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Synthesis of aromatic aldehydes by organocatalytic [4+2] and [3+3] cycloaddition of α,β-unsaturated aldehydes

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Abstract—Organocatalytic inter- and intramolecular [4+2] and [3+3] cycloadditions of α,β-unsaturated aldehydes to give polysubstituted aromatic aldehydes are described. High periselectivity for the cycloadditions, with catalyst effects exerted by L-proline and pyrrolidine–HOAc, as well as cocatalyst, additive effects, has been observed.

1. Introduction

Organocatalysis is emerging as a powerful tool in asymmetric synthesis and has attracted a great deal of attention recently.[1] Among the organocatalysts explored, secondary amines are of particular interest. For example, proline[2] and its derivatives,[3] MacMillan's catalyst,[4] dibenzylammonium trifluoroacetate,[5] and cysteine derivatives,[6] have all been used successfully in conjugated additions to α,β-unsaturated compounds. Chiral amino sulfonamide has been used effectively in Mannich reactions.[7] Friedel–Crafts alkylation of indoles with nitroalkenes was accomplished using a thiourea derivative.[8] 5,5-Dimethyl-thiazolidine-4-carboxylic acid (MDTP) was employed in the aldol reaction.[9] Even simple achiral secondary amines (e.g., pyrrolidine) have been reported in the catalyzation of a [2,3] Wittig rearrangement,[10] the Mannich reaction,[11] the epoxidation of alkenes,[12] and the domino reaction,[13] and have been applied in the synthesis of BIRT-377, as well.[14]

Although organocatalytic reactions have been extensively reported in the literature, their application in the efficient synthesis of aromatic aldehydes, compounds of longstanding interest in both organic and medicinal chemistry,[15] has remained elusive. Of the various methods developed for the preparation of these compounds, most depend upon the formylation of an aromatic precursor, a process that usually requires harsh reaction conditions and notorious reagents.[16] Thus, the efficient synthesis of aromatic aldehydes from commercially available compounds (e.g., α,β-unsaturated aldehydes) under mild reaction conditions remains a primary target.

Keywords: Organocatalysis; Proline; Cycloaddition; Unsaturated aldehyde.
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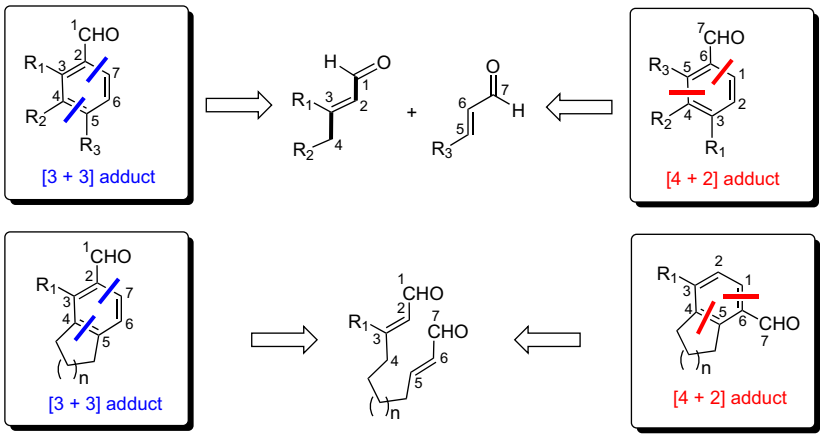
Recently, we reported on the proline-catalyzed [3+3] and [4+2] cycloadditions of α,β-unsaturated aldehydes, a methodology successfully applied in the synthesis of (−)-isopulegol hydrate and (−)-cubebaol.[17] From these results it could be suggested that aromatic aldehydes might also be synthesized by this route, using a secondary amine as catalyst (Scheme 1). Herein, we report an efficient and novel methodology for the synthesis of aromatic aldehydes from organocatalyzed [3+3] and [4+2] reactions of α,β-unsaturated aldehydes. The reaction proceeds under ambient and operationally simple conditions, requiring neither strong acids nor active reagents that are usually seen in the formylation reactions of aromatic compounds.

2. Results and discussion

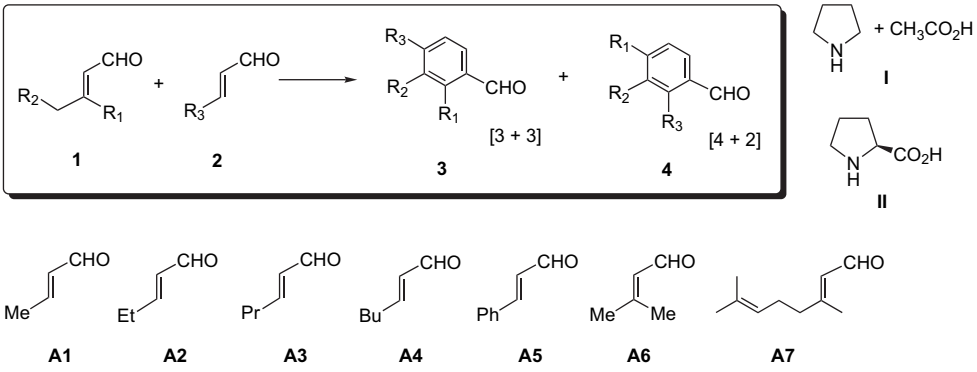
2.1. Organocatalyzed intermolecular cycloadditions of α,β-unsaturated aldehydes

Reaction of crotonaldehyde **A1** with pyrrolidine (**I**, 25 mol %) and HOAc (25 mol %) in CH_3CN at ambient temperature for 24 h afforded *p*-tolualdehyde **3a** in 81% yield (Table 1, entry 1).[18] Reaction of crotonaldehyde **A1**, pyrrolidine (**I**, 25 mol %), HOAc (25 mol %), and MnO_2 (25 mol %) under reflux, however, gave the [3+3] adduct **3a** and [4+2] adduct **4a** in the ratio 2:1 (entry 2, Table 1). This result implies that, prior to the aromatization step, [3+3] rather than [4+2] cycloaddition is favored at lower reaction temperatures. A series of α,β-unsaturated aldehydes were caused to react in the presence of **I** or **II** under various conditions; selected results are summarized in Table 1. In some cases, aromatization of the adducts occurred spontaneously without the addition of the aromatization agent (method A, Table 1). In many cases, the reaction of



Scheme 1. Retrosynthetic analysis of aromatic aldehydes by [3+3] and [4+2] transformations.

Table 1. Organocatalyzed intramolecular cycloadditions of α,β-unsaturated aldehydes



Entry	Aldehydes (**1**, **2**)	Meth.	*t* (h)	*T* (°C)	Product(s)	Ratio[b] (**3**:**4**)		Yield[c] (%)	
						I	**II**	**I**	**II**
1	**A1**, **A1**	A	24	25	R_1=R_2=H, R_3=CH_3, **3a**	96:4	100:0	81	20[d]
2	**A1**, **A1**	B	4	81	R_1=R_2=H, R_3=CH_3, **3a**:**4a**	66:34	65:35	84	63
3	**A1**, **A5**	A	18	25	R_1=R_2=H, R_3=Ph, **3b**	100:0	100:0	78	23[d]
4	**A1**, **A5**	C	(6, 3)	25[a]	R_1=R_2=H, R_3=Ph, **3b**	100:0	48:52	80	40
5	**A2**, **A2**	C	(1, 8)	81[a]	R_1=H, R_2=CH_3, R_3=Et, **3c**:**4c**	22:78	11:89	75	80
6	**A2**, **A2**	C	(6, 8)	32[a]	R_1=H, R_2=CH_3, R_3=Et, **3c**:**4c**	42:58	14:86	78	78
7	**A2**, **A2**	C	(6, 8)	0[a]	R_1=H, R_2=CH_3, R_3=Et, **3c**:**4c**	82:18	16:74	75	80[f]
8	**A3**, **A3**	C	(1, 8)	81[a]	R_1=H, R_2=Et, R_3=Pr, **3d**:**4d**	10:90	1:99	71	76
9	**A3**, **A3**	C	(6, 8)	32[a]	R_1=H, R_2=Et, R_3=Pr, **3d**:**4d**	18:82	3:97	75	78
10	**A3**, **A3**	C	(6, 8)	0[a]	R_1=H, R_2=Et, R_3=Pr, **3d**:**4d**	40:60	4:96	71	82[f]
11	**A4**, **A4**	C	(1, 8)	81[a]	R_1=H, R_2=Pr, R_3=Bu, **3e**:**4e**	10:90	1:99	71	75
12	**A4**, **A4**	C	(6, 8)	32[a]	R_1=H, R_2=Pr, R_3=Bu, **3e**:**4e**	20:80	3:97	76	78
13	**A4**, **A4**	C	(6, 8)	0[a]	R_1=H, R_2=Pr, R_3=Bu, **3e**:**4e**	38:62	9:91	71	80[f]
14	**A6**, **A1**	A	72	25	R_2=H, R_1=R_3=CH_3, **4f**	0:100	NA[g]	82	NA[g]
15	**A6**, **A1**	B	5	81	R_2=H, R_1=R_3=CH_3, **4f**	0:100	ND[e]	83	ND[e]
16	**A6**, **A5**	B	4	81	R_1=CH_3, R_2=H, R_3=Ph, **4g**	0:100	ND[e]	86	ND[e]
17	**A6**, **A2**	B	6	81	R_1=CH_3, R_2=H, R_3=Et, **4h**	0:100	ND[e]	77	ND[e]
18	**A6**, **A3**	B	7	81	R_1=CH_3, R_2=H, R_3=Pr, **4i**	0:100	ND[e]	72	ND[e]
19	**A6**, **A4**	B	10	81	R_1=CH_3, R_2=H, R_3=Bu, **4j**	0:100	ND[e]	68	ND[e]
20	**A7**, **A1**	B	8	81	R_1=Me_2C=$CHCH_2CH_2$, R_2=H, R_3=CH_3, **4k**; R_1=R_3=CH_3, R_2=Me_2C=$CHCH_2$, **4l**, **4k**:**4l**=71:29	0:100	ND[e]	82	ND[e]
21	**A7**, **A5**	B	7	81	R_1=Me_2C=$CHCH_2CH_2$, R_2=H, R_3=Ph, **4m**	0:100	ND[e]	76	ND[e]
22	**A7**, **A2**	B	9	81	R_1=Me_2C=$CHCH_2CH_2$, R_2=H, R_3=Et, **4n**; R_1=CH_3, R_2=Me_2C=$CHCH_2$, R_3=Et, **4o**, **4n**:**4o**=67:33	0:100	ND[e]	72	ND[e]

Method A: catalyst, CH_3CN, 25 °C. Method B: catalyst, MnO_2, CH_3CN, reflux. Method C: (1) catalyst, CH_3CN, 25 °C and (2) DDQ, C_6H_6, reflux.

[a] Reaction temperature prior to the exposure of MnO_2 or DDQ (aromatization step).

[b] The ratios were determined by ^1H NMR.

[c] Isolated yields.

[d] Isolated with large amounts of the [3+3] alcohol adducts and dienes, see Ref. 18.

[e] Not determined; complicated mixtures of self- and cross-condensations, and dienes.

