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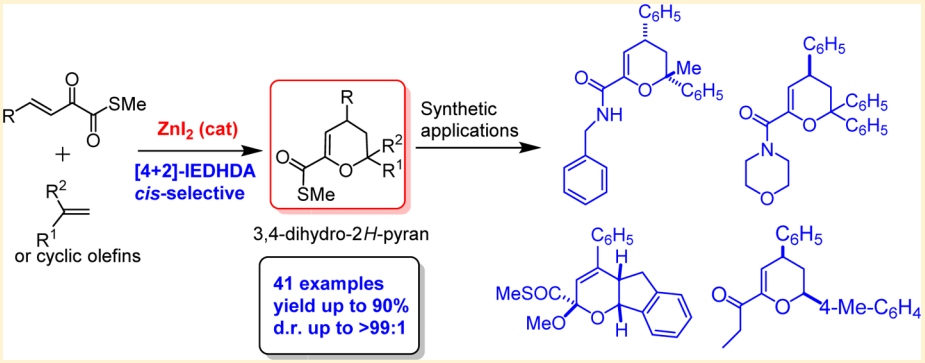
ZnI_2-Catalyzed Diastereoselective [4 + 2] Cycloadditions of β,γ-Unsaturated α-Ketothioesters with Olefins

Kanchan Mal,[†] Supriya Das,[‡] Nakul C. Maiti,[‡] Ramalingam Natarajan,[†] and Indrajit Das*[,†]

[†]Chemistry Division, CSIR-Indian Institute of Chemical Biology, 4, Raja S. C. Mullick Road, Jadavpur, Kolkata 700 032, India

[‡]Structural Biology & Bio-Informatics Division, CSIR-Indian Institute of Chemical Biology, 4, Raja S. C. Mullick Road, Jadavpur, Kolkata 700 032, India

Supporting Information



ABSTRACT: The potential of β,γ-unsaturated α-ketothioesters participating in hetero-Diels–Alder reaction has remained unexplored. We report herein the first study of a ZnI_2-catalyzed highly diastereoselective inverse electron demand hetero-Diels–Alder reaction of β,γ-unsaturated α-ketothioesters with olefins to access highly substituted 3,4-dihydro-2*H*-pyrans. All the reactions proceed with *cis*-selectivity in moderate to excellent yields. Under similar reaction conditions, terminal alkynes undergo direct conjugate 1,4-addition to yield δ,ε-acetylenic α-ketothioesters. Furthermore, the utility of these cycloadducts has been demonstrated by an NBS-MeOH mediated stereospecific efficient access to fully substituted pyran rings. The product bromoethers undergo E_2 elimination with DBU, resulting in substituted 3,6-dihydro-2*H*-pyrans. In addition, the thioester moiety of the products has been used for further transformations, such as amidations and Fukuyama coupling reactions.

INTRODUCTION

Polysubstituted dihydro- and tetrahydropyrans form important structural motifs, prevalent in many bioactive natural products, with applications that span pharmaceuticals, pheromones, and plant protective agents (Figure 1).[1] They find widespread applications as potentially important building blocks,[2] and as versatile starting materials for the synthesis of heterocycles, such as carbohydrates, iridoids, and lignans.[3]

Among the numerous methods developed so far for their synthesis,[4] the catalytic inverse electron demand hetero-Diels–Alder (IEDHDA) reaction of α,β-unsaturated carbonyl compounds with electron-rich alkenes is more common.[5] Moreover, remarkable progress has also been made on the achiral as well as chiral Lewis acid catalyzed IEDHDA reactions providing highly regio-, diastereo-, and enantioselective entry into dihydro- and tetrahydropyran derivatives.[6] However, HDA reactions with electronically unbiased less nucleophilic olefins are very much underexplored, owing to the necessity of harsh reaction conditions (mostly under high pressure) and prolonged reaction time to activate poorly reactive dienophiles.[7] Very recently, a few examples of catalytic enantioselective IEDHDA reaction of β,γ-unsaturated α-ketoesters with simple olefins and allylsilanes have been disclosed.[8] However, the potential of the related β,γ-unsaturated α-ketothioesters, having a wide array of additional functionalities, have yet not been explored in any synthetic transformations. This is the first report of this α-ketothioesters participating in IEDHDA reaction. In addition, this work demonstrates significant strategic advantages of using α-ketothioesters compared to the parent α-ketoesters in terms of achieving higher yields and *cis*-selectivities in the [4 + 2]-cycloaddition reaction, and a higher versatility in subsequent chemical transformations of the products. The sulfur atom in the thioester moiety is less able to contribute electron delocalization through the adjacent keto group, making the thioester bond less stable and more reactive than oxoester. Due to the strategic advantage associated with the thioester moiety, it can be used in versatile direct synthetic modifications in mild conditions, which are relatively difficult in the case of oxoesters.[9a] It may be mentioned that we have recently

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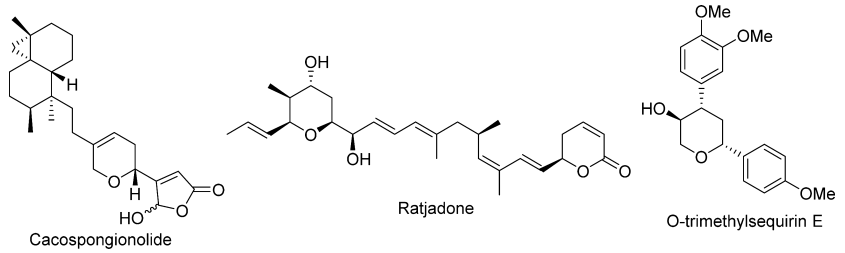
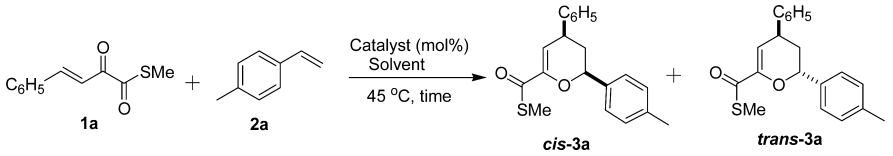


Figure 1. Selected examples of dihydro- and tetrahydropyran segments containing natural products.

Table 1. Optimization of the Reaction Conditions[a]



entry	catalyst	mol %	solvent	time (h)	yield[b] (%)	(*cis*:*trans*)[c]
1	$TiCl_4$	10	DCE	3	20	60:40
2	$InCl_3$	10	DCE	4	45	75:25
3	$InBr_3$	10	DCE	4	48	60:40
4	InI_3	10	DCE	3.5	45	72:28
5	$Zn(OTf)_2$	10	DCE	20	trace	
6	$ZnCl_2$	10	DCE	30	48	90:10
7	$ZnBr_2$	10	DCE	10	54	88:12
8	ZnI_2	10	DCE	5	87	88:12
9	ZnI_2	5	DCE	5	77	88:12
10[d]	ZnI_2	5	DCE	4	73	86:14
11[e]	ZnI_2	5	DCE	15	57	86:14
12	ZnI_2	1	DCE	8	64	86:14
13	ZnI_2/BINOL	10	DCE	3	78	86:14
14	ZnI_2/2,2′-biphenol	10	DCE	3	68	85:15
15[e]	ZnI_2/TFA	10	DCE	16	22	69:31
16	ZnI_2	10	toluene	20	55	75:25
17	ZnI_2	10	DCM	10	55	83:17
18	ZnI_2	10	CH_3CN	25	trace	
19[f]	ZnI_2	5	DCE	7	74	88:12

[a]By stirring a mixture of **1a** (0.05 g, 0.24 mmol, 1.0 equiv), 4-methylstyrene **2a** (0.064 mL, 0.48 mmol, 2.0 equiv), and catalyst (mol %) in 2.0 mL of dry 1,2-dichloroethane (DCE) under an Ar atmosphere at 45 °C for the designated time period. [b]Yield of isolated product *cis*-**3a**. [c]*cis*-**3a**:*trans*-**3a** (d.r.) was determined by ^{1}H NMR spectroscopic analysis of crude product mixtures. [d]The reaction was carried out at 60 °C. [e]The reaction was carried out at room temperature (30−35 °C). [f]For 0.5 g (2.42 mmol) of **1a**, batch size and DCE (20 mL) were used. Tf = trifluoromethane sulfonyl. BINOL = 1,1′-bi-2-naphthol. TFA = trifluoroacetic acid

disclosed a convenient method for synthesizing such α-ketothioesters in moderate to good yields.[9b]

Herein, we report the first IEDHDA reaction of β,γ-unsaturated α-ketothioesters with olefins using ZnI_2 as a catalyst to access highly substituted diastereomeric 3,4-dihydro-2*H*-pyrans. We also demonstrate that, under similar reaction conditions, terminal alkynes undergo direct conjugate 1,4-addition to yield δ,ε-acetylenic α-ketothioesters. Furthermore, the utility of these cycloadducts has been demonstrated by showing various synthetic applications, such as bromoetherification, followed by elimination, amidation, and palladium-catalyzed Fukuyama coupling reaction by using zinc reagents.

RESULTS AND DISCUSSION

To optimize the reaction conditions of IEDHDA reaction, we initiated a systematic study of γ-phenyl substituted β,γ-unsaturated α-ketomethylthioesters (**1a**) and 4-methylstyrene (**2a**) under different reaction conditions. As shown in Table 1, we observed that 10 mol % of $TiCl_4$, $InCl_3$, $InBr_3$, InI_3, or $Zn(OTf)_2$ could catalyze this transformation, but the product **3a** was formed either in lower yields (entries 1−4) or in trace amounts (entry 5), respectively. On the other hand, the use of 10 mol % $ZnCl_2$ (entry 6) or $ZnBr_2$ (entry 7) accelerated the transformation to afford the products in moderate yields with excellent *cis*-diastereoselctivity, but needed a longer reaction time. Interestingly, the use of 5 mol % ZnI_2 accelerated the transformation more readily (entry 9), and the reaction proceeded to completion within 5 h with excellent *cis*-diastereoselctivity (Table 1). The yield was further improved with 10 mol % of ZnI_2 (entry 8, 87%, *cis*-**3a**), but use of 1 mol % of the catalyst required a longer reaction time to furnish only a moderate yield (entry 12). However, the use of combined Lewis acid/Brønsted acid catalysts (ZnI_2/*rac*-BINOL, ZnI_2/*rac*-2,2′-biphenol, or ZnI_2/TFA) failed to improve the diastereoselectivity and yields of the reaction in any significant manner (entries 13−15). To study the temperature effect, we conducted the reaction at 60 °C (entry 10, 73%) and room temperature (entry 11, 57%). On the basis of the results

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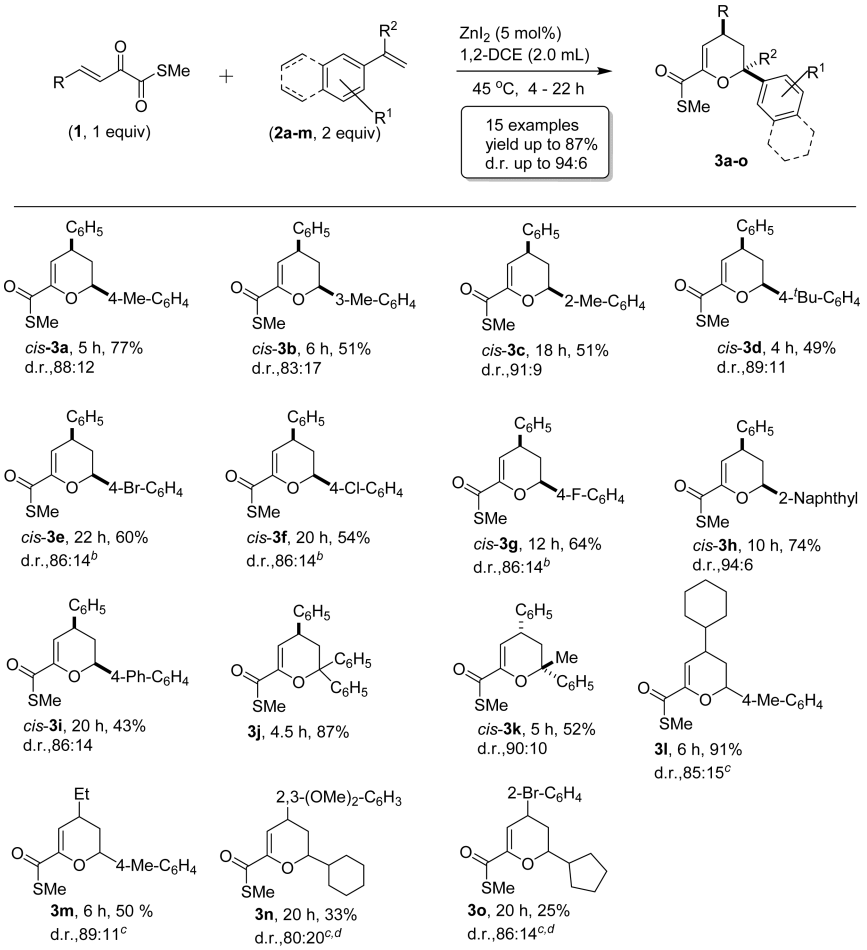
Table 2. Substrate Scope for Substituted Styrenes and α-Substituted Styrenes in IEDHDA Reaction[a]



[a]Yields are of isolated *cis* products after column purification; d.r. was determined by ^{1}H NMR analysis. [b]10 mol % ZnI_2. [c]Overall yield; inseparable mixture of two diastereomers. [d]Thioester (1.0 equiv), olefin (5.0 equiv), ZnI_2 (2.0 equiv), DCE (2.0 mL), 70 °C.

obtained (both yields and d.r.), we decided to carry out all the reactions at 45 °C. The use of other solvents (toluene, DCM, CH_3CN, and THF; entries 16−18) failed to deliver the required products **3a** in good yields. To demonstrate the feasibility of carrying out the transformation on a large scale, we conducted the reaction with 0.5 g of compound **1a** (2.42 mmol) to isolate *cis*-**3a** in 74% yield (entry 19, Table 1) without compromising the reaction efficiency. The reaction did not proceed when conducted at 45 °C or higher temperature for several hours either without catalyst or with different Lewis acids or metal salts, such as $MgBr_2$, CuI, $CuCl_2$, $NiBr_2$, Me_2AlCl, TMSOTf, $SnCl_4$, $Sc(OTf)_3$, $In(OTf)_3$, $Eu(OTf)_3$, $Yb(OTf)_3$, $ZnSO_4$, $Zn(OAc)_2$, and $Zn_3(PO_4)_2$; only starting materials were being recovered or decomposed.

Having established the optimized protocol (Table 1), we next investigated the substrate scope and generality for this transformation with substituted styrenes (**2a**−**m**). Table 2 summarizes the results. In general, the reaction is tolerant of variation in substituents in the styrenes. We found that, with 5 mol % ZnI_2, styrenes containing electron-donating (*cis*-**3a**−**d**, 49−77%, d.r., up to 91:9), fused aryl ring (*cis*-**3h**, 74%, d.r., 94:6), 4-phenyl (*cis*-**3i**, 43%, d.r, 86:14), or bulky substitution (**3j** and *cis*-**3k**, 52−87%) delivered the corresponding [4 + 2]-cycloadducts in moderate to excellent yields and with an excellent level of diastereoselectivity (*cis*-**3k**, d.r., 90:10). However, thioesters containing γ-aliphatic substituents (cyclohexyl and ethyl) delivered the corresponding cycloadducts (**3l**−**m**, 50−91%) as an inseparable mixture of two diastereomers. In addition, a catalytic amount of ZnI_2 was not enough to drive the reaction to completion for vinyl cyclo-alkyl substituents (**3n**−**o**). Only the use in stoichiometric ratios yielded the corresponding inseparable mixture of two diastereomers, albeit in poor yields (**3n**, 33% and **3o**, 25%). On the other hand, normal alkenes, such as *n*-octene, 4-phenyl-1-butene, and allylbenzene, did not result in the desired product even with the stoichiometric amount of ZnI_2 and at higher temperature. This may be due to the lack of sufficient electron density on olefins or plausible for oligomerization under the reaction conditions. Disappointedly, 5 mol % ZnI_2 was not sufficient to drive the reaction to completion for electron-deficient styrenes (**2e**−**g**). To our delight, the use of 10 mol % ZnI_2 ensured smooth conversion to their cycloadducts in moderate yields (*cis*-**3e**−**g**, 54−64%, d.r, up to 86:14).[10] In addition, we also provided the characterization data for separable *trans*-isomers (see the Supporting Information for details). The structure of *cis*-**3e** was confirmed by a single-crystal X-ray diffraction analysis of the corresponding bromoether adduct (**8c**, Scheme 1, *vide infra*), and the other products (*cis*-**3a** to **3j**) in Table 2 were assigned by analogy. In addition, 1D-NOE experiment of *cis*-**3f** also revealed the same configuration as described earlier. The exact configuration of *cis*-**3k** was assigned on the basis of a single-crystal X-ray analysis of the amidation product (**10a**,

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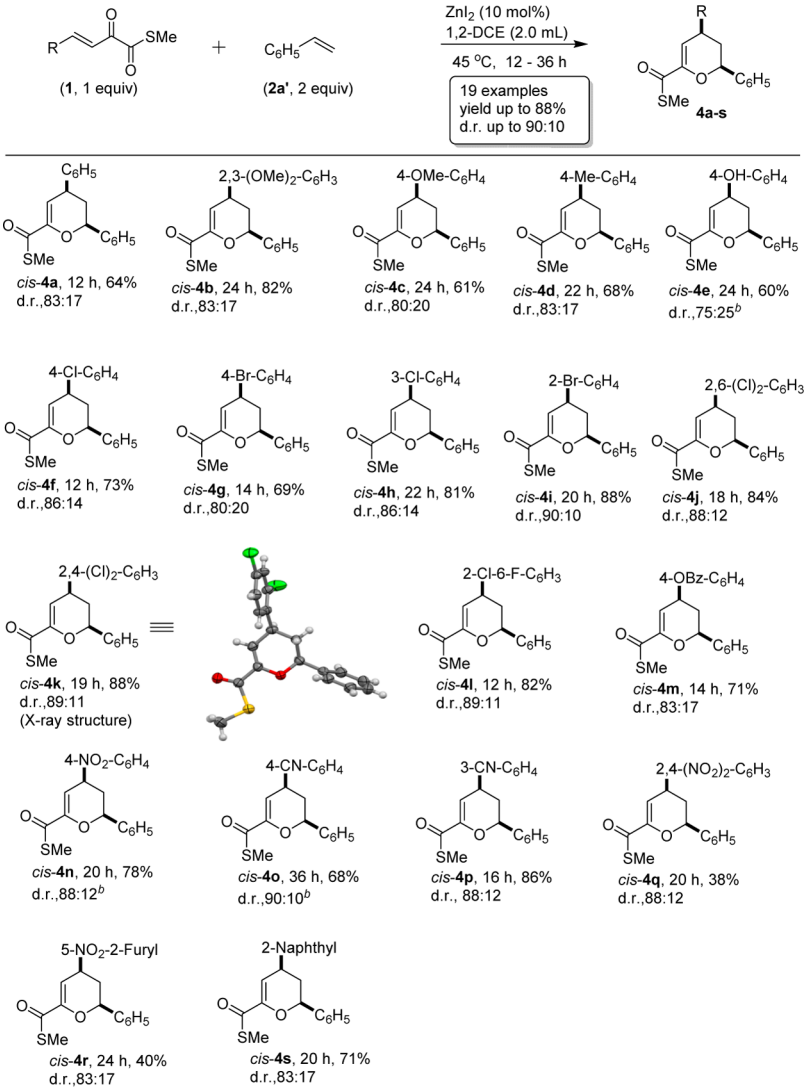
Table 3. Substrate Scope for β,γ-Unsaturated α-Ketomethylthioesters in IEDHDA Reaction[a]



[a]Yields are of isolated *cis* products after column purification; d.r. was determined by ^{1}H NMR analysis. [b]DCE (1.0 mL) + DCM (1.0 mL).

