Pergamon

SCIENCE DIRECT®

Tetrahedron 59 (2003) 9599–9607

TETRAHEDRON

A new synthesis, including asymmetric synthesis, of spiro[4.*n*]alkenones from three components: cyclic ketones, chloromethyl *p*-tolyl sulfoxide, and acetonitrile; and a formal total synthesis of racemic acorone

Tsuyoshi Satoh,[a,*] Tadashi Kawashima,[a] Satoru Takahashi[b] and Ken Sakai[b]

[a]*Department of Chemistry, Faculty of Science, Tokyo University of Science; Kagurazaka, Shinjuku-ku, Tokyo 162-8601, Japan*
[b]*Department of Applied Chemistry, Faculty of Science, Tokyo University of Science; Kagurazaka, Shinjuku-ku, Tokyo 162-8601, Japan*

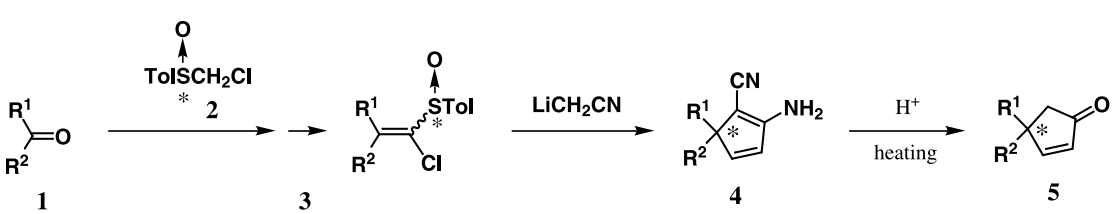
Received 4 September 2003; accepted 30 September 2003

Abstract—1-Chlorovinyl *p*-tolyl sulfoxides were synthesized from several kinds of cyclic ketones and chloromethyl *p*-tolyl sulfoxide in good yields. Treatment of the 1-chlorovinyl *p*-tolyl sulfoxides with cyanomethyllithium at −78°C to room temperature gave spirocyclic enaminonitriles in high yields. Acidic treatment of the enaminonitriles afforded spiro[4.*n*]alkenones in good yields. By using an unsymmetrical cyclic ketone, α-tetralone, and optically active chloromethyl *p*-tolyl sulfoxide, this procedure afforded enantiomerically pure spiro[4.5]decenone in good yield with excellent asymmetric induction from the sulfoxide chiral center. By using this method a formal total synthesis of a racemic spirocyclic sesquiterpene, acorone, was realized.

Spirocyclic compounds, which are compounds containing one carbon atom common to two rings, are structurally quite interesting. The spirocyclic structure is not unusual in natural products such as terpenes and terpenoids.[1] Many methods have been published for the synthesis of spirocyclic compounds;[1,2] however, in view of the interesting structure of the spirocyclic compounds, new methods are still eagerly studied.[3] The central carbon of the spirocycles is a quaternary carbon, and investigation of the stereoselective construction of the carbon is also challenging in its own right.[4]

We recently reported a new procedure for the synthesis, including asymmetric synthesis, of 4,4-disubstituted 2-cyclopentenones **5** by the reaction of cyanomethyllithium and 1-chlorovinyl *p*-tolyl sulfoxides **3** which were synthesized from acyclic ketones **1** and chloromethyl *p*-tolyl sulfoxide **2** (Scheme 1).[5]

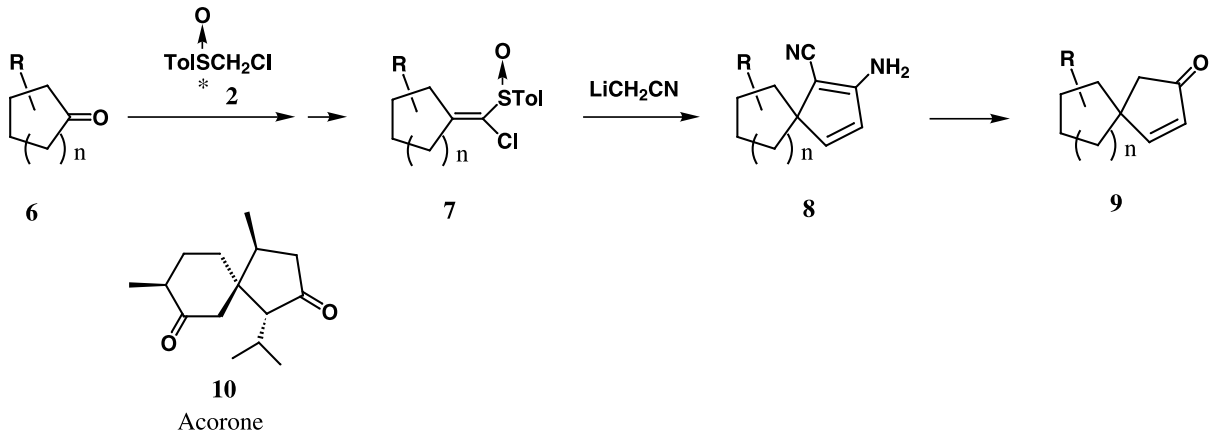
We thought that if cyclic ketones **6** could be used in these reactions, this procedure would give a new method for the synthesis of spiro[4.*n*]alkenones **9** through cyclic 1-chlorovinyl *p*-tolyl sulfoxides **7** and spirocyclic enaminonitriles **8**. This expectation was recently investigated, and quite interesting results were obtained. In this paper, detailed results of this study and a formal total synthesis of racemic spirocyclic sesquiterpene acorone **10** are reported (Scheme 2).



Scheme 1.

Keywords: spirocycle; spiro[4.*n*]alkenone; chiral sulfoxide; asymmetric synthesis; acorone.
* Corresponding author. Tel.: +81-3-5228-8272; fax: +81-3-3235-2214; e-mail: tsatoh@ch.kagu.tus.ac.jp

0040–4020/$ - see front matter © 2003 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2003.09.099



Scheme 2.

1. Results and discussion

1.1. Synthesis of 1-chlorovinyl *p*-tolyl sulfoxides from symmetrical and unsymmetrical cyclic ketones and synthesis of spiro[4.*n*]alkenones

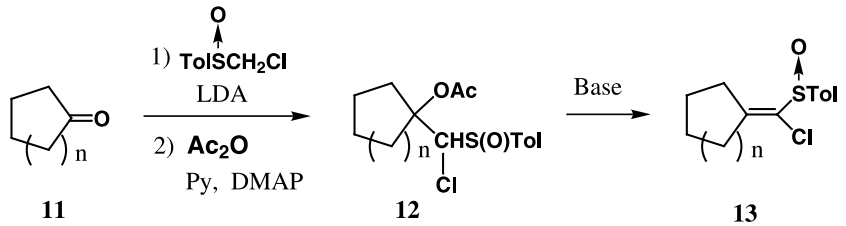
We started this study with cyclopentanone **11a**, cyclohexanone **11b**, cyclodecanone **11c**, and cyclopentadecanone **11d** as representative examples of symmetrical cyclic ketones (Table 1). First, chloromethyl *p*-tolyl sulfoxide was treated with LDA in THF at −78°C followed by cycloalkanones **11** to give the adducts, which were acetylated under usual conditions to afford the acetate **12** in over 90% yield in all cases. The elimination of acetic acid from **12** was carried out with three kind of bases (Ph_2NLi, dimsylsodium, and *N*-lithio 2-piperidone) and the desired 1-chlorovinyl *p*-tolyl sulfoxides **13** were obtained in good yields.

The selection of these three bases requires some comments. As the products, 1-chlorovinyl *p*-tolyl sulfoxides **13**, are sensitive to strong bases, the selection of the bases was found to be essential to the deacetylation. Previously, we used dimsylsodium in this elimination with special precautions.[5a] Later, in some cases lithium diphenylamide was found to work better than dimsylsodium.[5c] In the case of **12c**, both dimsylsodium and lithium diphenylamide worked; however, the yields were not satisfactory. We further investigated the bases and quite recently found that *N*-lithio 2-piperidone was the base of choice. By the use of this base at room temperature, 77% yield of **13c** was obtained with good reproducibility. In the case of entry 4, the elimination gave **13d** in quantitative yield without requiring special precautions. A further advantage of using this base is that it can be removed from the reaction mixture by simple washing with water.

The synthesized vinyl sulfoxides **13** were treated with 5 equiv. of cyanomethyllithium, obtained from acetonitrile and *n*-BuLi in THF at −78°C, and the reaction temperature was allowed to warm from −78°C to room temperature over 2 h. The reaction gave the desired enaminonitriles **14** up to 91% yields in all cases without any problem (Table 2).

