Palladium-catalyzed synthesis of indene derivatives *via* propargylic carbonates with *in situ* generated organozinc compounds†‡

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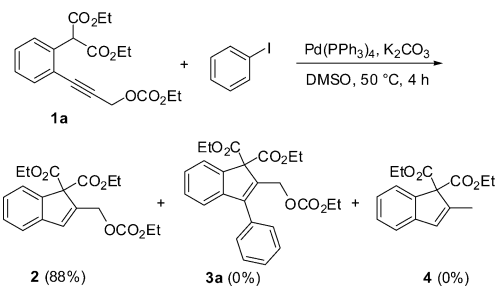
The palladium-catalyzed carboannulation and arylation reaction of propargylic carbonates with *in situ* generated organozinc compounds produced an important new class of indene derivatives. The reaction proceeded under mild conditions, and indene products were isolated in good to excellent yields.

Introduction

The indene ring system is present in drug candidates possessing interesting biological activities[1] and in metallocene complexes utilized in the catalysis of olefin polymerization.[2] Palladium-catalyzed carboannulation of propargylic carbonates[3] or alkynes[4], which has major advantages over traditional annulation methods, was proved to be one of the most useful tools for the construction of indene rings. In our recent reports,[3,4b,c] we prepared a variety of highly substituted indenes using this procedure. During our continuing studies in this research area, we examined the reaction of diethyl 2-{2-[3-(ethoxycarbonyloxy)prop-1-ynyl]phenyl}malonate **1a** with 1-iodobenzene under the carboannulation conditions shown in Scheme 1. Although diethyl 2-[(ethoxycarbonyloxy)methyl]-1*H*-indene-1,1-dicarboxylate **2** was isolated in 88% yield, neither the desired arylation product diethyl 2-[(ethoxycarbonyloxy)methyl]-3-phenyl-1*H*-indene-1,1-dicarboxylate **3a** nor the decarboxylation product diethyl 2-methyl-1*H*-indene-1,1-dicarboxylate **4** was observed.

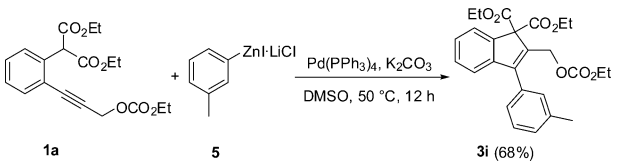


Scheme 1

Based on this observation, we envisioned that this reaction occurs predominantly between propargylic carbonates and nucleophiles, not electrophiles, such as aryl iodides. More recently, Knochel *et al.* have pioneered the development of a method for the preparation of functionalized organozinc reagents by the direct insertion of zinc powder into organic iodides in the presence of LiCl.[5] Considering the greater functional group tolerance of the coupling of aryl zinc reagents[6–8] than that of the coupling of aryl magnesium or lithium reagents,[9] we anticipated that the coupling of Knochel-type organozinc compounds could address the problem of functional group tolerance in the coupling of aryl nucleophiles.

Results and discussion

Our experiment was conducted by treating **1a** with isolated organozinc compound **5**[10] (Scheme 2). The reaction was first attempted using 1 equiv. of **1a** (0.1 mmol), 3 equiv. of organozinc compound **5**, 2 mol% of $Pd(PPh_3)_4$ as the catalyst, and 2 equiv. of K_2CO_3 in 2 mL of DMSO at 50 °C. Indeed, the reaction furnished a 68% yield of the indene product **3i** in 12 h.



Scheme 2

The conversion of this reaction into a synthetically useful process would provide a straightforward route to a new important class of indene derivatives. To the best of our knowledge, this reaction catalyzed by Pd represents the first example of a direct coupling of propargylic carbonates, diethyl malonate and organozinc compounds. In particular, the product containing two privileged substructures (the indene and the allyl ethyl carbonate nuclei) affords an important intermediate in the preparation of a wider variety of functionalized indene rings, which have attracted considerable attention in organic syntheses.[11]

However, the organozinc reagent decomposed slowly under our reaction conditions, and thus 3 or more equivalents of organozinc reagent were required for the reaction. We have to overcome this problem before we extend the scope of this process.

Since we felt that Knochel-type organozinc reagents might be achieved *in situ*, we envisioned that this carboannulation and arylation reaction might occur *via in situ* generated organozinc reagents, which form *in situ* from zinc powder and iodobenzene in

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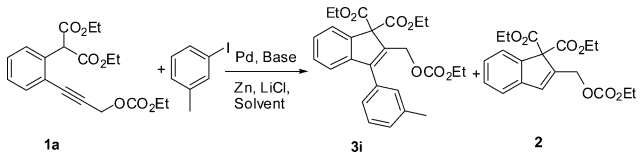
‡ Electronic supplementary information (ESI) available: Complete description of experimental details and product characterization. See DOI: 10.1039/b719957k

Table 1 Optimization of the palladium-catalyzed carboannulation and arylation of **1a**[a]