Scheme 4, *vide infra*). Interestingly, we found a different orientation of phenyl groups in *cis*-**3k** compared to the other products in Table 2. The reason behind this unusual approach of α-methylstyrene during cycloaddition reaction is not very clear at that moment.

In order to further broaden the substrate scope and establish the generality for this transformation, we investigated the reaction of several γ-substituted β,γ-unsaturated α-ketomethylthioesters with styrene (**2a′**) by using 10 mol % ZnI_2 as a catalyst. We observed that 5 mol % ZnI_2 was not sufficient to drive the reaction to completion and the necessity to conduct the reaction for a longer reaction time. As shown in Table 3, all of these reactions underwent *cis*-selective [4 + 2]-cycloaddition with an excellent level of diastereoselectivity and in moderate to good yields. In general, the reaction is tolerant of variation in substituents in the aryl ring. Substrates containing an electron-neutral (*cis*-**4a**, 64%, d.r., 83:17), electron-donating (*cis*-**4b**−**e**, 60−82%, d.r., up to 83:17), electron-deficient (*cis*-**4f**−**m**, 69−88%, d.r., up to 90:10), or strongly electron-withdrawing (*cis*-**4n**−**q**, 38−86%, d.r., up to 90:10) group on the aryl ring, or with a fused aryl ring (*cis*-**4s**, 71%, d.r, 83:17), delivered the corresponding cycloadducts in moderate to excellent yields. However, the reaction with a heteroaromatic substituent turned out to be rather sluggish (*cis*-**4r**, 40%, d.r., 83:17). The structure of *cis*-**4k** was established by a single-crystal X-ray diffraction analysis,[11] and the stereochemistry of other products in Table 3 was assigned by analogy, which all have similar ^{1}H NMR chemical shifts for the characteristic resonance. In addition, we also provided the characterization data for separable *trans*-isomers (see the Supporting Information for details)

On the basis of the promising results, we next explored the substrate scope and generality of the present IEDHDA reaction with 1*H*-indene **5a** under similar reaction conditions. As shown in Table 4, the reaction is tolerant of variation in substituents in the substituted thioesters, which were smoothly converted into the corresponding *cis*-selective [4 + 2]-cycloadducts in good to excellent yields and with high diastereoselectivity (*cis*-**6a**−**f**). However, the reaction with 1,2-dihydronaphthalene **5b** gave complicated product mixtures with 5−10 mol % of ZnI_2; with 15 mol % of ZnI_2, only a 30% yield of an inseparable mixture of two diastereomers (**6g**, d.r., 67:33) was obtained, ostensibly owing to the space-demanding nature of the *cis*-pathway. This consideration is consistent with the fact that the reaction did not work with highly substituted and sterically hindered

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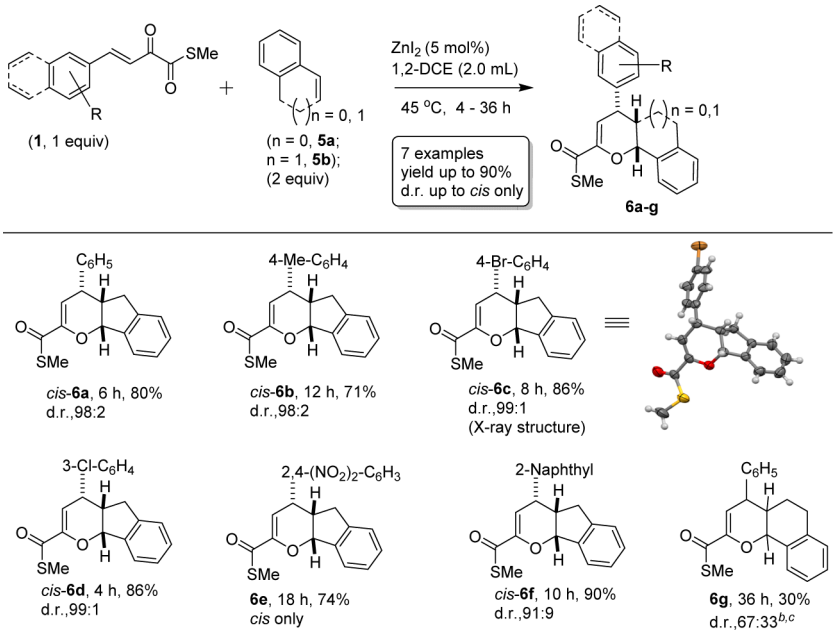
Table 4. Substrate Scope for 1*H*-Indene and 1,2-Dihydronaphthalene in IEDHDA Reaction[a]



[a]Yields are of isolated *cis* products after column purification; d.r. was determined by ^{1}H NMR analysis. [b]15 mol % ZnI_2. [c]Overall yield; inseparable mixture of two diastereomers.

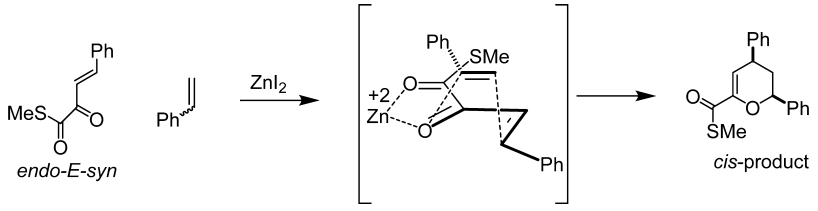


Figure 2. Plausible transition state for ZnI_2-catalyzed *cis*-selective IEDHDA reaction.

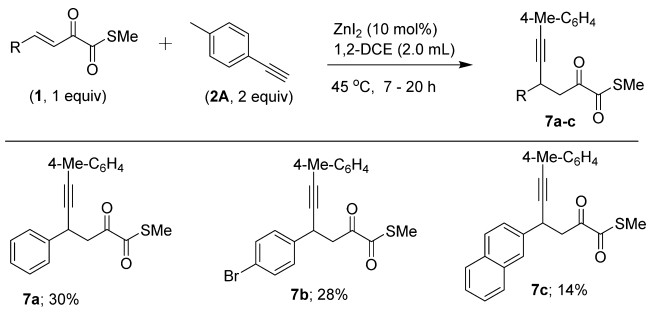
styrenes, such as *trans*-stilbene and *trans*-*β*-methylstyrene. The structure of *cis*-**6c** was established by a single-crystal X-ray diffraction analysis,[11] and the stereochemistry for the other products in Table 4 was tentatively assigned by analogy.

The highly *cis*-selective nature of this reaction can be explained as arising in consequence of the decrease in LUMO energy of the diene due to Zn^{2+} coordination with the diketo moiety of the substituted ketothioester, followed by [4 + 2]-cycloaddition with styrenes (Figure 2).[5d,l,8b]

Inspired by the above results, we examined the reaction of *γ*-substituted *β*,*γ*-unsaturated *α*-ketomethylthioesters with *p*-tolylacetylene (**2A**) using ZnI_2 as a catalyst. Interestingly, we isolated *δ*,*ε*-acetylenic *α*-ketothioesters (**7a**−**c**, 14−30%, Table 5), resulting from the conjugate addition of the triple bond to the electrophilic double bond.[12,13] Efforts are being made to develop a better catalyst.

To demonstrate the potential utility of the developed *cis*-selective [4 + 2]-cycloadduct, we treated *cis*-**6a** with NBS in MeOH, and this resulted in the stereospecific formation of separable diastereomeric bromoethers (**8a** and **8a′**, 2.5:1, Scheme 1). Interestingly, **8a** crystallized from a racemic solution in acetone as a conglomerate (**8a** and *ent*-**8a**). The structures of **8a** (**8a** and *ent*-**8a**) and **8a′** were established by single-crystal X-ray diffraction analyses (Scheme 1).[11] Under similar reaction conditions, *cis*-**4a** and *cis*-**3e** also yielded the corresponding separable diastereomeric bromoethers (**8b**: **8b′** = 9:1, and **8c**:**8c′** = 6.5:1, Scheme 1). The structures of major

Table 5. ZnI_2-Catalyzed Direct Conjugate Alkynylation of *γ*-Substituted *β*,*γ*-Unsaturated *α*-Ketomethylthioesters



diastereomer **8b** and **8c** were further established by single-crystal X-ray diffraction analysis (Scheme 1).[11]

The mechanistic pathway for bromoetherification of *cis*-**6a** can be explained on the basis of formation of a stereoelectronically more stable *α*-bromonium ion as a major intermediate and subsequent anti attack by methanol produced **8a** as the major diastereomer (**TS-I**, Figure 3) compared to **8a′** (**TS-II**, Figure 3).[14] On the other hand, bromoetherification of *cis*-**4a** and *cis*-**3e** might involve the formation of an open bromocarbonium ion intermediate, and incorporation of methanol preferentially occurred from the stereoelectronically assisted *α*-face, leading to **8b** and **8c** as major diastereomers, respectively (**TS-III**, Figure 3). It must be mentioned here that the stereochemical

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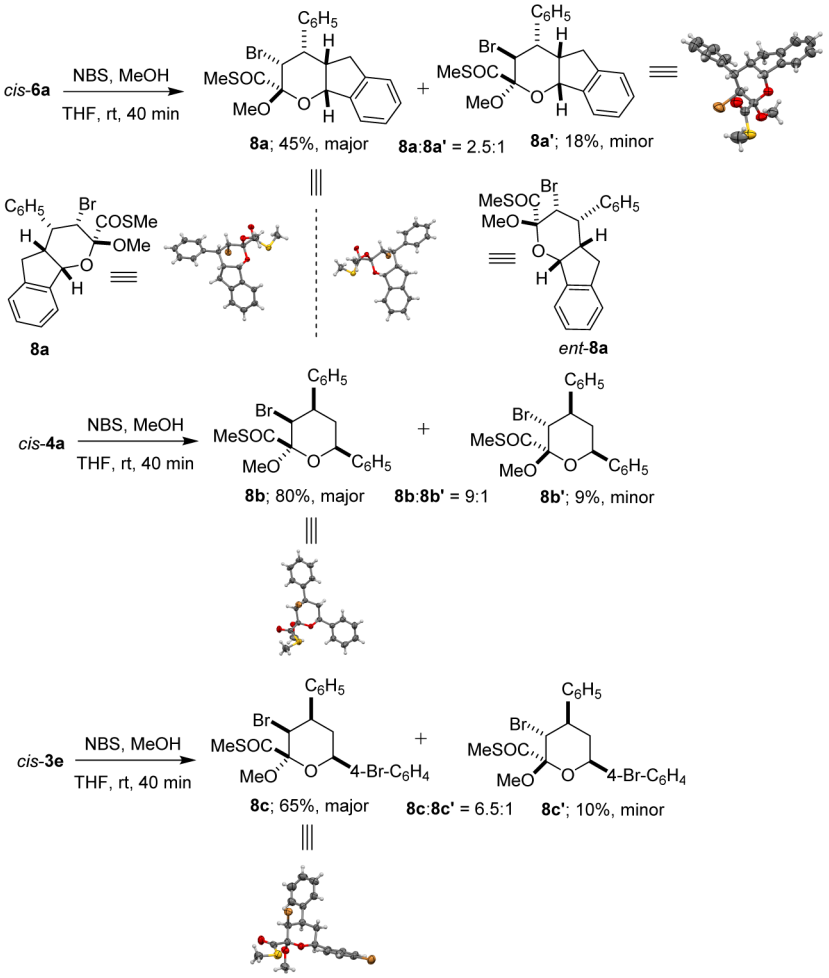
Scheme 1. Stereospecific Bromoetherification of Substituted 3,4-Dihydro-2*H*-pyrans with *N*-Bromosuccinimide (NBS)-MeOH. X-ray Determined Molecular Structures of 8a (8a and *ent*-8a as a Conglomerate), 8a′, 8b, and 8c



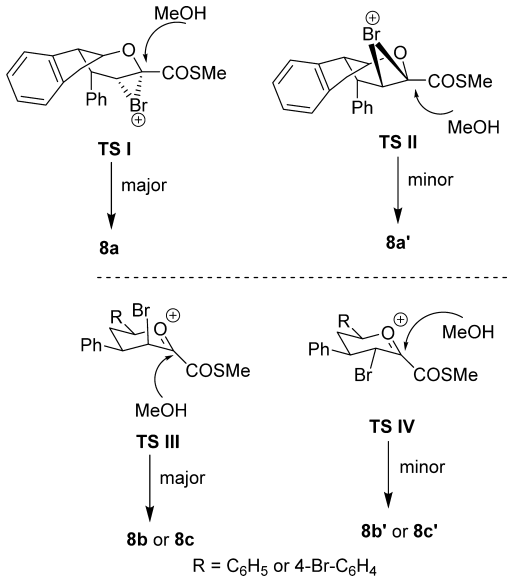
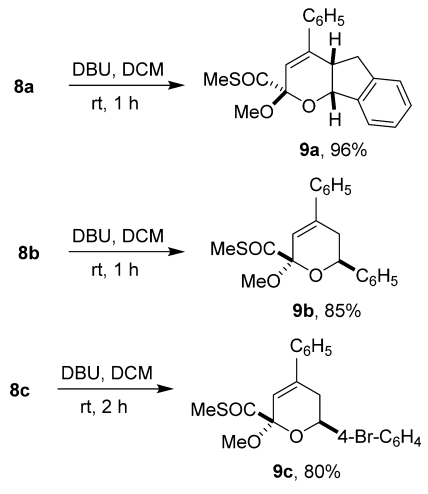


Figure 3. Mechanistic pathway for bromoetherification.

course for the bromine addition in methanol also depends on the solvent polarity, structure and substituents of enol ethers, and stereoelectronic α-anomeric effect.[14]

Further application of these bromoethers (**8a** and **8a′**) through E_2 elimination under DBU conditions was explored (Scheme 2). In the case of **8a**, the proton at C-4 is in an antiperiplanar orientation with C-3 bromine, and smooth elimination took place to furnish the substituted 3,6-dihydro-

Scheme 2. DBU (1,8-Diazabicycloundec-7-ene) Mediated Synthesis of Substituted 3,6-Dihydro-2*H*-pyrans



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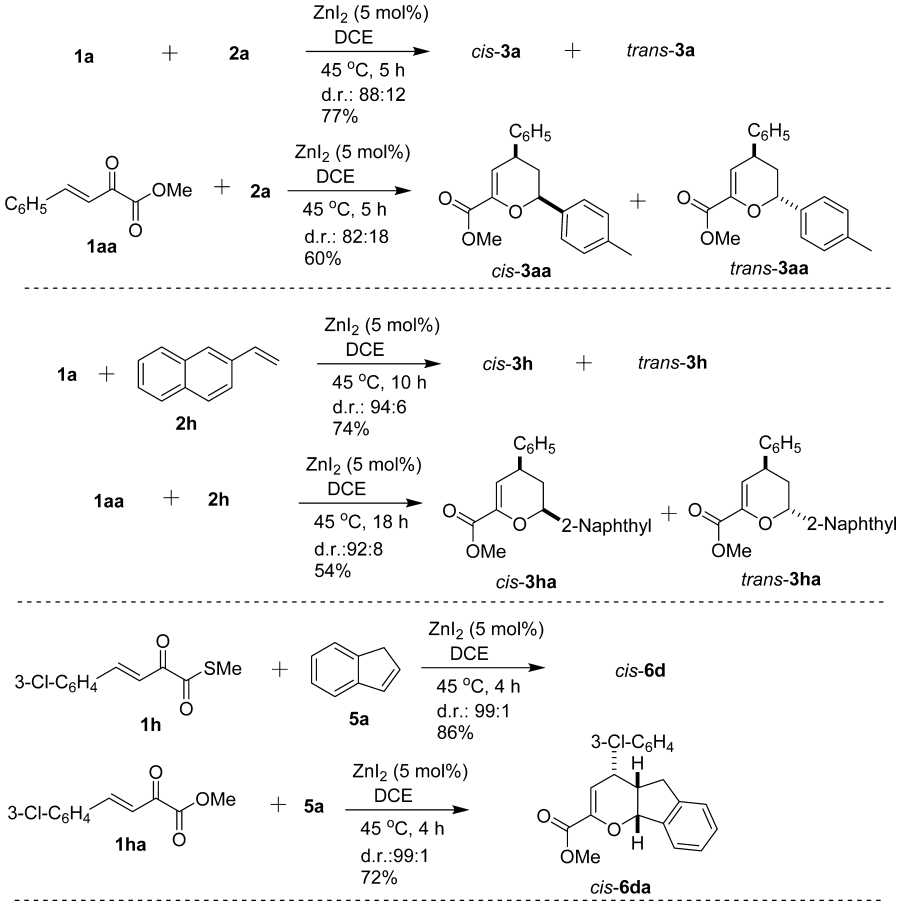
Scheme 3. Comparison of Reactivity between Thioesters and Oxoesters under Standard Reaction Conditions[a]



[a]Yields are of isolated *cis* products after column purification.

2*H*-pyran (**9a**, 96%). In contrast, no such elimination product was isolated from **8a′** due to lack of proper alignment of C_3-Br and C_4-H, and only starting material was recovered (Scheme 2). Similarly, **8b** and **8c** also produced the corresponding **9b** (85%) and **9c** (80%) under standard reaction conditions.

To reiterate the advantage and importance of the thioester compared to the oxoester, we treated oxoester (**1aa**, 0.05 g, 0.262 mmol) under the standard reaction conditions using 5 mol % ZnI_2 (Scheme 3). The corresponding major cycloadduct (*cis*-**3aa**) was isolated in relatively low yield (60%) and somewhat lower diastereoselectivity (d.r., 82:18) compared to the corresponding cycloadduct obtained from thioester (*cis*-**3a**, 77%, d.r., 88:12) under identical conditions. Similarly, we isolated major cycloadduct *cis*-**3ha** (54%, d.r., 92:8) and *cis*-**6da** (72%, d.r., 99:1) from oxoesters (**1aa** and **1ha**) in relatively low yield in comparison to the adducts obtained from thioesters (*cis*-**3h**, 74%, d.r., 94:6; and *cis*-**6d**, 86%, d.r., 99:1). Thus, we confirmed the advantage of thioesters in facilitating the cycloaddition reaction relative to oxoesters with consistently significant improvement. This may be due to that the sulfur atom in the thioester moiety is less able to contribute electron delocalization through the adjacent keto group, making the Zn^{2+} coordination with diketo of the thioester in the transition state more facile than the oxoester.

Furthermore, the thioester moiety of the cycloadducts was used for further transformations that are difficult to achieve using oxoesters.[9a] Direct amidation reaction with neat benzylamine and morpholine proceeded smoothly and produced the corresponding amide derivatives in excellent yields (**10a−d**, 88−95%, Scheme 4). To validate the superior reactivity of thioester compared to oxoester, we treated *cis*-**3aa** with neat benzylamine at rt (Scheme 4). In this case, the corresponding amide derivative **10e** was obtained in relatively low yield (40%), even conducting the reaction for a longer period of time (24 h). The structure of **10a** was established by a single-crystal X-ray diffraction analysis (Scheme 4).[11]

To further elaborate the significant reativity of *α*-ketothioesters compared to the parent *α*-ketoesters, Pd-catalyzed Fukuyama coupling reaction was accomplished for direct ketone synthesis, which was not affordable by the ketoester group.[15] Treatment of the thioesters *cis*-**3a** and *cis*-**4s** with EtZnI (3 equiv) using 10 mol % $PdCl_2(PPh_3)_2$ in THF at 40 °C under an argon atmosphere afforded the corresponding ketones (**11a**, 64% and **11b**, 85%) in good yields (Scheme 5).

