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Intramolecular Cyclization of 3,3-Diarylpropenylamides of Electron-deficient Alkenes: Stereoselective Synthesis of Functionalized Hexahydrobenzo[*f*]isoindoles

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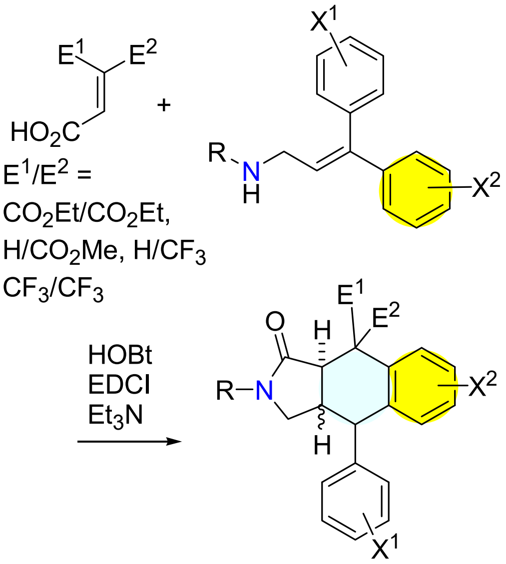
Graphical Abstract



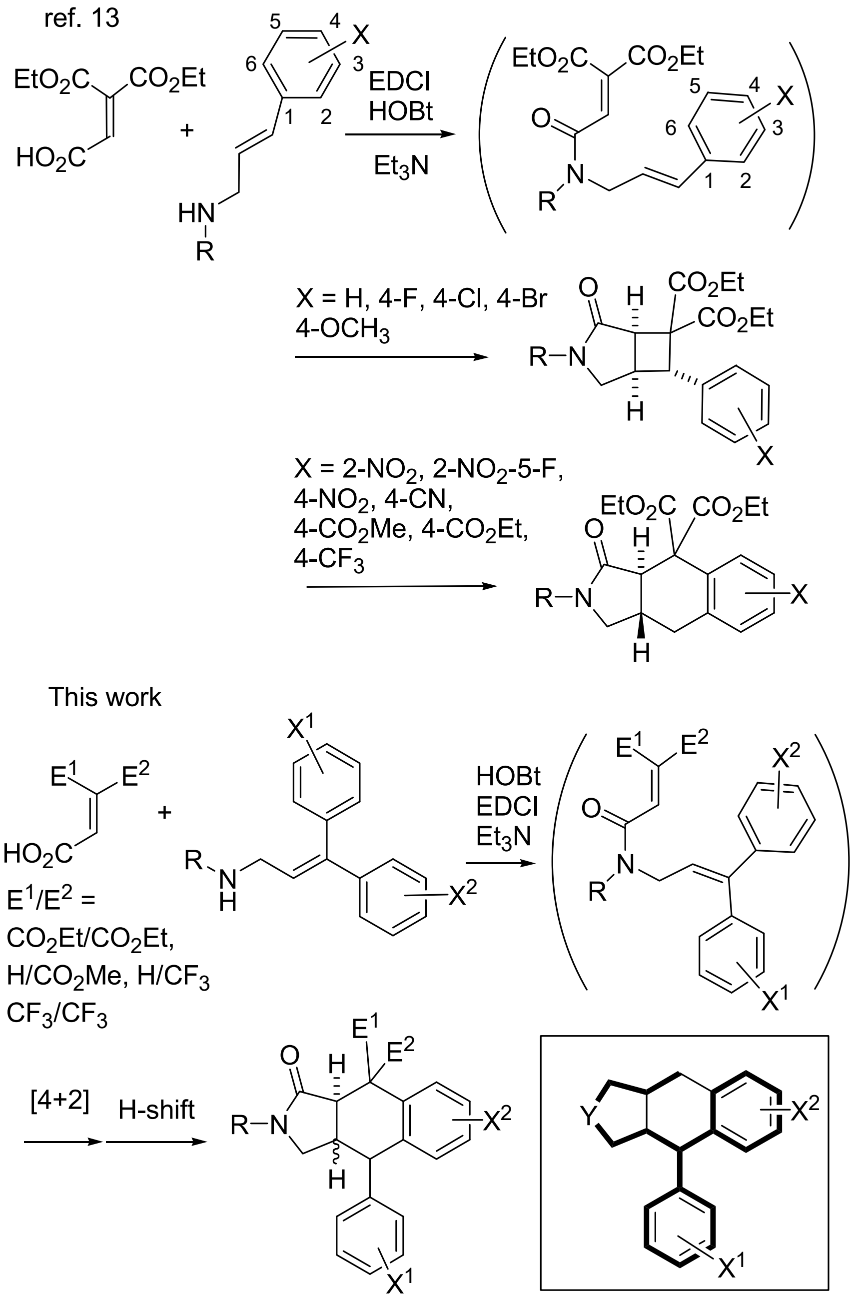
Abstract: Intramolecular Diels–Alder reactions of various 3,3-diarylpropenylamides of electron-deficient alkenes to give hexahydrobenzo[*f*]isoindoles were investigated. Reaction of 1,1,2-ethenetricarboxylic acid 1,1-diethyl ester with 3,3-diaryl-2-propen-1-amines under the amide formation conditions gave the tricyclic compounds in sequential processes involving intramolecular Diels-Alder reaction. The reaction gave *cis*- and *trans*-fused tricyclic compounds selectively, depending on the substituents on the benzene ring, reaction temperature and solvent. In the reaction with dissymmetrically substituted 3,3-diaryl-2-propen-1-amines, *E*-substituted aryl group reacted mainly as a styrene component. Amides of electron-deficient alkenic carboxylic acids such as fumarate do not undergo cyclization at room temperature sequentially and the reaction on heating gave trans-fused hexahydrobenzo[*f*]isoindoles. The origin of the observed stereoselectivity has been examined by the DFT calculations.

Introduction

The intramolecular [4+2] cycloaddition (Diels-Alder) reaction between alkenes and dienes is a powerful tool for the facile construction of multicyclic skeletons.[1] Vinyl heteroaromatic moieties such as vinyl pyrroles, thiophenes, furans,[2] imidazoles,[3] and benzothiophens[4] have been extensively used as dienes in the intramolecular Diels-Alder reaction. The intramolecular Diels-Alder reaction of vinyl benzene (styrene) as a diene requires relatively harsh conditions, because of involving dearomatization of benzene ring.[5]

The inter- and intramolecular reactions of styrenes diversely undergo [2+2] cycloadditions[6,7] and [4+2] cycloadditions as dienophile components.[8,9] Limited intermolecular [4+2] cycloadditions of styrenes as dienes were also reported.[10] In addition to the cycloaddition reactions of styrenes, the inter- and intramolecular reactions of diarylethenes were studied.[5c,11] Furthermore, one of the important selectivities of the intramolecular Diels-Alder reaction in general is formation of trans or cis fused ring,[1b,12] and the investigation on the stereoselectivity of the intramolecular [4+2] cycloaddition of styrenes with various substituents is of considerable interest.[5c,5k]

Recently, we have reported intramolecular [2+2] and [4+2] cycloaddition reactions of 1,1,2-ethenetricarboxylic acid 1,1-diethyl ester **1** with *E*-cinnamylamines under the amide formation conditions in sequential processes (Scheme 1).[13] Reaction of *E*-cinnamylamines without substituent on benzene ring and with halogens and OMe on *para* position at room temperature gave cyclobutane-fused pyrrolidines as major products via [2+2] cycloaddition. On the other hand, reaction of 1,1,2-ethenetricarboxylic acid 1,1-diethyl ester **1** and *E*-cinnamylamines bearing electron-withdrawing groups under the amide formation conditions gave trans-fused hexahydrobenzo[*f*]isoindoles via [4+2] cycloaddition as major products.



Scheme 1

In this work, the sequential amide formation/[4+2] cycloaddition/H-shift reactions of electron deficient alkenyl carboxylic acids with Z-cinnamyl amines and various 3,3-diaryl-2-propen-1-amines have been studied. This reaction proceeds to give tricyclic compounds, functionalized hexahydrobenzo[*f*]isoindoles. Some biologically active compounds such as podophyllotoxin[14] (Y=O) and 4-phenylbenzo[*f*]isoindoles[15] (Y=N) have the skeletons of the [4+2] cycloaddition products of 3,3-diaryl-2-propen-1-amines, shown in Scheme 1. In order to understand the factors to control *cis* and *trans*-fused stereochemistry in the present results, DFT calculations have been carried out.

Results and Discussion

We have previously reported that reactions of 1,1,2-ethenetricarboxylic acid 1,1-diethyl ester **1** and *E*-cinnamylamines bearing *p*-H, halogen and MeO groups in the presence of EDCI/HOBt/Et_3N at room temperature gave cyclobutane-fused pyrrolidines as major products.[13] The products may be formed via amide formation/intramolecular [2+2] cycloaddition. First, reaction with *Z*-cinnamylamines has been examined. Reaction with benzyl or cyclohexylmethyl cinnamylamines **2a,b** (*Z*:*E* = ca. 5:1) in the presence of EDCI/HOBt/Et_3N in THF at room temperature gave a complex mixture and the possible [2+2] cycloadducts were not detected. Intramolecular [2+2] cycloaddition reaction path for possible intermediate *Z*-amide was examined by DFT calculations according to the previously reported [2+2] cycloaddition path of *E*-amide.[13] The cyclobutane ring formation path is less stable than that of *E*-amide, probably because of the steric effect of Ph group.[16] The reaction at 80-110 °C gave [4+2] cycloadducts, *cis*-fused tricyclic compounds **3a,b** as major products (eq 1, Table 1). The *cis*-fused stereochemistry of **3a,b** was determined by NOEs in C_6D_6.

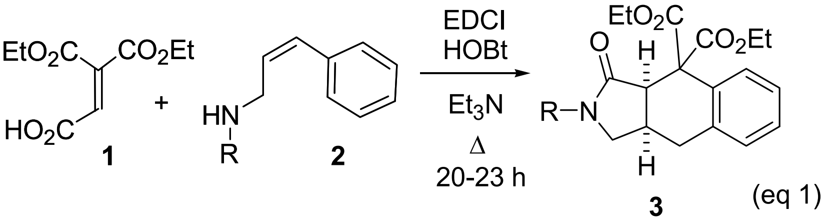


Table 1. Reactions of 1,1,2-ethenetricarboxylic acid 1,1-diethyl ester **1** and *Z*-cinnamylamines **2**

Entry	**2**	R	Solvent	Temp.	Product	**3** Yield (%)
1	**2a**[a]	CH_2Ph	THF	r.t.	[b]	-
2	**2a**[a]	CH_2Ph	Benzene	80°C	**3a**	62
3	**2a**[a]	CH_2Ph	Toluene	110 °C	**3a**	58
4	**2b**[a]	CH_2Cyclohexyl	THF	r.t.	[b]	-
5	**2b**[a]	CH_2Cyclohexyl	Benzene	80 °C	**3b**	50
6	**2b**[a]	CH_2Cyclohexyl	Toluene	110 °C	**3b**	61

[a] *Z*:*E* = 5:1. [b] A complex mixture.

Next, the reaction of **1** and 3,3-diaryl-2-propenylamines **4** in the presence of the amide condensation reagents has been examined (eq 2, Table 2). The influence of the second aromatic ring to stereochemistry by both steric and electronic effects is of mechanistic and synthetic interests.

The 3,3-diaryl-2-propen-1-amines **4** were prepared from the corresponding alcohols.[17] The reaction of **1** and *N*-benzyl 3,3-diphenyl-2-propen-1-amine **4a** with EDCI/HOBt/Et_3N in THF at room temperature gave a complex mixture. However, the reaction in DMF gave *trans*-fused hexahydrobenzo[*f*]isoindole **5a-trans** in 52% yield via [4+2] cycloaddition. Interestingly, the reaction of **4a,b** in benzene or toluene at 80 or 110 °C gave *cis*-fused hexahydrobenzo[*f*]isoindoles **5a,b-cis** as major products. Similarly, the reaction of *N*-benzyl-3,3-bis(4-fluorophenyl)-2-propenylamine **4c** in DMF at room temperature gave *trans*-fused tricyclic product **5c-trans** in 53% yield and the reaction of **4c** in benzene or toluene at 80 or 110 °C gave *cis*-fused product **5c-cis** in 87 and 98% yields, respectively. On the other hand, reaction of **1** and 4,4'-dichloro and 3,3'-di(trifluoromethyl) derivatives **4d,e** in THF, DMF and benzene at room temperature, 80 and 110 °C gave *trans*-fused tricyclic products **5d,e-trans** in high yields. Product **5e-trans** from 3,3'-CF_3 substituted amine substrate **4e** was obtained as a single regioisomer (3,3'-CF_3). The reaction of **1** and 4,4'-dimethyl derivative **4f** in DMF gave a complex mixture at room temperature and the reaction in DMF, benzene and toluene at 80 and 110 °C gave *cis*-fused tricyclic product **5f-cis** selectively. The relative configurations of **5** were determined by NOEs in $CDCl_3$ or C_6D_6. The reaction of **1** and 4,4'-dimethoxy derivative **4g** gave a complex mixture in THF, DMF, benzene and toluene at room temperature, 80 and 110 °C.

Thus, the reaction with 3,3-diaryl-2-propen-1-amines gave *cis*- and *trans*-fused tricyclic compounds selectively, depending on the substituents on the benzene ring, reaction temperature and solvent.

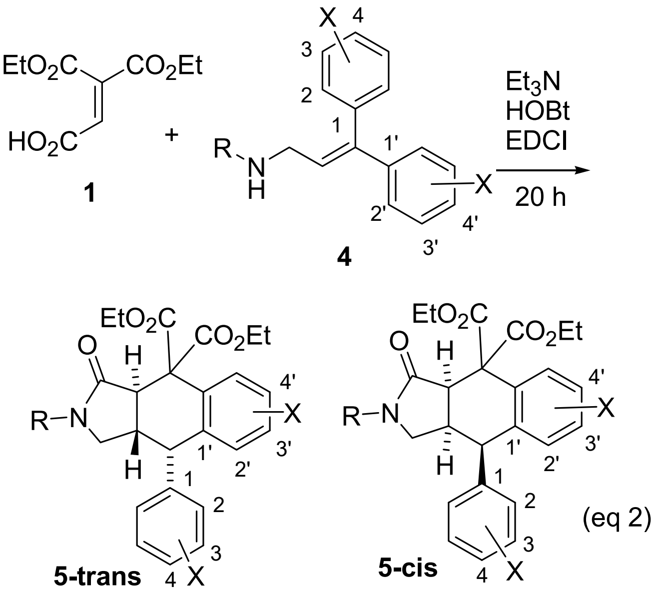


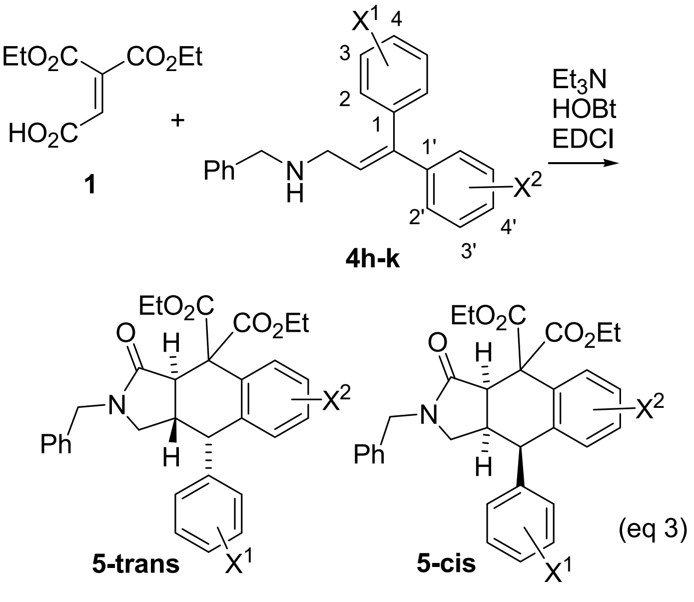
Table 2. Reactions of 1,1,2-ethenetricarboxylic acid 1,1-diethyl ester **1** and 3,3-diaryl-2-propen-1-amines **4**

Entry	**4**[a]	X	R	Solvent	Temp.	Product	Yield (%)
1	**4a**	H	CH_2Ph	THF	r.t.	[b]	-
2	**4a**	H	CH_2Ph	DMF[c]	r.t.	**5a-trans**	52
3	**4a**	H	CH_2Ph	Benzene	80 °C	**5a-cis**	48[d]
4	**4b**	H	CH_2Cyclohexyl	Benzene	80 °C	**5b-cis**	55[d]
5	**4c**	4,4'-F	CH_2Ph	THF	r.t.	[e]	-
6	**4c**	4,4'-F	CH_2Ph	DMF[c]	r.t.	**5c-trans**	53
7	**4c**	4,4'-F	CH_2Ph	Benzene	80 °C	**5c-cis**	87
8	**4c**	4,4'-F	CH_2Ph	Toluene	110 °C	**5c-cis**	98
9	**4d**	4,4'-Cl	CH_2Ph	THF	r.t.	**5d-trans**	89
10	**4d**	4,4'-Cl	CH_2Ph	DMF[f]	r.t.	**5d-trans**	93
11	**4d**	4,4'-Cl	CH_2Ph	Benzene	80 °C	**5d-trans**	67
12	**4e**	3,3'-CF_3	CH_2Ph	THF	r.t.	**5e-trans**	99
13	**4e**	3,3'-CF_3	CH_2Ph	DMF[f]	r.t.	**5e-trans**	93
14	**4e**	3,3'-CF_3	CH_2Ph	Benzene	80 °C	**5e-trans**	93
15	**4f**	4,4'-Me	CH_2Ph	Toluene	110 °C	**5f-cis**	48[g]
16	**4f**	4,4'-Me	CH_2Ph	DMF	110 °C	**5f-cis**	55

[a] The reaction of **4g** (X = 4,4'-OMe) gave a complex mixture. [b] A complex mixture. [c] The reaction in DMF at 80 or 110 °C gave a mixture of **5-cis** and **5-trans**. [d] The reaction in toluene at 110 °C gave **5-cis** in lower yields (**5a-cis** 32%, **5b-cis** 26%) and a complex mixture. [e] A mixture containing **5c-trans**. [f] The reaction in DMF at 80 or 110 °C also gave **5-trans** in 89-

95% yields. [g] The reaction in benzene at 80 °C gave **5f-cis** in lower yield (17%) and a complex mixture.

To obtain some insights into the mechanism, the reactions with dissymmetrically substituted 3,3-diaryl-2-propen-1-amines have been studied (eq 3, Table 3). Reaction of **1** with (*Z*) and (*E*)-3-(2- or 4-chlorophenyl)-3-phenyl-2-propen-1-amines **4h-j** in the presence of EDCI/HOBt/Et_3N at room temperature gave trans-fused hexahydrobenzo[*f*]isoindoles **5h,i,j-trans** stereoselectively in 30-86% yield (entries 1,2,5,6,11). At higher temperature in benzene or toluene, *cis*-fused hexahydrobenzo[*f*]isoindoles **5h,i,j-cis** were also formed (entries 3,4,8,9,13,14). Reaction of **1** with (*Z*)-3-(4-nitrophenyl)-3-phenyl-2-propen-1-amine **4k** in the presence of EDCI/HOBt/Et_3N at 110 °C gave *trans*-fused hexahydrobenzo[*f*]isoindoles **5k-trans** as a major product in 55% yield. Highly electron-deficient NO_2 group on phenyl group may decrease the [4+2] cycloaddition reaction rate. Thus, *E*-substituted aryl group reacted selectively as a styrene component.



(eq 3)

Table 3. Reactions of 1,1,2-ethenetricarboxylic acid 1,1-diethyl ester **1** and dissymmetrically substituted 3,3-diaryl-2-propen-1-amines **4h-k**

Entry	**4**	X^1	X^2	Solvent	Temp.	**5-trans** (Yield %)	**5-cis** (Yield %)
1	**4h**	2-Cl	H	THF	r.t.	**5h-trans** (30)	
2	**4h**	2-Cl	H	DMF	r.t.	**5h-trans** (33)	

3	**4h**	2-Cl	H	Benzene	80 °C	**5h-trans** (18)[a]	**5h-cis** (32)[a]
4	**4h**	2-Cl	H	Toluene	110 °C	**5h-trans** (28)[a]	**5h-cis** (56)[a]
5	**4i**	4-Cl	H	THF	r.t.	**5i-trans** (59)	
6	**4i**	4-Cl	H	DMF	r.t.	**5i-trans** (72)	
7	**4i**	4-Cl	H	DMF	80 °C	**5i-trans** (58)	
8	**4i**	4-Cl	H	Benzene	80 °C	**5i-trans** (48)[a]	**5i-cis** (27)[a]
9	**4i**	4-Cl	H	Toluene	110 °C	**5i-trans** (5)[a]	**5i-cis** (39)[a]
10	**4j**	H	4'-Cl	THF	r.t.	**5j-trans** (-)[b]	
11	**4j**	H	4'-Cl	DMF	r.t.	**5j-trans** (86)	
12	**4j**	H	4'-Cl	DMF	80 °C	**5j-trans** (71)	
13	**4j**	H	4'-Cl	Benzene	80 °C	**5j-trans** (61)[a]	**5j-cis** (18)[a]
14	**4j**	H	4'-Cl	Toluene	110 °C	**5j-trans** (47)[a]	**5j-cis** (31)[a]
15	**4k**	4-NO$_2$	H	THF	r.t.	**5k-trans** (32)[c]	
16	**4k**	4-NO$_2$	H	DMF	r.t.	**5k-trans** (34)[c]	
17	**4k**	4-NO$_2$	H	Toluene	110 °C	**5k-trans** (55)	
18	**4k**	4-NO$_2$	H	DMF	110 °C	**5k-trans** (36)[d]	

[a] The yields were calculated by ^{1}H NMR. [b] A complex mixture containing a small amount of **5j-trans**. [c] A complex mixture containing unidentified compounds was formed along with **5k-trans**. [d] A small amount of possible phenyl epimer of **5k-trans** was also formed but could not be purified.

Next the reactions of other electron-deficient alkenes **6** with carboxyl group and 3,3-diaryl-2-propen-1-amines **4** were carried out in order to examine the generality of the reaction (eq 4, Table 4). Reaction of β-substituted (CO$_2$Me, CF$_3$, bisCF$_3$) α,β-unsaturated carboxylic acids **6a-c** and 3,3-diaryl-2-propen-1-amines (Ar=Ph, C$_6$H$_4$-4-Cl) **4a,d** with EDCI/HOBt/Et$_3$N at room temperature gave the corresponding amides **7**.[18] On the other hand, the reaction of **6a,c** and **4a**, **6a-c** and **4d** on heating (at 60-160 °C) gave trans-fused tricyclic compounds **8** as major products.

