Tetrahedron 67 (2011) 179–192

Contents lists available at ScienceDirect

Tetrahedron

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

Tandem Wittig–intramolecular Diels–Alder cycloaddition of ester-tethered 1,3,9-decatrienes under microwave heating

Jinlong Wu [a], Xiuqing Jiang [a], Jingjing Xu [a], Wei-Min Dai [a,b,*]

[a] Laboratory of Asymmetric Catalysis and Synthesis, Department of Chemistry, Zhejiang University, Hangzhou 310027, China
[b] Department of Chemistry, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong SAR, China

ARTICLE INFO

Article history:
Received 20 August 2010
Received in revised form 22 October 2010
Accepted 29 October 2010
Available online 5 November 2010

Keywords:
1,3,9-Decatriene
Intramolecular Diels–Alder cycloaddition
Microwave
1-Oxo-3,4,4a,7,8,8a-hexahydro-1*H*-isochromene
Wittig olefination

ABSTRACT

Intramolecular Diels–Alder (IMDA) cycloaddition of the ester-tethered 1,3,9,-decatrienes possessing a carbonyl substituent at C10 has been investigated under controlled microwave heating (MeCN, 180 °C) to afford a variety of 3,4,4a,7,8,8a-hexahydroisochromen-1-ones in 53–89% yields and in 64:36–79:21 ratios for the cis and trans isomers. Under the same microwave heating conditions, a tandem Wittig–IMDA cycloaddition, starting from the α-bromoacetates of 3,5-hexadien-1-ols and glyoxalate/phenylglyoxal hydrates in the presence of PPh_3 and 2,6-lutidine, has been demonstrated, furnishing 3,4,4a,7,8,8a-hexahydroisochromen-1-one adducts in 73–91% yields in favor of the cis isomers. During this tandem process, three consecutive carbon–carbon bonds in the end products were efficiently formed with the aid of microwave irradiation within short reaction times.

1. Introduction

Intramolecular Diels–Alder (IMDA) cycloaddition is a versatile synthetic tool for enabling formation of polycyclic skeletons of structural complexity and has been widely used in total synthesis of natural products.[1] For example, IMDA cycloaddition of the ester-tethered 1,3,9-decartrienes **4a**,**b** have been studied under thermal,[2,3] Lewis acid catalysis, and non-conventional conditions[4] to afford the bicyclic lactones, such as **7** from **4b** (Fig. 1). This type of IMDA cycloaddition has been applied in total synthesis of alkaloids, such as lycorine[2c] and stenine,[3c,4b] and eleuthesides.[2d–f,3d] It has been established that cycloaddition of the trienes **4a** normally take place at higher temperatures (200–250 °C)[2] than the trienes **4b** possessing a C10-activating group. The latter undergo cycloaddition at 100–150 °C[3] or even at room temperature.[3d] The *cis*-fused bicyclic lactones are preferably formed under thermal conditions[5] but improved diastereoselectivity can be achieved under Lewis acid catalysis[4] or using ionic liquids as the reaction media,[4h] giving a single adduct in most cases. A boatlike-*cis* (*-endo*) transition state[5a] is energetically favored to form the *cis* adduct while the diastereoselectivity can be enhanced by incorporating a bulky R^4 substituent at C6 of **4**.[3d] We have reported

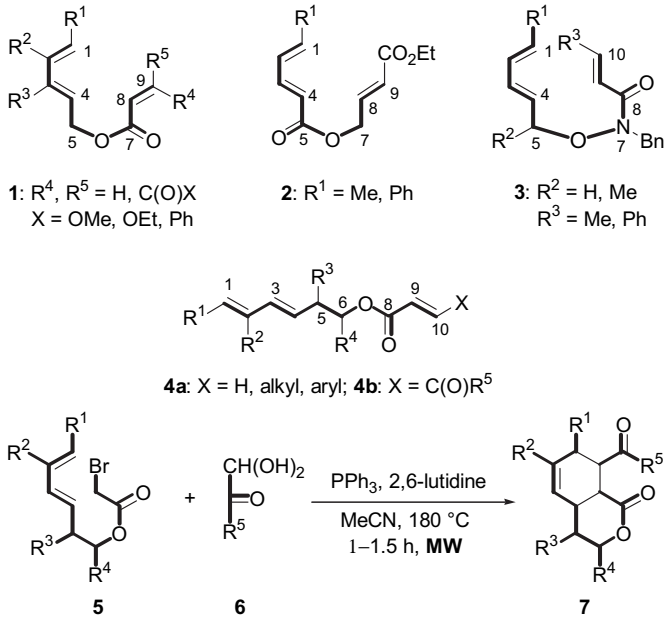


Fig. 1. Structures of the tethered 1,3,8-nonatrienes (**1** and **2**) and 1,3,9-decatrienes (**3** and **4**) and the tandem Wittig–IMDA cycloaddition for formation of 3,4,4a,7,8,8a-hexahydroisochromen-1-ones **7**.

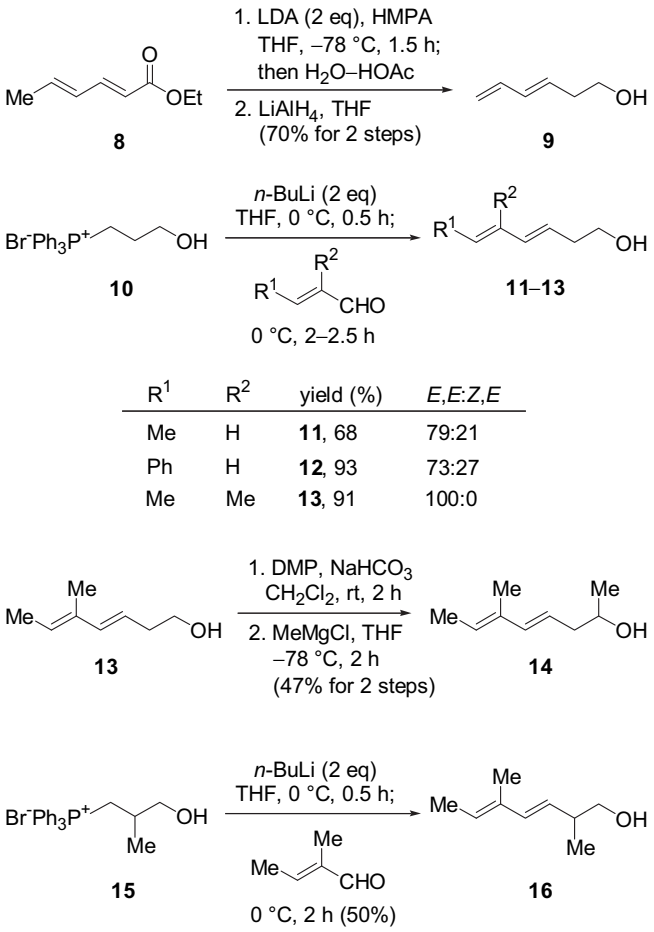
* Corresponding author. Tel./fax: +86 571 87953128; e-mail addresses: chdai@zju.edu.cn, chdai@ust.hk (W.-M. Dai).

0040-4020/$ – see front matter © 2010 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2010.10.088

IMDA cycloadditions of the ester-tethered 1,3,8-nonatrienes **1**[6a] and **2**[6b] and the hydroxamate-tethered 1,3,9-decatrienes **3**[6c] under controlled microwave heating. A tandem Wittig–IMDA cycloaddition of the trienes **1** has been developed. As a continuation of our studies on the tandem reaction protocol, we report here on microwave-assisted IMDA cycloaddition of the C10-activated trienes **4b** and one-pot synthesis of the bicyclic lactones **7** starting from 3,5-hexadien-1-yl α-bromoacetates **5** and glyoxalate or phenylglyoxal hydrates **6** (Fig. 1).

2. Results and discussion

We prepared (*E*)-3,5-hexadien-1-ol (**9**) from ethyl sorbate (**8**) according to the literature procedure (Scheme 1).[4i,7] Treatment of **8** with LDA/HMPA followed by aqueous quenching gave the corresponding deconjugate diene ester, which was then reduced by $LiAlH_4$ to furnish **9** in 70% overall yield. The diene alcohols **11**–**13** were synthesized in 68–91% yields by the Wittig olefination using 3-hydroxypropyltriphenylphosphonium bromide (**10**).[8] An inseparable mixture of (3*E*,5*E*)- and (3*Z*,5*E*)-isomers was obtained for **11** and **12**,[9] while **13**[10] was formed as a single (3*E*,5*E*)-isomer. Oxidation of **13** by Dess–Martin periodinane (DMP) followed by reaction of the aldehyde with MeMgCl afforded the racemic alcohol **14** in 47% overall yield (not optimized). Finally, the racemic alcohol **16** was synthesized in 50% yield from 3-hydroxy-2-methylpropyltriphenylphosphonium bromide (**15**) in a similar manner as described above for **10**.



R^1	R^2	yield (%)	*E*,*E*:*Z*,*E*
Me	H	**11**, 68	79:21
Ph	H	**12**, 93	73:27
Me	Me	**13**, 91	100:0

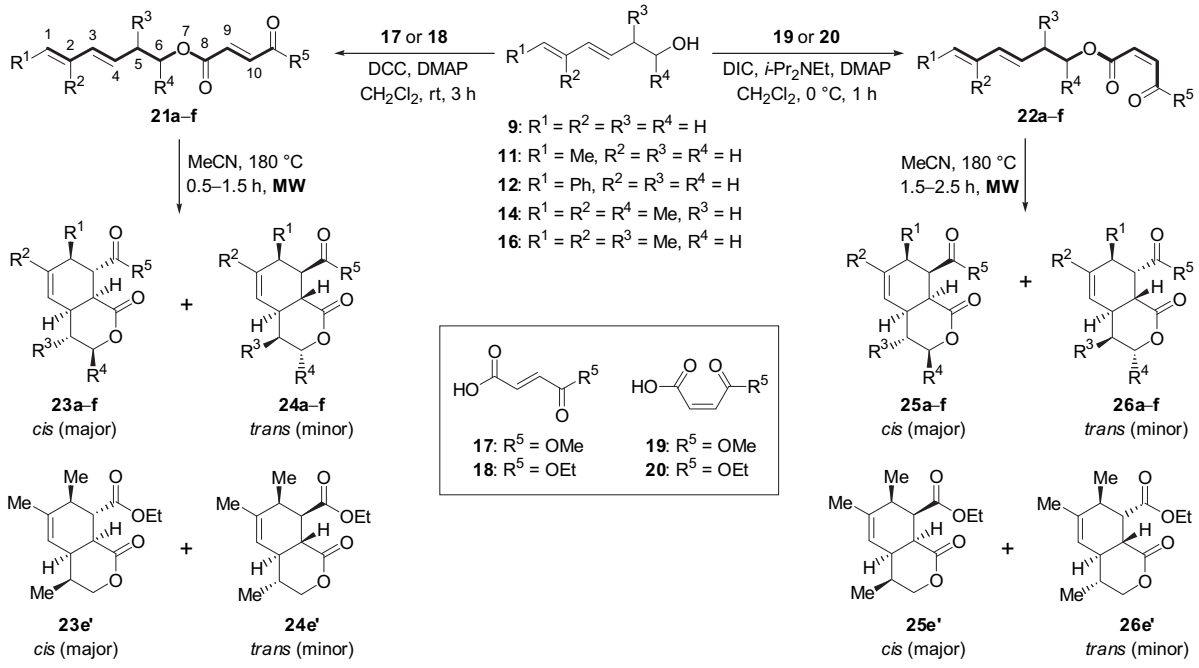
Scheme 1. Synthesis of the diene alcohols **9**, **11**–**14**, and **16**.

2.1. Microwave-assisted IMDA cycloadditions of ester-tethered 1,3,9-decatrienes

Fumaric and maleic acid monomethyl/monoethyl esters **17**/**18**[11] and **19**/**20**[12] were used to synthesize the ester-tethered 1,3,9-decatrienes possessing an ester activating group at C10 (Scheme 2). The *E*-substituted diesters **21a**–**f** were obtained in 79–93% yields by condensation of **17**/**18** with the diene alcohols **9**, **11**, **12**, **14**, and **16** in the presence of DCC–DMAP in CH_2Cl_2 at room temperature for 3 h (entries 1–6, Table 1). Similarly, the *Z*-substituted diesters **22a**–**f** were obtained in 56–71% yields from **19**/**20** and the diene alcohols in the presence of DIC/*i*-Pr_2NEt/DMAP[6a,13] in CH_2Cl_2 at 0 °C for 1 h (entries 7–12, Table 1).[14] Among these diesters, thermal IMDA cycloaddition of (*E*)-**21a**,**b** and (*Z*)-**22a** have been reported (Scheme 2); the values of diastereomer ratio (dr) for **23a**/**24a** and **23b**/**24b** are 83:17 (110 °C in PhMe)[5c] and 86:14 (70 °C in an ionic liquid),[4h] respectively, while dr for **25a**/**26a** is 70:30 (132 °C in PhCl).[5c] A slightly lower dr (78:22) was reported for **23a**/**24a** in refluxing xylene (bp=ca. 140 °C).[3c] We heated the diester (*E*)-**21a** at 180 °C in MeCN with microwave irradiation in a closed pressurized vial to afford **23a**/**24a** in 80% combined yield and in 79:21 dr (entry 1, Table 1). Thus, we confirmed that the *cis*-fused bicyclic lactone **23a** is the major adduct within the reaction temperatures ranged from 110 to 180 °C albeit the diastereoselectivity decreased slightly with increased temperatures. This temperature effect on diastereoselectivity was also observed in the cycloaddition of (*E*)-**21b**. We recorded 77:23 dr for **23b**/**24b** at 180 °C (entry 2, Table 1) as compared to 86:14 dr reported at 70 °C in an ionic liquid.[4h] The improved diastereoselectivity might also be contributed by using the ionic liquid. In contrast, the IMDA cycloaddition of (*Z*)-**22a**,**b** seems insensitive to reaction temperature; we obtained 74:26–75:25 dr for the adducts **25a**/**26a** and **25b**/**26b** at 180 °C, respectively, while 70:30 dr was reported at 132 °C for **25a**/**26a**[5c] (entries 7 and 8, Table 1).

IMDA cycloaddition of (*E*)-**21c**,**d** and (*Z*)-**22c**,**d** was performed under the same microwave heating conditions (Scheme 2). We found that the (3*Z*,5*E*)-hexadien-1-yl isomers of (*E*)-**21c**,**d** and (*Z*)-**22c**,**d** could not undergo the cycloaddition, and thus, they were recovered after the reaction. Yields of the adducts were then calculated according to the ratios of (3*E*,5*E*)-hexadien-1-yl isomers in the mixed trienes (*E*)-**21c**,**d** and (*Z*)-**22c**,**d** (entries 3, 4, 9, and 10, Table 1). The diastereoselectivity for (*E*)-**21c**,**d** is 71:29–75:25, being similar to the value of 77:23 obtained for (*E*)-**21b** (entries 2–4, Table 1). It implies that the C1-substituent (R^1=H, Me, Ph) is not influential on IMDA cycloaddition of the (*E*)-series of diesters. However, lower dr (64:36) was observed for the C1–Ph-substituted (*Z*)-**22d**, which also gave poorer yield (53%) for **25d**/**26d** (entry 4, Table 1). The relative stereochemistry of the major adduct **23d** was determined by X-ray crystal structural analysis.[15] The structures of other adducts were assigned analogously.

Inoue and co-workers[3e] examined the thermal IMDA cycloaddition of the ester-tethered 1,3,9-decatrienes of the type **21** (R^3=H, R^4=Me, R^5=Me or OEt) at 100–135 °C. Only one pair of *cis*/*trans* adducts of the types **23** and **24** was formed with diastereoselectivity of 70:30–80:20. The results suggest that the cycloaddition occurs via two boatlike-*cis* (-*endo*) and boatlike-*trans* (-*exo*) transition states[5a] where R^4 (=Me) sits in an equatorial position (see **TS-I** and **TS-II** in Fig. 2). Kurth and co-workers demonstrated that the bulky C6–*t*-Bu substituent could serve as an excellent *endo* and *boat* director, furnishing a singlet adduct via **TS-I**.[3d] We carried out the thermal IMDA cycloaddition of (*E*)-**21f** and (*Z*)-**22f** and obtained only one pair of *cis*/*trans* adducts **23f**/**24f** and **25f**/**26f**, respectively (entries 6 and 12, Table 1). For the adducts **23f**/**24f** a comparable diastereoselectivity (dr=72:28) to the literature data was observed while formation of the adducts **25f**/**26f**



Scheme 2. Synthesis and microwave-assisted IMDA cycloaddition of ester-tethered 1,3,9-decatrienes **21a**–**f** and **22a**–**f**.

was less diastereoselective (dr=65:35) as compared to the cycloaddition of (*Z*)-**22c** possessing the same C1-substituent (R^1=Me) (entry 12 vs entry 9, Table 1).

