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A novel synthesis, including asymmetric synthesis, of 2,4,4-trisubstituted 2-cyclopentenones based on the reaction of 1-chlorovinyl *p*-tolyl sulfoxides with acetonitrile and its homologues

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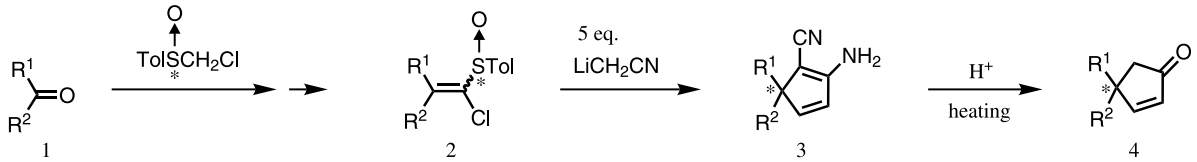
Abstract—Reaction of 1-chlorovinyl *p*-tolyl sulfoxides, which were synthesized from chloromethyl *p*-tolyl sulfoxide and ketones in high overall yields, with cyanomethyllithium (lithium α-carbanion of acetonitrile) gave adducts in high to quantitative yields. The adducts were treated with LDA followed by lithium α-carbanion of the homologues of acetonitrile to give 3,5,5-trisubstituted enaminonitriles in good to high yields. Hydrolysis of the enaminonitriles under acidic conditions gave 2,4,4-trisubstituted 2-cyclopentenones in good yields. By using the optically active chloromethyl *p*-tolyl sulfoxide and unsymmetrical ketones, this procedure gave the optically pure 2,4,4-trisubstituted 2-cyclopentenones. The scope and limitations of this method and the mechanism of the reactions are also discussed. These procedures offer a new and effective method for the synthesis of 2,4,4-trisubstituted 2-cyclopentenones from four components, ketones, chloromethyl *p*-tolyl sulfoxide, acetonitrile, and its homologues.

1. Introduction

The cyclopentane, including cyclopentanone and cyclopentenone, ring system is among the most widely found structures in natural compounds, especially in cyclopentanoid natural products.[1] 2-Cyclopentenones are undoubtedly one of the most versatile intermediates in the synthesis of cyclopentanes, because, the 3- and 5-positions of the 2-cyclopentenones are quite easily modified by a general method, for example, 1,4-addition of the enone system and aldol-type reaction, respectively. However, modification of the 2-position of the 2-cyclopentenones has been recognized to be relatively difficult.[2] In view of the importance of 2-cyclopentenones in organic synthesis, several methods such as the Nazarov cyclization[3] and the Pauson–Khand reaction[4] have been reported.

Recently, we reported a reaction of 1-chlorovinyl *p*-tolyl sulfoxides **2**, derived from ketones **1** and chloromethyl *p*-tolyl sulfoxide in three steps, with cyanomethyllithium to give 5,5-disubstituted enaminonitrile **3** in high to quantitative yield.[5] Acidic hydrolysis of **3** gave 4,4-disubstituted 2-cyclopentenones **4** in good yield (Scheme 1). Further, when unsymmetrical ketones and optically active chloromethyl *p*-tolyl sulfoxide were used in this procedure, an asymmetric synthesis of optically pure 4,4-disubstituted 2-cyclopentenones **4** was realized.[6]

Considering the usefulness of this procedure in the synthesis of 4,4-disubstitued 2-cyclopentenones and the proposed mechanism of the reaction from **2** to **3**,[5] we anticipated that if we used several kinds of nitriles other than acetonitrile in this reaction, highly substituted 2-cyclopentenones could be



1 2 3 4

Scheme 1.

Keywords: 2-Cyclopentenone; 2,4,4-Trisubstituted 2-cyclopentenone; Conjugate addition; Sulfoxide; Asymmetric synthesis.
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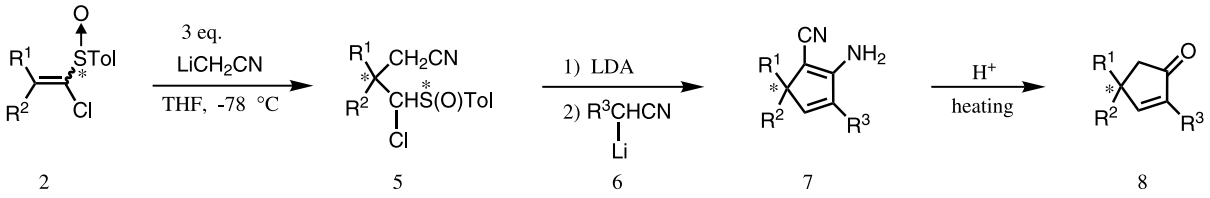


Scheme 2.

obtained. We investigated the reaction of 1-chlorovinyl *p*-tolyl sulfoxides **2** with several lithium α-carbanion of nitriles and found a quite versatile method for synthesis of 3,5,5-trisubstituted enaminonitriles **7** and 2,4,4-trisubstituted 2-cyclopentenones **8**. The whole sequence is shown in Scheme 2. Thus, the vinyl sulfoxides **2** was first treated with cyanomethyllithium at −78 °C to give the adducts **5**, which were treated with LDA followed by the lithium α-carbanion of the homologues of acetonitrile to afford 3,5,5-trisubstituted enaminonitriles **7**. The enaminonitriles were hydrolyzed to give 2,4,4-trisubstituted 2-cyclopentenones **8** in good to high yields. Herein we describe the details of this investigation and the application of this procedure to an asymmetric synthesis of optically active 2,4,4-trisubstituted 2-cyclopentenones.[7]

2. Results and discussion

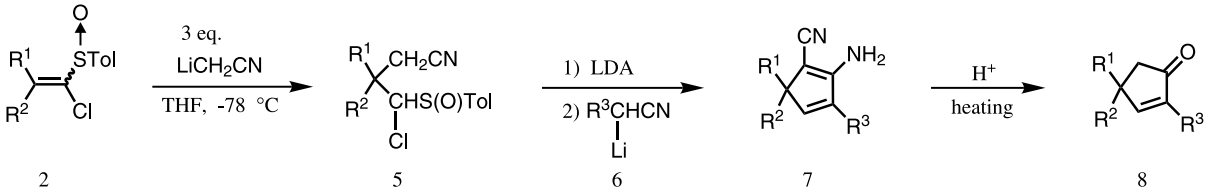
2.1. The reaction of lithium α-carbanion of acetonitrile and propionitrile with 1-chlorovinyl *p*-tolyl sulfoxides

As the substrate used in this investigation we selected three 1-chlorovinyl *p*-tolyl sulfoxides **2a–c** and synthesized them from the corresponding ketones and chloromethyl *p*-tolyl sulfoxide (see Table 1).[5,6] First, we studied the reaction of **2c** with lithium carbanion of propionitrile. We anticipated a product like **9** if the expected reaction worked (Scheme 3). Thus, 5 equiv of lithium α-carbanion of propionitrile was generated from propionitrile and *n*-butyllithium in THF at −78 °C. In this solution, a solution of **2c** in THF was added and the temperature of the reaction mixture was slowly allowed to warm to room temperature. However, only a complex mixture was obtained.

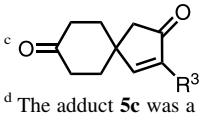
Next, to a solution of 3 equiv of lithium α-carbanion of propionitrile was added a solution of **2c** at −78 °C. The reaction was quenched with water after 10 min to give the adduct **10** in 91% yield.[5b] The adduct was treated with 3 equiv of LDA at −78 °C and to the solution was added a solution of 4 equiv of cyanomethyllithium. The reaction mixture was stirred and allowed to warm to room temperature. We anticipated a product like **11** in this treatment; however, we obtained a rather complex mixture with 27% of the enaminonitrile **3a**.

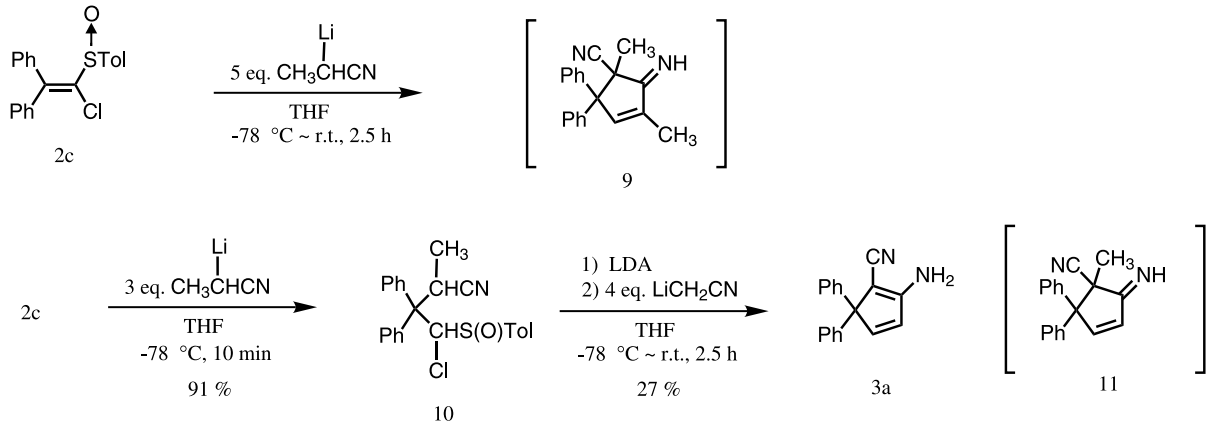
This rather unexpected result was explained as follows. Treatment of **10** with LDA afforded α-sulfinyl carbanion of **10**, from which the lithium α-carbanion of propionitrile was eliminated to give the vinyl sulfoxide **2c**. The cyanomethyllithium in the reaction mixture reacted with **2c** to give the enaminonitrile **3a**.[5]

Table 1. Synthesis of 3,5,5-trisubstituted enaminoitriles **7** and 2,4,4-trisubstituted 2- cyclopentenones **8** from the vinyl sulfoxides **2** by the reaction with acetonitrile followed by the homologues of acetonitrile



Entry	Vinyl sulfoxide **2**		Adduct **5**		R^3	Examinonitrile **7**		2-Cyclopentenone **8**	
	R^1	R^2		Yield/%			Yield/%		Yield/%
1	**2a**	$-(CH_2)_{14}-$	**5a**[a]	97	CH_3	**7a**	80	**8a**	93
2					CH_3CH_2	**7b**	76	**8b**	83
3	**2b**	$-(CH_2)_2C(CH_2)_2-$ (O,O)	**5b**[b]	99	CH_3	**7c**	76	**8c**[c]	87
4					CH_3CH_2	**7d**	75	**8d**[c]	89
5	**2c** Ph	Ph	**5c**[d]	93	CH_3	**7e**	62	**8e**	74
6					CH_3CH_2	**7f**	55	**8f**	72

[a] The adduct **5a** was 3:1 mixture of two diastereomers.
[b] The adduct **5b** was a 7:3 mixture of two diastereomers.
[c] 
[d] The adduct **5c** was a 13:3 mixture of two diastereomers.



