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Tuning the Reactivity of Oxygen/Sulfur by Acidity of the Catalyst in Prins Cyclization: Oxa- versus Thia-Selectivity

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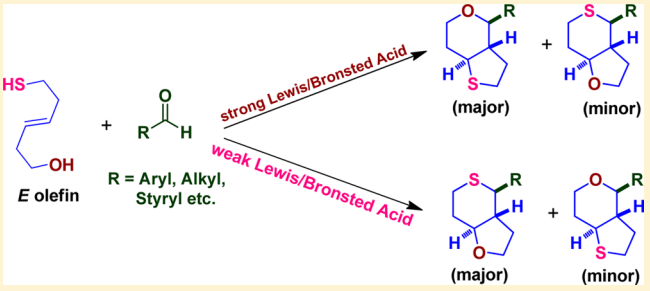
Supporting Information

ABSTRACT: An unprecedented oxa- versus thia-selectivity has been observed in Prins cyclization of 6-mercaptohex-3-en-1-ol with aldehydes. In the presence of a stoichiometric amount of strong Lewis or Brønsted acids, the reaction provides the hexahydro-2*H*-thieno[3,2-*c*]pyran skeleton predominantly via oxonium-Prins cyclization. In contrast, a catalytic amount of weak Lewis or Brønsted acids provides the hexahydro-2*H*-thiopyrano[4,3-*b*]furan preferentially through thionium-Prins cyclization.



Prins cyclization is a very useful strategy for the stereoselective synthesis of tetrahydropyran derivatives, a skeleton which is frequently present in natural products.[1] Aza- and thia-versions of Prins cyclization[2] are important approaches to generate the substituted piperidine and thiatetrahydropyran derivatives, respectively. In particular, thiatetrahydropyran plays an important role in pharmaceutical chemistry.[3−7] Though Prins cyclization is well-explored in organic synthesis, the thia-Prins cyclization is relatively less studied.[8] Inspired by a Prins bicyclization strategy with tethered nucleophiles,[9] we have successfully demonstrated the Prins cascade cyclization for the stereoselective synthesis of heterobicycles.[10] However, the scope of the reaction is still unexplored with 6-mercaptohex-3-en-1-ol. Recently, we reported the synergistic effects (cooperative catalysis) between the Lewis acids and Brønsted acids in Prins cyclization.[11] These observations encouraged us to study the effect of acidity of the catalyst in thia-Prins cyclization. During our study, we found very intriguing results dealing with the nature of acid catalysts in thia-Prins cyclization between 6-mercaptohex-3-en-1-ol and aldehydes. Under strong acidic conditions, the hexahydro-2*H*-thieno[3,2-*c*]pyran is formed predominantly through Prins cyclization, whereas the weak acid provides mainly hexahydro-2*H*-thiopyrano[4,3-*b*]furan via thia-Prins cyclization. To the best of our knowledge, there are no reports on such oxa- versus thia-selectivity and vice versa in Prins cyclization by tuning the reactivity of oxygen and sulfur with acidity of the catalyst. At first, we examined the reactivity of several Lewis and Brønsted acids in a model reaction between (*E*)-6-mercaptohex-3-en-1-ol (**1**) and 4-nitrobenzaldehyde in CH_2Cl_2 at 0 °C (entries 1−11, Table 1).

To our surprise, in the presence of 1 equiv of strong acid, a *trans*-fused hexahydro-2*H*-thieno[3,2-*c*]pyran **3a** was obtained as a major product via oxonium Prins pathway and hexahydro-2*H*-thiopyrano[4,3-*b*]furan **4a** as a minor product which arises from thionium-Prins cyclization, in moderate to high oxa- versus thia-selectivity (entries 4−11). Among the strong acids tested for this conversion, 1 equiv of $BF_3{\cdot}OEt_2$ gave the best result in terms of yield (85% of **3a**) with 9:1 oxa/thia-selectivity (entry 3). However, the selectivity of the reaction depends upon the amount of acid. As seen from Table 1, the selectivity was decreased to 1.2:1 (entry 1) when 0.1 equiv of $BF_3{\cdot}OEt_2$ was used. Next, we examined the reactivity of several weak Lewis/Brønsted acids in the above model reaction (entries 12−24, Table 1). Surprisingly, in the presence of weak Lewis/Brønsted acids, *trans*-hexahydro-2*H*-thiopyrano[4,3-*b*]furan **4a** was isolated as a major product. In the case of mild/weak acids (at 10 mol %), a predominant formation of product **4a** was observed over **3a** through thionium-Prins cyclization with moderate to good thia- vs oxa-selectivity (entries 12−24, Table 1). Among several mild/weak acids tested, $InCl_3$ gave excellent results in terms of yield (75% of **4a**) with 7.6:1 thia/oxa-selectivity (entry 16, Table 1). In this case also, the selectivity depends upon the quantity of acid but in the opposite direction. It decreased to 1.3:1 when 1 equiv of $InCl_3$ was used (entry 13). The two isomeric products could easily be separated by silica gel column chromatography. In each case, the ratio of two products was determined by crude ^1H NMR spectrum. Therefore, the selectivity of oxa versus thia and thia versus oxa can be changed in Prins bicyclization of 6-mercaptohex-3-en-1-ol with aldehyde by tuning the reactivity of oxygen and sulfur with strong and weak Lewis/Brønsted acids. Next, we examined the cooperative effect of two weaker acids. Interestingly, a combination of a weak Lewis acid with a

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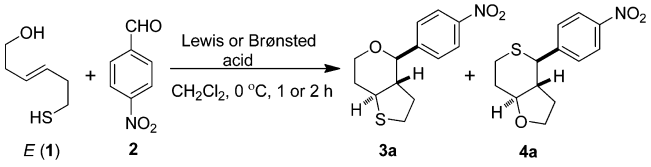
Table 1. Reactivity of Various Lewis and Brønsted Acids in Prins Cyclization of (*E*)-6-Mercaptohex-3-en-1-ol and 4-Nitrobenzaldehyde



E (**1**) **2** **3a** **4a**

Entry	Lewis/Brønsted acid[a]	Equiv.	Yield (%)[b] 3a	Yield (%)[b] 4a	3a:4a ratio[c]
1	$BF_3.OEt_2$	0.1	43	35	1.2 : 1
2	''	0.5	64	18	3.6 : 1
3	''	1	85	9	9 : 1
4	TfOH	''	78	10	7.9 : 1
5	TMSOTf	''	76	11	7 : 1
6	Tf_2NH	''	75	11	6.8 : 1
7	$SnCl_4$	''	74	12	6.2 : 1
8	$TiCl_4$	''	73	12	6.1 : 1
9	TMSCl	''	62	18	3.5 : 1
10	$Sc(OTf)_3$	''	50	20	2.6 : 1
11	TFA	''	45	20	2.3 : 1
12	$InBr_3$	1	40	50	1 : 1.3
13	''	0.5	22	65	1 : 3
14	''	0.1	10	73	1 : 7.4
15	$InCl_3$	''	10	75	1 : 7.6
16	$In(OTf)_3$	''	35	55	1: 2.2
17	$ZnCl_2$	''	12	62	1 : 5.2
18	$SnCl_2$	''	14	56	1 : 4.1
19	p-TSA	''	16	60	1 : 3.5
20	CSA	''	15	45	1 : 3.1
21	CuCl	''	< 5	25	1 : 3
22	AcOH	''	---	15	1 : 2.1
23	LiBr	''	---	< 10	----
24	BzOH	''	---	< 5	----
25	$InCl_3$+Camphor sulphonic acid	1.0+1.0	70	21	4.0:1.0
26	$InBr_3$+Camphor sulphonic acid	''	65	25	3.9:1.0
27	$InBr_3$+Acetic acid	''	55	21	3.7:1.0
28	$InBr_3$+4-Nitrobenzoic acid	''	51	27	3.3:1.0
29	$BiBr_3$+4-Nitrobenzoic acid	''	45	30	2.1:1.0
30	$ZnCl_2$+4-NitroBenzoic acid	''	40	35	0.6:1.0

