Tetrahedron 65 (2009) 3502–3508

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Second generation levoglucosenone-derived chiral auxiliaries. Scope and application in asymmetric Diels–Alder reactions

Ariel M. Sarotti, Rolando A. Spanevello, Alejandra G. Suárez *

Instituto de Química Rosario, Facultad de Ciencias Bioquímicas y Farmacéuticas, Universidad Nacional de Rosario-CONICET, Suipacha 531, S2002LRK Rosario, Argentina

ARTICLE INFO

Article history:
Received 20 November 2008
Received in revised form 11 February 2009
Accepted 11 February 2009
Available online 20 February 2009

ABSTRACT

Chiral alcohols were designed and easily prepared from levoglucosenone, a biomass-derived valuable synthon. These alcohols were tested as chiral auxiliaries in asymmetric Diels–Alder reactions between the corresponding acrylates with acyclic and cyclic dienes. The regio, stereo, and facial selectivity varied from very good to excellent, depending upon the benzylic substitution of the auxiliary and the diene employed. As a consequence, after removal of the auxiliary, the resulting carboxylic acid derivatives were obtained in 72–99% ee.

1. Introduction

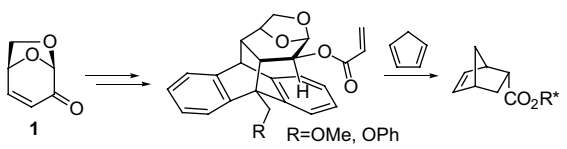
Chirality at the molecular level has emerged as one of the major issues in the development of chemical technology, especially in the areas of drug synthesis and advanced materials. The transfer of chirality through the use of chiral auxiliaries has been demonstrated as an effectual means for preparing enantiopure materials.[1] Most chiral auxiliaries reported in the literature are derived from natural occurring compounds.

Among the plethora of natural molecules, carbohydrates are the most prominent members of the chiral pool since they are major constituents of all foremost structural molecules in living systems. Levoglucosenone (1,6-anhydro-3,4-dideoxy-β-D-*glycero*-hex-3-enopyranos-2-ulose) (**1**) is a versatile and easily available chiral building block from the carbohydrate family.[2,3] Conventional pyrolysis of cellulose-containing materials such as waste paper is typically used to generate **1**,[2–4] but microwave irradiation of microcrystalline cellulose was recently found to be also effective.[5] The highly functionalized structure of **1** makes it an attractive chiral synthon for the synthesis of a wide variety of natural and unnatural compounds.[2,3]

In the context of our ongoing interest in the development new tools for asymmetric synthesis, we have recently reported the design and application of novel chiral auxiliaries derived from levoglucosenone and their application in Diels–Alder reactions.[6–8] Both stoichiometric (chiral auxiliaries) and catalytic (chiral Lewis acids) approaches to asymmetric Diels–Alder reaction have been developed with success.[9] For acrylates, several chiral auxiliaries such menthol derivatives, camphor derivatives[10] and oxazolidinones are available.[11] Carbohydrate compounds have also been reported, although the stereoselectivity was not always good.[1]

A systematic study was made in order to investigate the relationship between the structure of the synthetic chiral auxiliaries and their effectiveness in asymmetric Diels–Alder transformations. We found that the introduction of a substituent at the benzylic position closer to the ester group (Scheme 1), established a new key element of steric control, therefore imposing an additional restriction to the transition state. This structural modification allowed us to obtain excellent diastereoisomeric ratios (up to 98% de) in the cycloaddition reaction of the corresponding acrylic ester and cyclopentadiene (Scheme 1).[7,8]

The high levels of asymmetric induction achieved with the use of cyclopentadiene encouraged us to test the scope of this system with other dienes. Additionally, in an effort to develop new structurally related inductors we envisaged the synthesis of other two chiral auxiliaries bearing bulky groups at the benzylic position of the molecule. We considered that the presence of a *tert*-butyldimethylsilyloxy (OTBS) or a *tert*-butyldiphenylsilyloxy (OTPS) group would induce enhanced selectivity resulting from a larger difference in the steric environment of the two diastereofaces of the acrylate moiety.



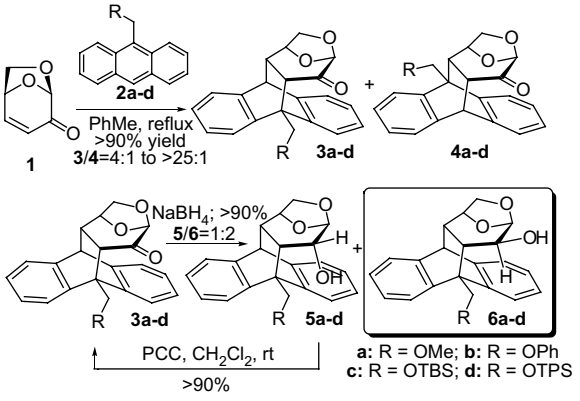
Scheme 1.

* Corresponding author. Tel./fax: +54 341 437 0477.
E-mail address: suarez@iquir-conicet.gov.ar (A.G. Suárez).

0040-4020/$ – see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2009.02.020

2. Results and discussion

Our strategy toward the preparation of the chiral auxiliaries **6a–d** was achieved using a general procedure, which started with a Diels–Alder reaction between levoglucosenone and the corresponding 9-substituted anthracene, followed by a diastereoselective reduction of the *ortho* adduct (Scheme 2). The 9-derived anthracenes **2a–d** were synthesized in a simple and efficient way from commercially available 9-anthracenemethanol.[12] Attempts to perform the cycloaddition step using Lewis acids as catalyst did not afford the desired product. However, this chemical transformation was accomplished in refluxing toluene with very good yields and *ortho* selectivity. Separation of both *ortho* **3a–d** and *meta* **4a–d** adducts was easily achieved by flash chromatography.

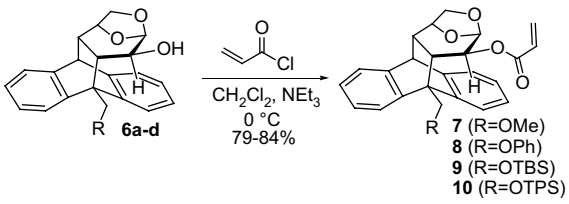


Scheme 2. Synthesis of chiral auxiliaries.

The reduction of ketones **3a–d** led to the formation of two epimeric alcohols **5a–d** and **6a–d**. Even though these compounds have the appropriate functionality to be tested as chiral auxiliaries, after extensive experimentation we found that esterification of isomers **5a–d** were notably difficult, probably due to the steric hindrance surrounding the α-alcohol. For this reason, we investigated reducing conditions toward the formation of **6a–d**. Reducing agents like DIBAL or L-Selectride afforded exclusively the α-alcohols **5a–d** due to the steric effect produced by the aromatic ring that overcomes the one exerted by the 1,6-anhydro bridge. With $NaBH_4$ instead, the outcome of the reduction was function of the $MeOH/CH_2Cl_2$ ratio employed. A low proportion of MeOH favored the product obtained from the attack of the hydride from the more crowded face of the carbonyl group at low MeOH concentration. This experimental result can be understood considering a coordination between the boron atom of the reducing agent and the oxygen at the homobenzylic position. The reaction of ketones **3a–d** with $NaBH_4$ in a mixture CH_2Cl_2/MeOH 95:5 at 0 °C afforded **5a–d**/**6a–d** in a 1:2 ratio, with excellent yields. The epimeric products were simply separated by flash chromatography. In order to improve the overall yield of **6a–d**, alcohols **5a–d** can be recycled by oxidation with PCC almost quantitatively to regenerate starting material.

Once the syntheses of inductors **6a–d** were achieved in a straightforward manner, the corresponding acrylates were prepared and tested as chiral dienophiles in asymmetric Diels–Alder cycloadditions. The acylation step was easily performed in good yields by reaction of acryloyl chloride with the corresponding alcohol in the presence of triethylamine at 0 °C (Scheme 3).