1a 3i 2

Entry	Pd	Base	Solvent	Additive	Yield (%)[b,c]
1	$Pd(PPh_3)_4$	K_2CO_3	DMF	Zn, LiCl	18 (0)
2	$Pd(PPh_3)_4$	K_2CO_3	CH_3CN	Zn, LiCl	15 (0)
3	$Pd(PPh_3)_4$	K_2CO_3	NMP	Zn, LiCl	<5 (0)
4	$Pd(PPh_3)_4$	K_2CO_3	DCE	Zn, LiCl	<5 (0)
5	$Pd(PPh_3)_4$	K_2CO_3	THF	Zn, LiCl	20 (0)
6	$Pd(PPh_3)_4$	K_2CO_3	Toluene	Zn, LiCl	12 (0)
7	$Pd(PPh_3)_4$	K_2CO_3	DMSO	Zn, LiCl	94 (0)
8[d]	$Pd(PPh_3)_4$	K_2CO_3	DMSO	Zn, LiCl	88 (0)
9	$Pd(PPh_3)_4$	K_2CO_3	DMSO	Zn	0 (72)
10	$Pd(PPh_3)_4$	K_2CO_3	DMSO	LiCl	0 (76)
11	$PdCl_2(PPh_3)_2$	K_2CO_3	DMSO	Zn, LiCl	31 (0)
12	$Pd(OAc)_2$	K_2CO_3	DMSO	Zn, LiCl	88 (0)
13[e]	$Pd(OAc)_2$	K_2CO_3	DMSO	Zn, LiCl, PPh_3	89 (0)
14	$Pd(dba)_2$	K_2CO_3	DMSO	Zn, LiCl	23 (0)
15	$Pd(PPh_3)_4$	Cs_2CO_3	DMSO	Zn, LiCl	40 (0)

[a] The reactions were run under the following conditions: 0.10 mmol of **1a**, 0.15 mmol of 1-iodo-3-methylbenzene, 0.30 mmol of zinc powder, 0.30 mmol of LiCl, 2 mol% of Pd catalyst, 0.20 mmol of base, stirred in 2 mL of solvent at 50 °C under an Ar atmosphere. [b] Yields are given for isolated product **3i**. [c] The numbers in parentheses are the isolated yields of product **2**. [d] 0.12 mmol of 1-iodo-3-methylbenzene was used. [e] 4 mol% of PPh_3 was added.

the presence of LiCl. Thus, a one-pot reaction of **1a**, zinc and aryl iodides would both address the problem and make the procedure more simple. The reaction was attempted using 1 equiv. of **1a** (0.1 mmol), 1.5 equiv. of 1-iodo-3-methylbenzene, 3 equiv. of Zn, 3 equiv. of LiCl, 2 mol% of $Pd(PPh_3)_4$, and 2 equiv. of K_2CO_3 in 2 mL of DMSO at 50 °C. To our delight, a 94% yield of the indene product **3i** was obtained without any side product (Table 1, entry 7).

Additional reaction parameters were also studied (Table 1). It is noteworthy that the choice of solvent and palladium catalyst turned out to be very important for the reaction's success. When other organic solvents, such as DMF, CH_3CN, NMP, DCE, THF and toluene, were used, the yield of the desired product was drastically reduced. Other Pd catalysts, such as $PdCl_2(PPh_3)_2$, $Pd(OAc)_2$, and $Pd(dba)_2$, have also been employed in this reaction. None of them gave a higher yield than $Pd(PPh_3)_4$. The use of other bases, such as Cs_2CO_3, provided a lower yield of the desired product. On the basis of these optimization efforts, the combination of the propargylic carbonate **1a** (0.1 mmol), 1.5 equiv. of the aryl iodide, 3 equiv. of Zn, 3 equiv. of LiCl, 2 mol% of $Pd(PPh_3)_4$, and 2 equiv. of K_2CO_3 in 2 mL of DMSO at 50 °C gave the best result.

Having gained an understanding of the factors that influence the carboannulation and arylation process, we have explored the scope and limitations of this method. The results are summarized in Table 2.

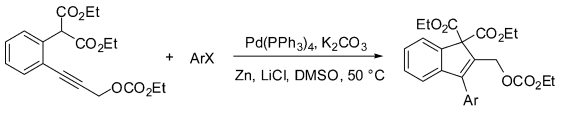
Aryl iodides bearing an electron-withdrawing group or an electron-donating group in the *para*, *meta*, and *ortho* positions afforded the corresponding multiply substituted indenes **3** in good to excellent yields. A broad range of functionalized aryl iodides bearing a methyl, an acetyl, or an ester group were all suitable for this reaction (Table 2, entries 2, 3, 7–9, 11, 12). Electron-rich aryl iodides such as methoxy derivatives are often poor substrates because of their low reactivity in the zinc insertion reaction. However, we were pleased to find that, using our conditions, this did not occur. These reactions also proceeded smoothly with high yields under our standard conditions (entries 6 and 14). In particular, even 2-iodophenol is also compatible with the mild reaction conditions, and **3m** was obtained in 65% yield (entry 13). The reaction also displays excellent chemoselectivity. Treating 3-chloro/4-chlorophenyl iodide or 4-bromophenyl iodide with **1a** resulted only in reaction at the C–I bond to give products **3j** (85%), **3d** (90%) and **3e** (87%) (entries 10, 4, 5). It is noteworthy that *ortho*-substituted aryl iodides required a slightly longer reaction time than that of *para*- or *meta*-substituted substrates. It can be inferred here that the sterically hindered aryl iodides slightly affect the rate of the arylation reaction. In addition, the use of 2-iodothiophene also afforded the indene **3o** in 86% yield (entry 15). The reaction of aryl bromides with **1a** is also possible in the case of activated aryl compounds. Thus, diethyl 3-(4-acetylphenyl)-2-[(ethoxycarbonyloxy)methyl]-1*H*-indene-1,1-dicarboxylate **3c** was formed in 50% yield starting from 4-bromophenyl ethanone (entry 16).