[f] Reaction for 64 h.

[g] The [4+2] diene product was obtained in 80% yield, see Ref. 17, which can be converted to **4f** by the reaction with DDQ.

aldehyde, catalyst, and MnO_2 in a one-pot reaction process provided the aromatic aldehydes (method B, Table 1). In certain cases, a strong reagent (e.g., DDQ) was required to promote aromatization of the diene adducts (method C, Table 1). Reaction of **A1** and **A5** with **I** gave the [3+3] adduct **3b**, predominantly (entries 3 and 4 Table 1). For self-condensation of the β-monoalkylaldehydes bearing γ-acidic protons (e.g., **A1**, **A2**, **A3**, and **A4**), reaction at lower temperature gave a higher ratio of [3+3] adducts **3a**, **3c**–**3e** (entries 1–2 and 5–13, Table 1). Reaction of prenal **A6** with **A1** (**A2**, **A3**, **A4** or **A5**), catalyzed by pyrrolidine–HOAc (**I**), afforded the [4+2] adducts **4f**–**4j** (entries 14–19). The same reactions, catalyzed by L-proline (**II**), afforded complicated diene mixtures arising from self- and cross-condensation of aldehydes. Reaction of geranial **A7** with **A1** (**A5** or **A2**), catalyzed by pyrrolidine–HOAc (**I**), provided the [4+2] adduct **4k**–**4o**, exclusively, albeit with regioisomers (entries 20–22, Table 1). L-Proline-catalyzed reaction of these substrates, however, gave complicated mixtures and low yields (entries 20–22, Table 1). The results in Table 1 imply that, in many cases, pyrrolidine–HOAc (**I**) is a superior catalyst to L-proline (**II**) in the preparation of these aromatic aldehydes.

2.2. Organocatalyzed intramolecular cycloadditions of α,β-unsaturated aldehydes

Periselectivity continues to be of great interest in organic chemistry.[19] Observing high periselectivity in the intermolecular cycloadditions of α,β-unsaturated aldehydes, we next turned our attention to achieve similar results in the analogous intramolecular reaction. Accordingly, dialdehydes **5** and **6** were prepared from cyclohexene and cycloheptene, respectively, in four steps (Scheme 2). Reaction of **5** in CH_3CN with 0.5 equiv of pyrrolidine and HOAc at 30 °C for 4 h, followed by the addition of DDQ (2 equiv) at 30 °C and stirring for 2 h, afforded an 83% yield of the aromatic aldehydes **13** ([3+3] adduct) and **14** ([4+2] adduct), in a ratio of 3:1 (Table 2, entry 1). Interestingly, the [3+3] product **13** was obtained exclusively, in 81% yield, when the reaction was conducted at −10 °C, followed by the addition of DDQ, with stirring, for an additional 2 h at ambient temperature (entry 2, Table 2). Even more interesting, reaction with L-proline at room temperature, followed by aromatization with DDQ gave the [4+2] product **14** exclusively, in 80% yield (entry 3, Table 2). Under the same reaction conditions but without the addition of DDQ, the [4+2] diene product **15** was isolated in 80% yield with 80% enantiomeric excess (entry 3, Table 2). The enantioselectivity increased to 85% ee when the reaction was run at −10 °C (entry 4, Table 2). From this study, we draw the general conclusion that the [3+3] adducts, i.e., **19** and **20**, are insufficiently stable to be observed or isolated under the reaction conditions, and spontaneously transform to the aromatic products, **13** or **16**. In contrast, the [4+2] adducts, **15** and **18**, were unreactive under the normal reaction conditions, and a strong aromatization agent, such as DDQ, was required to effect the aromatization.

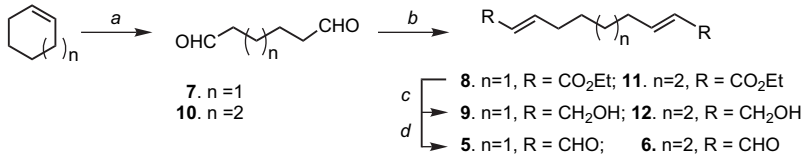
Recently, cocatalyst effects have been reported as instrumental in achieving enhanced chemoselectivity and stereoselectivity.[20] Accordingly, various additives (*t*-Bu_3P, pyrrolidine, Et_2NH, and imidazole) were introduced and their effects were examined in these reactions (entries 5–8, Table 2). Among these, it is noteworthy that diene **15** was isolated in 91% ee in the reaction with L-proline-*t*-Bu_3P (entry 6, Table 2). Addition of pyrrolidine in the presence of L-proline gave [3+3] product, exclusively (entry 8, Table 2). Reaction with the MacMillan's catalyst afforded [3+3] adduct **13**, exclusively, in 73% yield (entry 9, Table 2). Similar reaction conditions were applied to dienealdehyde **6** (entries 10–18, Table 2). Exclusive formation of [4+2] adducts **18** (and then **17**) was achieved by reaction with L-proline alone, or with the addition of imidazole or *t*-Bu_3P (entries 12–15, Table 2). Reaction with pyrrolidine–HOAc, MacMillan's catalyst or L-proline with the addition of Et_2NH and pyrrolidine, preferentially afforded [3+3] adduct **16** (entries 10, 11 and 16–18, Table 2).

2.3. Organocatalyzed intramolecular cycloadditions of α,β,γ,δ-unsaturated aldehydes

Dihydronaphthalenecarboxylic acid **21** was prepared and used in the synthesis of NaphMA for an ELISA (enzyme-linked immunosorbent assay) technique.[21] In a related application, ester **22** has been used for the preparation of a series of orally active platelet fibrinogen receptor glycoprotein IIb–IIIa antagonists.[22] It was our belief that the cycloaddition mechanism described herein might apply in the synthesis of these compounds (Scheme 3). Accordingly, trienedial **27** was prepared from **24** and caused to react with L-proline to give aromatic aldehyde **23** in 65% yield (Scheme 4). Chlorite oxidation of aldehyde **23** afforded the acid **21**, followed by reaction with diazomethane to give ester **22**. It is noteworthy that the inverse electron-demand Diels–Alder reaction was the predominant pathway in the reaction (Scheme 3).[23]

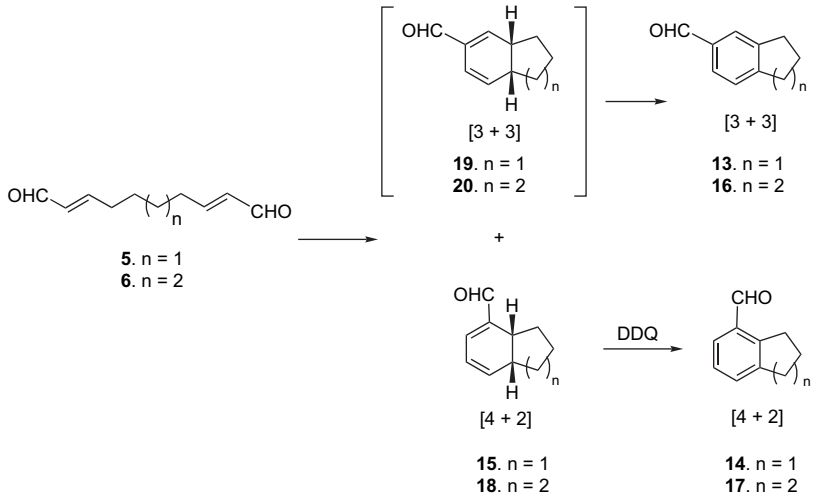
3. Conclusion

In summary, organocatalytic intermolecular [3+3] and [4+2] cycloadditions have been established as effective methodologies in the preparation of aromatic aldehydes. Further studies with the analogous intramolecular pathway were also conducted and high regioselectivity under certain catalyst



Scheme 2. Preparation of dienealdehydes **5** and **6**: (a) $RuCl_3$, $NaIO_4$, CH_2Cl_2–H_2O (2:1); 91% for **7**; 90% for **10**. (b) $(OEt)_2P(O)CH_2CO_2Et$, NaH, THF, 0 °C; 87% for **8**; 85% for **11**. (c) DIBAL-H, CH_2Cl_2, 0 °C; 81% for **9**; 80% for **12**. (d) MnO_2, CH_2Cl_2; 90% for **5**; 90% for **6**.

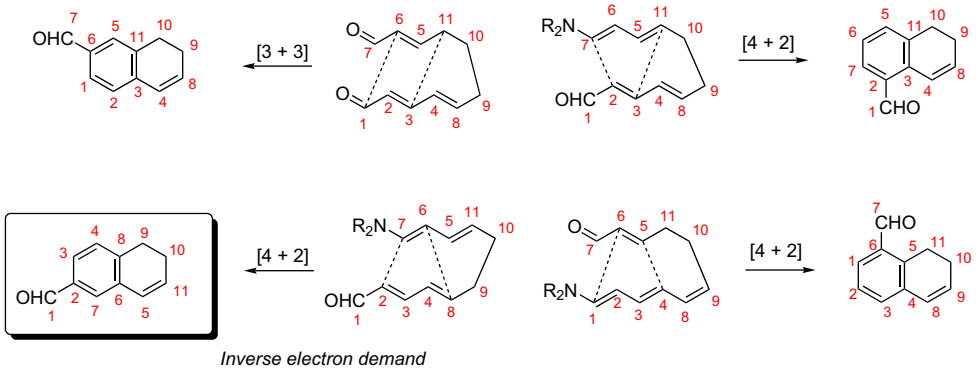
Table 2. Organocatalyzed intramolecular cycloadditions of α,β-unsaturated aldehydes



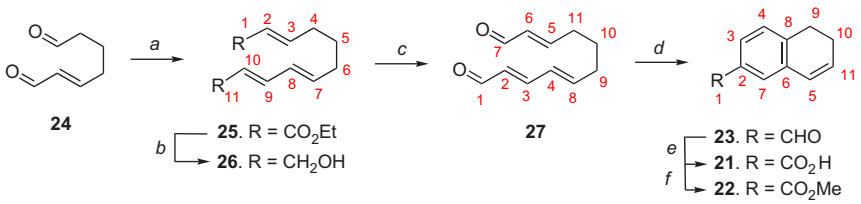
Entry	Aldehydes	T (°C)	t (h)	Method[b]	Additive	Products ratio ([3+3]/[4+2])	Yield[a] (%)	ee[c] (%)
1	**5**, n=1	(30, 30)	(4, 2)	A		13:14 (75:25)	83	NA
2	**5**, n=1	(−10, 30)	(6, 2)	A		13:14 (100:0)	81	NA
3	**5**, n=1	(30, 30)	(6, 2)	B		13:14 (0:100)	80	80[d]
4	**5**, n=1	(−10, 30)	(48, 2)	B		13:14 (33:67)	79	85[d]
5	**5**, n=1	(32, 30)	(2, 2)	C	Imidazole	13:14 (0:100)	48	52[d]
6	**5**, n=1	(30, 30)	(4, 2)	D	t-Bu_3P	13:14 (0:100)	77	91[d]
7	**5**, n=1	(30, 30)	(4, 2)	E	Et_2NH	13:14 (50:50)	70	20[d]
8	**5**, n=1	(30, 30)	(4, 2)	F	Pyrrolidine	13:14 (100:0)	75	NA
9	**5**, n=1	(30, 30)	(5, 2)	G		13:14 (100:0)	73	NA
10	**6**, n=2	(30, 30)	(2, 3)	A		16:17 (57:43)	74	NA
11	**6**, n=2	(0, 30)	(8, 3)	A		16:17 (66:34)	75	NA
12	**6**, n=2	(30, 30)	(5, 2)	B		16:17 (0:100)	80	83[e]
13	**6**, n=2	(32, 32)	(4, 2)	C	Imidazole	16:17 (0:100)	75	49[e]
14	**6**, n=2	(32, 30)	(2, 2)	D	t-Bu_3P	16:17 (4:96)	76	90[e]
15	**6**, n=2	(0, 30)	(66, 2)	D	t-Bu_3P	16:17 (0:100)	78	95[e]
16	**6**, n=2	(32, 32)	(4, 2)	E	Et_2NH	16:17 (62:38)	70	30[e]
17	**6**, n=2	(32, 32)	(2, 2)	F	Pyrrolidine	16:17 (72:28)	75	15[e]
18	**6**, n=2	(32, 32)	(3, 2)	G		16:17 (65:35)	75	~0[e]

