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Conjugate addition of lithium ester enolates to 1-chlorovinyl *p*-tolyl sulfoxides: a novel synthesis of functionalized esters and lactones having a tertiary or a quaternary carbon at the β-position

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Abstract—Addition of the lithium ester enolates to 1-chlorovinyl *p*-tolyl sulfoxides, which were synthesized from chloromethyl *p*-tolyl sulfoxide and ketones or aldehydes, gave esters having a tertiary or a quaternary carbon at the 3-position, and chlorine and sulfinyl groups at the 4-position in high to quantitative yields. The adducts were converted to various esters having methyl, formyl, and hydroxycarbonyl groups at the 3-position. A novel method for the synthesis of γ-lactones, including spiro-type γ-lactones and α-methylene γ-lactones, was realized from the adducts in good overall yields. The scope and limitations of this method and the mechanism of the reactions are also discussed.

Carboxylic acids and their derivatives are obviously among the most important and fundamental compounds in organic, bioorganic, and synthetic organic chemistry. Innumerable studies on the chemistry and synthesis of carboxylic acids and their derivatives have already been reported; however, in view of the importance of these compounds in organic chemistry, development of new synthetic methods is still eagerly awaited.[1] On the other hand, construction of the quaternary carbon center has been a formidable task and a quite interesting challenge in synthetic organic chemistry in its own right.[2]

Recently, we reported several new synthetic methods starting from 1-chlorovinyl *p*-tolyl sulfoxides **2** derived from ketones and aldehydes **1**, and chloromethyl *p*-tolyl sulfoxide.[3] In continuation of our studies for the development of a new synthetic method by using 1-chlorovinyl *p*-tolyl sulfoxides, herein we report a novel method for the synthesis of carboxylic acid derivatives **4** having a tertiary or a quaternary carbon at the 3-position and lactones **5**, and α-methylene γ-lactones **6** via the adduct **3** of the vinyl sulfoxide **2** with lithium ester enolates (Scheme 1).[4]

1. Results and discussion

1.1. The reaction of 1-chlorovinyl *p*-tolyl sulfoxides with lithium enolate of *tert*-butyl acetate, ethyl acetate, *tert*-butyl propionate and *tert*-butyl hexanoate

In previous studies, we have found that cyanomethyllithium (lithium carbanion of acetonitrile) added to the 1-chlorovinyl *p*-tolyl sulfoxides **2** in high yields.[3c–e] We further investigated the reaction of **2** with carbon nucleophiles, and the lithium enolate of acetic acid esters was found to work excellently. The results are summarized in Table 1.

The reaction was conducted simply by adding a THF solution of **2** to a solution of the lithium enolate of *tert*-butyl acetate or ethyl acetate derived from the acetates with LDA in THF at −75°C. The addition reaction was quite fast and found to be completed within 5 min except entries 4, 6, and 7. The yields of the adducts **7** were from 70% to quantitative in all cases that the addition reaction took place. The result of the reaction with the lithium enolate of ethyl acetate was quite interesting (entry 4). In this case, the reaction of vinyl sulfoxide **2c** with the enolate of ethyl acetate at −75°C did not take place at all. However, using 3 equiv. of the enolate and allowing the temperature of the reaction to warm to 0°C, the desired adduct **7d** was obtained in 80% yield. At present we have no explanation for the difference in reactivity of ethyl and *tert*-butyl acetate. The adducts have two or three chiral centers and theoretically two or four diastereomers should be produced. In these reactions, only two cases

Keywords: carboxylic acid; spiro-lactone; α-methylene γ-lactone; quaternary carbon; sulfoxide.

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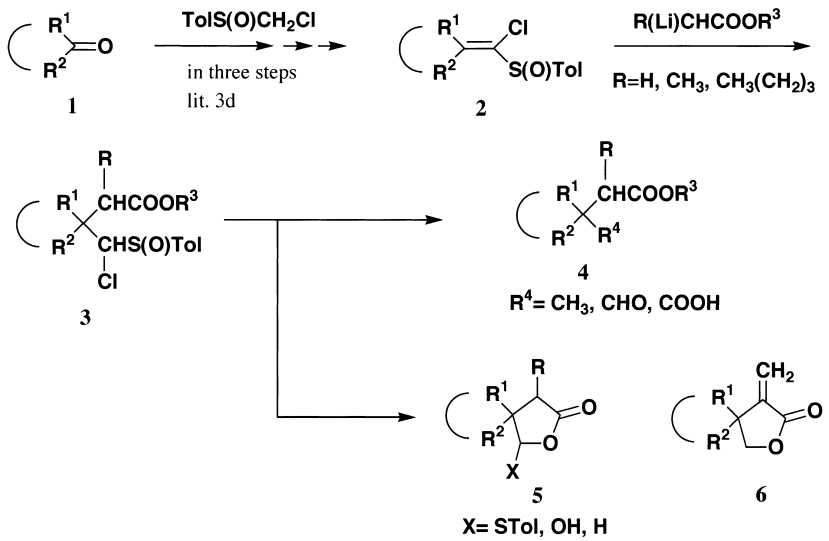


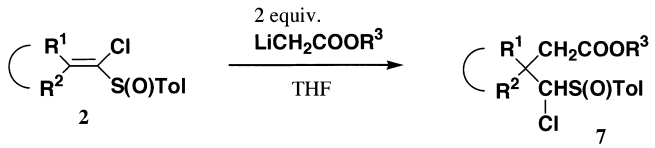
Scheme 1.

(entries 1 and 12) gave a mixture of the two diastereomers. All other adducts were obtained as a single isomer. This high stereoselectivity is quite interesting; however, we have no idea for the mechanism of the stereoselectivity of the reactions at present.

As shown in entries 1–9 in Table 1, the 1-chlorovinyl *p*-tolyl sulfoxides derived from ketones react with the lithium enolates of the acetate except entries 6 and 7. These results indicate that this procedure does not work when one or both of the substituents of the ketones are aromatic groups. Entries 10–12 show the results with the 1-chlorovinyl *p*-tolyl sulfoxides derived from aliphatic and aromatic aldehydes. These vinyl sulfoxides **2h** and **2i** gave the desired adducts **7g** and **7h**, respectively, in good yields even when one of the substituents is an aromatic ring. Entries 10 and 11 also indicate that this reaction shows no differences between two geometrical isomers.

Next, we were interested to see if this reaction would work with the higher homologue of the acetates. *tert*-Butyl propionate and *tert*-butyl hexanoate were selected as the esters and **2b**, **2c** and **2h**-*Z* as the 1-chlorovinyl *p*-tolyl sulfoxide. The results are summarized in Table 2.

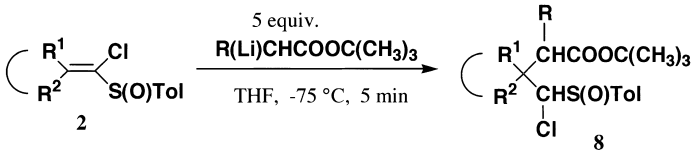
Table 1. Addition of lithium enolate of acetic acid esters to 1-chlorovinyl *p*-tolyl sulfoxides **2**



Entry	**2**	R^1	R^2	R^3	Conditions	**7**	Yield (%)
1	**2a**	—$(CH_2)_2C(CH_2)_2$— (O, O)		$C(CH_3)_3$	−75°C, 5 min	**7a**	99[a]
2	**2b**	$-(CH_2)_9-$		$C(CH_3)_3$	−75°C, 5 min	**7b**	97
3	**2c**	$-(CH_2)_{14}-$		$C(CH_3)_3$	−75°C, 5 min	**7c**	98
4	**2c**	$-(CH_2)_{14}-$		CH_2CH_3	−75–0°C, 1 h	**7d**	80[b]
5	**2d**	CH_3	CH_3	$C(CH_3)_3$	−75°C, 5 min	**7e**	99
6	**2e**	Ph	Ph	$C(CH_3)_3$	−75–0°C		0[c]
7	**2f**	CH_3	Ph	$C(CH_3)_3$	−75–0°C		0[c,d]
8	**2g**-*Z*	*n*-C_4H_9	CH_3	$C(CH_3)_3$	−75°C, 5 min	**7f**	97
9	**2g**-*E*	CH_3	*n*-C_4H_9	$C(CH_3)_3$	−75°C, 5 min	**7f**	72
10	**2h**-*Z*	$PhCH_2CH_2$	H	$C(CH_3)_3$	−75°C, 5 min	**7g**	99
11	**2h**-*E*	H	$PhCH_2CH_2$	$C(CH_3)_3$	−75°C, 5 min	**7g**	98
12	**2i**[e]	O, O	H	$C(CH_3)_3$	−75°C, 5 min	**7h**	95[f]

[a] The adduct **7a** was a mixture of two diastereomers; the ratio was 83:16. All other adducts (**7b**–**7g**) except **7h** were a single product.
[b] Three equivalents of lithium enolate of ethyl acetate was used.
[c] No reaction was observed.
[d] *E*-Isomer was used in this study.
[e] A mixture of *E*- and *Z*-isomers was used in this study.
[f] The adduct **7h** was a mixture of two diastereomers; the ratio was about 1:2.

