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One-Pot Synthesis of Five-Membered Cyclic Thioethers or Ethers via Intramolecular Nitrile Oxide-Olefin Cycloaddition (INOC) or Intramolecular Alkoxycarbonyl Nitronate-Olefin Cycloaddition (IAOC) by the Use of Methyl Chloroformate

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Abstract: Reaction of β -nitrostyrenes 1 with allyl mercaptan 2 in the presence of triethylamine generated unsaturated nitro sulfides 3 and then the solution was treated with methyl chloroformate (MCF) and was refluxed to obtain [3.3.0]bicyclic products *trans-6* and *cis-6* in one-pot. The ratios of *trans-6:cis-6* were from 1.1:1 to 1.8:1 and the mechanism of the formation 6 is proposed to proceed through the formation of nitrile oxides 5 to undergo intramolecular nitrile oxide-olefin cycloaddition (INOC). Nitronates 16, prepared from 1 with allyl alcohol and base, can be converted into methoxycarbonyl nitronates 22 by treating the solution with methyl chloroformate and catalytic amount of 4-dimethylaminopyridine (DMAP) in the presence of different amounts of triethylamine. Intermediates 22 can either undergo intramolecular alkoxycarbonyl nitronate-olefin cycloaddition (IAOC) to generate highly stereoselective product *trans-14* or undergo INOC to yield *trans-14* and *cis-14*. The application of this improved methodology to synthesize different heterocyclic products 10, 26, and 27 is reported. © 1999 Elsevier Science Ltd. All rights reserved.

Introduction

Nitro olefins are useful intermediates in organic synthesis.¹ Due to the strong electron-withdrawing property of the nitro group, conjugated nitroalkenes are excellent Michael acceptors and the nitro group can be further transformed into a host of reactive intermediates, including silyl nitronates,² nitrile oxides,³ and hydroximoyl chlorides.⁴ Intramolecular 1,3-dipolar cycloadditions have been proved to be useful in synthetic utility.⁵ Among these, intramolecular nitrile oxide-olefin cycloadditions (INOC),³⁻⁵ intramolecular silyl nitronate-olefin cycloadditions (ISOC),² and intramolecular oxime-olefin cycloadditions (IOOC)⁶ are useful methods to generate [n.3.0] bicyclic compounds which can be converted into different products.

Nitrile oxides are important intermediates in the synthesis of isoxazoles and of many five-membered heterocyclic system via 1,3-dipolar cycloaddition.² Two widely used methods to generate nitrile oxides are: (1) reaction of aldoximes with oxidizing agents⁷ or halogenating species⁸ and (2) reaction of primary nitroalkanes with different kinds of dehydrating agent such as aromatic isocyanates in the Mukaiyama-Hoshino method³ or ethyl chloroformate or benzenesulfonyl chloride in the Shimizu method.⁹

Our previous study found that medium to high yields of [3.3.0] and [4.3.0] bicyclic compounds or

tricyclic products could be obtained when 1-aryl-2-nitroethylene 1 reacted with diethyl allyl malonate anion 10a or alkenyl Grignard reagents 10b and then treated the nitronates with ethyl chloroformate and a catalytic amount of 4-dimethylaminopyridine (DMAP) in one-pot. In this paper, we report the preparation of five-membered cyclic thioethers or ethers from the reactions of 1 with allyl mercaptan or allyl alcohol and a base to form the nitronates and then treat the nitronates with methyl chloroformate (MCF), DMAP, and triethylamine in one-pot.

Results and Discussion

Sulfur as nucleophile

It has been reported that unsaturated nitro sulfides 3 react with Me₃SiCl-Et₃N^{2c} or PhNCO-Et₃N^{2d} at room temperature to provide cyclic sulfides *trans*-6 only or *trans*-6 and *cis*-6. Our study found that reaction of β -nitrostyrene 1a with allyl mercaptan 2 in the presence of triethylamine generated 3a almost quantitatively (check by NMR). Without isolation of 3a, the mixture was directly treated with MCF in one-pot and was refluxed for 3 hours to isolate 94% of *trans*-6a and *cis*-6a (Table 1, entry 1, 98% of NMR yield) and the ratio of *trans*-6a:*cis*-6a was 1.3:1 (equation 1). Not only 83% of the bicyclic products *trans*-6c and *cis*-6c but also 10% of 7c and 8c were isolated when 3c was used (entry 3). Similarly, 60% of the major products *trans*-6e and *cis*-6e and 30% of the minor products 7e and 8e were isolated when 1e was used (entry 4).



 Table 1 Reactions of 1 with Allyl Mercaptan 2 and Methyl Chloroformate to Generate Products 6-8

entry	substrate	6 yield ^a % (trans:cis) ^b	7 + 8 yield ^a %		
1	1 a	94 (1.3 : 1)			
2	1b	98 (1.1 : 1)	-		
3	lc	83 (1.3 : 1)	10		
4	le	60 (1.8 : 1)	30		

^a Isolated yield. ^b The ratios were measured by NMR.

The structure and the stereochemistry of compounds 6 can be assigned by comparing the spectral data with the literature reported.^{2d} The formation of the products 6-8 can be explained by converting 3 into 4 followed by elimination of carbon dioxide and methanol to generate nitrile oxides 5 that undergo INOC to yield the final products (Scheme 1). The following observation evidently supports this proposed mechanism. First, not only the major product 6 but also the minor products 7 and 8 were isolated when substrates 1 c and 1 e were used. The isolation of compounds 7 and 8 is significant evidence to support that the formation of the minor products proceeds through the trapping of the nitrile oxide 5 by methyl chloroformate or allyl mercaptan because similar products also have been reported.^{9,10} Second, the ratios of *trans*-6:*cis*-6 observed in this study are very closed to the ratios reported by Hassner et al. in the reaction of pure 3 with PhNCO-Et₃N (Mukaiyama-Hoshino method) at room temperature.^{2d}





After obtaining table 1, we tried applying this improved methodology to synthesize tricyclic compounds. Thus 1b was allowed to react with 3-acetylthiocyclohexene 9 and sodium ethoxide and then the solution was treated with MCF and triethylamine and was refluxed for 30 minutes as described above. As expected, 24% of *trans*-10 and 16% of *cis*-10 were isolated after the mixture was purified by flash column chromatography (equation 2).



Oxygen as nucleophile

It is reported that reaction of unsaturated alcohols with α -bromoalkanal O-(trimethylsilyl)oximes 11 in the presence of fluoride generate α -(allyloxy)alkanal oximes 12 and 12 can be converted into nitrile oxides 13 that undergo INOC to yield fused-ring tetrahydrofurans *trans*-14 and *cis*-14 by reaction with sodium hypochlorite (equation 3).¹¹



The preparation of 14 (n = 1) from the reaction of unsaturated nitroethers 15, prepared from the appropriate nitro olefins 1 and allyl alcohol in the presence of base, with phenyl isocyanate^{2c,12} or with 1,4-phenylene diisocyanate¹³ and triethylamine also has been reported (equation 4).



Hassner et al. also have reported either unsaturated nitroethers 15^{2c} or nitronates 16, ¹⁴ generated from nitroalkenes 1 and potassium allyloxide, can be converted into silyl nitronates 17 by treatment trimethylsilyl chloride to undergo ISOC reaction to yield N-trimethylsilyloxy isoxazolidines 18 and then the solution was workup with diluted hydrochloric acid solution, tetrabutylammonium fluoride, or anhydrous CsF to generate highly stereoselective product *trans*-14 only (equation 5).



After obtaining Table 1 by using allyl mercaptan as nucleophile, we tried to focus our study on the reaction of 1 with allyl alcohol and base under similar conditions. When 1b reacted with cinnamyl alcohol 19 and potassium *tert*-butoxide at -78 $^{\circ}$ C, the solution was workup with dilute acid solution to obtain 68% of 20. We were surprised to find that only quantitative of the highly stereoselective product *trans*-21 was generated when pure 20 was treated with methyl chloroformate (MCF) and triethylamine and the solution was refluxed for two hours according to literature procedures (equation 6).⁹



Based on equations 1 and 6, we decided not to isolate 20 but just to treat the nitronate with MCF, DMAP, and triethylamine in one-pot as described above. As expected, 79% (NMR yield) of *trans*-21 was generated after the solution was refluxed for 3 hours. The stereochemistry of *trans*-21 could be determined according to the NOESY studies. Thus, irradiation of H_{3a} caused enhancement of H_{4cis} only and irradiation of H_6 caused enhancement of both H_{4trans} and H_3 simultaneously.

It has been reported that β -nitrostyrene 1a undergoes 1,4-addition with potassium allyloxide at -20 or -98 ^oC to generate medium to high yields (77-90%) of 1-allyloxy-2-nitro-1-phenylethane 15a after adding the nitronate 16a to dilute aqueous acid solution.^{12,14} Based on equation 6 and literature report, ^{12,14} we added β -nitrostyrene 1a (1 equivalent) to potassium allyloxide (1.2 equivalents), prepared from allyl alcohol and potassium *tert*-butoxide, in a THF solution at -78 ^oC to generate nitronate 16a and then MCF (6 equivalents) and catalytic amount of DMAP (0.1 equivalent) were slowly added to the solution and the mixture was stirred for 1 hour at the same temperature. The solution was then refluxed for 10 hours to obtain 39% of *trans*-14a and 20% of nitroalkene 15a (equation 7, Table 2, entry 1). When 4.0 equivalents of Et₃N were added to the solution and the solution and the solution was refluxed for 2 hours, the yield of *trans*-14a was increased to 72% and the yield of 15a was decreased to 8% (entry 2). This result indicates that the addition of triethylamine to the solution not only can enhance the reaction but also can increase the yield of *trans*-14a.