Taguchi and co-workers[4d,e] reported IMDA cycloaddition of an ester-tethered 1,3,9-decatriene possessing a C5–Me substituent (R^3=Me, X=H) under thermal and Lewis acid catalysis conditions. Diastereoselectivity of 83:17–88:12 was observed for two *cis*-fused adducts formed via **TS-I** and **TS-I′**. Adducts via **TS-II** and **TS-II′** were not observed, being consistent with the selectivity order (*i*-Pr>H>CO_2Me/CO_2Et>COMe) for substituent X at C10.[3e] It is not surprising that four stereoisomers were detected in the crude cycloaddition mixtures of both (*E*)-**21e** and (*Z*)-**22e** (entries 5 and 11, Table 1). By referred to the above-mentioned results reported by Taguchi and co-workers,[4d,e] we tentatively assigned the two major adducts of (*E*)-**21e** as the *cis*-isomers **23e** and **23e′**, and the two minor adducts as the *trans*-isomers **24e** and **24e′**. All four adducts are formed via the boatlike transition states shown in Fig. 2 with **TS-I** and **TS-II** being favored over **TS-I′** and **TS-II′**, respectively. The estimated dr for the two *cis*-adducts **23e** and **23e′** is 77:23, which is close to that reported by Taguchi and co-workers for the C10-unactivated decatriene.[4d,e] Similarly, the four adducts from (*Z*)-**22e** are considered derived from the same types of

Table 1
Results of synthesis and microwave-assisted IMDA cycloaddition of ester-tethered 1,3,9-decatrienes **21a**–**f** and **22a**–**f**

Entry	R^1	R^2	R^3	R^4	R^5	Diesters	Yield (%)	Lactones	*t*[a] (h)	Yield[b] (%)	*cis*:*trans* ratio[c]
1	H	H	H	H	OMe	(*E*)-**21a**	79	**23a**+**24a**	1.5	80	79:21 (83:17)[d,e]
2	H	H	H	H	OEt	(*E*)-**21b**	83	**23b**+**24b**	0.5	80	77:23 (86:14)[f]
3	Me	H	H	H	OEt	(*E*)-**21c**	89[g]	**23c**+**24c**	1	82[h]	71:29
4	Ph	H	H	H	OEt	(*E*)-**21d**	92[g]	**23d**+**24d**	1	71[h]	75:25
5	Me	Me	Me	H	OEt	(*E*)-**21e**	93	**23e**+**24e**	1	87	86:14 (**23e′**:**24e′**=73:27)[i]
6	Me	Me	H	Me	OEt	(*E*)-**21f**	84	**23f**+**24f**	1	89	72:28
7	H	H	H	H	OMe	(*Z*)-**22a**	66	**25a**+**26a**	2.5	78	74:26 (70:30)[d]
8	H	H	H	H	OEt	(*Z*)-**22b**	62	**25b**+**26b**	1.5	76	75:25
9	Me	H	H	H	OEt	(*Z*)-**22c**	56[g]	**25c**+**26c**	2	80[h]	72:28
10	Ph	H	H	H	OEt	(*Z*)-**22d**	62[g]	**25d**+**26d**	2	53[h] (86)[i]	64:36 (62:38)[i]
11	Me	Me	Me	H	OEt	(*Z*)-**22e**	67	**25e**+**26e**	2	85	78:22 (**25e′**:**26e′**=77:23)[j]
12	Me	Me	H	Me	OEt	(*Z*)-**22f**	71	**25f**+**26f**	2	71	65:35

[a] IMDA cycloadditions were carried out in MeCN at 180 °C for the indicated time in a closed pressurized vial with temperature measured by an IR sensor.
[b] Combined yields of the isolated adducts.
[c] The ratio was determined by ^{1}H NMR spectrum of the crude product mixture.
[d] The numbers in the parentheses are taken from Ref. 5c. The IMDA cycloaddition was carried out in PhMe (110 °C, 22 h) and PhCl (132 °C, 72 h) for (*E*)-**21a** and (*Z*)-**22a**, respectively.
[e] The adducts **23a** and **24a** were obtained in 52% and 15% yields (dr=78:22) in refluxing xylene for 5 h as reported in Ref. 3c.
[f] The number in the parenthesis is taken from Ref. 4h. The adducts were obtained in 86% combined yield in [emim]BF_4 at 70 °C for 7 h.
[g] Obtained as an inseparable mixture of (3*E*,5*E*)- and (3*Z*,5*E*)-dien-1-yl esters.
[h] Calculated according to the (3*E*,5*E*)-dien-1-yl ester. The (3*Z*,5*E*)-dien-1-yl ester was recovered after the IMDA cycloaddition.
[i] The numbers in the parentheses are obtained for the IMDA reaction carried out at 200 °C for 2 h in MeCN using isomeric pure (*Z*)-**22d**. The latter was prepared from the isomeric pure **12** (see Ref. 9).
[j] Four inseparable diastereomers were found in the crude products due to the C5 stereogenic carbon attached with R^3 (=Me). The *cis*:*trans* ratios were tentatively assigned according to the isomer ratios (**23e**:**24e**:**23e′**:**24e′**=64:10:19:7 and **25e**:**25e**:**25e′**:**25e′**=54:15:24:7) measured by ^{1}H NMR spectra of the crude products.

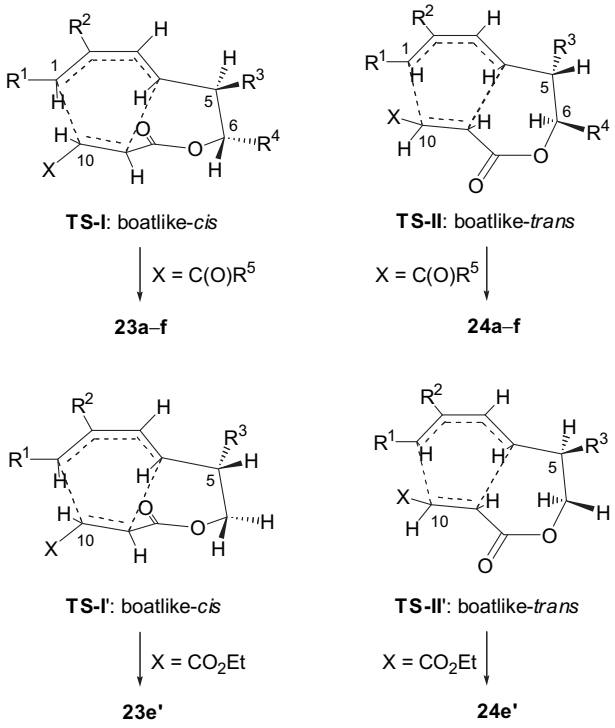
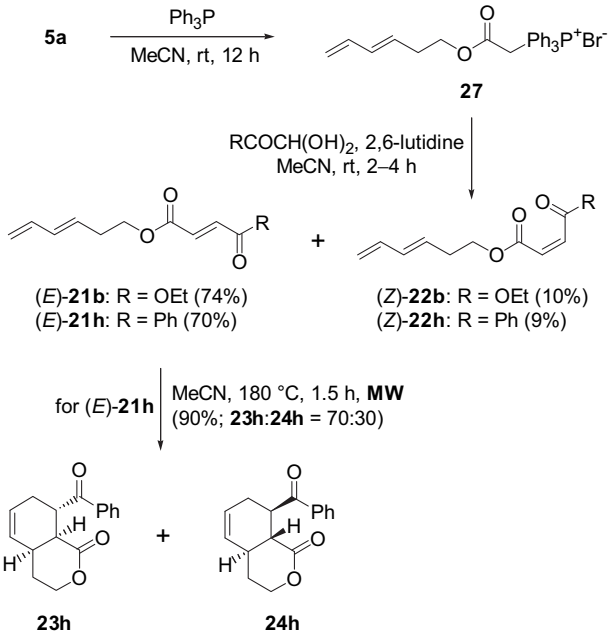


Fig. 2. Illustration of two favorable boatlike transition states for IMDA cycloaddition of (*E*)-**21a**–**f** with relative stereochemistry.



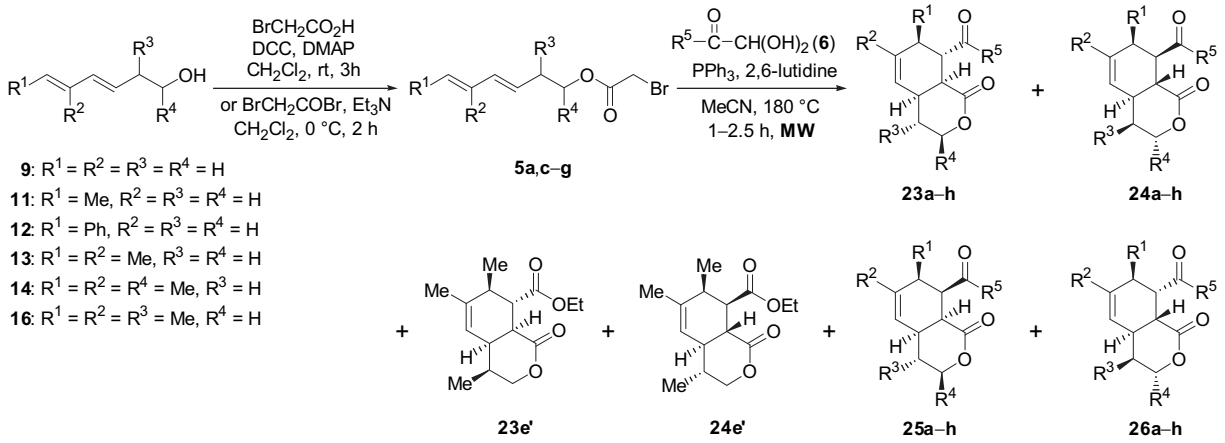
Scheme 3. Synthesis and IMDA cycloaddition of triene (*E*)-**21h**.

boatlike transition states shown in Fig. 2 but with altered positions for C10-H and C10-X. Therefore, our above described results have established that microwave heating at 180 °C in MeCN could facilitate IMDA cycloaddition of the ester-tethered 1,3,9-decatrienes possessing a C10-ester group. The reaction completes within 0.5–2.5 h to furnish the adducts in good yields in favor of the *cis*-fused adducts. Moreover, we have confirmed that a C6 alkyl substituent controls diastereoselectivity much efficiently than the same substituent at C5 of the ester-tethered 1,3,9-decatrienes.

2.2. Microwave-assisted tandem Wittig–IMDA cycloadditions of ester-tethered 1,3,9-decatrienes

Before investigating the tandem Wittig–IMDA protocol, stepwise formation and IMDA cycloaddition of the C10-activated trienes (*E*)-**21b**,**h** were first performed (Scheme 3). According to the similar procedure used in our previous study,[6a] α-bromoacetate **5a**, prepared from (*E*)-3,5-hexadien-1-ol (**9**) (see Scheme 4), was treated with PPh_3 in MeCN at room temperature for 12 h to give the corresponding phosphonium salt **27**. The latter was reacted with ethyl glyoxalate or phenylglyoxal hydrate in the presence of 2,6-lutidine as the base (MeCN, rt, 2–4 h) to afford the trienes (*E*)-**21b**,**h** and (*Z*)-**22b**,**h** in 70–74% and 9–10% overall yields for the two steps, respectively. The *E*/*Z* ratios are ca. 90:10 for both aldehydes. We found that (*E*)-**21h** underwent spontaneous IMDA cycloaddition at room temperature, being opposite to the related C9-keto-activated 1,3,8-nonatriene whose *Z*-isomer gave IMDA adducts at room temperature.[6a] Therefore, the freshly prepared (*E*)-**21h** was heated at 180 °C with microwave irradiation to give the adducts **23h** and **24h** in 90% combined yield and in 70:30 dr as checked by ^1H NMR analysis of the crude reaction mixture.

The requisite α-bromoacetates **5a**,**c**–**g** for studying the tandem protocol were prepared from the 3,5-hexadien-1-ols and bromoacetic acid (DCC/DMAP, rt) or bromoacetyl bromide (Et_3N, 0 °C) in 85–89% yields (Scheme 4 and Table 2). First, a mixture of **5a**, methyl or ethyl glyoxalate hydrate **6** (R^5=OMe or OEt),[16] PPh_3, and



Scheme 4. Synthesis and microwave-assisted tandem Wittig–IMDA cycloaddition of 3,5-hexadien-1-yl α-bromoacetates **5a**,**c**–**g**.

Table 2
Results of synthesis and microwave-assisted tandem Wittig–IMDA cycloaddition of 3,5-hexadien-1-yl α-bromoacetates **5a**,**c**–**g**

Entry	R^1	R^2	R^3	R^4	Acetates	Yield (%)	**6**: R^5	Lactones	t[a] (h)	Yield[b] (%)	dr[c]
1	H	H	H	H	**5a**	88	OMe	**23a**+**24a**+**25a**+**26a**	1.5	78	77:18:5:0
2	H	H	H	H	**5a**	—	OEt	**23b**+**24b**+**25b**+**26b**	1	84	72:24:4:0
3	Me	H	H	H	**5c**	86[d]	OEt	**23c**+**24c**+**25c**+**26c**	1	90[e]	51:34:8:7
4	Ph	H	H	H	**5d**	85[d]	OEt	**23d**+**24d**+**25d**+**26d**	1.5	85[e]	64:27:6:3
5	Me	Me	Me	H	**5e**	89	OEt	**23e**+**24e**+**23e′**+**24e′**+**25e**+**26e**	1	86[f]	53:11:18:10:5:3
6	Me	Me	H	Me	**5f**	87	OEt	**23f**+**24f**+**25f**+**26f**	1	73	63:31:4:0
7	Me	Me	H	H	**5g**	86	Ph	**23g**+**24g**+**25g**+**26g**	1	91	63:33:4:0
8	H	H	H	H	**5a**	—	Ph	**23h**+**24h**+**25h**+**26h**	1	77	65:32:3:0
9	Me	Me	H	H	**5g**	—	—[g]	**23i**+**24i**	2.5[h]	62 (58)[i]	88:12 (93:7)[i]

[a] All tandem Wittig–IMDA cycloadditions were carried out in MeCN at 180 °C for the indicated time in a closed pressurized vial with temperature measured by an IR sensor.
[b] Combined yield of the isolated adducts.
[c] The diastereomer ratio (dr) was calculated according to the isolated adducts. For entry 5, dr was estimated by ^{1}H NMR spectrum of the mixed products.
[d] Obtained as an inseparable mixture of (3*E*,5*E*)- and (3*Z*,5*E*)-dien-1-yl α-bromoacetates.
[e] Calculated according to the (3*E*,5*E*)-dien-1-yl α-bromoacetate.
[f] Combined yield of all adducts as an inseparable mixture.
[g] Aqueous formaldehyde (37 wt %, 3 equiv) was used instead of **6**.
[h] The tandem reaction was performed at 160 °C instead of 180 °C.
[i] The numbers in the parentheses are for the reaction using 37 wt % aqueous formaldehyde (8 equiv) carried out at 110 °C (oil bath) in MeCN for 36 h.

2,6-lutidine in MeCN was heated at 180 °C in a closed pressurized process vial with microwave irradiation for 1–1.5 h. In both cases, three adducts were identified among four possible diastereomers and the two major adducts were formed via (*E*)-**21a** and (*E*)-**21b**, respectively (entries 1 and 2, Table 2). The adducts **23a**,**b**, **24a**,**b**, and **25a**,**b** were isolated in the combined yields of 78–84% and their structures were confirmed by comparison with the authentic samples synthesized from the pre-isolated trienes (Scheme 2). These results confirmed that the Wittig olefination at 180 °C gave ca. 90% *E*-isomers of the trienes. Moreover, the *cis*/*trans* ratios of the ester adducts **23a**/**24a** (81:19) and **23b**/**24b** (75:25) for the tandem protocol are almost the same as those observed for the IMDA cycloaddition of the pre-isolated trienes (*E*)-**21a** and (*E*)-**21b** (entries 1 and 2 in Tables 1 and 2).

The tandem Wittig–IMDA cycloaddition using C6-Me- and C6-Ph-substituted 3,5-hexadien-1-yl α-bromoacetates **5c**,**d** and ethyl glyoxalate hydrate **6** (R^5=OEt) was carried out in a similar fashion as described above (Scheme 4). Four diastereomers **23c**,**d**, **24c**,**d**, **25c**,**d**, and **26c**,**d** were formed. The ratios of **23c**/**24c** (60:40) and **23d**/**24d** (70:30) are somewhat lower for the tandem protocol (entries 3 and 4, Table 2 vs entries 3 and 4, Table 1). In both cases, the trienes derived from the (3*Z*,5*E*)-hexadien-1-yl α-bromoacetates were recovered at the end of the reaction and the isolated yields were calculated according to the (3*E*,5*E*)-hexadien-1-yl α-bromoacetates **5c**,**d**.