Finally, **14** were heated under reflux in acetic acid containing H_3PO_4 and a small amount of water, for about 40 h. The desired spiro[4.*n*]alkenones **15** were obtained in somewhat variable yields from 66 to 91%. From these

Table 1. Synthesis of cyclic 1-chlorovinyl *p*-tolyl sulfoxides **13** from simple symmetrical cyclic ketones **11** and chloromethyl *p*-tolyl sulfoxide



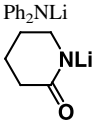
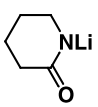
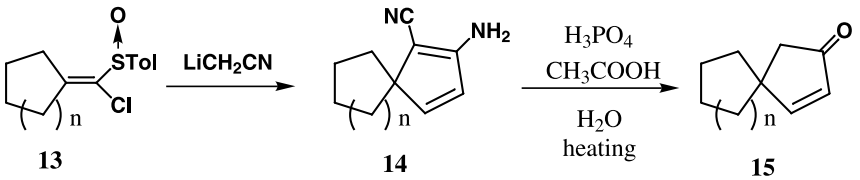
Entry	**11**, *n*	**12**, Yield (%)	Base	**13**, Yield (%)
1	**11a**, 1	**12a**, 93	Ph_2NLi	**13a**, 86
2	**11b**, 2	**12b**, 99	Ph_2NLi	**13b**, 94
3	**11c**, 6	**12c**, 92		**13c**, 77
4	**11d**, 11	**12d**, 93		**13d**, 98

Table 2. Synthesis of spiro[4.*n*]alkenone **15** from 1-chlorovinyl *p*-tolyl sulfoxides **13** and cyanomethyllithium through the spiro-enaminonitrile **14**



13 **14** **15**

Entry	**13**, *n*	**14**, Yield (%)	**15**, Yield (%)
1	**13a**, 1	**14a**, 85	**15a**, 91
2	**13b**, 2	**14b**, 91	**15b**, 76
3	**13c**, 6	**14c**, 71	**15c**, 66
4	**13d**, 11	**14d**, 83	**15d**, 90

results the method presented here is found to be quite general for the small to large-ringed ketones to give the spiro[4.*n*]alkenones in good overall yields.

Next, we investigated this procedure starting from unsymmetrical cyclic ketones. We selected 2-cyclohexenone **16a** and 4,4-ethylenedioxy 2-cyclohexenone **16b** as representative examples (Scheme 3). The reaction of the lithium α-carbanion of chloromethyl *p*-tolyl sulfoxide with **16a** and **16b** gave 1,2-adducts in quantitative yields without any 1,4-adducts. Acetylation of the adducts gave the acetates **17a** and **17b** as a mixture of two diastereomers in near quantitative yields.

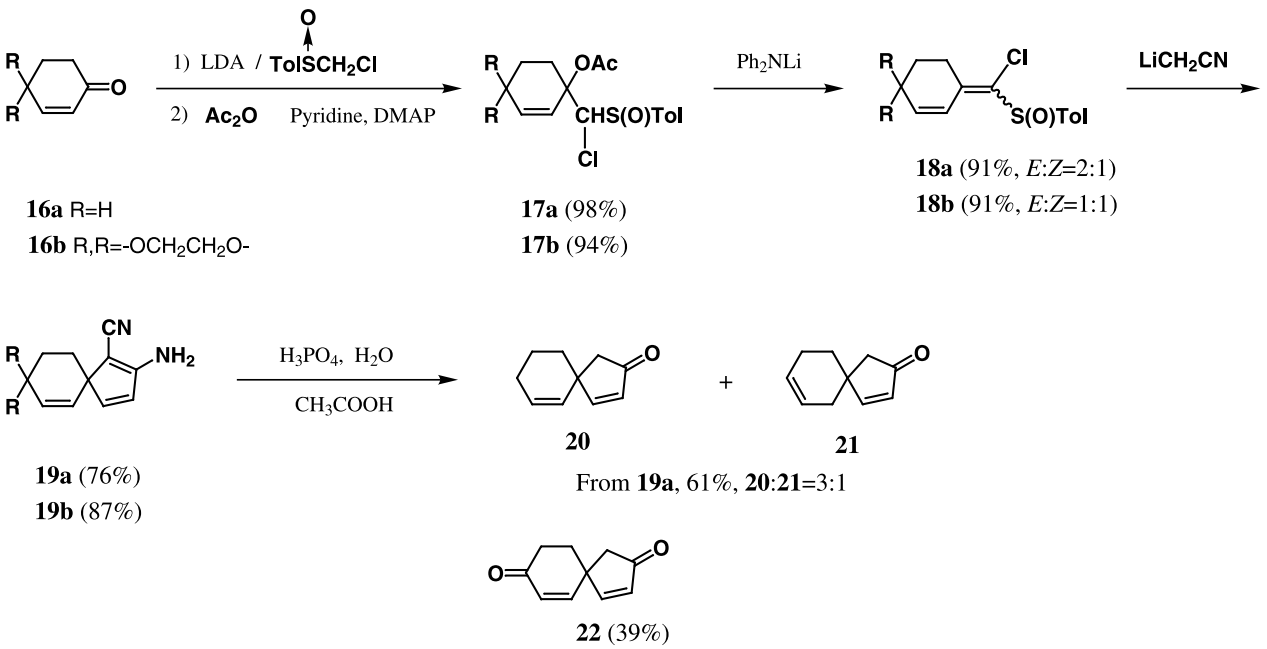
The deacetylation of these acetates **17a** and **17b** was conducted best with Ph_2NLi to give 91% yield of **18a** and **18b**. The 1-chlorovinyl *p*-tolyl sulfoxides **18a** and **18b** were obtained as separable geometrical isomers and the ratios are shown in Scheme 3. The reaction of these vinyl sulfoxides **18** (a mixture of two geometric isomers was used) with cyanomethyllithium gave the desired enaminonitriles **19a** and **19b** in 76 and 87% yields, respectively, without any problem.

Finally, the enaminonitrile **19a** was treated under the acidic conditions to give the desired spiro-enone in 61% yield; however, the product was found to be a mixture of two isomers **20** and **21**. These could be separated by silica gel column chromatography and the minor product **21** was found to be the spiro-enone whose double bond was migrated. The acidic treatment of **19b** gave the desired, structurally very interesting spiro dienedione **22**; 2-cyclopentenone and 2-cyclohexenone are connected by a carbon at each γ-position. However, the yield was somewhat lower than those of the other examples.

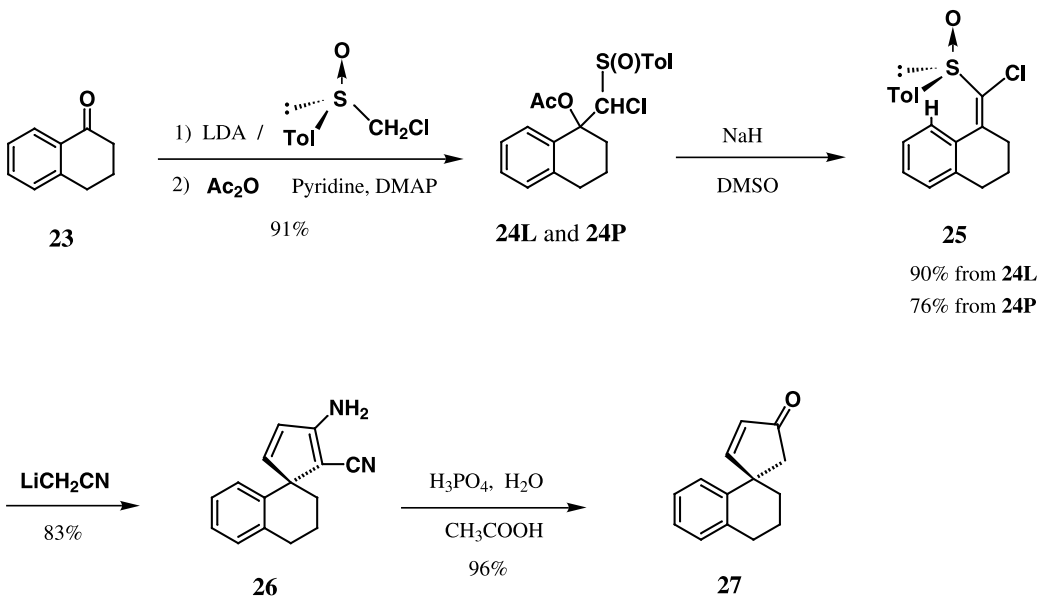
1.2. Asymmetric synthesis of optically pure spiro[4.5]-decenone from α-tetralone

Next, we planned the synthesis of optically active spiro[4.*n*]alkenones based on the above-mentioned method. We selected α-tetralone as an unsymmetrical cyclic ketone and optically pure (*R*)-chloromethyl *p*-tolyl sulfoxide[6] and the results are indicated in Scheme 4.

