but-1-en-1-yl)-3-phenyl-2H-azirine-2-carboxylate (**12b**) and methyl 5-ethyl-2-phenyl-1H-pyrrole-3-carboxylate (**9t**).* Compound **12b**, as a light yellow oil, yield 56 mg (57%), and compound **9t**, as a light yellow solid, mp 82-85 °C, yield 16 mg (16%), were obtained from (*E*/*Z*)-4-(but-1-en-1-yl)-5-methoxy-3-phenylisoxazole **8t** (99 mg, 0.43 mmol) and $FeCl_2 \cdot 4H_2O$ (9 mg, 0.045 mmol) in MeCN (3 mL) according to the general procedure D. The products were separated by column chromatography (light petroleum/ethyl acetate 8:1). Pyrrole **9t** was obtained as a sole product from (*E*/*Z*)-4-(but-1-en-1-yl)-5-methoxy-3-phenylisoxazole **8t** (118 mg, 0.52 mmol) and $FeCl_2 \cdot 4H_2O$ (11 mg, 0.055 mmol) in MeCN (4 mL) at 110 °C (a thick wall tube with a tightly sealed screw cap) for 5 h, yield 81 mg (69%). **12b**: ^{1}H NMR ($CDCl_3$): δ = 0.86 (t, *J* = 7.5 Hz, 3H), 2.02 (pd, *J* = 7.5, 1.6 Hz, 2H), 3.71 (s, 3H), 5.62 (dt, *J* = 11.4, 7.5 Hz, 1H), 5.94 (dt, *J* = 11.4, 1.6 Hz,

1H), 7.55-7.65 (m, 3H), 7.85-7.87 (m, 2H). ^{13}C NMR ($CDCl_3$): δ = 13.9 (CH_3), 21.8 (CH_2), 37.8 (C), 52.6 (CH_3), 122.6 (CH), 122.7 (C), 129.4 (CH), 130.1 (CH), 133.6 (CH), 138.2 (CH), 161.1 (C), 172.3 (C). HRMS (ESI-TOF) (m/z): 230.1176 Calcd. for $C_{14}H_{16}NO_2$ $[M+H]^+$; Found 230.1197. **9s**: ^{1}H NMR ($CDCl_3$): δ = 1.28 (t, J = 7.6 Hz, 3H), 2.62 (q, J = 7.6 Hz, 2H), 3.72 (s, 3H), 6.41 (d, J = 3.0 Hz, 1H), 7.30-7.41 (m, 3H), 7.56-7.59 (m, 2H), 8.26 (br.s., 1H). ^{13}C NMR ($CDCl_3$): δ = 13.2 (CH_3), 20.5 (CH_2), 50.8 (CH_3), 107.9 (CH), 111.5 (C), 127.9 (CH), 128.1 (CH), 128.7 (CH), 132.3 (C), 134.2 (C), 136.0 (C), 165.5 (C). HRMS (ESI-TOF) (m/z): $[M+H]^+$ Calcd. for $C_{14}H_{16}NO_2^+$ 230.1176; Found 230.1173.

Supporting Information.

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc….

NMR spectra for all new compounds and computation details: energies of compounds and their Cartesian coordinates (PDF)

Crystallographic data for **9e** (CIF)

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