Available online at www.sciencedirect.com
SCIENCE DIRECT®
Tetrahedron 61 (2005) 7087–7093
Tetrahedron
ELSEVIER

Intramolecular Diels–Alder reaction of 1,7,9-decatrienoates catalyzed by indium(III) trifluoromethanesulfonate in aqueous media

Hikaru Yanai, Akio Saito and Takeo Taguchi*

School of Pharmacy, Tokyo University of Pharmacy and Life Science, 1432-1 Horinouchi, Hachioji, Tokyo 192-0392, Japan

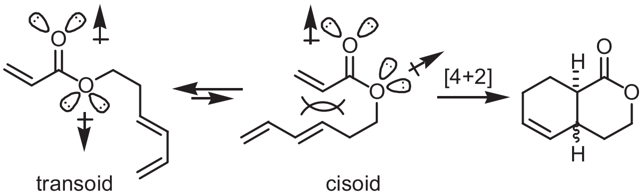
Received 30 April 2005; revised 16 May 2005; accepted 17 May 2005

Abstract—The intramolecular Diels–Alder reaction of ester-tethered 1,7,9-decatrienoate derivatives in a mixture of water and 2-propanol was catalyzed by indium(III) triflate to give the cycloadducts in good yield with perfect *endo*-selectivity.

1. Introduction

Nowadays, the use of aqueous media or water as a sole solvent has been attracting much interest not only from the viewpoint of green chemistry, but also due to a number of examples of highly regio- and/or stereoselective reactions achieved specifically in aqueous solvent.[1] These involves synthetically important carbon–carbon bond forming reactions such as allylation of carbonyl compounds,[2] aldol reaction,[3] Diels–Alder reaction[4] and the transition metal catalyzed cross-coupling reactions.[5,6] Furthermore, during these days extensive efforts have been made to develop a variety of Lewis acid catalyzed reactions using rare earth metal triflates[7,8] such as $Sc(OTf)_3$ and $Yb(OTf)_3$ or indium(III) salts[9] which are found to work efficiently in aqueous media or in water.

Study on the intramolecular Diels–Alder (IMDA) reactions of ester-tethered trienoate derivatives is one of our ongoing research projects. It is well documented that contrary to hydrocarbon substrates or amide-tethered substrates, ester-tethered triene compounds show lower reactivity in the IMDA reaction due to the conformational preference of the transoid form over the cisoid form in which the diene and dienophile are in close proximity required for the reaction to proceed. This fact is explained by repulsive dipole interaction between the two oxygen atoms in ester moiety and steric repulsion between the two alkyl substituents existing in the carboxylic acid part and in the alcohol part (Scheme 1).[10,11] Towards to this issue, we have reported that bis-aluminated triflic amide $TfN[Al(Me)Cl]_2$, a novel bidentate Lewis acid, efficiently promoted the IMDA reaction of 1,7,9-decatrienoate derivatives presumably due to the restriction to the cisoid conformation in some extent and decrease in LUMO level of dienophile part through the bidentate coordination of the ester group,[12,13] although in some cases stoichiometric amount of this aluminated triflic amide was essentially needed for the smooth reaction. Continuously, we have focused our attention to find out more efficient Lewis acid. It was demonstrated by several examples that in a highly polar solvent such as water or DMSO, repulsive dipole interaction between the two oxygen atoms in the ester moiety may be weakened, thereby the energy difference between the transoid geometry and the cisoid geometry in polar solvent should be smaller than that in non-polar solvent. For example, Jung et al. reported that the IMDA reaction of the ester-tethered trienoate derivatives in DMSO[14] and Oshima et al. reported the intramolecular radical addition reaction of alkenyl iodoacetate in water.[15] Both reactions were found to efficiently proceed by using such polar solvent. Taking into account this polar solvent effect on the conformation of ester compounds, we examined the IMDA reaction of 1,7,9-



Scheme 1. IMDA reaction of ester-tethered trienoate derivative.

Keywords: Intramolecular Diels–Alder reaction; 1,7,9-Decatrienoates; Indium(III)triflate; Aqueous media.

---

* Corresponding author. Tel./fax: +81 426 76 3257; e-mail: taguchi@ps.toyaku.ac.jp

0040–4020/$ - see front matter © 2005 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2005.05.062

decatrienoates in aqueous media using various water-compatible Lewis acids and as a result, $In(OTf)_3$ (20 mol%) was found to nicely catalyze the reaction. Detail is reported in this paper.