The Diels–Alder reactions between acrylates **7–10** and cyclopentadiene were first carried out under thermal conditions (Table 1, entries 1–4), affording the four expected diastereoisomers, two *endo* and two *exo* adducts. All cycloadditions were *endo* selective, as predicted by Alder's rule, which has been rationalized in terms of



Scheme 3.

interplay between stabilizing secondary orbital interactions and steric effects in the transition state.[13]

As shown in Table 1 (entries 1–4), an interesting π-facial selectivity favoring the *endo S*-adduct was observed (up to 76% de). It is generally accepted that the *s-cis*/*s-trans* conformation of the enoate moiety is not fixed in the absence of Lewis acids. However, the higher selectivity shown by these chiral auxiliaries compared to the one obtained with structurally related systems without a substituent at the benzylic position could be ascribed to the steric hindrance exerted by the substituent.[6a]

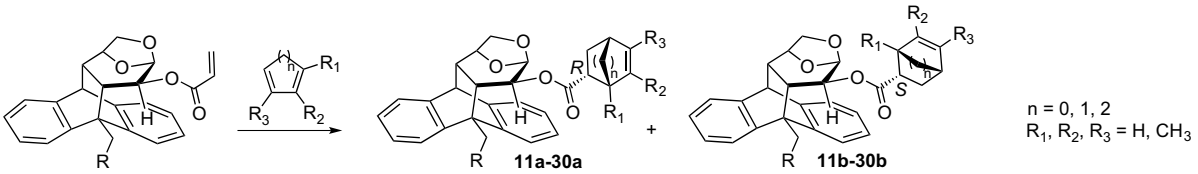
In order to improve the selectivity, the reactions were next carried out in the presence of Lewis acids. After extensive survey, Et_2AlCl and $EtAlCl_2$ demonstrated to be the most effective in this system and with structurally related dienophiles in terms of reactivity and selectivity.[6–8,14] All cycloaddition reactions of acrylates **7–10** with cyclopentadiene (entries 5–8) proceeded in very good yields with high *endo*/*exo* and π-facial selectivity (*endo R*/*S* ratio up to 99:1). It is important to point out that when employing Lewis acids a striking reversal of the stereoselectivity was obtained compared to the thermal conditions. This observation was interpreted in terms that the metal coordination plays a key role in the conformational preference of the enoate moiety, toward the attack of the diene.

With the high selectivity established in the Diels–Alder reactions of cyclopentadiene, our challenge was to test the effectiveness to less reactive cyclic dienes, such as cyclohexadiene (entries 9–12). Not unexpectedly, this reaction could not be carried out under thermal conditions. However, the addition of 3 equiv of Lewis acids proved to be effective in terms of reaction rate and yields. In all cases, the cycloaddition reaction showed excellent *endo* selectivity (*endo*/*exo* >99:1). The *endo R*/*S* ratios were very good (up to 92% de), except with the use of chiral acrylate **9** (R=OTBS), which was slightly decreased.

Chiral acrylates **7–10** were also found to accomplish high levels of regio- and diastereoselectivity when representative acyclic dienes were investigated (entries 13–24). Of the eight possible products, which might have been anticipated from the reaction using piperylene as diene, to our delight we found that only two of them were obtained, namely *ortho-endo* adducts (entries 13–16). The excellent regiocontrol was also achieved when isoprene was employed (*para*/*meta* >99:1, entries 17–20). The levels of π-facial selectivity with both dienes were high, particularly when using acrylates **7** (R=OMe) and **8** (R=OPh) (up to 92% de with piperylene, 94% de with isoprene). These experimental findings suggest that substitution at the benzylic position of chiral auxiliaries is a key element for facial discrimination, but the effectiveness does not rely on the bulkiness of the substituent group. In the case of 2,3-dimethyl-1,3-butadiene (entries 21–24) a lower π-facial selectivities were achieved (up to 72% de) than the ones observed for previous dienes. The lack of high selectivity in this case was not surprising, since it has already been reported a similar behavior when using this diene in asymmetric cycloaddition reactions.[15]

It is noteworthy to mention that the Diels–Alder reactions of the chiral acrylates with all dienes when tested at 25 °C in this study maintained almost the same diastereoselectivity observed at low temperatures.

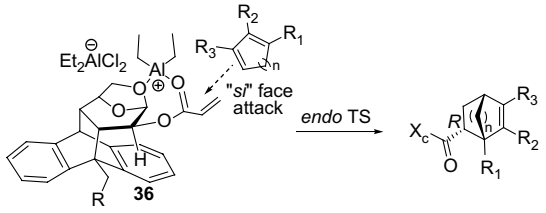
Table 1
Diels–Alder reactions of chiral acrylates **7**–**10** with different dienes[a]



Entry	Diene	Chiral acrylate	Lewis acid (equiv)	*T* (°C)	*t* (h)	Yield (%)[b]	Regio-selectivity[c]	*endo*/*exo*[c]	*endo R*/*S*[c]	Major product[d]	
1		**7**	—	25	48	95	—	76:24	23:77		**11b** (R=OMe)
2		**8**	—	25	48	91	—	78:22	13:87		**12b** (R=OPh)
3		**9**	—	25	48	91	—	78:22	12:88		**13b** (R=OTBS)
4		**10**	—	25	48	99	—	76:24	16:84		**14b** (R=OTPS)
5		**7**	Et_2AlCl (2)	−80	1	80	—	98:2	99:1		**11a** (R=OMe)
6		**8**	Et_2AlCl (2)	−80	1	82	—	96:4	97:3		**12a** (R=OPh)
7		**9**	Et_2AlCl (2)	−80	1	85	—	97:3	91:9		**13a** (R=OTBS)
8		**10**	Et_2AlCl (2)	−80	1	87	—	97:3	96:4		**14a** (R=OTPS)
9		**7**	Et_2AlCl (3)	0	6	90	—	>99:1	96:4		**15a** (R=OMe)
10		**8**	$EtAlCl_2$ (3)	0	20	92	—	>99:1	94:6		**16a** (R=OPh)
11		**9**	$EtAlCl_2$ (3)	0	20	89	—	>99:1	84:16		**17a** (R=OTBS)
12		**10**	Et_2AlCl (3)	0	20	86	—	>99:1	93:7		**18a** (R=OTPS)
13		**7**	$EtAlCl_2$ (3)	0	20	82	>99:1[e]	>99:1	95:5		**19a** (R=OMe)
14		**8**	Et_2AlCl (3)	0	20	86	>99:1[e]	>99:1	96:4		**20a** (R=OPh)
15		**9**	Et_2AlCl (3)	0	20	85	>99:1[e]	>99:1	89:11		**21a** (R=OTBS)
16		**10**	Et_2AlCl (3)	0	20	86	>99:1[e]	>99:1	83:17		**22a** (R=OTPS)
17		**7**	Et_2AlCl (3)	0	20	87	>99:1[f]	—	97:3		**23a** (R=OMe)
18		**8**	Et_2AlCl (3)	0	20	89	>99:1[f]	—	97:3		**24a** (R=OPh)
19		**9**	Et_2AlCl (3)	0	20	87	>99:1[f]	—	93:7		**25a** (R=OTBS)
20		**10**	Et_2AlCl (3)	0	20	83	>99:1[f]	—	92:8		**26a** (R=OTPS)
21		**7**	Et_2AlCl (3)	0	20	86	—	—	86:14		**27a** (R=OMe)
22		**8**	Et_2AlCl (3)	0	20	80	—	—	83:17		**28a** (R=OPh)
23		**9**	Et_2AlCl (3)	0	20	81	—	—	76:24		**29a** (R=OTBS)
24		**10**	Et_2AlCl (3)	0	20	79	—	—	69:31		**30a** (R=OTPS)

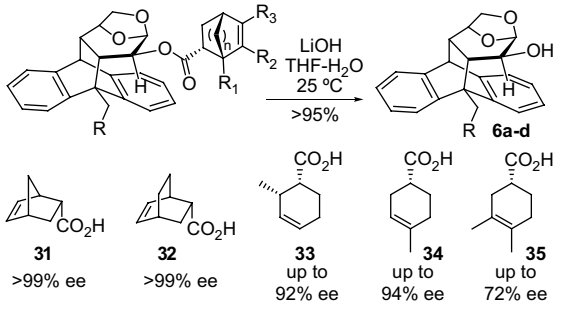
[a] Reactions run in CH_2Cl_2 with 10 equiv of diene.
[b] Overall isolated yield after flash column chromatography.
[c] Determined by NMR and HPLC (C-18 column, MeCN/H_2O 80/20, flow rate 1 mL/min).
[d] Major product absolute stereochemistry determined by hydrolysis and further comparison of the sign of the specific rotation of the isolated carboxylic acid to those reported in the literature (Ref. 15).
[e] *ortho*/*meta* ratio.
[f] *para*/*meta* ratio.