The results of tandem Wittig–IMDA cycloaddition starting with **5e**,**f** are summarized in entries 5 and 6 of Table 2. Since four diastereomers were observed for the IMDA cycloaddition of both (*E*)-**21e** and (*Z*)-**22e** (entries 5 and 11, Table 1), it was expected that a maximum of eight adducts could be formed. In fact, all four adducts **23e**, **24e**, **23e′**, and **24e′** from (*E*)-**21e**, and two major adducts **25e** and **26e** from (*Z*)-**22e** were isolated as an inseparable mixture in 86% yield. In contrast, the tandem Wittig–IMDA cycloaddition of **5f** was much more selective, providing three adducts **23f**, **24f**, and **25f** in 73% combined yield (entry 6, Table 2). The results are in agreement with those for IMDA cycloaddition of (*E*)-**21f** and (*Z*)-**22f** (entries 6 and 12, Table 1). Similar dr was noted for **23e**/**24e** (83:17) and **23f**/**24f** (67:33) via the tandem protocol (entries 5 and 6, Table 2).

The stepwise reactions starting from the α-bromoacetate **5a** as described in Scheme 3 above were now carried out in one-pot fashion under microwave heating at 180 °C (entry 8, Table 2). Three out of the four adducts expected for the trienes (*E*)-**21h** and (*Z*)-**22h** were isolated in 77% combined yield. The dr (**23h**/**24h**=67:33) is close to the ratio of 70:30 recorded for the pre-isolated (*E*)-**21h** (Scheme 3). Similar results were obtained for the tandem reaction of the α-bromoacetate **5g** and three adducts **23g**, **24g**, and **25g** were isolated in 91% combined yield (entry 7, Table 2). Moreover, the relative stereochemistry of the *trans* adduct **24g** was confirmed by X-ray crystallographic analysis as depicted in Fig. 3.[17]

The C10-unactivated 1,3,9-decatriene **21i** (Scheme 5), prepared from the alcohol **13** and acrylic acid, underwent IMDA cycloaddition at 160 °C for 3 h in MeCN with microwave irradiation, furnishing the *cis* and *trans* adducts **23i** and **24i** in 65% and 5% yields, respectively, with 92:8 dr for **23i**/**24i**. The results are consistent with IMDA cycloaddition of the parent triene **21j** carried out in PhCl (132 °C) for 47 h to afford the corresponding *cis* and *trans* adducts **23j** and **24j** in 70% combined yield and with **23j**/**24j** ratio of 92:8.[5c,18] We then investigated the tandem reaction of the α-bromoacetate **5g** with 37 wt % aqueous formaldehyde in the presence of 2,6-lutidine in MeCN at 110 °C (oil bath) for 36 h or at 160 °C for 2.5 h with microwave irradiation. In both cases, the adducts **23i** and **24i** were isolated in 58–62% combined yields and with dr of 88:12–93:7 (entry 9, Table 2). Better dr was observed for the cycloaddition at lower temperature. It should be mentioned that the *cis* adduct **23i** was reported as an intermediate in the synthesis

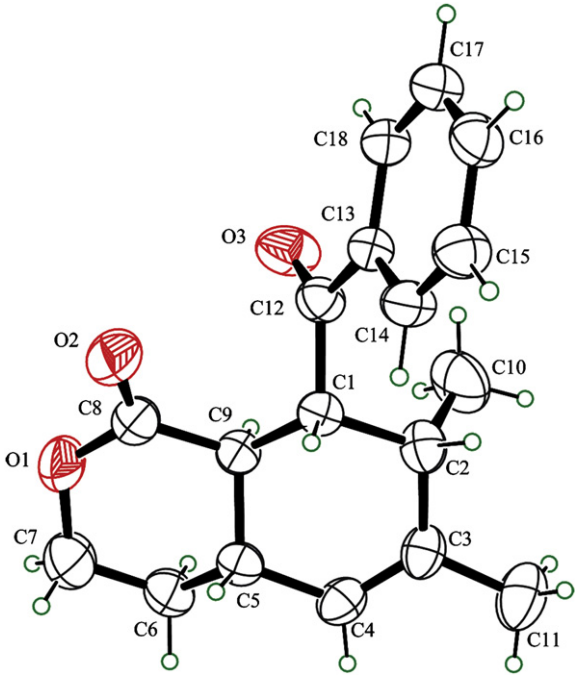
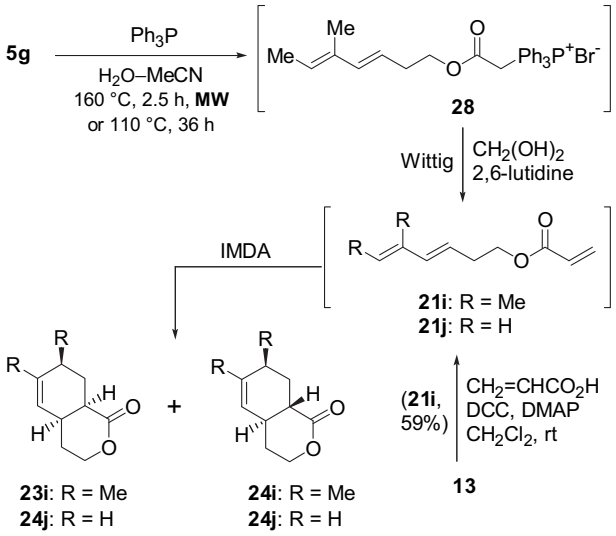


Fig. 3. X-ray crystal structure of the minor adduct **24g**.



Scheme 5. One-pot synthesis of **23i** and **24i** from **5g** and formaldehyde.

of the oxaspirobicyclic tetronic acid unit related to tetronothiodin, a CCK-B receptor antagonist.[10]

3. Conclusion

In summary, we have examined the intramolecular Diels–Alder (IMDA) cycloaddition of a series of ester-tethered 1,3,9-decatrienes in MeCN at 160–180 °C under controlled microwave heating. Stereoselectivity has been found to be similar to that reported for the thermal reactions carried out at lower temperatures. In general, the trienes **4** (Fig. 1) give slightly higher dr than the corresponding (9*Z*)-isomers in favor of the *cis*-adducts.[5c] Influence of the substituents on stereoselectivity varies: (a) dr increases for R^1 at C1 in the order of Me (71:29)<Ph (75:25)<H (77:23); (b) R^4 at C6 controls stereoselectivity better than R^3 at C5; and (c) dr increases for X at C10 in the order of COPh (70:30)≈CO_2Me/CO_2Et (71:29–77:23)<<H (92:8, at 160 °C). Moreover, we have established a microwave-assisted tandem Wittig–IMDA cycloaddition protocol.[6a] Starting from 3,5-hexadien-1-yl α-bromoacetates **5**, hydrated glyoxalate, phenylglyoxal, or formaldehyde, PPh_3, and 2,6-lutidine, 3,4,4a,7,8,8a-hexahydroisochromen-1-ones are prepared in 62–91% yields by heating in MeCN at 160–180 °C for 1–2.5 h with microwave irradiation. The main pair of *cis*/*trans* adducts are derived from the trienes **4** formed in situ in the tandem process. Three consecutive carbon–carbon bonds with up to four new stereogenic centers are installed onto the end products, demonstrating the high efficiency of the microwave-assisted synthesis.

4. Experimental

4.1. General methods

^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ or DMSO-d_6 (400, or 500 MHz for ^1H and 100 or 125 MHz for ^{13}C, respectively). IR spectra were taken on an FT-IR spectrophotometer. Mass spectra (MS) were measured by the ESI^+ or EI^+ method. Melting points are uncorrected. Silica gel plates pre-coated on glass were used for thin-layer chromatography using UV light, or 7% ethanolic phosphomolybdic acid and heating as the visualizing methods. Silica gel was used for flash column chromatography. Yields refer to chromatographically and spectroscopically (^1H NMR) homogeneous materials. Petroleum ether (PE) of 60–90 °C fraction was used in this work. Fumaric acid monoethyl ester **18**, phenylglyoxal hydrate **6** (R^3=Ph), and other reagents were obtained commercially and used as received. Fumaric acid monomethyl ester **17**,[11] maleic acid monomethyl ester **19**[12] and monoethyl ester **20**,[12] methyl glyoxalate hydrate **6** (R^3=OMe),[16] and ethyl glyoxalate hydrate **6** (R^3=OEt)[16] were prepared according to the reported procedures. The microwave-assisted reactions summarized in Tables 1 and 2, and Schemes 3 and 5 were carried out on an Emrys creator (single-mode microwave reactor) from Personal Chemistry AB (now under Biotage AB, Uppsala, Sweden) with temperature measured by an external IR sensor. The microwave-assisted reaction time is the hold time at the final temperature.

4.2. (*E*)-Hexa-3,5-dien-1-ol (9)[4i,7]

To a solution of diisopropyl amine (3.5 mL, 25.0 mmol) in dry THF (12 mL) cooled at −10 °C under a nitrogen atmosphere was added a solution of *n*-BuLi (10 mL, 2.5 M in hexanes, 25.0 mmol) followed by stirring for 30 min at the same temperature. The resultant LDA solution was then cooled to −78 °C, and, after adding HMPA (4 mL), was stirred for another 20 min at −78 °C.

To the above prepared LDA–HMPA solution was added a solution of ethyl sorbate (**8**, 1.50 mL, 10.0 mmol) in dry THF (5 mL). After stirring at −78 °C for 1.5 h, the reaction was quenched by adding a mixed solution of water (22 mL) and acetic acid (4 mL). The reaction mixture was extracted with hexane (30 mL×3) and the combined organic layer was washed with saturated aqueous $NaHCO_3$ and brine, dried over anhydrous Na_2SO_4, filtered off, and concentrated under reduced pressure to give the crude deconjugate ester, which was used for next reaction without purification.

To a suspension of $LiAlH_4$ (532.0 mg, 14 mmol) in dry THF (30 mL) cooled in an ice–water bath under a nitrogen atmosphere was added a solution of the above crude deconjugate ester in dry THF (5 mL). The resultant mixture was then stirred at room temperature for overnight (12 h). The reaction mixture was cooled in an ice–water bath and the reaction was quenched by carefully adding small amount of water. A saturated aqueous solution of potassium sodium tartrate was added to the above mixture followed by stirring at room temperature till the mixture became clear. The mixture was extracted with EtOAc (30 mL×3) and the combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, filtered off, and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, eluted with 20% EtOAc in PE) to give the alcohol **9** (686.0 mg, 70% for the two steps) as a colorless oil;[4i,7] R_f=0.39 (25% EtOAc in hexane); IR (film) 3345, 2919, 2865, 1648, 1603, 1050 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.33 (ddd, *J*=16.8, 10.4, 10.4 Hz, 1H), 6.16 (dd, *J*=15.2, 10.4 Hz, 1H), 5.68 (dt, *J*=15.2, 7.2 Hz, 1H), 5.14 (d, *J*=16.8 Hz, 1H), 5.02 (d, *J*=10.0 Hz, 1H), 3.69 (t, *J*=6.4 Hz, 2H), 2.36 (dt, *J*=6.4, 6.4 Hz, 2H), 1.50 (br s, 1H, O*H*); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.8, 133.7, 130.6, 115.9, 61.9, 35.9; MS (EI^+) *m*/*z* 98 (M^+, 20), 97 (M^+−H, 36), 71 (56), 59 (100).

4.3. General procedure A for synthesis of 3,5-hexadien-1-ols 11–13 via Wittig reaction of 10

To a suspension of (3-hydroxypropyl)triphenylphosphonium bromide (**10**)[8] (4.010 g, 10.0 mmol) in dry THF (25 mL) cooled in an ice–water bath (ca. 0 °C) was added a solution of *n*-BuLi (8.0 mL, 2.5 M in hexanes, 20.0 mmol) followed by stirring for 0.5 h at the same temperature. To the resultant mixture was added the aldehyde (12.0 mmol) in dry THF (5 mL) and the mixture was stirred for another 2–2.5 h at 0 °C. The reaction was quenched by adding saturated aqueous ammonium chloride. The aqueous layer was extracted with Et_2O (10 mL×2) and the combined organic layer was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. The residue was purified by flash column

chromatography (silica gel, eluted with 20% EtOAc in PE) to give the 3,5-hexadien-1-ols **11**–**13** in 68–91% yields (see Scheme 1).

*4.3.1. (3E,5E)-Hepta-3,5-dien-1-ol (**11**).* Prepared according to the general procedure A in 68% yield as a yellow oil; an inseparable mixture of two geometrical isomers [(3*E*,5*E*)/(3*Z*,5*E*)=79:21]; R_f=0.39 (20% EtOAc in hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.35 (dd, *J*=13.6, 12.4 Hz, 0.21H), 6.14–5.99 (m, 1.79H), 5.73 (dq, *J*=14.8, 6.8 Hz, 0.21H), 5.63 (dq, *J*=14.4, 6.4 Hz, 0.79H), 5.51 (dt, *J*=14.4, 7.6 Hz, 0.79H), 5.28 (dt, *J*=10.4, 6.8 Hz, 0.21H), 3.68–3.63 (m, 2H), 2.45 (dt, *J*=6.8, 6.8 Hz, 0.42H), 2.32 (dt, *J*=6.8, 6.8 Hz, 1.58H), 1.78 (d, *J*=6.2 Hz, 0.63H), 1.73 (d, *J*=6.8 Hz, 2.37H), 1.51 (br s, 1H, O*H*).

*4.3.2. (3E,5E)-6-Phenylhexa-3,5-dien-1-ol (**12**)*[9]. Prepared according to the general procedure A in 93% yield as a yellow oil; an inseparable mixture of two geometrical isomers [(3*E*,5*E*)/(3*Z*,5*E*)=73:27]; R_f=0.44 (25% EtOAc in hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43–7.19 (m, 5H), 7.08 (dd, *J*=15.6, 11.2 Hz, 0.27H), 6.77 (dd, *J*=15.6, 10.8 Hz, 0.73H), 6.58 (d, *J*=15.6 Hz, 0.27H), 6.49 (d, *J*=15.6 Hz, 0.73H), 6.34–6.29 (m, 1H), 5.80 (dt, *J*=14.8, 7.6 Hz, 0.73H), 5.54 (dt, *J*=10.8, 7.6 Hz, 0.27H), 3.75–3.70 (m, 2H), 2.58 (dt, *J*=6.8, 6.8 Hz, 0.54H), 2.43 (dt, *J*=6.8, 6.8 Hz, 1.46H) (OH signal is not identified).

*4.3.3. (3E,5E)-5-Methylhepta-3,5-dien-1-ol (**13**)*[10]. Prepared according to the general procedure A in 91% yield as a yellow oil; R_f=0.38 (20% EtOAc in hexane); IR (film) 3366 (br), 2921, 2875, 1651, 1633, 1435, 1379, 1048 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.12 (d, *J*=15.6 Hz, 1H), 5.51–5.43 (m, 2H), 3.62 (t, *J*=6.4 Hz, 2H), 2.32 (dt, *J*=6.8, 6.8 Hz, 2H), 2.17 (br s, 1H), 1.70–1.67 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.6, 134.1, 125.6, 122.2, 62.1, 36.1, 13.6, 11.9; MS (EI$^+$) *m*/*z* 126 (M$^+$, 34), 109 (M$^+$–OH, 52), 95 (96); HRMS (EI$^+$) calcd for $C_8H_{14}O$ (M$^+$) 126.1045, found 126.1041.

4.4. (4*E*,6*E*)-6-Methylocta-4,6-dien-2-ol (14)

To a solution of the alcohol **13** (940.0 mg, 7.5 mmol) in dry CH_2Cl_2 (40 mL) was added solid $NaHCO_3$ (5.040 g, 60.0 mmol) and Dess–Martin periodinane (0.3 M in CH_2Cl_2, 30 mL, 10.0 mmol). The resultant mixture was stirred at room temperature for 2 h and the reaction was quenched with saturated aqueous $Na_2S_2O_3$. The mixture was extracted with EtOAc (50 mL×3) and the combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, filtered, and condensed under reduced pressure. The crude aldehyde was used for the next step without further purification.

To a solution of the above aldehyde in dry THF (20 mL) under a nitrogen atmosphere cooled at −78 °C was added a solution of MeMgCl (0.33 M, 35.5 mL, 11.7 mmol) followed by stirring at the same temperature for 2 h. The reaction was quenched with saturated aqueous NH_4Cl, and the resultant mixture was extracted with EtOAc (30 mL×3) and the combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, filtered, and condensed under reduced pressure. The residue was purified by flash column chromatography (silica gel, eluted with 20% EtOAc in PE) to give the alcohol **14** (490.8 mg, 47% for the two steps) as a yellow oil; R_f=0.52 (25% EtOAc in hexane); IR (film) 3374 (br), 2969, 2920, 1454, 1377, 1125, 1076 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.14 (d, *J*=16.0 Hz, 1H), 5.55–5.47 (m, 2H), 3.86–3.78 (m, 1H), 2.30–2.14 (m, 2H), 1.79 (br s, 1H), 1.72–1.69 (m, 6H), 1.19 (d, *J*=6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.3, 134.1, 125.9, 122.2, 67.4, 42.7, 22.7, 13.7, 12.0; MS (EI$^+$) *m*/*z* 140 (M$^+$, 17), 81 (100); HRMS (EI$^+$) calcd for $C_9H_{16}O$ (M$^+$) 140.1201, found 140.1194.