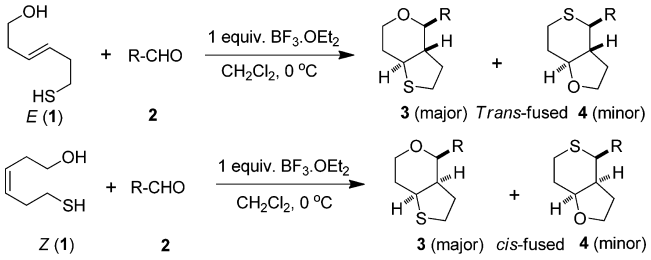
Strong acids: entries 1–11. Weak acids: entries 12–24. Weak Lewis + Brønsted acids: entries 25–30.

[a]The reaction was performed with strong acids for 1 h and with mild/weak acids for 2 h. [b]Isolated yields. [c]Ratio was determined by ^{1}H NMR of the crude product.

weak Brønsted acids (1:1 ratio) in most cases reversed the selectivity in favor of the oxonium pathway (entries 25−30, Table 1). This result is in line with our previous experimental studies[11] and the computational studies[12] indicating that such combinations could significantly increase the acidity of Brønsted acids.

Subsequently, we examined the scope of oxa-selectivity in the synthesis of *trans*/*cis*-fused hexahydro-2*H*-thieno[3,2-*c*]pyrans **3** by the coupling of (*E*)- and (*Z*)-6-mercaptohex-3-en-1-ols with aldehydes in the presence of a stoichiometric amount of BF_3·OEt_2, and the results are summarized in Table 2. This method is effective with aromatic aldehydes such as 4-bromobenzaldehyde, 2,5-dimethoxybenzaldehyde, and 4-chlorobenzaldehyde (entries 2−7, Table 2). Remarkably, acid-sensitive aldehydes such as cinnamaldehyde and phenylacetaldehyde participated well in this reaction (entries 8 and 9, Table 2). Aliphatic aldehyde, that is, *n*-hexanal, also gave the product in good yield (entry 10, Table 2). In all cases, product **3** was obtained predominantly via oxonium-Prins cyclization in good yields with excellent oxa- versus thia-selectivity. Furthermore, the structure of **3e** was confirmed by X-ray crystallography.[13]

Table 2. BF_3·OEt_2-Mediated Synthesis of Hexahydro-2*H*-thieno[3,2-*c*]pyran Scaffolds via Oxonium-Prins Cyclization



E (**1**) **2** **3** (major) *Trans*-fused **4** (minor)

Z (**1**) **2** **3** (major) *cis*-fused **4** (minor)

entry	olefin	R	major product[a]	time (h)	yield (%)[b]	3:4 ratio[c]
1	*E*	4-nitrophenyl	**3a**	1	85	9:1
2	*Z*	4-nitrophenyl	**3b**	1	86	10:1
3	*E*	4-bromophenyl	**3c**	1	82	8.5:1
4	*Z*	4-bromophenyl	**3d**	1	84	10:1
5	*E*	2,5-dimethoxyphenyl	**3e**	1.5	80	8:1
6	*Z*	2,5-dimethoxyphenyl	**3f**	1.5	78	8.2:1
7	*E*	4-chlorophenyl	**3g**	1	85	9:1
8	*Z*	benzyl	**3h**	2	75	6.5:1
9	*E*	styryl	**3i**	0.5	88	10:1
10	*Z*	*n*-pentyl	**3j**	2	70	10:1

[a]Products were characterized by ^{1}H and ^{13}C NMR, IR, and mass spectroscopy. [b]Yield refers to pure product after column chromatography. [c]Ratio was determined by ^{1}H NMR of the crude product.

The above examples were further studied with 10 mol % of $InCl_3$ for thia-selectivity. Accordingly, treatment of 6-mercaptohex-3-en-1-ol with different aldehydes afforded the hexahydro-2*H*-thiopyrano[4,3-*b*]furan derivatives **4** via thionium-Prins cyclization, and the results are illustrated in Table 3. In each case, product **4** was obtained predominantly with high thia-selectivity in good yields (Table 3, entries 1−9). As evident from Tables 2 and 3, the *trans*-fused products were obtained mainly from *E*-homoallylic substrate, while *cis*-fused products were formed selectively with *Z*-homoallylic substrate. 2-D NMR studies (NOESY and DQFCOSY) were used to establish the structure and stereochemistry of **3i** and **4i**.[14] The characteristic NMR peaks of **3i** and **4i** are shown in Figure 1.

In each case, the oxathioacetal was formed rapidly from 6-mercaptohex-3-en-1-ol and the aldehyde. It provides the clue to elucidate the role of this oxathioacetal intermediate in the reaction mechanism. Therefore, in order to obtain information on the reaction pathway, the oxathioacetal **A** was prepared separately from (*E*)-6-mercaptohex-3-en-1-ol and 4-nitrobenzaldehyde and then studied for its reactivity in Prins cyclization in the presence of a strong or weak Lewis/Brønsted acid (Table 4). A similar oxa- and thia-selectivity was observed even with this oxathioacetal, which is consistent with the results reported in Table 1. Therefore, product **3a** was formed in the presence of a stoichiometric amount of strong acid (BF_3·OEt_2 or TMSOTf) by oxonium-Prins cyclization (Table 4, entries 2 and 4), whereas product **4a** was formed under the influence of a catalytic amount of weak acid ($InCl_3$ or *p*-TSA) through thionium-Prins pathway (Table 4, entries 5 and 7) with good selectivity.