Scheme 3.

2.2. Consecutive reaction of 1-chlorovinyl *p*-tolyl sulfoxides with cyanomethyllithium and lithium α-carbanion of the homologues of acetonitrile.[7]

Finally, we tried the reaction shown in Table 1. 1-Chlorovinyl *p*-tolyl sulfoxide **2a**, derived from cyclopentadecanone, was treated with 3 equiv of cyanomethyllithium at −78 °C for 10 min to give the adduct **5a** in 97% yield as a 3:1 mixture of two diastereomers (Table 1, entry 1). A diastereomeric mixture of the adduct **5a** was treated with 3 equiv of LDA followed by lithium α-carbanion of propionitrile and the reaction mixture was stirred and slowly allowed to warm to room temperature. Fortunately, this reaction gave the desired 3,5,5-trisubstituted enaminonitrile **7a** in 80% yield as colorless crystals.

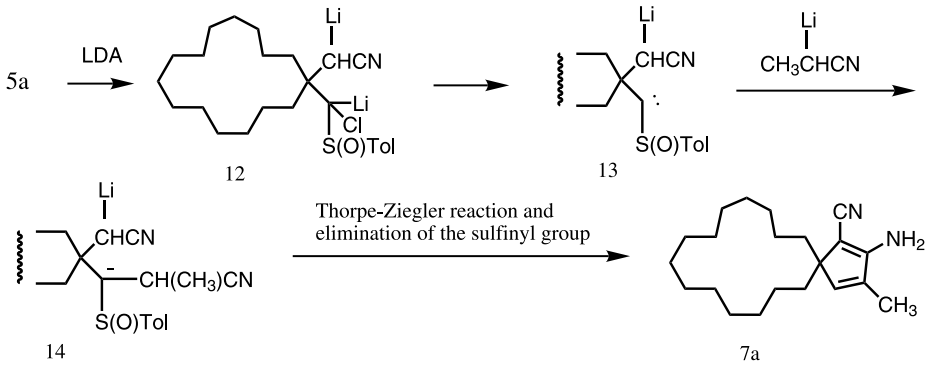
The presumed mechanism of this reaction is as follows (Scheme 4). Treatment of the adduct **5a** with 3 equiv of LDA afforded the lithium α-sulfinyl carbanion **12**. Upon warming the reaction mixture, α-elimination of LiCl took place to give α-sulfinyl carbenoid **13**. Addition of lithium α-carbanion of propionitrile to the electrophilic carbon of the carbenoid **13** resulted in the formation of the dinitrile **14**. Finally, the Thorpe–Ziegler reaction[8] of the dinitrile **14** with concomitant elimination of the *p*-tolylsulfinyl group took place to afford the enaminonitrile **7a**.

The enaminonitrile **7a** was heated under reflux in acetic acid containing H_3PO_4 and a small amount of water for 30 h to afford the desired 2,4,4-trisubstituted 2-cyclopentenone **8a** in 93% yield (Table 1, entry 1). The same reaction of **5a** with butyronitrile was carried out. As shown in Table 1, entry 2, the reaction of **5a** with lithium α-carbanion of butyronitrile gave **7b** in 76% yield, which was hydrolyzed to afford **8b** in somewhat lower yield compared with the yield in entry 1.

To ascertain the generality of this procedure, we investigated the reaction with other 1-chlorovinyl *p*-tolyl sulfoxides **2b** and **2c** with propionitrile and butyronitrile. The results are summarized in Table 1, entries 3–6. The addition reaction of **2b** and **2c** with cyanomethyllithium gave almost quantitative yields of **5b** and **5c**, respectively. In the next two steps, similar results were obtained with the adduct **5b** (entries 3 and 4). However, the reactions starting from the adduct **5c** (entries 5 and 6) showed somewhat lower yields of the enaminonitrile (**7e** and **7f**) and the 2-substituted 2-cyclopentenone (**8e** and **8f**). In any event, generality of this procedure was confirmed from the results described above.

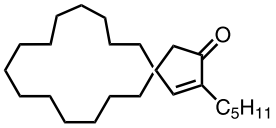
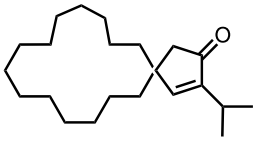
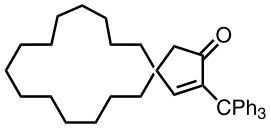
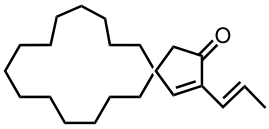
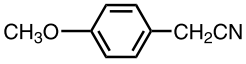
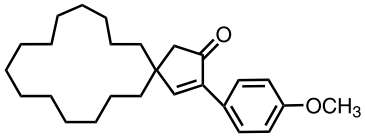
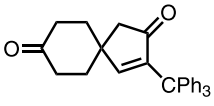
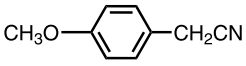
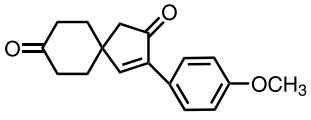
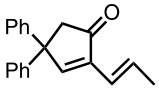
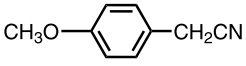
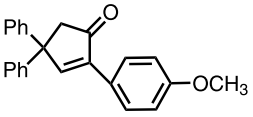
2.3. Investigation of the scope and limitation of the nitriles (R^3CH_2CN) used in this procedure

As described above, this procedure is quite a good way for the synthesis of 2,4,4-trisubstituted 2-cyclopentenones. It is interesting to investigate what kind of substituents could be introduced at the 2-position. We studied this procedure with heptanenitrile, isovaleronitrile, 3,3,3-triphenylpropionitrile,[9]



Scheme 4.

Table 2. Synthesis of 3,5,5-trisubstituted enaminonitriles **7** and 2,4,4-trisubstituted 2-cyclopentenones **8** from the adducts **5** and the homologues of acetonitrile

Entry	Adduct **5**	R^3CH_3CN	Enaminonitrile **7**		2,4,4-Trisubstituted 2-cyclopentenone **8**		Yield/%
			Yield/%				
1	**5a**	$C_6H_{13}CN$	**7g**	72	**8g**		87
2	**5a**	$(CH_3)_2CHCH_2CN$	**7h**	79	**8h**		91
3	**5a**	Ph_3CCH_2CN	**7i**	46	**8i**		51
4	**5a**	$CH_3CH{=}CHCH_2CN$	**7j**	76	**8j**		33
5	**5a**		**7k**	64	**8k**		93
6	**5b**	Ph_3CCH_2CN	**7l**	78	**8l**		89
7	**5b**		**7m**	90	**8m**		99
8	**5c**	Ph_3CCH_2CN	Complex mixture			—	
9	**5c**	$CH_3CH{=}CHCH_2CN$	**7n**	81	**8n**		61
10	**5c**		**7o**	91	**8o**		62

trans-3-pentenenitrile, and (4-methoxyphenyl)acetonitrile and the results are summarized in Table 2.

As shown in Table 2, entries 1–5, the reaction of the adduct **5a** with the five nitriles mentioned above gave the desired enaminonitriles **7g–k** in variable yields (46–79%). The acidic hydrolysis of **7g–k** gave the enones **8g–k**, respectively, in good to high yields except **8j**. Long-chain and branched-chain hydrocarbons were placed on the 2-position in good overall yields (entries 1 and 2). 2-Cyclopentenone having a quite bulky substituent (triphenylmethyl group) **8i** was also synthesized by this procedure though the overall yield was not satisfactory (entry 3). The enaminonitrile having an unsaturated carbon chain on the 2-position, **7j**, could be synthesized without problem (entry 4); however, the acidic hydrolysis gave a rather complex reaction mixture and only 33% of the 2-cyclopentenone **8j** could be obtained. Acetonitrile having an aromatic group could be used in this reaction and the 2-cyclopentenone directly combined with the aromatic ring at the 2-position **8k** could be obtained in good overall yield (entry 5).

Entries 6 and 7 show the results of the reaction of **5b** with 3,3,3-triphenylpropionitrile and (4-methoxyphenyl)acetonitrile. The desired enones **8l** and **8m** were obtained in high overall yields. Entries 8–10 show the results of the reaction of **5c** with 3,3,3-triphenylpropionitrile, *trans*-3-pentenenitrile, and (4-methoxyphenyl)acetonitrile. Interestingly, the reaction of **5c** with 3,3,3-triphenylpropionitrile only gave a complex mixture (entry 8). Two other reactions gave the desired enones **8n** and **8o** in moderate overall yields.

2.4. Synthesis of 2-(3-hydroxypropyl)-4,4-dimethyl-2-cyclopentenone from acetone by this procedure

Many cyclopentanoid natural products have geminal methyl groups on the cyclopentane ring.[1] As an application of our method described above, we planned to synthesize 2-(3-hydroxypropyl)-4,4-dimethyl-2-cyclopentenone **8q**, which was reported to be an intermediate in the total synthesis of alliacolide,[10] from acetone (Scheme 5).