In a similar manner, the addition reaction of lithium α-sulfinyl carbanion of (*R*)-chloromethyl *p*-tolyl sulfoxide



Scheme 3.



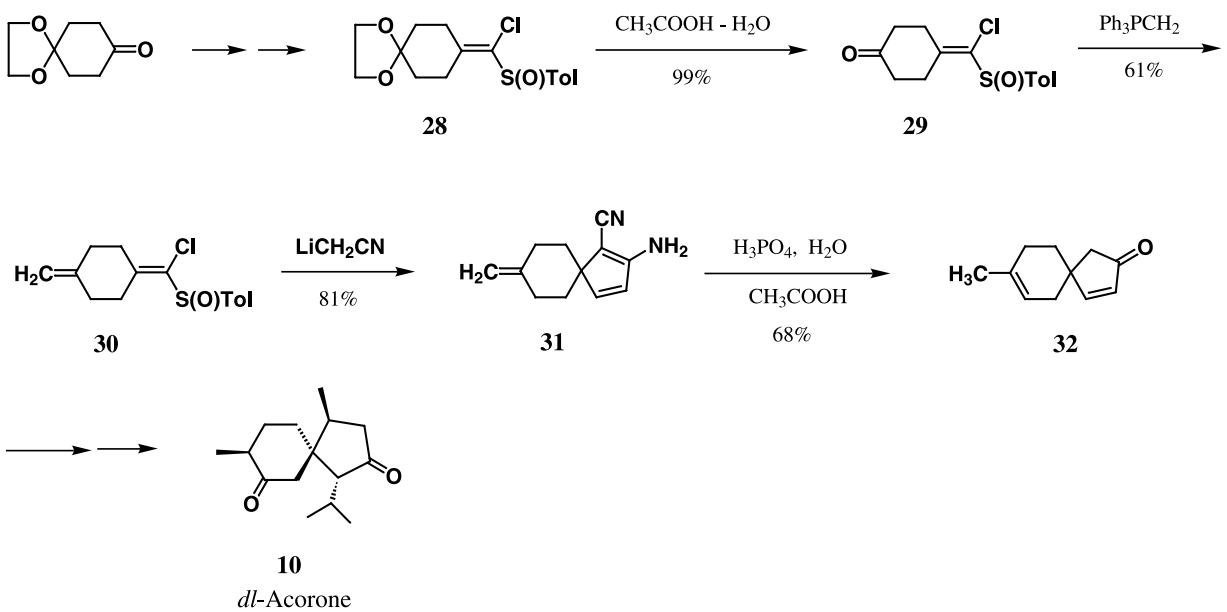
Scheme 4.

to α-tetralone gave the adduct, which was acetylated to give the acetate **24** in 91% overall yield. The acetate was a mixture of two diastereomers (the isomers are expressed as **L** and **P**), which were easily separated by silica gel column chromatography. The elimination of acetate was most conveniently carried out with dimsylsodium and the 1-chlorovinyl *p*-tolyl sulfoxide **25** was obtained in up to 90% yield. Quite interestingly, both acetates (**24L** and **24P**) gave the same vinyl sulfoxide **25**.

Determination of the stereochemistry of **25** is very important in the study of chiral induction. The NOESY spectrum of **25** was measured, and weak NOE was observed between the aromatic hydrogen depicted in Scheme 4 and the aromatic hydrogen on the tolyl group. Finally, the structure of the vinyl sulfoxide **25** was unambiguously determined to be *E* by X-ray crystallographic analysis[7] as shown in Scheme 4.

The 1-chlorovinyl *p*-tolyl sulfoxide **25** was treated with 5 equiv. of cyanomethyllithium in a similar way to that described above to afford optically active enaminonitrile **26** in 83% yield. The optical purity was determined by using HPLC with chiral stationary column (Daicel; CHIRALCEL OD) and the ee was found to be over 99%. The absolute configuration of the chiral center of this enaminonitrile **26** was established to be *S* as shown in Scheme 4 by X-ray crystallographic analysis.[8]

In the previous paper, we proposed a chelation model for the asymmetric induction of the optically active 1-chlorovinyl *p*-tolyl sulfoxides, derived from acyclic ketones, with the



Scheme 5.

cyanomethyllithium.[5b] From the absolute stereochemistries of the 1-chlorovinyl *p*-tolyl sulfoxide **25** and the enaminonitrile **26**, it was verified that the proposed model is quite general for the asymmetric induction even if the 1-chlorovinyl *p*-tolyl sulfoxide group is included in a cyclic carbon chain.

The optically pure enaminonitrile **26** was hydrolyzed and decyanated under the acidic conditions to give the optically pure spiro[4.5]decenone **27** in almost quantitative yield.

1.3. A formal total synthesis of racemic acorone 10

Finally, we studied an application of this method to a total synthesis of natural products. Sesquiterpene acorone **10** has a spiro[4.5]decenone carbon skeleton and is suitable for the application of our synthetic method. Several papers for the total synthesis of racemic acorone **10** have already been reported.[9] Herein we report a formal total synthesis of racemic acorone **10** from commercially available 1,4-cyclohexanedione mono-ethylene ketal (Scheme 5).

1-Chlorovinyl *p*-tolyl sulfoxide **28**[10] was synthesized from 1,4-cyclohexanedione mono-ethylene ketal by the above-mentioned procedure in high overall yield. The ketal group of **28** was deprotected in acetic acid containing water at 70°C for 1 h to give a ketone **29** in a quantitative yield. The Wittig methylenation of the ketone **29** was conducted in the usual way to afford the methylenated product **30**; however, the yield was somewhat lower than expected.

The synthesis of the cyclopentadienyl enaminonitrile was carried out by the above-mentioned procedure and the expected product **31** was obtained in 81% yield without problem. Finally, **31** was heated in acetic acid containing H_3PO_4 and a small amount of water. The hydrolysis of the enamine group, decyanation, and migration of the double bond from exomethylene to tri-substituted olefin occurred in one operation to give the desired enone **32** in 68% yield. From the enone **32** total synthesis of racemic acorone has already been reported by Dolby[9a] and Martin.[9b]

In conclusion, we have developed a new method for the synthesis of spiro[4.*n*]alkenones from several cyclic ketones and chloromethyl *p*-tolyl sulfoxide in relatively short steps. By using unsymmetrical cyclic ketones and optically active chloromethyl *p*-tolyl sulfoxide, an asymmetric synthesis of the spiro[4.*n*]alkenone was realized. A formal total synthesis of racemic acorone was successful by our method presented herein.

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. Silica gel 60 (MERCK) containing 0.5% fluorescence reagent 254 and a 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, acetonitrile, pyridine, and DMSO were distilled from CaH_2 and THF was distilled from diphenylketyl. Acetone was dried over $CaSO_4$ and distilled before use.

2.1.1. Acetic acid 1-[chloro-(toluene-4-sulfinyl)methyl]-cyclopentyl ester (12a). A solution of **2** (1.0 g; 5.3 mmol) in dry THF (1 ml) was added dropwise to a solution of LDA (6.4 mmol) in 14 ml of THF at −78°C. The solution was stirred at −78°C for 10 min, then cyclopentanone (0.56 ml; 6.4 mmol) in 1 ml of THF was added. The reaction mixture was stirred for 20 min and the reaction was quenched by sat. aq. NH_4Cl. The whole was extracted with $CHCl_3$. The organic layer was washed once with water and dried over $MgSO_4$. The solvent was evaporated to leave colorless crystals. The product was dissolved in a mixture of acetic anhydride (10 ml) and pyridine (21 ml). 4-Dimethylaminopyridine (108 mg; 0.88 mmol) was added to the solution and the reaction mixture was stirred at room temperature for 15 h. The acetic anhydride and pyridine were evaporated under vacuum and the residue was purified by silica gel column chromatography to give acetate **12a** (1.55 g; 93%) as colorless prisms; mp 87–88°C (AcOEt–hexane); IR (KBr) 2980, 2878, 1736 (CO), 1371, 1235, 1096, 1064 (SO), 1014, 822, 517 cm^{-1}; ^{1}H NMR δ 1.69–1.89 (4H, m), 2.12 (3H, s), 2.15–2.29 (3H, m), 2.40–2.46 (1H, m), 2.42 (3H, s), 5.60 (1H, s), 7.33, 7.45 (each 2H, d, J=8.0 Hz). Anal. calcd for $C_{15}H_{19}ClO_3S$: C, 57.23; H, 6.08; Cl, 11.26; S, 10.19. Found: C, 57.36; H, 6.12; Cl, 11.22; S, 9.95%.