 Table 2 Reactions of β-Nitrostyrenes 1 with Allyl Alcohol and Base and then the Solution was Treated with Methyl Chloroformate (MCF) and Catalytic Amount of 4-Dimethylaminopyridine (DMAP) (0.1 equivalent) in the Presence of Different Amount of Triethylamine

entry	1	alcohol (equiv)	base (equiv)	addition temp (°C)	MCF (equiv)	Et ₃ N (equiv)	hours (reflux)	14 (%) ^a	trans:cis	15 (%) ^a
1	1a	1.2	t-BuOK (2.0)	-78	6	0	10	39 ^b	> 99 : 1	20
2	1a	1.2	t-BuOK (2.0)	-78	6	4	2	72	> 99 : 1	8
3	1a	1.2	t-BuOK (2.0)	0	15	0	2	58	> 99 : 1	29
4	1a	1.2	t-BuOK (2.0)	0	15	4	2	88	> 99 : 1	-
5	1a	1.2	t-BuOK (2.0)	r.t.	15	4	2	75	> 99 : 1	-
6	1b	1.2	t-BuOK (2.5)	-78	3	0	1 ^c	44 ^b	> 99 : 1	29
7	1b	1.2	t-BuOK (2.5)	-78	6	0	5	9 0	> 99 : 1	tr
8	1b	1.2	t-BuOK (2.0)	0	15	3	1.5	87	> 99 : 1	tr
9	1b	1.2	t-BuOK (2.0)	r.t.	15	3	1.5	92	> 99 : 1	tr
10	1c	1.2	t-BuOK (2.0)	-78	15	4	9	86 ^b	> 99 : 1	-
11	1c	1.2	t-BuOK (2.0)	0	15	4	10	88	> 99 : 1	-
12	1c	1.2	t-BuOK (2.0)	r.t.	15	4	8	44	> 99 : 1	-
13	1d	3.0	NaH (5.0)	0	10	0 ^{<i>d</i>}	48 ^e	92 ^b	-	-
14	1d	1.2	t-BuOK (2.0)	0	15	4	4	99	-	-
15	1 d	1.2	t-BuOK (2.5)	r.t.	15	4	4	99	-	-
1 6	1e	1.2	t-BuOK (2.5)	-78	12	5	5	80 ^b	2.1 : 1	-
17	1e	1.2	t-BuOK (2.5)	0	12	5	5	tr	-	-
18	1f	1.2	t-BuOK (2.5)	-78	12	2	8⁄	39 ^b	19 : 1	-

^a Yields were measured by ¹H NMR from integrations with a known amount of dimethylformamide as an internal standard. ^b Isolation yields. ^c The solution was stirred for 1 hour at room temperature. ^dOne equivalent of DMAP was used. ^e The solution was stirred for 48 hours at room temperature. ^fThe solution was stirred for 8 hours at 40 °C. In order to gain more insight into the temperature effect to the reaction, the addition was performed at different temperatures and the nitronate 16a was also treated with different amounts of methyl chloroformate and triethylamine in the presence of catalytic amount of DMAP. When the addition was performed at 0 $^{\circ}$ C, 58% of *trans*-14a and 29% of 15a were obtained after adding 15 equivalents of MCF to the solution and refluxing the solution for 2 hours (entry 3). Only 88% of *trans*-14a was generated when 4 equivalents of Et₃N were added (entry 4). 75% Of *trans*-14a and trace amounts of unidentified by-products were obtained when the addition was performed at room temperature (entry 5). In addition to 1a, other substrates such as 1b-f were also used to react with potassium allyloxide under similar conditions as described above. Medium to high yields of fused-ring tetrahydrofurans 14b-f (entries 6-19) were generated and all the experimental data were shown in Table 2.

According to Table 2, we concluded that 1 undergo 1,4-addition reaction with potassium allyloxide at different temperature to generate nitronates 16. When nitronates 16 were treated with MCF and catalytic amount of DMAP in the presence of different amount of Et_3N , medium to high yields of 14 and 15 were obtained in one-pot. Usually better results are observed when the additions were performed at -90 $^{\circ}C^{11,13}$ or -78 $^{\circ}C$. Both crude NMR and GCMS analyses indicated that only the major products *trans*-14a-c could be observed when substrates 1a-c were used. On the contrary, *trans*-14e and *cis*-14f and *cis*-14f isomers were obtained under similar conditions when 1e or 1f was used (entries 16 and 18).

It has been reported that unsaturated nitroether 15a can react with phenyl isocyanate and triethylamine to generate product 14a in 87 or 89% and the ratio of *trans*-14a:*cis*-14a is 4:1 or 9:1.^{12a,b} Similarly, 88% of 14a also could be prepared when 15a reacts with 1,4-phenylene diisocyanate and the ratio of *trans*-14a:*cis*-14a was 9:1.¹³ All these results indicate that nitrile oxide 13a were formed during these reactions and the mechanism is proposed to proceed through INOC reaction to yield the heterocyclic products. Usually *trans* isomer predominates because the steric factor plays an important role in the INOC reaction according to the experimental results and model calculation.^{11,12,15}

Based on Table 2, we proposed that the formation of *trans*-14a-c proceeds through intramolecular alkoxycarbonyl nitronate-olefin cycloaddition (IAOC) reaction but the generation of *trans*-14e-f and *cis*-14e-f proceeds through INOC reaction. After adding substrate 1 to potassium allyloxide, nitronates 16 can either obtain a proton to yield nitroethers 15 or be converted into methoxycarbonyl nitronates 22 by reaction with MCF. Nitronates 22 can either undergo IAOC to produce intermediate 23 and then eliminate carbon dioxide and methanol (or MeOCOOH) to generate *trans*-14 only (pathway A) or eliminate carbon dioxide and methanol to generate nitrile oxide 13 to undergo INOC to yield compounds *trans*-14 and *cis*-14 (pathway B). Possible reaction mechanism is proposed as Scheme 2.

The stereochemistry of *trans* 14a-c can be explained by that the methoxycarbonyl nitronate olefin cycloaddition of the intermediate 22, in which the aryl group is assumed to take a pseudoequatorial orientation, probably proceed through the preferred *endo* transition state (Ar and H), which is similar to the literature report.^{14,2g} Direct evidence to support the assumption that the generation of products *trans*-14e-f and *cis*-14e-f proceeds through INOC pathway is the isolation of a trace amount of 24 when substrate 1e was used. The formation of the intermediate 24 also can be explained by the trapping of the intermediate nitrile oxide 13f with MCF. Similar results have also been reported to prove the presence of the nitrile oxides as intermediate in literature.^{9,10}



The roles of DMAP and Et_3N are important to the reaction system.^{3,9,10,12,13} DMAP is known to be an excellent catalyst for esterification of alcohols¹⁴ and should enhance the formation of 22. Furthermore, DMAP is also a strong base and can serve equally well in the elimination of the carbon dioxide and methanol (or MeOC(O)OH) to yield 13 or 14.^{15,16} In addition to DMAP, triethylamine also can be used as catalyst to enhance the reaction as well as base to deprotonate nitroethers 15 to generate nitronates 16.

It has been reported that α -bromopropanal O-(trimethylsilyl)oxime can react with cyclohexen-3-ol in the presence of fluoride ion to generate tricyclic ether *trans*-25 and *cis*-25 in 67% yield as 1:1 mixture of *trans*- and *cis*-diastereomers (equation 8).¹¹



Based on table 2 and equations 2 and 8, we tried to react 1b (1 equivalent) with cyclohexen-3-ol or cycloocten-3-ol (1.25 equivalents) and potassium *tert*-butoxide (2 equivalents) at -78 °C and then treat the solution with MCF (6 equivalents) and DMAP (0.1 equivalent). After the solution was refluxed for 5 hours, 33% of *trans*-26 and 48% of *cis*-26 or 21% of *trans*-27 and 44% of *cis*-27 were isolated (equation 9). The stereochemistry of 26 and 27 could be determined according to the NOESY studies. Thus, irradiation of H_{cis} caused enhancement of H_a', H_b', and H_c' but irradiation of H_{trans} had no effect on H_a, H_b, and H_c. The mechanism of the formation compounds 26 and 27 is also proposed to proceed through the generation of nitrile oxides to undergo INOC which is similar to equation 8.¹¹



Intramolecular 1,3-dipolar cycloaddition of nitrile oxides to a substituted double bond affords furoisoxazoles with excellent stereoselectivity.^{5,11} Hassner and Murthy found that nitrile oxide 13 ($R^1 = -CH_3$ or -Ph; $R^2 = -H$) delivers heterocycle 14 (C_6 -H trans to C_{3a} -H) selectively (equation 10).^{11,12a} Kurth also found that moving the alkyl substitutent from C_6 to C_4 (i.e., $R^1 = -H$; $R^2 = -CH_3$ or -Ph) results in complete diastereofacial selectivity in each case, only the *trans* isomer (C_4 -H trans to C_{3a} -H) was detected.^{12b}



Kurth et al. have reported that isoxazolines and furoisoxazoles are important intermediates in the synthesis of 2,5-disubstituted tetrahydrofurans.^{18,19} Based on equation 10, Kurth reported that compounds 31 and 32 can be synthesized from the reactions of nitroethers 29 and 30, prepared from the Michael addition of the derived potassium alkoxide of alcohols 28a-c and 1b, with phenyl isocyanate in the presence of triethylamine. For the C₄ phenyl-substituted system such as 29a and 30a, the reaction is 100% faceselective giving only furoisoxazole *trans*-31a and *cis*-31a in a 1:1 diastereomeric ratio and the total yield approximately equals to 53% from 1b to the final products 31a (Scheme 3).¹⁸ Based on our experimental results and Scheme 3, we thought it should be possible to obtain the same products under similar condition as described above. As expected, 47% of *trans*-31a and 35% of *cis*-31a were isolated when 1b reacted with potassium alkoxide of dienol 28a, MCF, DMAP and Et₃N in one-pot and the solution was refluxed for 45 hours (equation 11).