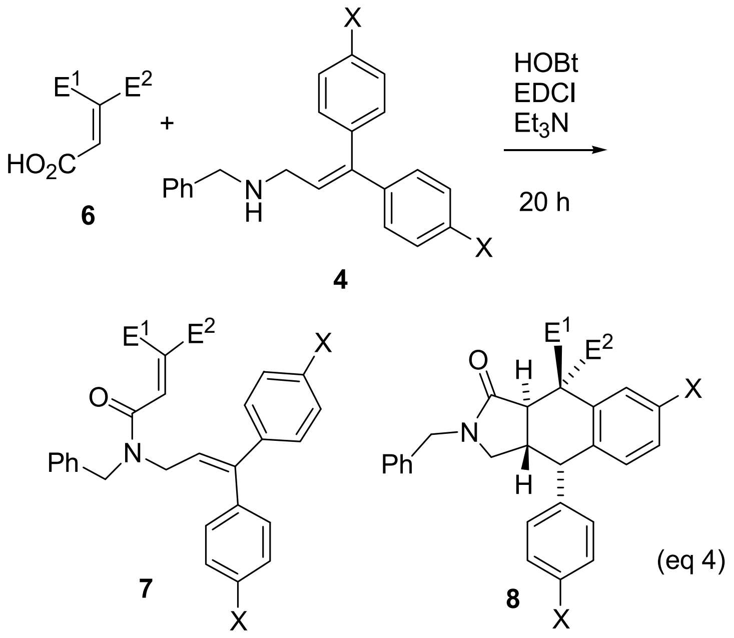
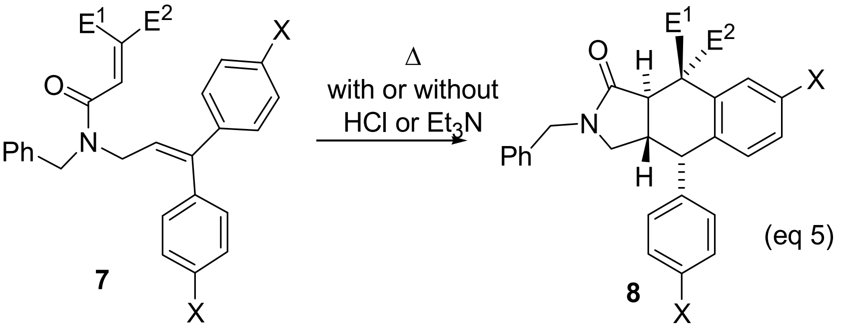


Table 4. Reactions of electron-deficient alkenes **6** and 3,3-diaryl-2-propen-1-amines **4**.

Entry	**6**	E^1	E^2	**4**	X	Solvent	Temp.	Product	Yield (%)
1	**6a**	H	CO_2Me	**4a**	H	THF	r.t.	**7a**[a]	ca. 77
2	**6a**	H	CO_2Me	**4a**	H	Toluene	110 °C	**8a**	47
3	**6b**	H	CF_3	**4a**	H	THF	r.t.	**7b**	89
4	**6b**	H	CF_3	**4a**	H	Xylene	140 °C	[c]	-
5	**6b**	H	CF_3	**4a**	H	Toluene[b]	160 °C	[c]	-
6	**6c**	CF_3	CF_3	**4a**	H	THF	r.t.	**7c**[a]	ca. 39
7	**6c**	CF_3	CF_3	**4a**	H	Benzene	80 °C	**8c**	37
8	**6c**	CF_3	CF_3	**4a**	H	Toluene	110 °C	**8c**	48
9	**6a**	H	CO_2Me	**4d**	Cl	THF	r.t.	**7d**[a]	ca. 86
10	**6a**	H	CO_2Me	**4d**	Cl	THF	60 °C	**8d**	80
11	**6a**	H	CO_2Me	**4d**	Cl	Benzene	80 °C	**8d**	75
12	**6a**	H	CO_2Me	**4d**	Cl	Toluene	110 °C	**8d**	69
13	**6b**	H	CF_3	**4d**	Cl	THF	r.t.	**7e**	77
14	**6b**	H	CF_3	**4d**	Cl	Toluene	110 °C	**7e**	67
15	**6b**	H	CF_3	**4d**	Cl	Xylene	140 °C	**8e**	27
16	**6b**	H	CF_3	**4d**	Cl	Toluene[b]	160 °C	**8e**	38
17	**6c**	CF_3	CF_3	**4d**	Cl	THF	r.t.	**7f**[a]	ca. 57
18	**6c**	CF_3	CF_3	**4d**	Cl	Benzene	80 °C	**8f**	53
19	**6c**	CF_3	CF_3	**4d**	Cl	Toluene	110 °C	**8f**	45

[a] Products **7a,c,d,f** are unstable and decompose to give complex mixtures gradually. [b] In a closed vessel. [c] A complex mixture.

Transformation of the amides **7** to the tricyclic compounds **8** was also examined. Thermal reaction of **7a,c,d,f** with and without acid or base gave **8** in 21-88% yield (eq 5, Table 5).



(eq 5)

Table 5. Transformation of amides **7** to hexahydrobenzo[*f*]isoindoles **8**.

Entry	7	E^1	E^2	X	Solvent	Additive	Temp.	Product	Yield (%)
1	**7a**	H	CO_2Me	H	Toluene	none	110 °C	**8a**	21
2	**7a**	H	CO_2Me	H	Toluene	HCl (1 equiv)[a]	110 °C	**8a**	67
3	**7a**	H	CO_2Me	H	Toluene	Et_3N (1 equiv)	110 °C	**8a**	83
4	**7b**	H	CF_3	H	Toluene	none	110 °C	**8b**	0[b]
5	**7b**	H	CF_3	H	Toluene	HCl (1 equiv)[a]	110 °C	**8b**	0[b]
6	**7b**	H	CF_3	H	Toluene	Et_3N (1 equiv)	110 °C	**8b**	0[b]
7	**7c**	CF_3	CF_3	H	Toluene	Et_3N (1 equiv)	110 °C	**8c**	55
8	**7d**	H	CO_2Me	Cl	THF	Et_3N (1 equiv)	60 °C	**8d**	88
9	**7e**	H	CF_3	Cl	Toluene	none	110 °C	**8e**	0[b]
10	**7e**	H	CF_3	Cl	Toluene	HCl (1 equiv)[a]	110 °C	**8e**	0[b]
11	**7e**	H	CF_3	Cl	Toluene	Et_3N (1 equiv)	110 °C	**8e**	0[b]
12	**7f**	CF_3	CF_3	Cl	Toluene	Et_3N (1 equiv)	110 °C	**8f**	87

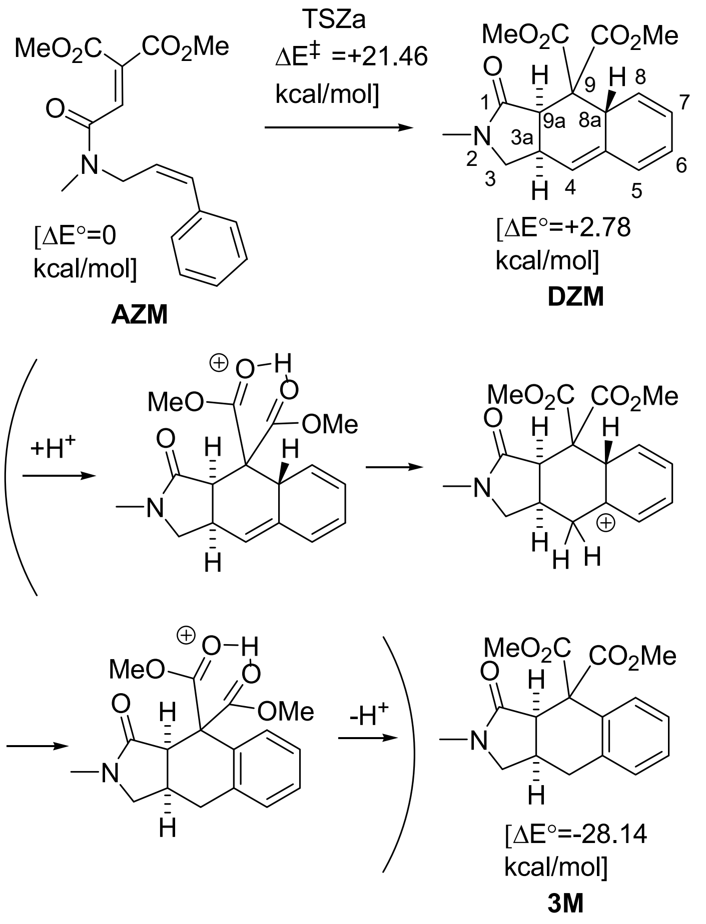
[a] 1M HCl in ether was added. [b] No reaction.

Theoretical study

In order to understand the reaction mechanism of the cycloadditions and find the factors to control *cis* and *trans*-fused stereochemistry, a theoretical study was carried out by DFT calculation. Some theoretical studies on *cis* and *trans*-fused stereoselectivity of intramolecular Diels-Alder reactions have been reported.[10c-f] The selectivity varies depending on the steric and electronic effects of linkers and substituents.

The reaction mechanism was examined using B3LYP/6-31G*[19,20] calculations including the PCM[21] solvent effect (solvent=THF). TS geometry was characterized by vibrational analysis, which checked whether the obtained geometry has single imaginary frequencies ($\nu^{\ddagger}$). From TSs, reaction paths were traced by the intrinsic reaction coordinate (IRC) method[22] to obtain the energy-minimum geometries. ΔE (sum of electronic and zero-point energies) for Schemes 2-4 were refined by single-point calculations of RB3LYP/6-311+G(d,p) SCRF = (PCM, solvent = THF).

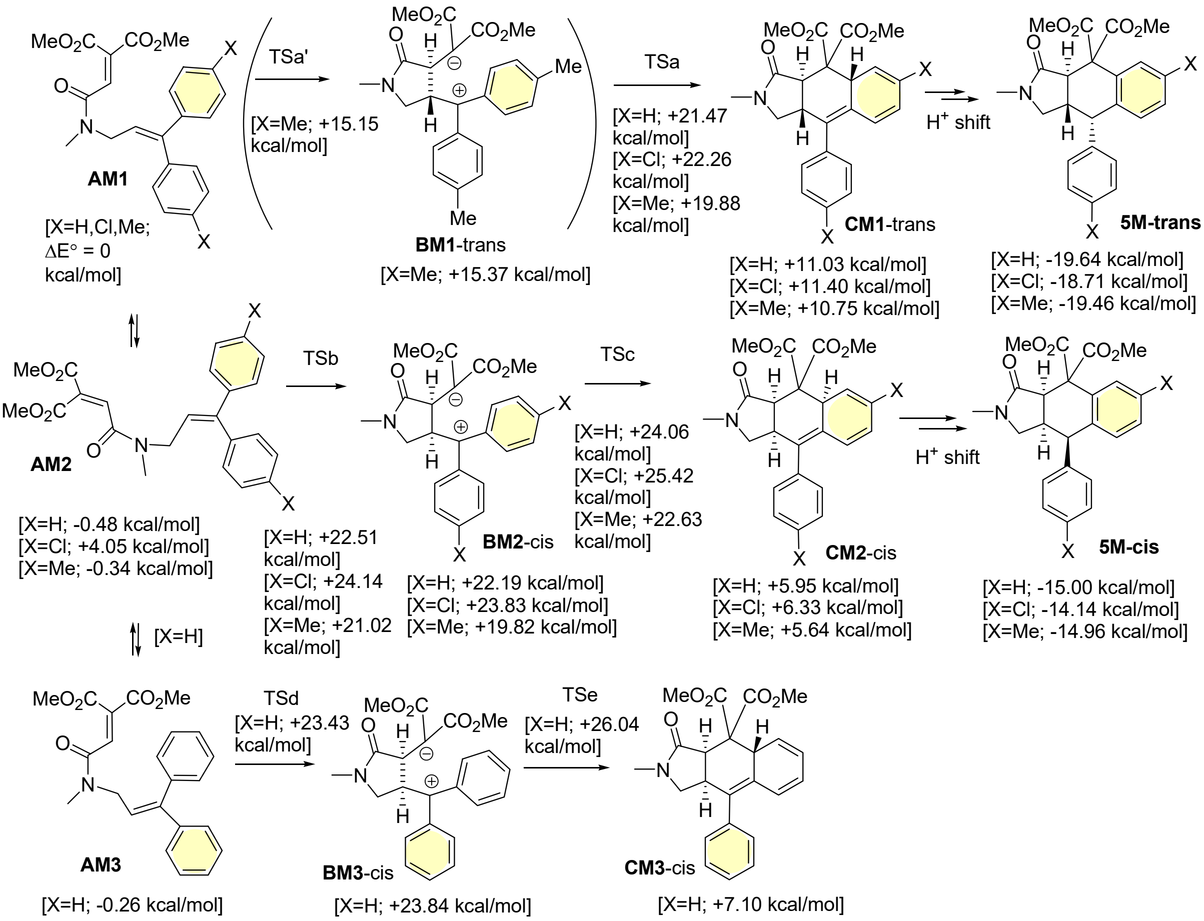
[4+2] Cycloadditions without acid catalyst for *Z*-cinnamyl amide models were calculated and the concerted path to 3a,9a-*cis*-fused and 8a,9a-*trans* [4+2] cycloadduct **DZM** was obtained and is shown in Scheme 2. The path to give 3a,9a-*trans*-fused and 8a,9a-cis cycloadduct could not be obtained because of the steric hindrance. Intermolecular proton transfer of **DZM** possibly leads to rearomatized product **3M**. A plausible mechanism involving stepwise proton transfer via CO_2R groups (R = Me in the model) could be included as shown in Scheme 2.



Scheme 2. [4+2] Cycloaddition path for Z-cinnamyl amide. ΔE's (sum of electronic and zero-point energies) by B3LYP/6-311+G(d,p) SCRF = (PCM, solvent = THF) // B3LYP/6-31G* SCRF = (PCM, solvent = THF) relative to **AZM** are shown.[23] The optimized structure of **3M** was obtained in the previous work.[13]

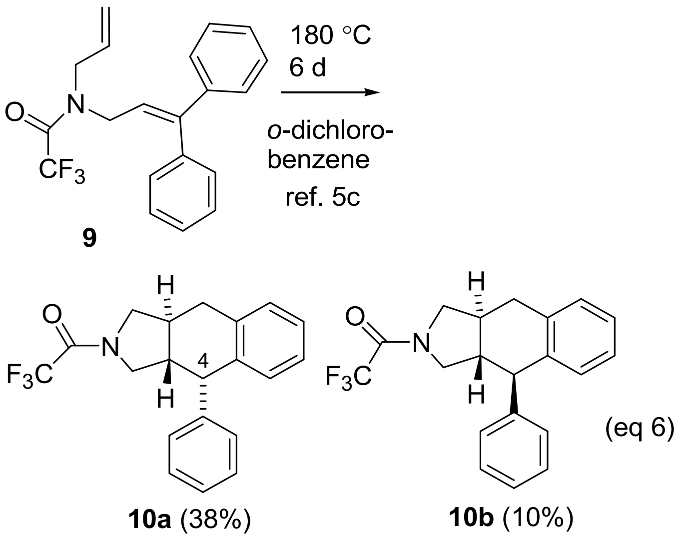
Next, the *cis* and *trans*-fused stereoselectivity for reaction of diaryl propenyl amides in the [4+2] cycloaddition path has been examined by DFT calculations (Scheme 3). For formation of *trans*-fused [4+2] cycloadduct CM1-trans, the asynchronous and concerted path for X = H was obtained. For formation of *cis*-fused [4+2] cycloadduct CM2-cis, stepwise path via zwitterionic intermediate BM2-cis was obtained.[24] The activation energy TSa (+21.47 kcal/mol) leading to CM1-trans is lower than TSb (+22.51 kcal/mol) and TSc (+24.06 kcal/mol) leading to CM2-cis. However, the cycloadduct CM2-cis (+5.96 kcal/mol) is more stable than CM1-trans (+11.03 kcal/mol). The stability of CM2-cis may be partially attributed to 8a,9a-*cis* (1,3-diequatorial-like) conformation of the cyclohexene ring. At higher temperature, the reaction leads to the more stable [4+2] cycloadduct CM2-cis. The path reacting with *Z*-phenyl group (via AM3 → BM3-cis → CM3-cis) was also calculated. However, the path to give CM3-cis with 8a,9a-*trans* stereochemistry is unfavorable. The paths reacting with *Z*-phenyl group to give 3a,9a-*trans* stereochemistry could not be obtained because of the steric hindrance, similar to the result of *Z*-cinnamyl amide. Thus, the reaction paths at *E*-substituted phenyl group of diphenyl propenyl substrates as a diene moiety were preferentially obtained for both *trans* and *cis*-fused products by the DFT calculations. This is in agreement with the experimental results of reactions of dissymmetrically substituted diaryl-2-propen-1-amines **4h-k**.

The reaction at room temperature proceeds favorably to give CM1-trans and the use of polar solvent such as DMF facilitates the stepwise protonation-deprotonation and leads to the *trans*-fused rearomatized product 5M-trans.



Scheme 3. [4 + 2] Cycloaddition reaction paths for model compounds of diaryl propenyl amides. ΔE's (sum of electronic and zero-point energies) by B3LYP/6-311+G(d,p) SCRF = (PCM, solvent = THF) // B3LYP/6-31G* SCRF = (PCM, solvent = THF) relative to AM1 are shown. The 3D-structures of intermediates and transition states are shown in Supporting Information.

The 1,3-H shift may not be a concerted process,[25] and the possible stepwise protonation-deprotonation (H^+ 1,3-shift)[26] is also considered to play an important role to *cis* and *trans* fused stereoselectivity in these cases. Selective formation of the stereochemistry at the 4-aryl group may arise from the protonation from less hindered side (*cis* to adjacent H). The result is in agreement with predominant formation of **10a** in the [4+2] cycloaddition reaction of *N*-allyl-*N*-diphenylallyl amide **9** at 180 °C for 6 days reported by Oppolzer et al. (eq 6).[5c] Intramolecular [4+2] cycloaddition of styrenes with [1,3]-hydrogen shift assisted di-t-butylhydroxytoluene at 160 °C was also reported and radical intermediates were postulated.[5j]



(eq 6)

The reaction of 4,4'-chlorophenyl and 4,4'-methylphenyl substrate models (X = Cl, Me) were also calculated. In the reaction of 4,4'-methylphenyl substrate model (X = Me), the path via intermediate BM1-trans was obtained.

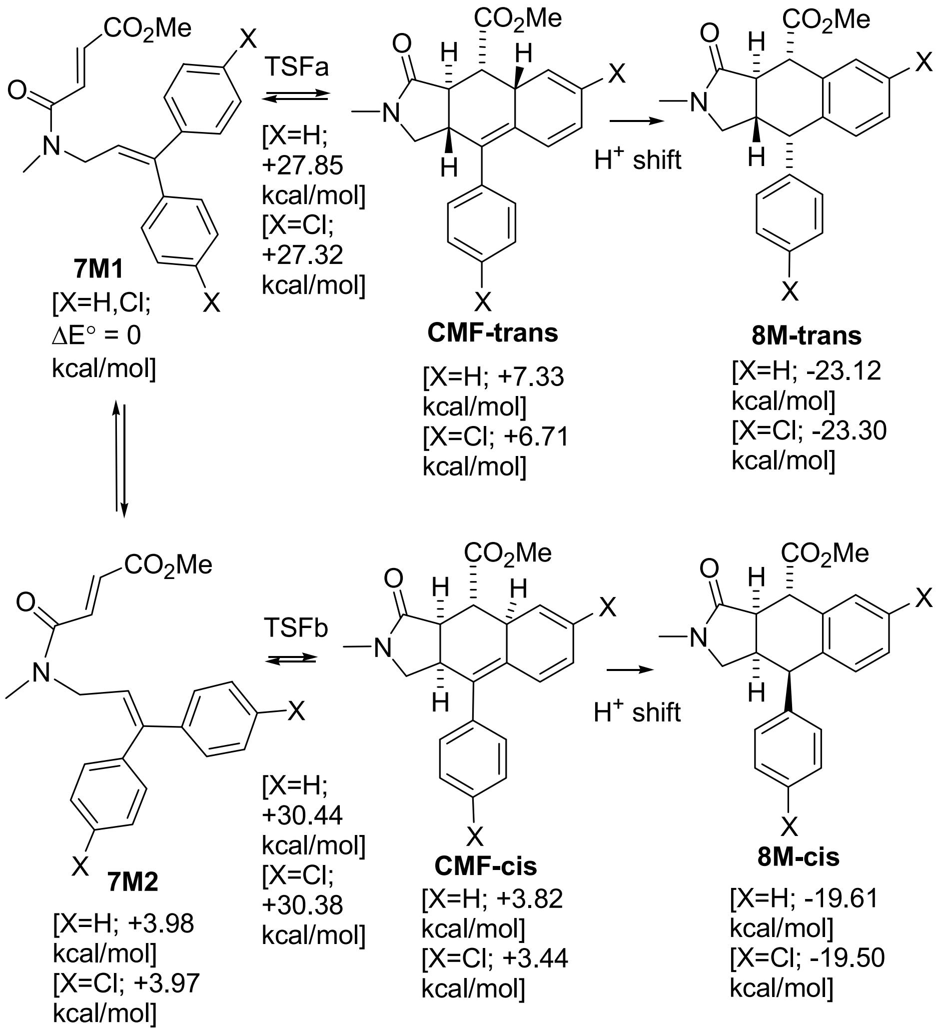
The stepwise H^+ 1,3-shift of CM2-cis (X = H and Me) by catalytic acid in situ leads to rearomatized 5M-cis. The path through TSb with partial ionic character and zwitterionic intermediate BM2-cis (X = Cl) is less stable than those of (X = H and Me) because of destabilization by electron-withdrawing chloro-substituents.

The observed difference on cis- and trans-fused selectivity by substituents in eq 2 and Table 2 may be correlated to the Hammet constants σ.[27] σ (*p*-Me, -0.07) gave *cis*-fused product. σ (H, 0, *p*-F, 0.06) gave *cis* and *trans*-fused products depending on the reaction conditions. Positive values of σ (*p*-Cl, 0.23, *m*-CF_3, 0.43) only gave *trans*-fused cycloadducts. Larger negative value of σ (*p*-OMe, -0.27) gave a complex mixture, probably because of the formation of the byproducts. The selective formation of *trans*-fused ring of mono-NO_2-substituted **5k-trans** (eq 3, Table 3) may be attributed to the destabilization of the cation intermediate BM2-cis similar to bis-Cl and CF_3-substituted substrates.