2.1.2. Acetic acid 1-[chloro-(toluene-4-sulfinyl)methyl]-cyclohexyl ester (12b). Colorless needles; mp 104–105°C (AcOEt–hexane); IR (KBr) 2958, 2940, 1733 (CO), 1371, 1224, 1088, 1062 (SO), 825, 515 cm^{-1}; ^{1}H NMR δ 1.22–1.78 (7H, m), 1.93–1.99 (1H, m), 2.17 (3H, s), 2.39–2.48 (2H, m), 2.41 (3H, s), 5.39 (1H, s), 7.32, 7.45 (each 2H, d, J=8.0 Hz). Calcd for $C_{16}H_{21}ClO_3S$: M, 328.0900. Found: m/z 328.0898; MS m/z (%) 328 (M^+, trace), 189 (67), 140 (86), 129 (72), 111 (12), 93 (45), 91 (34), 43 (100). Anal. calcd for $C_{16}H_{21}ClO_3S$: C, 58.44; H, 6.44; Cl, 10.78; S, 9.75. Found: C, 58.55; H, 6.48; Cl, 10.71; S, 9.81%.

The acetates **12c** and **12d** are known compounds.[10,11]

2.1.3. [Chloro-(*p*-tolylsulfinyl)methylidene]cyclopentane (13a). To a solution of **12a** (270 mg; 0.86 mmol) in 3 ml of dry THF was added dropwise with stirring a solution of Ph_2NLi (1.2 mmol) in 4 ml of THF at 0°C. After 10 min, the reaction was quenched by adding sat. aq. NH_4Cl. The whole was extracted with $CHCl_3$ and washed once with water. The organic layer was dried over $MgSO_4$ and the product was purified by silica gel flash column chromatography to give **13a** (188 mg, 86%) as colorless crystals; mp 86–87°C (AcOEt–hexane); IR (KBr) 2964, 2951, 1494, 1087, 1056 (SO), 880, 815 cm^{-1}; ^{1}H NMR δ 1.68–1.96 (4H, m), 2.42 (3H, s), 2.45–2.72 (3H, m), 3.04 (1H, dt, J=18.3, 6.0 Hz), 7.32, 7.50 (each 2H, d, J=8.0 Hz). Calcd for $C_{13}H_{15}ClOS$: M, 254.0531. Found: m/z 254.0534. MS m/z (%) 254 (M^+, 25), 239 (36), 237 (100), 201 (38), 123 (16), 91 (23), 79 (33). Anal. calcd for $C_{13}H_{15}ClOS$: C, 61.28; H, 5.93; Cl, 13.92; S, 12.59. Found: C, 61.30; H, 5.94; Cl, 13.78; S, 12.46%.

2.1.4. [Chloro-(*p*-tolylsulfinyl)methylidene]cyclohexane (13b). Colorless crystals; mp 83–84°C (AcOEt–hexane); IR (KBr) 2936, 2849, 1446, 1091, 1053 (SO), 857, 806, 530, 460 cm^{-1}; ^1H NMR δ 1.62–1.67 (5H, m), 1.79–1.82 (1H, m), 2.41 (3H, s), 2.41–2.51 (2H, m), 2.79–2.84, 2.88–2.93 (each 1H, m), 7.32, 7.46 (each 2H, d, J=8.0 Hz). Calcd for $C_{14}H_{17}ClOS$: M, 268.0606. Found: m/z 268.0696; MS m/z (%) 268 (M^+, 15), 253 (40), 251 (100), 215 (10), 159 (12), 139 (8), 123 (12), 91 (30), 77 (19). Anal. calcd for $C_{14}H_{17}ClOS$: C, 62.56; H, 6.37; Cl, 13.19; S, 11.93. Found: C, 62.68; H, 6.42; Cl, 13.44; S, 11.86%.

2.1.5. [Chloro-(*p*-tolylsulfinyl)methylidene]cyclodecane (13c). A solution of **12c** (211 mg, 0.55 mmol) in dry THF (4 ml) was added dropwise to *N*-lithio 2-piperidone [0.66 mmol; prepared from *n*-BuLi (0.66 mmol) and 2-piperidone (71 mg, 0.72 mmol) in THF (2 ml) at 0°C] in THF at 25°C. The reaction mixture was stirred at 25°C for 15 min. The reaction was quenched by sat. aq. NH_4Cl and the whole was extracted with $CHCl_3$ and washed with water three times. The organic layer was dried over $MgSO_4$. The solvent was evaporated to leave colorless crystals, which were purified by silica gel column chromatography to give 137 mg (77%) of **13c**.

The 1-chlorovinyl *p*-tolyl sulfoxides **13c** and **13d** are known compounds.[10,11]

2.1.6. 2-Aminospiro[4.4]nona-1,3-diene-1-carbonitirile (14a). Acetonitrile (0.19 ml; 3.6 mmol) was added to a solution of *n*-BuLi (3.5 mmol) in 8 ml of dry THF at −78°C with stirring. The solution was stirred for 10 min, then a solution of **13a** (181 mg; 0.71 mmol) in THF was added dropwise. The temperature of the reaction mixture was gradually allowed to warm to room temperature for 2 h and the reaction mixture was further stirred at room temperature for 30 min. The product was isolated by silica gel flash column chromatography to give 96 mg (85%) of **14a** as colorless plates; mp 110–111°C (AcOEt–hexane); IR (KBr) 3429, 3349, 3262 (NH), 2951, 2172 (CN), 1642, 1608, 1542, 1434, 771 cm^{-1}; ^1H NMR δ 1.70–2.00 (8H, m), 4.51 (2H, brs, NH_2), 5.97, 6.56 (each 1H, d, J=5.5 Hz). Calcd for $C_{10}H_{12}N_2$: M, 160.0999. Found: m/z 160.0995; MS m/z (%) 160 (M^+, 50), 132 (100), 118 (26), 106 (12), 91 (10). Anal. calcd for $C_{10}H_{12}N_2$: C, 74.97; H, 7.55; N, 17.48%. Found: C, 74.91; H, 7.33; N, 17.40%.

2.1.7. 2-Aminospiro[4.5]deca-1,3-diene-1-carbonitrile (14b). Colorless prisms; mp 135–136°C (AcOEt–hexane); IR (KBr) 3432, 3345, 3238 (NH), 2925, 2166 (CN), 1653, 1642, 1610, 1544, 1430, 770 cm^{-1}; ^1H NMR δ 1.37–1.54 (5H, m), 1.69–1.77 (3H, m), 1.82–1.88 (2H, m), 4.50 (2H, brs, NH_2), 6.04, 6.84 (each 1H, d, J=5.5 Hz). Calcd for $C_{11}H_{14}N_2$: M, 174.1155. Found: m/z 174.1150; MS m/z (%) 174 (M^+, 100), 159 (15), 145 (55), 131 (38), 118 (61), 106 (28), 91 (18). Anal. calcd for $C_{11}H_{14}N_2$: C, 75.82; H, 8.10; N, 16.08. Found: C, 75.80; H, 8.17; N, 15.93%.

2.1.8. 2-Aminospiro[4.9]tetradeca-1,3-diene-1-carbonitrile (14c). Colorless crystals; mp 132–133°C (AcOEt–hexane); IR (KBr) 3453, 3355 (NH), 2930, 2862, 2167 (CN), 1638, 1606, 1541, 1422, 771 cm^{-1}; ^1H NMR δ 1.51–1.84 (18H, m), 4.44 (2H, brs, NH_2), 5.97, 6.54 (each 1H, d, J=5.5 Hz). Calcd for $C_{15}H_{22}N_2$: M, 230.1781. Found: m/z 230.1778; MS m/z (%) 230 (M^+, 65), 187 (22), 173 (30), 159 (35), 145 (45), 133 (48), 118 (100), 106 (30), 94 (20). Anal. calcd for $C_{15}H_{22}N_2$: C, 78.21; H, 9.63; N, 12.16. Found: C, 78.28; H, 9.60; N, 12.07%.