Table 2. Addition of lithium enolate of *t*-butyl propionate and *t*-butyl hexanoate to 1-chlorovinyl *p*-tolyl sulfoxides **2**



Entry	2	R^1	R^2	R	8	Yield (%)
1	**2b**	$-(CH_2)_9-$		CH_3	**8a**	98
2	**2b**	$-(CH_2)_9-$		$CH_3CH_2CH_2CH_2$	**8b**	96[a]
3	**2c**	$-(CH_2)_{14}-$		CH_3	**8c**	95
4	**2c**	$-(CH_2)_{14}-$		$CH_3CH_2CH_2CH_2$	**8d**	71
5	**2h**-*Z*	$PhCH_2CH_2$	H	CH_3	**8e**	93
6	**2h**-*Z*	$PhCH_2CH_2$	H	$CH_3CH_2CH_2CH_2$	**8f**	93[b]

[a] The ester enolate of *t*-butyl hexanoate (7.4 equiv.) was used.
[b] The ester enolate of *t*-butyl hexanoate (10 equiv.) was used.

First, the reaction was conducted in the same way as described above (2 equiv. of the lithium enolate of the esters were used); however, under these conditions the reaction did not complete. Finally, use of over 5 equiv. of the esters gave good results. As shown in Table 2, the reaction with *tert*-butyl hexanoate was found to require additional amount of the ester enolate for completion.

1.2. Transformation of the adducts 7 and 8 to compounds that are of interest in organic chemistry

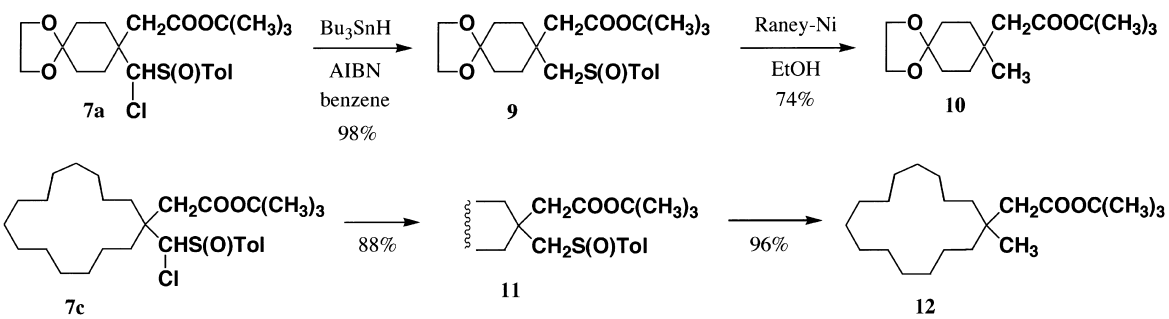
The adducts **7** and **8** (see Tables 1 and 2) are very interesting compounds in organic chemistry. First, the adducts have a tertiary or a quaternary carbon at the 3-position. Second, they have a highly functionalized carbon at the 4-position. By chemical modification of the carbon, the adducts **7** and **8** would be converted to various kinds of carboxylic acid derivatives. Based on this expectation, we investigated the chemistry of the adducts, and quite interesting results were obtained.

At first, transformation of the carbon having a chlorine atom and a sulfinyl group to a methyl group was investigated by using **7a** and **7c** as representative substrates (Scheme 2). Reduction of the chlorine atom of **7a** was successfully carried out under radical dehalogenation conditions[5] to give a sulfoxide **9** in a quantitative yield. Reduction of the sulfinyl group of **9** was easily carried out with Raney nickel W-2[6] in refluxing ethanol to afford the desired product **10** having the methyl group in good yield. In a similar way, the adduct **7c** gave the reduced product **12** in two steps in high overall yield via **11** without any problem.

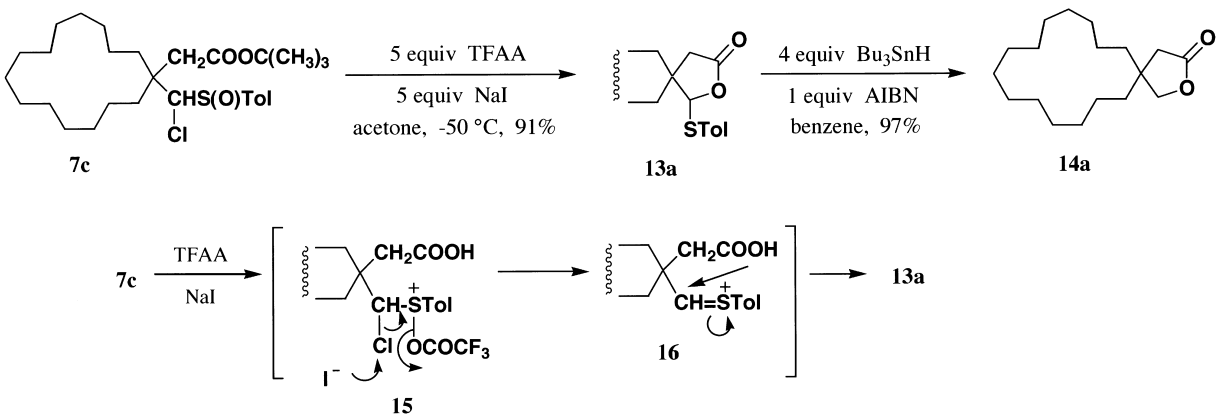
Next, we investigated the transformation of the carbon having the sulfinyl group to an aldehyde. As we have recognized that α-chlorinated sulfoxides are quite stable to an acid or a base, we tried to reduce the sulfoxide to sulfide. If this reduction would work, the obtained α-chlorosulfides have been known to be easily converted to aldehydes.[7] In some known reactions for the reduction of sulfoxide,[8] we tried to reduce **7c** with trifluoroacetic anhydride (TFAA) in the presence of NaI in acetone.[8c] Quite clean reaction took place to afford the unexpected spiro-γ-lactone **13a** having a tolylsulfanyl group at the 4-position in high yield (Scheme 3).

The presumed mechanism of this quite interesting reaction is shown in Scheme 3. First, the reaction of the sulfoxide **7c** gives an acyloxysulfonium ion.[9] At the same time, the *tert*-butyl ester is eliminated by trifluoroacetic acid to give carboxylic acid **15**. The iodide anion, then, attacks the chlorine atom to give thionium ion **16**. The oxygen of the carboxylic acid attacks intramolecularly the thionium ion[9d] to afford the spiro-lactone **13a**. Desulfurizaion of the tolylsulfanyl group of **13a** was successufully carried out with Bu_3SnH in the presence of 2,2′-azobisisobutyronitrile (AIBN)[10] to give the spiro-γ-lactone **14a** in quantitative yield.

This is a quite novel and good method for synthesis of γ-lactones, including a spiro-type, from ketones and



Scheme 2. Transformation of the 4-position of the adducts **7a** and **7c** to methyl group.



Scheme 3. Treatment of the adduct **7c** with TFAA and sodium iodide to give the spiro-lactone **13a** and a plausible mechanism.