It is generally accepted that the stereoselectivity in the Diels–Alder reaction depends upon the *s-trans*/*s-cis* conformation of the enoate.[16] Based on literature reports,[17] experimental evidences and detailed NMR studies, we can postulate that in this case, the reaction promoted with more than 1 equiv of Et_2AlCl (or $EtAlCl_2$) proceeds through the formation of a chelated complex like **36** in the *s-cis* conformation.[7,8] The addition of diene from the more accessible face of the Lewis acid–dienophile intermediate affords the predominant *R* isomers, as we observed experimentally (Scheme 4).



Scheme 4.

Aside from the excellent regio- and diastereocontrol, a salient feature of these chiral auxiliaries is their simple removal procedure. Treatment of adducts **11**–**30** with LiOH in THF/H_2O at 25 °C followed by a quench with 1 N HCl until pH=4 gave the corresponding free carboxylic acids **31**–**35** and allowed quantitative recovery of chiral auxiliaries (Scheme 5). No epimerization was observed at the stereogenic center α to the carboxylic acid. For that reason, acids **31**–**35** could be isolated in high enantiomeric purity, depending upon the diene employed. For instance, *endo R* adducts derived from reaction of acrylates **7**–**10** and cyclopentadiene (or cyclohexadiene), can be isolated in pure diastereoisomeric form after flash chromatography. Thus, the hydrolytic cleavage affords (2*R*)-*endo*-bicyclo[2.2.1]hept-5-ene-2-carboxylic acid (**31**) and (2*R*)-*endo*-bicyclo[2.2.2]oct-5-ene-2-carboxylic acid (**32**) in enantiomerically pure forms.[18] On the other hand, all attempts to separate pure major isomers derived from Diels–Alder reaction using piperylene, isoprene, and 2,3-dimethyl-1,3-butadiene met with no success. As a result, the cyclohexene carboxylic acids (**33**–**35**) obtained after hydrolysis could be only isolated in up to 94% ee.



Scheme 5.

3. Conclusion

In summary, we have described highly efficient regio- and diastereoselective Diels–Alder reactions using levoglucosenone-derived chiral auxiliaries. A systematic study was performed in order to investigate the relationship between the nature of the substituent at the benzylic position of chiral acrylates and its effectiveness in asymmetric Diels–Alder transformations. The sense of asymmetric induction depended upon the diene and the nature of the benzylic substituent of the chiral auxiliary, the smallest ones (R=OMe, R=OPh) being the most effective in terms of π-facial selectivity. Saponification of the obtained cycloadducts provided free carboxylic acids in high yields and enantiomeric purity. Chiral auxiliaries were recovered quantitatively after hydrolysis and could be reused.

4. Experimental

4.1. General methods

The melting points were taken on a Leitz Wetzlar Microscope Heating Stage Model 350 apparatus and are uncorrected. Optical rotations were recorded with a Jasco DIP 1000 polarimeter. Infrared spectra were obtained on an IRPrestige-21 Fourier Transform Spectrophotometer Shimadsu. High resolution mass spectrometry measurements were performed using a Waters AutoSpect equipment, Applied Biosystems MS, Micromass AutoSpec or Bruker micrOTOF-Q equipments. HPLC analyses were performed with a chromatograph Varian ProStar equipped with UV-V detector ProStar 320 at 270 nm. HPLC was performed on a Beckman C-18, 25 cm column. Acetonitrile and water HPLC grade were used as eluents in a mixture 80:20, respectively. Flow rate was 1 mL/min. Nuclear magnetic resonance spectra were recorded on a Bruker AC-200 or a Bruker Avance-300 DPX spectrometers with tetramethylsilane as internal standard and deuterochloroform as solvent. The NMR assignments were corroborated by NOE measurements, H,H- and H,C-correlations.

The reactions were monitored by thin layer chromatography carried out on 0.25 mm E. Merck silica gel plates ($60F_{254}$) that were developed using UV light and anisaldehyde–sulfuric acid–acetic acid with subsequent heating. Flash column chromatographies were performed using Merck silica gel 60H, by gradient elution created by mixtures of hexanes and increasing amounts of ethyl acetate. All reactions were carried out under argon atmosphere with dry, freshly distilled solvents under anhydrous conditions unless otherwise noted. Yields refer to chromatographically and spectroscopically (^{1}H NMR) homogeneous materials, unless otherwise stated.

Levoglucosenone (**1**) was synthesized according to the procedure described in literature[2,3] or following the procedure developed in our research group.[5]

4.2. Synthesis of chiral auxiliaries

4.2.1. General procedure

Levoglucosenone (**1**) and the corresponding 9-substituted anthracenes **2a–d** (2.8 equiv) were dissolved in toluene (*c* 0.2 M) at room temperature. The solution was heated under reflux for 7–10 days until completion by TLC analysis. Solvent was evaporated under reduced pressure and the solid residue was purified by flash chromatography to give adducts *ortho* **3a–d** and *meta* **4a–d** in >90% overall yield. The excess of the diene was recovered quantitatively and reused. Next, the major regioisomers *ortho* **3a–d** were dissolved in a CH_2Cl_2/MeOH 95:5 mixture (*c* 0.06 M), cooled at 0 °C and $NaBH_4$ (2.2 equiv) was incorporated. The solution was stirred 4–8 h and then water was added. The aqueous phase was extracted with CH_2Cl_2 (100 mL) and then with AcOEt (3×150 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash chromatography to afford alcohols **5a–d** and **6a–d** (major) in >90% overall yield. To recycle minor compounds **5a–d**, they were dissolved in CH_2Cl_2 (*c* 0.15 M) then PCC (2.7 equiv) was added in one portion and stirred overnight under argon atmosphere. The reaction mixture was diluted with CH_2Cl_2 and filtered through Florisil® contained in a sintered glass funnel. The filtrate was concentrated to give starting ketones **3a–d** in >95% yield.