2.1.9. 2-Aminospiro[4.14]nonadeca-1,3-diene-1-carbonitrile (14d). Colorless crystals; mp 152–154°C (AcOEt–hexane); IR (KBr) 3450, 3348 (NH), 2169 (CN), 1642 cm^{-1}; ^1H NMR δ 1.30–1.70 (28H, m), 4.48 (2H, brs, NH_2), 5.99, 6.55 (each 1H, d, J=5.6 Hz). MS m/z (%) 300 (M^+, 100), 119 (85), 118 (67). Anal. calcd for $C_{20}H_{32}N_2$: C, 79.94; H, 10.73; N, 9.32. Found: C, 79.53; H, 10.68; N, 9.20%.

2.1.10. Spiro[4.4]non-3-en-2-one (15a). To a solution of **14a** (88 mg; 0.55 mmol) in acetic acid (38 ml) was added phosphoric acid (85%; 17 ml) and water (3 ml). The reaction mixture was stirred and heated under reflux for 50 h. The reaction mixture was neutralized with 10% NaOH and the whole was extracted with Et_2O and washed with brine. The organic layer was dried over $MgSO_4$ and the product was purified by silica gel flash column chromatography to give 68.4 mg (91%) of **15a** as a colorless oil; IR (neat) 2954, 2871, 1715 (CO), 1586, 1407, 1180, 797 cm^{-1}; ^1H NMR δ 1.59–1.84 (8H, m), 2.26 (2H, s), 6.04, 7.50 (each 1H, d, J=5.5 Hz). Calcd for $C_9H_{12}O$: M, 136.0888. Found: m/z 136.0896; MS m/z (%) 136 (M^+, 100), 121 (36), 108 (64), 95 (98), 79 (76), 66 (40).

2.1.11. Spiro[4.5]dec-3-en-2-one (15b). Colorless oil; IR (neat) 2927, 2855, 1714 (CO), 1589, 1452, 1198, 924, 795 cm^{-1}; ^1H NMR δ 1.28–1.54 (8H, m), 1.63–1.73 (2H, m), 2.22 (2H, s), 6.03, 7.52 (each 1H, d, J=5.5 Hz). Calcd for $C_{10}H_{14}O$: M, 150.1043. Found: m/z 150.1040; MS m/z (%) 150 (M^+, 91), 135 (13), 122 (16), 107 (65), 95 (100), 82 (45), 68 (32).

2.1.12. Spiro[4.9]tetradec-3-en-2-one (15c). Colorless oil; IR (neat) 2926, 2863, 1716 (CO), 1587, 1482, 1445, 1188 cm^{-1}; ^1H NMR δ 1.53–1.67 (18H, m), 2.17 (2H, s), 6.01, 7.61 (each 1H, d, J=5.8 Hz). Calcd for $C_{14}H_{22}O$: M, 206.1670. Found: m/z 206.1675. MS m/z (%) 206 (M^+, 43), 163 (17), 149 (43), 135 (30), 121 (25), 109 (56), 95 (100), 79 (31), 66 (31), 55 (31).

2.1.13. Spiro[4.14]nonadec-3-en-2-one (15d). Colorless oil; IR (neat) 2929, 2857, 1717 (CO), 1588, 1459, 1350, 733 cm^{-1}; ^1H NMR δ 1.33–1.52 (28H, m), 2.17 (2H, s), 6.03, 7.60 (each 1H, d, J=5.5 Hz). Calcd for $C_{19}H_{32}O$: M, 276.2451. Found: m/z 276.2449; MS m/z (%) 276 (M^+, 85), 240 (25), 212 (26), 199 (81), 171 (55), 141 (35), 128 (30), 115 (49), 109 (88), 96 (100), 55 (38).

2.1.14. 1,4-Dioxaspiro[4.5]dec-6-en-8-one (16b). A solution of 1,4-cyclohexanedione monoethyleneketal (1.0 g; 6.4 mmol) in dry THF (5 ml) was added dropwise to a solution of LDA (7.7 mmol) in 40 ml of THF at −78°C for 30 min, then a solution of phenylselenenyl bromide (3.11 g, 12.8 mmol) in 5 ml of THF was added. The reaction mixture was stirred for 30 min and the reaction was quenched by sat. aq. NH_4Cl. The whole was extracted with $CHCl_3$ and washed with water. The organic layer was dried over

$MgSO_4$. The product was purified by silica gel column chromatography to give the selenate (1.51 g, 76%). To a solution of the selenate (3.0 g; 9.6 mmol) in 95 ml of THF was added acetic acid (2.5 ml) and 31% of hydrogen peroxide (14 ml). The reaction mixture was stirred at room temperature for 30 min and the reaction was quenched by $NaHCO_3$. The whole was extracted with Et_2O and washed with brine. The organic layer was dried over $MgSO_4$. The product was purified by silica gel flash column chromatography to give **16b** (926 mg; 62%) as a colorless oil; IR (neat) 2964, 2892, 1682 (CO), 1385, 1220, 1119, 1020, 914 cm^{-1}; ^1H NMR δ 2.20 (2H, t, J=6.1 Hz), 2.64 (2H, t, J=6.1 Hz), 4.05 (4H, m), 6.01, 6.61 (each 1H, d, J=10.4 Hz). Calcd for $C_8H_{10}O_3$: M, 154.0629. Found: m/z 154.0623; MS m/z (%) 154 (M^+, 13), 126 (100), 112 (12), 98 (53), 82 (10), 66 (10).

2.1.15. Acetic acid 1-[chloro-(toluene-4-sulfinyl)methyl]-cyclohex-2-enyl ester (17a). Colorless needles (about 4:1 diastereomeric mixture); mp 89–115°C (AcOEt–hexane); IR (KBr) 2941, 2915, 1726 (CO), 1370, 1237, 1086, 1059 (SO), 1018, 958, 821, 751 cm^{-1}; ^1H NMR δ 1.76–1.89 (2H, m), 2.05 (0.6H, s), 2.14 (2.4H, s), 2.0–2.2 (4H, m), 2.42 (3H, s), 5.45 (0.8H, s), 5.47 (0.2H, s), 6.05 (0.8H, brd, J=10.0 Hz), 6.11 (0.8H, ddd, J=10.0, 4.9, 2.5, Hz), 6.24 (0.2H, ddd, J=10.0, 4.8, 2.8 Hz), 6.33 (0.2H, brd, J=10.4 Hz), 7.32 (2H, d, J=8.2 Hz), 7.44 (1.6H, d, J=8.2 Hz), 7.49 (0.4H, d, J=8.2 Hz). Calcd for $C_{16}H_{18}ClO_3S$: M, 326.0744. Found: m/z 326.0741; MS m/z (%) 187 (M^+, 25), 182 (15), 140 (100), 139 (21), 109 (45), 91 (24), 81 (16). Anal. calcd for $C_{16}H_{19}ClO_3S$: C, 58.80; H, 5.86; Cl, 10.85; S, 9.81. Found: C, 58.74; H, 5.80; Cl, 10.74; S, 10.12%.

2.1.16. Acetic acid 8-[chloro-(toluene-4-sulfinyl)methyl]-1,4-dioxaspiro[4.5]dec-6-en-8-yl ester (17b). Colorless oil (about 2:1 diastereomeric mixture); IR (neat) 2977, 2885, 1733 (CO), 1398, 1370, 1243, 1211, 1092, 1064 (SO), 1018, 960, 822 cm^{-1}; ^1H NMR δ 1.90–1.93 (1H, m), 2.09 (1H, s), 2.15 (2H, s), 2.13–2.19 (1H, m), 2.42 (3H, s), 2.40–2.46 (1H, m), 2.58 (1H, dt, J=14.0, 3.4 Hz), 3.85–4.07 (4H, m), 5.42 (1H, s), 5.87 (0.7H, dd, J=10.0, 1.5 Hz), 5.94 (0.3H, d, J=10.4 Hz), 6.23 (0.7H, dd, J=10.0, 1.5 Hz), 6.46 (0.3H, d, J=10.4 Hz), 7.33 (2H, d, J=8.2 Hz), 7.43 (1.5H, d, J=8.2 Hz), 7.48 (0.5H, d, J=8.2 Hz). MS m/z (%) 245 ([M−TolS(O)]$^+$, 55), 167 (93), 140 (81), 139 (35), 87 (100), 43 (64).