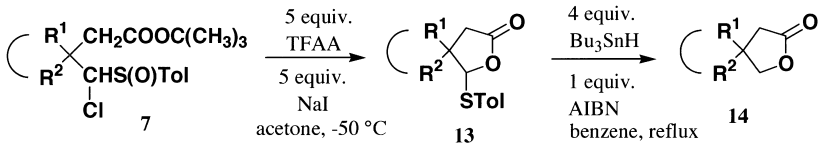
aldehydes via the adducts **7**. We investigated this procedure for the synthesis of lactones **14** with other adducts (**7a**, **7b**, and **7g**) and the results are summarized in Table 3. As shown in the table, the reaction gave the desired lactones **13** in good yields; however, in some cases the aldehydes (**17a** and **17b**) were obtained as by-products (entries 1 and 3). The reductive desulfurization took place without problem, but yields were found to be variable.

The spiro-lactone of the higher oxidation state (**19**) than **14a** was synthesized from **13a** via the sulfoxide **18** (Scheme 4). Thus, the sulfide **13a** was oxidized with *m*-chloroperbenzoic acid (*m*-CPBA) at −40°C to give the sulfoxide **18** as a mixture of two diastereoisomers in good yield. Treatment of the sulfoxide with TFAA in acetone gave the desired lactone having a hydroxyl group at the 4-position **19** through the Pummerer rearrangement.

Next, we investigated conversion of the carbon bearing the chlorine and the sulfinyl group to an aldehyde group (Scheme 4). As mentioned above, as the *tert*-butyl ester is easily eliminated by TFAA, we used the ethyl ester **7d**. Treatment of the ethyl ester **7d** with TFAA–NaI in the absence of a base gave the desired **20** in 60% yield; however, about 20% of the lactone **13a** was still present. We further investigated this reaction and found that excess organic base worked to give the desired aldehyde **20** in 85% yield without the lactone **13a**.

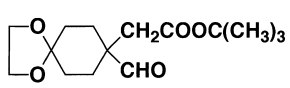
The mechanism of this reaction was presumed as shown in Scheme 4. By the same reaction as above, **7d** gave thionium ion **23** through **22**. As this reaction was carried out in the presence of excess organic base, and the ethyl ester was used, the ester remained unaffected by TFAA. Trifluoroacetic acid added to the thionium ion **23** to afford the sulfide

Table 3. Reaction of the adducts **7** with TFAA and sodium iodide to give γ-lactones having tolylthio group **13** and reductive desulfurization of **13** with tributyltin hydride to give **14**



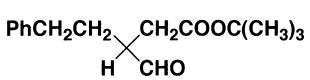
Entry	7	R^1	R^2	13	Yield (%)	14	Yield (%)
1	**7a**	—(CH2)2C(CH2)2— (O O)		**13b**	85[a]	**14b**	81
2	**7b**	–$(CH_2)_9$–		**13c**	83	**14c**	91
3	**7g**	$PhCH_2CH_2$	H	**13d**	65[b]	**14d**	62

[a] The aldehyde **17a** (15%) was also obtained.

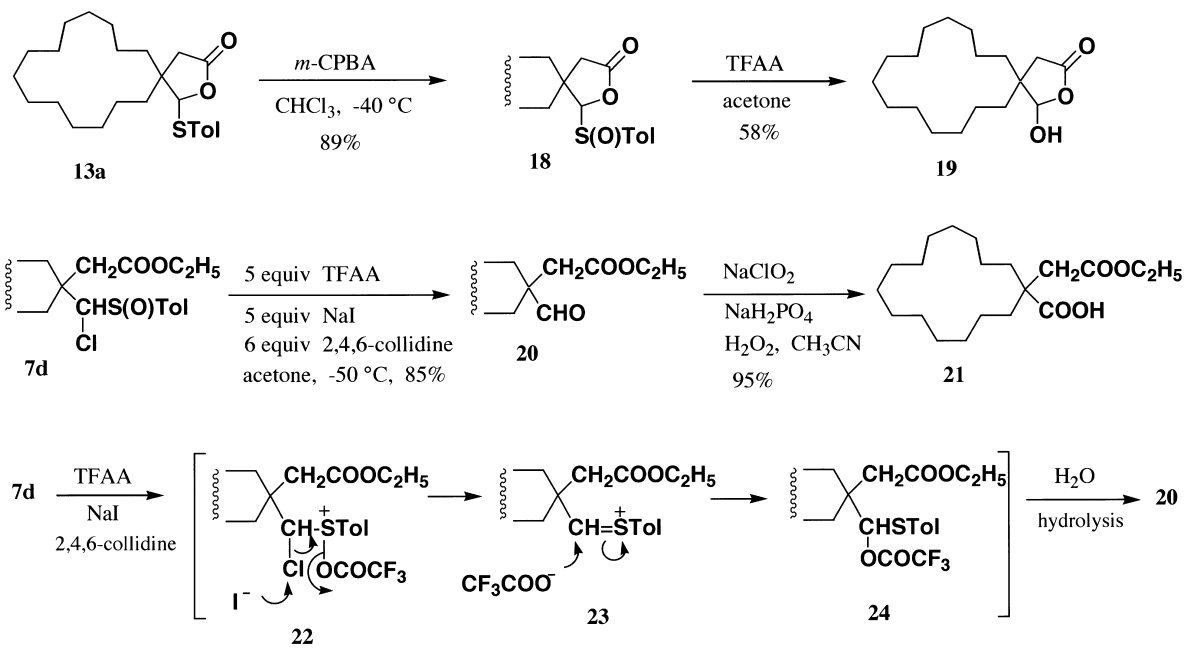


17a

[b] The aldehyde **17b** (30%) was also obtained.



17b



Scheme 4. Synthesis of various carboxylic acid derivatives.

having a trifluoroacetoxy group **24** on the same carbon, which was hydrolyzed in the work-up process to give the aldehyde **20**. Oxidation of this aldehyde **20** was carried out with $NaClO_2$[11] to give the desired carboxylic acid **21** in quantitative yield.

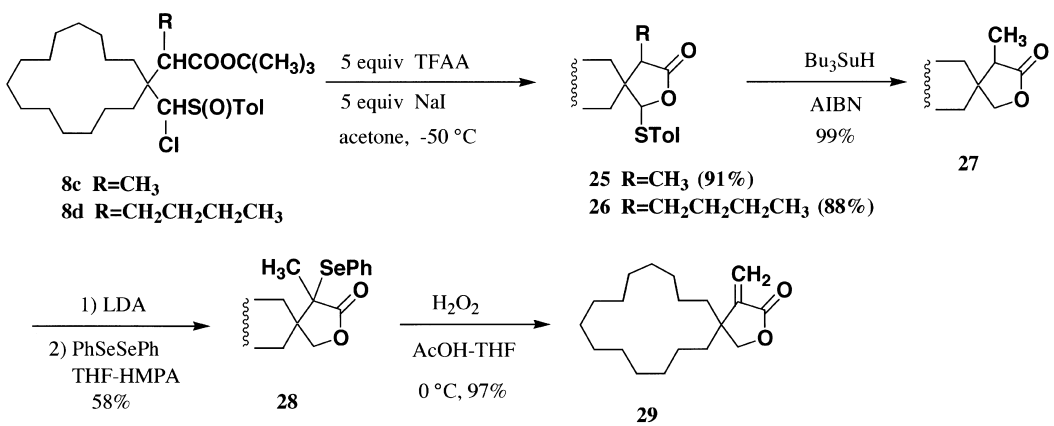
1.3. Synthesis of lactones, including α-methylene γ-lactones, from the adducts of the 1-chlorovinyl *p*-tolyl sulfoxides with *t*-butyl propionate and *t*-butyl hexanoate

Finally, we investigated conversion of the adducts of 1-chlorovinyl *p*-tolyl sulfoxides with the lithium enolate of the esters other than acetates to synthetically interesting compounds. The α-mthylene γ-lactone moiety is a quite interesting skeletal structure which often appears in biologically active terpenes and terpenoids.[12] As an extension of our new synthetic method we planned to synthesize a spiro-type α-methylene γ-lactone from the adduct with the lithium enolate of *tert*-butyl propionate (Scheme 5).