[a] Isolated yields.
[b] Method A: (1) pyrrolidine, HOAc, CH_3CN and (2) DDQ, CH_2Cl_2. Method B: (1) L-proline, CH_3CN and (2) DDQ, CH_2Cl_2. Method C: (1) L-proline, imidazole, CH_3CN and (2) DDQ, CH_2Cl_2. Method D: (1) L-proline, t-Bu_3P, CH_3CN and (2) DDQ, CH_2Cl_2. Method E: (1) L-proline, Et_2NH, CH_3CN and (2) DDQ, CH_2Cl_2. Method F: (1) L-proline, pyrrolidine, CH_3CN and (2) DDQ, CH_2Cl_2. Method G: MacMillan's catalyst, TFA, CH_3CN and (2) DDQ, CH_2Cl_2.
[c] The diene products, **15** and **18**, were isolated under the same reaction conditions without the treatment with DDQ and the enantiomeric excesses (ee) were measured by GC–MS (Shimadzu QP 5000, chiral capillary column, gamma-cyclodextrin trifluoroacetyl, Astec Type G-TA, size 30 m×0.25 mm, flow rate 24 mL/min, temperature range: 60–120 °C, gradient: 3 °C/min). Absolute configuration was not determined.
[d] ee of **15**.
[e] ee of **18**.

and temperature conditions was observed. The reaction proceeds under ambient conditions, precluding the need for harsh reagents and reaction conditions, and thus constituting an unprecedented and efficient synthesis of aromatic aldehydes from readily commercially available α,β-unsaturated aldehydes.



Scheme 3. Possible pathways for the intramolecular cycloaddition of **27**.



Scheme 4. Intramolecular cycloaddition of **27**: (a) $(OEt)_2P(O)CH_2CO_2Et$, NaH, THF, 0 °C; 87%. (b) DIBAL-H, CH_2Cl_2, 0 °C; 80%. (c) MnO_2, CH_2Cl_2; 90%. (d) L-Proline, CH_3CN; 65%. (e) $NaClO_2$, NaH_2PO_4, 2-methyl-2-butene, *t*-BuOH, 25 °C; 80%. (f) CH_2N_2, CH_2Cl_2; 90%.

4. Experimental

4.1. General

All solvents were reagent grade. All chemicals were purchased from Aldrich and Acros Chemical Co. Reactions were normally carried out under an argon atmosphere in flame-dried glassware. Merck silica gel 60 (particle size 0.04–0.063 mm) was employed for flash chromatography. HPLC was equipped with the ultraviolet and refractive index detectors. The sample was analyzed and/or separated on a Spherisorb-Si column (25 cm×10 mm, particle size 8 μm, pore size 60 Å) or a μ-Porasil column (25 cm×1.0 cm) using a flow rate of 5 mL/min and ultraviolet and refractive index detectors (ethyl acetate and hexane eluants). The flow rate of the indicated elution solvent is maintained at 5 mL/min or 1 mL/min and the retention time of a compound is recorded accordingly. Melting points are uncorrected. Most compounds were characterized by full spectroscopic (^{1}H NMR, ^{13}C NMR, DEPT, HMQC, COSY, and NOESY) data. ^{1}H NMR, COSY, and NOESY spectra were obtained in $CDCl_3$ unless otherwise noted at 400 MHz (Bruker DPX-400) or 500 MHz (Varian-Unity INOVA-500). ^{13}C NMR spectra were obtained at 100 MHz or 125 MHz.

4.2. Representative procedure for the synthesis of aromatic aldehyde from α,β-unsaturated aldehydes (reactions in Table 1)

Method A: to a solution of crotonaldehyde (70 mg, 1.0 mmol) and *trans*-cinnamaldehyde (132 mg, 1.0 mmol) in CH_3CN (14 mL) were added slowly pyrrolidine (71 mg, 1.0 mmol) and HOAc (60 mg, 1.0 mmol) at 25 °C. The solution was stirred at 25 °C for 18 h. The reaction was quenched by the addition of H_2O (10 mL). To the solution was added H_2O (10 mL) and extracted with EtOAc (50 mL×2). The organic solution was washed with brine (10 mL), dried over Na_2SO_4, and concentrated in vacuo to give the crude product. The residue was purified by flash column chromatography with 3% EtOAc–hexane to give adduct **3b** (141 mg, 78% yield; R_f=0.76 in 10% EtOAc–hexane) as a yellow oil.

Method B: to a solution of crotonaldehyde (70 mg, 1.0 mmol) and 3-methyl-2-butenal (84 mg, 1.0 mmol) in CH_3CN (14 mL) were added pyrrolidine (71 mg, 1.0 mmol), acetic acid (60 mg, 1.0 mmol), and MnO_2 (87 mg, 1.0 mmol). The solution was heated to reflux for 5 h until the reaction was completed, monitored by TLC. To the solution was added H_2O (10 mL) and extracted with EtOAc (50 mL×2). The organic solution was washed with brine (10 mL), dried over Na_2SO_4, and concentrated in vacuo to give the residue. The crude product was purified by flash column chromatography with 3% EtOAc–hexane to give adduct **4f** (111 mg, 83% yield; R_f=0.78 in 10% EtOAc–hexane) as a yellow oil.

Method C: a solution of *trans*-2-hexenyl aldehyde (196 mg, 2.0 mmol) and L-proline (115 mg, 1.0 mmol) in CH_3CN (14 mL) was stirred at 32 °C for 6 h until the reaction was completed, monitored by TLC. The solution was concentrated in vacuo to give the residue. A solution of the residue and DDQ (681 mg, 3.0 mmol) in C_6H_6 (5 mL) was heated to reflux for 8 h until the reaction was completed, monitored by TLC. The solution was concentrated in vacuo to give the residue. The crude product was purified by flash column chromatography with 3% EtOAc–hexane to give adduct **4d** (113 mg, 76% yield; R_f=0.69 in 10% EtOAc–hexane) as a yellow oil.

4.2.1. 4-Methyl-benzaldehyde (3a). Prepared from crotonaldehyde (**A1**) according to the procedure in Section 4.2. R_f=0.21 in 10% EtOAc–hexane, 81% yield, yellow oil;[24] IR (neat): 3043, 2927, 2826, 2737, 1695, 1515, 1211, 765, 676 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 9.94 (s, 1H), 7.75 (d, J=7.5 Hz, 2H), 7.30 (d, J=7.5 Hz, 2H), 2.41 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 191.99 (CH), 145.54 (C), 134.18 (C), 129.84 (2CH), 129.69 (2CH), 21.25 (CH_3); MS (*m*/*z*, relative intensity): 120 (M^+, 85), 91 (100), 65 (37), 63 (18); exact mass calculated for C_8H_8O (M^+): 120.0575; found: 120.0571.

4.2.2. 2-Methyl-benzaldehyde (4a). Prepared from crotonaldehyde (**A1**) according to the procedure in Section 4.2. R_f=0.21 in 10% EtOAc–hexane, 84% yield, yellow oil;[25] IR (neat): 3065, 2966, 2857, 2736, 1695, 1449, 1293, 835, 657 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 10.20 (s, 1H), 7.23 (d, J=7.5 Hz, 1H), 7.42 (dd, J=7.5, 7.5 Hz, 1H), 7.30 (dd, J=7.5, 7.5 Hz, 1H), 7.20 (d, J=7.5 Hz, 1H), 2.61 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 192.72 (CH), 140.64 (C), 133.95 (C), 133.54 (CH), 132.01 (CH), 131.65 (CH), 126.14 (CH), 19.42 (CH_3); MS (*m*/*z*, relative intensity): 120 (M^+, 85), 91 (100), 65 (37), 63 (18); exact mass calculated for C_8H_8O (M^+): 120.0575; found: 120.0582.

4.2.3. Biphenyl-4-carbaldehyde (3b). Prepared from crotonaldehyde (**A1**) and cinnamaldehyde (**A5**) according to the procedure in Section 4.2. R_f=0.76 in 10% EtOAc–hexane, 78% yield, yellow oil;[26] IR (neat): 3029, 2925, 2855, 2731, 1697, 1601, 1107, 967, 758, 726 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): 10.05 (s, 1H), 7.94 (d, J=8.0 Hz, 2H), 7.74 (d, J=8.0 Hz, 2H), 7.63 (d, J=7.0 Hz, 2H), 7.46 (dd, J=8.0, 8.0 Hz, 2H), 7.41 (d, J=8.0, 8.0 Hz, 1H); ^{13}C NMR

($CDCl_3$, 125 MHz): δ 191.96 (CH), 147.19 (C), 139.69 (C), 135.15 (C), 130.27 (2CH), 129.00 (2CH), 128.46 (CH), 127.68 (2CH), 127.36 (2CH); MS (*m/z*, relative intensity): 182 (M^+, 68), 181 (M^+-1, 72), 167 (42), 149 (100), 97 (38), 7 (56), 57 (80); exact mass calculated for $C_{13}H_{10}O$ (M^+): 182.0732; found: 182.0730.

4.2.4. 4-Ethyl-3-methyl-benzaldehyde (3c). Prepared from pent-2-enal (**A2**) according to the procedure in Section 4.2. R_f=0.69 in 10% EtOAc–hexane, yellow oil; IR (neat): 2967, 2925, 2865, 2709, 1694, 1604, 1379, 830, 786 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 9.92 (s, 1H), 7.63 (d, *J*=8.0 Hz, 1H), 7.63 (s, 1H), 7.29 (d, *J*=8.0 Hz, 1H), 2.66 (q, *J*=7.0 Hz, 2H), 2.66 (s, 3H), 1.22 (t, *J*=7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 192.31 (CH), 149.91 (C), 136.77 (C), 134.42 (C), 131.08 (CH), 128.52 (CH), 127.94 (CH), 26.55 (CH_2), 19.09 (CH_3), 13.94 (CH_3); MS (*m/z*, relative intensity): 148 (M^+, 6), 135 (43), 123 (32), 97 (60), 81 (60), 71 (60), 57 (100), 55 (94); exact mass calculated for $C_{10}H_{12}O$ (M^+): 148.0888; found: 148.0880.