2. Results and discussion

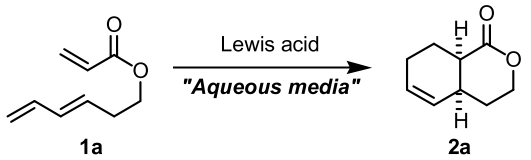
The IMDA reaction of (3*E*)-3,5-hexadienyl acrylate **1a** was conducted to examine the efficiency of various water-compatible Lewis acids. Results are summarized in Table 1. In a mixture of water and 2-propanol (6:1 v/v) reaction of **1a** in the presence of stoichiometric amount of $Sc(OTf)_3$ at 60 °C for 24 h gave the IMDA product **2a** in low yield (8% yield, entry 1). $Yb(OTf)_3$ also gave similar result (11% yield, entry 2). Any appreciable improvement in the yield of **2a** was not realized by the use of $Gd(OTf)_3$, $Ho(OTf)_3$, $Cu(OTf)_2$, $Zn(OTf)_2$, AgOTf. On the other hand, $InCl_3$ promoted the reaction efficiently to give **2a** in 51% yield with complete *endo*-selectivity after 12 h at 60 °C, although 100 mol% $InCl_3$ was used (entry 3). As shown in entries 4–6, with catalytic amount of $In(OTf)_3$ the reaction proceeded smoothly. That is, the use of 20 mol% $In(OTf)_3$ at 70 °C for 12 h resulted in the isolation of **2a** in 82% yield (entry 5), while in the cases of either 100 or 10 mol% of $In(OTf)_3$ yields of **2a** were lowered to 56 and 60%, respectively and in the latter case the reaction rate significantly decreased (entries 4 and 6).

Concerning the co-solvent, 2-propanol gave the best result (entry 5), while the product yield lowered to 39 and 52%, respectively when methanol or 2-methyl-2-propanol was used (entries 7 and 8). It should be noted that in the $In(OTf)_3$ catalyzed IMDA reaction of **1a** aqueous media is crucial to obtain the product **2a** in good yield. For example, reaction in 2-propanol under the similar conditions provided **2a** in low yield (39%, entry 9). Reaction in aprotic solvent such as 1,2-dichloroethane failed to obtain **2a**, but gave a complex mixture (entry 10). To check if a trace amount of trifluoromethanesulfonic acid (TfOH) liberated from $In(OTf)_3$ acts as a Brønsted acid catalyst, reaction was conducted in the presence of 0.6 M equiv of TfOH, but the yield of **2a** was only 47% (entry 11). This result should indicate that the IMDA reaction is catalyzed by $In(OTf)_3$ in this aqueous media.

Next, we examined the effect of the ratio of water on the product yield. Results are shown in Figure 1 by plotting the yield of **2a** on *y* axis and the water-content (H_2O in 2-propanol, vol%) on *x* axis. The best result was obtained when the ratio of H_2O–$^{i}PrOH$ was 6:1 (85.7 v/v%, 82% yield, entry 6). Increase in water content resulted in a remarkable drop of the product yield and without 2-propanol, namely in water **2a** was formed only in 20% yield (entries 7 and 8). As the water content decreased to 80, 75 and 50 v/v%, the yield of **2a** was also gradually lowered to 71, 64 and 34%, respectively (entries 3–5), and when the water content was between 50 and 0 v/v%, very little difference in the product yield was observed keeping in a range of 35–40% yield (entries 1–3).

To see the scope and limitation of the $In(OTf)_3$ catalyzed IMDA reaction in aqueous media, we examined the IMDA reaction of 1,7,9-decatrienoates **1b–g** having a different substituent pattern. Results are summarized in Table 2. Compared to the model substrate **1a**, 5-methyl derivative **1b** (R^1 = Me, $R^{2–5}$ = H) showed a similar reactivity to give the *endo*-adduct **2b** as a single isomer after 8 h at 70 °C (76% yield, entry 1). The IMDA reaction of 6,10-dimethylated substrate **1c** ($R^{2,4}$ = Me, $R^{1,3,5}$ = H) and 8-methylated substrate **1d** (R^3 = Me, $R^{1,2,4,5}$ = H) gave products **2c** and **2d** in 71 and 83% yield, respectively (entries 2 and 3). The IMDA adduct **2c** was a mixture of two diastereomers, and the stereochemistry of the major one was determined to have *cis*-relationship between angular hydrogen and 6-methyl group (*cis*/*trans* = 4.9:1). The reaction of 10-methyl derivative **1e** (R^4 = Me, $R^{1–3,5}$ = H) required longer time (24 h) and higher temperature (80 °C) to give the IMDA product **2e** in moderate yield (68%, entry 4), and the reaction of more lipophilic 10-propyl derivative **1f** required much longer reaction time even at higher temperature (under reflux condition) to give **2f** in only 18% yield (entry

Table 1. Effect of Lewis acids on IMDA reaction of (3*E*)-3,5-hexadienyl acrylate (**1a**)

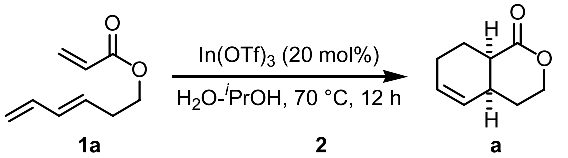


Entry	Lewis acid (mol%)	Solvent	Temp. (°C)	Time (h)	Yield (%)[a]
1	$Sc(OTf)_3$ (100)	H_2O–$^{i}PrOH$ (6:1)	60	24	8
2	$Yb(OTf)_3$ (100)	H_2O–$^{i}PrOH$ (6:1)	60	24	11
3	$InCl_3$ (100)	H_2O–$^{i}PrOH$ (6:1)	60	12	51
4	$In(OTf)_3$ (100)	H_2O–$^{i}PrOH$ (6:1)	70	12	56
5	$In(OTf)_3$ (20)	H_2O–$^{i}PrOH$ (6:1)	70	12	82
6[b]	$In(OTf)_3$ (10)	H_2O–$^{i}PrOH$ (6:1)	70	12	60
7	$In(OTf)_3$ (20)	H_2O–MeOH (6:1)	70	12	39
8	$In(OTf)_3$ (20)	H_2O–$^{t}BuOH$ (6:1)	70	12	52
9	$In(OTf)_3$ (20)	$^{i}PrOH$	70	12	39
10[c]	$In(OTf)_3$ (20)	$ClCH_2CH_2Cl$	70	12	—
11	TfOH (60)	H_2O–$^{i}PrOH$ (6:1)	70	12	47

