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CHIRAL FUNCTIONALIZATION OF 2(3*H*)-THIAZOLONE. NEW ROUTE TO CHIRAL SYNTHONS FOR 2-AMINO THIOLS[#]

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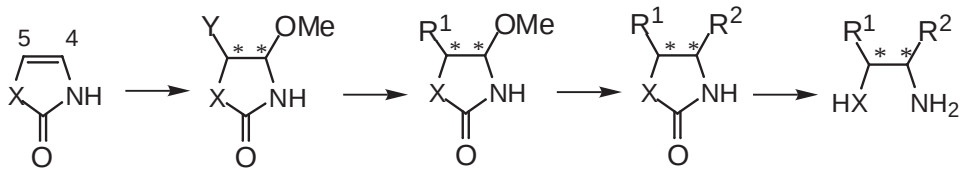
Abstract - Treatment of 3-[2(*R)*-methoxyethoxy- or 3-[2(*R)*-methoxyethoxyethoxy-7,7-dimethylbicyclo[2.2.1]heptane-1(*S)*-carbonyl]-2-thiazolones with Br_2 / $MeC(OMe)_3$ and C_6H_5SeCl / MeOH resulted in the diastereoselective formation of 4(*S)*-methoxy-5(*S)*-bromo- and 4(*R)*-methoxy-5(*R)*-phenylseleno-2-thiazolidinones, respectively, with high to excellent π-facial selectivity, but with opposite diastereofacial selection. The adducts thus obtained are potentially useful as chiral synthons for 2-amino thiols.

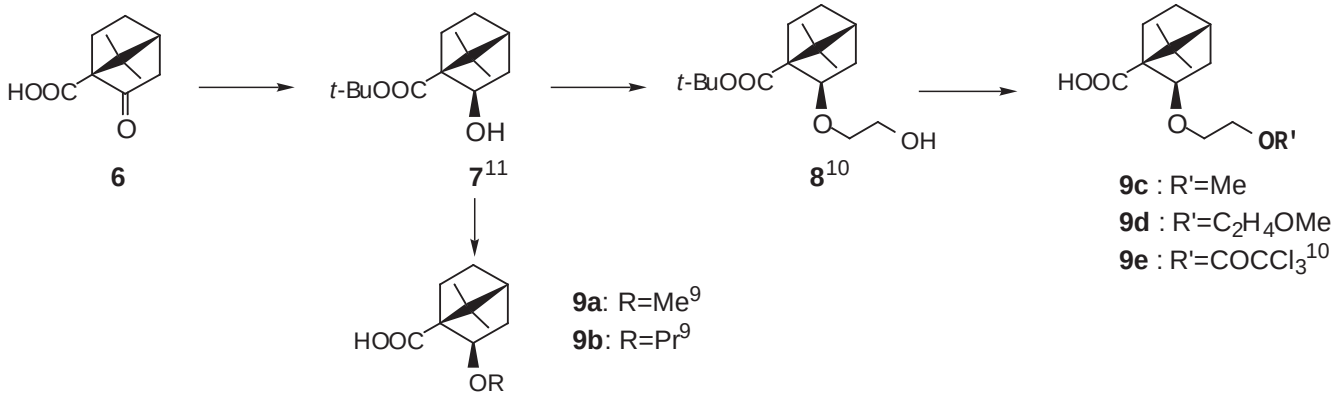
Simple five-membered heterocycles (**1**) such as 2(3*H*)-oxazolone (X=O), 1,3-dihydro-2-imidazolone (X=NH) and 2-thiazolone (X=S) hold considerable potential for use as important building blocks for the preparation of heterocyclic chiral auxiliaries,[1-3] and chiral synthons for polyfunctional compounds.[4,5] The synthetic potential of 2(3*H*)-oxazolone (**1**, X=O) and 1,3-dihydro-2-imidazolone (**1**, X=NH) has been verified by their facile conversion to enantioselectively functionalized compounds (**2**) with easily replaceable groups at the 4- and 5-positions, because of their high versatility and high degrees of asymmetric induction (Scheme 1). Thus, chiral 4-methoxy-5-bromo-,[6] 4-methoxy-5-phenylseleno-[6] and 4,5-dialkoxy-2-oxazolidinones (**2**) (X=O),[7] and 4,5-dimethoxy-2-imidazolidinone (**2**) (X=NH),[5b] are useful as synthons for the chiral synthesis of 2-amino alcohols and 1,2-diamines, respectively .



Scheme 1

[#] Dedicated to Professor Yuichi Kanaoka on the occasion of his 75th birthday.

