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Facile synthesis of benzo-fused 2,8-dioxabicyclo[3.3.1]nonane derivatives via a domino Knoevenagel condensation/hetero-Diels–Alder reaction sequence

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Abstract

A facile two-step synthesis of a series of benzo-fused 2,8-dioxabicyclo[3.3.1]nonane derivatives is described, featuring a domino Knoevenagel condensation/intramolecular hetero-Diels–Alder reaction sequence.

Keywords: Knoevenagel condensation; Hetero-Diels–Aldercycloaddition; Domino reaction; Benzo-fused 2,8-dioxabicyclo[3.3.1]nonanes; Proline

1. Introduction

The condensation reaction of carbonyl compounds with active methylene compounds in the presence of amines, known as the Knoevenagel condensation,[1] represents one of the most fundamental bond-forming reactions in organic chemistry.[2] Particularly, due to the fact that the resulting α,β-unsaturated dicarbonyl or related compounds are useful intermediates, combination of this reaction with other reactions in a domino fashion[3] has been increasingly employed, thereby making formation of multiple bonds possible.[4] For example, Knoevenagel condensation has been successfully combined with hetero-Diels–Alder reactions, Michael addition reactions, ene reactions, and/or sigmatropic rearrangements for the synthesis of highly functionalized molecules.[5] In the course of our investigation directed toward the efficient synthesis of heterocycles,[6] we discovered a new route to benzo-fused 2,8-dioxabicyclo[3.3.1]-nonane structures based upon Knoevenagel/hetero-Diels–Alder cascade reactions. Herein, we wish to describe our findings.

2. Results and discussion

As depicted in Scheme 1, domino Knoevenagel/hetero-Diels–Alder reactions have been extensively employed for the synthesis of polycyclic compounds since the pioneering work by Tietze. For instance, initial intermolecular Knoevenagel condensation of **1** with active methylene compounds generated a heterodiene **2**, which underwent intramolecular hetero-Diels–Alder cycloaddition with inverse electron demand to yield **3**.[7] As seen in (**2**), hetero-Diels–Alder reaction of the Knoevenagel product **5** with an enol ether moiety proceeded smoothly in an inter- or intramolecular fashion to furnish a dihydropyran ring system **6**.[8] However, to the best of our knowledge, no report on the Knoevenagel condensation/hetero-Diels–Alder cascade has been disclosed with substrate **7** where an enol ether functionality would act as a dienophile. Particularly, due to the short tether length and orientation of an enol ether group of **8**, a different conformation for the successful cycloaddition was envisaged as compared with **2** and **5**.

As illustrated in Scheme 2, facile intermolecular Knoevenagel condensation between an aldehyde moiety in **7** and active methylene compound was envisioned to set the stage for intramolecular hetero-Diels–Alder cycloaddition to give rise to

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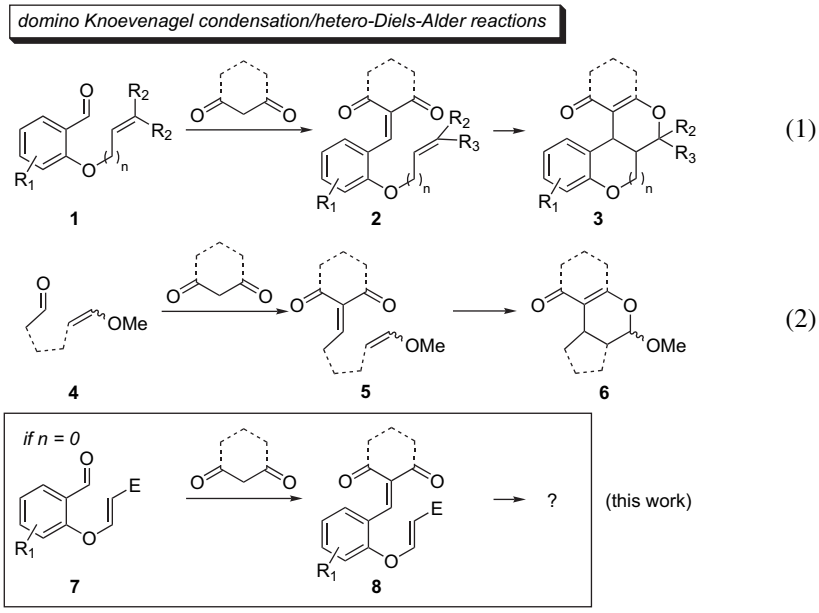
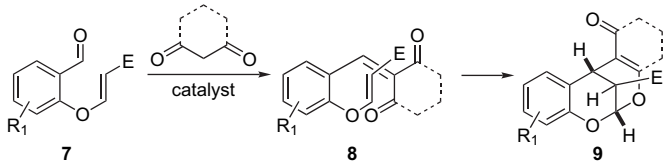


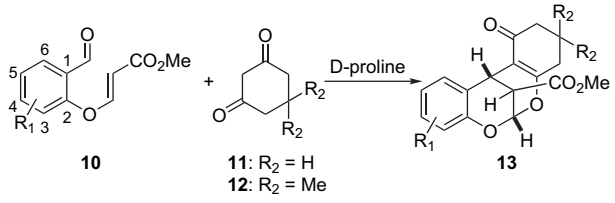
Scheme 1.