■ CONCLUSION

In conclusion, we have successfully developed the first diastereoselective IEDHDA reaction of *γ*-substituted *β,γ*-unsaturated *α*-ketothioesters and simple olefins using ZnI_2 as a catalyst. All the reactions proceed with *cis*-selectivity in moderate to excellent yields. Under similar standard reaction conditions, terminal alkynes undergo direct conjugate 1,4-addition to yield *δ,ε*-acetylenic *α*-ketothioesters. The potential of these cycloadducts has been extended by the preparation of a substituted 3,6-dihydro-2*H*-pyran derivative following a two-step reaction sequence. Thus, NBS-MeOH mediated reaction

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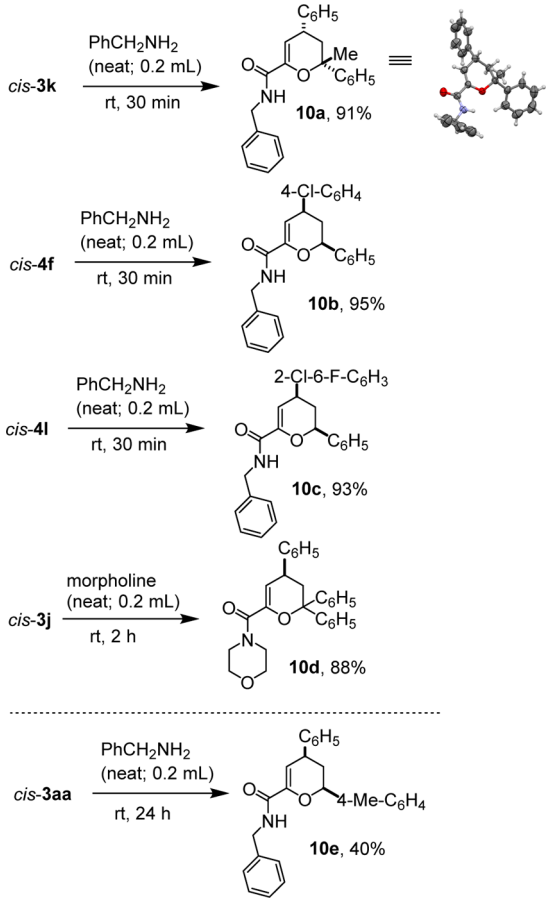
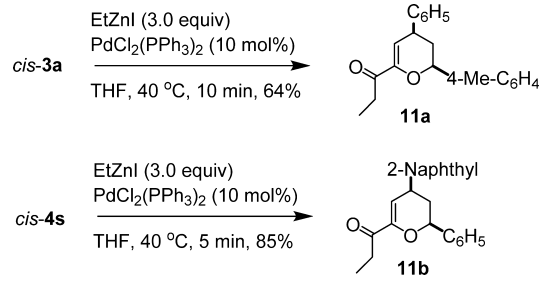
Scheme 4. Direct Transformations of Thioesters to Amides with Benzylamine and Morpholine



Scheme 5. Palladium-Catalyzed Direct Transformations of Thioesters to Ketones



of the [4 + 2]-cycloadduct produced separable diastereomeric bromoethers, the right stereoisomer from which underwent E_2 elimination with DBU to afford 3,6-dihydro-2*H*-pyran. In addition, the thioester moiety of the cycloadducts undergoes direct conversion to amides with benzylamine and morpholine in excellent yields. Furthermore, Pd-catalyzed Fukuyama coupling reaction was performed using zinc reagents to convert thioesters to ketones. Research is currently in progress to develop the asymmetric version of this IEDHDA reaction and advantages or synthetic utility of using these sulfur-derived substrates with respect to their oxygenated ketoester analogues.

EXPERIMENTAL SECTION

General Information. Melting points were determined in open-end-capillary tubes and are uncorrected. TLC was performed on silica gel plates (Merck silica gel 60, f_{254}), and the spots were visualized with UV light (254 and 365 nm) or by charring the plate dipped in 5% H_2SO_4–MeOH or vanillin charring solution. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ or DMSO-d_6 solvent using TMS as the internal standard. HRMS (*m*/*z*) were measured using EI (magnetic sector, positive ion) and ESI (Q-TOF, positive ion) techniques. Infrared (IR) spectra were recorded on Fourier transform infrared spectroscopy, and only intense peaks were reported.

General Procedure for the Synthesis of 3a–o, 4a–s, 6a–g, 7a–c, 3aa, 3ha, 6da. ZnI_2 (2.8 mg, 0.0087 mmol, 5 mol %) was taken in a 25 mL flame-dried, two-neck, round-bottomed flask, equipped with a magnetic stirring bar and a condenser, under an argon atmosphere and activated by heating in vacuum. The corresponding substituted thioester or ketoesters **1a–s** or **1aa** or **1ha** (0.05 g, 1.0 equiv) was dissolved in 1,2-DCE (2.0 mL) and introduced into the reaction mixtures. The corresponding alkene or alkyne (2.0 equiv or 5.0 equiv) was added successively, and the resulting reaction mixtures were stirred for the required temperatures and times. After completion of the reaction (TLC), saturated NH_4Cl solution was added, and the product was extracted with DCM. The combined organic layers were dried over anhydrous Na_2SO_4 and filtered, and the filtrate was concentrated under reduced pressure to obtain a residue. The crude residue was purified by using silica gel column chromatography [230–400 mesh particle size; eluent: ethyl acetate/*n*-hexane] to afford **3a–o**, **4a–s**, **6a–g**, **7a–c**, **3aa**, **3ha**, **6da**. All the d.r. (*cis*:*trans*) was determined by ^{1}H NMR spectroscopic analysis of crude product mixtures.

*4-Phenyl-6-p-tolyl-5,6-dihydro-4H-pyran-2-carbothioic Acid S-Methyl Ester (cis-**3a** and trans-**3a**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (2%); overall yield (*cis*:*trans*) = 0.075 g, 96%; isolated *cis* product yield = 0.060 g, 77%; isolated *trans* product yield = 0.007 g, 9%; *cis*-**3a**: yellow gum. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.30–7.34 (m, 4 H), 7.22–7.25 (m, 3 H), 7.19 (d, J = 7.8 Hz, 2 H), 6.09 (s, 1 H), 5.13 (d, J = 10.8 Hz, 1 H), 3.85 (ddd, J = 2.4, 6.6, 11.1 Hz, 1 H), 2.40 (dd, J = 6.6, 13.8 Hz, 1 H), 2.36 (s, 3 H), 2.34 (s, 3 H), 1.95 ppm (dt, J = 11.4, 13.8 Hz, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 189.6, 150.0, 143.0, 137.8, 137.2, 129.2 (2 CH), 128.7 (2 CH), 127.2 (2 CH), 126.9, 125.8 (2 CH), 109.2, 78.9, 39.8 (CH_2), 39.4, 21.2, 11.0 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1669, 1635 cm^{-1}; HRMS (EI): *m*/*z* calcd for $C_{20}H_{20}O_2S$ $[M]^+$: 324.1184; found: 324.1185. *trans*-**3a**: yellow gum. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.15–7.46 (m, 9 H), 6.23 (d, J = 4.5 Hz, 1 H),4.99 (dd, J = 2.1, 9.3 Hz, 1 H), 3.61–3.65 (m, 1 H), 2.37 (s, 3 H), 2.34 (s, 3 H), 2.27–2.32 (m, 1 H), 2.11–2.15 ppm (m, 1 H) ; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 189.6, 149.9, 144.0, 137.5, 137.3, 129.2 (2 CH), 128.6 (2 CH), 128.1 (2 CH), 126.8, 125.6 (2 CH), 107.1, 74.4, 37.7 (CH_2), 36.1, 21.1, 11.0 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1671, 1637, 1166 cm^{-1}; HRMS (EI): *m*/*z* calcd for $C_{20}H_{20}O_2S$ $[M]^+$: 324.1184; found: 324.1175.

*4-Phenyl-6-m-tolyl-5,6-dihydro-4H-pyran-2-carbothioic Acid S-Methyl Ester (cis-**3b** and trans-**3b**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (2.5%); overall yield (*cis*:*trans*) = 0.059 g, 75%; isolated *cis*-**3b** product yield = 0.04 g, 51%; isolated *trans*-**3b** product yield = 0.009 g, 11%; *cis*-**3b**: yellow gum. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.22–7.34 (m, 8 H), 7.13 (d, J = 6.6 Hz, 1 H), 6.10 (s, 1 H), 5.12 (dd, J = 1.2, 10.2 Hz, 1 H), 3.86 (ddd, J = 2.4, 6.3, 11.1 Hz, 1 H), 2.41 (dd, J = 6.3, 13.8 Hz, 1 H), 2.37 (s, 3 H), 2.34 (s, 3 H), 1.95 ppm (dt, J = 11.4, 14.1 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 189.6, 150.0, 142.9, 140.1, 138.2, 128.8 (3 CH), 128.4, 127.2 (2 CH), 126.9, 126.5, 122.9, 109.3, 79.0, 39.9 (CH_2), 39.4, 21.5, 11.0 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1673, 1638 cm^{-1}; HRMS (EI): *m*/*z* calcd for $C_{20}H_{20}O_2S$ $[M]^+$: 324.1184; found: 324.1180. *trans*-**3b**: yellow gum. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.34–7.37 (m, 2 H), 7.24–7.28 (m, 4 H), 7.11–7.14 (m, 3 H), 6.15 (dd, J = 1.2, 4.2 Hz, 1 H), 4.98 (dd, J = 2.4, 9.6 Hz, 1 H), 3.63–3.65 (m, 1 H), 2.38 (s, 3 H), 2.35 (s, 3 H), 2.29–2.33 (m, 1 H), 2.13–2.16 ppm (m, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 190.6, 150.9, 145.0, 141.3, 139.1, 129.7 (2 CH), 129.6, 129.4, 129.1 (2 CH), 127.8, 127.3, 123.7, 108.1, 75.5, 38.8 (CH_2), 37.2, 22.5, 12.1 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1672, 1637, 1052 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{20}H_{20}O_2SNa$ $[M + Na]^+$: 347.1082; found: 347.1101.

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*4-Phenyl-6-o-tolyl-5,6-dihydro-4H-pyran-2-carbothioic Acid S-Methyl Ester (cis-**3c** and trans-**3c**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (2.5%); overall yield (*cis*:*trans*) = 0.05 g, 64%; isolated *cis* product yield = 0.04 g, 51%; isolated *trans* product yield = 0.006 g, 7%. *cis*-**3c**: yellow gum. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.49−7.52 (m, 1 H), 7.16−7.35 (m, 8 H), 6.11 (d, J = 1.8 Hz, 1 H), 5.33 (dd, J = 1.2, 11.1 Hz, 1H), 3.86 (ddd, J = 2.4, 6.3, 11.1 Hz, 1 H), 2.41 (s, 3 H), 2.36−2.37 (m, 1 H), 2.33 (s, 3 H), 1.96 ppm (dt, J = 11.4, 13.8 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 189.5, 150.1, 142.9, 138.0, 134.9, 130.5, 128.7 (2 CH), 128.0, 127.2 (2 CH), 127.0, 126.3, 125.5, 109.2, 76.4, 39.6, 38.1 (CH_2), 19.0, 11.0 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1633 cm^{-1}; HRMS (EI): m/z calcd for $C_{20}H_{20}O_2S$ $[M]^+$: 324.1184; found: 324.1186. *trans*-**3c**: yellow gum. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.48 (d, J = 7.2 Hz, 1 H), 7.36 (t, J = 7.2 Hz, 2 H), 7.24−7.29 (m, 4 H), 7.20 (t, J = 7.8 Hz, 1 H), 7.10 (d, J = 7.8 Hz, 1 H), 6.21 (dd, J = 1.8, 5.4 Hz, 1 H), 5.05 (dd, J = 1.8, 10.8 Hz, 1 H), 3.73−3.75 (m, 1 H), 2.37 (s, 3 H), 2.19−2.26 (m, 1 H), 2.08−2.10 (m, 1 H), 1.99 ppm (s, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 190.6, 151.7, 145.1, 139.3, 135.5, 131.4, 129.6 (2 CH), 129.1 (2 CH), 128.7, 127.8, 127.3, 126.5, 107.5, 72.7, 37.9 (CH_2), 37.8, 19.5, 12.0 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1671, 1636, 1047 cm^{-1}; HRMS (ESI): m/z calcd for $C_{20}H_{20}O_2SNa$ $[M + Na]^+$: 347.1082; found: 347.1081.

*6-(4-tert-Butyl-phenyl)-4-phenyl-5,6-dihydro-4H-pyran-2-carbothioic Acid S-Methyl Ester (cis-**3d**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (2%); overall yield (*cis*:*trans*) = 0.052 g, 59%; isolated *cis* product yield = 0.043 g, 49%; yellow gum. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.22−7.49 (m, 9 H), 6.09 (s, 1 H), 5.13 (dd, J = 1.2, 10.2 Hz, 1 H), 3.86 (ddd, J = 2.4, 6.3, 11.1 Hz, 1 H), 2.36−2.47 (m, 1 H), 2.34 (s, 3 H), 1.95 (dt, J = 11.4, 13.8 Hz, 1 H), 1.32 ppm (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 189.6, 151.0, 149.9, 142.9, 137.2, 128.7 (2 CH), 127.2 (2 CH), 126.9, 125.5 (2 CH), 125.4 (2 CH), 109.2, 78.8, 39.7 (CH_2), 39.3, 34.5, 31.3 (3 CH_3), 11.0 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1664, 1631, 1166 cm^{-1}; HRMS (EI): m/z calcd for $C_{23}H_{26}O_2S$ $[M]^+$: 366.1653; found: 366.1656.

*6-(4-Bromo-phenyl)-4-phenyl-5,6-dihydro-4H-pyran-2-carbothioic Acid S-Methyl Ester (cis-**3e** and trans-**3e**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (2.5%); overall yield (*cis*:*trans*) = 0.083 g, 88%; isolated *cis* product yield = 0.056 g, 60%; isolated *trans* product yield = 0.012 g, 12%. *cis*-**3e**: colorless gum. ^{1}H NMR (300 MHz, d_6-DMSO): δ = 7.62 (d, J = 8.4 Hz, 2 H), 7.46 (d, J = 8.4 Hz, 2 H), 7.23−7.36 (m, 5 H), 5.94 (s, 1 H), 5.26 (d, J = 10.8 Hz, 1 H), 3.94−3.99 (m, 1 H), 2.41 (dd, J = 6.3, 13.5 Hz, 1 H), 2.29 (s, 3 H), 1.81 ppm (dt, J = 11.4, 12.9 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 189.3, 149.7, 142.6, 139.2, 131.7 (2 CH), 128.8 (2 CH), 127.6 (2 CH), 127.2 (2 CH), 127.1, 121.9, 109.5, 78.3, 39.7 (CH_2), 39.3, 11.0 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1664, 1633, 1165 cm^{-1}; HRMS (EI): m/z calcd for $C_{19}H_{17}BrO_2S$ $[M]^+$: 388.0133; found: 388.0132. *trans*-**3e**: yellow gum. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.48 (d, J = 8.4 Hz, 2 H), 7.35 (t, J = 7.8 Hz, 2 H), 7.28 (d, J = 7.2 Hz, 1 H), 7.24−7.26 (m, 2 H), 7.21 (d, J = 8.4 Hz, 2 H), 6.16 (dd, J = 1.2, 4.8 Hz, 1 H), 4.96 (dd, J = 2.4, 9.6 Hz, 1 H), 3.62−3.64 (m, 1 H), 2.38 (s, 3 H), 2.25−2.30 (m, 1 H), 2.11−2.14 ppm (m, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 190.3, 150.7, 144.7, 140.4, 132.6 (2 CH), 129.7 (2 CH), 129.1 (2 CH), 128.4 (2 CH), 128.0, 122.7, 108.2, 74.8, 38.7 (CH_2), 37.1, 12.1 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1671, 1638 cm^{-1}; HRMS (ESI): m/z calcd for $C_{19}H_{17}BrO_2SNa$ $[M+Na]^+$: 411.0031; found: 411.0039.

*6-(4-Chloro-phenyl)-4-phenyl-5,6-dihydro-4H-pyran-2-carbothioic Acid S-Methyl Ester (cis-**3f** and trans-**3f**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (2%); overall yield (*cis*:*trans*) = 0.05 g, 60%; isolated *cis* product yield = 0.045 g, 54%; isolated *trans* product yield = 0.0045 g, 5%; *cis*-**3f**: yellow gum. ^{1}H NMR (300 MHz, d_6-DMSO): δ = 7.46−7.54 (m, 4 H), 7.23−7.36 (m, 5 H), 5.94 (s, 1 H), 5.28 (d, J = 10.5 Hz, 1 H), 3.97 (ddd, J = 2.1, 6.2, 10.6 Hz, 1 H), 2.42 (dd, J = 6.3, 13.5 Hz, 1 H), 2.29 (s, 3 H), 1.82 ppm (dt, J = 11.4, 13.2 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 189.3, 149.7, 142.7, 138.7, 133.8, 128.8 (2 CH), 128.7 (2 CH), 127.2 (4 CH), 127.1, 109.4, 78.2, 39.8 (CH_2), 39.3, 11.0 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1664, 1632, 1165 cm^{-1}; HRMS (EI): m/z calcd for $C_{19}H_{17}ClO_2S$ $[M]^+$: 344.0638; found: 344.0636. *trans*-**3f**: yellow gum. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.32−7.37 (m, 4 H), 7.24−7.29 (m, 5 H), 6.16 (dd, J = 1.2, 4.8 Hz, 1 H), 4.98 (dd, J = 2.4, 9.6 Hz, 1 H), 3.62−3.65 (m, 1 H), 2.38 (s, 3 H), 2.25−2.30 (m, 1 H), 2.11−2.15 ppm (m, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 190.3, 150.7, 144.7, 139.8, 134.6, 129.7 (2 CH), 129.7 (2 CH), 129.1 (2 CH), 128.1 (2 CH), 128.0, 108.2, 74.8, 38.8 (CH_2), 37.1, 12.1 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1673, 1637 cm^{-1}; HRMS (ESI): m/z calcd for $C_{19}H_{17}ClO_2SNa$ $[M + Na]^+$: 367.0536; found: 367.0552.

*6-(4-Fluoro-phenyl)-4-phenyl-5,6-dihydro-4H-pyran-2-carbothioic Acid S-Methyl Ester (cis-**3g** and trans-**3g**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (2%); overall yield (*cis*:*trans*) = 0.062 g, 78%; isolated *cis* product yield = 0.051 g, 64%; isolated *trans* product yield = 0.006 g, 7%. *cis*-**3g**: white solid; mp 98 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.40−7.44 (m, 2 H), 7.22−7.34 (m, 5 H), 7.07 (t, J = 8.7 Hz, 2 H), 6.11 (s, 1 H), 5.15 (d, J = 11.4 Hz, 1 H), 3.86 (ddd, J = 2.1, 6.5, 11.2 Hz, 1 H), 2.40 (dd, J = 6.3, 13.8 Hz, 1 H), 2.35 (s, 3 H), 1.92 ppm (dt, J = 11.4, 13.8 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 189.3, 162.5 (d, J_{C-F} = 244.5 Hz, 1 C), 149.8, 142.7, 136.0 (d, J_{C-F} = 3.0 Hz, 1 C), 128.8 (2 CH), 127.6, 127.5, 127.2 (2 CH), 127.0, 115.6, 115.3, 109.4, 78.3, 39.9 (CH_2), 39.3, 11.0 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1665, 1633, 1511, 1222, 1163 cm^{-1}; HRMS (EI): m/z calcd for $C_{19}H_{17}FO_2S$ $[M]^+$: 328.0933; found: 328.0939. *trans*-**3g**: yellow gum. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.34−7.37 (m, 2 H), 7.25−7.32 (m, 5 H), 7.03−7.06 (m, 2 H), 6.16 (dd, J = 1.2, 5.4 Hz, 1 H), 4.97 (dd, J = 2.4, 10.2 Hz, 1 H), 3.64−3.66 (m, 1 H), 2.38 (s, 3 H), 2.27−2.32 (m, 1 H), 2.12−2.15 ppm (m, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 190.4, 163.3 (d, J_{C-F} = 244.5 Hz, 1 C), 150.8, 144.8, 137.1 (d, J_{C-F} = 3.0 Hz, 1 C), 129.7 (2 CH), 129.1 (2 CH), 128.5, 128.4, 127.9, 116.5, 116.3, 108.1, 74.8, 38.8 (CH_2), 37.2, 12.0 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1671, 1637, 1510, 1163, 1053 cm^{-1}; HRMS (ESI): m/z calcd for $C_{19}H_{17}FO_2SNa$ $[M + Na]^+$: 351.0831; found: 351.0839.