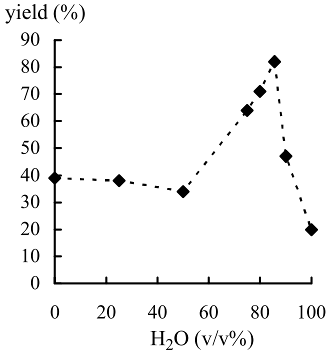
[a] Isolated yield.

[b] 87% conversion.

[c] Complex mixture was obtained.



1a **2** **a**



Entry	H_2O (v/v%)	Yield[a] (%)
1	0	39
2	25	38
3	50	34
4	75	64
5	80	71
6	85.7	82
7	90	47
8	100	20

[a] Isolated yield.

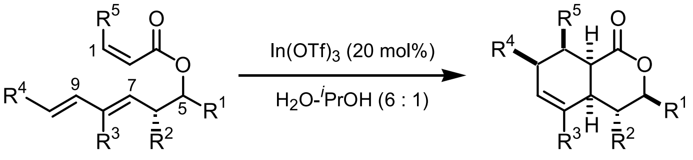
Figure 1. The plots of the yield and the water-content (H_2O in 2-propanol, volume %) on the IMDA reaction of **1a**.

5). The reaction of reactive maleic monoester **1g** proceeded at room temperature to give the product **2g** in 78% yield as a single isomer (entry 6).

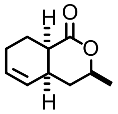
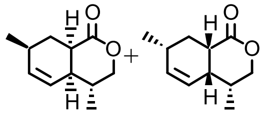
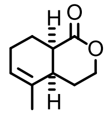
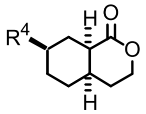
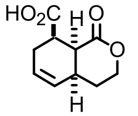
Since the present $In(OTf)_3$ catalyzed IMDA reaction smoothly proceeded with the 1,7,9-decatrienoate derivative having active hydrogen as in the case of carboxylic acid **1g**, the reaction of the substrate having C6-hydroxyl group **1h** was conducted (Scheme 2).[16] In this case the IMDA reaction and the simultaneous ring-contraction from the six membered lactone to the five membered lactone occurred to give the *cis*-fused oxabicyclo[4.3.0]nonene compound **2h** in 55% yield as a mixture of diastereomers in a ratio of *cis*/*trans*=2.8:1. Since the relative configuration between the angular hydrogen atom and the hydroxymethyl group in the major diastereomer was confirmed to be *cis*, this major isomer **2h**-*cis* was possibly formed through the IMDA reaction via *endo*-boat axial transition state leading to the *cis*-fused oxabicyclo[4.4.0]decene derivative **B**, which, in turn, re-lactonized stereospecifically to the thermodynamically stable five membered ring system **2h**-*cis*.[17] Likewise, the formation of the minor isomer **2h**-*trans*, which has the *trans* configuration between the hydroxymethyl group and the angular hydrogen atom, can be explained by considering the *endo*-boat equatorial transition state in the IMDA reaction steps followed by the re-lactonization. Since it was reported that diastereo (*endo*/*exo*) control in the IMDA reaction of 1,6,8-nonatrienoate derivatives is quite difficult, our present result provides a highly *endo*-selective and convenient mean for oxabicyclo[4.3.0]nonene system.[18]

Since certain examples demonstrated that indium(III) salts were recyclable Lewis acids,[9] we also examined recycling experiment of $In(OTf)_3$ used in the IMDA reaction of trienoate **1d** as a model substrate (Scheme 3). Extraction of the reaction mixture of the first run with diethyl ether left the aqueous phase, which without any modification was used for the second run giving rise to the IMDA product **2d** in the comparable yield (78%) to that obtained in the first run.