4.2.5. 2-Ethyl-3-methyl-benzaldehyde (4c). Prepared from pent-2-enal (**A2**) according to the procedure in Section 4.2. R_f=0.70 in 10% EtOAc–hexane, yellow oil;[27] IR (neat): 2962, 2925, 2857, 2709, 1694, 1604, 1455, 830, 756 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 10.29 (s, 1H), 7.66 (d, *J*=7.5 Hz, 1H), 7.37 (d, *J*=7.5 Hz, 1H), 7.24 (dd, *J*=7.5, 7.5 Hz, 1H), 3.05 (q, *J*=7.5 Hz, 2H), 2.37 (s, 3H), 1.19 (t, *J*=7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 192.79 (CH), 145.35 (C), 137.31 (C), 135.92 (CH), 133.69 (C), 129.65 (CH), 126.01 (CH), 21.14 (CH_2), 19.00 (CH_3), 15.21 (CH_3); MS (*m/z*, relative intensity): 148 (M^+, 100), 147 (M^+-1, 86), 119 (49), 105 (50), 91 (44), 77 (31); exact mass calculated for $C_{10}H_{12}O$ (M^+): 148.0888; found: 148.0886.

4.2.6. 3-Ethyl-4-propyl-benzaldehyde (3d). Prepared from hex-2-enal (**A3**) according to the procedure in Section 4.2. R_f=0.67 in 10% EtOAc–hexane, yellow oil; IR (neat): 2961, 2926, 2867, 1695, 1605, 1380, 1195, 901, 756 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 9.94 (s, 1H), 7.67 (s, 1H), 7.61 (d, *J*=7.5 Hz, 1H), 7.28 (d, *J*=7.5 Hz, 1H), 2.70 (q, *J*=7.5 Hz, 2H), 2.65 (t, *J*=7.5 Hz, 2H), 1.62 (q, *J*=7.5 Hz, 2H), 1.23 (t, *J*=7.5 Hz, 3H), 0.98 (t, *J*=7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 192.39 (CH), 147.91 (C), 142.80 (C), 134.63 (C), 129.77 (CH), 129.49 (CH), 127.50 (CH), 34.98 (CH_2), 25.13 (CH_2), 23.90 (CH_2), 14.98 (CH_3), 14.16 (CH_3); MS (*m/z*, relative intensity): 176 (M^+, 80), 147 (100), 129 (54), 119 (42), 105 (48), 57 (68); exact mass calculated for $C_{12}H_{16}O$ (M^+): 176.1201; found: 176.1206.

4.2.7. 3-Ethyl-2-propyl-benzaldehyde (4d). Prepared from hex-2-enal (**A3**) according to the procedure in Section 4.2. R_f=0.68 in 10% EtOAc–hexane, yellow oil; IR (neat): 2967, 1695, 1455, 1113 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 10.27 (s, 1H), 7.65 (d, *J*=7.0 Hz, 1H), 7.38 (d, *J*=7.5 Hz, 1H), 7.25 (dd, *J*=7.5, 7.0 Hz, 1H), 2.97 (t, *J*=8.0 Hz, 2H), 2.68 (q, *J*=8.0 Hz, 2H), 1.58–1.49 (m, 2H), 1.21 (t, *J*=8.0 Hz, 3H), 1.02 (t, *J*=8.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 192.70 (CH), 143.41 (C), 143.17 (C), 134.26 (CH and C), 129.29 (CH), 126.20 (CH), 29.25 (CH_2), 25.67 (CH_2), 25.28 (CH_2), 15.56 (CH_3), 14.38 (CH_3); MS (*m/z*, relative intensity): 176 (M^+, 21), 135 (21), 107 (59), 79 (100), 77 (45); exact mass calculated for $C_{10}H_{14}O$ (M^+): 176.1201; found: 176.1206.

4.2.8. 4-Butyl-3-propyl-benzaldehyde (3e). Prepared from hept-2-enal (**A4**) according to the procedure in Section 4.2. R_f=0.63 in 10% EtOAc–hexane, yellow oil; IR (neat): 2958, 2867, 1694, 1584, 1459, 1233, 756 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 9.95 (s, 1H), 7.66 (s, 1H), 7.63 (d, *J*=7.0 Hz, 1H), 7.30 (d, *J*=7.0 Hz, 1H), 2.70–2.60 (m, 4H), 1.68–1.60 (m, 2H), 1.58–1.55 (m, 2H), 1.44–1.40 (m, 2H), 1.01 (t, *J*=7.5 Hz, 3H), 0.96 (t, *J*=7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 192.41 (CH), 148.36 (C), 141.27 (C), 134.41 (C), 130.40 (CH), 129.79 (CH), 127.46 (CH), 34.49 (CH_2), 33.06 (CH_2), 32.72 (CH_2), 24.03 (CH_2), 22.78 (CH_2), 14.13 (CH_3), 13.96 (CH_3); MS (*m/z*, relative intensity): 204 (M^+, 4), 203 (M^+-1, 21), 173 (61), 148 (93), 69 (100); exact mass calculated for $C_{14}H_{20}O$ (M^+): 204.1514; found: 204.1507.

4.2.9. 2-Butyl-3-propyl-benzaldehyde (4e). Prepared from hept-2-enal (**A4**) according to the procedure in Section 4.2. R_f=0.64 in 10% EtOAc–hexane, yellow oil; IR (neat): 2966, 1696, 1456, 1112 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 10.28 (s, 1H), 7.66 (d, *J*=7.5 Hz, 1H), 7.36 (d, *J*=8.0 Hz, 1H), 7.24 (dd, *J*=8.0, 7.5 Hz, 1H), 3.00 (t, *J*=7.0 Hz, 2H), 2.62 (t, *J*=8.0 Hz, 2H), 1.65–1.41 (m, 6H), 0.99 (t, *J*=8.0 Hz, 3H), 0.94 (t, *J*=7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 192.7 (CH), 143.6 (C), 141.8 (C), 135.1 (CH), 134.1 (C), 129.3 (CH), 125.9 (CH), 34.7 (CH_2), 34.4 (CH_2), 27.1 (CH_2), 24.5 (CH_2), 23.1 (CH_2), 14.1 (CH_3), 13.8 (CH_3); MS (*m/z*, relative intensity): 204 (M^+, 4), 203 (M^+-1, 21), 173 (61), 148 (93), 69 (100); exact mass calculated for $C_{14}H_{20}O$ (M^+): 204.1514; found: 204.1511.

4.2.10. 2,4-Dimethyl-benzaldehyde (4f). Prepared from crotonaldehyde (**A1**) and 3-methyl-but-2-enal (**A6**) according to the procedure in Section 4.2. R_f=0.78 in 10% EtOAc–hexane, 82% yield, yellow oil;[28] IR ($CHCl_3$): 2966, 1696, 1232 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 10.81 (s, 1H), 7.67 (d, *J*=8.0 Hz, 1H), 7.14 (d, *J*=8.0 Hz, 1H), 7.04 (s, 1H), 2.61 (s, 3H), 2.36 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 192.38 (CH), 144.58 (C), 140.60 (C), 132.52 (CH), 132.37 (CH), 131.92 (C), 127.04 (CH), 21.65 (CH_3), 19.56 (CH_3); MS (*m/z*, relative intensity): 135 (M^++1, 33), 97 (21), 87 (75), 74 (100); exact mass calculated for $C_9H_{10}O$ (M^+): 134.0732; found 134.0729.

4.2.11. 5-Methyl-biphenyl-2-carbaldehyde (4g). Prepared from cinnamaldehyde (**A5**) and 3-methyl-but-2-enal (**A6**) according to the procedure in Section 4.2. R_f=0.69 in 10% EtOAc–hexane, 86% yield, yellow oil; IR (neat): 2849, 1689, 1603, 1395, 1119 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 9.92 (s, 1H), 7.93 (d, *J*=8.0 Hz, 1H), 7.47–7.40 (m, 3H), 7.38–7.33 (m, 2H), 7.31–7.26 (m, 1H), 7.23 (s, 1H), 2.45 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 192.12 (CH), 146.12 (C), 144.54 (C), 137.95 (C), 131.47 (C), 131.32 (CH), 130.00 (2CH), 128.64 (CH), 128.33 (2CH), 128.07 (CH), 127.65 (CH), 21.82 (CH_3); MS (*m/z*, relative intensity): 196 (M^+, 100), 195 (M^+-1, 100), 152 (45), 43 (80); exact mass calculated for $C_{14}H_{12}O$ (M^+): 196.0888; found 196.0891.

4.2.12. 2-Ethyl-4-methyl-benzaldehyde (4h). Prepared from pent-2-enal (**A2**) and 3-methyl-but-2-enal (**A6**)

according to the procedure in Section 4.2. R_f=0.71 in 10% EtOAc–hexane, 77% yield, yellow oil; IR (neat): 2966, 1696, 1455, 1232, 1112 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 10.19 (s, 1H), 7.69 (d, J=8.0 Hz, 1H), 7.13 (d, J=8.0 Hz, 1H), 7.07 (s, 1H), 3.00 (q, J=7.5 Hz, 2H), 2.37 (s, 3H), 1.23 (t, J=7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 192.0 (CH), 147.1 (C), 144.9 (C), 132.1 (CH), 131.2 (C), 130.9 (CH), 127.1 (CH), 25.7 (CH_2), 21.7 (CH_3), 16.3 (CH_3); MS (*m/z*, relative intensity): 148 (M^+, 100), 147 (M^+-1, 81), 119 (41), 77 (23); exact mass calculated for $C_{10}H_{12}O$ (M^+): 148.0888; found: 148.0887.

4.2.13. 4-Methyl-2-propyl-benzaldehyde (4i). Prepared from hex-2-enal (**A3**) and 3-methyl-but-2-enal (**A6**) according to the procedure in Section 4.2. R_f=0.69 in 10% EtOAc–hexane, 72% yield, yellow oil; IR (neat): 2966, 1696, 1455, 1112, 817 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 10.19 (s, 1H), 7.70 (d, J=8.0 Hz, 1H), 7.12 (d, J=8.0 Hz, 1H), 7.04 (s, 1H), 2.93 (t, J=8.0 Hz, 2H), 2.36 (s, 3H), 1.62 (q, J=7.5 Hz, 2H), 0.86 (t, J=7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 192.1 (CH), 145.8 (C), 144.9 (C), 132.0 (CH), 131.9 (CH), 131.7 (C), 127.5 (CH), 34.9 (CH_2), 25.6 (CH_2), 20.0 (CH_3), 14.4 (CH_3); MS (*m/z*, relative intensity): 162 (M^+, 84), 161 (M^+-1, 53), 147 (100), 119 (33), 77 (25); exact mass calculated for $C_{11}H_{14}O$ (M^+): 162.1045; found: 162.1045.