On the basis of these results, we propose a tentative mechanism for the observed oxa- versus thia-selectivity in Prins cyclization of 6-mercaptohex-3-en-1-ol with aldehydes, as depicted in Schemes 1 and 2. Under acid catalysis, 6-

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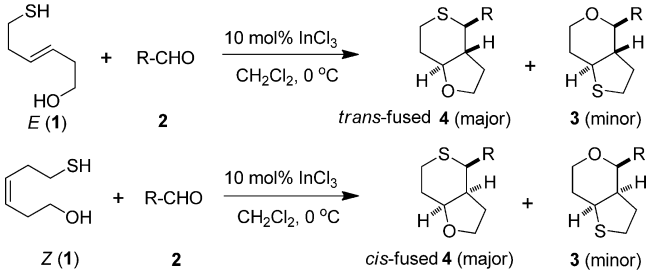
Table 3. $InCl_3$-Catalyzed Synthesis of Hexahydro-2*H*-thiopyrano[4,3-*b*]furan Scaffolds via Thionium-Prins Cyclization



entry	olefin	R	major product[a]	time (h)	yield (%)[b]	4:3 ratio[c]
1	*E*	4-nitrophenyl	**4a**	2	75	7.6:1
2	*Z*	4-nitrophenyl	**4b**	2	76	7.8:1
3	*E*	4-bromophenyl	**4c**	2	80	7.4:1
4	*Z*	4-bromophenyl	**4d**	2	78	7.2:1
5	*E*	2,5-dimethoxyphenyl	**4e**	3	74	6:1
6	*Z*	2,5-dimethoxyphenyl	**4f**	3	72	6.2:1
7	*E*	4-chlorophenyl	**4g**	2	78	7.5:1
8	*Z*	benzyl	**4h**	4	68	5.4:1
9	*E*	styryl	**4i**	1	82	7.5:1

[a]Products were characterized by ^1H and ^{13}C NMR, IR, and mass spectroscopy. [b]Yield refers to pure product after column chromatography. [c]Ratio was determined by ^1H NMR of the crude product.

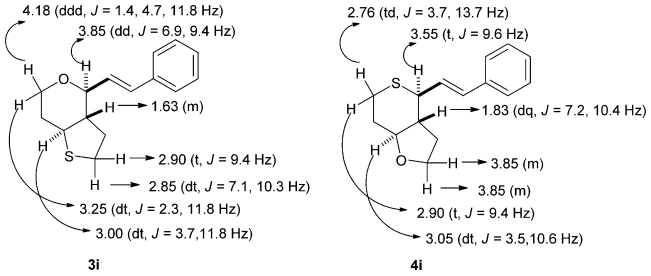


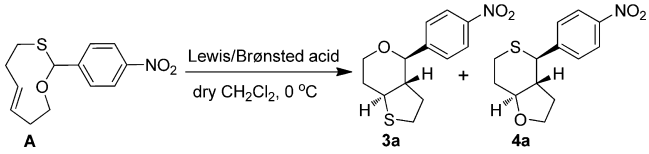
Figure 1. Characteristic NMR data of **3i** and **4i**.

mercaptohex-3-en-1-ol and the aldehyde will give first the intermediates hemiacetal (**X**) and hemithioacetal (**W**) and then the corresponding oxonium ion (**B**) and thionium ion (**C**).[15] Latter derivatives can afford bicycles **3** and **4** via Prins-type reactions and/or give oxathioacetal **A** by intramolecular cyclization (Scheme 1).

In preceding results, we have shown that (i) the intermediate **A** is formed very quickly during the synthesis, and (ii) similar results are obtained if the reaction is performed starting either from 6-mercaptohex-3-en-1-ol or from oxathioacetal **A**. Therefore, it appears logical to consider that this latter intermediate plays a key role in the selectivity. After formation of **A**, the complexation of sulfur by the acid induces the C−O bond cleavage of the thioacetal to generate an oxonium ion, affording the hexahydro-2*H*-thieno[3,2-*c*]pyran derivative **3**. On the other hand, complexation onto the oxygen by the acid will cleave the C−S bond and generate a thiocarbenium ion to provide the respective hexahydro-2*H*-thiopyrano[4,3-*b*]furan derivative **4** (Scheme 2).[16]

From our results, complexation to sulfur is favored in the case of strong acids or Lewis acids such as $BF_3{\cdot}OEt_2$, while coordination to oxygen is preferred for weaker acids or Lewis

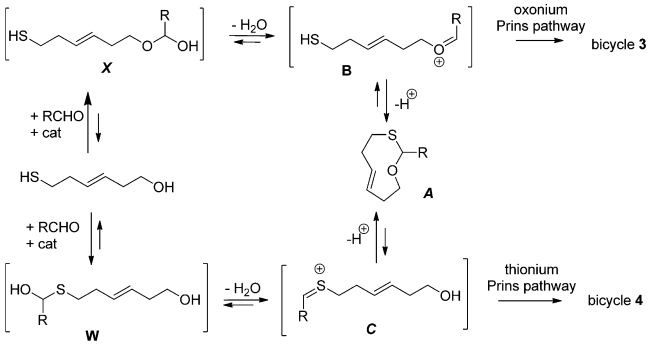
Table 4. Prins Cyclization of Oxathioacetal (A) with Strong and Weak Lewis/Brønsted Acids



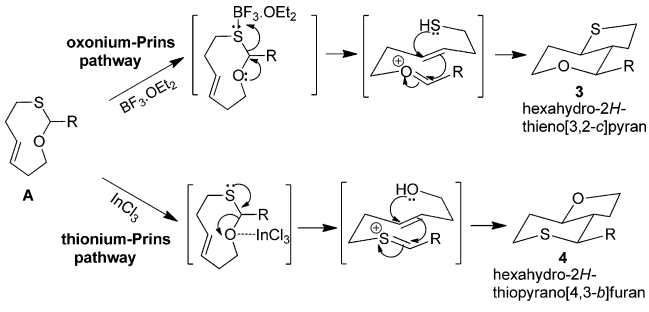
				yield (%)[a]		
entry	acid	equiv	time (h)	**3a**	**4a**	**3a**:**4a** ratio[b]
1	$BF_3{\cdot}OEt_2$	0.1	1	60	30	63:37
2	$BF_3{\cdot}OEt_2$	1	0.5	85	10	89:11
3	TMSOTf	0.1	1	50	35	55:45
4	TMSOTf	1	0.5	76	11	82:18
5	$InCl_3$	0.1	2	10	75	12:88
6	$InCl_3$	1	1	30	56	33:67
7	$InBr_3$	0.1	2	10	73	11:89
8	$InBr_3$	1	1	40	50	44:56
9	*p*-TSA	0.1	2	16	60	23:77
10	*p*-TSA	1	1	30	45	35:65

[a]Isolated yields. [b]Ratio was determined by ^1H NMR of the crude product.