*6-Naphthalen-2-yl-4-phenyl-5,6-dihydro-4H-pyran-2-carbothioic Acid S-Methyl Ester (cis-**3h**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (3%); overall yield (*cis*:*trans*) = 0.079 g, 90%; isolated *cis* product yield = 0.065 g, 74%; yellow gum. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.83−7.92 (m, 4 H), 7.47−7.57 (m, 3 H), 7.22−7.35 (m, 5 H), 6.15 (s, 1 H), 5.33 (d, J = 11.1 Hz, 1 H), 3.92 (ddd, J = 2.4, 6.3, 11.1 Hz, 1 H), 2.52 (dd, J = 6.3, 14.1 Hz, 1 H), 2.36 (s, 3 H), 2.05 ppm (dt, J = 11.4, 13.8 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 189.5, 150.0, 142.9, 137.6, 133.2, 133.1, 128.8 (2 CH), 128.4, 128.1, 127.7, 127.3 (2 CH), 127.0, 126.3, 126.1, 124.9, 123.9, 109.4, 79.1, 39.8 (CH_2), 39.4, 11.0 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1668, 1634 cm^{-1}; HRMS (EI): m/z calcd for $C_{23}H_{20}O_2S$ $[M]^+$: 360.1184; found: 360.1180.

*6-Biphenyl-4-yl-4-phenyl-5,6-dihydro-4H-pyran-2-carbothioic Acid S-Methyl Ester (cis-**3i** and trans-**3i**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (2%); overall yield (*cis*:*trans*) = 0.055 g, 59%; isolated *cis* product yield = 0.04 g, 43%; isolated *trans* product yield = 0.007 g, 7%. *cis*-**3i**: yellow gum. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.60 (t, J = 8.1 Hz, 5 H), 7.52 (d, J = 8.1 Hz, 2 H), 7.44 (t, J = 7.2 Hz, 2 H), 7.30−7.37 (m, 4 H), 7.24 (m, 1 H), 6.12 (s, 1 H), 5.22 (d, J = 10.5 Hz, 1 H), 3.86−3.92 (m, 1 H), 2.47 (dd, J = 6.6, 14.1 Hz, 1 H), 2.36 (s, 3 H), 1.99 ppm (dt, J = 11.4, 13.8 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 189.5, 149.9, 142.9, 141.0, 140.7, 139.2, 128.8 (4 CH), 127.4, 127.3 (2 CH), 127.3 (2 CH), 127.1 (2 CH), 127.0, 126.3 (2 CH), 109.3, 78.8, 39.8 (CH_2), 39.4, 11.0 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1669, 1635 cm^{-1}; HRMS (ESI): m/z calcd for $C_{25}H_{22}O_2SNa$ $[M + Na]^+$: 409.1238; found: 409.1228. *trans*-**3i**: yellow gum. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.58−7.59 (m, 4 H), 7.40−7.45 (m, 4 H), 7.35−7.38 (m, 3 H), 7.27−7.29 (m, 3 H), 6.17 (d, J = 4.8 Hz, 1 H), 5.07 (dd, J = 2.4, 9.6 Hz, 1 H), 3.66−3.68 (m, 1 H), 2.39 (s, 3 H), 2.34−2.38 (m, 1 H), 2.18−2.21 ppm (m, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 190.5, 150.9, 144.9, 141.8, 141.7, 140.3, 129.8 (2 CH), 129.7 (2 CH), 129.1 (2 CH), 128.4, 128.3 (2 CH), 128.1 (2 CH), 127.9, 127.1 (2 CH), 108.2, 75.3, 38.7 (CH_2), 37.2, 12.1 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1670, 1637, 1166, 1054 cm^{-1}; HRMS

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(ESI): m/z calcd for $C_{25}H_{22}O_2SNa$ $[M + Na]^+$: 409.1238; found: 409.1230.

*4,6,6-Triphenyl-5,6-dihydro-4H-pyran-2-carbothioic Acid S-Methyl Ester (**3j**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (2%); isolated product yield = 0.081 g, 87%; yellow gum. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.57 (d, J = 7.5 Hz, 2 H), 7.48 (d, J = 7.5 Hz, 2 H), 7.39 (t, J = 7.2 Hz, 2 H), 7.20−7.31 (m, 9 H), 6.01 (s, 1 H), 3.40−3.47 (m, 1 H), 3.10−3.16 (m, 1 H), 2.42 (s, 3 H), 2.28 ppm (dd, J = 12.0, 14.1 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 189.4, 148.0, 144.9, 142.8, 142.7, 128.9 (2 CH), 128.8 (2 CH), 128.4 (2 CH), 127.6 (3 CH), 127.4, 127.0, 125.6 (2 CH), 125.2 (2 CH), 109.7, 83.9, 41.3 (CH_2), 36.9, 11.1 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1669, 1633, 698 cm^{-1}; HRMS (EI): m/z calcd for $C_{25}H_{22}O_2S$ $[M]^+$: 386.1340; found: 386.1337.

*6-Methyl-4,6-diphenyl-5,6-dihydro-4H-pyran-2-carbothioic Acid S-Methyl Ester (cis-**3k**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (1.5%); overall yield (*cis*:*trans*) = 0.073 g, 93%; isolated *cis* product yield = 0.041 g, 52%; colorless gum. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.50−7.52 (m, 2 H), 7.34−7.37 (m, 2 H), 7.25−7.30 (m, 3 H), 7.19−7.23 (m, 3 H), 6.09 (dd, J = 1.8, 2.4 Hz, 1 H), 3.71 (ddd, J = 2.4, 6.0, 11.4 Hz, 1 H), 2.38 (s, 3 H), 2.36 (td, J = 1.2, 7.8 Hz, 1 H), 1.90 (dd, J = 11.4, 13.8 Hz, 1 H), 1.68 ppm (s, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 191.1, 148.7, 146.8, 143.8, 129.7 (2 CH), 129.3 (2 CH), 128.5 (2 CH), 128.2, 127.8, 125.2 (2 CH), 108.3, 80.9, 44.2 (CH_2), 37.7, 25.3, 12.0 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1672, 1637, 1283, 1175, 699 cm^{-1}; HRMS (ESI): m/z calcd for $C_{20}H_{20}O_2SNa$ $[M + Na]^+$: 347.1082; found: 347.1102.

*4-Cyclohexyl-6-p-tolyl-5,6-dihydro-4H-pyran-2-carbothioic Acid S-Methyl Ester (**3l**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (1%); overall yield (*cis*:*trans*) = 0.070 g, 91%; colorless gum. Inseparable mixture of major and minor diastereomers: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.99−7.44 (m, 4 H), 5.99 (s, 1 H), 4.93 (d, J = 10.2 Hz, 1 H), 2.38−2.46 (m, 1 H), 2.37 (s, 3 H), 2.30 (s, 3 H), 1.97−2.09 (m, 1 H), 1.61−1.82 (m, 6 H), 0.95−1.45 ppm (m, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 189.7, 149.5, 138.0, 137.5, 129.1 (2 CH), 125.7 (2 CH), 109.5, 78.8, 41.7, 38.7, 34.1 (CH_2), 30.1 (CH_2), 29.8 (CH_2), 26.4 (CH_2), 26.4 (CH_2), 21.1, 10.9 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1670, 1634 cm^{-1}; HRMS (ESI): m/z calcd for $C_{20}H_{26}O_2SNa$ $[M + Na]^+$: 353.1551; found: 353.1549.

*4-Ethyl-6-p-tolyl-5,6-dihydro-4H-pyran-2-carbothioic Acid S-Methyl Ester (**3m**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (1%); overall yield (*cis*:*trans*) = 0.044 g, 50%; colorless gum. Inseparable mixture of major and minor diastereomers: ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.31 (d, J = 7.8 Hz, 2 H), 7.20 (d, J = 7.8 Hz, 2 H), 5.92 (t, J = 1.8 Hz, 1 H), 4.95 (d, J = 9.6 Hz, 1 H), 2.45−2.54 (m, 1 H), 2.37 (s, 3 H), 2.30 (s, 3 H), 2.16 (ddt, J = 1.8, 6.0, 13.8 Hz, 1 H), 1.47−1.54 (m, 2 H), 1.39−1.46 (m, 1 H), 0.98 ppm (t, J = 7.2 Hz, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 190.8, 150.1, 139.0, 138.6, 130.1 (2 CH), 126.7 (2 CH), 111.3, 79.7, 37.9 (CH_2), 35.7, 28.9 (CH_2), 22.2, 12.3, 11.9 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1670, 1635 cm^{-1}; HRMS (ESI): m/z calcd for $C_{16}H_{20}O_2SNa$ $[M + Na]^+$: 299.1082; found: 299.1088.

*6-Cyclohexyl-4-(2,3-dimethoxy-phenyl)-5,6-dihydro-4H-pyran-2-carbothioic Acid S-Methyl Ester (**3n**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (4%); overall yield (*cis*:*trans*) = 0.023 g, 33%; colorless gum. Inseparable mixture of major and minor diastereomers: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.99 (t, J = 8.1 Hz, 1 H), 6.83 (dd, J = 1.2, 8.1 Hz, 1 H), 6.71−6.74 (m, 1 H), 5.95 (d, J = 4.8 Hz, 1 H), 3.78−3.97 (m, 7 H), 3.62−3.66 (m, 1 H), 2.31−2.38 (m, 4 H), 1.98−2.10 (m, 2 H), 1.06−1.85 ppm (m, 10 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 190.0, 152.6, 150.0, 146.4, 137.9, 123.5, 121.4, 111.1, 107.0, 77.8, 60.7, 55.7, 40.9, 31.9 (CH_2), 30.1, 28.7 (CH_2), 28.6 (CH_2), 26.4 (CH_2), 26.1 (CH_2), 25.9 (CH_2), 10.9 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1672, 1637, 1586, 1475, 1277, 1075 cm^{-1}; HRMS (ESI): m/z calcd for $C_{21}H_{28}O_4SNa$ $[M + Na]^+$: 399.1606; found: 399.1630.

*4-(2-Bromo-phenyl)-6-cyclopentyl-5,6-dihydro-4H-pyran-2-carbothioic Acid S-Methyl Ester (**3o**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (1.5%); overall yield (*cis*:*trans*) = 0.017 g, 25%; colorless gum. Inseparable mixture of major and minor diastereomers: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.57 (dd, J = 0.9, 7.8 Hz, 1 H), 7.19−7.29 (m, 2 H), 7.08−7.14 (m, 1 H), 5.95 (dd, J = 0.9, 4.8 Hz, 1 H), 3.99−4.04 (m, 1 H), 3.67−3.73 (m, 1 H), 2.35 (s, 3 H), 1.62−2.27 ppm (m, 11 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 189.9, 150.4, 142.9, 133.1, 130.3, 128.3, 127.4, 124.1, 105.7, 77.2, 43.1, 35.8, 32.8 (CH_2), 29.7 (CH_2), 28.9 (CH_2), 28.7 (CH_2), 25.5 (CH_2), 11.0 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1673, 1638, 1463, 1435, 1025 cm^{-1}; HRMS (ESI): m/z calcd for $C_{18}H_{21}BrO_2SNa$ $[M + Na]^+$: 403.0344; found: 403.0350.

*4,6-Diphenyl-5,6-dihydro-4H-pyran-2-carbothioic Acid S-Methyl Ester (cis-**4a**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (2%); overall yield (*cis*:*trans*) = 0.069 g, 92%; isolated *cis* product yield = 0.048 g, 64%; yellow gum. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.44−7.46 (m, 2 H), 7.37−7.40 (m, 2 H), 7.30−7.34 (m, 3 H), 7.23−7.25 (m, 3 H), 6.11 (t, J = 1.8 Hz, 1 H), 5.18 (dd, J = 1.8, 11.4 Hz, 1 H), 3.87 (ddd, J = 2.4, 6.0, 11.4 Hz, 1 H), 2.43 (ddt, J = 1.8, 6.6, 14.4 Hz, 1 H), 2.35 (s, 3 H), 1.95 ppm (dt, J = 11.4, 14.4 Hz, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 189.5, 149.9, 142.9, 140.2, 128.8 (2 CH), 128.5 (2 CH), 128.0, 127.2 (2 CH), 127.0, 125.8 (2 CH), 109.3, 78.9, 39.9 (CH_2), 39.4, 11.0 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1662, 1632 cm^{-1}; HRMS (ESI): m/z calcd for $C_{19}H_{18}O_2SNa$ $[M + Na]^+$: 333.0925; found: 333.0907.

*4-(2,3-Dimethoxy-phenyl)-6-phenyl-5,6-dihydro-4H-pyran-2-carbothioic Acid S-Methyl Ester (cis-4b and trans-**4b**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (10%); overall yield (*cis*:*trans*) = 0.068 g, 98%; isolated *cis* product yield = 0.057 g, 82%; isolated *trans* product yield = 0.006 g, 8%. *cis*-**4b**: colorless gum. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.28−7.45 (m, 5 H), 7.01 (t, J = 8.1 Hz, 1 H), 6.79 (t, J = 9.0 Hz, 2 H), 6.05 (s, 1 H), 5.18 (d, J = 10.2 Hz, 1 H), 4.27 (ddd, J = 2.4, 6.3, 11.1 Hz, 1 H), 3.86 (s, 6 H), 2.42 (dd, J = 6.3, 13.5 Hz, 1 H), 2.34 (s, 3 H), 1.88 ppm (dt, J = 11.4, 13.8 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 189.5, 152.6, 150.0, 146.8, 140.3, 136.4, 128.4 (2 CH), 127.9, 125.8 (2 CH), 124.3, 119.6, 111.0, 109.8, 79.0, 61.1, 55.7, 38.4 (CH_2), 32.8, 10.9 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1670, 1635, 1516 cm^{-1}; HRMS (EI): m/z calcd for $C_{21}H_{22}O_4S$ $[M]^+$: 370.1239; found: 370.1240. *trans*-**4b**: yellow gum. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.35 (d, J = 4.2 Hz, 4 H), 7.27−7.30 (m, 1 H), 7.04 (t, J = 7.8 Hz, 1 H), 6.87 (dd, J = 1.8, 8.4 Hz, 1 H), 6.82 (dd, J = 1.8, 7.8 Hz, 1 H), 6.08 (d, J = 4.8 Hz, 1 H), 5.03 (dd, J = 2.4, 9.6 Hz, 1 H), 3.96−3.99 (m, 1 H), 3.88 (s, 3 H), 3.84 (s, 3 H), 2.37 (s, 3 H), 2.30−2.35 (m, 1 H), 2.10−2.14 ppm (m, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 190.5, 153.7, 151.1, 147.4, 141.4, 138.4, 129.4 (2 CH), 128.7, 126.7 (2 CH), 124.7, 122.3, 112.3, 108.6, 75.7, 61.7, 56.8, 37.6 (CH_2), 31.5, 12.0 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1671, 1637, 1475, 1278 cm^{-1}; HRMS (ESI): m/z calcd for $C_{21}H_{22}O_4SNa$ $[M + Na]^+$: 393.1137; found: 393.1138.

*4-(4-Methoxy-phenyl)-6-phenyl-5,6-dihydro-4H-pyran-2-carbothioic Acid S-Methyl Ester (cis-**4c**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (4%); overall yield (*cis*:*trans*) = 0.051 g, 70%; isolated *cis* product yield = 0.044 g, 61%; yellow gum. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.29−7.46 (m, 5 H), 7.15 (d, J = 8.4 Hz, 2 H), 6.85 (d, J = 8.7 Hz, 2 H), 6.08 (s, 1 H), 5.16 (d, J = 11.4 Hz, 1 H), 3.81−3.89 (m, 1 H), 3.79 (s, 3 H), 2.36−2.46 (m, 1 H), 2.34 (s, 3 H), 1.91 ppm (dt, J = 11.4, 13.8 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 189.5, 158.5, 149.7, 140.3, 134.9, 128.5 (2 CH), 128.2 (2 CH), 128.0, 125.8 (2 CH), 114.1 (2 CH), 109.7, 79.0, 55.3, 40.0 (CH_2), 38.6, 11.0 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1609, 1670, 1635, 1514 cm^{-1}; HRMS (EI): m/z calcd for $C_{20}H_{20}O_3S$ $[M]^+$: 340.1133; found: 340.1131.

*6-Phenyl-4-p-tolyl-5,6-dihydro-4H-pyran-2-carbothioic Acid S-Methyl Ester (cis-4d and trans-**4d**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (2.5%); overall yield (*cis*:*trans*) = 0.072 g, 98%; isolated *cis* product yield = 0.05 g, 68%; isolated *trans* product yield = 0.009 g, 12%; *cis*-**4d**: yellow gum. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.29−7.46 (m, 5 H), 7.12 (m, 4 H), 6.09 (s, 1 H), 5.16 (dd, J = 11.4 Hz, 1 H), 3.83 (ddd, J = 2.4, 6.5, 11.3 Hz, 1 H), 2.40 (dd, J = 6.3, 13.8 Hz, 1 H), 2.34 (s, 3 H), 2.32 (s, 3 H), 1.93 (dt, J = 11.4, 13.8 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ =

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189.5, 149.8, 140.3, 139.9, 136.6, 129.4 (2 CH), 128.5 (2 CH), 128.0, 127.1 (2 CH), 125.8 (2 CH), 109.6, 79.0, 39.9 (CH_2), 39.0, 21.0, 11.0 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1671, 1636, 1161, 1049, 754 cm^{-1}; HRMS (EI): *m/z* calcd for $C_{20}H_{20}O_2S$ $[M]^+$: 324.1184; found: 324.1184. *trans*-**4d**: yellow liquid. ^1H NMR (600 MHz, $CDCl_3$): δ = 7.32−7.37 (m, 4 H), 7.28−7.31 (m, 1 H), 7.13−7.16 (m, 4 H), 6.14 (d, *J* = 4.8 Hz, 1 H), 5.01 (dd, *J* = 2.4, 9.6 Hz, 1 H), 3.58−3.61 (m, 1 H), 2.37 (s, 3 H), 2.35 (s, 3 H), 2.27−2.33 (m, 1 H), 2.12−2.15 ppm (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 190.6, 150.8, 141.9, 141.4, 137.5, 130.3 (2 CH), 129.5 (2 CH), 129.0 (2 CH), 128.7, 126.6 (2 CH), 108.5, 75.4, 38.9 (CH_2), 36.8, 22.0, 12.0 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1672, 1638, 1167, 912 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{20}H_{20}O_2SNa$ $[M + Na]^+$: 347.1082; found: 347.1080.

*4-(4-Hydroxy-phenyl)-6-phenyl-5,6-dihydro-4H-pyran-2-carbothioic Acid S-Methyl Ester (cis-**4e**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (20%); overall yield (*cis*:*trans*) = 0.055 g, 75%; isolated *cis* product yield = 0.044 g, 60%; yellow gum. ^1H NMR (600 MHz, $CDCl_3$): δ = 7.44 (d, *J* = 7.2 Hz, 2 H), 7.39 (t, *J* = 7.2 Hz, 2 H), 7.32 (t, *J* = 7.2 Hz, 1 H), 7.09 (d, *J* = 7.8 Hz, 2 H), 6.77 (d, *J* = 8.4 Hz, 2 H), 6.07 (t, *J* = 1.8 Hz, 1 H), 5.15 (d, *J* = 10.8 Hz, 1 H), 4.98 (br s, 1 H), 3.80 (ddd, *J* = 2.4, 6.6, 11.4 Hz, 1 H), 2.39 (ddt, *J* = 1.8, 6.6, 13.5 Hz, 1 H), 2.35 (s, 3 H), 1.90 ppm (dt, *J* = 11.4, 13.8 Hz, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 189.9, 154.5, 149.7, 140.2, 135.0, 128.5 (2 CH), 128.4 (2 CH), 128.0, 125.8 (2 CH), 115.5 (2 CH), 109.7, 79.0, 40.1 (CH_2), 38.6, 11.0 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1614, 1632, 1514 cm^{-1}; HRMS (EI): *m/z* calcd for $C_{19}H_{18}O_3S$ $[M]^+$: 326.0977; found: 326.0959.