4.2.14. 2-Butyl-4-methyl-benzaldehyde (4j). Prepared from hept-2-enal (**A4**) and 3-methyl-but-2-enal (**A6**) according to the procedure in Section 4.2. R_f=0.74 in 10% EtOAc–hexane, 68% yield, yellow oil; IR (neat): 2966, 1696, 1455, 1112 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 10.16 (s, 1H), 7.68 (d, J=7.5 Hz, 1H), 7.11 (d, J=7.5 Hz, 1H), 7.03 (s, 1H), 2.95 (t, J=7.5 Hz, 2H), 2.35 (s, 3H), 1.59–1.51 (m, 2H), 1.41–1.33 (m, 2H), 0.90 (t, J=7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 192.13 (CH), 146.15 (C), 144.98 (C), 131.94 (2CH), 131.86 (C), 127.47 (CH), 34.83 (CH_2), 32.48 (CH_2), 22.92 (CH_2), 22.06 (CH_3), 14.27 (CH_3); MS (*m/z*, relative intensity): 176 (M^+, 81), 161 (45), 147 (100), 105 (45), 77 (41); exact mass calculated for $C_{12}H_{16}O$ (M^+): 176.1201; found: 176.1201.

4.2.15. 2-Methyl-4-(4-methyl-pent-3-enyl)-benzaldehyde (4k). Prepared from crotonaldehyde (**A1**) and geranial (**A7**) according to the procedure in Section 4.2. R_f=0.65 in 10% EtOAc–hexane, yellow oil;[29] IR (neat): 2965, 2922, 2858, 2726, 1692, 1383, 814 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 10.21 (s, 1H), 7.71 (d, J=7.5 Hz, 1H), 7.17 (d, J=7.5 Hz, 1H), 7.07 (s, 1H), 5.14 (t, J=7.0 Hz, 1H), 2.67–2.64 (m, 2H), 2.65 (s, 3H), 2.30 (t, J=7.5 Hz, 2H), 1.68 (s, 3H), 1.55 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): 192.49 (CH), 148.95 (C), 140.61 (C), 132.69 (C), 132.35 (CH), 132.15 (C), 131.98 (CH), 126.47 (CH), 123.06 (CH), 36.17 (CH_2), 29.48 (CH_2), 25.65 (CH_3), 19.63 (CH_3), 17.66 (CH_3), 14.33 (CH_3); MS (*m/z*, relative intensity): 202 (M^+, 26), 159 (100), 131 (58), 115 (35); exact mass calculated for $C_{14}H_{18}O$ (M^+): 202.1358; found: 202.1366.

4.2.16. 2,4-Dimethyl-3-(3-methyl-but-2-enyl)-benzaldehyde (4l). Prepared from crotonaldehyde (**A1**) and geranial (**A7**) according to the procedure in Section 4.2. R_f=0.65 in 10% EtOAc–hexane, yellow oil; IR (neat): 2965, 2922, 2858, 2726, 1692, 1383, 814 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 10.24 (s, 1H), 7.55 (d, J=8.0 Hz, 1H), 7.14 (d, J=8.0 Hz, 1H), 4.90 (t, J=7.5 Hz, 1H), 3.37 (d, J=7.5 Hz, 2H), 2.59 (s, 3H), 2.35 (s, 3H), 1.77 (s, 3H), 1.68 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 193.01 (CH), 143.21 (C), 140.26 (C), 138.90 (C), 132.94 (C), 132.68 (C), 129.91 (CH), 128.17 (CH), 121.14 (CH), 28.33 (CH_2), 25.64 (CH_3), 21.02 (CH_3), 18.04 (CH_3), 14.35 (CH_3); MS (*m/z*, relative intensity): 202 (M^+, 26), 159 (100), 131 (58), 115 (35); exact mass calculated for $C_{14}H_{18}O$ (M^+): 202.1358; found: 202.1366.

4.2.17. 5-(4-Methyl-pent-3-enyl)-biphenyl-2-carbaldehyde (4m). Prepared from cinnamaldehyde (**A5**) and geranial (**A7**) according to the procedure in Section 4.2. R_f=0.67 in 10% EtOAc–hexane, 82% yield, yellow oil; IR (neat): 2849, 1689, 1485, 1119 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 9.92 (s, 1H), 7.94 (d, J=8.0 Hz, 1H), 7.48–7.30 (m, 5H), 7.30 (d, J=8.0 Hz, 1H), 7.24 (s, 1H), 5.15 (t, J=6.5 Hz, 1H), 2.71 (t, J=7.5 Hz, 2H), 2.41–2.29 (m, 2H), 1.676 (s, 3H), 1.53 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 192.2 (CH), 148.9 (C), 146.1 (C), 138.0 (C), 132.8 (C), 131.6 (C), 130.8 (CH), 130.1 (2CH), 128.3 (2CH), 128.1 (CH), 128.0 (CH), 127.6 (CH), 123.0 (CH), 36.3 (CH_2), 29.5 (CH_2), 25.7 (CH_3), 17.7 (CH_3); MS (*m/z*, relative intensity): 264 (M^+, 14), 135 (100), 107 (54), 77 (31); exact mass calculated for $C_{19}H_{20}O$ (M^+): 264.1514; found: 264.1513.

4.2.18. 2-Ethyl-4-(4-methyl-pent-3-enyl)-benzaldehyde (4n). Prepared from pent-2-enal (**A2**) and geranial (**A7**) according to the procedure in Section 4.2. R_f=0.63 in 10% EtOAc–hexane, yellow oil; IR (neat): 2967, 2924, 2724, 1692, 1600, 1384, 823 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz, 2:1 ratio): δ 10.21 (s, 1H), 7.71 (d, J=7.5 Hz, 1H), 7.15 (d, J=7.5 Hz, 1H), 7.07 (s, 1H), 5.12 (t, J=7.0 Hz, 1H), 3.02 (m, 2H), 2.65 (t, J=7.0 Hz, 2H), 2.29 (q, J=7.5 Hz, 2H), 1.66 (s, 3H), 1.52 (s, 3H), 1.24 (t, J=7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 192.22 (CH), 149.09 (C), 147.09 (C), 132.69 (C), 132.05 (CH), 131.43 (C), 130.43 (CH), 126.56 (CH), 123.07 (CH), 36.24 (CH_2), 29.48 (CH_2), 25.77 (CH_2), 25.67 (CH_3), 17.65 (CH_3), 16.38 (CH_3); MS (*m/z*, relative intensity): 216 (M^+, 10), 121 (53), 93 (49), 69 (41); exact mass calculated for $C_{15}H_{20}O$ (M^+): 216.1515; found: 216.1514.

4.2.19. 2-Ethyl-4-methyl-3-(3-methyl-but-2-enyl)-benzaldehyde (4o). Prepared from pent-2-enal (**A2**) and geranial (**A7**) according to the procedure in Section 4.2. R_f=0.63 in 10% EtOAc–hexane; IR (neat): 2967, 2924, 2724, 1692, 1600, 1384, 823 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 10.22 (s, 1H), 7.59 (d, J=7.5 Hz, 1H), 7.14 (d, J=7.5 Hz, 1H), 4.93 (t, J=6.0 Hz, 1H), 3.37 (d, J=6.0 Hz, 2H), 3.04 (q, J=7.5 Hz, 2H), 2.34 (s, 3H), 1.78 (s, 3H), 1.68 (s, 3H), 1.19 (t, J=7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 192.63 (CH), 145.17 (C), 143.90 (C), 139.41 (C), 132.44 (C), 132.15 (C), 129.75 (CH), 128.45 (CH), 122.07 (CH), 27.69 (CH_2), 25.62 (CH_3), 21.02 (CH_2), 20.98 (CH_3), 18.02 (CH_3), 16.19 (CH_3); MS (*m/z*, relative intensity): 216 (M^+, 10), 121 (53), 93 (49), 69 (41); exact mass calculated for $C_{15}H_{20}O$ (M^+): 216.1515; found: 216.1514.

4.2.20. Hexanedial (7). To a solution of cyclohexene (2.5 g, 30.5 mmol) in CH_2Cl_2–H_2O (2:1, 200 mL) were added ruthenium (III) chloride (2.4 g, 11.8 mmol) and $NaIO_4$

(9.8 g, 46.0 mmol) at 25 °C. The solution was stirred for 3 h at the same temperature until the reaction was completed, monitored by TLC. The reaction was quenched by the addition of saturated aqueous $Na_2S_2O_3$ solution (50 mL). The solution was extracted with EtOAc (100 mL×2), washed with brine, dried over Na_2SO_4, and concentrated in vacuo to give the crude product. The residue was purified by flash column chromatography with 20% EtOAc–hexane (R_f=0.31 in 30% EtOAc–hexane) to give **7** as a light yellow oil (3.1 g, 91% yield);[30] IR (neat): 2952, 2726, 1736, 1365, 1173 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 9.68 (br s, 2H), 2.42–2.38 (m, 4H), 1.61–1.54 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 201.9 (2CH), 43.4 ($2CH_2$), 21.3 ($2CH_2$); MS (*m*/*z*, relative intensity): 114 (M^+, 3), 99 (42), 81 (86), 70 (79), 43 (100); exact mass calculated for $C_6H_{10}O_2$ (M^+): 114.0681; found: 114.0681.

4.2.21. Deca-2,8-dienedioic acid dimethyl ester (8). To a solution of NaH (1.3 g, 52.5 mmol) in THF (50 mL) was slowly added diethylphosphonoacetic acid ethyl ester (11.8 g, 52.5 mmol) at 0 °C under N_2. The solution was stirred for 10 min, followed by the slow addition of dialdehyde **7** (2.0 g, 17.5 mmol) and stirred for 2 h at 25 °C until the reaction was completed, monitored by TLC. The reaction was quenched by the addition of H_2O (50 mL). The solution was extracted with EtOAc (50 mL×2), washed with brine, dried over Na_2SO_4, and concentrated in vacuo to give the crude product. The residue was purified by flash column chromatography with 10% EtOAc–hexane (R_f=0.21 in 10% EtOAc–hexane) to give **8** as a light yellow oil (3.9 g, 87% yield);[31] IR (neat): 2952, 1736, 1437, 1172 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 6.85 (dt, J=16.0, 7.0 Hz, 2H), 5.73 (d, J=16.0 Hz, 2H), 4.10 (q, J=7.0 Hz, 4H), 2.18–2.09 (m, 4H), 1.45–1.36 (m, 4H), 1.20 (t, J=7.0 Hz, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 166.40 (2C), 148.44 (2CH), 121.46 (2CH), 59.98 ($2CH_2$), 31.69 ($2CH_2$), 27.28 ($2CH_2$), 14.08 ($2CH_3$); MS (*m*/*z*, relative intensity): 254 (M^+, 6), 135 (100), 107 (54), 57 (45); exact mass calculated for $C_{14}H_{22}O_4$ (M^+): 254.1518; found: 254.1517.