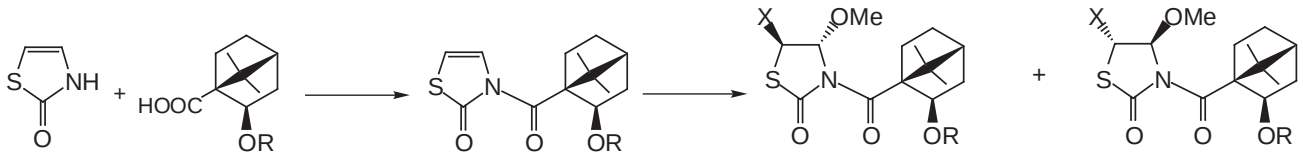
This paper describes the chiral functionalization of a simple 2(3*H*)-thiazolone heterocycle (**10**) which serves as a building block for a variety of chiral 2-amino thiols. Previous findings suggest that the chiral conversion of 2-thiazolone to type (**2)** thiazolidinone synthons could be readily performed in a diastereoselective manner by use of the camphor-derived auxiliaries, 2*R*-alkoxy-7,7-dimethylbicyclo[2.2.1]heptane-1*S*-carboxylic acids (2*R*-alkoxy-1*S*-apocamphanecarboxylic acids) (**9a-e**), due to the high diastereoselectivity attained and the ease of purification of the diastereomeric adducts.[6] Thus, a series of 2-alkoxy-1-apocamphanecarboxylic acids involving 2*R*-methoxy (MAC) (**9a**),[8,9] 2*R*-propoxy (**9b**),[9] 2*R*-methoxyethoxy (MOE) (**9c**),[6] and 2*R*-methoxyethoxyethoxy (MEE) (**9d**) and 2*R*-trichloroacetoxyethoxy derivatives (**9e**),[10] were readily synthesized by the alkylation of the 2*R*-hydroxy (**7**)[11] and 2*R*-(2-hydroxyethoxy) compounds(**8**),[10] as outlined in Scheme 2.



Scheme 2

The condensation of the 2*R*-alkoxy-1*S*-apocamphanecarboxylic acids (**9a-e**) with 2-thiazolone (**10**),[3] which is readily available by the hydrolysis of commercial 2-bromothiazole, proceeded smoothly *via* the carbonyl chlorides to give the corresponding 3-(2*R*-alkoxy-1*S*-apocamphanecarbonyl)-2-thiazolones (**11a-e**). The methoxy-bromination of **11a** and **11c** with *N*-bromosuccinimide (NBS) or bromine in methanol resulted in the highly regioselective formation of *trans*-5-bromo-4-methoxy-2-thiazolidinone adducts, (**12a**) and (**12c**), respectively, but with a rather low diastereoselectivity (less than 68% de). On the other hand, the diastereoselectivity was greatly improved, when the 2-thiazolone derivatives (**11c**) and (**11d**) containing ethereal methoxyethoxy (MOE) and methoxyethoxyethoxy (MEE) pendant groups, respectively, were treated with bromine in an aprotic solution of trimethyl orthoesters[6] (Table 1). Among the methoxy-donating agents examined, including tetramethoxysilane, the trimethyl orthoacetate was the compound of choice for achieving the highest degree of selectivity up to 94.5% de. The effect of an additive, such as TMSOTf, was negligible.

Similarly, the treatment of the 2-thiazolone derivatives (**11a-e**) with phenylselenenyl chloride in methanol resulted in the preferential formation of 4*R*-methoxy-5*R*-phenylseleno-2-thiazolidinone (**13a-e**) (Table 1).



10 **9a-e** **11a-e** **12a-e** **13a-e**

a: R=Me **b**: R=Pr **c**: R=C_2H_4OMe **d**: R=$C_2H_4OC_2H_4OMe$ **e**: R=$C_2H_4OCOCCl_3$

Scheme 3

Table 1. Regio- and Diastereoselective Methoxybromination and Methoxyselenenylation of 3-Acyl-2-thiazolones (**11a-e**)

Compound: R	Reagents(equiv) /Solvent	Temp (°C)	Time (h)	X	Yield (%)	Ratio[a] **1 2**:**1 3**
a:Me	NBS(1.4)/ MeOH	rt	3	Br	89	2:1
	Br_2 (1.2)/ $MeC(OMe)_3$	-78	2	Br	66	3:1
	PhSeCl/MeOH, CH_2Cl_2	-20	24	PhSe	90	1:2
b: Pr	Br_2 (1.2)/$MeC(OMe)_3$	-78	2	Br	59	2:1
	PhSeCl/MeOH, CH_2Cl_2	-20	24	PhSe	82	1:3
c: C_2H_4OMe	NBS(1.4)/ MeOH	-20	3	Br	82	5:1
	Br_2 (1.2)/MeOH	-78	2	Br	62	5:1
	Br_2 (3.0)/ $MeC(OMe)_3$	-78	2	Br	60	20:1[b]
	PhSeCl/MeOH, CH_2Cl_2	-20	24	PhSe	86	1:6
	PhSeCl/MeOH, CH_2Cl_2	-50	48	PhSe	81	1:9
d: $C_2H_4OC_2H_4OMe$	Br_2 (1.0)/ $HC(OMe)_3$	-78	2	Br	36(38)[c]	25:1[b]
	Br_2 (2.0)/ $MeC(OMe)_3$	-78	2	Br	70	35:1[b]
	Br_2(1.2), TMSOTf(0.5) / $MeC(OMe)_3$	-78	2	Br	75	30:1[b]
	Br_2 (1.2)/ $Si(OMe)_4$	-78	2	Br	67	9:1
	PhSeCl/MeOH, CH_2Cl_2	-50	48	PhSe	84	1:7
e: $C_2H_4OCOCCl_3$	Br_2 (1.2)/ $MeC(OMe)_3$	-78	2	Br	66	6:1
	PhSeCl/MeOH, CH_2Cl_2	-20	24	PhSe	58	1:2