Although the NMR spectroscopic data support the formation of the products **3**, the structure was unambiguously secured by an X-ray crystal structure analysis of compound **3f** (Fig. 1).†

We then turned our attention to the carboannulation and arylation reaction using secondary carbonates and propargylic carbonate with different electron-withdrawing groups. As described in Table 3, these trials also gave satisfactory yields.

As observed in our previous studies on the carboannulation route to indenes, the propargylic carbonates were found to play a crucial role.[3] No reaction occurred when diethyl 2-[2-(3-acetoxyprop-1-ynyl)phenyl]malonate **1d** was subjected to aryl zinc

Table 2 Palladium-catalyzed carboannulation and arylation of diethyl 2-{2-[3-(ethoxycarbonyloxy)prop-1-ynyl]phenyl}malonate with *in situ* generated organozinc reagents[a]



1a 3

Entry	ArX	Ar (**3**)	Time/h	Yield (%)[b]
1	PhI	Ph (**3a**)	7	96
2	*p*-$CH_3C_6H_4I$	*p*-$CH_3C_6H_4$ (**3b**)	11	88
3	*p*-$CH_3COC_6H_4I$	*p*-$CH_3COC_6H_4$ (**3c**)	9	92
4	*p*-ClC_6H_4I	*p*-ClC_6H_4 (**3d**)	7	90
5	*p*-BrC_6H_4I	*p*-BrC_6H_4 (**3e**)	9	87
6	*p*-$CH_3OC_6H_4I$	*p*-$CH_3OC_6H_4$ (**3f**)	7	86
7	*p*-$CF_3C_6H_4I$	*p*-$CF_3C_6H_4$ (**3g**)	11	97
8	*p*-$CH_3O_2CC_6H_4I$	*p*-$CH_3O_2CC_6H_4$ (**3h**)	10	94
9	*m*-$CH_3C_6H_4I$	*m*-$CH_3C_6H_4$ (**3i**)	12	94
10	*m*-ClC_6H_4I	*m*-ClC_6H_4 (**3j**)	9	85
11	*o*-$CH_3C_6H_4I$	*o*-$CH_3C_6H_4$ (**3k**)	18	85
12	*o*-$CH_3O_2CC_6H_4I$	*o*-$CH_3O_2CC_6H_4$ (**3l**)	32	63
13	*o*-HOC_6H_4I	*o*-HOC_6H_4 (**3m**)	28	65
14	*o*-$CH_3OC_6H_4I$	*o*-$CH_3OC_6H_4$ (**3n**)	32	90
15	2-Iodothiophene	2-Thienyl (**3o**)	6	86
16	*p*-$CH_3COC_6H_4Br$	*p*-$CH_3COC_6H_4$ (**3c**)	95	50

[a] The reactions were run under the following conditions: 0.10 mmol of **1a**, 0.15 mmol of the aryl halide, 0.30 mmol of zinc powder, 0.30 mmol of LiCl, 2 mol% of $Pd(PPh_3)_4$, 0.20 mmol of K_2CO_3, stirred in 2 mL of DMSO at 50 °C under an Ar atmosphere. [b] Yields are given for isolated products.

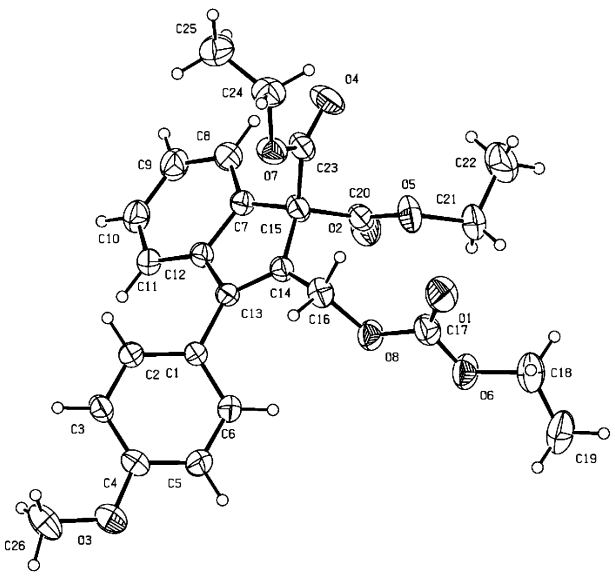
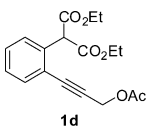


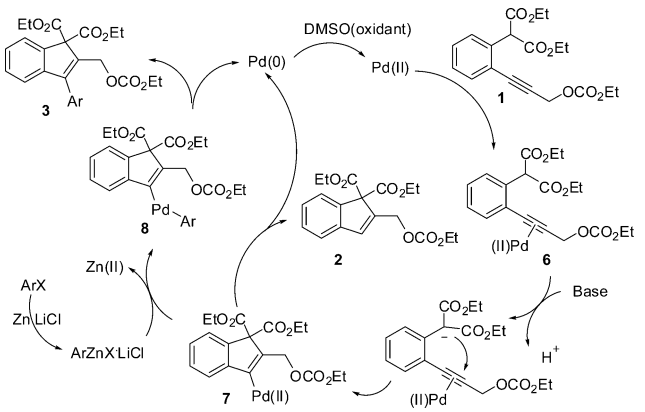
Fig. 1 ORTEP representation of **3f** at 30% probability thermal ellipsoids.

reagents under our standard conditions. This is presumably due to the incoordination of Pd(II) to the propargylic acetate.