1-Chlorovinyl *p*-tolyl sulfoxide **2d** was synthesized from acetone in high overall yield.[5b] The vinyl sulfoxide **2d** was treated with cyanomethyllithium to give the adduct **5d** in quantitative yield as a 17:4 mixture of two diastereomers. First, **5d** was treated with 3 equiv of LDA followed by the dianion of 5-hydroxypentanenitrile under the conditions described above. The desired enaminonitrile bearing a 3-hydroxypropyl group at the 3-position **7p** was obtained; however, the yield was not satisfactory. The presence of the free hydroxyl group in the reaction was thought to be the reason for the lowered yield.

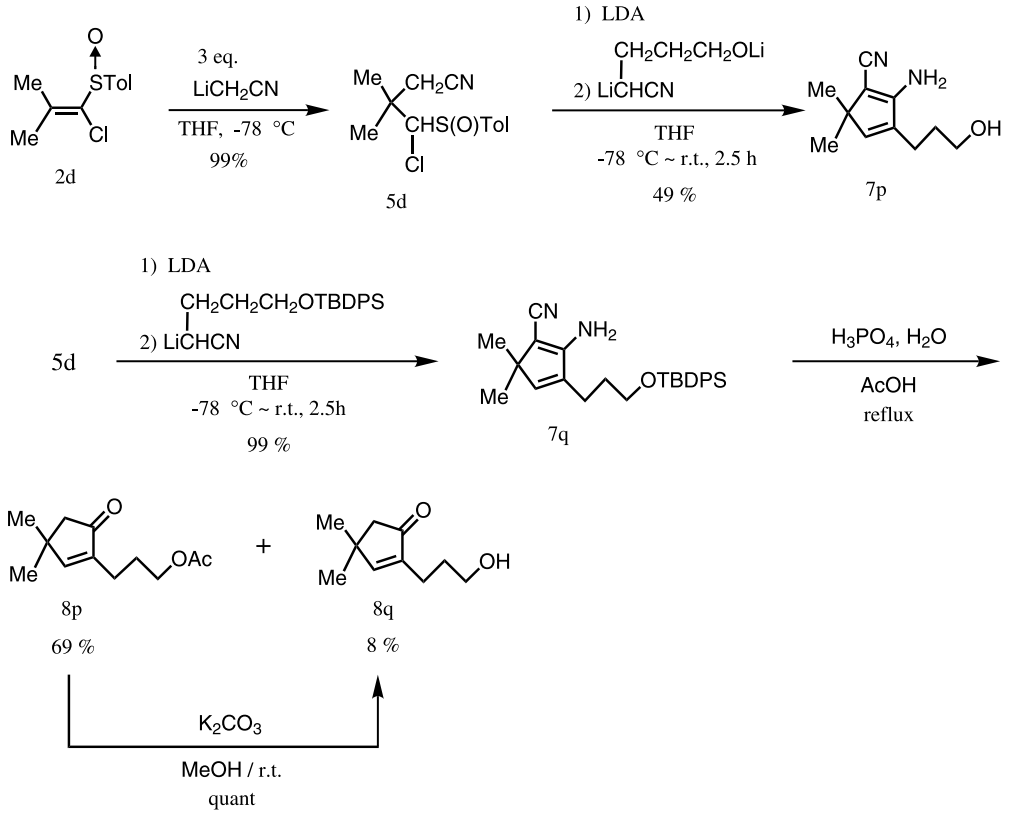
Next, O-protected 5-hydroxypentanenitrile was reacted with **5d** under the same conditions described above. As expected, the desired enaminonitrile **7q** was obtained in quantitative yield. Finally, **7q** was heated under reflux in acetic acid containing H_3PO_4 and water. We obtained the desired 2-(3-hydroxypropyl)-4,4-dimethyl-2-cyclopentenone **8q**; however, the main product was found to be the acetate **8p**. The acetate **8p** was transformed, in the usual manner, to give the alcohol **8q** in a quantitative yield. As a whole, the desired **8q**[10] was obtained from **7q** in 77% yield.

2.5. Asymmetric synthesis of optically active 3,5,5-trisubstituted enaminonitriles and 2,4,4-trisubstituted 2-cyclopentenones

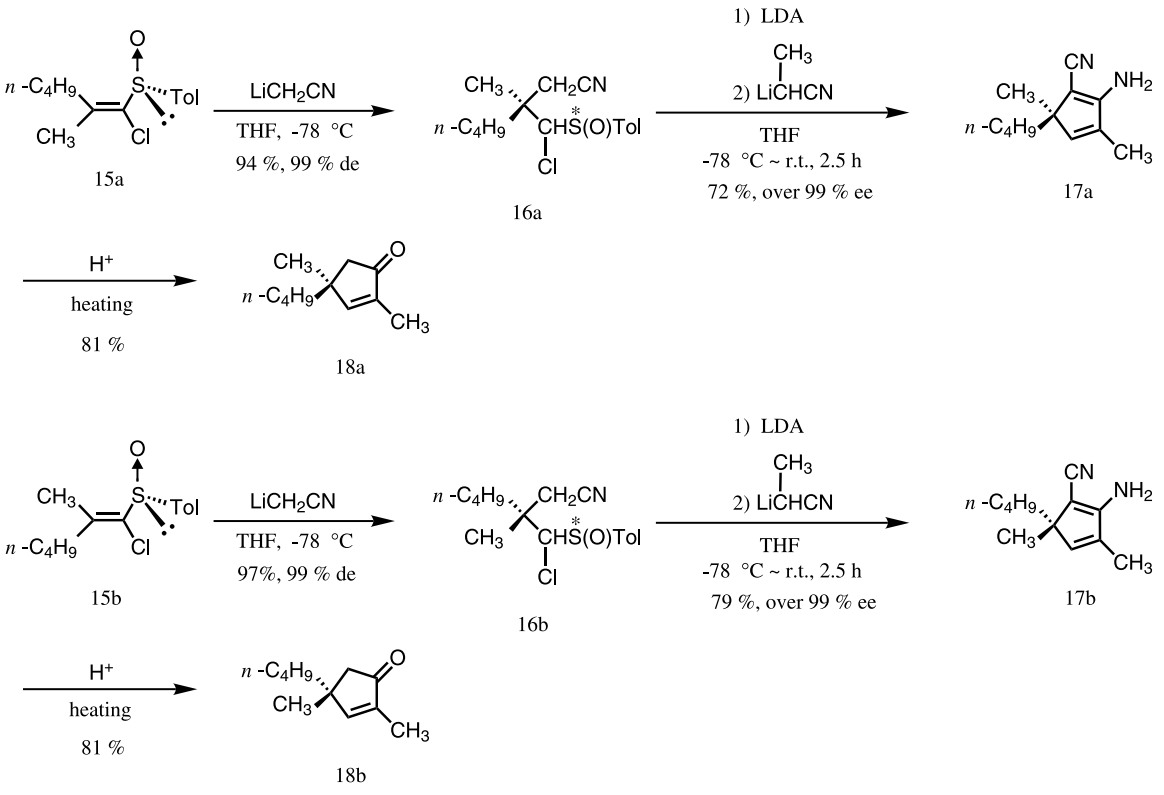
We previously reported an asymmetric synthesis of 4,4-disubstituted 2-pentenones **4** from the optically active 1-chlorovinyl *p*-tolyl sulfoxides **2** via the optically active enaminonitriles **3** (Scheme 1).[6] As an extension of our new synthetic method described above, we investigated the feasibility for the asymmetric synthesis of the 2,4,4-trisubstituted 2-cyclopentenones (Scheme 6).

Optically pure *E*-1-chloro-1-hexenyl *p*-tolyl sulfoxide **15a** and its *Z*-isomer **15b** were synthesized from 2-hexanone and (*R*)-chloromethyl *p*-tolyl sulfoxide[11] as reported before.[6b] First, **15a** was treated with cyanomethyllithium at −78 °C for 10 min to afford the adduct **16a** as a 17:4 mixture of two diastereomers. These diastereomers could be separated by column chromatography and from the ^{1}H NMR spectrum of each diastereomers, they were found to be diastereomerically pure. The diastereomers are thought to be based on the two chiral carbons. This meant that the diastereomeric excess of these isomers was over 99%.

Next, a mixture of the adduct **16a** was treated with 3 equiv of LDA at −78 °C followed by lithium α-carbanion of propionitrile in a similar manner described above. This reaction gave optically active **17a** as an oil in 72% yield. We measured the optical purity of the product using HPLC with CHIRALCEL OD and found that it was over 99%. As the stereochemistry of the asymmetric induction of the reaction of the vinyl sulfoxides **15** and cyanomethyllithium was

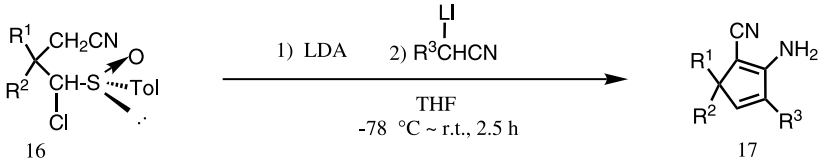


Scheme 5.



Scheme 6.

Table 3. Synthesis of optically 3,5,5-trisubstituted cyclopentadienyl enaminonitriles **17** from the optically active adduct **16** with lithium α-carbanion of heptanenitrile and isovaleronitrile



Entry	Adduct **16**	Nitrile	Enaminonitrile **17**	Yield/%	Enantiomeric excess/% ee[a]
1	**16a**	$C_6H_{13}CN$	**17c**	88	98
2	**16b**	$C_6H_{13}CN$	**17d**	81	99
3	**16a**	$(CH_3)_2CHCH_2CN$	**17e**	83	>99
4	**16b**	$(CH_3)_2CHCH_2CN$	**17f**	89	>99

[a] The enantiomeric excess was measured by using HPLC with CHIRALCEL OD (hexane/2-propanol=20:1).

already established by our previous work,[6b] the absolute configuration of **17a** is *R*. Finally, the optically active **17a** was treated in the acidic media to give optically pure (*S*)-4-butyl-2,4-dimethyl-2-cyclopentenone **18a** in 81% yield ($[\alpha]_D^{30} = -46.7$).