Table 2. IMDA reaction of 1,7,9-decatrienoate derivatives in aqueous media

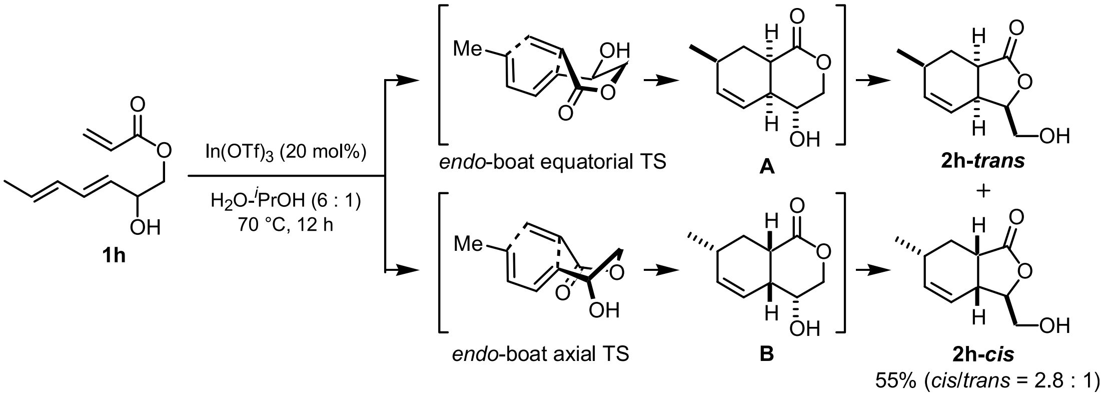


1 **2**

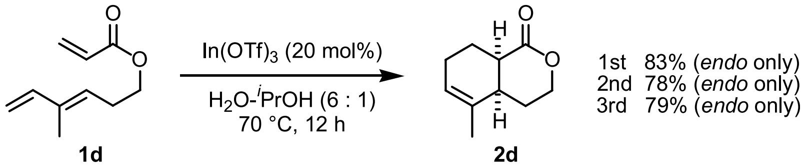
Entry	**1**	R^1	R^2	R^3	R^4	R^5	Temp. (°C)	Time (h)	Products **2**		Yield (%)[a]
1	**1b**	Me	H	H	H	H	70	8	**2b**		76
2	**1c**	H	Me	H	Me	H	70	14	**2c**		71[b]
3	**1d**	H	H	Me	H	H	70	12	**2d**		83
4	**1e**	H	H	H	Me	H	80	24	**2e**		68
5	**1f**	H	H	H	*n*-Pr	H	Reflux	24	**2f**		18
6	**1g**	H	H	H	H	CO_2H	rt	24	**2g**		78

[a] Isolated yield.

[b] *cis*/*trans*=4.9:1 based on isolated yield.



Scheme 2. IMDA reaction of 6-hydroxy substrate (**1h**).



Scheme 3. Recycling experiment of In(OTf)$_3$.

Likewise, in the third run **2d** was also isolated in essentially similar yield (79%), indicating that In(OTf)$_3$ was recyclable catalyst for the present IMDA reaction.

Finally, the effect of In(OTf)$_3$ on the IMDA reaction of acrylamide derivative **1i** was examined (Scheme 4). The IMDA reaction of amide-tethered substrate **1i** under thermal conditions was reported by Martin et al.[19] to proceed in toluene at 85 °C for 12 h to give a mixture of **2i**-*endo* and **2i**-*exo* in 63% yield (*endo*/*exo* = 6.9:1). 20 mol% In(OTf)$_3$ catalyzed reaction in a mixture of water and 2-propanol (6:1 v/v) proceeded at lower temperature (50 °C, 12 h) to give the cycloadduct **2i**-*endo* as a sole stereoisomer (74% yield). On the other hand, the use of bidentate Lewis acid TfN[Al(Me)Cl]$_2$ reduced the yield of product **2i** (41% yield).

3. Conclusion

We have demonstrated that catalytic amount of In(OTf)$_3$ in a mixture of water and 2-propanol can promote the IMDA reaction of the various 1,7,9-decatrienoate derivatives to give the corresponding cycloadducts in good yield with perfect *endo*-selectivity. Since the present reaction proceeds quite nicely in water and 2-propanol as environmentally friendly solvents and In(OTf)$_3$ used as the catalyst is recyclable without troublesome purification, these results provide useful examples from a viewpoint of green chemistry.

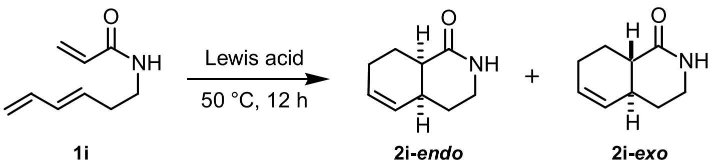
4. Experimental

4.1. General

Indium(III) trifluoromethanesulfonate is available commercially. All reactions were carried out under argon atmosphere. ^1H NMR (400 MHz) and ^{13}C NMR (100.6 MHz) spectra were recorded on a 400 MHz spectrometer, and chemical shifts were reported in parts per million (ppm) using $CHCl_3$ (7.26 ppm) in $CDCl_3$ for ^1H NMR, and $CDCl_3$ (77.01 ppm) for ^{13}C NMR as an internal standard, respectively. Mass spectra (MS) were obtained by EI or ESI technique. Medium pressure liquid chromatography (MPLC) was performed using pre-packed column (silica gel, 50 μm) with UV or RI detector.

4.2. General procedure for preparation of 1,7,9-decatrienoate derivatives: (3*E*,5*E*)-3,5-heptadienyl acrylate (1e)

After a suspension of (3-hydroxypropyl)triphenyl-phosphonium bromide[20] (7.06 g, 17.0 mmol) in THF (25 mL)



In(OTf)$_3$ (20 mol%)	H_2O-^{i}PrOH (6 : 1)	50 °C	74% (*endo* only)
TfN[Al(Me)Cl]$_2$ (110 mol%)	$ClCH_2CH_2Cl$	50 °C	41% (*endo* only)
none (ref. 19)	toluene	85 °C	63% (*endo*/*exo* = 6.9 : 1)

Scheme 4. IMDA reaction of N–H acrylamide derivative (**1i**).