4.2.22. Deca-2,8-diene-1,10-diol (9). To a solution of **8** (1.0 g, 3.94 mmol) in CH_2Cl_2 (30 mL) was added a solution of DIBAL-H (1 M in hexane, 11.8 mL, 11.8 mmol) at −78 °C. The solution was stirred for 2 h at 0 °C until the reaction was completed, monitored by TLC. The reaction was quenched by the addition of saturated aqueous potassium sodium tartrate (10 mL). The solution was extracted with 10% *t*-BuOH–EtOAc (50 mL×2), dried over Na_2SO_4, and concentrated in vacuo to give the crude product. The residue was purified by flash column chromatography with 50% EtOAc–hexane (R_f=0.24 in 50% EtOAc–hexane) to give alcohol **9** as a colorless oil (542 mg, 81% yield);[32] IR (neat): 3342, 2930, 1691, 1462, 970 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 5.64–5.46 (m, 4H), 4.01–3.88 (m, 4H), 3.04 (br s, 2H), 2.01–1.88 (m, 4H), 1.34–1.28 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 132.52 (2CH), 128.90 (2CH), 63.10 ($2CH_2$), 31.83 ($2CH_2$), 28.41 ($2CH_2$); MS (*m*/*z*, relative intensity): 170 (M^+, 3), 135 (23), 83 (51), 57 (89), 41 (100); exact mass calculated for $C_{10}H_{14}O_2$ (M^+): 170.1307; found: 170.1305.

4.2.23. Deca-2,8-dienedial (5). To a solution of diol **9** (500 mg, 2.94 mmol) in CH_2Cl_2 (50 mL) was added MnO_2 (1.28 g, 14.7 mmol) and the solution was stirred at 30 °C under N_2 for 2 h. The solution was filtered through filter paper, washed with EtOAc, and the filtrate was concentrated in vacuo to give the crude product. The residue was purified by flash column chromatography with 15% EtOAc–hexane (R_f=0.38 in 20% EtOAc–hexane) to give dialdehyde **5** as a light yellow oil (439 mg, 90% yield);[33] IR (neat): 2952, 1736, 1173, 1091 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 9.33 (d, J=7.5 Hz, 2H), 6.75–6.64 (m, 2H), 6.01–5.89 (m, 2H), 2.24–2.19 (m, 4H), 1.46–1.38 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 193.57 (2CH), 157.80 (2CH), 132.69 (2CH), 31.91 ($2CH_2$), 26.82 ($2CH_2$); MS (*m*/*z*, relative intensity): 166 (M^+, 1), 121 (27), 108 (23), 67 (90), 41 (100); exact mass calculated for $C_{10}H_{14}O_2$ (M^+): 166.0994; found: 166.0993.

4.2.24. Heptanedial (10). Prepared from cycloheptene according to the procedure in Section 4.2.20. R_f=0.66 in 66% EtOAc–hexane, 85% yield, yellow oil;[34] IR (neat): 2936, 2861, 1716, 1365, 1404, 1134, 954 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 9.92 (br s, 2H), 2.41 (t, J=7.0 Hz, 4H), 1.65–1.58 (m, 4H), 1.36–1.27 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 202.24 (2CH), 43.53 ($2CH_2$), 28.52 (CH_2), 21.68 ($2CH_2$); MS (*m*/*z*, relative intensity): 128 (M^+, 5), 111 (17), 101 (40), 83 (51), 73 (100), 57 (65), 55 (78); exact mass calculated for $C_7H_{12}O_2$ (M^+): 128.0837; found: 128.0831.

4.2.25. Undeca-2,9-dienedioic acid diethyl ester (11). Prepared from **10** according to the procedure in Section 4.2.21. R_f=0.88 in 33% EtOAc–hexane, 87% yield, yellow oil;[34] IR (neat): 2931, 2860, 1719, 1635, 1268, 982, 771 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 6.88 (dt, J=16.0, 7.0 Hz, 2H), 5.74 (d, J=16.0 Hz, 2H), 4.41 (q, J=7.0 Hz, 4H), 2.15–2.11 (m, 4H), 1.44–1.27 (m, 6H), 1.22 (t, J=7.0 Hz, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 166.50 (2C), 148.82 (2CH), 121.30 (2CH), 59.97 ($2CH_2$), 31.86 ($2CH_2$), 28.46 (CH_2), 27.64 ($2CH_2$), 14.11 ($2CH_3$); MS (*m*/*z*, relative intensity): 268 (M^+, 1), 222 (14), 177 (100), 176 (76), 150 (98), 149 (70), 121 (67), 79 (29); exact mass calculated for $C_{15}H_{24}O_4$ (M^+): 268.1675; found: 268.1680.

4.2.26. Undeca-2,9-diene-1,11-diol (12). Prepared from **11** according to the procedure in Section 4.2.22. R_f=0.26 in 50% EtOAc–hexane, 83% yield, yellow oil;[32] IR (neat): 3336, 2924, 2854, 1667, 736 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 5.66–5.61 (m, 4H), 4.06 (d, J=5.5 Hz, 4H), 2.04–2.01 (m, 4H), 1.50 (br s, 2H), 1.36–1.31 (m, 4H), 1.31–1.28 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 133.18 (2CH), 128.94 (2CH), 63.65 ($2CH_2$), 31.98 ($2CH_2$), 28.76 ($2CH_2$), 28.37 (CH_2); MS (*m*/*z*, relative intensity): 184 (M^+, 1), 137 (17), 123 (25), 111 (40), 97 (68), 83 (63), 57 (100), 55 (87); exact mass calculated for $C_{11}H_{20}O_2$ (M^+): 184.1463; found: 184.1473.

4.2.27. Undeca-2,9-dienedial (6). Prepared from **12** according to the procedure in Section 4.2.23. R_f=0.63 in 63% EtOAc–hexane, 90% yield, yellow oil;[32] IR (neat): 2926, 2856, 1686, 1455, 799, 659 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 9.40 (d, J=8.0 Hz, 2H), 6.76 (dt, J=15.5, 6.5 Hz, 2H), 6.04–6.00 (m, 2H), 2.28–2.24 (m, 4H), 1.48–1.42 (m, 4H), 1.34–1.30 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 193.81 (2CH), 158.26 (2CH), 132.83 (2CH),

32.28 ($2CH_2$), 28.38 (CH_2), 27.31 ($2CH_2$); MS (*m/z*, relative intensity): 180 (M^+, 2), 138 (14), 98 (49), 97 (35), 82 (100), 71 (66), 70 (57), 67 (67); exact mass calculated for $C_{11}H_{16}O_2$ (M^+): 180.1150; found: 180.1158.

4.3. Representative procedure for the intramolecular reaction of α,β-unsaturated aldehydes (reactions in Table 2)

Method A: to a solution of **5** (33.2 mg, 0.2 mol) in CH_3CN (5 mL) were added slowly pyrrolidine (7.1 mg, 0.1 mmol) and HOAc (6 mg, 0.1 mmol) at 30 °C. The solution was stirred at 30 °C for 4 h. To the solution was added H_2O (10 mL) and extracted with EtOAc (50 mL×2). The organic solution was washed with brine (10 mL), dried over Na_2SO_4, and concentrated in vacuo to give the crude product. A solution of the crude **15** and DDQ (136 mg, 0.3 mmol) in CH_2Cl_2 (2 mL) was stirred for 2 h until the reaction was completed, monitored by TLC. The solution was concentrated in vacuo and the crude product was purified by flash column chromatography with 3% EtOAc–hexane to give **13** and **14** (24 mg, 83% yield; R_f=0.64 in 10% EtOAc–hexane) as a yellow oil.

Method B (without aromatization): a solution of **5** (33.2 mg, 0.2 mmol) and L-proline (11.4 mg, 0.1 mg) in CH_3CN (5 mL) was stirred at 30 °C for 6 h until the reaction was completed, monitored by TLC. To the solution was added H_2O (10 mL) and extracted with EtOAc (50 mL×2). The organic solution was washed with brine (10 mL), dried over Na_2SO_4, and concentrated in vacuo to give the residue. The crude product was purified by flash column chromatography with 20% EtOAc–hexane to give adduct **15** (24 mg, 80% yield; R_f=0.64 in 10% EtOAc–hexane) as a yellow oil.

Method B (with aromatization): diene **15** was prepared from the above procedure without the purification by flash column chromatography. A solution of the crude **15** and DDQ (136 mg, 0.3 mmol) in CH_2Cl_2 (2 mL) was stirred for 2 h until the reaction was completed, monitored by TLC. The solution was concentrated in vacuo and the crude product was purified by flash column chromatography with 3% EtOAc–hexane to give **14** (13.1 mg, 80% yield; R_f=0.64 in 10% EtOAc–hexane) as a yellow oil.

Method C: the same procedure as method B was employed, except that imidazole was added with L-proline in the reaction.

Method D: the same procedure as method B was employed, except that *t*-Bu_3P was added with L-proline in the reaction.

Method E: the same procedure as method B was employed, except that Et_2NH was added with L-proline in the reaction.

Method F: the same procedure as in method B was employed, except that pyrrolidine was added with L-proline in the reaction.

Method G: the same procedure as method B was employed, except that L-proline was replaced by (2*S*,5*S*)-2-*tert*-butyl-3-methyl-5-phenylmethyl-4-imidazolidinone (MacMillan's Imidazolidinone OrganoCatalysts™) and trifluoroacetic acid in the reaction.

4.3.1. Indan-5-carbaldehyde (13). Prepared from **5** according to the procedure in Section 4.3. R_f=0.64 in 10% EtOAc–hexane, 75% yield, yellow oil; IR (neat): 2967, 1696, 1455, 1112 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 9.94 (s, 1H), 7.71 (s, 1H), 7.64 (d, *J*=8.0 Hz, 1H), 7.34 (d, *J*=8.0 Hz, 1H), 2.95 (m, 4H), 2.12 (tt, *J*=7.5, 7.5 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 192.37 (CH), 152.08 (C), 145.29 (C), 135.22 (C), 128.92 (CH), 125.17 (CH), 124.80 (CH), 33.16 (CH_2), 32.36 (CH_2), 25.35 (CH_2); MS (*m/z*, relative intensity): 146 (M^+, 86), 145 (M^+-1, 37), 117 (100), 91 (39), 77 (20); exact mass calculated for $C_{10}H_{10}O$ (M^+): 146.0732; found: 146.0735.

4.3.2. Indan-4-carbaldehyde (14). Prepared from **5** according to the procedure in Section 4.3, with DDQ. R_f=0.64 in 10% EtOAc–hexane, 80% yield, yellow oil; IR (neat): 2967, 1696, 1456, 1112 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 10.13 (s, 1H), 7.61 (d, *J*=8.0 Hz, 1H), 7.45 (d, *J*=7.5 Hz, 1H), 7.30 (dd, *J*=8.0, 7.5 Hz, 1H), 3.27 (t, *J*=8.0 Hz, 2H), 2.92 (t, *J*=7.5 Hz, 2H), 2.13 (tt, *J*=8.0, 7.5 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 193.07 (CH), 146.64 (C), 146.51 (C), 132.52 (C), 130.19 (CH), 129.45 (CH), 126.93 (CH), 32.29 (CH_2), 31.98 (CH_2), 25.46 (CH_2); MS (*m/z*, relative intensity): 146 (M^+, 97), 145 (M^+-1, 51), 117 (100), 91 (24); exact mass calculated for $C_{10}H_{10}O$ (M^+): 146.0732; found: 146.0735.