[a] Determined by ^{1}H-NMR (500 MHz) analysis, unless otherwise stated.

[b] Determined by HPLC analysis.

[c] Recovery in parenthesis

The use of a chiral auxiliary having MOE and MEE pendant groups gave a selectivity of up to 80% de. The configurational assignment of the adducts thus formed was made on the basis of an X-ray crystal analysis of compound (**12a**) (Figure 1) and their chemical conversions to 5-allyl-4-methoxy-2-thiazolidinones (**14** and **15**), indicative of the reversed configuration of the adducts, as summarized in Scheme 4. Thus, the bromo-methoxy (**12**) and the seleno-methoxy adducts (**13**), formed as the major isomers, were treated with allyltributyltin under radical conditions, followed by removal of the acyl auxiliary, resulting in the distinct formation of enantiomeric products, ((-)-**14**) and ((+)-**15**), respectively.

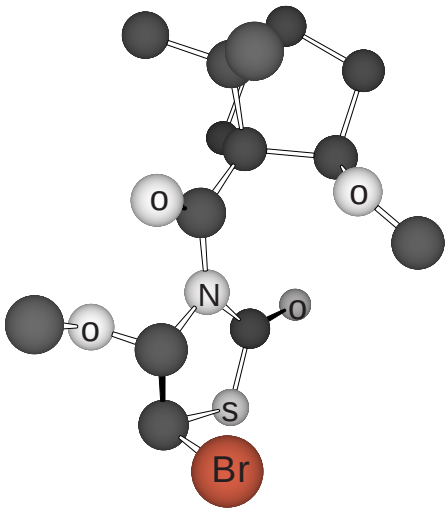
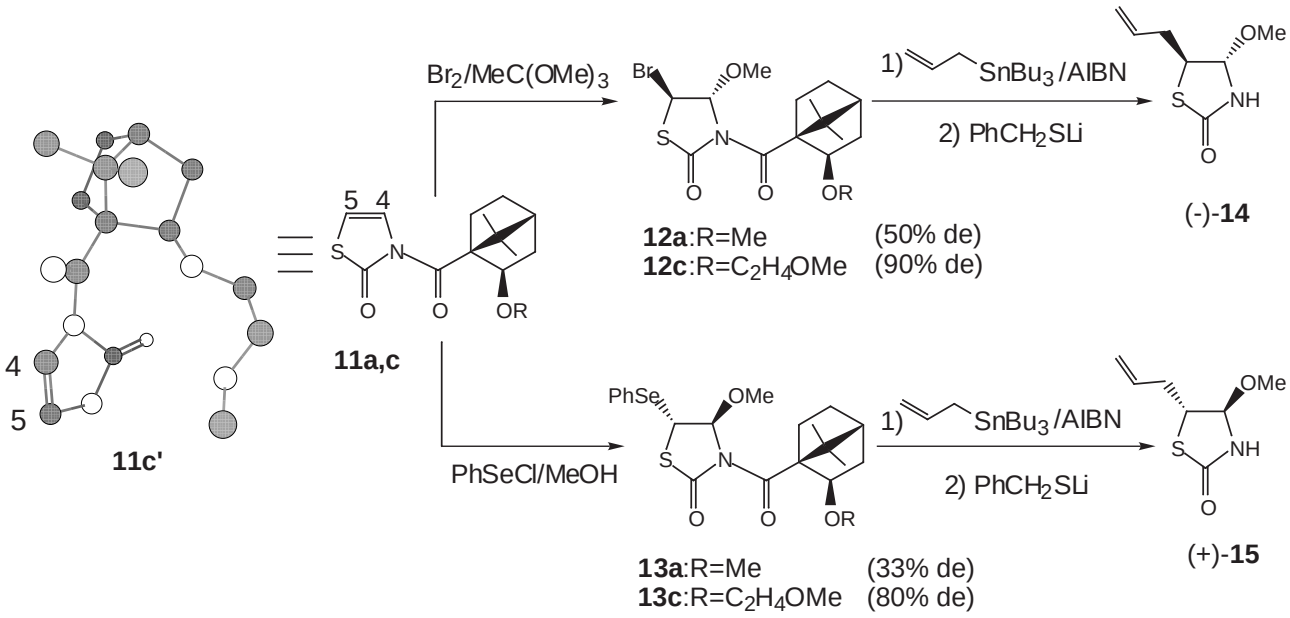