1d

Based on our experimental results and other related studies,[4a,12,13] we propose the general reaction mechanism shown in Scheme 3. The first step of this mechanism is the oxidation of Pd(0) to form Pd(II) by DMSO, and then coordination of Pd(II) to the propargylic carbonates to give complex **6**. The use of DMSO as a solvent is crucial since Pd(0) promotes decarboxylation of propargylic carbonate **1a**, as observed in our previous studies.[3] The second step is the intramolecular nucleophilic attack of the carbanion on the activated carbon–carbon triple bond to afford a vinylic palladium intermediate **7**. Then, transmetallation of **7** with *in situ* generated organozinc compounds affords **8**, and reductive elimination of the intermediate **8** furnishes the indene **3** and regenerates the Pd(0) catalyst.

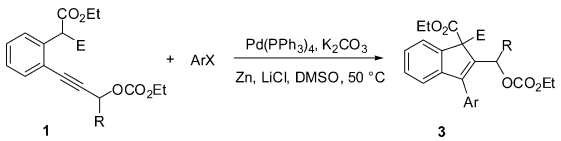


Scheme 3

Conclusion

In conclusion, we have developed a straightforward, very useful approach to a new, important class of indene derivatives. The reaction not only represents the first example of a direct coupling of propargylic carbonates, diethyl malonate and organozinc

Table 3 Palladium-catalyzed carboannulation and arylation of propargylic carbonates with *in situ* generated organozinc reagents[a]



Entry	1	ArX	Ar (3)	Time/h	Yield (%)[a]
1	E = CO_2Et R = Me (**1b**)	PhI	Ph (**3p**)	35	52
2	**1b**	*p*-$CH_3COC_6H_4I$	*p*-$CH_3COC_6H_4$ (**3q**)	24	89
3	**1b**	*p*-ClC_6H_4I	*p*-ClC_6H_4 (**3r**)	31	46
4	**1b**	*p*-$CH_3OC_6H_4I$	*p*-$CH_3OC_6H_4$ (**3s**)	31	22
5	**1b**	*m*-$CH_3C_6H_4I$	*m*-$CH_3C_6H_4$ (**3t**)	24	60
6	E = SO_2Ph R = H (**1c**)	*p*-$CH_3COC_6H_4I$	*p*-$CH_3COC_6H_4$ (**3u**)	24	74

[a] The reactions were run under the following conditions: 0.10 mmol of **1**, 0.15 mmol of the aryl iodide, 0.30 mmol of zinc powder, 0.30 mmol of LiCl, 2 mol% of $Pd(PPh_3)_4$, 0.20 mmol of K_2CO_3, stirred in 2 mL of DMSO at 50 °C under an Ar atmosphere. [b] Yields are given for isolated products.

compounds, but also demonstrates for the first time that allyl ethyl carbonates can be achieved from propargylic carbonates in the presence of Pd. The procedure was simple, the reaction proceeded under mild conditions, and indene products were isolated in good to excellent yields. Further investigations on the application of this method to the assembly of other functionalized indene products are currently in progress.

Experimental

General details

Column chromatography was carried out on silica gel. ^1H NMR spectra were recorded at 300 MHz or 400 MHz in $CDCl_3$ and ^{13}C NMR spectra were recorded at 75 MHz or 100 MHz in $CDCl_3$ using TMS as internal standard. IR spectra were recorded on a FT-IR spectrometer and only major peaks are reported in cm^{-1}. Melting points were determined on a microscopic apparatus and were uncorrected. All new compounds were further characterized by elemental analysis; copies of their ^1H NMR and ^{13}C NMR spectra are provided in the ESI‡. Unless otherwise stated, all aryl halides were purchased from commercial suppliers and used without further purification. Propargylic carbonates were prepared according to the literature.[3]

Typical procedure for preparation of 5 and synthesis of 3i

Anhydrous LiCl (7 mmol) was placed in an Ar-flushed flask and dried for 20 min at 150–170 °C under high vacuum (1 mbar). Zinc powder (7 mmol, 1.4 equiv., 325 mesh, Strem) was added under Ar and the heterogeneous mixture of Zn and LiCl was dried again for 10–20 min at 150–170 °C under high vacuum (1 mbar). The reaction flask was evacuated and refilled with argon three times. THF (5 mL) was added and the Zn was activated with $BrCH_2CH_2Br$ (5 mol%) and Me_3SiCl (1 mol%). 1-Iodo-3-methylbenzene (5 mmol) was then added neat at room temperature. The insertion reaction was complete after 48 h and afforded a solution of **5**.