4.3.3. 5,6-Dihydro-naphthalene-2-carboxylic acid methyl ester (15). Prepared from **5** according to the procedure in Section 4.3, without aromatization. R_f=0.64 in 10% EtOAc–hexane, 73% yield, yellow oil; IR (neat): 2960, 2714, 1674, 1457, 1112 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 9.37 (s, 1H), 6.08–6.00 (m, 2H), 5.75–5.68 (m, 1H), 2.53–2.45 (m, 2H), 1.98–1.89 (m, 1H), 1.86–1.78 (m, 1H), 1.58–1.35 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 191.67 (CH), 143.54 (C), 142.76 (CH), 140.73 (CH), 125.38 (CH), 44.67 (CH), 41.89 (CH), 26.29 (CH_2), 25.81 (CH_2), 23.16 (CH_2); MS (*m/z*, relative intensity): 148 (M^+, 53), 119 (48), 91 (100); exact mass calculated for $C_{10}H_{12}O$ (M^+): 148.0888; found: 148.0886.

4.3.4. 5,6,7,8-Tetrahydro-naphthalene-2-carbaldehyde (16). Prepared from **6** according to the procedure in Section 4.3. R_f=0.91 in 33% EtOAc–hexane, 75% yield, yellow oil; IR (neat): 2960, 2625, 2721, 1694, 1604, 1568, 1455, 1045, 753, 676 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 9.90 (s, 1H), 7.58–5.55 (m, 2H), 7.18 (d, *J*=8.0 Hz, 1H), 2.82–2.80 (m, 4H), 1.80–1.81 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 192.37 (CH), 144.89 (C), 138.01 (C), 134.18 (C), 130.81 (CH), 129.81 (CH), 126.60 (CH), 29.86 (CH_2), 29.21 (CH_2), 22.82 (CH_2), 22.70 (CH_2); MS (*m/z*, relative intensity): 160 (M^+, 71), 131 (100), 115 (20), 104 (19), 92 (37); exact mass calculated for $C_{11}H_{12}O_2$ (M^+): 160.0888; found: 160.0885.

4.3.5. 5,6,7,8-Tetrahydro-naphthalene-1-carbaldehyde (17). Prepared from **6** according to the procedure in Section 4.3, without aromatization. R_f=0.58 in 10% EtOAc–hexane, 85% yield, yellow oil; IR (neat): 2928, 2857, 2753, 1693, 1584, 1295, 1023, 889, 777 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 10.24 (s, 1H), 7.60 (d, *J*=7.0 Hz, 1H), 7.28 (d, *J*=7.0 Hz, 1H), 7.25 (dd, *J*=7.0, 7.0 Hz, 1H), 3.18 (t, *J*=6.0 Hz, 2H), 2.81 (t, *J*=6.0 Hz, 2H), 1.84–1.78 (m, 4H);

^{13}C NMR ($CDCl_3$, 125 MHz): δ 193.20 (CH), 139.62 (C), 138.63 (C), 135.08 (CH), 133.96 (C), 130.60 (CH), 125.50 (CH), 29.92 (CH_2), 26.28 (CH_2), 22.73 (CH_2), 22.19 (CH_2); MS (*m*/*z*, relative intensity): 160 (M^+, 76), 131 (100), 129 (19), 115 (24), 91 (47); exact mass calculated for $C_{11}H_{12}O$ (M^+): 160.0888; found: 160.0833.

4.3.6. 4a,5,6,7,8,8a-Hexahydro-naphthalene-1-carbaldehyde (18). Prepared from **6** according to the procedure in Section 4.3, without aromatization. R_f=0.52 in 33% EtOAc–hexane, 80% yield, yellow oil; IR (neat): 2922, 2856, 1644, 1463, 1384, 677 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 9.50 (s, 1H), 6.70 (dd, *J*=9.5, 2.0 Hz, 1H), 6.15–6.12 (m, 1H), 6.04 (d, *J*=9.5 Hz, 1H), 2.95 (m, 1H), 2.29–2.23 (m, 1H), 2.10–2.06 (m, 1H), 1.89–1.87 (m, 1H), 1.80–1.74 (m, 2H), 1.37–1.15 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 193.72 (CH), 145.00 (CH), 142.84 (CH), 140.87 (C), 123.30 (CH), 41.08 (CH), 39.96 (CH), 32.46 (CH_2), 28.76 (CH_2), 26.51 (CH_2), 26.44 (CH_2); MS (*m*/*z*, relative intensity): 162 (M^+, 23), 119 (17), 115 (12), 91 (100); exact mass calculated for $C_{11}H_{14}O$ (M^+): 162.1045; found: 162.1049.

4.3.7. Undeca-2,4,9-trienedioic acid diethyl ester (25). Prepared from **24**[35] according to the procedure in Section 4.2.21. R_f=0.70 in 33% EtOAc–hexane, 87% yield, yellow oil; IR (neat): 2987, 1763, 1712, 1375, 1242, 468, 677 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.21 (dd, *J*=15.5, 11.0 Hz, 1H), 6.90 (dt, *J*=16.0, 7.0 Hz, 1H), 6.14 (dd, *J*=15.5, 11.0 Hz, 1H), 6.07–6.03 (m, 1H), 5.80–5.74 (m, 2H), 4.18–4.12 (m, 4H), 2.20–2.14 (m, 4H), 1.60–1.54 (m, 2H), 1.26–1.22 (m, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 167.09 (C), 166.48 (C), 148.82 (CH), 144.55 (CH), 143.02 (CH), 128.95 (CH), 121.76 (CH), 119.64 (CH), 60.12 ($2CH_2$), 32.12 (CH_2), 31.39 (CH_2), 26.90 (CH_2), 14.11 (CH_3), 14.17 (CH_3); MS (*m*/*z*, relative intensity): 266 (M^+, 7), 221 (21), 119 (61), 114 (40), 81 (88), 67 (69); exact mass calculated for $C_{15}H_{22}O_4$ (M^+): 266.1518; found: 266.1523.

4.3.8. Undeca-2,4,9-triene-1,11-diol (26). Prepared from **25** according to the procedure in Section 4.2.22. R_f=0.54 in 66% EtOAc–hexane, 80% yield, yellow oil; IR (neat): 3353, 3015, 2925, 2856, 1663, 1444, 1370, 1217, 990, 668 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 6.16 (dd, *J*=15.5, 10.5 Hz, 1H), 6.00 (dd, *J*=15.5, 10.5 Hz, 1H), 5.69–5.58 (m, 4H), 4.10 (d, *J*=6.0 Hz, 2H), 4.04–4.02 (m, 2H), 2.08–2.01 (m, 4H), 1.96 (s, 2H), 1.47–1.41 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 134.66 (CH), 132.39 (CH), 131.50 (CH), 129.71 (CH), 129.64 (CH), 129.17 (CH), 63.65 (CH_2), 62.97 (CH_2), 31.98 (CH_2), 31.51 (CH_2), 28.48 (CH_2); MS (*m*/*z*, relative intensity): 182 (M^+, 1), 107 (25), 95 (35), 93 (41), 83 (54), 67 (100), 55 (77); exact mass calculated for $C_{11}H_{18}O_2$ (M^+): 182.1307; found: 182.1297.

4.3.9. Undeca-2,4,9-trienedial (27). Prepared from **26** according to the procedure in Section 4.2.23. R_f=0.36 in 33% EtOAc–hexane, 90% yield, yellow oil; IR (neat): 2926, 2857, 2810, 2730, 1682, 1636, 1446, 769, 677 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 9.54–9.49 (m, 2H), 7.06 (dd, *J*=15.0, 10.5 Hz, 1H), 6.82 (dt, *J*=15.5, 7.0 Hz, 1H), 6.35–6.30 (m, 1H), 6.25–6.21 (m, 1H), 6.14–6.06 (m, 2H), 2.39–2.34 (m, 2H), 2.29–2.25 (m, 2H), 1.72–1.66 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 193.81 (CH), 193.59 (CH), 157.41 (CH), 152.07 (CH), 145.21 (CH), 133.06 (CH), 130.22 (CH), 129.20 (CH), 32.19 (CH_2), 31.77 (CH_2), 26.39 (CH_2); MS (*m*/*z*, relative intensity): 178 (M^+, 3), 149 (8), 97 (28), 83 (100), 57 (49), 55 (43); exact mass calculated for $C_{11}H_{14}O_2$ (M^+): 178.0994; found: 178.1000.

4.3.10. 5,6-Dihydro-naphthalene-2-carbaldehyde (23). Prepared from **27** according to the procedure in Section 4.3, method B, without the addition of DDQ. R_f=0.79 in 33% EtOAc–hexane, 65% yield, yellow oil; IR (neat): 2922, 2854, 1762, 1688, 1625, 1241, 770 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 9.92 (s, 1H), 7.61 (d, *J*=7.5 Hz, 1H), 7.49 (s, 1H), 7.23 (d, *J*=7.5 Hz, 1H), 6.51 (d, *J*=9.5 Hz, 1H), 6.12–6.01 (m, 1H), 2.86 (t, *J*=7.5 Hz, 2H), 2.36–2.32 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 192.16 (CH), 142.89 (C), 135.23 (C), 134.83 (C), 130.17 (CH), 128.81 (CH), 128.17 (CH), 126.36 (CH), 27.85 (CH_2), 22.70 (CH_2); MS (*m*/*z*, relative intensity): 158 (M^+, 80), 129 (89), 109 (42), 103 (66), 95 (60), 94 (63), 83 (94), 55 (100); exact mass calculated for $C_{11}H_{10}O$ (M^+): 158.0732; found: 158.0773.

4.3.11. 5,6-Dihydro-naphthalene-2-carboxylic acid (21). To a solution of **23** (48 mg, 0.30 mmol) and 2-methyl-2-butene (2 mL, 18.8 mmol) in *t*-BuOH (7 mL) was added a freshly prepared solution of sodium chlorite (140 mg, 1.55 mmol) in 20% w/w aqueous NaH_2PO_4 (2.4 g in 12 mL of H_2O) at room temperature and the resulting solution was stirred for 4 h. The mixture was diluted with ethyl acetate (30 mL) and washed with water (4 mL). The aqueous phase was extracted with ethyl acetate (30 mL) and the combined organic layers were dried over Na_2SO_4 and concentrated in vacuo to give the crude product. The residue was purified by flash column chromatography with 30% EtOAc–hexane (R_f=0.45 in 33% EtOAc–hexane) to give diol **21** as a yellow oil (42 mg, 80% yield); IR (neat): 3029, 2927, 2857, 1689, 1431, 1279, 1020, 771 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.84 (d, *J*=8.0 Hz, 1H), 7.72 (s, 1H), 7.17 (d, *J*=8.0 Hz, 1H), 6.50 (d, *J*=9.5 Hz, 1H), 6.09–6.07 (m, 1H), 2.85 (t, *J*=8.5 Hz, 2H), 2.36–2.31 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 171.03 (CH), 141.68 (C), 134.28 (C), 129.39 (CH), 128.73 (CH), 127.72 (C), 127.65 (CH), 127.22 (CH), 127.16 (CH), 27.67 (CH_2), 22.75 (CH_2); MS (*m*/*z*, relative intensity): 174 (M^+, 73), 129 (100), 115 (17), 77 (13), 57 (12); exact mass calculated for $C_{11}H_{10}O_2$ (M^+): 174.0681; found: 174.0672.