Figure 1. Crystal structure of diastereomer (**12a**)



Scheme 4

Both addition reactions might involve the participation of three-membered cyclic intermediates, bromonium and episeleniranium ions, followed by an *anti*-periplanar attack by nucleophiles. The observed addition of electrophilic bromonium and selenenium species in the opposite direction may be

rationalized by postulating a favorable conformer such as **11'** (Scheme 4), as previously pointed out for similar heterocyclic systems,[6a] in which the attack of a bromine molecule at the shielded diastereotopic face-side is accelerated through coordination with the ethereal oxygen atoms on the pendant groups, while phenylselenenium ions approach from the less hindered side.

Substitution of the bromo-methoxy and the seleno-methoxy adducts thus formed would be expected to proceed smoothly under nucleophilic and radical conditions. Thus, the 4-methoxy groups of compounds (**14** and **15)** were readily displaced by *prim* to *tert*-alkyl groups as well as aryl moieties on treatment with organocuprates in the presence of Lewis acids with full retention of configuration,[6] suggesting that these compounds represent promising chiral synthons leading to a variety of optically active 2-amino thiols.

In conclusion, an effective chiral functionalization of simple 2-thiazolone skeleton can be achieved by the electrophilic addition of bromine and phenylselenenyl chloride in the presence of methoxy-donating agents with the aid of camphor-based chiral auxiliaries to give both enantiomers of the 2-thiazolidinone synthons, either of which may be used for the chiral synthesis of 2-amino thiols, depending on the stereochemistry required.

EXPERIMENTAL

Melting points were determined on a Yanaco micro melting point apparatus and are uncorrected. ^{1}H-NMR spectra were recorded in $CDCl_3$ with tetramethylsilane as the internal standard on a JEOL ALPHA-500 (500 MHz) spectrometer. Optical rotations were measured in $CHCl_3$ with a JASCO DIP-370 polarimeter. HRMS spectra were obtained with a JOEL JMS-DX303HF mass spectrometer. The solvents other than anhydrous dichloromethane, which was purchased in a prepurified form, were distilled prior to use: THF over Na / benzophenone, benzene over CaH_2 and MeOH over MeONa.

(1*S*,2*R*,4*R*)-2-Alkoxy-7,7-dimethylbicyclo[2.2.1]heptane-1-carboxylic Acids [(1*S*,2*R*)-2-Alkoxy-1-apocamphanecarboxylic Acids] (9)

A series of 2*R*-methoxy (MAC) (9a)[8,9] and 2*R*-propoxy-1-apocamphanecarboxylic acids (9b),[9] and 2*R*-(2-trichloroacetoxyethoxy)-1-apocamphanecarboxylic acids (9e)[10] were prepared from 2*R*-hydroxy- (7)[11] and 2*R*-(2-hydroxyethoxy)-1*S*-apocamphanecarboxylic esters (8),[10] respectively, as previously reported.

(1*S*,2*R*)-2-Methoxyethoxy-1-apocamphanecarboxylic Acid (9c): This was prepared in 73 % yield by methylation of the 2-hydroxyethoxy *tert*-butyl ester (**8)**[10] with CH_3I / NaH, followed by deprotection with CF_3COOH in CH_2Cl_2, as a colorless oil, $[\alpha]_D^{25}$ –52.0 ° (*c* 1.0). ^{1}H-NMR, δ: 1.04 (3H, s), 1.06-1.17 (1H,

m), 1.19 (3H, s), 1.24-1.31 (1H, m), 1.77-1.87 (3H, m), 2.00-2.04 (1H, m), 2.38-2.42 (1H, m), 3.38 (3H, s), 3.55-3.62 (3H, m), 3.74-3.78 (2H, m), 3.81 (1H, dd, *J* = 3.50 Hz, *J'*= 7.83 Hz), 11.0 (1H, br). HRMS, Calcd for $C_{13}H_{22}O_4Cs$ (MCs^+): m/z 375.0613. Found: 375.0568.

(1*S*,2*R*)-2-(2-Methoxyethoxy)ethoxy-1-apocamphanecarboxylic Acid (9d): Analogous to the conversion of alcohol (**7**) to the 2-MOE-derivative (**9c**), this was prepared by the allylation (allyl bromide / NaH) of **8**, followed by successive treatment with ozone gas / $NaBH_4$ and MeI / NaH, as a colorless oil, $[\alpha]_D^{25}$ +62.8 ° (*c* 1.0). ^{1}H-NMR, δ: 1.04 (3H, s), 1.07-1.14 (1H, m), 1.18 (3H, s), 1.25-1.29 (1H, m), 1.76-1.80 (1H, m), 1.83-1.89 (1H, m), 1.98-2.02 (1H, m), 2.37-2.43 (1H, m), 3.38 (3H, s), 3.52-3.78 (7H, m), 3.81 (2H, dd, J=3.36 Hz, J=4.37 Hz). HRMS, Calcd for $C_{15}H_{26}O_5Na$ (MNa^+): m/z 309.1651. Found: m/z 309.1678.