Scheme 2.

a benzo-fused 2,8-dioxabicyclo[3.3.1]nonane system **9**.[9] Notably, one diastereomer was anticipated from this step due to the restricted conformation of **8**.

To validate this hypothesis, **10a**[10] and **11** were chosen for the Knoevenagel condensation partners and with proline as the catalyst (Scheme 3).[11]

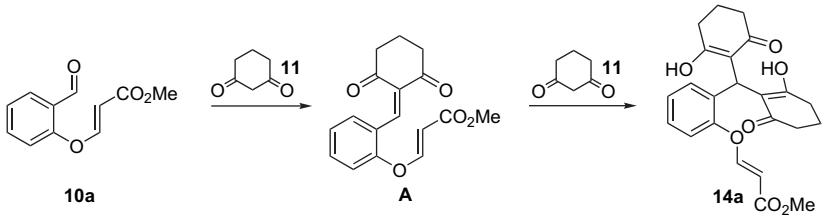


Scheme 3.

We were pleased to find that the reaction of **10a** and **11** in CH_3CN in the presence of D-proline (Table 1, entry 1) gave an approximately 45% yield of **13a**, the structure of which was initially assigned by NMR and mass spectroscopy but later unambiguously established on the basis of an X-ray crystallographic analysis (Fig. 1).[12]

As expected, only one diastereomer was formed as confirmed by X-ray crystallographic, ^1H, and ^{13}C NMR data. The other detectable side product was **14a** as a result of direct attack of another equivalent of cyclohexane-1,3-dione (**11**) to an enedione unit in **A** (Eq. 1).

To optimize the reaction conditions, we screened several solvents and catalysts (Table 1). Surprisingly, no desired product was formed with pyrrolidine, which is commonly used for Knoevenagel condensations (entry 3). Among the solvents examined, ethyl acetate provided the best yield.



Due to the formation of **14a**, one more equivalent of cyclohexane-1,3-dione (**11**) was added to the reaction mixture for the reaction with the remaining **10a** after no detection of **11** was confirmed by TLC (after 6 h), which resulted in increased yield of the desired product (entry 7). Mild heating at 50 °C was also found to be beneficial (entries 11 and 12). At this point, the following procedure gave the best result. A mixture of **10a** (0.48 mmol), cyclohexane-1,3-dione (**11**) (0.96 mmol), and D-proline (0.14 mmol) in ethyl acetate (3 mL) was stirred at 50 °C for 24 h. After the completion of reaction, the solvent was evaporated in vacuo and the resulting residue was directly purified by silica gel column chromatography (hexanes/ethyl acetate=10:1) to give **13a** in 89% yield.

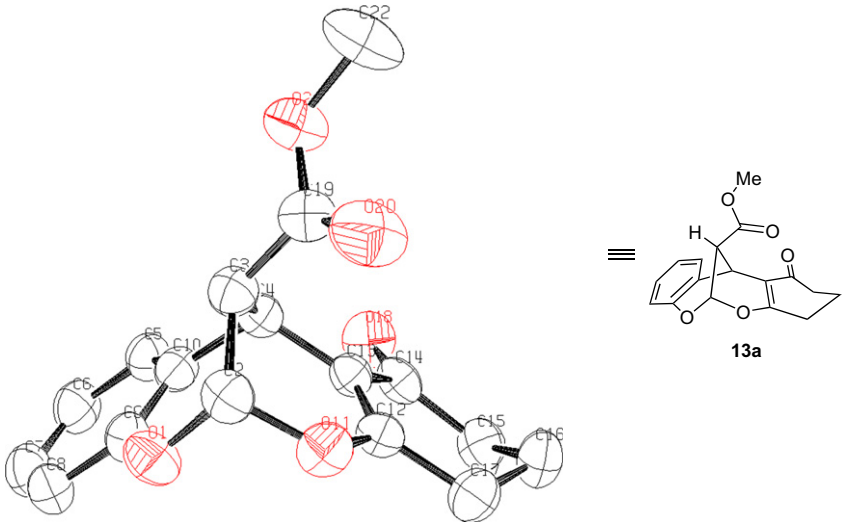
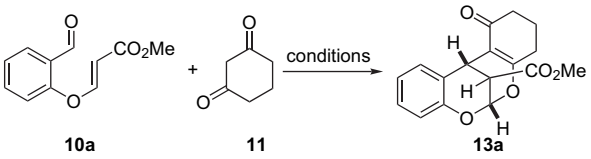


Figure 1. Crystal structure of **13a**.