The stereochemistry of the two different products was determined using the NOESY technique and the results were all consistent with literature report.¹⁸ The formation of the two diastereomers indicates that the reaction proceeds through the generation of nitrile oxides to undergo INOC reaction and the mechanism is similar to equations 8-10 and literature reports.^{11,19} Possible and reasonable explanation is that the increase of the steric hindrance of the bulky enol **28a** will retard the intermediate alkoxycarbonyl nitronate to undergo IAOC reaction and only INOC reactions could occur.

To prove the effect of the steric hindrance in the determining of the different isomers, we tried to react 1b (1.0 equivalent) with 3-methyl-1-buten-1-ol 33 (1.25 equivalents) and potassium *tert*-butoxide (2.5 equivalents) and treat the nitronate with MCF (6 equivalents), DMAP (0.1 equivalent), and Et₃N (10 equivalents) in one-pot. After the solution was refluxed for 6 hours, not only 55% of *trans*-34 and 21% of *cis*-34 but also 13% of 35 were isolated and the formation of the the different products is the significant evidence to support the assumption that the use of the bulky alkoxide may convert the reaction mechanism form IAOC into INOC due to the steric hindrance effect (equation 12).



Conclusion

An improved, easy, and efficient method affords medium to high yields of cyclic sulfides 6 or cyclic ethers 14 from the reactions of β -nitrostyrenes 1 with allyl mercaptan or allyl alcohol and base and then treating the nitronates with methyl chloroformate (MCF) and catalytic amount of 4-dimethylaminopyridine (DMAP) in the presence of different amount of triethylamine in one-pot. The generation of the cyclic sulfides *trans*-6 and *cis*-6 is proposed to proceed through the formation of the nitrile oxides as intermediate to undergo intramolecular nitrile oxide-olefin cycloaddition (INOC). The formation of highly stereoselective products *trans*-14 only can be explained by intramolecular alkoxycarbonyl nitronate-olefin cycloaddition (IAOC) reaction and the formation of *trans*-14 and *cis*-14 is proposed to proceed through INOC reaction. The application of this improved methodology to synthesize heterocyclic compounds such as 10, 26, and 27 is reported and the formation of both *trans*- and *cis*-isomer can be explained by the INOC mechanism. The converting of the reaction mechanism from IAOC into INOC can be explained by the steric effect of the bulky alkoxides which were generated from different alcohols such as cyclohexen-3-ol, cycloocten-3-ol, 1-phenyl-2,6-heptadien-1-ol 28a, and 3-methyl-1-buten-1-ol 33 with potassium *tert*-butoxide.

Experimental Section

General. All reactions were performed in flame or oven-dried glassware under a positive pressure of nitrogen. Air and moisture sensitive compounds were introduced by the use of a syringe or cannula through a rubber septum. THF and diethyl ether were distilled from sodium/benzophenone ketyl. Analytical thin layer chromatography was performed with E. Merck silica gel 60F glass plates and flash chromatography by the use of E. Merck silica gel 60 (230-400 mesh). GCMS were recorded on a HP 5890 GC/HP 5970B MSD, MS or HRMS were measured by JEOL JMS-D300 or JEOL JMS-HX110 spectrometer. ¹H and ¹³C NMR spectra were recorded with a Varian Gemini-200. All NMR data were obtained in CDCl₃ solution and chemical shifts (δ) were given in ppm relative to TMS. Elemental Analysis was performed by a Perkin-Elmer 2400 instrument. All melting points were determined on a MEL-TEMP II melting point apparatus and were uncorrected.

Materials. Compounds 1a-c, 1e, allyl mercaptan, cinnamyl alcohol, allyl alcohol, cyclohexen-3-ol, methyl chloroformate, potassium *tert*-butoxide, triethylamine, 4-dimethylaminopyridine, and 3-methyl-1-buten-1-ol 33 were purchased from Aldrich Chemical Co and were used without further purification. Compounds 1d, ²¹ 1f, ²² 3-acetylthiocyclohexene 9, ²³ and dienol $28a^{24,19}$ were prepared by modifying or according to the literature procedures.

Typical Experimental Procedures for the One-Pot Synthesis of 6-Aryl-3,3a,4,6tetrahydrothiopheno[3,4-c]isoxazole from the Reaction of β -Nitrostyrenes 1 and Allyl Mercaptan in the Presence of Triethylamine and then Treating the Nitronates with Methyl chloroformate (Table 1)

 β -Nitrostyrene 1a (3 mmol), allyl mercaptan 2 (3.3 mmol) and triethylamine (10.0 mmol) were dissolved in 30 mL diethyl ether and the solution was stirred at room temperature for 1 hour. After the starting material 1a disappeared by checking with TLC and crude NMR, 20 mmol of methyl chloroformate (MCF) were added to the solution and the solution was refluxed for 3 hours. The solution was poured into the ice-cold dilute acid solution, extracted with dichloromethane, dried over MgSO₄, filtered and the solvent was evaporated to obtain 56% of *trans*-6a and 42% of *cis*-6a (the yield was measured by NMR). The purification of the products was carried out by flash column chromatography by using hexane and ethyl acetate as eluent to obtain 94% of pure products *trans*-6a and *cis*-6a. The spectral data of *trans*-6a and *cis*-6a were consistent with literature report.^{2d} Not only 83% of the major products *trans*-6c and *cis*-6c but also 10% of the minor products 7c and 8c were isolated when 1c reacted with allyl mercaptan and MCF under similar conditions as described above.

trans-6-Phenyl-3,3a,4,6-tetrahydrothiopheno[3,4-c]isoxazole (*trans*-6a):^{2d} This compound is colorless liquid. ¹H NMR (200 MHz, CDCl₃) 7.49-7.24 (m, 5H), 5.22 (s, 1H), 4.56 (dd, J = 9.6, 7.8 Hz, 1H), 4.37-4.18 (m, 1H), 4.10 (dd, J = 10.0, 7.6 Hz, 1H), 3.20 (dd, J = 10.0, 7.8 Hz, 1H), 2.86 (dd, J = 10.0, 9.0 Hz, 1H). ¹³C NMR (50 MHz, CDCl₃) 168.2, 138.9, 128.8, 127.9, 127.3, 74.7, 55.1, 43.3, 31.6. MS *m*/z (relative intensity) 205 (M⁺, 70), 174 (63), 160 (29), 141 (18), 121 (100), 103 (39), 89 (50), 77 (61), 63 (40), 51 (58). HRMS calcd for C₁₁H₁₁NOS (M⁺) 205.0561, found 205.0570.

cis-6-Phenyl-3,3a,4,6-tetrahydrothiopheno[3,4-*c*]isoxazole (*cis*-6a):^{2d} This compound is colorless liquid. ¹H NMR (200 MHz, CDCl₃) 7.50-7.29 (m, 5H), 5.16 (d, J = 1.0, 1H), 4.61 (dd, J = 9.8, 7.6 Hz, 1H), 4.46-4.26 (m, 1H), 4.18 (dd, J = 10.0, 7.6 Hz, 1H), 3.16 (dd, J = 10.0, 7.8 Hz, 1H), 3.04 (dd, J = 10.0, 9.0 Hz, 1H). ¹³C NMR (50 MHz, CDCl₃) 168.4, 137.1, 128.8, 128.7, 128.3, 75.1, 57.0, 44.2, 31.5. MS *m/z* (relative intensity) 205 (M⁺, 77), 174 (58), 160 (21), 141 (20), 121 (100), 103 (48), 89 (63), 77 (65), 63 (43), 51 (60). HRMS calcd for C₁₁H₁₁NOS (M⁺) 205.0561, found 205.0566.

trans-6-(4-Methoxyphenyl)-3,3a,4,6-tetrahydrothiopheno[3,4-c]isoxazole (*trans*-6b):^{2d} This compound is colorless solid and the melting point is 112-113 ^OC after recrystallized from hexane and ethyl acetate solution. ¹H NMR (200 MHz, CDCl₃) 7.39 (dt, J = 8.8, 3.0 Hz, 2H), 6.88 (dt, J = 8.8, 3.0 Hz, 2H), 5.18 (s, 1H), 4.56 (dd, J = 10.0, 7.8 Hz, 1H), 4.37-4.18 (m, 1H), 4.09 (dd, J = 10.0, 7.8 Hz, 1H), 3.80 (s, 3H), 3.17 (dd, J = 10.0, 8.0 Hz, 1H), 2.84 (dd, J = 10.0, 9.0 Hz, 1H). ¹³C NMR (50 MHz, CDCl₃) 168.5, 159.4, 131.0, 128.5, 114.2, 74.7, 55.3, 55.1, 42.8, 31.6. MS *m*/z (relative intensity) 235 (M⁺, 100), 204 (39), 190 (30), 174 (30), 172 (36), 151 (84), 146 (65), 135 (21), 115 (17), 91 (13), 77 (10). HRMS calcd for C₁₂H₁₃NO₂S (M⁺) 235.0667, found 235.0665. Anal. Calcd for: C, 61.28; H, 5.53; N, 5.96. Found: C, 61.24; H, 5.53; N, 5.78.