3-[(1*S*,2*R*)-2-Alkoxy-1-apocamphanecarbonyl]-2-thiazolones (11).

***General Procedure*:**: To a solution of 2-*exo*-alkoxy-1*S*-apocamphanecarbonyl chloride (1 mmol), derived from the carboxylic acids (**9**) and thionyl chloride, in THF (5 mL) were added the lithium salts, derived from the reaction of 2-thiazolone (**10**) (1 mmol) with BuLi (1.1 mmol), dissolved in THF (5 mL), at -78° C under an argon atmosphere. The mixture was stirred at 0°C for 1 h and then passed through a silica gel pad with AcOEt as an eluent. Usual work-up followed by chromatographic purification on silica gel (CH_2Cl_2) gave the 3-acyl-2-thiazolone derivatives (**11**) in good yields.

3-[(1*S*,2*R*)-2-Methoxy-1-apocamphanecarbonyl]-2-thiazolone (11a: R=Me): This was obtained in 90% yield as colorless crystals, mp 46.5-48.0° C (from hexane), $[\alpha]_D^{27}$ -59.1 ° (*c* 1.0). ^{1}H-NMR, δ: 1.13 (3H s), 1.59 (3H s), 168 (1H s), 1.69-1.92 (5H, m), 3.18 (3H, s), 4.39 (1H, q, *J* = 3.66 Hz), 6.13 (1H, d, *J* = 6.10 Hz), 7.19 (1H, d, *J* = 5.49 Hz). *Anal*. Calcd for $C_{14}H_{19}NO_3S$: C, 59.76; H, 6.80; N, 4.97. Found: C, 59.89; H, 6.85; N, 4.79.

3-[(1*S*,2R)-2-Propoxy-1-apocamphanecarbonyl]-2-thiazolone (11b: R=Pr): This was obtained in 98% yield as colorless crystals, mp 48.0-49.0° C (from hexane), $[\alpha]_D^{27}$ –72.5 ° (*c* 1.0). ^{1}H-NMR, δ: 0.78 (3H, t, J=7.34 Hz), 1.15 (4H s), 1.30 (3H, s), 1.40-1.43 (2H, m), 1.57-1.70 (2H, m), 1.78-1.90 (3H, m), 2.30-2.35 (1H m), 3.09-3.13 (1H, m), 3.33-3.37 (1H, m), 4.41 (1H, q, *J* = 3.66 Hz), 6.12 (1H, d, *J* = 5.50 Hz), 7.18 (1H, d, *J* = 5.49 Hz). *Anal*. Calcd for $C_{16}H_{23}NO_3S$: C, 62.10; H, 7.81; N, 4.52. Found: C, 62.38, H, 7.58, N, 4.22.

3-[(1*S*,2*R*)-2-(2-Methoxyethoxy)-1-apocamphanecarbonyl]-2-thiazolone (11c: R=C_2H_4OMe): This

was obtained in 73% yield as pale yellow crystals, mp 55-56 °C (from hexane), $[\alpha]_D^{27}$ –69.5 ° (*c* 1.0). ^{1}H-NMR, δ: 1.15 (3H s), 1.31 (3H, s), 1.58 (1H, s), 1.67-1.94 (5H, m), 3.28 (3H, s), 3.37-3.39 (3H, m), 3.53-3.57 (1H, m), 4.47 (1H, dd, *J* = 3.66 Hz, *J'* = 7.93 Hz), 6.13 (1H, d, *J* = 5.49 Hz), 7.19 (1H, d, *J* = 5.50 Hz). *Anal*. Calcd for $C_{16}H_{23}NO_4S$: C, 59.05, H, 7.12, N, 4.3. Found: C, 58.92; H, 7.02; N, 4.07.

3-[(1*S*,2*R*)-2-Methoxyethoxyethoxy-1-apocamphanecarbonyl]-2-thiazolone (11d: R=$(C_2H_4O)_2$ Me): This was obtained in 76% yield as a colorless oil, $[\alpha]_D^{28}$ –58.0° (c 1.0). ^{1}H-NMR, δ: 1.14 (3H, s), 1.16-1.18 (1H, m), 1.67-1.72 (2H, m), 1.78-1.95 (3H, m), 2.25-2.30 (1H, m), 3.35 (3H, s), 3.36-3.39 (1H, m), 3.45-3.59 (7H, m), 4.46 (1H, dd, *J* = 3.66 Hz, *J'* = 4.37 Hz), 6.13 (1H, d, *J* = 6.10 Hz), 7.19 (1H, d, *J* = 5.49 Hz). HRMS, Calcd for $C_{18}H_{27}NO_5NaS$ (MNa^+) : m/z 392.1445. Found: m/z 392.1507.