In a similar way, the addition reaction of **15b** with cyanomethyllithium gave the adduct **16b** as a 7:2 mixture of two diastereomers with 99% diastereomeric excess. From **16b** the enaminonitrile **17b** and the optically pure (*R*)-4-butyl-2,4-dimethyl-2-cyclopentenone **18b** (the enantiomer of **18a**) were synthesized in similar chemical yields. The specific rotation of **18b** showed +43.4.

Table 3 shows the results for the asymmetric synthesis of optically active enaminonitriles **17c–f** from **16a** and **16b** with hexanenitrile and isovaleronitrile. As shown in the table, both enantiomers of the enaminonitriles were obtained in 81–89% yield with over 98% enantiomeric excess. These results show that the procedure described above is a quite versatile and reliable method for the preparation of optically active 2,4,4-trisubstituted 2-cyclopentenones.

3. Experimental

3.1. General

All melting points are uncorrected. ^{1}H NMR spectra were measured in a $CDCl_3$ solution with JEOL JNM-LA 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 was 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 and chloromethyl *p*-tolyl sulfoxide as reported before.[5,6]

2a, **2b**, **2c**, **2d**, **3a**, **10**, **15a**, and **15b** are known compounds.[5,6]

3.1.1. {1-[Chloro(*p*-tolylsulfinyl)methyl]cyclopentadecyl}acetonitrile (5a). Acetonitrile (0.096 ml; 1.80 mmol) was added to a solution of *n*-BuLi (1.80 mmol) in 10 ml of dry THF at −78 °C with stirring. The solution was stirred for 10 min and a solution of **2a** (237.0 mg; 0.60 mmol) in 2 ml of dry THF was added. The reaction mixture was stirred for 10 min and the reaction was quenched by adding satd aq. NH_4Cl. The whole was extracted with $CHCl_3$. The products (less polar product **5a-L** and more polar product **5a-P**) were isolated by silica gel column chromatography to give **5a-L** (190.8 mg; 73%) and **5a-P** (61.9 mg; 23%) as a colorless oil.

Compound **5a-L**. IR (neat) 2930, 2858, 2243 (CN), 1461, 1083, 1054 (SO), 812, 756 cm^{-1}; ^{1}H NMR δ 1.31–1.44 (24H, m), 1.73 (2H, br t, J=11.6 Hz), 1.99 (2H, br quintet, J=14.3 Hz), 2.44 (3H, s), 2.65, 3.24 (each 1H, d, J=17.1 Hz), 4.56 (1H, s), 7.35, 7.74 (each 2H, d, J=8.3 Hz). MS *m*/*z* (%) 435 (M^+, 1.4), 419 (1.8), 385 (4), 296 (4), 260 (7), 248 (5), 141 (9), 140 (100), 139 (10). Calcd for $C_{25}H_{38}ClNOS$: M, 435.2363. Found: *m*/*z* 435.2376.

Compound **5a-P**. IR (neat) 2929, 2858, 2242 (CN), 1461, 1089, 1060 (SO), 811, 756 cm^{-1}; ^{1}H NMR δ 1.31–1.59 (24H, m), 1.76–1.79 (2H, m), 1.88–1.98 (2H, m), 2.44 (3H, s), 2.80, 2.85 (each 1H, d, J=17.1 Hz), 4.26 (1H, s), 7.36, 7.48 (each 2H, d, J=8.3 Hz). MS *m*/*z* (%) 435 (M^+, 1.5), 419 (2.2), 385 (7), 296 (4), 260 (7), 248 (4), 221 (4), 140 (100), 139 (10). Calcd for $C_{25}H_{38}ClNOS$: M, 435.2363. Found: *m*/*z* 435.2372.

3.1.2. {8-[Chloro(*p*-tolylsulfinyl)methyl]-1,4-dioxaspiro[4.5]dec-8-yl}acetonitrile (5b). *Compound* **5b-L**. Colorless crystals, mp 110–111 °C (AcOEt–hexane); IR (KBr) 2948, 2881, 2243 (CN), 1454, 1107, 1082, 1053 (SO), 813, 503 cm^{-1}; ^{1}H NMR δ 1.61–1.79 (4H, m), 1.85–1.88 (1H, m), 2.01–2.05 (1H, m), 2.25–2.31 (1H, m), 2.36–2.41 (1H, m), 2.44 (3H, s), 2.90, 3.46 (each 1H, d, J=17.1 Hz), 3.96 (4H, s), 4.69 (1H, s), 7.35, 7.75 (each 2H, d, J=8.3 Hz). MS *m*/*z* (%) 367 (M^+, 11), 230 (32), 228 (100), 200 (16), 192 (49), 184 (40), 148 (26), 140 (66), 139 (35), 120 (16). Anal. Calcd for $C_{18}H_{22}ClNO_3S$: C, 58.77; H, 6.03; Cl, 9.64; N, 3.81; S, 8.72%. Found: C, 58.80; H, 5.78; Cl, 9.55; N, 3.74; S, 8.70%.

Compound **5b-P**. Colorless crystals, mp 166–167 °C (AcOEt–hexane); IR (KBr) 2940, 2897, 2239 (CN), 1114, 1085, 1053 (SO), 820, 515 cm^{-1}; ^{1}H NMR δ 1.67–2.20 (6H, m), 2.32–2.42 (2H, m), 2.44 (3H, s), 2.90, 2.99 (each 1H, d, J=17.4 Hz), 3.97 (4H, s), 4.48 (1H, s), 7.36, 7.48 (each 2H, d, J=8.2 Hz). MS *m*/*z* (%) 367 (M^+, 15), 230 (32), 228 (100), 192 (61), 184 (38), 148 (30), 140 (68), 139 (34), 120 (16). Anal. Calcd for $C_{18}H_{22}ClNO_3S$: C, 58.77; H, 6.03; Cl, 9.64; N, 3.81; S, 8.72%. Found: C, 58.77; H, 5.91; Cl, 9.55; N, 3.73; S, 8.72%.

3.1.3. 4-Chloro-3,3-diphenyl-4-(*p*-tolylsulfinyl)butyronitrile (5c). *Compound* **5c-L**. Colorless crystals, mp 198–199 °C (AcOEt–hexane); IR (KBr) 2950, 2926, 2247 (CN), 1595, 1494, 1443, 1083, 1051 (SO), 705 cm^{-1}; ^{1}H NMR δ 2.44 (3H, s), 3.54, 4.34 (each 1H, d, J=16.2 Hz), 5.31 (1H, s), 7.22 (2H, d, J=6.7 Hz), 7.29–7.35 (5H, m), 7.49 (3H, m), 7.60–7.63 (2H, m), 7.72 (2H, d, J=8.0 Hz). MS *m*/*z* (%) 393 (M^+, trace), 254 (73), 214 (54), 179 (66), 178 (65), 140 (100), 139 (26). Anal. Calcd for $C_{23}H_{20}ClNOS$: C, 70.13; H, 5.12; Cl, 9.00; N, 3.56; S, 8.14%. Found: C, 70.01; H, 4.94; Cl, 8.93; N, 3.57; S, 8.16%.

Compound **5c-P**. Colorless crystals, mp 68–69 °C (AcOEt–hexane); IR (KBr) 2926, 2852, 2241 (CN), 1632, 1495, 1447, 1087, 1058 (SO), 700 cm^{-1}; ^{1}H NMR δ 2.41 (3H, s), 3.57, 3.85 (each 1H, d, J=17.1 Hz), 5.01 (1H, s), 7.26–7.48 (14H, m). MS *m*/*z* (%) 393 (M^+, trace), 256 (31), 254 (95), 218 (40), 214 (69), 179 (78), 178 (77), 140 (100), 139 (30). Anal. Calcd for $C_{23}H_{20}ClNOS$: C, 70.13; H, 5.12; Cl, 9.00; N, 3.56; S, 8.14%. Found: C, 69.94; H, 5.25; Cl, 8.94; N, 3.58; S, 7.76%.

3.1.4. 2-Amino-3-methylspiro[4.14]nonadeca-1,3-diene-1-carbonitrile (7a). To a solution of LDA (0.23 mmol) in

2 ml of dry THF was added a solution **5a** (33.1 mg; 0.076 mmol) in 1 ml of dry THF at −78 °C and the reaction mixture was stirred for 30 min. To the reaction mixture was added lithium α-carbanion of propionitrile (0.30 mmol), which was generated from propionitrile and *n*-BuLi at −78 °C, through a cannula and the temperature of the reaction mixture was slowly allowed to warm to room temperature for 2.5 h. The reaction mixture was quenched by satd aq. NH_4Cl. The whole was extracted with $CHCl_3$. The product was isolated by silica gel column chromatography to give 19.0 mg (80%) of **7a** as colorless crystals; mp 162–164 °C (AcOEt–hexane); IR (KBr) 3424 (NH), 3346 (NH), 2930, 2854, 2168 (CN), 1648, 1623, 1565, 1451, 1421 cm^{-1}; ^1H NMR δ 1.34–1.59 (28H, m), 1.85 (3H, d, $J=1.3$ Hz), 4.42 (2H, br s, NH), 6.20 (1H, q, $J=1.3$ Hz). MS *m/z* (%) 315 (25), 314 (M^+, 100), 147 (20), 134 (24), 133 (38), 132 (17). Anal. Calcd for $C_{21}H_{34}N_2$: C, 80.20; H, 10.90; N, 8.91%. Found: C, 80.18; H, 10.94; N, 8.91%.