cis-6-(4-Methoxyphenyl)-3,3a,4,6-tetrahydrothiopheno[3,4-*c*]isoxazole (*cis*-6b):^{2d} This compound is colorless solid and the melting point is 105-106 ^{O}C after recrystallized from hexane and ethyl acetate solution. ¹H NMR (200 MHz, CDCl₃) 7.38 (dt, J = 8.8, 3.0 Hz, 2H), 6.88 (dt, J = 8.8, 3.0 Hz, 2H), 5.13 (s, 1H), 4.58 (dd, J = 9.8, 7.6 Hz, 1H), 4.41-4.22 (m, 1H), 4.16 (dd, J = 10.2, 7.6 Hz, 1H), 3.79 (s, 3H), 3.12 (dd, J = 10.0, 8.0 Hz, 1H), 3.00 (dd, J = 10.0, 9.0 Hz, 1H). ¹³C NMR (50 MHz, CDCl₃) 168.4, 159.5, 129.9, 128.6, 114.0, 75.1, 56.6, 55.2, 43.8, 31.2. MS *m/z* (relative intensity) 235 (M⁺, 100), 204 (33), 190 (23), 174 (25), 172 (29), 151 (58), 146 (53), 135 (18), 115 (13), 91 (11), 77 (9). HRMS calcd for C₁₂H₁₃NO₂S (M⁺) 235.0667, found 235.0666. Anal. Calcd for: C, 61.28; H, 5.53; N, 5.96. Found: C, 61.20; H, 5.55; N, 5.82.

trans-6-(4-Fluorophenyl)-3,3a,4,6-tetrahydrothiopheno[3,4-c]isoxazole (*trans*-6c): This compound is colorless liquid. ¹H NMR (200 MHz, CDCl₃) 7.49-7.39 (m, 2H), 7.11-6.99 (m, 2H), 5.20 (s, 1H), 4.57 (dd, J = 9.6, 7.6 Hz, 1H), 4.35-4.16 (m, 1H), 4.11 (dd, J = 10.0, 7.6 Hz, 1H), 3.18 (dd, J = 10.0, 8.0 Hz, 1H), 2.86 (dd, J = 10.0, 9.0 Hz, 1H). ¹³C NMR (50 MHz, CDCl₃) 168.1, 162.4 (d, J = 245.8), 134.7 (d, J = 3.0), 129.0 (d, J = 7.6), 115.7 (d, J = 21.2), 74.7, 55.0, 42.6, 31.7. MS *m/z* (relative intensity) 223 (M⁺, 1), 192 (2), 148 (1), 146 (13), 134 (13), 120 (14), 107 (42), 95 (27), 75 (18), 58 (11). HRMS calcd for C₁₁H₁₀FNOS (M⁺) 223.0457, found 223.0459. Anal. Calcd for: C, 59.18; H, 4.52; N, 6.27. Found: C, 59.34; H, 4.58; N, 6.04.

cis-6-(4-Fluorophenyl)-3,3a,4,6-tetrahydrothiopheno[3,4-c]isoxazole (*cis*-6c): This compound is colorless liquid. ¹H NMR (200 MHz, CDCl₃) 7.50-7.40 (m, 2H), 7.10-6.98 (m, 2H), 5.15 (s, 1H), 4.61 (dd, J = 9.6, 7.6 Hz, 1H), 4.47-4.25 (m, 1H), 4.18 (dd, J = 10.0, 7.6 Hz, 1H), 3.16 (dd, J = 10.0,

8.0 Hz, 1H), 3.02 (dd, J = 10.0, 9.0 Hz, 1H). ¹³C NMR (50 MHz, CDCl₃) 168.1, 162.4 (d, J = 246.7), 132.6 (d, J = 3.1), 130.4 (d, J = 8.4), 115.4 (d, J = 21.2), 75.0, 56.5, 43.4, 31.2. MS *m*/z (relative intensity) 223 (M⁺, 100), 192 (54), 148 (44), 146 (27), 139 (88), 123 (31), 107 (29), 95 (15), 75 (9), 57 (6). HRMS calcd for C₁₁H₁₀FNOS (M⁺) 223.0467, found 223.0458. Anal. Calcd for: C, 59.18; H, 4.52; N, 6.27. Found: C, 59.21; H, 4.58; N, 5.93.

trans-6-(2-Thienyl)-3,3a,4,6-tetrahydrothiopheno[3,4-c]isoxazole (*trans*-6e): This compound is colorless liquid. ¹H NMR (200 MHz, CDCl₃) 7.26 (dd, J = 5.2, 1.2 Hz, 1H), 7.07 (dt, J = 3.6, 1.2 Hz, 1H), 6.96 (dd, J = 5.2, 3.6 Hz, 1H), 5.40 (s, 1H), 4.56 (dd, J = 10.0, 8.0 Hz, 1H), 4.44-4.25 (m, 1H), 4.11 (dd, J = 9.6, 8.0 Hz, 1H), 3.21 (dd, J = 10.0, 8.0 Hz, 1H), 2.83 (dd, J = 10.0, 9.0 Hz, 1H). ¹³C NMR (50 MHz, CDCl₃) 167.2, 143.8, 127.3, 125.8, 125.6, 74.7, 54.0, 38.5, 31.5. MS *m/z* (relative intensity) 211 (M⁺, 100), 181 (23), 180 (26), 154 (11), 148 (15), 136 (20), 127 (78), 122 (27), 109 (18), 96 (21), 69 (37), 58 (44). HRMS calcd for C₉H₉NOS₂ (M⁺) 211.0126, found 211.0120.

cis-6-(2-Thienyl)-3,3a,4,6-tetrahydrothiopheno[3,4-*c*]isoxazole (*cis*-6e): This compound is colorless liquid. ¹H NMR (200 MHz, CDCl₃) 7.31 (dd, J = 5.4, 1.2 Hz, 1H), 7.15 (dt, J = 3.6, 1.2 Hz, 1H), 6.96 (dd, J = 5.4, 3.6 Hz, 1H), 5.50 (s, 1H), 4.62 (dd, J = 10.0, 7.8 Hz, 1H), 4.44-4.25 (m, 1H), 4.19 (dd, J = 10.0, 7.8 Hz, 1H), 3.13 (dd, J = 10.0, 7.8 Hz, 1H), 3.06 (dd, J = 10.0, 9.0 Hz, 1H). ¹³C NMR (50 MHz, CDCl₃) 167.7, 140.2, 127.2, 126.8, 126.3, 75.3, 56.7, 39.4, 31.5. MS *m/z* (relative intensity) 211 (M⁺, 100), 181 (21), 180 (18), 154 (8), 148 (18), 136 (22), 127 (34), 122 (27), 109 (18), 96 (25), 69 (11), 58 (6). HRMS calcd for C₉H₉NOS₂ (M⁺) 211.0126, found 211.0125.

2-Allylthio-1-chloro-1-(methoxycarbonyloxyimino)-2-(4-fluorophenyl)ethane (7c): This compound is colorless liquid. ¹H NMR (200 MHz, CDCl₃) 7.50-7.40 (m, 2H), 7.11-7.00 (m, 2H), 5.90-5.69 (m, 1H), 5.27-5.17 (m, 2H), 5.05 (s, 1H), 3.94 (s, 3H), 3.25 (ddt, J = 14.0, 7.8, 1.0 Hz, 1H), 3.15 (ddt, J =14.0, 5.4, 1.0 Hz, 1H). ¹³C NMR (50 MHz, CDCl₃) 162.8 (d, J = 248.8), 153.2, 149.8, 132.6, 130.6 (d, J =3.1), 130.3 (d, J = 8.4), 119.2, 115.7 (d, J = 22.1), 55.8, 51.6, 34.7. MS *m/z* (relative intensity) 319 [(M+2)⁺, tr], 317 (M⁺, tr), 247 (11), 245 (22), 169 (45), 168 (42), 134 (100), 107 (6), 59 (22). HRMS calcd for C₁₃H₁₃ClFNO₃S [(M+2)⁺] 319.0259, found 319.0273; calcd (M⁺) 317.0288, found 317.0280.