was treated with lithium bis(trimethylsilyl)amide (LHMDS, 35 mL, 1.0 M in THF) for 1 h at 0 °C, crotonaldehyde (2.80 g, 40.0 mmol) was added at 0 °C. The reaction mixture was stirred for 3 h at 0 °C. After usual work-up (extracted with Et_2O, dried over $MgSO_4$, and concentrated under reduced pressure), the residue was purified by flash column chromatography on silica gel (hexane/Et_2O = 15:1) to give (3*E*,5*E*)-3,5-heptadien-1-ol (1.03 g, 9.18 mmol, 54% yield) as colorless oil. ^1H NMR spectrum of this compound was identical with that reported in the literature.[21] To a solution of this dienyl alcohol (561 mg, 5.0 mmol) in CH_2Cl_2 (10 mL), acryloyl chloride (0.45 mL, 5.5 mmol) and triethylamine (0.83 mL, 6.0 mmol) were added at 0 °C. After being stirred at room temperature for 2 h, the reaction mixture was quenched by H_2O and extracted with Et_2O (10 mL × 3). The organic layer was washed with brine and dried over $MgSO_4$. Purification by column chromatography (hexane/Et_2O = 50:1) gave the product **1e** (689 mg, 85% yield). Colorless oil. IR (neat) ν cm^{-1}; 1726. ^1H NMR (400 MHz, $CDCl_3$) δ 1.72 (3H, d, J = 6.9 Hz), 2.42 (2H, q, J = 6.8 Hz), 4.18 (2H, t, J = 6.9 Hz), 5.45–5.55 (1H, m), 5.57–5.68 (1H, m), 5.81 (1H, dd, J = 10.4, 1.5 Hz), 5.96–6.14 (2H, m), 6.12 (1H, dd, J = 17.3, 10.4 Hz), 6.39 (1H, dd, J = 17.3, 1.5 Hz). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 18.0, 31.9, 63.9, 126.1, 128.3, 128.5, 130.6, 131.2, 132.9, 166.2. EI-MS *m/z*: 166 $[M]^+$. Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.17; H, 8.24.

The substrates **1a–d**, **1h**[12a,b] and **1i**[19] were prepared according to the reported procedure. The physical data of **1a–d**, **1h** and **1i** were reported previously.

4.2.1. (3*E*,5*E*)-3,5-Nonadienyl acrylate (1f). In a similar manner for the preparation of (3*E*,5*E*)-3,5-heptadien-1-ol, reaction of (3-hydroxypropyl)triphenylphosphonium bromide (7.06 g, 17.0 mmol) with LHMDS (35 mL, 1.0 M in THF) and *E*-2-hexenal (4.60 mL, 40 mmol), and the subsequent purification by flash column chromatography on silica gel (hexane/EtOAc = 25:1) gave (3*E*,5*E*)-3,5-nonadien-1-ol (1.19 g, 8.5 mmol, 50% yield) as colorless oil. IR (neat) ν cm^{-1}; 3340, 3016, 1653, 986. ^1H NMR (400 MHz, $CDCl_3$) δ 0.90 (3H, t, J = 7.4 Hz), 1.42 (2H, qt, J = 7.4, 7.2 Hz), 2.04 (2H, q, J = 7.2 Hz), 2.29–2.39 (2H, m), 3.66 (2H, bs), 5.48–5.68 (2H, m), 5.97–6.18 (2H, m). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 13.7, 22.5, 34.6, 36.0, 62.1, 127.2, 130.0, 133.6, 133.7. EI-MS *m/z*: 140 $[M]^+$. Anal. Calcd for $C_9H_{16}O$: C, 77.09; H, 11.50. Found: C, 77.16; H, 11.63. To a solution of this dienyl alcohol (701 mg, 5.0 mmol) in CH_2Cl_2 (10 mL), acryloyl chloride (0.45 mL, 5.5 mmol) and triethylamine (0.83 mL, 6.0 mmol) were added at 0 °C. After being stirred at room temperature for 2.5 h, the reaction mixture was quenched by H_2O and extracted with Et_2O (10 mL × 3). The organic layer was washed with brine and dried over $MgSO_4$. Purification by column chromatography on silica gel (hexane/Et_2O = 50:1) gave the product **1f** (93% yield). Colorless oil. IR (neat) ν cm^{-1}; 1727. ^1H NMR (400 MHz, $CDCl_3$) δ 0.91 (3H, t, J = 7.4 Hz), 1.42 (2H, qt, J = 7.4, 7.2 Hz), 2.04 (2H, q, J = 7.2 Hz), 2.43 (2H, q, J = 6.9 Hz), 4.19 (2H, t, J = 6.9 Hz), 5.49–5.67 (2H, m), 5.82 (1H, dd, J = 10.4, 1.5 Hz), 5.97–6.15 (2H, m), 6.12 (1H, dd, J = 17.3, 10.4 Hz), 6.40 (1H, dd, J = 17.3, 1.5 Hz). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 13.7, 22.5, 31.9, 34.7, 63.9, 126.3, 128.5, 130.1, 130.6, 133.1, 133.7, 166.2. ESI-MS *m/z*: 195 $[M+H]^+$. HRMS Calcd for $C_{12}H_{19}O_2$ $[M+H]^+$: 195.1385, Found: 195.1400.