*4-(4-Chloro-phenyl)-6-phenyl-5,6-dihydro-4H-pyran-2-carbothioic Acid S-Methyl Ester (cis-**4f** and trans-**4f**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (2.5%); overall yield (*cis*:*trans*) = 0.062 g, 87%; isolated *cis* product yield = 0.052 g, 73%; isolated *trans* product yield = 0.004 g, 5%; *cis*-**4f**: yellow gum. ^1H NMR (600 MHz, $CDCl_3$): δ = 7.43−7.44 (m, 2 H), 7.38−7.40 (m, 2 H), 7.31−7.34 (m, 1 H), 7.27−7.29 (m, 2 H), 7.16−7.17 (m, 2 H), 6.04 (t, *J* = 1.8 Hz, 1 H), 5.16 (d, *J* = 1.2, 11.5 Hz, 1 H), 3.85 (ddd, *J* = 3.0, 6.3, 11.3 Hz, 1 H), 2.40 (ddt, *J* = 1.8, 6.0, 13.8 Hz, 1 H), 2.35 (s, 3 H), 1.89 ppm (dt, *J* = 12.0, 13.8 Hz, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 189.5, 150.1, 141.4, 140.0, 132.7, 128.9 (2 CH), 128.6 (2 CH), 128.6 (2 CH), 128.1, 125.7 (2 CH), 108.4, 78.9, 39.8 (CH_2), 38.8, 11.0 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1663, 1629 cm^{-1}; HRMS (EI): *m/z* calcd for $C_{19}H_{17}ClO_2S$ $[M]^+$: 344.0638; found: 344.0630. *trans*-**4f**: yellow gum. ^1H NMR (600 MHz, $CDCl_3$): δ = 7.35−7.38 (m, 2 H), 7.31−7.33 (m, 5 H), 7.18−7.20 (m, 2 H), 6.10 (dd, *J* = 0.6, 4.8 Hz, 1 H), 4.98 (dd, *J* = 2.4, 9.6 Hz, 1 H), 3.59−3.61 (m, 1 H), 2.38 (s, 3 H), 2.29−2.34 (m, 1 H), 2.09−2.12 ppm (m, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 190.5, 151.0, 143.4, 141.1, 133.7, 130.4 (2 CH), 129.8 (2 CH), 129.6 (2 CH), 128.9, 126.6 (2 CH), 107.4, 75.4, 38.7 (CH_2), 36.5, 12.1 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1672, 1638, 1165 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{19}H_{17}ClO_2SNa$ $[M + Na]^+$: 367.0536; found: 367.0522.

*4-(4-Bromo-phenyl)-6-phenyl-5,6-dihydro-4H-pyran-2-carbothioic Acid S-Methyl Ester (cis-**4g** and trans-**4g**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (2.5%); overall yield (*cis*:*trans*) = 0.063 g, 92%; isolated *cis* product yield = 0.047 g, 69%; isolated *trans* product yield = 0.007 g, 10%. *cis*-**4g**: colorless gum. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.30−7.45 (m, 7 H), 7.19 (d, *J* = 8.1 Hz, 2 H), 6.03 (s, 1 H), 5.16 (d, *J* = 11.1 Hz, 1 H), 3.83 (ddd, *J* = 2.4, 6.3, 11.0 Hz, 1 H), 2.40 (dd, *J* = 6.3, 13.8 Hz, 1 H), 2.35 (s, 3 H), 1.89 ppm (dt, *J* = 11.4, 13.8 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 189.5, 150.1, 141.9, 140.0, 131.9 (2 CH), 129.0 (2 CH), 128.6 (2 CH), 128.2, 125.8 (2 CH), 120.7, 108.4, 78.9, 39.8 (CH_2), 38.9, 11.0 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1661, 1628, 1160 cm^{-1}; HRMS (EI): *m/z* calcd for $C_{19}H_{17}BrO_2S$ $[M]^+$: 388.0133; found: 388.0140. *trans*-**4g**: yellow gum. ^1H NMR (600 MHz, $CDCl_3$): δ = 7.47−7.48 (m, 2 H), 7.35−7.38 (m, 2 H), 7.31−7.32 (m, 3 H), 7.12−7.14 (m, 2 H), 6.10 (dd, *J* = 0.6, 4.8 Hz, 1 H), 4.98 (dd, *J* = 2.4, 9.6 Hz, 1 H), 3.57−3.60 (m, 1 H), 2.38 (s, 3 H), 2.29−2.34 (m, 1 H), 2.10 ppm (dt, *J* = 2.4, 14.4 Hz, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 190.5, 151.1, 143.9, 141.0, 132.8 (2 CH), 130.8 (2 CH), 129.6 (2 CH), 128.9, 126.6 (2 CH), 121.8, 107.2, 75.4, 38.7 (CH_2), 36.6, 12.1 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1670, 1638, 1165 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{19}H_{17}BrO_2SNa$ $[M + Na]^+$: 411.0031; found: 411.0041.

*4-(3-Chloro-phenyl)-6-phenyl-5,6-dihydro-4H-pyran-2-carbothioic Acid S-Methyl Ester (cis-**4h** and trans-**4h**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (2.5%); overall yield (*cis*:*trans*) = 0.065 g, 91%; isolated *cis* product yield = 0.058 g, 81%; isolated *trans* product yield = 0.004 g, 5%. *cis*-**4h**: yellow gum. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.30−7.45 (m, 6 H), 7.22−7.27 (m, 2 H), 7.10−7.15 (m, 1 H), 6.05 (s, 1 H), 5.16 (d, *J* = 11.1 Hz, 1 H), 3.85 (ddd, *J* = 2.4, 6.3, 11.1 Hz, 1 H), 2.38−2.45 (m, 1 H), 2.35 (s, 3 H), 1.91 ppm (dt, *J* = 11.4, 13.8 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 189.5, 150.1, 144.9, 140.0, 134.6, 130.1, 128.6 (2 CH), 128.1, 127.5, 127.2, 125.8 (2 CH), 125.5, 108.1, 78.8, 39.7 (CH_2), 39.0, 11.0 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1672, 1636 cm^{-1}; HRMS (EI): *m/z* calcd for $C_{19}H_{17}ClO_2S$ $[M]^+$: 344.0638; found: 344.0639. *trans*-**4h**: yellow gum. ^1H NMR (600 MHz, $CDCl_3$): δ = 7.36−7.38 (m, 2 H), 7.32−7.34 (m, 2 H), 7.27−7.31 (m, 2 H), 7.24−7.26 (m, 2 H), 7.13−7.15 (m, 1 H), 6.10 (dd, *J* = 1.2, 4.8 Hz, 1 H), 5.00 (dd, *J* = 3.0, 9.6 Hz, 1 H), 3.59−3.61 (m, 1 H), 2.38 (s, 3 H), 2.30−2.35 (m, 1 H), 2.12−2.15 ppm (m, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 189.4, 150.1, 145.9, 140.0, 134.5, 129.9, 128.5 (2 CH), 128.2, 127.9, 127.1, 126.2, 125.5 (2 CH), 106.0, 74.3, 37.5 (CH_2), 35.8, 11.0 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1670, 1638, 1051 cm^{-1}; HRMS (EI): *m/z* calcd for $C_{19}H_{17}ClO_2S$ $[M]^+$: 344.0638; found: 344.0630.

*4-(2-Bromo-phenyl)-6-phenyl-5,6-dihydro-4H-pyran-2-carbothioic Acid S-Methyl Ester (cis-**4i**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (2%); overall yield (*cis*:*trans*) = 0.064 g, 94%; isolated *cis* product yield = 0.060 g, 88%; yellow gum. ^1H NMR (600 MHz, $CDCl_3$): δ = 7.55 (dd, *J* = 1.2, 8.4 Hz, 1 H), 7.45−7.46 (m, 2 H), 7.37−7.40 (m, 2 H), 7.31−7.34 (m, 1 H), 7.26−7.29 (m, 1 H), 7.24 (dd, *J* = 1.8, 7.2 Hz, 1 H), 7.10 (ddd, *J* = 1.8, 6.3, 8.7 Hz, 1 H), 6.08 (t, *J* = 2.4 Hz, 1 H), 5.20 (dd, *J* = 1.8, 11.4 Hz, 1 H), 4.33 (ddd, *J* = 2.4, 6.0, 11.1 Hz, 1 H), 2.60 (ddt, *J* = 1.8, 6.6, 13.8 Hz, 1 H), 2.36 (s, 3 H), 1.74 ppm (dt, *J* = 11.4, 13.8 Hz, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 189.4, 150.6, 142.0, 140.0, 132.9, 128.6, 128.6 (4 CH), 128.2, 128.1 (2 CH), 125.9, 108.5, 79.0, 38.6, 37.5 (CH_2), 11.1 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1668, 1635 cm^{-1}; HRMS (EI): *m/z* calcd for $C_{19}H_{17}BrO_2S$ $[M]^+$: 388.0133; found: 388.0140.

*4-(2,6-Dichloro-phenyl)-6-phenyl-5,6-dihydro-4H-pyran-2-carbothioic Acid S-Methyl Ester (cis-**4j**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (2%); overall yield (*cis*:*trans*) = 0.060 g, 87%; isolated *cis* product yield = 0.058 g, 84%; yellow gum. ^1H NMR (600 MHz, $CDCl_3$): δ = 7.49 (d, *J* = 7.2 Hz, 2 H), 7.40 (t, *J* = 7.2 Hz, 2 H), 7.32−7.34 (m, 2 H), 7.24−7.28 (m, 1 H), 7.12 (t, *J* = 7.8 Hz, 1 H), 6.10 (t, *J* = 1.8 Hz, 1 H), 5.19 (dd, *J* = 1.8, 11.4 Hz, 1 H), 4.76 (ddd, *J* = 3.0, 6.3, 11.2 Hz, 1 H), 2.39−2.46 (m, 1 H), 2.34 (s, 3 H), 2.22 ppm (ddt, *J* = 1.8, 6.6, 13.5 Hz, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 189.1, 149.3, 140.2, 136.7, 128.6, 128.5 (3 CH), 128.1, 125.9 (3 CH), 109.0, 78.9, 36.3, 33.0 (CH_2), 10.9 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1668, 1638 cm^{-1}; HRMS (EI): *m/z* calcd for $C_{19}H_{16}Cl_2O_2S$ $[M]^+$: 378.0248; found: 378.0247.

*4-(2,4-Dichloro-phenyl)-6-phenyl-5,6-dihydro-4H-pyran-2-carbothioic Acid S-Methyl Ester (cis-**4k**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (20%); overall yield (*cis*:*trans*) = 0.068 g, 98%; isolated *cis* product yield = 0.061 g, 88%; light yellow solid, mp 115 °C. ^1H NMR (600 MHz, $CDCl_3$): δ = 7.43−7.45 (m, 2 H), 7.38−7.40 (m, 3 H), 7.31−7.34 (m, 1 H), 7.17−7.22 (m, 2 H), 6.02 (t, *J* = 1.8 Hz, 1 H), 5.19 (dd, *J* = 1.2, 11.4 Hz, 1 H), 4.30 (ddd, *J* = 2.4, 6.6, 11.1 Hz, 1 H), 2.55 (ddt, *J* = 1.8, 6.6, 13.8 Hz, 1 H), 2.36 (s, 3 H), 1.72 ppm (dt, *J* = 11.4, 13.8 Hz, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 189.4, 150.8, 139.8, 138.9, 134.1, 133.2, 129.3, 129.0, 128.6 (2 CH), 128.2, 127.7, 125.8 (2 CH), 107.6, 78.9, 37.3 (CH_2), 35.4, 11.0 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1663, 1631, 1164 cm^{-1}; HRMS (EI): *m/z* calcd for $C_{19}H_{16}Cl_2O_2S$ $[M]^+$: 378.0248; found: 378.0248.

*4-(2-Chloro-6-fluoro-phenyl)-6-phenyl-5,6-dihydro-4H-pyran-2-carbothioic Acid S-Methyl Ester (cis-**4l**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (2%); overall yield (*cis*:*trans*) = 0.063 g, 90%; isolated *cis* product yield =

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0.058 g, 82%; light yellow solid, mp 94 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.48 (d, J = 7.2 Hz, 2 H), 7.30−7.42 (m, 3 H), 7.12−7.20 (m, 2 H), 6.92−7.00 (m, 1 H), 6.01 (s, 1 H), 5.17 (dd, J = 3.9, 9.6 Hz, 1 H), 4.45−4.53 (m, 1 H), 2.34 (s, 3 H), 2.23−2.40 ppm (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 189.2, 161.8 (d, J_{C-F} = 249.8 Hz, 1 C), 149.2, 140.1, 134.7 (d, J_{C-F} = 6.0 Hz, 1 C), 128.7 (d, J_{C-F} = 9.7 Hz, 1 C), 128.5 (2 CH), 128.0, 127.6 (d, J_{C-F} = 14.2 Hz, 1 C), 125.8 (2 CH), 125.7 (d, J_{C-F} = 3.7 Hz, 1 C), 114.9 (d, J_{C-F} = 22.5 Hz, 1 C), 108.3, 78.9, 34.5 (CH_2), 33.2, 10.9 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1659, 1632, 1604, 1449 cm^{-1}; HRMS (EI): m/z calcd for $C_{19}H_{16}ClFO_2S$ $[M]^+$: 362.0544; found: 362.0544.

*Benzoic Acid 4-(6-Methylsulfanylcarbonyl-2-phenyl-3,4-dihydro-2H-pyran-4-yl)-phenyl Ester (cis-**4m**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (8%); overall yield (*cis*:*trans*) = 0.059 g, 89%; isolated *cis* product yield = 0.047 g, 71%; yellow gum. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.19−8.20 (m, 2 H), 7.62−7.65 (m, 1 H), 7.50−7.52 (m, 2 H), 7.45−7.46 (m, 2 H), 7.39−7.41 (m, 2 H), 7.29−7.35 (m, 3 H), 7.16−7.18 (m, 2 H), 6.11 (t, J = 1.8 Hz, 1 H), 5.18 (dd, J = 1.8, 11.4 Hz, 1 H), 3.91 (ddd, J = 2.4, 6.0, 10.8 Hz, 1 H), 2.43−2.47 (m, 1 H), 2.35 (s, 3 H), 1.97 ppm (dt, J = 11.4, 13.8 Hz, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 189.5, 165.2, 150.0, 149.8, 140.5, 140.1, 133.6, 130.2 (2 CH), 129.5, 128.6 (4 CH), 128.3 (2 CH), 128.1, 125.8 (2 CH), 122.0 (2 CH), 108.9, 78.9, 39.9 (CH_2), 38.9, 11.0 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1736, 1672, 1636, 1504, 1266, 1207 cm^{-1}; HRMS (ESI): m/z calcd for $C_{26}H_{22}O_4SNa$ $[M + Na]^+$: 453.1137; found: 453.1115.

*4-(4-Nitro-phenyl)-6-phenyl-5,6-dihydro-4H-pyran-2-carbothioic Acid S-Methyl Ester (cis-**4n** and trans-**4n**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (10%); overall yield (*cis*:*trans*) = 0.067 g, 95%; isolated *cis* product yield = 0.055 g, 78%; isolated *trans* product yield = 0.005 g, 7%. *cis*-**4n**: yellow gum. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.17−8.19 (m, 2 H), 7.39−7.45 (m, 6 H), 7.32−7.35 (m, 1 H), 6.04 (t, J = 1.8 Hz, 1 H), 5.20 (dd, J = 1.8, 11.4 Hz, 1 H), 4.00 (ddd, J = 3.0, 6.3, 11.1 Hz, 1 H), 2.45 (ddt, J = 1.8, 6.0, 13.8 Hz, 1 H), 2.36 (s, 3 H), 1.92 ppm (dt, J = 11.4, 14.4 Hz, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 189.3, 150.5, 150.5, 147.0, 139.6, 128.7 (2 CH), 128.3, 128.2 (2 CH), 125.7 (2 CH), 124.1 (2 CH), 106.8, 78.7, 39.5 (CH_2), 39.2, 11.0 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1636, 1517, 1348 cm^{-1}; HRMS (ESI): m/z calcd for $C_{19}H_{17}NO_4SNa$ $[M + Na]^+$: 378.0776; found: 378.0810. *trans*-**4n**: yellow liquid. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.22 (d, J = 8.4 Hz, 2 H), 7.44 (d, J = 8.4 Hz, 2 H), 7.36−7.39 (m, 2 H), 7.31−7.33 (m, 3 H), 6.10 (d, J = 4.2 Hz, 1 H), 5.01 (dd, J = 2.4, 9.0 Hz, 1 H), 3.71−3.73 (m, 1 H), 2.36−2.42 (m, 1 H), 2.39 (s, 3 H), 2.13−2.17 ppm (m, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 190.4, 152.3, 151.4, 148.0, 140.6, 130.0 (2 CH), 129.7 (2 CH), 129.1, 126.5 (2 CH), 125.0 (2 CH), 106.0, 75.4, 38.3 (CH_2), 36.9, 12.1 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1671, 1639, 1519, 1347, 1166 cm^{-1}; HRMS (ESI): m/z calcd for $C_{19}H_{17}NO_4SNa$ $[M + Na]^+$: 378.0776; found: 378.0764.

*4-(4-Cyano-phenyl)-6-phenyl-5,6-dihydro-4H-pyran-2-carbothioic Acid S-Methyl Ester (cis-**4o** and trans-**4o**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (10%); overall yield (*cis*:*trans*) = 0.063 g, 87%; isolated *cis* product yield = 0.049 g, 68%; isolated *trans* product yield = 0.006 g, 8%. *cis*-**4o**: yellow gum. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.61 (d, J = 8.4 Hz, 2 H), 7.32−7.44 (m, 7 H), 6.02 (t, J = 1.8 Hz, 1 H), 5.18 (dd, J = 1.8, 11.4 Hz, 1 H), 3.94 (ddd, J = 2.4, 6.6, 11.4 Hz, 1 H), 2.43 (ddt, J = 1.8, 6.0, 13.8 Hz, 1 H), 2.35 (s, 3 H), 1.90 ppm (dt, J = 11.4, 13.8 Hz, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 189.4, 150.5, 148.4, 139.7, 132.6 (2 CH), 128.6 (2 CH), 128.3, 128.1 (2 CH), 125.7 (2 CH), 118.7, 111.0, 107.0, 78.7, 39.5 (CH_2), 39.4, 11.0 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 2227, 1607, 1669, 1636 cm^{-1}; HRMS (EI): m/z calcd for $C_{20}H_{17}NO_2S$ $[M]^+$: 335.0980; found: 335.0979. *trans*-**4o**: yellow gum. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.65 (d, J = 8.4 Hz, 2 H), 7.36−7.39 (m, 4 H), 7.31−7.33 (m, 3 H), 6.08 (d, J = 4.8 Hz, 1 H), 4.99 (dd, J = 3.0, 10.2 Hz, 1 H), 3.65−3.68 (m, 1 H), 2.38 (s, 3 H), 2.34−2.37 (m, 1 H), 2.11−2.14 ppm (m, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 190.3, 151.4, 150.3, 140.7, 133.5 (2 CH), 129.9 (2 CH), 129.6 (2 CH), 129.1, 126.5 (2 CH), 119.7, 111.9, 106.1, 75.4, 38.3 (CH_2), 37.1, 12.1 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1670, 1639, 1164 cm^{-1}; HRMS (EI): m/z calcd for $C_{20}H_{17}NO_2S$ $[M]^+$: 335.0980; found: 335.0969.