*4.2.1.1. Alcohol **6c**.* Colorless oil; $[\alpha]_D^{25}$ +6.4 (*c* 0.64, $CHCl_3$); IR (film) ν_{max}: 3462 (OH), 3072, 3023, 2953, 2928, 1457, 1254, 1102, 1056, 835, 749 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.53–7.02 (m, 8H, aromatic), 4.98 (d, J_{1-2}=3.4 Hz, 1H, H-1), 4.86 (d, J_{gem}=10.7 Hz, 1H, H-7), 4.73 (d, J_{gem}=10.7 Hz, 1H, H-7), 4.65 (d, J_{5-6exo}=4.7 Hz, 1H, H-5), 4.13 (d, J_{4-4a}=0.9 Hz, 1H, H-4a), 3.74 (dd, J_{gem}=7.1 Hz, J_{5-6exo}=4.7 Hz, 1H, H-6*exo*), 3.66 (d, J_{gem}=7.1 Hz, 1H, H-6*endo*), 2.99–2.91 (m, 1H, H-2), 2.32–2.21 (m, 2H, H-3 and OH), 2.08 (d, J_{3-4}=10.5 Hz, 1H, H-4), 0.98 (s, 9H, H-10), 0.33 (s, 3H, H-8a), 0.28 (s, 3H, H-8b); ^{13}C NMR ($CDCl_3$) δ 146.5 (C, aromatic), 141.9 (C, aromatic), 141.4 (C, aromatic), 141.2 (C, aromatic), 126.0 (CH, aromatic), 125.4 (CH, 3C, aromatic), 124.9 (CH, aromatic), 123.9 (CH, aromatic), 122.9 (CH, aromatic), 121.8 (CH, aromatic), 99.8 (CH, C-1), 76.7 (CH, C-5), 70.2 (CH_2, C-6), 68.7 (CH, C-2), 61.9 (CH_2, C-7), 50.8 (C, C-3a), 50.5 (CH, C-4a), 47.6 (CH, C-4), 41.2 (CH, C-3), 25.8 (CH_3, C-10), 18.2 (C, C-9), −5.5 (CH_3, C-8a), −5.6 (CH_3, C-8b). HRMS calcd for $C_{27}H_{34}O_4SiNa$ $[M+Na]^+$ 473.2124; found 473.2144.

*4.2.1.2. Alcohol **6d**.* Colorless oil; $[\alpha]_D^{16}$ +9.7 (*c* 1.80, $CHCl_3$); IR (film) ν_{max}: 3473 (OH), 3071, 2930, 2857, 1457, 1426, 1103, 1056, 750, 702 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.86–7.81 (m, 4H, aromatic), 7.49–7.41 (m, 6H, aromatic), 7.33–7.30 (m, 1H, aromatic), 7.19–6.87 (m, 7H, aromatic), 4.98 (d, J_{1-2}=3.3 Hz, 1H, H-1), 4.88 (s, 2H, H-7), 4.65 (d, J_{5-6exo}=4.7 Hz, 1H, H-5), 4.11 (d, J_{4-4a}=1.0 Hz, 1H, H-4a), 3.74 (dd, J_{gem}=7.1 Hz, J_{5-6exo}=4.7 Hz, 1H, H-6*exo*), 3.67 (d, J_{gem}=7.1 Hz, 1H, H-6*endo*), 2.94 (br s, 1H, H-2), 2.33–2.26 (m, 2H, H-3 and OH), 2.10 (d, J_{3-4}=10.4 Hz, 1H, H-4), 1.16 (s, 9H, H-9); ^{13}C NMR ($CDCl_3$) δ 146.3 (C, aromatic), 141.7 (C, aromatic), 141.3 (C, aromatic), 140.8 (C, aromatic), 136.2 (CH, 2C, aromatic), 136.1 (CH, 2C, aromatic), 133.0 (C, aromatic), 132.9 (C, aromatic), 130.0 (CH, aromatic), 129.8 (CH, aromatic), 127.7 (CH, 2C, aromatic), 127.6 (CH, 2C, aromatic), 125.9 (CH, aromatic), 125.3 (CH, aromatic), 125.2 (CH, 2C, aromatic), 124.8 (CH, aromatic), 124.3 (CH, aromatic), 123.1 (CH, aromatic), 121.6 (CH, aromatic), 99.8 (CH, C-1), 76.7 (CH, C-5), 70.1 (CH_2, C-6), 68.5 (CH, C-2), 62.7 (CH_2, C-7), 51.2 (C, C-3a), 50.4 (CH, C-4a), 47.7 (CH, C-4), 41.4 (CH, C-3), 27.2 (CH_3, C-9), 19.3 (C, C-8). HRMS calcd for $C_{37}H_{38}O_4SiNa$ $[M+Na]^+$ 597.2437; found 597.2426.

4.3. Synthesis of chiral acrylates

4.3.1. General procedure

Each alcohol **6a–d** (3 mmol) was dried azeotropically with dry benzene, dissolved in CH_2Cl_2 to afford a 0.70 mM solution which was cooled at 0 °C. Triethylamine (21 mmol) and acryloyl chloride (13 mmol) were added and stirred for 1 h under argon atmosphere. The mixture was diluted with water (50 mL) and extracted several times with 50 mL portions of CH_2Cl_2. The combined organic extracts were dried (Na_2SO_4) and concentrated. The residue was purified by flash chromatography to afford acrylates **7–10** in 79–84% yield.

*4.3.1.1. Acrylate **9**.* Colorless oil; $[\alpha]_D$ −14.3 (*c* 1.95, $CHCl_3$); IR (film) ν_{max}: 3074, 2955, 2857, 1722 (C=O), 1464, 1405, 1259, 1194, 1104, 1012, 838, 733 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.57–7.05 (m, 8H, aromatic), 6.48 (dd, J_{vic}=17.3 Hz, J_{gem}=1.4 Hz, 1H, H-3′*cis*), 6.19 (dd,

J_{vic}=17.3 Hz, J_{vic}=10.3 Hz, 1H, H-2′), 5.88 (dd, J_{vic}=10.3 Hz, J_{gem}=1.4 Hz, 1H, H-3′*trans*), 5.09 (d, J_{1-2}=3.1 Hz, 1H, H-1), 4.66 (d, J_{5-6exo}=4.0 Hz, 1H, H-5), 4.55 (d, J_{gem}=10.7 Hz, 1H, H-7), 4.42 (d, J_{gem}=10.7 Hz, 1H, H-7), 4.32 (dd, J_{2-3}=6.1 Hz, J_{1-2}=3.1 Hz, 1H, H-2), 4.16 (s, 1H, H-4a), 3.75–3.69 (m, 2H, H-6), 2.45 (br s, 1H, H-3), 2.18 (d, J_{3-4}=10.4 Hz, 1H, H-4), 0.92 (s, 9H, H-10), 0.24 (s, 3H, H-8a), 0.15 (s, 3H, H-8b); ^{13}C NMR ($CDCl_3$) δ 165.2 (C, C-1′), 146.0 (C, aromatic), 141.1 (C, aromatic), 141.0 (C, aromatic), 140.8 (C, aromatic), 131.5 (CH_2, C-3′), 128.2 (CH, C-2′), 126.1 (CH, aromatic), 125.8 (CH, aromatic), 125.6 (CH, aromatic), 125.3 (CH, aromatic), 124.8 (CH, aromatic), 124.6 (CH, aromatic), 123.6 (CH, aromatic), 121.8 (CH, aromatic), 96.8 (CH, C-1), 76.6 (CH, C-5), 70.8 (CH, C-2), 70.1 (CH_2, C-6), 61.2 (CH_2, C-7), 51.5 (C, C-3a), 50.7 (CH, C-4a), 47.8 (CH, C-4), 37.1 (CH, C-3), 25.8 (CH_3, C-10), 18.0 (C, C-9), −5.6 (CH_3, C-8a), −5.9 (CH_3, C-8b). HRMS calcd for $C_{30}H_{36}O_5SiNa$ $[M+Na]^+$ 527.2230; found 527.2219.