The lactonization of the adduct **8c** was carried out under the same conditions as described for the synthesis of **13a** to give the desired γ-lactone having a methyl group at the 2-position and a *p*-tolylsulfanyl group at the 4-position **25** in high yield. The reductive desulfurization of **25** also took place smoothly to give the desired lactone **27** in quantitative yield. Selenenylation[13] of the lactone **27** gave the α-seleno lactone **28** in 58% yield. Oxidation of the selenenyl group of **28** with hydrogen peroxide followed by syn-elimination[14] afforded the desired spiro-α-methylene γ-lactone **29** in quantitative yield.

The lactonization was found to take place with the higher homologue **8d** to give the lactone **26** in 88% yield without any problem.

In conclusion, we have developed a novel and versatile procedure for the synthesis of carboxylic acid derivatives having a tertiary or a quaternary carbon at the 3-position from 1-chlorovinyl *p*-tolyl sulfoxides with several esters.



Scheme 5. Synthesis of spiro-type α-methylene γ-lactone **29** from the adduct **8c**.

These carboxylic acid derivatives, in addition, have various kinds of functional groups with a different oxidation state at the 4-position. The novel synthesis of γ-lactones including α-methylene γ-lactone also was realized.

2. Experimental

2.1. General

All melting points are uncorrected. ^{1}H NMR spectra were measured in a $CDCl_3$ solution with JEOL JNM-LA 400 and 500 spectrometer. Electron-impact mass spectra (MS) were obtained at 70 eV by direct insertion. Silical gel 60 (Merck) containing 0.5% fluorescence reagent 254 and quartz column were used for column chromatography and the products having UV absorption were detected by UV irradiation. In experiments requiring a dry reagent and solvent, diisopropylamine, HMPA, 2,4,6-collidine, and benzene were distilled from CaH_2 and THF was distilled from diphenylketyl. Acetone was dried over $CaSO_4$ and distilled before use. 1-Chlorovinyl *p*-tolyl sulfoxides **2** used in this study were synthesized from the corresponding ketones or aldehydes and chloromethyl *p*-tolyl sulfoxide as reported before.[3d]

2.1.1. *tert*-Butyl {8-[chloro(*p*-tolylsulfinyl)methyl]-1,4-dioxaspiro[4.5]dec-8-yl}acetate (7a). *tert*-Butyl acetate (0.04 ml; 0.3 mmol) was added to a solution of LDA (0.3 mmol) in 4 ml of dry THF at −78°C with stirring. The solution was stirred for 10 min, then a solution of **2a** (49 mg; 0.15 mmol) in THF (1 ml) was added. The solution was stirred for 5 min, then the reaction was quenched by adding sat. aq. NH_4Cl. The whole was extracted with hexane–AcOEt. The products (less polar product **7a-L**, and more polar product **7a-P**) were purified and separated by silica gel column chromatography to afford **7a-L** (55.2 mg; 83%) and **7a-P** (10.6 mg; 16%). **7a-L**: Colorless crystals; mp 108–111°C (hexane). IR (KBr) 2977, 1707 (CO), 1458, 1364, 1168, 1064, 940, 813 cm^{-1}; ^{1}H NMR δ 1.47 (9H, s), 1.7–2.3 (8H, m), 2.42 (3H, s), 2.75, 3.27 (each 1H, d, *J*=15.4 Hz), 3.96 (4H, s), 5.31 (1H, s), 7.31, 7.74 (each 2H, d, *J*=8.0 Hz). MS *m/z* (%) 442 (M^+, 1.3), 369 (15), 247 (58), 211 (59), 140 (100), 99 (43), 57 (49). Calcd for $C_{22}H_{31}ClO_5S$: *M*, 442.1581. Found: *m/z* 442.1560. Anal. Calcd for $C_{22}H_{31}ClO_5S$: C, 59.65; H, 7.05; Cl, 8.00; S, 7.24. Found: C, 59.89; H, 6.89; Cl, 8.08; S, 7.37. **7a-P**: Colorless crystals; mp 153–155°C (hexane). IR (KBr) 2936, 1701 (CO), 1438, 1366, 1217, 1152, 1105, 1064, 814 cm^{-1}; ^{1}H NMR δ 1.46 (9H, s), 1.7–2.3 (8H, m), 2.41 (3H, s), 2.90 (2H, s), 3.95 (4H, s), 5.02 (1H, s), 7.33, 7.55 (each 2H, d, *J*=8.3 Hz). MS *m/z* (%) 443 ($[M+H]^+$, trace), 369 (30), 247 (100), 211 (99), 140 (100), 99 (63). Calcd for $C_{22}H_{32}ClO_5S$: *M*, 443.1659. Found: *m/z* 443.1666. Anal. Calcd for $C_{22}H_{31}ClO_5S$: C, 59.65; H, 7.05: Cl, 8.00; S, 7.24. Found: C, 59.86; H, 6.87; Cl, 7.96; S, 7.24.

2.1.2. *tert*-Butyl {1-[chloro(*p*-tolylsulfinyl)methyl]cyclodecyl}acetate (7b). Colorless oil; IR (neat) 2926, 1722 (CO), 1484, 1446, 1366, 1150, 1054, 811, 756 cm^{-1}; ^{1}H NMR δ 1.46 (9H, s), 1.5–1.9 (16H, m), 2.06 (1H, m), 2.19 (1H, m), 2.39 (3H, s), 2.46 (1H, d, *J*=15.9 Hz), 3.05 (1H, d, *J*=15.9 Hz), 5.29 (1H, s), 7.31, 7.73 (each 2H, d, *J*=7.7 Hz). MS *m/z* (%) 440 (M^+, 1.3), 367 (99), 245 (99), 209 (100), 140 (100). Calcd for $C_{24}H_{37}ClO_3S$: *M*, 440.2152. Found: *m/z* 440.2160.

2.1.3. *tert*-Butyl {1-[Chloro(*p*-tolylsulfinyl)methyl]cyclopentadecyl}acetate (7c). Colorless oil; IR (neat) 2929, 1721 (CO), 1362, 1146, 1052, 760 cm^{-1}; ^{1}H NMR δ 1.3–1.6 (28H, m), 1.46 (9H, s), 2.41 (3H, s), 2.50, 3.09 (each 1H, d, *J*=15.6 Hz), 5.27 (1H, s), 7.30, 7.74 (each 2H, d, *J*=8.3 Hz). MS *m/z* (%) 510 (M^+, 0.3) 279 (38), 219 (40), 140 (100), 57 (54). Calcd for $C_{29}H_{47}ClO_3S$: *M*, 510.2934. Found: *m/z* 510.2939.

2.1.4. Ethyl {1-[chloro(*p*-tolylsulfinyl)methyl]cyclopentadecyl}acetate (7d). Ethyl acetate (0.146 ml; 1.5 mmol) was added to a solution of LDA (1.5 mmol) in 4 ml of dry THF at −78°C with stirring. The solution was stirred for 10 min, then a solution of **2c** (197.6 mg; 0.5 mmol) in THF (1 ml) was added. The solution was stirred for 5 min. The temperature of the reaction mixture was gradually allowed to warm to 0°C. The reaction was quenched by adding sat. aq. NH_4Cl. The whole was extracted with hexane–AcOEt. The product was purified by silica gel column chromatography to afford **7d** (194 mg; 80%) as a colorless oil; IR (neat) 2929, 1730 (CO), 1461, 1180, 1056, 811, 723 cm^{-1}; ^{1}H NMR δ 0.88 (3H, t, *J*=6.8 Hz), 1.2–1.4 (28H, m), 2.42 (3H, s), 2.59, 3.19 (each 1H, d, *J*=15.6 Hz), 4.15 (2H, dq, *J*=8.0, 1.7 Hz), 5.26 (1H, s), 7.31, 7.73 (each 2H, *J*=8.3 Hz). MS *m/z* (%) 483 ($[M+H]^+$, 0.6), 437 (11), 343 (67), 307 (82), 261 (41), 219 (100), 140 (26), 95 (30), 81 (31). Calcd for $C_{27}H_{44}ClO_3S$: *M*, 483.2699. Found: *m/z* 483.2692.