*4-(3-Cyano-phenyl)-6-phenyl-5,6-dihydro-4H-pyran-2-carbothioic Acid S-Methyl Ester (cis-**4p**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (10%); overall yield (*cis*:*trans*) = 0.070 g, 97%; isolated *cis* product yield = 0.062 g, 86%; yellow gum. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.33−7.56 (m, 9 H), 6.02 (s, 1 H), 5.19 (d, J = 11.1 Hz, 1 H), 3.92 (ddd, J = 2.1, 6.5, 11.0 Hz, 1 H), 2.43 (dd, J = 6.3, 13.8 Hz, 1 H), 2.36 (s, 3 H), 1.90 ppm (dt, J = 11.4, 13.8 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 189.3, 150.5, 144.4, 139.7, 131.8, 131.0, 130.8, 129.6, 128.6 (2 CH), 128.2, 125.7 (2 CH), 118.6, 112.9, 107.1, 78.7, 39.7 (CH_2), 38.9, 11.0 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 2229, 1670, 1636 cm^{-1}; HRMS (EI): m/z calcd for $C_{20}H_{17}NO_2S$ $[M]^+$: 335.0980; found: 335.0974.

*4-(2,4-Dinitro-phenyl)-6-phenyl-5,6-dihydro-4H-pyran-2-carbothioic Acid S-Methyl Ester (cis-**4q**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (10%); overall yield (*cis*:*trans*) = 0.035 g, 52%; isolated *cis* product yield = 0.026 g, 38%; yellow solid; mp 80 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.75 (d, J = 2.1 Hz, 1 H), 8.39 (dd, J = 2.1, 8.4 Hz, 1 H), 7.69 (d, J = 8.4 Hz, 1 H), 7.32−7.46 (m, 5 H), 5.96 (s, 1 H), 5.23 (dd, J = 1.2, 9.9 Hz, 1 H), 4.54 (ddd, J = 2.4, 6.4, 10.9 Hz, 1 H), 2.77 (dd, J = 6.3, 13.8 Hz, 1 H), 2.38 (s, 3 H), 1.85 ppm (dt, J = 10.8, 13.8 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 189.2, 151.4, 149.3, 146.7, 144.8, 139.1, 131.1, 128.7 (2 CH), 128.4, 127.5, 125.7 (2 CH), 120.2, 105.5, 78.8, 38.5 (CH_2), 35.0, 11.1 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1670, 1639, 1605, 1533, 1348 cm^{-1}; HRMS (EI): m/z calcd for $C_{19}H_{16}N_2O_6S$ $[M]^+$: 400.0729; found: 400.0727.

*4-(5-Nitro-furan-2-yl)-6-phenyl-5,6-dihydro-4H-pyran-2-carbothioic Acid S-Methyl Ester (cis-**4r**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (15%); overall yield (*cis*:*trans*) = 0.036 g, 50%; isolated *cis* product yield = 0.029 g, 40%; yellow gum. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.33−7.42 (m, 5 H), 7.24 (d, J = 3.6 Hz, 1 H), 6.34 (d, J = 3.6 Hz, 1 H), 6.04 (d, J = 1.5 Hz, 1 H), 5.18 (dd, J = 1.5, 10.8 Hz, 1 H), 4.04−4.10 (m, 1 H), 2.58−2.65 (m, 1 H), 2.36 (s, 3 H), 2.10 ppm (dt, J = 11.1, 13.5 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 189.1, 159.2, 150.5, 139.1, 128.6 (2 CH), 128.3, 125.6 (2 CH), 112.6, 108.8, 102.3, 78.0, 35.0 (CH_2), 32.8, 11.0 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1671, 1641, 1495, 1355 cm^{-1}; HRMS (EI): m/z calcd for $C_{17}H_{15}NO_5S$ $[M]^+$: 345.0671; found: 345.0673.

*4-Naphthalen-2-yl-6-phenyl-5,6-dihydro-4H-pyran-2-carbothioic Acid S-Methyl Ester (cis-**4s** and trans-**4s**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (3%); overall yield (*cis*:*trans*) = 0.063 g, 90%; isolated *cis* product yield = 0.050 g, 71%; isolated *trans* product yield = 0.006 g, 8%; *cis*-**4s**: yellow solid; mp 124 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.79−7.82 (m, 3 H), 7.69 (s, 1 H), 7.44−7.48 (m, 4 H), 7.39−7.41 (m, 2 H), 7.32−7.37 (m, 2 H), 6.21 (s, 1 H), 5.23 (d, J = 10.8 Hz, 1 H), 4.04 (ddd, J = 2.4, 6.0, 8.4 Hz, 1 H), 2.51 (dd, J = 6.0, 13.8 Hz, 1 H), 2.37 (s, 3 H), 2.04 ppm (dt, J = 11.4, 13.8 Hz, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 189.6, 150.0, 140.3, 140.2, 133.5, 132.5, 128.6 (2 CH), 128.5, 128.1, 127.6, 127.6, 126.2, 125.8 (2 CH), 125.7, 125.7, 125.6, 109.1, 79.0, 39.8 (CH_2), 39.5, 11.0 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1665, 1633 cm^{-1}; HRMS (EI): m/z calcd for $C_{23}H_{20}O_2S$ $[M]^+$: 360.1184; found: 360.1182. *trans*-**4s**: yellow liquid. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.82−7.85 (m, 3 H), 7.67 (s, 1 H), 7.47−7.51 (m, 2 H), 7.28−7.40 (m, 6 H), 6.27 (d, J = 5.4 Hz, 1 H), 5.05 (dd, J = 2.4, 9.6 Hz, 1 H), 3.80−3.82 (m, 1 H), 2.41 (s, 3 H), 2.35−2.40 (m, 1 H), 2.23−2.26 ppm (m, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 190.6, 151.1, 142.3, 141.3, 134.3, 133.4, 129.6, 129.5 (2 CH), 128.8, 128.8, 128.6, 127.9, 127.3, 127.3, 126.9, 126.6 (2 CH), 107.9, 75.4, 38.7 (CH_2), 37.3, 12.1 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1672, 1636, 1594 cm^{-1}; HRMS (ESI): m/z calcd for $C_{23}H_{20}O_2SNa$ $[M + Na]^+$: 383.1082; found: 383.1089.

*4-Phenyl-4,4a,5,9b-tetrahydro-indeno[1,2-b]pyran-2-carbothioic Acid S-Methyl Ester (**6a**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (2%); overall yield (*cis*:*trans*) = 0.068 g, 87%; isolated *cis* product yield = 0.063 g, 80%; yellow solid; mp 97 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.53−7.56 (m, 1 H), 7.21−7.39 (m, 7 H), 7.11−7.13 (m, 1 H), 6.17 (d, J = 1.8 Hz, 1 H), 5.34 (d, J = 4.8 Hz, 1 H), 4.18−4.21 (m, 1 H), 2.96−3.04

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(m, 1 H), 2.72 (dd, J = 10.8, 15.6 Hz, 1 H), 2.28 (s, 3 H), 2.21 ppm (dd, J = 7.2, 15.6 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 189.4, 151.1, 144.2, 141.6, 141.4, 129.3, 128.6 (2 CH), 127.8 (2 CH), 126.8, 126.7, 125.4, 125.0, 105.7, 81.4, 45.2, 38.3, 33.1 (CH_2), 11.0 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1662, 1636, 1166 cm^{-1}; HRMS (EI): m/z calcd for $C_{20}H_{18}O_2S$ $[M]^+$: 322.1027; found: 322.1025.

*4-p-Tolyl-4,4a,5,9b-tetrahydro-indeno[1,2-b]pyran-2-carbothioic Acid S-Methyl Ester (**6b**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (2%); overall yield (*cis*:*trans*) = 0.061 g, 80%; isolated *cis* product yield = 0.054 g, 71%; yellow solid; mp 144 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.52−7.55 (m, 1 H), 7.23−7.28 (m, 2 H), 7.10−7.21 (m, 5 H), 6.15 (d, J = 1.5 Hz, 1 H), 5.42 (d, J = 4.5 Hz, 1 H), 4.13−4.17 (m, 1 H), 2.96−3.01 (m, 1 H), 2.71 (dd, J = 10.5, 15.3 Hz, 1 H), 2.36 (s, 3 H), 2.28 (s, 3 H), 2.21 ppm (dd, J = 6.9, 15.6 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 189.4, 151.0, 144.2, 141.5, 138.5, 136.4, 129.3, 129.3 (2 CH), 127.7 (2 CH), 126.7, 125.5, 125.0, 106.1, 81.4, 45.3, 37.9, 33.2 (CH_2), 21.1, 11.0 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1663, 1637, 1166 cm^{-1}; HRMS (ESI): m/z calcd for $C_{21}H_{20}O_2SNa$ $[M + Na]^+$: 359.1082; found: 359.1113.

*4-(4-Bromo-phenyl)-4,4a,5,9b-tetrahydro-indeno[1,2-b]pyran-2-carbothioic Acid S-Methyl Ester (**6c**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (2%); overall yield (*cis*:*trans*) = 0.062 g, 88%; isolated *cis* product yield = 0.060 g, 86%; yellow solid; mp 135 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.47−7.55 (m, 3 H), 7.22−7.30 (m, 2 H), 7.12−7.15 (m, 3 H), 6.08 (d, J = 1.5 Hz, 1 H), 5.42 (d, J = 4.5 Hz, 1 H), 4.13−4.16 (m, 1 H), 2.93−3.02 (m, 1 H), 2.68 (dd, J = 10.5, 15.3 Hz, 1 H), 2.28 (s, 3 H), 2.22 ppm (dd, J = 7.2, 15.6 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 189.3, 151.3, 143.9, 141.2, 140.6, 131.7 (2 CH), 129.5 (2 CH), 129.4, 126.8, 125.4, 125.0, 120.7, 104.7, 81.3, 44.8, 37.8, 33.1 (CH_2), 11.0 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1659, 1636, 1482, 1164 cm^{-1}; HRMS (EI): m/z calcd for $C_{20}H_{17}BrO_2S$ $[M]^+$: 400.0133; found: 400.0130.

*4-(3-Chloro-phenyl)-4,4a,5,9b-tetrahydro-indeno[1,2-b]pyran-2-carbothioic Acid S-Methyl Ester (**6d**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (2%); overall yield (*cis*:*trans*) = 0.068 g, 92%; isolated *cis* product yield = 0.064 g, 86%; yellow solid; mp 112 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.52−7.55 (m, 1 H), 7.22−7.32 (m, 5 H), 7.14−7.16 (m, 2 H), 6.09 (d, J = 1.8 Hz, 1 H), 5.42 (d, J = 4.5 Hz, 1 H), 4.15−4.18 (m, 1 H), 2.94−3.04 (m, 1 H), 2.70 (dd, J = 10.5, 15.3 Hz, 1 H), 2.28 (s, 3 H), 2.24 ppm (dd, J = 7.2, 15.6 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 189.3, 151.3, 143.9, 143.7, 141.2, 134.5, 129.9, 129.4, 128.0, 127.1, 126.8, 126.0, 125.4, 125.0, 104.5, 81.4, 44.8, 38.1, 33.1 (CH_2), 11.0 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1666, 1642, 1175 cm^{-1}; HRMS (ESI): m/z calcd for $C_{20}H_{17}ClO_2SNa$ $[M + Na]^+$: 379.0536; found: 379.0562.

*4-(2,4-Dinitro-phenyl)-4,4a,5,9b-tetrahydro-indeno[1,2-b]pyran-2-carbothioic Acid S-Methyl Ester (**6e**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (10%); overall yield (*cis* only) = 0.051 g, 74%; yellow solid; mp 172 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.81 (d, J = 2.4 Hz, 1 H), 8.43 (dd, J = 2.4, 8.4 Hz, 1 H), 7.65 (d, J = 8.4 Hz, 1 H), 7.55−7.57 (m, 1 H), 7.28−7.30 (m, 2 H), 7.13 (d, J = 6.0 Hz, 1 H), 5.92 (d, J = 1.8 Hz, 1 H), 5.44 (d, J = 4.2 Hz, 1 H), 4.82 (dd, J = 3.0, 7.2 Hz, 1 H), 3.31−3.35 (m, 1 H), 2.72 (dd, J = 10.8, 15.0 Hz, 1 H), 2.31 (s, 3 H), 2.21 ppm (dd, J = 7.2, 15.0 Hz, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 190.3, 152.9, 150.5, 147.9, 144.4, 144.0, 141.6, 133.1, 130.8, 128.3, 128.1, 126.5, 126.0, 121.2, 103.8, 82.4, 43.0, 35.9, 34.0 (CH_2), 12.1 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1669, 1638, 1527, 1349 cm^{-1}; HRMS (EI): m/z calcd for $C_{20}H_{16}N_2O_6S$ $[M]^+$: 412.0729; found: 412.0728.

*4-Naphthalen-2-yl-4,4a,5,9b-tetrahydro-indeno[1,2-b]pyran-2-carbothioic Acid S-Methyl Ester (**6f**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (2%); overall yield (*cis*:*trans*) = 0.071 g, 98%; isolated *cis* product yield = 0.065 g, 90%; yellow gum. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.83−7.86 (m, 3 H), 7.70 (s, 1 H), 7.46−7.57 (m, 3 H), 7.41 (dd, J = 1.5, 8.7 Hz, 1 H), 7.23−7.26 (m, 2 H), 7.06−7.09 (m, 1 H), 6.29 (d, J = 1.8 Hz, 1 H), 5.48 (d, J = 4.5 Hz, 1 H), 4.34−4.37 (m, 1 H), 3.09−3.14 (m, 1 H), 2.75 (dd, J = 10.5, 15.6 Hz, 1 H), 2.31 (s, 3 H), 2.18 ppm (dd, J = 7.2, 15.6 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 189.6, 151.2, 144.1, 141.4, 139.1, 133.4, 132.4, 129.4, 128.3, 127.8, 127.6, 126.7, 126.4, 126.2, 125.9, 125.7, 125.4, 125.0, 105.5, 81.5, 45.1, 38.3, 33.2 (CH_2), 11.0 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1662, 1632 cm^{-1}; HRMS (EI): m/z calcd for $C_{24}H_{20}O_2S$ $[M]^+$: 372.1184; found: 372.1184.

*4-Phenyl-4a,5,6,10b-tetrahydro-4H-benzo[h]chromene-2-carbothioic Acid S-Methyl Ester (**6g**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (2%); overall yield (*cis*:*trans*) = 0.025 g, 30%; yellow gum. Inseparable mixture of two diastereomers: ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.42 (dd, J = 1.2, 7.8 Hz, 1 H), 7.36 (t, J = 7.2 Hz, 2 H), 7.28−7.30 (m, 2 H), 7.21−7.25 (m, 3 H), 7.12 (d, J = 7.8 Hz, 1 H), 6.14 (dd, J = 1.2, 2.4 Hz, 1 H), 5.13 (s, 1 H), 4.18 (dd, J = 1.8, 6.0 Hz, 1 H), 2.85 (dd, J = 5.4, 17.4 Hz, 1 H), 2.64 (ddd, J = 6.6, 12.0, 17.7 Hz, 1 H), 2.30 (s, 3 H), 2.25−2.28 (m, 1 H), 1.61 (ddd, J = 6.0, 13.2, 25.8 Hz, 1 H), 1.14−1.17 ppm (m, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 190.3, 150.3, 141.6, 138.5, 135.1, 131.9, 130.0 (2 CH), 129.5 (2 CH), 129.3 (2 CH), 127.8, 127.1, 108.2, 78.2, 43.0, 38.6, 30.0 (CH_2), 19.2 (CH_2), 11.9 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1671, 1638, 1162 cm^{-1}; HRMS (EI): m/z calcd for $C_{21}H_{20}O_2S$ $[M]^+$: 336.1184; found: 336.1183.

*2-Oxo-4-phenyl-6-p-tolyl-hex-5-ynethioic Acid S-Methyl Ester (**7a**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (1.5%); isolated yield = 0.024 g, 30%; yellow gum. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.45−7.47 (m, 2 H), 7.33−7.36 (m, 2 H), 7.30 (dt, J = 1.8, 8.4 Hz, 2 H), 7.27 (dt, J = 1.2, 7.2 Hz, 1 H), 7.09 (d, J = 7.8 Hz, 2 H), 4.45 (dd, J = 6.6, 8.4 Hz, 1 H), 3.46 (dd, J = 7.8, 16.2 Hz, 1 H), 3.30 (dd, J = 6.0, 16.8 Hz, 1 H), 2.33 (s, 3 H), 2.33 ppm (s, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 193.3, 192.5, 141.3, 139.2, 132.5 (2 CH), 129.9 (2 CH), 129.8 (2 CH), 128.5 (2 CH), 128.3, 121.0, 89.6, 85.1, 46.3 (CH_2), 34.2, 22.4, 12.3 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1722, 1670, 1504 cm^{-1}; HRMS (ESI): m/z calcd for $C_{20}H_{18}O_2SNa$ $[M + Na]^+$: 345.0925; found: 345.0909.

*4-(4-Bromo-phenyl)-2-oxo-6-p-tolyl-hex-5-ynethioic Acid S-Methyl Ester (**7b**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (1.5%); isolated yield = 0.02 g, 28%; yellow gum. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.46 (dt, J = 3.0, 8.4 Hz, 2 H), 7.34 (dt, J = 2.4, 9.0 Hz, 2 H), 7.28−7.29 (m, 2 H), 7.09−7.10 (m, 2 H), 4.41 (t, J = 7.2 Hz, 1 H), 3.42 (dd, J = 7.8, 16.8 Hz, 1 H), 3.29 (dd, J = 6.6, 17.4 Hz, 1 H), 2.33 ppm (s, 6 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 193.0, 192.4, 140.3, 139.4, 132.8 (2 CH), 132.5 (2 CH), 130.3 (2 CH), 130.0 (2 CH), 122.2, 120.7, 89.0, 85.4, 46.0 (CH_2), 33.7, 22.4, 12.3 ppm; IR (Neat): $\tilde{\nu}_{max}$ = 1723, 1670, 1486 cm^{-1}; HRMS (ESI): m/z calcd for $C_{20}H_{17}BrO_2SNa$ $[M + Na]^+$: 423.0031; found: 423.0048.

*4-Naphthalen-2-yl-2-oxo-6-p-tolyl-hex-5-ynethioic Acid S-Methyl Ester (**7c**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (14%); isolated yield = 0.01 g, 14%; yellow gum. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.90 (s, 1 H), 7.81−7.85 (m, 3 H), 7.58 (dd, J = 1.8, 8.4 Hz, 1 H), 7.45−7.50 (m, 2 H), 7.32 (d, J = 8.4 Hz, 2 H), 7.10 (d, J = 7.8 Hz, 2 H), 4.62 (dd, J = 6.6, 7.8 Hz, 1 H), 3.53 (dd, J = 8.4, 17.4 Hz, 1 H), 3.41 (dd, J = 6.6, 17.4 Hz, 1 H), 2.34 (s, 3 H), 2.32 ppm (s, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 193.3, 192.5, 139.2, 138.6, 134.4, 133.6, 132.6 (2 CH), 130.0 (2 CH), 129.6, 128.9, 128.6, 127.3, 127.2, 127.0, 126.5, 120.9, 89.6, 85.4, 46.1 (CH_2), 34.4, 22.4, 12.3 ppm; IR (Neat): $\tilde{\nu}_{max}$ = 1722, 1670, 1508 cm^{-1}; HRMS (ESI): m/z calcd for $C_{24}H_{20}O_2SNa$ $[M + Na]^+$: 395.1082; found: 395.1079.

*3-Bromo-2-methoxy-4-phenyl-2,3,4,4a,5,9b-hexahydro-indeno-[1,2-b]pyran-2-carbothioic Acid S-Methyl Ester (**8a** and **8a′**).* In a 25 mL flame-dried, two-neck, round-bottomed flask equipped with a magnetic stir bar, compound **6a** (0.05 g, 0.155 mmol, 1 equiv) was dissolved in dry THF (2 0.0 mL) under an Ar atmosphere and cooled to 0 °C. *N*-Bromosuccinimide (0.055 g, 0.310 mmol, 2 equiv) was added, followed by addition of dry MeOH (1.0 mL). After completion of the addition, the resulting reaction mixtures were stirred at room temperature for 40 min. After completion of the reaction (TLC), saturated NH_4Cl solution was added, and the product was extracted with EtOAc. The combined organic layers were dried over anhydrous Na_2SO_4 and filtered, and the filtrate was concentrated under reduced

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pressure to obtain a residue. The crude residue was purified by using silica gel column chromatography [230−400 mesh particle size; eluent: EtOAc/*n*-hexane (2−4%)] to obtain **8a** (0.030 g, 45%) as major diastereomer and **8a′** (0.012 g, 18%) as minor diastereomer.