The solution of **5** (0.3 mmol, 0.38 mL, titration with iodine) was carefully separated from the remaining zinc powder using a syringe and transferred to a mixture of diethyl 2-{2-[3-(ethoxycarbonyloxy)prop-1-ynyl]phenyl}malonate **1a** (36.2 mg, 0.10 mmol), $Pd(PPh_3)_4$ (2.3 mg, 0.002 mmol, 2 mol%) and K_2CO_3 (27.6 mg, 0.20 mmol) in DMSO (2.0 mL) under an argon atmosphere. The resulting mixture was stirred for 12 h at 50 °C. Then, the reaction mixture was allowed to cool to room temperature, quenched with water and extracted with EtOAc (2 mL × 3). The combined organic extracts were washed with water and saturated brine. The organic layer was dried over Na_2SO_4 and filtered. Solvents were evaporated under reduced pressure. The residue was purified by chromatography on silica gel to afford the corresponding indene product **3i** in 68% yield (hexanes–EtOAc 15 : 1).

Typical procedure for indene synthesis *via in situ* organozinc compounds

A solution of the propargylic carbonate **1** (0.10 mmol), aryl iodine (0.15 mmol), Zn powder (19.5 mg, 0.30 mmol), anhydrous LiCl (12.8 mg, 0.30 mmol), $Pd(PPh_3)_4$ (2.3 mg, 0.002 mmol, 2 mol%) and K_2CO_3 (27.6 mg, 0.20 mmol) in DMSO (2.0 mL) was stirred under an argon atmosphere at 50 °C. When the reaction was considered complete as determined by TLC analysis, the reaction mixture was allowed to cool to room temperature, quenched with water and extracted with EtOAc (2 mL × 3). The combined organic extracts were washed with water and saturated brine. The organic layer was dried over Na_2SO_4 and filtered. Solvents were evaporated under reduced pressure. The residue was purified by chromatography on silica gel to afford the corresponding indene product **3**.

3a. Mp: 50–51 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 7.75–7.72 (m, 1H), 7.48–7.42 (m, 5H), 7.35–7.32 (m, 2H), 7.25–7.21 (m, 1H), 5.15 (s, 2H), 4.31–4.12 (m, 6H), 1.30–1.24 (m, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.7, 154.8, 149.5, 143.9, 140.5, 133.5, 132.6, 128.9, 128.6, 127.2, 125.3, 121.5, 70.2, 63.8, 62.7, 62.2, 14.2, 13.8. IR (KBr, cm^{-1}) 2983, 1744, 1252, 1050. Anal. calcd for $C_{25}H_{26}O_7$: C 68.48, H 5.98; found: C 68.27, H 5.69%.

3b. Mp: 80–80.5 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 7.74–7.71 (m, 1H), 7.36–7.22 (m, 7H), 5.14 (s, 2H), 4.30–4.12 (m, 6H), 2.42 (s, 3H), 1.30–1.25 (t, J = 6.9 Hz, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.8, 154.8, 149.6, 144.0, 140.6, 138.4, 133.1, 129.6, 129.3, 128.8,

128.5, 127.2, 125.3, 121.5, 70.2, 63.8, 62.8, 62.2, 21.3, 14.2, 13.8. IR (KBr, cm^{-1}) 2979, 1730, 1261, 1046. Anal. calcd for $C_{26}H_{28}O_7$: C 69.01, H 6.24; found: C 68.75, H 5.96%.

3c. Mp: 90.5–91 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.09–8.06 (d, $J = 8.1$ Hz, 2H), 7.75–7.72 (m, 1H), 7.55–7.57 (d, $J = 8.1$ Hz, 2H), 7.36–7.33 (m, 2H), 7.18–7.15 (m, 1H), 5.11 (s, 2H), 4.31–4.18 (m, 4H), 4.18–4.11 (q, $J = 6.9$ Hz, 2H), 2.66 (s, 3H), 1.30–1.24 (m, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.6, 167.4, 154.7, 148.4, 143.4, 140.5, 137.6, 137.0, 134.6, 129.2, 128.7, 128.6, 127.6, 125.5, 121.3, 70.4, 63.9, 62.4, 62.3, 26.7, 14.2, 13.8. IR (KBr, cm^{-1}) 3428, 2992, 1742, 1259. Anal. calcd for $C_{27}H_{28}O_8$: C 67.49, H 5.87; found: C 67.64, H 5.66%.

3d. Mp: 77–78 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74–7.71 (m, 1H), 7.48–7.45 (d, $J = 8.4$ Hz, 2H), 7.41–7.38 (d, $J = 8.4$ Hz, 2H), 7.36–7.33 (m, 2H), 7.18–7.16 (m, 1H), 5.11 (s, 2H), 4.31–4.12 (m, 6H), 1.32–1.25 (m, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.5, 154.7, 148.4, 143.5, 140.4, 134.6, 134.0, 131.0, 130.3, 128.9, 128.7, 127.5, 125.4, 121.3, 70.3, 63.9, 62.5, 62.3, 14.3, 13.8. IR (KBr, cm^{-1}) 2978, 1727, 1261, 1044. Anal. calcd for $C_{25}H_{25}ClO_7$: C 63.49, H 5.33; found: C 63.37, H 5.38%.