3-[(1*S*,2*R*)-2-(2-Trichloroacetoxyethoxy)-1-apocamphanecarbonyl]-2-thiazolone (11e: R= $C_2H_4OCOCCl_3$): This was obtained in 83% yield as a colorless oil, $[\alpha]_D^{28}$ –55.1° (c 1.0). ^{1}H-NMR, δ: 1.13 (3H, s), 1.14-1.27 (1H, m), 1.30 (3H, s), 1.58-2.05 (5H, m), 2.25-2.30 (1H, m), 3.54-3.58 (1H, m), 3.68-3.72 (1H, m), 4.34-4.36 (2H, m), 4.59 (1H, dd, *J* = 3.66 Hz, *J'* = 7.93 Hz), 6.15 (1H, d, *J* = 6.60 Hz) 7.19 (1H, d, *J* = 6.60 Hz). HRMS, Calcd for $C_{17}H_{20}NO_5Cl_3S$ (MNa^+): m / z 454.0058. Found: m / z 454.0049.

(4*S*,5*S*)-5-Bromo-4-methoxy-3-(,2*R*-alkoxy-1*S*-apocamphanecarbonyl)-2-thiazolidinones (12, X=Br). ***General Procedure for Methoxybrominations*:** A solution of bromine (0.64 g, 4.0 mmol) in trimethyl orthoacetate (20 mL) was added dropwise over a period of 30 min to the 3-acyl-2-thiazolones (**11**) (3.5 mmol) in trimethyl orthoacetate (20 mL) at –78°C under an argon atmosphere. The mixture was quickly passed through a short silica gel column with CH_2Cl_2 as the eluent followed by evaporation of the eluate *in vacuo*. Chromatography on silica gel with CH_2Cl_2 gave the diastereomeric mixture of **12** and **13** (X=Br), the ratio of which was determined by HPLC analysis on a COSMOSIL column as well as ^{1}H-NMR (500 MHz) spectral analysis, based on the singlet peaks due to the C4-proton (Table 2).

Table 2. Chemical Shifts (δ) for Singlet Peak Assignable to the C4-Proton of 2-Thiazolidinones (**12**) and (**13**)

Compound		a	b	c	d	e
12(X=Br)	**δ**	5.92	6.05	6.03	6.02	5.99
13(X=Br)	**δ**	5.91	5.97	5.96	5.94	5.91
12(X=PhSe)	**δ**	5.67	5.77	5.76	5.73	5.69
13(X=PhSe)	**δ**	5.73	5.85	5.77	5.78	5.74

(4*S*,5*S*)-5-Bromo-4-methoxy-3-(2*R*-methoxy-1*S*-apocamphanecarbonyl)-2-thiazolidinone (12a, X=Br): This was obtained in 66% yield as colorless crystals, mp 84-85 °C (from hexane), $[\alpha]_D^{26}$ –136° (c 1.0). ^{1}H-NMR, δ: 1.20 (3H, s), 1.24 (3H, s), 1.56 (1H, s), 1.62 -1.67 (2H, m), 1.81-1.96 (3 H, m), 2.25-2.30 (1H, m), 3.21 (3H, s), 3.54 (3H, s), 4.05 (1H, dd, *J* = 3.66 Hz, *J'* = 4.27 Hz), 5.41 (1H, s), 5.92 (1H, s). *Anal.* Calcd for $C_{15}H_{22}NO_4BrS$: C, 45.92 ; H, 5.65 ; N, 3.57. Found: C, 45.78; H, 5.60; N, 3.45.

X-Ray Crystal Data: monoclinic, $P2_1$, a = 12.700 (7) Å, b = 10.468 (8) Å, c = 13.313 (6) Å, V = 1769 (1) Å, Z = 4, μ(MoKα) = 24.63 cm^{-1}, R = 0.17.

(4*S*,5*S*)-5-Bromo-4-methoxy-3-(2*R*-methoxyethoxy-1*S*-apocamphanecarbonyl)-2-thiazolidinone (12c, X=Br): This was obtained in 88 % yield as colorless crystals, mp 50-51 °C (from hexane), $[\alpha]_D^{26}$ –151° (c 1.0). ^{1}H-NMR, δ: 1.18 (3H, s), 1.29 (3Hs), 1.56 (1H, s), 1.65-1.96 (5H, m), 2.04-2.30 (1H, m), 3.33 (3H, s), 3.47-3.55 (4H, m), 4.29 (1H, t, *J* = 3.67 Hz), 5.42 (1H, s), 6.30 (1H, s). *Anal.* Calcd for $C_{17}H_{26}NO_5BrS$: C, 46.79; H, 6.01; N, 3.21. Found: C, 46.70; H, 6.11; N, 3.21.