2-Allylthio-1-chloro-1-(methoxycarbonyloxyimino)-2-(2-thienyl)ethane (7e): This compound is colorless liquid. ¹H NMR (200 MHz, CDCl₃) 7.31 (dd, J = 5.4, 1.2 Hz, 1H), 7.13 (dt, J = 3.6, 1.2 Hz, 2H), 6.98 (dd, J = 5.4, 3.6 Hz, 1H), 5.91-5.71 (m, 1H), 5.33 (d, J = 0.6 Hz, 1H), 5.30-5.17 (m, 2H), 3.94 (s, 3H), 3.28 (ddt, J = 13.6, 6.8, 1.0, 1H), 3.19 (ddt, J = 13.6, 6.8, 1.0, 1H). ¹³C NMR (50 MHz, CDCl₃) 153.2, 149.3, 137.4, 132.4, 127.6, 127.0, 126.6, 119.3, 55.8, 47.8, 35.1. MS *m/z* (relative intensity) 307 [(M⁺), tr], 305 (M⁺, tr), 234 (32), 232 (91), 158 (35), 156 (100), 122 (58), 108 (14), 73 (9), 59 (12). HRMS calcd for C₁₁H₁₂CINO₃S₂ (M⁺) 304.9947, found 304.9940.

1,2-Diallylthio-1-(methoxycarbonyloxyimino)-2-(4-fluorophenyl)ethane (8c): This compound is colorless liquid. ¹H NMR (200 MHz, CDCl₃) 7.50-7.41 (m, 2H), 7.11-6.99 (m, 2H), 5.92-5.51 (m, 2H), 5.26-5.06 (m, 4H), 4.95 (s, 1H), 3.92 (s, 3H), 3.60 (ddt, J = 13.6, 6.8, 1.0, 1H), 3.43 (ddt, J = 13.6, 7.0, 1.0, 1H), 3.29 (ddt, J = 13.6, 7.6, 1.0, 1H), 3.12 (ddt, J = 13.6, 6.8, 1.0, 1H).

¹³C NMR (50 MHz, CDCl₃) 162.5 (d, J = 246.6), 162.4, 153.7, 133.1, 132.1, 131.9 (d, J = 3.1), 130.2 (d, J = 8.4), 119.3, 118.8, 115.6 (d, J = 21.3), 55.4, 50.2, 34.7. MS *m/z* (relative intensity) 355 (M⁺, tr), 314 (M⁺, tr), 206 (4), 181 (11), 166 (56), 139 (60), 107 (17), 73 (29), 59 (100). HRMS calcd for C₁₆H₁₈FNO₃S₂ (M⁺) 355.0713, found 355.0693.

1,2-Diallylthio-1-(methoxycarbonyloxyimino)-2-(2-thienyl)ethane (8e): This compound is colorless liquid. ¹H NMR (200 MHz, CDCl₃) 7.29 (dd, J = 5.4, 1.2 Hz, 1H), 7.11 (dt, J = 3.6, 1.2 Hz, 2H), 6.97 (dd, J = 5.4, 3.6 Hz, 1H), 5.94-5.61 (m, 2H), 5.30-5.08 (m, 5H), 3.90 (s, 3H), 3.72 (ddt, J = 13.6, 6.8, 1.0, 1H), 3.50 (ddt, J = 13.6, 6.8, 1.0, 1H), 3.32 (ddt, J = 13.6, 6.8, 1.0, 1H), 3.50 (ddt, J = 13.6, 6.8, 1.0, 1H), 3.32 (ddt, J = 13.6, 6.8, 1.0, 1H). ¹³C NMR (50 MHz, CDCl₃) 162.3, 153.7, 139.6, 132.8, 132.1, 127.0, 126.9, 126.3, 119.4, 119.1, 55.4, 47.1, 35.1, 30.0. MS *m/z* (relative intensity) 343 (M⁺, tr), 302 (tr), 272 (10), 270 (7), 194 (24), 169 (43), 161 (22), 154 (100), 135 (53), 127 (99), 122 (68), 73 (78), 59 (88). HRMS calcd for C₁₄H₁₇NO₃S₃ (M⁺) 343.0371, found 343.0361.

Typical Experimental Procedures for the One-Pot Synthesis of *trans*-10 and *cis*-10 from the Reaction of 1b and 3-Acetylthiocyclohexene 9 in the Presence of Sodium Ethoxide and then Treating the Nitronate with MCF and Triethylamine (equation 2)

A solution of fresh sodium ethoxide prepared from 3 mmol of metallic sodium in dry ether 30 mL was treated dropwise with 2 mmol of 3-acetylthiocyclohexene 9 in 10 mL of ether. The reaction mixture was refluxed for 10 minutes and then cooled to 0 $^{\circ}$ C. To this solution of the sodium mercaptide was added dropwise 1 mol of **1b** dissolved in 10 mL of ether. The solution was stirred for 10 minutes at 0 $^{\circ}$ C and was warmed to room temperature and then 2 mmol of triethylamine were added to stir for 30 minutes. After adding 10 mmol of MCF, the solution was refluxed for 5 hours and was poured into the ice water, extracted with dichloromethane, dried over MgSO₄, filtered and the solvent was evaporated to isolate 24% of *trans*-10 and 16% of *cis*-10 after flash column chromatography purification.

trans-10: This compound is colorless solid and the melting point is 129-131 °C after recrystallized from hexane and ethyl acetate solution. ¹H NMR (200 MHz, CDCl₃) 7.34 (dt, J = 8.8, 3.0 Hz, 2H), 6.87 (dt, J = 8.8, 3.0 Hz, 2H), 5.21 (d, J = 1.6, 1H), 4.80 (dt, J = 10.0, 7.4 Hz, 1H), 4.34 (td, J = 10.0, 1.6 Hz, 1H), 3.79 (s, 3H), 3.45 (ddd, J = 10.0, 8.4, 6.4 Hz, 1H), 2.19-1.93 (m, 2H), 1.78-1.43 (m, 3H), 1.26-1.05 (m, 1H). ¹³C NMR (50 MHz, CDCl₃) 170.4, 159.3, 130.9, 128.7, 114.2, 80.0, 58.3, 55.3, 42.5, 40.9, 33.1, 28.3, 19.9. MS *m/z* (relative intensity) 275 (M⁺, 84), 260 (24), 231 (11), 218 (15), 204 (84), 188 (18), 162 (14), 151 (100), 136 (58), 121 (25), 91 (12). HRMS calcd for C₁₅H₁₇NO₂S (M⁺) 275.0980, found 275.0985. Anal. Calcd for C₁₅H₁₇NO₂S: C, 65.43; H, 6.22; N, 5.09. Found: C, 65.17; H, 6.20; N, 4.94.

cis-10: This compound is colorless liquid. ¹H NMR (200 MHz, CDCl₃) 7.43 (dt, J = 8.8, 3.0 Hz, 2H), 6.89 (dt, J = 8.8, 3.0 Hz, 2H), 5.19 (d, J = 1.6, 1H), 4.84 (dt, J = 10.0, 7.4 Hz, 1H), 4.29 (td, J = 10.0, 1.6 Hz, 1H), 3.80 (s, 3H), 3.39 (ddd, J = 10.0, 8.4, 6.4 Hz, 1H), 2.27-1.94 (m, 2H), 1.80-1.43 (m, 3H), 1.27-1.07 (m, 1H). ¹³C NMR (50 MHz, CDCl₃) 169.1, 159.4, 129.8, 129.4, 114.1, 80.2, 58.5, 55.2, 43.8, 40.1, 34.4, 28.5, 19.5. MS *m/z* (relative intensity) 275 (M⁺, 66), 260 (21), 218 (18), 204 (100), 188 (18), 151

(88), 135 (59), 121 (17), 77 (25). HRMS calcd for $C_{15}H_{17}NO_2S$ (M⁺) 275.0980, found 275.0977. Anal. Calcd for $C_{15}H_{17}NO_2S$: C, 65.43; H, 6.22; N, 5.09. Found: C, 65.16; H, 6.22; N, 4.89.

Typical Experimental Procedures (A) for the Preparation of Nitro Compound 20 from the Reaction of 1b and Cinnamyl Alcohol and Potassium *tert*-Butoxide and (B) for the Converting of Nitronate into Bicyclic Product 21 with MCF and Triethylamine (equation 6)

(A): To a stirred solution contained cinnamyl alcohol (6 mmol) and potassium *tert*-butoxide (7 mmol) in dried THF 30 mL was added β -nitrostyrene 1b (5 mmol) in THF 20 mL at -78 °C. After the starting material 1b disappeared, the solution was poured into the ice-cold dilute acid aqueous solution, extracted with dichloromethane, dried over MgSO₄, filtered and the solvent was evaporated to obtain oily residue. The mixture was purified by flash column to obtain 68% of 20 in isolation yield.

(B): To a 50 mL of benzene solution was added pure compound 20 (2 mmol), MCF (4 mmol) and triethylamine (4 mmol) at room temperature and then the mixture was refluxed for 2 hours. After filtration of triethylamine hydrochloride, the filtrate was evaporated to give oily residue, which was purified by flash column chromatography to give 100% (NMR yield) of *trans*-21.