Diels–Alder reactions of furan with halogen substituents have been found to increase rates and yields.[28] Nitrofurans also undergo intramolecular Diels–Alder reactions more rapidly and in higher yield than non-nitrated furans.[29] Further study for the effects of the electron-withdrawing groups to styrene moiety as dienes in the Diels-Alder reaction is under investigation.

Next, the [4+2] cycloaddition reaction path of less reactive methyl (2*E*)-4-amino-4-oxo-2-butenoates **7** has been examined (Scheme 4). For **7M**, the models of **7a,d**, the concerted paths lead to both *cis* and *trans* adducts. The activation energies of TSFa and TSFb for **7M** leading to cycloadducts CMF-trans and CMF-cis are substantially higher than those of TSa, TSb, and TSc in Scheme 3. The path with lower activation barrier TSFa may give *trans*-[4+2] cycloadduct CMF-trans and the final stable aromatic ring-reproduced product 8M-trans by the stepwise protonation-deprotonation (H^+ 1,3-shift) under the reaction conditions.

The reaction of less reactive amides **7a,c,d,f** with HCl or Et_3N has been shown to give the cyclized products. The 1,3-H shift under thermal conditions without acid or base for **7a** may proceed intermolecularly as well. The [4+2] cycloaddition may be reversible and the catalysts accelerate the 1,3-H shift step.



Scheme 4. [4 + 2] Cycloaddition reaction paths for the models of **7a,d**. ΔE's (sum of electronic and zero-point energies) by B3LYP/6-311+G(d,p) SCRF = (PCM, solvent = THF) // B3LYP/6-31G* SCRF = (PCM, solvent = THF) are shown. The 3D-structures of intermediates and transition states are shown in Supporting Information.

Conclusions

In summary, intramolecular Diels–Alder reactions of various 3,3-diarylpropenylamides of electron-deficient alkenes to give hexahydrobenzo[*f*]isoindoles were investigated. Reaction of 1,1,2-ethenetricarboxylic acid 1,1-diethyl ester with 3,3-diarylpropenylamines or *Z*-cinnamyl amines under the amide formation conditions gave the tricyclic compounds in sequential processes involving intramolecular Diels-Alder reaction. When the electron-withdrawing substituents (positive values of Hammet constants σ) are present on benzene ring, the [4+2] cycloaddition proceeds in *trans*-fused manner. When the substituents such as H and F (σ near 0) are present, the reaction gives *cis* and *trans*-fused products depending on the reaction conditions. When the substituents (slightly negative values of σ) are present, the reaction gives *cis*-fused product. These processes are controlled by the substituents on the benzene ring, reaction temperature and solvent. Reaction of electron-deficient alkenic carboxylic acids such as fumarate and 3,3-diaryl-2-propen-1-amines under the amide formation conditions at room temperature gave the corresponding amides, and the reaction on heating gave trans-fused hexahydrobenzo[*f*]isoindoles. The origin of observed stereoselectivity of the fused rings has been examined by the DFT calculations.

Experimental Section

General Methods. ^{1}H Chemical shifts are reported in ppm relative to Me_4Si. ^{13}C Chemical shifts are reported in ppm relative to $CDCl_3$ (77.1 ppm). ^{19}F Chemical shifts are reported in ppm relative to $CFCl_3$. ^{13}C multiplicities were determined by DEPT and HSQC. Mass spectra were recorded at an ionizing voltage of 70 eV by EI, FAB or ESI. Mass analyzer type used for EI and FAB is double-focusing and that for ESI is TOF in the HRMS measurements. All reactions were carried out under a nitrogen atmosphere. Column chromatography was performed on silica gel (75-150 μm).

1,1,2-Ethenetricarboxylic acid 1,1-diethyl ester **1** was prepared according to the literature.[30] (*Z*)-Cinnamyl alcohol[31] was prepared by hydrogenation of 3-phenyl-2-propyn-1-ol with Lindlar catalyst in methanol.

(*Z*)-Cinnamyl bromide[32] was prepared by reaction of (*Z*)-cinnamyl alcohol with PBr_3 and pyridine in ether and used without further purification. *Z*-Cinnamylamines **2a-b** were prepared by reaction of benzylamine or cyclohexylamine (2 equiv) with (*Z*)-cinnamyl bromide in ether according to the literature procedure.[33]

(*Z*)-**Benzyl cinnamylamine (2a):** *Z*:*E* = 5:1 (2.4 mmol scale, 274 mg, 51%); R_f = 0.1 (hexane-ether = 1 : 1); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) For a major isomer, 1.68 (bs, 1H), 3.55 (dd, J = 6.6, 1.9 Hz, 2H), 3.77 (s, 2H), 5.65 (dt, J = 11.6, 6.6 Hz, 1H), 6.53 (d, J =

11.6 Hz, 1H), 7.19-7.37 (m, 10H). Selected NOEs are between δ 5.65 (=C-*H*) and δ 6.53 (=C-*H*).; ^{13}C NMR (100.6 MHz, $CDCl_3$) *δ* (ppm) For a major isomer, 46.99 (CH_2), 53.53 (CH_2), 126.93 (CH), 127.01 (CH), 128.19 (CH), 128.27 (CH), 128.41 (CH), 128.80 (CH), 130.78 (CH), 130.94 (CH), 137.07 (C), 140.04 (C); IR (neat) 3313, 3024, 2831, 1599, 1494, 1453, 1115, 1028 cm^{-1}; MS (EI) *m/z* 223 (M^+, 35), 222 (17), 132 (100%); HRMS (EI) *m/z* 223.1372 (calcd for $C_{16}H_{17}N$ 223.1361).

(*Z*)-**Cinnamyl cyclohexylmethylamine** (**2b**): *Z*:*E* = 5:1 (20 mmol scale, 2.24 g, 49%); R_f = 0.4 (hexane-ether = 1 : 4); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* (ppm) For a major isomer, 0.834-0.957 (m, 2H), 1.08-1.29 (m, 3H), 1.36-1.48 (m, 1H), 1.62-1.77 (m, 5H), 2.43 (d, *J* = 6.6 Hz, 2H), 3.50 (dd, *J* = 6.5, 1.9 Hz, 2H), 5.76 (dt, *J* = 11.7, 6.5 Hz, 1H), 6.49 (d, *J* = 11.7 Hz, 1H), 7.16-7.37 (m, 5H). Selected NOEs are between δ 5.76 (=C-*H*) and δ 6.49 (=C-*H*) and between δ 3.50 (CH_2) and δ 7.16-7.37 (Ph).; ^{13}C NMR (100.6 MHz, $CDCl_3$) *δ* (ppm) For a major isomer, 26.03 (CH_2), 26.66 (CH_2), 31.45 (CH_2), 38.01 (CH), 47.92 (CH_2), 56.48 (CH_2), 126.76 (CH), 128.08 (CH), 128.74 (CH), 130.14 (CH), 131.56 (CH), 137.18 (C); IR (neat) 3323, 3023, 2923, 1600, 1494, 1447, 1124 cm^{-1}; MS (EI) *m/z* 229 (M^+, 9.3), 146 (19), 117 (100%); HRMS (EI) *m/z* 229.1836 (calcd for $C_{16}H_{23}N$ 229.1830).

Typical experimental procedure for eq 1 (eq 1, Table 1, entry 2). To a solution of 1,1,2-ethenetricarboxylic acid 1,1-diethyl ester (**1**) (prepared from 1,1-diethyl 2-*tert*-butyl ethenetricarboxylate (272 mg, 1 mmol) upon treatment with CF_3CO_2H (4 mL))[30] in benzene (0.7 mL) were added *Z*-benzyl cinnamylamine (**2a**) (223 mg, 1 mmol) in benzene (0.7 mL), Et_3N (0.14 mL, 102 mg, 1 mmol), HOBt (1-hydroxybenzotriazole) (270 mg, 2 mmol) and EDCI (1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride) (199 mg, 1.04 mmol) at 0 °C. The reaction mixture was stirred for 1 h at 0 °C, and then heated at 80 °C and stirred for 20 h. The reaction mixture was diluted with CH_2Cl_2. The organic phase was washed with saturated aqueous $NaHCO_3$ solution, 2M aqueous citric acid, saturated aqueous $NaHCO_3$ and water, dried (Na_2SO_4), and evaporated *in vacuo*. The residue was purified by column chromatography over silica gel eluting with hexane-Et_2O to give **3a** (261 mg, 62%).

3a: R_f = 0.5 (hexane-ether = 1 : 4); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.17 (t, *J* = 7.1 Hz, 3H), 1.33 (t, *J* = 7.1 Hz, 3H), 2.34 (dd, *J* = 17.4, 11.1 Hz, 1H), 2.86-2.98 (m, 3H), 3.49 (dd, *J* = 8.5, 8.5 Hz, 1H), 3.59 (d, *J* = 11.1 Hz, 1H), 4.07-4.26 (m, 2H), 4.27 (d, *J* = 14.7 Hz, 1H), 4.35-4.40 (m, 2H), 4.67 (d, *J* = 14.7 Hz, 1H), 7.08 (d, *J* = 7.2 Hz, 1H), 7.15-7.18 (m, 2H), 7.20-7.30 (m, 5H), 7.53 (dd, *J* = 7.7, 1.3 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.80 (CH_3), 13.99 (CH_3), 29.05 (CH), 33.21 (CH_2), 46.85 (CH_2), 48.41 (CH), 52.48 (CH_2), 60.72 (C), 61.72 (CH_2), 62.29 (CH_2), 126.96 (CH), 127.34 (CH), 127.77 (CH), 127.82 (CH), 127.97 (CH), 128.22 (CH), 128.49 (CH), 135.36 (C), 136.14 (C), 136.35 (C), 168.81 (C), 169.88 (C), 172.77 (C); ^{1}H NMR (400 MHz, C_6D_6) δ (ppm) 0.843 (t, *J* = 7.1 Hz, 3H), 0.949 (t, *J* = 7.1 Hz, 3H), 2.09 (dd, *J* = 14.8, 8.6 Hz, 1H), 2.35 (ddddd, *J* = 11.5, 9.0, 8.6, 7.2, 6.4 Hz, 1H), 2.50 (dd, *J* = 14.8, 7.2 Hz, 1H), 2.58 (dd, *J* = 9.0 Hz, 6.4 Hz, 1H), 2.88 (dd, *J* = 9.0, 9.0 Hz, 1H), 3.62 (d, *J* = 11.5 Hz, 1H), 3.81-3.89 (m, 1H), 4.01-4.17 (m, 3H), 4.17 (d, *J* = 14.8 Hz, 1H), 4.35 (d, *J* = 14.8 Hz, 1H), 6.78 (d, *J* = 7.0 Hz, 1H), 6.93-7.08 (m, 7H), 7.83 (dd, *J* = 7.8, 1.0 Hz, 1H). Selected NOEs are between δ 2.35 (C3a-*H*) and δ 3.62 (C9a-*H*), 2.88 (C3-H*H*) and 2.50 (C4-H*H*). Atom numbering is shown in Supporting Information.; ^{13}C NMR (100.6 MHz, C_6D_6) δ (ppm) 13.85 (CH_3), 13.95 (CH_3), 29.30 (CH), 33.24 (CH_2), 46.94 (CH_2), 48.68 (CH), 52.21 (CH_2), 61.08 (C), 61.61 (CH_2), 62.17 (CH_2), 127.13 (CH), 127.38 (CH), 127.89 (CH), 128.24 (CH), 128.49 (CH), 128.66 (CH), 128.73 (CH), 136.15 (C), 136.78 (C), 137.29 (C), 168.87 (C), 169.95 (C), 172.26 (C). Selected HMBC correlations are between δ 2.35 (C4-*H*H), 2.50 (C4-H*H*), 2.58 (C3-*H*H), 2.88 (C3-H*H*), 3.62 (C9a-*H*) and δ 29.30 (*C*3a), δ 2.58 (C3-*H*H), 2.88 (C3-H*H*), 3.62 (C9a-*H*), 6.78 (C5-*H*) and δ 33.24 (*C*4), and between δ 3.62 (C9a-*H*) and δ 61.08 (*C*9).; IR (neat) 2980, 1734, 1689, 1485, 1444, 1247, 1096, 1031 cm^{-1}; MS (EI) *m/z* 421 (M^+, 45), 347 (8.4), 303 (14), 301 (12), 91 (100%); HRMS (EI) *m/z* 421.1906 (calcd for $C_{25}H_{27}NO_5$ 421.1889).

3b: (1 mmol scale, toluene, 110 °C, 262 mg, 61%); R_f = 0.3 (hexane-ether = 1 : 4); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.803-0.925 (m, 2H), 1.09-1.20 (m, 3H), 1.17 (t, *J* = 7.0 Hz, 3H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.43-1.70 (m, 6H), 2.40 (dd, *J* = 17.5, 11.0 Hz, 1H), 2.87 (dd, *J* = 13.5, 6.7 Hz, 1H), 2.96-3.01 (m, 2H), 3.05 (dd, *J* = 9.0, 5.9 Hz, 1H), 3.30 (dd, *J* = 13.5, 7.8 Hz, 1H), 3.55 (d, *J* = 10.7 Hz, 1H), 3.66 (dd, *J* = 9.0, 8.6 Hz, 1H), 4.08-4.26 (m, 2H), 4.34

(q, *J* = 7.1 Hz, 2H), 7.11-7.13 (m, 1H), 7.20-7.28 (m, 2H), 7.54-7.57 (m, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.83 (CH_3), 13.98 (CH_3), 25.77 (CH_2), 25.83 (CH_2), 26.38 (CH_2), 29.17 (CH), 30.74 (CH_2), 30.78 (CH_2), 33.34 (CH_2), 35.85 (CH), 48.52 (CH), 49.40 (CH_2), 54.10 (CH_2), 60.54 (C), 61.65 (CH_2), 62.24 (CH_2), 126.94 (CH), 127.71 (CH), 127.95 (CH), 127.97 (CH), 135.36 (C), 136.14 (C), 168.75 (C), 169.90 (C), 172.96 (C); ^{1}H NMR (400 MHz, C_6D_6) δ (ppm) 0.689-0.850 (m, 2H), 0.965-1.12 (m, 3H), 0.938 (t, *J* = 7.1 Hz, 3H), 0.993 (t, *J* = 7.0 Hz, 3H), 1.36-1.45 (m, 2H), 1.49-1.63 (m, 4H), 2.26 (dd, *J* = 14.8, 8.2 Hz, 1H), 2.53 (ddddd, *J* = 11.3, 8.8, 8.2, 7.0, 6.4 Hz, 1H), 2.69 (dd, *J* = 14.8, 7.0 Hz, 1H), 2.73 (dd, *J* = 9.0, 6.4 Hz, 1H), 2.90 (dd, *J* = 13.5, 6.8 Hz, 1H), 3.04 (dd, *J* = 9.0, 8.8 Hz, 1H), 3.12 (dd, *J* = 13.5, 7.2 Hz, 1H), 3.71 (d, *J* = 11.3 Hz, 1H), 3.91-3.99 (m, 1H), 4.07-4.24 (m, 3H), 6.92 (d, *J* = 7.4, 0.6 Hz, 1H), 7.05 (ddd, *J* = 7.6, 7.4, 1.2 Hz, 1H), 7.14 (ddd, *J* = 7.8, 7.6, 1.4 Hz, 1H), 8.01 (d, *J* = 7.8 Hz, 1H). Selected NOEs are between δ 2.53 (C3a-*H*) and δ 3.71 (C9a-*H*), 3.04 (C3-H*H*) and 2.69 (C4-H*H*).; ^{13}C NMR (100.6 MHz, C_6D_6) δ (ppm) 13.85 (CH_3), 13.90 (CH_3), 26.15 (CH_2), 26.70 (CH_2), 29.43 (CH), 30.88 (CH_2), 31.06 (CH_2), 33.44 (CH_2), 36.16 (CH), 48.76 (CH), 49.47 (CH_2), 53.77 (CH_2), 60.88 (C), 61.53 (CH_2), 62.10 (CH_2), 127.14 (CH), 127.76 (CH), 128.24 (CH), 128.98 (CH), 136.10 (C), 136.71 (C), 168.76 (C), 169.93 (C), 172.34 (C). Selected HMBC correlations are between δ 2.26 (C4-*H*H), 2.69 (C4-H*H*), 2.73 (C3-*H*H), 3.04 (C3-H*H*), 3.71 (C9a-*H*) and δ 29.30 (*C*3a), δ 2.58 (C3-*H*H), 2.88 (C3-H*H*), 3.62 (C9a-*H*), 6.92 (C5-*H*) and δ 29.43 (*C*4), and between δ 3.62 (C9a-*H*) and δ 60.88 (*C*9).; IR (neat) 2925, 2852, 1733, 1690, 1485, 1448, 1366, 1236, 1118, 1095, 1035 cm^{-1}; MS (EI) *m/z* 427 (M^+, 9.9), 345 (11), 117 (10), 84 (100%); HRMS (EI) *m/z* 427.2368 (calcd for $C_{25}H_{33}NO_5$ 427.2359).

Arylpropenyl esters, ethyl 3,3-diphenylacrylate **Xa** (for **4a-b**), ethyl 3,3-bis-(4-fluorophenyl)acrylate **Xc** (for **4c**), ethyl 3,3-bis-(4-chlorophenyl)acrylate **Xd** (for **4d**), ethyl 3,3-bis[3-(trifluoromethyl)phenyl]acrylate **Xe** (for **4e**) and ethyl (2Z)-3-(2-chlorophenyl)-3-phenylprop-2-enoate **Xh** (for **4h**) and the corresponding alcohols, 3,3-diphenylprop-2-en-1-ol **Ya**, 3,3-bis(4-fluorophenyl)prop-2-en-1-ol **Yc**, 3,3-bis(4-chlorophenyl)prop-2-en-1-ol **Yd**, 3,3-bis[3-(trifluoromethyl)phenyl]prop-2-en-1-ol **Ye**, and 3-(2-chlorophenyl)-3-phenylprop-

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2-en-1-ol **Yh** were prepared according to the literature.[17] Arylpropenyl esters **Xf** (for **4f**), **Xg** (for **4g**), **Xi** (for **4i**), **Xj** (for **4j**), **Xk** (for **4k**) and the corresponding alcohols **Yf** (for **4f**), **Yg** (for **4g**), **Yi** (for **4i**), **Yk** (for **4k**) were prepared by the literature methods.[17]

The stereochemistry of ethyl 3-(2-chlorophenyl)-3-phenylprop-2-enoate **Xh** obtained as a major product by the literature method was reported as *E*[17] but it was found to be *Z* by the observed NOE's in C_6D_6. The ^{1}H NMR spectra of **Xh** in $CDCl_3$ were in accord with the reported data.

(2*E*)-3-(4-chlorophenyl)-3-phenylprop-2-en-1-ol (**Yj**) (for **4j**) was prepared by the Suzuki cross-coupling reaction of (*E*)-3-bromo-3-phenylprop-2-en-1-ol and 4-chlorophenylboronic acid by the literature method.[34]

Ethyl 3,3-bis-(4-methylphenyl)acrylate (**Xf**): (2.7 mmol scale, 721 mg, 95%); $R_f = 0.4$ (hexane-ether = 4 : 1); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.14 (t, *J* = 7.1 Hz, 3H), 2.34 (s, 3H), 2.39 (s, 3H), 4.06 (q, *J* = 7.1 Hz, 2H), 6.30 (s, 1H), 7.08-7.12 (m, 4H), 7.17-7.20 (m, 4H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 14.13 (CH_3), 21.29 (CH_3), 21.44 (CH_3), 59.96 (CH_2), 116.22 (CH), 128.38 (CH), 128.59 (CH), 129.09 (CH), 129.21 (CH), 136.16 (C), 137.94 (C), 138.34 (C), 139.61 (C), 156.94 (C), 166.31 (C); IR (neat) 2980, 1723, 1604, 1508, 1368, 1264, 1160, 1038 cm^{-1}; MS (EI) *m/z* 280 (M^+, 98), 235 (100%); HRMS (EI) *m/z* 280.1459 (calcd for $C_{19}H_{20}O_2$ 280.1463).

Ethyl 3,3-bis-(4-methoxyphenyl)acrylate (**Xg**): (2.7 mmol scale, 537 mg, 64%); $R_f = 0.4$ (hexane-ether = 1 : 1); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.16 (t, *J* = 7.1 Hz, 3H), 3.81 (s, 3H), 3.84 (s, 3H), 4.07 (q, *J* = 7.1 Hz, 2H), 6.23 (s, 1H), 6.84 (d-like, *J* = 9.0 Hz, 2H), 6.91 (d-like, *J* = 8.7 Hz, 2H), 7.15 (d-like, *J* = 8.7 Hz, 2H), 7.24 (d-like, *J* = 9.0 Hz, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 14.21 (CH_3), 55.27 (CH_3), 55.39 (CH_3), 59.90 (CH_2), 113.26 (CH), 113.74 (CH), 114.97 (CH), 130.04 (CH), 130.91 (CH), 131.33 (C), 133.89 (C), 156.43 (C), 159.71 (C), 160.79 (C), 166.50 (C); IR (neat) 2979, 2837, 1717, 1600, 1513, 1250, 1174, 1149, 1034 cm^{-1}; MS (EI) *m/z* 312 (M^+, 100), 267 (33), 240 (49%); HRMS (EI) *m/z* 312.1357 (calcd for $C_{19}H_{20}O_4$ 312.1362).

Ethyl (2Z)-3-(2-chlorophenyl)-3-phenylprop-2-enoate (**Xh**): ^{1}H NMR (400 MHz, C_6D_6) δ (ppm) 0.824 (t, J = 7.1 Hz, 3H), 3.88 (q, J = 7.1 Hz, 2H), 6.61 (s, 1H), 6.86 (ddd, J = 7.6, 7.5, 2.0 Hz, 1H), 6.91 (ddd, J = 7.5, 7.4, 1.4 Hz, 1H), 6.95-7.03 (m, 5H), 7.18-7.20 (m, 2H), 7.24 (dd, J = 7.6, 1.4 Hz, 1H). Selected NOEs are between δ 6.61 (C2-*H*) and δ 7.18-7.20 (2-*H* of Ph).; ^{13}C NMR (100.6 MHz, C_6D_6) δ (ppm) 13.99 (CH_3), 59.91 (CH_2), 119.56 (CH), 126.54 (CH), 127.67 (CH), 128.79 (CH), 129.05 (CH), 129.57 (CH), 130.62 (CH), 133.14 (C), 138.74 (C), 139.06 (C), 153.03 (C), 164.89 (C).

Xi and **Xj** were obtained as a ca. 1:1 mixture. (20 mmol scale, 5.46 g, 95%). **Xi** (2.15 g, 38%) was partially isolated by fractional crystallization of the mixture (from hexane). **Xj** (3:1 (**Xj**:**Xi**) mixture) was obtained from the filtrates. The stereochemistries of **Xi** and **Xj** were assigned by the NOE's of the corresponding alcohols **Yi** and **Yj** obtained by DIBAL-H reduction. The spectral data for **Yj** obtained from **Xj** were in accord with those by the Suzuki cross-coupling reaction.