(4*R*,5*R*)-4-Methoxy-3-[2*R*-alkoxy-1*S*-apocamphanecarbonyl]-5-phenylselenenyl-2-thiazolidinone (13, X=PhSe).

General Procedure for Methoxyselenenylation: Phenylselenenyl chloride (0.24 g, 1.0 mmol), dissolved in CH_2Cl_2 (1 mL), was added to a solution of 3-acyl-2-thiazolones (**11**) (0.5 mmol) in MeOH (1 mL) and CH_2Cl_2 (1 mL) at -50°C under an argon atmosphere and the resulting solution stirred for 48 h. The mixture was passed through a short silica gel column with CH_2Cl_2 as an eluent followed by concentration *in vacuo*. Chromatography on silica gel (CH_2Cl_2) gave a diastereomeric mixture of **12** and **13** (X=PhSe), the ratio of which was determined based on the singlet peaks assignable to the C4-proton in the ^{1}H-NMR (500 MHz) spectrum (Table 2).

(4*R*,5*R*)-4-Methoxy-3-(2*R*-methoxy-1*S*-apocamphanecarbonyl)-5-phenylselenenyl-2-thiazolidinone (13a, X=PhSe): This was obtained in 90% yield for the major isomer as pale yellow crystals, mp 85.5°C (from hexane), $[\alpha]_D^{28}$ -67.15° (*c* 1.0). ^{1}H-NMR, δ: 1.06 (3H, s), 1.36 (3H, s), 1.56 (1H, s), 1.64-1.74 (4H, m), 1.87-1.91 (2H, m), 3.22 (3H, s), 3.36 (3H, s), 4.33 (1H, dd, *J* = 3.66 Hz, *J'* = 4.27 Hz), 4.71 (1H, s), 5.73 (1H, s), 7.33-7.41 (3H, m), 7.61-7.62 (2H, m). *Anal.* Calcd for $C_{21}H_{27}NO_4SSe$: C, 53.96; H, 5.60; N, 3.05. Found: C, 53.84; H, 5.81; N, 2.99.

(4*R*,5*R*)-4-Methoxy-3-(2*R*-methoxyethoxy-1*S*-apocamphanecarbonyl)-5-phenylselenenyl-2-thiazolidinone (13c, X=PhSe): This was obtained in 81 % yield as colorless crystals, mp 73 °C (from hexane), $[\alpha]_D^{26}$ –37.5 ° (c 1.0). ^{1}H-NMR, δ: 1.07 (3H, s), 1.37 (3H, s), 1.57 (2H, s), 1.67-1.72 (3H, m), 1.86-1.90 (2H, m), 3.29 (3H, s), 3.34 (3H, s), 3.42-3.54 (2H, m), 3.55-3.58 (1H, m), 4.46 (1H, dd, *J* = 3.66 Hz, *J'* = 4.28 Hz), 4.70 (1H, s), 5.78 (1H, s) 7.35-7.40 (3H, m), 7.61-7.62 (2H, m). *Anal.* Calcd for

$C_{23}H_{31}NO_5SSe$: C, 53.89; H, 6.09; N, 2.73. Found: C, 54.00; H, 5.96; N, 2.78.

(4*S*,5*S*)-5-Allyl-4-methoxy2-thiazolidinone (14)

a) From **12a** (X=Br): A solution of compound (**12a**) (56 mg, 0.14 mmol) and allyltributylstannane (140 mg, 0.43 mmol) in benzene (1.4 mL) was refluxed in the presence of AIBN (7 mg) for 2 h under an argon atmosphere. Removal of the solvent *in vacuo* followed by chromatography on silica gel (CH_2Cl_2) gave (4*S*,5*S*)-5-allyl-4-methoxy-3-(2*R*-methoxy-1*S*-apocamphanecarbonyl)-2-thiazolidinone (36 mg, 74 %) as colorless crystals, mp 70.5-72 °C (from hexane), $[\alpha]_D^{26}$ +20.8° (c 0.9). ^{1}H-NMR, δ: 1.20 (3H, s), 1.21 (3H, s), 1.54 (1H, s), 1.55-1.64 (3H, m), 1.84-1.96 (2H, m), 2.24-2.29 (1H, m), 2.45-3.15 (2H, m), 3.18 (3H, d, *J* = 2.44 Hz), 3.47 (3H, d, *J* = 2.44 Hz), 4.01-4.03 (1H, m), 5.10-5.18 (2H, m), 5.58 (1H, s), 5.74-5.77 (1H, m). *Anal*. Calcd for $C_{18}H_{27}NO_4S$: C, 61.16; H, 7.70; N, 3.96. Found: C, 61.01; H, 7.85; N, 3.76.