3.1.5. 2-Amino-3-ethylspiro[4.14]nonadeca-1,3-diene-1-carbonitrile (7b). Colorless crystals; mp 132–134 °C (AcOEt–hexane); IR (KBr) 3427 (NH), 3347 (NH), 2932, 2855, 2166 (CN), 1646, 1563, 1459, 1423, 842 cm^{-1}; ^1H NMR δ 1.16 (3H, t, $J=7.3$ Hz), 1.26–1.54 (28H, m), 2.16 (2H, q, $J=7.3$ Hz), 4.40 (2H, br s, NH), 6.18 (1H, s). MS *m/z* (%) 329 (26), 328 (M^+, 100), 161 (18), 159 (15), 148 (24), 147 (43), 146 (22). Anal. Calcd for $C_{22}H_{36}N_2$: C, 80.43; H, 11.04; N, 8.53%. Found: C, 80.30; H, 11.10; N, 8.43%.

3.1.6. 10-Amino-11-methyl-1,4-dioxa-dispiro[4.2.4.2]-tetradeca-9,11-diene-9-carbonitrile (7c). Colorless crystals; mp 243–244 °C ($CHCl_3$–hexane); IR (KBr) 3405 (NH), 3356 (NH), 3245, 2929, 2165 (CN), 1663, 1560, 1452, 1092 cm^{-1}; ^1H NMR δ 1.45 (2H, br d, $J=12.8$ Hz), 1.73 (2H, dt, $J=12.8$, 4.1 Hz), 1.89 (3H, s), 1.92 (2H, m), 2.02 (2H, br t, $J=12.4$ Hz), 3.97 (4H, s), 4.46 (2H, br s, NH), 6.49 (1H, s). MS *m/z* (%) 246 (M^+, 32), 218 (26), 145 (15), 133 (15), 132 (100), 131 (14). Anal. Calcd for $C_{14}H_{18}N_2O_2$: C, 68.27; H, 7.37; N, 11.37%. Found: C, 67.88; H, 7.32; N, 11.30%.

3.1.7. 10-Amino-11-ethyl-1,4-dioxa-dispiro[4.2.4.2]tetradeca-9,11-diene-9-carbonitrile (7d). Colorless crystals; mp 195–196 °C (AcOEt–hexane); IR (KBr) 3410 (NH), 3354 (NH), 3245, 2964, 2162 (CN), 1661, 1557, 1436, 1090 cm^{-1}; ^1H NMR δ 1.18 (3H, t, $J=7.3$ Hz), 1.45 (2H, br d, $J=12.9$ Hz), 1.75 (2H, dt, $J=12.9$, 4.2 Hz), 1.92 (2H, br d, $J=13.2$ Hz), 2.03 (2H, br t, $J=10.4$ Hz), 2.19 (2H, dt, $J=7.3$, 1.8 Hz), 3.97 (4H, s), 4.48 (2H, br s, NH), 6.46 (1H, br s). MS *m/z* (%) 261 (9), 260 (M^+, 40), 232 (27), 147 (20), 146 (100), 131 (15). Calcd for $C_{15}H_{20}N_2O_2$: M, 260.1524. Found: *m/z* 260.1525.

3.1.8. 2-Amino-3-methyl-5,5-diphenylcyclopenta-1,3-diene-1-carbonitrile (7e). Colorless crystals; mp 171–172 °C (AcOEt–hexane); IR (KBr) 3456 (NH), 3366 (NH), 3232, 2166 (CN), 1654, 1624, 1563, 1445, 698 cm^{-1}; ^1H NMR δ 1.96 (3H, d, $J=1.5$ Hz), 4.69 (2H, br s, NH), 6.62 (1H, q, $J=1.5$ Hz), 7.21–7.29 (10H, m). MS *m/z* (%) 273 (23), 272 (M^+, 100), 258 (21), 257 (52), 195 (15). Anal. Calcd for $C_{19}H_{16}N_2$: C, 83.79; H, 5.92; N, 10.29%. Found: C, 83.38; H, 5.76; N, 10.19%.

3.1.9. 2-Amino-3-ethyl-5,5-diphenylcyclopenta-1,3-diene-1-carbonitrile (7f). Colorless crystals; mp 164–165 °C (AcOEt–hexane); IR (KBr) 3352 (NH), 3232 (NH), 2969, 2175 (CN), 1651, 1562, 1490, 1445, 758, 699 cm^{-1}; ^1H NMR δ 1.24 (3H, t, $J=7.3$ Hz), 2.26 (2H, q, $J=7.3$ Hz), 4.69 (2H, br s, NH), 6.58 (1H, s), 7.22–7.29 (10H, m). MS *m/z* (%) 287 (25), 286 (M^+, 95), 271 (62), 256 (34), 257 (100). Anal. Calcd for $C_{20}H_{18}N_2$: C, 83.88; H, 6.34; N, 9.78%. Found: C, 83.63; H, 6.09; N, 9.75%.

3.1.10. 3-Methylspiro[4.14]nonadec-3-en-2-one (8a). To a solution **7a** (97.2 mg; 0.31 mmol) in 21 ml acetic acid was added phosphoric acid (85%, 9 ml) and water (2 ml). The reaction mixture was stirred and heated under reflux for 32 h. The reaction mixture was neutralized with 10% aq. NaOH and the whole was extracted with $CHCl_3$. The product was isolated by silica gel column chromatography to give 83.3 mg (93%) of **8a** as a colorless oil; IR (neat) 2929, 2857, 1709 (CO), 1639, 1459, 1330, 756 cm^{-1}; ^1H NMR δ 1.31–1.44 (28H, m), 1.73 (3H, d, $J=1.3$ Hz), 2.19 (2H, s), 7.23 (1H, q, $J=1.3$ Hz). MS *m/z* (%) 291 (16), 290 (M^+, 69), 262 (28), 123 (27), 110 (39), 109 (100), 108 (35). Calcd for $C_{20}H_{34}O$: M, 290.2608. Found: *m/z* 290.2625.

3.1.11. 3-Ethylspiro[4.14]nonadec-3-en-2-one (8b). Colorless oil; IR (neat) 2930, 2857, 1709 (CO), 1460 cm^{-1}; ^1H NMR δ 1.07 (3H, t, $J=7.5$ Hz), 1.33–1.44 (28H, m), 2.15 (2H, dq, $J=7.5$, 1.1 Hz), 2.21 (2H, s), 7.19 (1H, t, $J=1.1$ Hz). MS *m/z* (%) 305 (25), 304 (M^+, 100), 137 (24), 124 (53), 123 (80), 122 (24). Calcd for $C_{21}H_{36}O$: M, 304.2764. Found: *m/z* 304.2774.

3.1.12. 3-Methylspiro[4.5]dec-3-ene-2,8-dione (8c). Colorless crystals; mp 84–85 °C (AcOEt–hexane); IR (KBr) 2963, 2946, 2868, 1712 (CO), 1701 (CO), 1637, 1069, 977 cm^{-1}; ^1H NMR δ 1.80 (3H, d, $J=1.2$ Hz), 1.82–1.86 (2H, m), 1.94–2.00 (2H, m), 2.44–2.51 (4H, m), 2.49 (2H, s), 7.21 (1H, q, $J=1.2$ Hz). MS *m/z* (%) 179 (14), 178 (M^+, 100), 122 (42), 121 (31), 108 (92). Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92%. Found: C, 73.90; H, 7.80%.

3.1.13. 3-Ethylspiro[4.5]dec-3-ene-2,8-dione (8d). Colorless crystals; mp 58–59 °C (AcOEt–hexane); IR (KBr) 2970, 2933, 1698 (CO), 1337, 970 cm^{-1}; ^1H NMR δ 1.11 (3H, t, $J=7.5$ Hz), 1.81–1.85 (2H, m), 1.94–2.00 (2H, m), 2.21 (2H, q, $J=7.5$ Hz), 2.44–2.48 (4H, m), 2.50 (2H, s), 7.15 (1H, s). MS *m/z* (%) 193 (10), 192 (M^+, 100), 164 (32), 136 (73), 135 (45), 123 (18), 122 (74), 121 (20), 107 (23). Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39%. Found: C, 74.92; H, 8.30%.

3.1.14. 2-Methyl-4,4-diphenyl-2-cyclopentenone (8e). Colorless crystals; mp 91–92 °C (hexane); IR (KBr) 1697 (CO), 1493, 1445, 752, 704 cm^{-1}; ^1H NMR δ 1.88 (3H, d, $J=1.2$ Hz), 3.17 (2H, s), 7.14–7.33 (10H, m), 7.63 (1H, d, $J=1.2$ Hz). MS *m/z* (%) 249 (22), 248 (M^+, 100), 220 (39), 205 (93), 171 (35), 129 (21), 128 (35), 115 (25). Anal. Calcd for $C_{18}H_{16}O$: C, 87.06; H, 6.49%. Found: C, 86.83; H, 6.26%.

3.1.15. 2-Ethyl-4,4-diphenyl-2-cyclopentenone (8f). Colorless oil; IR (neat) 3059, 3026, 2969, 2935, 1709 (CO), 1634, 1597, 1493, 1446, 761, 700 cm^{-1}; ^1H NMR δ

1.17 (3H, t, J=7.4 Hz), 2.30 (2H, dq, J=7.4, 1.2 Hz), 3.18 (2H, s), 7.13–7.33 (10H, m), 7.58 (1H, br t, J=1.2 Hz). MS *m/z* (%) 263 (22), 262 (M^+, 100), 261 (53), 233 (39), 205 (68), 185 (18), 157 (39), 129 (18), 115 (26). Calcd for $C_{19}H_{18}O$: M, 262.1356. Found: *m/z* 262.1342.

3.1.16. 2-Amino-3-pentylspiro[4.14]nonadeca-1,3-diene-1-carbonitrile (7g). Colorless crystals; mp 109–110 °C (hexane); IR (KBr) 3424 (NH), 3359 (NH), 2929, 2857, 2165 (CN), 1673, 1648, 1557 cm^{-1}; ^1H NMR δ 0.91 (3H, t, J=6.9 Hz), 1.33–1.57 (34H, m), 2.12 (2H, dt, J=7.7, 1.4 Hz), 4.39 (2H, br s, NH), 6.17 (1H, t, J=1.4 Hz). MS *m/z* (%) 371 (29), 370 (M^+, 100), 313 (32), 189 (18), 145 (10), 132 (12). Anal. Calcd for $C_{25}H_{42}N_2$: C, 81.02; H, 11.42; N, 7.56%. Found: C, 81.12; H, 11.63; N, 7.48%.