4.2.2. (*Z*)-4-[(3*E*)-3,5-Hexadienyloxy]-4-oxo-2-butenoic acid (1g). After a solution of 3,5-hexadien-1-ol (981 mg, 10.0 mmol) in CH_2Cl_2 (25 mL) was treated with maleic anhydride (981 mg, 10.0 mmol) and 4-dimethylaminopyridine (DMAP, 24.5 mg, 0.20 mmol) for 3 h at 0 °C, the reaction mixture was extracted with EtOAc (10 mL × 3). The organic layer was washed with brine, dried over $MgSO_4$, and purified by silica gel column chromatography (hexane/EtOAc = 3:1) to give **1g** (746 mg, 3.8 mmol, 38% yield) and 3,5-hexadien-1-ol (549 mg, 5.6 mmol). Colorless oil. IR (neat) ν cm^{-1}; 3025, 1731, 1712. ^1H NMR (400 MHz, $CDCl_3$) δ 2.51 (2H, t, J = 6.7 Hz), 4.33 (2H, t, J = 6.7 Hz), 5.05 (1H, d, J = 10.1 Hz), 5.16 (1H, d, J = 14.8 Hz), 5.69–5.74 (1H, m), 6.14 (1H, dd, J = 14.8, 10.4 Hz), 6.24–6.35 (1H, m), 6.37 (1H, d, J = 12.7 Hz), 6.47 (1H, d, J = 12.7 Hz). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 31.4, 66.1, 116.8, 128.2, 128.9, 134.2, 136.4, 137.1, 167.0, 171.2. ESI-MS *m/z*: 197 $[M+H]^+$. HRMS Calcd for $C_{10}H_{13}O_4$ $[M+H]^+$: 197.0798, Found: 197.0814.

4.3. Typical procedure for IMDA reaction of 1,7,9-decatrienoate derivatives in aqueous media: (4a*S**,7*S**,8a*R**)-7-methyl-3,4,4a,7,8,8a-hexahydro-1*H*-isochromen-1-one (2e)

To a solution of indium(III) triflate (56.0 mg, 0.1 mmol) in H_2O (6.0 mL), a solution of 1,7,9-decatrienoate **1e** (83.1 mg, 0.5 mmol) in 2-propanol (1.0 mL) was added at room temperature and then the reaction mixture was stirred at 80 °C for 24 h. After the resulting mixture was extracted with Et_2O (5 mL × 3), the organic layer was washed with brine and dried over $MgSO_4$. Purification by column chromatography on silica gel (hexane/EtOAc = 3:1) gave the product **2e** (56.5 mg, 68% yield) as colorless oil. IR (neat) ν cm^{-1}; 1732. ^1H NMR (400 MHz, $CDCl_3$) δ 1.02 (3H, d, J = 7.1 Hz), 1.38 (1H, ddd, J = 12.7, 10.3, 10.2 Hz), 1.67–1.80 (1H m), 1.81–1.89 (1H, m), 2.10 (1H, dt, J = 12.7, 4.3 Hz), 2.24–2.37 (1H, m), 2.47–2.58 (1H, m), 2.77–2.86 (1H, m), 4.26 (1H, td, J = 11.5, 3.3 Hz), 4.41 (1H, ddd, J = 11.5, 4.6, 2.8 Hz), 5.53–5.58 (1H, m), 5.64 (1H, bd, J = 10.0 Hz). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 21.2, 27.3, 30.7, 32.2, 32.4, 40.2, 69.2, 126.9, 134.8, 174.1. EI-MS *m/z*: 166 $[M]^+$. Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.16; H, 8.20.

The cycloadducts **2a–d**, **2h**[12a,b] and **2i**[19] were reported previously.

4.3.1. (4a*S,7*S**,8a*R**)-7-Propyl-3,4,4a,7,8,8a-hexahydro-1*H*-isochromen-1-one (2f).** Yield 18%. Colorless crystals. Mp 31–32 °C. IR (KBr) ν cm^{-1}; 1731. ^1H NMR (400 MHz, $CDCl_3$) δ 0.91 (3H, t, J = 6.7 Hz), 1.19–1.46 (6H, m), 1.67–1.80 (1H, m), 1.81–1.89 (1H, m), 2.08–2.26 (2H, m), 2.49–2.59 (1H, m), 2.67–2.76 (1H, m), 4.27 (1H, td, J = 11.6, 3.3 Hz), 4.41 (1H, ddd, J = 11.6, 4.6, 2.5 Hz), 5.58 (1H, ddd, J = 10.0, 4.2, 2.5 Hz), 5.68 (1H, bd, J = 10.0 Hz). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 14.1, 19.7, 27.3, 30.1, 32.8, 35.4, 38.1, 40.1, 69.2, 127.1, 133.7, 174.3. ESI-MS *m/z*: 195 $[M+H]^+$. HRMS Calcd for $C_{12}H_{19}O_2$ $[M+H]^+$: 195.1385, Found: 195.1402.