The (4*S*,5*S*)-3-acyl-5-allyl-4-methoxy-2-thiazolidinone derivative thus obtained (0.56 g 1.6 mmol) was added to a solution of $PhCH_2SLi$, prepared from $PhCH_2SH$ (0.39 g, 3.2 mmol) and BuLi (0.10 g, 1.7 mmol) in THF (6 mL) at 0 °C under an argon atmosphere. It was gently refluxed for 2 h to complete the deacylation. The usual work-up followed by chromatographic purification on silica gel yielded compound (**14**) in 68 % yield as a colorless oil, $[\alpha]_D^{28}$ –195.1° (c 1.0), in addition to quantitative amounts of the benzyl thioester. ^{1}H-NMR, δ: 2.46-2.55 (2H, m), 3.35 (3H, s), 3.67 (1H, t, *J* = 7.34 Hz), 4.70 (1H, s), 5.11-5.20 (2H, m), 5.75-5.89 (1H, m), 7.87 (1H, br). HRMS, Calcd for $C_7H_{11}NO_2NaS$ (MNa^+): m/z 173.0523. Found: m/z 173.0510.

b) From **12c** (X=Br): Analogous to the above, the 5-allylation of compound (**12c**) gave (4*S*,5*S*)-5-allyl-4-methoxy-3-(2*R*-methoxyethoxy-1*S*-apocamphanecarbonyl)-2-thiazolidinone in 74 % yield as a colorless oil, $[\alpha]_D^{26}$ +10.5° (*c* 1.0). ^{1}H-NMR, δ: 1.18 (3H, s), 1.25 (3H, s), 1.60 (1H, s), 1.63-1.67 (2H, m), 1.80-1.92 (3H, m), 2.26-2.31 (1H, m), 2.46-2.57 (2H, m), 3.30 (3H, s), 3.43-3.51 (7H, m), 4.25 (1H, dd, *J* = 3.66 Hz, *J'* = 4.27 Hz), 5.13-5.20 (2H, m), 5.71 (1H, s), 5.77-5.79 (1H, m). HRMS, Calcd for $C_{20}H_{31}NO_5NaS$ (MNa^+): m/z 420.1820. Found: m/z 420.1796. Subsequent deacylation with $PhCH_2Li$ gave product **14** in 50 % yield.

(4*R*,5*R*)-5-Allyl-4-methoxy-2-thiazolidinone (15)

a) From **13a** (X=PhSe): Treatment of compound (**13a**) with allyltributyltin in the presence of AIBN gave (4*R*,5*R*)-5-allyl-4-methoxy-3-(2*R*-methoxy-1*S*-apocamphanecarbonyl)-2-thiazolidinone in 75 % yield as colorless crystals, mp 53-54 °C (from hexane), $[\alpha]_D^{24}$ –18.9 ° (c 1.0). ^{1}H-NMR, δ: 1.03 (3H, s), 1.36 (3H, s), 1.60 (1H, s), 1.64-1.74 (4H, m), 1.88 (1H, s), 2.01-2.03 (1H, m), 2.42-2.45 (2H, m), 3.24 (3H, s), 3.47 (3H, s), 4.41 (dd, 1H, *J* = 3.66 Hz, *J'* = 4.27 Hz), 5.17-5.18 (2H, m), 5.66 (1H, s), 5.78 (1H, dd, *J* = 10.37 Hz, *J'* = 6.72 Hz). *Anal*. Calcd for $C_{18}H_{27}NO_4S$: C, 61.16; H, 7.70; N, 3.96. Found: C, 61.24; H, 7.84; N,

3.94.

Subsequent deacylation with $PhCH_2SLi$ in THF gave compound (**15**) in 61 % yield as a colorless oil, $[\alpha]_D^{28}$ +194.6° (c 1.0). The ^{1}H-NMR (500 MHz) spectrum was identical with that of (4*S*,5*S*)-isomer (**14**).

b) From **13c** (X=PhSe): The allylation of compound (**13c**) (X=PhSe) as above gave (4*R*,5*R*)-5-allyl-4-methoxy-3-(2*R*-methoxyethoxy-1*S*-apocamphanecarbonyl)-2-thiazolidinone in 85% yield as a colorless oil, $[\alpha]_D^{28}$ -10.2° (*c* 1.0). ^{1}H-NMR, δ: 1.04 (3H, s), 1.38 (3H, s), 1.58 (1H, s), 1.63-1.73 (3H, m), 1.92-2.02 (2H, m), 2.24-2.45 (2H, m), 3.31 (3H, s), 3.43-3.50 (7H, m), 4.53 (1H, dd, *J* = 3.66 Hz, *J'* = 4.27 Hz), 5.13-5.18 (2H, m), 5.69 (1H, s), 5.77 (1H, dd, *J* = 10.37 Hz, *J'* = 6.72 Hz). HRMS, Calcd for $C_{20}H_{31}NO_5NaS$ (MNa^+): m/z 420.1820. Found: m/z 420.1768. Subsequent deacylation with $PhCH_2Li$ gave product (**15**) in 40 % yield.

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