2.1.17. (*E*)-1-(Chloro-cyclohex-2-enylidene-methanesulfinyl)-4-methylbenzene (18a-*E*). Colorless needles; mp 128–129°C (AcOEt–hexane); IR (KBr) 2954, 2922, 2911, 1615, 1493, 1084, 1057 (SO), 886, 877, 811, 746, 527 cm^{-1}; ^1H NMR δ 1.66–1.77 (1H, m), 1.79–1.86 (1H, m), 2.22–2.26 (2H, m), 2.41 (3H, s), 2.53–2.64 (2H, m), 6.26 (1H, dt, J=10.0, 4.3 Hz), 7.13 (1H, dt, J=10.0, 2.2 Hz), 7.30 (2H, d, J=8.0 Hz), 7.48 (2H, d, J=8.0 Hz). Calcd for $C_{14}H_{15}ClOS$: M, 266.0530. Found: m/z 266.0529; MS m/z (%) 266 (M^+, 10), 250 (10), 218 (100), 183 (33), 139 (12), 124 (37), 123 (22), 91 (65), 79 (25), 65 (25). Anal. calcd for $C_{14}H_{15}ClOS$: C, 63.03; H, 5.67; Cl, 13.29, S, 12.02. Found: C, 62.60; H, 5.54; Cl, 13.30, S, 12.16%

2.1.18. (*Z*)-1-(Chloro-cyclohex-2-enylidene-methanesulfinyl)-4-methylbenzene (18a-*Z*). Colorless prisms; mp 125–126°C (AcOEt–hexane); IR (KBr) 2942, 2865, 1610, 1492, 1428, 1083, 1056 (SO), 957, 877, 807, 749, 523 cm^{-1}; ^1H NMR δ 1.80–1.91 (2H, m), 2.26–2.31 (2H, m), 2.41 (3H, s), 2.73 (1H, ddd, J=15.3, 10.0, 5.0 Hz), 3.21 (1H, ddd, J=15.3, 7.0, 4.0 Hz), 6.33 (1H, dt, J=10.0, 4.3 Hz), 6.55 (1H, dt, J=10.0, 1.9 Hz), 7.30 (2H, d, J=8.0 Hz), 7.47 (2H, d, J=8.0 Hz). Calcd for $C_{14}H_{15}ClOS$: M, 266.0530. Found: m/z 266.0523; MS m/z (%) 266 (M^+, 73), 249 (81), 218 (42), 183 (25), 169 (13), 139 (20), 124 (40), 123 (32), 91 (100), 65 (62). Anal. calcd for $C_{14}H_{15}ClOS$: C, 63.03; H, 5.67; Cl, 13.29, S, 12.02. Found: C, 62.89; H, 5.53; Cl, 13.05, S, 12.30%

2.1.19. 8-[Chloro-(toluene-4-sulfinyl)methylene]-1,4-dioxaspiro[4.5]dec-6-ene (18b). Colorless crystals (about 1:1 mixture of two diastereomers); mp 84–95°C (AcOEt–hexane); IR (KBr) 2965, 2891, 1397, 1187, 1109, 1087, 1056 (SO), 1022, 906, 805, 532 cm^{-1}; ^1H NMR δ 1.88–2.07 (2H, m), 2.41 (3H, s), 2.71–2.84 (1H, m), 2.96 (0.5H, ddd, J=15.5, 10.0, 4.6 Hz), 3.32 (0.5H, ddd, J=15.5, 6.5, 1.8 Hz), 3.98–4.07 (4H, m), 5.99, 6.03, 6.66, 7.26 (each 0.5H, d, J=10.0 Hz), 7.31 (2H, d, J=8.0 Hz), 7.47, 7.48 (each 1H, d, J=8.0 Hz). Calcd for $C_{16}H_{17}ClO_3S$: M, 324.0587. Found: m/z 324.0583; MS m/z (%) 324 (M^+, 10), 308 (17), 276 (100), 261 (12), 241 (20), 232 (15), 204 (40), 169 (15), 165 (15), 139 (24), 123 (31), 91 (28), 77 (32).

2.1.20. 2-Aminospiro[4.5]deca-1,3,6-triene-1-carbonitrile (19a). Colorless crystals; mp 126–127°C (AcOEt–hexane); IR (KBr) 3443, 3354, 3260, 3237 (NH), 2929, 2174 (CN), 1645, 1609, 1540, 1430, 778 cm^{-1}; ^1H NMR δ 1.67–2.19 (6H, m), 4.57 (2H, brs, NH_2), 5.08 (1H, dt, J=10.0, 2.2 Hz), 5.94 (1H, dt, J=10.0, 3.9 Hz), 6.03, 6.45 (each 1H, d, J=5.4 Hz). Calcd for $C_{11}H_{12}N_2$: M, 172.0999. Found: m/z 172.0996; MS m/z (%) 172 (M^+, 100), 157 (68), 144 (35), 130 (26), 118 (17), 103 (8), 91 (10), 77 (10). Anal. calcd for $C_{11}H_{12}N_2$: C, 76.71; H, 7.02; N, 16.27. Found: C, 76.77; H, 7.01; N, 16.20%.

2.1.21. 10-Amino-1,4-dioxadispiro[4.2.4.2]tetradeca-6,9,11-triene-9-carbonitrile (19b). Colorless prisms; mp 172°C (AcOEt–hexane); IR (KBr) 3421, 3349, 3239 (NH), 2173 (CN), 1658, 1611, 1541, 1432, 1137, 1102, 945 cm^{-1}; ^1H NMR δ 1.86–1.97 (2H, m), 2.07–2.20 (2H, m), 3.96–4.06 (4H, m), 4.66 (2H, brs, NH_2), 5.29 (1H, d, J=9.8 Hz), 5.79 (1H, d, J=9.8 Hz), 6.11, 6.48 (each 1H, d, J=5.5 Hz). Calcd for $C_{13}H_{14}N_2O_2$: M, 230.1054. Found: m/z 230.1056; MS m/z (%) 230 (M^+, 100), 202 (40), 186 (55), 171 (18), 158 (50), 143 (12), 130 (35), 118 (20), 103 (13), 77 (8). Anal. calcd for $C_{13}H_{14}N_2O_2$: C, 67.81; H, 6.13; N, 12.17. Found: C, 67.63; H, 5.91; N, 12.12%.

2.1.22. Spiro[4.5]deca-3,6-dien-2-one (20). Colorless oil; IR (neat) 3018, 2927, 2859, 1717 (CO), 1584, 1406, 1340, 1205, 1179, 938, 802 cm^{-1}; ^1H NMR δ 1.60–1.86 (4H, m), 2.06 (2H, m), 2.31 (2H, d, J=2.0 Hz), 5.37 (1H, brd, J=10.0 Hz), 5.82 (1H, dt, J=10.0, 3.9 Hz), 6.08, 7.45 (each 1H, d, J=5.5 Hz). Calcd for $C_{10}H_{12}O$: M, 148.0887. Found: m/z 148.0887; MS m/z (%) 148 (M^+, 83), 133 (25), 120 (71), 105 (39), 91 (100), 79 (44), 65 (18).

2.1.23. Spiro[4.5]deca-3,7-dien-2-one (21). Colorless oil; IR (neat) 3026, 2919, 2842, 1714, 1588, 1439, 1408, 1189,

944, 796 cm^{-1}; ^1H NMR δ 1.63–1.72 (3H, m), 1.94–2.05 (1H, m), 2.16–2.28 (4H, m), 5.71, 5.77 (each 1H, brd, J=10.0 Hz), 6.09, 7.57 (each 1H, d, J=5.5 Hz). Calcd for $C_{10}H_{12}O$: M, 148.0887. Found: m/z 148.0884; MS m/z (%) 148 (M^+, 100), 133 (12), 120 (28), 105 (11), 94 (68), 79 (20), 66 (67), 54 (95).

2.1.24. Spiro[4.5]deca-3,6-diene-2,8-dione (22). Colorless plates; mp 84–85°C (AcOEt–hexane); IR (KBr) 2927, 1712 (CO), 1683 (CO), 1583, 1390, 1347, 1208, 822 cm^{-1}; ^1H NMR δ 2.09–2.26 (2H, m), 2.50 (2H, d, J=2.4 Hz), 2.49–2.71 (2H, m), 6.05 (1H, d, J=10.0 Hz), 6.29 (1H, d, J=5.5 Hz), 6.59 (1H, d, J=10.0 Hz), 7.57 (1H, d, J=5.5 Hz). Calcd for $C_{10}H_{10}O_2$: M, 162.0680. Found: m/z 162.0686; MS m/z (%) 162 (M^+, 100), 134 (99), 120 (29), 106 (85), 91 (48), 78 (85), 77 (19), 51 (22). Anal. calcd for $C_{10}H_{10}O_2$: C, 74.06; H, 6.21. Found: C, 74.04; H, 6.04%.