3.1.17. 2-Amino-3-isopropylspiro[4.14]nonadeca-1,3-diene-1-carbonitrile (7h). Colorless crystals; mp 113–115 °C (AcOEt–hexane); IR (KBr) 3434 (NH), 3349 (NH), 2932, 2852, 2165 (CN), 1643, 1559, 1459, 1420 cm^{-1}; ^1H NMR δ 1.14 (6H, d, J=6.7 Hz), 1.34–1.55 (28H, m), 2.41 (1H, septet, J=6.7 Hz), 4.44 (2H, br s, NH), 6.17 (1H, s). MS *m/z* (%) 343 (28), 342 (M^+, 100), 327 (28), 299 (22), 161 (24). Anal. Calcd for $C_{23}H_{38}N_2$: C, 80.64; H, 11.18; N, 8.18%. Found: C, 80.77; H, 11.41; N, 8.08%.

3.1.18. 2-Amino-3-(triphenylmethyl)spiro[4.14]nonadeca-1,3-diene-1-carbonitrile (7i). Colorless crystals; mp 202–203 °C (AcOEt–hexane); IR (KBr) 3483 (NH), 2930, 2856, 2182 (CN), 1637, 1552, 1492, 1445, 702 cm^{-1}; ^1H NMR δ 1.26–1.66 (28H, m), 3.87 (2H, br s, NH), 6.18 (1H, s), 7.16 (6H, m), 7.24–7.34 (9H, m). MS *m/z* (%) 543 (43), 542 (M^+, 100), 456 (16), 243 (37), 165 (11). Anal. Calcd for $C_{39}H_{46}N_2$: C, 86.30; H, 8.54; N, 5.16%. Found: C, 85.83; H, 8.50; N, 5.00%.

3.1.19. (*E*)-2-Amino-3-propenylspiro[4.14]nonadeca-1,3-diene-1-carbonitrile (7j). Colorless crystals; mp 92–93 °C (hexane); IR (KBr) 3484 (NH), 3342 (NH), 2930, 2856, 2177 (CN), 1662, 1557, 1423, 961 cm^{-1}; ^1H NMR δ 1.34–1.54 (28H, m), 1.84 (3H, d, J=6.4 Hz), 4.50 (2H, br s, NH), 5.97 (1H, d, J=15.9 Hz), 6.06 (1H, dq, J=15.9, 6.4 Hz), 6.37 (1H, s). MS *m/z* (%) 341 (26), 340 (M^+, 100), 173 (16), 160 (18), 159 (18), 111 (13). Anal. Calcd for $C_{23}H_{36}N_2$: C, 81.12; H, 10.66; N, 8.23%. Found: C, 81.20; H, 10.89; N, 8.07%.

3.1.20. 2-Amino-3-(4-methoxyphenyl)spiro[4.14]nonadeca-1,3-diene-1-carbonitrile (7k). Colorless crystals; mp 164–165 °C (AcOEt–hexane); IR (KBr) 3459 (NH), 2930, 2855, 2173 (CN), 1645, 1603, 1509, 1247, 832 cm^{-1}; ^1H NMR δ 1.27–1.70 (28H, m), 3.84 (3H, s), 4.55 (2H, br s, NH), 6.44 (1H, s), 6.94, 7.28 (each 2H, d, J=8.6 Hz). MS *m/z* (%) 407 (29), 406 (M^+, 100), 304 (7), 225 (12), 224 (5), 146 (6). Anal. Calcd for $C_{27}H_{38}N_2O$: C, 79.76; H, 9.42; N, 6.89%. Found: C, 79.79; H, 9.47; N, 6.74%.

3.1.21. 10-Amino-11-(triphenylmethyl)-1,4-dioxa-dispiro[4.2.4.2]tetradeca-9,11-diene-9-carbonitrile (7l). Colorless crystals; mp > 300 °C (AcOEt–hexane); IR (KBr) 3478 (NH), 3336 (NH), 2941, 2893, 2180 (CN), 1653, 1556, 1491, 1099, 750, 703 cm^{-1}; ^1H NMR δ 1.57–1.67 (4H, m), 1.90–1.93 (2H, m), 2.05–2.10 (2H, m), 3.91 (2H, br s, NH), 3.92–3.98 (4H, m), 6.43 (1H, s), 7.14–7.32 (15H, m). MS *m/z* (%) 475 (37), 474 (M^+, 100), 360 (17), 242 (15), 243 (57), 165 (17). Calcd for $C_{32}H_{30}N_2O_2$: M, 474.2305. Found: *m/z* 474.2299.

3.1.22. 10-Amino-11-(4-methoxyphenyl)-1,4-dioxa-dispiro[4.2.4.2]tetradeca-9,11-diene-9-carbonitrile (7m). Colorless crystals; mp 223 °C (AcOEt–hexane); IR (KBr) 3462 (NH), 3353 (NH), 2937, 2893, 2169 (CN), 1647, 1509, 1247, 1106, 1031, 837 cm^{-1}; ^1H NMR δ 1.55–1.62 (2H, m), 1.79 (2H, dt, J=12.7, 3.7 Hz), 1.96 (2H, br d, J=13.1 Hz), 2.12 (2H, br t, J=11.3 Hz), 3.84 (3H, s), 3.98 (4H, s), 4.61 (2H, br s, NH), 6.71 (1H, s), 6.96, 7.29 (each 2H, d, J=8.9 Hz). MS *m/z* (%) 339 (24), 338 (M^+, 100), 294 (28), 293 (22), 276 (28), 237 (35), 246 (66). Anal. Calcd for $C_{20}H_{22}N_2O_3$: C, 70.99; H, 6.55; N, 8.28%. Found: C, 71.04; H, 6.59; N, 8.14%.

3.1.23. (*E*)-2-Amino-5,5-diphenyl-3-propenylcyclopenta-1,3-diene-1-carbonitrile (7n). Colorless crystals; mp 146–147 °C (AcOEt–hexane); IR (KBr) 3474 (NH), 3421 (NH), 3330 (NH), 3230 (NH), 3026, 2183 (CN), 1657, 1557, 761, 701 cm^{-1}; ^1H NMR δ 1.86 (3H, d, J=6.4 Hz), 4.77 (2H, br s, NH), 6.03 (1H, d, J=15.9 Hz), 6.17 (1H, dq, J=15.9, 6.4 Hz), 6.75 (1H, s), 7.22–7.30 (10H, m). MS *m/z* (%) 299 (25), 298 (M^+, 100), 297 (38), 283 (26), 205 (13). Calcd for $C_{21}H_{18}N_2$: M, 298.1468. Found: *m/z* 298.1462.

3.1.24. 2-Amino-3-(4-methoxyphenyl)-5,5-diphenylcyclopenta-1,3-diene-1-carbonitrile (7o). Colorless crystals; mp 171–173 °C (AcOEt–hexane); IR (KBr) 3465 (NH), 3344 (NH), 3058, 2179 (CN), 1650, 1621, 1604, 1508, 1242, 1027, 831, 701 cm^{-1}; ^1H NMR δ 3.84 (3H, s), 4.84 (2H, br s, NH), 6.84 (1H, s), 6.96 (2H, d, J=8.6 Hz), 7.25–7.32 (10H, m), 7.34 (2H, d, J=8.6 Hz). MS *m/z* (%) 365 (28), 364 (M^+, 100), 349 (8), 287 (11). Anal. Calcd for $C_{25}H_{20}N_2O$: C, 82.39; H, 5.53; N, 7.69%. Found: C, 82.35; H, 5.47; N, 7.63%.

3.1.25. 3-Pentylspiro[4.14]nonadec-3-en-2-one (8g). Colorless oil; IR (neat) 2929, 2857, 1709 (CO), 1460 cm^{-1}; ^1H NMR δ 0.89 (3H, t, J=7.0 Hz), 1.24–1.49 (34H, m), 2.11 (2H, dt, J=15.4, 1.3 Hz), 2.20 (2H, s), 7.19 (1H, t, J=1.3 Hz). MS *m/z* (%) 347 (28), 346 (M^+, 100), 166 (13), 165 (32), 163 (12), 151 (12), 109 (10). Calcd for $C_{24}H_{42}O$: M, 346.3233. Found: *m/z* 346.3226.

3.1.26. 3-Isopropylspiro[4.14]nonadec-3-en-2-one (8h). Colorless oil; IR (neat) 2930, 2858, 1708 (CO), 1460, 1369, 1002 cm^{-1}; ^1H NMR δ 1.07 (6H, d, J=6.7 Hz), 1.33–1.44 (28H, m), 2.20 (2H, s), 2.59 (1H, double septet, J=6.7, 1.0 Hz), 7.15 (1H, d, J=1.0 Hz). MS *m/z* (%) 319 (26), 318 (M^+, 100), 276 (20), 275 (15), 138 (32), 137 (40). Calcd for $C_{22}H_{38}O$: M, 318.2920. Found: *m/z* 318.2913.

3.1.27. 3-(Triphenylmethyl)spiro[4.14]nonadec-3-en-2-one (8i). Colorless crystals; mp 144–145 °C (AcOEt–hexane); IR (KBr) 3056, 3029, 2928, 2855, 1715 (CO), 1492, 1446, 746, 699 cm^{-1}; ^1H NMR δ 1.27–1.50 (28H, m), 2.30 (2H, s), 7.12–7.26 (15H, m), 7.32 (1H, s). MS *m/z* (%) 519 (40), 518 (M^+, 100), 441 (8), 296 (30), 268 (9), 243 (11), 215 (7), 165 (10). Anal. Calcd for $C_{38}H_{46}O$: C, 87.98; H, 8.94%. Found: C, 88.06; H, 8.97%.