Table 1



Entry	Equiv of **11**	Catalyst (equiv)	Solvent	Time (h)	Yield of **13a** (%)
1	1	D-Proline (0.3)	CH_3CN	5	45
2	1	DBU (1.0)	CH_3CN	5	—
3	1	Pyrrolidine (1.0)	CH_3CN	5	—
4	1	D-Proline (0.3)	DMSO	5	6.8
5	1+1[a]	D-Proline (1.0)	DMF	24	25
6	1+1[a]	D-Proline (1.0)	EtOH	24	22
7	1+1[a]	D-Proline (0.3)	CH_3CN	24	60
8	1+1[a]	D-Proline (0.3)	$CHCl_3$	24	58
9	1+1[a]	D-Proline (1.0)	Benzene	24	57
10	1+1[a]	D-Proline (0.3)	EtOAc	24	77
11	1+1[a]	D-Proline (0.3)	EtOAc[b]	24	85
12	2	D-Proline (0.3)	EtOAc[b]	24	89

[a] One more equivalent of **11** was added after 6 h.
[b] The reaction temperature was 50 °C.

Having the optimal conditions in hand, other benzaldehydes were tested with **11** or **12** as summarized in Table 2.

Overall, the highly functionalized benzo-fused 2,8-dioxabicyclo[3.3.1]nonanes[13] were obtained in good yields. When benzaldehyde bearing an electron-donating group such as methoxyl at the C4 position was used, modest yields of the corresponding 2,8-dioxabicyclo[3.3.1]nonanes were obtained (entries 2 and 7). Substrate **10e** derived from naphthaldehyde also provided **13e** and **13j** in acceptable yields (entries 4 and 9). It should be mentioned that coupling with **12** gave better yields of the products **13** than that with **11**.

To expand the reaction scope, reactions with other active methylene compounds were attempted (Scheme 4). The reaction of **10a** with the unsymmetrical active methylene compound, 4-hydroxycoumarin (**15**),[14] proceeded well to afford two pentacyclic compounds, **16a** and **16b**, in a 2:1 ratio. Interestingly, exposure of **10a** and Meldrum's acid (**17**) to our reaction conditions delivered **18** instead of **19**. The formation of **18** can be explained by the sequence depicted in Scheme 5.[15]

Thus, the expected product **19** was indeed produced as a consequence of the domino Knoevenagel/hetero-Diels–Alder reaction. However, **19** would lose acetone via a retro-Diels–Alder reaction to give ketene **20**. Hydrolysis of the unstable ketene **20** followed by decarboxylation of the intermediate carboxylic acid **21** would result in lactone **18**.

However, the expected domino sequence did not occur when cyclopentane-1,3-dione was subjected to our conditions. Only **22** was isolated as a major product (Fig. 2). Acyclic active methylene compounds such as pentane-2,4-dione and dimethyl malonate were also examined. Unfortunately, only Knoevenagel condensation took place from **10a** and pentane-2,4-dione under our conditions, delivering adduct **23** in low yield while reaction with dimethyl malonate yielded a complex mixture of products. Certainly, the rigid conformation and the bond angles of the heterodiene group in Knoevenagel adducts derived from cyclic active methylene compounds seemed crucial for the subsequent hetero-Diels–Alder reaction (see the lower box of Fig. 2).

3. Conclusions

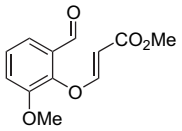
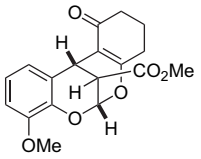
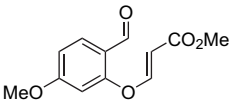
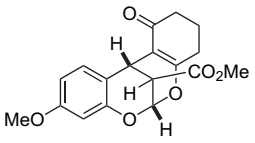
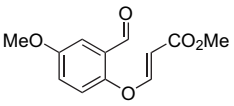
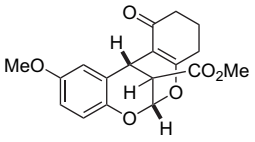
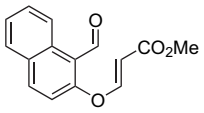
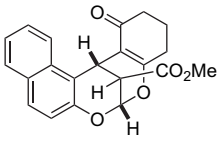
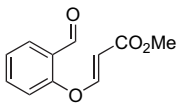
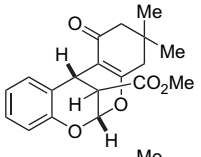
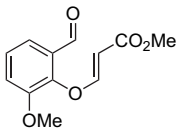
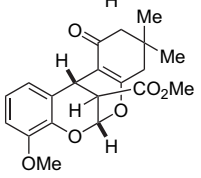
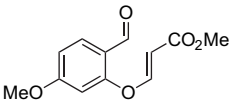
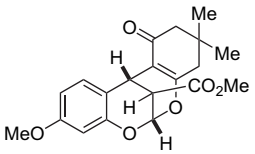
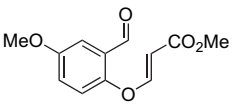
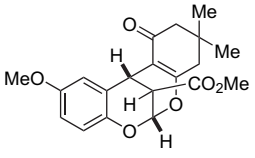
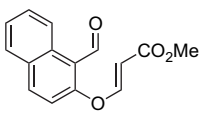
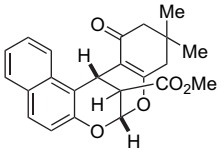
In summary, we describe here for the first time the stereoselective construction of the bridged and fused 2,8-dioxabicyclo[3.3.1]nonane ring system in two steps from commercially available 2-hydroxybenzaldehydes, utilizing a domino Knoevenagel condensation/hetero-Diels–Alder process as a key step. Currently, efforts are being made to apply this protocol to the synthesis of other novel heterocycles and will be reported in due course.