Scheme 1. Formation of Intermediate A and Bicycles 3 and 4 Starting from 6-Mercaptohex-3-en-1-ol and Aldehydes



Scheme 2. Plausible Mechanism for Oxa- and Thia-Selectivity



acids such as $InCl_3$. In the case of oxa-aza or thia-aza homoallylic trifunctional susbstrate, no aza-Prins cyclization was observed either by strong or by weak acid even with stoichiometric amounts.[17]

In summary, we demonstrated a remarkable oxa- and thia-selectivity in Prins cyclization by changing the acidity of the catalyst. The reaction follows the oxonium-Prins pathway preferentially in the presence of a strong acid to provide the hexahydro-2*H*-thieno[3,2-*c*]pyran derivatives. Conversely, in the presence of a weak acid as catalyst, the reaction mainly

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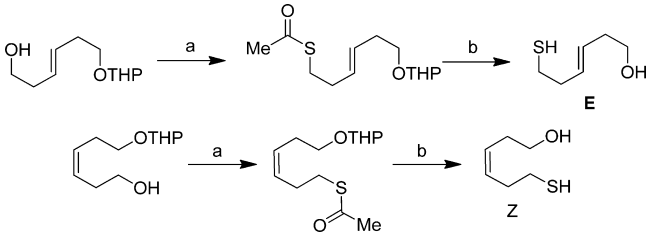
follows the thionium-Prins pathway, affording the hexahydro-2*H*-thiopyrano[4,3-*b*]furan derivatives. By using a combination of two weak acids, the reaction follows again the oxonium-Prins pathway. Further, the reaction is stereoselective to provide useful *cis*- and *trans*-fused oxa-thia and thia-oxa bicycles in a single-step process.

EXPERIMENTAL SECTION

General. Dichloromethane was dried according to a standard literature procedure. Reactions were performed in an oven-dried round-bottom flask; the flasks were fitted with rubber septa, and the reactions were conducted under nitrogen atmosphere. Glass syringes were used to transfer the solvent. Crude products were purified by column chromatography on silica gel of 100−200 mesh. Thin layer chromatography plates were visualized by exposure to ultraviolet light and/or by exposure to iodine vapors and/or by exposure to methanolic acidic solution of *p*-anisaldehyde (anis) followed by heating (<1 min) on a hot plate (∼250 °C). Organic solvents were concentrated on rotary evaporator at 35−40 °C. IR spectra were recorded on a FT-IR spectrometer. ^{1}H NMR and ^{13}C NMR (proton-decoupled) spectra were recorded in $CDCl_3$ on 300, 500, 600, or 700 MHz NMR spectrometers. Chemical shifts (δ) were reported in parts per million (ppm) with respect to TMS as an internal standard. Coupling constants (J) are quoted in hertz (Hz). Mass spectra were recorded on mass spectrometer by gas chromatography electron impact mass spectrometry (GC-EI-MS) or electrospray ionization mass spectrometry (ESI-MS) technique.

Procedure. To a stirred solution of (*E*)- or (*Z*)-6-(tetrahydro-2*H*-pyran-2-yloxy)hex-3-enyl 4-methylbenzenesulfonate [obtained via tosylation of (*E*)- or (*Z*)-6-(tetrahydro-2*H*-pyran-2-yloxy)hex-3-en-1-ol][1] (15 mmol) in *N*,*N*-dimethylformamide (30 mL) was added potassium thioacetate (23 mmol) (Scheme 3). The reaction mixture was stirred at room temperature for 3 h. After completion of the reaction as indicated by TLC, the reaction mixture was diluted with water and extracted with ether (3 × 40 mL). The organic layer was washed with brine (2 × 15 mL), dried over anhydrous Na_2SO_4, and concentrated in vacuo. The resulting crude product was purified by column chromatography (silica gel, 60−120 mesh) using ethyl acetate/*n*-hexane gradients to afford the pure thioacetic acid esters, (*E*)- or (*Z*)-*S*-6-(tetrahydro-2*H*-pyran-2-yloxy)hex-3-enyl esters as a liquid in 80−82% yields, respectively. To a stirred solution of the above thioacetic acid ester in methanol (15 mL) was added Amberlyst-15 (2 g), and the mixture was stirred for 2−3 h at ambient temperature. After completion, the mixture was filtered, washed with methanol, and the filtrate was concentrated in vacuo. The resulting crude product was purified by column chromatography (silica gel, 60−120 mesh) using ethyl acetate/*n*-hexane gradients to afford the pure (*E*)- or (*Z*)-*S*-6-hydroxyhex-3-enyl ethanethioate as a liquid in 90% yield. The above hydroxy compound was dissolved in 5 mL of anhydrous tetrahydrofuran and was added dropwise to a suspension of lithium aluminum hydride (2 equiv) in anhydrous tetrahydrofuran (15 mL) under a nitrogen atmosphere at 0 °C.[2] The resulting mixture was stirred at ambient temperature for 1 h, and the excess lithium aluminum hydride was quenched by adding anhydrous sodium sulfate. Then the mixture was filtered through Celite, and the residue was washed with hot ethyl acetate. The filtrate was dried over anhydrous Na_2SO_4 and concentrated in vacuo, and the resulting crude product was purified by column chromatography (silica gel, 60−120 mesh) using ethyl acetate/*n*-hexane gradients to afford the corresponding pure (*E*)-or (*Z*)-6-mercaptohex-3-en-1-ol.

Scheme 3. Preparation of the Starting Material[a]



[a]Reagents and conditions: (a) (i) TsCl, Et_3N, DMAP, dichloromethane, rt, 4−5 h (90%); (ii) CH_3COSK, *N*,*N*-dimethylformamide, rt, 3 h (80−82%); (b) (i) Amberlyst-15, methanol, 1 h (90%); (ii) lithium aluminium hydride, dry THF, 0 °C to rt, 1 h (82−85%).

Typical Procedure for Prins Cyclization in the Presence of Strong Lewis or Brønsted Acid (entries 1−12, Table 1). To a stirred solution of (*E*)-6-mercaptohex-3-en-1-ol (**1**) (0.5 mmol, 1 equiv) and 4-nitrobenzaldehyde (**2a**) (0.525 mmol, 1.05 equiv) in dry dichloromethane (5 mL) under nitrogen atmosphere was added strong Lewis or Brønsted acid (1 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 1 h and then quenched with saturated aqueous $NaHCO_3$ solution (1 mL), diluted with water (2−3 mL), and extracted with dichloromethane (2 × 5 mL). The organic phases were combined, washed with brine (2 × 2 mL), dried over anhydrous Na_2SO_4, and concentrated in vacuo. The resulting crude mixture was purified by column chromatography (silica gel of 100−200 mesh) using ethyl acetate/*n*-hexane gradients to afford **3a** (major) and **4a** (minor) as pure products (Table 1).

Typical Procedure for Prins Cyclization in the Presence of Mild/Weak Lewis or Brønsted Acid (entries 13−25, Table 1). To a stirred solution of (*E*)-6-mercaptohex-3-en-1-ol (**1**) (0.5 mmol, 1 equiv) and 4-nitrobenzaldehyde (**2a**) (0.525 mmol, 1.05 equiv) in dry dichloromethane (5 mL) under nitrogen atmosphere was added mild/weak Lewis or Brønsted acid (10 mol %) at 0 °C. The reaction mixture was stirred at the same temperature for 2 h and then quenched with saturated aqueous $NaHCO_3$ solution (0.5 mL), diluted with water (2−3 mL), and extracted with dichloromethane (2 × 5 mL). The organic phases were combined, washed with brine (2 × 2 mL), dried over anhydrous Na_2SO_4, and concentrated in vacuo. The resulting crude mixture was purified by column chromatography (silica gel of 100−200 mesh) using ethyl acetate/*n*-hexane gradients to afford **4a** (major) and **3a** (minor) as pure products (Table 1).