Ethyl (2*Z*)-3-(4-chlorophenyl)-3-phenylprop-2-enoate (**Xi**): R_f = 0.5 (hexane-ether = 4 : 1); colorless crystals; mp 67-68 °C (hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.16 (t, J = 7.1 Hz, 3H), 4.07 (q, J = 7.1 Hz, 2H), 6.37 (s, 1H), 7.15 (d-like, J = 8.4 Hz, 2H), 7.26-7.39 (m, 7H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 14.12 (CH_3), 60.27 (CH_2), 117.92 (CH), 128.24 (CH), 128.33 (CH), 128.56 (CH), 129.69 (CH), 130.69 (CH), 134.26 (C), 137.43 (C), 140.49 (C), 155.46 (C), 165.96 (C); IR (KBr) 2981, 1718, 1488, 1368, 1271, 1157, 1089 cm^{-1}; MS (EI) *m/z* 288 (M$^+$, 27), 286 (M$^+$, 81), 241 (100%); HRMS (EI) *m/z* 286.0759, 288.0732 (calcd for $C_{17}H_{15}ClO_2$ 286.0761, 288.0731); Anal. Calcd for $C_{17}H_{15}ClO_2$: C, 71.20; H, 5.27. Found: C, 71.27; H, 5.29.

Ethyl (2*E*)-3-(4-chlorophenyl)-3-phenylprop-2-enoate (**Xj**): R_f = 0.4 (hexane-ether = 4 : 1); pale yellow oil; (**Xj**:**Xi** = 3:1) ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.10 (t, J = 7.1 Hz, 3H), 4.04 (q, J = 7.1 Hz, 2H), 6.33 (s, 1H), 7.14-7.23 (m, 3H), 7.25-7.39 (m, 6H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.98 (CH_3), 60.14 (CH_2), 117.81 (CH), 128.00 (CH), 128.61 (CH), 129.08 (CH), 129.55 (CH), 130.62 (CH), 135.50 (C), 138.51 (C), 139.26 (C), 155.10 (C), 165.86 (C); IR (neat) 2981, 1724, 1618, 1489, 1368, 1263, 1165, 1092 cm^{-1}; MS (EI) *m/z* 288

(M^+, 27), 286 (M^+, 79), 241 (89), 214 (51), 178 (100%); HRMS (EI) *m/z* 286.0767, 288.0743 (calcd for $C_{17}H_{15}ClO_2$ 286.0761, 288.0731).

Ethyl (2*Z*)-3-(4-nitrophenyl)-3-phenylprop-2-enoate (**Xk**): (2.7 mmol scale, 424 mg, purified by recrystalization, 52%); R_f = 0.4 (hexane- AcOEt = 4 : 1); yellow crystals; mp 88.5-90.0 °C (hexane-MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.17 (t, J = 7.1 Hz, 3H), 4.07 (d, J = 7.1 Hz, 2H), 6.48 (s, 1H), 7.24-7.27 (m, 2H), 7.33-7.43 (m, 5H), 8.27 (d-like, J = 8.8 Hz, 2H). Selected NOEs are between δ 6.48 (C2-*H*) and δ 7.24-7.27 (2-*H* of Ph).; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 14.12 (CH_3), 60.54 (CH_2), 118.62 (CH), 123.34 (CH), 128.08 (CH), 128.81 (CH), 130.08 (CH), 130.14 (CH), 139.24 (C), 146.13 (C), 147.57 (C), 154.50 (C), 165.49 (C). Selected HMBC correlations are between δ 6.48 (C2-*H*) and δ 139.24 (1-*C* of Ph), and δ 7.24-7.27 (2-*H* of Ph) and δ 154.50 (*C*3).; IR (KBr) 2985, 1719, 1619, 1594, 1515, 1350, 1267, 1172, 1034 cm^{-1}; MS (EI) *m/z* 297 (M^+, 80), 252 (100%); HRMS (EI) *m/z* 297.1010 (calcd for $C_{17}H_{15}NO_4$ 297.1001).

3,3-Bis(4-methylphenyl)prop-2-en-1-ol (**Yf**): (26 mmol scale, 5.915 g, 95%); colorless crystals: mp 68.5-69.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.57 (bs, 1H), 2.33 (s, 3H), 2.37 (s, 3H), 4.19 (d, J = 6.8 Hz, 2H), 6.17 (t, J = 6.8 Hz, 1H), 7.04 (d-like, J = 8.0 Hz, 2H), 7.08 (d-like, J = 8.0 Hz, 2H), 7.13-7.17 (m, 4H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 21.15 (CH_3), 21.29 (CH_3), 60.81 (CH_2), 126.46 (CH), 127.62 (CH), 128.91 (CH), 129.72 (CH), 136.28 (C), 137.26 (C), 137.42 (C), 139.27 (C), 144.13 (C); IR (KBr) 3267, 2916, 1510, 1012 cm^{-1}; MS (EI) *m/z* 238 (M^+, 60), 223 (68), 195 (100%); HRMS (EI) *m/z* 238.1361 (calcd for $C_{17}H_{18}O$ 238.1358).

3,3-Bis(4-methoxyphenyl)prop-2-en-1-ol (**Yg**): (19.4 mmol scale, 5.26 g, 100%); R_f = 0.1 (hexane-ether = 1 : 1); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.75 (bs, 1H), 3.79 (s, 3H), 3.82 (s, 3H), 4.20 (d. J = 7.0 Hz, 2H), 6.09 (t, J = 7.0 Hz, 1H), 6.81 (d-like, J = 8.9 Hz, 2H), 6.88 (d-like, J = 8.8 Hz, 2H), 7.07 (d-like, J = 8.8 Hz, 2H), 7.18 (d-like, J = 8.9 Hz, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 55.29 (CH_3), 55.31 (CH_3), 60.81 (CH_2), 113.54 (CH), 113.56 (CH), 125.46 (CH), 128.92 (CH), 131.01 (CH), 131.60 (C), 134.86 (C), 143.48 (C), 159.01 (C), 159.24 (C); IR (neat) 3344, 2933, 2835, 1607, 1511, 1245, 1174, 1034 cm^{-1}; MS

(EI) *m/z* 270 (M^+, 52), 242 (29), 227 (100), 135 (65%); HRMS (EI) *m/z* 270.1253 (calcd for $C_{17}H_{18}O_3$ 270.1256).

(2*Z*)-3-(2-chlorophenyl)-3-phenylprop-2-en-1-ol (**Yh**): (11.4 mmol scale, 2.67 g, 96%); R_f = 0.1 (hexane-ether = 1 : 1); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.55 (bs, 1H), 4.03-4.08 (m, 2H), 6.44 (t, *J* = 6.8 Hz, 1H), 7.18-7.20 (m, 1H), 7.22-7.33 (m, 7H), 7.43-7.48 (m, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 60.99 (CH_2), 126.58 (CH), 126.96 (CH), 127.83 (CH), 128.46 (CH), 128.60 (CH), 129.15 (CH), 129.82 (CH), 131.50 (CH), 133.61 (C), 137.75 (C), 139.66 (C), 140.79 (C); IR (neat) 3327, 3056, 2867, 1597, 1494, 1472, 1446, 1052, 1035 cm^{-1}; MS (EI) *m/z* 246 (M^+, 11), 244 (M^+, 32), 209 (100%); HRMS (EI) *m/z* 244.0651, 246.0625 (calcd for $C_{15}H_{13}ClO$ 244.0655, 246.0625); ^{1}H NMR (400 MHz, C_6D_6) δ (ppm) 0.43 (bs, 1H), 3.93 (bs, 2H), 6.33-6.39 (m, 1H), 6.78-6.88 (m, 2H), 6.92-6.97 (m, 1H), 7.00-7.09 (m, 3H), 7.19 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.22-7.25 (m, 2H). Selected NOEs are between δ 6.33-6.39 (C*H*=CPh) and δ 7.22-7.25 (2'-*H* of CH=C*Ph*) and between δ 3.93 (C*H*$_2$) and δ 6.92-6.97 (6-*H* of 2-chlorophenyl) in C_6D_6.; ^{13}C NMR (100.6 MHz, C_6D_6) δ (ppm) 60.75 (CH_2), 126.82 (CH), 126.90 (CH), 127.76 (CH), 128.65 (CH), 129.05 (CH), 129.89 (CH), 129.91 (CH), 131.77 (CH), 134.08 (C), 138.37 (C), 140.17 (C), 140.25 (C).

(2*Z*)-3-(4-chlorophenyl)-3-phenylprop-2-en-1-ol (**Yi**): (8.75 mmol scale, 2.37 g, 94%); R_f = 0.4 (hexane-ether = 1 : 1); colorless crystals; mp 88.5-89.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.48 (bs, 1H), 4.20 (d, *J* = 6.8 Hz, 2H), 6.24 (t, *J* = 6.8 Hz, 1H), 7.11 (d-like, *J* = 8.6 Hz, 2H), 7.22-7.32 (m, 5H), 7.35 (d-like, *J* = 8.6 Hz, 2H). Selected NOEs are between δ 4.20 (C*H*$_2$) and δ 7.11 (2-*H* of 4-chlorophenyl).; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 60.66 (CH_2), 127.88 (CH), 127.91 (CH), 128.02 (CH), 128.37 (CH), 128.57 (CH), 131.21 (CH), 133.67 (C), 137.55 (C), 141.47 (C), 143.26 (C); IR (KBr) 3270, 2860, 1594, 1491, 1091, 1015 cm^{-1}; MS (EI) *m/z* 246 (M^+, 23), 244 (M^+, 70), 201 (100%); HRMS (EI) *m/z* 244.0647, 246.0615 (calcd for $C_{15}H_{13}ClO$ 244.0655, 246.0625).

(2*Z*)-3-(4-Nitrophenyl)-3-phenylprop-2-en-1-ol (**Yk**): (5 mmol scale, 854 mg, 88%); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 2.12 (bs, 1H), 4.19 (d, *J* = 6.9 Hz, 2H), 6.34 (t, *J* = 6.9 Hz, 1H), 7.18-7.21 (m, 2H), 7.28-7.32 (m, 3H), 7.35 (d-like, *J* = 8.8 Hz, 2H), 8.21 (d-like, *J* = 8.8 Hz, 2H). Selected NOEs are between δ 6.34 (C*H*=CPh) and δ 7.18-7.21 (2'-*H* of CH=C*Ph*) between δ 4.19 (C*H*$_2$) and δ 7.35 (2-*H* of 4-nitrophenyl).; ^{13}C NMR (100.6 MHz, CDCl$_3$) *δ* (ppm) 60.27 (CH$_2$), 123.53 (CH), 127.56 (CH), 128.21 (CH), 128.51 (CH), 129.34 (CH), 130.75 (CH), 140.57 (C), 142.29 (C), 146.10 (C), 147.21 (C); IR (neat) 3359, 3078, 1520, 1347, 1107, 1014 cm^{-1}; MS (EI) *m/z* 255 (M$^+$, 100), 237 (79), 212 (61), 165 (78%); HRMS (EI) *m/z* 255.0892 (calcd for $C_{15}H_{13}NO_3$ 255.0895).

Preparation of Yj. A mixture of Pd(OAc)$_2$ (22 mg, 0.1 mmol), PPh$_3$ (52 mg, 0.2 mmol), 4-chlorophenylboronic acid (2.4 mmol), KOH (224 mg, 4 mmol), MeOH (8 mL), and THF (8 mL) was heated at 60 °C overnight. After cooling to room temperature, the solution was taken up in Et$_2$O (30 mL) and the Et$_2$O layer was washed with aq 1.0 M NaOH (10 mL) and brine (2 × 5mL). The organic layer was dried (MgSO$_4$), filtered, concentrated under reduced pressure. The crude material was purified by column chromatography on silica gel using hexane/ethyl acetate as eluent. The *E*-configuration of the products was assigned by 2D-NOESY.

(2*E*)-3-(4-chlorophenyl)-3-phenylprop-2-en-1-ol (**Yj**): (6.8 mmol scale, 1.49 g, 90%); R$_f$ = 0.3 (hexane-AcOEt = 1 : 1); colorless crystals; mp 72.0-73.0 °C; ^{1}H NMR (400 MHz, CDCl$_3$) *δ* (ppm) 1.53 (bs, 1H), 4.21 (d, *J* = 6.8 Hz, 2H), 6.22 (t, *J* = 6.8 Hz, 1H), 7.12-7.15 (m, 2H), 7.18 (d-like, *J* = 8.6 Hz, 2H), 7.25 (d-like, *J* = 8.6 Hz, 2H), 7.32-7.40 (m, 3H). Selected NOEs are between δ 4.21 (C*H*$_2$) and δ 7.12-7.15 (2'-*H* of CH=C*Ph*) and between δ 6.22 (C*H*=CAr) and δ 7.18 (2-*H* of 4-chlorophenyl).; ^{13}C NMR (100.6 MHz, CDCl$_3$) *δ* (ppm) 60.71 (CH$_2$), 127.88 (CH), 127.97 (CH), 128.42 (CH), 128.95 (CH), 129.73 (CH), 133.57 (C), 138.64 (C), 140.33 (C), 143.15 (C); IR (neat) 3261, 2848, 1488, 1092, 1010 cm^{-1}; MS (EI) *m/z* 246 (M$^+$, 22), 244 (M$^+$, 67), 226 (37), 209 (61), 201 (100%); HRMS (EI) *m/z* 244.0651, 246.0625 (calcd for $C_{15}H_{13}ClO$ 244.0655, 246.0625).

The 3,3-diaryl-2-propen-1-amines **4a-k** were prepared from the corresponding alcohols **Ya**, **Yc-k**. The corresponding bromides were prepared by reaction of the alcohols with PBr$_3$ in ether and used without further purification. The 3,3-diaryl-2-propen-1-amines **4a-k** were prepared by reaction of benzylamine (2 equiv) with the corresponding bromide in ether according to the literature procedure.[33]

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4a: (1.5 mmol scale, 216 mg, 48%); R_f = 0.1 (hexane-ether = 1 : 1); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 2.00 (bs, 1H), 3.35 (d, J = 7.0 Hz, 2H), 3.75 (s, 2H), 6.22 (t, J = 7.0 Hz, 1H), 7.14-7.16 (m, 2H), 7.19-7.36 (m, 13H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 48.02 (CH_2), 53.43 (CH_2), 127.05 (CH), 127.30 (CH), 127.34 (CH), 127.48 (CH), 128.19 (CH), 128.24 (CH), 128.26 (CH), 128.44 (CH), 129.81 (CH), 139.64 (C), 139.99 (C), 142.21 (C), 143.83 (C); IR (neat) 3330, 3026, 2836, 1598, 1495, 1443, 1114, 1073, 1028 cm^{-1}; MS (EI) *m/z* 299 (M$^+$, 70), 298 (21), 222 (30), 208 (66), 132 (49), 91 (100%); HRMS (EI) *m/z* 299.1678 (calcd for $C_{22}H_{21}N$ 299.1674).

4b: (10 mmol scale, 1.31 g, 43%); R_f = 0.1 (hexane-ether = 1 : 1); colorless crystals; mp 67.5-68.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.803-0.901 (m, 2H), 1.06-1.24 (m, 4H), 1.31-1.42 (m, 1H), 1.62-1.70 (m, 5H), 2.38 (d, J = 6.6 Hz, 2H), 3.27 (d, J = 6.8 Hz, 2H), 6.18 (t, J = 6.8 Hz, 1H), 7.14-7.34 (m, 5H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 25.93 (CH_2), 26.57 (CH_2), 31.29 (CH_2), 37.80 (CH), 48.60 (CH_2), 56.19 (CH_2), 126.99 (CH), 127.20 (CH), 127.94 (CH), 127.98 (CH), 128.04 (CH), 129.60 (CH), 139.61 (C), 142.06 (C), 142.96 (C); IR (neat) 3317, 3076, 2925, 2846, 1596, 1493, 1444, 1363, 1118 cm^{-1}; MS (EI) *m/z* 305 (M$^+$, 46), 302 (11), 222 (11), 193 (100%); HRMS (EI) *m/z* 305.2145 (calcd for $C_{22}H_{27}N$ 305.2143); Anal. Calcd for $C_{22}H_{27}N$: C, 86.51; H, 8.91; N, 4.59. Found: C, 86.35; H, 8.66; N, 4.49.

4c: (2 mmol scale, 501 mg, 74%); R_f = 0.4 (hexane-ether = 4 : 1); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.60 (bs, 1H), 3.32 (d, J = 6.8 Hz, 2H), 3.75 (s, 2H), 6.13 (t, J = 6.8 Hz, 1H), 6.92-6.98 (m, 2H), 7.01-7.06 (m, 2H), 7.07-7.12 (m, 2H), 7.14-7.19 (m, 2H), 7.21-7.32 (m, 5H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 48.00 (CH_2), 53.59 (CH_2), 115.10 (CH, d, J_{FC} = 21 Hz), 115.27 (CH, d, J_{FC} = 21 Hz), 127.09 (CH), 127.90 (CH), 128.19 (CH), 128.47 (CH), 129.03 (CH, d, J_{FC} = 8.4 Hz), 131.39 (CH, d, J_{FC} = 8.4 Hz), 135.28 (C, d, J_{FC} = 3.1 Hz), 138.22 (C, d, J_{FC} = 3.1 Hz), 140.06 (C), 141.63 (C), 162.13 (C, d, J_{FC} = 247 Hz), 162.32 (C, d, J_{FC} = 247 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) -115.14 (m), -114.68 (m); IR (neat) 3330, 3028, 2835, 1601, 1508, 1453, 1224, 1159, 1095 cm^{-1}; MS (EI) *m/z* 335 (M$^+$, 94), 244 (70), 132 (67), 91 (100%); HRMS (EI) *m/z* 335.1482 (calcd for $C_{22}H_{19}F_2N$ 335.1486).

4d: (2.5 mmol scale, 446 mg, 48%); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.61 (bs, 1H), 3.31 (d, J = 6.8 Hz, 2H), 3.73 (s, 2H), 6.17 (t, J = 6.8 Hz, 1H), 7.05 (d-like, J = 8.7

Hz, 2H), 7.11 (d-like, *J* = 8.7 Hz, 2H), 7.20-7.32 (m, 9H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 47.98 (CH_2), 53.62 (CH_2), 127.08 (CH), 128.15 (CH), 128.43 (CH), 128.47 (CH), 128.60 (CH), 128.69 (CH), 128.89 (CH), 131.10 (CH), 133.41 (C), 133.49 (C), 137.57 (C), 140.09 (C), 140.29 (C), 141.37 (C); IR (neat) 3028, 2837, 1591, 1492, 1091, 1014 cm^{-1}; MS (EI) *m/z* 369 (M^+, 6.5), 367 (M^+, 10), 278 (7.3), 276 (10), 165 (60), 164 (58), 106 (100%); HRMS (EI) *m/z* 367.0887, 369.0887 (calcd for $C_{22}H_{19}Cl_2N$ 367.0895, 369.0865).

4e: (1.9 mmol scale, 592 mg, 72%); R_f = 0.3 (hexane-ether = 1 : 4); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.52 (bs, 1H), 3.34 (d, *J* = 6.8 Hz, 2H), 3.76 (s, 2H), 6.30 (t, *J* = 6.8 Hz, 1H), 7.22-7.34 (m, 7H), 7.39 (dd, *J* = 7.7, 7.7 Hz, 1H), 7.41 (s, 1H), 7.47-7.53 (m, 3H), 7.61 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 47.98 (CH_2), 53.75 (CH_2), 123.96 (CH, q, J_{FC} = 3.8 Hz), 124.08 (C, q, J_{FC} = 272 Hz), 124.12 (C, q, J_{FC} = 273 Hz), 124.37 (CH, q, J_{FC} = 3.8 Hz), 124.64 (CH, q, J_{FC} = 3.8 Hz), 126.46 (CH, q, J_{FC} = 3.8 Hz), 127.19 (CH), 128.19 (CH), 128.53 (CH), 128.89 (CH), 129.05 (CH), 130.84 (CH), 130.92 (C, q, J_{FC} = 32 Hz), 130.96 (CH), 130.99 (C, q, J_{FC} = 32 Hz), 133.17 (CH), 139.59 (C), 140.00 (C), 141.05 (C), 142.31 (C); ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) -62.62, -62.69; IR (neat) 3030, 2836, 1608, 1589, 1495, 1331, 1168, 1125, 1074 cm^{-1}; MS (EI) *m/z* 435 (M^+, 24), 344 (18), 132 (33), 91 (100%); HRMS (EI) *m/z* 435.1418 (calcd for $C_{24}H_{19}F_6N$ 435.1422).

4f: (2 mmol scale, 234 mg, 35%); R_f = 0.2 (hexane-ether = 1 : 4); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.44 (bs, 1H), 2.31 (s, 3H), 2.37 (s, 3H), 3.35 (d, *J* = 6.8 Hz, 2H), 3.74 (s, 2H), 6.14 (t, *J* = 6.8 Hz, 1H), 7.02-7.07 (m, 4H), 7.12-7.15 (m, 4H), 7.19-7.30 (m, 5H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 21.13 (CH_3), 21.31 (CH_3), 48.24 (CH_2), 53.59 (CH_2), 126.73 (CH), 126.92 (CH), 127.41 (CH), 128.20 (CH), 128.40 (CH), 128.85 (CH), 129.72 (CH), 136.83 (C), 136.85 (C), 136.99 (C), 139.69 (C), 140.41 (C), 143.38 (C); IR (neat) 3316, 3024, 2919, 1512, 1453, 1111 cm^{-1}; MS (EI) *m/z* 327 (M^+, 26), 236 (27), 195 (42), 119 (69), 91 (100%); HRMS (EI) *m/z* 327.1985 (calcd for $C_{24}H_{25}N$ 327.1987).

4g: (2.9 mmol scale, 365 mg, 35%); R_f = 0.2 (hexane-ether = 1 : 4); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.48 (bs, 1H), 3.35 (d, *J* = 7.0 Hz, 2H), 3.75 (s, 2H), 3.79 (s, 3H), 3.84 (s, 3H), 6.07 (t, *J* = 7.0 Hz, 1H), 6.80 (d-like, *J* = 8.9 Hz, 2H), 6.87 (d-like, *J* = 8.8 Hz 2H), 7.07 (d-like, *J* = 8.8 Hz, 2H), 7.17 (d-like, *J* = 8.9 Hz, 2H), 7.21-7.31 (m, 5H); ^{13}C NMR

(100.6 MHz, $CDCl_3$) *δ* (ppm) 48.26 (CH_2), 53.62 (CH_2), 55.31 (CH_3), 55.33 (CH_3), 113.51 (CH), 113.53 (CH), 125.76 (CH), 126.94 (CH), 128.22 (CH), 128.42 (CH), 128.68 (CH), 130.99 (CH), 132.20 (C), 135.32 (C), 140.41 (C), 142.69 (C), 158.77 (C), 159.01 (C); IR (neat) 3328, 2953, 2834, 1606, 1511, 1246, 1173, 1035 cm^{-1}; MS (EI) *m/z* 359 (M^+, 100), 268 (52%); HRMS (EI) *m/z* 359.1878 (calcd for $C_{24}H_{25}NO_2$ 359.1887).