3e. Mp: 87–88 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75–7.72 (m, 1H), 7.64–7.61 (m, 2H), 7.37–7.32 (m, 4H), 7.19–7.16 (m, 1H), 5.11 (s, 2H), 4.31–4.12 (m, 6H), 1.30–1.25 (m, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.5, 154.7, 148.3, 143.5, 140.4, 134.0, 131.8, 131.5, 130.6, 128.7, 127.5, 125.4, 122.8, 121.3, 70.3, 63.9, 62.5, 62.3, 14.2, 13.8. IR (KBr, cm^{-1}) 2978, 1745, 1725, 1260. Anal. calcd for $C_{25}H_{25}BrO_7$: C 58.04, H 4.87; found: C 58.01, H 5.01%.

3f. Mp: 94–95 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74–7.71 (m, 1H), 7.42–7.39 (d, $J = 8.7$ Hz, 2H), 7.35–7.32 (m, 2H), 7.27–7.24 (m, 1H), 7.03–7.00 (d, $J = 8.7$ Hz, 2H), 5.14 (s, 2H), 4.31–4.13 (m, 6H), 3.86 (s, 3H), 1.30–1.25 (t, $J = 6.9$ Hz, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.8, 159.7, 154.8, 149.3, 144.0, 140.5, 132.7, 130.2, 128.5, 127.2, 125.3, 124.8, 121.5, 114.0, 70.1, 63.8, 62.9, 62.2, 55.3, 14.3, 13.8. IR (KBr, cm^{-1}) 2994, 1741, 1241, 1044. Anal. calcd for $C_{26}H_{28}O_8$: C 66.66, H 6.02; found: C 66.38, H 5.75%. Crystal data: $C_{26}H_{28}O_8$, $M = 468.48$, orthorhombic, $Pca2_1$, $a = 8.5186(6)$, $b = 14.4133(11)$, $c = 19.6340(15)$ Å, $V = 2410.7(3)$ Å^3, $T = 294(2)$ K, $Z = 4$, μ (Mo Kα) = 0.096 mm^{-1}, 11809 reflections measured, 4476 unique ($R_{int} = 0.0346$), $R1$ [$I > 2\sigma(I)$] = 0.0449, $wR2$ [$I > 2\sigma(I)$] = 0.1131.

3g. Mp: 91–92 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.77–7.74 (m, 3H), 7.60–7.57 (d, $J = 8.4$ Hz, 2H), 7.37–7.34 (m, 2H), 7.17–7.14 (m, 1H), 5.12 (s, 2H), 4.32–4.11 (m, 6H), 1.31–1.24 (m, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.4, 154.7, 148.0, 143.4, 140.4, 136.4, 134.8, 129.4, 128.8, 127.6, 125.6, 125.6, 125.5, 121.2, 70.4, 64.0, 62.4, 14.2, 13.8. IR (KBr, cm^{-1}) 2978, 1745, 1725, 1257, 1116. Anal. calcd for $C_{26}H_{25}F_3O_7$: C 61.66, H 4.98; found: C 61.47, H 4.68%.

3h. Mp: 71–72 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.18–8.15 (d, $J = 8.1$ Hz, 2H), 7.76–7.73 (m, 1H), 7.56–7.53 (d, $J = 8.4$ Hz, 2H), 7.37–7.34 (m, 2H), 7.19–7.17 (m, 1H), 5.12 (s, 2H), 4.30–4.12 (m, 6H), 3.96 (s, 3H), 1.31–1.25 (m, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.5, 166.7, 154.7, 148.5, 143.4, 140.5, 137.4, 134.6, 130.2, 129.9, 129.0, 128.7, 127.5, 125.5, 121.3, 70.4, 63.9, 62.5, 62.4, 52.3, 14.2, 13.9. IR (KBr, cm^{-1}) 2923, 1739, 1258, 1046. Anal. calcd for $C_{27}H_{28}O_9$: C 65.31, H 5.68; found: C 65.60, H 5.74%.

3i. Mp: 102–103 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74–7.71 (m, 1H), 7.39–7.30 (m, 3H), 7.25–7.21 (m, 4H), 5.14 (s, 2H), 4.31–4.12 (m, 6H), 2.41 (s, 3H), 1.30–1.25 (t, $J = 7.5$ Hz, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.8, 154.8, 149.7, 144.0, 140.6, 138.2, 133.4, 132.5, 129.5, 129.3, 128.6, 128.5, 127.2, 126.0, 125.3, 121.6, 70.2, 63.8, 62.8, 62.2, 21.5, 14.3, 13.9. IR (KBr, cm^{-1}) 3001, 1735, 1255, 1044. Anal. calcd for $C_{26}H_{28}O_7$: C 69.01, H 6.24; found: C 68.78, H 6.12%.

3j. Mp: 70–70.5 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75–7.72 (m, 1H), 7.45–7.42 (m, 3H), 7.37–7.32 (m, 3H), 7.20–7.17 (m, 1H), 5.13 (s, 2H), 4.29–4.13 (m, 6H), 1.31–1.26 (m, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.4, 154.7, 148.0, 143.4, 140.4, 134.5, 134.4, 130.0, 128.9, 128.7, 127.5, 127.1, 125.4, 121.3, 70.3, 63.9, 62.4, 62.3, 14.2, 13.8. IR (KBr, cm^{-1}) 2987, 1735, 1255, 1043. Anal. calcd for $C_{25}H_{25}ClO_7$: C 63.49, H 5.33; found: C 63.52, H 5.04%.