2.1.5. *tert*-Butyl 4-chloro-3,3-dimethyl-4-(*p*-tolylsulfinyl)butyrate (7e). Colorless oil; IR (neat) 2976, 1722 (CO), 1471, 1368, 1227, 1144, 1055, 812, 756 cm^{-1}; ^{1}H NMR δ 1.32 (3H, s), 1.45 (3H, s), 1.46 (9H, s), 2.41 (3H, s), 2.54, 2.92 (each 1H, d, *J*=15.6 Hz), 5.09 (1H, s), 7.31, 7.72 (each 2H, d, *J*=8.6 Hz). MS *m/z* (%) 344 (M^+, trace), 271 (17), 140 (100), 113 (21), 92 (16), 57 (55). Calcd for $C_{17}H_{25}ClO_3S$: *M*, 344.1213. Found: *m/z* 344.1219.

2.1.6. *tert*-Butyl 3-[chloro(*p*-tolylsulfinyl)methyl]-3-methylheptanoate (7f). Colorless oil; IR (neat) 2961, 2934, 1728 (CO), 1456, 1368, 1216, 1143, 1056, 812 cm^{-1}; ^{1}H NMR δ 0.91 (3H, t, *J*=7.0 Hz), 1.2–1.4 (4H, m), 1.42 (3H, s), 1.45 (9H, s), 1.68–1.71 (2H, m), 2.41 (3H, s), 2.69, 2.94 (each 1H, d, *J*=15.6 Hz), 5.08 (1H, s), 7.31, 7.73 (each 2H, d, *J*=8.0 Hz). MS *m/z* (%) 386 (M^+, trace), 313 (14), 191 (11), 140 (100), 57 (33). Calcd for $C_{20}H_{31}ClO_3S$: *M*, 386.1682. Found: *m/z* 386.1686.

2.1.7. *tert*-Butyl 3-[chloro(*p*-tolylsulfinyl)methyl]-5-phenylpentanoate (7g). Colorless crystals; mp 83–84°C (hexane); IR (KBr) 2978, 2930, 1731 (CO), 1455, 1368, 1257, 1151, 1055, 812 cm^{-1}; ^{1}H NMR δ 1.46 (9H, s), 1.8–2.0 (2H, m), 2.39 (1H, q, *J*=7.1 Hz), 2.44 (3H, s), 2.66 (2H, t, *J*=8.3 Hz), 2.8–2.9 (1H, m), 3.0–3.1 (1H, m), 4.46 (1H, d, *J*=2.2 Hz), 7.1–7.2 (3H, m), 7.2–7.3 (2H, m), 7.33, 7.63 (each 2H, d, *J*=8.3 Hz). MS *m/z* (%) 420 (M^+, trace), 347 (10), 207 (10), 188 (29), 140 (69), 129 (37), 91 (100), 57 (22). Calcd for $C_{23}H_{29}ClO_3S$: *M*, 420.1526. Found: *m/z* 420.1573. Anal. Calcd for $C_{23}H_{29}ClO_3S$: C, 65.62; H, 6.94; Cl, 8.42; S, 7.62. Found: C, 65.71; H, 6.8; Cl, 8.51; S, 7.72.

2.1.8. *tert*-Butyl 3-(3,4-methylenedioxyphenyl)-4-chloro-4-(*p*-tolylsulfinyl)butyrate (7h). Colorless oil (about 1:2 diastereomeric mixture); IR (neat) 2979, 1728 (CO) 1491, 1252, 1150, 1042, 757 cm^{-1}; ^1H NMR δ 1.30 (3H, s), 1.34 (6H, s), 2.42 (3H, s), 2.74–3.07 (2H, m), 4.48 (0.32H, d, J=2.8 Hz), 4.63 (0.63H, d, J=3.1 Hz), 5.94 (0.63H, s), 5.98 (1.25H, s), 6.75–7.64 (7H, m). MS m/z (%) 436 (M^+, 1.4), 384 (7), 363 (7), 328 (10), 241 (23), 204 (41), 140 (67), 91 (17), 57 (100). Calcd for $C_{22}H_{25}ClO_5S$: M, 436.1111. Found: m/z 436.1105.

2.1.9. *tert*-Butyl 2-{1-[chloro(*p*-tolylsulfinyl)methyl]-cyclodecyl}propionate (8a). Colorless oil; IR (neat) 2926, 1725 (CO), 1484, 1445, 1367, 1148, 1057, 811, 755 cm^{-1}; ^1H NMR δ 1.34 (3H, d, J=7.0 Hz), 1.47 (9H, s), 1.5–1.7 (12H, m), 1.8–2.1 (5H, m), 2.15 (1H, m), 2.43 (3H, s), 3.01 (1H, q, J=7.0 Hz), 4.54 (1H, s), 7.32, 7.70 (each 2H, d, J=8.0 Hz). MS m/z (%) 455 ($[M+H]^+$, trace), 381 (8), 259 (17), 223 (55), 140 (100), 95 (33), 57 (74). Calcd for $C_{25}H_{40}ClO_3S$: M, 455.2386. Found m/z 455.2400.

2.1.10. *tert*-Butyl 2-{1-[chloro(*p*-tolylsulfinyl)methyl]cyclodecyl}hexanoate (8b). Colorless oil; IR (neat) 2928, 1724 (CO), 1484, 1455, 1367, 1149, 1082, 1056, 811, 756 cm^{-1}; ^1H NMR δ 0.85–1.92 (24H, m), 0.92 (3H, t, J=7.3 Hz), 1.49 (9H, s), 2.42 (3H, s), 2.86 (1H, t, J= 7.6 Hz), 4.48 (1H, s), 7.31, 7.70 (each 2H, d, J=8.0 Hz). MS m/z (%) 497 ($[M+H]^+$, trace), 301 (28), 265 (65), 247 (22), 219 (22), 140 (100), 139 (30), 81 (26), 57 (63). Calcd for $C_{28}H_{46}ClO_3S$: M, 497.2816. Found: m/z 497.2861.

2.1.11. *tert*-Butyl 2-{1-[chloro(*p*-tolylsulfinyl)methyl]cyclopentadecyl}propionate (8c). Colorless oil; IR (neat) 2929, 1727 (CO), 1459, 1369, 1241, 1150, 1059 cm^{-1}; ^1H NMR δ 1.37 (3H, d, J=7.1 Hz), 1.2–1.4 (28H, m), 1.47 (9H, s), 2.43 (3H, s), 3.03 (1H, q, J=7.1 Hz), 4.60 (1H, s), 7.35, 7.71 (each 2H, d, J=8.3 Hz). MS m/z (%) 525 ($[M+H]^+$, 1), 451 (24), 329 (80), 293 (100), 275 (43), 219 (100), 140 (100), 95 (40), 57 (100). Calcd for $C_{30}H_{50}ClO_3S$: M, 525.3169. Found: m/z 525.3185.

2.1.12. *tert*-Butyl 2-{1-[chloro(*p*-tolylsulfinyl)methyl]-cyclopentadecyl}hexanoate (8d). Colorless oil; IR (neat) 2929, 1727 (CO), 1462, 1367, 1148, 1059 cm^{-1}; ^1H NMR δ 0.93 (3H, t, J=7.3 Hz), 1.2–1.5 (28H, m), 1.48 (9H, s), 1.67 (2H, d, J=10 Hz), 1.7–1.9 (4H, m), 2.10 (1H, m), 2.43 (3H, s), 4.53 (1H, s), 7.31, 7.71 (each 2H, d, J=8.0 Hz). MS m/z (%) 567 ($[M+H]^+$, trace), 493 (21), 371 (69), 335 (100), 289 (45), 267 (19), 219 (100), 140 (100), 57 (100).

2.1.13. *tert*-Butyl 3-[chloro(*p*-tolylsulfinyl)methyl]-2-methyl-5-phenylpentanoate (8e). Colorless oil; IR (neat) 2977, 2934, 1726 (CO), 1597, 1454, 1367, 1149, 1055, 812, 753 cm^{-1}; ^1H NMR δ 1.42 (3H, d, J=7.0 Hz), 1.45 (9H, s), 2.0–2.1 (2H, m), 2.47 (3H, s), 2.73 (2H, t, J=7.4 Hz), 2.84 (1H, m), 2.91 (1H, quint, J=7.1 Hz), 4.56 (1H, d, J=3.1 Hz), 7.2–7.3 (7H, m), 7.62 (2H, d, J=8.3 Hz). MS m/z (%) 434 (M^+, trace), 361 (15), 203 (23), 157 (26), 140 (100), 129 (53), 91 (68). Calcd for $C_{24}H_{31}ClO_3S$: M, 434.1682. Found: m/z 434.1686.