4h: (3.1 mmol scale, 515 mg, 50%); $R_f = 0.4$ (hexane-ether = 1 : 4); pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) *δ* (ppm) 1.49 (bs, 1H), 3.17-3.21 (m, 2H), 3.73 (s, 2H), 6.41 (t, *J* = 6.8 Hz, 1H), 7.14-7.16 (m, 1H), 7.17-7.29 (m, 12H), 7.41-7.44 (m, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) *δ* (ppm) 48.27 (CH_2), 53.59 (CH_2), 126.35 (CH), 126.78 (CH), 126.91 (CH), 127.40 (CH), 128.08 (CH), 128.34 (CH), 128.37 (CH), 128.82 (CH), 129.00 (CH), 129.72 (CH), 131.49 (CH), 133.73 (C), 138.22 (C), 139.99 (C), 140.25 (C), 140.35 (C); IR (neat) 3026, 2835, 1597, 1495, 1445, 1362, 1125, 1050 cm^{-1}; MS (EI) *m/z* 335 (M^+, 7.5), 333 (M^+, 18), 298 (42), 91 (100%); HRMS (EI) *m/z* 333.1282, 335.1245 (calcd for $C_{22}H_{20}ClN$ 333.1284, 335.1255).

4i: (3.5 mmol scale, 531 mg, 45%); $R_f = 0.5$ (hexane-AcOEt = 1 : 4); pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) *δ* (ppm) 1.59 (bs, 1H), 3.33 (d, *J* = 6.8 Hz, 2H), 3.75 (s, 2H), 6.21 (t, *J* = 6.8 Hz, 1H), 7.08 (d-like, *J* = 8.4 Hz, 2H), 7.19-7.33 (m, 12H). Selected NOEs are between δ 3.33 (C*H*2-CH=) and δ 7.08 (2'-*H* of 4-chlorophenyl).; ^{13}C NMR (100.6 MHz, $CDCl_3$) *δ* (ppm) 48.01 (CH_2), 53.59 (CH_2), 127.09 (CH), 127.47 (CH), 127.55 (CH), 128.21 (CH), 128.31 (CH), 128.49 (CH), 131.21 (CH), 133.25 (C), 138.08 (C), 140.14 (C), 141.82 (C), 142.55 (C); IR (neat) 3316, 3027, 2833, 1597, 1489, 1445, 1090, 1015 cm^{-1}; MS (EI) *m/z* 335 (M^+, 16), 333 (M^+, 16), 242 (41), 132 (49), 91 (100%); HRMS (EI) *m/z* 333.1277, 335.1266 (calcd for $C_{22}H_{20}ClN$ 333.1284, 335.1255).

4j: (2.4 mmol scale, 805 mg, 41%); $R_f = 0.3$ (hexane-AcOEt = 1 : 1); pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) *δ* (ppm) 1.50 (bs, 1H), 3.34 (d, *J* = 6.8 Hz, 2H), 3.74 (s, 2H), 6.18 (t, *J* = 6.8 Hz, 1H), 7.11-7.16 (m, 4H), 7.20-7.37 (m, 10H); ^{13}C NMR (100.6 MHz, $CDCl_3$) *δ* (ppm) 48.14 (CH_2), 53.63 (CH_2), 127.02 (CH), 127.51 (CH), 128.18 (CH), 128.32 (CH), 128.34 (CH), 128.45 (CH), 128.73 (CH), 129.74 (CH), 133.15 (C), 139.18 (C), 140.24 (C), 140.73 (C), 142.46 (C); IR (neat) 3323, 3027, 2836, 1599, 1488, 1453, 1442, 1092, 1012 cm^{-1}; MS (EI) *m/z* 335 (M^+, 23), 333 (M^+, 65), 242 (55), 132 (69), 91 (100%); HRMS (EI) *m/z* 333.1279, 335.1266 (calcd for $C_{22}H_{20}ClN$ 333.1284, 335.1255).

4k: (2.6 mmol scale, 432 mg, 48%); R_f = 0.2 (hexane-AcOEt = 1 : 4); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.54 (bs, 1H), 3.31 (d, *J* = 7.0 Hz, 2H), 3.76 (s, 2H), 6.30 (t, *J* = 7.0 Hz, 1H), 7.16-7.18 (m, 2H), 7.23-7.32 (m, 10H), 8.18 (d-like, *J* = 8.8 Hz, 2H). Selected NOEs are between δ 6.30 (C*H*=CPh) and δ 7.16-7.18 (2-*H* of CH=C*Ph*).; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 47.78 (CH_2), 53.53 (CH_2), 123.48 (CH), 127.12 (CH), 127.41 (CH), 127.88 (CH), 128.13 (CH), 128.45 (CH), 129.69 (CH), 130.72 (CH), 139.88 (C), 140.94 (C), 141.75 (C), 146.64 (C), 147.02 (C); IR (neat) 3026, 2838, 1598, 1516, 1346, 1107 cm^{-1}; MS (EI) *m/z* 344 (M^+, 31), 253 (22), 132 (35), 91 (100%); HRMS (EI) *m/z* 344.1521 (calcd for $C_{22}H_{20}N_2O_2$ 344.1525).

Typical experimental procedure for eq 2 (Table 2, entry 2). To a solution of 1,1,2-ethenetricarboxylic acid 1,1-diethyl ester (**1**) (prepared from 1,1-diethyl 2-*tert*-butyl ethenetricarboxylate (136 mg, 0.5 mmol) upon treatment with CF_3CO_2H (2 mL))[29] in DMF (0.7 mL) were added *N*-benzyl 3,3-diphenyl-2-propen-1-amine (**4a**) (150 mg, 0.5 mmol) in DMF (0.7 mL), Et_3N (0.07 mL, 51 mg, 0.5 mmol), HOBt (1-hydroxybenzotriazole) (135 mg, 1 mmol) and EDCI (1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride) (100 mg, 0.5 mmol) at 0 °C. The reaction mixture was stirred for 1 h at 0 °C, and was allowed to warm to room temperature and stirred for 20 h. The reaction mixture was diluted with CH_2Cl_2. The organic phase was washed with saturated aqueous $NaHCO_3$ solution, 2M aqueous citric acid, saturated aqueous $NaHCO_3$ and water, dried (Na_2SO_4), and evaporated *in vacuo*. The residue was purified by column chromatography over silica gel eluting with hexane-Et_2O to give **5a-trans** (129 mg, 52%).

5a-trans: R_f = 0.4 (hexane-ether = 1 : 4); colorless crystals; mp 159.5-160 °C (hexane-AcOEt); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.25 (t, *J* = 7.1 Hz, 3H), 1.38 (t, *J* = 7.1 Hz, 3H), 2.60 (dd, *J* = 9.6, 9.0 Hz, 1H), 2.96 (dddd, *J* = 13.5, 9.6, 8.0, 6.3 Hz, 1H), 3.24 (dd, *J* = 9.0, 8.0 Hz, 1H), 3.48 (d, *J* = 13.5 Hz, 1H), 3.78 (d, *J* = 15.0 Hz, 1H), 4.16 (qd, *J* = 10.8, 7.1 Hz, 1H), 4.29-4.48 (m, 4H), 4.90 (d, *J* = 15.0 Hz, 1H), 6.90 (d, *J* = 6.8 Hz, 2H), 6.98 (d, *J* = 7.6 Hz, 1H), 7.18-7.32 (m, 10H), 7.53 (dd, J = 8.0, 1.0 Hz, 1H). Selected NOEs are between δ 2.96 (C3a-*H*) and δ 3.24 (C3-H*H*), and between δ 2.60 (C3-*H*H) and δ 3.48 (C9a-*H*), and between δ 2.60 (C3-*H*H) and δ 6.90 (*o*-H of C4-*Ph*). Atom numbering is shown in Supporting Information.; ^{13}C NMR (100.6 MHz, CDCl$_3$) *δ* (ppm) 14.00 (CH$_3$), 14.13 (CH$_3$), 36.37 (CH), 43.81 (CH), 46.15 (CH$_2$), 46.91 (CH), 47.32 (CH$_2$), 60.32 (C), 62.03 (CH$_2$), 62.51 (CH$_2$), 126.99 (CH), 127.01 (CH), 127.39 (CH), 127.92 (CH), 128.41 (CH), 128.50 (CH), 128.61 (CH), 130.25 (CH), 130.52 (CH), 131.45 (CH), 134.64 (CH), 136.80 (C), 138.80 (C), 141.18 (C), 168.44 (C), 170.96 (C), 171.86 (C). Selected HMBC correlations are between δ 2.96 (C9a-*H*) and δ 36.37 (*C*3a), between δ 2.60 (C3-*H*H), 2.96 (C3a-*H*), 6.98 (C5-*H*) and δ 46.91 (*C*4), and between δ 2.96 (C3a-*H*), 3.48 (C9a-*H*) and δ 60.32 (*C*9).; IR (KBr) 2977, 1735, 1691, 1496, 1441, 1249, 1025 cm^{-1}; MS (EI) *m/z* 497 (M$^+$, 75), 394 (45), 91 (100%); HRMS (EI) *m/z* 497.2201 (calcd for $C_{31}H_{31}NO_5$ 497.2202).

5a-cis: (1 mmol scale, benzene, 80 °C, 247 mg, 48%); R$_f$ = 0.2 (hexane-ether = 1 : 8); pale yellow viscous oil; ^{1}H NMR (400 MHz, CDCl$_3$) *δ* (ppm) 1.15 (t, J = 7.0 Hz, 3H), 1.36 (t, J = 7.2 Hz, 3H), 3.00 (dd, J = 9.6, 7.4 Hz, 1H), 3.14 (dd, J = 9.6, 8.2 Hz, 1H), 3.35 (dddd, J = 10.0, 8.2, 7.4, 5.1 Hz, 1H), 4.03-4.09 (m, 1H), 4.10 (d, J = 15.2 Hz, 1H), 4.20 (d, J = 10.0 Hz, 1H), 4.18-4.27 (m, 1H), 4.29 (d, J = 5.1 Hz, 1H), 4.31 (d, J = 15.2 Hz, 1H), 4.33-4.46 (m, 2H), 6.87 (d, J = 7.8 Hz, 1H), 6.93-6.95 (m, 2H), 7.06-7.08 (m, 2H), 7.13-7.33 (m, 8H), 8.09 (dd, J = 8.0, 1.0 Hz, 1H). Selected NOEs are between δ 3.35 (C3a-*H*) and δ 4.20 (C9a-*H*), 4.29 (C4-*H*) (overlapped), and between δ 4.29 (C4-*H*) and δ 6.87 (C5-*H*), 7.06-7.08 (*o*-H of C4-*Ph*).; ^{13}C NMR (100.6 MHz, CDCl$_3$) *δ* (ppm) 13.80 (CH$_3$), 14.05 (CH$_3$), 36.38 (CH), 45.08 (CH), 46.40 (CH$_2$), 47.58 (CH), 48.49 (CH$_2$), 59.24 (C), 61.94 (CH$_2$), 62.39 (CH$_2$), 126.66 (CH), 127.19 (CH), 127.31 (CH), 127.57 (CH), 127.76 (CH), 128.58 (CH), 128.66 (CH), 129.84 (CH), 130.94 (CH), 132.54 (C), 135.93 (C), 138.18 (C), 139.90 (C), 168.70 (C), 169.71 (C), 172.70 (C). Selected HMBC correlations are between δ 3.00 (C3-*H*H), 3.52 (C3-H*H*), 4.20 (C9a-*H*), 4.29 (C4-*H*) and δ 36.38 (*C*3a), between δ 3.00 (C3-*H*H), 3.52 (C3-H*H*), 3.35 (C3a-*H*), 7.06-7.08 (*o*-H of C4-*Ph*) and δ 45.08 (*C*4), and between δ 4.20 (C9a-*H*) and δ 59.24 (*C*9).; IR (KBr) 2980, 1729, 1694, 1495, 1445, 1239, 1029 cm^{-1}; MS (EI) *m/z* 497 (M$^+$, 46), 423 (6.4), 350 (13), 276 (22), 91 (100%); HRMS (EI) *m/z* 497.2195 (calcd for $C_{31}H_{31}NO_5$ 497.2202).

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5b-cis: (1 mmol scale, benzene, 80 °C, 277 mg, 55%); $R_f = 0.2$ (hexane-ether = 1 : 1); pale yellow crystals; mp 47.5-48.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.669-0.825 (m, 2H), 0.959-1.11 (m, 3H), 1.14 (t, $J = 7.1$ Hz, 3H), 1.22-1.26 (m, 1H), 1.33 (t, $J = 7.2$ Hz, 3H), 1.36-1.43 (m, 2H), 1.51-1.61 (m, 3H), 2.72 (dd, $J = 13.6$, 7.3 Hz, 1H), 2.95 (dd, $J = 13.6$, 7.5 Hz, 1H), 3.05 (dd, $J = 9.3$, 7.5 Hz, 1H), 3.26 (dd, $J = 9.3$, 8.2 Hz, 1H), 3.36 (dddd, $J = 9.6$, 8.2, 7.5, 4.9 Hz, 1H), 4.01-4.09 (m, 1H), 4.12 (d, $J = 9.6$ Hz, 1H), 4.18-4.26 (m, 1H), 4.31 (d, $J = 4.9$ Hz, 1H), 4.31-4.43 (m, 2H), 6.92 (d, $J = 7.6$ Hz, 1H), 7.15-7.18 (m, 3H), 7.24-7.33 (m, 2H), 7.36-7.40 (m, 2H), 8.04 (dd, $J = 8.0$, 1.2 Hz, 1H). Selected NOEs are between δ 3.36 (C3a-*H*) and δ 4.12 (C9a-*H*), 4.31 (C4-*H*), and between δ 4.31 (C4-*H*) and δ 6.92 (C5-*H*).; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.80 (CH_3), 14.05 (CH_3), 25.75 (CH_2), 26.38 (CH_2), 30.34 (CH_2), 30.61 (CH_2), 35.55 (CH), 36.45 (CH), 45.09 (CH), 47.73 (CH), 48.92 (CH_2), 49.83 (CH_2), 59.13 (C), 61.81 (CH_2), 62.35 (CH_2), 126.64 (CH), 127.23 (CH), 127.48 (CH), 127.67 (CH), 128.73 (CH), 129.86 (CH), 130.97 (CH), 132.66 (C), 138.20 (C), 140.11 (C), 168.56 (C), 169.81 (C), 172.60 (C). Selected HMBC correlations are between δ 3.05 (C3-*H*H), 3.26 (C3-H*H*), 4.12 (C9a-*H*), 4.31 (C4-*H*) and δ 36.45 (*C*3a), between δ 3.05 (C3-*H*H), 6.92 (C5-*H*) and δ 45.09 (*C*4), and between δ 4.12 (C9a-*H*) and δ 59.13 (*C*9).; IR (KBr) 2924, 1730, 1695, 1448, 1238, 1038 cm^{-1}; MS (EI) *m/z* 503 (M^+, 5.3), 205 (6.9), 86 (100%); HRMS (EI) *m/z* 503.2672 (calcd for $C_{31}H_{37}NO_5$ 503.2672).

5c-trans: (0.5 mmol scale, DMF, r.t., 141 mg, 53%); $R_f = 0.2$ (hexane-ether = 1 : 8); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.27 (t, $J = 7.1$ Hz, 3H), 1.39 (t, $J = 7.1$ Hz, 3H), 2.58 (dd, $J = 9.7$, 9.1 Hz, 1H), 2.94 (dddd, $J = 13.5$, 9.7, 7.7, 6.1 Hz, 1H), 3.24 (dd, $J = 9.1$, 7.7 Hz, 1H), 3.37 (d, $J = 13.5$ Hz, 1H), 3.83 (d, $J = 15.0$ Hz, 1H), 4.17 (dq, $J = 10.7$, 7.1 Hz, 1H), 4.30-4.50 (m, 4H), 4.88 (d, $J = 15.0$ Hz, 1H), 6.86 (dd, $J = 8.6$, 5.3 Hz, 2H), 6.93-7.00 (m, 4H), 7.21-7.32 (m, 6H). Selected NOEs are between δ 2.94 (C3a-*H*) and δ 3.24 (C3-H*H*) and between δ 2.58 (C3-*H*H) and δ 3.37 (C9a-*H*), and between δ 2.58 (C3-*H*H) and δ 6.86 (*o*-H of C4-*Ar*).; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.98 (CH_3), 14.12 (CH_3), 36.42 (CH), 43.48 (CH), 45.57 (CH), 46.17 (CH_2), 47.13 (CH_2), 60.14 (C), 62.29 (CH_2), 62.85 (CH_2), 115.54 (CH, d, $J_{FC} = 21$ Hz), 116.28 (CH, d, $J_{FC} = 21$ Hz), 116.92 (CH, d, $J_{FC} = 23$ Hz), 127.50 (CH), 127.91 (CH), 128.66 (CH), 131.54 (CH, d, $J_{FC} = 8.4$ Hz), 132.74 (CH, d, $J_{FC} = 7.7$ Hz),

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134.47 (C, d, J_{FC} = 3.1 Hz), 136.43 (C, d, J_{FC} = 7.7 Hz), 136.55 (C), 136.57 (C), 161.25 (C, d, J_{FC} = 246 Hz), 161.85 (C, d, J_{FC} = 247 Hz), 167.79 (C), 170.48 (C), 171.38 (C). Selected HMBC correlations are between δ 2.58 (C3-*H*H), 3.24 (C3-H*H*) and δ 36.42 (*C*3a), between δ 6.86 (*o*-H of C4-*Ph*) and δ 45.57 (*C*4), and between δ 2.94 (C3a-*H*), 3.37 (C9a-*H*) and δ 60.14 (*C*9).; ^{19}F NMR (376 MHz, $CDCl_3$) *δ* (ppm) -114.56 (ddd, *J* = 10.3, 6.9, 6.9 Hz), -115.29 (m); IR (KBr) 2979, 1735, 1691, 1507, 1495, 1260, 1161, 1028 cm^{-1}; MS (EI) *m/z* 533 (M^{+}, 18), 430 (12), 57 (100%); HRMS (EI) *m/z* 533.2013 (calcd for $C_{31}H_{29}F_2NO_5$ 533.2014).

5c-cis: (0.54 mmol scale, toluene, 110 °C, 282 mg, 98%); R_f = 0.5 (hexane-ether = 1 : 4); pale yellow viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* (ppm) 1.17 (t, *J* = 7.0 Hz, 3H), 1.37 (t, *J* = 7.1 Hz, 3H), 2.93 (dd, *J* = 9.6, 7.0 Hz, 1H), 3.13 (dd, *J* = 9.6, 8.3 Hz, 1H), 3.33 (dddd, *J* = 9.8, 8.3, 7.0, 5.1 Hz, 1H), 4.03-4.11 (m, 1H), 4.18-4.28 (m, 5H), 4.34-4.50 (m, 2H), 6.79 (dd, *J* = 8.5, 6.0 Hz, 1H), 6.88 (ddd, *J* = 8.5, 8.2, 2.7 Hz, 1H), 6.92-6.94 (m, 2H), 7.00-7.02 (m, 4H), 7.19-7.22 (m, 3H), 8.01 (dd, J_{FH} = 11.0, J_{HH} = 2.7 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) *δ* (ppm) 13.80 (CH_3), 14.05 (CH_3), 36.13 (CH), 43.78 (CH), 46.36 (CH_2), 47.36 (CH), 48.08 (CH_2), 58.77 (C), 62.18 (CH_2), 62.67 (CH_2), 114.79 (CH, d, J_{FC} = 21 Hz), 115.66 (CH, d, J_{FC} = 21 Hz), 118.07 (CH, d, J_{FC} = 25 Hz), 127.49 (CH), 127.56 (CH), 128.65 (CH), 128.69 (CH, d, J_{FC} = 9.2 Hz), 131.27 (CH, d, J_{FC} = 8.4 Hz), 133.71 (C, d, J_{FC} = 3.1 Hz), 134.29 (C, d, J_{FC} = 8.4 Hz), 135.14 (C, d, J_{FC} = 3.1 Hz), 135.62 (C), 161.52 (C, d, J_{FC} = 245 Hz), 161.92 (C, d, J_{FC} = 246 Hz), 168.15 (C), 168.95 (C), 172.25 (C); ^{19}F NMR (376 MHz, $CDCl_3$) *δ* (ppm) -115.06 ~ -114.93 (m, 2F); ^{1}H NMR (400 MHz, C_6D_6) *δ* (ppm) 0.787 (t, *J* = 7.0 Hz, 3H), 1.16 (t, *J* = 7.2 Hz, 3H), 2.62 (dd, *J* = 9.4, 8.4 Hz, 1H), 2.69 (dd, *J* = 9.4, 7.0 Hz, 1H), 2.85 (dddd, *J* = 9.6, 8.4, 7.0, 4.9 Hz, 1H), 3.70 (dq, *J* = 10.7, 7.0 Hz, 1H), 3.94 (d, *J* = 15.0 Hz, 1H), 4.02 (dq, *J* = 10.7, 7.0 Hz, 1H), 4.14 (d, *J* = 15.0 Hz, 1H), 4.21 (d, *J* = 4.9 Hz, 1H), 4.38 (d, *J* = 9.6 Hz, 1H), 4.38-4.51 (m, 2H), 6.56-6.60 (m, 3H), 6.65-6.70 (m, 3H), 6.88-6.96 (m, 3H), 7.01-7.05 (m, 2H), 8.54 (dd, J_{FH} = 11.1, J_{HH} = 2.7 Hz, 1H). Selected NOEs are between δ 2.85 (C3a-*H*) and δ 4.38 (C9a-*H*), 4.21 (C4-*H*), and between δ 4.21 (C4-*H*) and δ 4.38 (C9a-*H*).; ^{13}C NMR (100.6 MHz, C_6D_6) *δ* (ppm) 13.57 (CH_3), 13.98 (CH_3), 36.44 (CH), 44.09 (CH), 46.37 (CH_2), 47.54 (CH), 47.85 (CH_2), 59.30 (C), 62.36 (CH_2), 62.47 (CH_2), 114.86 (CH, d, J_{FC} = 21 Hz), 115.61 (CH, d, J_{FC} = 21 Hz), 118.68 (CH, d, J_{FC} = 25 Hz), 127.59 (CH), 127.72 (CH), 128.78 (CH), 129.04 (CH, d, J_{FC} = 7.7 Hz), 131.45 (CH, d, J_{FC} = 7.7 Hz), 134.45 (C, d, J_{FC} = 3.1 Hz), 135.30 (C, d, J_{FC} = 8.4 Hz), 135.58 (C, d, J_{FC} = 3.1 Hz), 136.41 (C), 161.97 (C, d, J_{FC} = 244 Hz), 162.14 (C, d, J_{FC} = 245 Hz), 168.29 (C), 169.31 (C), 171.83 (C). Selected HMBC correlations are between δ 2.69 (C3-H*H*), 4.38 (C9a-*H*), 4.21 (C4-*H*) and δ 36.44 (*C*3a), between δ 2.69 (C3-H*H*) and δ 44.09 (*C*4), and between δ 2.85 (C3a-*H*), 4.38 (C9a-*H*), 8.54 (C8-*H*) and δ 59.30 (*C*9).; ^{19}F NMR (376 MHz, C_6D_6) *δ* (ppm) -114.89 (m, 1F), -115.20 (m, 1F); IR (neat) 2982, 1732, 1699, 1604, 1511, 1445, 1161, 1039 cm^{-1}; MS (EI) *m/z* 533 (M$^+$, 52), 312 (29), 267 (25), 253 (23), 91 (100%); HRMS (EI) *m/z* 533.2019 (calcd for $C_{31}H_{29}NO_5$ 533.2014).