4. Experimental

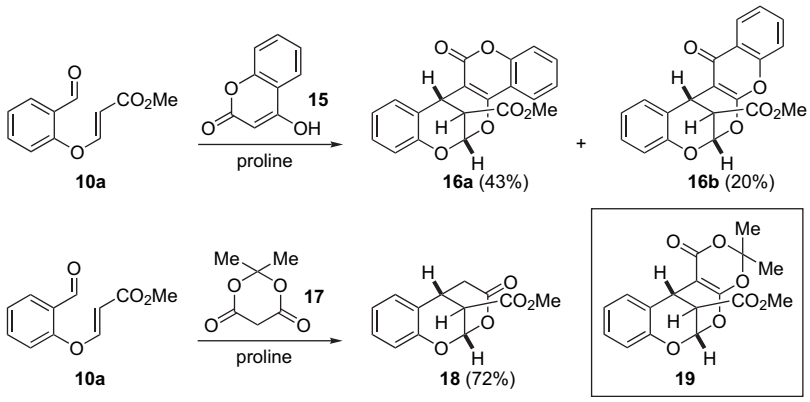
4.1. General procedure

Thin layer chromatography was carried out with E. Merck (Darmstadt) TLC plates precoated with silica gel 60 F_{254}.

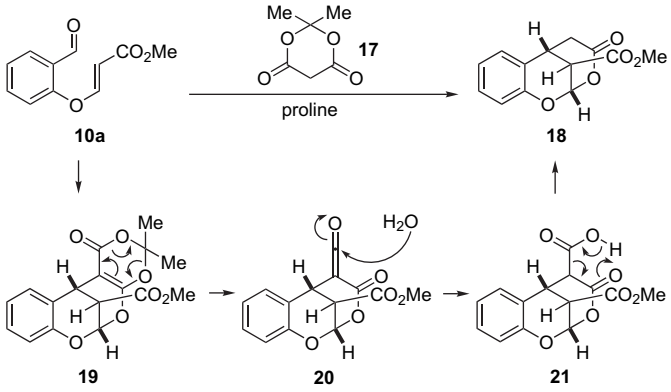
Table 2

Entry	10		11 or 12	13		Yield (%)
1		**10b**	**11**		**13b**	77
2		**10c**	**11**		**13c**	52
3		**10d**	**11**		**13d**	76
4		**10e**	**11**		**13e**	40
5		**10a**	**12**		**13f**	90
6		**10b**	**12**		**13g**	95
7		**10c**	**12**		**13h**	54
8		**10d**	**12**		**13i**	76
9		**10e**	**12**		**13j**	46

Visualization was accomplished using a UV lamp, iodine vapors, and/or a *p*-anisaldehyde (PAA) stain. Flash column chromatography was accomplished with Silicycle silica gel 60 (230–400 mesh). Proton nuclear magnetic resonance spectra were recorded in deuterated solvents on a VARIAN systems-300 (300 MHz) instrument. Chemical shifts are reported in parts per million (ppm, δ) relative to tetramethylsilane (TMS, δ 0.00). Carbon nuclear magnetic resonance spectra were recorded in deuterated solvents on a VARIAN systems-300 (75 MHz) instrument. Infrared spectra were measured on a Mattson Polaris FT-IR spectrometer, and signals are recorded in wavenumbers. High resolution mass spectra (HRMS) using electron ionization (EI) were measured on a Micromass mass spectrometer.



Scheme 4.



Scheme 5.

4.2. General procedure for the synthesis of **10**

To a stirred solution of 2-hydroxybenzaldehyde (5.0 mmol) in CH_2Cl_2 (9 mL) were added *N*-methylmorpholine (1.2 equiv) and methyl propiolate (1.2 equiv) at rt. After being stirred at rt overnight, the reaction mixture was concentrated in vacuo. The resulting residue was purified by silica gel column chromatography (hexanes/ethyl acetate/dichloromethane=10:1:2) to afford **10**.