4.3.1.2. Acrylate ***10****.* Colorless oil; $[\alpha]_D$ −17.7 (*c* 0.78, $CHCl_3$); IR (film) ν_{max}: 3072, 2929, 2857, 1724 (C=O), 1458, 1405, 1189, 1105, 1011, 749, 702 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.72–7.66 (m, 4H, aromatic), 7.49–7.33 (m, 9H, aromatic), 7.21–6.94 (m, 5H, aromatic), 6.31 (dd, J_{vic}=17.2 Hz, J_{gem}=1.5 Hz, 1H, H-3′*cis*), 5.99 (dd, J_{vic}=17.2 Hz, J_{vic}=10.4 Hz, 1H, H-2′), 5.74 (dd, J_{vic}=10.4 Hz, J_{gem}=1.5 Hz, 1H, H-3′*trans*), 5.11 (d, J_{1-2}=3.1 Hz, 1H, H-1), 4.63 (d, J_{5-6exo}=4.4 Hz, 1H, H-5), 4.59 (d, J_{gem}=11.5 Hz, 1H, H-7), 4.55 (d, J_{gem}=11.5 Hz, 1H, H-7), 4.16–4.13 (m, 2H, H-2 and H-4a), 3.69 (dd, J_{gem}=7.0 Hz, J_{5-6exo}=4.4 Hz, 1H, H-6*exo*), 3.64 (d, J_{gem}=7.0 Hz, 1H, H-6*endo*), 2.20 (dd, J_{3-4}=10.6 Hz, J_{2-3}=6.1 Hz, 1H, H-3), 2.10 (d, J_{3-4}=10.6 Hz, 1H, H-4), 1.12 (s, 9H, H-9); ^{13}C NMR ($CDCl_3$) δ 164.9 (C, C-1′), 145.7 (C, aromatic), 140.7 (C, 2C, aromatic), 140.3 (C, aromatic), 136.0 (CH, 2C, aromatic), 135.9 (CH, 2C, aromatic), 133.2 (C, aromatic), 132.9 (C, aromatic), 131.2 (CH_2, C-3′), 129.8 (CH, aromatic), 129.7 (CH, aromatic), 127.9 (CH, C-2′), 127.7 (CH, 2C, aromatic), 127.5 (CH, 2C, aromatic), 126.0 (CH, aromatic), 125.8 (CH, aromatic), 125.6 (CH, aromatic), 125.3 (CH, aromatic), 124.8 (CH, aromatic), 124.7 (CH, aromatic), 124.6 (CH, aromatic), 121.7 (CH, aromatic), 96.6 (CH, C-1), 76.4 (CH, C-5), 71.1 (CH, C-2), 70.3 (CH_2, C-6), 62.7 (CH_2, C-7), 52.4 (C, C-3a), 50.6 (CH, C-4a), 48.1 (CH, C-4), 38.3 (CH, C-3), 27.1 (CH_3, C-9), 19.5 (C, C-8). HRMS calcd for $C_{40}H_{40}O_5SiNa$ $[M+Na]^+$ 651.2543; found 651.2554.

4.4. Asymmetric Diels–Alder reactions

Each acrylic ester **7**–**10** (0.1 mmol) was dried azeotropically with dry benzene and dissolved in the CH_2Cl_2 to give a 0.2 M solution. When the reaction was promoted by Lewis acid the appropriate amount was added under nitrogen and stirred for 20 min at the corresponding temperature. The diene (1 mmol) was added dropwise and the mixture was stirred at the temperature and time indicated in Table 1. The cycloaddition reactions carried out without Lewis acid were concentrated after completion to afford a solid residue. The reactions promoted by Lewis acids were quenched by the addition of water (10 mL) and HCl 0.1 N (10 mL), then extracted with CH_2Cl_2 (3×30 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated. The solid residue was purified by flash chromatography to separate the excess of diene and to recover the product mixture. Diastereoselectivities were determined by HPLC and NMR analysis.

4.4.1. Adduct ***15a***

Colorless oil; $[\alpha]_D^{23}$ +9.8 (*c* 0.71, $CHCl_3$); IR (film) 3041, 3022, 2941, 2868, 1729 (C=O), 1458, 1191, 1160, 1147, 1111, 1053, 1004, 748 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.44–7.05 (m, 8H, aromatic), 6.36 (dd, $J_{4'-5'}$=$J_{5'-6'}$=7.0 Hz, 1H, H-5′), 6.28 (dd, $J_{5'-6'}$=$J_{6'-7'}$=7.0 Hz, 1H, H-6′), 4.99 (d, J_{1-2}=3.3 Hz, 1H, H-1), 4.58 (d, J_{5-6exo}=4.4 Hz, 1H, H-5), 4.26–4.18 (m, 3H, H-2 and H-7), 4.13 (s, 1H, H-4a), 3.67 (dd, J_{gem}=7.2 Hz, J_{5-6exo}=4.4 Hz, 1H, H-6*exo*), 3.63 (d, J_{gem}=7.2 Hz, 1H, H-6*endo*), 3.59 (s, 3H, H-8), 3.01 (br s, 1H, H-7′), 2.68 (td, $J_{2'-3'exo}$=9.9 Hz, $J_{2'-3'endo}$=5.5 Hz, $J_{2'-7'}$=2.2 Hz, 1H, H-2′), 2.60 (br s, 1H, H-4′), 2.35 (dd, J_{3-4}=10.4 Hz, J_{2-3}=6.0 Hz, 1H, H-3), 2.10 (d, J_{3-4}=10.4 Hz, 1H, H-4), 1.79 (td, J_{gem}=12.9 Hz, $J_{2'-3'exo}$=9.9 Hz, $J_{3'exo-4'}$=2.6 Hz, 1H, H-3′*exo*), 1.66 (td, J_{gem}=12.9 Hz, $J_{2'-3'endo}$=5.5 Hz, $J_{3'endo-4'}$=2.8 Hz, 1H, H-3′*endo*), 1.60–1.24 (m, 4H, H-8′ and H-9′); ^{13}C NMR ($CDCl_3$) δ 174.4 (C, C-1′), 145.6 (C, aromatic), 140.8 (C, aromatic), 140.6 (C, aromatic), 140.4 (C, aromatic), 135.3 (CH, C-5′), 131.1 (CH, C-6′), 126.1 (CH, aromatic), 125.9 (CH, aromatic), 125.7 (CH, 2C, aromatic), 124.6 (CH, aromatic), 123.9 (CH, aromatic), 123.5 (CH, aromatic), 121.8 (CH, aromatic), 96.6 (CH, C-1), 76.3 (CH, C-5), 71.3 (CH_2, C-7), 70.1 (CH, C-2), 70.1 (CH_2, C-6), 59.0 (CH_3, C-8), 50.5 (CH, C-4a), 50.4 (C, C-3a), 47.5 (CH, C-4), 42.7 (CH, C-2′), 37.6 (CH, C-3), 32.1 (CH, C-7′), 30.0 (CH_2, C-3′), 29.2 (CH, C-4′), 25.3 (CH_2, C-9′), 24.0 (CH_2, C-8′).

4.4.2. Adduct ***16a***

Colorless oil; $[\alpha]_D^{24}$ −6.5 (*c* 0.99, $CHCl_3$); IR (film) 3042, 3023, 2944, 2868, 1728 (C=O), 1599, 1499, 1478, 1244, 1160, 1147, 1052, 753 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.42–7.01 (m, 13H, aromatic), 6.17 (dd, $J_{5'-6'}$=$J_{4'-5'}$=7.2 Hz, 1H, H-5′), 6.05 (dd, $J_{5'-6'}$=$J_{6'-7'}$=7.2 Hz, 1H, H-6′), 5.00 (d, J_{gem}=9.8 Hz, 1H, H-7), 4.95 (d, J_{1-2}=3.2 Hz, 1H, H-1), 4.69 (d, J_{gem}=9.8 Hz, 1H, H-7), 4.65 (dd, J_{5-6exo}=3.5 Hz, $J_{5-6endo}$=2.1 Hz, 1H, H-5), 4.28 (dd, J_{2-3}=6.3 Hz, J_{1-2}=3.2 Hz, 1H, H-2), 4.21 (d, J_{4-4a}=1.2 Hz, 1H, H-4a), 3.74–3.69 (m, 2H, H-6), 2.80 (br s, 1H, H-3), 2.44 (br s, 2H, H-4′ and H-7′), 2.24 (d, J_{3-4}=10.9 Hz, 1H, H-4), 1.97 (br s, 1H, H-2′), 1.64 (td, J_{gem}=11.6 Hz, $J_{2'-3'exo}$=11.6 Hz, $J_{3'exo-4'}$=2.3 Hz, 1H, H-3′*exo*), 1.36–1.01 (m, 5H, H-3′*endo*, H-8′ and H-9′); ^{13}C NMR ($CDCl_3$) δ 174.9 (C, C-1′), 158.5 (C, aromatic), 145.9 (C, aromatic), 141.0 (C, aromatic), 140.5 (C, 2C, aromatic), 134.3 (CH, C-5′), 132.0 (CH, C-6′), 129.5 (CH, 2C, aromatic), 126.4 (CH, aromatic), 126.0 (CH, aromatic), 125.9 (CH, aromatic), 125.8 (CH, aromatic), 125.0 (CH, aromatic), 124.0 (CH, aromatic), 122.7 (CH, aromatic), 122.0 (CH, aromatic), 121.1 (CH, aromatic), 114.3 (CH, 2C, aromatic), 97.0 (CH, C-1), 76.6 (CH, C-5), 70.3 (CH_2, C-6), 69.9 (CH, C-2), 65.5 (CH_2, C-7), 50.6 (CH, C-4a), 49.7 (C, C-3a), 47.4 (CH, C-4), 42.3 (CH, C-2′), 36.5 (CH, C-3), 31.2 (CH, C-7′), 31.0 (CH_2, C-3′), 29.2 (CH, C-4′), 24.9 (CH_2, C-9′), 23.8 (CH_2, C-8′).