Typical Procedure for Prins Cyclization in the Presence of Mild/Weak Lewis and Brønsted Acid (entries 26-31, Table 1). To a stirred solution of (*E*)-6-mercaptohex-3-en-1-ol (**1**) (0.5 mmol, 1 equiv) and 4-nitrobenzaldehyde (**2a**) (0.525 mmol, 1.05 equiv) in dry dichloromethane (5 mL) under nitrogen atmosphere were added mild/weak Lewis (1.0 equiv) and Brønsted acid (1.0 equiv) at 0 °C. The reaction mixture was stirred at same temperature for 2 h and then quenched with saturated aqueous $NaHCO_3$ solution (0.5 mL), diluted with water (2−3 mL), and extracted with dichloromethane (2 × 5 mL). The organic phases were combined, washed with brine (2 × 2 mL), dried over anhydrous Na_2SO_4, and concentrated in vacuo. The resulting crude mixture was purified by column chromatography (silica gel of 100−200 mesh) using ethyl acetate/*n*-hexane gradients to afford pure products (Table 1).

Procedure for the Synthesis of Hexahydro-2*H*-thieno[3,2-*c*]pyrans (3, Table 2). To a stirred solution of (*E*)- or (*Z*)-6-mercaptohex-3-en-1-ol (**1**) (0.5 mmol, 1 equiv) and aldehyde (**2**) (0.525 mmol, 1.05 equiv) in dry dichloromethane (5 mL) under nitrogen atmosphere was added $BF_3{\cdot}Et_2O$ (1 mmol) at 0 °C. The reaction mixture was stirred at room temperature for specified time. After completion, as indicated by TLC, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ solution (1 mL), diluted with water (2−3 mL), and extracted with dichloromethane (2 × 5 mL). The organic phases were combined, washed with brine (2 × 2 mL), dried over anhydrous Na_2SO_4, and concentrated in vacuo. The resulting crude product was purified by column chromatography (silica gel of 100−200 mesh) using ethyl acetate/*n*-hexane gradients to afford **3** as a pure product (Table 2).

Procedure for the Synthesis of Hexahydro-2*H*-thiopyrano-[4,3-*b*]furans (4, Table 3). To a stirred solution of (*E*)-6-mercaptohex-3-en-1-ol (**1**) (0.5 mmol, 1 equiv) and 4-nitrobenzaldehyde (**2a**) (0.525 mmol, 1.05 equiv) in dry dichloromethane (5 mL) under nitrogen atmosphere was added $InCl_3$ (10 mol %) at 0

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°C. The reaction mixture was stirred at room temperature for specified time. After completion, as indicated by TLC, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ solution (0.5 mL), diluted with water (2−3 mL), and extracted with dichloromethane (2 × 5 mL). The organic phases were combined, washed with brine (2 × 2 mL), dried over anhydrous Na_2SO_4, and concentrated in vacuo. The resulting crude product was purified by column chromatography (silica gel of 100−200 mesh) using ethyl acetate/*n*-hexane gradients to afford **4** as a pure product (Table 3).

(E)-6-Mercaptohex-3-en-1-ol: 1.22 g, yield 85%; liquid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.62−5.42 (m, 2H), 3.65 (t, J = 6.8 Hz, 2H), 2.75−2.60 (m, 2H), 2.43−2.35 (m, 2H), 2.33−2.24 (m, 2H), 1.70 (br s, 1H), 1.46 (t, J = 7.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 131.1, 128.4, 61.8, 38.6, 35.9, 32.2; IR (neat) ν_{max} 2924, 2854, 1373, 1165, 1085, 811, 662 cm^{-1}; GC-EI-MS m/z 132 (M)$^+$; HRMS (TOF GC-EI) calcd for $C_6H_{12}OS$ 132.0609 (M)$^+$, found 132.0607.

6(Z)-6-Mercaptohex-3-en-1-ol: 1.18 g, yield 82%; liquid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.60−5.45 (m, 2H), 3.67 (t, J = 6.8 Hz, 2H), 2.63−2.54 (m, 2H), 2.46−2.30 (m, 4H), 1.76 (br s, 1H), 1.44 (t, J = 7.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 130.2, 127.9, 62.1, 31.5, 30.9, 24.5; IR (neat) ν_{max} 2924, 2854, 1373, 1165, 1085, 811, 662 cm^{-1}; GC-EI-MS m/z 132 (M)$^+$; HRMS (TOF GC-EI) calcd for $C_6H_{12}OS$ 132.0609 (M)$^+$, found 132.0608.

(3aS,4R*,7aS*)-4-(4-Nitrophenyl)hexahydro-2H-thieno[3,2-c]pyran (**3a**; Table 2, entry 1):* 118 mg, yield 85%; solid; mp 100−102 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.28−8.18 (m, 2H), 7.56−7.46 (m, 2H), 4.35−4.23 (m, 2H), 3.61 (dt, J = 12.1 and 2.3 Hz, 1H), 3.17−3.05 (m, 1H), 2.94−2.84 (m, 1H), 2.83−2.70 (m, 1H), 2.17−2.07 (m, 1H), 1.94−1.45 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.3, 148.3, 127.1, 123.7, 83.4, 67.6, 55.7, 49.5, 32.8, 30.8, 28.3; IR (KBr) ν_{max} 2925, 2855, 1519, 1350, 1247, 1069, 852, 695 cm^{-1}; GC-EI-MS m/z 265 (M)$^+$; HRMS (TOF GC-EI) calcd for $C_{13}H_{15}NO_3S$ 265.0772 (M)$^+$, found 265.0773.

(3aR,4R*,7aS*)-4-(4-Nitrophenyl)hexahydro-2H-thieno[3,2-c]pyran (**3b**; Table 2, entry 2):* 119 mg, yield 86%; solid; mp 118−120 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.27−8.17 (m, 2H), 7.54−7.44 (m, 2H), 4.88 (d, J = 3.0 Hz, 1H), 4.18 (ddd, J = 12.1, 4.5, and 1.5 Hz, 1H), 3.59 (dt, J = 12.1 and 3.0 Hz, 1H), 3.53−3.42 (m, 1H), 3.00−2.89 (m, 1H), 2.76 (dt, J = 10.6 and 7.6 Hz, 1H), 2.54−2.42 (m, 1H), 2.02−1.79 (m, 3H), 1.46−1.34 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.2, 147.0, 125.8, 123.6, 78.0, 68.3, 49.4, 44.3, 32.9, 29.1, 25.7; IR (KBr) ν_{max} 2925, 2850, 1520, 1346, 1249, 1084, 855, 708 cm^{-1}; GC-EI-MS m/z 265 (M)$^+$; HRMS (TOF GC-EI) calcd for $C_{13}H_{15}NO_3S$ 265.0771 (M)$^+$, found 265.0772.