5d-trans: (1 mmol scale, DMF, r.t., 526 mg, 93%); R$_f$ = 0.6 (hexane-ether = 1 : 4); colorless crystals; mp 130-131 °C (hexane-AcOEt); ^{1}H NMR (400 MHz, $CDCl_3$) *δ* (ppm) 1.26 (t, *J* = 7.1 Hz, 3H), 1.39 (t, *J* = 7.1 Hz, 3H), 2.58 (dd, *J* = 9.7, 9.1 Hz, 1H), 2.93 (dddd, *J* = 13.5, 9.7, 7.7, 6.1 Hz, 1H), 3.24 (dd, *J* = 9.1, 7.7 Hz, 1H), 3.34 (d, *J* = 13.5 Hz, 1H), 3.80 (d, *J* = 14.9 Hz, 1H), 4.14-4.22 (m, 1H), 4.29-4.50 (m, 3H), 4.33 (d, *J* = 6.1 Hz, 1H), 4.89 (d, *J* = 14.9 Hz, 1H), 6.83 (d, *J* = 8.4 Hz, 2H), 6.89 (d, *J* = 8.4 Hz, 1H), 7.18 (dd, *J* = 8.4, 2.1 Hz, 1H), 7.22-7.32 (m, 7H), 7.52 (d, *J* = 2.1 Hz, 1H). Selected NOEs are between δ 2.93 (C3a-*H*) and δ 3.24 (C3-H*H*), 4.33 (C4-*H*) and between δ 2.58 (C3-*H*H) and δ 3.34 (C9a-*H*), 6.83 (*o*-H of C4-*Ar*).; ^{13}C NMR (100.6 MHz, $CDCl_3$) *δ* (ppm) 13.95 (CH_3), 14.09 (CH_3), 36.21 (CH), 43.56 (CH), 45.90 (CH), 46.21 (CH_2), 47.07 (CH_2), 60.06 (C), 62.29 (CH_2), 62.86 (CH_2), 127.51 (CH), 127.92 (CH), 128.66 (CH), 128.83 (CH), 128.91 (CH), 130.49 (CH), 131.39 (CH), 132.46 (CH), 132.94 (C), 133.28 (C), 136.32 (C), 136.58 (C), 136.90 (C), 139.07 (C), 167.73 (C), 170.33 (C), 171.17 (C). Selected HMBC correlations are between δ 2.58 (C3-*H*H), 3.24 (C3-H*H*), 3.34 (C9a-*H*) and δ 36.21 (*C*3a), between δ 6.83 (*o*-H of C4-*Ph*) and δ 45.90 (*C*4), and between δ 2.93 (C3a-*H*), 3.34 (C9a-*H*) and δ 60.06 (*C*9).; IR (KBr) 2979, 1734, 1686, 1596, 1488, 1442, 1364, 1253, 1186, 1013 cm^{-1}; MS (EI) *m/z* 567 (M$^+$, 50), 565 (72), 464 (26), 462 (31), 91 (100%); HRMS (EI) *m/z* 565.1407, 567.1392 (calcd for $C_{31}H_{29}Cl_2NO_5$ 565.1423, 567.1393).

5e-trans: (1.02 mmol scale, THF, r.t., 644 mg, 99%); R$_f$ = 0.6 (hexane-ether = 1 : 4); colorless crystals; mp 134-135 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* (ppm) 1.26 (t, *J* = 7.1 Hz, 3H), 1.37 (t, *J* = 7.1 Hz, 3H), 2.53 (dd, *J* = 9.7, 9.2 Hz, 1H), 3.01 (dddd, *J* = 13.7, 9.7, 7.8, 5.9 Hz, 1H), 3.31 (dd, J = 9.2, 7.8 Hz, 1H), 3.37 (d, J = 13.7 Hz, 1H), 3.84 (d, J = 15.0 Hz, 1H), 4.18 (dq, J = 10.7, 7.1 Hz, 1H), 4.30-4.48 (m, 3H), 4.51 (d, J = 5.9 Hz, 1H), 4.88 (d, J = 15.0 Hz, 1H), 7.05 (d, J = 7.8 Hz, 1H), 7.18-7.32 (m, 7H), 7.43 (dd, J = 7.8, 7.7 Hz, 1H), 7.53-7.58 (m, 2H), 7.71 (d, J = 8.4 Hz, 1H). Selected NOEs are between δ 3.01 (C3a-*H*) and δ 3.31 (C3-H*H*), 4.51 (C4-*H*) and between δ 2.53 (C3-*H*H) and δ 3.37 (C9a-*H*), 7.05 (6-H of C4-*Ar*).; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.95 (CH_3), 14.00 (CH_3), 36.17 (CH), 43.37 (CH), 46.20 (CH_2), 46.84 (CH), 46.89 (CH_2), 60.24 (C), 62.50 (CH_2), 62.95 (CH_2), 123.63 (C, q, J_{FC} = 272 Hz), 123.85 (C, q, J_{FC} = 273 Hz), 124.12 (CH, q, J_{FC} = 3.1 Hz), 124.46 (CH, q, J_{FC} = 3.8 Hz), 126.59 (CH, q, J_{FC} = 3.8 Hz), 127.57 (CH), 127.93 (CH), 128.08 (CH, q, J_{FC} = 3.8 Hz), 128.68 (CH), 129.46 (CH), 130.89 (C, q, J_{FC} = 33 Hz), 131.12 (C, q, J_{FC} = 33 Hz), 131.61 (CH), 133.46 (CH), 136.41 (C), 138.46 (C), 138.77 (C), 141.07 (C), 167.53 (C), 170.05 (C), 170.97 (C). Selected HMBC correlations are between δ 2.53 (C3-*H*H), 3.31 (C3-H*H*) and δ 36.17 (*C*3a), between δ 7.05 (6-H of C4-*Ar*) and δ 46.84 (*C*4), and between δ 3.01 (C3a-*H*), 3.37 (C9a-*H*), 7.71 (C8-*H*) and δ 60.24 (*C*9).; ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) -62.70, -62.89; IR (KBr) 3062, 2984, 1739, 1704, 1620, 1607, 1415, 1330, 1253, 1166, 1132 cm^{-1}; MS (EI) *m/z* 633 (M^+, 84), 530 (29), 149 (14), 118 (16), 91 (100%); HRMS (EI) *m/z* 633.1951 (calcd for $C_{33}H_{29}F_6NO_5$ 633.1950); Anal. Calcd for $C_{33}H_{29}F_6NO_5$: C, 62.56; H, 4.61; N, 2.21. Found: C, 62.60; H, 4.66; N, 2.21.

5f-cis: (1 mmol scale, DMF, 110 °C, 292 mg, 55%); R_f = 0.7 (hexane-ether = 1 : 4); pale yellow viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.16 (t, J = 7.0 Hz, 3H), 1.36 (t, J = 7.2 Hz, 3H), 2.33 (s, 3H), 2.39 (s, 3H), 3.00 (d, J = 9.6, 7.6 Hz, 1H), 3.12 (dd, J = 9.6, 8.3 Hz, 1H), 3.30 (dddd, J = 9.8, 8.3, 7.6, 5.1 Hz, 1H), 4.06 (dq, J = 10.7, 7.0 Hz, 1H), 4.11 (d, J = 15.2 Hz, 1H), 4.18 (d, J = 9.8 Hz, 1H), 4.22 (d, J = 5.1 Hz, 1H), 4.25 (dq, J = 10.7, 7.0 Hz, 1H), 4.35 (d, J = 15.2 Hz, 1H), 4.35-4.46 (m, 2H), 6.78 (d, J = 7.8 Hz, 1H), 6.92-6.97 (m, 5H), 7.11 (d, J = 7.8 Hz, 2H), 7.16-7.19 (m, 3H), 7.94 (d, J = 1.0 Hz, 1H). Selected NOEs are between δ 3.30 (C3a-*H*) and δ 4.18 (C9a-*H*), 4.22 (C4-*H*), 3.12 (C3-H*H*).; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.78 (CH_3), 14.04 (CH_3), 21.02 (CH_3), 21.42 (CH_3), 36.36 (CH), 44.19 (CH), 46.29 (CH_2), 47.68 (CH), 48.40 (CH_2), 59.12 (C), 61.82 (CH_2), 62.32 (CH_2), 127.26 (CH), 127.33 (CH), 127.51 (CH), 128.47 (CH), 128.50 (CH), 129.26 (CH), 129.62 (CH), 131.21 (CH), 132.18 (C), 135.23 (C), 135.88 (C), 136.06 (C), 136.68 (C), 136.81 (C), 168.74 (C), 169.65 (C), 172.83 (C). Selected HMBC correlations are between δ 3.00 (C3-*H*H), 3.12 (C3-H*H*), 4.18 (C9a-*H*) and δ 36.36 (*C*3a), between δ 6.78 (C5-*H*) and δ 44.19 (*C*4), and between δ 4.18 (C9a-*H*), 7.94 (C8-*H*) and δ 59.12 (*C*9).; IR (KBr) 2980, 1730, 1696, 1495, 1444, 1237, 1041 cm^{-1}; MS (EI) *m/z* 525 (M$^+$, 15), 304 (13), 84 (100%); HRMS (EI) *m/z* 525.2523 (calcd for $C_{33}H_{35}NO_5$ 525.2515).

5h-trans: (0.73 mmol scale, DMF, r.t., 126 mg, 33%); R$_f$ = 0.6 (hexane-AcOEt = 1 : 1); colorless crystals; mp 183.0-183.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* (ppm) 1.25 (t, *J* = 7.1 Hz, 3H), 1.38 (t, *J* = 7.1 Hz, 3H), 2.58 (dd, *J* = 9.9, 9.4 Hz, 1H), 3.03 (dddd, *J* = 13.5, 9.9, 7.8, 6.1 Hz, 1H), 3.43 (d, *J* = 13.5 Hz, 1H), 3.48 (dd, *J* = 9.4, 7.8 Hz, 1H), 3.79 (d, *J* = 15.2 Hz, 1H), 4.17 (dq, *J* = 10.7, 7.1 Hz, 1H), 4.29-4.49 (m, 3H), 4.91 (d, *J* = 15.2 Hz, 1H), 4.96 (d, *J* = 6.1 Hz, 1H), 6.69 (dd, *J* = 7.4, 2.0 Hz, 1H), 6.91 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.11-7.33 (m, 9H), 7.39 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.53 (dd, *J* = 8.0, 1.2 Hz, 1H). Selected NOEs are between δ 3.03 (C3a-*H*) and δ 3.48 (C3-H*H*), 4.96 (C4-*H*) and between δ 3.43 (C9a-*H*) and δ 2.58 (C3-*H*H), 6.69 (6-H of C4-*Ar*).; ^{13}C NMR (100.6 MHz, $CDCl_3$) *δ* (ppm) 14.02 (CH_3), 14.15 (CH_3), 36.20 (CH), 43.13 (CH), 43.83 (CH), 46.11 (CH_2), 47.53 (CH_2), 60.25 (C), 62.10 (CH_2), 62.59 (CH_2), 127.22 (CH), 127.31 (CH), 127.41 (CH), 127.89 (CH), 128.29 (CH), 128.57 (CH), 128.63 (CH), 129.23 (CH), 130.60 (CH), 131.42 (CH), 132.74 (CH), 134.85 (C), 134.99 (C), 136.82 (C), 138.47 (C), 139.00 (C), 168.30 (C), 171.02 (C), 171.67 (C). Selected HMBC correlations are between δ 2.58 (C3-*H*H), 3.48 (C3-H*H*), 3.43 (C9a-*H*), 4.96 (C4-*H*) and δ 36.20 (*C*3a), between δ 6.69 (6-H of C4-*Ar*) and δ 43.13 (*C*4), and between δ 3.43 (C9a-*H*), 7.53 (C8-*H*) and δ 60.25 (*C*9).; IR (KBr) 2976, 1747, 1724, 1702, 1433, 1250, 1044 cm^{-1}; MS (EI) *m/z* 533 (M$^+$, 9.4), 531 (M$^+$, 24), 428 (24), 202 (21), 91 (100%); HRMS (EI) *m/z* 531.1807, 533.1794 (calcd for $C_{31}H_{30}ClNO_5$ 531.1813, 533.1783).

5h-cis: (1 mmol scale, toluene, 110 °C, 445 mg, 84% (**5h-cis**:**5h-trans**=56:28), **5h-cis** was partially isolated by removal of **5h-trans** by crystallization of the mixture and the subsequent column chromatography of the filtrate. 116 mg, 22%); R$_f$ = 0.7 (hexane-AcOEt = 1 : 1); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* (ppm) 1.18 (t, *J* = 7.1 Hz, 3H), 1.34 (t, *J* = 7.1 Hz, 3H), 2.89 (dd, *J* = 9.8, 6.4 Hz, 1H), 3.24 (dd, *J* = 9.8, 7.9 Hz, 1H), 3.43 (dddd, *J* = 9.6, 7.9, 6.4, 6.1 Hz, 1H), 3.94 (d, *J* = 15.0 Hz, 1H), 4.10-4.18 (m, 1H), 4.16 (d, *J* = 9.6 Hz, 1H), 4.20-4.28 (m, 1H), 4.32-4.45 (m, 2H), 4.33 (d, *J* = 15.0 Hz, 1H), 4.93 (d, *J* = 6.1 Hz, 1H), 6.75 (d, *J* = 7.8 Hz, 1H), 6.85 (dd, *J* = 7.8, 1.8 Hz, 1H), 6.90-6.93 (m, 2H), 7.12-7.21 (m, 6H), 7.30-7.34 (m, 1H), 7.42 (dd, *J* = 7.8, 1.6 Hz, 1H), 8.11 (dd, *J* = 8.0, 1.2 Hz, 1H). Selected NOEs are between δ 3.43 (C3a-*H*) and δ 4.16 (C9a-*H*), 4.93 (C4-*H*), 3.24 (C3-H*H*) and between δ 4.16 (C9a-*H*) and δ 4.93 (C4-*H*).; ^{13}C NMR (100.6 MHz, $CDCl_3$) *δ* (ppm) 13.89 (CH_3), 14.05 (CH_3), 34.38 (CH), 40.88 (CH), 46.36 (CH_2), 47.62 (CH), 48.59 (CH_2), 58.96 (C), 61.94 (CH_2), 62.54 (CH_2), 126.75 (CH), 126.80 (CH), 127.33 (CH), 127.60 (CH), 127.80 (CH), 127.92 (CH), 128.28 (CH), 128.59 (CH), 129.88 (CH), 130.48 (CH), 130.75 (CH), 132.62 (C), 135.13 (C), 135.87 (C), 137.31 (C), 138.35 (C), 168.64 (C), 169.82 (C), 172.36 (C). Selected HMBC correlations are between δ 2.89 (C3-*H*H), 3.24 (C3-H*H*), 4.16 (C9a-*H*), 4.93 (C4-*H*) and δ 34.38 (*C*3a), between δ 6.75 (C5-*H*) and δ 40.88 (*C*4), and between δ 4.16 (C9a-*H*), 8.11 (C8-*H*) and δ 58.96 (*C*9).; IR (neat) 2981, 1730, 1697, 1443, 1237, 1039 cm^{-1}; MS (EI) *m/z* 533 (M^+, 22), 531 (M^+, 56), 384 (28), 91 (100%); HRMS (EI) *m/z* 531.1805, 533.1780 (calcd for $C_{31}H_{30}ClNO_5$ 531.1813, 533.1783);

5i-trans: (0.80 mmol scale, DMF, r.t., 306 mg, 72%); R_f = 0.6 (ether); colorless crystals; mp 154-156 °C (hexane-AcOEt); ^{1}H NMR (400 MHz, $CDCl_3$) *δ* (ppm) 1.25 (t, *J* = 7.1 Hz, 3H), 1.38 (t, *J* = 7.1 Hz, 3H), 2.59 (dd, *J* = 9.7, 9.1 Hz, 1H), 2.96 (dddd, *J* = 13.7, 9.7, 7.7, 6.1 Hz, 1H), 3.24 (dd, *J* = 9.1, 7.7 Hz, 1H), 3.38 (d, *J* = 13.7 Hz, 1H), 3.82 (d, *J* = 15.0 Hz, 1H), 4.15 (dq, *J* = 10.7, 7.1 Hz, 1H), 4.28-4.48 (m, 4H), 4.89 (d, *J* = 15.0 Hz, 1H), 6.84 (d, *J* = 8.4 Hz, 2H), 6.94 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.19-7.32 (m, 9H), 7.53 (dd, *J* = 7.9, 1.3 Hz, 1H). Selected NOEs are between δ 2.96 (C3a-*H*) and δ 3.24 (C3-H*H*), between δ 3.38 (C9a-*H*) and δ 2.59 (C3-*H*H), 6.84 (*o*-H of C4-*Ar*), and between δ 2.59 (C3-*H*H) and δ 6.84 (*o*-H of C4-*Ar*).; ^{13}C NMR (100.6 MHz, $CDCl_3$) *δ* (ppm) 13.99 (CH_3), 14.13 (CH_3), 36.19 (CH), 43.79 (CH), 46.19 (CH_2), 46.31 (CH), 47.20 (CH_2), 60.21 (C), 62.10 (CH_2), 62.60 (CH_2), 127.25 (CH), 127.47 (CH), 127.94 (CH), 128.54 (CH), 128.66 (CH), 128.71 (CH), 130.65 (CH), 131.31 (CH), 131.50 (CH), 133.02 (C), 134.60 (C), 136.66 (C), 138.30 (C), 139.66 (C), 168.30 (C), 170.91 (C), 171.64 (C). Selected HMBC correlations are between δ 2.59 (C3-*H*H), 3.24 (C3-H*H*), 3.38 (C9a-*H*) and δ 36.19 (*C*3a), between δ 6.84 (*o*-H of C4-*Ar*) and δ 46.31 (*C*4), and between δ 3.38 (C9a-*H*), 7.53 (C8-*H*), 2.96 (C3a-*H*) and δ 60.21 (*C*9).; IR (KBr) 2979, 1735, 1693, 1490, 1256 cm^{-1}; MS (EI) m/z 533 (M$^+$, 15), 531 (M$^+$, 39), 428 (21), 91 (100%); HRMS (EI) m/z 531.1803, 533.1790 (calcd for $C_{31}H_{30}ClNO_5$ 531.1813, 533.1783).

5i-cis: (0.80 mmol scale, toluene, 110 °C, 166 mg, 39%); R$_f$ = 0.6 (ether); colorless crystals; mp 157-159 °C (hexane-AcOEt); ^{1}H NMR (400 MHz, $CDCl_3$) *δ* (ppm) 1.15 (t, *J* = 7.1 Hz, 3H), 1.36 (t, *J* = 7.1 Hz, 3H), 2.95 (dd, *J* = 9.6, 7.4 Hz, 1H), 3.11 (dd, *J* = 9.6, 8.2 Hz, 1H), 3.31 (dddd, *J* = 9.6, 8.2, 7.4, 5.1 Hz, 1H), 4.06 (dq, *J* = 10.7, 7.1 Hz, 1H), 4.11 (d, *J* = 14.9 Hz, 1H), 4.17 (d, *J* = 9.6 Hz, 1H), 4.23 (dq, *J* = 10.7, 7.1 Hz, 1H), 4.27 (d, *J* = 5.1 Hz, 1H), 4.31 (d, *J* = 14.9 Hz, 1H), 4.33-4.47 (m, 2H), 6.83 (d, *J* = 7.8 Hz, 1H), 6.93-6.95 (m, 2H), 7.00 (d-like, *J* = 8.4 Hz, 2H), 7.15-7.21 (m, 4H), 7.25-7.34 (m, 3H), 8.09 (dd, *J* = 8.1, 1.1 Hz, 1H). Selected NOEs are between δ 3.11 (C3a-*H*) and δ 4.17 (C9a-*H*), 4.27 (C4-*H*), 3.11 (C3-H*H*) and between δ 4.17 (C9a-*H*) and δ 4.27 (C4-*H*).; ^{13}C NMR (100.6 MHz, $CDCl_3$) *δ* (ppm) 13.82 (CH_3), 14.08 (CH_3), 36.26 (CH), 44.45 (CH), 46.40 (CH_2), 47.41 (CH), 48.30 (CH_2), 59.10 (C), 62.04 (CH_2), 62.50 (CH_2), 126.92 (CH), 127.44 (CH), 127.60 (CH), 127.92 (CH), 128.66 (CH), 128.84 (CH), 131.07 (CH), 131.17 (CH), 132.39 (C), 133.09 (C), 135.78 (C), 137.62 (C), 138.38 (C), 168.67 (C), 169.66 (C), 172.60 (C). Selected HMBC correlations are between δ 2.95 (C3-*H*H), 3.11 (C3-H*H*), 4.17 (C9a-*H*) and δ 36.26 (*C*3a), between δ 6.83 (C5-*H*) and δ 44.45 (*C*4), and between δ 4.17 (C9a-*H*), 8.09 (C8-*H*) and δ 59.10 (*C*9).; IR (KBr) 2978, 2935, 1731, 1685, 1492, 1450, 1292, 1231, 1094, 1036 cm^{-1}; MS (EI) *m/z* 533 (M$^+$, 45), 531 (M$^+$, 23), 430 (23), 149 (34), 91 (82), 57 (100%); HRMS (EI) *m/z* 531.1809 (calcd for $C_{31}H_{30}ClNO_5$ 531.1813).