4.4.3. Adducts ***19a*** *and* ***19b***

Colorless oil; IR (film) 3071, 3021, 2960, 2923, 2892, 1725, 1458, 1305, 1228, 1145, 1115, 1020, 734 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.44–7.34 (m, 2H, aromatic), 7.27–7.06 (m, 6H, aromatic), 5.72–5.48 (m, 2H, H-4′ and H-5′), 5.12 (d, J_{1-2}=3.5 Hz, 1H, H-1 of **19a**), 5.08 (d, J_{1-2}=3.3 Hz, 1H, H-1 of **19b**), 4.64 (d, J_{5-6exo}=4.4 Hz, 1H, H-5), 4.32–4.23 (m, 3H, H-2 and H-7), 4.17 (d, J_{4-4a}=1.3 Hz, 1H, H-4a), 3.72 (dd, J_{gem}=7.1 Hz, J_{5-6exo}=4.4 Hz, 1H, H-6*exo*), 3.67 (dd, J_{gem}=7.1 Hz, $J_{5-6endo}$=1.1 Hz, 1H, H-6*endo*), 3.59 (s, 3H, H-8), 2.77–2.64 (m, 2H, H-2′ and H-3′), 2.42 (dd, *J*=10.3, 5.9 Hz, 1H, H-3), 2.16 (d, J_{3-4}=10.5 Hz, 1H, H-4), 2.09–1.75 (m, 4H, H-6′ and H-7′), 1.09 (d, $J_{3'-8'}$=7.2 Hz, H-8′ of **19b**), 1.06 (d, $J_{3'-8'}$=7.0 Hz, 3H, H-8′ of **19a**); ^{13}C NMR ($CDCl_3$) δ 174.9 (C, C-1′ of **19b**), 173.8 (C, C-1′ of **19a**), 145.6 (C, aromatic), 140.9 (C, aromatic), 140.7 (C, aromatic), 140.5 (C, aromatic), 131.5 (CH, C-4′), 126.2 (CH, aromatic), 125.9 (CH, aromatic), 125.8 (CH, 2C, aromatic), 125.7 (CH, C-5′), 124.7 (CH, aromatic), 123.9 (CH, aromatic), 123.3 (CH, aromatic), 121.9 (CH, aromatic), 96.6 (CH, C-1), 76.4 (CH, C-5), 71.3 (CH_2, C-7), 70.3 (CH, C-2), 70.2 (CH_2, C-6), 58.9 (CH_3, C-8), 50.6 (CH, C-4a), 50.2 (C, C-3a), 47.5 (CH, C-4), 43.9 (CH, C-2′), 37.4 (CH, C-3), 31.8 (CH, C-3′ of **19b**), 31.0 (CH, C-3′ of **19a**), 24.6 (CH_2, C-6′ of **19a**), 24.3 (CH_2, C-6′ of **19b**), 19.4 (CH_2, C-7′), 16.7 (CH_3, C-8′).

4.4.4. Adducts ***20a*** *and* ***20b***

Colorless oil; IR (film) 3065, 3021, 2960, 2893, 1722, 1599, 1478, 1245, 1145, 1020, 909, 752, 734 cm^{-1}; ^{1}H NMR ($CDCl_3$)

δ 7.43–7.00 (m, 13H, aromatic), 5.50–5.36 (m, 2H, H-4′ and H-5′), 5.09 (d, J_{1-2}=3.2 Hz, 1H, H-1), 4.99 (d, J_{gem}=9.7 Hz, 1H, H-7), 4.76 (d, J_{gem}=9.7 Hz, 1H, H-7), 4.69 (dd, J_{5-6exo}=2.8 Hz, $J_{5-6endo}$ =2.8 Hz, 1H, H-5), 4.36 (dd, J_{2-3}=6.2 Hz, J_{1-2}=3.2 Hz, 1H, H-2 of **20a**), 4.33 (dd, J_{1-2}=3.2 Hz, J_{2-3}=6.2 Hz, 1H, H-2 of **20b**), 4.23 (d, J_{4-4a}=1.0 Hz, 1H, H-4a), 3.77–3.72 (m, 2H, H-6), 2.85 (br s, 1H, H-3), 2.31–2.17 (m, 3H, H-2′, H-3′ and H-4), 1.88–1.56 (m, 4H, H-6′ and H-7′), 0.79 (d, $J_{3'-8'}$=6.8 Hz, 3H, H-8′); ^{13}C NMR ($CDCl_3$) δ 174.0 (C, C-1′), 158.3 (C, aromatic of **20b**), 158.2 (C, aromatic of **20a**), 145.9 (C, aromatic), 141.1 (C, aromatic), 140.6 (C, aromatic), 140.4 (C, aromatic), 131.5 (CH, C-4′), 129.5 (CH, 2C, aromatic), 126.4 (CH, aromatic), 126.0 (CH, aromatic), 125.9 (CH, C-5′), 125.8 (CH, aromatic), 125.4 (CH, aromatic), 125.1 (CH, aromatic), 124.0 (CH, aromatic), 122.6 (CH, aromatic), 122.0 (CH, aromatic), 121.1 (CH, aromatic), 114.2 (CH, 2C, aromatic), 96.9 (CH, C-1), 76.6 (CH, C-5), 70.2 (CH_2, C-6), 70.2 (CH, C-2), 65.3 (CH_2, C-7), 50.6 (CH, C-4a), 49.69 (C, C-3a), 47.5 (CH, C-4), 43.5 (CH, C-2′), 36.3 (CH, C-3), 30.7 (CH, C-3′), 24.5 (CH_2, C-6′ of **20a**), 24.0 (CH_2, C-6′ of **20b**), 20.1 (CH_2, C-7′ of **20b**), 19.2 (CH_2, C-7′ of **20a**), 16.4 (CH_3, C-8′).