2.1.14. *tert*-Butyl 2-{1-[Chloro(*p*-tolylsulfinyl)methyl]-3-phenylpropyl}hexanoate (8f). Colorless oil; IR (neat) 2958, 2931, 1725 (CO), 1597, 1455, 1367, 1149, 1055, 812 cm^{-1}; ^1H NMR δ 0.90 (3H, t, J=7.0 Hz), 1.44 (9H, s), 1.64–1.67 (1H, m), 1.78–1.80 (1H, m), 2.44 (3H, s), 2.57–2.63 (1H, m), 2.67–2.73 (1H, m), 2.80–2.82 (2H, m), 4.46 (1H, d, J=1.9 Hz), 7.1–7.3 (7H, m), 7.65 (2H, d, J=8.2 Hz). MS m/z (%) 476 (M^+, trace), 403 (13), 281 (13), 245 (40), 199 (22), 140 (100), 129 (67), 91 (90), 57 (96). Calcd for $C_{27}H_{37}ClO_3S$: M, 476.2125. Found: m/z 476.2149.

2.1.15. *tert*-Butyl {[8-(*p*-tolylsulfinyl)methyl]-1,4-dioxaspiro[4.5]dec-8-yl}acetate (9). AIBN (9.8 mg; 0.06 mmol) was added to a solution of **7a** (88.6 mg; 0.2 mmol) and Bu_3SnH (0.083 ml; 0.3 mmol) in 4 ml of dry benzene. The atmosphere in the flask was replaced with Ar, and the reaction mixture was stirred and refluxed for 20 min. The benzene was evaporated, and the residue was purified by silica gel column chromatography to give 9 (80.4 mg; 98%) as a colorless oil; IR (neat) 2935, 1716 (CO), 1367, 1246, 1147, 1106, 1043, 813 cm^{-1}; ^1H NMR δ 1.45 (9H, s), 1.5–2.0 (8H, m), 2.41 (3H, s), 2.64, 2.75 (each 1H, d, J=14.8 Hz), 2.96, 3.07 (each 1H, d, J=13.9 Hz), 3.96 (4H, s), 7.32, 7.57 (each 2H, d, J=7.0 Hz). MS m/z (%) 408 (M^+, trace), 392 (13), 335 (24), 213 (100), 151 (23), 123 (22), 99 (38). Calcd for $C_{22}H_{32}O_5S$: M, 408.1986. Found: m/z 408.1978.

2.1.16. *tert*-Butyl (8-methyl-1,4-dioxaspiro[4.5]dec-8-yl)acetate (10). A solution of **9** (71 mg; 0.17 mmol) and excess of Raney-Ni in 8 ml of EtOH was stirred and refluxed for 15 min. The Raney Ni was filtered off, and the filtrate was evaporated to give a residue, which was purified by silica gel column chromatography to afford **10** (37.0 mg; 74%) as a colorless oil; IR (neat) 2951, 1727 (CO), 1366, 1257, 1159, 1107 cm^{-1}; ^1H NMR δ 1.06 (3H, s), 1.44 (9H, s), 1.5–1.7 (8H, m), 2.17 (2H, s), 3.93 (4H, s). MS m/z (%) 270 (M^+, 1.7), 197 (8), 99 (100), 86 (13), 57 (5). Calcd for $C_{15}H_{26}O_4$: M, 270.1829. Found: m/z 270.1836.

2.1.17. *tert*-Butyl {1-[(*p*-tolylsulfinyl)methyl]cyclopentadecyl}acetate (11). Colorless oil; IR (neat) 2932, 1718 (CO), 1143, 1042 cm^{-1}; ^1H NMR δ 1.2–1.4 (28H, m), 1.45 (9H, s), 2.40 (3H, s), 2.57, 2.67 (each 1H, d, J=15.0 Hz). 2.90, 3.02 (each 1H, d, J=14.0 Hz), 7.31, 7.60 (each 2H, d, J=7.9 Hz). MS m/z (%) 476 (M^+, 2), 281 (100), 140 (70), 57 (40). Calcd for $C_{29}H_{48}O_3S$: M, 476.3324. Found: m/z 476.3313.

2.1.18. *tert*-Butyl (1-methylcyclopentadecyl)acetate (12). Colorless oil; IR (neat) 2930, 1727 (CO), 1461, 1367, 1258, 1140 cm^{-1}; ^1H NMR δ 0.97 (3H, s), 1.2–1.3 (28H, m), 1.44 (9H, s), 2.07 (2H, s). MS m/z (%) 338 (M^+, 4), 282 (20), 222 (100), 57 (42). Calcd for $C_{22}H_{42}O_2$: M, 338.3185. Found: m/z 338.3194.

2.1.19. 1-(*p*-Tolylsulfanyl)-2-oxaspiro[4.14]nonadecan-3-one (13a). TFAA (0.66 ml; 3.35 mmol) was added dropwise with stirring to a suspension of **7c** (344.2 mg; 0.67 mmol) and NaI (508 mg; 3.35 mmol) in 5 ml of dry acetone at −55°C. The reaction mixture turned from yellow to black-green in color. The reaction mixture was stirred at −55°C for 5 min and the reaction was quenched by sat. aq. $NaHCO_3$ and sat. aq. Na_2SO_3. The whole was extracted with

ether–benzene. The organic layer was washed with sat. aq. $NaHCO_3$ and dried over $MgSO_4$. The solvent was evaporated, and the residue was purified by silica gel column chromatography to give **13a** (247 mg; 91%) as a colorless oil; IR (neat) 2930, 1790 (CO), 1459, 1155, 958, 812 cm^{-1}; ^1H NMR δ 1.2–1.4 (28H, m), 2.34, 2.80 (each 1H, d, J=17.0 Hz), 2.34 (3H, s), 5.44 (1H, s), 7.14, 7.43 (each 2H, d, J=7.8 Hz). MS m/z (%) 402 (M^+, 7), 279 (100), 219 (9), 55 (15). Calcd for $C_{25}H_{38}O_2S$: M, 402.2593. Found: m/z 402.2589.

2.1.20. 9-(*p*-Tolylsulfanyl)-1,4,10-trioxadispiro[4.2.4.2]-tetradecan-11-one (13b). Colorless crystals; mp 118–119°C (AcOEt–hexane); IR (KBr) 2934, 1769 (CO), 1190, 1156, 1078, 947 cm^{-1}; ^1H NMR δ 1.6–2.0 (8H, m), 2.35 (3H, s), 2.41, 2.64 (each 1H, d, J=17.3 Hz), 3.97 (4H, s), 5.48 (1H, s), 7.15, 7.44 (each 2H, d, J=8.3 Hz). MS m/z (%) 334 (M^+, 18), 211 (100), 183 (7), 149 (28), 121 (15), 99 (32). Calcd for $C_{18}H_{22}O_4S$: M, 334.1237. Found: m/z 334.1232. Anal Calcd C, 64.65; H, 6.63; S, 9.59. Found: C, 64.76; H, 6.44; S, 9.73.

2.1.21. 1-(*p*-Tolylsulfanyl)-2-oxaspiro[4.9]tetradecan-3-one (13c). Colorless crystals; mp 86–87°C (AcOEt–hexane); IR (KBr) 2922, 1786 (CO), 1493, 1481, 1180, 952, 804 cm^{-1}; ^1H NMR δ 1.6–1.8 (17H, m), 1.91 (1H, m), 2.32 (1H, d, J=17.1 Hz), 2.34 (3H, s), 2.50 (1H, d, J=17.1 Hz), 5.41 (1H, s), 7.14, 7.43 (each 2H, d, J=8.3 Hz). MS m/z (%) 332 (M^+, 12), 209 (96), 149 (19), 123 (14), 95 (18), 81 (28), 55 (19), 41 (14). Calcd for $C_{20}H_{28}O_2S$: M, 332.1810. Found: m/z 332.1804. Anal. Calcd C, 72.25; H, 8.49; S, 9.64. Found: C, 72.21; H, 8.51; S, 9.62.