1-(Cinnamoxy)-2-nitro-1-(4-methoxyphenyl)ethane (20): This compound is colorless liquid. ¹H NMR (200 MHz, CDCl₃) 7.39-7.19 (m, 7H), 6.93 (dt, J = 8.8, 3.0 Hz, 2H), 6.50 (d, J = 16.2 Hz, 1H), 6.18 (ddd, J = 16.2, 6.6, 5.4 Hz, 1H), 5.14 (dd, J = 10.2, 3.6 Hz, 1H), 4.67 (dd, J = 12.8, 10.2 Hz, 1H), 4.38 (dd, J = 12.8, 3.6 Hz, 1H), 4.13 (ddd, J = 12.6, 5.4, 1.4 Hz, 1H), 3.96 (ddd, J = 12.6, 6.6, 1.0 Hz, 1H), 3.82 (s, 3H). ¹³C NMR (50 MHz, CDCl₃) 160.3, 136.5, 133.0, 128.6, 128.3, 128.1, 127.8, 126.6, 125.1, 114.5, 80.4, 76.8, 69.2, 55.2. MS *m*/z (relative intensity) 313 (M⁺, 11), 253 (19), 224 (3), 180 (45), 159 (17), 134 (97), 117 (100), 105 (49), 91 (68), 77 (34). HRMS calcd for C₁₈H₁₉NO₄ (M⁺) 313.1274, found 313.1294. Anal. Calcd for C₁₈H₁₉NO₄: C, 69.00; H, 6.11; N, 4.47. Found: C, 68.90; H, 6.20; N, 4.64.

trans-3a,4-Dihydro-3-diphenyl-6-(4-methoxyphenyl)-6H-furo[3,4-c]isoxazole (*trans*-21): This compound is colorless liquid. ¹H NMR (200 MHz, CDCl₃) 7.39-7.19 (m, 7H), 6.94 (dt, J = 8.8, 2.2 Hz, 2H), 5.60 (s, 1H), 5.53 (d, J = 11.4 Hz, 1H), 4.43 (dd, J = 9.0, Hz, 1H), 4.33-4.18 (m, 1H), 3.98 (dd, J = 9.0, 8.0 Hz, 1H), 3.81 (s, 3H). ¹³C NMR (50 MHz, CDCl₃) 171.3, 159.9, 136.9, 129.4, 128.9, 127.2, 126.7, 114.3, 89.1, 73.2, 69.4, 60.6, 55.3. MS *m/z* (relative intensity) 295 (M⁺, 5), 189 (10), 152 (13), 135 (100), 97 (6), 85 (10), 77 (17), 70 (16). HRMS calcd for C₁₈H₁₇NO₃ (M⁺) 295.1190, found 295.1199. Anal. Calcd for C₁₈H₁₇NO₃: C, 73.20; H, 5.80; N, 4.74. Found: C, 73.10; H, 5.73; N, 4.64.

Typical Experimental Procedures for the One-Pot Synthesis of Tetrahydrofurans 14 from the Reaction of β -Nitrostyrenes 1 and Potassium Allyloxide and then Treating the Nitronates with MCF and Catalytic Amount of 4-Dimethylaminopyridine (DMAP) in the Presence of Different Amounts of Triethylamine (Table 2)

To a stirred solution of the potassium alloxide (2.4 mmol), prepared from allyl alcohol (2.4 mmol) and potassium *tert*-butoxide (4.0 mmol), in dried THF 30 mL was added β -nitrostyrene **1a** (2 mmol) in THF 20 mL at -78 °C. After the starting material **1a** disappeared, 0.2 mmol of the 4-dimethylaminopyridine (DMAP) and 6

mmol of MCF were slowly added to the solution at -78 $^{\circ}$ C and the solution was stirred for 1 hour at the same temperature. The solution was warmed to room temperature and then 6 mmol of methyl chloroformate and 4 mmol of triethylamine were slowly added to the mixture. The solution was refluxed for 2 hours and was poured into the ice water, extracted with dichloromethane, dried over MgSO₄, filtered and the solvent was evaporated to obtain 72% of *trans*-14a and 8% of 15a (the yield was measured by NMR). GCMS analysis indicated only the *trans*-14a isomer could be detected and none of the *cis*-14a was observed. The purification of the mixture was carried out by flash column chromatography (95:5 hexane/ethyl acetate) to obtain pure products *trans*-14a and the trans-14a a

15a. The spectral data of *trans*-14a and 15a were consistent with the literature reports.¹¹⁻¹³ Similar procedures were enacted when substrate 1b-f reacted with the potassium allyloxide under similar conditions as described above. Not only the major product *trans*-14e but also the minor product *cis*-14e was isolated when 1e was used. Similarly, not only *trans*-14f and *cis*-14f but also trace amount of 24 were isolated when 1f was used.

trans-3a,4-Dihydro-6-phenyl-3H,6H-furo[3,4-c]isoxazole (*trans*-14a):¹¹⁻¹³ This compound is colorless liquid. ¹H NMR (200 MHz, CDCl₃) 7.47-7.28 (m, 5H), 5.61 (s, 1H), 4.59 (dd, J = 8.6, 7.4 Hz, 1H), 4.44 (t, J = 7.8 Hz, 1H), 4.34-4.15 (m, 1H), 4.07 (dd, J = 12.0, 7.4 Hz, 1H), 3.82 (dd, J = 8.8, 8.0 Hz, 1H). ¹³C NMR (50 MHz, CDCl₃) 170.4, 137.4, 128.8, 128.5, 125.7, 73.7, 72.9, 69.9, 54.5. MS *m/z* (relative intensity) 189 (M⁺, 5), 188 (46), 175 (23), 105 (100), 91 (7), 77 (65). HRMS calcd for C_{11H10}NO₂ [(M-1)⁺] 188.0712, found 188.0712.

trans-3a,4-Dihydro-6-(4-methoxyphenyl)-3H,6H-furo[3,4-c]isoxazole (*trans*-14b):^{11a} This compound is colorless liquid. ¹H NMR (200 MHz, CDCl₃) 7.33 (dt, J = 8.2, 1.6 Hz, 2H), 6.91 (dt, J = 8.2, 1.6 Hz, 2H), 5.56 (s, 1H), 4.60 (dd, J = 8.6, 7.6 Hz, 1H), 4.42 (t, J = 7.8 Hz, 1H), 4.36-4.17 (m, 1H), 4.07 (dd, J = 12.8, 7.4 Hz, 1H), 3.81 (s, 3H), 3.80 (t, J = 8.0 Hz, 1H). ¹³C NMR (50 MHz, CDCl₃) 170.6, 159.7, 129.4, 127.1, 114.0, 73.4, 72.6, 69.6, 55.1, 54.6. MS *m/z* (relative intensity) 219 (M⁺, 29), 189 (95), 188 (25), 160 (21), 147 (18), 135 (100), 115 (9), 92 (8), 77 (13). HRMS calcd for C₁₂H₁₃NO₃ (M⁺) 219.0896, found 219.0898.

trans-3a,4-Dihydro-6-(4-fluorophenyl)-3H,6H-furo[3,4-c]isoxazole (*trans*-14c):^{4g} This compound is colorless liquid. ¹H NMR (200 MHz, CDCl₃) 7.45-7.36 (m, 2H), 7.13-7.02 (m, 2H), 5.58 (s, 1H), 4.66 (dd, J = 8.6, 7.4 Hz, 1H), 4.43 (td, J = 8.0, 0.8 Hz, 1H), 4.33-4.14 (m, 1H), 4.07 (dd, J = 12.0, 7.4 Hz, 1H), 3.81 (dd, J = 9.0, 8.0 Hz, 1H). ¹³C NMR (50 MHz, CDCl₃) 170.3, 162.8 (d, J = 246.5 Hz), 133.2 (d, J = 3.0 Hz), 127.6 (d, J = 7.6 Hz), 115.7 (d, J = 21.3 Hz), 73.6, 72.4, 69.9, 54.4. MS *m/z* (relative intensity) 206 (M⁺, 10), 177 (48), 123 (100), 107 (8), 95 (39). HRMS calcd for C₁₁H₉FNO₂ [(M-1)⁺] 206.0617, found: 206.0615.

3a,4-Dihydro-6,6-diphenyl-4H-furo[3,4-c]isoxazole (14d):^{4g} This compound is colorless solid and the melting point is 69-70 °C after recrystallized from hexane and ethyl acetate solution. ¹H NMR (200 MHz, CDCl₃) 7.58-7.20 (m, 10H), 4.62-4.50 (m, 1H), 4.50-4.17 (m, 2H), 4.07-3.88 (m, 2H). ¹³C NMR (50 MHz, CDCl₃) 171.6, 141.3, 141.2, 128.6, 128.4, 128.2, 127.7, 126.4, 125.8, 82.4, 74.1, 68.2, 55.7. MS m/z (relative intensity) 265 (M⁺, 1), 235 (18), 206 (15), 115 (2), 77 (37). HRMS calcd for C₁₇H₁₅NO₂ (M⁺) 265.1103, found: 265.1110. Anal. Calcd for C₁₇H₁₅NO₂: C, 76.96; H, 5.70; N, 5.28. Found: C, 76.99; H,

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5.61; N, 5.60.

trans-3a,4-Dihydro-6-(2-thienyl)-3H,6H-furo[3,4-c]isoxazole (*trans*-14e): This compound is colorless liquid. ¹H NMR (200 MHz, CDCl₃) 7.31 (dd, J = 5.0, 1.2 Hz, 1H), 7.21 (dd, J = 3.4, 1.2 Hz, 1H), 6.99 (dd, J = 5.0, 3.4 Hz, 1H), 5.79 (s, 1H), 4.68-4.52 (m, 1H), 4.45-4.24 (m, 2H), 4.14-3.99 (m, 1H), 3.82-3.67 (m, 1H). ¹³C NMR (50 MHz, CDCl₃) 169.3, 140.7, 127.0, 126.1, 125.0, 73.7, 69.7, 69.1, 53.9. MS *m/z* (relative intensity) 195 (M⁺, 3), 178 (4), 153 (7), 136 (8), 122 (12), 112 (16), 111 (100), 96 (13), 84 (9), 69 (4). HRMS calcd for C₉H₉NO₂S (M⁺) 195.0354, found 195.0341.