2.1.25. (−)-Acetic acid 1-[chloro-(toluene-4-sulfinyl)-methyl]-1,2,3,4-tetrahydronaphthalen-1-yl ester (24L). Colorless amorphous; IR (KBr) 2940, 1747 (CO), 1492, 1451, 1367, 1234, 1089, 1063 (SO), 812, 753 cm^{-1}; ^1H NMR δ 1.96–2.04 (1H, m), 2.00 (3H, s), 2.08–2.18 (1H, m), 2.40 (3H, s), 2.42–2.55 (2H, m), 2.86–2.97 (2H, m), 5.32 (1H, s), 7.26–7.33 (7H, m), 7.50 (1H, d, J=7.4 Hz). MS m/z (%) 237 ([M−TolS(O)]$^+$, 20), 178 (82), 159 (100), 129 (80), 83 (64), 43 (55). $[\alpha]_D^{23}$=−5.68 (c 0.41, acetone).

2.1.26. (−)-Acetic acid 1-[chloro-(toluene-4-sulfinyl)-methyl]-1,2,3,4-tetrahydronaphthalen-1-yl ester (24P). Colorless crystals; mp 111–112°C (AcOEt–hexane); IR (KBr) 2926, 1752 (CO), 1495, 1366, 1226, 1091, 1068 (SO), 1017, 974, 820, 773, 743, 513 cm^{-1}; ^1H NMR δ 1.93–2.02 (1H, m), 2.10–2.19 (1H, m), 2.13 (3H, s), 2.43 (3H, s), 2.57 (1H, ddd, J=14.7, 11.0, 4.3 Hz), 2.63 (1H, dt, J=14.7, 4.6 Hz), 2.77 (1H, ddd, J=16.5, 11.0, 5.5 Hz), 2.85 (1H, dt, J=16.5, 5.0 Hz), 5.41 (1H, s), 7.13–7.25 (3H, m), 7.34 (2H, d, J=8.0 Hz), 7.48 (1H, d, J=8.0 Hz), 7.53 (2H, d, J=8.0 Hz). MS m/z (%) 182 (42), 140 (100), 131 (40), 91 (25). Anal. calcd for $C_{20}H_{21}ClO_3S$, C, 63.73; H, 5.62; Cl, 9.41; S, 8.51. Found: C, 63.69; H, 5.49; Cl, 9.27; S, 8.48%. $[\alpha]_D^{23}$=−111.9 (c 0.42, acetone).

2.1.27. (+)-(*E*)-1-[Chloro-(toluene-4-sulfinyl)methylene]-1,2,3,4-tetrahydronaphthalene (25). Colorless needles; mp 147.5–148°C (AcOEt–hexane); IR (KBr) 2949, 1084, 1056 (SO), 863, 815, 763, 534 cm^{-1}; ^1H NMR δ 1.80–1.88 (2H, m), 2.41 (3H, s), 2.61–2.69, 2.71–2.77 (each 1H, m), 2.82 (2H, t, J=7.0 Hz), 7.24–7.32 (2H, m), 7.31 (2H, d, J=8 Hz), 7.37 (1H, dt, J=6.5, 1.0 Hz), 7.47 (2H, d, J=8.0 Hz), 7.62 (1H, d, J=7.7 Hz). Calcd for $C_{18}H_{17}ClOS$: M, 316.0688. Found: m/z 316.0688: MS m/z (%) 316 (M^+, 28), 300 (100), 265 (30), 237 (25), 207 (18), 181 (28), 141 (94), 115 (58), 91 (32). Anal. calcd for $C_{18}H_{17}ClOS$: C, 68.23; H, 5.41; Cl, 11.19; S, 10.12. Found: C, 68.24; H, 5.26; Cl, 11.17; S, 10.09%. $[\alpha]_D^{24}$=+394.6 (c 0.40, acetone).

2.1.28. (−)-(*S*)-Spiro[4.5]enaminonitrile (26). Colorless needles; mp 225–226°C (AcOEt–hexane); IR (KBr) 3439, 3357, 3240 (NH), 2929, 2166 (CN), 1659, 1641, 1609, 1540, 1421, 759 cm^{-1}; ^1H NMR δ 1.85–1.95 (2H, m), 2.09–2.19 (2H, m), 2.83 (1H, dt, J=16.8, 5.5 Hz), 2.90–2.96 (1H, m), 4.64 (2H, brs, NH_2), 6.05, 6.73 (each 1H, d, J=5.5 Hz), 6.84 (1H, d, J=7.7 Hz), 7.00–7.04 (1H, m), 7.10 (2H, d, J=4.0 Hz). Calcd for $C_{15}H_{14}N_2$: M, 222.1156. Found: m/z 222.1150: MS m/z (%) 222 (M^+, 100), 207 (22), 194 (36), 180 (24), 167 (8). Anal. calcd for $C_{15}H_{14}N_2$: C, 81.05; H, 6.35; N, 12.60. Found: C, 80.89; H, 6.30; N, 12.36%. $[\alpha]_D^{24}$=−430.5 (c 0.41, acetone; over 99% ee).

2.1.29. (−)-(*S*)-Spiro[4.5]alkenone (27). Colorless needles; mp 108–109°C (AcOEt–hexane); IR (KBr) 2923, 1706 (CO), 1586, 1490, 1448, 1399, 1181, 817, 759 cm^{-1}; ^1H NMR δ 1.76–1.88 (2H, m), 1.92–2.05 (2H, m), 2.52 (1H, d, J=18.6 Hz), 2.56 (1H, d, J=18.6 Hz), 2.81–2.90 (2H, m), 6.25 (1H, d, J=5.5 Hz), 6.97–6.99 (1H, m), 7.11–7.17 (3H, m), 7.54 (1H, d, J=5.5 Hz). Calcd for $C_{14}H_{14}O$: M, 198.1044. Found: m/z 198.1051: MS m/z (%) 198 (100), 183 (12), 169 (16), 155 (17), 141 (31), 128 (22), 115 (20). Anal. calcd for $C_{14}H_{14}O$; C, 84.81; H, 7.12. Found: C, 84.74; H, 7.13%. $[\alpha]_D^{23}$=−135.9 (c 0.40, acetone).

2.1.30. 4-[Chloro-(toluene-4-sulfinyl)methylene]cyclohexanone (29). The ketal **28**[10] (700 mg, 2.14 mmol) was dissolved in a mixture of acetic acid (18 ml) and water (4.5 ml) and the reaction mixture was stirred and heated at 75°C for 2 h. The reaction mixture was neutralized with 10% NaOH and the whole was extracted with $CHCl_3$ and the organic layer was washed with water. The organic layer was dried over $MgSO_4$. The product was purified by silica gel flash column chromatography to give **29** (599 mg, 99%) as colorless needles; mp 108–109°C (AcOEt–hexane); IR (KBr) 2970, 1711 (CO), 1085, 1053 (SO), 872, 807, 528 cm^{-1}; ^1H NMR δ 2.43 (3H, s), 2.50–2.64 (4H, m), 2.78 (1H, dt, J=17.1, 7.0 Hz), 2.86–2.93 (1H, m), 3.07 (1H, ddd, J=15.6, 9.6, 5.5 Hz), 3.45 (1H, dt, J=15.6, 6.1 Hz), 7.34, 7.50 (each 2H, d, J=8.0 Hz). Calcd for $C_{14}H_{15}ClO_2S$: M, 282.0481. Found: m/z 282.0487: MS m/z (%) 282 (M^+, 45), 265 (80), 229 (95), 223 (21), 187 (20), 139 (35), 123 (100), 105 (22), 91 (43), 79 (33), 77 (32). Anal. calcd for $C_{14}H_{15}ClO_2S$; C, 59.46; H, 5.35; Cl, 12.54; S, 11.34. Found: C, 59.52; H, 5.32; Cl, 12.51; S, 11.32%.