(3aS,4R*,7aS*)-4-(4-Bromophenyl)hexahydro-2H-thieno[3,2-c]pyran (**3c**; Table 2, entry 3):* 128 mg, yield 82%; solid; mp 68−70 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52−7.45 (m, 2H), 7.25−7.18 (m, 2H), 4.24 (ddd, J = 12.1, 4.5, and 1.5 Hz, 1H), 4.14 (d, J = 9.8 Hz, 1H), 3.57 (dt, J = 12.1 and 2.3 Hz, 1H), 3.13−3.01 (m, 1H), 2.91−2.70 (m, 2H), 2.13−2.04 (m, 1H), 1.91−1.62 (m, 3H), 1.55−1.37 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.2, 131.6, 128.1, 121.8, 83.9, 67.6, 55.8, 49.6, 32.9, 31.0, 28.4; IR (KBr) ν_{max} 2938, 2860, 1491, 1344, 1228, 1156, 1087, 1024, 818, 763, 664 cm^{-1}; GC-EI-MS m/z 298 (M)$^+$; HRMS (TOF GC-EI) calcd for $C_{13}H_{15}BrOS$ 298.0027 (M)$^+$, found 298.0014.

(3aR,4R*,7aS*)-4-(4-Bromophenyl)hexahydro-2H-thieno[3,2-c]pyran (**3d**; Table 2, entry 4):* 131 mg, yield 84%; solid; mp 72−74 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50−7.43 (m, 2H), 7.22−7.14 (m, 2H), 4.74 (d, J = 2.8 Hz, 1H), 4.14 (ddd, J = 11.8, 4.7, and 1.5 Hz, 1H), 3.56 (dt, J = 11.8 and 2.6 Hz, 1H), 3.49−3.39 (m, 1H), 2.98−2.88 (m, 1H), 2.81−2.68 (m, 1H), 2.47−2.34 (m, 1H), 2.03−1.75 (m, 3H), 1.55−1.42 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.0, 131.3, 126.7, 120.7, 78.2, 68.3, 49.8, 44.2, 33.1, 29.2, 25.7; IR (KBr) ν_{max} 2925, 1487, 1046, 1007, 835, 729 cm^{-1}; GC-EI-MS m/z 298 (M)$^+$; HRMS (TOF GC-EI) calcd for $C_{13}H_{15}BrOS$ 298.0027 (M)$^+$, found 298.0020.

(3aS,4R*,7aS*)-4-(2,5-Dimethoxyphenyl)hexahydro-2H-thieno-[3,2-c]pyran (**3e**; Table 2, entry 5):* 117 mg, yield 80%; solid; mp 104−106 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.06−7.00 (m, 1H), 6.83−6.74 (m, 2H), 4.71 (d, J = 8.9 Hz, 1H), 4.23 (ddd, J = 11.9, 4.5, and 1.3 Hz, 1H), 3.79 (s, 3H), 3.76 (s, 3H), 3.58 (dt, J = 11.9 and 2.3 Hz, 1H), 3.18−3.05 (m, 1H), 2.89−2.68 (m, 2H), 2.13−2.03 (m, 1H), 1.91−1.48 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.0, 150.3, 130.7, 113.6, 112.4, 111.6, 76.9, 67.6, 56.2, 56.0, 55.8, 49.6, 33.1, 30.8, 28.6; IR (KBr) ν_{max} 2924, 2853, 1498, 1463, 1279, 1232, 1048, 1022, 794, 709 cm^{-1}; GC-EI-MS m/z 280 (M)$^+$; HRMS (TOF GC-EI) calcd for $C_{15}H_{20}O_3S$ 280.1133 (M)$^+$, found 280.1143.

(3aR,4R*,7aS*)-4-(2,5-Dimethoxyphenyl)hexahydro-2H-thieno-[3,2-c]pyran (**3f**; Table 2, entry 6):* 114 mg, yield 78%; solid; mp 96−98 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.04−6.98 (m, 1H), 6.83−6.71 (m, 2H), 5.02 (br s, 1H), 4.17−4.07 (m, 1H), 3.77 (s, 6H), 3.64−3.53 (m, 1H), 3.49−3.39 (m, 1H), 2.95−2.86 (m, 1H), 2.79−2.68 (m, 1H), 2.66−2.56 (m, 1H), 2.05−1.87 (m, 2H), 1.85−1.75 (m, 1H), 1.51−1.41 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.7, 149.4, 131.5, 112.5, 111.9, 110.9, 74.1, 68.3, 55.8, 47.1, 44.2, 33.5, 29.3, 26.4; IR (KBr) ν_{max} 2928, 2841, 1500, 1464, 1276, 1216, 1086, 1047, 1023, 793, 711 cm^{-1}; GC-EI-MS m/z 280 (M)$^+$; HRMS (TOF GC-EI) calcd for $C_{15}H_{20}O_3S$ 280.1133 (M)$^+$, found 280.1136.

(3aS,4R*,7aS*)-4-(4-Chlorophenyl)hexahydro-2H-thieno[3,2-c]pyran (**3g**; Table 2, entry 7):* 113 mg, yield 85%; solid; mp 76−78 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39−7.23 (m, 4H), 4.29−4.19 (m, 1H), 4.15 (d, J = 9.3 Hz, 1H), 3.57 (dt, J = 11.9 and 2.1 Hz, 1H), 3.13−3.01 (m, 1H), 2.92−2.70 (m, 2H), 2.14−2.04 (m, 1H), 1.91−1.62 (m, 3H), 1.54−1.38 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.6, 133.6, 128.6, 127.7, 83.8, 67.6, 55.7, 49.6, 32.8, 30.9, 28.4; IR (KBr) ν_{max} 2922, 2855, 1485, 1251, 1080, 1019, 819 cm^{-1}; GC-EI-MS m/z 254 (M)$^+$; HRMS (TOF GC-EI) calcd for $C_{13}H_{15}ClOS$ 254.0532 (M)$^+$, found 254.0533.

(3aR,4S*,7aS*)-4-Benzylhexahydro-2H-thieno[3,2-c]pyran (**3h**; Table 2, entry 8):* 92 mg, yield 75%; viscous liquid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36−7.16 (m, 5H), 3.96−3.91 (m, 1H), 3.91−3.85 (m, 1H), 3.36 (dt, J = 12.5 and 2.1 Hz, 1H), 3.28−3.22 (m, 1H), 3.08−3.01 (m, 1H), 2.97−2.80 (m, 2H), 2.73−2.66 (m, 1H), 2.25−2.03 (m, 3H), 1.88−1.77 (m, 1H), 1.76−1.66 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.5, 128.9, 128.4, 126.3, 78.7, 68.2, 47.6, 44.7, 41.3, 33.4, 29.6, 25.1; IR (neat) ν_{max} 2924, 2851, 1452, 1161, 1084, 700 cm^{-1}; GC-EI-MS m/z 234 (M)$^+$; HRMS (TOF GC-EI) calcd for $C_{14}H_{18}OS$ 234.1078 (M)$^+$, found 234.1085.