4.5. (3*E*,5*E*)-2,5-Dimethylhepta-3,5-dien-1-ol (16)

To a solution of 2-methyl-1,3-propanediol (1.350 g, 15.0 mmol) in dry CH_2Cl_2 (100 mL) cooled in an ice–water bath (ca. 0 °C) was added pyridine (2.42 mL, 20 mmol) and *p*-toluenesulfonyl chloride (3.15 g, 16.5 mmol) followed by stirring at room temperature for overnight (12 h). The reaction was quenched with saturated aqueous NH_4Cl, and the resultant mixture was extracted with EtOAc (100 mL×3). The combined organic layer was washed with 10% aqueous HCl, saturated aqueous $NaHCO_3$, and brine, and dried over anhydrous Na_2SO_4. The solid was filtered off and filtrate was condensed under reduced pressure. The residue was purified by flash column chromatography (silica gel, eluted with gradient from 20% EtOAc in PE to 100% EtOAc) to give, along with the bis-tosylate, the mono-tosylate (2.500 g, 68%) as a colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J*=7.6 Hz, 2H), 7.35 (d, *J*=8.4 Hz, 2H), 4.02 (d, *J*=5.6 Hz, 2H), 3.60–3.49 (m, 2H), 2.45 (s, 3H), 2.04–1.96 (m, 1H), 0.92 (d, *J*=6.8 Hz, 3H) (OH signal is not identified).

A solution of the above mono-tosylate (4.150 g, 17.0 mmol) and LiI (2.70 g, 20.4 mmol) in dry THF (150 mL) was heated under reflux for 30 min. After cooling, the resultant yellow suspension was filtered off through a plug of Celite with washing by EtOAc. The combined filtrate was diluted with EtOAc (200 mL), washed with water and brine, dried over anhydrous Na_2SO_4, filtered, and condensed under reduced pressure. The residue was purified by flash column chromatography (silica gel, eluted with gradient from 9% to 50% EtOAc in PE) to give the mono-iodide (2.860 g, 84%) as a colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.52 (m, 2H), 3.29 (d, *J*=5.6 Hz, 2H), 1.88 (br s, 1H), 1.70–1.62 (m, 1H), 0.98 (d, *J*=6.4 Hz, 3H).

A solution of the above mono-iodide (200.0 mg, 1.0 mmol) and PPh_3 (314.6 mg, 1.2 mmol) in dry MeCN (10 mL) was heated under reflux for 40 h. The solvent was removed under reduced pressure to give a white solid. The solid was washed with toluene and ether until PPh_3 was completely removed. The solid was thoroughly dried in a vacuum oven (100 °C) to give the phosphonium salt **15** (374.5 mg, 81%) as a white solid.

The alcohol **16** was prepared, by following the general procedure A as described in Section 4.2 above, in 50% yield from the phosphonium salt **15** and *trans*-2-methyl-2-butenal as a yellow oil; R_f=0.47 (25% EtOAc in hexane); IR (film) 3354 (br), 2959, 2923, 1453, 1380, 1033 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.16 (d, *J*=15.6 Hz, 1H), 5.52 (q, *J*=6.4 Hz, 1H), 5.36 (dd, *J*=15.2, 8.0 Hz, 1H), 3.52 (dd, *J*=10.8, 5.6 Hz, 1H), 3.40 (dd, *J*=10.8, 8.0 Hz, 1H), 2.45–2.33 (m, 1H), 1.80–1.60 (br s, 1H), 1.73–1.70 (m, 6H), 1.02 (d, *J*=6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.1, 134.0, 128.5, 126.0, 67.5, 39.9, 16.7, 13.7, 12.0; MS (EI$^+$) *m*/*z* 140 (M$^+$, 25), 109 (100); HRMS (EI$^+$) calcd for $C_9H_{16}O$ (M$^+$) 140.1201, found 140.1205.

4.6. General procedure B for synthesis of α-bromoacetates 5a,c–g

To a suspension of the alcohol (**9**, **11**–**14**, or **16**) (1.5 mmol), 4-dimethylaminopyridine (DMAP, 0.15 mmol), and bromoacetic acid (2.0 mmol) in dry CH_2Cl_2 (15 mL) cooled in an ice–water bath (0 °C) under a nitrogen atmosphere was added *N*,*N*′-dicyclohexylcarbodiimide (DCC, 2.0 mmol) in one portion. After stirring for 30 min at 0 °C, the reaction was allowed to warm up to room temperature followed by stirring for another 3 h. Celite was added to the reaction vessel and the mixture, after stirring for 30 min, was then filtered off with washing by CH_2Cl_2. The combined filtrate was evaporated under reduced pressure and the residue was purified by flash column chromatography (silica gel, eluted with 5–10% EtOAc in PE) to provide the α-bromoacetates **5a**,**c**–**g**. The latter could be prepared from the alcohols and bromoacetyl bromide in the presence of Et_3N in CH_2Cl_2 at 0 °C for 2 h. But the acylation should be quenched at 0 °C in order to suppress decomposition of the dienes by the acidic species in the reaction mixture. The yields of **5a**,**c**–**g** are listed in Table 2.

*4.6.1. (E)-Hexa-3,5-dien-1-yl α-bromoacetate (**5a**).* Prepared from the alcohol **9** according to the general procedure B in 88% yield as

a pale yellow oil; R_f=0.62 (25% EtOAc in hexane); IR (film) 2961, 1738, 1282, 1164, 1005 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.31 (ddd, J=16.4, 10.4, 10.4 Hz, 1H), 6.14 (dd, J=14.8, 10.8 Hz, 1H), 5.65 (dt, J=15.2, 6.8 Hz, 1H), 5.15 (d, J=16.8 Hz, 1H), 5.04 (d, J=10.0 Hz, 1H), 4.22 (t, J=6.4 Hz, 2H), 3.83 (s, 2H), 2.46 (dt, J=6.8, 6.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.2, 136.6, 133.8, 128.9, 116.3, 65.2, 31.6, 25.7; MS (ESI^+) m/z 241 ($M+Na^+$, 100), 218 ($M+H^+$, 26); HRMS (EI^+) calcd for $C_8H_{11}BrO_2$ 217.9942 (M^+), found 217.9927.

*4.6.2. (3E,5E)-Hepta-3,5-dien-1-yl α-bromoacetate (**5c**).* Prepared from the alcohol **11** according to the general procedure B in 86% yield as a pale yellow oil; an inseparable mixture of two geometrical isomers [(3*E*,5*E*)/(3*Z*,5*E*)=77:23]; R_f=0.73 (20% EtOAc in hexane); ^1H NMR (400 MHz, $CDCl_3$) δ 6.30 (dd, J=13.2, 12.8 Hz, 0.23H), 6.12–5.98 (m, 1.77H), 5.74 (dq, J=14.8, 6.8 Hz, 0.23H), 5.64 (dq, J=14.8, 6.8 Hz, 0.77H), 5.48 (dt, J=14.8, 6.8 Hz, 0.77H), 5.28–5.21 (m, 0.23H), 4.20 (t, J=6.8 Hz, 2H), 3.83 (s, 2H), 2.54 (dt, J=6.8, 6.8 Hz, 0.46H), 2.42 (dt, J=6.8, 6.8 Hz, 1.54H), 1.79 (d, J=6.8 Hz, 0.69H), 1.74 (d, J=6.4 Hz, 2.31H).

*4.6.3. (3E,5E)-6-Phenylhexa-3,5-dien-1-yl α-bromoacetate (**5d**).* Prepared from the alcohol **12** according to the general procedure B in 85% yield as a pale yellow oil; an inseparable mixture of two geometrical isomers [(3*E*,5*E*)/(3*Z*,5*E*)=79:21]; R_f=0.63 (20% EtOAc in hexane); ^1H NMR (400 MHz, $CDCl_3$) δ 7.44–7.20 (m, 5H), 7.03 (dd, J=15.6, 11.2 Hz, 0.21H), 6.75 (dd, J=15.6, 10.4 Hz, 0.79H), 6.58 (d, J=15.6 Hz, 0.21H), 6.49 (d, J=15.6 Hz, 0.79H), 6.33–6.27 (m, 1H), 5.76 (dt, J=15.2, 7.2 Hz, 0.79H), 5.52–5.46 (m, 0.21H), 4.26 (t, J=6.4 Hz, 2H), 3.85 (s, 1.58H), 3.83 (s, 0.42H), 2.68 (dt, J=7.2, 7.2 Hz, 0.42H), 2.53 (dt, J=6.8, 6.8 Hz, 1.58H).

*4.6.4. (3E,5E)-2,5-Dimethylhepta-3,5-dien-1-yl α-bromoacetate (**5e**).* Prepared from the alcohol **16** according to the general procedure B in 87% yield as a yellow oil; R_f=0.61 (17% EtOAc in hexane); IR (film) 2967, 1738, 1281, 1165, 1110 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.11 (d, J=16.0 Hz, 1H), 5.50 (q, J=6.8 Hz, 1H), 5.39 (dd, J=15.6, 7.2 Hz, 1H), 4.10 and 4.01 (ABqd, J=10.0, 7.2 Hz, 2H), 3.83 (s, 2H), 2.65–2.54 (m, 1H), 1.71 (br s, 6H), 1.07 (d, J=6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.2, 135.5, 134.1, 127.1, 126.1, 70.4, 36.2, 25.9, 17.0, 13.7 12.0; HRMS (EI^+) calcd for $C_{11}H_{17}BrO_2$ 260.0412 (M^+) and 262.0391 (M^++2), found 260.0416 and 262.0396.

*4.6.5. (4E,6E)-6-Methylocta-4,6-dien-2-yl α-bromoacetate (**5f**).* Prepared from the alcohol **14** according to the general procedure B in 89% yield as a yellow oil; R_f=0.50 (11% EtOAc in hexane); IR (film) 2981, 2933, 1738, 1283, 1171, 1109 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.10 (d, J=15.0 Hz, 1H), 5.50–5.41 (m, 2H), 4.99 (tq, J=6.5, 6.5 Hz, 1H), 3.79 (s, 2H), 2.42–2.30 (m, 2H), 1.71–1.70 (m, 6H), 1.25 (d, J=7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.7, 138.1, 134.1, 125.9, 120.6, 72.9, 39.0, 26.3, 19.2, 13.7 12.0; HRMS (EI^+) calcd for $C_{11}H_{17}BrO_2$ 260.0412 (M^+) and 262.0391 (M^++2), found 260.0414 and 262.0387.

*4.6.6. (3E,5E)-5-Methylhepta-3,5-dien-1-yl α-bromoacetate (**5g**).* Prepared from the alcohol **13** according to the general procedure B in 86% yield as a pale yellow oil; R_f=0.68 (20% EtOAc in hexane); IR (film) 2959, 2913, 1738, 1280, 1163, 1110 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.13 (d, J=16.0 Hz, 1H), 5.51–5.43 (m, 2H), 4.21 (t, J=6.8 Hz, 2H), 3.83 (s, 2H), 2.45 (dt, J=6.8, 6.8 Hz, 2H), 1.71–1.70 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.2, 137.7, 134.0, 126.1, 120.8, 65.8, 31.9, 25.9, 13.7, 12.0; HRMS (EI^+) calcd for $C_{10}H_{15}BrO_2$ 246.0255 (M^+), found 246.0258.

4.7. General procedure C for synthesis of *E*-substituted 1,3,9-decatrienes (*E*)-21a–f and 21i

To a solution of the alcohol (**9**, **11**, **12**, **14**, or **16**) (1.5 mmol), 4-dimethylaminopyridine (DMAP, 0.15 mmol), and fumaric acid monomethyl ester **17**[11] or monoethyl ester **18**[11] (2 mmol) in dry CH_2Cl_2 (20 mL) cooled in an ice–water bath (0 °C) under a nitrogen atmosphere, was added *N*,*N*′-dicyclohexylcarbodiimide (DCC, 2.2 mmol) in one portion. After stirring for 30 min at the same temperature, the reaction mixture was allowed to warm up to room temperature followed by stirring for another 3 h. Celite was added to the reaction vessel and the mixture, after stirring for 30 min, was then filtered off with washing by CH_2Cl_2. The combined filtrate was evaporated under reduced pressure and the residue was purified by flash column chromatography (silica gel, eluted with 9% EtOAc in PE) to provide the product (*E*)-**21a**–**f**. The yields are given in Table 1.

*4.7.1. Methyl (E)-hexa-3,5-dien-1-yl fumarate [(E)-**21a**][5c].* Prepared from the alcohol **9** according to the general procedure C in 79% yield as a colorless oil; R_f=0.70 (25% EtOAc in hexane); IR (film) 2954, 1730, 1646, 1437, 1301, 1260, 1157, 1009 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.84 (br s, 2H), 6.30 (ddd, J=16.8, 10.0, 10.0 Hz, 1H), 6.13 (dd, J=15.2, 10.4 Hz, 1H), 5.65 (dt, J=14.8, 6.8 Hz, 1H), 5.13 (d, J=16.8 Hz, 1H), 5.02 (d, J=10.4 Hz, 1H), 4.24 (t, J=6.8 Hz, 2H), 3.80 (s, 3H), 2.46 (dt, J=6.8, 6.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 164.8, 136.6, 133.6 (2×), 133.3, 129.1, 116.3, 64.4, 52.3, 31.7; MS (EI^+) m/z 211 ($M+H^+$, 5), 113 (72), 105 (70), 80 (100).

*4.7.2. Ethyl (E)-hexa-3,5-dien-1-yl fumarate [(E)-**21b**][4h,i].* Prepared from the alcohol **9** according to the general procedure C in 83% yield as a colorless oil; R_f=0.71 (25% EtOAc in hexane); IR (film) 2961, 1732, 1652, 1259, 1162, 1038 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.84 (br s, 2H), 6.30 (ddd, J=16.8, 10.0, 10.0 Hz, 1H), 6.13 (dd, J=15.2, 10.4 Hz, 1H), 5.66 (dt, J=15.2, 6.8 Hz, 1H), 5.14 (d, J=17.2 Hz, 1H), 5.03 (d, J=10.0 Hz, 1H), 4.28–4.20 (m, 4H), 2.47 (dt, J=6.8, 6.8 Hz, 2H), 1.31 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.9 (2×), 136.6, 133.8, 133.6, 133.3, 129.1, 116.3, 64.3, 61.3, 31.7, 14.0; MS (EI^+) m/z 225 ($M+H^+$, 19), 179 (71), 127 (79), 105 (100), 79 (96); HRMS (ESI^+) calcd for $C_{12}H_{16}O_4Na^+$ ($M+Na^+$) 247.0946, found 247.0937.

*4.7.3. Ethyl (3E,5E)-hepta-3,5-dien-1-yl fumarate [(E)-**21c**].* Prepared from the alcohol **11** according to the general procedure C in 89% yield as a colorless oil; an inseparable mixture of two geometrical isomers [(3*E*,5*E*)/(3*Z*,5*E*)=77:23]; R_f=0.71 (20% EtOAc in hexane); ^1H NMR (400 MHz, $CDCl_3$) δ 6.83 (s, 2H), 6.30 (dd, J=14.0, 11.6 Hz, 0.23H), 6.11–5.98 (m, 1.77H), 5.74 (dq, J=14.8, 6.8 Hz, 0.23H), 5.63 (dq, J=14.0, 6.8 Hz, 0.77H), 5.49 (dt, J=14.4, 6.8 Hz, 0.77H), 5.28 (dt, J=11.6, 6.8 Hz, 0.23H), 4.28–4.20 (m, 4H), 2.55 (dt, J=6.8, 6.8 Hz, 0.46H), 2.43 (dt, J=6.8, 6.8 Hz, 1.54H), 1.78 (d, J=6.4 Hz, 0.69H), 1.73 (d, J=7.2 Hz, 2.31H), 1.31 (t, J=6.8 Hz, 3H).

Ethyl (3*Z*,5*E*)-hepta-3,5-dien-1-yl fumarate was recovered from IMDA cycloaddition given in entry 3 of Table 1. ^1H NMR (400 MHz, $CDCl_3$) δ 6.84 (s, 2H), 6.30 (dd, J=14.4, 11.6 Hz, 1H), 6.07 (dd, J=11.2, 10.4 Hz, 1H), 5.74 (dq, J=14.8, 6.4 Hz, 1H), 5.25 (dt, J=10.4, 6.8 Hz, 1H), 4.28–4.21 (m, 4H), 2.55 (dt, J=6.8, 6.8 Hz, 2H), 1.79 (d, J=6.8 Hz, 3H), 1.32 (t, J=7.2 Hz, 3H).

*4.7.4. Ethyl (3E,5E)-5-phenylhexa-3,5-dien-1-yl fumarate [(E)-**21d**].* Prepared from the alcohol **13** according to the general procedure C in 92% yield as a colorless oil; an inseparable mixture of two geometrical isomers [(3*E*,5*E*)/(3*Z*,5*E*)=74:26]; R_f=0.62 (20% EtOAc in hexane); ^1H NMR (400 MHz, $CDCl_3$) δ 7.43–7.19 (m, 5H), 7.03 (dd, J=14.8, 10.8 Hz, 0.26H), 6.89–6.84 (m, 2H), 6.77 (dd, J=16.0, 10.0 Hz, 0.74H), 6.58 (d, J=15.2 Hz, 0.26H), 6.49 (d, J=15.6 Hz, 0.74H), 6.33–6.26 (m, 1H), 5.77 (dt, J=14.8, 7.6 Hz, 0.74H), 5.50 (dt, J=10.8, 7.6 Hz, 0.26H), 4.30–4.21 (m, 4H), 2.69 (dt, J=6.8, 6.8 Hz, 0.52H), 2.54 (dt, J=6.8, 6.8 Hz, 1.48H), 1.33–1.24 (m, 3H).