4.3.12. 5,6-Dihydro-naphthalene-2-carboxylic acid methyl ester (22). To a solution of **21** (30 mg, 0.17 mmol) in CH_2Cl_2 (10 mL) was added a freshly prepared solution of CH_2N_2 in Et_2O at room temperature and the resulting solution was stirred for 30 min. The solution was concentrated in vacuo to give the crude product. The residue was purified by flash column chromatography with 10% EtOAc–hexane (R_f=0.81 in 33% EtOAc–hexane) to give diol **22** as a yellow oil (28 mg, 90% yield); IR (neat): 3029, 2928, 2860, 1721, 1436, 1280, 1194 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.76 (d, *J*=8.0 Hz, 1H), 7.66 (s, 1H), 7.13 (d, *J*=8.0 Hz, 1H), 6.47 (d, *J*=9.5 Hz, 1H), 6.06 (dd, *J*=9.5, 5.0 Hz, 1H), 3.88 (s, 3H), 2.83 (t, *J*=8.0 Hz, 2H), 2.34–2.30 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 167.22 (CH), 140.90 (C), 134.20 (C), 129.51 (CH), 128.40 (C), 127.72 (C), 127.56 (CH), 127.23 (CH), 126.74 (CH), 51.98 (CH_3), 27.60 (CH_2), 22.80 (CH_2); MS (*m*/*z*, relative intensity): 188 (M^+, 46), 157 (21), 129 (100), 85 (11), 71 (19), 64 (25); exact

mass calculated for $C_{12}H_{12}O_2$ (M^+): 188.0837; found: 188.0834.

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Supplementary data

Selected spectral data for the compounds (**3**–**27**). Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2007.01.039.

References and notes

1. For recent review, see: (a) Dalko, P. I.; Moisan, L. *Angew. Chem., Int. Ed.* **2004**, *43*, 5138; (b) Notz, W.; Tanaka, F.; Barbas, C. F., III. *Acc. Chem. Res.* **2004**, *37*, 580; (c) Seayad, J.; List, B. *Org. Biomol. Chem.* **2005**, *3*, 719; (d) Berkessel, A.; Gröger, H. *Asymmetric Organocatalysis: From Biomimetic Concepts to Applications in Asymmetric Synthesis*; Wiley: New York, NY, 2005; For a recent example in aqueous media, see: Hayashi, Y.; Sumiya, T.; Takahashi, J.; Gotoh, H.; Urushima, T.; Shoji, M. *Angew Chem., Int. Ed.* **2006**, *45*, 958.
2. Fonseca, M. T. H.; List, B. *Angew. Chem., Int. Ed.* **2004**, *43*, 3958.
3. (a) Brandau, S.; Landa, A.; Franzén, J.; Marigo, M.; Jørgensen, K. A. *Angew. Chem., Int. Ed.* **2006**, *45*, 4305; (b) Knudsen, K. R.; Mitchell, C. E. T.; Ley, S. V. *Chem. Commun.* **2006**, 66; (c) Cobb, A. J.; Shaw, D. M.; Longbottom, D. A.; Gold, J. B.; Ley, S. V. *Org. Biomol. Chem.* **2005**, *3*, 84.
4. Brown, S. P.; Goodwin, N. C.; David, W. C.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2003**, *125*, 1192.
5. Yang, J. W.; Fonseca, M. T. H.; List, B. *Angew. Chem., Int. Ed.* **2004**, *43*, 6660.
6. Hayashi, Y.; Gotoh, H.; Tamura, T.; Yamaguchi, H.; Masui, R.; Shoji, M. *J. Am. Chem. Soc.* **2005**, *127*, 16028.
7. Kano, T.; Yamaguchi, Y.; Tokuda, O.; Maruoka, K. *J. Am. Chem. Soc.* **2006**, *127*, 16408.
8. Herrera, R. P.; Sgarzani, V.; Bernardi, L.; Ricci, A. *Angew. Chem., Int. Ed.* **2005**, *44*, 6576.
9. Sakthivel, K.; Notz, W.; Bui, T.; Barbas, C. F., III. *J. Am. Chem. Soc.* **2001**, *123*, 5260.
10. McNally, A.; Evans, B.; Gaunt, M. J. *Angew. Chem., Int. Ed.* **2006**, *45*, 2116.
11. Zhuang, W.; Jørgensen, A. *Angew. Chem., Int. Ed.* **2004**, *43*, 4476.
12. (a) Armstrong, A. *Angew Chem., Int. Ed.* **2004**, *43*, 1460; (b) Aggarwal, V. K.; Lopin, C.; Sandrinelli, F. *J. Am. Chem. Soc.* **2003**, *125*, 7596.
13. Ramachary, D. B.; Barbas, C. F. *J. Org. Chem.* **2004**, *69*, 5838.
14. Chowdari, N. S.; Barbas, C. F. *Org. Lett.* **2005**, *7*, 807.
15. (a) Sano, Y.; Shiina, I. *Tetrahedron Lett.* **2006**, *47*, 1631; (b) Peng, X.; Shindo, K.; Kanoh, K.; Inomata, Y.; Choi, S.-K.; Misawa, N. *Appl. Microbiol. Biotechnol.* **2005**, *69*, 141; (c) Bolm, C.; Zani, L.; Rudolph, J.; Schiffers, I. *Synthesis* **2004**, 2173; (d) Wroczynski, P.; Wierzchowski, J. *Analyst* **2000**, *125*, 511; (e) Lee, K.; Maleczka, R. E., Jr. *Org. Lett.* **2006**, *8*, 1887; (f) Wang, Y.-G.; Cui, S.-L.; Lin, X.-F. *Org. Lett.* **2006**, *8*, 1241; (g) Godet, T.; Bonvin, Y.; Vincent, G.; Merle, D.; Thozet, A.; Ciufolini, M. A. *Org. Lett.* **2004**, *6*, 3281; (h) Fan, Q.; Lin, L.; Liu, J.; Huang, Y.; Feng, X.; Zhang, G. *Org. Lett.* **2004**, *6*, 2185; (i) Gröger, H. *Adv. Synth. Catal.* **2001**, *343*, 547.
16. For recent review, see: (a) Kantlehner, W. *Eur. J. Org. Chem.* **2003**, 2530; (b) Lücke, B.; Narayana, K. V.; Martin, A.; Jähnisch, K. *Adv. Synth. Catal.* **2004**, *346*, 1407; (c) de Angelis, A.; Ingallina, P.; Perego, C. *Ind. Eng. Chem. Res.* **2004**, *43*, 1169; (d) Ryu, I.; Sonoda, N. *Angew. Chem., Int. Ed.* **1996**, *35*, 1050.
17. Hong, B.-C.; Wu, M.-F.; Tseng, H.-C.; Liao, J.-H. *Org. Lett.* **2006**, *8*, 2217.
18. For promising examples in organocatalysis by pyrrolidine and acetic acid, see: (a) See Ref. 10; (b) Erkkilae, A.; Pihko, P. M. *J. Org. Chem.* **2006**, *71*, 2538; (c) Li, D.-P.; Guo, Y.-C.; Ding, Y.; Xiao, W.-J. *Chem. Commun.* **2006**, 799; (d) Ramachary, D. B.; Ramakumar, K.; Kishor, M. *Tetrahedron Lett.* **2005**, *46*, 7037; (e) Ji, C.; Peng, Y.; Huang, C.; Wang, N.; Jiang, Y. *Synlett* **2005**, 986; (f) Mase, N.; Tanaka, F.; Barbas, C. F. *Org. Lett.* **2003**, *5*, 4369.
19. For selected examples, see: (a) Ussing, B. R.; Hang, C.; Singleton, D. A. *J. Am. Chem. Soc.* **2006**, *128*, 7594; (b) Nakazaki, A.; Nakai, T.; Tomooka, K. *Angew. Chem., Int. Ed.* **2006**, *45*, 2235; (c) Marmsaeter, F. P.; Vanecko, J. A.; West, F. G. *Org. Lett.* **2004**, *6*, 1657; (d) Deubel, D. V.; Schlecht, S.; Frenking, G. *J. Am. Chem. Soc.* **2001**, *123*, 10085; (e) Leach, A. G.; Houk, K. N.; Davies, I. W. *Synthesis* **2005**, 3463; (f) Fujita, M.; Oshima, M.; Okuno, S.; Sugimura, T.; Okuyama, T. *Org. Lett.* **2006**, *8*, 4113.
20. Peelen, T. J.; Chi, Y.; Gellman, S. H. *J. Am. Chem. Soc.* **2005**, *127*, 11598; Mase, N.; Nakai, Y.; Ohara, N.; Yoda, H.; Takabe, K.; Tanaka, F.; Barbas, C. F., III. *J. Am. Chem. Soc.* **2006**, *128*, 734.
21. Marco, M.-P.; Hammock, B. D.; Kurth, M. J. *J. Org. Chem.* **1993**, *58*, 7548.
22. (a) Okumura, K.; Shimazaki, T.; Aoki, Y.; Yamashita, H.; Tanaka, E.; Banba, S.; Yazawa, K.; Kibayashi, K.; Banno, H. *J. Med. Chem.* **1998**, *41*, 4036; (b) Okumura, K.; Yokoyama, I.; Shimazaki, T.; Miyamoto, M.; Yamashita, H.; Kibayashi, K.; Yutaka, T.; Yazawa, K. Eur. Pat. Appl. EP 709370, 1996.
23. For organocatalytic inverse electron-demand Diels–Alder reactions, see: Juhl, K.; Jørgensen, K. A. *Angew. Chem., Int. Ed.* **2003**, *42*, 1498 and Ref. 6.
24. The NMR spectrum of **3a** was identical with that of an authentic sample purchased from Aldrich Chem. Co.
25. The NMR spectrum of **4a** was identical with that of an authentic sample purchased from Aldrich Chem. Co.
26. Su, W.; Urgaonkar, S.; Verkade, J. G. *Org. Lett.* **2004**, *6*, 1421.
27. Flippin, L. A.; Muchowski, J. M.; Carter, D. S. *J. Org. Chem.* **1993**, *58*, 2463.
28. The NMR spectrum of **4f** was identical with that of an authentic sample purchased from TCI Chem. Co.
29. Thomas, A. F.; Guntz-Dubini, R. *Helv. Chim. Acta* **1976**, *59*, 2261.
30. Lopez, S.; Fermandez-Trillo, F.; Castedo, L.; Saa, C. *Org. Lett.* **2003**, *5*, 3725.
31. Hon, Y.-S.; Chu, K.-P.; Hong, P.-C.; Lu, L. *Synth. Commun.* **1992**, 429.
32. Iriye, R.; Toya, T.; Makino, J.; Aruga, R.; Doi, Y.; Handa, S.; Tanaka, H. *Agric. Biol. Chem.* **1988**, *52*, 989.
33. Nicolaou, K. C.; Montagnon, T.; Baran, P. S. *Angew. Chem., Int. Ed.* **2002**, *41*, 993.
34. Roels, J.; Metz, P. *Synlett* **2001**, 789.
35. Chen, S.-H.; Hong, B.-C.; Su, C.-F.; Sarshar, S. *Tetrahedron Lett.* **2005**, *51*, 8899.