(3aS,4S*,7aS*)-4-Styrylhexahydro-2H-thieno[3,2-c]pyran (**3i**; Table 2, entry 9):* 113 mg, yield 88%; solid; mp 90−92 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44−7.20 (m, 5H), 6.64 (d, J = 15.9 Hz, 1H), 6.23 (dd, J = 15.9 and 6.8 Hz, 1H), 4.18 (ddd, J = 12.1, 4.5, and 1.5 Hz, 1H), 3.89−3.80 (m, 1H), 3.52 (dt, J = 12.1 and 2.3 Hz, 1H), 3.06−2.94 (m, 1H), 2.93−2.80 (m, 2H), 2.24−2.12 (m, 1H), 2.09−1.98 (m, 1H), 1.85−1.39 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.5, 131.7, 128.5, 127.8, 126.5, 82.7, 67.1, 54.4, 49.5, 32.8, 30.9, 28.6; IR (KBr) ν_{max} 2927, 2855, 1443, 1239, 1071, 9970, 749, 692 cm^{-1}; GC-EI-MS m/z 246 (M)$^+$; HRMS (TOF GC-EI) calcd for $C_{15}H_{18}OS$ 246.1078 (M)$^+$, found 246.1079.

(3aR,4S*,7aS*)-4-Pentylhexahydro-2H-thieno[3,2-c]pyran (**3j**; Table 2, entry 10):* 78 mg, yield 70%; viscous liquid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.97−3.90 (m, 1H), 3.61−3.55 (m, 1H), 3.37 (dt, J = 12.5 and 2.1 Hz, 1H), 3.32−3.24 (m, 1H), 3.06−2.99 (m, 1H), 2.93−2.83 (m, 1H), 2.14−1.91 (m, 3H), 1.85−1.65 (m, 2H), 1.50−1.17 (m, 8H), 0.89 (t, J = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 77.8, 68.0, 48.1, 44.7, 35.0, 33.7, 31.9, 29.7, 25.7, 25.1, 22.6, 14.0; IR (neat) ν_{max} 2928, 2860, 1459, 1376, 1261, 1088, 768 cm^{-1}; GC-EI-MS m/z 214 (M)$^+$; HRMS (TOF GC-EI) calcd for $C_{12}H_{22}OS$ 214.1391 (M)$^+$, found 214.1390.

(3aR,4R*,7aS*)-4-(4-Nitrophenyl)hexahydro-2H-thiopyrano-[4,3-b]furan (**4a**; Table 3, entry 1):* 104 mg, yield 75%; solid; mp 118−120 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.23−8.17 (m, 2H), 7.57−7.51 (m, 2H), 3.91 (d, J = 10.7 Hz, 1H), 3.86−3.81 (m, 2H), 3.19−3.12 (m, 1H), 3.02−2.95 (m, 1H), 2.88−2.82 (m, 1H), 2.55−2.48 (m, 1H), 2.16−2.07 (m, 1H), 1.88−1.76 (m, 2H), 1.56−1.45 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.1, 147.0, 128.7, 124.0, 82.2, 65.0, 50.6, 32.4, 29.8, 29.5; IR (KBr) ν_{max} 2925, 1516, 1345, 1117, 1029, 860, 731 cm^{-1}; GC-EI-MS m/z 265 (M)$^+$; HRMS (TOF GC-EI) calcd for $C_{13}H_{15}NO_3S$ 265.0772 (M)$^+$, found 265.0774.

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(3aS,4R*,7aS*)-4-(4-Nitrophenyl)hexahydro-2H-thiopyrano-[4,3-b]furan (**4b**; Table 3, entry 2):* 105 mg, yield 76%; solid; mp 135−137 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.23−8.16 (m, 2H), 7.54−7.46 (m, 2H), 4.54 (d, J = 3.8 Hz, 1H), 4.20−4.00 (m, 2H), 3.85−3.73 (m, 1H), 2.85−2.58 (m, 3H), 2.48−2.31 (m, 1H), 2.12−2.00 (m, 1H), 1.85−1.70 (m, 1H), 1.51−1.38 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.3, 147.1, 128.5, 123.8, 76.9, 66.4, 46.9, 44.7, 28.0, 26.2, 23.9; IR (KBr) ν_{max} 2930, 2888, 1514, 1346, 1258, 1045, 850, 705 cm^{-1}; GC-EI-MS m/z 265 (M)$^+$; HRMS (TOF GC-EI) calcd for $C_{13}H_{15}NO_3S$ 265.0772 (M)$^+$, found 265.0773.

(3aR,4R*,7aS*)-4-(4-Bromophenyl)hexahydro-2H-thiopyrano-[4,3-b]furan (**4c**; Table 3, entry 3):* 125 mg, yield 80%; solid; mp 92−94 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51−7.41 (m, 2H), 7.29−7.20 (m, 2H), 3.87−3.74 (m, 3H), 3.18−3.07 (m, 1H), 3.01−2.88 (m, 1H), 2.85−2.75 (m, 1H), 2.54−2.43 (m, 1H), 2.19−2.00 (m, 1H), 1.91−1.70 (m, 2H), 1.57−1.40 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.7, 131.8, 129.4, 121.5, 82.4, 65.0, 50.9, 50.7, 32.6, 29.9, 29.4; IR (KBr) ν_{max} 2925, 2875, 1484, 1072, 1000, 844, 750 cm^{-1}; GC-EI-MS m/z 298 (M)$^+$; HRMS (TOF GC-EI) calcd for $C_{13}H_{15}BrOS$ 298.0027 (M)$^+$, found 298.0029.

(3aS,4R*,7aS*)-4-(4-Bromophenyl)hexahydro-2H-thiopyrano-[4,3-b]furan (**4d**; Table 3, entry 4):* 116 mg, yield 78%; solid; mp 74−76 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50−7.41 (m, 2H), 7.24−7.16 (m, 2H), 4.40 (d, J = 3.6 Hz, 1H), 4.15−3.99 (m, 2H), 3.83−3.71 (m, 1H), 2.80−2.53 (m, 3H), 2.48−2.27 (m, 1H), 2.09−1.97 (m, 1H), 1.82−1.66 (m, 1H), 1.55−1.42 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.0, 131.6, 129.2, 121.1, 77.0, 66.5, 46.8, 45.1, 28.1, 26.3, 24.0; IR (KBr) ν_{max} 2923, 2849, 1482, 1246, 1132, 1085, 1004, 824, 726, 663 cm^{-1}; GC-EI-MS m/z 298 (M)$^+$; HRMS (TOF GC-EI) calcd for $C_{13}H_{15}BrOS$ 298.0027 (M)$^+$, found 298.0025.

(3aR,4R*,7aS*)-4-(2,5-Dimethoxyphenyl)hexahydro-2H-thiopyrano[4,3-b]furan (**4e**; Table 3, entry 5):* 108 mg, yield 74%; solid; mp 90−92 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.01 (d, J = 3.0 Hz, 1H), 6.86−6.72 (m, 2H), 4.42 (d, J = 11.0 Hz, 1H), 3.88−3.74 (m, 2H), 3.81 (s, 3H), 3.78 (s, 3H), 3.23−3.11 (m, 1H), 3.04−2.90 (m, 1H), 2.84−2.73 (m, 1H), 2.53−2.42 (m, 1H), 2.19−2.01 (m, 1H), 1.95−1.71 (m, 2H), 1.61−1.44 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.9, 150.9, 129.0, 114.3, 113.0, 112.1, 82.5, 65.0, 56.4, 55.7, 50.9, 42.5, 32.8, 29.7, 29.3; IR (KBr) ν_{max} 2932, 2830, 1500, 1482, 1227, 1181, 1074, 1046, 813, 711 cm^{-1}; GC-EI-MS m/z 280 (M)$^+$; HRMS (TOF GC-EI) calcd for $C_{15}H_{20}O_3S$ 280.1133 (M)$^+$, found 280.1126.