4.3.2. (4a*S,8*R**,8a*S**)-1-Oxo-3,4,4a,7,8,8a-hexahydro-1*H*-isochromene-8-carboxylic acid (2g).** Yield 78%. Colorless crystals. Mp 177–178 °C. IR (KBr) ν cm^{-1}; 3023, 1734, 1709, 946. ^{1}H NMR (400 MHz, CDCl$_3$) δ 1.70–1.81 (1H, m), 2.18–2.29 (1H, m), 2.30–2.53 (2H, m), 2.62–2.72 (1H, m), 2.96 (1H, bs), 3.41–3.49 (1H, m), 4.16–4.25 (1H, m), 4.26–4.35 (1H, m), 5.54 (1H, bd, $J=10.0$ Hz), 5.79–5.88 (1H, m), 11.2 (1H, bs, CO$_2$*H*). ^{13}C NMR (100.6 MHz, CDCl$_3$) δ 22.9, 28.5, 32.6, 40.1, 40.9, 66.3, 128.0, 128.2, 171.5, 178.7. ESI-MS m/z: 197 $[M+H]^+$. HRMS Calcd for $C_{10}H_{13}O_4$ $[M+H]^+$: 197.0814, Found: 197.0810. Anal. Calcd for $C_{10}H_{12}O_4$: C, 61.22; H, 6.16. Found: C, 61.01; H, 6.19.

4.4. Recycling procedure of In(OTf)$_3$: IMDA reaction of 1-methyl-3,5-hexadienyl acrylate (1d)

To a solution of indium(III) triflate (56 mg, 0.1 mmol) in H$_2$O (6.0 mL), a solution of 1,7,9-decatrienoate **1d** (83 mg, 0.5 mmol) in 2-propanol (1.0 mL) was added at room temperature, and then the whole was stirred at 70 °C for 12 h. When the consumption of **1d** was confirmed by monitoring the reaction mixture by TLC, the reaction mixture was carefully extracted with Et$_2$O (5 mL × 2). Usual work-up of the organic extracts (washed with brine, dried over MgSO$_4$ and evaporated) and purification by column chromatography gave the cycloadduct **2d** (68.7 mg, 83% yield). To the aqueous layer (ca. 6 mL), a solution of substrate **1d** (83 mg, 0.5 mmol) in 2-propanol (1.0 mL) was added and the mixture was stirred under the similar conditions for the first run. After extractive work-up and purification by column chromatography on silica gel, the organic phase gave the product **2d** (64.7 mg, 78% yield). In a similar manner, the resulting aqueous layer was used for the third reaction (**1d**; 83 mg, 0.5 mmol) to obtain **2d** (65.3 mg) in 79% yield.