4.2.1. Compound ***10a***

^{1}H NMR (300 MHz, $CDCl_3$) δ 10.37 (d, J=0.6 Hz, 1H), 7.94 (dd, J=7.8, 1.8 Hz, 1H), 7.86 (d, J=12.3 Hz, 1H), 7.65 (ddd, J=9.3, 7.5, 2.1 Hz, 1H), 7.33 (t, J=7.5 Hz, 1H), 7.16 (dd, J=8.1, 0.9 Hz, 1H), 5.66 (d, J=12.0 Hz, 1H), 3.75 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 188.3, 167.1, 158.3, 157.7, 136.2, 129.2, 126.7, 125.6, 118.4, 104.0, 51.7; IR (KBr) 3100, 1705, 1648, 1598, 1482, 1303 cm^{-1}; HRMS (EI) calcd for $[C_{11}H_{10}O_4]^+$: *m*/*z* 206.0579, found 206.0575.

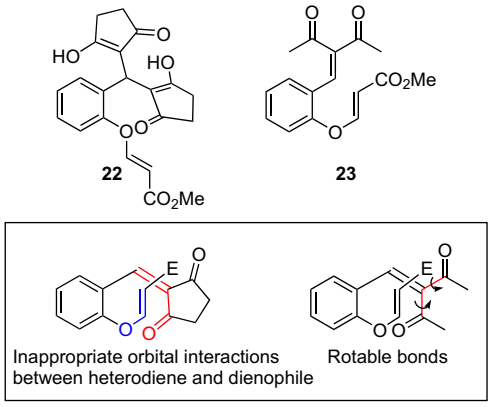


Figure 2.

4.2.2. Compound ***10b***

^{1}H NMR (300 MHz, $CDCl_3$) δ 10.24 (d, J=0.9 Hz, 1H), 7.80 (d, J=12.3 Hz, 1H), 7.49 (dd, J=6.0, 1.5 Hz, 1H), 7.32 (dt, J=8.2, 0.7 Hz, 1H), 7.25 (dd, J=8.2, 1.6 Hz, 1H), 5.31 (d, J=12.3 Hz, 1H), 3.90 (s, 3H), 3.72 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 188.5, 167.5, 161.7, 151.5, 146.1, 129.2, 127.0, 120.0, 118.6, 101.0, 56.6, 51.6; IR (KBr) 3011, 1700, 1650, 1530, 1455, 1320 cm^{-1}; HRMS (EI) calcd for $[C_{12}H_{12}O_5]^+$: *m*/*z* 236.0685, found 236.0686.

4.2.3. Compound ***10c***

^{1}H NMR (300 MHz, $CDCl_3$) δ 10.21 (s, 1H), 7.89 (d, J=9.0 Hz, 1H), 7.82 (d, J=12.3 Hz, 1H), 6.82 (dd, J=8.7, 2.1 Hz, 1H), 6.59 (d, J=2.1 Hz, 1H), 5.68 (d, J=12.3 Hz, 1H), 3.90 (s, 3H), 3.76 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 188.1, 167.3, 159.8, 157.3, 151.8, 127.5, 123.6, 120.7, 111.0. 103.0, 56.1, 51.7; IR (KBr) 3051, 1705, 1626, 1520, 1400, 1330 cm^{-1}; HRMS (EI) calcd for $[C_{12}H_{12}O_5]^+$: *m*/*z* 236.0685, found 236.0688.

*4.2.4. Compound **10d***

^{1}H NMR (300 MHz, $CDCl_3$) δ 10.28 (d, 9.0 Hz, 1H), 7.81 (d, J=12.3 Hz, 1H), 7.38 (d, J=3.0 Hz, 1H), 7.18 (dd, J=9.0, 3.1 Hz, 1H), 7.08 (d, J=9.0 Hz, 1H), 5.52 (d, J=12.3 Hz, 1H), 3.85 (s, 3H), 3.74 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 187.0, 167.2, 166.1, 160.0, 158.1, 131.0, 120.0, 111.4, 104.1, 103.8, 56.2, 51.8; IR (KBr) 3023, 1736, 1658, 1511, 1456, 1345 cm^{-1}; HRMS (EI) calcd for $[C_{12}H_{12}O_5]^+$: *m/z* 236.0685, found 236.0683.

*4.2.5. Compound **10e***

^{1}H NMR (300 MHz, $CDCl_3$) δ 10.77 (s, 1H), 9.26 (dd, J=8.7, 0.5 Hz, 1H), 8.14 (d, J=9.0 Hz, 1H), 7.92 (d, J=12.3 Hz, 1H), 7.87 (d, J=8.1 Hz, 1H), 7.71 (dt, J=6.9, 1.4 Hz, 1H), 7.56 (dt, J=6.9, 1.3 Hz, 1H), 7.29 (d, J=9.0 Hz, 1H), 5.64 (d, J=12.0 Hz, 1H), 3.76 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 190.7, 167.1, 159.4, 158.8, 137.9, 131.3, 131.2, 130.5, 128.7, 126.8, 125.8, 120.0, 117.8, 104.2, 51.8; IR (KBr) 3048, 1721, 1648, 1566, 1422, 1372 cm^{-1}; HRMS (EI) calcd for $[C_{15}H_{12}O_4]^+$: *m/z* 256.0736, found 256.0739.