(3aS,4R*,7aS*)-4-(2,5-Dimethoxyphenyl)hexahydro-2H-thiopyrano[4,3-b]furan (**4f**; Table 3, entry 6):* 105 mg, yield 72%; solid; mp 84−86 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.96−6.93 (m, 1H), 6.80−6.78 (m, 1H), 6.76−6.73 (m, 1H), 4.93 (d, J = 3.8 Hz, 1H), 4.16−3.97 (m, 2H), 3.83−3.73 (m, 8H), 2.76−2.64 (m, 2H), 2.50−2.30 (m, 1H), 2.09−1.97 (m, 1H), 1.80−1.66 (m, 1H), 1.51−1.39 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.4, 150.1, 130.3, 114.8, 112.1, 111.2, 77.0, 66.5, 55.9, 55.7, 42.7, 39.9, 28.4, 26.5, 24.3; IR (KBr) ν_{max} 2943, 2833, 1498, 1461, 1276, 1219, 1247, 1076, 1049, 1023, 877, 799, 713 cm^{-1}; GC-EI-MS m/z 280 (M)$^+$; HRMS (TOF GC-EI) calcd for $C_{15}H_{20}O_3S$ 280.1132 (M + H)$^+$, found 280.1133.

(3aR,4R*,7aS*)-4-(4-Chlorophenyl)hexahydro-2H-thiopyrano-[4,3-b]furan (**4g**; Table 3, entry 7):* 104 mg, yield 78%; solid; mp 80−82 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30 (s, 4H), 3.86−3.77 (m, 3H), 3.17−3.09 (m, 1H), 3.02−2.88 (m, 1H), 2.85−2.75 (m, 1H), 2.54−2.43 (m, 1H), 2.19−2.00 (m, 1H), 1.92−1.71 (m, 2H), 1.58−1.40 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.2, 133.4, 129.1, 128.8, 82.4, 65.0, 50.9, 50.6, 32.6, 29.9, 29.4; IR (KBr) ν_{max} 2926, 2878, 1488, 1077, 1032, 844, 753 cm^{-1}; GC-EI-MS m/z 254 (M)$^+$; HRMS (TOF GC-EI) calcd for $C_{13}H_{15}ClOS$ 254.0532 (M)$^+$, found 254.0534.

(3aS,4S*,7aS*)-4-Benzylhexahydro-2H-thiopyrano[4,3-b]furan (**4h**; Table 3, entry 8):* 83 mg, yield 68%; viscous liquid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36−7.16 (m, 5H), 4.09−4.00 (m, 1H), 3.99−3.89 (m, 1H), 3.88−3.76 (m, 1H), 3.54−3.45 (m, 1H), 2.87−2.67 (m, 2H), 2.66−2.55 (m, 1H), 2.53−2.22 (m, 3H), 1.99−1.88 (m, 2H), 1.75−1.60 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.7, 128.8, 128.4, 126.6, 76.7, 66.3, 44.1, 41.9, 40.4, 28.3, 25.3, 23.4; IR (neat) ν_{max} 2923, 1450, 1267, 1128, 1054, 756, 700 cm^{-1}; GC-EI-MS m/z 234 (M)$^+$; HRMS (TOF GC-EI) calcd for $C_{14}H_{18}OS$ 234.1078 (M)$^+$, found 234.1069.

(3aR,4S*,7aS*)-4-Styrylhexahydro-2H-thiopyrano[4,3-b]furan (**4i**; Table 2, entry 9):* 105 mg, yield 82%; solid; mp 74−76 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45−7.20 (m, 5H), 6.62 (d, J = 15.9 Hz, 1H), 6.13 (dd, J = 15.9 and 9.1 Hz, 1H), 3.90−3.81 (m, 2H), 3.55 (t, J = 9.8 Hz, 1H), 3.11−3.00 (m, 1H), 2.91 (dt, J = 13.6 and 3.0 Hz, 1H), 2.75 (td, J = 13.6 and 3.4 Hz, 1H), 2.47−2.37 (m, 1H), 2.20−2.07 (m, 1H), 1.92−1.52 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.4, 132.5, 128.5, 127.8, 127.5, 126.4, 81.8, 65.1, 50.4, 49.7, 32.3, 30.3, 28.6; IR (KBr) ν_{max} 2929, 2878, 1446, 1068, 963, 761, 690 cm^{-1}; GC-EI-MS m/z 246 (M)$^+$; HRMS (TOF GC-EI) calcd for $C_{15}H_{18}OS$ 246.1078 (M)$^+$, found 246.1079.

*(E)-2-(4-Nitrophenyl)-4,5,8,9-tetrahydro-1,3-oxathionine (**A**; Table 4) (Spectral Data Represents a Crude Oxathioacetal):* To a stirred solution of (*E*)-6-mercaptohex-3-en-1-ol (**1**) (0.5 mmol, 1 equiv) and 4-nitrobenzaldehyde (**2a**) (0.525 mmol, 1.05 equiv) in dry dichloromethane (5 mL) under nitrogen atmosphere was added strong Lewis or Brønsted acid (0.05 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 25 min and then quenched with saturated aqueous $NaHCO_3$ solution (1 mL), diluted with water (2−3 mL), and extracted with dichloromethane (2 × 5 mL). The organic phases were combined, washed with brine (2 × 2 mL), dried over anhydrous Na_2SO_4, and concentrated in vacuo to afford the oxathioacetal **A** in quantitative yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.20 (d, J = 9.0 Hz, 2H), 7.61 (d, J = 9.0 Hz, 2H)5.57−5.42 (m, 2H), 4.97 (s, 1H), 3.63 (t, J = 6.8 Hz, 2H), 2.76−2.53 (m, 2H), 2.35−2.22 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.8, 147.2, 130.9, 128.5, 123.8, 61.7, 52.9, 38.5, 35.7, 32.1: IR (KBr) ν_{max} 2930, 2988, 1564, 1336, 1258, 945, 850, 705 cm^{-1}; GC-EI-MS m/z 265 (M)$^+$; HRMS (TOF GC-EI) calcd for $C_{13}H_{15}NO_3S$ 265.0872 (M)$^+$, found 265.0873.

■ ASSOCIATED CONTENT

Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra of products (**3a−3j**, **4a−4i**, ***E*1**,***Z*1**, and **A**), NOESY and DQFCOSY study of compounds (**3i** and **4i**), ORTEP diagram of **3e**, and X-ray data of compounds **3e** are provided in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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(13) The supplementary crystallographic data (CIF file) and respective ORTEP diagram of **3e** are provided in Supporting Information.

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