3k. Oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74–7.72 (m, 1H), 7.34–7.23 (m, 5H), 7.20–7.18 (m, 1H), 6.90–6.87 (m, 1H), 5.08–5.04 (d, $J = 12.3$ Hz, 1H), 5.00–4.97 (d, $J = 12.3$ Hz, 1H), 4.30–4.17 (m, 4H), 4.12–4.05 (q, $J = 6.9$ Hz, 2H), 2.15 (s, 3H), 1.32–1.20 (m, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.0, 167.5, 154.8, 149.3, 144.4, 140.4, 136.6, 134.6, 132.3, 130.1, 129.2, 128.6, 128.4, 127.1, 125.8, 125.0, 121.3, 70.2, 63.7, 62.8, 62.2, 19.5, 14.2, 13.9. IR (KBr, cm^{-1}) 2983, 1746, 1252, 1051. Anal. calcd for $C_{26}H_{28}O_7$: C 69.01, H 6.24; found: C 68.83, H 5.98%.

3l. Oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11–8.09 (m, 1H), 7.73–7.70 (m, 1H), 7.63–7.59 (m, 1H), 7.54–7.50 (m, 1H), 7.36–7.34 (m, 1H), 7.30–7.26 (m, 2H), 6.84–6.82 (m, 1H), 5.10–5.07 (dd, $J_1 = 0.9$ Hz, $J_2 = 8.4$ Hz, 1H), 5.00–4.97 (dd, $J_1 = 0.9$ Hz, $J_2 = 8.4$ Hz, 1H), 4.31–4.20 (m, 4H), 4.11–4.06 (m, 2H), 3.48 (s, 3H), 1.32–1.21 (m, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.8, 167.6, 167.2, 154.8, 149.6, 145.0, 140.0, 133.7, 133.1, 132.2, 130.9, 130.6, 128.6, 128.6, 127.0, 125.1, 120.7, 70.4, 63.7, 62.7, 62.2, 51.9, 14.2, 13.9. IR (KBr, cm^{-1}) 2983, 1740, 1258, 1042. Anal. calcd for $C_{27}H_{28}O_9$: C 65.31, H 5.68; found: C 65.29, H 5.92%.

3m. Oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73–7.70 (m, 1H), 7.33–7.30 (m, 2H), 7.26–7.19 (m, 1H), 7.12–7.07 (m, 2H), 6.84–6.77 (m, 2H), 5.10 (s, 2H), 4.34–4.07 (m, 6H), 3.74 (s, 1H), 1.32–1.21 (m, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.1, 167.3, 154.7, 146.5, 144.3, 143.6, 140.7, 136.1, 129.9, 129.7, 128.7, 127.4, 125.1, 121.7, 118.0, 117.4, 115.4, 70.2, 63.8, 63.0, 62.4, 62.3, 14.2, 13.9. IR (KBr, cm^{-1}) 3471, 3379, 2983, 1744, 1253. Anal. calcd for $C_{25}H_{26}O_8$: C 66.07, H 5.77; found: C 66.33, H 5.95%.

3n. Mp: 76–77 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72–7.69 (m, 1H), 7.42–7.37 (m, 1H), 7.30–7.26 (m, 3H), 7.06–6.99 (m, 3H), 5.23–5.19 (d, $J = 12.3$ Hz, 1H), 5.01–4.97 (d, $J = 12.3$ Hz, 1H), 4.30–4.06 (m, 6H), 3.74 (s, 3H), 1.31–1.21 (m, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.0, 167.7, 157.1, 154.8, 145.7, 144.3, 140.3, 134.8, 130.8, 130.0, 128.3, 126.7, 125.0, 121.6, 120.5, 111.3, 70.2, 63.7, 63.4, 62.2, 62.1, 55.5, 14.2, 13.9, 13.8. IR (KBr, cm^{-1}) 2927, 1741, 1247. Anal. calcd for $C_{26}H_{28}O_8$: C 66.66, H 6.02; found: C 66.59, H 5.83%.

3o. Mp: 80–80.5 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74–7.72 (m, 1H), 7.59–7.56 (m, 1H), 7.51–7.49 (m, 1H), 7.42–7.33 (m, 3H), 7.20–7.17 (m, 1H), 5.24 (s, 2H), 4.30–4.16 (m, 6H), 1.32–1.25 (m, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.4, 154.8, 143.1, 142.5, 140.2, 134.1, 132.9, 128.7, 128.6, 127.5, 127.2, 125.4, 121.7, 70.4,

63.9, 62.7, 62.3, 14.3, 13.8. IR (KBr, cm^{-1}) 2983, 1742, 1251, 1043. Anal. calcd for $C_{23}H_{24}O_7S$: C 62.15, H 5.44; found: C 61.86, H 5.24%.

3p. Mp: 78–80 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68–7.66 (m, 1H), 7.48–7.42 (m, 5H), 7.31–7.26 (m, 2H), 7.05–7.02 (m, 1H), 5.95–5.93 (m, 1H), 4.30–4.10 (m, 6H), 1.37–1.35 (m, 3H), 1.30–1.22 (m, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.9, 167.8, 154.4, 147.5, 145.3, 140.0, 138.4, 134.0, 129.2, 128.6, 128.4, 128.2, 127.0, 124.7, 121.2, 71.4, 63.6, 62.1, 19.3, 14.3, 13.9, 13.8. IR (KBr, cm^{-1}) 2985, 1741, 1265, 1047. Anal. calcd for $C_{26}H_{28}O_7$: C 69.01, H 6.24; found: C 69.25, H 6.06%.