*4.7.5. Ethyl (3E,5E)-2,5-dimethylhepta-3,5-dien-1-yl fumarate [(E)-**21e**].* Prepared from the alcohol **16** according to the general procedure C in 93% yield as a colorless oil; R_f=0.68 (11% EtOAc in hexane); IR (film) 2978, 1724, 1646, 1297, 1259, 1154, 1031 cm^{-1}; ^1H

NMR (400 MHz, $CDCl_3$) δ 6.86 and 6.81 (ABq, J=16.8 Hz, 2H), 6.11 (d, J=16.0 Hz, 1H), 5.49 (q, J=6.4 Hz, 1H), 5.39 (dd, J=16.0, 7.2 Hz, 1H), 4.25 (q, J=7.2 Hz, 2H), 4.12 and 4.03 (ABqd, J=10.4, 7.2 Hz, 2H), 2.63–2.56 (m, 1H), 1.70 (br s, 6H), 1.31 (t, J=7.2 Hz, 3H), 1.07 (d, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.0 (2×), 135.4, 134.0, 133.6, 133.5, 127.3, 126.1, 69.6, 61.3, 36.2, 17.1, 14.1, 13.7, 12.0; MS (ESI^-) m/z 265 (M−H, 100); HRMS (ESI^+) calcd for $C_{15}H_{22}O_4Na^+$ ($M+Na^+$) 289.1416, found 289.1407.

*4.7.6. Ethyl (4E,6E)-6-methylocta-4,6-dien-2-yl fumarate [(E)-**21f**].* Prepared from the alcohol **14** according to the general procedure C in 84% yield as a colorless oil; R_f=0.65 (14% EtOAc in hexane); IR (film) 2980, 2936, 1723, 1647, 1296, 1259, 1156, 1034 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.82 (s, 2H), 6.09 (d, J=15.2 Hz, 1H), 5.47–5.40 (m, 2H), 5.07–5.00 (m, 1H), 4.25 (q, J=7.2 Hz, 2H), 2.45–2.30 (m, 2H), 1.70 (br s, 6H), 1.30 (t, J=7.2 Hz, 3H), 1.26 (d, J=6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.1, 164.5, 138.1, 134.1, 134.0, 133.4, 125.9, 120.8, 71.9, 61.3, 39.2, 19.3, 14.1, 13.7, 12.0; MS (ESI^+) m/z 555 ($2M+Na^+$, 38), 289 ($M+Na^+$, 100); HRMS (ESI^+) calcd for $C_{15}H_{22}O_4Na^+$ ($M+Na^+$) 289.1416, found 289.1409.

*4.7.7. (3E,6E)-6-Methylhapta-4,6-dien-2-yl acrylate (**21i**).* Prepared from the alcohol **13** and acrylic acid according to the general procedure C in 59% yield as a colorless oil; R_f=0.63 (4.8% EtOAc in PE); IR (film) 2955, 2920, 1727, 1636, 1408, 1272, 1187, 1059 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.38 (dd, J=17.2, 1.6 Hz, 1H), 6.14–6.07 (m, 2H), 5.79 (dd, J=10.4, 1.6 Hz, 1H), 5.52–5.44 (m, 2H), 4.18 (t, J=6.8 Hz, 2H), 2.44 (dt, J=6.8 Hz, 2H), 1.70 (s, 3H), 1.67 (d, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 137.3; 134.0; 130.4; 128.4; 125.6; 121.2; 64.0; 32.0; 13.5; 11.8; HRMS (EI^+) calcd for $C_{11}H_{16}O_2$ (M^+) 180.1150, found 180.1150.

4.8. General procedure D for synthesis of *Z*-substituted 1,3,9-decatrienes (*Z*)-22a–f

To a solution of maleic acid monomethyl ester **19** or monoethyl ester **20**[12] (3.0 mmol) in dry CH_2Cl_2 (10 mL) was added *N,N′*-diisopropylcarbodiimide (DIC, 1.5 mmol) and the mixture was stirred at 0 °C for 1 h. The insoluble urea was filtered off through a plug of Celite and the filtrate was added to a solution of the alcohol (**9**, **11**, **12**, **14**, or **16**) (1.0 mmol) in dry CH_2Cl_2 (6 mL), followed by addition of *i*-Pr_2NEt (DIEA, 3.0 mmol) and 4-dimethylaminopyridine (DMAP, 0.1 mmol). The resultant mixture was stirred at 0 °C for 1 h. The reaction mixture was diluted with CH_2Cl_2 and successively washed with saturated aqueous NH_4Cl and brine. The organic layer was dried over anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure. The residue was purified by column chromatography (silica gel, eluted with 9% EtOAc in PE) to provide the product (*Z*)-**22a**–**f**. The yields are given in Table 1.

*4.8.1. Methyl (E)-hexa-3,5-dien-1-yl maleate [(Z)-**22a**][5c].* Prepared from the alcohol **9** according to the general procedure D in 66% yield as a pale yellow oil; R_f=0.42 (18% EtOAc in hexane); IR (film) 2955, 1732, 1651, 1436, 1398, 1218, 1163, 1006 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.29 (ddd, J=16.8, 10.0, 10.0 Hz, 1H), 6.24 (s, 2H), 6.12 (dd, J=15.2, 10.4 Hz, 1H), 5.65 (dt, J=14.8, 7.2 Hz, 1H), 5.13 (d, J=16.8 Hz, 1H), 5.01 (d, J=10.0 Hz, 1H), 4.22 (t, J=7.2 Hz, 2H), 3.77 (s, 3H), 2.46 (dt, J=6.8, 6.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6, 165.1, 136.6, 133.5, 129.8, 129.6, 129.3, 116.1, 64.3, 52.1, 31.5; MS (EI^+) m/z 113 ($C_5H_5O_3^+$, 100), 80 (47).

*4.8.2. Ethyl (E)-hexa-3,5-dien-1-yl maleate [(Z)-**22b**].* Prepared from the alcohol **9** according to the general procedure D in 62% yield as a colorless oil; R_f=0.69 (25% EtOAc in hexane); IR (film) 2983, 1731, 1645, 1405, 1212, 1162, 1006 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.30 (dt, J=17.2, 10.4 Hz, 1H), 6.23 (s, 2H), 6.14 (dd, J=15.2, 11.2 Hz, 1H), 5.66 (dt, J=15.6, 6.8 Hz, 1H), 5.14 (d, J=17.2 Hz, 1H), 5.02 (d, J=10.4 Hz, 1H), 4.28–4.22 (m, 4H), 2.47 (dt, J=6.8, 6.8 Hz, 2H), 1.31 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.1, 165.1, 136.6, 133.4, 129.9, 129.5, 129.3, 116.1, 64.3, 61.1, 31.5, 13.9; MS (EI^+) m/z 224 (M^+, 4), 179 (12), 127 (15), 105 (45), 99 (38), 80 (100); HRMS (ESI^+) calcd for $C_{12}H_{16}O_4Na^+$ ($M+Na^+$) 247.0946, found 247.0942.

*4.8.3. Ethyl (3E,5E)-hepta-3,5-dien-1-yl maleate [(Z)-**22c**].* Prepared from the alcohol **11** according to the general procedure D in 56% yield as a colorless oil; an inseparable mixture of two geometrical isomers [(3*E*,5*E*)/(3*Z*,5*E*)=78:22]; R_f=0.65 (20% EtOAc in hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.29 (dd, J=13.6, 12.8 Hz, 0.22H), 6.22 (s, 2H), 6.11–5.98 (m, 1.78H), 5.73 (dq, J=14.8, 6.8 Hz, 0.22H), 5.63 (dq, J=14.4, 6.8 Hz, 0.78H), 5.49 (dt, J=14.4, 7.2 Hz, 0.78H), 5.25 (dt, J=10.4, 6.8 Hz, 0.22H), 4.27–4.19 (m, 4H), 2.55 (dt, J=6.8, 6.8 Hz, 0.44H), 2.42 (dt, J=6.8, 6.8 Hz, 1.56H), 1.77 (d, J=6.4 Hz, 0.66H), 1.73 (d, J=6.4 Hz, 2.34H), 1.32–1.25 (m, 3H).

*4.8.4. Ethyl (3E,5E)-5-phenylhexa-3,5-dien-1-yl maleate [(Z)-**22d**].* Prepared from the alcohol **12** according to the general procedure D in 62% yield as a colorless oil; an inseparable mixture of two geometrical isomers [(3*E*,5*E*)/(3*Z*,5*E*)=72:28]; R_f=0.58 (20% EtOAc in hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43–7.21 (m, 5H), 7.03 (dd, J=14.8, 10.8 Hz, 0.28H), 6.75 (dd, J=15.6, 10.8 Hz, 0.72H), 6.57 (d, J=16.0 Hz, 0.28H), 6.48 (d, J=15.6 Hz, 0.72H), 6.35–6.23 (m, 3H), 5.77 (dt, J=14.8, 7.6 Hz, 0.72H), 5.50 (dt, J=10.8, 7.2 Hz, 0.28H), 4.29–4.23 (m, 4H), 2.69 (dt, J=7.2, 7.2 Hz, 0.56H), 2.53 (dt, J=6.8, 6.8 Hz, 1.44H), 1.33–1.26 (m, 3H).

*4.8.5. Ethyl (3E,5E)-2,5-dimethylhepta-3,5-dien-1-yl maleate [(Z)-**22e**].* Prepared from the alcohol **16** according to the general procedure D in 67% yield as a colorless oil; R_f=0.54 (11% EtOAc in hexane); IR (film) 2978, 1732, 1645, 1404, 1211, 1163, 1027 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.23 (br s, 2H), 6.10 (d, J=15.6 Hz, 1H), 5.50–5.49 (q, J=6.8 Hz, 1H), 5.40 (dd, J=15.6, 7.2 Hz, 1H), 4.24 (q, J=7.2 Hz, 2H), 4.11 and 4.01 (ABqd, J=10.8, 6.8 Hz, 2H), 2.64–2.54 (m, 1H), 1.70 (br s, 6H), 1.30 (t, J=7.2 Hz, 3H), 1.06 (d, J=6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 165.2, 135.3, 134.1, 129.9, 129.6, 127.5, 125.9, 69.6, 61.2, 36.0, 17.2, 14.0, 13.7, 11.9; MS (ESI^+) m/z 555 ($2M+Na^+$, 100), 289 ($M+Na^+$, 54); HRMS (ESI^+) calcd for $C_{15}H_{22}O_4Na^+$ ($M+Na^+$) 289.1416, found 289.1408.

*4.8.6. Ethyl (4E,6E)-6-methylocta-4,6-dien-2-yl maleate [(Z)-**22f**].* Prepared from the alcohol **14** according to the general procedure D in 71% yield as a colorless oil; R_f=0.50 (17% EtOAc in hexane); IR (film) 2982, 2935, 1723, 1642, 1403, 1384, 1213, 1166, 1028 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.20 (br s, 2H), 6.09 (d, J=16.0 Hz, 1H), 5.49–5.42 (m, 2H), 5.04 (sextet, J=6.0 Hz, 1H), 4.24 (q, J=7.0 Hz, 2H), 2.44 and 2.31 (ABqdd, J=21.0, 7.0, 7.0 Hz, 2H), 1.70 (s, 3H), 1.70 (d, J=6.5 Hz, 3H), 1.30 (t, J=7.5 Hz, 3H), 1.26 (d, J=6.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.2, 164.7, 137.9, 134.2, 130.1, 129.5, 125.7, 121.0, 71.9, 61.1, 39.0, 19.1, 14.0, 13.7, 12.0; MS (ESI^+) m/z 555 ($2M+Na^+$, 100), 289 ($M+Na^+$, 70); HRMS (ESI^+) calcd for $C_{15}H_{22}O_4Na^+$ ($M+Na^+$) 289.1416, found 289.1406.

4.9. General procedure E for synthesis of the ester-tethered 1,3,9-decatrienes via Wittig olefination

A solution of (*E*)-hexa-3,5-dien-1-yl α-bromoacetate **5a** (0.30 mmol) and PPh_3 (0.33 mmol) in MeCN (10 mL) was stirred at room temperature for overnight (12 h). The reaction mixture was evaporated under reduced pressure to give a white solid, which was washed with dry benzene (9 mL×3) and dried in vacuum to provide quantitatively the salt **27**. The phosphonium salt was used without further purification.

A solution of the above phosphonium salt **27** (0.20 mmol), ethyl glyoxalate or phenylglyoxal hydrate (0.22 mmol), and 2,6-lutidine

(0.26 mmol) in MeCN (5 mL) was stirred for 2–4 h at room temperature. The reaction mixture was diluted with EtOAc (30 mL) and washed with 6% aqueous HCl and brine. The organic layer was dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. The residue was purified by flash column chromatography (silica gel, 9% EtOAc in PE) to give (*E*)-**21b** (74%) and (*Z*)-**22b** (10%) or (*E*)-**21h** (70%) and (*Z*)-**22h** (9%), respectively (see Scheme 3 for detail).

*4.9.1. (E)-Hexa-3,5-dien-1-yl (E)-4-phenyl-4-oxo-2-butenoate [(E)-**21h**].* Prepared from the phosphonium salt **27** and phenylglyoxal hydrate according to the general procedure E in 70% yield as a colorless oil; R_f=0.74 (20% EtOAc in hexane); IR (film) 2958, 1720, 1678, 1593, 1459, 1299, 1173, 1014 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 8.02 (d, *J*=7.2 Hz, 2H), 7.93 (d, *J*=15.6 Hz, 1H), 7.70 (t, *J*=7.6 Hz, 1H), 7.57 (dd, *J*=7.6, 7.6 Hz, 2H), 6.72 (d, *J*=15.6 Hz, 1H), 6.33 (ddd, *J*=17.2, 10.0, 10.0 Hz, 1H), 6.17 (dd, *J*=15.2, 10.8 Hz, 1H), 5.75 (dt, *J*=15.6, 6.8 Hz, 1H), 5.15 (d, *J*=16.8 Hz, 1H), 5.01 (d, *J*=10.4 Hz, 1H), 4.24 (t, *J*=6.4 Hz, 2H), 2.47 (dt, *J*=6.8, 6.8 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 189.7, 165.3, 137.3 (2×), 136.5, 134.5, 133.6, 131.8, 130.7, 129.5 (2×), 129.2 (2×), 116.7, 64.5, 31.7; MS (ESI$^+$) *m*/*z* 279 (M+Na$^+$, 100); HRMS (ESI$^+$) calcd for $C_{16}H_{16}O_3Na^+$ (M+Na$^+$) 279.0997, found 279.0986.

*4.9.2. (E)-Hexa-3,5-dien-1-yl (Z)-4-phenyl-4-oxo-2-butenoate [(Z)-**22h**].* Prepared from the phosphonium salt **27** and phenylglyoxal hydrate according to the general procedure E in 9% yield as a colorless oil; R_f=0.66 (20% EtOAc in hexane); IR (film) 2958, 2926, 1724, 1674, 1598, 1449, 1213, 1166, 1005 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.87 (d, *J*=7.6 Hz, 2H), 7.67 (t, *J*=7.6 Hz, 1H), 7.55 (dd, *J*=7.6, 7.6 Hz, 2H), 7.27 (d, *J*=11.6 Hz, 1H), 6.38 (d, *J*=12.0 Hz, 1H), 6.23 (ddd, *J*=16.8, 10.0, 10.0 Hz, 1H), 6.02 (dd, *J*=14.8, 10.4 Hz, 1H), 5.53 (dt, *J*=15.6, 6.8 Hz, 1H), 5.10 (d, *J*=16.8 Hz, 1H), 5.00 (d, *J*=10.0 Hz, 1H), 3.98 (t, *J*=6.4 Hz, 2H), 2.12 (dt, *J*=6.4, 6.4 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 194.1, 165.0, 142.4, 137.1, 135.9, 134.1, 133.2, 130.5, 129.2 (2×), 128.8 (2×), 126.0, 116.5, 64.1, 31.3; MS (ESI$^+$) *m*/*z* 256 (M$^+$, 100); HRMS (ESI$^+$) calcd for $C_{16}H_{16}O_3Na^+$ (M+Na$^+$) 279.0997, found 279.0990.