*4.3. General procedure for the synthesis of **13***

To a stirred solution of **10** (0.48 mmol) and **11** or **12** (2 equiv) in ethyl acetate (3 mL) was added D-proline (0.3 equiv) at rt. After being stirred at 50 °C for 24 h, the reaction mixture was concentrated in vacuo. The residue was purified by silica gel column chromatography (hexanes/ethyl acetate=10:1) to give **13**.

*4.3.1. Compound **13a***

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36 (dd, J=7.8, 1.8 Hz, 1H), 7.13 (dt, J=8.2, 1.8 Hz, 1H), 6.93–6.88 (m, 2H), 6.30 (t, J=2.1 Hz, 1H), 4.54 (t, J=2.4 Hz, 1H), 3.72 (s, 3H), 3.12 (t, J=2.3 Hz, 1H), 2.43–2.38 (m, 2H), 2.35–2.27 (m, 2H), 1.94–1.85 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.8, 168.9, 168.6, 150.3, 128.7, 128.2, 125.7, 122.1, 116.3, 115.0, 92.1, 52.7, 40.3, 36.5, 27.6, 25.6, 20.8; IR (KBr) 2953, 1741, 1628, 1482, 1388, 1231 cm^{-1}; HRMS (EI) calcd for $[C_{17}H_{16}O_5]^+$: *m/z* 300.0998, found 300.0995.

*4.3.2. Compound **13b***

^{1}H NMR (300 MHz, $CDCl_3$) δ 6.98 (dd, J=7.6, 1.5 Hz, 1H), 6.86 (t, J=7.7 Hz, 1H), 6.75 (dd, J=8.1, 1.5 Hz, 1H), 6.39 (t, J=2.1 Hz, 1H), 4.54 (t, J=2.1 Hz, 1H), 3.87 (s, 3H), 3.72 (s, 3H), 3.13 (t, J=2.2 Hz, 1H), 2.43–2.39 (m, 2H), 2.34–2.27 (m, 2H), 1.93–1.83 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.8, 168.8, 147.9, 139.5, 126.7, 122.1, 120.5, 114.9, 110.4, 92.0, 56.1, 52.7, 40.2, 36.5, 27.5, 25.5, 20.7; IR (KBr) 2945, 1750, 1645, 1436, 1385, 1226 cm^{-1}; HRMS (EI) calcd for $[C_{18}H_{18}O_6]^+$: *m/z* 330.1103, found 330.1105.

*4.3.3. Compound **13c***

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25 (d, J=8.6 Hz, 1H), 6.50–6.46 (m, 2H), 6.27 (t, J=1.8 Hz, 1H), 4.47 (t, J=2.4 Hz, 1H), 3.74 (s, 3H), 3.71 (s, 3H), 3.10 (t, J=2.3 Hz, 1H), 2.42–2.38 (m, 2H), 2.35–2.27 (m, 2H), 1.93–1.85 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.9, 169.0, 168.4, 159.8, 151.1, 129.1, 118.1, 115.5, 108.2, 101.9, 92.1, 55.6, 52.7, 40.7, 36.5, 27.6, 25.0, 20.8; IR (KBr) 3003, 2975, 1752, 1678, 1455, 1356 cm^{-1}; HRMS (EI) calcd for $[C_{18}H_{18}O_6]^+$: *m/z* 330.1103, found 330.1108.

*4.3.4. Compound **13d***

^{1}H NMR (300 MHz, $CDCl_3$) δ 6.86 (d, J=3.0 Hz, 1H), 6.79 (d, J=8.7 Hz, 1H), 6.64 (dd, J=8.7, 3.0 Hz, 1H), 6.22 (t, J=1.8 Hz, 1H), 4.45 (t, J=2.1 Hz, 1H), 3.70 (s, 3H), 3.68 (s, 3H), 3.07 (t, J=2.3 Hz, 1H), 2.39–2.35 (m, 2H), 2.32–2.25 (m, 2H), 1.91–1.82 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.8, 168.9, 154.6, 144.0, 126.2, 117.0, 114.8, 114.6, 112.7, 92.2, 55.9, 52.7, 40.4, 36.5, 27.6, 25.9, 20.8; IR (KBr) 2980, 1726, 1653, 1467, 1326, 1252 cm^{-1}; HRMS (EI) calcd for $[C_{18}H_{18}O_6]^+$: *m/z* 330.1103, found 330.1101.