References and notes

1. For reviews, see: (a) Li, C. *Chem. Rev.* **1993**, *93*, 2023. (b) Lubineau, A. *Chem. Ind.* **1996**, 123. (c) Engberts, J. B. N.; Feringa, B. L.; Keller, E.; Otto, S. *Recl. Trav. Chim. Pays-Bas* **1996**, *115*, 457. (d) Cornils, B.; Herrmann, W. A.; Eckl, R. W. *J. Mol. Catal., A* **1997**, *116*, 27. (e) Li, C.; Chen, T.-H. *Organic Synthesis in Water*; Wiley: New York, 1997. (f) Grieco, P. A. *Organic Reaction in Aqueous Media*; Blackie Academic and Professinal: London, 1998.
2. For recent examples of the allylation of carbonyl compounds mediated by indium, see: (a) Tan, K.-T.; Chng, S.-S.; Cheng, H.-S.; Loh, T.-P. *J. Am. Chem. Soc.* **2003**, *125*, 2958. (b) Foubelo, F.; Yus, M. *Tetrahedron: Asymmetry* **2004**, *15*, 3823. Bismuth mediated reactions, see: (c) Smith, K.; Lock, S.; El-Hiti, G. A.; Wada, M.; Miyoshi, N. *Org. Biomol. Chem.* **2004**, *2*, 935. (d) Xu, X.; Zha, Z.; Miao, Q.; Wang, Z. *Synlett* **2004**, 1171. Other metal salts mediated reactions, see: (e) Wang, Z.; Yuan, S.; Li, C.-J. *Tetrahedron Lett.* **2002**, *43*, 5097. (f) Fukuma, T.; Lock, S.; Miyoshi, N.; Wada, M. *Chem. Lett.* **2002**, 376.
3. For recent examples, see: (a) Tian, H.-Y.; Chen, Y.-J.; Wang, D.; Bu, Y.-P.; Li, C.-J. *Tetrahedron Lett.* **2001**, *42*, 1803. (b) Darbre, T.; Machuqueiro, M. *Chem. Commun.* **2003**, 1090. (c) Nyberg, A. I.; Usano, A.; Pihko, P. M. *Synlett* **2004**, 1891. (d) Iimura, S.; Manabe, K.; Kobayashi, S. *Tetrahedron* **2004**, *60*, 7673.
4. For recent examples, see: (a) Loh, T.-P.; Pei, J.; Lin, M. *Chem. Commun.* **1996**, 2315. (b) Otto, S.; Engberts, J. B. F. N. *J. Am. Chem. Soc.* **1999**, *121*, 6798. (c) Amantini, D.; Fringuelli, F.; Piermatti, O.; Pizzo, F.; Vaccaro, L. *J. Org. Chem.* **2003**, *68*, 9263.
5. Reviews on Pd-catalyzed cross coupling reactions in water, see: (a) Pierre Genet, J.; Savignac, M. *J. Organometal. Chem.* **1999**, *576*, 305. (b) Beletskaya, I. P.; Cheprakov, A. V. In Negishi, E., Ed.; Handbook of organopalladium chemistry for organic synthesis; Wiley: New York, 2002; Vol. 2, pp 2957–3006. (c) Uozumi, Y. *J. Synth. Org. Chem., Jpn.* **2002**, *60*, 1063.
6. Recent examples, see: (a) Morin Deveau, A.; MacDonald, T. L. *Tetrahedron Lett.* **2004**, *45*, 803. (b) Wolf, C.; Lerebours, R. *Org. Lett.* **2004**, *6*, 1147. (c) Friesen, R. W.; Trimble, L. A. *Can. J. Chem.* **2004**, *82*, 206. (d) DeVasher, R. B.; Moore, L. R.; Shaughnessy, K. H. *J. Org. Chem.* **2004**, *69*, 7919.
7. For reviews on synthetic utility of lanthanoid triflates, see: (a) Kobayashi, S.; Ishitani, H. *J. Synth. Org. Chem., Jpn.* **1998**, *56*, 357. (b) Kobayashi, S. In Yamamoto, H., Ed.; Lewis Acids in Organic Synthesis; Wiley: Weinheim, Germany, 2000; Vol. 2, pp 883–910. (c) Kobayashi, S.; Sugiura, M.; Kitagawa, H.; Lam, W. W.-L. *Chem. Rev.* **2002**, *102*, 2227.
8. For some examples, see: (a) Kobayashi, S.; Iwamoto, S.; Nagayama, S. *Synlett* **1997**, 1099. (b) Nagayama, S.; Kobayashi, S. *J. Am. Chem. Soc.* **1997**, *119*, 10049. (c) Kobayashi, S.; Busujima, T.; Nagayama, S. *Chem. Commun.* **1998**, 19.
9. (a) Kobayashi, S.; Busujima, T.; Nagayama, S. *Tetrahedron Lett.* **1998**, *39*, 1579. (b) Munoz-Muniz, O.; Quintanar-Audelo, M.; Juaristi, E. *J. Org. Chem.* **2003**, *68*, 1622. (c) Ding, R.; Zhang, H. B.; Chen, Y. J.; Liu, L.; Wang, D.; Li, C. J. *Synlett* **2004**, 555.
10. For a review on conformation and stereoelectronic effect of ester compounds, see: Deslongchamps, P. *Stereoelectric Effects in Organic Chemistry*; Pergamon: Oxford, 1983; pp 54–100.
11. Cain, D.; Pawar, D. M.; Stewart, M.; Billings, H., Jr.; Noe, E. A. *J. Org. Chem.* **2001**, *66*, 6092.
12. For examples of IMDA reaction, see: (a) Saito, A.; Ito, H.; Taguchi, T. *Org. Lett.* **2002**, *4*, 4619. (b) Saito, A.; Yanai, H.; Taguchi, T. *Tetrahedron* **2004**, *60*, 12239.(c) Saito, A.; Yanai, H.; Sakamoto, W.; Takahashi, K.; Taguchi, T. *J. Fluorine Chem.* **2005**, *126*, 709.
13. For example of intermolecular version, see: Saito, A.; Yanai, H.; Taguchi, T. *Tetrahedron Lett.* **2004**, *45*, 9439.
14. (a) Jung, M. E.; Gervay, J. *J. Am. Chem. Soc.* **1989**, *111*, 5469. (b) Jung, M. E. *Synlett* **1990**, 186. (c) Giessner-Prettre, C.; Hückel, S.; Maddaluno, J.; Jung, M. E. *J. Org. Chem.* **1997**, *62*, 1439. (d) Jung, M. E. *Synlett* **1999**, 843.
15. (a) Yorimitsu, H.; Nakamura, T.; Shinokubo, H.; Oshima, K. *J. Org. Chem.* **1998**, *63*, 8604. (b) Yorimitsu, H.; Nakamura, T.; Shinokubo, H.; Oshima, K.; Omoto, K.; Fujimoto, H. *J. Am. Chem. Soc.* **2000**, *122*, 11041. (c) Yorimitsu, H.; Shinokubo, H.; Oshima, K. *Synlett* **2002**, 674.
16. The reaction of 6-hydroxy substrate **1h** with TfN(AlMe$_2$)$_2$ resulted in decomposition of the substrate **1h**.
17. We have already reported that stereoselective construction of oxabicyclo[4.3.0]nonene derivatives was achieved by the

IMDA reaction of 6-silyloxy derivative followed by the desilylation reaction of the cycloadducts with fluoride ion. In these cases, re-lactonization reactions also proceeded in stereospecificic manner. See, Ref. 12b.

18. White, J. D.; Nolen, E. G., Jr.; Miller, C. H. *J. Org. Chem.* **1986**, *51*, 1150.
19. Martin, S. F.; Williamson, S. A.; Gist, R. P.; Smith, K. M. *J. Org. Chem.* **1983**, *48*, 5170.
20. Page, P. C. B.; Vahedi, H.; Batchelor, K. J.; Hindley, S. J.; Edgar, M.; Beswick, P. *Synlett* **2003**, 1022.
21. Snider, B. B.; Phillips, G. B.; Cordova, R. *J. Org. Chem.* **1983**, *48*, 3003.