5j-trans: (0.43 mmol scale, DMF, r.t., 229 mg, 86%); R$_f$ = 0.7 (hexane-AcOEt = 1 : 1); colorless crystals; mp 182.0-182.5 °C (hexane-AcOEt); ^{1}H NMR (400 MHz, $CDCl_3$) *δ* (ppm) 1.27 (t, *J* = 7.1 Hz, 3H), 1.39 (t, *J* = 7.1 Hz, 3H), 2.59 (dd, *J* = 9.7, 9.0 Hz, 1H), 2.92 (dddd, *J* = 13.5, 9.7, 7.8, 6.3 Hz, 1H), 3.24 (dd, *J* = 9.0, 7.8 Hz, 1H), 3.44 (d, *J* = 13.5 Hz, 1H), 3.77 (d, *J* = 15.0 Hz, 1H), 4.19 (dq, *J* = 10.7, 7.1 Hz, 1H), 4.29-4.50 (m, 4H), 4.90 (d, *J* = 15.0 Hz, 1H), 6.88-6.90 (m, 2H), 6.92 (d, *J* = 8.4 Hz, 1H), 7.18 (dd, *J* = 8.4, 2.1 Hz, 1H), 7.21-7.32 (m, 8H), 7.51 (d, *J* = 2.1 Hz, 1H). Selected NOEs are between δ 2.92 (C3a-*H*) and δ 3.24 (C3-H*H*), between δ 3.44 (C9a-*H*) and δ 2.59 (C3-*H*H), 6.88-6.90 (*o*-H of C4-*Ar*), and between δ 2.59

(C3-*H*H) and δ 6.88-6.90 (*o*-H of C4-*Ar*).; ^{13}C NMR (100.6 MHz, $CDCl_3$) *δ* (ppm) 13.96 (CH_3), 14.09 (CH_3), 36.35 (CH), 43.56 (CH), 46.14 (CH_2), 46.45 (CH), 47.18 (CH_2), 60.14 (C), 62.27 (CH_2), 62.80 (CH_2), 127.23 (CH), 127.44 (CH), 127.89 (CH), 128.63 (CH), 128.79 (CH), 130.14 (CH), 130.32 (CH), 132.61 (CH), 132.65 (C), 136.27 (C), 136.65 (C), 137.38 (C), 140.55 (C), 167.88 (C), 170.41 (C), 171.44 (C). Selected HMBC correlations are between δ 2.59 (C3-*H*H), 3.24 (C3-H*H*), 3.44 (C9a-*H*) and δ 36.35 (*C*3a), between δ 6.88-6.90 (*o*-H of C4-*Ar*) and δ 46.45 (*C*4), and between δ 3.44 (C9a-*H*), 7.51 (C8-*H*), 2.92 (C3a-*H*) and δ 60.14 (*C*9).; IR (KBr) 2979, 2902, 1741, 1699, 1596, 1492, 1434, 1362, 1250, 1199, 1115, 1026 cm^{-1}; MS (EI) *m/z* 533 (M^+, 19), 531 (M^+, 48), 428 (25), 191 (26), 91 (100%); HRMS (EI) *m/z* 531.1803, 533.1790 (calcd for $C_{31}H_{30}ClNO_5$ 531.1813, 533.1783).

5j-cis: (1 mmol scale, toluene, 110 °C, 241 mg, 78% (**5j-cis**:**5j-trans**=31:47), **5j-cis** was partially isolated by column chromatography. 84 mg, 16%); R_f = 0.62 (benzene-ether = 1 : 1); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* (ppm) 1.17 (t, *J* = 7.0 Hz, 3H), 1.37 (t, *J* = 7.2 Hz, 3H), 2.95 (dd, *J* = 9.8, 7.0 Hz, 1H), 3.16 (dd, *J* = 9.8, 8.3 Hz, 1H), 3.31 (dddd, *J* = 9.8, 8.3, 7.0, 5.1 Hz, 1H), 4.09 (dq, *J* = 10.7, 7.0 Hz, 1H), 4.17-4.29 (m, 5H), 4.35-4.49 (m, 2H), 6.80 (dd, *J* = 8.3, 0.9 Hz, 1H), 6.91-6.93 (m, 2H), 7.03-7.06 (m, 2H), 7.00-7.02 (m, 4H), 7.13 (dd, *J* = 8.3, 2.3 Hz, 1H), 7.16-7.23 (m, 3H), 7.25-7.34 (m, 3H), 8.26 (d, *J* = 2.3 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) *δ* (ppm) 13.80 (CH_3), 14.04 (CH_3), 35.88 (CH), 44.66 (CH), 46.36 (CH_2), 47.55 (CH), 48.29 (CH_2), 58.84 (C), 62.16 (CH_2), 62.66 (CH_2), 127.41 (CH), 127.44 (CH), 127.51 (CH), 127.92 (CH), 128.63 (CH), 128.74 (CH), 128.80 (CH), 129.71 (CH), 130.76 (CH), 132.69 (C), 134.14 (C), 135.65 (C), 136.81 (C), 139.12 (C), 168.08 (C), 169.02 (C), 172.28 (C); ^{1}H NMR (400 MHz, C_6D_6) *δ* (ppm) 0.779 (t, *J* = 7.1 Hz, 3H), 1.16 (t, *J* = 7.2 Hz, 3H), 2.69 (dd, *J* = 9.4, 8.2 Hz, 1H), 2.76 (dd, *J* = 9.4, 7.0 Hz, 1H), 2.92 (dddd, *J* = 9.6, 8.2, 7.0, 4.7 Hz, 1H), 3.70 (dq, *J* = 10.7, 7.1 Hz, 1H), 3.94 (d, *J* = 15.1 Hz, 1H), 3.99 (dq, *J* = 10.7, 7.1 Hz, 1H), 4.07 (d, *J* = 15.1 Hz, 1H), 4.28 (d, *J* = 4.7 Hz, 1H), 4.39 (d, *J* = 9.6 Hz, 1H), 4.37-4.53 (m, 2H), 6.66 (dd, *J* = 8.4, 0.6 Hz, 1H), 6.80-6.82 (m, 2H), 6.89 (d, *J* = 7.2 Hz, 2H), 6.93 (dd, *J* = 8.4, 2.3 Hz, 1H), 6.93-7.06 (m, 6H), 8.83 (d, *J* = 2.3 Hz, 1H). Selected NOEs are between δ 2.92 (C3a-*H*) and δ 4.39 (C9a-*H*), 4.28 (C4-*H*), and between δ 4.28 (C4-*H*) and δ 4.39 (C9a-*H*).; ^{13}C NMR (100.6 MHz, C_6D_6) *δ* (ppm) 13.57 (CH_3), 13.98 (CH_3), 36.20 (CH), 45.08 (CH), 46.36 (CH_2), 47.68 (CH), 48.07 (CH_2), 59.33 (C), 62.35 (CH_2), 62.46 (CH_2), 127.32 (CH), 127.51 (CH), 127.76 (CH), 128.06 (CH), 128.76 (CH), 128.83 (CH), 129.21 (CH), 129.91 (CH), 131.54 (CH), 132.97 (C), 135.12 (C), 136.49 (C), 137.56 (C), 139.73 (C) 168.26 (C), 169.43 (C), 171.79 (C). Selected HMBC correlations are between δ 2.69 (C3-*H*H), 2.76 (C3-H*H*), 4.39 (C9a-*H*), 4.28 (C4-*H*) and δ 36.20 (*C*3a), between δ 2.69 (C3-*H*H), 2.76 (C3-H*H*) and δ 45.08 (*C*4), and between δ 2.92 (C3a-*H*), 4.39 (C9a-*H*), 8.83 (C8-*H*) and δ 59.33 (*C*9).; IR (neat) 2982, 1731, 1693, 1596, 1495, 1475, 1445, 1365, 1240, 1173, 1101, 1038 cm^{-1}; MS (EI) *m/z* 533 (M^+, 30), 531 (M^+, 78), 310 (28), 91 (100%); HRMS (EI) *m/z* 531.1808, 533.1808 (calcd for $C_{31}H_{30}ClNO_5$ 531.1813, 533.1783).

5k-trans: (1 mmol scale, toluene, 110 °C, 292 mg, 55%); $R_f = 0.5$ (hexane-AcOEt = 1 : 1); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.26 (t, J = 7.1 Hz, 3H), 1.40 (t, J = 7.1 Hz, 3H), 2.53 (dd, J = 9.7, 9.2 Hz, 1H), 3.07 (dddd, J = 13.7, 9.7, 8.0, 6.4 Hz, 1H), 3.30 (dd, J = 9.2, 8.0 Hz, 1H), 3.34 (d, J = 13.7 Hz, 1H), 3.84 (d, J = 14.9 Hz, 1H), 4.16 (dq, J = 10.6, 7.1 Hz, 1H), 4.30-4.49 (m, 3H), 4.51 (d, J = 6.4 Hz, 1H), 4.87 (d, J = 14.9 Hz, 1H), 6.91 (dd, J = 7.7, 1.1 Hz, 1H), 7.10 (d, J = 8.7 Hz, 2H), 7.22-7.35 (m, 7H), 7.57 (dd, J = 8.0, 1.2 Hz, 1H), 8.14 (d, J = 8.7 Hz, 2H). Selected NOEs are between δ 3.07 (C3a-*H*) and δ 3.30 (C3-H*H*), 4.51 (C4-*H*) and between δ 2.53 (C3-*H*H) and δ 3.34 (C9a-*H*), 7.10 (*o*-H of C4-*Ar*).; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.98 (CH_3), 14.15 (CH_3), 35.99 (CH), 43.87 (CH), 46.21 (CH_2), 46.74 (CH), 47.04 (CH_2), 60.09 (C), 62.19 (CH_2), 62.75 (CH_2), 123.73 (CH), 127.57 (CH), 127.72 (CH), 127.96 (CH), 128.69 (CH), 128.80 (CH), 130.94 (CH), 131.07 (CH), 131.17 (CH), 134.69 (C), 136.46 (C), 137.31 (C), 146.96 (C), 148.66 (C), 168.10 (C), 170.82 (C), 171.26 (C). Selected HMBC correlations are between δ 2.53 (C3-*H*H), 3.30 (C3-H*H*) and δ 35.99 (*C*3a), between δ 6.91 (C5-H), 7.10 (*o*-H of C4-*Ar*) and δ 46.74 (*C*4), and between δ 3.07 (C3a-*H*), 3.34 (C9a-*H*), 7.57 (C8-*H*) and δ 60.09 (*C*9).; IR (KBr) 2981, 1730, 1697, 1604, 1521, 1348, 1257, 1110, 1051, 1026 cm^{-1}; MS (FAB) *m/z* 565 ($[M+Na]^+$), 543 ($[M+H]^+$); HRMS (FAB) *m/z* 565.1956 (calcd for $C_{31}H_{30}N_2O_7Na$ $[M+Na]^+$ 565.1951), 543.2137 (calcd for $C_{31}H_{31}N_2O_7$ $[M+H]^+$ 543.2131).

Typical experimental procedure for eq 4 (Table 4, entry 2). To a solution of monomethyl fumarate (**6a**) (299 mg, 1 mmol) and *N*-benzyl 3,3-diphenyl-2-propen-1-amine (**4a**) (299 mg, 1 mmol) in toluene (1.6 mL) were added, Et_3N (0.14 mL, 101 mg, 1 mmol), HOBt (270 mg, 2 mmol) and EDCI (199 mg, 1 mmol) at 0 °C. The reaction mixture was stirred for 5 min. at 0 °C, and then heated at 110 °C and stirred for 20 h. The reaction mixture was diluted with CH_2Cl_2. The organic phase was washed with saturated aqueous $NaHCO_3$ solution, 2M aqueous citric acid, saturated aqueous $NaHCO_3$ and water, dried (Na_2SO_4), and evaporated *in vacuo*. The residue was purified by column chromatography over silica gel eluting with hexane-Et_2O to give **8a** (194 mg, 47%).

8a: R_f = 0.5 (hexane-ether = 1 : 4); colorless crystals; mp 164.5-165.5 °C; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 2.60 (dddd, J = 13.7, 9.8, 6.8, 5.5 Hz, 1H), 2.74 (dd, J = 9.8, 8.7 Hz, 1H), 3.21 (dd, J = 8.7, 6.8 Hz, 1H), 3.25 (dd, J = 13.7, 11.5 Hz, 1H), 3.92 (d, J = 14.8 Hz, 1H), 3.93 (s, 3H), 4.02 (d, J = 11.5 Hz, 1H), 4.37 (d, J = 5.5 Hz, 1H), 4.74 (d, J = 14.8 Hz, 1H), 6.97-6.99 (m, 2H), 7.02 (dd, J = 7.7, 1.3 Hz, 1H), 7.15-7.31 (m, 10H), 7.41 (d, J = 7.8 Hz, 1H). Selected NOEs are between δ 2.60 (C3a-*H*) and δ 3.21 (C3-H*H*), 4.37 (C4-*H*), 4.02 (C9-*H*), and between δ 3.25 (C9a-*H*), 2.74 (C3-*H*H) and δ 6.97-6.99 (*o*-H of C4-*Ph*). Atom numbering is shown in Supporting Information.; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 40.34 (CH), 40.41 (CH), 46.34 (CH_2), 46.69 (CH), 46.88 (CH), 47.69 (CH_2), 52.64 (CH_3), 126.97 (CH), 127.57 (CH), 127.63 (CH), 127.65 (CH), 127.79 (CH), 128.08 (CH), 128.47 (CH), 128.74 (CH), 130.36 (CH), 131.65 (CH), 133.92 (C), 136.53 (C), 138.45 (C), 140.84 (C), 173.40 (C), 173.90 (C). Selected HMBC correlations are between δ 4.02 (C9-*H*) and δ 40.34, 40.41 (*C*3a, *C*9a), between δ 2.74 (C3-*H*H), 3.21 (C3-H*H*), 2.60 (C3a-*H*), 4.02 (C9-*H*) and δ 46.69 (*C*4), and between δ 3.25 (C9a-*H*) and δ 46.88 (*C*9).; IR (KBr) 3024, 1735, 1685, 1494, 1430, 1309, 1205, 1161 cm^{-1}; MS (EI) *m/z* 411 (M^+, 47), 351 (23), 205 (22), 118 (24), 91 (100%); HRMS (EI) *m/z* 411.1845 (calcd for $C_{27}H_{25}NO_3$ 411.1834); Anal. Calcd for $C_{27}H_{25}NO_3$: C, 78.81; H, 6.12; N, 3.40. Found: C, 78.89; H, 6.22; N, 3.41.

7b: (1 mmol scale, THF, r.t., 188 mg, 89%); R_f = 0.6 (hexane-ether = 1 : 1); colorless oil; ^1H NMR (400 MHz, $CDCl_3$) (2 rotamers, ratio 1.9:1) δ (ppm) 3.99 (d, J = 6.6 Hz, 2H×0.66, major rotamer), 4.18 (d, J = 7.0 Hz, 2H×0.34, minor rotamer), 4.47 (s, 2H×0.34), 4.66 (s, 2H×0.66), 5.90 (t, J = 6.6 Hz, 2H×0.66), 6.07 (t, J = 7.0 Hz, 2H×0.34), 6.73 (dq, J = 13.6, 1.7 Hz, 1H×0.66), 6.77-6.99 (m, 1H+1H×0.34), 7.06-7.41 (m, 15H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 45.32 (CH_2), 46.54 (CH_2), 49.76 (CH_2), 51.03 (CH_2), 122.59 (C, q, J_{FC} = 270 Hz), 122.61 (C, q, J_{FC} = 270 Hz), 122.86 (CH), 122.97 (CH), 126.67 (CH), 127.41 (CH), 127.55 (CH), 127.80 (CH), 128.02 (CH), 128.09 (CH), 128.12 (CH), 128.20 (CH), 128.22 (CH), 128.38 (CH), 128.43 (CH), 128.51 (CH), 128.67 (CH), 128.75 (CH), 129.00 (CH), 129.42-130.59 (m), 129.72 (CH), 129.76 (CH), 130.11 (CH), 135.95 (C), 136.65 (C), 138.19 (C), 138.75 (C), 140.98 (C), 141.39 (C), 145.68 (C), 163.55 (C), 163.66 (C); ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) -64.72 (d, J_{FH} = 5.7 Hz, 3F×0.66), -65.01 (d, J_{FH} = 5.7 Hz, 3F×0.34); IR (neat) 3060, 1681, 1633, 1495, 1445, 1303, 1266, 1132 cm^{-1}; MS (EI) *m/z* 421 (M^+, 18), 330 (29), 191 (100%); HRMS (EI) *m/z* 421.1656 (calcd for $C_{26}H_{22}F_3NO$ 421.1653).

8c: (1 mmol scale, toluene, 110 °C, 237 mg, 48%); R_f = 0.5 (hexane-ether = 1 : 4); pale yellow crystals; mp 84-85 °C; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 2.68-2.72 (m, 1H), 3.13-3.26 (m, 3H), 3.81 (d, J = 14.8 Hz, 1H), 4.41 (d, J = 4.1 Hz, 1H), 4.92 (d, J = 14.8 Hz, 1H), 6.83-6.85 (m, 2H), 7.10 (dd, J = 7.5, 1.9 Hz, 1H), 7.15-7.17 (m, 2H), 7.22-7.39 (m, 7H), 7.91 (d, J = 7.6 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 36.74 (CH, q, J_{FC} = 1.5 Hz), 40.39 (CH), 45.95 (CH_2), 46.45 (CH), 46.80 (CH_2), 56.47 (C, septet, J_{FC} = 26 Hz), 123.59 (C, q, J_{FC} = 288 Hz), 125.01 (C, q, J_{FC} = 287 Hz), 127.41 (CH), 127.51 (CH), 127.66 (CH), 127.89 (CH), 128.73 (CH), 128.77 (CH), 129.90 (CH), 130.05 (CH), 130.97 (CH, septet, J_{FC} = 3.8 Hz), 132.12 (CH), 136.34 (C), 139.51 (C), 140.85 (C), 167.96 (C); ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) -61.15 (q, J_{FH} = 6.9 Hz, 3F), -64.20 (q, J_{FH} = 6.9 Hz, 3F); ^1H NMR (400 MHz, C_6D_6) δ (ppm) 2.31 (dd, J = 9.5, 8.6 Hz, 1H), 2.65 (dd, J = 8.6, 7.4 Hz, 1H), 2.75 (dddd, J = 13.9, 9.5, 7.4, 5.7 Hz, 1H), 3.12 (d, J = 13.9 Hz, 1H), 3.14 (d, J = 15.0 Hz, 1H), 3.73 (d, J = 5.7 Hz, 1H), 4.82 (d, J = 15.0 Hz, 1H), 6.64-6.66 (m, 2H), 6.72 (dd, J = 7.4, 2.0 Hz, 1H). 6.91-7.10 (m, 9H), 7.98 (d, J = 7.2 Hz, 1H). Selected NOEs are between δ 2.75 (C3a-*H*), 2.65 (C3-H*H*) and δ 3.73 (C4-*H*), between δ 2.31 (C3-*H*H) and δ 3.12 (C9a-*H*) and between δ 2.31 (C3-*H*H), 3.12 (C9a-*H*) and δ 6.64-6.66 (*o*-H of C4-*Ph*).; ^{13}C NMR (100.6 MHz, C_6D_6) δ (ppm) 36.90 (CH, q, J_{FC} = 2.3 Hz), 40.66 (CH), 45.47 (CH_2), 46.28 (CH), 46.47 (CH_2), 56.93 (C, septet, J_{FC} = 26 Hz), 124.88 (C, q, J_{FC} = 289 Hz), 125.85 (C, q, J_{FC} = 289 Hz), 127.33 (CH), 127.62 (CH), 127.64 (CH), 128.00 (CH), 128.76 (CH), 128.81 (CH), 129.82 (CH), 130.23 (CH), 131.27 (CH, septet, J_{FC} = 3.8 Hz), 132.29 (CH), 137.36 (C), 140.15 (C), 141.32 (C), 166.98 (C). Selected HMBC correlations are between δ 2.65 (C3-H*H*), 3.73 (C4-*H*) and δ 36.90 (*C*3a), between δ 2.65 (C3-H*H*), 3.73 (C4-*H*) and δ 40.66 (*C*9a), and between δ 3.12 (C9a-*H*) and δ 56.93 (*C*9).; IR (KBr) 3030, 2888, 1711, 1496, 1258, 1200, 1161 cm^{-1}; MS (EI) *m/z* 489 (M$^+$, 61), 91 (100%); HRMS (EI) *m/z* 489.1527 (calcd for $C_{27}H_{21}F_6NO$ 489.1527).

8d: (1 mmol scale, THF, 60 °C, 388 mg, 80%); R$_f$ = 0.6 (hexane-ether = 1 : 4); colorless crystals; mp 202-203 °C; ^{1}H NMR (400 MHz, CDCl$_3$) *δ* (ppm) 2.56 (dddd, *J* = 13.8, 9.9, 7.0, 5.5 Hz, 1H), 2.72 (dd, *J* = 9.9, 9.2 Hz, 1H), 3.15 (dd, *J* = 13.8, 11.6 Hz, 1H), 3.21 (dd, *J* = 9.2, 7.0 Hz, 1H), 3.94 (s, 3H), 3.95 (d, *J* = 14.8 Hz, 1H), 3.96 (d, *J* = 11.6 Hz, 1H), 4.31 (d, *J* = 5.5 Hz, 1H), 4.71 (d, *J* = 14.8 Hz, 1H), 6.90 (d-like, *J* = 8.4 Hz, 2H), 6.92 (d, *J* = 8.4 Hz, 1H), 7.14-7.17 (m, 3H), 7.24-7.32 (m, 5H), 7.39-7.40 (m, 1H). Selected NOEs are between δ 2.56 (C3a-*H*) and δ 3.21 (C3-H*H*), 4.31 (C4-*H*), 3.96 (C9-*H*), between δ 3.15 (C9a-*H*) and δ 2.72 (C3-*H*H), and between δ 3.15 (C9a-*H*), 2.72 (C3-*H*H) and δ 6.90 (*o*-H of C4-*Ar*).; ^{13}C NMR (100.6 MHz, CDCl$_3$) *δ* (ppm) 39.99 (CH), 40.16 (CH), 45.63 (CH), 46.40 (CH$_2$), 46.54 (CH), 47.43 (CH$_2$), 52.89 (CH$_3$), 127.70 (CH), 127.73 (CH), 128.08 (CH), 128.27 (CH), 128.79 (CH), 131.49 (CH), 132.69 (CH), 133.22 (C), 133.51 (C), 135.63 (C), 136.30 (C), 136.56 (C), 138.70 (C), 172.76 (C), 173.17 (C). Selected HMBC correlations are between δ 2.72 (C3-*H*H), 3.21 (C3-H*H*), 3.15 (C9a-*H*), 3.96 (C9-*H*) and δ 40.16 (*C*3a), between δ 3.21 (C3-H*H*), 3.15 (C9a-*H*) and δ 45.63 (*C*4), and between δ 3.15 (C9a-*H*) and δ 46.54 (*C*9).; IR (KBr) 2946, 2912, 1740, 1698, 1560, 1485, 1436, 1273, 1118, 1014 cm^{-1}; MS (EI) *m/z* 481 (M$^+$, 69), 479 (M$^+$, 100), 419 (27), 118 (34%); HRMS (EI) *m/z* 479.1049, 481.1028 (calcd for $C_{27}H_{23}Cl_2NO_3$ 479.1055, 481.1025); Anal. Calcd for $C_{27}H_{23}Cl_2NO_3$: C, 67.51; H, 4.83; N, 2.92. Found: C, 67.51; H, 4.84; N, 2.95.