*4.4.5. Adducts **23a** and **23b***

Colorless oil; IR (film) 3072, 3022, 2957, 2925, 2894, 2853, 1729, 1458, 1306, 1222, 1147, 1114, 1013, 735 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.43–7.33 (m, 2H, aromatic), 7.21–7.06 (m, 6H, aromatic), 5.40 (br s, 1H, H-4′), 5.05 (d, J_{1-2}=3.5 Hz, 1H, H-1), 4.64 (d, J_{5-6exo}=4.2 Hz, 1H, H-5), 4.31–4.16 (m, 4H, H-2, H-4a and H-7), 3.72 (dd, J_{gem}=7.1 Hz, J_{5-6exo}=4.2 Hz, 1H, H-6*exo*), 3.68 (dd, J_{gem}=7.1 Hz, $J_{5-6endo}$=1.2 Hz, 1H, H-6*endo*), 3.56 (s, 3H, H-8), 2.61–2.45 (m, 2H, H-2′ and H-3), 2.31–2.29 (m, 2H, H-3′), 2.16 (d, J_{3-4}=10.6 Hz, 1H, H-4), 2.08–1.99 (m, 3H, H-6′, H-7′), 1.77–1.69 (m, 1H, H-7′), 1.65 (s, 3H, H-8′); ^{13}C NMR ($CDCl_3$) δ 175.1 (C, C-1′), 145.7 (C, aromatic), 141.0 (C, aromatic), 140.8 (C, aromatic), 140.7 (C, aromatic), 133.8 (C, C-5′ of **23a**), 133.5 (C, C-5′ of **23b**), 126.2 (CH, aromatic), 125.9 (CH, aromatic), 125.8 (CH, aromatic), 125.7 (CH, aromatic), 124.8 (CH, aromatic), 123.9 (CH, aromatic), 123.1 (CH, aromatic), 121.9 (CH, aromatic), 119.1 (CH, C-4′ of **23a**), 118.8 (CH, C-4′ of **23b**), 96.8 (CH, C-1), 76.5 (CH, C-5), 71.2 (CH_2, C-7), 70.2 (CH, C-2), 70.1 (CH_2, C-6), 59.1 (CH_3, C-8), 50.5 (CH, C-4a), 50.1 (C, C-3a), 47.5 (CH, C-4), 39.2 (CH, C-2′ of **23b**), 39.0 (CH, C-2′ of **23a**), 37.1 (CH, C-3), 29.3 (CH_2, C-6′ of **23b**), 29.1 (CH_2, C-6′ of **23a**), 27.6 (CH_2, C-3′ of **23b**), 27.3 (CH_2, C-3′ of **23a**), 25.5 (CH_2, C-7′ of **23a**), 25.2 (CH_2, C-7′ of **23b**), 23.4 (CH_3, C-8′).

*4.4.6. Adducts **24a** and **24b***

Colorless oil; IR (film) 3071, 3041, 2958, 2927, 2854, 1729, 1600, 1499, 1478, 1456, 1305, 1243, 1160, 1012, 910, 753 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.42–6.98 (m, 13H, aromatic), 5.20 (br s, 1H, H-4′ of **24b**), 5.13 (br s, 1H, H-4′ of **24a**), 5.03–4.98 (m, 2H, H-1 and H-7), 4.72–4.68 (m, 2H, H-5 and H-7), 4.35 (dd, J_{2-3}=6.2 Hz, J_{1-2}=3.3 Hz, 1H, H-2), 4.23 (d, J_{4-4a}=1.1 Hz, 1H, H-4a), 3.77–3.72 (m, 2H, H-6), 2.85 (br s, 1H, H-3), 2.27 (d, J_{3-4}=10.4 Hz, 1H, H-4), 1.93–1.43 (m, 10H, H-2′, H-3′, H-6′, H-7′ and H-8′); ^{13}C NMR ($CDCl_3$) δ 175.3 (C, C-1′), 158.4 (C, aromatic), 145.9 (C, aromatic), 141.1 (C, aromatic), 140.6 (C, aromatic), 140.5 (C, aromatic), 133.5 (C, C-5′ of **24b**), 133.1 (C, C-5′ of **24a**), 129.5 (CH, aromatic), 126.5 (CH, aromatic), 126.0 (CH, aromatic), 125.9 (CH, aromatic), 125.8 (CH, aromatic), 125.1 (CH, aromatic), 124.0 (CH, aromatic), 122.6 (CH, aromatic), 122.0 (CH, aromatic), 121.0 (CH, aromatic), 118.9 (CH, C-4′ of **24a**), 118.8 (CH, C-4′ of **24b**), 114.2 (CH, aromatic), 97.0 (CH, C-1), 76.6 (CH, C-5), 70.3 (CH_2, C-6), 69.9 (CH, C-2), 65.5 (CH_2, C-7), 50.6 (CH, C-4a), 49.7 (C, C-3a), 47.4 (CH, C-4), 38.8 (CH, C-2′ of **24b**), 38.6 (CH, C-2′ of **24a**), 36.4 (CH, C-3), 28.9 (CH_2, C-6′), 26.8 (CH_2, C-3′), 25.4 (CH_2, C-7′), 23.3 (CH_3, C-8′).

*4.4.7. Adducts **27a** and **27b***

Colorless oil; IR (film) 3072, 3021, 2923, 1728 (C=O), 1458, 1386, 1316, 1220, 1147, 1114, 1006, 749 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.43–7.34 (m, 2H, aromatic), 7.23–7.05 (m, 6H, aromatic), 5.05 (d, J_{1-2}=3.1 Hz, 1H, H-1), 4.62 (d, J_{5-6exo}=4.3 Hz, 1H, H-5), 4.31–4.15 (m, 4H, H-2, H-4a and H-7), 3.71 (dd, J_{gem}=7.0 Hz, J_{5-6exo}=4.3 Hz, 1H, H-6*exo*), 3.66 (dd, J_{gem}=7.0 Hz, $J_{5-6endo}$=0.9 Hz, 1H, H-6*endo*), 3.57 (s, 3H, H-8), 2.65–2.55 (m, 1H, H-2′), 2.48 (dd, J_{3-4}=10.3 Hz, J_{2-3}=6.0 Hz, 1H, H-3), 2.35–2.00 (m, 6H, H-4, H-3′, H-6′ and H-7′a), 1.73–1.61 (m, 7H, H-7′b, H-8′ and H-9′); ^{13}C NMR ($CDCl_3$) δ 175.1 (C, C-1′), 145.8 (C, aromatic), 141.0 (C, aromatic), 140.8 (C, aromatic), 140.7 (C, aromatic), 126.2 (CH, aromatic), 125.9 (CH, aromatic), 125.8 (CH, aromatic), 125.7 (CH, aromatic), 125.4 (C, C-5′ of **27a**)$^+$, 125.1 (C, C-5′ of **27b**)$^{++}$, 124.8 (CH, aromatic), 123.9 (CH, aromatic), 123.8 (C, C-4′ of **27b**)$^{++}$, 123.5 (C, C-4′ of **27a**)$^+$, 123.1 (CH, aromatic), 121.9 (CH, aromatic), 96.9 (CH, C-1), 76.5 (CH, C-5), 71.2 (CH_2, C-7), 70.2 (CH_2, C-6), 70.1 (CH, C-2), 59.1 (CH_3, C-8), 50.6 (CH, C-4a), 50.1 (C, C-3a), 47.5 (CH, C-4), 40.2 (CH, C-2′ of **27b**), 40.1 (CH, C-2′ of **27a**), 37.0 (CH, C-3), 33.6 (CH_2, C-3′ of **27b**)*, 33.4 (CH_2, C-3′ of **27a**)**, 31.0 (CH_2, C-6′ of **27b**)*, 30.8 (CH_2, C-6′ of **27a**)**, 25.8 (CH_2, C-7′ of **27a**), 25.6 (CH_2, C-7′ of **27b**), 18.9 (CH_3, C-8′)***, 18.7 (CH_3, C-9′)*** ($^+$,* interchangeable signals).