2.1.22. 4-(2-Phenylethyl)-5-(*p*-tolylsulfanyl)dihydrofuran-2-one (13d). Colorless oil (about 10:3 mixture of diastereomers); IR (neat) 2925, 1790 (CO), 1495, 1456, 1206, 1151, 958, 813 cm^{-1}; ^1H NMR δ 1.70–1.77 (1H, m), 2.33 (3H, s), 2.03–2.76 (6H, m), 5.33 (0.77H, d, J=7.0 Hz), 5.77 (0.23H, d, J=6.4 Hz), 7.11–7.44 (9H, m). MS m/z (%) 312 (M^+, 4), 189 (16), 143 (15), 129 (100), 124 (35), 91 (68). Calcd for $C_{19}H_{20}O_2S$: M, 312.1182. Found: m/z 312.1160.

2.1.23. 2-Oxaspiro[4.14]nonadecan-3-one (14a). AIBN (34.5 mg; 0.21 mmol) was added to a solution of **13a** (85.4 mg; 0.21 mmol) and Bu_3SnH (0.234 ml; 0.84 mmol) in 7 ml of dry benzene. The atmosphere in the flask was replaced with Ar, and the reaction mixture was stirred and refluxed for 4 h. The benzene was evaporated, and the residue was purified by silica gel column chromatography to give **14a** (56.9 mg; 97%) as colorless crystals; mp 53–54°C (EtOH–H_2O); IR (KBr) 2929, 1787 (CO), 1459, 1170, 1025 cm^{-1}; ^1H NMR δ 1.3–1.5 (28H, m), 2.32 (2H, s), 4.01 (2H, s). MS m/z 280 (M^+, 22), 249 (100), 222 (29), 55 (47), 41 (45). Calcd for $C_{18}H_{32}O_2$: M, 280.2401. Found: m/z 280.2412. Anal Calcd C, 77.09; H, 11.50. Found: C, 77.32 H, 11.21.

2.1.24. 1,4,10-Trioxadispiro[4.2.4.2]tetradecan-11-one (14b). Colorless crystals; mp 79–81°C (hexane); IR (KBr) 2975, 2879, 1787 (CO), 1175, 1096, 1024 cm^{-1}; ^1H NMR δ 1.60–1.75 (8H, m), 2.42 (2H, s), 3.95 (4H, s), 4.08 (2H, s). MS m/z (%) 212 (M^+, 0.6), 182 (0.6), 99 (100), 86 (15), 55 (9). Calcd for $C_{11}H_{16}O_4$: M, 212.1047. Found: m/z 212.1061. Anal. Calcd for $C_{11}H_{16}O_4$: C, 62.24; H, 7.60. Found: C, 62.25; H, 7.55.

2.1.25. 2-Oxaspiro[4.9]tetradecan-3-one (14c). Colorless oil; IR (neat) 2931, 1781 (CO), 1482, 1177, 1014 cm^{-1}; ^1H NMR δ 1.5–2.3 (18H, m), 2.31 (2H, s), 3.98 (2H, s). MS m/z (%) 210 (M^+, 11), 179 (37), 152 (62), 137 (100), 124 (22), 96 (57), 81 (83), 67 (65), 55 (68). Calcd for $C_{13}H_{22}O_2$: M, 210.1620. Found: m/z 210.1611.

2.1.26. 4-(2-Phenylethyl)dihydrofuran-2-one (14d). Colorless oil; IR (neat) 2924, 1777 (CO), 1172, 1022, 701 cm^{-1}; ^1H NMR δ 1.80–1.84 (2H, m), 2.18–2.23 (1H, m), 2.5–2.7 (4H, m), 3.94, 4.39 (each 1H, t, J=7.6 Hz), 7.15–7.31 (5H, m). MS m/z (%) 190 (M^+, 42), 159 (19), 130 (12), 104 (48), 91 (100), 65 (11), 41 (9). Calcd for $C_{12}H_{14}O_2$: M, 190.0992. Found: m/z 190.0990.

2.1.27. *tert*-Butyl (8-formyl-1,4-dioxaspiro[4.5]dec-8-yl)acetate (17a). Colorless oil; IR (neat) 2935, 2703 (CHO), 1732 (CO), 1455, 1369, 1259, 1157, 1110 cm^{-1}; ^1H NMR δ 1.42 (9H, s), 1.6–2.0 (8H, m), 2.47 (2H, s), 3.93 (4H, s), 9.63 (1H, s). MS m/z (%) 284 (M^+, trace), 256 (16), 211 (29), 200 (24), 155 (17), 99 (57), 86 (100), 57 (26). Calcd for $C_{15}H_{24}O_5$: M, 284.1623. Found: m/z 284.1601.

2.1.28. *tert*-Butyl 3-formyl-5-phenylpentanoate (17b). Colorless oil; IR (neat) 2978, 2928, 2714 (CHO), 1725 (CO), 1455, 1367, 1251, 1152 cm^{-1}; ^1H NMR δ 1.43 (9H, s), 1.77 (1H, m), 2.06 (1H m), 2.43 (1H, dd, J=16.5, 5.5 Hz), 2.62–2.69 (3H, m), 2.779 (1H, m), 7.17–7.31 (5H, m), 9.71 (1H, d, J=1.3 Hz). MS m/z (%) 262 (M^+, trace), 222 (54), 204 (22), 187 (48), 118 (73), 91 (99), 57 (86).

2.1.29. 1-(*p*-Tolylsulfinyl)-2-oxaspiro[4.14]nonadecan-3-one (18). The sulfide **13a** (212 mg; 0.53 mmol) was dissolved in 6 ml of chloroform and the solution was cooled to −40°C. To this was added *m*CPBA (335 mg; 1.36 mmol) and the suspension was stirred at −40°C for 1 h. The reaction was quenched by sat. aq. $Na_2S_2O_3$. The whole was extracted with chloroform. The organic layer was washed with aq. 5% NaOH and dried over $MgSO_4$. The solvent was evaporated, and the residue was purified by silica gel column chromatography to give **18** (198 mg; 89%) as a colorless oil (about 4:1 diastereomeric mixture); IR (neat) 2930, 1800 (CO), 1459, 1140, 1055 (SO), 1031, 811 cm^{-1}; ^1H NMR δ 1.2–1.5 (28H, m), 2.26, 2.89 (each 0.8H, d, J=17.4 Hz), 2.40, 2.64 (each 0.2H, d, J=17.7 Hz), 2.42 (2.4H, s), 2.43 (0.6H, s), 4.49 (1H, s), 7.34, 7.52 (each 1.6H, d, J=8.0 Hz), 7.35, 7.58 (0.4H, d, J=8.0 Hz). MS m/z (%) 418 (M^+, trace), 279 (100), 249 (12), 219 (8), 124 (25), 91 (33), 55 (27). Calcd for $C_{25}H_{38}O_3S$: M, 418.2542. Found: m/z 418.2540.

2.1.30. 1-Hydroxy-2-oxaspiro[4.14]nonadecan-3-one (19). TFAA (0.078 ml; 0.39 mmol) was added dropwise with stirring to a solution of 18 (55.3 mg; 0.13 mmol) in 4 ml of dry acetone at −50°C. The temperature of the reaction mixture was gradually allowed to warm to 0°C. The reaction was quenched by sat. aq. $NaHCO_3$. The whole was extracted with ether–benzene. The organic layer was washed with sat. aq. $NaHCO_3$ and dried over $MgSO_4$. The

solvent was evaporated, and the residue was purified by silica gel column chromatography to give **19** (22.3 mg; 58%) as colorless crystals; mp 111–112°C (hexane); IR (KBr) 3325 (OH), 2928, 1765 (CO), 1459, 934 cm^{-1}; ^1H NMR δ 1.2–1.4 (28H, m), 2.28, 2.47 (each 1H, d, J=17.3 Hz), 3.76 (1H, s), 5.44 (1H, s). MS m/z (%) 296 (M^+, trace), 268 (39), 222 (80), 208 (33), 97 (56), 83 (55), 69 (62), 55 (98), 41 (100). Calcd for $C_{18}H_{32}O_3$: M, 296.2350. Found: m/z 296.2355. Anal. Calcd for $C_{18}H_{32}O_3$: C, 72.93; H, 10.88. Found: C, 72.83; H, 10.69.