7e: (1 mmol scale, THF, r.t., 376 mg, 77%); R$_f$ = 0.8 (hexane-ether = 1 : 4); pale yellow oil; ^{1}H NMR (400 MHz, CDCl$_3$) (2 rotamers, ratio 1.3:1) *δ* (ppm) 4.00 (d, *J* = 6.4 Hz, 2H×0.57, major rotamer), 4.16 (d, *J* = 6.8 Hz, 2H×0.43, minor rotamer), 4.49 (s, 2H×0.43), 4.66 (s, 2H×0.57), 5.87 (t, *J* = 6.4 Hz, 1H×0.57), 6.04 (t, *J* = 6.8 Hz, 1H×0.43), 6.72 (dq, J_{HH} = 15.2, J_{FH} = 1.8 Hz, 1H×0.57), 6.79-6.90 (m, 1H), 6.96-7.36 (m, 13H+1H×0.43); ^{13}C NMR (100.6

MHz, CDCl$_3$) δ (ppm) 45.31 (CH$_2$), 46.42 (CH$_2$), 49.78 (CH$_2$), 51.28 (CH$_2$), 122.46 (C, q, J_{FC} = 270 Hz), 122.49 (C, q, J_{FC} = 270 Hz), 124.07 (CH), 124.17 (CH), 126.57 (CH), 127.78 (CH), 127.96 (CH, q, J_{FC} = 6.1 Hz), 128.05 (CH), 128.30 (CH), 128.34 (CH), 128.51 (CH), 128.55 (CH), 128.67 (CH), 128.69 (CH), 128.92 (CH), 128.96 (CH), 129.91 (CH, q, J_{FC} = 35 Hz), 130.10 (CH, q, J_{FC} = 35 Hz), 130.93 (CH), 133.66 (C), 133.76 (C), 134.11 (C), 134.41 (C), 135.67 (C), 135.99 (C), 136.46 (C), 136.59 (C), 138.96 (C), 139.42 (C), 142.98 (C), 143.14 (C), 163.36 (C), 163.57 (C); ^{19}F NMR (376 MHz, CDCl$_3$) δ (ppm) -64.67 (d, J_{FH} = 5.7 Hz, 3F×0.57), -64.90 (d, J_{FH} = 4.6 Hz, 3F×0.43); IR (neat) 3064, 1681, 1638, 1493, 1303, 1134, 1091, 1014 cm^{-1}; MS (EI) *m/z* 491 (M$^+$, 13), 489 (M$^+$, 20), 400 (29), 398 (41), 261 (70), 259 (100%); HRMS (EI) *m/z* 489.0880, 491.0849 (calcd for $C_{26}H_{20}Cl_2F_3NO$ 489.0874, 491.0845).

8e: (0.5 mmol scale, toluene in a closed vessel, 160 °C, 94 mg, 38%); R$_f$ = 0.7 (hexane-AcOEt = 1 : 1); colorless crystals; mp 198.5-199.0 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ (ppm) 2.56 (dddd, *J* = 14.2, 9.7, 6.3, 4.5 Hz, 1H), 2.62 (dd, *J* = 14.2, 9.7 Hz, 1H), 2.93 (dd, *J* = 9.7, 9.2 Hz, 1H), 3.22 (dd, *J* = 9.2, 6.3 Hz, 1H), 4.05 (dq, *J* = 9.7, J_{FC} = 9.2 Hz, 1H), 4.05 (d, *J* = 14.8 Hz, 1H), 4.27 (d, *J* = 4.5 Hz, 1H), 4.73 (d, *J* = 14.8 Hz, 1H), 6.88 (d-like, *J* = 8.4 Hz, 2H), 7.01 (d, *J* = 8.4 Hz, 1H), 7.18-7.20 (m, 2H), 7.25-7.33 (m, 6H), 7.63 (bs, 1H); ^{13}C NMR (100.6 MHz, CDCl$_3$) δ (ppm) 37.47 (CH), 42.04 (CH), 43.30 (CH, q, J_{FC} = 27 Hz), 45.49 (CH), 46.63 (CH$_2$), 46.78 (CH$_2$), 126.59 (C, q, J_{FC} = 282 Hz), 128.12 (CH), 128.76 (CH), 128.81 (CH), 128.85 (CH), 130.02 (CH, q, J_{FC} = 3.1 Hz), 131.22 (CH), 132.09 (C, q, J_{FC} = 1.6 Hz), 132.42 (CH), 133.41 (C), 133.56 (C), 136.30 (C), 136.98 (C), 138.00 (C), 171.85 (C); ^{19}F NMR (376 MHz, CDCl$_3$) δ (ppm) -65.57 (d, J_{FH} = 9.2 Hz); ^{1}H NMR (400 MHz, C_6D_6) δ (ppm) 1.57 (dddd, *J* = 14.5, 10.5, 6.4, 4.9 Hz, 1H), 2.23 (dd, *J* = 10.5, 9.0 Hz, 1H), 2.30 (dd, *J* = 14.5, 10.0 Hz, 1H), 2.49 (dd, *J* = 9.0, 6.4 Hz, 1H), 3.30 (d, *J* = 4.9 Hz, 1H), 3.38 (d, *J* = 14.9 Hz, 1H), 3.74 (dq, *J* = 10.0, J_{FH} = 8.9 Hz, 1H), 4.81 (d, *J* = 14.9 Hz, 1H), 6.34 (d, *J* = 8.3 Hz, 1H), 6.43 (d, *J* = 8.5 Hz, 2H), 6.94 (dd, *J* = 8.3, 2.1 Hz, 1H), 6.98 (d-like, *J* = 8.5 Hz, 2H), 7.05-7.16 (m, 5H), 7.58 (s, 1H). Selected NOEs are between δ 1.57 (C3a-*H*) and δ 2.49 (C3-H*H*), 3.30 (C4-*H*), 3.74 (C9-*H*), between δ 2.49 (C3-H*H*) and δ 3.30 (C4-*H*), and between δ 2.30 (C9a-*H*) and δ 6.43 (*o*-H of C4-*Ar*).; ^{13}C NMR (100.6 MHz, C_6D_6) δ (ppm) 37.26 (CH), 41.52 (CH), 43.38 (CH, q, J_{FC} = 27 Hz), 45.23 (CH), 45.82 (CH$_2$), 46.50 (CH$_2$), 127.25 (C, q, J_{FC} = 282 Hz), 127.89 (CH), 128.33 (CH). 128.49 (CH), 128.74 (CH), 128.91 (CH), 130.49 (CH, q, J_{FC} = 3.1 Hz), 131.31 (CH). 132.38 (CH), 132.68 (C, q, J_{FC} = 1.6 Hz), 133.37 (C), 133.49 (C), 137.30 (C), 137.49 (C), 138.27 (C), 170.91 (C). Selected HMBC correlations are between δ 2.23 (C3-*H*H), 2.49 (C3-H*H*), 2.30 (C9a-*H*), 3.30 (C4-*H*) and δ 41.52 (*C*3a), between δ 2.23 (C3-*H*H), 2.30 (C9a-*H*), 1.57 (C3a-*H*) and δ 45.23 (*C*4), and between δ 2.30 (C9a-*H*) and δ 43.38 (*C*9).; IR (KBr) 2912, 1696, 1491, 1243, 1165, 1097 cm^{-1}; MS (EI) *m/z* 491 (M$^+$, 59), 489 (M$^+$, 88), 91 (100%); HRMS (EI) *m/z* 489.0880, 491.0862 (calcd for $C_{26}H_{20}Cl_2F_3NO$ 489.0874, 491.0845).

8f: (1 mmol scale, benzene, 80 °C, 298 mg, 53%); R_f = 0.3 (hexane-ether = 1 : 4); pale yellow viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* (ppm) 2.68 (dd, *J* = 9.4, 9.1 Hz, 1H), 3.04 (d, *J* = 13.9 Hz, 1H), 3.15 (dddd, *J* = 13.9, 9.4, 7.2, 5.3 Hz, 1H), 3.25 (dd, *J* = 9.1, 7.2, 1H), 3.84 (d, *J* = 14.8 Hz, 1H), 4.36 (d, *J* = 5.3 Hz, 1H), 4.88 (d, *J* = 14.8 Hz, 1H), 6.76 (d, *J* = 8.6 Hz, 2H), 7.03 (d, *J* = 8.6 Hz, 1H), 7.14-7.16 (m, 2H), 7.24-7.34 (m, 6H), 7.89 (s, 1H). Selected NOEs are between δ 3.15 (C3a-*H*) and δ 3.25 (C3-H*H*), and between 3.15 (C3a-*H*) and δ 4.36 (C4-*H*), between δ 2.68 (C3-*H*H) and δ 3.04 (C9a-*H*), and between δ 2.68 (C3-*H*H), 3.04 (C9a-*H*) and δ 6.76 (*o*-H of C4-*Ar*).; ^{13}C NMR (100.6 MHz, $CDCl_3$) *δ* (ppm) 36.56 (CH, q, J_{FC} = 2.3 Hz), 40.08 (CH), 45.38 (CH), 45.72 (CH), 46.85 (CH_2), 56.37 (C, septet, J_{FC} = 26 Hz), 123.75 (C, q, J_{FC} = 288 Hz), 124.70 (C, q, J_{FC} = 288 Hz), 127.76 (CH), 127.88 (CH), 128.81 (CH), 128.99 (C), 129.05 (CH), 130.50 (CH), 130.95 (CH, septet, J_{FC} = 3.7 Hz), 131.17 (CH), 133.09 (CH), 133.67 (C), 133.74 (C), 136.08 (C), 137.39 (C), 138.94 (C), 167.24 (C). Selected HMBC correlations are between δ 2.68 (C3-*H*H), 3.25 (C3-H*H*), 3.04 (C9a-*H*), 4.36 (C4-*H*) and δ 36.56 (*C*3a), between δ 3.25 (C3-H*H*), 4.36 (C4-*H*), 3.15 (C3a-*H*) and δ 40.08 (*C*9a), and between δ 3.04 (C9a-*H*) and δ 56.37 (*C*9).; ^{19}F NMR (376 MHz, $CDCl_3$) *δ* (ppm) -61.06 (q, J_{FF} = 6.9 Hz), -64.31 (q, J_{FF} = 6.9 Hz); IR (KBr) 3031, 2888, 1711, 1596, 1491, 1259, 1203, 1163, 1015 cm^{-1}; MS (EI) *m/z* 559 (M$^+$, 43), 557 (M$^+$, 63), 91 (100%); HRMS (EI) *m/z* 557.0755, 559.0730 (calcd for $C_{27}H_{19}Cl_2F_6NO$ 557.0748, 559.0718).

7a,c,d,f are unstable and decompose to give complex mixtures gradually. They are freshly prepared and used immediately in eq 5. For **7a**, ^{1}H and ^{13}C NMR and mass spectra and for **7d**,

^{1}H and ^{13}C NMR spectra were measured. For **7c** and **7f**, copy of ^{1}H NMR are shown in Supporting Information.

7a: (1 mmol scale, THF, r.t., 318 mg, 77%); R$_f$ = 0.3 (hexane-ether = 1 : 1); pale yellow oil; ^{1}H NMR (400 MHz, CDCl$_3$) (2 rotamers, ratio 1.5:1) δ (ppm) 3.72 (s, 3H×0.4, minor rotamer), 3.74 (s, 3H×0.6, major rotamer), 4.01 (d, J = 6.4 Hz, 2H×0.6), 4.17 (d, J = 7.0 Hz, 2H×0.4), 4.48 (s, 2H×0.4), 4.62 (s, 2H×0.6), 5.91 (t, J = 6.4 Hz, 1H×0.6), 6.08 (t, J = 7.0 Hz, 1H×0.4), 6.89 (d, J = 15.2 Hz, 1H×0.6), 6.94 (d, J = 15.2 Hz, 1H×0.4), 6.97 (dd, J =7.5, 1.9 Hz, 2H×0.4), 7.05-7.13 (m, 4H+2H×0.6), 7.20-7.40 (m, 9H), 7.30 (d, J = 15.2 Hz, 1H×0.6), 7.44 (d, J = 15.2 Hz, 1H×0.4); ^{13}C NMR (100.6 MHz, CDCl$_3$) δ (ppm) 44.83 (CH$_2$), 46.37 (CH$_2$), 49.19 (CH$_2$), 50.83 (CH$_2$), 51.96 (CH$_3$), 52.02 (CH$_3$), 123.11 (CH), 123.16 (CH), 126.67 (CH), 127.23 (CH), 127.34 (CH), 127.39 (CH), 127.46 (CH), 127.69 (CH), 127.80 (CH), 127.83 (CH), 128.02 (CH), 128.15 (CH), 128.22 (CH), 128.34 (CH), 128.41 (CH), 128.47 (CH), 128.70 (CH), 129.56 (CH), 129.61 (CH), 131.29 (CH), 131.54 (CH), 133.86 (CH), 133.89 (CH), 135.99 (C), 136.69 (C), 138.20 (C), 138.61 (C), 140.89 (C), 141.28 (C), 145.21 (C), 145.38 (C), 164.49 (C), 164.57 (C), 165.80 (C), 165.89 (C); MS (EI) *m/z* 411 (M$^+$, 28), 298 (18), 191 (100%); HRMS (EI) *m/z* 411.1845 (calcd for $C_{27}H_{25}NO_3$ 411.1834).

7c: (1 mmol scale, THF, r.t., 149 mg, 39%); R$_f$ = 0.6 (hexane-ether = 1 : 1); pale yellow oil.

7d: (1 mmol scale, THF, r.t., 415 mg, 86%); R$_f$ = 0.7 (hexane-ether = 1 : 4); pale yellow oil; ^{1}H NMR (400 MHz, CDCl$_3$) (2 rotamers, ratio 1:1) δ (ppm) 3.76 (s, 3H×0.5), 3.77 (s, 3H×0.5), 4.00 (d, J = 6.4 Hz, 2H×0.5), 4.13 (d, J = 6.8 Hz, 2H×0.5), 4.51 (s, 2H×0.5), 4.63 (s, 2H×0.5), 5.87 (t, J = 6.4 Hz, 1H×0.5), 6.03 (t, J = 6.8 Hz, 1H×0.5), 6.87 (d, J = 15.2 Hz, 1H), 6.92 (d, J = 15.2 Hz, 1H), 6.95-7.05 (m, 4H+2H×0.5), 7.09-7.12 (m, 2H×0.5), 7.18-7.35 (m, 5H+2H×0.5+1H×0.5), 7.37 (d-like, J = 8.4 Hz, 2H×0.5), 7.42 (d, J = 15.2 Hz, 1H); ^{13}C NMR (100.6 MHz, CDCl$_3$) δ (ppm) 45.11 (CH$_2$), 46.52 (CH$_2$), 49.54 (CH$_2$), 51.36 (CH$_2$), 52.15 (CH$_3$), 124.45 (CH), 126.74 (CH), 127.72 (CH), 128.00 (CH), 128.34 (CH), 128.37 (CH), 128.53 (CH), 128.58 (CH), 128.68 (CH), 128.93 (CH), 130.99 (CH), 131.03 (CH), 131.61 (CH), 131.88 (CH), 133.68 (C), 133.73 (C), 133.76 (CH), 134.09 (C), 134.27 (C), 135.90 (C), 136.22 (C), 136.65 (C), 136.69 (C), 139.05 (C), 139.51 (C), 142.85 (C), 143.14 (C), 164.64 (C), 164.82 (C), 165.89 (C), 165.96 (C).

7f: (1 mmol scale, THF, r.t., 320 mg, 57%); R_f = 0.7 (hexane-ether = 1 : 4); pale yellow oil.

11:[18] (1 mmol of acrylic acid **6** ($E^1 = E^2$ = H), 1mmol of **4d**, THF, r.t., 320 mg, 82%); R_f = 0.8 (hexane-ether = 1 : 4); pale yellow viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$) (2 rotamers, ratio 1.1:1) δ (ppm) 2.32 (t, *J* = 7.2 Hz, 2H×0.52, major rotamer), 2.45 (t, *J* = 7.2 Hz, 2H×0.48, minor rotamer), 2.88 (t, *J* = 7.2 Hz, 2H×0.52), 2.91 (t, *J* = 7.2 Hz, 2H×0.48), 3.09 (d, *J* = 6.6 Hz, 2H×0.52), 3.13 (d, *J* = 6.6 Hz, 2H×0.48), 3.48 (s, 2H×0.52), 3.55 (s, 2H×0.48), 3.79 (d, *J* = 6.6 Hz, 2H×0.52), 4.04 (d, *J* = 6.8 Hz, 2H×0.48), 4.30 (s, 2H×0.48), 4.54 (s, 2H×0.52), 5.79 (t, *J* = 6.6 Hz, 1H×0.52), 5.99 (t, *J* = 6.8 Hz, 1H×0.48), 6.16 (t, *J* = 6.6 Hz, 1H×0.52), 6.18 (t, *J* = 6.6 Hz, 1H×0.48), 6.89-6.98 (m, 6H+2H×0.48), 7.05-7.11 (m, 2H+2H×0.52), 7.15-7.27 (m, 14H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 31.30 (CH_2), 31.44 (CH_2), 44.80 (CH_2), 46.13 (CH_2), 48.83 (CH_2), 50.16 (CH_2), 50.26 (CH_2), 51.07 (CH_2), 52.52 (CH_2), 52.72 (CH_2), 58.77 (CH_2), 58.92 (CH_2), 124.91 (CH), 125.52 (CH), 126.43 (CH), 126.99 (CH), 127.44 (CH), 127.63 (CH), 128.13 (CH), 128.28 (CH), 128.34 (CH), 128.47 (CH), 128.49 (CH), 128.52 (CH), 128.56 (CH), 128.61 (CH), 128.69 (CH), 128.79 (CH), 128.81 (CH), 130.97 (CH), 131.00 (CH), 131.11 (CH), 133.27 (C), 133.30 (C), 133.33 (C), 133.51 (C), 133.58 (C), 133.96 (C), 134.11 (C), 136.36 (C), 136.50 (C), 136.81 (C), 137.49 (C), 137.51 (C), 139.23 (C), 139.27 (C), 139.67 (C), 140.25 (C), 141.57 (C), 142.14 (C), 142.55 (C), 171.69 (C), 172.03 (C); IR (neat) 3029, 2919, 2826, 1652, 1591, 1495, 1455, 1363, 1265, 1090, 1014 cm^{-1}; MS (EI) *m/z* 788 (M^+, 1.6), 701 (96), 699 (100%); HRMS (ESI) *m/z* 793.1963, 791.1946, 789.1964 (calcd for $C_{47}H_{41}Cl_4N_2O$ $[M+H]^+$ 793.1914, 791.1943, 789.1973).

Transformation of 7 to 8 (eq 5, Table 5, entry 8): To a solution of **7d** (415 mg, 0.86 mmol, freshly prepared under the conditions of Table 4, entry 9) in THF (2 mL) was added Et_3N (0.12 mL, 87 mg, 0.86 mmol). The mixture was stirred at 60 °C for 20 h. The reaction mixture was concentrated under reduced pressure. The residue was purified by column chromatography over silica gel eluting with hexane-Et_2O to give **8d** (365 mg, 88%).

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Supporting Information available: Optimized structures of Schemes S1-S3 and Schemes 2-4, Cartesian coordinates of the optimized geometries, copies of the ^{1}H and ^{13}C NMR, and 2D NOESY spectra.

Keywords: Alkenes; Cycloaddition; Nitrogen heterocycles; Stereoselectivity; Substituent effects

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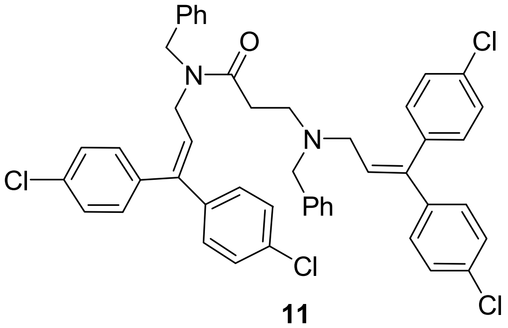
[18] The reaction of maleic acid monomethyl ester **6** (E^1 = CO_2Me, E^2 = H) with **4d** in THF at room temperature gave a complex mixture, possibly including **7d** and the reaction in toluene at 110 °C gave an complex mixture possibly including **8d**. The *Z*/*E* isomerization of the amide in the reaction conditions is likely. The reaction of acrylic acid **6** (E^1 = E^2 = H) in THF at room temperature and in toluene at 110 °C with **4d** gave only aza-Michael adduct **11** in 82 and 34% yields, respectively.



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[23] Calculations of AZM → DZM process and 3M by the use of the functionals ωB97X-D[35] and B3LYP-D3[36] which include the dispersion correction were also carried out. The calculations gave the path via a strongly interacted intermediate BZM, similar to BM3-cis in Scheme 3. Geometries of the transition states and intermediates obtained by IRC, such as C-C distances by ωB97X-D and B3LYP-D3, are slightly different from those by B3LYP. However, the stepwise path via intermediate with very small energy barriers is essentially similar to the concerted path calculated by B3LYP (see Scheme S2 of Supporting Information). The ωB97X-D and B3LYP-D3 structures have been shown in Figure S5. Although the degree of the asynchronicity and the presence or absence of the intermediates with very small energy barriers may depend on the calculation methods, the steric effect and the polar asynchronous nature of the intramolecular cycloaddition control the observed stereochemistry.

[24] B3LYP/6-311+G(d,p) SCRF = (PCM, solvent = THF), B3LYP/6-31G* SCRF = (PCM, solvent = benzene), B3LYP/6-31G* SCRF = (PCM, solvent = n,n-DiMethylFormamide), and B3PW91[37]/6-31G* SCRF = (PCM, solvent = THF) geometry optimizations of TSb (X=H) and the IRC calculations were also carried out. These calculations gave the zwitterionic intermediates BM2-cis as the energy-minimum geometries similarly (see Scheme S3 of Supporting Information).

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