8a: white solid; mp 180 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.53 (t, J = 7.8 Hz, 3 H), 7.39 (t, J = 7.2 Hz, 2 H), 7.28−7.36 (m, 4 H), 5.24 (d, J = 4.8 Hz, 1 H), 4.62 (d, J = 3.6 Hz, 1 H), 4.26−4.27 (m, 1 H), 4.09 (dd, J = 10.8, 15.6 Hz, 1 H), 3.54 (s, 3 H), 3.10 (dd, J = 8.4, 16.2 Hz, 1 H), 2.90−2.95 (m, 1 H), 2.29 ppm (s, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 199.8, 145.1, 140.2, 139.4, 129.3, 128.3 (2 CH), 128.3 (2 CH), 127.1, 126.7, 125.5, 125.2, 101.7, 78.0, 51.9, 51.3, 40.9, 39.2, 33.4 (CH_2), 11.2 ppm; IR (Neat): $\tilde{\nu}_{max}$ = 1681, 1054, 753 cm^{-1}; HRMS (ESI): m/z calcd for $C_{21}H_{21}BrO_3SNa$ $[M + Na]^+$: 455.0293; found: 455.0307.

8a′: white solid; mp 140 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.40 (t, J = 7.2 Hz, 3 H), 7.29−7.32 (m, 3 H), 7.25−7.27 (m, 1 H), 7.17−7.22 (m, 2 H), 5.47 (d, J = 4.2 Hz, 1 H), 4.69 (d, J = 12.0 Hz, 1 H), 4.51 (dd, J = 5.4, 12.6 Hz, 1 H), 3.41 (s, 3 H), 3.08 (dd, J = 10.8, 15.0 Hz, 1 H), 2.68−2.73 (m, 1 H), 2.37 (s, 3 H), 2.28−2.34 ppm (m, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 200.7, 144.7, 142.1, 141.2, 130.2, 129.6 (2 CH), 128.6, 128.2 (2 CH), 127.8, 126.7, 125.8, 100.1, 80.7, 50.6, 48.7, 47.6, 47.2, 32.5 (CH_2), 12.4 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1679, 1035, 933 cm^{-1}; HRMS (ESI): m/z calcd for $C_{21}H_{21}BrO_3SNa$ $[M + Na]^+$: 455.0293; found: 455.0305.

*3-Bromo-2-methoxy-4,6-diphenyl-tetrahydro-pyran-2-carbothioic Acid S-Methyl Ester (**8b** and **8b′**).* Prepared according to the procedure discussed above. After completion of the reaction, the residue was purified by using silica gel column chromatography [230−400 mesh particle size; eluent: EtOAc/*n*-hexane (2−4%)] to obtain **8b** (0.054 g, 80%) as major diastereomer and **8b′** (0.006 g, 9%) as minor diastereomer.

8b: white solid; mp 145 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.57 (d, J = 7.2 Hz, 2 H), 7.45 (t J = 7.2 Hz, 2 H), 7.21−7.39 (m, 6 H), 5.02 (dd, J = 2.7, 11.7 Hz, 1 H), 4.53 (d, J = 1.8 Hz, 1 H), 3.84−3.88 (m, 1 H), 3.40 (s, 3 H), 2.38−2.50 (m, 1 H), 2.36 (s, 3 H), 1.96−2.01 ppm (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 200.0, 141.1, 140.4, 128.6 (2 × CH), 128.3 (2 × CH), 127.9, 127.5 (2 × CH), 127.1, 125.8 (2 × CH), 101.4, 74.4, 56.2, 51.6, 39.7, 32.5 (CH_2), 11.3 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1684, 1153, 1049 cm^{-1}; HRMS (ESI): m/z calcd for $C_{20}H_{21}BrO_3SNa$ $[M + Na]^+$: 443.0293; found: 443.0298.

8b′: colorless gum. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.27−7.37 (m, 10 H), 5.33 (dd, J = 2.4, 11.4 Hz, 1 H), 4.32 (d, J = 12.0 Hz, 1 H), 4.14 (td, J = 3.6, 12.3 Hz, 1 H), 3.68 (s, 3 H), 2.32 (s, 3 H), 2.22−2.26 (m, 1 H), 1.92−1.98 ppm (m, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 200.8, 142.8, 141.7, 129.7 (2 × CH), 129.5 (2 × CH), 128.9, 128.4, 128.3 (2 × CH), 126.6 (2 × CH), 100.4, 76.6, 52.7, 50.8, 47.1, 44.1 (CH_2), 12.3 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1676 cm^{-1}; HRMS (ESI): m/z calcd for $C_{20}H_{21}BrO_3SNa$ $[M + Na]^+$: 443.0293; found: 443.0301.

*3-Bromo-6-(4-bromo-phenyl)-2-methoxy-4-phenyl-tetrahydro-pyran-2-carbothioic Acid S-Methyl Ester (**8c** and **8c′**).* Prepared according to the procedure discussed above. After completion of the reaction, the residue was purified by using silica gel column chromatography [230−400 mesh particle size; eluent: EtOAc/*n*-hexane (2−5%)] to obtain **8c** (0.042 g, 65%) as major diastereomer and **8c′** (0.007 g, 10%) as minor diastereomer.

8c: white solid; mp 160 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.57 (d, J = 8.4 Hz, 2 H), 7.44 (d, J = 8.4 Hz, 2 H), 7.29−7.35 (m, 3 H), 7.20−7.24 (m, 2 H), 4.97 (dd, J = 2.7, 11.7 Hz, 1 H), 4.51 (d, J = 2.4 Hz, 1 H), 3.82−3.86 (m, 1 H), 3.39 (s, 3 H), 2.36 (s, 3 H), 2.33−2.46 (m, 1 H), 1.93−1.97 ppm (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 199.7, 140.2, 140.1, 131.7 (2 CH), 128.4 (2 CH), 127.6 (2 CH), 127.5 (2 CH), 127.2, 121.8, 101.3, 73.8, 56.1, 51.7, 39.6, 32.4 (CH_2), 11.3 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1685, 1061 cm^{-1}; HRMS (ESI): m/z calcd for $C_{20}H_{20}Br_2O_3SNa$ $[M + Na]^+$: 520.9398; found: 520.9397.

8c′: white solid. mp 125 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.46 (d, J = 8.4 Hz, 2 H), 7.35 (t, J = 7.2 Hz, 2 H), 7.28 (d, J = 7.2 Hz, 1 H), 7.22−7.26 (m, 4 H), 5.31 (dd, J = 1.8, 11.4 Hz, 1 H), 4.29 (d, J = 11.4 Hz, 1 H), 4.11 (td, J = 4.2, 12.0 Hz, 1 H), 3.66 (s, 3 H), 2.32 (s, 3 H), 2.20−2.23 (m, 1 H), 1.86−1.92 ppm (m, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 200.8, 142.6, 140.7, 132.6 (2 CH), 129.8 (2 CH), 128.5, 128.3 (2 CH), 128.3 (2 CH), 122.7, 100.4, 75.9, 52.4, 50.9, 46.9, 43.9 (CH_2), 12.3 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1675, 1490 cm^{-1}; HRMS (ESI): m/z calcd for $C_{20}H_{20}Br_2O_3SNa$ $[M + Na]^+$: 520.9398; found: 520.9395.

General Procedure for the Synthesis of 9a−c. In a 25 mL flame-dried, two-neck, round-bottomed flask equipped with a magnetic stir bar, compound **8a**, **8b**, or **8c** (0.050 g, 1 equiv) was dissolved in dry DCM (2 0.0 mL) under an Ar atmosphere. The resulting reaction mixture was cooled to 0 °C, and DBU (2 equiv/mmol) was added dropwise. After completion of the addition, the solution was stirred at room temperature for 1−2 h. After completion of the reaction (TLC), saturated NH_4Cl solution was added, and the product was extracted with EtOAc. The combined organic layers were dried over anhydrous Na_2SO_4 and filtered, and the filtrate was concentrated under reduced pressure to obtain a residue. The crude residue was purified by using silica gel column chromatography [230−400 mesh particle size; eluent: EtOAc/*n*-hexane] to obtain **9a−c**.

*2-Methoxy-4-phenyl-2,4a,5,9b-tetrahydro-indeno[1,2-b]pyran-2-carbothioic Acid S-Methyl Ester (**9a**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (4%); isolated yield = 0.0385 g, 96%; colorless gum. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.56 (d, J = 7.2 Hz, 1 H), 7.49−7.50 (m, 2 H), 7.34−7.40 (m, 4 H), 7.32 (d, J = 7.2 Hz, 1 H), 7.29 (d, J = 7.8 Hz, 1 H), 6.12 (d, J = 0.6 Hz, 1 H), 5.28 (d, J = 4.8 Hz, 1 H), 3.46 (s, 3 H), 3.37 (dddd, J = 0.6, 4.2, 7.8, 9.6 Hz, 1 H), 3.21 (dd, J = 7.8, 15.6 Hz, 1 H), 3.02 (dd, J = 10.2, 15.6 Hz, 1 H), 2.22 ppm (s, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 201.3, 145.9, 143.5, 141.9, 139.0, 130.3, 129.7 (3 CH), 128.0, 127.1 (2 CH), 126.8, 125.9, 121.0, 101.7, 76.9, 52.2, 41.4, 37.5 (CH_2), 12.5 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1691, 1063, 889 cm^{-1}; HRMS (ESI): m/z calcd for $C_{21}H_{20}O_3SNa$ $[M + Na]^+$: 375.1031; found: 375.1060.

*2-Methoxy-4,6-diphenyl-5,6-dihydro-2H-pyran-2-carbothioic Acid S-Methyl Ester (**9b**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (3%); isolated yield = 0.034 g, 85%; white solid; mp 112 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.58 (d, J = 7.5 Hz, 2 H), 7.31−7.48 (m, 8 H), 6.17 (s, 1 H), 5.04−5.09 (m, 1 H), 3.34 (s, 3 H), 2.73−2.77 (m, 2 H), 2.32 ppm (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 200.6, 141.0, 140.9, 138.4, 128.6 (2 × CH), 128.6 (3 × CH), 128.0, 126.1 (2 × CH), 125.3 (2 × CH), 120.1, 100.9, 71.7, 51.1, 34.8 (CH_2), 11.7 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1678, 1066 cm^{-1}; HRMS (ESI): m/z calcd for $C_{20}H_{20}O_3SNa$ $[M + Na]^+$: 363.1031; found: 363.1039.

*6-(4-Bromo-phenyl)-2-methoxy-4-phenyl-5,6-dihydro-2H-pyran-2-carbothioic Acid S-Methyl Ester (**9c**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (4%); isolated yield = 0.034 g, 80%; colorless gum. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.56−7.58 (m, 2 H), 7.41−7.46 (m, 4 H), 7.31−7.36 (m, 3 H), 6.16 (t, J = 1.2 Hz, 1 H), 5.02 (t, J = 6.6 Hz, 1 H), 3.33 (s, 3 H), 2.70 (dd, J = 1.8, 7.8 Hz, 2 H), 2.32 ppm (s, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 201.2, 141.8, 141.0, 139.3, 132.8 (2 CH), 129.7, 129.6 (2 CH), 128.8 (2 CH), 126.3 (2 CH), 122.9, 121.1, 101.9, 72.2, 52.1, 35.7 (CH_2), 12.7 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1684, 1069 cm^{-1}; HRMS (ESI): m/z calcd for $C_{20}H_{19}BrO_3SNa$ $[M + Na]^+$: 441.0136; found: 441.0138.

*4-Phenyl-6-p-tolyl-5,6-dihydro-4H-pyran-2-carboxylic Acid Methyl Ester (cis-**3aa**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (5%); overall yield (*cis*:*trans*) = 0.073 g, 90%; isolated *cis*-**3aa** product yield = 0.049 g, 60%; colorless gum. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.23−7.35 (m, 7 H), 7.16 (d, J = 7.8 H, 2 H), 6.22 (s, 1 H), 5.06 (d, J = 10.8 Hz, 1 H), 3.83−3.90 (m, 1 H), 3.81 (s, 3 H), 2.36−2.39 (m, 1 H), 2.34 (s, 3 H), 1.94−2.03 ppm (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.5, 145.1, 143.1, 137.9, 137.2, 129.3 (2 CH), 128.8 (2 CH), 127.2 (2 CH), 126.9, 126.2 (2 CH), 114.4, 78.8, 52.3, 39.6, 39.4 (CH_2), 21.2 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1733, 1292, 1253 cm^{-1}; HRMS (ESI): m/z calcd for $C_{20}H_{20}O_3Na$ $[M + Na]^+$: 331.1310; found: 331.1312.

*6-Naphthalen-2-yl-4-phenyl-5,6-dihydro-4H-pyran-2-carboxylic Acid Methyl Ester (cis-**3ha**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (7%); overall yield (*cis*:*trans*) = 0.066 g, 73%; isolated *cis*-**3ha** product yield = 0.049

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g, 54%; yellow gum. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.81−7.90 (m, 4 H), 7.46−7.60 (m, 4 H), 7.22−7.45 (m, 4 H), 6.28 (s, 1 H), 5.27 (d, J = 10.5 Hz, 1 H), 3.87−3.96 (m, 1 H), 3.84 (s, 3 H), 2.47 (dd, J = 6.3, 13.8 Hz, 1 H), 2.00−2.12 ppm (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.4, 145.1, 143.0, 137.6, 133.2, 133.2, 128.8 (2 CH), 128.3, 128.0, 127.6, 127.2 (2 CH), 127.0, 126.2, 126.0, 125.2, 124.1, 114.5, 79.0, 52.3, 39.6, 39.5 (CH_2) ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1730, 1644, 1292, 1253, 1044 cm^{-1}; HRMS (ESI): m/z calcd for $C_{23}H_{20}O_3Na$ [M + Na]$^+$: 367.1310; found: 367.1305.

*4-(3-Chloro-phenyl)-4,4a,5,9b-tetrahydro-indeno[1,2-b]pyran-2-carboxylic Acid Methyl Ester (cis-**6da**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (8%); overall yield (*cis*:*trans*) = 0.067 g, 88%; isolated *cis*-**6da** product yield = 0.055 g, 72%; yellow gum. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.54−7.57 (m, 1 H), 7.20−7.33 (m, 5 H), 7.12−7.17 (m, 2 H), 6.20−6.22 (m, 1 H), 5.38 (d, J = 4.2 Hz, 1 H), 4.18−4.21 (m, 1 H), 3.79 (s, 3 H), 2.90−2.97 (m, 1 H), 2.66−2.75 (m, 1 H), 2.22 ppm (dd, J = 6.9, 15.3 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.1, 146.2, 143.9, 143.8, 141.3, 134.4, 129.8, 129.4, 127.8, 127.0, 126.8, 126.0, 125.5, 125.0, 109.0, 80.8, 52.3, 44.5, 38.1, 32.8 (CH_2) ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1731, 1651, 1243, 1098 cm^{-1}; HRMS (ESI): m/z calcd for $C_{20}H_{17}ClO_3Na$ [M + Na]$^+$: 363.0764; found: 363.0764.

General Procedure for the Synthesis of 10a−e. A mixture of *cis*-**3k**, *cis*-**4f**, *cis*-**4l**, *cis*-**3j**, or *cis*-**3aa** (0.05 g, 1 equiv) and the appropriate amine (neat; 0.2 mL) was stirred at ambient temperature. After completion of the reaction (TLC), satd NH_4Cl solution was added, and the mixture was extracted with EtOAc. The combined organic layers were dried over anhydrous Na_2SO_4 and filtered, and the filtrate was concentrated under reduced pressure to get a residue. The residue was purified over silica gel column chromatography [230−400 mesh particle size; eluent: ethyl acetate/*n*-hexane] to afford **10a−e**.

*6-Methyl-4,6-diphenyl-5,6-dihydro-4H-pyran-2-carboxylic Acid Benzylamide (**10a**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (15%); isolated yield = 0.054 g, 91%; white solid; mp 168 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.17−7.42 (m, 15 H), 7.01−7.03 (m, 1 H), 6.29 (s, 1 H), 4.59 (d, J = 6.0 Hz, 2 H), 3.67−3.74 (m, 1 H), 2.19−2.26 (m, 1 H), 1.83−1.92 (m, 1 H), 1.70 ppm (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.5, 145.7, 144.4, 143.0, 138.2, 128.7 (2 CH), 128.5 (2 CH), 128.3 (2 CH), 127.7 (2 CH), 127.5 (2 CH), 127.4, 127.3, 126.6, 124.3 (2 CH), 108.4, 79.6, 44.0 (CH_2), 43.1 (CH_2), 36.6, 23.3 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1648, 1516 cm^{-1}; HRMS (ESI): m/z calcd for $C_{26}H_{25}NO_2Na$ [M + Na]$^+$: 406.1783; found: 406.1791.

*4-(4-Chloro-phenyl)-6-phenyl-5,6-dihydro-4H-pyran-2-carboxylic Acid Benzylamide (**10b**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (15%); isolated yield = 0.055 g, 95%; white solid; mp 160 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.36−7.39 (m, 4 H), 7.30−7.34 (m, 5 H), 7.26−7.28 (m, 3 H), 7.18−7.20 (m, 2 H), 6.92 (br. s., 1 H), 6.22 (s, 1 H), 5.06 (d, J = 11.4 Hz, 1 H), 4.49−4.58 (m, 2 H), 3.83−3.86 (m, 1 H), 2.30−2.33 (m, 1 H), 1.88−1.94 ppm (m, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 162.9, 147.9, 142.7, 141.1, 139.1, 133.5, 129.8 (2 CH), 129.7 (4 CH), 129.6 (2 CH), 129.5, 128.9 (2 CH), 128.5, 127.2 (2 CH), 110.4, 80.3, 44.2 (CH_2), 40.8 (CH_2), 39.7 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1649, 1518, 1454 cm^{-1}; HRMS (ESI): m/z calcd for $C_{25}H_{22}ClNO_2Na$ [M + Na]$^+$: 426.1237; found: 426.1245.

*4-(2-Chloro-6-fluoro-phenyl)-6-phenyl-5,6-dihydro-4H-pyran-2-carboxylic Acid Benzylamide (**10c**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (15%); isolated yield = 0.054 g, 93%; white solid; mp 142 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.11−7.42 (m, 12 H), 6.89−6.99 (m, 2 H), 6.20 (d, J = 1.2 Hz, 1 H), 5.07 (dd, J = 2.1, 11.1 Hz, 1 H), 4.44−4.63 (m, 3 H), 2.25−2.33 (m, 1 H), 2.16−2.23 ppm (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.0, 145.9, 140.2, 138.2, 134.7 (d, J_{C-F} = 6.7 Hz, 1 C), 128.6, 128.5, 128.4, 127.9, 127.4, 126.3, 125.6, 114.9 (d, J_{C-F} = 22.5 Hz, 1 C), 109.2, 79.3, 43.1 (CH_2), 34.4 (CH_2), 33.3 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1652, 1517, 1453 cm^{-1}; HRMS (EI): m/z calcd for $C_{25}H_{21}ClFNO_2$ [M]$^+$: 421.1245; found: 421.1236.