4.10. General procedure F for microwave-assisted IMDA cycloaddition of (*E*)-21a–f,h,i and (*Z*)-22a–f

To a 10-mL pressurized process vial was added the 1,3,9-decatriene (0.30–0.90 mmol) and CH_3CN (4 mL). The loaded vial was then sealed with a cap containing a silicon septum, and put into the microwave cavity and heated at 180 °C for 0.5–2.5 h. The reaction mixture was evaporated under reduce pressure. The residue was checked for adduct isomer ratio by ^1H NMR spectrum and was then purified by flash column chromatography (silica gel, eluted with 5–20% EtOAc in PE) to give the desired products. The structures, isomer ratios, and yields are found in Schemes 2, 3, and 5, and Table 1.

4.10.1. Methyl (4aS,8S*,8aS*)-1-oxo-3,4,4a,7,8,8a-hexahydro-1H-isochromene-8-carboxylate (**23a**)[5c].* The major adduct obtained, according to the general procedure F, from the triene (*E*)-**21a** in 58% isolated yield as a colorless oil; R_f=0.29 (20% EtOAc in hexane); IR (film) 2953, 2920, 1731 (br), 1436, 1275, 1155 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.82 (br dd, *J*=4.8, 2.8 Hz, 1H), 5.50 (br d, *J*=9.6 Hz, 1H), 4.34–4.20 (m, 2H), 3.69 (s, 3H), 3.47–3.45 (m, 1H), 3.26 (dd, *J*=6.4, 2.8 Hz, 1H), 2.93–2.85 (br s, 1H), 2.52 (br d, *J*=18.4 Hz, 1H), 2.29 (dm, *J*=18.4 Hz, 1H), 2.16 (dddd, *J*=14.0, 9.6, 5.2, 5.2 Hz, 1H), 1.71 (dddd, *J*=14.4, 5.2, 5.2, 5.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.8, 172.1, 127.8, 127.6, 66.4, 52.1, 40.3, 38.9, 28.6, 28.2, 22.9; MS (EI$^+$) *m*/*z* 210 (M$^+$, 15), 178 (M$^+$–MeOH, 100), 150 (97), 122 (42), 105 (74), 91 (95), 78 (96).

4.10.2. Methyl (4aS,8R*,8aR*)-1-oxo-3,4,4a,7,8,8a-hexahydro-1H-isochromene-8-carboxylate (**24a**)[5c].* The minor adduct obtained, according to the general procedure F, from the triene (*E*)-**21a** in 22% yield as colorless needles; mp 100–101 °C (EtOAc–hexane); R_f=0.21 (20% EtOAc in hexane); IR (KBr) 2922, 1735 (br), 1432, 1411, 1313, 1199, 1168, 1101, 1066, 1008 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.72 (br d, *J*=11.6 Hz, 1H), 5.61 (br d, *J*=9.2 Hz, 1H), 4.39 (t, *J*=7.2 Hz, 2H), 3.74 (s, 3H), 2.80–2.69 (m, 2H), 2.48–2.44 (m, 2H), 2.29–2.20 (m, 2H), 1.73–1.66 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.5, 173.0, 128.5, 125.5, 66.2, 52.0, 43.1, 40.0, 32.9, 29.2, 28.1; MS (EI$^+$) *m*/*z* 210 (M$^+$, 8), 178 (M$^+$–MeOH, 45), 150 (73), 122 (55), 105 (38), 91 (100), 78 (77).

4.10.3. Methyl (4aS,8R*,8aS*)-1-oxo-3,4,4a,7,8,8a-hexahydro-1H-isochromene-8-carboxylate (**25a**)[5c].* The major adduct obtained, according to the general procedure F, from the triene (*Z*)-**22a** in 58% yield as a colorless solid; mp 92–93 °C (EtOAc/hexane); R_f=0.12 (20% EtOAc in hexane); IR (KBr) 2949, 1732 (br), 1433, 1209, 1184, 1146, 1002 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.85 (ddd, *J*=7.2, 5.2, 2.4 Hz, 1H), 5.53 (br dd, *J*=10.0, 2.4 Hz, 1H), 4.30 (ddd, *J*=11.6, 4.8, 4.8 Hz, 1H), 4.21 (ddd, *J*=11.6, 10.0, 4.4 Hz, 1H), 3.74 (s, 3H), 3.46 (dd, *J*=6.4, 3.2 Hz, 1H), 3.00–2.92 (br s, 1H), 2.63 (ddd, *J*=9.6, 6.0, 3.2 Hz, 1H), 2.52–2.32 (m, 2H), 2.21 (dddd, *J*=14.0, 10.0, 5.6, 4.0 Hz, 1H), 1.75 (dddd, *J*=14.4, 5.6, 5.6, 4.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.3, 171.3, 128.4, 127.9, 66.2, 52.0, 41.1, 40.1, 32.6, 28.5, 23.2; MS (EI$^+$) *m*/*z* 210 (M$^+$, 3), 178 (M$^+$–MeOH, 85), 150 (57), 105 (53), 91 (100), 78 (100).

4.10.4. Methyl (4aS,8S*,8aR*)-1-oxo-3,4,4a,7,8,8a-hexahydro-1H-isochromene-8-carboxylate (**26a**)[5c].* The minor adduct obtained, according to the general procedure F, from the triene (*Z*)-**22a** in 20% yield as a colorless solid; mp 91–92 °C (EtOAc/hexane); R_f=0.15 (20% EtOAc in hexane); IR (KBr) 2960, 1727 (br), 1403, 1211, 1174, 1104, 1066 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.72–5.67 (m, 1H), 5.60 (br d, *J*=10.0 Hz, 1H), 4.50 (ddd, *J*=12.8, 6.8, 4.4 Hz, 1H), 4.42 (dd, *J*=11.2, 3.6 Hz, 1H), 3.69 (s, 3H), 3.55 (dd, *J*=7.2, 3.2 Hz, 1H), 2.94 (br t, *J*=11.2 Hz, 1H), 2.67 (br d, *J*=18.8 Hz, 1H), 2.53–2.45 (m, 1H), 2.27 (dd, *J*=12.4, 3.6 Hz, 1H), 2.04 (dm, *J*=18.0 Hz, 1H), 1.70 (dddd, *J*=12.4, 12.4, 12.4, 6.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.3, 171.4, 129.0, 126.0, 69.4,. 52.0, 44.7, 37.0, 31.2, 29.8, 28.1; MS (EI$^+$) *m*/*z* 211 (M+H$^+$, 3), 179 (M$^+$–OMe, 85), 152 (100), 122 (55), 106 (68), 91 (72), 78 (92).

4.10.5. Ethyl (4aS,8S*,8aS*)-1-oxo-3,4,4a,7,8,8a-hexahydro-1H-isochromene-8-carboxylate (**23b**)[4h].* The major adduct obtained, according to the general procedure F, from the triene (*E*)-**21b** in 62% yield as a colorless oil; R_f=0.22 (20% EtOAc in hexane); IR (film) 2980, 2906, 1728 (br), 1274, 1196, 1155, 1093, 1034 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.85–5.81 (m, 1H), 5.50 (br d, *J*=10.0 Hz, 1H), 4.31–4.23 (m, 2H), 4.14 (q, *J*=7.0 Hz, 2H), 3.43 (br dd, *J*=2.8, 2.8 Hz, 1H), 3.26 (dd, *J*=6.4, 2.8 Hz, 1H), 2.89 (br s, 1H), 2.52 (dm, *J*=18.2 Hz, 1H), 2.28 (dm, *J*=18.8 Hz, 1H), 2.20–2.11 (m, 1H), 1.74–1.67 (m, 1H), 1.23 (t, *J*=7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.3, 172.1, 127.9, 127.6, 66.3, 60.9, 40.3, 39.0, 28.5, 28.2, 22.9, 14.1; MS (EI$^+$) *m*/*z* 224 (M$^+$, 4), 178 (M$^+$–EtOH, 31), 150 (65), 122 (20), 105 (39), 91 (87), 78 (100); HRMS (ESI$^+$) calcd for $C_{12}H_{16}O_4Na^+$ (M+Na$^+$) 247.0946, found 247.0940.

4.10.6. Ethyl (4aS,8R*,8aR*)-1-oxo-3,4,4a,7,8,8a-hexahydro-1H-isochromene-8-carboxylate (**24b**).* The minor adduct obtained, according to the general procedure F, from the triene (*E*)-**21b** in 18% yield as colorless needles; mp 76–78 °C (EtOAc/hexane); R_f=0.14 (20% EtOAc in hexane); IR (KBr) 2991, 2932, 1736 (br), 1412, 1255, 1185, 1090, 1038 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.73–5.70 (m, 1H), 5.60 (br d, *J*=10.0 Hz, 1H), 4.38 (t, *J*=7.2 Hz, 2H), 4.26–4.13 (m, 2H), 2.77–2.68 (m, 2H), 2.51–2.40 (m, 2H), 2.30–2.17 (m, 2H), 1.73–1.64 (m, 1H), 1.28 (t, *J*=7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.0, 173.0, 128.5, 125.5, 66.2, 60.7, 43.0, 40.2, 32.9, 29.2, 28.1, 14.0; MS (EI$^+$) *m*/*z* 224 (M$^+$, 10), 179 (M$^+$–OEt, 30), 150 (62), 122 (57), 105

(35), 91 (100), 78 (79). Anal. Calcd for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19, found: C, 64.20; H, 7.02.

4.10.7. Ethyl (4aS,8R*,8aS*)-1-oxo-3,4,4a,7,8,8a-hexahydro-1H-isochromene-8-carboxylate (**25b**).* The major adduct obtained, according to the general procedure F, from the triene (*Z*)-**22b** in 57% yield as colorless needles; mp 80–82 °C (EtOAc/hexane); R_f=0.21 (20% EtOAc in hexane); IR (film) 2980, 2925, 1732 (br), 1393, 1207, 1183, 1137, 1034 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.83 (br s, 1H), 5.52 (br d, *J*=10.0 Hz, 1H), 4.30–4.26 (m, 1H), 4.21–4.16 (m, 3H), 3.44 (br d, *J*=3.6 Hz, 1H), 2.95 (br s, 1H), 2.62–2.57 (m, 1H), 2.48–2.31 (m, 2H), 2.24–2.15 (m, 1H), 1.76–1.71 (m, 1H), 1.25 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.7, 171.3, 128.4, 127.9, 66.2, 60.7, 41.1, 40.2, 32.7, 28.5, 23.2, 14.0; MS (EI^+) *m*/*z* 224 (M^+, 1), 178 (M^+–EtOH, 39), 150 (30), 105 (25), 91 (56), 78 (100). Anal. Calcd for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19, found: C, 64.23; H, 7.07.

4.10.8. Ethyl (4aS,8S*,8aR*)-1-oxo-3,4,4a,7,8,8a-hexahydro-1H-isochromene-8-carboxylate (**26b**).* The minor adduct obtained, according to the general procedure F, from the triene (*Z*)-**22b** in 19% yield as a colorless oil; R_f=0.26 (20% EtOAc in hexane); IR (film) 2979, 2928, 1731 (br), 1403, 1201, 1168, 1090 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.70–5.68 (m, 1H), 5.60 (br d, *J*=10.0 Hz, 1H), 4.51–4.38 (m, 2H), 4.20–4.09 (m, 2H), 3.52 (dd, *J*=7.6, 2.8 Hz, 1H), 2.93 (br t, *J*=11.2 Hz, 1H), 2.68 (br d, *J*=18.4 Hz, 1H), 2.47 (dm, *J*=18.8 Hz, 1H), 2.26 (dd, *J*=11.2, 2.8 Hz, 1H), 2.03 (dm, *J*=13.2 Hz, 1H), 1.73 (dddd, *J*=13.2, 13.2, 13.2, 6.0 Hz, 1H), 1.24 (t, *J*=6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.8, 171.4, 129.0, 126.2, 69.4, 60.9, 44.8, 37.2, 31.3, 29.9, 28.1, 14.1; MS (EI^+) *m*/*z* 224 (M^+, 1), 179 (M^+–OEt, 100), 166 (70), 150 (51), 122 (45), 105 (65), 91 (64), 79 (96); HRMS (ESI^+) calcd for $C_{12}H_{16}O_4Na^+$ (M+Na^+) 247.0946, found 247.0940.

4.10.9. Ethyl (4aS,7R*,8S*,8aS*)-7-methyl-1-oxo-3,4,4a,7,8,8a-hexahydro-1H-isochromene-8-carboxylate (**23c**).* The major adduct obtained, according to the general procedure F, from the triene (*E*)-**21c** in 58% yield as a colorless oil; R_f=0.46 (20% EtOAc in hexane); IR (film) 2964, 2932, 1732, 1403, 1265, 1179, 1087 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.70 (br d, *J*=9.6 Hz, 1H), 5.53 (br d, *J*=10.0 Hz, 1H), 4.42–4.30 (m, 1H), 4.29–4.25 (m, 1H), 4.21–4.15 (m, 2H), 3.17 (dd, *J*=7.6, 6.8 Hz, 1H), 2.72–2.60 (m, 3H), 2.02–1.95 (m, 1H), 1.77–1.67 (m, 1H), 1.26 (t, *J*=7.2 Hz, 3H), 1.02 (d, *J*=6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.8, 171.5, 133.4, 126.2, 68.0, 60.9, 46.9, 41.3, 32.3, 31.0, 27.8, 20.3, 14.1; MS (EI^+) *m*/*z* 192 (M^+–EtOH, 52), 164 (47), 105 (49), 92 (100); HRMS (ESI^+) calcd for $C_{13}H_{18}O_4Na^+$ (M+Na^+) 261.1103, found 261.1090.

4.10.10. Ethyl (4aS,7R*,8R*,8aR*)-7-methyl-1-oxo-3,4,4a,7,8,8a-hexahydro-1H-isochromene-8-carboxylate (**24c**).* The minor adduct obtained, according to the general procedure F, from the triene (*E*)-**21c** in 24% yield as a colorless oil; R_f=0.40 (20% EtOAc in hexane); IR (film) 2971, 2927, 1738 (br), 1397, 1316, 1260, 1162, 1086, 1032 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.69 (br d, *J*=9.6 Hz, 1H), 5.54 (br d, *J*=9.6 Hz, 1H), 4.42–4.38 (m, 2H), 4.23–4.17 (m, 2H), 2.88 (dd, *J*=11.6, 6.4 Hz, 1H), 2.76–2.68 (m, 2H), 2.42–2.25 (m, 2H), 1.67–1.59 (m, 1H), 1.28 (t, *J*=7.2 Hz, 3H), 0.93 (d, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.1, 173.0, 131.9, 126.8, 65.2, 60.5, 43.5, 38.0, 33.1, 31.0, 27.6, 17.6, 14.2; MS (EI^+) *m*/*z* 238 (M^+, 25), 193 (M^+–OEt, 100), 163 (72), 149 (70), 119 (50), 105 (50), 91 (52); HRMS (ESI^+) calcd for $C_{13}H_{18}O_4Na^+$ (M+Na^+) 261.1103, found 261.1090.

4.10.11. Ethyl (4aS,7R*,8R*,8aS*)-7-methyl-1-oxo-3,4,4a,7,8,8a-hexahydro-1H-isochromene-8-carboxylate (**25c**).* The major adduct obtained, according to the general procedure F, from the triene (*Z*)-**22c** in 58% yield as a colorless oil; R_f=0.15 (20% EtOAc in hexane); IR (film) 2977, 2934, 1731 (br), 1402, 1261, 1187, 1090, 1036 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.81 (br d, *J*=10.0 Hz, 1H), 5.47 (br d, *J*=10.0 Hz, 1H), 4.40–4.26 (m, 2H), 4.18 (q, *J*=7.2 Hz, 2H), 3.38 (dd, *J*=7.6, 4.4 Hz, 1H), 3.00 (dd, *J*=4.4, 4.4 Hz, 1H), 2.85 (br s, 1H), 2.65 (br s, 1H), 2.08–2.01 (m, 1H), 1.91–1.86 (m, 1H), 1.26 (t, *J*=7.2 Hz, 3H), 1.15 (d, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.0, 171.8, 134.5, 126.6, 67.2, 60.4, 44.8, 39.8, 33.0, 30.5, 28.2, 17.9, 14.1; MS (EI^+) *m*/*z* 238 (M^+, 13), 192 (M^+–EtOH, 88), 164 (56), 119 (65), 105 (65), 92 (100); HRMS (ESI^+) calcd for $C_{13}H_{18}O_4Na^+$ (M+Na^+) 261.1103, found 261.1090.

4.10.12. Ethyl (4aS,7R*,8S*,8aR*)-7-methyl-1-oxo-3,4,4a,7,8,8a-hexahydro-1H-isochromene-8-carboxylate (**26c**).* The minor adduct obtained, according to the general procedure F, from the triene (*Z*)-**22c** in 22% yield as a white solid; mp 54–55 °C (EtOAc/hexane); R_f=0.22 (20% EtOAc in hexane); IR (KBr) 2961, 1732 (br), 1403, 1231, 1171, 1080, 1026 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.62 (br d, *J*=10.0 Hz, 1H), 5.55 (br d, *J*=10.0 Hz, 1H), 4.52–4.38 (m, 2H), 4.19–4.08 (m, 2H), 3.20 (d, *J*=2.4 Hz, 1H), 2.94–2.88 (m, 2H), 2.23 (dd, *J*=12.0, 3.6 Hz, 1H), 2.03 (br d, *J*=13.6 Hz, 1H), 1.75 (dddd, *J*=12.8, 12.8, 12.8, 6.0 Hz, 1H), 1.24 (t, *J*=7.2 Hz, 3H), 1.17 (d, *J*=6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.6, 171.9, 132.1, 128.1, 69.4, 60.8, 44.3, 41.5, 32.9, 31.5, 29.8, 22.0, 14.1; MS (EI^+) *m*/*z* 238 (M^+, 1), 193 (M^+–OEt, 98), 164 (67), 136 (85), 119 (87), 105 (100), 91 (90). Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61; found: C, 65.46; H, 7.63.