2.1.31. Ethyl (1-formylcyclopentadecyl)acetate (20). TFAA (0.187 ml; 0.95 mmol) was added dropwise with stirring to a solution of **7d** (92.2 mg; 0.19 mmol) and 2,4,6-collidine (0.151 ml; 1.14 mmol) and NaI (144 mg; 0.95 mmol) in 5 ml of dry acetone at −50°C. The reaction mixture turned from yellow to black–green in color. The reaction mixture was stirred at −50°C for 5 min. The temperature of the reaction mixture was gradually allowed to warm to 0°C. The reaction was quenched by sat. aq. $NaHCO_3$ and sat. aq. Na_2SO_3. The whole was extracted with benzene. The organic layer was washed with sat. aq. $NaHCO_3$ and dried over $MgSO_4$. The benzene was evaporated, and the residue was purified by silica gel column chromatography to give **20** (52.6 mg; 85%) as a colorless oil; IR (neat) 2930, 2696 (CHO), 1733 (CO), 1461, 1370, 1205, 1033, 757 cm^{-1}; ^1H NMR δ 1.2–1.4 (28H, m), 1.22 (3H, t, J=7.0 Hz), 2.53 (2H, s), 4.10 (2H, q, J=7.0 Hz), 9.58 (1H, s). MS m/z (%) 324 (M^+, 2). 296 (85), 279 (32), 222 (22), 109 (29), 88 (82), 69 (58), 55 (100), 41 (87). Calcd for $C_{20}H_{36}O_3$: M, 324.2662. Found: m/z 324.2664.

2.1.32. (1-Ethoxycarbonylmethyl)cyclopentadecanecarboxylic acid (21). A solution of $NaClO_2$ (91.4 mg; 0.8 mmol) in 2 ml of water was added dropwise in 2 h to a stirred mixture of **20** (25.9 mg; 0.08 mmol) in 4 ml of acetonitrile and NaH_2PO_4 (115.2 mg; 0.96 mmol) in 2 ml water and 35% H_2O_2 (0.072 ml; 0.8 mmol), keeping the temperature at 10°C. The reaction mixture was stirred at 10°C for 16 h. A small amount of Na_2SO_3 was added to destroy the unreacted HOCl and H_2O_2. Acidification with 10% aqueous HCl afforded **21** (26 mg; 95%) as a colorless oil; IR (neat) 2928, 1732 (CO), 1693 (CO), 1462, 1237, 1176 cm^{-1}; ^1H NMR δ 1.23 (3H, t, J=7.1 Hz), 1.20–1.73 (28H, m), 2.62 (2H, s), 4.11 (2H, q, J=7.1 Hz). MS m/z (%) 340 (M^+, 21), 322 (31), 294 (100), 253 (84), 235 (31), 206 (48), 184 (35), 138 (23). Calcd for $C_{20}H_{36}O_4$: M, 340.2611. Found: m/z 340.2605.

2.1.33. 4-Methyl-1-(*p*-tolylsulfanyl)-2-oxaspiro[4.14]nonadecan-3-one (25). Colorless oil (about 1:1 mixture of two diastereomers); IR (neat), 2930, 1785 (CO), 1461, 1162, 970, 811 cm^{-1}; ^1H NMR δ 1.21, 1.34 (each 1.5H, d, J=7.3 Hz), 1.2–1.5 (28H, m), 2.38, 2.68 (each 0.5H, q, J=7.3 Hz), 5.41, 5.48 (each 0.5H, s), 7.13, 7.44 (each, 2H J=8.0 Hz). MS m/z (%) 416 (M^+, 5), 293 (100), 282 (14), 69 (14), 55 (15). Calcd for $C_{26}H_{40}O_2S$: M, 416.2749. Found: m/z 416.2738.

2.1.34. 4-Butyl-1-(*p*-tolylsulfanyl)-2-oxaspiro[4.14]nonadecan-3-one (26). Colorless oil (about 1:1 mixture of two diastereomers); IR (neat) 2929, 1779 (CO), 1495, 1463, 1151, 970, 812 cm^{-1}; ^1H NMR δ 0.91–0.95 (3H, m), 1.2–1.5 (28H, m), 1.5–1.8 (9H, m), 2.33 (3H, s), 2.19 (0.5H, m), 2.44 (0.5H, m), 5.38 (0.5H, s), 5.42 (0.5H, s), 7.12–7.15 (2H, m), 7.42 (1H, d, J=7.6 Hz), 7.43 (1H, d, J=7.6 Hz). MS m/z (%) 458 (M^+, 3), 335 (100), 267 (37), 116 (24), 99 (23), 55 (37). Calcd for $C_{29}H_{46}O_2S$: M, 458.3219. Found: m/z 458.3216.

2.1.35. 4-Methyl-2-oxaspiro[4.14]nonadecan-3-one (27). Colorless oil; IR (neat) 2930, 1779 (CO), 1462, 1382, 1171, 1015 cm^{-1}; ^1H NMR δ 1.18 (3H, d, J=7.4 Hz), 1.2–1.5 (28H, m), 2.37 (1H, q, J=7.4 Hz), 3.81, 4.05 (each 1H, d, J=8.9 Hz). MS m/z (%) 294 (M^+, 21), 263 (100), 236 (16), 95 (27), 83 (32), 69 (42), 55 (55), 41 (52). Calcd for $C_{19}H_{34}O_2$: M, 294.2556. Found: m/z 294.2550.

2.1.36. 4-Methyl-4-phenylselenenyl-2-oxaspiro[4.14]nonadecan-3-one (28). The enolate of lactone **27** was prepared by adding a solution of **27** (41 mg; 0.14 mmol) in 1 ml of THF to 0.42 mmol of LDA in 3 ml of THF at −75°C. After 10 min, 134 mg (0.43 mmol) of diphenyl diselenide in 1.0 ml of THF containing 0.14 ml (0.42 mmol) of HMPA was rapidly added at −75°C. The reaction mixture was stirred at −75°C for 40 min, then warmed to 0°C, and kept at that temperature for 1 h. The reaction was quenched by 0.1N HCl solution. Usual work-up afforded a yellow oil, which was purified by silica gel column chromatography to afford **28** (36 mg; 58%) as a light yellow oil; IR (neat) 2930, 1771 (CO), 1463, 1380, 1224, 1084, 1023, 741 cm^{-1}; ^1H NMR δ 1.2–1.7 (28H, m), 1.49 (3H, s), 4.08 (2H, s), 7.31–7.35 (2H, m), 7.40–7.44 (1H, m), 7.59–7.61 (2H, m). MS m/z (%) 450 (M^+, 12), 293 (100), 265 (35), 247 (11), 157 (10), 95 (13), 69 (15). Calcd for $C_{25}H_{38}O_2Se$: M, 450.2037. Found: m/z 450.2029.

2.1.37. 4-Methylene-2-oxaspiro[4.14]nonadecan-3-one (29). To a solution of **28** (50 mg; 0.11 mmol) in 2.0 ml of THF containing 0.05 ml of acetic acid cooled to 0°C was added 0.2 ml of 30% hydrogen peroxide. The reaction mixture was stirred for 30 min at 0°C, then poured into cold saturated sodium bicarbonate solution, and extracted with ether. The solution was dried over $MgSO_4$ and the solvent was evaporated. The product was purified by silica gel column chromatography to give **29** (31.3 mg; 97%) as colorless crystals. Mp 59–60°C (ethanol); IR (KBr) 2925, 1770 (CO), 1458, 1023, 812, 711 cm^{-1}; ^1H NMR δ 1.2–1.7 (28H, m), 4.05 (2H, s), 5.47, 6.24 (each 1H, s). MS m/z (%) 292 (M^+, 61), 125 (49), 112 (100), 95 (36), 81 (40), 67 (41), 55 (67), 41 (78). Calcd for $C_{19}H_{32}O_2$: M, 292.2400. Found: m/z 292.2394. Anal. Calcd for $C_{19}H_{32}O_2$: C, 78.03; H, 11.03. Found: C, 78.41; H, 11.02.

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