3q. Mp: 85–86 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.10–8.05 (m, 2H), 7.74–7.68 (m, 1H), 7.60–7.57 (m, 2H), 7.32–7.27 (m, 2H), 6.99–6.97 (m, 1H), 5.95–5.92 (m, 1H), 4.32–4.10 (m, 6H), 2.67 (s, 3H), 1.37–1.25 (m, 12H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.6, 167.6, 167.4, 154.2, 146.4, 144.7, 139.8, 139.2, 139.0, 136.7, 129.5, 128.9, 128.7, 128.3, 127.2, 124.9, 120.9, 71.3, 71.0, 63.6, 62.3, 26.6, 19.4, 14.2, 13.8, 13.7. IR (KBr, cm^{-1}) 2988, 1730, 1682, 1260. Anal. calcd for $C_{28}H_{30}O_8$: C 68.00, H 6.11; found: C 68.29, H 6.05%.

3r. Mp: 96–97 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69–7.66 (m, 1H), 7.47–7.45 (m, 2H), 7.42–7.39 (m, 2H), 7.33–7.29 (m, 2H), 7.01–6.99 (m, 1H), 5.94–5.89 (m, 1H), 4.32–4.09 (m, 6H), 1.41–1.35 (m, 3H), 1.33–1.20 (m, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.8, 167.5, 154.3, 146.4, 145.0, 139.9, 138.9, 134.3, 132.4, 130.6, 128.7, 127.2, 124.9, 121.0, 109.8, 71.1, 63.6, 62.2, 19.4, 14.3, 13.9, 13.8. IR (KBr, cm^{-1}) 2984, 1743, 1260, 1048. Anal. calcd for $C_{26}H_{27}ClO_7$: C 64.13, H 5.59; found: C 64.43, H 5.68%.

3s. Mp: 66–67 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68–7.65 (m, 1H), 7.42–7.39 (d, J = 8.7 Hz, 2H), 7.31–7.28 (m, 2H), 7.09–7.06 (m, 1H), 7.02–7.00 (d, J = 8.1 Hz, 2H), 5.95–5.93 (m, 1H), 4.31–4.10 (m, 6H), 3.87 (s, 3H), 1.39–1.36 (d, J = 6.9 Hz, 3H), 1.31–1.23 (m, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.0, 167.9, 159.6, 154.4, 147.3, 145.5, 140.0, 137.9, 130.4, 128.5, 126.9, 126.1, 124.7, 121.2, 113.9, 71.4, 63.5, 62.1, 55.2, 19.1, 14.3, 13.9, 13.8. IR (KBr, cm^{-1}) 2984, 1730, 1251, 1049. Anal. calcd for $C_{27}H_{30}O_8$: C 67.21, H 6.27; found: C 67.04, H 5.98%.

3t. Mp: 94–95 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68–7.65 (m, 1H), 7.36–7.21 (m, 6H), 7.05–7.02 (m, 1H), 5.94–5.92 (m, 1H), 4.31–4.09 (m, 6H), 2.41 (s, 3H), 1.39–1.37 (d, J = 6.6 Hz, 3H), 1.31–1.23 (m, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.0, 167.8, 154.3, 147.6, 145.3, 139.9, 138.1, 137.9, 133.7, 129.7, 128.9, 128.5, 128.2, 126.9, 126.2, 124.6, 121.2, 71.4, 71.0, 63.5, 62.1, 21.4, 19.3, 14.3, 13.9, 13.8. IR (KBr, cm^{-1}) 2986, 1731, 1258, 1042. Anal. calcd for $C_{27}H_{30}O_7$: C 69.51, H 6.48; found: C 69.35, H 6.24%.

3u. Oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10–8.08 (d, J = 7.6 Hz, 1H), 7.98–7.96 (d, J = 7.6 Hz, 2H), 7.50–7.41 (m, 2H), 7.33–7.28 (m, 3H), 7.23–7.19 (m, 2H), 7.05–7.03 (d, J = 8.0 Hz, 2H), 6.77–6.75 (d, J = 7.6 Hz, 1H), 5.54–5.12 (d, J = 12.8 Hz, 1H), 5.08–5.05 (d, J = 12.4 Hz, 1H), 4.45–4.41 (m, 2H), 4.17–4.12 (q, J = 7.2 Hz, 2H), 2.63 (s, 3H), 1.41–1.38 (m, 3H), 1.29–1.25 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.3, 163.2, 151.5, 143.8, 137.2, 136.9, 136.7, 134.2, 133.8, 131.4, 130.0, 129.8, 128.6, 128.4, 127.9, 127.8, 127.5, 121.2, 74.2, 64.0, 63.4, 61.5, 26.6, 14.3, 13.9. IR (KBr, cm^{-1}) 3411, 2923, 1741, 1249. Anal. calcd for $C_{30}H_{28}O_8S$: C 65.68, H 5.14; found: C 65.78, H 5.37%.

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