4.10.13. Ethyl (4aS,7R*,8S*,8aS*)-1-oxo-7-phenyl-3,4,4a,7,8,8a-hexahydro-1H-isochromene-8-carboxylate (**23d**)*[14]. The major adduct obtained, according to the general procedure F, from the triene (*E*)-**21d** in 53% yield as colorless needles; mp 119–121 °C (EtOAc/hexane); R_f=0.17 (20% EtOAc in hexane); IR (KBr) 2990, 2954, 2899, 1725 (br), 1404, 1374, 1221, 1179, 1087 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.31–7.21 (m, 3H), 7.16 (d, *J*=6.8 Hz, 2H), 5.87–5.80 (m, 2H), 4.47 (ddd, *J*=11.2, 4.4, 4.4 Hz, 1H), 4.33 (ddd, *J*=11.2, 3.2, 3.2 Hz, 1H), 4.09–4.01 (m, 2H), 3.87 (dd, *J*=8.4, 1.6 Hz, 1H), 3.28 (dd, *J*=10.0, 7.2 Hz, 1H), 2.91 (dd, *J*=10.0, 8.8 Hz, 1H), 2.80 (br s, 1H), 2.07–2.03 (m, 1H), 1.91–1.81 (m, 1H), 1.09 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.0, 170.6, 141.9, 130.7, 128.5 (2×), 128.0, 127.8 (2×), 127.1, 68.5, 60.8, 48.0, 44.1, 41.8, 31.6, 27.7, 13.9; MS (EI^+) *m*/*z* 300 (M^+, 2), 254 (M^+–EtOH, 50), 226 (32), 154 (100). Anal. Calcd for $C_{18}H_{20}O_4$: C, 71.98; H, 6.71; found C, 71.92; H, 6.71. The relative stereochemistry of **23d** has been confirmed by X-ray crystal structural analysis.[15]

4.10.14. Ethyl (4aS,7R*,8R*,8aR*)-1-oxo-7-phenyl-3,4,4a,7,8,8a-hexahydro-1H-isochromene-8-carboxylate (**24d**).* The minor adduct obtained, according to the general procedure F, from the triene (*E*)-**21d** in 18% yield as a colorless oil; R_f=0.19 (20% EtOAc in hexane); IR (film) 2930, 1732 (br), 1454, 1394, 1273, 1085 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.31–7.25 (m, 3H), 7.13 (d, *J*=6.8 Hz, 2H), 5.89 (dm, *J*=10.0 Hz, 1H), 5.77 (ddd, *J*=7.2, 4.8, 2.4 Hz, 1H), 4.45 (dd, *J*=8.4, 5.2 Hz, 2H), 3.95–3.92 (m, 1H), 3.86–3.73 (m, 2H), 3.13 (dd, *J*=12.0, 7.2 Hz, 1H), 2.84 (dd, *J*=12.0, 12.0 Hz, 1H), 2.56–2.37 (m, 2H), 1.86–1.77 (m, 1H), 0.96 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.8, 171.7, 139.2, 129.2 (2×), 128.7, 128.2 (2×), 128.1, 127.4, 65.3, 60.3, 45.4, 42.9, 37.9, 33.0, 27.7, 13.7; MS (EI^+) *m*/*z* 300 (M^+, 9), 254 (M^+–EtOH, 35), 226 (61), 156 (100), 91 (71); HRMS (ESI^+) calcd for $C_{18}H_{20}O_4Na^+$ (M+Na^+) 323.1259; found 323.1252.

4.10.15. Ethyl (4aS,7R*,8R*,8aS*)-1-oxo-7-phenyl-3,4,4a,7,8,8a-hexahydro-1H-isochromene-8-carboxylate (**25d**).* The major adduct obtained, according to the general procedure F, from the triene (*Z*)-**22d** in 34% yield as a colorless oil; R_f=0.38 (25% EtOAc in hexane); IR (film) 2981, 1728 (br), 1454, 1403, 1247, 1188, 1157, 1086, 1022 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.33–7.20 (m, 5H), 6.03 (dt, *J*=10.4, 2.0 Hz, 1H), 5.86 (dt, *J*=10.0, 3.0 Hz, 1H), 4.49 (ddd, *J*=10.8,

4.4, 2.4 Hz, 1H), 4.36 (ddd, *J*=12.0, 12.0, 2.8 Hz, 1H), 3.87–3.75 (m, 2H), 3.69–3.60 (m, 2H), 3.33 (dd, *J*=9.2, 5.6 Hz, 1H), 2.85–2.76 (m, 1H), 2.35 (dddd, *J*=12.8, 12.8, 12.8, 4.4 Hz, 1H), 1.87 (dm, *J*=14.0 Hz, 1H), 0.82 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 171.6, 141.3, 129.7, 128.3 (2×), 128.0 (2×), 127.4, 126.7, 69.5, 60.1, 46.9, 42.5, 41.1, 32.6, 26.9, 13.4; HRMS (TOF-CI$^+$) calcd for $C_{18}H_{21}O_4^+$ (M+H$^+$) 301.1440, found 301.1437.

4.10.16. Ethyl (4aS,7R*,8S*,8aR*)-1-oxo-7-phenyl-3,4,4a,7,8,8a-hexahydro-1H-isochromene-8-carboxylate (**26d**).* The minor adduct obtained, according to the general procedure F, from the triene (*Z*)-**22d** in 19% yield as a colorless solid; mp 95–96 °C (EtOAc/hexane); R_f=0.39 (25% EtOAc in hexane); IR (KBr) 2992, 2918, 1724 (br), 1450, 1407, 1244, 1220, 1194, 1068, 1029 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.24 (m, 5H), 5.92 (ddd, *J*=9.6, 1.6, 1.2 Hz, 1H), 5.80 (ddd, *J*=11.6, 4.0, 2.8 Hz, 1H), 4.52–4.40 (m, 2H), 4.27–4.16 (m, 3H), 3.44 (d, *J*=2.8 Hz, 1H), 3.07–3.00 (m, 1H), 2.25 (dd, *J*=12.0, 3.2 Hz, 1H), 2.14 (dm, *J*=12.8 Hz, 1H), 1.81 (dddd, *J*=12.4, 12.4, 12.4, 6.4 Hz, 1H), 1.31 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1, 171.5, 142.9, 130.7, 128.7 (2×), 128.0 (2×), 127.7, 127.0, 69.3, 61.1, 46.1, 43.2, 40.4, 31.4, 29.8, 14.1; MS (EI$^+$) *m*/*z* 300 (M$^+$, 5), 254 (M$^+$–EtOH, 66), 226 (100), 198 (65), 181 (62), 167 (52), 154 (45), 91 (46). Anal. Calcd for $C_{18}H_{20}O_4$: C, 71.98; H, 6.71; found C, 71.88; H, 6.68.

*4.10.17. Ethyl 4,6,7-trimethyl-1-oxo-3,4,4a,7,8,8a-hexahydro-1H-isochromene-8-carboxylates (**23e**, **24e**, **23e′**, **24e′**).* An inseparable mixture of four adducts obtained, according to the general procedure F, from the triene (*E*)-**21e** in 87% yield as a colorless oil. The ratio of **23e**/**24e**/**23e′**/**24e′** is 60:10:19:7 as measured by ^{1}H NMR spectrum of the crude products. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.35 (br s, 0.19H), 5.30 (br s, 0.64H), 5.27 (br s, 0.10H), 5.21 (br s, 0.07H) (for the vinyl protons of the four diastereomeric adducts).

*4.10.18. Ethyl 4,6,7-trimethyl-1-oxo-3,4,4a,7,8,8a-hexahydro-1H-isochromene-8-carboxylates (**25e**, **26e**, **25e′**, **26e′**).* An inseparable mixture of four adducts obtained, according to the general procedure F, from the triene (*Z*)-**22e** in 85% yield as a colorless oil. The ratio of **25e**/**26e**/**25e′**/**26e′** is 54:15:24:7 as measured by ^{1}H NMR spectrum of the crude products. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.44 (br s, 0.24H), 5.25 (br s, 0.15H), 5.22 (br s, 0.54H), 5.20 (br s, 0.07H) (for the vinyl protons of the four diastereomeric adducts).

4.10.19. Ethyl (3S,4aS*,7S*,8S*,8aS*)-3,6,7-trimethyl-1-oxo-3,4,4a,7,8,8a-hexahydro-1H-isochromene-8-carboxylates (**23f**).* The major adduct obtained, according to the general procedure F, from the triene (*E*)-**21f** in 64% yield as a colorless oil; R_f=0.41 (25% EtOAc in hexane); IR (film) 2981, 1731, 1715, 1446, 1250, 1224, 1150, 1037 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.28 (br s, 1H), 4.45–4.38 (m, 1H), 4.26–4.11 (m, 2H), 3.08 (dd, *J*=8.4, 8.4 Hz, 1H), 2.66–2.52 (m, 3H), 1.94 (ddd, *J*=10.8, 3.2, 3.2 Hz, 1H), 1.68 (s, 3H), 1.36 (d, *J*=6.4 Hz, 3H), 1.32 (br d, *J*=14.0 Hz, 1H), 1.26 (t, *J*=7.2 Hz, 3H), 1.02 (d, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.3, 172.3, 137.1, 122.1, 76.3, 60.9, 47.5, 40.4, 36.4, 35.7, 32.0, 21.6, 21.2, 17.9, 14.1; MS (EI$^+$) *m*/*z* 266 (M$^+$, 5), 220 (M$^+$–EtOH, 90), 192 (65), 177 (57), 151 (100), 133 (77), 119 (71), 106 (100), 91 (95); HRMS (EI$^+$) calcd for $C_{15}H_{22}O_4$ (M$^+$) 266.1518, found 266.1516.

4.10.20. Ethyl (3R,4aS*,7S*,8R*,8aR*)-3,6,7-trimethyl-1-oxo-3,4,4a,7,8,8a-hexahydro-1H-isochromene-8-carboxylates (**24f**).* The minor adduct obtained, according to the general procedure F, from the triene (*E*)-**21f** in 25% yield as a colorless oil; R_f=0.53 (25% EtOAc in hexane); IR (film) 2976, 2935, 1732 (br), 1449, 1385, 1256, 1186, 1122, 1054 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.25 (br s, 1H), 4.63–4.58 (m, 1H), 4.20 (q, *J*=7.0 Hz, 2H), 2.83 (dd, *J*=12.0, 6.0 Hz, 1H), 2.75 (dd, *J*=12.0, 12.0 Hz, 1H), 2.50–2.29 (m, 2H), 1.92 (ddd, *J*=12.8, 10.0, 10.0 Hz, 1H), 1.74–1.67 (m, 1H), 1.72 (s, 3H), 1.39 (d, *J*=6.4 Hz, 3H), 1.28 (t, *J*=7.2 Hz, 3H), 0.96 (d, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.7, 173.0, 137.5, 122.3, 72.4, 60.5, 44.3, 37.0, 35.6, 35.3, 33.6, 21.8, 21.0, 15.8, 14.2; MS (EI$^+$) *m*/*z* 266 (M$^+$, 16), 220 (M$^+$–EtOH, 57), 192 (40), 177 (48), 147 (95), 119 (77), 107 (100), 91 (81); HRMS (EI$^+$) calcd for $C_{15}H_{22}O_4$ (M$^+$) 266.1518, found 266.1522.

4.10.21. Ethyl (3S,4aS*,7S*,8R*,8aS*)-3,6,7-trimethyl-1-oxo-3,4,4a,7,8,8a-hexahydro-1H-isochromene-8-carboxylates (**25f**).* The major adduct obtained, according to the general procedure F, from the triene (*Z*)-**22f** in 46% yield as a colorless oil; R_f=0.52 (33% EtOAc in hexane); IR (film) 2975, 2937, 1732 (br), 1447, 1386, 1226, 1192, 1097, 1035 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.17 (br s, 1H), 4.45–4.42 (m, 1H), 4.21–4.08 (m, 2H), 3.30 (dd, *J*=10.0, 5.0 Hz, 1H), 2.93–2.84 (m, 2H), 2.58–2.51 (m, 1H), 2.05 (dd, *J*=14.0, 7.0 Hz, 1H), 1.71 (s, 3H), 1.37–1.32 (m, 1H), 1.34 (d, *J*=7.0 Hz, 3H), 1.24 (t, *J*=7.5 Hz, 3H), 1.15 (d, *J*=7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.6, 172.2, 138.2, 122.1, 74.5, 60.4, 44.5, 38.1, 37.0, 34.1, 32.3, 21.5, 21.1, 16.4, 14.1; MS (EI$^+$) *m*/*z* 266 (M$^+$, 21), 220 (M$^+$–EtOH, 72), 192 (41), 147 (86), 119 (49), 107 (100), 91 (76); HRMS (EI$^+$) calcd for $C_{15}H_{22}O_4$ (M$^+$) 266.1518, found 266.1519.

4.10.22. Ethyl (3R,4aS*,7S*,8S*,8aR*)-3,6,7-trimethyl-1-oxo-3,4,4a,7,8,8a-hexahydro-1H-isochromene-8-carboxylates (**26f**).* The minor adduct obtained, according to the general procedure F, from the triene (*Z*)-**22f** in 25% yield as a colorless oil; R_f=0.58 (33% EtOAc in hexane); IR (film) 2976, 2935, 1732 (br), 1454, 1380, 1220, 1183, 1156, 1127, 1028 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.24 (br s, 1H), 4.72 (qdd, *J*=6.5, 6.5, 4.0 Hz, 1H), 4.18–4.08 (m, 2H), 3.12 (d, *J*=3.0 Hz, 1H), 3.10–3.04 (m, 1H), 2.65 (q, *J*=7.0 Hz, 1H), 2.27 (dd, *J*=12.0, 3.0 Hz, 1H), 1.86 (ddd, *J*=13.3, 5.5, 4.0 Hz, 1H), 1.80–1.74 (m, 1H), 1.70 (br s, 3H), 1.45 (d, *J*=7.0 Hz, 3H), 1.24 (t, *J*=7.5 Hz, 3H), 1.20 (d, *J*=7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.9, 172.5, 137.6, 123.7, 74.7, 60.7, 44.6, 40.0, 37.0, 35.2, 27.9, 22.0, 21.9, 20.5, 14.1; MS (EI$^+$) *m*/*z* 266 (M$^+$, 5), 220 (M$^+$–EtOH, 47), 192 (45), 147 (100), 119 (85), 107 (89), 91 (67); HRMS (EI$^+$) calcd for $C_{15}H_{22}O_4$ (M$^+$) 266.1518, found 266.1522.

4.10.23. (4aS,8S*,8aS*)-8-Benzoyl-3,4,4a,7,8,8a-hexahydro-1H-isochromene-1-one (**23h**).* The major adduct obtained, according to the general procedure F, from the triene (*E*)-**21h** in 63% yield as a colorless solid; mp 95–96 °C (EtOAc/hexane); R_f=0.33 (20% EtOAc in hexane); IR (KBr) 2958, 2908, 1725, 1683, 1445, 1265, 1148 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J*=7.2 Hz, 2H), 7.57 (t, *J*=7.2 Hz, 1H), 7.48 (dd, *J*=7.6, 7.6 Hz, 2H), 5.88–5.84 (m, 1H), 5.54 (dd, *J*=10.4, 2.0 Hz, 1H), 4.46–4.45 (m, 1H), 4.30 (dd, *J*=9.2, 4.0 Hz, 2H), 3.20 (dd, *J*=7.2, 2.0 Hz, 1H), 2.94 (br s, 1H), 2.46–2.44 (m, 2H), 2.17–2.09 (m, 1H), 1.77–1.71 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.1, 172.3, 135.3, 132.9, 128.7 (2×), 128.3 (2×), 127.4, 127.2, 66.4, 41.0, 40.5, 28.4, 28.2, 23.2; MS (EI$^+$) *m*/*z* 256 (M$^+$, 11), 228 (M$^+$–CO, 15), 183 (11), 151 (90), 105 (100), 77 (83). Anal. Calcd for $C_{16}H_{16}O_3$: C, 74.98; H, 6.29; found C, 74.92; H, 6.07.