*4.3.5. Compound **13e***

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.81 (d, J=8.4 Hz, 1H), 7.73 (td, J=8.0, 0.6 Hz, 1H), 7.66 (d, J=8.8 Hz, 1H), 7.58 (ddd, J=9.9, 6.9, 1.2 Hz, 1H), 7.37 (ddd, J=8.1, 6.9, 1.2 Hz, 1H), 7.13 (d, J=8.8 Hz, 1H), 6.35 (t, J=1.8 Hz, 1H), 5.29 (t, J=2.4 Hz, 1H), 3.74 (s, 3H), 3.19 (t, J=2.3 Hz, 2H), 2.43 (t, J=5.9 Hz, 2H), 2.28–2.34 (m, 2H), 1.76–1.93 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.1, 170.4, 169.1, 148.1, 131.6, 129.9, 129.1, 128.2, 127.2, 124.6, 118.4, 117.8, 114.8, 91.7, 52.8, 40.8, 36.7, 28.0, 22.0, 20.4; IR (KBr) 3056, 2981, 1755, 1645, 1488, 1356 cm^{-1}; HRMS (EI) calcd for $[C_{21}H_{18}O_5]^+$: *m/z* 350.1154, found 350.1149.

*4.3.6. Compound **13f***

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33 (d, J=7.5 Hz, 1H), 7.10 (t, J=8.4 Hz, 1H), 6.91–6.86 (m, 2H), 6.30 (d, J=0.6 Hz, 1H), 4.53 (s, 1H), 3.71 (s, 3H), 3.12 (s, 1H), 2.35–2.03 (m, 4H), 0.98 (s, 3H), 0.95 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.5, 168.9, 166.9, 150.3, 128.5, 128.2, 125.5, 122.1, 116.3, 114.1, 92.4, 52.6, 50.4, 41.3, 40.2, 32.7, 29.5, 27.0, 25.5; IR (KBr) 3063, 2985, 1753, 1655, 1485, 1326 cm^{-1}; HRMS (EI) calcd for $[C_{19}H_{20}O_5]^+$: *m/z* 328.1311, found 328.1315.

*4.3.7. Compound **13g***

^{1}H NMR (300 MHz, $CDCl_3$) δ 6.96 (d, J=7.8 Hz, 1H), 7.86 (dt, J=7.8, 0.9 Hz, 1H), 6.74 (d, J=8.4 Hz, 1H), 6.41 (t, J=1.5 Hz, 1H), 4.55 (s, 1H), 3.87 (s, 3H), 3.71 (s, 3H), 3.14 (t, J=1.2 Hz, 1H), 2.36–2.04 (m, 4H), 0.98 (s, 3H), 0.95 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.5, 168.8, 167.1, 147.9, 139.4, 126.5, 122.1, 120.3, 113.9, 110.4, 92.2, 56.0, 52.6, 50.3, 41.2, 40.1, 32.6, 29.4, 27.0, 25.3; IR (KBr) 3025, 2866, 1732, 1676, 1385, 1216 cm^{-1}; HRMS (EI) calcd for $[C_{20}H_{22}O_6]^+$: *m/z* 358.1416, found 358.1412.

*4.3.8. Compound **13h***

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23 (d, J=9.3 Hz, 1H), 6.48–6.45 (m, 2H), 6.41 (dd, J=1.8, 1.2 Hz, 1H), 4.47 (s, 1H), 3.73 (s, 3H), 3.70 (s, 3H), 3.11 (t, J=1.8 Hz, 1H), 2.35–2.04 (m, 4H), 1.00 (s, 3H), 0.96 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.6, 169.0, 166.7, 159.7, 151.1, 128.9, 117.9, 114.6, 108.2, 101.9, 92.3, 55.6, 52.6, 50.4, 41.3, 40.6,

32.7, 29.5, 27.0, 24.8; IR (KBr) 3055, 2980, 1752, 1686, 1495, 1336 cm^{-1}; HRMS (EI) calcd for $[C_{20}H_{22}O_6]^+$: *m/z* 358.1416, found 358.1420.

*4.3.9. Compound **13i***

^1H NMR (300 MHz, $CDCl_3$) δ 6.88–6.80 (m, 2H), 6.67 (dd, *J*=9.0, 3.0 Hz, 1H), 6.27 (t, *J*=1.5 Hz, 1H), 4.49 (s, 1H), 3.73 (s, 3H), 3.71 (s, 3H), 3.11 (t, *J*=1.8 Hz, 1H), 2.35–2.04 (m, 4H), 0.98 (s, 3H), 0.96 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.4, 168.9, 167.2, 154.5, 144.0, 126.0, 116.9, 114.5, 113.8, 112.5, 92.4, 55.8, 52.6, 50.3, 41.3, 40.2, 32.7, 29.5, 26.9, 25.7; IR (KBr) 3035, 2875, 1782, 1698, 1461, 1308 cm^{-1}; HRMS (EI) calcd for $[C_{20}H_{22}O_6]^+$: *m/z* 358.1416, found 358.1415.