cis-3a,4-Dihydro-6-(2-thienyl)-3H,6H-furo[3,4-c]isoxazole (cis-14e): This compound is colorless liquid. ¹H NMR (200 MHz, CDCl₃) 7.34 (dd, J = 5.0, 1.2 Hz, 1H), 7.07 (dd, J = 3.4, 1.2 Hz, 1H), 7.01 (dd, J = 5.0, 3.4 Hz, 1H), 5.84 (s, 1H), 4.70-4.56 (m, 1H), 4.47-4.26 (m, 2H), 4.18-4.03 (m, 1H), 3.96-3.80 (m, 1H). ¹³C NMR (50 MHz, CDCl₃) 170.4, 139.8, 126.9, 126.6, 126.5, 74.1, 69.3, 68.8, 55.9. MS m/z (relative intensity) 195 (M⁺, 5), 165 (4), 136 (6), 122 (6), 111 (100), 105 (8), 96 (7). HRMS calcd for C₉H₉NO₂S (M⁺) 195.0354, found 195.0336.

trans-3a,4-Dihydro-6-(2-furyl)-3H,6H-furo[3,4-c]isoxazole (*trans*-14f): This compound is colorless liquid. ¹H NMR (200 MHz, CDCl₃) 7.43 (dd, J = 1.8, 0.8 Hz, 1H), 6.41 (dd, J = 3.4, 0.8 Hz, 1H), 6.37 (dd, J = 3.4, 1.8 Hz, 1H), 5.54 (s, 1H), 4.67 (dd, J = 9.2, 7.8 Hz, 1H), 4.58-4.35 (m, 2H), 4.08 (dd, J = 10.4, 7.8 Hz, 1H), 3.77 (dd, J = 8.4, 7.8 Hz, 1H). ¹³C NMR (50 MHz, CDCl₃) 168.1, 149.9, 143.6, 110.5, 109.1, 74.0, 69.7, 66.5, 54.7. MS *m/z* (relative intensity) 179 (M⁺, 18), 149 (100), 120 (51), 95(87). HRMS calcd for C₉H₉NO₃ (M⁺) 179.0583, found 179.0601.

cis-3a,4-Dihydro-6-(2-furyl)-3H,6H-furo[3,4-c]isoxazole (*cis*-14f): This compound is colorless liquid. ¹H NMR (200 MHz, CDCl₃) 7.47 (dd, J = 1.8, 0.8 Hz, 1H), 6.51 (dd, J = 3.0, 0.8 Hz, 1H), 6.38 (dd, J = 3.0, 1.8 Hz, 1H), 5.63 (s, 1H), 4.65 (dd, J = 8.6, 7.6 Hz, 1H), 4.44-4.09 (m, 3H), 3.94-3.76 (m, 1H). ¹³C NMR (50 MHz, CDCl₃) 169.0, 149.6, 143.9, 110.4, 109.9, 73.8, 69.0, 66.8, 56.0. MS *m/z* (relative intensity) 179 (M⁺, 71), 149 (63), 120 (100), 95(77). HRMS calcd for C₉H₉NO₃ (M⁺) 179.0583, found 179.0580.

2-Alloxy-1-chloro-2-(2-furyl)-1-(methoxycarbonyloxyimino)ethane (24): This compound is colorless liquid. ¹H NMR (200 MHz, CDCl₃) 7.43 (dd, J = 1.8, 0.8 Hz, 1H), 6.53 (dd, J = 3.4, 0.8 Hz, 1H), 6.40 (dd, J = 3.4, 1.8 Hz, 1H), 6.03-5.83 (m, 1H), 5.48 (s, 1H), 5.40-5.24 (m, 2H), 4.20-4.02 (m, 2H), 3.95 (s, 3H). ¹³C NMR (50 MHz, CDCl₃) 153.2, 148.6, 148.0, 143.4, 132.9, 119.0, 110.6, 109.7, 74.9, 70.4, 55.9. MS *m*/z (relative intensity) 307 [(M⁺), tr], 305 (M⁺, tr), 234 (32), 232 (91), 158 (35), 156 (100), 122 (58), 108 (14), 73 (9), 59 (12). HRMS calcd for C₁₁H₁₂CINO₅ (M⁺) 304.9947, found 304.9940.

Typical Experimental Procedures for the One-Pot Synthesis of Compounds 26 and 27 from the Reaction of 1b with 2-Cyclohexen-1-ol or 2-Cycloocten-1-ol and Potassium *tert*-Butoxide and then Treating the Nitronate with MCF, DMAP, and Triethylamine (equation 9)

To a stirred solution of the potassium 2-cyclohexen-1-oxide (6.25 mmol), prepared from 2-cyclohexen-1ol (6.25 mmol) and potassium *tert*-butoxide (12.5 mmol), in dried THF 30 mL was added β -nitrostyrene 1b (5 mmol) in THF 20 mL at -78 °C. After the starting material 1b disappeared, 0.5 mmol of the DMAP and 30 mmol of MCF were slowly added to the solution at -78 °C and the solution was stirred for 1 hour at the same temperature. The solution was heated and was refluxed for 5 hours. The solution was poured into the ice water, extracted with dichloromethane, dried over MgSO₄, filtered and the solvent was evaporated to obtain compound **26**. Purification of the mixture was carried out by flash column chromatography (5:95 ethyl acetate/hexane) to isolate 32% of *trans*-26 and 56% of *cis*-26. Similarly, 21% of *trans*-27 and 44% of *cis*-27 were isolated when 1b reacted with 2-cycloocten-1-ol under similar conditions.

trans-26: This compound is colorless solid and the melting point is 124-125.5 °C after recrystallized from hexane and ethyl acetate solution. ¹H NMR (200 MHz, CDCl₃) 7.32 (dt, J = 8.2, 3.0 Hz, 2H), 6.90 (dt, J = 8.2, 3.0 Hz, 1H), 5.60 (s, 1H), 4.89 (ddd, J = 10.4, 6.2, 5.6 Hz, 1H), 4.53 (dt, J = 8.4, 6.6 Hz, 1H), 4.13 (t, J = 9.0, 1H), 3.80 (s, 3H), 2.02-1.52 (m, 5H), 1.25-1.07 (m, 1H). ¹³C NMR (50 MHz, CDCl₃) 168.9, 159.7, 129.8, 127.0, 114.1, 80.5, 72.8, 71.4, 55.2, 53.7, 29.9, 29.3, 17.0. MS *m/z* (relative intensity) 259 (M⁺, 4), 188 (100), 161 (9), 146 (7), 135 (47), 133 (21), 121 (10), 77 (13). HRMS calcd for C₁₅H₁₇NO₃ (M⁺) 259.1209, found 259.1203. Anal. Calcd for C₁₅H₁₇NO₃: C, 69.59; H, 6.56; N, 5.41. Found: C, 69.57; H, 6.73; N, 5.38.

cis-26: This compound is colorless liquid. ¹H NMR (200 MHz, CDCl₃) 7.32 (dt, J = 8.4, 3.0Hz, 2H), 6.91 (dt, J = 8.4, 3.0Hz, 2H), 5.45 (s, 1H), 4.94 (dt, J = 10.6, 5.0 Hz, 1H), 4.49 (dt, J = 9.0, 5.4 Hz, 1H), 4.30 (t, J = 9.0, 1H), 3.81 (s, 3H), 1.90-1.52 (m, 4H), 1.40-1.16 (m, 2H). ¹³C NMR (50 MHz, CDCl₃) 167.0, 159.7, 128.5, 128.3, 113.8, 80.1, 72.3, 70.9, 55.1, 53.5, 31.2, 29.4, 15.9. MS *m/z* (relative intensity) 259 (M⁺, 46), 204 (7),188 (24), 174 (8),160 (19), 146 (18), 135 (100), 133 (28), 121 (15), 107 (8), 77 (20). HRMS calcd for C₁₅H₁₇NO₃ (M⁺) 259.1209, found 259.1211. Anal. Calcd for C₁₅H₁₇NO₃: C, 69.59; H, 6.56; N, 5.41. Found: C, 69.49; H, 6.55; N, 5.32.

trans-27: ¹H NMR (200 MHz, CDCl₃) 7.35 (dt, J = 8.8, 2.8 Hz, 2H), 6.90 (dt, J = 8.8, 2.8 Hz, 1H), 5.53 (s, 1H), 4.63 (dt, J = 4.2, 10.8 Hz, 1H), 4.04 (dt, J = 3.8, 10.2 Hz, 1H), 3.81 (s, 3H), 3.72 (dd, J = 10.8, 10.2 Hz, 1H), 2.20-1.36 (m, 10H). ¹³C NMR (50 MHz, CDCl₃) 168.0, 159.8, 130.1, 127.5, 114.1, 83.1, 78.3, 73.2, 60.8, 55.3, 33.2, 28.5, 26.0, 24.7, 23.4. MS *m*/z (relative intensity) 287 (M⁺, 39), 258 (18), 216 (17), 202 (17), 188 (85), 160 (98), 146 (69), 135 (100), 121 (80), 91 (28), 77 (39). HRMS calcd for C₁₇H₂₁NO₃ (M⁺) 287.1522, found 287.1539.

cis-27: ¹H NMR (200 MHz, CDCl₃) 7.37 (dt, J = 8.2, 3.0 Hz, 2H), 6.90 (dt, J = 8.2, 3.0 Hz, 1H), 5.54 (s, 1H), 4.65 (dt, J = 4.2, 11.0 Hz, 1H), 4.15 (dt, J = 4.0, 10.2 Hz, 1H), 3.78 (s, 3H), 3.77 (dd, J = 11.0, 10.2 Hz, 1H), 2.09-1.32 (m, 10H). ¹³C NMR (50 MHz, CDCl₃) 167.8, 159.6, 130.0, 128.1, 113.9, 83.2, 77.2, 73.2, 61.9, 55.1, 32.9, 28.5, 25.8, 24.5, 23.3. MS *m*/z (relative intensity) 287 (M⁺, 57), 188 (53), 160 (100),133 (88), 121 (46), 91 (13), 77 (17). HRMS calcd for C₁₇H₂₁NO₃ (M⁺) 287.1522, found 287.1514.