4.10.24. (4aS,8R*,RaS*)-8-Benzoyl-3,4,4a,7,8,8a-hexahydro-1H-isochromene-1-one (**24h**).* The minor adduct obtained, according to the general procedure F, from the triene (*E*)-**21h** in 27% yield as a colorless solid; mp 74–76 °C (EtOAc/hexane); R_f=0.22 (20% EtOAc in hexane); IR (KBr) 2924, 1733, 1679, 1296, 1206, 1178 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J*=7.6 Hz, 2H), 7.57 (t, *J*=7.6 Hz, 1H), 7.48 (dd, *J*=7.6, 7.6 Hz, 2H), 5.77–5.74 (m, 1H), 5.68 (d, *J*=9.6 Hz, 1H), 4.44–4.40 (m, 2H), 3.81 (ddd, *J*=16.0, 5.2, 5.2 Hz, 1H), 3.10 (dd, *J*=12.0, 11.2 Hz, 1H), 2.63–2.55 (m, 1H), 2.50–2.44 (m, 1H), 2.33 (dddd, *J*=13.6, 8.0, 8.0, 8.0 Hz, 1H), 2.20–2.12 (m, 1H), 1.78–1.69 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.7, 173.6, 136.5, 132.9, 128.5 (3×), 128.3 (2×), 125.5, 65.7, 43.2, 40.7, 32.8, 29.8, 27.8; MS (EI$^+$) *m*/*z*

256 (M^+, 44), 151 (25), 105 (100), 77 (94). Anal. Calcd for $C_{16}H_{16}O_3$: C, 74.98; H, 6.29; found: C, 74.91; H, 6.23.

4.10.25. (4aS,7S*,8aR*)-6,7-Dimethyl-3,4,4a,7,8,8a-hexahydro-1H-isochromene-1-one (**23i**).* The major adduct obtained, according to the general procedure F, from the triene (*E*)-**21i** in 65% yield as a colorless oil; R_f=0.30 (20% EtOAc in hexane); IR (film) 2961, 1731 (br), 1444, 1399, 1247, 1213, 1089, 1066 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.27 (br s, 1H), 4.38 (ddd, *J*=11.2, 4.4, 4.4 Hz, 1H), 4.24 (ddd, *J*=10.8, 10.8, 3.2 Hz, 1H), 2.78 (ddd, *J*=10.8, 6.0, 3.6 Hz, 1H), 2.55 (br s, 1H), 2.23–2.17 (m, 1H), 2.06 (ddd, *J*=13.2, 4.8, 4.4 Hz, 1H), 1.84 (dq, *J*=14.4, 3.6 Hz, 1H), 1.77–1.70 (m, 1H), 1.68 (s, 3H), 1.67–159 (m, 1H), 1.02 (d, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.4, 140.3, 122.6, 68.8, 39.7, 33.6, 32.9, 27.5, 21.1, 19.2; MS (EI^+) *m*/*z* 180 (M^+, 78), 152 (M^+–CO, 47), 121 (40), 107 (100), 93 (100), 79 (66); HRMS (ESI^+) calcd for $C_{11}H_{17}O_2$ ($M+H^+$): 181.1229; found 181.1216.

4.10.26. (4aS,7S*,8aS*)-6,7-Dimethyl-3,4,4a,7,8,8a-hexahydro-1H-isochromene-1-one (**24i**).* The minor adduct obtained, according to the general procedure F, from the triene (*E*)-**21i** in 5% yield as a white solid; mp 72–74 °C (EtOAc/hexane); R_f=0.38 (20% EtOAc in hexane); IR (KBr) 2961, 1732 (br), 1454, 1399, 1273, 1191, 1124, 1078 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.25 (s, 1H), 4.45–4.32 (m, 2H), 2.40–2.01 (m, 5H), 1.74 (dd, *J*=12.8, 6.4 Hz, 1H), 1.70–1.64 (m, 1H), 1.69 (s, 3H), 1.08 (d, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.4, 139.9, 123.4, 68.0, 38.5, 35.2, 33.5, 30.1, 29.2, 21.8, 19.8; MS (EI^+) *m*/*z* 180 (M^+, 35), 152 (M^+–CO, 37), 135 (55), 121 (40), 107 (100), 93 (80), 79 (51); HRMS (ESI^+) calcd for $C_{11}H_{17}O_2$ ($M+H^+$): 181.1229; found 181.1219.

4.11. General procedure G for microwave-assisted tandem Wittig–IMDA cycloaddition

To a 10-mL pressurized process vial was added the 3,5-hexadien-1-yl α-bromoacetate **5** (0.30 mmol), PPh_3 (0.39 mmol), 2,6-lutidine (0.39 mmol), methyl/ethyl glyoxalate or phenylglyoxal hydrate **6** (0.9 mmol), and MeCN (4 mL). The loaded vial was then sealed with a cap containing a silicon septum, and put into the microwave cavity and heated at 180 °C for 1–1.5 h. The reaction mixture was diluted with EtOAc and washed with saturated aqueous NH_4Cl and brine. The organic layer was dried over anhydrous Na_2SO_4, filtered, and evaporated under reduce pressure. The residue was checked for adduct isomer ratio by ^1H NMR spectrum and was then purified by flash column chromatography (silica gel, eluted with 10–20% EtOAc in PE) to give the desired products. The structures, isomer ratios, and yields are found in Scheme 4 and entries 1–8 of Table 2. For the reaction in entry 9 of Table 2, 37 wt % aqueous formaldehyde solution (0.9 mmol) was used and the reaction was carried out at 160 °C for 2.5 h.

4.11.1. (4aS,7S*,8S*,8aS*)-8-Benzoyl-6,7-dimethyl-3,4,4a,7,8,8a-hexahydro-1H-isochromene-1-one (**23g**).* The major adduct obtained, according to the general procedure G, from the α-bromoacetate **5g** and phenylglyoxal hydrate in 60% yield as a colorless oil; R_f=0.46 (25% EtOAc in hexane); IR (film) 2967, 2918, 1728, 1682, 1447, 1272, 1169, 1149 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J*=7.6 Hz, 2H), 7.56 (t, *J*=7.2 Hz, 1H), 7.47 (dd, *J*=7.6, 7.2 Hz, 2H), 5.17 (br s, 1H), 4.40–4.25 (m, 3H), 3.16 (dd, *J*=8.0, 3.2 Hz, 1H), 2.86 (br s, 1H), 2.49 (q, *J*=7.6 Hz, 1H), 2.10–2.01 (m, 1H), 1.78–1.68 (m, 1H), 1.73 (s, 3H), 1.18 (d, *J*=7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.2, 172.8, 140.3, 135.7, 133.0, 128.8 (2×), 128.4 (2×), 121.2, 66.5, 49.0, 39.0, 34.2, 29.6, 28.5, 22.2, 20.1; MS (ESI^+) *m*/*z* 307 ($M+Na^+$, 100); HRMS (ESI^+) calcd for $C_{18}H_{20}O_3Na^+$ ($M+Na^+$) 307.1310; found 307.1296.

4.11.2. (4aS,7S*,8R*,8aR*)-8-Benzoyl-6,7-dimethyl-3,4,4a,7,8,8a-hexahydro-1H-isochromene-1-one (**24g**).* The minor adduct obtained, according to the general procedure G, from the α-bromoacetate **5g** and phenylglyoxal hydrate in 31% yield as a white solid; R_f=0.36 (25% EtOAc in hexane); IR (KBr) 2970, 2937, 1743, 1682, 1449, 1299, 1171 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J*=7.6 Hz, 2H), 7.57 (t, *J*=7.2 Hz, 1H), 7.47 (dd, *J*=7.6, 7.2 Hz, 2H), 5.35 (br s, 1H), 4.46–4.42 (m, 2H), 3.89 (dd, *J*=11.2, 5.6 Hz, 1H), 3.06 (dd, *J*=12.0, 12.0 Hz, 1H), 2.52–2.23 (m, 3H), 1.74 (s, 3H), 1.69–1.60 (m, 1H), 0.85 (d, *J*=6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.3, 174.7, 137.9, 136.5, 133.0, 128.7 (2×), 128.3 (2×), 122.5, 65.0, 45.2, 38.0, 35.6, 33.8, 27.7, 22.0, 15.7; MS (EI^+) *m*/*z* 284 (M^+, 20), 179 (25), 150 (15), 133 (20), 105 (100), 77 (65). Anal. Calcd for $C_{18}H_{20}O_3$: C, 76.03; H, 7.09; found C, 76.05; H, 7.03. The relative stereochemistry of **24g** has been confirmed by X-ray crystal structural analysis.[17]

Acknowledgements

The Laboratory of Asymmetric Catalysis and Synthesis is established under the Cheung Kong Scholars Program of The Ministry of Education of China. This work is supported in part by the research grants from The National Natural Science Foundation of China (Grant No. 20572092), Zhejiang University, and Zhejiang University Education Foundation. The authors thank Mr. Jianming Gu of the X-ray crystallographic facility of Zhejiang University for assistance on crystal structure analysis. Dr. Jian Jin is thanked for helping on some experiments.

Supplementary data

Supplementary data associated with this article can be found in online version at doi:10.1016/j.tet.2010.02.096. These data include MOL files and InChIKeys of the most important compounds described in this article.

References and notes

1. For selected reviews on IMDA reaction, see: (a) Taber, D. F. *Intramolecular Diels–Alder and Alder Ene Reactions*; Springer: Berlin, 1984; (b) Fallis, A. G. *Can. J. Chem.* **1984**, *62*, 183–234; (c) Ciganek, E. *Org. React.* **1984**, *32*, 1–374; (d) Craig, D. *Chem. Soc. Rev.* **1987**, 187–238; (e) Roush, W. R. In *Advances in Cycloaddition*; Curran, D. P., Ed.; JAI: Greenwich, CT, 1990; Vol. 2, pp 91–142; (f) Roush, W. R. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Paquette, L. A., Eds.; Pergamon: Oxford, 1991; Vol. 5, pp 513–550; (g) Craig, D. Stereoselective Synthesis (Houben-Weyl) No E21c In *Methods of Organic Chemistry*, 4th ed.; Helmchen, G., Hoffmann, R. W., Mulzer, J., Schumann, E., Eds.; Thieme: Stuttgart, 1995, pp 2872–2904; (h) Fallis, A. G. *Acc. Chem. Res.* **1999**, *32*, 464–474; (i) Bear, B.; Sparks, S. M.; Shea, K. J. *Angew. Chem., Int. Ed.* **2001**, *40*, 820–849; (j) Stocking, E. M.; Williams, R. M. *Angew. Chem., Int. Ed.* **2003**, *42*, 3078–3115; (k) Takao, K.; Munakata, R.; Tadano, K. *Chem. Rev.* **2005**, *105*, 4779–4807.
2. For thermal IMDA of ester-tethered 1,3,9-decatrienes, see: (a) Martin, S. F.; Williamson, S. A.; Gist, R. P.; Smith, K. M. *J. Org. Chem.* **1983**, *48*, 5170–5180; (b) Nugent, W. A.; Thorn, D. L.; Harlow, R. L. *J. Am. Chem. Soc.* **1987**, *109*, 2788–2796; (c) Hoshino, O.; Ishizaki, M.; Kamei, K.; Taguchi, M.; Nagao, T.; Iwaoka, K.; Sawaki, S.; Umezawa, B.; Iitaka, Y. *J. Chem. Soc., Perkin Trans. 1* **1996**, 571–580; (d) Jung, M. E.; Huang, A.; Johnson, T. W. *Org. Lett.* **2000**, *2*, 1835–1837; (e) Ritter, N.; Metz, P. *Synlett* **2003**, 2422–2424; (f) Bruyère, H.; Samaritani, S.; Ballereau, S.; Tomas, A.; Royer, J. *Synlett* **2005**, 1421–1424.
3. For thermal IMDA of ester-tethered 1,3,9-decatrienes possessing a C10-activating group, see: (a) Boeckman, R. K., Jr.; Demko, D. M. *J. Org. Chem.* **1982**, *47*, 1789–1792; (b) Mori, K.; Gupta, A. K. *Tetrahedron* **1985**, *41*, 5295–5299; (c) Chen, C.-Y.; Hart, D. J. *J. Org. Chem.* **1993**, *58*, 3840–3849; (d) Kim, P.; Hantz, M. H.; Kurth, M. J.; Olmstead, M. M. *Org. Lett.* **2000**, *2*, 1831–1834; (e) Inoue, S.; Yin, C.; Kosugi, H.; Nabeta, A.; Sakai, Y.; Honda, K.; Hoshino, Y. *Bull. Chem. Soc. Jpn.* **2008**, *81*, 1308–1314.
4. For IMDA of ester-tethered 1,3,9-decatrienes under Lewis acid catalysis or non-conventional conditions, see: (a) Alexakis, A.; Jachiet, D.; Toupet, L. *Tetrahedron* **1989**, *45*, 6203–6210; (b) Chen, C.-Y.; Hart, D. J. *J. Org. Chem.* **1990**, *55*, 6236–6240; (c) Saito, A.; Ito, H.; Taguchi, T. *Org. Lett.* **2002**, *4*, 4619–4621; (d) Saito, A.; Yanai, Y.; Taguchi, T. *Tetrahedron* **2004**, *60*, 12239–12247; (e) Saito, A.; Yanai, H.; Sakamoto, W.; Takahashi, K.; Taguchi, T. *J. Fluorine Chem.* **2005**, *126*, 709–714; (f) Yanai, H.; Saito, A.; Taguchi, T. *Tetrahedron* **2005**, *61*, 7087–7093; (g) Taguchi, T.; Saito, A.; Yanai, H. *Chem. Rec.* **2007**, *7*, 167–179; (h) Yanai, H.; Ogura, H.; Taguchi, T. *Org. Biomol. Chem.* **2009**, *7*, 3657–3659 For IMDA cycloaddition catalyzed by an *N*-protonated chiral oxazaborolidine, see: (i) Zhou, G.; Hu, Q.-Y.; Corey, E. J. *Org. Lett.* **2003**, *5*, 3979–3982 Also see Refs. 2e,3c.

5. For computational calculations on IMDA of ester-tethered 1,3,9-decatrienes, see: (a) Tantillo, D. J.; Houk, K. N.; Jung, M. E. *J. Org. Chem.* **2001**, *66*, 1938–1940; (b) Jones, G. A.; Paddon-Row, M. N.; Sherburn, M. S.; Turner, C. I. *Org. Lett.* **2002**, *4*, 3789–3792 and correction,; *Org. Lett.* **2005**, *7*, 4547; (c) Pearson, E. L.; Kwan, L. C. H.; Turner, C. I.; Jones, G. A.; Willis, A. C.; Paddon-Row, M. N.; Sherburn, M. S. *J. Org. Chem.* **2006**, *71*, 6099–6109; (d) Pearson, E. L.; Willis, A. C.; Sherburn, M. S.; Paddon-Row, M. N. *Org. Biomol. Chem.* **2008**, *6*, 513–522.
6. (a) Wu, J.; Sun, L.; Dai, W.-M. *Tetrahedron* **2006**, *62*, 8360–8372; (b) Wu, J.; Yu, H.; Wang, Y.; Xing, X.; Dai, W.-M. *Tetrahedron Lett.* **2007**, *48*, 6543–6547; (c) Wang, Y.; Wu, J.; Dai, W.-M. *Synlett* **2009**, 2862–2866.
7. Martin, S. F.; Tu, C.-Y.; Chou, T.-S. *J. Am. Chem. Soc.* **1980**, *102*, 5274–5279.
8. Couturier, M.; Dory, Y. L.; Rouillard, F.; Deslongchamps, P. *Tetrahedron* **1998**, *54*, 1529–1562.
9. Wu, P.-L.; Chung, T.-H.; Chou, Y. *J. Org. Chem.* **2001**, *66*, 6585–6594.
10. Page, P. C. B.; Vahedi, H.; Batchelor, K. J.; Hindley, S. J.; Edgar, M.; Beswick, P. *Synlett* **2003**, 1022–1024.
11. Spate, S. M.; Stone, H. *J. Org. Chem.* **1958**, *23*, 1559–1560.
12. Sabitha, G.; Srividya, R.; Yadav, J. S. *Tetrahedron* **1999**, *55*, 4015–4018. Also see Ref. 11.
13. Paulvannan, K.; Jacobs, J. W. *Tetrahedron Lett.* **1999**, *55*, 7433–7440.
14. The *E*- and *Z*-substituted diesters of the diene alcohol **13** were prepared similarly. But the results are not included here because their IMDA adducts could not be separated by flash column chromatography.
15. Jiang, X. Q.; Wu, J.-L. *Acta Crystallogr.* **2010**, *E66*, o1367.
16. (a) Hursthouse, M. B.; Malik, K. M. A.; Hibbs, D. E.; Roberts, S. M.; Seago, A. J. H.; Sik, V.; Storer, R. *J. Chem. Soc., Perkin Trans. 1* **1995**, 2419–2425; (b) Bailey, P. D.; Smith, P. D.; Pederson, F.; Clegg, W.; Rosaira, G. M.; Teat, S. J. *Tetrahedron Lett.* **2002**, *43*, 1067–1070.
17. The X-ray crystal data (excluding structure factors) of compound **24g**, given in Fig. 3, have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no CCDC 785558. Copy of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44 (0) 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk).
18. The adducts **23j**/**24j** were obtained from the triene **21j** in 42% combined yield and in 90:10 dr by heating in xylene at 210 °C for 5 h as reported in Ref. 2a.