*Morpholin-4-yl-(4,6,6-triphenyl-5,6-dihydro-4H-pyran-2-yl)-methanone (**10d**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (25%); isolated yield = 0.048 g, 88%; yellow gum. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.19−7.56 (m, 15 H), 5.33 (s, 1 H), 3.72 (br. s., 8 H), 3.33−3.38 (m, 1 H), 3.09 (dd, J = 6.0, 13.8 Hz, 1 H), 2.26−2.35 ppm (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.8, 146.6, 144.9, 143.3, 142.9, 128.7 (4 CH), 128.3 (2 CH), 127.5 (2 CH), 127.3 (2 CH), 126.9, 125.6 (2 CH), 125.5 (2 CH), 108.1, 83.2, 66.9 (4 CH_2), 41.1 (CH_2), 36.2 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1637, 1446, 1280, 1114, 1026, 753, 700 cm^{-1}; HRMS (ESI): m/z calcd for $C_{28}H_{27}NO_3Na$ [M + Na]$^+$: 448.1889; found: 448.1888.

*4-Phenyl-6-p-tolyl-5,6-dihydro-4H-pyran-2-carboxylic Acid Benzylamide (**10e**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (16%); isolated yield = 0.025 g, 40%; colorless gum. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.15−7.37 (m, 14 H), 6.90−6.92 (m, 1 H), 6.26 (d, J = 1.5 Hz, 1 H), 5.03 (dd, J = 1.2, 10.2 Hz, 1 H), 4.45−4.59 (m, 2 H), 3.82−3.89 (m, 1 H), 2.35 (s, 3 H), 2.28−2.37 (m, 1 H), 1.91−2.03 ppm (m, 1 H) ; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.1, 146.7, 143.3, 138.3, 138.2, 137.3, 129.3 (2 CH), 128.6 (3 CH), 127.9 (2 CH), 127.4, 127.2 (2 CH), 126.8, 126.3 (2 CH), 120.7, 110.0, 79.2, 43.1 (CH_2), 39.7 (CH_2), 39.3, 21.2 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1677, 1649, 1518 cm^{-1}; HRMS (EI): m/z calcd for $C_{26}H_{25}NO_2$ [M]$^+$: 383.1885; found: 383.1884.

General Procedure for the Synthesis of 11a−b. *cis*-**3a** or *cis*-**4s** (0.05 g, 1 equiv) was dissolved in THF (2 mL) and was added to a stirred solution of EtZnI (3 equiv; prepared according to the literature procedure)[15] under an argon atmosphere at 40 °C. $PdCl_2(PPh_3)_2$ (10 mol %) was added into the reaction mixtures and stirred at that temperature for 5−10 min. After completion of the reaction (TLC), the mixtures were filtered through a Celite pad, saturated NH_4Cl solution was added to the filtrate portion, and the product was extracted with EtOAc. The combined organic layers were dried over anhydrous Na_2SO_4 and filtered, and the filtrate was concentrated under reduced pressure to obtain a residue. The residue was purified by using silica gel column chromatography [230−400 mesh particle size; eluent: EtOAc/*n*-hexane (4%)] to obtain **11a** or **11b**.

*1-(4-Phenyl-6-p-tolyl-5,6-dihydro-4H-pyran-2-yl)-propan-1-one (**11a**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (4%); isolated yield = 0.03 g, 64%; yellow gum. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.30−7.33 (m, 4 H), 7.23−7.26 (m, 3 H), 7.19 (d, J = 7.2 Hz, 2 H), 6.09 (t, J = 2.4 Hz, 1 H), 5.06 (dd, J = 1.2, 11.4 Hz, 1 H), 3.86 (ddd, J = 2.4, 6.6, 11.3 Hz, 1 H), 2.74 (q, J = 7.2, 14.4 Hz, 2 H), 2.36 (s, 3 H), 2.34−2.38 (m, 1 H), 1.88−1.95 (m, 1 H), 1.11 ppm (t, J = 7.8 Hz, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 199.0, 152.6, 144.3, 138.8, 138.7, 130.2 (2 CH), 129.7 (2 CH), 128.2 (2 CH), 127.9, 126.9 (2 CH), 111.7, 79.3, 40.6 (CH_2), 40.5, 32.3 (CH_2), 22.2, 8.7 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1700, 1629, 1042 cm^{-1}; HRMS (ESI): m/z calcd for $C_{21}H_{22}O_2Na$ [M + Na]$^+$: 329.1518; found: 329.1514.

*1-(4-Naphthalen-2-yl-6-phenyl-5,6-dihydro-4H-pyran-2-yl)-propan-1-one (**11b**).* Prepared according to the general procedure discussed above: eluent, EtOAc/*n*-hexane (4%); isolated yield = 0.04 g, 85%; yellow gum. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.78−7.82 (m, 3 H), 7.68 (m, 1 H), 7.43−7.48 (m, 4 H), 7.38−7.41 (m, 2 H), 7.31−7.36 (m, 2 H), 6.20 (t, J = 1.8 Hz, 1 H), 5.15 (dd, J = 1.8, 11.4 Hz, 1 H), 4.04 (ddd, J = 3.0, 6.6, 11.3 Hz, 1 H), 2.78 (q, J = 7.2, 15.0 Hz, 2 H), 2.47 (ddt, J = 1.8, 6.0, 13.8 Hz, 1 H), 1.97−2.04 (m, 1 H), 1.14 ppm (t, J = 7.2 Hz, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 198.9, 152.6, 141.7, 141.6, 134.6, 133.5, 129.6 (2 CH), 129.5, 129.1, 128.6, 128.6, 127.2, 126.9 (2 CH), 126.7, 126.7, 126.5, 111.7, 79.4, 40.6 (CH_2), 40.6, 32.4 (CH_2), 8.7 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1699, 1629, 1048 cm^{-1}; HRMS (ESI): m/z calcd for $C_{24}H_{22}O_2Na$ [M + Na]$^+$: 365.1518; found: 365.1521.

■ ASSOCIATED CONTENT

Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra for all new compounds; ORTEP diagrams of **4k**, **6c**, **8a**, *ent*-**8a**, **8a′**, **8b**, **8c**, and **10a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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AUTHOR INFORMATION

Corresponding Author

*E-mail: id@csiriicb.in. Fax: (+91) 33 2473 5197 (I.D.).

Notes

The authors declare no competing financial interest.

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REFERENCES

(1) For selected references, see: (a) De Rosa, S.; De Stefano, S.; Zavodnik, N. *J. Org. Chem.* **1988**, *53*, 5020−5023. (b) Tezuka, Y.; Gewali, M. B.; Ali, M. S.; Banskota, A. H.; Kadota, S. *J. Nat. Prod.* **2001**, *64*, 208−213. (c) Kinoshita, K.; Khosla, C.; Cane, D. E. *Helv. Chim. Acta* **2003**, *86*, 3889−3907. (d) Ruijter, E.; Schültingkemper, H.; Wessjohann, L. A. *J. Org. Chem.* **2005**, *70*, 2820−2823. (e) Gunatilaka, A. A. L. *J. Nat. Prod.* **2006**, *69*, 509−526. (f) Li, P.-L.; Wang, C.-M.; Zhang, Z.-X.; Jia, Z.-J. *Tetrahedron* **2007**, *63*, 12665−12670. (g) Laurent, M. Y.; Stocker, V.; Temgoua, V. M.; Dujardin, G.; Dhal, R. *Tetrahedron Lett.* **2011**, *52*, 1608−1611.

(2) For selected references, see: (a) Boger, D. L.; Robarge, K. D. *J. Org. Chem.* **1988**, *53*, 5793−5796. (b) Bednarski, M. D.; Lyssikatos, J. P. In *Comprehensive Organic Synthesis*; Trost, B. M., Heathcock, C. H., Eds.; Pergamon Press: New York, 1991; Vol. *2*, pp 661−706. (c) Mack, D. J.; Guo, B.; Njardarson, J. T. *Chem. Commun.* **2012**, *48*, 7844−7846. (d) Sultana, S.; Indukuri, K.; Deka, M. J.; Saikia, A. K. *J. Org. Chem.* **2013**, *78*, 12182−12188.

(3) For selected references, see: (a) Desimoni, G.; Tacconi, G. *Chem. Rev.* **1975**, *75*, 651−692. (b) Beracierta, A. P.; Whiting, D. A. *J. Chem. Soc., Perkin Trans. 1* **1978**, 1257−1263. (c) Apparao, S.; Maier, M. E.; Schmidt, R. R. *Synthesis* **1987**, 900−904. (d) Brown, E.; Dujardin, G.; Maudet, M. *Tetrahedron* **1997**, *53*, 9679−9694. (e) Tietze, L. F.; Kettschau, G. In *Topics in Current Chemistry*; Metz, P., Ed.; Springer-Verlag: Berlin, 1997; Vol. *189*, pp 1−120. (f) Dujardin, G.; Rossignol, S.; Brown, E. *Synthesis* **1998**, 763−770. (g) Audrain, H.; Thorhauge, J.; Hazell, R. G.; Jørgensen, K. A. *J. Org. Chem.* **2000**, *65*, 4487−4497.

(4) For selected references, see: (a) Boger, D. L.; Weinreb, S. M. In *Hetero Diels-Alder Methodology in Organic Synthesis*; Wasserman, H. H., Ed.; Academic Press: San Diego, CA, 1987; Vol. *47*. (b) Boivin, T. L. B. *Tetrahedron* **1987**, *43*, 3309−3362. (c) Yang, W.; Shang, D.; Liu, Y.; Du, Y.; Feng, X. *J. Org. Chem.* **2005**, *70*, 8533−8537. (d) Clarke, P. A.; Santos, S. *Eur. J. Org. Chem.* **2006**, 2045−2053. (e) Larrosa, I.; Romea, P.; Urpí, F. *Tetrahedron* **2008**, *64*, 2683−2723. (f) Franke, P. T.; Richter, B.; Jørgensen, K. A. *Chem.—Eur. J.* **2008**, *14*, 6317−6321. (g) Smith, A. B., III; Dong, S.; Fox, R. J.; Brenneman, J. B.; Vanecko, J. A.; Maegawa, T. *Tetrahedron* **2011**, *67*, 9809−9828. (h) Hanessian, S.; Focken, T.; Oza, R. *Tetrahedron* **2011**, *67*, 9870−9884. (i) Giguère, D.; Martel, J.; Shiao, T. C.; Roy, R. *J. Org. Chem.* **2011**, *76*, 9687−9698. (j) Liu, Y.; Liu, X.; Wang, M.; He, P.; Lin, L.; Feng, X. *J. Org. Chem.* **2012**, *77*, 4136−4142. (k) Yadav, J. S.; Reddy, G. M.; Anjum, S. R.; Reddy, B. V. S. *Eur. J. Org. Chem.* **2014**, 4389−4397. (l) Zeng, J.; Tan, Y. J.; Ma, J.; Leow, M. L.; Tirtorahardjo, D.; Liu, X.-W. *Chem.—Eur. J.* **2014**, *20*, 405−409.

(5) For selected references, see: (a) Gu, J.; Ma, C.; Li, Q.-Z.; Du, W.; Chen, Y.-C. *Org. Lett.* **2014**, *16*, 3986−3989. (b) Yang, L.; Wang, F.; Lee, R.; Lv, Y.; Huang, K.-W.; Zhong, G. *Org. Lett.* **2014**, *16*, 3872−3875. (c) Weise, C. F.; Lauridsen, V. H.; Rambo, R. S.; Iversen, E. H.; Olsen, M.-L.; Jørgensen, K. A. *J. Org. Chem.* **2014**, *79*, 3537−3546. (d) Jiang, X.; Wang, R. *Chem. Rev.* **2013**, *113*, 5515−5546. (e) Desimoni, G.; Faita, G.; Quadrelli, P. *Chem. Rev.* **2013**, *113*, 5924−5988. (f) Sinha, D.; Perera, S.; Zhao, J. C.-G. *Chem.—Eur. J.* **2013**, *19*, 6976−6979. (g) Li, J.-L.; Liu, T.-Y.; Chen, Y.-C. *Acc. Chem. Res.* **2012**, *45*, 1491−1500. (h) Fujiwara, K.; Kurahashi, T.; Matsubara, S. *J. Am. Chem. Soc.* **2012**, *134*, 5512−5515. (i) Dong, S.; Liu, X.; Chen, X.; Mei, F.; Zhang, Y.; Gao, B.; Lin, L.; Feng, X. *J. Am. Chem. Soc.* **2010**, *132*, 10650−10651. (j) Barroso, S.; Blay, G.; Muñoz, M. C.; Pedro, J. R. *Adv. Synth. Catal.* **2009**, *351*, 107−111. (k) Lin, L.; Liu, X.; Feng, X. *Synlett* **2007**, 2147−2157. (l) Gouverneur, V.; Reiter, M. *Chem.—Eur. J.* **2005**, *11*, 5806−5815. (m) Iwakura, I.; Ikeno, T.; Yamada, T. *Angew. Chem., Int. Ed.* **2005**, *44*, 2524−2527. (n) Jørgensen, K. A. In *Cycloaddition Reactions in Organic Synthesis*; Kobayashi, S., Jørgensen, K. A., Eds.; Wiley-VCH: Weinheim, Germany, 2002; p 151. (o) Tietze, L. F.; Saling, P. *Synlett* **1992**, 281−282.

(6) For selected references, see: (a) Kagan, H. B.; Riant, O. *Chem. Rev.* **1992**, *92*, 1007−1019. (b) Tietze, L. F.; Schneider, C.; Grote, A. *Chem.—Eur. J.* **1996**, *2*, 139−148. (c) Thorhauge, J.; Johannsen, M.; Jørgensen, K. A. *Angew. Chem., Int. Ed.* **1998**, *37*, 2404−2406. (d) Evans, D. A.; Johnson, J. S.; Olhava, E. J. *J. Am. Chem. Soc.* **2000**, *122*, 1635−1649. (e) Jørgensen, K. A. *Angew. Chem., Int. Ed.* **2000**, *39*, 3558−3588. (f) Gademann, K.; Chavez, D. E.; Jacobsen, E. N. *Angew. Chem., Int. Ed.* **2002**, *41*, 3059−3061. (g) Jørgensen, K. A. *Eur. J. Org. Chem.* **2004**, 2093−2102. (h) Reymond, S.; Cossy, J. *Chem. Rev.* **2008**, *108*, 5359−5406. (i) Pellissier, H. *Tetrahedron* **2009**, *65*, 2839−2877. (j) Zhu, Y.; Xie, M.; Dong, S.; Zhao, X.; Lin, L.; Liu, X.; Feng, X. *Chem.—Eur. J.* **2011**, *17*, 8202−8208. (k) Xu, Z.; Liu, L.; Wheeler, K.; Wang, H. *Angew. Chem., Int. Ed.* **2011**, *50*, 3484−3488. (l) Xu, Z.; Wang, H. *Synlett* **2011**, 2907−2912. (m) Erdmann, N.; Atodiresei, I.; Enders, D. *Synthesis* **2012**, *44*, 2107−2113. (n) Gao, S.; Chen, J.-R.; Hu, X.-Q.; Cheng, H.-G.; Lu, L.-Q.; Xiao, W.-J. *Adv. Synth. Catal.* **2013**, *355*, 3539−3544. (o) Hu, Y.; Xu, K.; Zhang, S.; Guo, F.; Zha, Z.; Wang, Z. *Org. Lett.* **2014**, *16*, 3564−3567. (p) Viglianisi, C.; Sinni, A.; Menichetti, S. *Heteroat. Chem.* **2014**, *25*, 361−366. (q) Matsuo, K.; Ohta, M.; Hasuike, Y.; Ueno, S.; Tateishi, Y.; Arase, T.; Tanaka, K. *Chem. Express* **1993**, *8*, 293−296.

(7) (a) Smith, C. W.; Norton, D. G.; Ballard, S. A. *J. Am. Chem. Soc.* **1951**, *73*, 5273−5280. (b) Fehr, C.; Galindo, J.; Ohloff, G. *Helv. Chim. Acta* **1981**, *64*, 1247−1256. (c) Dvořák, D.; Arnold, Z. *Tetrahedron Lett.* **1982**, *23*, 4401−4402. (d) Schmidt, R. R.; Frick, W.; Haag-Zeino, B.; Apparao, S. *Tetrahedron Lett.* **1987**, *28*, 4045−4048. (e) Sera, A.; Ohara, M.; Yamada, H.; Egashira, E.; Ueda, N.; Setsune, J.-i. *Chem. Lett.* **1990**, 2043−2046. (f) Dujardin, C.; Maudet, M.; Brown, E. *Tetrahedron Lett.* **1994**, *35*, 8619−8622. (g) Wijnen, J. W.; Zavarise, S.; Engberts, J. B. F. N. *J. Org. Chem.* **1996**, *61*, 2001−2005. (h) Brown, E.; Dujardin, G.; Maudet, M. *Tetrahedron* **1997**, *53*, 9679−9694. (i) Leconte, S.; Dujardin, G.; Brown, E. *Eur. J. Org. Chem.* **2000**, 639−643. (j) Maingot, L.; Leconte, S.; Chataigner, I.; Martel, A.; Dujardin, G. *Org. Lett.* **2009**, *11*, 1619−1622.

(8) (a) Lv, J.; Zhang, L.; Hu, S.; Cheng, J.-P.; Luo, S. *Chem.—Eur. J.* **2012**, *18*, 799−803. (b) Lv, J.; Zhang, L.; Luo, S.; Cheng, J.-P. *Angew. Chem., Int. Ed.* **2013**, *52*, 9786−9790. (c) Matsumura, Y.; Suzuki, T.; Sakakura, A.; Ishihara, K. *Angew. Chem., Int. Ed.* **2014**, *53*, 6131−6134.

(9) (a) Zhou, G.; Lim, D.; Coltart, D. M. *Org. Lett.* **2008**, *10*, 3809−3812. (b) For the synthesis of γ-substituted β,γ-unsaturated α-ketomethylthioesters, see: Mal, K.; Sharma, A.; Maulik, P. R.; Das, I. *Chem.—Eur. J.* **2014**, *20*, 662−667.

(10) The reaction did not work with highly electron-rich styrenes, such as 4-methoxystyrene and 2,4,6-trimethylstyrene, due to the tendency of oligomerization of these olefins under the reaction conditions, or with highly electron-deficient styrene, such as 4-nitrostyrene, due to the lack of sufficient electron density on olefins.

(11) CCDC 1019429 (**4k**), 1019430 (**6c**), 1019431 (**8a**), 1019433 (*ent*-**8a**), 1019432 (**8a′**), 1043255 (**8b**), 1043257 (**8c**), and 1043254 (**10a**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. See also the Supporting Information.

(12) Other unidentified minor products were also isolated in all cases.

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(13) For selected references, see: (a) Sanz-Marco, A.; García-Ortiz, A.; Blay, G.; Pedro, J. R. *Chem. Commun.* **2014**, *50*, 2275−2278. (b) Sanz-Marco, A.; García-Ortiz, A.; Blay, G.; Fernández, I.; Pedro, J. R. *Chem.—Eur. J.* **2014**, *20*, 668−672. (c) Chinchilla, R.; Nájera, C. *Chem. Rev.* **2014**, *114*, 1783−1826. (d) Blay, G.; Muñoz, M. C.; Pedro, J. R.; Sanz-Marco, A. *Adv. Synth. Catal.* **2013**, *355*, 1071−1076. (e) Blay, G.; Cardona, L.; Pedro, J. R.; Sanz-Marco, A. *Chem.—Eur. J.* **2012**, *18*, 12966−12969. (f) Yazaki, R.; Kumagai, N.; Shibasaki, M. *Chem.—Asian J.* **2011**, *6*, 1778−1790.

(14) (a) Boschi, A.; Chiappe, C.; De Rubertis, A.; Ruasse, M. F. *J. Org. Chem.* **2000**, *65*, 8470−8477. (b) Bellucci, G.; Chiappe, C.; D'Andrea, F.; Lo Moro, G. *Tetrahedron* **1997**, *53*, 3417−3424.

(15) (a) Tokuyama, H.; Yokoshima, S.; Yamashita, T.; Fukuyama, T. *Tetrahedron Lett.* **1998**, *39*, 3189−3192. (b) Shimizu, T.; Seki, M. *Tetrahedron Lett.* **2000**, *41*, 5099−5101.

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J. Org. Chem. 2015, 80, 2972−2988