Typical Experimental Procedures for the One-Pot Synthesis of Compounds 31 from the Reaction of 1b with 1-phenyl-2,6-heptadien-1-ol 28a and Potassium *tert*-Butoxide and then

Treating the Nitronate with MCF, DMAP and Triethylamine (equation 11)

To a stirred solution of the 1-phenyl-2,6-heptadien-1-ol 28a (4 mmol) and potassium *tert*-butoxide (9 mmol) in dried THF 30 mL was added β -nitrostyrene 1b (3 mmol) in THF 20 mL at -78 °C. After the starting material 1b disappeared, 4.9 mmol of the DMAP and 30 mmol of MCF were slowly added to the solution at -78

^oC and the solution was stirred for 1 hour at the same temperature and then 10 mmol of triethylamine was added. The solution was refluxed for 45 hours and then was poured into the ice water, extracted with dichloromethane, dried over MgSO₄, filtered and the solvent was evaporated to obtain compound 31. Purification of the mixture was carried out by flash column chromatography (5:95 ethyl acetate/hexane) to isolate 47% of *trans*-31a and 35% of *cis*-31a.

trans -3- (3-Butenyl)-3a, 4-dihydro-6-(4-methoxyphenyl)-4-phenyl-3H, 6H-furo [3, 4c]isoxazole (*trans*-31a):¹⁸: This compound is colorless liquid. ¹H NMR (200 MHz, CDCl₃) 7.47-7.31 (m, 7H), 6.96 (dt, J = 8.8, 3.0 Hz, 2H), 5.78-5.58 (m, 1H), 5.71 (s, 1H), 4.96 (d, J = 9.4, 1H), 4.95-4.83 (m, 2H), 4.76-4.64 (m, 1H), 3.83 (s, 3H), 3.90-3.75 (m, 1H), 1.98-1.66 (m, 4H). ¹³C NMR (50 MHz, CDCl₃) 171.0, 159.9, 138.2, 136.9, 129.7, 128.9, 127.5, 126.4, 115.5, 114.2, 85.7, 83.3, 73.9, 66.0, 55.3, 32.3, 29.7. MS *m*/z (relative intensity) 349 (M⁺, 1), 264 (3), 243 (16), 214 (14), 188 (30), 172 (18), 171 (13), 160 (34), 135 (100), 121 (17), 105 (15), 77 (29). HRMS calcd for C₂₂H₂₃NO₃ (M⁺) 349.1678, found 349.1676.

cis-3-(3-Butenyl)-3a, 4-dihydro-6-(4-methoxyphenyl)-4-phenyl-3H, 6H-furo[3, 4*c*]isoxazole (*cis*-31a):¹⁸ This compound is colorless liquid. ¹H NMR (200 MHz, CDCl₃) 7.48-7.33 (m, 7H), 6.93 (dt, J = 8.8, 3.0 Hz, 2H), 5.82 (s, 1H), 5.79-5.59 (m, 1H), 5.05 (d, J = 9.6 Hz, 1H), 4.96-4.86 (m, 2H), 4.75-4.63 (m, 1H), 3.97-3.83 (m, 1H), 3.81 (s, 3H), 2.04-1.70 (m, 4H). ¹³C NMR (50 MHz, CDCl₃) 171.2, 159.9, 138.8, 137.0, 129.6, 128.9, 128.8, 128.1, 126.3, 115.5, 114.1, 86.2, 82.3, 74.1, 67.2, 55.3, 32.3, 29.7. MS *m*/z (relative intensity) 349 (M⁺, 2), 291 (4), 243 (11), 214 (10), 188 (20), 172 (20), 160 (35), 135 (100), 129 (5), 105 (28), 77 (35). HRMS calcd for C₂₂H₂₃NO₃ (M⁺) 349.1630, found 349.1654.

Typical Experimental Procedures for the One-Pot Synthesis of Compounds 34 and 35 from the Reaction of 1b with 3-Methyl-2-buten-1-ol and Potassium *tert*-Butoxide and then Treating the Nitronates with MCF and Catalytic Amount of DMAP in the Presence of Triethylamine (equation 12)

To a stirred solution of the 3-methyl-2-buten-1-ol (1.25 mmol) and potassium *tert*-butoxide (2.5 mmol) in dried THF 30 mL was added 1b (1.0 mmol) in THF 20 mL at -78 °C. After the starting material 1b disappeared, 0.1 mmol of the DMAP and 6 mmol of MCF were slowly added to the solution at -78 °C and the solution was stirred for 30 minutes at the same temperature. After adding 10 mmol of triethylamine, the solution was refluxed for 6 hours and was poured into the ice water, extracted with dichloromethane, dried over MgSO₄, filtered and the solvent was evaporated to obtain 55% of *trans*-34, 21% of *cis*-34, and 13% of 35 (the yield was measured by NMR). The purification of the mixture was carried out by flash column chromatography (5:95 ethyl acetate/hexane) to obtain pure products.

trans -3 a, 4 - Di hy dro -3, 3 - di methyl-6 - (4 - metho xy phenyl) - δH - furo [3, 4 - c] iso x az ole (*trans*-34): This compound is colorless liquid. ¹H NMR (200 MHz, CDCl₃) 7.33 (dt, J = 8.8, 2.8 Hz, 2H), 6.91 (dt, J = 8.8, 2.8 Hz, 2H), 5.49 (s, 1H), 4.21 (t, J = 13.0 Hz, 1H), 3.93 (d, J = 13.0 Hz, 1H), 3.89 (

13.0 Hz, 1H), 3.81 (s, 3H), 1.58 (s, 3H), 1.35 (s, 3H). ¹³C NMR (50 MHz, $CDCl_3$) 170.5, 159.2, 129.1, 126.8, 113.5, 87.9, 72.7, 64.9, 60.7, 54.6, 26.1, 21.8. MS *m/z* (relative intensity) 247 (M⁺, 100), 216 (54), 200 (67), 187 (87), 184 (99), 171 (59), 154 (56), 142 (29), 129 (22). HRMS calcd for $C_{14}H_{17}NO_3$ (M⁺) 247.1219, found 247.1214.

cis-3a,4-Dihydro-3,3-dimethyl-6-(4-methoxyphenyl)-6*H*-furo[3,4-c]isoxazole (*cis*-34): This compound is colorless liquid. ¹H NMR (200 MHz, CDCl₃) 7.38 (d, J = 8.4, 2H), 6.91 (d, J = 8.4 Hz, 2H), 5.45 (s, 1H), 4.17 (t, J = 4.6 Hz, 1H), 4.09-3.94 (m, 2H), 3.81 (s, 3H), 1.60 (s, 3H), 1.31 (s, 3H). ¹³C NMR (50 MHz, CDCl₃) 170.9, 159.7, 129.0, 128.0, 113.9, 88.9, 73.2, 64.4, 62.0, 55.0, 26.4, 21.9. MS *m/z* (relative intensity) 247 (M⁺, 32), 216 (12), 187 (30), 174 (20), 159 (10), 146 (10), 135 (100), 77 (26), 44 (26). HRMS calcd for C₁₄H₁₇NO₃ (M⁺) 247.1210, found 247.1209.

2 - (3 - Me th y l - 2 - b ut en - 1 - ox y) - 1 - ch lor o - 2 - (4 - me th ox y ph en y l) - 1 - (methoxycarbonyloxyimino)ethane (35): This compound is colorless liquid. ¹H NMR (200 MHz, CDCl₃) 7.40 (dt, J = 8.8, 2.0 Hz, 2H), 6.89 (dt, J = 8.8, 2.0 Hz, 2H), 5.42-5.35 (m, 1H), 5.39 (s, 1H), 4.12-4.06 (m, 2H), 3.94 (s, 3H), 3.81 (s, 3H), 1.76 (s, 3H), 1.66 (s, 3H). ¹³C NMR (50 MHz, CDCl₃) 160.0, 153.4, 151.2, 138.9, 128.0, 127.5, 119.7, 113.9, 79.3, 65.8, 55.8, 55.2, 25.8, 18.0. MS *m/z* (relative intensity) 341 (M⁺, tr), 321 (4), 219 (3), 162 (33), 135 (100), 103 (14), 77 (31), 55 (23). Anal. Calcd for C₁₆H₂₀CINO₅: C, 56.23; H, 5.90; N, 4.10. Found: C, 56.38; H, 5.80; N, 4.07.

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