*4.3.10. Compound **13j***

^1H NMR (300 MHz, $CDCl_3$) δ 8.79 (d, *J*=8.7 Hz, 1H), 7.72 (d, *J*=8.4 Hz, 1H), 7.64 (d, *J*=9.0 Hz, 1H), 7.58 (t, *J*=7.8 Hz, 1H), 7.36 (t, *J*=7.5 Hz, 1H), 7.12 (d, *J*=8.7 Hz, 1H), 6.38 (t, *J*=1.8 Hz, 1H), 5.28 (s, 1H), 3.74 (s, 3H), 3.18 (t, *J*=1.8 Hz, 1H), 2.39–2.04 (m, 4H), 0.97 (s, 3H), 0.93 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.0, 169.1, 168.6, 148.2, 131.5, 129.9, 129.1, 128.1, 127.2, 124.5, 118.3, 117.7, 113.8, 91.9, 52.7, 50.8, 41.7, 40.7, 33.0, 29.6, 26.9, 21.8; IR (KBr) 3077, 3015, 2936, 1746, 1685, 1456 cm^{-1}; HRMS (EI) calcd for $[C_{23}H_{22}O_5]^+$: *m/z* 378.1467, found 378.1469.

*4.3.11. Compound **16a***

^1H NMR (300 MHz, $CDCl_3$) δ 7.81 (dd, *J*=8.7, 1.8 Hz, 1H), 7.53–7.45 (m, 2H), 7.26–7.14 (m, 3H), 6.99–6.94 (m, 2H), 6.12 (t, *J*=1.8 Hz, 1H), 4.70 (t, *J*=2.1 Hz, 1H), 3.72 (s, 3H), 3.35 (t, *J*=2.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.3, 161.4, 157.5, 152.5, 150.3, 132.4, 129.0, 128.7, 124.5, 124.3, 123.2, 122.7, 116.9, 116.6, 114.7, 104.8, 92.6, 53.0, 40.4, 27.5; IR (KBr) 2953, 1714, 1635, 1488, 1402, 1222 cm^{-1}; HRMS (EI) calcd for $[C_{20}H_{14}O_6]^+$: *m/z* 350.0790, found 350.0793.

*4.3.12. Compound **16b***

^1H NMR (300 MHz, $CDCl_3$) δ 8.14 (dd, *J*=8.4, 1.8 Hz, 1H), 7.61–7.51 (m, 2H), 7.38–7.33 (m, 2H), 7.15 (ddd, *J*=9.0, 7.8, 1.8 Hz, 1H), 6.97–6.93 (m, 2H), 6.59 (t, *J*=1.5 Hz, 1H), 4.89 (t, *J*=2.1 Hz, 1H), 3.72 (s, 3H), 3.36 (t, *J*=2.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.9, 168.3, 162.6, 153.1, 149.9, 133.5, 128.8, 128.6, 126.0, 125.6, 125.5, 122.9, 122.8, 117.7, 116.6, 99.5, 94.9, 53.1, 40.6, 26.3; IR (KBr) 2935, 1741, 1626, 1567, 1426, 1218 cm^{-1}; HRMS (EI) calcd for $[C_{20}H_{14}O_6]^+$: *m/z* 350.0790, found 350.0789.

*4.3.13. Compound **18***

^1H NMR (300 MHz, $CDCl_3$) δ 7.24 (ddd, *J*=9.3, 8.1, 0.6 Hz, 1H), 7.11 (dd, *J*=7.8, 1.8 Hz, 1H), 7.02 (dt, *J*=7.2, 0.9 Hz, 1H), 6.94 (d, *J*=8.1 Hz, 1H), 6.39 (t, *J*=1.8 Hz, 1H), 3.85 (s, 3H), 3.61 (dd, *J*=3.3, 1.8 Hz, 1H), 3.25 (dd, *J*=3.3, 1.5 Hz, 1H), 3.10 (dd, *J*=18.3, 5.4 Hz, 1H), 2.72 (td, *J*=18.6, 1.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.8, 167.1, 149.0, 130.0, 128.7, 124.2, 123.3, 117.9, 95.0, 53.2, 40.7, 36.2, 30.0; IR (KBr) 3004, 2980, 1740, 1434, 1360, 1221 cm^{-1}; HRMS (EI) calcd for $[C_{13}H_{12}O_5]^+$: *m/z* 248.0685, found 248.0689.

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Supplementary data

Copies of ^1H and ^{13}C NMR spectra for **10**, **13**, **16**, and **18**. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2007.11.036.

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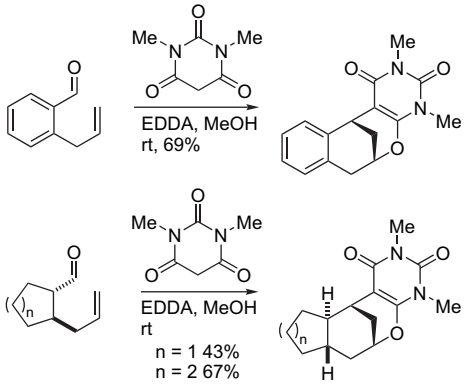

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