3.1.28. (*E*)-3-Propenylspiro[4.14]nonadec-3-en-2-one (8j). Colorless oil; IR (neat) 2930, 2857, 1709 (CO), 1459, 971 cm^{-1}; ^1H NMR δ 1.33–1.46 (28H, m), 1.78 (3H, dd, J=6.7, 1.5 Hz), 2.25 (2H, s), 6.04 (1H, dd, J=15.3, 1.5 Hz), 6.62 (1H, dq, J=15.3, 6.7 Hz), 7.26 (1H, s). MS *m/z* (%) 317 (26), 316 (M^+, 100), 149 (18), 136 (25), 121 (9), 105 (8). Calcd for $C_{22}H_{36}O$: M, 316.2765. Found: *m/z* 316.2772.

3.1.29. 3-(4-Methoxyphenyl)spiro[4.14]nonadec-3-en-2-one (8k). Colorless crystals; mp 54–55 °C (hexane); IR (KBr) 2928, 2854, 1698 (CO), 1600, 1509, 831 cm^{-1}; ^1H NMR δ 1.35–1.54 (28H, m), 2.38 (2H, s), 3.82 (3H, s), 6.90 (2H, d, J=8.6 Hz), 7.64 (1H, s), 7.67 (2H, d, J=8.6 Hz). MS *m/z* (%) 383 (29), 382 (M^+, 100), 354 (18), 201 (18), 159 (7), 121 (8). Anal. Calcd for $C_{26}H_{38}O_2$: C, 81.62; H, 10.01%. Found: C, 81.74; H, 10.14%.

3.1.30. 3-(Triphenylmethyl)spiro[4.5]dec-3-ene-2,8-dione (8l). Colorless crystals; mp 242–243 °C (AcOEt–hexane); IR (KBr) 3050, 2933, 1712 (CO), 1490, 1444, 751, 702 cm^{-1}; ^1H NMR δ 1.88 (2H, m), 1.96–2.04 (2H, m), 2.40–2.46 (4H, m), 2.60 (2H, s), 7.11–7.28 (16H, m). MS *m/z* (%) 407 (33), 406 (M^+, 100), 329 (28), 296 (68), 268 (30), 243 (24), 165 (31). Anal. Calcd for $C_{29}H_{26}O_2$: C, 85.68; H, 6.45%. Found: C, 85.30; H, 6.51%.

3.1.31. 3-(4-Methoxyphenyl)spiro[4.5]dec-3-ene-2,8-dione (8m). Colorless crystals; mp 106–107 °C (AcOEt–hexane); IR (KBr) 2944, 2872, 1709 (CO), 1693 (CO), 1612, 1599, 1510, 1256, 833 cm^{-1}; ^1H NMR δ 1.91–1.95 (2H, m), 2.03–2.09 (2H, m), 2.45–2.56 (4H, m), 2.68 (2H, s), 3.83 (3H, s), 6.93 (2H, d, J=9.2 Hz), 7.59 (1H, s), 7.71 (2H, d, J=9.2 Hz). MS *m/z* (%) 271 (19), 270 (M^+, 100), 212 (63), 213 (88), 200 (28). Anal. Calcd for $C_{17}H_{18}O_3$: C, 75.53; H, 6.71%. Found: C, 75.69; H, 6.73%.

3.1.32. (*E*)-4,4-Diphenyl-2-propenyl-2-cyclopentenone (8n). Colorless crystals; mp 59–60 °C (AcOEt–hexane); IR (KBr) 3023, 2933, 1705 (CO), 1489, 1444, 976, 764, 701 cm^{-1}; ^1H NMR δ 1.84 (3H, dd, J=6.7, 1.5 Hz), 3.21 (2H, s), 6.15 (1H, dd, J=15.9, 1.5 Hz), 6.75 (1H, dq, J=15.9, 6.7 Hz), 7.14–7.32 (10H, m), 7.62 (1H, s). MS *m/z* (%) 275 (25), 274 (M^+, 100), 231 (72), 217 (48), 170 (45), 155 (38), 142 (32), 128 (38), 115 (37). Anal. Calcd for $C_{20}H_{18}O$: C, 87.56; H, 6.61%. Found: C, 87.64; H, 6.46%.

3.1.33. 2-(4-Methoxyphenyl)-4,4-diphenyl-2-cyclopentenone (8o). Colorless crystals; mp 159–160 °C (AcOEt–hexane); IR (KBr) 2835, 1702 (CO), 1605, 1509, 1254, 1035, 835, 758, 701 cm^{-1}; ^1H NMR δ 3.34 (2H, s), 3.83 (3H, s), 6.93 (2H, d, J=8.9 Hz), 7.21–7.27 (6H, m), 7.32–7.35 (4H, m), 7.76 (2H, d, J=8.9 Hz), 8.01 (1H, s). MS *m/z* (%) 341 (28), 340 (M^+, 100), 312 (15), 281 (16), 263 (16), 235 (21), 221 (25). Anal. Calcd for $C_{24}H_{20}O_2$: C, 84.68; H, 5.92%. Found: C, 84.36; H, 5.88%.

3.1.34. 3-Chloro-2,2-dimethyl-3-(*p*-tolylsulfinyl)propionitrile (5d). *Compound* **5d-L**. Colorless crystals, mp 62 °C (AcOEt–hexane); IR (KBr) 2973, 2939, 2243 (CN), 1082, 1046 (SO), 809, 501 cm^{-1}; ^1H NMR δ 1.41 (3H, s), 1.52 (3H, s), 2.44 (3H, s), 2.76, 3.12 (each 1H, d, J=16.8 Hz), 4.44 (1H, s), 7.34, 7.73 (each 2H, d, J=8.2 Hz). MS *m/z* (%) 269 (M^+, 9), 140 (100), 139 (56), 92 (43), 91 (22). Anal. Calcd for $C_{13}H_{16}ClNOS$: C, 57.88; H, 5.98; Cl, 13.14; N, 5.19; S, 11.88%. Found: C, 57.84; H, 5.88; Cl, 13.08; N, 5.11; S, 11.74%.

Compound **5d-P**. Colorless crystals, mp 136 °C (AcOEt–hexane); IR (KBr) 2980, 2946, 2239 (CN), 1087, 1054 (SO), 811, 515 cm^{-1}; ^1H NMR δ 1.48 (3H, s), 1.51 (3H, s), 2.44 (3H, s), 2.71, 2.76 (each 1H, d, J=16.8 Hz), 4.24 (1H, s), 7.36, 7.49 (each 2H, d, J=8.2 Hz). MS *m/z* (%) 269 (M^+, 9), 140 (100), 139 (54), 92 (44), 91 (17). Anal. Calcd for $C_{13}H_{16}ClNOS$: C, 57.88; H, 5.98; Cl, 13.14; N, 5.19; S, 11.88%. Found: C, 57.71; H, 5.85; Cl, 13.08; N, 5.05; S, 11.82%.

3.1.35. 2-Amino-3-(3-hydroxypropyl)-5,5-dimethylcyclopenta-1,3-diene-1-carbonitrile (7p). Colorless oil; IR (neat) 3361 (OH), 2930, 2173 (CN), 1652, 1565 cm^{-1}; ^1H NMR δ 1.23 (6H, s), 1.77–1.82 (2H, m), 2.31 (2H, t, J=7.3 Hz), 2.42 (1H, t, J=7.0 Hz), 3.69–3.73 (2H, m), 4.68 (2H, br s, NH), 6.12 (1H, s). MS *m/z* (%) 192 (M^+, 61), 177 (41), 159 (23), 147 (100), 133 (54), 132 (31), 131 (22). Calcd for $C_{11}H_{16}N_2O$: M, 192.1262. Found: *m/z* 192.1261.

3.1.36. 2-Amino-3-[3-(*tert*-butyldiphenylsilanyloxy)propyl]-5,5-dimethylcyclopenta-1,3-diene-1-carbonitrile (7q). Colorless oil; IR (neat) 3355 (NH), 3072, 2931, 2859, 2177 (CN), 1651, 1567, 1428, 1111 (OSi), 702 cm^{-1}; ^1H NHR δ 1.07 (9H, s), 1.20 (6H, s), 1.70–1.76 (2H, m), 2.29 (2H, t, J=6.7 Hz), 3.70 (2H, t, J=5.8 Hz), 4.59 (2H, br s, NH), 6.03 (1H, s), 7.38–7.46 (6H, m), 7.64–7.66 (4H, m). MS *m/z* (%) 430 (M^+, 14), 374 (24), 373 (100), 295 (17), 199 (35). Calcd for $C_{27}H_{34}N_2OSi$: M, 430.2441. Found: *m/z* 430.2434.

3.1.37. 3-(3,3-Dimethyl-5-oxocyclopent-1-enyl)propyl acetate (8p). Colorless oil; IR (neat) 2959, 2867, 1741 (CO), 1706 (CO), 1242 (COC), 1044, 756 cm^{-1}; ^1H NMR δ 1.20 (6H, s), 1.69–1.75 (2H, m), 2.05 (3H, s), 2.22 (2H, dt, J=7.6, 1.3 Hz), 2.28 (2H, s,), 4.07 (2H, t, J=6.6 Hz), 7.07 (1H, t, J=1.3 Hz). MS *m/z* (%) 210 (M^+, trace), 151 (16), 150 (100), 135 (95), 107 (44). Calcd for $C_{12}H_{18}O_3$: M, 210.1256. Found: *m/z* 210.1259.

3.1.38. 2-(3-Hydroxypropyl)-4,4-dimethyl-2-cyclopentenone (8q). To a solution of **8p** (12.9 mg; 0.061 mmol) in MeOH (3 ml) was added aq. K_2CO_3 (0.5 M, 0.4 ml) at room temperature and the reaction mixture was stirred for 40 min. The whole was extracted with $CHCl_3$. The product was isolated by silica gel column chromatography to give **8q** (10.2 mg; 99%) as a colorless oil; IR (neat) 3419 (OH), 2958, 2869, 1695 (CO), 1060 cm^{-1}; ^1H NMR δ 1.21 (6H, s), 1.80–1.85 (2H, m), 2.04 (1H, br s, OH), 2.26 (2H, t, J=7.3 Hz), 2.30 (2H, s), 3.59 (2H, br t, J=5.3 Hz), 7.10 (1H, s). MS *m/z* (%) 168 (M^+, 8), 150 (90), 135 (100), 125 (15), 122 (24), 112 (30), 109 (67), 107 (62). Calcd for $C_{10}H_{16}O_2$: M, 168.1148. Found: *m/z* 168.1133.