2.1.31. 1-[Chloro-(4-methylene-cyclohexylidene)-methanesulfinyl]-4-methylbenzene (30). A solution of **29** (89.6 mg, 0.32 mmol) in dry THF (1 ml) was added dropwise to a solution of methylenetriphenylphosphorane (0.7 mmol; prepared from n-BuLi (0.7 mmol) and methyltriphenylphosphonium bromide (274 mg, 0.77 mmol) in THF (1.5 ml)) in THF at room temperature. The reaction mixture was stirred at room temperature for 3 h and the reaction was quenched by sat. aq. NH_4Cl. The whole was extracted with $CHCl_3$ and washed with water. The organic layer was dried over $MgSO_4$. The product was purified by silica gel flash column chromatography to give **30** (54.5 mg; 61%) as colorless crystals; mp 94–95°C (AcOEt–hexane); IR (KBr) 2941, 1651, 1491, 1438, 1087, 1058 (SO), 892, 867, 813 cm^{-1}; ^1H NMR δ 2.26–2.41 (3H, m), 2.41 (3H, s), 2.43–2.53 (2H, m), 2.62 (1H, ddd, J=13.9, 7.8, 5.2 Hz), 2.86 (1H, ddd, J=13.7, 8.7, 5.0 Hz), 3.04 (1H, ddd, J=13.7, 7.8, 5.0 Hz), 4.80 (2H, s), 7.32, 7.48 (each 2H, d, J=8.2 Hz). Calcd for $C_{15}H_{17}ClOS$: M, 280.0687. Found: m/z 280.0685: MS m/z (%) 280 (M^+, 33), 263 (100), 227 (33), 171 (20), 139 (28), 124 (21), 105 (34), 91 (45), 77 (30), 65 (20). Anal.

calcd for $C_{15}H_{17}ClOS$; C, 64.16; H, 6.10; Cl, 12.62; S, 11.42. Found: C, 64.32; H, 6.08; Cl, 12.53; S, 11.36%.

2.1.32. 2-Amino-8-methylenespiro[4.5]deca-1,3-diene-1-carbonitrile (31). Colorless plates; mp 167–168°C (AcOEt–hexane); IR (KBr) 3435, 3345, 3237 (NH), 2935, 2167 (CN), 1651, 1610, 1547, 1430, 885, 775 cm^{-1}; ^1H NMR δ 1.53–1.57 (2H, m), 1.86 (2H, dt, J=12.5, 4.3 Hz), 2.26 (2H, dt, J=12.0, 4.3 Hz), 2.48 (2H, dt, J=14.0, 4.6 Hz), 4.54 (2H, brs, NH_2), 4.72 (2H, s), 6.09, 6.89 (each 1H, d, J=5.5 Hz). Calcd for $C_{12}H_{14}N_2$: M, 186.1157. Found: m/z 186.1160: MS m/z (%) 186 (M^+, 100), 171 (38), 131 (35), 118 (88), 91 (19). Anal. calcd for $C_{12}H_{14}N_2$; C, 77.38; H, 7.58; N, 15.04. Found: C, 77.06; H, 7.36; N, 14.70.

2.1.33. (±)-8-Methylspiro[4.5]deca-3,7-dien-2-one (32). Colorless oil; IR (KBr) 2918, 1716 (CO), 1587, 1439, 1188, 795 cm^{-1}; ^1H NMR δ 1.61–1.71 (2H, m), 1.70 (3H, s), 1.93 (1H, brd, J=16.8 Hz), 2.00–2.22 (3H, m), 2.16 (1H, d, J=18.5 Hz), 2.23 (1H, d, J=18.5 Hz), 5.39 (1H, m), 6.07, 7.56 (each 1H, d, J=5.5 Hz). Calcd for $C_{11}H_{14}O$: M, 162.1044. Found: m/z 162.1049: MS m/z (%) 162 (M^+, 72), 95 (40), 91 (13), 68 (100), 67 (20).

Acknowledgements

This work was supported by a Grant-in-Aid for Scientific Research No. 11640545 from the Ministry of Education, Culture, Sports, Science and Technology, Japan, which is gratefully acknowledged.

References

1. Ho, T.-L. *Carbocyclic Construction in Terpene Synthesis*; VCH: Weinheim, 1988.
2. A review for the stereocontrolled synthesis of spirocycles: Sannigrahi, M. *Tetrahedron* **1999**, *55*, 9007.
3. Some selected recent papers for the synthesis of spirocycles: (a) Fujioka, H.; Kitagaki, S.; Imai, R.; Kondo, M.; Okamoto, S.; Yoshida, Y.; Akai, S.; Kita, Y. *Tetrahedron Lett.* **1995**, *36*, 3219. (b) Srikrishna, A.; Kumar, P. P.; Viswajanani, R. *Tetrahedron Lett.* **1996**, *37*, 1683. (c) Kita, Y.; Kitagaki, S.; Yoshida, Y.; Mihara, S.; Fang, D.-F.; Kondo, M.; Okamoto, S.; Imai, R.; Akai, S.; Fujioka, H. *J. Org. Chem.* **1997**, *62*, 4991. (d) Pohmakotr, M.; Bunlaksananusorn, T.; Tuchinda, P. *Tetrahedron Lett.* **2000**, *41*, 377. (e) Srikrishna, A.; Kumar, P. P. *Tetrahedron* **2000**, *56*, 8189. (f) Clive, D. L. J.; Huang, X. *Tetrahedron* **2001**, *57*, 3845. (g) Oesterreich, K.; Klein, I.; Spitzner, D. *Synlett* **2002**, 1712. (h) Du, Y.; Lu, X.; Yu, Y. *J. Org. Chem.* **2002**, *67*, 8901.
4. (a) Martin, S. F. *Tetrahedron* **1980**, *36*, 419. (b) Fuji, K. *Chem. Rev.* **1993**, *93*, 2037. (c) Corey, E. J.; Guzman-Perez, A. *Angew Chem. Int. Ed.* **1998**, *37*, 388.
5. (a) Satoh, T.; Ota, H. *Tetrahedron* **2000**, *56*, 5113. (b) Satoh, T.; Yoshida, M.; Ota, H. *Tetrahedron Lett.* **2001**, *42*, 9241. (c) Satoh, T.; Yoshida, M.; Takahashi, Y.; Ota, H. *Tetrahedron: Asymmetry* **2003**, *14*, 281.
6. (a) Satoh, T.; Oohara, T.; Ueda, Y.; Yamakawa, K. *Tetrahedron Lett.* **1988**, *29*, 313. (b) Satoh, T.; Oohara, T.; Ueda, Y.; Yamakawa, K. *J. Org. Chem.* **1989**, *54*, 3130.
7. Crystallographic data for **25**. $C_{18}H_{17}ClOS$, M=316.83, orthorhombic, space group $P2_12_12_1$ (#19), a=8.0065(7), b=12.4937(11), c=15.9413(14) Å, V=1594.6(2) $Å^3$, Z=4, F(000)=664, D_{calc}=1.320 g cm^{-3}, μ(Mo Kα)=3.66 cm^{-1}, T=296 K, radiation=0.71073 Å, $R1$=0.0620 for $I>2.0\sigma(I)$, $wR2$=0.1328 for all data (3648 reflections), GOF=1.105 (219 parameters), crystal dimensions 0.35×0.10×0.10 mm^3. A quality single crystal of **25** was mounted on a glass fiber. Diffraction data were measured on a Bruker APEX CCD-Detector X-ray diffractometer with monochromated Mo Kα radiation. A part of the cyclohexane methylene moiety was treated as being disordered over two sites (C3A, C4A, C5A; C3B, C4B, C5B), where the occupation factors of two sites were refined and converged at 42(2) and 58(2)%, respectively. The data reduction, structure solution and refinement, and all the necessary computational data processes were performed using SMART, SAINT, SHELXTL, KENX, and TEXSAN programs. Data deposited at the Cambridge Crystallographic Data Centre; deposition number CCDC 214890.
8. Crystallographic data for **26**. $C_{15}H_{14}N_2$, M=222.28, orthorhombic, space group $P2_12_12_1$ (#19), a=6.8893(6), b=11.5269(10), c=15.5172(13) Å, V=1232.26(18) $Å^3$, Z=4, F(000)=472, D_{calc}=1.198 g cm^{-3}, μ(Mo Kα)=0.72 cm^{-1}, T=296 K, radiation=0.71073 Å, $R1$=0.0638 for $I>2.0\sigma(I)$, $wR2$=0.1458 for all data (2840 reflections), GOF=1.173 (154 parameters), crystal dimensions 0.341×0.215×0.070 mm^3. Other details are similar to those described above for **25**. Data deposited at the Cambridge Crystallographic Data Centre; deposition number CCDC 214891.
9. (a) McCrae, D. A.; Dolby, L. *J. Org. Chem.* **1977**, *42*, 1607. (b) Martin, S. F.; Chou, T.-S. *J. Org. Chem.* **1978**, *43*, 1027. (c) Srikrishna, A.; Kumar, P. P. *Tetrahedron* **2000**, *56*, 8189. (d) Srikrishna, A.; Rao, M. S.; Gharpure, S. J.; Babu, N. C. *Synlett* **2001**, 1986.
10. Satoh, T.; Takano, K.; Ota, H.; Someya, H.; Matsuda, K.; Koyama, M. *Tetrahedron* **1998**, *54*, 5557.
11. Satoh, T.; Sugiyama, S.; Kamide, Y.; Ota, H. *Tetrahedron* **2003**, *59*, 4327.