*4.4.8. Adducts **28a** and **28b***

Colorless oil; IR (film) 3071, 3023, 2925, 1726 (C=O), 1600, 1499, 1476, 1243, 1147, 1012, 753 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.42–6.97 (m, 13H, aromatic), 5.02–4.97 (m, 2H, H-1 and H-7), 4.74–4.68 (m, 2H, H-5 and H-7), 4.37 (dd, J_{2-3}=6.0 Hz, J_{1-2}=3.4 Hz, 1H, H-2), 4.22 (s, 1H, H-4a), 3.77–3.72 (m, 2H, H-6), 2.84 (br s, 1H, H-3), 2.26 (d, J_{3-4}=10.5 Hz, 1H, H-4), 2.03–1.26 (m, 13H, H-2′, H-3′, H-6′, H-7′, H-8′ and H-9′); ^{13}C NMR ($CDCl_3$) δ 175.4 (C, C-1′), 158.4 (C, aromatic), 145.9 (C, aromatic), 141.1 (C, aromatic), 140.6 (C, aromatic), 140.5 (C, aromatic), 129.5 (CH, 2C, aromatic), 126.4 (CH, aromatic), 126.0 (CH, aromatic), 125.9 (CH, aromatic), 125.8 (CH, aromatic), 125.0 (CH, aromatic), 125.0 (C, C-5′ of **28a**)$^+$, 124.6 (C, C-5′ of **28b**)$^+$, 124.0 (CH, aromatic), 123.4 (C, C-4′)$^+$, 122.6 (CH, aromatic), 122.0 (CH, aromatic), 121.0 (CH, aromatic), 114.3 (CH, 2C, aromatic), 97.0 (CH, C-1), 76.6 (CH, C-5), 70.3 (CH_2, C-6), 69.8 (CH, C-2), 65.5 (CH_2, C-7), 50.6 (CH, C-4a), 49.7 (C, C-3a), 47.4 (CH, C-4), 39.9 (CH, C-2′ of **28b**), 39.7 (CH, C-2′ of **28a**), 36.4 (CH, C-3), 33.8 (CH_2, C-3′ of **28b**)*, 32.8 (CH_2, C-3′ of **28a**)**, 30.6 (CH_2, C-6′ of **28a**)*, 29.5 (CH_2, C-6′ of **28b**)**, 25.9 (CH_2, C-7′ of **28a**), 24.9 (CH_2, C-7′ of **28b**), 18.6 (CH_3, C-8′ and C-9′) ($^+$,* interchangeable signals).

4.5. Hydrolysis of Diels–Alder adducts

Each adduct **11**–**30** was dissolved in THF/H_2O 2:1 and LiOH·H_2O (6 equiv) was added. The reaction was stirred at room temperature until no starting material was detected by TLC. The solution was neutralized with HCl 0.1 N to reach pH=4 and extracted with ether (5×40 mL). The combined organic extracts were dried (Na_2SO_4) and the solvent was evaporated. The resulting residue was purified by flash chromatography to obtain the chiral auxiliary **6** (>95%) and the corresponding carboxylic acid **31**–**35** (80–90%).

Acknowledgements

This research was supported by grants from Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Agencia Nacional de Promoción Científica y Tecnológica (ANPCyT), The International Foundation for Science (IFS) and the Organization for the Prohibition of Chemical Weapons (OPCW), The Netherlands to A.G.S. and R.A.S. A.M.S. thanks CONICET and Fundación Josefina Prats for the award of a fellowship. We also thank Dr. Alejandra Rodríguez, Uruguay for the HRMS.

Supplementary data

Experimental procedures for the synthesis of all compounds, characterization data, and copies of ^{1}H NMR and ^{13}C NMR spectra of new compounds. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2009.02.020.

References and notes

1. Lin, G. Q.; Li, Y. M.; Chan, A. S. C. *Principles and Applications of Asymmetric Synthesis*; John Wiley and Sons: New York, NY, 2001.
2. *Levoglucosenone and Levoglucosans: Chemistry and Applications*; Witczak, Z. J., Ed.; ATL: Mount Prospect, IL, 1994.
3. *Carbohydrate Synthons in Natural Products Chemistry. Synthesis, Functionalization, and Applications*; Witczak, Z. J., Tatsuta, K., Eds. ACS Symposium Series; American Chemical Society: Washington, DC, 2003.
4. Swenton, J. S.; Freskos, J. N.; Dalidowicz, P.; Kerns, M. L. *J. Org. Chem.* **1996**, *61*, 459.
5. Sarotti, A. M.; Spanevello, R. A.; Suárez, A. G. *Green Chem.* **2007**, *9*, 1137.
6. (a) Sarotti, A. M.; Spanevello, R. A.; Duhayon, C.; Tuchagues, J. P.; Suárez, A. G. *Tetrahedron* **2007**, *63*, 241; (b) Sarotti, A. M.; Spanevello, R. A.; Suárez, A. G. *Tetrahedron Lett.* **2005**, *46*, 6987; (c) Sarotti, A. M.; Spanevello, R. A.; Suárez, A. G. *Tetrahedron Lett.* **2004**, *45*, 8203.
7. Sarotti, A. M.; Spanevello, R. A.; Suárez, A. G. *Org. Lett.* **2006**, *8*, 1487.
8. Sarotti, A. M.; Fernández, I.; Spanevello, R. A.; Sierra, M. A.; Suárez, A. G. *Org. Lett.* **2008**, *10*, 3389.
9. Kagan, H. B.; Riant, O. *Chem. Rev.* **1992**, *92*, 1007.
10. (a) Tanaka, K.; Uno, H.; Osuga, H.; Suzuki, H. *Tetrahedron: Asymmetry* **1993**, *4*, 629; (b) Oppolzer, W. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 876.
11. Evans, D. A.; Chapman, K. T.; Bisaha, J. *J. Am. Chem. Soc.* **1988**, *110*, 1238.
12. See Supplementary data.
13. Fringuelli, F.; Taticchi, A. *The Diels-Alder Reaction. Selected Practical Methods*; John Wiley & Sons: New York, NY, 2002; Chapter 1.
14. After an extensive screening of Lewis acids (Et_2AlCl, $EtAlCl_2$, $TiCl_4$, $AlCl_3$) the former two were selected based on the yields and selectivities achieved. See Supplementary data.
15. Evans, D. A.; Barnes, D. M.; Johnson, J. S.; Lectka, T.; von Matt, P.; Miller, S. J.; Murry, J. A.; Norcross, R. D.; Shaughnessy, E. A.; Campos, K. R. *J. Am. Chem. Soc.* **1999**, *121*, 7582.
16. Shambayati, S.; Schreiber, S. L. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 1, Chapter 1.10.
17. (a) Cipiciani, A.; Fringuelli, F.; Piermatti, O.; Pizzo, F.; Ruzziconi, R. *J. Org. Chem.* **2002**, *67*, 2665; (b) Ferreira, M. L. G.; Pinheiro, S.; Perrone, C. C.; Costa, P. R. R.; Ferreira, V. F. *Tetrahedron: Asymmetry* **1998**, *9*, 2671; (c) Shida, N.; Kabuto, C.; Niwa, T.; Ebata, T.; Yamamoto, Y. *J. Org. Chem.* **1994**, *59*, 4068; (d) Gras, J. L.; Poncet, A.; Nouguier, R. *Tetrahedron Lett.* **1992**, *33*, 3323.
18. Absolute stereochemistry of **31**–**35** were assigned by comparing the sign of the specific rotations to that reported in the literature: Chang, H.; Zhou, L.; McCargar, R. D.; Mahmud, T.; Hirst, I. *Org. Process Res. Dev.* **1999**, *3*, 289 (for **31**); Hansen, M. M.; Bertsch, C. F.; Harkness, A. R.; Huff, B. E.; Hutchison, D. R.; Khau, V. V.; LeTourneau, M. E.; Martinelli, M. J.; Misner, J. W.; Peterson, B. C.; Rieck, J. A.; Syllivan, K. A.; Wright, I. G. *J. Org. Chem.* **1998**, *63*, 775 (for **32**); Davies, I. W.; Senanayake, C. H.; Castonguay, L.; Larsen, R. D.; Verhoeven, T. R.; Reider, P. J. *Tetrahedron Lett.* **1995**, *36*, 7619 (for **33**); Poll, T.; Sobczak, A.; Hartmann, H.; Helmchen, G. *Tetrahedron Lett.* **1985**, *26*, 3095 (for **34**); Akkari, R.; Calmès, M.; Escale, F.; Iapichella, J.; Rolland, M.; Martínez, J. *Tetrahedron: Asymmetry* **2004**, *15*, 2515 (for **35**).