3.1.39. (*S*)-(R_S)-2-[Chloro(*p*-tolylsulfinyl)methyl]-2-methylhexanenitrile (16a). 16a-L/16a-P=17:4.

Compound **16a-L**. Colorless oil; IR (neat) 2959, 2872, 2243 (CN), 1462, 1055 (SO), 813 cm^{-1}; ^1H NMR δ 0.96 (3H, t,

J=7.0 Hz), 1.32–1.47 (4H, m), 1.39 (3H, s), 1.85–1.91 (1H, m), 1.97–2.03 (1H, m), 2.44 (3H, s), 2.64, 3.18 (each 1H, d, J=16.8 Hz), 4.55 (1H, s), 7.35, 7.74 (each 2H, d, J=8.0 Hz). MS *m/z* (%) 311 (M^+, 4), 142 (5), 141 (9), 140 (100), 139 (18), 123 (5). Calcd for $C_{16}H_{22}ClNOS$: M, 311.1111. Found: *m/z* 311.1115.

Compound **16a-P**. Colorless oil; IR (neat) 2933, 2864, 2238 (CN), 1089, 1060 (SO), 813, 514 cm^{-1}; ^1H NMR δ 0.97 (3H, t, J=7.0 Hz), 1.32–1.44 (4H, m), 1.40 (3H, s), 1.82–1.88 (1H, m), 1.92–1.98 (1H, m), 2.44 (3H, s), 2.79, 2.85 (each 1H, d, J=17.1 Hz), 4.35 (1H, s), 7.36, 7.48 (each 2H, d, J=8.3 Hz).

Racemic **16a-P**. Colorless crystals; mp 67–68 °C (AcOEt–hexane); IR (KBr) 2943, 2870, 2236 (CN), 1084, 1047 (SO), 816, 517 cm^{-1}; Anal. Calcd for $C_{16}H_{22}ClNOS$: C, 61.62; H, 7.11; Cl, 11.37; N, 4.49; S, 10.28%. Found: C, 61.63; H, 7.07; Cl, 11.24; N, 4.49; S, 10.09%.

3.1.40. (*R*)-(*R*$_S$)-2-[Chloro(*p*-tolylsulfinyl)methyl]-2-methylhexanenitrile (16b). 16b-L/16b-P=7:2.

Compound **16b-L**. Colorless oil; IR (neat) 2960, 2865, 2243 (CN), 1597, 1463, 1082, 1051 (SO), 813, 756 cm^{-1}; ^1H NMR δ 0.93 (3H, t, J=6.9 Hz), 1.20–1.39 (4H, m), 1.48 (3H, s), 1.71–1.80 (2H, m), 2.44 (3H, s), 3.00, 3.05 (each 1H, d, J=16.8 Hz), 4.42 (1H, s), 7.35, 7.73 (each 2H, d, J=8.0 Hz). MS *m/z* (%) 311 (M^+, 4), 142 (5), 141 (9), 140 (100), 139 (18), 124 (5), 123 (5). Calcd for $C_{16}H_{22}ClNOS$: M, 311.1110. Found: *m/z* 311.1120.

Compound **16b-P**. Colorless crystals; mp 120–121 °C (AcOEt–hexane); IR (KBr) 2940, 2872, 2240 (CN), 1463, 1087, 1050 (SO), 816, 518 cm^{-1}; ^1H NMR δ 0.96 (3H, t, J=7.2 Hz), 1.27–1.34 (2H, m), 1.37–1.43 (2H, m), 1.47 (3H, s), 1.78–1.84 (1H, m), 1.88–1.95 (1H, m), 2.44 (3H, s), 2.68, 2.81 (each 1H, d, J=17.1 Hz), 4.27 (1H, s), 7.36, 7.48 (each 2H, d, J=8.2 Hz). Anal. Calcd for $C_{16}H_{22}ClNOS$: C, 61.62; H, 7.11; Cl, 11.37; N, 4.49; S, 10.28%. Found: C, 61.57; H, 7.03; Cl, 11.31; N, 4.47; S, 10.15%.

Racemic **16b-P**. Colorless crystals; mp 94–95 °C (AcOEt–hexane).

3.1.41. (*R*)-2-Amino-5-butyl-3,5-dimethylcyclopenta-1,3-diene-1-carbonitrile (17a) and (*S*)-2-amino-5-butyl-3,5-dimethylcyclopenta-1,3-diene-1-carbonitrile (17b).

Colorless oil; IR (neat) 3446 (NH), 3359 (NH), 3242 (NH), 2959, 2929, 2862, 2175 (CN), 1652, 1568, 1456, 828 cm^{-1}; ^1H NMR δ 0.85 (3H, t, J=7.3 Hz), 1.07–1.12 (2H, m), 1.20 (3H, s), 1.22–1.28 (2H, m), 1.53–1.61 (2H, m), 1.87 (3H, d, J=1.6 Hz), 4.42 (2H, br s, NH), 6.07 (1H, q, J=1.6 Hz). MS *m/z* (%) 191 (5), 190 (M^+, 29), 147 (45), 134 (60), 133 (100), 118 (22). Calcd for $C_{12}H_{18}N_2$: M, 190.1469. Found: *m/z* 190.1469.

Compound **17a**. $[\alpha]_D^{27}=-122.1$ (c 2.0, acetone).

Compound **17b**. $[\alpha]_D^{27}=+119.4$ (c 1.11, acetone).

3.1.42. (*S*)-4-Butyl-2,4-dimethylcyclopent-2-enone (18a) and (*R*)-4-butyl-2,4-dimethylcyclopent-2-enone (18b).

Colorless oil; IR (neat) 2958, 2928, 1713 (CO), 1640, 1456, 1328 cm^{-1}; ^1H NMR δ 0.89 (3H, t, J=7.2 Hz), 1.16 (3H, s), 1.18–1.32 (4H, m), 1.38–1.50 (2H, m), 1.74 (3H, d, J=1.2 Hz), 2.14, 2.32 (each 1H, d, J=18.6 Hz), 7.05 (1H, q, J=1.2 Hz). MS *m/z* (%) 166 (M^+, 25), 123 (10), 110 (32), 109 (100). Calcd for $C_{11}H_{18}O$: M, 166.1356. Found: *m/z* 166.1356.

Compound **18a**. $[\alpha]_D^{30}=-46.7$ (c 0.88, acetone).

Compound **18b**. $[\alpha]_D^{30}=+43.4$ (c 1.55, acetone).

3.1.43. (*R*)-2-Amino-5-butyl-5-methyl-3-pentylcyclopenta-1,3-dienecarbonitrile (17c) and (*S*)-2-amino-5-butyl-5-methyl-3-pentyl-cyclopenta-1,3-dienecarbonitrile (17d).

Colorless oil; IR (neat) 3462 (NH), 3358 (NH), 3252 (NH), 2929, 2860, 2175 (CN), 1651, 1564, 1457, 1417, 1379 cm^{-1}; ^1H NMR δ 0.85 (3H, t, J=7.3 Hz), 0.90–0.92 (3H, m), 1.06–1.13 (2H, m), 1.21 (3H, s), 1.22–1.26 (2H, m), 1.21–1.35 (6H, m), 1.51–1.55 (2H, m), 2.14 (2H, t, J=7.6 Hz), 4.42 (2H, br s, NH), 6.04 (1H, s). MS *m/z* (%) 246 (M^+, 40), 203 (44), 190 (77), 189 (100), 165 (28), 133 (89), 132 (31). Calcd for $C_{16}H_{26}N_2$: M, 246.2094. Found: *m/z* 246.2097.

Compound **17c**. $[\alpha]_D^{27}=-64.2$ (c 0.65, acetone).

Compound **17d**. $[\alpha]_D^{27}=+63.9$ (c 1.14, acetone). Racemic compound is colorless crystals, low melting solid; IR (KBr) 3451 (NH), 3355 (NH), 3250 (NH), 2929, 2860, 2170 (CN), 1651, 1567, 1467, 1419, 1379 cm^{-1}.

3.1.44. (*R*)-2-Amino-5-butyl-3-isopropyl-5-methylcyclopenta-1,3-dienecarbonitrile (17e) and (*S*)-2-amino-5-butyl-3-isopropyl-5-methylcyclopenta-1,3-dienecarbonitrile (17f).

Colorless oil; IR (neat) 3445 (NH), 3359 (NH), 3249 (NH), 2962, 2929, 2175 (CN), 1652, 1615, 1558, 1417 cm^{-1}; ^1H NMR δ 0.85 (3H, t, J=7.3 Hz), 1.02–1.13 (2H, m), 1.15 (6H, d, J=7.0 Hz), 1.19–1.26 (2H, m), 1.20 (3H, s), 1.56–1.61 (2H, m), 2.42 (1H, septet, J=7.0 Hz), 4.45 (2H, br s, NH), 6.03 (1H, s). MS *m/z* (%) 219 (10), 218 (M^+, 44), 203 (35), 175 (60), 162 (68), 161 (100), 147 (55), 146 (57). Calcd for $C_{14}H_{22}N_2$: M, 218.1781. Found: *m/z* 218.1778.

Compound **17e**. $[\alpha]_D^{29}=-80.7$ (c 0.91, acetone).

Compound **17f**. $[\alpha]_D^{28}=+86.6$ (c 1.48, acetone). Racemic compound is colorless crystals; mp 66–67 °C (hexane); IR (KBr) 3440 (NH), 3354 (NH), 3251 (NH), 2963, 2928, 2164 (CN), 1671, 1648, 1560, 1419 cm^{-1}.

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